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ABSTRACTS

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317 Prognostic Significance of the Single Cell Pattern in Fine-Needle Aspirations Diagnostic of PapillaryThyroid Carcinoma

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Disclosures: Amrou Abdelkader: None; Mohamed Mostafa: None; Christopher Hartley: None

Background: The initial diagnosis of papillary thyroid carcinoma (PTC) is frequently made via Fine-Needle Aspiration (FNA). FNAs exert physical strain on epithelial clusters and represent a test of cohesion. Some tumors resist the strain and remain in tightly-packed clusters, while others exhibit discohesion, with single cells shedding off of cellular groups. The single cell pattern (SCP) is a correlate of the epithelial-mesenchymal transition (EMT), a concept best described and understood in lobular breast carcinoma and hereditary signet ring cell gastric adenocarcinoma. To our knowledge, no studies have addressed the prognostic significance of the SCP in PTC. Our aim was to correlate SCP in FNAs diagnostic of PTC with aggressive features at the time of resection and with local recurrence free survival.

Design: 87 consecutive FNAs diagnostic of PTC ("Suspicious for PTC" or "Positive for PTC") with confirmatory surgical resections were identified and retrieved from the pathology archives. Slides were reviewed and the presence of the SCP was recorded. SCP was defined as single cells readily visible separate from clusters at 4x (Figure 1). Presence of SCP was compared to clincopathologic features gathered from chart review.

Results: The SCP was observed in 42/87 (48%) FNAs diagnostic of PTC. Median follow-up of the SCP group was 4.9 years (range 1.2-7.9) and 5.9 years (range 0.4-8.2) in the group without SCP. The average age at FNA was 50.5 years, and the F:M ratio was 4:1. The single cell pattern was associated with a 2.6 times greater rate of lymph node positivity at resection (p=0.04, 95% CI 1.1-6.4). However, SCP was not significantly correlated with tumor size or lymphovascular invasion at resection (Table 1). A non-significant trend of local recurrence in the SCP group was noted (Figure 2).
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Table 1: Summary of Clinicopathologic Features in Correlation with the Single Cell Pattern

	SCP present (n=42)	SCP absent (n=45)	All Cases	Statistics for SCP presence vs. absence	Statistical Method
Positive LN at Resection	26/42(62%)	18/45(40%)	44/87(51%)	**p=0.04, OR=2.6, 95% CI 1.1-6.4**	Logistic regression
Resection Tumor size (cm), mean±SD(range)	2.0±1.4(0.2-5.5)	1.6±1.2(0.25-7.5)	1.8±1.3(0.2-7.5)	p=0.11	t-test
LVI at Resection	2/42(4.8%)	2/45(4.4%)	4.87(4.6%)	p=1	Fisher's exact test
Local Recurrence	2/42(9.5%)	2/45(4.4%)	6/87(6.9%)	p=0.1	Log rank test (Kaplan-Meier curve, Figure 2)
Female	31/42(74%)	34/45(75%)	64/87(75%) F:M ratio 4:1	p=1	Fisher's exact test
Age at time of FNA (years), mean	47.6	53.3	50.5	p=0.1	t-test

Legend: SCP=single cell pattern; LN= lymph node, LVI= lymphovascular invasion; FNA=fine-needle aspiration; SD=standard deviation; OR=odds ratio; CI=confidence interval.

Figure 1 - 317

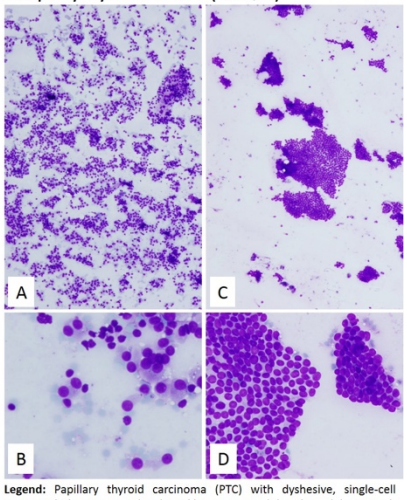

Figure 1: Fine-Needle Aspiration Smears Diagnostic of Papillary Thyroid Carcinoma (Diff Quik)

Legend: Papillary thyroid carcinoma (PTC) with dyshesive, single-cell cytomorphologic pattern (SCP) readily seen on 4X (A) and 20X (B). PTC with cohesive groups of cells (SCP absent) seen on 4X (C) and 20X (D).

Figure 2 - 317

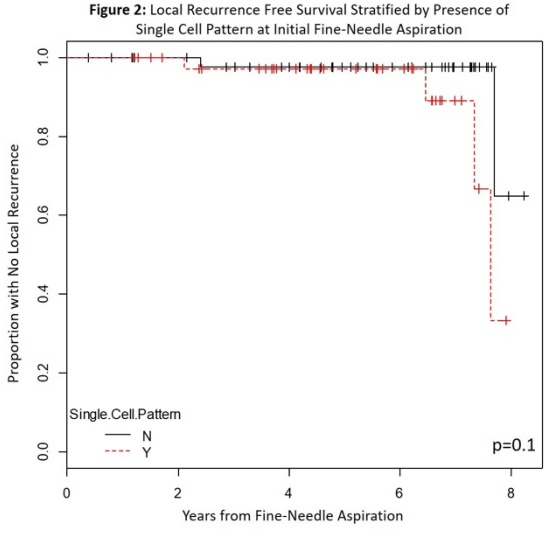

Figure 2: Local Recurrence Free Survival Stratified by Presence of Single Cell Pattern at Initial Fine-Needle Aspiration

Conclusions: The SCP is readily appreciated in FNAs diagnostic of PTC, and is significantly correlated with LN positivity at resection, and shows a trend of increased local recurrence. SCP may indicate a more aggressive phenotype in PTC. Due to the indolent course of PTC, a larger cohort with longer follow-up will be pursued to further evaluate the significance of the SCP in PTC FNAs.

318 Can Human Papillomavirus (HPV) in Cytology Material be a Substitute Marker for p16 Expression in Oropharyngeal Squamous Cell Carcinoma?

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Disclosures: Rita Abi-Raad: None; Guoping Cai: None; Deborah Barlow: None; Adebowale Adeniran: None; Manju Prasad: None

Background: Human papillomavirus (HPV) has been implicated in the pathogenesis of oropharyngeal squamous cell carcinoma (OPSCC) where p16+ is considered a surrogate marker for HPV in surgical specimens. p16 overexpression has also been shown to be a prognostic marker of favorable outcome regardless of HPV status, and is therefore often requested as part of the initial work-up in anticipation of neo-adjuvant therapy. Patients with head and neck squamous cell carcinoma (HNSCC) often present with a neck mass and Fine Needle Aspiration (FNA) may be the only specimen available for assessment. Interpretation of immunohistochemistry (IHC) for p16 in cytology specimens is however not well established. Furthermore, cytology cell block (CB) may be frequently paucicellular precluding IHC and HPV status by PCR may be the only information available. This study aims to assess whether HPV assessment in FNA specimens can be used as a substitute for p16+ status in OPSCC.

Design: The institutional pathology database was searched for HNSCC diagnosed by FNA of neck masses between January 2016 and June 2018. OPSCC cases with available HPV status and corresponding surgical resection/biopsy with p16 IHC were included in the study. We correlated HPV status, performed by PCR on residual FNA material with p16 IHC on surgical specimens. p16 was interpreted as positive if ? 70% of tumor cells showed staining in surgical specimens.

Results: 50 matched cases of OPSCC were identified including 38 (76%) HPV-positive, 11 (22%) HPV-negative cases and one (2%) HPV-indeterminant case. All HPV+ cases were p16+ on surgical specimens. Of 11 HPV- cases, 10 were p16- and one was p16+ on surgical excision. A repeat HPV test on surgical specimen of the latter case was positive. One HPV-indeterminant case was p16+ on surgical specimen. HPV PCR correlated with p16 in surgical specimens with a positive predictive value (PPV) of 100% and a negative predictive value (NPV) of 91%. Only 11 cases had available and adequate CB material. HPV status predicted p16 status regardless of cellularity or preservation on cytology CB.

Conclusions: HPV status in FNA correlates to p16 status on surgical specimens and can be used as an alternative to immunohistochemistry in cytology specimens in OPSCC regardless of CB adequacy to predict p16 status.

319 Comparison of Different Molecular Testing Platforms in Thyroid Fine Needle Aspiration Cytology

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Disclosures: Rita Abi-Raad: None; Guoping Cai: None; Adebowale Adeniran: None

Background: The indeterminate categories within the Bethesda Reporting System for fine needle aspiration (FNA) of the thyroid include follicular lesion of undetermined significance (FLUS), follicular neoplasm (FN), and suspicious for malignancy (SFM), which may present challenges for clinical management. The advent of molecular mutational panels has been shown to be useful in helping guide management decisions. The most common molecular tests in clinical use are ThyroSeq, ThyGenX/ThyraMir and Afirma Gene Expression Classifier (GEC). This study was designed to compare the performance indices of these different platforms at a large academic institution.

Design: The institutional pathology database was searched for thyroid cytology cases in which molecular testing was performed using ThyroSeq, ThyGenX/ThyraMir or Afirma GEC panels. Cytology diagnosis, molecular test results and subsequent surgical specimen diagnosis were reviewed.

Results: Between January 2015 and August 2018, 287 FNA samples were sent for molecular testing. Of those, 94 samples were sent for ThyGenX, 136 were sent for ThyroSeq and 57 were sent for Afirma GEC. 175 cases (61%) corresponded to FLUS diagnosis: 61 ThyGenX, 81 Thyroseq and 33 Afirma GEC. FN accounted for 71 cases (25%): 20, 35 and 16 cases underwent ThyGenX, ThyroSeq and Afirma GEC testing respectively. SFM accounted for 14 cases (5%) – 6 ThyGenX, 5 ThyroSeq and 3 Afirma GEC. 96 patients underwent subsequent surgical resection. In the ThyGenX cohort, 25 patients underwent surgery, including 14 patients with genetic alteration (10 malignant) and 11 without genetic alteration (4 malignant). In the ThyroSeq group, 44 patients had surgery including 20 patients with genetic alteration (9 malignant) and 24 without alteration (1 malignant). Of the cases sent to Afirma GEC, 27 underwent surgery. 22 patients had a suspicion for alteration (5 malignant) and 5 were negative for alteration (1 malignant). ThyGenX/ThyraMir, ThyroSeq and

Afirma GEC showed a positive predictive value of 71%, 45% and 23%, respectively, and a negative predictive value of 64%, 96% and 80%, respectively. The sensitivity for malignancy detection in ThyGenX/ThyraMir, ThyroSeq and Afirma GEC was 71%, 90% and 83%, respectively while the specificity was 64%, 68% and 19%, respectively.

Conclusions: Different molecular tests performed on thyroid FNAs have different positive and negative predictive values and rates of malignancy detection. Tests should be chosen based on specific clinical questions to be resolved.

320 Malignant Mesothelioma in Effusion Cytology and a Tale of Two Proteins – The CD47 'Don't Eat Me Signal' and BAP-1

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Disclosures: Tanupriya Agrawal: None; Patricia Fetsch: None; Mark Roth: None; Raffit Hassan: None; Armando Filie: None

Background: Malignant mesothelioma (MM) is a rare aggressive disease that cytomorphologically may be very difficult to differentiate from benign reactive mesothelial cell proliferations in effusion samples. The application of new immunomarkers may be helpful in achieving a more definitive cytologic diagnosis on these challenging effusions. In this study, we intended to determine the utility of BAP-1 and CD47 for detecting MM in effusion samples.

Design: We searched our database from 2013-2018 for benign and positive/suspicious MM cases. Twenty-eight MM cases and 5 benign effusions were selected for immunocytochemistry (ICC) staining with antibodies to BAP-1 (Santa Cruz) and CD47 (Sigma). Negative nuclear staining was considered loss of BAP1 expression and is the expected pattern in MM. Positive $\geq$2+ membranous staining (on an intensity scale of 0 – 3+) was the expected positive pattern for CD47. The percentage of CD47 positive tumor cells for each case was also determined.

Results: BAP1 expression was lost in 24/28 (86%) of the MM cases, retained in two cases, and noncontributory in two cases. The ICC staining for CD47 showed a predominant 2+ membranous pattern in 24/28 (86%) of the MM cases; 3+ in 2/28 (7%) of the MM cases and a 0-1+ membranous pattern in 2/28 (7%) of the MM cases; consequently, positive staining was seen in 26/28 (92%) of MM cases. All benign effusions showed a 0-1+ CD47 membranous pattern. BAP-1 loss with CD47 positive staining was seen in 25/26 (96%) of MM cases. All benign effusions retained BAP-1 expression and were CD47 negative.

Figure 1 - 320

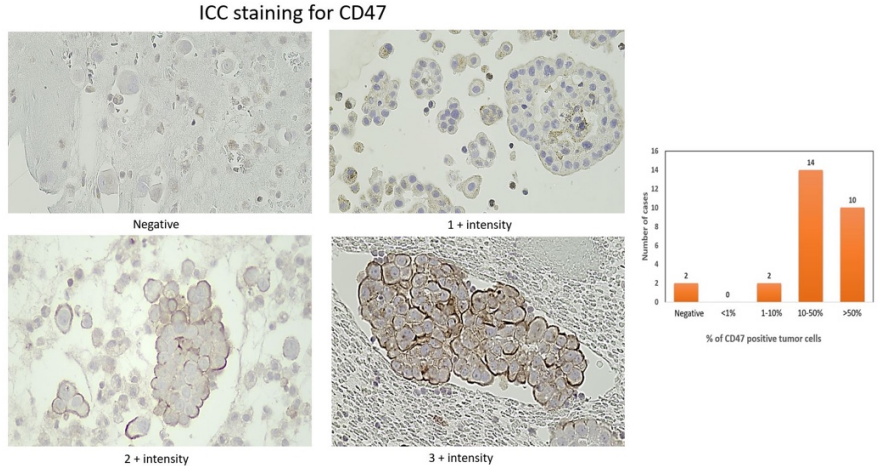
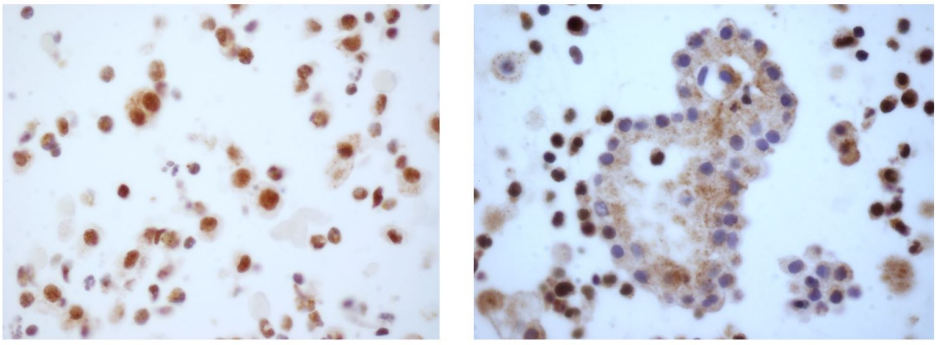


Figure 2 - 320

ICC staining for BAP-1



Benign Effusion | Malignant Mesothelioma Effusion

Conclusions: ICC for BAP1 and CD47 are independently helpful immunomarkers for the detection of MM in effusions samples. ICC panel with BAP-1 in combination with CD47 is very helpful for detecting MM and may serve as a valuable ancillary tool in the diagnosis of MM in effusion samples.

321 A Novel Approach for BRAF V600E Mutation Analysis of Routine Thyroid Fine Needle Aspirates

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Disclosures: Tanupriya Agrawal: None; Liqiang Xi: None; Mark Raffeld: None; Mark Roth: None; Armando Filie: None

Background: BRAF V600E (BRAF) mutation is highly specific for malignancy in thyroid neoplasms seen in approximately 40-45% of papillary thyroid carcinomas (PTC). Recent proposed management for thyroid aspirates state that BRAF mutation positive cases can be followed by thyroidectomy without frozen section. Molecular testing for genetic alterations seen in thyroid neoplasms, including BRAF mutation, are often applied to thyroid aspirates that fall into the indeterminate categories of the Bethesda System for reporting thyroid cytology. However, current methods typically require dedicated aspirated material for analysis, without morphologic determination if this material contains the follicular cells of interest and often at elevated cost. Here, we show our experience with BRAF mutation analysis on material obtained from routine clinical Papanicolaou-stained ThinPrep (TP) slides after diagnostic morphologic evaluation.

Design: 83 cases collected between 2012-2018 were selected for analysis. An electronic record consisting of a whole slide scan was made of the TP slide for each case and the percentage of follicular versus all cells was documented. The coverslips were removed and DNA was extracted from material scraped from each TP slide using the Qiagen QIAamp DNA FFPE Tissue Kit. BRAF V600E test was performed with a high-sensitive mutation detection assay either with COLD-PCR, castPCR or droplet digital PCR.

Results: 17 out of 83 (20%) cases harbored BRAF mutation. Of these, 10 were cytomorphologically classified as atypia of undetermined significance/suspicious for malignancy from which follow-up resection showed PTC in 6 out of 8 (78%) available cases. Surgical pathology follow-up in 36 out of the 66 (54%) BRAF mutation negative cases identified one PTC [1 out 36 (3%)].

Figure 1 - 321

BRAF Mutation Analysis from TP Slides of Thyroid Aspirates

Cytology	BRAF Positive	Surgical Follow-up	BRAF Negative	Surgical Follow-up
Benign	0	0	16 (24%)	Benign - 4 (6%) FA - 2 (3%) NA - 10 (15%)
AUS	4 (23%)	PTC - 3 (17%) NA - 1 (6%)	34 (52%)	Benign - 10 (15%) PTC-M - 4 (6%) FA - 3 (4.5%) FNUS - 1 (1.5%) PTC - 1 (1.5%) PTC-F - 1 (1.5%) NA - 14 (19%)
FLUS	0	0	10 (15%)	PTC-F - 2 (3%) FA - 1 (1.5%) Benign - 1 (1.5%) NA - 6 (9%)
Suspicious	6 (36%)	PTC - 3 (17%) PTC-F - 1 (6%) FA - 1 (6%) NA - 1 (6%)	5 (7.5%)	FA - 3 (4.5%) PTC-F-1 (1.5%) PTC-M-1 (1.5%) Benign - 1 (1.5%) Hashimoto's - 1 (1.5%)
PTC	7 (41%)	PTC - 6 (36%) NA - 1 (6%)	1 (1.5%)	PTC - 1 (1.5%)
Total	17 (100%)	17 (100%)	66 (100%)	66 (100%)

Abbreviations: **TP** - ThinPrep; **AUS** - Atypia of Undetermined Significance; **FLUS** - Follicular Lesion of Undetermined Significance; **PTC** - Papillary Thyroid Carcinoma; **PTC-M** - Papillary Thyroid Microcarcinoma; **PTC-F** - Papillary Thyroid Carcinoma, Follicular Variant; **FA** - Follicular Adenoma; **FNUS** - Follicular Neoplasm of Undetermined significance; **NA** - No surgical follow up

Conclusions: Our study demonstrates that BRAF mutation analysis can be reliably performed on material obtained from TP slides. This novel approach for BRAF mutation analysis, as a first step, may reduce costs related to the molecular evaluation of thyroid aspirates and provides the opportunity for cytomorphologic confirmation that the cells of interest are present.

322 Comparative Test Performance of ThyroSeq® and Afirma®, Including Their Newer Versions, in Indeterminate Thyroid Fine-Needle Aspiration

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Disclosures: Josephine Aguilar-Jakthong: None; Brian Chang: None; Dipti Sajed: None; Melissa Cobarrubias: None; Rekha Govind: None; Neda Moatamed: None

Background: Up to 25% of the thyroid fine-needle aspiration (FNA) diagnoses are categorized as indeterminate, including atypia of undetermined significance (AUS), follicular lesion of undetermined significance (FLUS), suspicious for a follicular neoplasm (SFN), and follicular neoplasm (FN). Indeterminate diagnoses are a challenge for clinicians in management decisions. Molecular studies were developed to address this issue for ultimate clinical outcome. The two most prevalent molecular methods currently in use are Afirma® and ThyroSeq® each with different versions. In this study, we compared the diagnostic performance of the two molecular tests, each with two versions, in indeterminate FNA of thyroid nodules.

Design: We retrospectively reviewed cases from our departmental database, under IRB approval. Cases with thyroid FNA between May 2016 and June 2018 were reviewed. Patients with an indeterminate cytologic diagnosis who had either ThyroSeq or Afirma tests and subsequent surgery were selected. Cases meeting the criteria were divided into two groups: one with ThyroSeq and the other with Afirma. The ThyroSeq group was subdivided into versions 2 and 3. The Afirma group was subdivided into Gene Expression Classifier (**GEC**) and Genomic Sequencing Classifier (**GSC**) versions. Each subdivision had two FNA-diagnostic subgroups: AUS/FLUS and SFN/FN. Using the histopathology diagnoses as the gold standard, true positive, true negative, false positive, or false negative was assigned to each individual test result from which sensitivity, specificity, negative predictive value, positive predictive value, and diagnostic accuracy were calculated (Tables 1&2).

Results: Of 2190, 102 cases met selection criteria, 48 of which had ThyroSeq and 54 had Afirma testing. Combined versions of ThyroSeq had a total diagnostic accuracy (DA) of 81% vs 56% for Afirma. Specifically, DA of AUS/FLUS was 91% for ThyroSeq version 3 and 50% for Afirma GSC. Conversely, DA of FSN/FN was 100% for Afirma GSC and 67% for ThyroSeq version 3. The test parameters are detailed in Tables 1&2.

Table 1. ThyroSeq® Test Performance for Versions (Vs) 2 and 3 (V2 & V3)

Vs	Diagnoses	n	Sn	Sp	PPV	NPV	DA
V2	AUS/FLUS	27	**87%**	**83%**	**87%**	**83%**	**85%**
	SFN/FN	7	**100%**	**40%**	**40%**	**100%**	**57%**
	Combined	34	**88%**	**71%**	**75%**	**86%**	**79%**
V3	AUS/FLUS	11	**100%**	**50%**	**90%**	**100%**	**91%**
	SFN/FN	3	**100%**	**0%**	**67%**	NV	**67%**
	Combined	14	**100%**	**33%**	**85%**	**100%**	**86%**
V2 + V3	AUS/FLUS	38	**92%**	**79%**	**88%**	**85%**	**87%**
	SFN/FN	10	**100%**	**33%**	**50%**	**100%**	**60%**
	Combined	48	**93%**	**65%**	**79%**	**87%**	**81%**

Sn, sensitivity; **Sp**, specificity; **PPV**, positive predictive value; **NPV**, negative predictive value; **DA**, diagnostic accuracy; **NV,** no value

Table 2. Afirma® Test Performance for Gene Expression Classifier (GEC) and Genomic Sequencing Classifier (GSC) Versions (Vs)

Vs	Diagnoses	n	Sn	Sp	PPV	NPV	DA
GEC	AUS/FLUS	31	**92%**	**11%**	**43%**	**67%**	**45%**
	SFN/FN	3	**100%**	**0%**	**67%**	NV	**67%**
	Combined	34	**93%**	**11%**	**45%**	**67%**	**47%**
GSC	AUS/FLUS	12	**100%**	**0%**	**50%**	NV	**50%**
	SFN/FN	8	**100%**	**100%**	**100%**	**100%**	**100%**
	Combined	20	**100%**	**33%**	**65%**	**100%**	**70%**
GEC + GSC	AUS/FLUS	43	**95%**	**8%**	**45%**	**67%**	**47%**
	SFN/FN	11	**100%**	**75%**	**88%**	**100%**	**91%**
	Combined	54	**96%**	**18%**	**52%**	**83%**	**56%**

Conclusions: Overall, the newer versions of ThyroSeq and Afirma show improvement in sensitivity and diagnostic accuracy. Our results indicate that ThyroSeq is best suited for AUS/FLUS evaluation while Afirma provides a superior diagnostic accuracy for SFN/FN lesions.

323 Multiplex Immunofluorescence-Based Approach for Body Fluid Cytological Analysis

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Disclosures: Josephine Aguilar-Jakthong: None; Jianyu Rao: None

Background: Distinguishing adenocarcinoma from reactive mesothelial cells in body fluid cytology may be challenging and diagnosis may be dependent on a panel of immunohistochemical (IHC) stains. However, IHC based stain are non-quantitative, require multiple sections, and it is often difficult to match the staining pattern of the cells of interest. This is especially problematic in cases with limited cellularity for evaluation.

Multiplex fluorescence image (MFI) analysis allows simultaneous detection with high resolution up to seven targets with quantification capabilities on a single cell basis. This approach has been shown to be applicable in a variety of tissue-based settings, yet there is limited data on its use on cytology specimens. The goal of this preliminary study is to determine the feasibility of performing MFI analysis on cell block sections of pleural fluid samples.

Design: In this study, cases with malignant and benign pleural fluid cytology diagnosis were randomly selected from our institution between 2015-2018. Of these cases those with equivocal diagnosis (atypical or suspicious) were excluded. A single section of the cell block from each case was used for multiplex staining and analysis of three markers: MOC31, BerEP4 and Calretinin. Cases were scored as positive if MFI analysis showed positive for MOC31 and/or BerEP4 (Figure 1) and negative if MFI analysis showed positive for Calretinin and negative for both MOC31 and BerEP4 (Figure 2). Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were calculated to evaluate test performance.

Results: A total of 41 cases of pleural fluids including 20 malignant and 21 benign were selected for the study. 7 of the 21 benign cases were noted to have only red blood cells on cell block. These cases were excluded, leaving a total of 14 benign cases. 34 of the 34 total cases (20 malignant, 14 benign) were concordant to the previous cytological diagnosis. Sensitivity, specificity, PPV, NPV and accuracy were 100%.

		Multiplex Fluorescence Analysis		
Case #	**Primary Diagnosis**	**Calretinin**	**MOC31/ BerEP4**	**Concordance**
1	Adenocarcinoma	Negative	Positive	Concordant
2	Adenocarcinoma	Negative	Positive	Concordant
3	Adenocarcinoma	Negative	Positive	Concordant
4	Adenocarcinoma	Negative	Positive	Concordant
5	Adenocarcinoma	Positive	Positive	Concordant
6	Adenocarcinoma	Negative	Positive	Concordant
7	Adenocarcinoma	Positive	Positive	Concordant
8	Adenocarcinoma	Positive	Positive	Concordant
9	Adenocarcinoma	Positive	Positive	Concordant
10	Adenocarcinoma	Positive	Positive	Concordant
11	Adenocarcinoma	Positive	Positive	Concordant
12	Adenocarcinoma	Positive	Positive	Concordant
13	Adenocarcinoma	Positive	Positive	Concordant
14	Adenocarcinoma	Positive	Positive	Concordant
15	Adenocarcinoma	Negative	Positive	Concordant
16	Adenocarcinoma	Negative	Positive	Concordant
17	Adenocarcinoma	Positive	Positive	Concordant
18	Supportive of carcinoma	Positive	Positive	Concordant
19	Adenocarcinoma	Positive	Positive	Concordant
20	Adenocarcinoma	Positive	Positive	Concordant
21	Negative	Positive	Negative	Concordant
22	Reactive changes	Positive	Negative	Concordant
23	Negative	Positive	Negative	Concordant
24	Negative	Positive	Negative	Concordant
25	Negative	Positive	Negative	Concordant
26	Reactive changes	Positive	Negative	Concordant
27	Negative	Positive	Negative	Concordant
28	Negative	Positive	Negative	Concordant
29	Negative	Positive	Negative	Concordant
30	Negative	Positive	Negative	Concordant
31	Negative	Positive	Negative	Concordant
32	Negative	Positive	Negative	Concordant
33	Negative	Positive	Negative	Concordant
34	Negative	Positive	Negative	Concordant
35	Negative	Non-contributory	Non-contributory	RBC only
36	Negative	Non-contributory	Non-contributory	RBC only
37	Negative	Non-contributory	Non-contributory	RBC only
38	Negative	Non-contributory	Non-contributory	RBC only
39	Negative	Non-contributory	Non-contributory	RBC only
40	Negative	Non-contributory	Non-contributory	RBC only
41	Negative	Non-contributory	Non-contributory	RBC only

Figure 1 - 323

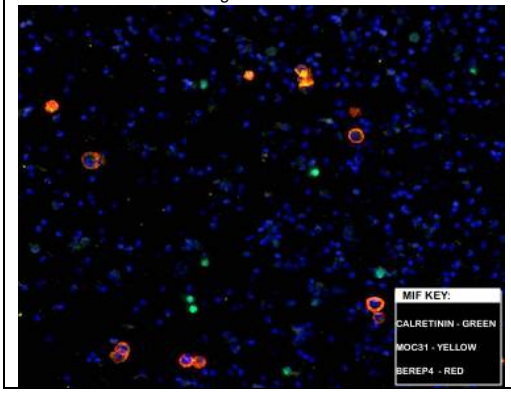
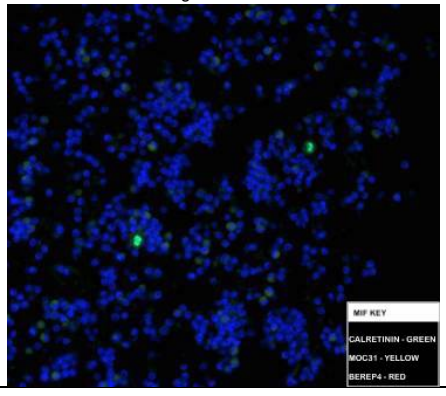


Figure 2 - 323



Conclusions: MFI analysis of cytology specimens on cell block section is a valuable option for the detection of malignant cells in pleural fluid samples. Further studies are warranted to determine if this approach can be used for diagnosing cases with limited cellularity and equivocal cytological diagnosis.

324 Noninvasive follicular thyroid neoplasm with papillary-like nuclear features versus Follicular variant of papillary thyroid carcinoma: Cytomorphologic limitations in thyroid fine needle aspirations

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Disclosures: Oluwadamilare Ajayi: None; Paul Lee: None; Shobha Parajuli: None

Background: The reclassification of a subset of follicular variant papillary thyroid carcinoma (FVPTC) as non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) has resulted in a shift for the evaluation of thyroid nodules that recognizes NIFTP's indolent course. This distinction has created a diagnostic dilemma for cytopathologists for preoperative fine needle aspirations (FNAs). The aim of this study is to assess whether there are specific morphologic or clinical characteristics on thyroid FNA specimens that can distinguish between NIFTP and FVPTC.

Design: Cases between 1/2015 and 10/2018 of surgical pathology diagnosis of NIFTPs and FVPTCs with prior in-house thyroid FNA cytology were included. Exclusion criteria included: non-diagnostic FNAs and discordant FNA site compared to histologic tumor location. Of the 63 cases found, 21 cases were eligible for the study (10 NIFTPs and 11 FVPTCs). The available Diff-Quik, alcohol-fixed, ThinPrep, and cell block slides were evaluated by 2 board certified cytopathologists who were blinded to the final diagnosis. Each thyroid FNA was evaluated for the presence of 10 selected morphologic classifiers. A two-tail t-test was performed for the age, tumor size distribution; Chi-squared analysis was performed tumor location, distribution of cytology diagnosis within the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) and architecture; the remaining morphologic classifiers were analyzed using Fisher exact test.

Results: The average age of the NIFTP cohort was 44.4 years old, which was lower compared with the FVPTC cohort at 58 years old. The sex ratio, tumor size, tumor location, and predominant architecture were matched between the two cohorts.The distribution of TBSRTC classifications were as follows in the NIFTP vs FVPTC cohorts respectively: benign follicular nodule (10%, 0%); Atypia of undetermined significance (50%, 55%); Suspicious for follicular neoplasm (30%, 18%), Suspicious for papillary neoplasm (10%, 27%), and Malignant (0%, 0%). Of the ten morphologic classifiers, none were statistically significant to distinguish between the NIFTP vs FVPTC cohorts.

	Giant cells	Intranuclear pseudo-inclusions	Nuclear crowding	Prominent nucleoli	Anisonucleosis	Nuclear membrane irregularity	Chromatin clearing	Nuclear grooves	Macrophages	Colloid
NIFTP	2/10 (0.20)	1/10 (0.10)	6/10 (0.60)	5/10 (0.50)	5/10 (0.50)	6/10 (0.60)	1/10 (0.10)	4/10 (0.40)	6/10 (0.60)	8/10 (0.80)
FVPTC	3/11 (0.27)	2/11 (0.18)	9/11 (0.81)	5/11 (0.45)	7/11 (0.64)	7/11 (0.64)	4/11 (0.36)	4/11 (0.36)	4/11 (0.36)	7/11 (0.64)
p value	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05

Conclusions: The limitation discovered by this study is that morphologic distinctions between NIFTP and FVPTC are not feasible. Although preoperative thyroid cytology evaluation has demonstrated utility in triaging thyroid nodules, recognition of limitations of thyroid cytology can help cytopathologist develop areas for further research.

325 The Cobas HPV Test on SurePath Collection Media as a Primary Screening Test: a Histologic Correlation Study

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Disclosures: Fatimah Alruwaii: None; Khaleel Al-Obaidy: None; Harvey Cramer: None; Melissa Randolph: None; Howard Wu: None

Background: The Cobas HPV test has been recently approved by the FDA as a primary screening test to be used on specimens collected in SurePath media. Herein, we present our experience with Cobas HPV test on SurePath specimens in correlation with follow-up histologic

diagnoses. We also evaluate its sensitivity in detecting high grade squamous intraepithelial lesion or carcinoma (HSIL+) in comparison with cytology alone and co-testing

Design: 602 SurePath specimens with subsequent tissue specimen were selected. For each case, the cytology diagnosis, Cobas HPV testing status and biopsy/LEEP diagnosis were recorded. Cases with the results of unsatisfactory and glandular pathology were excluded. For the cytology results, any case with at least atypical squamous cells of undetermined significance (ASCUS+) diagnosis was considered positive. The sensitivity of each method was calculated

Results: (Table.1) 591 cases met the selection criteria (mean age=38, age range 20-72). Concurrent Cobas HPV testing was done on 287 cases. Of these, 242 were positive for one or more high risk HPV (16, 18 and others) and 45 were negative. Correlation with histology showed that 16.1% (n=39) and 4.4% (n=2) were of HSIL+ category in the positive and negative groups, respectively. Of the positive cases, 106 cases were of HPV 16 or/and 18 subtypes (16/18 +) and 136 cases were positive for other high risk group (16/18-Other +), and correlation with histology showed HSIL+ in 22.6% (n=24) and 11% (n=15), respectively. Analysis of cases by cytology only (n=591), showed that 19.6% (n=90) of the ASCUS+ category and 10.4% (n=14) of the negative cytology were HSIL+ on histology. Of the 14 false negative cases, 7 had concurrent Cobas HPV testing, which showed high risk HPV in 5 cases and was negative in 2. The two false negative cases constituted 12.9% (n=16) of the total negative cases on both cytology and Cobas. The sensitivity was 86.5% for Cytology alone, 95% for Cobas HPV alone, and 95% for co-testing. The positive predictive value (PPV) of Cobas HPV+ (all types), HPV 16/18+, and HPV others+ was 19%, 29%, and 12%, respectively

		No	Histologic diagnosis			% HSIL+
			NSILM	LSIL	HSIL+	
Cytology alone (n=591)	ASCUS+	457	93	274	90	19.60%
	NSILM	134	63	57	14	10.40%
Cobas alone (n=287)	Cobas HPV-	45	36	7	2	4.4%
	Cobas HPV+	242	127	76	39	16.1%
	16/18 +	106	53	29	24	22.6%
	16/18 -Other +	136	74	47	15	11%
Co-testing (ASCUS+ or Cobas HPV+)		260	140	81	39	15%
NSILM on cytology and Cobas HPV+		63	26	30	7	11.00%
NSILM on cytology and Cobas HPV-		16	12	2	2	12.50%

LSIL: low grade squamous intraepithelial lesion, HSIL: high grade squamous intraepithelial lesion, NSILM: negative for squamous intraepithelial lesion or malignancy

Conclusions: Cobas testing on SurePath media has an overall superior sensitivity (95%) for detection of HSIL+ when compared to cytology alone (86.5%). In our study, HPV 16/18 genotypes identified twice amount of HSIL+ lesions than HPV others (22.6% vs 11%) that justified the strategy of referring HP16/18 positive patients for colposcopy and reflex cytology for patients who are 16/18 negative and others positive

326 Pathologist-Related Factors Associated with Indeterminate Diagnoses ("Atypical" and "Suspicious") in Body Fluid Cytology

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Disclosures: Safa Alshaikh: None; Razvan Lapadat: None; Mohammed Atieh: None; Swati Mehrotra: None; Guliz A. Barkan: None; Eva Wojcik: None; Stefan Pambuccian: None

Background: Although the diagnoses of “atypical” or “suspicious” are made daily in effusion cytology and pelvic washings, very little is known about the factors contributing to these diagnoses. The aim of this study was to review our experience with such diagnoses, and determine if pathologist-related factors contributed to these diagnoses, by comparing the pathologists' rates of indeterminate (IND) and MAL diagnoses and their in IND/MAL ratios.

Design: We searched the electronic records of our academic pathology department and retrieved all cases diagnosed from 1/1/2013 to 6/30/2018 as “atypical” or “suspicious” in BFC. Individual pathologists’ rates of indeterminate diagnoses were calculated and correlated (bivariate, Pearson) with their volume of BCF, years of experience and rates of “positive for malignancy” (MAL) diagnoses.

Results: Of the 4156 BFC cases diagnosed during the study period, 122 (2.94%) had indeterminate diagnoses (100 “atypical” and 22 “suspicious”) and 561 (13.54%) were diagnosed as MAL. Of the 8 board cerified cytopathologists with 6 to over 20 years experience who diagnosed these cases, 2 (P3 and P4), who had reviewed 17 and respectively 49 cases, were excluded from further analysis. Indeterminate diagnoses showed an almost 4-fold inter-pathologist variation, from 1.37% to 5.45%, which was accompanied by a similarly large variation of the indeterminate/malignant ratio (Table 1). Higher IND rates correlated significantly with less experience (r=-0.51, p<0.05), and weakly (not statistically significantly) with BFC volume (r=0.35). The IND/MAL ratio varied within a relatively narrow range, from 0.1 to 0.2 for 5 of 6 pathologists, but was significantly higher (0.42) for the sixth pathologist.

	P1	P2	P5	P6	P7	P8	All
All BFC cases	918	1104	146	604	527	779	4144
Atypical	42 (4.6%)	14 (1.3%)	2 (1.4%)	14 (2.3%)	12 (2.3%)	15 (1.9%)	100 (2.4%)
Suspicious	8 (0.9%)	5 (0.5%)	0 (0.0%)	2 (0.3%)	4 (0.8%)	3 (0.4%)	22 (0.5%)
Indeterminate	50 (5.5%)	19 (1.7%)	2 (1.4%)	16 (2.6%)	16 (3.0%)	18 (2.3%)	122 (2.9%)
Malignant	120 (13.1%)	123 (11.1%)	20 (13.7%)	96 (15.9%)	93 (17.7%)	94 (12.1%)	561 (13.5%)
IND/MAL ratio	0.42	0.15	0.10	0.17	0.17	0.19	0.22

Conclusions: Although the percentage of IND diagnoses in BFC is lower than in other cytology specimens, there is a high interpathologist variation. The rates of IND diagnoses correlate inversely with experience. The IND/MAL ratio could be used, in analogy to the ASC/SIL ratio, for interpathologist and interlaboratory comparisons.

327 Patient and Specimen-Related Factors Associated with Indeterminate Diagnoses (“Atypical” and “Suspicious for Malignancy”) in Body Fluid Cytology (BFC)

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Disclosures: Safa Alshaikh: None; Razvan Lapadat: None; Mohammed Atieh: None; Guliz A. Barkan: None; Swati Mehrotra: None; Eva Wojcik: None; Stefan Pambuccian: None

Background: Although the indeterminate (IND) diagnoses of “atypical” or “suspicious” are routinely used in cytology practice in BFC (pleural, peritoneal, pericardial fluids and pelvic washings), very little is known about the factors contributing to these diagnoses. The aim of this study was to determine the patient-and specimen-related factors that have contributed to IND diagnoses by comparing cases with IND diagnoses to “negative for malignancy” (NEG) cases.

Design: We identified all cases diagnosed as IND in BFC from 2013 to 2018 and matched them with contemporaneous site-matched NEG cases, which were used as a control group. We reviewed all cases and recorded the number and appearance of the atypical/suspicious cells and background features (RBCs, PMNs, lymphocytes, eosinophils, mesothelial cells and macrophages), which were evaluated semiquantitatively (0-3+). The cytologic features, sites, and patient’s history were compared between the two groups, using the Fisher exact text.

Results: Of the 4156 BFC cases diagnosed during the study period, 122 (2.94%) had IND diagnoses (100 "atypical" and 22 "suspicious") and 561 (13.54%) were diagnosed as "positive for malignancy" (MAL). Of the 122 IND cases 47 (38.5%) were pleural, 5 (4.1%) pericardial, 41 (33.6%) peritoneal and 29 (23.8%) pelvic BFC. IND diagnosis were more frequently made in peritoneal/ascitic fluid (46/1075, 3.63% vs. 76/2993, 2.48% all other BFC, p=0.004). The IND/MAL ratio was, however, highest for pelvic (0.30) and pericardial (0.28) BFC and lower for peritoneal (0.24) and pleural (0.17) BFC. There was no difference between the background cytomorphologic features of IND and NEG cases, except for the presence of macrophages in IND. [Table]. IND cases were more frequently from patients with a history of malignancy and had IHC stains done more frequently. On review, the factors most commonly considered to have caused the IND diagnosis were few (<10) atypical/suspicious cells, atypical lymphoid cells, poor cell preservation, and rarely poor preparation/stain quality.

Cytologic Feature	Negative (n=116)	Indeterminate (n=110)	P value (two-tailed)
Cellularity 2-3+	65.6%	74.3%	0.19
RBCs 2-3+	7.7%	9.3%	0.81
PMNs 2-3+	16.4%	14.7%	0.85
Lymphocytes 2-3+	41.9%	55.1%	0.06
Mesothelial cells 2-3+	50.4%	56.0%	0.43
Macrophages 1,2,3+	42.2%	58.3%	0.02
History of Malignancy	43.2%	80.6%	0.0001
IHC stains performed	18.6%	51.4%	0.0001

Conclusions: The most common causes of IND diagnoses were rare atypical cells or poor preservation/staining of cells. Patients with IND diagnoses in BFC frequently have history of malignancy, which may bias the pathologist. IND diagnoses were most frequent in peritoneal BFC, but the IND/MAL ratio was highest in pelvic and pericardial BFC. Apart from the presence of macrophages, background cytomorphologic features are not associaan IND diagnosis in BFC

328 The Utilization of Immunostains in Body Fluid Cytology

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Disclosures: Safa Alshaikh: None; Razvan Lapadat: None; Mohammed Atieh: None; Swati Mehrotra: None; Guliz A. Barkan: None; Eva Wojcik: None; Stefan Pambuccian: None

Background: Immunohistochemistry (IHC) is a valuable ancillary study in cytology in general and plays an important role in body fluid cytology (BFC) in differentiating between negative and positive BFC, and determining the tumor type and primary site. Although a large number of studies have addressed the value of individual immunohistochemical stains or combinations in BFC, little is known about the frequency of the actual use of these stains in routine practice. The aim of this study was to evaluate the utilization of IHC stains in an academic institution.

Design: We performed a retrospective analysis of BFC diagnosed at our institution from 2013 to 2018. The following information was extracted for each case: diagnosis, site (pleural, pericardial, peritoneal, pelvic), number and type of IHC stains performed and their indication.

Results: During the six-year period of this study 4156 BFC cases were diagnosed; 1989 individual IHC stains were performed on 442 cases, representing 10.6% of all BFC cases. 66 individual IHC antibodies were used, with an average of 4.5 stains per case. The most commonly used antibodies were MOC31 (86.9%), calretinin (80%), Ber-Ep4 (44.3%), CD68 (42.9%), and D2-40 (41.1%). IHC stains were most commonly used to rule out malignancy, i.e. to distinguish between reactive mesothelial cells and malignant epithelial cells (%), to determine the type of malignancy (adenocarcinoma vs. squamous cell carcinoma, vs. other malignancies) or to determine the primary site of malignancy.

Diagnoses	IHC	Total	%
Unsatisfactory	0	12	0%
Negative	231	3461	6.67%
Atypical	37	100	37.00%
Suspicious	5	22	22.73%
Positive	169	561	30.12%
Total	442	4156	10.64%
Specimen sites			
Pleural	234	1639	14.28%
Pericardial	34	193	17.62%
Peritoneal	145	1078	13.45%
Pelvic	29	1246	2.33%
Total	442	4156	10.64%

Conclusions: The rate of IHC stain use varied by specimen site, being highest in pericardial specimens, supporting the contention that these fluids contain the most reactive mesothelial cells. The most common indication of IHC stain use was differentiating between benign/reactive "atypical" mesothelial cells and malignant cells; consequently the most commonly used antibodies were MOC31, calretinin, Ber-Ep4, CD68, and D2-40. IHC stains were used most commonly in cases with final indeterminate (atypical/suspicious) diagnoses, suggesting that their use was not entirely successful in separating benign/reactive "atypical" mesothelial cells from malignant cells.

329 Reliability of Combined Fine Needle Aspiration and Core Needle Biopsy in the Diagnosis of Liver Lesions: An Eight-Year Institutional Experience

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Disclosures: Evgeniya Angelova: None; Cecilia Clement: None; Ranjana Nawgiri: None; Heather Stevenson-Lerner: None; Jing He: None

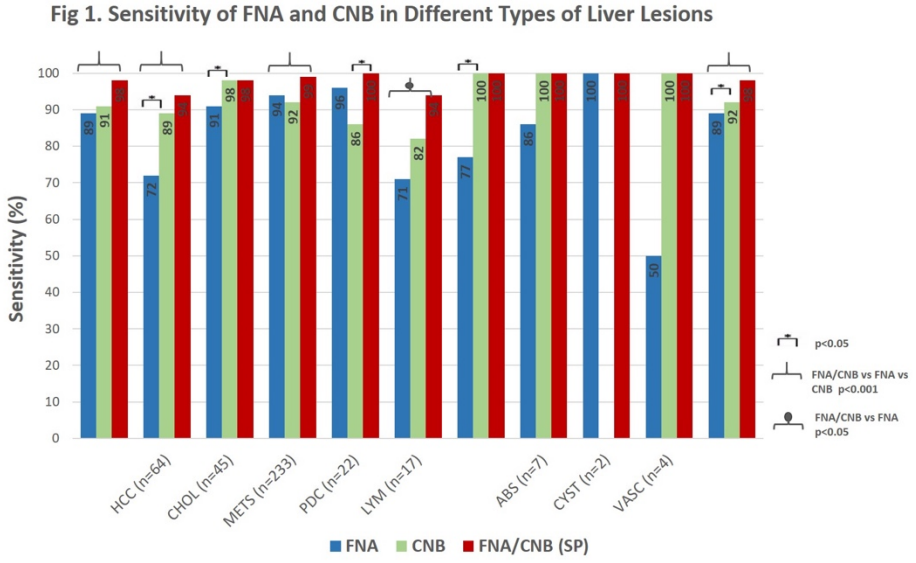
Background: Fine needle aspiration (FNA) followed by core needle biopsy (CNB) when needed, based on rapid on-site evaluation (ROSE), was adopted as a standard of care in our institution for patients with liver lesions. With respect to liver diagnosis this combined FNA and CNB approach has not been systemically evaluated in the literature. This study aims to explore the diagnostic efficacy of image-guided FNA and CNB in the diagnosis of suspected liver lesions.

Design: We retrospectively reviewed all liver FNA performed in our institution between January 2010 and September 2018. A total of 550 cases from 531 patients (358 males and 173 females) with median age of 59 years (range, 13-90) were identified. A total of 459 cases with FNA and concurrent CNB (n=433) or subsequent (n=26) confirmation histology (CNB or resection) were selected. All FNA were assessed with ROSE. Both FNA and CNB in the paired sampling were read by cytopathologist with an expert consultation used as needed. Cytology diagnoses were categorized as benign, malignant, atypical/suspicious, and non-diagnostic.

Results: Malignant diagnoses (83%) included hepatocellullar carcinoma (HCC), cholangiocarcinoma (CHOL), metastatic tumors (MET), poorly differentiated carcinoma (PDC) and lymphomas (LYM). Benign results (17%) included abscess, cysts, benign vascular lesions and non-neoplastic liver. The diagnostic consistency between the FNA and CNB was 85% with significantly discordant results in only 5.3% of cases. Figure 1 shows the distribution of paired FNA and histology diagnostic categories. Combined FNA and CNB shows a higher efficacy for all malignant and benign liver lesions than FNA or CNB alone (Figure 1). However, the false negative rate (FNR) of CNB was lower than FNA for HCC and CHOL, and benign vascular lesions ($p<0.05$). The liver FNA has a slightly better sensitivity than CNB in the metastatic and PDC groups, however not significant. In the entire studied group FNR was significantly lower for combined FNA-CNB (2%) than FNA (11%, $p<.0001$) or CNB (9%, $P<001$) alone.

Categories	FNA/CNB (SP)	Number of cases (%)
Concordant	Malignant/ Malignant	310 (67.5%)
	Benign/ Benign	71 (15.5%)
	Atypical/ Atypical	9 (2%)
Discrepant with 1 tier difference	Malignant/Atypical	10 (2.2%)
	Atypical/Malignant	27 (5.9%)
	Atypical/ Benign	4 (0.9%)
	Benign/ Atypical	0
Discordant	Malignant/ Benign	14 (3.1%)
	Benign/ Malignant	10 (2.2%)
Non-diagnostic FNA	Non-diagnostic/ Malignant	2 (0.4%)
	Non-diagnostic/ Benign	2 (0.4%)

Figure 1 - 329



Conclusions: Combined FNA and CNB approach in our institution provides a high diagnostic efficacy for malignant and benign liver lesions with reduction of FNR of standalone FNA or CNB. This combined diagnostic technique ensures efficient use of tissue, tumor subtyping and ancillary testing by saving health care resources and should therefore be recommended for the evaluation and workup of liver nodules.

330 Is Ultrasound-Guided Fine Needle Aspiration Biopsy of Axillary Lymph Nodes a Viable Alternative to Sentinel Lymph Node Biopsy?

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Disclosures: Kristine Astvatsaturyan: None; Shikha Bose: None

Background: Sentinel lymph node (SLN) status determines the need for axillary dissection in patients with breast cancer. With the improvement in radiologic techniques, it is possible that ultrasound-guided fine needle aspiration biopsy (USG FNAB), a minimally invasive procedure that has successfully replaced many diagnostic surgical interventions, may be used for the preoperative evaluation of axillary lymph nodes (ALN) status. Despite the relative ease of use and low cost, the utility of FNAB is still controversial in evaluation of SLN. Paucity of comparative studies and wide variation in the reported accuracy of FNAB preclude its clinical utility. This study aims to assess the accuracy of USG FNAB in detecting metastatic disease in ALN and to determine if USG FNAB should be considered a viable alternative to SLN excision.

Design: 225 consecutive cases of USG FNAB of ALNs with subsequent histologic follow-up performed in our institution from 2005 to 2018 in patients with primary breast carcinoma were retrospectively evaluated. Results of the FNAB were correlated with histologic diagnosis. Sensitivity, specificity, positive and negative predictive values (PPV and NPV), false-positive and -negative (FP and FN) rates of FNAB were calculated and compared to final ALN status.

Results: FNAB was diagnostic in 202 (90%) patients and inadequate in 23 (10%) patients. In 156 cases (69%) results of the FNAB were concordant with the histologic diagnosis: 83 true negative - TN and 73 true positive- TP cases. No FP result had been rendered. 10 patients with diagnosis of metastatic carcinoma on FNAB were administered neoadjuvant chemotherapy. Subsequent axillary dissection revealed negative ALN. A 100% specificity and PPV were obtained. 25 cases were FN on FNAB, in 16 of these the metastatic deposits were small varying in size from 0.1 to 0.8 cm. Additionally, 11 cases were diagnosed as equivocal on FNAB due to the presence of atypical cells. 5 (45%) of these were negative on histopathology, the remaining 6 cases (55%) had metastatic carcinoma. This yielded a NPV of 77%., and sensitivity of 74.5%.

COMPARISON OF CYTOPATHOLOGIC AND HISTOPATOLOGIC DATA

Cytology	Histology		
	Benign	Metastatic	Total (FNA)
Benign	83	25	108
Metastatic	10	73	83
Equivocal	5	6	11
Non-Diagnostic	12	11	23
Total (Surgical)	110	115	225

Figure 1 - 330

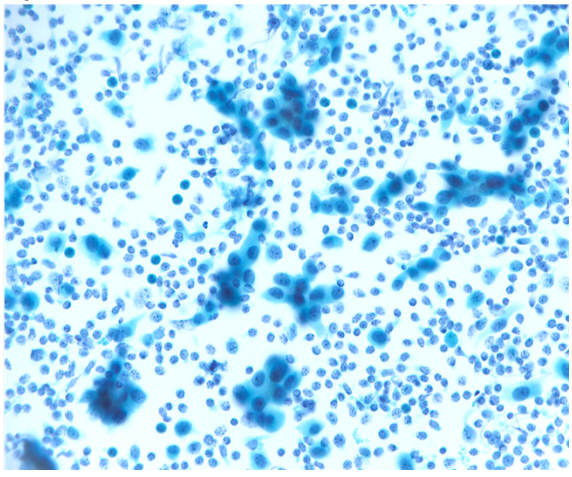
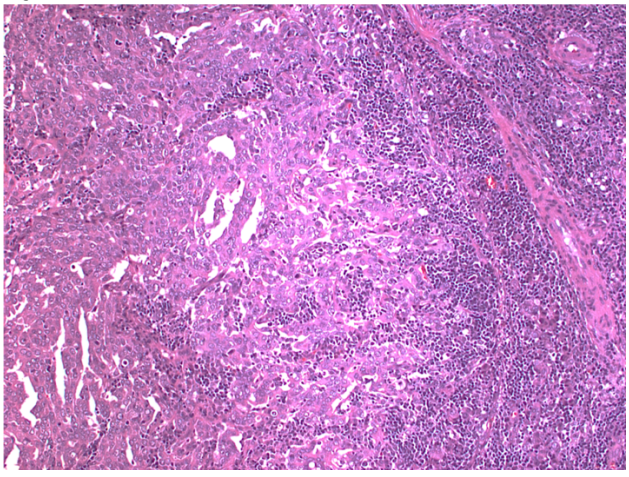


Figure 2 - 330



Conclusions: FNAB of ALN is highly specific with a PPV of 100%.

A negative FNAB result does not exclude the existence of metastatic carcinoma. Correlation with US findings is required for adequate evaluation of these cases.

FNAB of ALN may be used as an initial diagnostic step, thus reducing management cost and improving time to definitive therapy.

331 Noninvasive Follicular Variant of Papillary Thyroid Carcinoma: Impact on Risk of Malignancy Stratification in Thyroid Fine Needle Aspiration Cytology with Histopathologic Correlation

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Disclosures: Kristine Astvatsaturyan: None; Rania Bakkar: None

Background: The term noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) has replaced noninvasive encapsulated follicular variant of papillary thyroid carcinoma (EFVPTC), reflecting indolent behavior of this lesion and identifying it as a neoplasm rather than carcinoma. The aim of our study is to assess the impact of re-classification on risk of malignancy (ROM) for each fine needle aspiration (FNA) diagnostic category and to correlate the histologically proved NIFTP cases with FNA samples.

Design: A cohort of 200 thyroid FNA cases with subsequent resection specimens performed in our institution from 2016 to 2018 was retrospectively evaluated. The FNA diagnoses were reported according to the Bethesda System for Reporting Thyroid Cytopathology. For patients with more than one FNA procedure performed on the same area, the FNA with diagnosis associated with the highest risk of malignancy was included in the study. Results of all FNA cytology were correlated with resection diagnoses. The risk of malignancy was calculated for each category applying NIFTP in malignant (Method 1) and non-malignant (Method 2) groups. The results for two methods were compared. NIFTP resection specimens were correlated with FNA samples.

Results: Cytologic evaluation showed 7 (3.5%) non-diagnostic cases (Category 1), 43 (21.5%) benign (Category 2), 63 (31.5%) atypia/follicular lesion of undetermined significance (AUS/FLUS, Category 3), 26 (13%) follicular neoplasm or suspicious for follicular neoplasm (FN/SFN, Category 4), 17 (8.5%) suspicious for malignancy (SUS, Category 5), and 44 (22%) malignant cases (Category 6). Histopathology revealed 94 (47%) benign cases, 88 (44%) malignant cases and 18 (9%) NIFTP cases. When NIFTP termed as malignant, ROM for Bethesda Categories 1, 2, 3, 4, 5, and 6 was 0%, 11.6%, 46.0%, 46.15%, 94.1%, and 100%, respectively. If NIFTP termed non-malignant, ROM for Bethesda Categories 1, 2, 3, 4, 5, and 6 changed to 0% (no change), 4.65% (6.95% decrease), 28.6% (17.4% decrease) 38.5% (7.65% decrease), 82.4% (11.7% decrease), and 100% (no change), respectively. Review of FNA cytology from 18 NIFTP cases yielded the diagnosis of AUS/FLUS in 11 (61%) cases, benign in 3 (27%), FN/SFN and SUS in 2 (18%) cases each.

Comparison of Risk of Malignancy in Two Methods

Bethesda Category	Total Number of Cases	Method 1: NIFTP = Carcinoma	Method 2: NIFTP = Neoplasm	Decrease in ROM
1	7	0 (0%)	0 (0%)	0 (0%)
2	43	5 (11.6%)	2 (4.65%)	3 (6.95%)
3	63	29 (46.0%)	18 (28.6%)	11 (17.4%)
4	26	12 (46.15%)	10 (38.5%)	2 (7.65%)
5	17	16 (94.1%)	14 (82.4%)	2 (11.7%)
6	44	44 (100%)	44 (100%)	0 (0%)

Figure 1 - 331

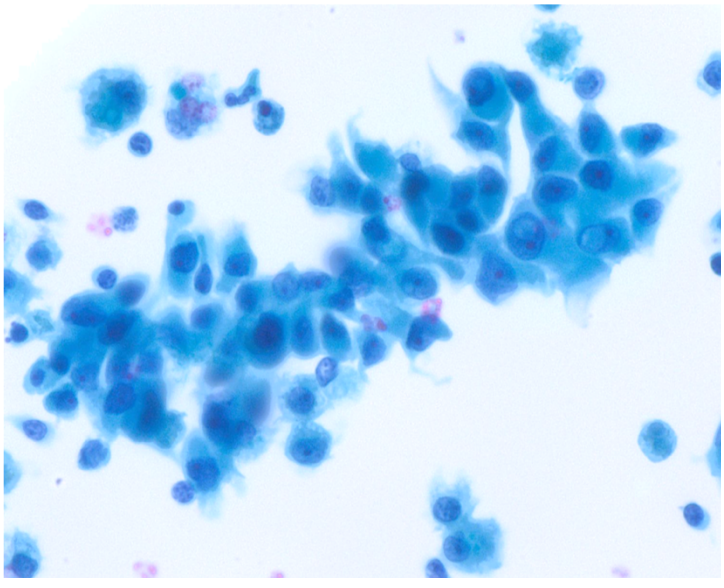
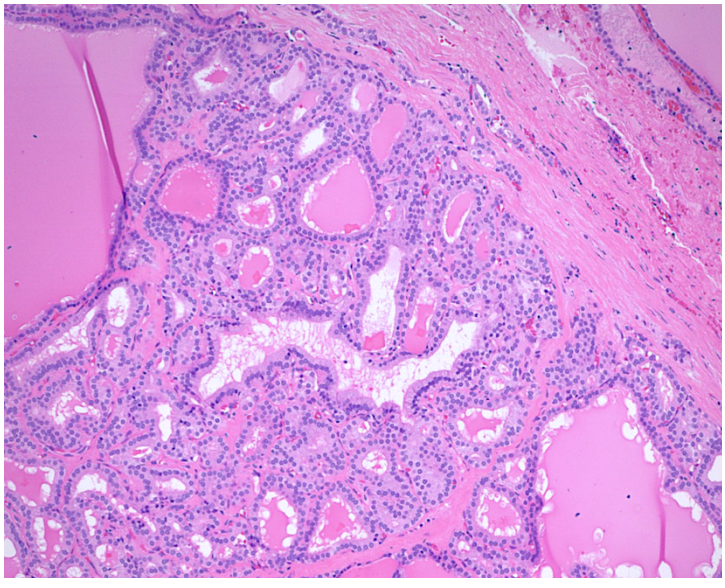


Figure 2 - 331



Conclusions: From out institution experience, the impact of re-classifying NIFTP on the ROM was most pronounced in AUS/FLUS and SUS categories. The majority of NIFTP nodules yielded AUS/FLUS cytological diagnosis in preoperative FNA specimens.

332 Detection of Gene Fusions and Hotspot Mutations in Salivary Gland Tumors Using Cytology Smears and a Custom-Designed Next-Generation Sequencing-Based Assay

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Disclosures: Ava Bhattarai: None; Natalya Guseva: None; Aaron Stence: None; Ramakrishna Sompallae: None; Krishnaveni Sompallae: None; Aaron Bossler: None; Robert Robinson: None; Deqin Ma: None

Background: Salivary gland tumors (SGT) represent 3-6% of head and neck tumors. Fine needle aspirate (FNA) is routinely used as the first diagnostic procedure. Accurate diagnosis can be challenging due to the diversity of these tumors, morphologic overlap between different tumor types and limited immunohistochemistry for differential diagnosis. Identification of recurrent gene fusions in SGTs may serve as diagnostic and prognostic markers. We tested RNA extracted from cytology smears using a custom-designed, next generation sequencing (NGS)-based assay for detection of gene fusions and hotspot mutations associated with SGTs.

Design: Fourteen genes (*ETV6, EWSR1, HMGA2, HRAS, MAML2, MYB, MYBL1, NFIB, NTRK3, NUTM1, PLAG1, PRKD1, PRKD2, PRKD3)* were selected based on extensive literature review. An RNA-based panel was designed using the Archer Assay Designer. Fifteen FNA cases including 7 mucoepidermoid carcinoma (MEC), 5 adenoid cystic carcinoma (AdCC), 1 secretory carcinoma (SC), 1 basal cell carcinoma (BCC), and 1 pleomorphic adenoma (PA) were tested. Total RNA was used to generate NGS libraries and sequencing was performed on Illumina MiSeq. Data were analyzed using the Archer Analysis platform. Corresponding FFPE tissues were tested as well.

Results: Expected gene fusions were identified in each tumor type (Table 1). Specific fusions were confirmed by RT-PCR followed by Sanger sequencing and *PRKD1* mutation was confirmed by Sanger sequencing. Limit of detection was defined as 10% tumor content for fusion and 1% for point mutation. Concordance with FFPE was seen in 12/13 cases. One MEC had low level of *CRTC1/MAML2* fusion detected in the FFPE but not from the smear, likely due to low cellularity in the smear (<10%). Two AdCC cases in which *MYB* fusions were detected in the cytology smear, the corresponding FFPE tissue had insufficient RNA quality or quality.

Tumor	Fusion/mutation in smear	Fusion/mutation in FFPE tissue	Cytology/FFPE concordance
MEC-1	*CRTC1/MAML2*	*CRTC1/MAML2*	YES
MEC-2	*CRTC1/MAML2*	*CRTC1/MAML2*	YES
MEC-3	*CRTC1/MAML2*	*CRTC1/MAML2*	YES
MEC-4	*CRTC1/MAML2*	*CRTC1/MAML2*	YES
MEC-5	*CRTC1/MAML2*	*CRTC1/MAML2*	YES
MEC-6	None	*CRTC1/MAML2*	NO
MEC-7	None	None	YES
AdCC-1	MYB/NFIB	*MYB/NFIB*	YES
AdCC-2	MYB/NFIB	*MYB/NFIB*	YES
AdCC-3	*MYB/NFIB*	QC failed	NA
AdCC-4	*MYB/NFIB*	QC failed	NA
AdCC-5	None	None	YES
SC	*ETV6/NTRK3*	*ETV6/NTRK3*	YES
BCC	*PRKD1* p.E710D	*PRKD1* p.E710D	YES
PA	*GEM/PLAG1*	*GEM/PLAG1*	YES

Conclusions: This study showed that gene fusions and mutations can be reliably detected from cytology smears of various types of SGT using this custom-designed NGS assay. Interestingly, cytology smears yielded better quality RNA than FFPE tissue. The ability of this assay to detect novel fusions without prior knowledge of their partners will expand our understanding of genomic aberrations in SGTs and be beneficial for diagnosis of challenging cases.

333 Biliary Tract Involvement by Hepatocellular Carcinoma (HCC): An Under-Appreciated Phenomenon and Potential Diagnostic Pitfall in the Evaluation of Bile Duct Brushings

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Disclosures: Shristi Bhattarai: None; Rondell Graham: None; Carlie Sigel: None; Jiaqi Shi: None; Raul Gonzalez: None; Yue Xue: None; Alyssa Krasinskas: None; Kim HooKim: None; Michelle Reid: None

Background: Bile duct brushings (BDBs) are often used as the initial investigative pathology test for pancreatobiliary tract lesions. Most biliary lesions/tumors are first diagnosed on BDB or biopsies and are pancreatic in origin/cholangiocarcinoma (CC), and less frequently intraductal papillary neoplasms of bile duct (IPNB). Biliary tract involvement by HCC however is highly unusual and a rare source of malignant cells on BDB.Their clinicocytopathologic features have not been elucidated.

Design: A multi-institutional archival search yielded 12 such cases.

Results: HCC involving common bile duct (CBD) (n=10) and right hepatic duct (n=2) was identified in 10 males and 2 females, of mean age 48 yrs (range 46-80). MRI/CT results were available in 6 and revealed masses consistent with HCC in 6; 1 presented with an ill-defined portal hepatis mass arising from the CBD/liver. ERCP results were available in 7 and revealed an intraductal papillary frond-like/polypoid mass in 3, a stricture in 2 and no lesion was seen in 2 cases. On BDB 8 cases were diagnosed as HCC, 1 as CC, 2 as atypical cells ppresent and 1 as negative. Urovysion FISH was done in 2 and was (+) in 1 (polysomy of chr 3, 7,17). Cytologic findings were similar across cases which showed a 2-cell population of ductal cells and large poylgonal cells in 3-D clusters or singly. These had abundant granular, oncocytic (n=11) to pure clear/mixed cytoplasm, N/C of 0.5 and oval nuclei with large central nucleoli. Nuclear irregularity (n=6), pleomorphism (n=3), endothelial wrapping (n=2) and cytoplasmic bile pigment (n=2) were less common; 1 HCC had large papillae lined by clear cytoplasm consistent with steatohepatitic HCC (Table 1).

Cytological findings of Hepatocellular Carcinoma on Bile Duct Brushing (n=12)

Variables	**Cases**											
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Hypercellularity	0	0	1	1	0	0	0	1	1	1	0	1
3D cluster	1	1	1	1	1	1	1	1	1	1	1	1
Single cell	1	1	1	1	1	1	1	1	1	1	1	1
NC ratio	High	High	High	High	Low	Low	High	High	High	High	High	High
Cytoplasm	Granular	Granular	Granular/ Clear	Granular	Granular/ Clear/oncocytic	Granular/ Clear/oncocytic	Granular/oncocytic	Granular/ Clear	Granular/ Clear	Granular/ Clear	Granular	Granular
Nucleoli	1	1	1	1	1	1	0	1	0	1	1	1
Endothelial Wrapping	0	0	0	0	0	0	0	1	0	0	0	1
Chromatin	0/1	1	0/1	0/1	0/1	0/1	1	1	1	0/1	0/1	0/1
Papillae	0	0	0	1	1	1	1	0	0	1	0	0
Necrosis	0	0	0	1	1	1	1	1	0	0	0	0
Cytoplasmic Bile Pigment	0	0	0	1	0	0	1	0	0	0	0	0
Nuclear Irregularity	0	0	1	0	1	1	0	0	1	1	0	1
Pleomorphism	0	0	0	1	0	0	0	1	0	0	0	1
2 cell population	0	0	0	1	0	0	0	1	0	0	0	1

0, absent; 1, present; 0/1, hypochromatic and hypochromatic; 3D, 3-dimensional cell clusters; 2 cell population, tumor cells and benign ductal cells.

Conclusions: HCC may occasionally extend into the intra/extrahepatic biliary tree and may present as polypoid intraductal lesions simulating IPNB, particularly oncocytic type or less commonly an oncocytic neuroendocrine tumor. As a result tumors are sometimes sampled on BDB. Because of the monotony of well-differentiated HCC and the rarity of endothelial wrapping in liquid-based samples HCC may be mistakenly classified as benign or indeterminate, while more pleomorphic examples may be misclassified as adenocarcinoma. Cytopathologists should be mindful of this differential when evaluating BDBs, particularly in patients with concomitant liver lesions or risk factors for HCC.

334 Pelvic Mass Fine Needle Aspiration in Men: A Multi-institutional Retrospective Analysis of 107 Cases

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Disclosures: Shristi Bhattarai: None; Kim HooKim: None; Mohammad Mohammad: None; Michelle Reid: None

Background: Pelvic masses are commonly seen in women and are usually of metastatic origin. Fine needle aspiration (FNA) plays a critical role in the diagnosis, providing material for possible molecular testing, guiding biopsy of target site and clinical management. However, FNA experience in the assessment of pelvic masses in men is not well established as it is in women. In addition, the diagnosis may be challenging if the mass presents years after primary diagnosis. The goal of this study was to evaluate pathologic features of pelvic masses in males sampled by FNA with clinical and pathologic correlation.

Design: Pelvic mass FNAs performed on men over the age of 18 years were identified. The pertinent clinical and pathologic data were reviewed and correlated with corresponding surgical diagnosis when available.

Results: There were 107 patients of median age 59 years (age range 18- 93 years); the median mass size was 5.3 cm (range 1.1-17.5 cm). FNA diagnoses included 56 (52.3%) malignant FNAs, 3 (2.8%) suspicious for carcinoma, 15 (15.0%) atypical, 24 (22.4%) negative, and 8 (7.5%) non-diagnostic specimens. There were 23 (41.1%) soft tissue tumors {16 malignant and 7 benign (all schwannomas)}, 8 (14.3%) lymphomas and 25 (44.6%) adenocarcinomas {7 (28%) of them not otherwise specified (NOS) and 18 (72%) metastases from prostate (3, 16.6%), colorectal (6, 33.3%), lung (1, 5.5%), upper gastrointestinal tract (4, 22.2%), and urothelial (4, 22.2%)}. In 32 (57.14%) cases, the pelvic mass represented the first time diagnosis of malignancy, while 24 (42.86%) patients had a known cancer history prior to FNA.

Conclusions: Pelvic masses are rarely seen in men. When these occur, roughly 40% of them are soft tissue tumors (most of them malignant) while almost half of them represent metastatic adenocarcinomas mainly from the gastrointestinal tract and prostate. FNA is an effective diagnostic tool in the assessment of these masses and plays a critical role in clinical management. Cytopathologists should be aware of the spectrum of clinical presentation and broad differential diagnosis of lesions that maybe seen, including metastatic tumors from as far away as the lung.

335 Evaluation of NSCLC Cytology Cell Block Specimens Using Ventana PD-L1 SP263 Immunohistochemistry Assay

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Disclosures: Aastha Chauhan: None; Emilian Racila: None; Jimmie Stewart: None; Khalid Amin: None

Background: Introduction of immune checkpoint inhibitors, including programmed death-1(PD-1) and programmed death–ligand 1 (PD-L1) inhibitors, has rapidly altered the treatment protocol of non-small cell lung carcinomas (NSCLC). Since endobronchial ultrasound guided fine needle aspiration is the mainstay of diagnosis and staging of NSCLC, cytology material in many cases is the only available specimen for ancillary testing of NSCLC. This study was undertaken to determine the adequacy of Ventana SP263 PD-L1 Assay in cytology cell blocks.

Design: Forty cytology NSCLC cases with matching histology specimens (biopsies and resections) obtained between 2014 and 2018 were identified. After assessing for adequacy, the cytology and histology specimens from each case were stained with Ventana SP263 PD-L1 assay. Adequate cases with 100 or more tumor cells (32 cell blocks) were evaluated for tumor proportion scores (TPS) and staining intensity scores (SIS). TPS was determined by enumeration of the percentage of PD-L1 tumor cells with any amount of membrane positivity expressed as a whole number relative to all viable tumor cells in the specimen. The scoring system for PD-L1 expression was divided into three groups: a) High expressor, TPS ≥ 50%; b) Low expressor, TPS of ≥1%-49%; and c) Negative, TPS <1%. SIS was evaluated on a scale of 0-3 as follows: 0-negative, 1-weak, 2-moderate, 3-strong.

Results: Out of 40 cases, 32 had adequate cellularity on both cytology and histology. There were 12 adenocarcinomas and 20 squamous cell carcinomas. Overall concordance between cytology and histology was 60% (19/32). Of the 25(78%) positive cytology cases, 17 showed low expression and 8 high expression of PD-L1. SIS was 1+ in 7 cases, 2+ in 11 cases, and 3+ in 7 cases. Of the 20(62.5%) positive histology specimens, 14 were low expressors and 6 were high expressors. There was 100% concordance of SIS between positive cytology and histology specimens. The 13 of 32 cases (40%) that were discordant included 8 biopsies and 5 resections: 9 cytology cases were positive for PD-L1 while corresponding histology specimens were negative; similarly, 4 cases that were negative on cytology were positive for PD-L1 on histology.

Conclusions: This study showed a 60% concordance of PDL-1 expression in NSCLC between cytology and histology specimens. Since 8 of the discordant specimens were biopsy samples, the results can be, at least in part, attributed to tumor heterogeneity and tumor sampling. Cytology cell blocks can potentially be considered

336 Non-invasive Follicular Thyroid Neoplasm with Papillary-like Nuclear Features (NIFTP): Impact on FNA Diagnoses of Thyroid Nodules and its Molecular Profile

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Disclosures: Li Chen: None; Lina Liu: None; Bing Leng: None

Background: Fine needle aspiration (FNA) and its on site evaluation is a reliable and indispensable procedure for diagnosing thyroid nodules. In 2016 a new diagnostic entity of non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) has been proposed. NIFTP is the category for neoplasms previously classified as noninvasive follicular variant of papillary thyroid carcinoma (FVPTC) characterized by its extremely indolent behavior. NIFTP is considered as a neoplasm with very low malignant potential, instead of a benign nodule, due to its underlying mutations. The main goals of this study are to investigate the impact of NIFTP diagnosis on FNA evaluation of thyroid nodules and subsequent clinical management and to identify its molecular profile.

Design: 308 cases previously diagnosed as FVPTC from the year 2005 to 2015 were reevaluated by two pathologists independently. After NIFTP has been introduced and applied in our practice (2016 to present), 10 cases were diagnosed as NIFTP. The presurgical FNA diagnoses were reviewed. Demographic information, treatment, tumor metastasis and tumor related death were collected. DNA and RNA were extracted, libraries were prepared, sequencing was performed to target 52 genes relevant to solid tumors (Oncomine™ Focus Assay, ThermoFisher) and data were analyzed using Ion Reporter.

Results: Totally 32 cases were diagnosed/reclassified as NIFTP from 2005 to present. Among them, 22 cases were previously (year 2005 to 2015) diagnosed as FVPTC and reclassified as NIFTP. 10 cases were diagnosed as NIFTP since 2016. The average size of the tumors is 1.2 cm. Majority of these NIFTP patients are female (81.2%, 26/32) and the median age is 54 year old. There are no tumor metastases or tumor related death in any of these cases. The comparison of FNA diagnoses for surgical NIFTP cases before and after 2016 is summarized in Table 1. Before 2016, 28.8% (6/21) NIFTP cases were diagnosed as PTC (Bethesda category 6) and all of these patients were treated with total thyroidectomy. Interestingly, since 2016, only 10% (1/10) NIFTP case was diagnosed as PTC by FNA and treated with total thyroidectomy. The molecular study showed RAS mutations (KRAS or NRAS) in 42.9% NIFTP cases.

Table 1: The comparison of FNA cytology diagnoses of NIFTP cases before and after NIFTP introduction in 2016.

FNA cytology dianosis	benign	AUS/FLUS	FN	Suspicous for PTC	PTC	FNA not performed
Before NIFTP introduction	28.5% (6/21)	4.7% (1/21)	19.0% (4/21)	19.0% (4/21)	28.5% (6/21)	4.8% (1/21)
After NIFTP introduction	40% (4/10)	10% (1/10)	30% (3/10)	0 (0/10)	10% (1/10)	10.0% (1/10)

Conclusions: Our study demonstrates the big impact of the concept of NIFTP on FNA diagnosis of thyroid nodule with reduced PTC FNA diagnosis after introduction of NIFTP. The presence of nuclear features of PTC, but rare or absence of nuclear inclusions, predominantly microfollicular growth<

337 Cytomorphologic and Molecular Analyses of Fallopian Tube Fimbrial Brushings for Diagnosis of Serous Tubal Intraepithelial Carcinoma

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Disclosures: Michael Herman Chui: None; Russell Vang: None; Tian-Li Wang: None; Ie-Ming Shih: None; Christopher VandenBussche: None

Background: The paradigm shift localizing the origin of ovarian high-grade serous carcinoma (HGSC) to the fimbriated end of the fallopian tube underscores the rationale for meticulous microscopic examination of salpingectomy specimens. The precursor, termed “serous intraepithelial carcinoma” (STIC), often presents as a focal lesion, which poses difficulties for histologic diagnosis. In this study, we describe a method to examine exfoliated epithelial cells from fallopian tube fimbria by gentle brushing, thereby enabling thorough sampling of the mucosal surface.

Design: Fimbrial brushings were collected from 20 fresh salpingectomy specimens from 15 patients, including 5 with pathologically-confirmed ovarian HGSC. Samples, taken only from tubes grossly negative for tumor, were processed for Papanicolaou staining, p53 immunocytochemistry, and *TP53* mutation analysis.

Results: Cells with malignant cytomorphologic features were found only in tubal brushings from patients with ovarian HGSC. Rare cell clusters composed of malignant cells juxtaposed with normal epithelial cells were identified and interpreted as evidence consistent with STIC or mucosal colonization by carcinoma (Figure 1 - Case #15, cytologic preparation). In all cases, atypical/malignant cells detected by cytology corresponded to lesions with similar morphology and immunostaining pattern in permanent sections, demonstrating the sensitivity of the technique, while providing reassurance that specimen integrity is not disrupted by the procedure (Figure 2 - Case #15, tissue section). Targeted next-generation sequencing confirmed the presence of *TP53* mutations in fimbrial brushings from HGSC, but not benign cases, and demonstrated concordance with the immunostaining pattern. Identical mutations were found in matched lesions microdissected from formalin-fixed tissue sections.

Figure 1 - 337

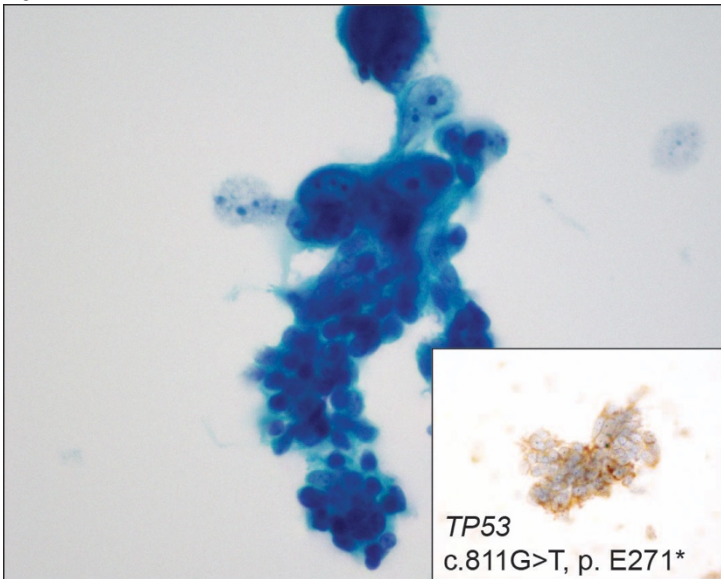
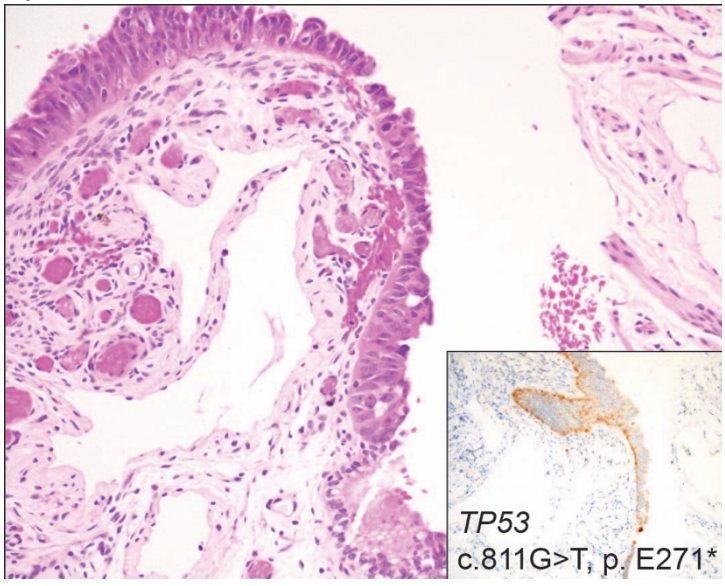


Figure 2 - 337



Conclusions: The described technique enables cytomorphologic evaluation of the fallopian tube fimbria for diagnosis of STIC, serving as a complement to histology, while offering distinct advantages with respect to procurement of cellular material for ancillary testing and research.

338 ASC-US: A Diagnosis of High Clinical and Diagnostic Significance from Anal Pap Tests in HIV-Positive Patient Population

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Disclosures: Adela Cimic: None; Jonas Heymann: None; Susan Alperstein: None; Momin Siddiqui: None

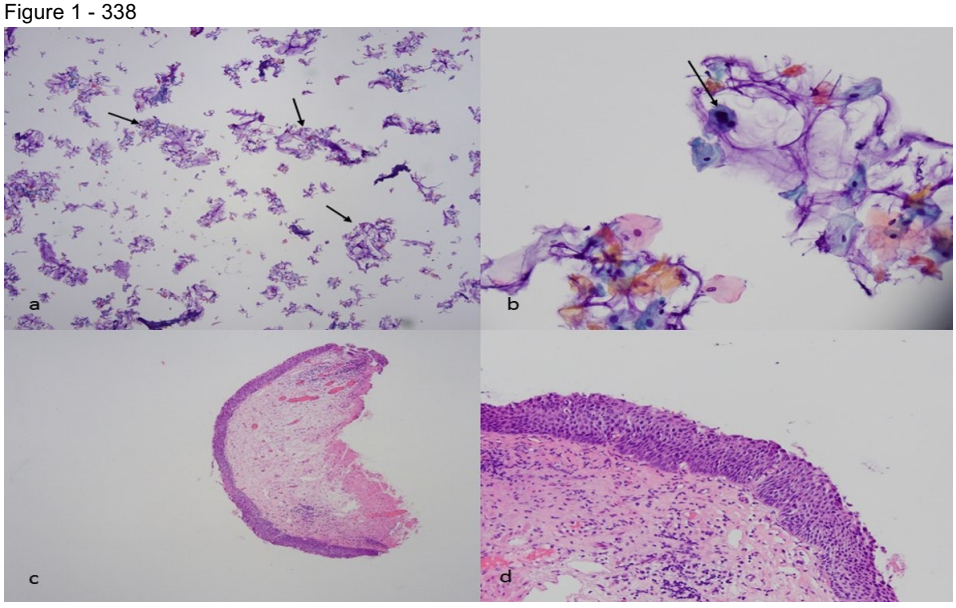
Background: The incidence of squamous cell carcinoma of the anus (SCCA) is increasing. The main risk factors for SCCA are HPV infection, anal intercourse, HIV infection, and smoking. There is no consensus on screening for anal SCCA, and the most commonly accepted first-step screening modality is Pap test alone or combined with digital anorectal examination.

Design: A retrospective search at our institution over a 5 year period, identified 5982 HIV positive patients. Of those, 1754 patients with a follow-up biopsy within 6 months, were identified. The specimens were collected with a Dacron swab and processed as a single ThinPrep slide. HR-HPV testing was not performed on this cohort. We focused on the interpretation of ASC-US and its follow-up. To our knowledge, this is the largest anal cytology study of HIV positive patients.

Results: Of 5982 patients, 37.7% were women while 62.3% were men with an average age of 49.4 years. Our five-year ASC-US/SIL ratio is 1.3. The distribution of diagnostic categories and correlation with high-grade histologic findings is presented in Table 1. The sensitivity of the anal Pap test is 93.1% but with low specificity at 22.9% in predicting the severity of dysplasia in the follow-up biopsy.

Cytologic diagnosis	Number of cases (%)	Number and (%) of cases histologically diagnosed as AIN 2/3
NILM	169 (9.6)	39 (23)
ASC-US	771 (43.9)	333 (43.1)
ASC-H	308 (17.5)	178 (58)
LSIL	329 (18.7)	189 (57.7)
HSIL	177 (10.1)	117 (66.6)

Figure 1 - 338



Conclusions: ASC-US is the most frequent interpretation rendered on anal cytology. Corresponding biopsies show high-grade disease in 43% of the cases. Failure to detect high-grade disease in these specimens can be attributed to thicker preparations due to presence of mucous and profoundly degenerated cells, resulting in ASC-US as the most frequent interpretation being rendered in anal cytology specimens (figure 1: a. low-power view shows abundant mucous b. rare ASC-US cells entangled with mucous c. follow-up biopsy shows AIN2-low power view d. follow-up biopsy shows AIN2-high-power view). The results highlight the need for HR-HPV testing even in HPV positive patients. Having the results of HR-HPV testing would likely improve the specificity of ASC-US diagnosis. In addition, patient education on preparing for the anal Pap test, along with improvement in collection practices may lead to a reduction in ASC-US diagnosis and a higher yield of diagnostic cells displaying features of high-grade disease and more unequivocal clinical diagnosis.

339 Anal Cytology in Correlation with HPV Negative Cervical cytology in HIV Positive Women: A Separate Infection or Viral Clearing?

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Disclosures: Adela Cimic: None; Jonas Heymann: None; Susan Alperstein: None; Momin Siddiqui: None

Background: Risk factors for squamous cell carcinoma of the anus (SCCA) are HPV infection, anal intercourse, HIV infection, and smoking. A positive correlation between cervical dysplasia and anal lesions has been reported and we decided to investigate the correlation between cervical lesions, cervical HPV status and anal lesions in HIV positive women. To our knowledge, this is the first study to correlate HPV negative cervical cytology with anal lesions in HIV positive population.

Design: A retrospective database search identified 571 HIV positive patients with anal Pap tests in 2017; 84 patients have a follow-up biopsy within 6 months and for 59 patients long-term gynecologic follow-up is available (>10 years) with two or more HPV results. The highest grade cervical dysplasia is recorded. 39 patients have at least one HR-HPV positive result, while 20 patients have negative HPV results.

Results: The average patient's age at the time of diagnosis of anal high-grade dysplasia is 50.7. Of all the cases with histologic follow-up, the cytologic results included NILM: 6.4%, ASCUS: 46.4 %, ASC-H: 14,3 %, LSIL: 18.9 %, HSIL: 11.8 %. Patients with gynecologic history along with cervical HPV results and follow-up anal cytology/ histology are presented in Table 1. HPV status for anal specimens is not available.

Cytology/histopathology		**HPV negative patients**		HPV positive patients	
Cervical pathology	Anal pathology	**Number**	**%**	Number	%
Benign/NILM	Benign/NILM	**4**	**20**	2	5.1
Benign/NILM	LSIL	**1**	**5**	0	0
Benign/NILM	HSIL	**6**	**30**	4	10.2
LSIL	Benign/NILM	**4**	**20**	3	7.6
LSIL	LSIL	**1**	**5**	2	5.1
LSIL	HSIL	**4**	**20**	9	23
HSIL	Benign/NILM	**0**	**0**	3	7.6
HSIL	LSIL	**0**	**0**	2	5.1
HSIL	HSIL	**0**	**0**	14	35.8

Conclusions: HIV positive women with cervical dysplasia along with HR-HPV positive results are likely to develop anal disease. However, in HPV negative patients anal lesions appear to be largely independent in HIV positive population. Our study shows that 50% of all cervical HPV negative patients with low-grade or negative for dysplasia cervical cytology develop high-grade anal lesions. The results suggest that cervical and anal lesions could be due to separate infections or a separate process of viral clearing. This pilot study highlights the need for independent HPV testing and screening for cervical and anal specimens.

340 Reliability of Thyroid Imaging Reporting and Data System (TI-RADS) in Predicting Malignancy in Thyroid Fine Needle Aspirations (FNA)

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Disclosures: Leah Commander: None; Shikhar Vyas: None; Kevin Greene: None

Background: In 2017, the American College of Radiology (ACR) developed a risk stratification scoring system for thyroid ultrasounds (US) called the Thyroid Imaging Reporting and Data System (TI-RADS). This system assigns points to five different ultrasonographic features within a thyroid lesion, which are combined into a total score. Based on the total score, the lesion is placed into one of five risk categories, ranging from “benign” (TR1) to “highly suspicious” (TR5). TI-RADS category and lesion size determine whether clinical follow up or FNA are recommended. These guidelines were adopted at our institution in 2017. In this study, we seek to evaluate the concordance between TI-RADS category and Bethesda category in US-guided FNAs.In 2017, the American College of Radiolo

Design: We performed a retrospective review of the pathology reports from all US-guided thyroid FNAs collected at our institution over a two-month period in 2018, as well as the US reports conducted prior to the FNAs. When applicable, subsequent surgical pathology reports were also reviewed. Cases without a documented TI-RADS score were excluded, as were FNAs interpreted as Bethesda Category I (Unsatisfactory). We calculated the unweighted kappa between TI-RADS category and Bethesda category, as well as the median Bethesda category for cases within each TI-RADS catego

Results: We identified 94 thyroid FNAs, 52 of which were accompanied by TI-RADS-compliant US reports. FNAs from two of the cases were unsatisfactory and excluded from our analysis. The median Bethesda category was II for each TI-RADS category. The unweighted kappa between TI-RADS category and Bethesda category was 0.0145. Three cases had a subsequent surgical resection. Two of the three surgical specimens showed papillary thyroid carcinoma (TR5/Bethesda V and TR3/Bethesda VI). The other surgical specimen showed an adenomatoid nodule in a multinodular goiter (TR4/Bethesda III).

Figure 1 - 340

Diagnostic Category		TI-RADS				
		2 *Not Suspicious*	3 *Mildly Suspicious*	4 *Moderately Suspicious*	5 *Highly Suspicious*	*Total*
Bethesda	II	5 (100%)	13 (81%)	14 (66%)	5 (63%)	*37*
	III	0	2 (13%)	6 (28%)	2 (25%)	*10*
	IV	0	0	0	0	*0*
	V or VI*	0	1 (6%)	1 (5%)	1 (12%)	*3*
	Total	*5*	*16*	*21*	*8*	*50*

* Bethesda categories V (suspicious for malignancy) and VI (malignant) were considered equivalent for analysis purposes

Conclusions: TI-RADS scoring plays a critical role in determining which thyroid nodules receive an FNA; however, in our experience, it does not correlate well with the FNA results. The identical median Bethesda category (II), regardless of TI-RADS category, suggests that the current TI-RADS scoring system may be suboptimal at determining which patients would most benefit from an FNA. Cytopathologists should take care to avoid bias based on the reported TI-RADS score of the lesion. A larger study to expand the number of cases, including those with subsequent surgical specimens, may be valuable.

341 Defining Thyroid "Spherules": a Benign Cytomorphologic Feature that Mimics Microfollicles

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Disclosures: Danielle Costigan: None; Mohanad Shaar: None; Mary Frates: None; Erik Alexander: None; Edmund Cibas: None

Background: We have observed distinctive rounded structures in thyroid fine needle aspirations (FNAs) we have termed "spherules." Although often small and interpreted as microfollicles, spherules are notable for the even spacing of the follicular cells along the perimeter of the structure. Because they have an orderly architectural arrangement, we hypothesize that spherules are non-neoplastic and do not carry the same risk of neoplasia as do traditional microfollicles. The aim of this study was to identify the clinical significance and histopathologic correlate of spherules.

Design: 420 thyroid FNAs with an interpretation of atypia of undetermined significance (AUS) were reviewed for the presence of spherules, defined as small follicles with a rounded, smooth, sharply defined outer contour, evenly spaced nuclei, and a three-dimensional appearance. Cases were included if spherules accounted for most of the cellular sample (>50% of follicular cell arrangements). Cases were assessed for cellularity using a three-tier system (low, medium, high cellularity). Clinical, histopathologic, molecular testing, and sonographic follow-up data were obtained.

Results: Twenty-one spherule cases were identified, representing 5% of all AUS cases reviewed. All twenty cases with follow-up had a benign outcome. Eleven were tested by the Afirma® gene expression classifier (GEC); 8 were GEC benign and 3 suspicious but histologically benign following surgical resection. 2 additional cases (total =5) were histologically benign following surgery. Four patients had repeat benign cytology. Three patients had repeat stable ultrasound findings. The histopathology of spherules recapitulated the cytomorphology; in resected specimens, spherules were often associated with hyalinization. Cellularity was evaluated in all available cases (n=18) and was mostly low (13/18; 72%). The remainder were moderately cellular (5/18; 28%); no cases were markedly cellular.

Conclusions: Thyroid nodules comprised of spherules are uncommon but appear to be associated with benign outcome. Recognizing this distinctive cytomorphologic finding may help reduce the number of thyroid FNAs interpreted as AUS and save patients unnecessary additional testing and surgery.

342 The Value of Peritoneal Washing Cytology in Staging of Ovarian Tumor: A 16-Year Institutional Experience

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Disclosures: Ding Dai: None; Rongqin Ren: None; Qiang Wu: None; Heng Hong: None

Background: Peritoneal washing cytology (PWC) is a routine procedure in staging of ovarian neoplasms according to American Joint Committee on Cancer (AJCC). The purpose of this study was to evaluate PWC in ovarian tumors by comparing the results of PWC and corresponding histopathological specimens. A positive PWC may upstage ovarian tumor into T1c3. We reviewed the cases of ovarian tumor in our institution from 2003 to 2018, and compared the histologic and cytological features with other entities. The study analyzed the risk factors for a positive PWC and its significance in the pathological staging of malignant ovarian tumors.

A total of 918 ovarian neoplasm specimens with surgical resection and PWC performed from 2003 to 2018 in our institution were collected, reviewed, categorized and statistically analyzed retrospectively. All the cases have histological diagnoses and concurrent PWC results.

Total 712 benign ovarian neoplasms showed negative PWC except 2 cases with atypical changes. Among borderline and malignant ovarian epithelial neoplasms, 7 of the 53 borderline cases showed positive PWC (13.2%), while 51 of 120 malignant cases showed positive PWC (42.5%). None of the 31 cases of germ cell and sex cord-stromal tumors had positive PWC (0%). High grade and smaller tumor size of epithelial ovarian tumors were related to a higher rate of positive PWC ($p<0.01$). Other histological risk factors related to positive PWC included positivity of capsular involvement by tumor, angiolymphatic invasion, ovarian rupture, and bilateral ovarian involvement (all $p<0.01$). As for the role of PWC in the pathological staging of ovarian tumors, among the 196 cases of malignant ovarian tumors with pathological stage in this study, all T2 and T3 tumors were staged based on histological results. Furthermore, of the 25 cases of T1c tumors could be correctly staged under the current AJCC system based only on the presence of the either capsular rupture or capsular involvement on histological examination. Only 10 showed positive PWC, in which 4 cases of T1c3 were determined by positive PWC.

Figure 1 - 342

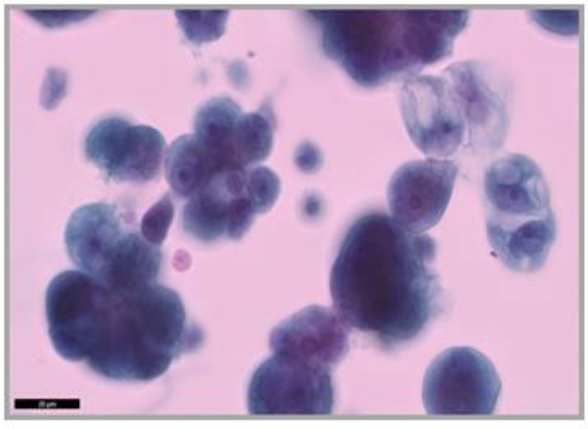
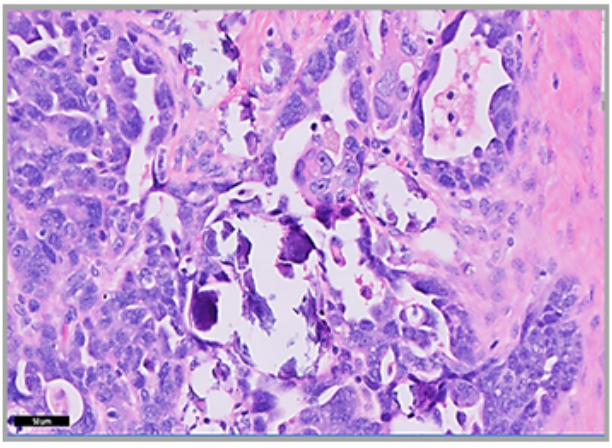


Figure 2 - 342



Positive PWC is closely related to many risk factors which can be determined by histological examination of ovarian tumor. Most ovarian tumors can be correctly staged in the current AJCC system based on histological findings without PWC. The current AJCC staging criteria supports our findings.

343 DICER1 Mutation in Follicular Neoplasm of the Thyroid

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Disclosures: Armine Darbinyan: None; Manju Prasad: None; Guoping Cai: None; Adebowale Adeniran: None

Background: Autosomal dominant hereditary pleiotropic tumor syndrome caused by germline *DICER1* mutations is a genetic disorder which is associated with development of tumors and dysplasias with onset in childhood, adolescence, or early adulthood, including

pleuropulmonary blastoma, cystic nephroma, and lesions involving endocrine organs. Recent studies show that incidence of multinodular goiter (MNG) is elevated in patients with *DICER1* syndrome significantly with 16-fold increased risk of thyroid cancer.

Design: Cytological analysis of FNA of the thyroid from three patients with *DICER1* mutations (two adolescent female siblings and one adult female patient) was performed. Results were correlated with clinical/imaging findings and histological evaluation of corresponding thyroidectomy specimens.

Results: Cytologic preparations from all three patients showed moderately cellular specimen with altered architecture displaying uniform follicular cells arranged in small crowded and overlapping groups and microfollicles. Follicular cells showed slight size variation, had round nuclei, evenly dispersed finely granular chromatin and small, inconspicuous nucleoli. Colloid was scant, although some microfollicles contained small amounts of inspissated colloid. No definite nuclear features of papillary thyroid carcinoma were identified. Based on cytological features these lesions were diagnosed as follicular neoplasm. The diagnoses on histological examination of thyroid tissue received after thyroidectomies were follicular adenoma, follicular carcinoma and follicular variants of papillary carcinoma. Genetic studies identified two different somatic variants of *DICER1* gene: transcript variants c.5428G>T in two patients (adult patient and one of sisters) and c.5113G>A (the second adolescent patient).

Conclusions: Thyroid nodules are rare in children but carry a high risk for malignancy. We describe three cases of follicular thyroid neoplasm with two different *DICER1* somatic variants in two adolescent siblings and one adult, suggesting that follicular neoplasm of the thyroid is an emerging phenotype of *DICER1* syndrome. Our findings provide new information regarding association of specific *DICER1* variants with neoplastic transformation in patients with *DICER1* syndrome. Although all three neoplasms are follicular patterned, there is the possibility of another mutation driving tumor differentiation in these patients. FNA is important in the surveillance and monitoring of patients with *DICER1* syndrome.

344 A Minimally Invasive Approach to Evaluate the DNA Methylation Status in Patients with Non-Small-Cell Lung Cancer

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Disclosures: Carlos de Andrea: None; Francisco Exposito: None; Maria Lozano: None

Background: Aberrant patterns of DNA methylation of certain genes are currently used as a prognostic biomarker, as well as a diagnostic marker in non-small-cell lung cancers (NSCLCs). *TMPRSS4* promoter DNA methylation is an independent prognostic factor indicator of reduced survival in patients with squamous NSCLC at early stages.

Design: We have developed and optimised a *TMPRSS4* promoter DNA methylation droplet digital PCR (ddPCR) assay for samples with a very low input of DNA and plasma analysis able to detect genomic alteration at low allele frequencies and with high sensitivity. Two lung cancer cell lines harbouring aberrant DNA hypomethylation of the TMPRSS4 promoter region were used to optimize such a methylation-specific ddPCR assay, as well as to determine the sensitivity and specificity of the assay. 10 squamous NSCLC cytologies were then evaluated and compared to 10 non-tumoral lung cytologies.

Results: Using ddPCR for the detection of DNA methylation in the *TMPRSS4* promoter gene in bisulfite-converted samples, we were able to detect *TMPRSS4* promoter hypomethylation with very low input of DNA as low as 0.5ng (3.3 copies/ul). We also showed that ddPCR can detect amounts as low as 0.5% methylated DNA in the background of a nonmethylated control DNA. The squamous NSCLC cytologies showed lower *TMPRSS4* promoter DNA methylaton when compared to the non-tumoral lung cytologies.

Conclusions: ddPCR has shown to reliably detect genomic alteration at low allele frequencies and with high sensitivity. Therefore, ddPCR is a very promising tool, suitable for measuring methylation in samples with low DNA concentrations, including lung cytology samples.

345 Bile Duct Brushing Cytology: A Large, Single Institutional Retrospective Review with an Emphasis on Sensitivity, Specificity, and Positive Predictive Value

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Disclosures: Carlo De la Sancha: None; Harvey Cramer: None; Howard Wu: None

Background: Brushing cytology remains the predominant technique for the cytologic evaluation of bile duct strictures despite the fact that the reported sensitivities for the technique are relatively low, ranging from 30 to 60 percent.

Design: An electronic search of our department's cytology records was performed to identify all bile duct brushing cytology cases with follow-up surgical resections that occurred between January 2010 and September 2018. The cytologic diagnoses were classified as benign, atypical, suspicious, positive, and insufficient for diagnosis. These results were correlated with subsequent surgical pathology diagnoses. Diagnostic sensitivity, specificity, and positive predictive value were calculated and chi-square analysis was performed.

Results: One hundred and nineteen resections were benign while 298 were malignant. Of the proven malignant cases, cytologic diagnosis was positive (56), suspicious (50), atypical (85), negative (98), and insufficient (9). When only positive results were considered malignant, the sensitivity was 19% (56/289), the specificity was 100% (114/114), and the positive predictive value was 100% (56/56). When suspicious and positive results were considered malignant, the sensitivity was 37% (106/289) the specificity was 94% (107/114), and the positive predicted value was 94% (106/113). When atypical, suspicious and positive results were considered positive, the sensitivity was 66% (191/289), the specificity was 71% (81/114), and the positive predicted value was 85% (191/224). The atypical and worse cytologic diagnosis is significantly associated with malignant outcome compared with the negative result ($p<0.05$).

Correlation between cytological dx and final surgical pathology dx in 416 patients

	Cytological diagnosis				
Surgical pathology diagnosis	**Negative**	**Atypical**	**Suspicious**	**Positive**	**Insufficient for dx**
Benign (**n=118**)	81	26	7	0	4
Malignant (**n=298**)					
Liver, Hepatocellular carcinoma (5)	2	2	1	0	0
Liver, Cholangiocarcinoma (13)	4	3	1	4	1
Liver, Adenocarcinoma NOS (8)	2	3	1	2	0
Liver, Diffuse large B cell lymphoma (1)	0	1	0	0	0
Gallbladder, Adenocarcinoma (10)	2	4	3	1	0
Bile duct, Extrahepatic Cholangiocarcinoma (28)	9	7	8	4	0
Bile duct, Extrahepatic Adenocarcinoma NOS (1)	1	0	0	0	0
Bile duct, Extrahepatic Well-differentiated neuroendocrine tumor (1)	1	0	0	0	0
Pancreas, Adenocarcinoma (194)	65	56	31	35	7
Pancreas, Neuroendocrine carcinoma (6)	2	2	1	0	1
Pancreas, Adenosquamous carcinoma (2)	1	0	1	0	0
Pancreas, Mixed acinar-ductal carcinoma (1)	1	0	0	0	0
Pancreas, Colloid carcinoma (1)	0	1	0	0	0
Ampulla, Adenocarcinoma (10)	3	4	1	2	0
Metastatic (17)					
Liver, Metastatic (15)	4	1	2	8	0
Pancreas, Metastatic (1)	1	0	0	0	0
Abdominal mass, Metastatic (1)	0	1	0	0	0
Total malignant cases	**98**	**85**	**50**	**56**	**9**

Conclusions: At our institution, the diagnostic sensitivity of brushing cytology for biliary tract strictures is disappointingly low (19%-66%), but the diagnostic specificity and positive predictive value remains good or excellent whether or not atypical and suspicious results are counted as positive or not (specificity: 71%-100%; positive predictive value: 85%-100%).

346 Outcomes of Patients with Radiologically Suspicious Pancreatic Lesions and a "Benign" FNA Diagnosis: A Multi-Institutional Study with Cyto-Histologic Correlation

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Disclosures: Teena Dhir: None; Austin Goetz: None; Alex Clavijo: None; Shannon O'Brien: None; Sonal Pandya: None; Barbara Centeno: None; Michelle Reid: None; Kim HooKim: None

Background: Fine needle aspiration (FNA) is the main diagnostic tool for assessing pancreatic lesions. However, several factors may limit diagnostic accuracy, such as size, location, and secondary changes from chronic pancreatitis. Benign and malignant lesions may also show similar radiologic and cytological features. Therefore, inaccurate diagnosis can lead to either overtreatment or under treatment of patients. The goal of this study was to evaluate the clinical significance of benign pancreatic FNAs that are suspicious for adenocarcinoma (ADC) through correlation with follow-up resections or repeat FNA or biopsy.

Design: This is a 6-10 year multi-institutional retrospective review of all pancreatic FNAs performed on lesions suspicious for ADC. Metastatic tumors and pancreatic neuroendocrine tumors were excluded. We analyzed clinical and pathologic reports for pertinent data, including age, gender, race, radiological features, cytology and surgical diagnoses, date and type of surgery, and last known clinical status.

Results: 185 of 1225 FNAs (15%) were reported as "benign" (47 (11%), 45 (5.6%), 93 (8%), per institution). 89 cases (48%) had a follow-up biopsy or resection: 28 (15%) were non-neoplastic lesions (20 chronic pancreatitis, 2 retention cysts, 2 pseudocysts, 1 accessory spleen, 1 endometriotic cyst, and 2 Rosai-Dorfman disease); 50 (27%) were neoplastic (35 (70%), 7 (16%), and 8 (18%), per institution). The tumors ranged from 0.6-8.5 cm (mean 2.3 cm); the histologic diagnoses were 17 IPMNs, 2 serous cystadenomas, 1 fibromatosis, and 29 malignancies (27 ADC, 1 adenosquamous, 1 myeloid sarcoma), resulting in false negative rate of 33%).

Conclusions: Overall, 15% of pancreatic lesions that were radiologically suspicious for ADC had a “benign” FNA diagnosis. The false negative rate in this cohort was concerningly high (33%). This raises the possibility of overusage of the negative diagnostic category. In radiologically suspicious lesions, a “non-diagnostic” interpretation may be more appropriate to ensure a close follow-up and repeat tissue sampling given the grave clinical implications.

347 Surgical Follow-Up of Indeterminate Pancreatic Fine Needle Aspirations Suspicious for Pancreatic Adenocarcinoma.

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Disclosures: Teena Dhir: None; Austin Goetz: None; Charalambos Solomides: None; Kim HooKim: None

Background: Fine needle aspiration (FNA) cytology is the most useful diagnostic tool for evaluating pancreatic lesions. Confirmation of malignancy is usually necessary before initiating treatment for pancreatic adenocarcinoma (ADC). However, tumor size, location, tumor heterogeneity, and secondary changes from chronic pancreatitis may limit diagnostic accuracy. Also, some tumors may mimic benign pancreatic or gastrointestinal tissue. In these cases, a definitive diagnosis might not be possible and the FNA result is signed out as “atypical” or "suspicious for neoplasm or malignancy".The goal of this study was to evaluate the clinical significance of indeterminate pancreatic FNAs in lesions that are suspicious for adenocarcinoma through correlation with follow-up resections.

Design: This is an eleven-year retrospective study on pancreatic FNAs performed from 2005-2015 for lesions suspicious for ADC and with follow-up resection. Metastatic tumors and pancreatic neuroendocrine tumors were excluded. All cases represented the most recent FNA sample before surgical resection. Pertinent clinical and pathologic data was reviewed, including age, gender, race, radiological features, cytology and surgical diagnoses, date and type of surgery, and last known clinical status.

Results: 423 FNAs were performed on pancreatic lesions suspicious for ADC with follow-up resections. Overall, 147 (34.8%) were "atypical" or "suspicious for neoplasm or malignancy" (atypical: 83, 56.5%; suspicious: 64, 43.5%). Of the 147 cases, 133 (90.5%) were neoplasms (atypical: 71, 85.5%; suspicious: 62, 96.9%). The remaining 14 FNA cases were non-neoplastic (atypical: 12, 14.6%; suspicious: 2, 3.1%). The non-neoplastic lesions included 7 chronic pancreatitis, 4 autoimmune pancreatitis, 1 lymphoepithelial cyst and benign lymph node, respectively, and 1 with no identifiable lesion. Of the 133 neoplasms, there were 104 (78.2%) ADCs, 25 (18.8%) intraductal papillary mucinous neoplasms, 2 (1.5%) mucinous cystic neoplasms, and 1 (0.8%) serous and acinar cystadenoma, respectively.

Conclusions: The overall neoplastic rate was 90.5%, with the majority (87.1%) of FNAs previously reported as "suspicious". Chronic and autoimmune pancreatitis was the most common mimicker of malignancy and likely represented examples of pseudotumoral pancreatitis. A large patient population referred to an academic institution with pancreatic oncology expertise may have caused the high malignancy rate in this study.

348 A Worm in the Cytology Laboratory: A Root Cause Analysis Case Study

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Disclosures: Siba El Hussein: None; Dominick Guerrero: None; Stefano Rozental: None; Louis Weiss: None; Shweta Gera: None; Mark Suhrland: None; Alaaeddin Fatyan: None; Samer Khader: None

Background: Beginning in the spring of 2018, nematode-like organisms were first noted at the time of microscopic diagnosis on gynecologic (GYN) and anal pap specimens in our institution's cytopathology department. Due to their morphology and specimen source, we considered a diagnosis of pinworm. However, after identifying at least thirty more cases over three months from patients living in a variety of distant locations, the likelihood of a contaminant existing in our laboratory was favored.

Design: Each step in processing GYN and anal pap specimens was analyzed together with the director, lab supervisor, and directly involved technicians. Within our cytology lab, the use of filtered and UV radiated water for processing was unique to these specimens. A sample from this water was processed alone without patient tissue, revealing the worm in question. Another sample was collected directly from the downstream filter, which was found bathing in opaque, dirty water. Although none were seen macroscopically, multiple worms at various stages of development were identified on light microscopy. Purified C. elegans genomic DNA was prepared for use as a positive control. Genomic DNA was then extracted and amplified from the contaminated water. Purified DNA was submitted to the GENEWIZ Corporation for Sanger sequencing.

Results: The nucleotide sequences were compared to existing, known sequences using NCBI BLAST. Our positive control was a 100% match for C. elegans and our unknown worm results returned 100% for GeneBank Poikilolaimus oxycercus subunit rRNA gene partial sequences, a free-living non-pathogenic nematode of the family Rhabditiae.

Figure 1 - 348

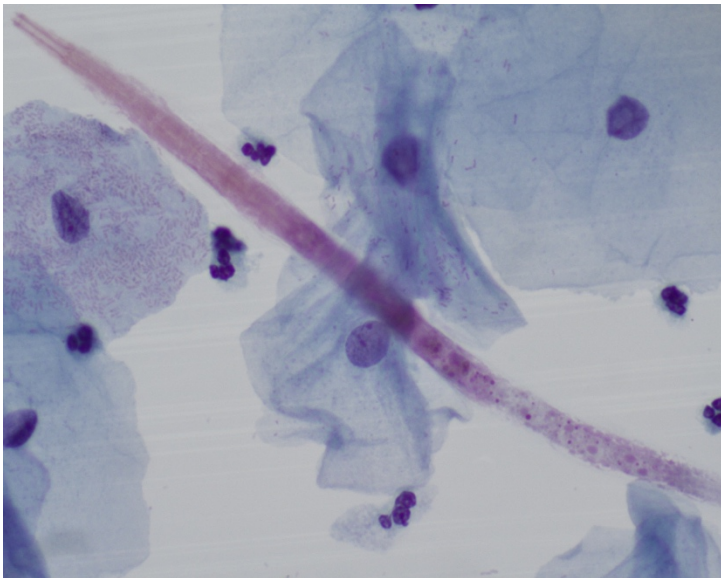
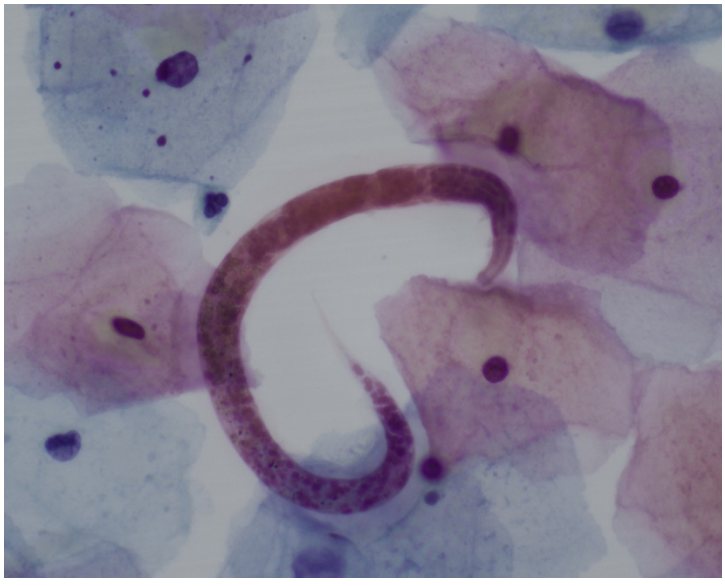


Figure 2 - 348



Conclusions: This case highlights the danger of overlooking areas in a laboratory that lie under no specific jurisdiction of supervision. The water filtration system was located in a "grey zone" of the hospital, shared by multiple departments. Areas like this are commonly encountered in hospital systems where there are many moving parts, which cumulatively pose a challenge to accurate surveillance.

349 Retrospective study of 40,328 liquid based cervical cytology: assessment of the relevance of computer assisted evaluation in the identification and ranking of lesions

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Disclosures: Caroline Eymerit-Morin: None; Caroline Hugonin Ohana: None; Anne BARRES: None

Background: Liquid Based Cytology (LBC) and automated screening devices are increasingly used in cervical screening. Computer-assisted screening seems as sensitive as manual screening, and more sensitive for high-grade lesions. Moreover, this technology can be used to identify slides as normal for No Further Review (NFR) or ranked into 5 quintile at risk of neoplasia (quintile 1 indicates the highest risk of abnormality).We do not use the NFR category as a precaution to avoid false negatives. The objective of our study was to assess distribution of epithelial lesions, and to verify if rank in "quintiles" correlated to the abnormality and more specialy in the quintile 5.

Design: We retrospectively included all LCB diagnosed between July 2017 to July 2018 in our institute. We analyzed the distribution of epithelial lesions, according to 2014 Bethesda System and HPV status as appropriate, depending on the quintile (1 to 5). The reading assistance system used was the BD FocalPoint ™ GS imaging system (BDFP).

Results: We evaluated 40328 LCB. Of these cases, 84% (n=33946) were classified into FocalPoint quintiles and were interpreted by computer-assisted, field-of-view screening. In total 1440 cases were diagnosed as abnormal : 1079 ASCUS (3%), 253 LSIL, 49 ASCH, 16 HSIL, 26 AGC and 10 adenocarcinomas. 54% of epithelial lesions were classified as quintile 1 (n=789). We found 22.1% (n = 318) in quintile 2, 11.8% (n = 170) in quintile 3 and 7.1% (n = 102) in quintile 4. Only 3.8% (n = 54) were found in quintile 5. No HSIL, AGC or malignant lesion were identified in quintile 5. The lesions identified in quintile 5 corresponded to 49 ASCUS including 26 high-risk HPV and 4 LSIL. Moreover, when HPV test was performed according to guidelines, it was positive in 53% without significant difference depending on the quintile.

	Lesion and quintile						
	quintile 1	quintile 2	quintile 3	quintile 4	quintile 5	total quintiles (n ; %)	
NILM	5600	6829	7074	7167	7276	33946	95,93%
ASCUS	555	250	132	93	49	1079	3,00%
ASCH	38	9	1	0	1	49	0,14%
LSIL	133	52	30	8	3	226	0,63%
LSIL+ASCH	23	3	0	0	1	27	0,08%
HSIL	15	1	0	0	0	16	0,04%
AGC	15	3	7	1	0	26	0,07%
Adenocarcinoma	10	0	0	0	0	10	0,03%
total lesion (n ; %)	789 ; 2,19%	318 ; 0,88%	170 ; 0,47%	102 ; 0,28%	54 ; 0,15%	1440	4,07%
NILM : Negative for Intraepithelial Lesion or Malignancy							
ASCUS :Atypical Squamous Cells of Undetermined Significance							
AGC : Atypical Glandular Cell							
LSIL : Low Grade Saquamous intraepithelial Lesion							
HSIL : High Grade Squamous intraepithelial Lesion							

	quintile 1	quintile 2	quintile 3	quintile 4	quintile 5	total quintiles (n)	
total HPV testing	734	282	152	97	56	1321	
high risk HPV +	412	158	87	56	29	742	
% high risk HPV+	56,13%	56,03%	57,24%	57,73%	51,79%	56,17%	

Conclusions: The BDFP GS imaging system allows for a relevant identification of squamous lesions, especially high grade lesions. However, in quintiles 4 and 5 with a lower risk of abnormality, a not insignificant number of ASCUS and low-grade lesions are diagnosed, some of which are related to HPV infection. This results invite to remain cautious about the practical application of NFR category that would not identify these patients. This information has to be considered in the choice in clinical practice.

350 Are we ready to develop a tiered reporting scheme for effusion cytology? "A systematic review and meta-analysis of the literature."

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Disclosures: Sahar Farahani: None; Tom Hu: None; Sharon Song: None; Zubair Baloch: None

Background: Serous effusion cytology (SEC) has been widely utilized in the initial evaluation of the etiology of fluid accumulation in the body cavities. However, the data on the accuracy of body fluid cytology is heterogeneous. Recently, an international cytopathology panel proposed a reporting system for SEC. The aim of this study was to determine the accuracy of cytology in distinguishing between benign and malignant body cavity effusions in the reported literature.

Design: A systematic review of the literature was conducted to identify the publications which evaluated the accuracy of SEC against tissue biopsy/resection histology, imaging or clinical follow-up as the reference test. The number of cases categorized as inadequate, negative, atypical, suspicious, and positive for malignancy was extracted. Risk of publication bias and level of heterogeneity in the included studies was assessed. A Bi-variate mixed-effect model was used to calculate pooled measures of cytology accuracy in SEC. Meta-regression was used to assess the effect of various variables on the accuracy of SEC.

Results: Seventy studies comprising a total of 20501 cases met the inclusion criteria for meta-analysis; 1.0%, 65%, <1%, 3%, 13%, and 18% were reported as inadequate, negative, atypical, suspicious, suspicious or positive, and positive for malignancy, respectively. The risk of malignancy (ROM) for negative, atypical, suspicious, suspicious or positive, and positive for malignancy categories was 29%, 75%, 69%,97%, and 99%, respectively. High level of heterogeneity was detected in the included studies (P-value: 0.00). Funnel plot demonstrated a significant publication bias, however, trim and fill test showed that publication bias did not have any significant effect on the results of the study. Pooled sensitivity, specificity, diagnostic odds ratio, and positive and negative likelihood ratio of body cavity cytology in differentiating between malignant and benign effusion were 71.2%, 99.8%, 2182.1, 628.8, and 0.29, respectively. Summary estimates of sensitivity and specificity of cytology were the highest in pericardial effusions followed by peritoneal effusions. Meta-regression did not recognize any variable impacting the accuracy of cytology.

Reference Test†	Cytology						
		Inadequate	NM	Atypical	SM	SM or M	M
	N° Studies	7	70	6	26	6	64
	N° Cases (Percentage)	208 (1.0%)	13,365 (65.2%)	32 (0.2%)	530 (2.6%)	2,634 (12.8%)	3,732 (18.2%)
	N° Benign Cases (Percentage)	-	9,476 (70.9%)	8 (25.0%)	164 (30.9%)	74 (2.8%)	54 (1.4%)
	N° Malignant Cases (Percentage)	-	3,889 (29.1%)	24 (75.0%)	366 (69.1%)	2560 (97.2%)	3,679 (98.6%)

NM=negative for malignancy; SM=suspicious for malignancy; M=malignant

†Reference test considered as biopsy/resection tissue histology and/or radiological and clinical examination and follow-up.

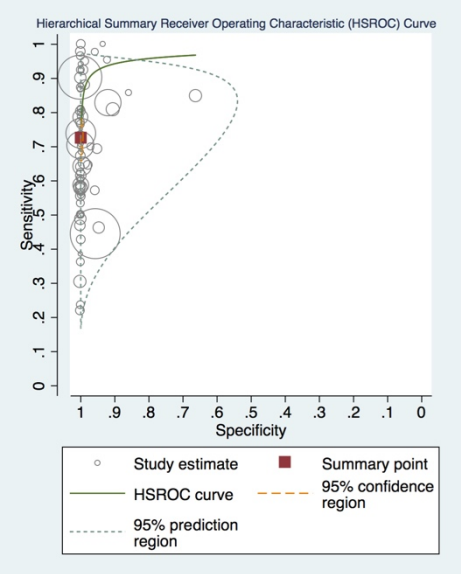
Figure 1 - 350

Summary Test Characteristics of Serous Effusion Cytology

Fluid	N° Studies	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	DOR (95% CI)	PLR (95% CI)	NLR (95% CI)
All	64	**71.2** (65.7-76.1)	**99.8** (99.5-99.9)	**2182.1** (522.9-9104.6)	**628.8** (150.7-2624.5)	**0.29** (0.24-0.35)
Pleural	26	**68.3** (60.4-75.3)	**99.8** (99.3-99.9)	**1557** (304.9-7853.6)	**490.7** (97.3-2476.1)	**0.32** (0.25-0.40)
Peritoneal	23	**72.0** (63.1-79.5)	**99.8** (98.1-99.9)	**1496.6** (149.2-15016.8)	**419.7** (38.5-4576.3)	**0.28** (0.21-0.38)
Pericardial	7	**79.1** (52.9-92.7)	**99.7** (94.7-99.9)	**1624.9** (68.1-38794.8)	**340.2** (14.9-7780.2)	**0.21** (0.08-0.55)

CI=Confidence Interval; DOR=Diagnostic Odds Ratio; PLR=Positive Likelihood Ratio; NLR=Negative Likelihood Ratio

Figure 2 - 350



Conclusions: The SEC is a moderately sensitive and highly specific diagnostic tool in the initial evaluation of body cavity fluids. A tiered classification scheme may prove to be helpful in creating uniformity in reporting SEC specimens for better patient management.

351 Individualized Bayesian Risk Assessment for Cervical Squamous Neoplasia

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Disclosures: Lama Farchoukh: None; Agnieszka Onisko: None; R. Marshall Austin: None

Background: Cervical screening strives to prevent cervical cancer and minimize morbidity and mortality while also limiting harms and controlling costs. Despite success in preventing cervical squamous carcinoma (SCC), cervical cancer has never been completely eradicated in any system. Cervical screening could potentially be improved by better stratifying individual risk for development of cervical cancer or precancer, possibly even allowing follow-up of individual patients differently than proposed under current guidelines that focus primarily on recent screening test results. We explore the use of a Bayesian decision science model to quantitatively stratify individual risk for development of cervical squamous neoplasia.

Design: We previously developed a dynamic multivariate Bayesian network model that uses cervical screening and histopathologic data collected over 13 years in our system to quantitatively estimate the risk of individuals for development of cervical precancer or invasive cervical cancer. Unlike current guidelines, risk stratifications utilizing the model are able to take into consideration extended cervical screening histories, prior cervical biopsy findings, and other clinical factors beyond recent screening test results, while targeting risk assessment for important but uncommon histopathologic outcomes.

Results: Using our Bayesian model, cumulative 5-year risk assessments with varying patient histories were determined for histopathologic outcomes of SCC and CIN3. Selected results are shown in Figures 1 and 2. Historical data affected 5-year cumulative risk for both SCC and CIN3. The greatest risk for subsequent documentation of system histopathology diagnoses of both SCC and CIN3 were seen with HSIL cytology results. Persistent abnormal cervical screening test results, either abnormal cytology results and/or HPV-positive results, were generally associated with increasing risk for subsequent documentation of squamous neoplasia. Varying extended screening histories were associated with different risk estimates. Different quantitative risks were also documented with prior histopathologic diagnoses of precancer, including CIN2, CIN3, and AIS. Risk projections reflected both risk of disease progression as well as the success or failure of ablative treatments.

Figure 1 - 351

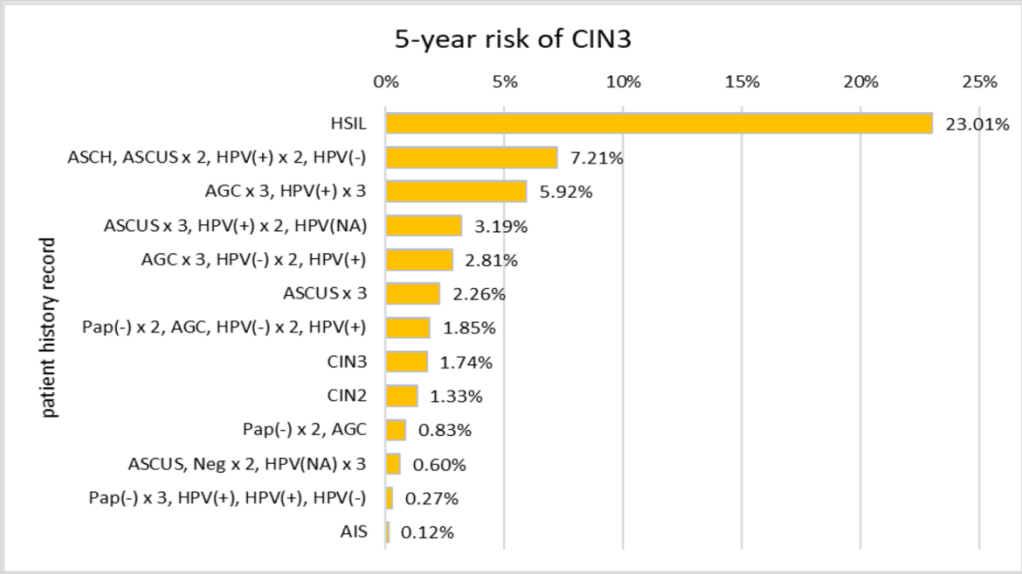
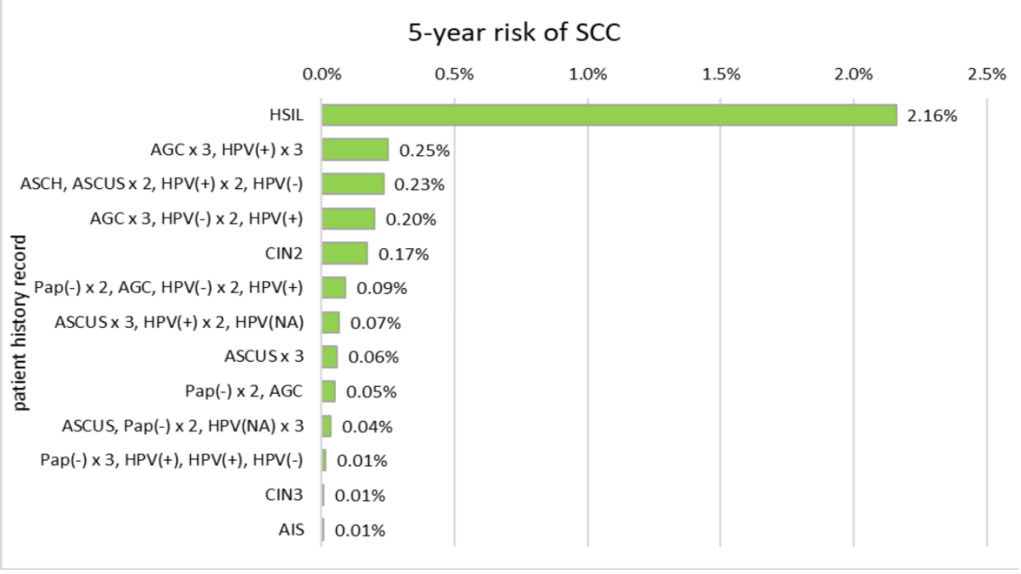


Figure 2 - 351



Conclusions: Bayesian modelling allows for individualized quantitative risk assessments of system patients for histopathologic diagnoses of significant cervical squamous neoplasia, including very rare outcomes such as SCC.

352 Cytotechnologist (CT) Dots and CT Interpretations Correlate with Cytopathologist Upgrade in Anal Pap Smears

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Disclosures: Youssef Farhat: None; Gustavo Moreno: None; Christopher Hartley: None

Background: All anal Pap smears are sent for cytopathologist (CP) review, regardless of cytotechnologist (CT) interpretation. CT indicate squamous cells of concern via “dots” to aid the accuracy of CP interpretation. To our knowledge, only one previous study has undertaken a formal assessment of dots, focusing only on cervicovaginal Pap smears (Bongiovanni et al, Acta Cytologica, 2009: PubMed ID 20014554). Our aim was to evaluate CT dots in relation to CT interpretation and CP diagnosis in anal Pap smears at our institution, to gauge their utility and influence on the final CP diagnosis.

Design: Consecutive anal Pap smears (n=600) were reviewed from 12/2015 to 12/2016. Eighty cases interpreted as "Unsatisfactory" were excluded. On the remaining 520 cases, the number of dots was recorded along with the CT interpretation and CP diagnosis. Dots were correlated with an upgrade and downgrade in final CP diagnosis, controlling for CT interpretation via bivariate logistic regression. CT interpretation was coded on an ordinal scale according to diagnosis as follows: NILM=0; ASC-US=1, LSIL=2, ASC-H=3, and HSIL=4.

Results: A summary of dots in relation to CT interpretation and CP diagnosis is presented in Table 1. HSIL showed the highest concordance (2/2, 100%), with the most dots (mean 10.5), but represented only 2 cases. LSIL showed the second highest concordance (91/109, 83%). Dots were significantly correlated with both CT interpretation (p<0.001, ANOVA) and CP diagnosis (p<0.001, ANOVA). Each increase on the ordinal CT interpretation axis (NILM->ASC-US->LSIL->ASC-H->HSIL) was negatively correlated with CP upgraded diagnosis (p<0.01, odds ratio (OR) 0.3 95% CI 0.2-0.5), while each additional dot was positively correlated with CP upgrade (p<0.01, OR 1.2, 95% CI 1.1-1.3). Only ordinal CT interpretation was correlated with CP downgrade, with each ordinal increase conferring a 2.2 times odds ratio of downgrade (p=0.004, 95% CI 1.6-8.9). Dots were not correlated with downgrade (p=0.16, OR-0.9, 95% CI 0.8-1.03).

Table 1: Correlation of Cytotechnologist Interpretation and Cytopathologist Diagnosis with Summary of Dots

Dots: Mean±SD(range),n(concordance%)	**Cytotechnologist Interpretation**					
Cytopathologist Diagnosis	NILM	ASC-US	LSIL	ASC-H	HSIL	All
NILM	**0.8±1.2(0-6),n=253(81%)**	1.5±0.7(1-2),n=2	1 case, 3 dots	None	None	0.8±1.3(0-6),n=256
ASC-US	1.3±1.8(0-7),n=54	**5.2±3.2(0-14),n=58 (62%)**	6.1±3.2(2-14),n=15	None	None	3.6±3.4(0-14),n=127
LSIL	0.3±0.6(0-1),n=3	6.6±4.6(1-16),n=31	**6.4±3.4(0-17),n=91(83%)**	1 case, 5 dots	None	6.3±3.8(0-17),n=126
ASC-H	1±0(1-1),n=2	9.3±3.1(6-12),n=3	None	**9.5±4.9(6-13),n=2(25%)**	None	7.0±4.9(1-13),n=7
HSIL	None	None	7±2.8(5-9),n=2	None	**10.5±7.8(5-16),n=2(100%)**	8.8±5.2(5-16),n=4
Total	0.9±1.4(0-7),n=312	5.7±3.8(0-16),n=94	6.3±3.3(0-17),n=109	8±4.4(5-13),n=3	10.5±7.8(5-16),n=2(100%)	**3.0±3.6(0-17),n=520 (78%)**

Legend: NILM=Negative for intraepithelial lesion or malignancy; ASC-US=Atypical squamous cell of uncertain significance; LSIL=Low-grade squamous intraepithelial lesion; ASC-H=Atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion; HSIL=High-grade squamous intraepithelial lesion; SD=standard deviation.

Conclusions: The fact that dots correlate with both CT interpretation and CP diagnosis suggests overall accurate and efficient dotting by CTs in anal Pap smears. The CP decision to upgrade cases appears to occur in a dot-dependent manner, while downgrade occurs independently of dots. Additional follow-up with biopsy diagnosis will be used to further evaluate these trends.

353 Exploring the Heterogeneity of Risk of Malignancy Associated with the Cytologic Categories of The Bethesda System for Reporting Thyroid Cytology: A Meta-Analysis

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Disclosures: Huma Fatima: None; Isam-Eldin Eltoum: None; Mohammad Abdelgawwad: None

Background: The Bethesda System for Reporting Thyroid Cytology (TBSRTC) suggests risk of malignancy (ROM) for each categories based on a few large studies. The objective of this study is to explore the heterogeneity among different studies reporting ROM associated with TBSRTC categories.

Design: PubMed and Scopus were searched focusing on articles that used TBSRTC with surgical outcome and no molecular studies for triage of indeterminate categories. We excluded cases that classified non-invasive follicular neoplasm with papillary feature as benign. Data collected included: ROM, geographic location, gender ratio and mean age of the study population. Missing data was imputed using 'mice' R-Package. L'Abbe plot was used to demonstrate variations and overlap of ROM among different TBSRTC categories and their relation to the base risk. Comprehensive Meta-Analysis software was used to estimate the mean (95% CI) ROM and to test meta-regression between the categories. Because of the ordinal nature of the categories, we used a recently described multivariate Poisson correlated gamma-frailty (PCGF) model to assess the extent of heterogeneity, threshold effects and the main covariates that predict diagnostic performance.

Results: 53 studies fulfilled our selection criteria. L' Abbe' plot shows marked overlap of ROM of adjacent categories and positive correlation with base risk which is statistically significant for the unsatisfactory (UNS), follicular lesion of undetermined significant (FLUS) and follicular neoplasm (FN) categories (p .05), but not significant for suspicious (SUS) and positive (POS) for malignancy, Figure 1. There is significant heterogeneity of ROM for all categories, Q statistic = 119 to 415; I-square statistic = 59 to 88, table. This is confirmed further by PCGF model with a frailty variances (SE) for histologically positive and negative cases of 0.57 (0.1) and 0.22 (0.04), respectively. The correlations (SE) between sensitivities and specificities across thresholds and that across studies at each threshold were high, 0.98 (0.00)

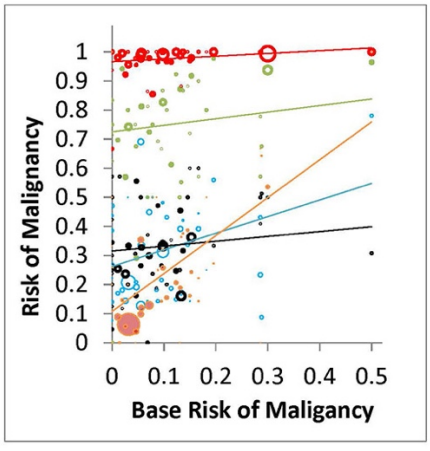
and 0.57 (0.17), respectively. The PCGF shows diagnostic performance to be affected by study size and geographic location but not by the mean age or gender distribution of the study population.

Table: Pooled ROM, test of heterogeneity and pooled sensitivity and specificity at different category cut-off of TBSRTTC

Category	Pooled Risk	I-squared	Q	P-value	Pooled Specificity	Pooled Sensitivity
Unsatisfactory	22% (17%, 29%)	84	273	<.001	NA	NA
Negative	8% (7%, 10%)	88	415	<.001	NA	NA
FLUS	28% (25%, 35%)	87	308	<.001	42% (5%, 79%)	93% (85%, 100%)
FN	32% (29%, 36%)	66	147	<.001	71% (62%, 80%)	80% (60%, 100%)
SUSP	79% (73%, 83%)	82	277	<.001	94% (83%, 100%)	67% (38%, 96%)
POSITIVE	97% (96%, 98%)	59	119	<.001	99% (95%, 100%)	46% (7%, 85%)

Figure 1 - 353

Figure1: L' Abbe' plot for risk of malignancy (ROM) associated with each cytologic diagnostic categories in 53 studies (Unsatisfactory, FLUS, FN, SUSP and POS against base risk (ROM in NEG). Size of the mark is proportional to study weight.



Conclusions: There is marked heterogeneity of ROM across the studies and significant overlap between different diagnostic categories. Some of the variation among studies could be explained by base risk, study volume and geographic location.

354 Next generation sequencing identified novel fusion partners for HMGA2 and PLAG1 genes in salivary gland pleomorphic adenomas

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Disclosures: Aisha Fatima: None; Jie-Gen Jiang: None; Neena Mirani: None; Bei You: None

Background: Pleomorphic adenoma (PA) is the most common salivary gland tumor with variegated morphologies. Two types of characteristic gene fusions involving pleomorphic adenoma gene 1 (PLAG1) and high mobility group AT-hook 2 (HMGA2) have been reported in 35% -90% of PAs, helping to establish diagnosis in challenging cases. The fusion partners for PLAG1 and HMGA2 have been well characterized, but new ones emerge occasionally.

Design: From tissue archive of our institution of last 48 months, we identified 17 PA cases (5 fine needle aspiration cell blocks and 12 surgical biopsies). PLAG1-related gene fusion was tested by traditional fluorescence in situ hybridization (FISH) using a PLAG1 Break-Apart probe from Empire Genomics (New York). The exact same cases and diagnostic material were also sent for Next Generation Sequencing (including both RNA-seq and DNA-seq) using PredicinePLUS from Predicine Inc. (California).

Results: RNA-seq results indicate 1 out of 17 PAs (5.9%) show PLAG1-related fusion, with a novel partner protein-L-isoaspartate (D-aspartate) O-methyltransferase domain containing 1(PCMTD1); 11 of the 17 (64.7%) PAs show HMGA2-related gene fusion, 1 case with novel partner transmembrane and tetratricopeptide repeat domains-containing protein 2(TMTC2), 2 cases with new partner FLJ41278. The PLAG1-related gene fusion was confirmed by FISH analysis. No case show double gene fusions, but DNA-Seq shows genetic mutations in genes including: FGFR3 (p.Asn4238Ser); NF1 (p.Ser1933Ter), PTPN11 (p.Val181Ile), MSH6(p.Arg1242His), PMS2 (p.Arg315Ter).

Conclusions: Our results indicate HMGA2 or PLAG1-related gene fusions are present in 70.6% of PAs; novel partners for PLAG1 and HMAG2-related gene fusions and their function deserve further investigation. In addition, our results suggest both RNA-seq and FISH are sensitive methods to detect gene fusions. However, next generation sequencing in the platform of PredicinePLUS has the additional advantage to identify other genetic mutations and locate unexpected gene fusion(s)

355 Role of Cytology in the Diagnosis of Subcentimeter Indeterminate Thyroid Lesions

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Disclosures: Vincenzo Fiorentino: None; Teresa Musarra: None; Marco Dell'Aquila: None; Luigi Maria Larocca: None; Guido Fadda: None; Liron Pantanowitz: None; N. Paul Ohori: None; Esther Rossi: None

Background: Thyroid nodules are common and detected in nearly 4.7% of patients by palpation alone and 10-67% by ultrasound (US). Guidelines have been clearly defined for managing large thyroid nodules, but controversy exists about nodules smaller than 1cm. For small nodules with suspicious US features referral for US-FNA seems feasible. Also problematic is the recent introduction of NIFTP that is defined as a thyroid lesion greater than 1cm. The purpose of this study was to evaluate subcentimeter thyroid nodules to determine their rate of malignancy (ROM) and indeterminate as well as NIFTP diagnoses

Design: The thyroid archival databases were searched at two tertiary medical centres (for a 40 month timeframe (January 2015-May 2018). A total of 363 thyroid FNA cases of lesions smaller or equal to 1 cm with available histological follow-up were identified. All nodules were aspirated with US guidance and processed with either conventional smears and/or liquid based cytology. Cases were classified according to The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC).

Results: The series included lesions $\leq$1cm (363 cases). According to TBSRTC we found: 36 cases in category I (10%), 67 in category II-Benign Lesion (BL, 18.4%), 44 in III- Atypia of undetermined significance/follicular lesion of undetermined significance (AUS/FLUS, 12%), 23 in IV-Follicular Neoplasm/Suspicious for follicular neoplasm (FN/SFN, 6.3%), 71 in V-Suspicious for malignancy (SM, 19.5%) and 127 in VI-Positive for malignancy (PM, 35%)The malignant rate for indeterminate lesions (III+IV) was 22.3%; with 20.4% for category III and 26% for category IV. The malignant rate for the malignant categories (V plus VI) was 98.3%, with only three follicular adenomas diagnosed in the category V

Conclusions: Aspirates of many small lesions are often unsatisfactory, most likely because these small nodules are hard to biopsy. Furthermore, a large proportion (35%) of subcentimeter lesions were malignant, perhaps indicating that subcentimeter lesions selected for fine needle aspiration are more clinically suspicious for malignancy

356 Comparison of Cytological and Histological Diagnosis of Pancreatic Cystic Lesions in a Large Cancer Center

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Disclosures: Qiong Gan: None; Nancy Caraway: None; Minhua Wang: None; Huamin Wang: None

Background: More incidental pancreatic cystic lesions are detected by imaging in patients who are worked up for other diseases. Endoscopic ultrasound guided fine needle aspiration (EUS-FNA) is particularly valuable in assessing diagnostic features of cystic pancreatic lesions, acquiring material for cytological evaluation, and biochemical analysis, and management of these patients. The aim of this study is to compare the cytological and histological diagnosis of pancreatic cystic lesions; and to determine the sensitivity of detecting high-grade dysplasia or carcinoma by EUS-FNA in our clinic settings.

Design: We searched all cystic pancreatic lesions sampled by EUS-FNA in our institute between 2002 and 2018 following IRB approval. The cases with subsequent surgical resection were selected to compare the cytological and histological diagnosis. Other data including the imaging findings, carcinoembryonic antigen (CEA) level of cystic fluid, size and location of the lesion, were also collected from the electronic medical record.

Results: 658 cases of pancreatic cystic lesions were found in this study to include 357 (54.3%) female and 301 (45.7%) male patients with mean age of 68 years old. 101 patients (15.3%) had subsequent surgical resection of the pancreatic cystic lesions. The mean size of resected cysts is significantly larger (2.89 cm vs 2.12 cm, p=0.0001) than those without surgery. CEA level were available in 336 (51%) patients and 128 (38%) of them with a CEA level ?192 ng/ml. The diagnosis and grading correlation between cytology and surgical resection specimens were listed in Tables 1 and 2 respectively.

Figure 1 - 356

Table 1. Diagnosis correlation between cytology and histology.

Histological diagnosis	Cytological diagnosis
Mucinous cystadenoma (n=21)	A. Mucinous cystadenoma/MCL(n=13) B. Descriptive but no mentioning of mucinous lesion (n=6) C. Pseudocyst (n=1) D. Non-diagnostic (n=1)
IPMN (n=40)	A. IPMN/MCL (n=37) B. Descriptive but no mentioning of mucinous lesion (n=3)
Serous cystadenoma (n=11)	A. MCL (n=4) B. Possible serous cystadenoma (n=5) C. Descriptive (n=2)
Adenocarcinoma or adenocarcinoma arising from IPMN (n=16)	A. Adenocarcinoma (n=8) B. IPMN with high-grade dysplasia (n=3) C. IPMN with no to low-grade dysplasia (n=4) D. Non-diagnostic (n=1)
Cystic PanNET (n=8)	PanNET (n=8)
Solid pseudopapillary tumor (n=4)	Solid pseudopapillary tumor (n=4)

Abbreviation: PanNET: pancreatic neuroendocrine tumor; MCL: mucinous cystic lesion; IPMN: intraductal papillary mucinous neoplasm

Figure 2 - 356

Table 2. Dysplasia grading between cytological specimen and surgical resection.

Histological diagnosis and grading	Cytological diagnosis and grading
Mucinous cystadenoma (n=21) 1. No dysplasia or LGD (n=21)	A. Mucinous cystadenoma/MCL(n=13) 1. No dysplasia or LGD (n=13) B. Descriptive but no mentioning of mucinous lesion (n=6) 1. No dysplasia (n=6) C. Pseudocyst (n=1) 1. No dysplasia (n=1) D. Non-diagnostic (n=1) 1. Not applicable (n=1)
IPMN (n=40) 1. No dysplasia or LGD (n=20) 2. HGD (n=20)	A. IPMN/MCL (n=37) 1. No dysplasia or LGD (n=28) 2. HGD (n=9) B. Descriptive but no mentioning of mucinous lesion (n=3) 1. No dysplasia (n=3)
Adenocarcinoma (n=14)	A. Adenocarcinoma (n=8) B. IPMN with HGD (n=3) C. IPMN with no to LGD (n=4) D. Non-diagnostic (n=1)
Serous cystadenoma (n=11) 1. No dysplasia or LGD (n=11)	A. MCL (n=4) 1. No dysplasia or LGD (n=4) B. Possible serous cystadenoma (n=5) 1. No dysplasia (n=5) C. Descriptive (n=2) 1. No dysplasia (n=2)

Abbreviation: PanNET: pancreatic neuroendocrine tumor; MCL: mucinous cystic lesion; IPMN: intraductal papillary mucinous neoplasm; LGD: low-grade dysplasia; HGD: high-grade dysplasia

Conclusions: Majority of pancreatic cystic lesions could be accurately classified as neoplastic mucinous cysts by combining cytology, imaging, and biochemical analysis. The false positive rate for high-grade dysplasia or carcinoma is low on cytology specimens (2.87%), while a portion (14.5%) of cases had high-grade dysplasia or carcinoma on surgical resection specimens but not on cytology specimens. The accuracy to diagnose cystic PanNET and solid pseudopapillary tumor on EUS-FNA cytology is very high (100%).

357 Cytologic Evaluation of Basaloid Salivary Gland Neoplasms and Correlation with Surgical Outcomes: What are the Cytomorphologic Predictors of a High Grade Basaloid Malignancy?

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Disclosures: Stacey Gargano: None; Christopher Sebastiano: None; Emilio Madrigal: None; Charalambos Solomides: None; Christopher Griffith: None; Kim HooKim: None

Background: Basaloid salivary gland neoplasms (BSG) include benign primary tumors and primary or metastatic malignancies that show overlapping cytologic features in fine needle aspirations (FNA). Confirmation of malignancy and tumor grade of BSGs affect surgical planning, and thus grading is recommended by the Milan System. We sought to identify cytomorphologic features in salivary gland FNAs showing basaloid morphology that may help favor a high-grade over a low-grade malignancy or benign tumor.

Design: FNAs of BSG seen at 2 institutions from 2012-2018 were collected, and those with corresponding surgical resections were selected for analysis. Two pathologists performed a double-blinding cytologic review, which included evaluation of nuclear and architectural atypia. The diagnosis based on the Milan system was correlated with final surgical diagnosis and grade.

Results: Of 132 BSG FNA cases, 87 patients underwent surgical resection, and 49 of those had cytology slides available for review. The cyto-histologic correlation is shown in Table 1. The risk of malignancy for benign neoplasm, SUMP, SFM and malignant were 13.6%, 22%, 100% and 100%, respectively. The sensitivity, specificity, negative and positive predictive values were 83%, 100%, 86% and 100%, respectively. Favoring high-grade malignancy on FNA had 80% (4/5) accuracy, with one case showing intermediate-grade resection. Favoring low-grade malignancy on FNA had 75% (6/8) accuracy; misclassification of 2 tumors was attributed to FNA sampling error. The 3 false negative cytologic diagnoses were all low-grade adenoid cystic carcinomas on resection; one was hypocellular, mimicked pleomorphic adenoma with fibrillar stroma, and lacked cribriform architecture. The most helpful cytomorphologic clues that predicted high-grade malignancy were necrotic/apoptotic debris, prominent nucleoli, mitotic activity and discohesion (Figures 1 and 2).

Surgical pathology diagnosis	# of cases	Cytology diagnosis (Milan)			
Benign		BN	SUMP	SFM	M
Pleomorphic adenoma	34	14	20		
Basal cell adenoma	22	5	17		
Myoepithelioma	2		2		
TOTAL	58	19	39		
Malignant					
Adenoid cystic carcinoma	13	3	4	4	2
Basal cell adenocarcinoma	3		2		1
Myoepithelial carcinoma	3		1		2
Adenocarcinoma NOS ex PA	2		1		1
Epithelial-myoepithelial carcinoma	2		2		
Recurrent/metastatic basal cell carcinoma of cutaneous origin	2			1	1
Salivary duct carcinoma	1		1		
Polymorphous adenocarcinoma	1			1	
Metastatic large cell neuroendocrine carcinoma	1				1
Basaloid carcinoma with skin adnexal-type features	1				1
TOTAL	29	3	11	6	9

Table 1. *Surgical outcomes of basaloid salivary neoplasms and the corresponding cytology diagnoses.* BN = Benign Neoplasm; SUMP = Salivary Gland Neoplasm of Uncertain Malignant Potential; SFM = Suspicious for Malignancy; M = Malignant.

Figure 1 - 357

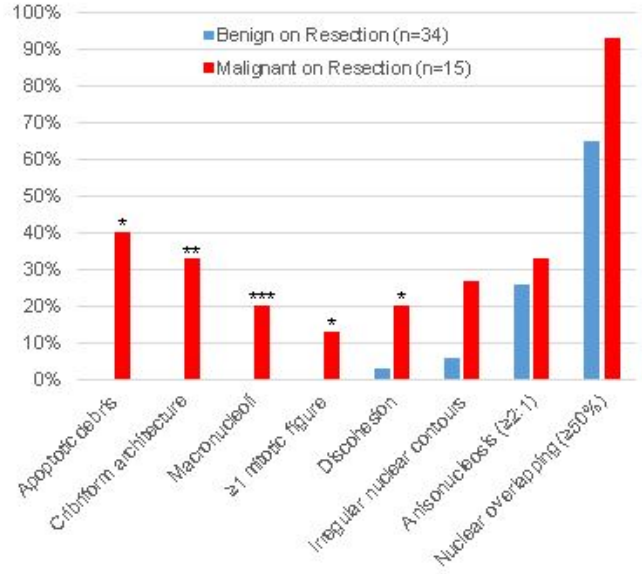

Figure 1. *Frequency of cytomorphologic features in confirmed benign and malignant basaloid neoplasms.* *All were high-grade. **All were low-grade. ***2/3 tumors were high-grade.

Figure 2 - 357

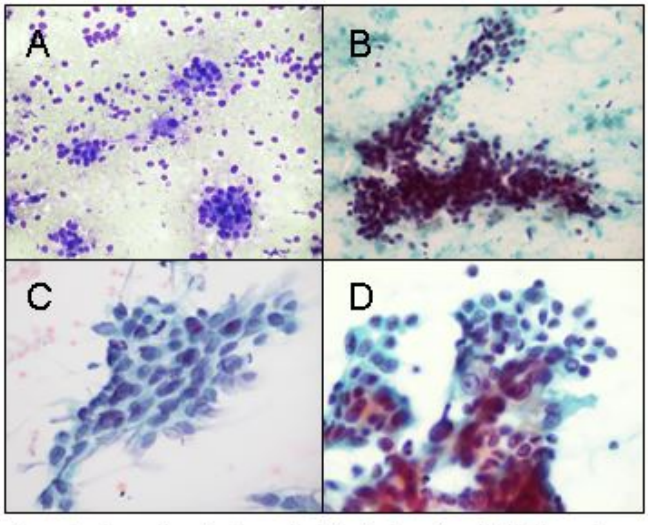

Figure 2. *Examples of cytomorphologic features found in high-grade malignant basaloid neoplasms.* A. Discohesion in high-grade adenoid cystic carcinoma (Diff-Quik, 20x). B. Apoptotic debris in high-grade myoepithelial carcinoma (Pap, 40x). C and D. Mitoses and prominent nucleoli, respectively, in high-grade adenocarcinoma NOS ex PA (Pap, 60x).

Conclusions: Cytologically BSGs encompass a broad spectrum of primary and metastatic tumors. The Milan system recommends grading malignancies, but this may not be possible in predominantly low-grade tumors due to sampling error, for instance in carcinoma ex PA or a

tumor with focal high-grade transformation. Necrotic/apoptotic debris, prominent nucleoli, mitotic activity and discohesion, alone or especially in combination, should make a cytopathologist suspect high-grade malignancy and thus help guide surgical management.

358 Age-stratified 3-year Cumulative Risk of Cervical Cancer and High-Grade Dysplasia Among Women who Underwent HPV-Cytology Co-testing

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Disclosures: Yimin Ge: None; Paul Christensen: None; Donna Armylagos: None; Mary Schwartz: None; Dina Mody: None

Background: HPV-Pap co-testing has been increasingly used in cervical cancer screening for women 30 years or older. The purpose of this study was to analyze the effectiveness of co-testing in risk management among different age groups.

Design: Retrospective review of a cytology database from March 1, 2013 to March 1, 2018 identified 10,435 women with HPV-Pap co-testing and cervical biopsy follow-up up to 3 years. Pap+ was defined as any epithelial cell abnormality at baseline using the Bethesda System for Reporting Cervical Cytology. Baseline HPV results on either Cobas or Aptima HPV platforms were recorded as HPV+ or HPV-. Aptima HPV test was performed on cases with ASC-H or higher cytology diagnoses if initial Cobas test was negative. The 3-year cumulative risk of developing cervical cancer and high-grade dysplasia was analyzed with age stratification.

Results: All women with biopsy-confirmed high grade cervical lesions (HGCLs, ?HSIL) had abnormal baseline co-testing results. The 3-year cumulative risk of developing HGCLs in women with baseline co-testing results of HPV+/Pap+, HPV+/Pap- and HPV-/Pap+ were 19.9%, 7.8% and 2.6%, respectively ($p<0.0001$). The age-stratified 3-year cumulative risk of HGCLs in women with baseline HPV+/Pap+ or HPV+/Pap- peaked at 30-39 years (23% and 11%, respectively) and decreased significantly at 50-59 years (11% and 4%, respectively, $p<0.0001$). Women with HPV-/Pap+ carried a lower risk of HGCLs (?3%), especially in women over age 60. The HPV-positive rates were trending lower with age in women with benign or low-grade lesions (average 83.8%), but they stayed significantly higher in women with HGCLs across age groups (average 97.3%, $p<0.0001$).

Conclusions: HPV-Pap co-testing with 3-year intervals is a very safe practice and provides an effective tool for risk stratification with the highest 3-year cumulative risk of HGCLs in women with HPV+/Pap+ followed by HPV+/Pap- and HPV-/Pap+. The effectiveness in risk assessment peaked at age 30-39 years followed by a significant decrease after age 50 years. This may be attributed to significantly reduced specificity of HPV testing in women over age 60 considering the extremely high HPV-positive rates in women with HGCLs across age groups. Women with HPV-/Pap+ carried a low risk of HGCLs that approached zero in women over age 60.

359 Cytohistological Correlation and HPV Status of Low-Grade Squamous Intraepithelial Lesion, Cannot Rule Out High Grade Lesion

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Disclosures: Akisha Glasgow: None; Claire Michael: None; Philip Bomeisl: None; Aparna Harbhajanka: None

Background: The 2014 Bethesda System for Reporting Cervical Cytology classifies squamous intraepithelial lesions (SILs) of cervix in 2 main categories: Low-grade SIL (LSIL) and High-grade SIL (HSIL). In some clinical practices, “LSIL cannot rule out high grade lesion (LSIL-H)” interpretive category is used in cases with LSIL and findings that may raise the possibility of HSIL. The purpose of this study is to assess follow-up histopathology and high-risk human papillomavirus (hrHPV) results in patients with LSIL-H and compare it with LSIL, atypical squamous cells, cannot rule out HSIL (ASC?H), and HSIL.

Design: Cervical Pap tests with LSILH, LSIL, ASC?H and HSIL interpretation, surgical follow-up, and hrHPV status were retrieved from the computer database from January 2012?December 2017. A total of 646 LSIL-H ThinPrep cases with histologic follow up were identified. hrHPV testing was available in 248 patients.

Results: There were a total of 10527 Paps with histological follow-up. LSIL-H comprised 6.1%, ASCUS 24.8%, LSIL 28.7%, ASCH 4.9% and HSIL 8.2%. The risk of histologic cervical intraepithelial neoplasia (CIN) 2 or worse (CIN 2+) associated with LSIL-H (214/646 [33.1%]) was higher than LSIL (294/3026 [9.7%]) and ASC-H (132/515 [25.6%]) while lower than HSIL (550/865 [63.6%]). Also, LSIL-H was more frequently associated with a definitive histologic diagnosis of CIN1 than ASC-H (257/646 [39.8%] vs 167/515 [32.4%]). If LSIL-H cases are reported as ASC-H, the rate of CIN 2+ for the ASC-H category would increase from 25.6% to 29.8%. Alternatively, if LSIL-H cases are downgraded to LSIL, the rate of HGD+ for the LSIL category would rise from 9.7% to 13.8%. Moreover, the prevalence of HR-HPV was significantly greater in patients with LSIL-H than in patients with ASC-H (210/248 [84.7%] vs 177/253 [70%]). Approximately 62% of cases were hrHPV positive. Of LSIL-H cases with surgical follow-up, 84.7% tested hrHPV positive, accounting for the second most common positive group after HSIL (91.1%).

Table 1. Histological outcome in patients with Pap diagnosis.				
Thin prep Pap diagnosis	HPV Negative	HPV Positive	Total	p value
Negative	1857(85.3%)	320(14.7%)	2177(30.8%)	<0.0001
ASCUS	324(12.8%)	2206(87.2%)	2530(24.9%)	
LSIL	382(22.5%)	1316(77.5%)	1698(24%)	
ASC-H	76(30%)	177(70%)	253(3.6%)	
HSIL	15(8.9%)	154(91.1%)	169(2.4%)	
LSIL-H	38(15.3%)	210(84.7%)	248(3.5%)	
Total	2692	4383	7075	

Table 2. Histological outcome in patients with Pap diagnosis.					
Thin prep Pap diagnosis	Negative/Benign	CIN1	CIN2+	Total	p value
Negative	2658(93%)	157(5.5%)	44(1.6%)	2856(27.2%)	<0.0001
ASCUS	1449(55.4%)	963(36.8%)	204(7.8%)	2616(24.9%)	
LSIL	1264(41.8%)	1468(48.5%)	294(9.7%)	3026(28.7%)	
ASC-H	216(41.9%)	167(32.4%)	132(25.6%)	515(4.9%)	
HSIL	133(15.4%)	182(21%)	550(63.6%)	865(8.2%)	
LSIL-H	175(27.1%)	257(39.8%)	214(33.1%)	646(6.1%)	
Total	5895	3194	1438	10527	

Conclusions: “LSIL-H” category is associated with a higher number of CIN 2 or higher lesions on follow-up compared to patients with LSIL ($p<0.0001$) and ASC-H, while fewer than HSIL. It is associated with a significant percentage of positive hrHPV, supporting LSIL-H as a useful diagnostic category with distinctive features that are different from LSIL or ASC-H. LSIL-H needs further follow-up for the proper management.

360 Improving The Accuracy of Nuclear to Cytoplasmic Ratio Estimations

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Disclosures: Ryan Glass: None; Oana Rosca: None; Karen Chau: None; Silvat Sheikh-Fayyaz: None; Rubina Cocker: None

Background: The Paris System for Reporting Urinary Cytology utilizes nuclear to cytoplasmic (N/C) ratios to stratify cases into diagnostic categories. However, some studies have called into question the accuracy of visually estimating N/C ratios. If we model cells and nuclei as concentric ovals, the N/C ratio can be estimated as the product of the ratios of their diameters (Figure 1). As visual estimates within one dimension may be more reliable, we sought to determine if estimating the ratio of the N/C diameters is more accurate than estimating the ratio of N/C areas.

Design: 24 cells from urine cytologies were assessed using the Adobe Photoshop Histogram tool for nuclear and cell areas to calculate the N/C ratio. Visual estimates of the N/C ratios were made by 4 pathologists. They were then instructed to estimate the N/C diameter ratios along short and long axes. These estimations were multiplied to yield an alternate N/C ratio. Statistical analysis was performed to determine accuracy and precision.

Results: Estimates of N/C ratio made using the diameters (Figure 2B) were more accurate than those made using the areas (Figure 2A), though precision was similar in both groups. Using areas, the median bias was 11% and the limits of agreement of the percent differences were -11% to 33%. Using diameters, however, the median bias was 1% and limits of agreement were-27% to 28%). When evaluating classification accuracy, both methods were similar overall (Table 1). However, the diameter method was more accurate for N/C ratios less than 0.5 (0.63 vs 0.38) and between 0.5 and 0.7 (0.47 vs 0.22), while the area method was more accurate for N/C ratios greater than 0.7 (0.90 vs 0.58)

Area estimation

		Actual		
Estimated	<0.5	0.5-0.7	>0.7	Total
<0.5	6	1	0	7
0.5-0.7	6	7	5	18
>0.7	4	24	43	71
Total	16	32	48	96
Accuracy	0.38	0.22	0.90	0.58

Diameter Estimation

		Actual		
Estimated	<0.5	0.5-0.7	>0.7	Total
<0.5	10	6	3	19
0.5-0.7	6	15	17	38
>0.7	0	11	28	39
Total	16	32	48	96
Accuracy	0.63	0.47	0.58	0.55

Figure 1 - 360

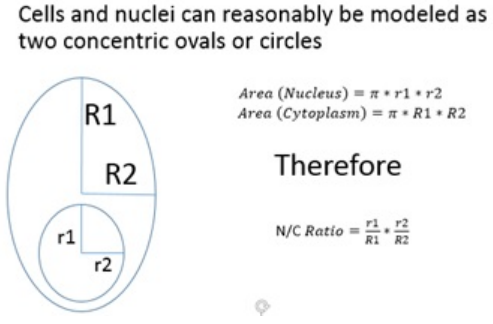
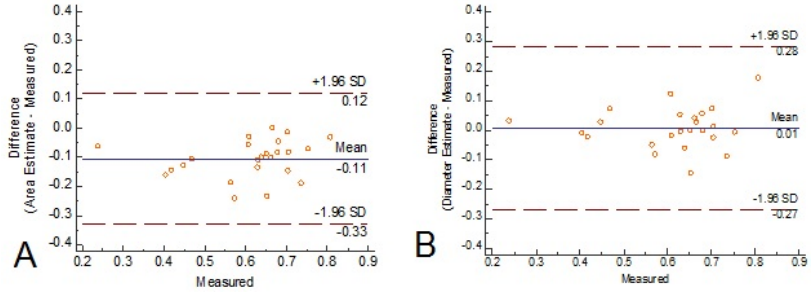


Figure 2 - 360



Conclusions: Use of N/C diameter ratios provides more accurate assessments of N/C ratios than the conventional N/C area ratios. Additional practice using this method may be helpful to achieve the precise categorization required for implementation of The Paris System.

361 Surgical Follow-Up of Non-diagnostic Pancreatic Fine Needle Aspirations Concerning for Pancreatic Adenocarcinoma

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Disclosures: Austin Goetz: None; Teena Dhir: None; Charalambos Solomides: None; Kim HooKim: None

Background: Fine needle aspiration (FNA) is the main diagnostic tool for evaluating pancreatic lesions. Accurate diagnosis and classification of lesions suspicious for adenocarcinoma (ADC) are essential for guiding appropriate clinical management and treatment. However, despite clinical concern, some FNAs maybe non-diagnostic even with additional sampling. The goal of this study was to evaluate the clinical significance of non-diagnostic pancreatic FNAs that are suspicious for adenocarcinoma through correlation with follow-up resections.

Design: This is an eleven-year retrospective study on pancreatic FNAs performed from 2005-2015 for lesions suspicious for ADC with follow-up resection. Metastatic tumors and pancreatic neuroendocrine tumors were excluded. All non-diagnostic FNA cases represented the most recent FNA sample before surgical resection. Pertinent clinical and pathologic data, including age, gender, race, radiological features, cytologic and surgical pathology diagnoses, date and type of surgery, and last known clinical status was reviewed.

Results: There were 423 FNAs performed on pancreatic lesions suspicious for ADC with follow-up resections. Twenty cases (4.7%) were reported as “non-diagnostic”. All twenty cases were neoplastic on resection. The tumors ranged from 0.8-9 cm (mean 3.6 cm), the majority were located in the head and tail (8, 40%, respectively), the others were located in the neck (1, 5%) and body/tail (3, 15%). The tumors were 8 (40%) ADC, 4 (20%) intraductal papillary mucinous neoplasms (IPMN), 3 (15%) mucinous cystic neoplasms and serous cystadenomas, respectively, and 2 (10%) solid-pseudopapillary neoplasms.

Conclusions: The majority of pancreatic lesions that were suspicious for ADC had diagnostic FNAs performed prior to surgical resection, with only 4.7% reported as "non-diagnostic". Despite a non-diagnostic result, these patients underwent surgical excision due to a high index of clinical suspicion. All cases were neoplastic and most were benign (50%). However, 40% were malignant and 10% were solid-pseudopapillary tumors of low malignant potential. Following the most recent guidelines for IPMN, all except 2 resections were performed on tumors greater than 3 cm. A large patient population referred to an academic institution with pancreatic oncology expertise may have caused the high neoplastic rate in this study.

362 Institutional Experience with Ki-67 Grading of Gastroenteropancreatic Well-Differentiated Neuroendocrine Tumor Cytology Specimens Since the Implementation of WHO 2010

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Disclosures: Matthew Gosse: None; Neha Dhungana: None; Chris Jensen: None; Kim Lake: None; Andrew Bellizzi: None

Background: The Ki-67 proliferation index (PI) is essential for grading gastroenteropancreatic neuroendocrine tumors (GEP-NET), and uptake of this practice has increased substantially since the introduction of the 2010 WHO Classification of GEP-NETs. The first specimen from these patients is often a cytology, usually an EUS-FNA. A recent editorial advocated abandoning EUS-FNA for EUS-guided core biopsy for the purpose of more accurate grading based on limited data (PMID: 25493252), while a recent meta-analysis espoused the prevailing practice (PMID: 26713749). Herein, we describe our institutional experience with Ki-67 grading of GEP-NETs since WHO 2010, including correlation with results in surgically resected specimens.

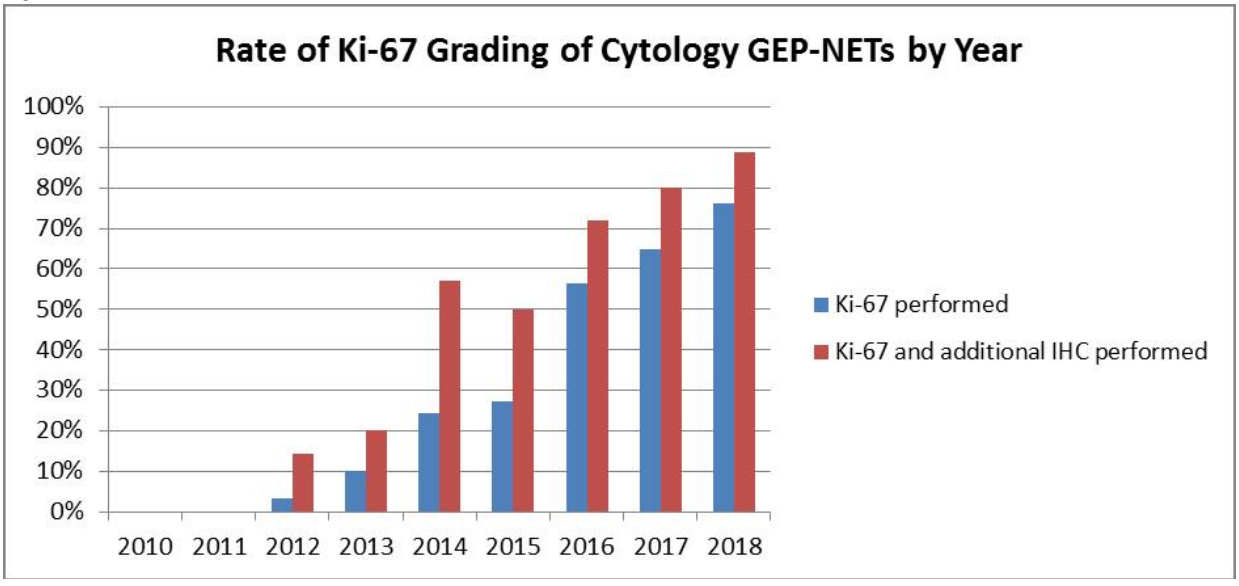
Design: Our anatomic pathology database was searched for all GEP-NET cytology specimens from January 2010 to August 2018. The following were extracted from the electronic medical record: specimen site; results of immunohistochemistry (IHC), including Ki-67 PI; determination whether Ki-67 PI was a formal count or "eyeball estimate." Patients with subsequent surgical pathology material were identified and Ki-67 results recorded. We compared cytology-surgical pathology Ki-67 grade concordance at 3% and 5% cutoffs and in cytology specimens that were formally counted vs. eyeball-estimated.

Results: We identified 251 GEP-NET cytology specimens (combined in-house and outside slides cases) since January 2010. IHC was performed on 53% (n=135), and among this subset Ki-67 was performed on 59% (n=79). There has been substantial uptake of Ki-67 grading from 2010 (0%), with a point of inflection in 2014 (57% in cases with cell block) and a 2018 peak of 89% (see Table and Figure).

33 cases had subsequent surgical pathology material. Rates of grade concordance were similar at 3% and 5% cutoffs: 67% and 70%. Concordance appeared more frequent when the cytology Ki-67 PI was formally counted (79%) vs eyeball-estimated (58%), but this result did not achieve significance. All disagreements were 1 grade apart.

Year	Total GEP-NETs	Ki-67 performed	Ki-67 and other IHC performed (as a surrogate for the presence of adequate material for IHC)
2010	19	0%	0%
2011	16	0%	0%
2012	30	3%	14%
2013	30	10%	20%
2014	33	24%	57%
2015	33	27%	50%
2016	32	56%	72%
2017	37	65%	80%
2018	21	76%	89%

Figure 1 - 362



Conclusions: We have experienced substantial uptake of Ki-67 grading of GEP-NET cytology specimens since the implementation of WHO 2010. Although grades may be discordant between cytology and surgical pathology specimens, they were always increments of 1, which is rarely clinically significant. We are currently further exploring the significance of eyeball-estimated cytology Ki-67 PIs in this grade discordance.

363 Correlation Between Cytologic, ThyroSeq Next Generation Sequencing Assay, and Definitive Surgical Histopathologic Diagnosis In Thyroid Nodules--A Multi-Institutional Experience

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Disclosures: Dominick Guerrero: None; Roshan Raza: None; Siba El Hussein: None; Wenjing Shi: None; Samer Ali: None; Manju Harshan: None

Background: Fine needle aspiration (FNA) biopsy with cytologic evaluation is the first approach to most nodules of the thyroid gland, and integral in directing the next step of clinical management. In recent years, the use of ThyroSeq molecular testing has increased in Bethesda category 3 and 4 lesions—diagnoses that provide relatively less guidance for clinical management—and previous research has shown high sensitivity and specificity in classifying malignant thyroid nodules with this molecular testing. Our study further assesses the accuracy of ThyroSeq testing for thyroid nodules at our institutions.

Design: Between February 2014 and August 2018, 454 FNA biopsies of thyroid nodules diagnosed as primarily Bethesda category 3 (83%), but also 1 (<1%), 2 (5%), 4 (9%), 5 (2%), and 6 (<1%) were sent for ThyroSeq v2 panel molecular testing. 4 specimens resulted as inadequate for molecular analysis. Of the remaining 450 nodules, 63 (14%) underwent subsequent definitive surgical follow-up.

Results: Of the 450 nodules, 150 (34%) were positive for one or more mutations that included 12 point mutations (most commonly NRAS and HRAS), and 3 gene fusions. Upon analysis of the 63 nodules with definitive surgical follow-up, 33 (52%) were diagnosed histologically as malignant. In 31 of these malignant nodules, Thyroseq testing identified a mutation. However, in 2 malignant cases (6%)—one a follicular variant of papillary thyroid carcinoma (PTC), and the other an incidentally found PTC micro carcinoma—ThyroSeq did not identify a mutation or translocation. Mutations were also identified in 15 of the remaining histologically benign nodules. In this data, the sensitivity was 94%, and the specificity 50%.

Figure 1 - 363

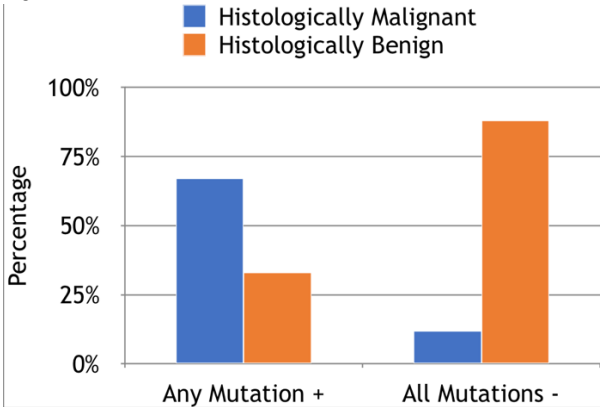
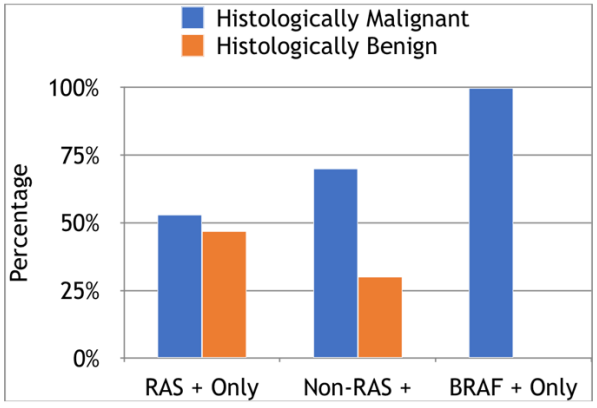


Figure 2 - 363



Conclusions: Our data correlates with the high sensitivity of ThyroSeq testing, although our specificity was lower than expected. Inter-observer variability in identifying category 3 lesions and sample size may have impacted the results. Notably, of the 15 "false positives," 9 had RAS mutations. Further investigation into the specific biology and clinical implications of RAS mutations is an important field of research and may hold relevance to our results.

364 The Diagnostic Utility of Next-Generation Sequencing on Fine Needle Aspiration Biopsies of Melanocytic Uveal Lesions

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Disclosures: Lucy Han: None; Elham Khanafshar: None; Sarah Calkins: None

Background: Uveal melanoma (UM) is the most common intraocular malignancy and is highly aggressive with propensity to metastasize. UM harbors a unique set of genetic abnormalities, separate from cutaneous melanoma. Mutation status correlates with disease-free survival and overall prognosis, which often guides follow-up management. Fine needle aspiration (FNA) biopsies play an important role in obtaining fresh tissue specimen for both cytologic diagnosis of melanoma and molecular studies. It has been suggested that while FNA usually provides high diagnostic accuracy, there may be limited cellularity, which may compromise the diagnostic potential for molecular studies. This study evaluates FNA biopsies of uveal melanocytic lesions to assess the sample adequacy for both cytologic evaluation and next-generation sequencing (NGS).

Design: We retrospectively evaluated FNA cases of melanocytic uveal lesions from 2015-2018. Samples were obtained by ophthalmologist-performed FNA. Using ROSE, samples were aliquoted for cytologic and NGS testing. Cytologic preparations included varying combinations of direct smears, ThinPrep slides, and cell blocks. Immunohistochemical stains for melanocytic markers were performed in select cases. Samples were additionally submitted for hybrid-capture based NGS to evaluate for molecular alterations.

Results: Thirty-six cases of melanocytic uveal lesions were reviewed. There was sufficient material for cytologic diagnosis in 33/36 cases (92%) and for NGS testing in 30/36 cases (83%). Sufficient material for both cytologic diagnosis and NGS testing was present in 28/36 cases (78%). Of the 7 cases cytologically categorized as "atypical" or "non-diagnostic", NGS testing was sufficient and diagnostic for melanoma in 5 cases. Twenty-three cases were diagnostic of melanoma by cytology alone. Of these cases, 20 (87%) had concordant NGS results, 2 lacked molecular alterations, and 1 was insufficient for testing.

Conclusions: FNA sampling of melanocytic uveal lesions is adequate for both cytologic diagnosis and next generation sequencing testing. In a subset of cases where pathologic findings were indeterminate, either diagnosed as "atypical" or "non-diagnostic", NGS results were clarifying for diagnosis. In addition, specific molecular alterations identified using NGS testing can aid in evaluating prognosis and guide further management.

365 Use of Next Generation Sequencing for Detection of Somatic Mutations in Centrifugation Supernatant of specimens from Pancreaticobiliary lesions.

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Background: Bile duct brushing (BDB) and pancreatic fine needle aspiration (PFNA) is used to evaluate pancreatobiliary lesions as they widely sample the lesions with low complication rate. Cytological evaluation of PFNA or BDB is a specific, but not very sensitive test. However, there is minimal literature on the use of postcentrifugation supernatant which is usually discarded for next-generation sequencing (NGS) as adjunct to cytological diagnosis of BDB and PFNA. We investigate the use of supernatants for detection of clinically relevant biomarkers by NGS.

Design: After cell pellet removal, cytocentrifugation supernatant from 8 PFNA rinses and 20 BDB specimens from 27 patients were retained. DNA was extracted from the supernatant and tested with in-house focused solid tumor assay by Ion Torrent platform. The NGS results were compared with an orthogonal method. Specimens were placed into negative/atypical (negative) or suspicious/positive (positive) categories on cytology. Performance characteristics for each diagnostic modality were calculated on the basis of clinicopathologic follow-up.

Results: There were 12 malignant (11 PDA and 1 cholangiocarcinoma) and 15 benign. NGS revealed mutations in 10/12 malignant cases (83.3%), including KRAS (9/12), TP53 (6/12), SMAD4 (1/12), CCND1 (2/12), CDKN2A (1/12), FBXW7 (1/12). Other mutations are U2AF1, ERBB2, BRAF, PIK3CA in 1 case each. 9/12 malignant cases showed more than 2 mutations. Out of 5 cases which showed atypical cells on cytology, NGS showed mutations in 3 cases including case 8 (KRAS, TP53, U2AF1), case 9 (KRAS, ERBB2) and case 28 (KRAS, TP53) (Table 1). The follow up of 2 cases with atypical cytology and negative NGS were cholangiocarcinoma and pancreatitis. Cytology had a sensitivity of 75% and a specificity of 100%. When added to cytology, NGS increased the sensitivity to 91.6%. All cytology negative cases were also negative by NGS except one which showed KRAS mutation and follow up was pancreatitis.

7	Sample	Diagnosis on Cytology	cytology	NGS	KRAS	TP53	SMAD4	CDKN2A	Other	CNV	diagnosis
1	Bile duct brush	NMCI	neg	neg							Benign
2	pancrease FNA	ADENOCARCINOMA	pos	neg							PDA
3	Bile duct brush	NMCI	neg	neg							Benign
4	Bile duct brush	NMCI	neg	neg							Benign
5	Pancreas brush	NMCI	neg	neg							Benign
6	Pancreas FNA	ADENOCARCINOMA	pos	pos	c.35G>T : p.G12V : 45.9 : (1999)			CDKN2A : c.151-2A>G : 35.8			PDA
7	Pancreas FNA	ADENOCARCINOMA	pos	pos	c.35G>T : p.G12V : 48.4 : (1996)	c.817C>T : p.R273C : 21.7 : (295)				MYC amp	PDA
8	Bile duct brush	Rare atypical cells	atypical	pos	c.34G>T : p.G12C : 6.8 : (1608)	c.524G>A : p.R175H : 12.3 : (1397)			U2AF1 : c.101C>T : p.S34F : 3.9 : (458)		PDA
9	Bile duct brush	Rare atypical cells	atypical	pos	c.35G>A : p.G12D : 3.1 : (1399)				ERBB2:c.2524G>A : p.V842I : 3.1 : (1486)		PDA
10	Pancreas FNA	ADENOCARCINOMA	pos	pos	c.35G>T : p.G12V : 19.9 : (1259)	c.700T>A : p.Y234N : 31.1 : (1060)	c.1051G>T : p.D351Y : 29.2 : (408)		FBXW7 : c.1394G>A :p.R465H :19.2 : (526)		PDA
11	Bile duct brush	ADENOCARCINOMA	pos	pos	c.35G>T : p.G12V : 4.3 : (1943)	c.700T>A : p.Y234N : 4.8 : (1970)	SMAD4 : c.1051G>T : p.D351Y : 4.3 : (974)		FBXW7 : c.1394G>A : p.R465H : 3.0 : (929)		PDA
12	Hepatic ductbrush	NMCI	neg	neg							Benign
13	Pancreas brush	NMCI	neg	neg							Benign
14	Hepatic ductbrush	NMCI	neg	neg							Benign
15	Bile duct brush	ADENOCARCINOMA	pos	pos					BRAF: c.1803A>C : p.K601N : 34.7 : (300)	CCND1 amp	PDA
16	Bile duct brush	NMCI	neg	neg							Benign
17	pancrease FNA	NMCI	neg	neg							Benign
18	Bile duct brush	NMCI	neg	neg							Benign
19	pancrease FNA	ADENOCARCINOMA	pos	pos	c.34G>C : p.G12R : 31.0 : (1742)	c.714T>G : p.C238W : 49.0 : (1608)			PIK3CA: c.1624G>A : p.E542K : 7.4 : (1843)		PDA
20	Pancreas FNA	NMCI	neg	neg							Benign
21	Pancreas FNA	PD Carcinoma	pos	pos	c.35G>A : p.G12D : 41.0 : (960)						PDA
22	Bile duct brush	ADENOCARCINOMA	pos	pos	c.35G>A : p.G12D : 17.3 : (1652)	c.529_546del18 : p.P177_C182delPHHERC : 12.4 : (1256)					PDA
23	Bile duct brush	NMCI	neg	neg							Benign
24	Bile duct brush	Atypical cells	atypical	neg							CLC
25	Bile duct brush	NMCI	neg	neg							Benign
26	Bile duct brush	NMCI	neg	pos	c.34G>C : p.G12R : 2.2 : (1999)						pancreatitis
27	Bile duct brush	Atypical cells	atypical	neg							pancreatitis
28	Bile duct brush	Atypical cells	atypical	pos	c.183A>C : p.Q61H : 21.0 : (1996)	c.817C>T : p.R273C : 13.9 : (1997)					PDA

NMCI- No malignant cells identified, PDA - Pancreatic ductal carcinoma, CLC- CHOLANGIOCARCINOMA

Conclusions: This study represents a significant advance as it presented mutations other than KRAS and TP53. Thus, NGS offers advantages as it increased the sensitivity of cytology, although studies with larger cohorts are needed to verify these findings. Use of cytocentrifugation supernatant for molecular testing can reduce the need for repeat invasive procedures and conservation of the tissue for other diagnostic purposes.

366 Scoring of Programmed Death-Ligand 1 (PD-L1) Immunohistochemistry (IHC) on Cytology Specimens in Non-Small Cell Lung Carcinoma (NSCLC): An Inter-observer Agreement Study

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Background: Studies evaluating PD-L1 immunohistochemistry (IHC) testing in patients with non-small cell lung carcinoma (NSCLC) have shown good correlations between cytology and surgical pathology specimens. Inter-observer agreement when evaluating PD-L1 IHC in cytology cell blocks (CBs) has yet to be explored. Our study aimed to determine the reproducibility of PD-L1 IHC scoring in CBs. Our secondary aim was to evaluate the impact of CB cellularity, method of sample collection and observer subspecialty on scoring agreement.

Design: PD-L1 IHC was performed on 54 NSCLC CBs using the DAKO 22C3 clone (Vantana platform). Specimens included 21 pleural effusions, 32 fine needle aspirations (FNA), and 1 bronchial brush. 14 cases had <100 tumor cells (TCs) and 40 had ≥100 TCs. PD-L1 staining was scored independently by 7 cytopathologists, 3 of whom also have expertise in pulmonary pathology. Scoring was done in three tiers; negative (<1%), low positive (1-49%) and high positive (≥50%). Sample collection type was compared between FNA vs effusion. Fleiss' kappa statistics was used to measure the reliability of agreement among observers. Total agreement was defined as exact scores between all observers and majority agreement was defined as exact score agreement between 4 of 7 observers. Fischer's exact test was used to measure the impact of specimen collection type, number of TCs and added pulmonary subspecialty expertise.

Results: There was 48% and 98% total and majority agreement, respectively, in PD-L1 scores between observers. When agreement was measured between pathologists specializing in both pulmonary pathology and cytology, there was a total and majority agreement of 67% and 98%, respectively. See table. The number of TCs (p=0.36) and sample collection type (p=0.59) had no statistically significant impact on total inter-observer agreement. The same was observed when scoring was performed by pathologists specializing in both pulmonary and cytopathology (p=0.26 and p=0.39, respectively).

Table. Inter-observer Agreement: PD-L1 Scoring in Cell Blocks

	Total Agreement	Majority Agreement	Kappa*	Fleiss' kappa (95% confidence interval)
All cytopathologists (7)	48%	98%	0.608*	(0.50-0.72)
Cytopathologists with added pulmonary pathology expertise (3)	67%	98%	0.633*	(0.51-0.76)

*substantial agreement

Conclusions: Our study demonstrates that there is substantial agreement in PD-L1 IHC scoring in cytology cell blocks among cytopathologists. Additional expertise in pulmonary pathology has no statistically significant benefit. The sample collection type and the number of TCs are not associated with differing inter-observer scores at a 5% significance level. The number of TCs or sample collection type do not interfere with the ability to obtain compatible inter-observer agreements in PD-L1 scoring.

367 Application of The Milan System for Reporting Salivary Gland Cytopathology in Cystic Lesions

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Disclosures: Monica Hill: None; Derek Allison: None; Liron Pantanowitz: None; Zahra Maleki: None

Background: Fine needle aspiration (FNA) is a well-accepted diagnostic modality for the preoperative management of salivary gland lesions. The subset of salivary gland lesions that are cystic present diagnostic challenges related to sampling, confounded by a broad differential diagnosis. In this study, we evaluate the benefit of applying The Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) to a series of cystic salivary gland lesions.

Design: The pathology archive at a large academic institution was searched for cystic salivary gland FNAs over a 15 year period (2000 – 2015). Patient demographics, anatomic site of the lesion, cytology and histopathology reports, as well as clinical and surgical follow-up were recorded. MSRSGC was newly applied to each case and the risk of malignancy (ROM) and risk of neoplasia (RON) for each category was calculated.

Results: There were 145 cases aspirated from 80 males and 65 females with a mean age of 53 years (range 4 – 90 years). The most common anatomic site was the parotid gland (96.6%) followed by the submandibular (2.8%) and submental glands (0.7%). After applying MSRSGC, there were 37 (25.5%) non-diagnostic, 72 (49.7%) non-neoplastic, 28 (19.3%) atypia of undetermined significance (AUS), 1 (0.7%) benign neoplasm, 2 (1.4%) salivary gland neoplasms of uncertain malignant potential (SUMP), 4 (2.8%) suspicious for malignancy (SFM), and 1 (0.7%) malignant case(s) (Figure 1). Of these 145 cases, 123 patients (84.8%) with follow-up data available showed an overall RON and ROM of 18.7% and 9.8%, respectively. The RON and ROM were 8.8%/5.9%, 13.8%/6.2%, 38.9%/16.7%, 0.0%/0.0%, 100.0%/50.0% and 66.7%/66.7% for each category, respectively (Figure 2). The RON and ROM could not be calculated for the single case categorized as malignant due to lack of follow-up data.

Figure 1 - 367

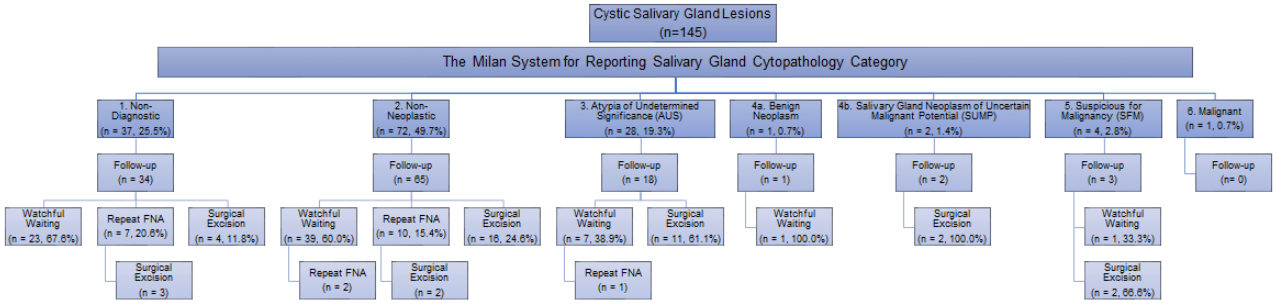

Figure 1: Clinical management and follow-up of patients with cystic salivary gland lesions after initial fine needle aspiration (FNA)

Figure 2 - 367

The Milan System for Reporting Salivary Gland Cytopathology Category		Non-diagnostic		Non-neoplastic		Atypia of Undetermined Significance (AUS)		Benign Neoplasm		Salivary Gland Neoplasm of Uncertain Malignant Potential (SUMP)		Suspicious for Malignancy		Malignant
Total patients with any follow-up		n = 34		n = 65		n = 18		n = 1		n = 2		n = 3		n = 0
Watchful Waiting Only: Assumed Benign														
	n (%)	23	67.6%	37	56.9%	6	33.3%	1	100.0%	0	0.0%	1	33.3%	
Diagnosis on Repeat FNA or Surgical Excision														
Benign non-neoplastic	n (%)	8	23.5%	19	29.2%	5	27.8%	0	0.0%	0	0.0%	0	0.0%	
	Surgical Diagnosis	Salivary duct cyst (3) Retention cyst (1)		Lymphoepithelial cyst (4) Salivary duct cyst (4) Branchial cleft cyst (2)		Lymphoepithelial cyst (2) Benign squamous-lined cyst (1) Parotid tissue with no cystic lesion (1) Fibrous walled cyst with keratin debris and reactive atypia (1)								
	Repeat FNA Diagnosis	Acellular debris (1) Blood and macrophages (1) Vascular lesion or leiomyoma (1) Cyst content (1)		Lymphoepithelial cyst (4) Inflammatory cells and debris (3) Lymphocytes, fibrosis and parotid tissue (1) Blood, macrophages and rare atypical cells (1)										N/A No follow-up
Benign neoplastic	n (%)	1	2.9%	5	7.7%	4	22.2%	0	0.0%	1	50.0%	0	0.0%	
	Surgical Diagnosis	Pleomorphic adenoma (1)		Warthin's tumor (3) Cystic sebaceous lymphadenoma (1)		Warthin's tumor (1) Hemangioma (1) Pleomorphic adenoma (1)				Warthin's tumor (1)				
	Repeat FNA Diagnosis			Warthin's tumor (1)		Warthin's tumor (1)								
Malignant	n (%)	2	5.9%	4	6.2%	3	16.7%	0	0.0%	1	50.0%	2	66.7%	
	Surgical Diagnosis	Mucoepidermoid carcinoma (1) Acinic cell carcinoma, papillary cystic variant (1)		EBV-associated smooth muscle tumor (1) EBV (+) diffuse large B cell lymphoma (1) Squamous cell carcinoma (1) Extranodal marginal zone lymphoma (1)		Mucoepidermoid carcinoma (1) Acinic cell carcinoma (1) Squamous cell carcinoma (1)				Mucoepidermoid carcinoma (1)		Mucoepidermoid carcinoma (2)		
Risk of neoplasm		8.8%		13.8%		38.9%		0.0%		100.0%		66.7%		N/A No follow-up
Risk of malignancy		5.9%		6.2%		16.7%		0.0%		50.0%		66.7%		

Figure 2: Follow-up diagnosis in patients after clinical, surgical or additional cytology follow-up

Conclusions: After applying MSRSGC to cystic salivary gland lesions the majority of cases fell in the non-neoplastic category (49.7%). The RON was highest in the SUMP category (100.0%), followed by the SFM, AUS, non-neoplastic, non-diagnostic and benign neoplasm categories. The ROM was highest in the SFM category (66.7%), followed by the SUMP, AUS, non-neoplastic, non-diagnostic and benign neoplasm categories. In summary, applying MSRSGC can provide useful information for the management of cystic salivary gland lesions; however, the diagnostic challenge of these under sampled lesions may result in an increase in the rate of AUS diagnoses.

368 Risk of Malignancy in the Categories of the Papanicolaou Society of Cytopathology System for Reporting Pancreaticobiliary Cytology

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Disclosures: Raza Hoda: None; Elizabeth Finer: None; Ronald Arpin: None; Matthew Rosenbaum: None; Martha Pitman: None

Background: Management of pancreatic lesions depends on risk of malignancy (ROM), which is primarily based on cytologic and radiologic evaluation. The Papanicolaou Society of Cytopathology (PSC) has proposed a six-tier classification system for reporting pancreaticobiliary cytology. The PSC system categories include Nondiagnostic, Negative, Atypical, Neoplastic: Benign or Other, Suspicious, and Positive. Neoplastic: Other lesions can be further stratified by presence of high-grade atypia. Studies on the ROM associated with each category is limited.

Design: All patients who underwent fine-needle aspiration (FNA) biopsy for a pancreatic lesion at a single institution from 01/2016 to 12/2016 were evaluated. Clinical data, radiographic impressions, endoscopic findings, next-generation sequencing results, biochemical analyses and cytologic diagnoses were reviewed. Pancreatic lesions were prospectively classified according to the PSC system. Epithelial atypia in Neoplastic: Other lesions was categorized as low- and high-grade. Low-grade atypia was defined as low-to-intermediate grade mucinous dysplasia, and high-grade atypia denoted high-grade mucinous dysplasia, adenocarcinoma or neuroendocrine tumors (NETs). ROM was determined by histological outcome or definitive clinical follow-up.

Results: 334 pancreatic FNA biopsies from 323 patients were reviewed. Pancreatic lesions were cystic in 171 (51.2%) and solid in 163 (48.8%). Cytology interpretations included 39 Nondiagnostic, 100 Negative, 25 Atypical, 4 Neoplastic: Benign, 66 Neoplastic: Other, 6 Suspicious and 94 Positive (Table 1). Histology was obtained in 138 (41.3%) cases, and clinical follow-up was used in 196 (58.7%) (mean 15 months). Absolute ROM for Nondiagnostic was 7.7%, Negative 3.0%, Atypical 36.0%, Neoplastic: Benign 0.0%, Neoplastic: Other 33.3%, Suspicious 100% and Positive 100%. Within the Neoplastic: Other category, ROM for low-grade cysts was 4.8%, while ROM for high-grade lesions was 83.3%. Of the patients with Neoplastic: Other interpretations, 48.4% were managed conservatively. 8 Neoplastic: Other lesions with high-grade atypia were managed conservatively, 7 of which were NETs. 60.6% of patients in the Neoplastic: Other category had benign follow-up.

Table 1. Correlation of Cytologic Classification with Histologic and Clinical Follow-up of 334 Pancreatic FNAs from 323 Patients.

Cytologic Classification	Benign *n* (%)	Malignant *n* (%)	Total Cases *n* (%)
I. Nondiagnostic	36 (92.3)	3 (7.7)	39 (11.7)
II. Negative	97 (97.0)	3 (3.0)	100 (29.9)
III. Atypical	16 (64.0)	9 (36.0)	25 (7.5)
IV. Neoplastic: Benign	4 (100.0)	0 (0)	4 (1.2)
IV. Neoplastic: Other	44 (66.7)	22 (33.3)	66 (19.8)
With Low-Grade Atypia	40 (95.2)	2 (4.8)	42 (12.6)
With High-Grade Atypia	4 (16.7)	20 (83.3)	24 (7.2)
V. Suspicious	0 (0)	6 (100)	6 (1.8)
VI. Malignant	0 (0)	94 (100)	94 (28.1)
Total Cases	**197 (59.0)**	**137 (41.0)**	**334 (100)**

Conclusions: The PSC classification system for reporting pancreatic FNAs demonstrates the expected gradation of ROM among the six tiers. The Neoplastic: Other category gives accurate ROM while allowing for flexibility in patient management.

369 Quantification of Colloid and its Use in the Classification of Hurthle Cell Fine Needle Aspirations

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Disclosures: Melissa Hogan: None; Kim Ely: None; Alice Coogan: None; Vivian Weiss: None

Background: It is common practice, as mentioned in The Bethesda System for Reporting thyroid Cytopathology (TBSRCT), that a pure population of Hurthle/oncocytic cells in the presence of abundant colloid will be interpreted as benign rather than follicular neoplasm oncocytic type/suspicious for follicular neoplasm oncocytic type (FNHCT/SFNHCT). However, a macrofollicular component has been described in oncocytic carcinomas (Yang et al. Cytopathol. 2013) and the presence of abundant colloid does not assure a benign lesion. Here we evaluate the utility of colloid quantification in predicting the malignancy risk of FNHCT/SFNHCT lesions.

Design: A retrospective chart review was performed for consecutive FNHCT/SFNHCT thyroid FNAs with follow-up resection (23 patients, 24 cases 2008-2016). Quantification of colloid on diagnostic slides was performed by 2 cytopathologists. Colloid was scored as

absent/scant (A/S)=less than a 3-4 clusters/slide, moderate (Mod)= more readily identifiable clusters of colloid/slide, and abundant (AB)=colloid occupying > half the slide.

Results: The average age of patients was 57 (41-78 years, 3:1 female:male ratio). The colloid content of FNHCT/SFNHCT FNAs at our institution was: 83% A/S (20/24), 8.3% mod (2/24), and 8.3% AB (2/24). Twenty-five percent of the cases A/S cases were malignant and 58% with A/S colloid were benign on surgical resection. Of the malignant resections, 14 % had Mod or AB colloid (1/6 cases) on FNA as compared to 18% of cases with benign surgical resection diagnoses (3/14, p=1). Similarly, for neoplastic surgical resection diagnoses, 17% had Mod or AB colloid (3/15 cases) on FNA as compared to 17% of cases with non-neoplastic surgical resection diagnoses (1/6 cases). There was no significant difference in colloid quantity or quality between neoplastic or malignant lesions and benign lesions on FNA.

Conclusions: Here we demonstrate that the majority (83%) of FNAs meeting criteria for FNHCT/SFNHCT, moderately to markedly cellular sample containing a pure population of oncocytic (Hurthle) follicular cells, at our institution have A/S colloid. However, an equal number of cases of both malignant and benign Hurthle cell lesions contained Mod-to-AB colloid on FNA (14% and 18% respectively). In the setting of a moderate to markedly cellular consisting exclusively of Hurthle cells, the presence of abundant colloid should not preclude a diagnosis of FNHCT/SFNHCT.

370 Aero Sample Preparation System (ASPS, Preora Healthcare®): Early Report of a Novel Automated Approach to Rapid and Uniform Cytology Slide Preparation with High Diagnostic Concordance

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Disclosures: Yanjun Hou: None; Michael Verleye: *Employee*, Preora HealthCare; Hariharan Subramanian: *Major Shareholder*, Preora HealthCare; Jeffrey Mueller: None; Charles Sturgis: None

Background: In recent years, cytopreparatory laboratories have transitioned from direct smears and cytocentrifuge preparations to liquid-based systems such as ThinPrep (Hologic) and SurePath (BD). Scientists at Preora Healthcare have devised an innovative aerosol-powered cytology specimen preparation device that combines deposition and staining into a single automated Aero Sample Prep System (ASPS) in which samples such as FNAs and fluids are injected into a proprietary desktop device that utilizes an aerosol method to uniformly distribute cells onto a circular region in the center of a microscope slide. The slide is stained within the machine and is available for rapid review within 2.5 minutes.

Design: Cytology specimens (102 total, including residua of 68 EBUS samples, 15 bench top FNAs, and residua of 19 serous fluids) were prepared using Preora's system. Slides were reviewed for preparation and stain quality, cellularity, cytodiagnosis, and concordance with reference diagnoses. Bronchial and fluid slides were reviewed by one pathologist (CDS). Bench top FNAs were reviewed by two (CDS and YH) (Figure 1).

Results: Slides made from Cytolyt residua of 68 bronchoscopic specimens (46 EBUS nodal FNAs / 9 EBUS lung FNAs / 13 bronchial brushings) were prepared using the ASPS. These slides showed 85% diagnostic concordance with historical results (Table 1). All discordant cases were malignant / atypical by original studies but showed no lesional cells on Preora slides, with all discrepancies attributed to low residual cellularity. Slides from 19 body fluids were prepared using Preora's system with 100% diagnostic concordance. Fifteen benchtop FNAs of malignancies (9 different organs) were performed using 23g needles with samples split into direct smears and Preora preparations. Diagnostic concordance was 93% (14/15), with the single discordant case, a primary renal cell carcinoma, showing fewer intact cells in the Preora preparation. This case was diagnosed as carcinoma on direct smear and atypical cells by ASPS. The intrinsic Preora cyto-staining module was used for bench top FNAs with excellent quality Diff-Quik staining.

Table 1. Preora System Diagnostic Accuracy.

Specimen Types	Number of Cases	Diagnostic Concordance	Diagnostic Concordance Corrected for Cellularity
EBUS FNAs neoplastic and benign	68	58/68 (85%)	58/58 (100%)
Benchtop FNAs neoplastic	15	14/15 (93%)	14/15 (93%)
Fluids neoplastic and benign	19	19/19 (100%)	19/19 (100%)
Total	102	91/102 (89%)	91/92 (99%)

Figure 1 - 370

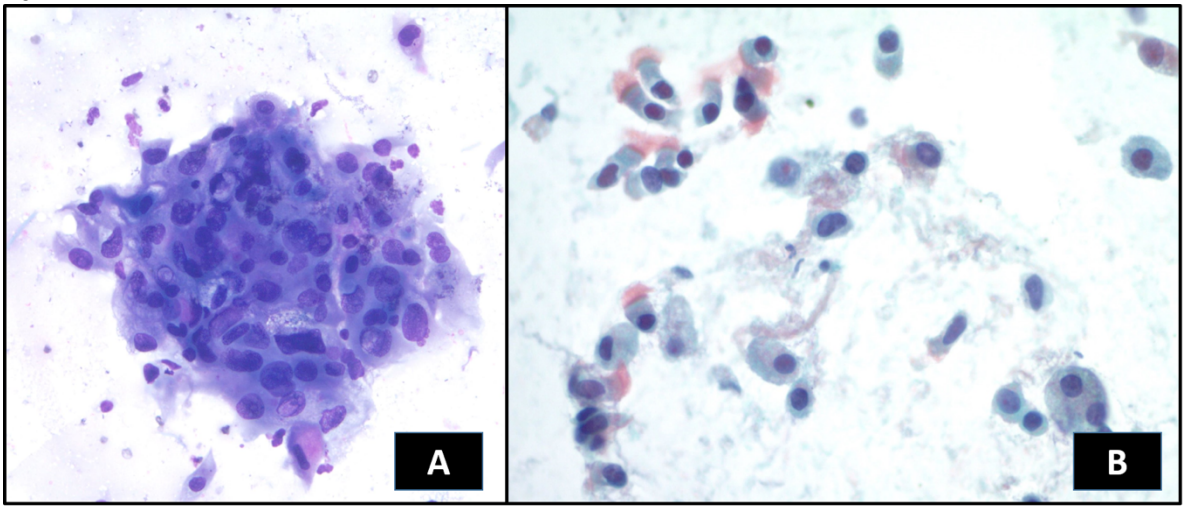

Figure 1. A. Non-small cell carcinoma of lung, bench top FNA, Preora AeroDep & AeroStain, Diff-Quik stain, magnification 40X. B. Benign bronchial cells, EBUS FNA, Preora AreoDep, Papanicolaou stain, magnification 60X

Conclusions: Preora's ASPS is a small-footprint desktop device that harnesses the power of specimen aerosolization to create and then stain high quality microscope slides. High concordance is observed with paired conventional preparations and historical results. This technology could be applied during routine processing or at the time of rapid on site evaluations.

371 The Diagnostic Value of Ancillary Studies in Serous Effusion Cytology: Comprehensive Review of the Recent Literature

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Disclosures: Tom Hu: None; Sahar Farahani: None; Sharon Song: None; Zubair Baloch: None

Background: The cytologic evaluation of serous effusion specimens, while highly specific (89-98%), is only moderately sensitive (40-80%) in identifying malignancy due to morphologic overlap between benign and malignant conditions. Ancillary techniques (e.g. immunocytochemistry (ICC) and molecular markers (MM)) substantially improve the performance characteristics of this common but challenging specimen, particularly in morphologically ambiguous cases. The aim of this study was to perform a systematic review of the recent effusion cytology literature and evaluate the diagnostic value of the newer ICC and MM in use today.

Design: A PubMed search of the English literature from the past five years (1/1/2013-8/25/2018) was conducted using the following search terms: “Adenocarcinoma,” “mesothelioma,” “effusion,” “pericardial,” “peritoneal,” “pleural,” “fluid,” and “cytology.” Only studies on serous effusion specimens were included in our analysis; studies that examined both tissue and effusion specimens were included if the effusion specimen data could be reliably extracted. The numbers of true positives/negatives and false positives/negatives were noted. The weighted mean sensitivity and specificity were calculated for each marker.

Results: The final analysis included 30 studies exploring the diagnostic value of ICC and/or MM in effusion cytology. 2 investigated EZH2 in distinguishing malignant from benign effusions; 5 evaluated Claudin-4 (4 studies) and MMP-7 (1 study) in differentiate carcinomatous from non-carcinomatous effusions; 10 studied BAP1 and/or p16 FISH to distinguish malignant from reactive mesothelial cells; and 13 reviewed various organ-specific markers to determine the etiological site of carcinomatous effusions. Table 1 summarizes our findings.

Marker (# of Studies)	TP†	FP†	FN†	TN†	Sensitivity‡(%±SE)	Specificity‡(%±SE)	PPV‡(±SE)	NPV‡ (±SE)
Differentiating Malignant from Benign Effusions - ICC								
EZH2 *(2)* §	126	0	11	101	91.4 ± 1.8	100	100	90.2 ± 0.3
Differentiating Reactive from Malignant Mesothelial Cells - ICC								
BAP-1 *(9)*	285¶	18	149	566	64.2 ± 3.7	96.3 ± 1.8	94.3 ± 2.7	64.4 ± 6.6
Differentiating Reactive from Malignant Mesothelial Cells - FISH								
p16 *(3 Sensitivity, 2 Specificity*)*	29¶	0	19	24	61.3 ± 10.1	100	100	58.9 ± 8.9
Differentiating Carcinoma from Non-Carcinomatous Effusions – ICC								
Claudin-4 *(4)*	477	0	17	335	95.1 ± 3.4	100	100	94.8 ± 3.0
MMP-7 *(1)*°	124	0	183	49	40.4	100	100	21.2
Lung Specific Markers - ICC								
TTF1 *(4 Sensitivity, 3 Specificity*)*	76	5	29	175	69.5 ± 10.1	96.3 ± 1.0	88.2 ± 1.6	86.7 ± 1.8
Napsin-A *(3)*	44	2	21	176	69.9 ± 3.9	99.4 ± 0.6	96.5 ± 3.4	88.4 ± 2.7
Breast Specific Marker - ICC								
GATA-3 *(5 Sensitivity, 3 Specificity*)*	145	30	18	269	88.4 ± 6.3	93.7 ± 2.6	86.7 ± 9.6	92.5 ± 3.0
Thyroid Specific Markers - ICC								
Thyroglobulin *(3 Sensitivity only*)*	7	-*	-*	4	63.6	-*	-*	-*
TTF-1 *(4 Sensitivity, 1 Specificity*)*	10	6	0	20	100	76.9	62.5	100
PAX-8 *(3 Sensitivity, 1 Specificity*)*	9	15	0	17	100	53.1	37.5	100
Kidney (Renal Cell Carcinoma) Specific Marker - ICC								
PAX-8 *(1)*°	8	23	0	56	100	70.9	25.8	100
PAX-2 *(1)*°	8	8	0	71	100	89.9	50	100
Müllerian System Specific Marker - ICC								
PAX-8 *(1)*°	20	11	0	56	100	84.1	64.5	100

TP true positive, FP false positive, FN false negative, TN true negative, PPV positive predictive value, NPV negative predictive value, SE standard error, ICC immunocytochemistry

†Values are totaled across all studies included in the analysis ‡Simple weighted means §EZH2 positivity was seen in 1/1 peritoneal malignant mesothelioma only; all other positives were carcinomas. ¶Positivity was defined as loss of BAP-1 staining by ICC and homozygous deletion of p16 by FISH. *Only sensitivity was able to be calculated when just the number of true positive and false negative was available. ° These calculations were made from the data found in only one study.

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Marker (# of Studies)	TP†	FP†	FN†	TN†	Sensitivity‡ (%±SE)	Specificity‡ (%±SE)	PPV‡ (±SE)	NPV‡ (±SE)
Differentiating Malignant from Benign Effusions - ICC								
EZH2 (2) §	126	0	11	101	91.4±1.8	100	100	90.2 ±0.3
Differentiating Reactive from Malignant Mesothelial Cells - ICC								
BAP-1 (9)	285¶	18	149	566	64.2±3.7	96.3±1.8	94.3±2.7	64.4±6.6
Differentiating Reactive from Malignant Mesothelial Cells - FISH								
p16 (3 Sensitivity, 2 Specificity*)	29¶	0	19	24	61.3±10.1	100	100	58.9±8.9
Differentiating Carcinoma from Non-Carcinomatous Effusions – ICC								
Claudin-4 (4)	477	0	17	335	95.1±3.4	100	100	94.8±3.0
MMP-7 (1)#	124	0	183	49	40.4	100	100	21.2
Lung Specific Markers - ICC								
TTF1 (4 Sensitivity, 3 Specificity*)	76	5	29	175	69.5±10.1	96.3±1.0	88.2±1.6	86.7±1.8
Napsin-A (3)	44	2	21	176	69.9 ±3.9	99.4±0.6	96.5±3.4	88.4±2.7
Breast Specific Marker - ICC								
GATA-3 (5 Sensitivity, 3 Specificity*)	145	30	18	269	88.4 ±6.3	93.7±2.6	86.7±9.6	92.5±3.0
Thyroid Specific Markers - ICC								
Thyroglobulin (3 Sensitivity only*)	7	-*	-*	4	63.6	-*	-*	-*
TTF-1 (4 Sensitivity, 1 Specificity*)	10	6	0	20	100	76.9	62.5	100
PAX-8 (3 Sensitivity, 1 Specificity*)	9	15	0	17	100	53.1	37.5	100
Kidney (Renal Cell Carcinoma) Specific Marker - ICC								
PAX-8 (1)#	8	23	0	56	100	70.9	25.8	100
PAX-2 (1)#	8	8	0	71	100	89.9	50	100
Müllerian System Specific Marker - ICC								
PAX-8 (1)#	20	11	0	56	100	84.1	64.5	100

TP true positive, FP false positive, FN false negative TN true negative PPV positive predictive value, NPV negative predictive value, SE standard error, ICC immunocytochemistry
†Values are totaled across all studies included in the analysis, ‡Simple weighted means, §EZH2 positivity was seen in 1/1 peritoneal malignant mesothelioma only; all other positives were carcinomas.
¶Positivity is defined as loss of BAP-1 staining by ICC and homozygous deletion of p16 by FISH, #Only sensitivity was able to be calculated when just the number of true positive and false negative was available.
*These calculations were made from the data found in only one study.

Conclusions: Our review highlights the utility of several key ICC and MM in classifying disease in effusion cytology specimens. EZH2 positive is almost exclusively seen in the setting of malignant effusions. Claudin-4 and MMP-7 are highly specific and sensitive markers for detecting carcinoma. Homozygous deletion of p16 by FISH and BAP-1 loss by ICC confirm the diagnosis of malignant mesothelioma. Finally, several organ-specific markers that are helpful in the evaluation of tissue specimens also perform well in effusion fluid specimens.

372 Distinct Expression Pattern of PDL-1 in Primary and Metastatic Colorectal Carcinoma and Correlated with Microsatellite Instability Status

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Disclosures: Xiao Huang: None; Guang-Yu Yang: None; Ritu Nayar: None

Background: Microsatellite instability (MSI) is a marker of dysfunctional mismatch repair proteins within a tumor, and 15% of colorectal carcinomas (CRCs) are noted to be MSI-H. It has been shown that MSI-H was found to be more frequent in the primary tumor compared to the metastatic lesions. PDL-1 expression on tumor cells in non-small cell lung cancer reveals intratumoral heterogeneity, and can differ between surgical and biopsy specimen. Thus, it is interesting to investigate if there is a different expression level or status of the PDL-1 between primary and metastatic CRCs. PD-1 inhibitor has been used to treat the patients with locally unresectable or metastatic CRC with or without MMR deficiency. And it has been reported that anti PDL-1 antibody is effective even in patients without PDL-1 expression that are MSI-H. Understanding why this subgroup of MSI-H tumors are responsive to immunotherapy will help develop better treatment options for all patients with metastatic CRC.

Design: The pathology database was searched for metastatic colorectal adenocarcinoma diagnosed between 2017 and 2018. Clinicopathologic data was recorded. PD-L1 expression in tumor cells (TCs) and immune cells (TILs) were assessed as percentages of positive tumor cells. The percentage of PD-L1 positive TC or TIL cells was categorized as: 0 (<1%), 1 (1-10%), and 2(>10%). MMR expression was characterized as stable when >10% of tumor cell nuclei stained positive.

Results: Thirty-five cases of metastatic colorectal adenocarcinoma, with corresponding specimens of the primary colorectal adenocarcinoma were identified. Three of 35 cases showed MSI-H (MLH1 and PMS2 loss), which was also present in the metastatic tumor. Two of the 3 MSI-H cases showed PDL-1 expression in the metastatic lesion but not in the primary tumor (figure 1). Of 35 cases, metastasis showed higher PDL1 expression in tumor associated immune cells than primary tumor (p value: 0.02, Table 1).

Table 1. Comparison of PDL1 expression between primary CRC and metastasis

	Primary (%)	Metastasis (%)
TC0	27/35 (77.1)	22/35 (62.9)
TC1	6/35 (17.1)	11/35 (31.4)
TC2	2/35 (5.7)	2/35 (5.7)
p-value: 0.06		
TIL0	20/35 (57.1)	16/35 (45.7)
TIL1	12/35 (34.3)	11/35 (31.4)
TIL2	3/35 (8.6)	8/35 (22.9)
p-value: 0.02		

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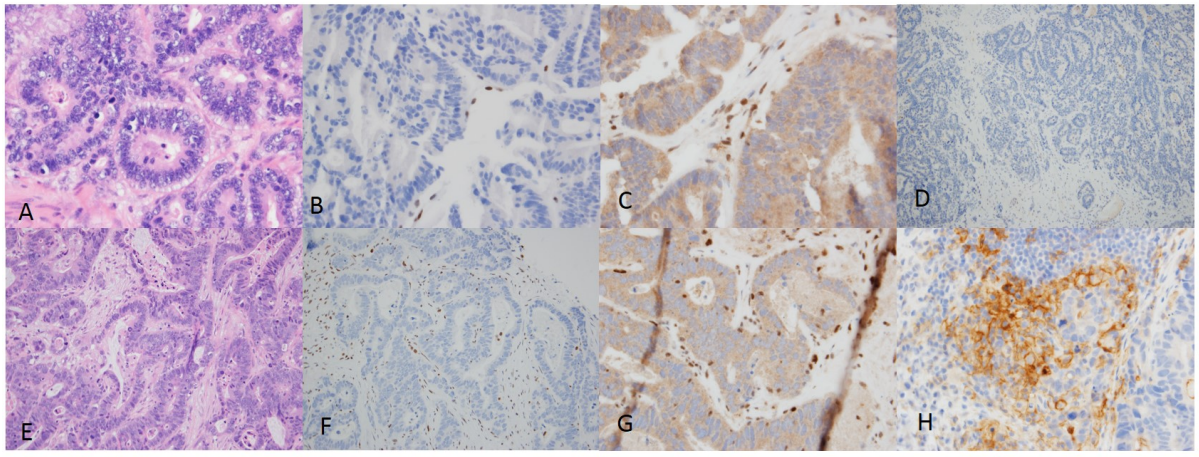
Figure 1: Comparison between primary CRC and metastasis of one patient. A-D. H&E, MLH1, PMS2 and PDL1 of primary CRC respectively. E-H. H&E, MLH1, PMS2 and PDL1 of metastasis respectively.



Metastatic CRCs were not more microsatellite stable, compared to the primary tumors. However metastatic MSI-H CRCs demonstrate higher PDL1 expression level in both tumor cells and immune cells compared to primary tumor. We did not find evidence of change in microsatellite stability in metastasis. Our results suggest that PD-L1 testing should be performed in both primary and remote metastatic tumors, even if the primary tumor is negative and PDL1 blockade is a potential therapeutic approach for the advanced/metastatic CRC.

373 The Utility of Fine Needle Aspiration Biopsy in the Diagnosis of Hematolymphoid Neoplasms: A Retrospective Study of 148 Cases

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Disclosures: Kimberly Ingersoll: None; Grant Harrison: None; Endi Wang: None

Background: The utility of fine needle aspiration (FNA) in the diagnosis of hematolymphoid processes is challenging due to limited cellularity for ancillary testing and architectural evaluation. However, if FNA is able to render a diagnosis, it saves the patient from a more invasive procedure.

Design: We retrospectively analyzed 148 hematolymphoid FNA cases from January 2017 – August 2018, correlating the diagnostic features with clinicopathologic factors.

Results: Of the 148 cases, 120 (81%) resulted in a diagnosis without subsequent biopsy. The diagnostic categories of these cases include: recurrent/residual lymphoma (43/43, 100%), initial diagnosis of lymphoma (77/105, 73%), and patients at a high risk of developing lymphoma (5/5, 100%). Twenty-eight cases required a subsequent biopsy, including 6 cases without flow cytometry (21%), 7 cases without sufficient tissue for immunohistochemistry (25%) and 15 cases due to other causes (54%). Of these 28 cases, 23 resulted in a concordant diagnosis with FNA, whereas 5 cases yielded a discordant diagnosis with FNA. The 5 cases with diagnostic discordance involved histologic grading differences (2 cases), incorrect lymphoma classification (2 cases), and missing a neoplastic component in a composite lymphoma (1 case). The diagnostic capabilities of FNA depend somewhat on the type of lymphoma (*Table 1)*. Age, gender, symptoms, site, imaging, and type of biopsy have no impact on the need for subsequent biopsy.

Table 1: Diagnostic categories in cases not requiring a subsequent biopsy versus cases requiring a subsequent biopsy.

Subsequent biopsy not required/performed (120)	Subsequent biopsy required (28)
- Malignant hematologic B-cell disorder (86): DLBCL, CHL, small mature B-cell lymphoma (SLL/CLL, FL (LG and HG), MZL/MALT, LPL, MCL), HG B-cell lymphoma, PTLD (monomorphic and polymorphic), EBV-associated lymphoproliferative disorder, PCN **- Malignant hematologic non-B-cell disorder (6)**: AML, T-LBL, suspicious for T-cell lymphoma - **Malignant non-hematologic disorder (3):** metastatic neuroendocrine tumor, metastatic small cell carcinoma, metastatic breast carcinoma - **Benign (22)**: RFH, granulomas, chronic inflammation in tissue, normal lymph node - **Descriptive (3):** scattered atypical mononuclear cells (spleen), suspicious for lymphoma, indeterminant suggest re-biopsy	**Concordant biopsy diagnoses (23):** - **Malignant hematologic B-cell disorder (15):** DLBCL, CHL, small mature B-cell lymphoma (FL, MALT, MCL), NLPHL - **Malignant hematologic non-B-cell disorder (1):** Atypical T-cells consistent with PTCL - **Malignant non-hematologic disorder (1):** metastatic small cell carcinoma - **Benign (5):** RFH, granulomas - **Descriptive (1):** florid FH with PTGC-like changes **Discordant biopsy diagnoses (5):** -Excision diagnosis: CHL • FNA: atypical T-cells of uncertain significance -Excision diagnosis: SLL/CLL • FNA: suspicious for T-cell lymphoproliferative disorder - Excision diagnosis: Composite HG FL + TFH lymphoma • FNA: MZL vs. LPL -Excision diagnosis: DLBCL + HG FL • FNA: suggestive of LG FL - Excision diagnosis: EBV-associated B-cell lymphoproliferative disorder • FNA: mixed lymphoid population with small lymphocytes

Abbreviations: **DLBCL** = diffuse large B-cell lymphoma; **CHL** = Classic Hodgkin lymphoma; **SLL/CLL** = small lymphocytic lymphoma/chronic lymphocytic leukemia; **FL** = follicular lymphoma; **LG** = low-grade; **HG** = high-grade; **MZL** = marginal zone lymphoma; **MALT** = mucosa-associated lymphoid tissue lymphoma; **LPL** = lymphoplasmacytic lymphoma; **MCL** = mantle cell lymphoma; **PTLD** = post-transplant lymphoproliferative disorder; **PCN** = plasma cell neoplasm; **AML** = acute myeloid neoplasm; **T-LBL** = T-cell lymphoblastic lymphoma; **RFH** = reactive follicular hyperplasia; **NLPHL** = nodular lymphocyte predominant Hodgkin lymphoma; **PTCL** = peripheral T-cell lymphoma; **FH** = follicular hyperplasia; **PTGC** = progressive transformation of germinal centers; **TFH** = T follicular helper cell

Conclusions: FNA is effective in the diagnosis of hematolymphoid neoplasms, with 81% of cases resulting in a diagnosis. FNA can provide a diagnosis in cases of persistent/recurrent lymphoma, histologic transformation of an indolent lymphoma, and those at high risk of developing lymphoma. Flow cytometry and a sufficient tissue core for ancillary studies greatly contribute to the likelihood of rendering a diagnosis in these cases. Therefore, initially performing an FNA is the best course of action in most patients with a suspicion of lymphoma as it often saves the patient from a more invasive procedure. Pathologists should use caution when evaluating an FNA with limited tissue available for ancillary testing. Excisional biopsy should be considered in patients with a possible initial diagnosis of T-cell lymphoma, T-cell rich nodular lymphocyte predominant Hodgkin lymphoma, T-cell rich B-cell lymphoma, composite lymphomas, or lymphomas with unclear histologic grading or growth pattern, as these cases are often unclear or misleading on FNA evaluation.

374 Evaluating MSI/MMR Status using Cytology Effusion Specimens to Determine Eligibility for Immunotherapy

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Disclosures: Elizabeth Jacobi: None; Gene Landon: None; Russell Broaddus: None; Sinchita Roy-Chowdhuri: None

Background: Mismatch repair (MMR) is routinely evaluated in surgical biopsy or resection specimens of colorectal and endometrial cancers for the evaluation of Lynch Syndrome. The approval of pembrolizumab for patients with microsatellite instability-high (MSI-H) or MMR deficient advanced cancers has led to increased requests for MSI and/or MMR immunohistochemistry (IHC). MMR IHC is often preferred, as it is widely available and less costly than PCR-based MSI testing. Since advanced stage cancer patients are frequently diagnosed on cytology specimens, we evaluated the feasibility of using a cell block (CB) preparation of effusions for MMR IHC testing.

Design: Surgical pathology (SP) cases of colorectal and endometrial carcinomas with known MSI/MMR status from 2000-2017 and matched effusions with available CBs from the same patient were identified. H&E stained CB sections were evaluated for adequacy. CBs with both tumor and normal cells were selected for MMR IHC (MSH2, MSH6, MLH1, and PMS2). Three pathologists, blinded to the corresponding SP results, reviewed cases, quantified the number of tumor cells (< 10, 10-50, 50-300, >300) and interpreted MMR IHC as either retained, lost, suboptimal (tumor with questionable staining or focal staining in cells indefinite for tumor), or non-contributory (both tumor and internal control without staining).

Results: We identified 748 cases with MSI/MMR testing on surgical specimens and matched effusions. Of these, 131 cases (18%) had an available CB and 53 cases were deemed adequate for MMR IHC. These included ascitic (n=30), pleural (n=21), and pericardial (n=2) fluids. MMR IHC results between effusion CBs and surgical specimens were concordant in 45/53 (85%) cases, discordant in 2/53 (4%) cases, and inconclusive in 6/53 (11%) cases. All inconclusive cases had ≥2 retained MMR IHC and 5/6 (83%) cases had retention of MLH1 (Table 1).

Table 1. Comparison of MMR IHC on Cytology Cell Block Sections and Surgical Specimens

Case	Cancer Type	# of Tumor Cells	MMR IHC Cell Block				MMR/MSI Surgical	Concordant
			MLH1	PMS2	MSH2	MSH6		
1	CRC	10-50	R	R	R	R	Intact	Yes
2	CRC	10-50	R	R	R	R	Intact	Yes
3	CRC	>300	R	R	R	R	Intact	Yes
4	CRC	10-50	R	R	R	S-CIFT	Intact	Inconclusive
5	CRC	50-300	R	R	R	R	Intact	Yes
6	CRC	< 10	R	R	R	R	Intact	Yes
7	CRC	>300	R	R	R	R	Intact	Yes
8	CRC	10-50	R	R	S-CIFT	L	L MSH2/6	Inconclusive
9	CRC	>300	R	R	R	R	Intact	Yes
10	CRC	>300	R	R	R	R	Intact	Yes
11	CRC	50-300	R	R	R	S-CIFT	Intact	Inconclusive
12	CRC	< 10	R	R	R	R	Intact	Yes
13	EC	10-50	R	R	L	L	L MSH2/6	Yes
14	CRC	>300	R	R	R	R	Intact	Yes
15	CRC	>300	R	R	R	R	Intact	Yes
16	CRC	>300	R	R	R	R	Intact	Yes
17	CRC	50-300	R	R	R	R	Intact	Yes
18	EC	>300	R	R	R	R	Intact	Yes
19	CRC	>300	R	R	R	R	Intact	Yes
20	CRC	10-50	R	R	R	NC	Intact	Inconclusive
21	CRC	50-300	R	R	R	R	Intact	Yes
22	CRC	10-50	R	R	R	R	Intact	Yes
23	CRC	>300	R	R	R	R	Intact	Yes
24	CRC	50-300	R	R	R	L	Intact	No
25	CRC	10-50	R	R	R	R	Intact	Yes
26	CRC	50-300	R	R	R	R	Intact	Yes
27	CRC	50-300	R	R	R	R	Intact	Yes
28	EC	10-50	R	R	R	R	Intact	Yes
29	CRC	>300	R	R	R	R	Intact	Yes
30	CRC	10-50	R	R	R	R	Intact	Yes
31	CRC	< 10	R	R	R	R	Intact	Yes
32	CRC	>300	R	R	R	R	Intact	Yes
33	CRC	>300	R	R	R	R	MSS	Yes
34	CRC	>300	R	R	R	R	Intact	Yes
35	CRC	10-50	R	R	R	R	Intact	Yes
36	EC	>300	R	R	R	R	Intact	Yes
37	EC	>300	R	R	R	R	Intact	Yes
38	CRC	10-50	R	R	R	R	Intact	Yes
39	CRC	50-300	R	R	R	R	Intact	Yes
40	EC	50-300	S-CIFT	R	R	NC	Intact	Inconclusive
41	CRC	50-300	R	R	R	R	Intact	Yes
42	CRC	< 10	R	R	R	R	Intact	Yes
43	CRC	50-300	R	R	R	R	Intact	Yes
44	CRC	50-300	R	R	R	R	Intact	Yes
45	EC	10-50	R	R	R	R	Intact	Yes
46	CRC	10-50	S-QS	L	R	R	Intact	No
47	CRC	>300	R	R	R	R	Intact	Yes
48	CRC	10-50	R	R	R	R	Intact	Yes
49	CRC	>300	R	R	R	R	Intact	Yes
50	CRC	50-300	R	R	R	R	Intact	Yes
51	CRC	10-50	R	R	R	R	Intact	Yes
52	CRC	10-50	R	R	R	S-QS	Intact	Inconclusive
53	CRC	50-300	R	R	R	R	Intact	Yes

Abbreviations: CRC = Colorectal carcinoma; EC = Endometrial carcinoma; L = Lost; MSS = MSI-Stable by PCR; NC = Non-contributory; NP= Not performed; R = Retained; S-CIFT = Suboptimal-focal staining in cells indefinite for tumor; S-QS = Suboptimal-tumor with questionable staining

Conclusions: In CBs that were evaluated, there was high concordance of MMR IHC testing between cytology and surgical specimens, with 2 false negative and no false positive CB results. IHC analysis of slides with limited tumor cells, staining in cells indefinite as tumor, tumor staining heterogeneity, and lack of internal control staining were problematic in some cases. In such cases, even one or more interpretable markers (i.e. MLH1) yielded useful information. Our findings indicate that cytologic effusion specimens may be suitable substrates for MMR IHC biomarker testing. Inconclusive cases need to be interpreted with caution.

375 Cytopathologic Features of SMARCA4-Deficient Neoplasms

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Disclosures: Tyler Janovitz: None; Lynette Sholl: *Consultant*, Foghorn Therapeutics; *Speaker*, Astra Zeneca Pharmaceuticals; *Advisory Board Member*, Loxo Oncology; Xiaohua Qian: None

Background: Recurrent inactivating alterations in *SMARCA4* are frequently observed in a broad range of solid malignancies. Recently, *SMARCA4* loss of function has been described as one of the defining features of a novel aggressive neoplasm, SMARCA4-deficient thoracic sarcomas. However, the recognition and characterization of SMARCA4-deficient neoplasms from cytology material has not been investigated.

Design: We retrospectively analyzed all institutional cytology cases on which SMARCA4 immunohistochemistry was performed, resulting in a case series of SMARCA4-deficient neoplasms including 8 fine needle aspiration (FNA) samples and 1 ascites fluid from 8 patients. The eight SMARCA4-deficient neoplasms included SMARCA4-deficient thoracic sarcoma (n=4), poorly differentiated lung adenocarcinoma (n=3), metastatic undifferentiated endometrial carcinoma (n=1), and metastatic small cell carcinoma of the ovary, hypercalcemic type (SCCOHT, n=1). The cytopathologic analysis was performed with review of patient demographics, clinical data and targeted next-generation sequencing (NGS).

Results: The 8 FNAs were derived from mediastinal and hilar lymph nodes (n=5), lung (n=2), and bone metastasis (n=1) in two male and five female patients (age range 43-83 years, median age 72.5 years). The peritoneal fluid was from a 23-year-old woman with SCCOHT. All tumors, except for SCCOHT, demonstrated overlapping cytologic features including intermediate to large epithelioid cells with moderate amounts of eosinophilic cytoplasm, vesicular chromatin, and prominent nucleoli. However, the SMARCA4-deficient thoracic sarcomas all demonstrated focal rhabdoid features, which were absent in the carcinomas. In addition to loss of SMARCA4 expression, all 4 SMARCA4-deficient thoracic sarcomas were also positive for SOX2 and negative to focal positive for cytokeratins, while the carcinomas were frequently diffusely keratin positive (3/4; 75%) and lacked SOX2 expression in all tested cases. NGS was performed in 5 cases and the genomic basis of *SMARCA4* inactivation was confirmed in all tested cases. Inactivation occurred most commonly via frameshift alterations (50%), with less frequent nonsense (33.3%) and splice site mutations (16.7%).

Conclusions: SMARCA4-deficient neoplasms form a clinical and morphologic spectrum of high grade epithelioid malignancy. Immunohistochemistry for SMARCA4 in cytology specimens is useful to identify SMARCA4-deficient malignancies and correlates with genomic loss of function alterations.

376 Detection of Atypical Glandular Cells (AGC) with the ThinPrep Imaging System.

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Disclosures: Joshua Jeanty: None; Stacy Eaton: None; Cherie Paquette: None

Background: The 2003 FDA approval for the ThinPrep Imaging System (TIS) device was based on increased sensitivity in detection of precursor lesions, primarily squamous, in cervical cytology specimens. Atypical glandular cells (AGC) were rare in the original TIS studies and AGC in 2003 were defined slightly differently under Bethesda 2001 criteria. Subsequent to TIS approval, detection of AGC by TIS has not been well-established in the literature. The aim of this study is to evaluate the accuracy of the TIS in highlighting AGC (as defined by Bethesda 2014).

Design: This was a retrospective review of 48 cases (collected January-October 2011) initially screened using the TIS and diagnosed as AGC or variant of AGC. The cell or cell groups with best morphologic features supporting an AGC diagnosis or “diagnostic AGC” (up to 9) were highlighted on the slide prior to re-review on TIS. The 22 fields of view (FOV) selected by TIS were reviewed to see if they included diagnostic AGC.

The cases were divided up into 3 groups: Group 1: Cases with at least 1 group of “best diagnostic AGC” in the 22 fields. Group 2: Cases where “best diagnostic AGC” were not found in the 22 FOV, but an AGC diagnosis could be made with other cell/groups within the 22 FOV. Group 3: Cases where neither “best diagnostic AGC” or any other AGC present in the 22 FOV, precluding a diagnosis of AGC.

Results: The TIS accurately detected the “best diagnostic AGC” in 83% (40/48) of cases. Of the remaining cases, 50% (4/8) had other diagnostic AGC highlighted in the 22 FOV. In 8.3% of total cases (4/48) diagnostic AGC were not seen in the 22 FOV.

Figure 1 - 376

Figure 1. Images of cases in group 3 (60x).

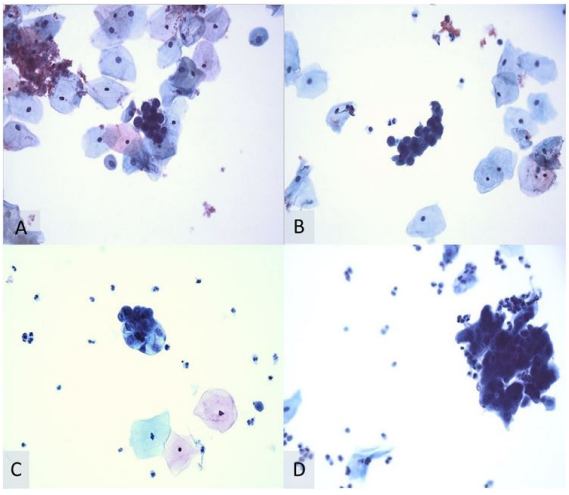

Figure: Group 3: cases without diagnostic AGC in any of the 22 FOV (ThinPrep Papanicolaou x400) .

Conclusions: Overall, the TIS accurately highlighted within the 22 FOV either the “best diagnostic AGC” or other AGC in 91.6% of the cases. A minority of the cases (8.3%) did not have AGC highlighted within the 22 FOV. Highlighting AGC is only the first step in the process as the cells within the FOV must also be interpreted correctly as AGC. With changing demographics, increasing HPV vaccination rates, and recent shifts in screening intervals, a close look at how the TIS highlights AGC is needed in order to show test performance for glandular lesions, particularly as many AGC-related entities are unrelated to human papillomavirus and so would not be caught with molecular based HPV tests used without cytology.

377 Single Smear Total Nucleic Acid Extraction for Molecular Testing: Shooting FISH in a Barrel

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Disclosures: Rachel Jester: None; Jake Emanuel: None; Julie Hirschhorn: None; Kathryn Lindsey: None; Olga Chajewski: None; Jack Yang: None; W Bailey Glen Jr.: None; Cynthia Schandl: None

Background: Molecular analysis is a component in the standard of care for the work-up of non-small cell lung cancer. Obtaining sufficient amounts and quality of tumor is often the burden of molecular cytopathology, with ever-increasing amounts of clinical information expected from smaller biopsies. The guideline-driven algorithm of testing in lung adenocarcinomas traditionally has required multiple cytology smears and/or unstained slides and a cell block. As the era of personalized medicine matures, it is likely that the number and variety of molecular tests will escalate. Accordingly, the ability to efficiently utilize the cytologic material for molecular testing has become increasingly important. We hypothesized that total nucleic acid extraction from a single cytologic smear could serve as a source of DNA and RNA for PCR-based downstream molecular analyses.

Design: By searching the laboratory information system, we identified eight fine needle aspirations and three bronchoalveolar lavage specimens that had corresponding results for both ALK rearrangement by FISH and a solid tumor panel by next-generation sequencing. Each smear was assessed for cell number and tumor percentage independently by two pathologists. Following this, the smears were destained and we performed total nucleic acid extraction using the Maxwell RSC DNA FFPE kit from Promega.

Results: We found that the smears with 500 or more cells yielded concentrations of nucleic acids sufficient for most PCR-based downstream molecular analyses, such as DNA and RNA fusions. The smears determined to have over 500 cells and an average tumor percentage greater than 20 had a DNA concentration range of 7.4-9.1 ng/µL and an RNA concentration range of 142-285 ng/µL. Comparatively, smears with fewer cells showed a statistically significant decrease in the extracted nucleic acid material.

Conclusions: These results indicate that PCR-based assays are likely to be successful in a some single smear cytology specimens. The next steps will include running assays (AmpliSeq Focus Panel, Illumina) for PCR-based structural aberrations using the nucleic acids obtained from the smears, followed by a comparison of these results with known variants previously detected in these samples by solid tumor panel and FISH studies. Our final results will show whether clinically useful information can be obtained from a single cytology smear, which would have profound diagnostic and treatment implications while also decreasing time, cost, and effort of testing.

378 Lung adenocarcinoma with isolated P53 gene mutation: cytomorphology and immunohistochemical profile

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Disclosures: Daniel Johnson: None; Lauren Ritterhouse: None; Tatjana Antic: None

Background: Recurrent molecular alterations in lung adenocarcinoma include well-known alterations such as *ALK* and *ROS* fusion genes as well as *EGFR*, *KRAS,* and *BRAF* mutations. Mutations in the *TP53* gene are also common and sometimes occur with other alterations, but isolated *TP53* mutations have been reported in a subset of lung adenocarcinomas showing some fetal lung-like morphology with supra- or subnuclear cytoplasmic clearing and complex glandular architecture. Aberrant SALL4 and/or CDX2 expression has been reported in these tumors. For now, tumors with fetal-like morphology have been considered rare and not well described. In this study we attempt to describe those cases regarding their cytomorphology and immunohistochemical profile.

Design: The molecular reports from 2014 to September 2018 were searched for lung adenocarcinomas diagnosed on cytology material with *TP53* mutation and no other well-known driver mutations. The cytology reports were reviewed for the patient demographics, clinical history, location of the tumor, and immunohistochemical findings. The cytomorphology was also reviewed and recorded.

Results: Eight cases were identified. Patient's age ranged from 51 to 75 years (average 62.75 years); 5 were male, 3 female. All patients had smoking history and lung masses (range 1.8 to 7.7 cm, average 4.5 cm) on imaging at time of diagnosis and molecular testing. Testing was performed on lung masses in 3 cases and mediastinal lymph nodes in 5. One case did not have sufficient tissue left in the cell block for additional immunohistochemistry. Two of 7 cases were positive for SALL4 and CDX2 immunohistochemistry [Table 1]. One of these was TTF1 positive and had marked nuclear pleomorphism; the other was TTF1 negative and exhibited supra- or subnuclear cytoplasmic clearing and complex glandular architecture consistent with fetal-lung type morphology. The other 5 were TTF1, CDX2, and SALL4 negative and had non-specific adenocarcinoma morphology.

Age	Sex	Pathogenic Variants Detected	Tested Site	Primary Lung Tumor Location	Mass size (cm)	Immunohistochemistry
67	M	TP53 c.475G>C	Right middle Lobe	Right middle lobe	4.3	TTF-1 - / CDX-2 - / SALL4 -
62	M	TP53 c.193A>T	Paratracheal lymph node	Left upper lobe	5.5	TTF-1 - / CDX-2 - / SALL4 -
60	M	TP53 c.527G>T	Subcarinal lymph node	Right upper lobe	2	TTF-1 - / CDX-2 - / SALL4 -
65	M	TP53 c.482_490del; TP53 c.745A>T	Left lower lobe	Left lower lobe	7.7	TTF-1 - / CDX-2 + / SALL4 +
75	F	TP53 c.883C>G	Paratracheal lymph node	Left upper lobe	1.8	TTF-1 + / CDX-2 - / SALL4 -
51	F	TP53 c.329G>T	Subcarinal lymph node	Right upper lobe	2.2	TTF-1 + / CDX-2 + / SALL4 +
55	F	TP53 c.1025G>C	Paratracheal lymph node	Left hilum	5.1	TTF-1 - / CDX-2 - / SALL4 -
67	M	TP53 c.488A>G	Left upper lobe	Left upper lobe	7.4	TTF-1 + / CDX-2 not done / SALL4 not done

Conclusions: Patients in this group with isolated *TP53* mutations are smokers and older (average 62.75 years) with a slightly increased male to female ratio. These features are shared with other lung adenocarcinoma patient cohorts, but within this subset there appears to be two smaller subsets. The first contains tumors with TTF1-/CDX-/SALL4- immunohistochemical profile and the second, tumors that aberrantly express SALL4 and CDX2. Additional larger studies are needed to further characterize these tumors.

379 Personalized Medicine and Cervical Screening: Development of Individualized Quantitative Risk Assessments for Cervical Adenocarcinoma In Situ and Cervical Adenocarcinoma

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Disclosures: Terrell Jones: None; Agnieszka Onisko: None; R. Marshall Austin: None

Background: Cervical screening has decreased the incidence of cervical carcinoma around the world primarily by preventing cervical squamous carcinoma, with significantly less measurable protective benefits in prevention of cervical adenocarcinoma. In this study, we apply Bayesian modeling on cervical clinical, screening, and biopsy data from a large integrated health system to explore the feasibility of calculating personalized risk assessments on screened system patients for subsequent histopathologic diagnoses of cervical adenocarcinoma *in situ* (AIS) and/or cervical adenocarcinoma (AdCa).

Design: Diagnoses of cervical AIS or AdCa rendered between 2005 and 2017 were identified in our large health system database with 1,053,713 cytology results, 354,843 high risk Human Papillomavirus (HPV) test results, and 99,012 cervical histopathologic results. Using our continuously updated Bayesian cervical screening model which includes clinical data, cervical screening results, and cervical biopsy results, we projected quantitative estimates of patients' five-year cumulative risk for cervical AIS or AdCa.

Results: 161 patients were identified with AIS (ages 17 to 75, mean 37 years) and 99 patients had diagnoses of cervical AdCa (ages 26 to 91, mean 48 years). Quantitative 5 year cumulative risk estimates for diagnoses of cervical AdCa or AIS in patients with different cervical screening test and biopsy histories are shown in Table 1. The highest patient risk estimates for subsequent cervical AdCa and/or AIS histopathologic diagnoses were associated with prior cervical screening test results of HPV-positive atypical glandular cells (AGC). Prior squamous cytologic abnormalities were associated with lower risk estimates. Prior histopathologic diagnoses of squamous abnormalities also influenced quantitative risk. A prior histopathologic diagnosis of AIS was associated with a very low risk of subsequent AdCa, consistent with effective excisional treatment. AdCa risk was greatest in women age 30-65 with prior CIN3 biopsy results, whereas AIS risk was greatest in women less than 30 (Figures 1,2).

Table 1. Five year risk of AdCa and AIS development given patient history record

Patient history record (number or consecutive cytology/HPV interpretations or histopathologic diagnoses)	5-year risk of AdCa (%)
AGC(1), HPV+ (1)	1.59
AGC (2), HPV+ (2)	0.82
AGC (1)	0.81
Neg (2), AGC (1) , HPV- (2), HPV+ (1)	0.77
AGC (2)	0.70
AGC (3), HPV+ (3)	0.47
AGC (3), HPV- (2), HPV+ (1)	0.45
Neg (2), AGC (1)	0.30
HSIL (1)	0.25
CIN3 (1)	0.14
ASCH (1), ASCUS (2), HPV- (3)	0.07
ASCUS (1)	0.06
ASCUS (1) , Neg (2), HPV N/A (2), HPV+ (1)	0.05
ASCH (1), ASCUS (2), HPV+ (2), HPV- (1)	0.04
ASCUS (3)	0.04
ASCUS (1), Neg (2), HPV N/A (3)	0.04
Neg (3), HPV+ (2), HPV- (1)	0.03
ASCUS (3), HPV+ (2), HPV N/A (1)	0.02
LSIL (1)	0.01
CIN2 (1)	0.01
AIS (1)	0.01
Patient history record (number or consecutive cytology/HPV interpretations or histopathologic diagnoses	**5-year risk of AIS (%)**
AGC (3), HPV+ (3)	56.40
AGC (3), HPV- (2), HPV+ (1)	33.02
AGC (2), HPV+ (2)	6.95
Neg (2), AGC (1), HPV- (2), HPV+ (1)	4.51
AGC (2)	4.44
AGC (1), HPV+ (1)	2.56
ASCH (1), ASCUS (2), HPV+ (2), HPV- (1)	2.29
ASCH (1), ASCUS(2), HPV-(3)	1.93
AGC (1)	1.15
Neg (2), AGC (1)	0.93
ASCUS (3), HPV+ (2), HPV N/A (1)	0.79
ASCUS (3), HPV N/A (2), HPV+ (1)	0.76
HSIL (1)	0.55
ASCUS (3)	0.55
ASCUS (1), HPV+ (1)	0.27
ASCUS (1), Neg (2), HPV N/A (2), HPV+ (1)	0.22
Neg (3), HPV+ (2), HPV- (1)	0.18
ASCUS (1)	0.12
LSIL (1)	0.11
ASCUS (1), Neg (2), HPV N/A (3)	0.06
CIN2 (1)	0.04
AIS (1)	0.03
CIN3 (1)	0.02

Figure 1 - 379

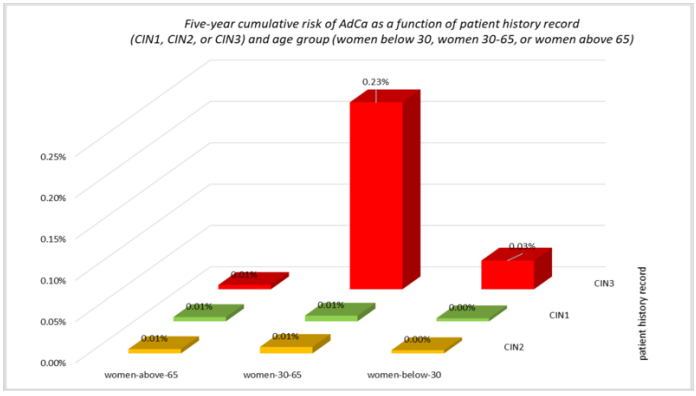
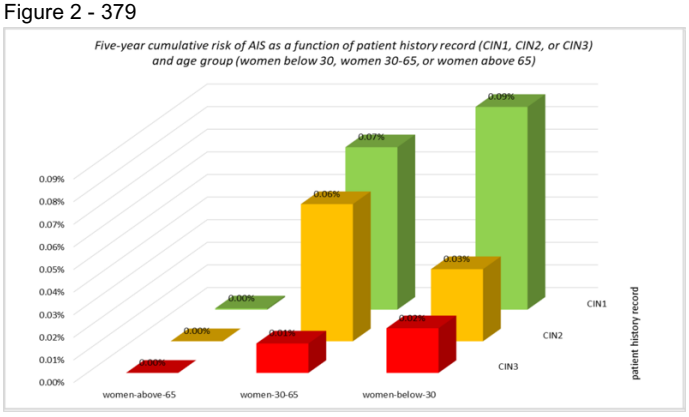


Figure 2 - 379



Conclusions: Prevention of cervical adenocarcinoma in screened patients remains a major challenge for cervical screening. Individualized risk projections for cervical glandular neoplasia reflecting patient age, prior cervical screening test results, and prior cervical biopsy history are feasible using Bayesian modelling of health system data.

380 Molecular Triage of Indeterminate Thyroid Nodule Aspirates: Initial Findings from a Large Academic Medical Center

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Disclosures: Joshua Kagan: None; Michelle Reid: None; Amy Chen: None; Christopher Griffith: None

Background: Molecular triage of indeterminate thyroid aspirates is increasingly popular and gaining acceptance from professional associations. However, the American Thyroid Association guidelines note the need for additional data examining these ancillary testing strategies. Additionally, each individual institution should examine their own results when implementing such testing as pre-test and post-test factors can effect positive and negative predictive values for these assays. Here we examine our initial experience with ThyroSeq at a large academic medical center.

Design: In 9/2017 we began offering the option of collecting and reflexively submitting for ThyroSeq testing of indeterminate thyroid aspirates. Through 8/2018, 483 ThyroSeq samples were collected. ThyroSeq samples were reflexively submitted for testing on indeterminate aspirates (Bethesda categories III, IV, V). Occasional samples from other categories were also submitted. FNA and molecular results were correlated with histologic follow-up when available. NIFTP was considered benign in calculation of risk of malignancy (ROM). Molecular alterations were divided into low- and high-risk. Low-risk was defined as predicted ROM <90% and/or RAS-like; high-risk was defined as predicted ROM at least 90% and/or BRAF-like.

Results: 106 samples from 102 patients were submitted for ThyroSeq testing. Average age was 53.7 years (range 21-85 years) and male:female ratio was 1:3.25. 73 aspirates (Bethesda: 2-non-diagnostic; 1-negative; 58-AUS; 5-SFN; 4-SFN, oncocytic; 3-suspicious for PTC) were negative by ThyroSeq and 30 samples (Bethesda:1-negative; 18-AUS; 5-SFN; 1-SFN, oncocytic; 4-suspicious for PTC; 1-PTC) were positive for a molecular alteration (25 low-risk alterations; 5 high-risk mutations). 3 samples (Bethesda:1-non-diagnostic; 1-AUS; 1-suspicious for PTC) were inadequate for ThyroSeq . RON and ROM for cases with surgical follow-up are summarized in the table.

Table: Bethesda Categories and Risk by Mutation Category									
		ThyroSeq Negative			Low Risk Mutation		High Risk Mutation		
Bethesda categories	Cases with F/U	N	RON, N (%)	ROM, N (%)	RON, N (%)	ROM, N (%)	N	RON, N (%)	ROM, N (%)
Total	26	9	2 (22.2%)	0	11 (84.6%)	6 (46.2%)	4	4 (100%)	4 (100%)
Benign (II)	2	1	0	0	1 (100%)	0			
AUS (III)	12	6	2 (33.3%)	0	5 (100%)	2 (40%)	1	1 (100%)	1 (100%)
SFN (IV)	6	2	0	0	3 (100%)	3 (100%)	1	1 (100%)	1 (100%)
SFN, oncocytic (IV)	1				1 (100%)	0			
Suspicious for PTC (V)	4				1 (33.3%)	1 (33.3%)	1	1 (100%)	1 (100%)
Malignant PTC (VI)	1						1	1 (100%)	1 (100%)
high-risk mutations = BRAF V600E (n=2), isolated TERT p.C228T (n=1), NRAS+TERT p.C228T (n=1), ETV6/NTRK3 (n=1)									
low-risk mutations = N/K/HRAS (n=17), copy number alterations (n=4), PAX8/PPARG (n=1), THADA/IGF2BP3 (n=1), DICER1 p.D1810Y (n=1), low level TERT p.C228A (n=1)									

Conclusions: All samples with negative ThyroSeq results were found to be benign on histologic follow-up (i.e. no false-negative cases). Two cases considered false positive were suspicious for PTC on FNA and had low-risk alterations by ThyroSeq but were non-neoplastic on follow-up. One was likely due to sampling of an adjacent microcarcinoma and the other showed borderline overexpression of RET resulting in positive ThyroSeq. Division of ThyroSeq alterations into low- and high-risk is useful to stratify RON and ROM on excised nodules and can guide surgical management.

381 Correlation Between The TIRADS Ultrasound Criteria and The Bethesda Cytology Criteria in Malignant Risk Stratification in Thyroid Nodules.

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Disclosures: Hatem Kaseb: None; Ahmad Charifa: None; Guoping Cai: None; Rita Abi-Raad: None; Lynwood Hammers: None; Manju Prasad: None; Adebowale Adeniran: None

Background: Ultrasound is the most commonly used imaging technique for the evaluation of thyroid nodules. Sonographic findings are often not specific, and definitive diagnosis is usually made through fine-needle aspiration biopsy or surgery. Thyroid imaging report and data system (TIRADS) is helpful in differentiating between benign and malignant thyroid nodules by offering a risk stratification model using a score. The primary aim of our study was to determine if TIRADS in conjunction with the findings on fine-needle aspiration cytology (FNAC) could be used to stratify the malignancy risk of these nodules and to help in their clinical management.

Design: Single-center retrospective study of a cohort of 670 patients who were referred for ultrasound-guided fine-needle aspiration from June 2017 to February 2018. TIRADS score was prospectively determined for all patients included. Cytologic evaluation was done using the Bethesda System. Follow-up information on the patient including surgical resection when applicable was obtained from the Pathology database.

Results: We evaluated 670 cases of thyroid FNA (n=513 female, median age=56 years; and n=157 male, median age=61 years). TIRADS 1 nodules were predominantly benign nodules on FNA (45/56), with non-diagnostic, follicular lesion of undetermined significance (FLUS) accounting for 6 and 4 cases, respectively. One case was positive for PTC and confirmed on resection. In 189 TIRADS 2 nodules, 148 were benign nodules on FNA, while non-diagnostic, and FLUS accounted for 17 and 18 cases, respectively. TIRADS 3 nodules were predominantly benign (148/255), while non-diagnostic FLUS and follicular neoplasm (FN) accounted for 29, 50 and 16 cases, respectively. TIRADS score was positively correlated with the malignancy rate. Rate of positive FNA call in TIRADS 1, 2, 3, 4 and 5 nodules were 1.5%, 1.1%, 4.7%, 12.5% and 54.5%, respectively. Thirty eight cases with suspicious and positive calls on FNA had surgical follow-up, 37 of which were positive for malignancy. These were mostly TIRADS 4-5 nodules.

Conclusions: The TIRADS criteria has a good concordance with the Bethesda system. The ultrasound findings of benign pathology in TIRADS 1 and 2 nodules are aligned with the cytology results. The correct interpretation of the two findings helps the clinician to reduce the risk of unnecessary invasive procedures in patients with a low probability of presenting thyroid cancer, while facilitating the identification of patients at higher risk of cancer.

382 Assessment of Cellularity in Pediatric Thyroid Cytology: A Comparison Between Adult and Pediatric Populations

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Disclosures: Sarah Kassaby: None; Huiying Wang: None; Vivian Weiss: None

Background: The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) diagnostic criteria have been equally applied to adult and pediatric thyroid lesions without addressing whether there is a significant difference between the two populations. One such criteria is overall cellularity. The TBSRTC defines benign thyroid nodules as sparsely-moderately cellular. We assess whether non-neoplastic pediatric thyroid fine needle aspirations (FNAs) have similar cellularity to adult FNAs and whether the TBSRTC benign criteria can be applied effectively to pediatric thyroid nodules.

Design: Sequential/retrospective benign cytology cases with corresponding non-neoplastic thyroid resections were retrieved including: 20 pediatric (4-20 yrs, 16:5 F:M ratio) and 43 adults (35-61 yrs, 9:3 F:M ratio) FNAs. Criteria for exclusion included adenomas, cysts, and history of Hashimoto's thyroiditis. The cellularity was defined based on the number of groups of 10 or more well-visualized/well-preserved follicular cells. Grading/scoring was as follows: Scant(score 0; ≤8 groups), mild(score 1; 9-16 groups), moderate(score 2; 17-24 groups), and high(score 3; >24 groups) across the case.

Results: The pediatric FNAs had significantly higher cellularity with an overall score of 1.95 ±1.1 compared to the adult FNAs with an overall score of 0.9 ±0.8 (p=.0005). The adult cellularity was scored: 39% scant/score=0 (17/43), 33% mild/score=1 (14/43), 26% moderate/score=2 (11/43) and 2% high/score=3 (1/43). The pediatric cellularity was scored: 15% scant/score=0 (3/20), 10% mild/score=1 (2/20), 40% moderate/score=2 (8/20) and 35% high/score=3 (7/20). The average number of passes in pediatric cases was higher than adults (2.7 vs. 2.1, p=0.02) resulting in an increased number of pediatric slides/case (5.2 vs 4.1 in adults, p=0.01). However, the average number of groups of follicular cells per slide and per pass was still higher in pediatric cases compared to adults (6.3 vs 3.8, p=0.02, and 12.7 vs 7.2, p=0.008).

Conclusions: Hypercellularity is considered a concerning feature by many pathologists in adult thyroid FNAs. However, we demonstrate that benign non-neoplastic pediatric thyroid FNAs have increased cellularity compared to adult FNAs. The increased cellularity of pediatric thyroid FNAs should not dissuade pathologists from diagnosing them as benign in the absence of cytologic/architectural atypia. Further guidance on how to interpret pediatric thyroid cytopathology in TBSRTC is needed to improve the care of our youngest patients.

383 Cytopathologic Characterization of SMARCB1-deficient Malignancies of the Head and Neck Region

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Disclosures: Brie Kezlarian: None; Snjezana Dogan: None; Oscar Lin: None

Background: SMARCB1 is a tumor suppressor and a member of the SWI/SNF complex, which is found deleted or mutated in multiple cancer types. In head and neck (H&N), SMARCB1-deficient carcinomas typically arise in the sinonasal tract but may also occur in the thyroid and skin. Although the majority of SMARCB1-deficient sinonasal carcinomas (SNC) display basaloid or "rhabdoid" morphology, they are histologically diverse and may show (pseudo)glandular or clear cell features. Cytopathology reports on these tumors in H&N are limited and thus far focused exclusively on SMARCB1-deficient SNC.

Design: A total of 18 SMARCB1-deficient H&N carcinomas with a confirmed SMARCB1-deficient status by MSK-IMPACT molecular assay or FISH, and by INI1 immunohistochemistry were reviewed. The corresponding cytology specimens were retrieved and evaluated for: cellularity, cell size, nuclear morphology, nucleolar findings, chromatin pattern, multinucleation, presence of glandular or squamous differentiation.

Results: Cytology specimens from 13 patients were available (24 Diff-Quick, 15 alcohol fixed, 17 monolayer and 15 cell block slides) encompassing sinonasal (n=7), thyroid (n=3) skin (n=2), and unknown primary (n=1) sites. All tumors were originally diagnosed as carcinomas (see table 1). The most consistent cytologic features included presence of nucleoli (n=13, 100% cases), bi- or multinucleation (n=11, 85%), and presence of nuclear grooves and indentations (n=11, 85%). Most (n=8, 62%) cases showed no discernable differentiation. "Rhabdoid" morphology and glandular and/or signet ring features were each seen in 31% (n=4) cases. Cytoplasm was either delicate with indistinct nuclear borders (n=7, 54%) or dense with distinct nuclear borders (n=6, 46%). This dichotomous appearance was also confirmed in the histologic sections. Cytoplasmic vacuoles (n=9, 69%) and dense eosinophilic bodies (n=2, 15%) were seen. Cell shape (round, plasmacytoid or polygonal), size (small to large), and quantity of cytoplasm (scant to abundant) were variable. Necrosis (n=7, 54%) and mitotic figures (n=7, 54%) were frequent.

	Primary Site	Age	Clinical Diagnosis	Specimen Site	Specimen Type
1	Sinonasal	53	Poorly differentiated / Undifferentiated carcinoma	Preauricular mass	FNA
2	Sinonasal	54	Poorly differentiated squamous cell carcinoma with basaloid features	Shoulder fluid collection	FNA
3	Sinonasal	54	Poorly differentiated carcinoma with focal glandular and clear cell features	Bone lytic lesion	FNA
4	Sinonasal	66	Poorly differentiated carcinoma, favor adenocarcinoma	Lymph node, neck	FNA
5	Sinonasal	33	Poorly differentiated non-keratinizing squamous cell carcinoma	Lung	FNA and touch prep
6	Sinonasal	79	Poorly differentiated carcinoma with glandular features, SMARCB-1 deficient	Liver	Touch prep
7	Sinonasal	26	Poorly differentiated carcinoma	Lung	Touch Prep
8	Thyroid	59	Anaplastic carcinoma	Peritoneal fluid	Fluid
9	Thyroid	67	Anaplastic carcinoma	Thyroid	FNA
10	Thyroid	50	Undifferentiated neoplasm admixed with cribriform morular variant of papillary thyroid carcinoma	Lymph node	FNA
				Lung	FNA
11	Skin	18	Poorly differentiated carcinoma	Lymph node	FNA and touch prep
12	Skin	76	Poorly differentiated carcinoma, SMARCB1 (INI1)-deficient	Soft tissue mass	Touch prep
13	Unknown	52	Poorly differentiated carcinoma	Lymph node, neck	FNA
				Liver	Touch prep
				Lung	BAL
				Lung	Brush

Conclusions: Similar to their histologic counterpart, the cytomorphologic features of SMARCB1-deficient H&N carcinomas are heterogenous. SMARCB1-deficient carcinoma would be in the differential cytologic diagnosis of any high-grade/poorly-differentiated carcinoma in the H&N region, with or without rhabdoid features; in cases of metastasis/unknown primary, H&N primary sites other than sinonasal tract also need to be considered.

384 Optimal CEA Cut Off Values in the Diagnosis of Mucinous Cystic Lesions of the Pancreas Differ by Assays

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Disclosures: David Kim: None; Elizabeth Margolskee: None; Jonas Heymann: None; June Koizumi: None; Abha Goyal: None; Momin Siddiqui: None; Joshua Hayden: None; Rema Rao: None

Background: Pancreatic cyst fluid carcinoembryonic antigen (CEA) values have been shown to be a pivotal test in the diagnosis and management of mucinous cystic lesions of the pancreas (MCL). Varying cyst fluid CEA cut off values have been reported in the literature. Cyst fluid CEA levels of 192ng/mL have been widely used in cytology to differentiate mucinous from non-mucinous pancreatic cysts. However, the CEA values are unique to the assays used and significantly differ between assays. Here, we investigate the significance of CEA cut off values of pancreatic cysts from two different assays.

Design: The results of pancreatic cyst fluid CEA, endoscopic ultrasound imaging, cytology, surgical resections, and the type of assay used, either Beckman Dxl® (BD) or the newer Siemens Centaur XP® (SC) were retrospectively collected (01/2012 - 08/2018). Final histology was used as the gold standard where available. In cases where histologic correlation was not available, a combination of cytology with clinical and imaging findings was used for correlation. The diagnostic categories included MCL versus non-MCL. CEA values of MCL were compared with CEA values from non-MCL to determine an optimal cut off value for distinction. A receiver operator characteristic (ROC) curve was plotted and an area under the curve (AUC) was calculated for all samples, then separately by test platforms. An optimal CEA cutoff was determined using the distance to corner method. Curves were compared using Delong's test.

Results: We identified 140 pancreatic cystic lesions with concurrent CEA values (SC: n= 39; BD: n=101). Histologic correlation was available for 25 specimens (17% of cystic lesions). When all MCL were compared with non-MCL, an optimal CEA cutoff value of 45.9 ng/mL (AUC = 86, Se = 85.7%, Sp = 73.8%) was determined (fig. 1). When analyzed separately for the assays, cut-off values of 45.9 ng/mL (AUC = 84.27, Se = 89.7%, Sp = 71.4%) for the BD and 24.4 ng/mL (AUC = 77, Se = 81.8%, Sp = 75%) for the SC were determined (p=0.48, fig. 2).

Figure 1 - 384

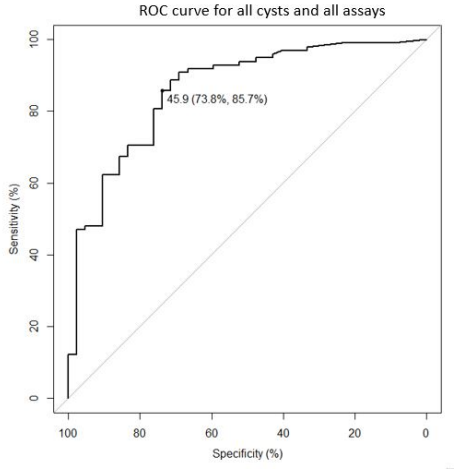
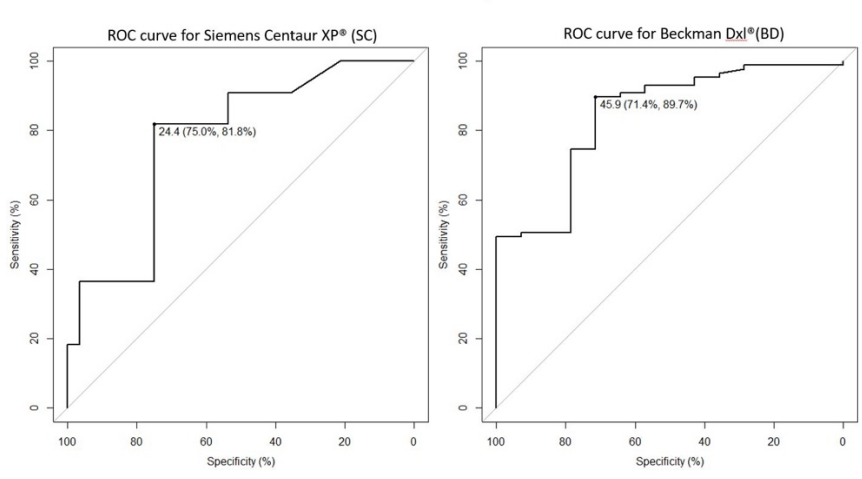


Figure 2 - 384



Conclusions: Our optimal pancreas cyst CEA cut off is 45.9 ng/mL, which is lower than commonly cited in the literature. The cut off values also differed on the two separate assays used. As future directions, we aim to prospectively use the cut off values obtained in our institution, to determine the optimal sensitivity and specificity of cyst fluid CEA in the diagnosis of pancreatic MCL and further investigate these differences through collaborative multi-institutional studies.

385 Rapid On-Site Evaluation (ROSE) of breast masses in Tanzania

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Background: Fine needle aspiration biopsy (FNAB) is a rapid, minimally invasive and cost-effective technique ideal for low resource settings. Breast FNAB has high accuracy when performed by a trained operator. FNAB can be combined with rapid on-site evaluation (ROSE) to assess adequacy, triage for ancillary testing, and determine preliminary diagnoses. Feasibility and accuracy of ROSE in determining cellular adequacy and preliminary diagnoses in a low-resource setting was evaluated at an FNA clinic at a national hospital in Dar es Salaam, Tanzania.

Design: Adult patients with a breast mass who presented to the clinic were enrolled in the study with informed consent from Nov 2017 to Sept 2018. ROSE and FNABs were performed by a Tanzanian pathologist who received intensive training at the affiliated institution in the United States. ROSE using toluidine blue stain on alcohol-fixed smears was performed to determine adequacy, and categorized as low, moderate or high cellularity. Preliminary diagnoses were categorized as benign or malignant and were compared to the final diagnoses.

Results: A total of 88 female patients were enrolled with a median age of 49 years (range 23-78). All cases were adequate in cellularity. ROSE was malignant in 63 (72%) and benign in 25 (28%) patients. The concordance between ROSE and final diagnosis was 96% (85/88). The 3 discordant cases were reported as malignant at ROSE, but diagnosed as benign on final review of the Pap stained slides. Diagnoses included fat necrosis, proliferative fibrocystic change, and benign breast tissue. Only 1 pass was performed in 28 cases (32%), 2 passes in 24 (27%), 3 passes in 30 (34%) , and 4 passes in 6 (7%). All malignant cases had at least one pass with moderate or high cellularity.

Conclusions: ROSE is a simple, cost-effective method to determine adequacy and cellularity in a low-resource setting. With training, ROSE can be used to determine preliminary diagnoses with high accuracy. Accurate ROSE has the potential to optimize the use of limited resources by allowing for triage for ancillary testing, reducing inadequate FNAB rates and the need for repeat biopsies, and expediting the referral of patients for specialized cancer care.

386 Live Digital Telecytology for Rapid On-Site Evaluation of Touch Preparation Smears of Needle Core Biopsies: An Appraisal of Four Years Utilization at an Academic Institution

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Background: Telecytology (TC) is important tool as interventional procedures tax the ability of laboratories to provide personnel support for rapid on-site evaluation (ROSE). We retrospectively analyzed the utilization of live digital TC for ROSE, employed for evaluation of computerized tomography-guided needle core biopsies (CT-CNB). The goal was to review its procedural components and assess the overall impact on technical and professional personnel involved in the procedure.

Design: TC was implemented exclusively for touch preparations of CT-CNB. All CT-CNB cases with associated TC (July 2014 to July 2018) were identified and minutes of laboratory meetings were reviewed regarding TC-related difficulties reported. Equipment employed is listed in Table 1. Validation was performed by seven pathologists who each evaluated 20 TC cases, correlating their ROSE and final adequacy statements. Directed interviews regarding procedure components were conducted with the laboratory technical director, Cytopathology fellows (CF), Cytotechnologists (CT), Cytology supervisor and Cytopathology faculty involved in TC.

Results: Of a total 1770 CT-CNBs, TC was utilized in 1149 (65%). Of those 978 (85%) were evaluated on-site by CFs and 171 (15%) by CTs. They all reported TC as useful because of perceived increased training and supervision, assistance for better specimen triage as well as improved communication with radiologists. The disadvantages were TC set-up time, equipment, internet or communication failures. On the pathologist side, the time perceived as spent on TC per ROSE procedure varied from 1 to 5 minutes (70%), 5 to 10 minutes (20%), and more than 10 minutes (10%). The remote pathologist confirmed the adequacy interpretation by the on-site TC operator in 80-90% of cases, concurred with the triage strategy proposed by the on-site TC operator in 70-80% of cases. Overall correlation of TC-based ROSE with final adequacy statement was higher than 95%. Both by on site and remote operators considered that the pathologist input makes a significant contribution in approximately 20% of cases.

Camera	Nikon DS-Fi2
Dedicated camera controller	Nikon DS-L3
Internet connection	Wired, fixed IP
Software	Brower-based system
Additional monitor in CT suite	50 inch, wall mounted
Communication	Vocera VOIP-based personal 2-way digital voice communicator

Table 1: Telecytology Equipment

Figure 1 - 386

Conclusions: TC is a useful tool, assisting in correct adequacy ROSE and specimen triage. It is impactful for the pathologists, who can supervise the procedure remotely and in a time saving fashion. TC is particularly useful for supervision of junior CTs and fellows at the beginning of training. Its utility however decreases for experienced, skilled ROSE on-site operators with increased diagnostic skills.

387 The Role of Repeat Endoscopic retrograde cholangiopancreatography (ERCP)-guided biliary brush cytology for Suspected Pancreatico-biliary Malignancy

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Disclosures: Vinita Kukkar: None; Kamal Khurana: None

Background: Brush cytology performed during ERCP serves as a valuable tool for diagnosis and management of pancreaticobiliary diseases. The diagnostic sensitivity of brush cytology has been reported between 18% and 70% for malignant strictures/ masses involving pancreatico-biliary tract. The role of repeat ERCP guided brush cytology in improving the yield for pancreatic-biliary malignancies has not been well established. The goal of our study was to ascertain the additional yield and success of repeat brush cytology

Design: A retrospective review of our University center electronic database for patients that underwent ERCP-guided brush cytology from January 2007 to August 2018 was performed. All patients that had more than one ERCP-guided brush cytology for evaluation of suspected neoplastic process were included. Chi-squared test was used to compare the frequencies of malignant neoplasm in patients with initial diagnosis of atypical /suspicious or benign. Cytologic material was also reviewed to determine the cause of failed ERCP-guided brush cytology.

Results: A total of 672 patients underwent 800 procedures. Repeat ERCP-guided brush was performed on 85 (12.6%) patients and included 213 (26.62%) procedures. Initial brush cytology was reported as atypical/suspicious in 20 (23.5%) patients and benign in 65 (76.5%) patients. Repeat brush cytology revealed malignant neoplasm in 12 (14.2%) patients. Eight of 20 (40%) patients with atypical/

suspicious cytology at the first brush cytology were diagnosed with adenocarcinoma on repeat brush cytology. Of the 65 patients with benign disease at the initial procedure, repeat diagnosis was adenocarcinoma in 4 (6.1%), atypical/suspicious in 7 (13.8%), and the rest remained negative on follow up 52 (64.19%). The yield of malignant neoplasm in atypical/suspicious and benign category was statistically significant (40% vs 6%, p<.0002). Reason for failed initial ERCP guided brush cytology was attributed to sampling error (n=4, 33.3%) and paucity of tumor cells precluding definitive diagnosis of neoplastic process (n=8, 66.7%).

Conclusions: Repeat ERCP-guided brush cytology improves the yield of diagnosis in patients with continued suspicion of pancreaticobiliary cancer. Hence this procedure is warranted especially in patients with initial ERCP-guide brush cytology findings of atypical/suspicious.

388 Diagnostic Accuracy of Fine-Needle Aspiration Cytology for Discrimination of Squamous Cell Carcinoma from Adenocarcinoma in Pulmonary Cytology Samples: A systemic review and meta-analysis

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Disclosures: Lester Layfield: None; Lauren Pearson: None

Background: Fine-needle aspiration (FNA) represents a cornerstone for diagnosis of pulmonary nodules. Historically, separation of carcinomas into non-small cell and small cell types was required but recent developments demand separation of squamous cell carcinoma (SCC) from adenocarcinoma (AC). Because cytology specimens are often of limited cellularity and preservation of sufficient material for molecular testing is a priority, it is desirable to limit the amount of specimen utilized for histologic typing. Immunohistochemistry for p40 and TTF-1 improves accuracy of separation but utilizes material otherwise available for molecular testing. Reported accuracy of purely cytologic separation of AC and SCC has been variable. We undertook a meta-analysis to determine the accuracy of cytologic distinction of AC from SCC.

Design: A literature search was executed in December 2017 to identify diagnostic accuracy studies on FNA in lung cancer. Medline, Embase, and Scopus databases were searched and studies reviewed using Endnote. Titles and abstracts were screened independently by 2 reviewers for relevance. Full text review selected studies included for analysis. Meta-analysis used the midas package of stata version 14.

Results: 2877 entries were screened and 34 potentially relevant studies identified. Seventeen studies (2,235 cases) were utilized after full text review. A forest plot of included studies with reported sensitivities and specificities showed a pooled diagnostic accuracy for AC with sensitivity of 63% and a specificity of 95%. Pooled diagnostic accuracy for SCC showed a sensitivity of 84% and specificity of 90%.

Conclusions: Identification of AC had poor sensitivity and good specificity. Identification of SCC showed good sensitivity and specificity. Statistically significant levels of heterogeneity occurred among studies. Sensitivity for identification of AC was poor suggesting that immunocytochemistry plays an important role in identification of pulmonary adenocarcinomas. Accuracy of carcinoma typing varied significantly by location so accuracy expectations need to be determined for individual laboratories.

389 Cytomorphologic Criteria for Separation of Pulmonary Adenocarcinomas from Squamous Cell Carcinomas: A Linear Regression Analysis

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Disclosures: Lester Layfield: None

Background: Current therapy requires separation of non-small cell carcinomas into adenocarcinomas (AC) and squamous cell carcinomas (SCC). A meta-analysis has shown a pooled diagnostic sensitivity of 63% and specificity of 95% for AC. While a number of cytomorphologic features have been proposed for separation of AC from SCC, we are unaware of a statistically-based analysis of cytomorphologic features useful for separation. We performed logistic regression analysis of cytologic features useful in classifying SCC and AC.

Design: 61 Papanicolaou stained FNA specimens (29 AC/32 SCC) were reviewed by two board-certified cytopathologists for 9 features (eccentric nuclei, vesicular chromatin, prominent nucleoli, vacuolated cytoplasm, 3-dimensional cell balls, dark non-transparent chromatin, central nuclei, single malignant cells, and spindle cells). All cytologic specimens had surgical biopsy results. Inter-rater agreement was assessed by Cohen's kappa. Association between features and AC was determined using hierarchical logistic regression model where feature scores were nested within reviewers. A model to classify cases as SCC or AC was developed and verified by k-fold verification (k=5). Classification performance was assessed using the area under the ROC curve.

Results: Observed rater agreement ranged from 49% to 82%. Kappa scores were clustered in three groups. Raters demonstrated good agreement for prominent nucleoli, vesicular chromatin, and eccentric nuclei. Fair agreement was seen for 3-dimensional cell balls, dark non-transparent chromatin, and presence of spindle cells. Association of features with adenocarcinoma showed four statistically significant associations ($p<0.001$) with adenocarcinoma. These were prominent nucleoli, vesicular chromatin, eccentric nuclei, and three dimensional cell balls. Spindle cells and dark non-transparent chromatin were negatively associated with adenocarcinoma.

Conclusions: Logistics regression analysis demonstrated six features helpful in separation of AC from SCC. Prominent nuclei, vesicular chromatin, cell balls and eccentric nuclei were positively associated with AC and demonstrated a p value of 0.001 or less. The presence of dark, non-transparent chromatin and spindle cells favored the diagnosis of SCC.

390 Histologic Features in Endoscopic Ultrasound-Guided Fine Needle (ProCore) Biopsies with Autoimmune Pancreatitis type I and II

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Background: Autoimmune pancreatitis (AIP) is a recently introduced unique pancreatic inflammatory disease. With recent advances of development of new EUS-guided biopsy needles such as ProCore needle, Fine needle biopsy (FNB) has enabled to obtain core samples suitable for histologic evaluation. However, only limited data regarding the utility of EUS-FNB for histologic diagnosis of AIP has reported. We investigate histologic features of AIP and it diagnostic accuracy of EUS-FNB used by 19G or 22G ProCore.

Design: We retrospectively reviewed cases of clinically confirmed AIP and selected 53 cases of EUS-FNB using 19 or 22 G ProCore needle and performed serial sections and immunohistochemistry for CD138, CD3, IgG, IgG4, neutrophil elastase antibody and Verhoeff's elastic stain.

Results: Study patients comprised of 41 (77%) males and 12 (23%) females aged 54.5 year. The study group consists of 44 (83%) type I patients and 9 (17%) type II patients. Among forty-four type I patients, eighteen (41%) patients have been diagnosed with systemic IgG4 related disease at the time of diagnosis of AIP. Six (67%) of nine patients with type II have a history of ulcerative colitis. One to eight cores of tissue were obtained for examination. The size of core ranges from 0.1 to 3.0 cm. Histologically, forty-two (95%) cases of forty-four type I AIP have shown dense lymphoplasmacytic infiltration with 5 to 100 IgG4 positive plasma cells/high power field and thirty-eight (86%) cases demonstrated stromal fibrosis and obstructive phlebitis was found in only two (5%) cases. In nine cases of type II AIP, eight (89%) cases have shown GEN in FNBs. The sensitivity of EUS-FNB is 90.6% and its specificity is 100%. The tissue retrieved by EUS-FNB was judged adequate for diagnosis of 48 of 53 cases (90.6%) on initial EUS guided FNB. Only one (3%) FNB specimen obtained by 19G procure was not diagnosed as AIP. In contrast, four (18%) FNB specimens acquired by using 22G procure were failed to be diagnosed as AIP.

Conclusions: Our results suggested that EUS-FNB using ProCore needle is effective and highly useful for histologic diagnosis of type I and II AIP and differentiation from a mass forming lesion, importantly pancreatic cancer. In type I AIP cases, lymphoplasmacytic infiltration and increased IgG4 positive cells (95%) are the most frequently identified histologic feature followed by stromal fibrosis (86%) and phlebitis (5%) with specificity 100%. Eight (89%) of nine type II AIP cases showed GEN in FNB specimens.

391 Pattern of cervical biopsy results in cases with cervical cytology interpretation as higher than low-grade in the background of atrophic cellular changes

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Disclosures: Yilan Li: None; Olubunmi Shoyele: None; Vinod Shidham: None

Background: The changes associated with *atrophic cellular pattern* (ACP) in *cervical cytology smears* (PAP smears) may mimic high-grade squamous intraepithelial lesion (HSIL) with higher chances of cytomorphologic over-interpretation. *Estrogen therapy (topical or systemic)* (ET) would reverse the changes related to ACP and repeat Pap smear after ET would correct the false positives. This approach would minimize the unindicated invasive interventions. However, performing immediate biopsies following higher than *LSIL (ASC-H, LSIL-H and HSIL) interpretations* (HGI) in such cases with ACP is relatively frequent practice.

Design: PAP smears with HGI in association with ACP over a period of 10 years were selected. The follow up biopsy material was reviewed with other clinical details including *high risk HPV test* (HT) results as applicable.

Results: Total 657,871 cases over 10 years were reviewed. Out of these 188 PAP Smears with HGI in association with ACP, 67 underwent biopsies (Figure 1). Out of 67, 36 were diagnosed as positive and 31 were negative. Out of these 31 cases, 19 biopsies with adequate squamous component were reviewed further. p16 were evaluated in 11 cases with indeterminate histomorphology (11/11 (100%) were p16 negative). High risk HPV testing was performed in 14 cases (11/14 (79%) were with negative HPV test). Six cases demonstrated simultaneous negativity for HT and p16.

Figure 1 - 391

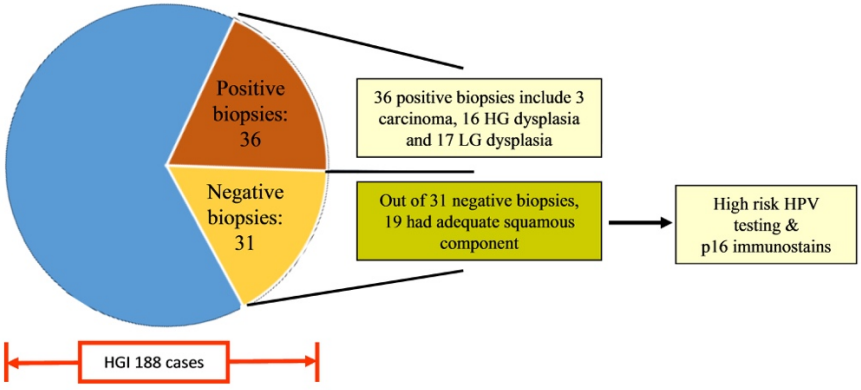

Figure 1: Distribution of biopsy results. The total pie represents 188 cases of positive PAP smear with HGI diagnosis.

Conclusions: The above results indicate that atrophic PAP smears have higher frequency of false positive HGI. Approaches such as repeating Pap smears after ET may decrease the chances of false positivity in concert with high risk HPV testing as clinically indicated.

392 Deconvolution Microscopy as a Simple Platform for Non-Destructive Rapid On-Site Evaluation (ROSE) of Fine Needle Aspiration (FNA) Specimens

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Disclosures: Haihui Liao: None; Todd Sheridan: None; Kevin Fogarty: None; Karl Bellve: None; Ediz Cosar: None; Tao Zuo: None; Xiaofei Wang: None; Ali Akalin: None; Dina Kandil: None; Andrew Fischer: None

Background: ROSE is needed to optimize the diagnostic performance of FNA microbiopsies. ROSE requires skilled triage and technical production of smears, and the material that is smeared may not be available for ancillary tests. There is a need to facilitate ROSE in a manner that does not sacrifice diagnostic material. We evaluated fluorescence microscopy techniques because fluorescence staining is compatible with rapid one-step staining, and imaging living cells. Conventional epifluorescence microscopy has poor resolution due to out of plane signal. Other optical sectioning technologies such as confocal or two photon microscopy are impractically expensive.

Design: We emulated a process for ROSE using residual material remaining from 14 FNA samples. Fragments were stained with Hoechst 33342 (DNA stain, blue emission) and sypro-red (protein stain, red emission). The process places fragments at an optical surface in an inverted epifluorescent microscope equipped with a motorized Z-axis to acquire a series of planes through the fragments. A deconvolution algorithm was applied to digitally obtain virtual “optical” sections through the stacks. The deconvolved images were pseudocolored to resemble an H&E section. 4 cytopathologists blindly diagnosed 2 to 4 representative image stacks per case, and later compared them to conventional epifluorescent images.

Results: Compared to the reference diagnoses (4 benign and 10 malignant cases), accurate definitive categorical diagnoses (negative or positive) in deconvolved cases were rendered in 36 of 56 (64%) total evaluations, equivocal diagnoses (atypical or suspicious) were rendered in 17 of 56 (30%). Two false positive and one false negative definite diagnoses (5%) were rendered. Limitations leading to equivocal or erroneous diagnoses were described by participants as due to case-specific difficulty (follicular variant papillary thyroid carcinoma vs goiter or specimen overrun by necrosis), need for IHC (7/17, 41%), poor image quality (6/17, 35%) and sampling limitation (4/17, 24%). Cytopathologists preferred the deconvolved images compared to the raw epifluorescent images ($p < 0.01$) (see Figure A and B). The examined sample was recovered and used to make either a thinprep (see Figure C) or cell block.

Figure 1 - 392

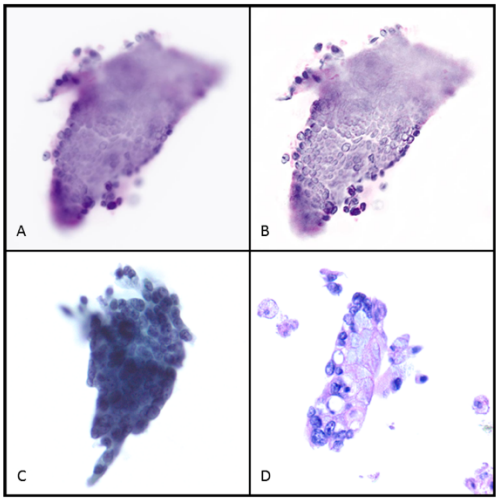

Figure. A) An optical section of pancreatic adenocarcinoma B) The same optical section as A processed with deconvolution algorithm. C) ThinPrep (Papanicolaou stain) made from the recovered sample. D) Cell block section (H&E stain) of the original sample.

Conclusions: A deconvolution algorithm improves image quality of FNA fragments compared to epifluorescence, allowing frequent definitive diagnosis for a non-destructive ROSE.

393 Rapid onside evaluation with telecytology significantly reduced unsatisfactory rates of thyroid FNA: A case control study

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Disclosures: Diana Lin: None; Jessica Tracht: None; Erik Kouba: None; Deepti Bahl: None; Anish Patel: None; Isam-Eldin Eltoum: None

Background: Rapid onsite evaluation (ROSE) for thyroid ultrasound guided fine-needle aspirations (UG-FNA) has been shown to significantly reduce the unsatisfactory/no-diagnostic (UN/ND) rate, both in national studies and at our own institution. However, providing an on-site pathologist for all thyroid FNAs is challenging. ROSE for UG-FNA was introduced in our institution's Thyroid Endocrinology Clinic, first with a pathologist on-site and then with a pathologist using telecytology. In this case control study, we compared Endocrinology Clinic results to another thyroid UG-FNA clinic at our institution where ROSE was not performed.

Design: We reviewed thyroid UG-FNA performed 12 months before introduction of ROSE in the Endocrinology Clinic and analyzed follow-up data for 6 months after the introduction of on-site ROSE and 12 months after the introduction of telecytology. Our institution's Ultrasound Clinic, where ROSE is not provided, was used as a control group. Telecytology was performed in real time with a video monitor connected to a microscope.

Results: 954 patients were seen in Endocrinology Clinic (509 before ROSE, 184 after on-site ROSE, and 261 after telecytology ROSE). As a control for both periods, we included 1,434 patients from Ultrasound Clinic, all UG-FNA without ROSE (860 before ROSE introduction in Endocrinology Clinic, 181 after 6 months, and 393 cases 12 months after telecytology began in Endocrinology Clinic). In both clinic groups, the UN/ND before ROSE was not significantly different. After implementation of on-site ROSE, the rate of UN/ND was significantly reduced to 1.6% in the Endocrinology Clinic ($P < .05$) as compared to in the Ultrasound Clinic (previously reported). Our new data reveal that after telecytology, the UN/ND rate in Endocrinology Clinic was still significantly reduced to 4.2% ($p<0.05$). There was no significant difference between the UN/ND rates at Endocrinology Clinic between on-site ROSE and telecytology ROSE periods ($p>0.05$).

	Thyroid Clinic			Ultrasound Clinic		
Bethesda Category	Before ROSE (%)	After onsite ROSE (%)	After telecytology (%)	Before (%)	After onsite ROSE(%)	After Telecytology(%)
Unsatisfactory	45(8.8)	3(1.6)	11 (4.2)	69(8.0)	13(7.2)	29 (7.4)
Benign	417(81.9)	160(87)	216(82.8)	628(73)	132(72.9)	282 (71.8)
Atypical	32(6.3)	16(9)	23 (8.8)	103(12)	23(12.7)	49 (12.5)
Follicular neoplasm	1(0.2)	4(2.1)	6 (2.3)	10(1.2)	5(2.8)	7 (1.7)
Suspicious	3(0.6)	1(0.5)	3 (1.2)	7(0.8)	2(1.1)	10 (2.5)
Malignant	11(2.2)	1(0.5)	2 (0.8)	43(5.0)	6(3.3)	16 (4.1)
Total	509(100)	184(100)	261 (100)	860(100)	181(100)	393 (100)

Conclusions: ROSE reduces unsatisfactory rates in UG-FNA. Telecytology is as helpful as having a pathologist on-site.

394 Comparison of Diagnostic Accuracy between ThyroSeq v2 and ThyroSeq v3 Molecular Test for Indeterminate Thyroid Nodules

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Disclosures: Benjamin Lin: None; Michele Zelonis: None; Fan Lin: None; Haiyan Liu: None

Background: A significant percentage of fine needle aspirations (FNAs) of thyroid nodules fall into the indeterminate categories, which include atypia of undetermined significance/or follicular lesion of undetermined significance (AUS/FLUS) and (suspicious for) follicular neoplasm (FN/SFN). Molecular testing such as ThyroSeq has been suggested as a reflex test for indeterminate specimens to improve diagnostic accuracy. ThyroSeq v3 was developed to improve the lower positive predictive value (PPV) of ThyroSeq v2. In this study, we compared the PPV of ThyroSeq v3 and ThyroSeq v2 for AUS/FLUS and FN/SFN FNA samples.

Design: Between June 2017 and August 2018 in our institution, 240 AUS/FLUS or FN/SFN cases were sent for ThyroSeq testing (University of Pittsburgh). Of 240 cases, 81 cases had subsequent surgical resections. Within those 81 cases, 44 were subject to ThyroSeq v2 testing (Group 1) and 37 cases were done with ThyroSeq v3 testing (Group 2).

Results: Within Group 1, 33 of 44 cases were positive for ThyroSeq v2 testing, and 11 cases were negative. Of the 33 positive cases, 19 (57.6%) were positive for malignancy, and 14 (42.4%) were benign. The 19 malignant cases included 11 papillary thyroid carcinoma (PTC), 7 non-invasive follicular thyroid neoplasm with papillary like nuclear features (NIFTP), and 1 follicular carcinoma (FCA). The 14 benign lesions included 6 follicular adenomas (FAs), 7 nodular goiters (NGs), and 1 parathyroid adenoma (PTA). The 11 cases that were negative on ThyroSeq testing were diagnosed on surgical resection as 1 PTC, 1 NIFTP, 1 metastatic renal cell carcinoma (RCC), 4 FAs, and 4 NGs.

Within Group 2, 28 of 37 cases were positive for ThyroSeq v3 testing, and 9 were negative. Of the 28 positive cases, 15 (53.6%) were positive for malignancy, and 13 (46.4%) were benign. The 15 malignant cases included 11 PTCs and 4 NIFTPs. The 13 benign lesions included 8 NGs and 5 FAs. The 9 cases that were negative for ThyroSeq v3 were diagnosed on surgical resection as 1 NIFTP, 1 B-cell lymphoma, 4 FAs, and 3 NGs.

Of 27 lesions (from Groups 1 and 2) that were positive for ThyroSeq testing and benign on follow-up surgical resection, the mutations identified as: 8 NRAS, 4 HRAS, 4 IGF2BP3, 2 KRAS, 2 BRAF (K601E), 1 RAS, 1 MET, 1 DICER1, 1 EIF1AX, and 3 chromosome copy changes.

Conclusions: Our data suggest that both ThyroSeq v3 and v2 testing have a similar PPV of about 55%, which is significantly lower than the previous reports. A further study to confirm this finding is warranted.

395 Role of DNA Ploidy Quantitative Analysis in Opportunistic Screening of Cervical Cancer in Clinic

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Disclosures: Long-teng Liu: None; Fei Su: None; Jing Wang: None; Lan Chen: None

Background: DNA ploidy quantitative analysis can identify abnormal cells. It is an automatic test and not subject to a pathologist's experiences. Its clinical implication, particularly with regard to opportunistic screening of cervical cancer in clinic, has yet to be confirmed.

Design: 2768 cervical cancer screening samples, on both Hologic liquid based pap smear and Fulgen DNA smear, were collected from April to November in 2016, with an average age of 44.3 years. Cytology was performed on pap smear according to Bethesda reporting system. DNA ploidy analysis was made on Fulgen smear (Heer, Wuhan, China). For cases whose DNA Index is ? 2.5, depending on the number of abnormal cells, they were divided into negative, suspicious and positive for cervical lesions. 167 cases had biopsy follow-up and 2086 had High Risk HPV (HC2) tests. A comparative analysis was made based on biopsy and HPV results.

Results: Out of 2768 cases, DNA ploidy analysis identified 218 positive cases (7.9%); cytology had 190 positive cases (?LSIL) (6.9%). The two methods enjoyed a good statistical consistency (Kappa=0.6919, Chi-square, $P<0.05$). With biopsy confirmed HSIL or invasive cancer as gold standard, cytology achieved 100% sensitivity and 100% specificity whilst DNA ploidy analysis had 100% sensitivity and a statistically much lower 33.3% specificity (Pearson's Chi-squared test, $P=1.3X10^{-5}$). HPV infection rate was 84.1% in abnormal cytology cases and 11.3% in NILM whereas it was 81.1% in DNA ploidy analysis of positive cases and 11.3% in negative, so HPV infection rate was insignificantly different between the two methods (Fisher's exact test, $P>0.05$). When combined with positive HPV status, DNA ploidy analysis had no enhanced specificity to detect HSIL as compared to that without HPV status (35.7% vs. 33.3%, Pearson's Chi-squared test, $P=0.9536$).

Conclusions: Our research indicated that DNA ploidy analysis had a lower specificity for HSIL compared with cytology. The specificity is not improved even if complimented by HPV tests. However, it is as sensitive as cytology. So cytology screening may start from abnormal cases detected by DNA ploidy analysis. Combination of two methods will reduce the work load as well as keep the same clinical guidelines as for cytology.

396 Are All High Grade Urothelial Carcinomas Following the Paris System?

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Background: The implementation of the Paris System Criteria (PSC) for reporting urine cytology has improved interobserver reproducibility for reporting urine cytology. The criteria for the cytologic diagnosis of High Grade Urothelial Carcinoma (HGUC) and Suspicious for High Grade Urothelial Carcinoma (SHGUC) are nuclear to cytoplasmic (N/C) ratio >0.7 and hyperchromasia (major criteria, required), in addition to irregular clumpy chromatin and/or irregular nuclear membranes (minor criteria, at least one required). The aim of this study is to investigate the usefulness of the current nuclear features as established by the PSC.

Design: The urinary cytology results of 78 patients with concomitant surgical diagnosis of high grade urothelial carcinoma obtained from 2015 to 2017, were re-reviewed by two pathologists (a cytopathology fellow and an experienced cytopathologist and genitourinary pathologist). The presence or absence of hyperchromasia or other nuclear characteristics were noted.

Results: Of a total of 78 patients with high grade urothelial carcinomas by tissue diagnosis, 40 were diagnosed as SHGUC and 38 were diagnosed as HGUC. Of all the cases, 26 cases (33.3%) demonstrated hyperchromasia and the remaining cases, in addition to demonstrating a N/C ratio >0.7, displayed nuclear characteristics such as smooth, glassy nuclei (n=27, 34.6%) and/or coarse, clumpy chromatin (n=25, 32.1%).

Conclusions: The preliminary findings of this study show a large proportion of urinary cytologies with diagnosis of HGUC or SHGUC with concomitant diagnosis of high grade urothelial carcinoma in tissue samples that may display nuclear characteristics other than hyperchromasia, such as coarse chromatin and smooth chromatin/glassy nuclei. These findings should be considered when interpreting urine cytology to avoid false negative diagnoses.

397 Splenic Fine Needle Aspiration: A Single-Institution 25-Year Retrospective Analysis of 125 Cases

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Disclosures: Martin Magers: None; Adam Miller: None; Howard Wu: None; Harvey Cramer: None

Background: While uncommonly performed, fine needle aspiration (FNA) of the spleen is sometimes utilized to investigate patients presenting with mass lesions of the spleen or diffuse splenomegaly.

Design: Electronic records of an academic pathology department were queried for all splenic FNAs (1993-2018). The FNA reports including all ancillary studies and any associated surgical pathology reports were reviewed. Hospital records were searched for procedural complications.

Results: 125 splenic FNAs were identified. 58% of the patients were female. The median patient age was 58 years (range: 7-88). Diagnostic material was obtained in 113 cases (90%). Diagnostic categories included benign spleen (n=46, 41%), atypical/malignant (n=41, 36%), and inflammatory/infectious (n=26, 23%). The majority of the atypical/malignant cases were lymphoid (76%) with metastases (carcinoma 12%, melanoma 7%, and sarcoma 2%) accounting for the majority of the remaining cases. Most of the atypical/malignant lymphoid cases were broadly classified as classic Hodgkin lymphoma (10%), B-cell lymphoma (39%), or large cell lymphoma (6%); the remaining cases were not further classified. Breast, lung, liver, and cervix were the sites of origin of metastatic carcinoma. A cell block was created in 43% of cases; special stains were performed in 41% of those cases which had a cell block. Flow cytometry was performed in 34% of cases; 53% were negative for immunophenotypic abnormalities, 42% were at least suspicious for a monoclonal B-cell population, 1 case was suspicious for an NK/T-cell disorder, and 1 case was inadequate for analysis. Microbiologic studies were performed in 25 cases (20%); of 4 cases with available results, 1 case was positive for *Bartonella* spp. and 3 were negative. A concurrent surgical pathology biopsy was performed in 18% of cases, a subsequent resection in 14%, and both a biopsy and resection in 5%; most surgical pathology diagnoses were either benign spleen (42%) or an atypical/malignant lymphoid process (44%). Most cases (96%) had no immediate complications following FNA; the 3 patients with complications had pain and minor bleeding but no life-threatening complications.

Conclusions: Splenic FNA can be a safe procedure which typically yields diagnostic material on which ancillary tests (ie flow cytometry, special stains, and microbiologic studies) may be performed. Lymphoma is frequently diagnosed, and metastatic disease occasionally occurs. Splenic FNA should be considered in patients with splenic lesions.

398 Cytomorphologic Comparison of Type 1 and Type 2 Papillary Renal Cell Carcinoma: A Retrospective Analysis of 28 Cases

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Disclosures: Martin Magers: None; Carmen Perrino: None; Harvey Cramer: None; Howard Wu: None

Background: Papillary renal cell carcinoma (pRCC) is classified as type 1 or type 2 on the basis of histomorphologic features, predominantly the presence or absence of nuclear pseudostratification. Because type 1 pRCC is associated with a better prognosis, this distinction is important. Furthermore, RCC is often diagnosed by fine needle aspiration (FNA). Thus, we sought to characterize cytomorphologic features present in FNA cases which discriminate between type 1 and type 2 pRCC.

Design: Electronic records of an academic pathology department were searched for all FNA cases with pRCC (2007-2018). Corresponding surgical pathology reports were reviewed to classify all patients as either type 1 or type 2 pRCC. FNA slides were reviewed to assess cytomorphologic features (ie nuclear grade; cell size; cytoplasm volume and quality; and the presence of single cells, papillary clusters, nuclear grooves, foamy histiocytes, hemosiderin pigment, psammoma bodies, and hyaline globules). A semi-quantitative score was assigned to each feature. Nuclear grade was assigned using the Fuhrman/ISUP grading system. Cell size was scored as 1 (equivalent to <3 red blood cells [RBCs]), 2 (3-5 RBCs), or 3 (>5 RBCs). The remaining cytomorphologic features were assigned 0 (absent), 1 (scant), 2 (moderate), or 3 (abundant). The cytomorphologic features of type 1 and type 2 pRCC were compared using a two-tailed T-Test with a significance of $p<0.05$.

Results: 16 patients with type 1 pRCC and 12 patients with type 2 pRCC were included in the study. Type 2 pRCC had higher nuclear grade (all type 2 pRCC grade ≥3 compared to 15% of type 1 pRCC, $p<0.05$), higher volume of cytoplasm (50% of type 2 pRCC abundant cytoplasm compared to 19% of type 1 pRCC, $p<0.05$), and more granular cytoplasm (all type 2 pRCC had granular cytoplasm compared to 56% of type 1 pRCC, $p<0.05$). Type 1 papillary RCC more frequently had nuclear grooves (63% of type 1 pRCC compared to 17% of type 2 pRCC, $p<0.05$) and clear cytoplasm (75% of type 1 pRCC compared to 19% of type 2 pRCC, $p<0.05$). The remaining features (ie cell size, papillary clusters, single cells, foamy histiocytes, hemosiderin pigment, psammoma bodies, and hyaline globules) were not statistically significant.

Conclusions: Nuclear grade, cytoplasmic volume and granularity or clarity, and nuclear grooves are all cytomorphologic features which may aid in the distinction of type 1 versus type 2 pRCC. Prospective validation of these features may yield clinical utility of application of these features.

399 Sclerosing Pneumocytoma of Lung: Cytomorphologic Findings and Immunoprofile of a Rare Entity

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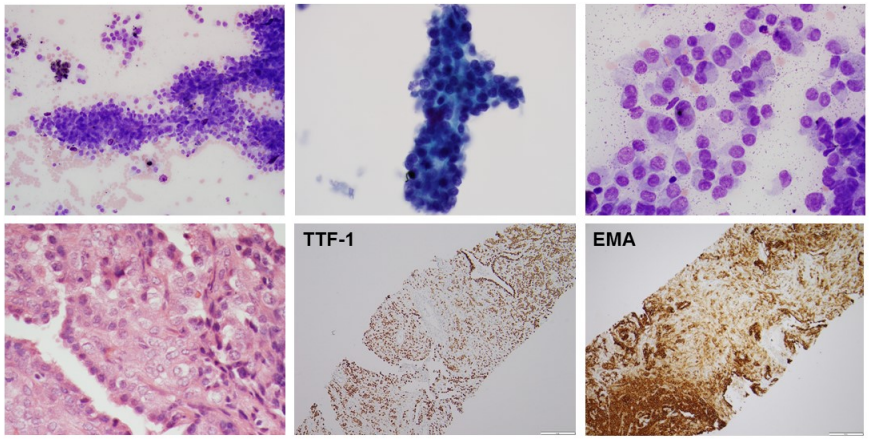
Background: Sclerosing pneumocytoma (SP), previously called sclerosing hemangioma, is an extremely rare tumor of lung origin. To date, there has been no published series on the cytopathology of this entity. Herein, we evaluate for the first time the cytomorphologic findings and immunoprofile of SP in a series of such cases.

Design: Seven fine needle aspiration (FNA) cases of SP collected from 5 pathology departments were included along with corresponding histopathology and immunohistochemical (IHC) stains. CT-guided FNA was performed in 6 cases and EBUS-guided in one case. Slides were reviewed and the cytomorphologic, histopathologic and immunostaining findings recorded.

Results: The female to male ratio for patients was 6:1, with a mean age of 58 years (min 27, max 73 years). Six tumors presented as lung masses and one was mediastinal, and these were of mean size 2.5 cm (range 1.1 - 5 cm). All cases were interpreted as atypical on rapid on site evaluation and the final diagnoses were favor adenocarcinoma (n=1), well differentiated lung adenocarcinoma (n=1), low grade epithelial neoplasm (n=1) and sclerosing pneumocytoma (n=4). Samples were moderately cellular consisting of round epithelioid cells with clear cell features, columnar cells and spindle cells. A papillary arrangement with prominent hyalinized fibrovascular cores was the most common architectural pattern (figures 1-4) followed by flat sheets and acinar formation. Tumor cells exhibited mild to focally moderate nuclear pleomorphism with prominent nucleoli, hyperchromasia, nuclear elongation, and nuclear overlap. Occasional nuclear inclusions and grooves were noted. All cases contained foamy macrophages and 6 cases had hemosiderin pigment and hemosiderin-laden cells. No mitoses or necrosis was noted. Hyalinized papillae were detached or attached to cells. Three cases had associated lymphoid aggregates. The most notable IHC finding was that surface cells and underlying round cells were positive for both TTF-1 and EMA (figures TTF-1 and EMA) in all cases.

Figure 1 - 399



Conclusions: Sclerosing pneumocytoma is a rare benign tumor of pneumocytic origin that presents with cytomorphological findings such as papillary features and nuclear pleomorphism that make it difficult to discriminate from well differentiated lung adenocarcinoma. Awareness of these cytomorphologic findings and immunoprofile of the two cell types found in SP should prevent a misdiagnosis and unnecessary aggressive treatment.

400 Reporting "ASC-H With Coexistent LSIL" versus "ASC-H" in Pap Tests: Is There A Difference?

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Background: The 2001 Bethesda System (TBS) for cervical cytology reporting categorizes squamous abnormalities into atypical squamous cells of undetermined significance (ASCUS), low or high grade squamous intraepithelial lesions (LSIL or HSIL), or atypical squamous cells, cannot exclude HSIL (ASC-H). A diagnostically challenging group of cases exists that shows features of unequivocal LSIL with findings of ASC-H (reported as "ASC-H, background LSIL" at Yale). The goals of this study were to determine if reporting "ASC-H, background LSIL" provides added value compared to a diagnosis of "ASC-H" alone, what criteria could help consistently distinguish reporting "ASC-H, background LSIL" from "ASC-H" alone.

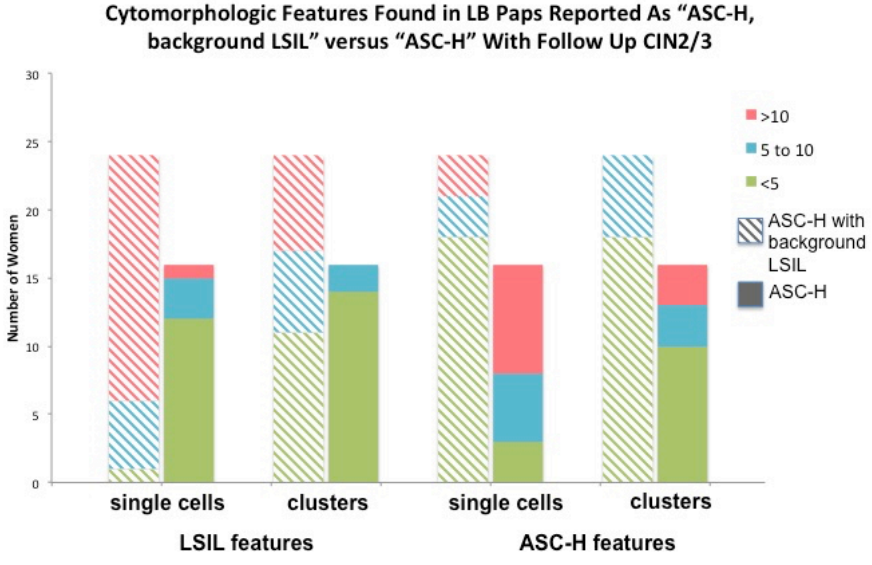
Design: The Yale Pathology database was searched for liquid-based (LB) Pap tests (SurePap and ThinPrep) with a cytologic interpretation of ASC-H with or without background LSIL during a 1 year period from January - December 2017. Pap interpretations were made as part of clinical practice by 1 of 6 fellowship trained and boarded cytopathologists. Fifty random Pap cases were selected from each category ("ASC-H" and "ASC-H, background LSIL") to total 100 cases, which were re-reviewed by two pathologists. Cytologic features described by TBS as LSIL and ASC-H were used to identify LSIL and ASC-H foci and semi-quantitated based on occurrence as single cells versus crowded groups. Patients' follow-up surgical specimen reports were reviewed and the most severe lesion on histologic follow-up within 1 year from Pap tests was recorded. Histologic tissues were from cervical/cone biopsy, endocervical curettage, and hysterectomies.

Results: A total of 255 cases of ASC-H, 88 of which had background LSIL were identified. Follow up of both cohorts (Table 1) were similar (ASC-H with LSIL: 42 of 50, 84%; and ASC-H: 40 of 50, 80%). Histologic follow up in patients with ASC-H background LSIL (n=50) revealed 24(57%) CIN2/3 and 13(31%) CIN1. In patients with only ASC-H (n=50), 16(40%) had follow up of CIN2/3 and 13(32.5%) had follow up showing CIN1. Women aged 20-29 with a Pap reported as "ASC-H, background LSIL" had the highest rate of CIN2/3 (13 of 18, 72.2%). Cytomorphological review of LB Paps with correlation to histological follow-up is depicted in Figure 1.

Table 1: Follow-up results

Age	ASC-H with background LSIL				ASC-H			
	F/u No (%)	Benign	CIN1 (%)	CIN2/3 (%)	F/u No (%)	Benign	CIN1 (%)	CIN2/3 (%)
20-29	18 (82)	2(11)	3(16.7)	13(72.2)	10 (71)	4(40)	3(30)	3(30)
30-39	8 (80)	1(12.5)	2(25)	5(62.5)	9 (90)	3(33.3)	2(22.2)	4(44.4)
40-49	7 (87.5)	1(14.3)	4(57)	2(28.6)	12 (100)	0(0)	6(50)	6(50)
50-59	5 (100)	1(20)	2(40)	2(40)	4 (80)	2(50)	1(25)	1(25)
>60	4 (83)	0(0)	2(50)	2(50)	5 (56)	2(40)	1(20)	2(40)
Total	42(84)	5(12)	13(31)	24(57)	40(80)	11(27.5)	13(32.5)	16(40)

Figure 1 - 400



Conclusions: This study highlights that in Paps with ASC-H it appears valuable to report "background LSIL" when present in >10 foci as there may be increased progression to CIN2/3 in women < 30 years.

401 Concordance of Breast Fine Needle Aspiration Biopsy Interpretation with Subsequent Surgical Pathology: An 18 Year 9 Month Retrospective Review from a Single Sub-Saharan African Institution

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Disclosures: Kelsey McHugh: None; Peter Bird: None; Charles Sturgis: None

Background: There are many merits to fine needle aspiration biopsy (FNAB) as a diagnostic modality in evaluation of palpable breast lesions. We set out to determine the concordance of breast FNAB interpretation with subsequent surgical pathology diagnoses in the resource-limited healthcare setting of rural Kenya.

Design: A retrospective review of the electronic pathology files at African Inland Church (AIC) Kijabe Hospital was performed from 1/1999 through 9/2017. All breast FNAB cases and associated subsequent surgical pathology specimens were identified. FNAB interpretations were retrospectively categorized according to the International Academy of Cytology (IAC) Yokohama codes: insufficient, benign, atypical favor benign, suspicious favor malignant, and malignant. All surgical pathology results fell into 1 of 2 diagnostic categories: benign or malignant. Surgical pathology interpretation served as the diagnostic gold standard.

Results: 695 total breast FNABs were identified. 219 (31.5%) had subsequent surgical pathology. The average patient age was 39 years (range 13-88); 95% were female. Nearly all (98%) lesions were palpable. FNAB interpretive categorization according to the Yokohama system was as follows: 20 (9%) insufficient, 103 (47%) benign, 16 (7%) atypical, 24 (11%) suspicious, and 56 (26%) malignant. On histology, there were 141 (64%) benign cases and 78 (36%) malignancies (Table 1). With atypical and above on cytology considered a non-benign interpretation, the sensitivity of FNAB for detecting malignancy was 85% and the specificity was 75%. Positive and negative predictive values were 69% and 88%. Overall diagnostic concordance between FNAB and surgical pathology was 79%. When only considering definitively diagnostic FNAB categories, benign and malignant, diagnostic concordance was 89%.

Table 1.

	Diagnosis in Histology					Total	Probability of Malignancy
Diagnosis in Cytology	**Invasive Carcinoma**	**In Situ Carcinoma**	**Sarcoma**	**Melanoma**	**Benign**		
C1: insufficient	0 (0%)	0 (0%)	0 (0%)	0 (0%)	20 (100%)	20	0%
C2: benign	9 (9%)	2 (2%)	1 (1%)	0 (0%)	91 (88%)	103	12%
C3: atypical	3 (19%)	1 (6%)	0 (0%)	0 (0%)	12 (75%)	16	25%
C4: suspicious	10 (42%)	1 (4%)	0 (0%)	0 (0%)	13 (54%)	24	46%
C5: malignant	48 (86%)	0 (0%)	2 (3%)	1 (2%)	5 (9%)	56	91%
					Total	219	

Conclusions: On histopathology, malignant diagnoses were given in 0 insufficient, 12 (12%) benign, 4 (25%) atypical, 11 (46%) suspicious, and 51 (91%) malignant cases. There were 5 false-positives diagnosed as malignancy on cytology with subsequent benign surgical pathology (2 fibroadenomas, 1 lactating adenoma, 1 gynecomastia, 1 fat necrosis). There were 12 false-negatives with malignancy found on subsequent histology after benign cytology (9 infiltrating carcinomas, 2 ductal carcinoma in-situs, 1 malignant phyllodes tumor). The vast majority of discrepancies were minor, where FNAB with indeterminate interpretations (atypical or suspicious) were ultimately found to be benign on subsequent histology.

402 Digital Image Analysis Reveals that High-Grade Urothelial Carcinomas of the Upper Urothelial Tract have Different Cytomorphological Features than those of the Lower Urothelial Tract in Urine Cytology Samples

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Background: The Paris System for Report Urinary Cytology (TPS) was introduced to standardize the reporting of urinary cytology. TPS placed an emphasis on characterization and reporting of high-grade urothelial carcinomas (HGUC). A requirement for diagnosing HGUC is

that the N:C ratio should be ≥ 0.7. Cellular and nuclear size is not included in the criteria. Recent studies have suggested that upper tract urothelial carcinomas (UTUC) and lower tract urothelial carcinomas (LTUC) are morphologically and genetically different entities. However, TPS does not account for these differences.

Design: Urine cytology diagnoses of HGUC, with biopsy proven HGUC follow-up, were identified in the pathology files at our institution. ThinPrep™ urine cytology slides were scanned into whole-slide digital images at 40X magnification. Digital annotations of nuclear and cytoplasmic membranes were manually conducted by a single pathologist and IA software performed cellular enumeration. A total of 10 cells per case were enumerated. Cells with indistinct cell borders, disrupted cytoplasmic membranes or marked nuclear degeneration were excluded. A two-sample T-test (Student's T-test) was conducted and two sided, alpha level of 0.05 was the significance cutoff.

Results: The final cohort consisted of 49 HGUCs from 42 patients for a total of 490 analyzed cells. There were 17 cases of UTUC and 32 of LTUC. For UTUC, the average N:C ratio was 0.58 (range: 0.27 – 0.91) and the average nuclear area was 129.0 μm^2 (range: 42.5 μm^2 – 404.7 μm^2). The average cellular circumference was 59.6 µm (range: 35.9 µm – 104.9 µm) and the average cytoplasmic area was 222.0 μm^2 (range: 72.5 μm^2 – 712.4 μm^2). **Table 1**. For LTUC, the average N:C ratio was 0.55 (range: 0.21 – 0.93) and the average nuclear area was 168.5 μm^2 (range: 39.8 μm^2 – 2451.5 μm^2). The average cellular circumference was 65.8 µm (range: 32.2 µm – 280.5 µm) and the average cytoplasmic area was 306.0 μm^2 (range: 72.3 μm^2 – 4635.5 μm^2). **Table 1**. When comparing the cohorts, UTUC had a higher N:C ratio (p=0.02), less nuclear area (p=0.007), less cytoplasmic area (p<0.001) and lower cellular circumference (p<0.001).

Table 1: Summary of Nuclear-to-Cytoplasm Ratios, Nuclear and Cytoplasmic Area Based on Location of Biopsy Proven High-Grade Urothelial Carcinomas

Variable	Upper Tract	Lower Tract	p-value
N:C (range)	0.58 (0.27 – 0.91) n = 170	0.55 (0.21 – 0.93) n = 320	0.02
Nuclear Area (µm2) (range)	129.0 (42.4 – 404.74) n = 170	168.5 (39.8 – 2451.5) n = 320	0.007
Cytoplasmic Area (µm2) (range)	222.0 (72.5 – 712.4) n = 170	306.0 (72.3 – 4635.5) n = 320	<0.001
Cell Circumference (µm) (range)	59.6 (35.9 – 104.9) n = 170	65.8 (32.2 – 280.5) n = 320	<0.001
Maximum N:C (range)	0.74 (0.53 – 0.91) n = 17	0.73 (0.56 – 0.93) n = 32	0.6
Maximum Nuclear Area (µm2) (range)	235.4 (102.3 – 404.7) n = 17	421.4 (118.0 – 2451.5) n = 32	0.03
Maximum Cytoplasmic Area (µm2) (range)	392.5 (196.6 – 712.4) n = 17	707.5 (174.7 – 4635.4) n = 32	0.04

Conclusions: Morphologically, the malignant cells seen in urine cytology samples from tumors originating in the upper tract were smaller with less cytoplasm and nuclear area but had a higher N:C ratio when compared to the lower tract. These are important diagnostic findings which may play a role in refining the already existing TPS criteria for diagnosing HGUC.

403 Urinary Cytology has an Excellent Negative Predictive Value Following Implementation of The Paris System for Reporting Urinary Cytology

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Disclosures: Patrick McIntire: None; Ayse Irem Kilic: None; Reema Khan: None; Reza Eshraghi: None; Eva Wojcik: None; Stefan Pambuccian: None; Guliz A. Barkan: None

Background: The Paris System for Reporting Urinary Cytology (TPS) was introduced to provide clear diagnostic criteria and reporting methods for urinary cytology specimens. By placing the main emphasis on detection of high-grade urothelial carcinoma (HGUC), TPS has reduced the rates of the "atypical" or indeterminate diagnostic category. Implementation of TPS usually leads to a reduction of the "atypical" rate through the reallocation to the "negative" category. Previously, our institution has reported an overall NPV of 96.7% prior to TPS implementation (years 2012-2013).

Design: Patients with "negative for HGUC" urinary cytology specimens were identified in the pathology files from 1/1/2016 to 12/31/2017 at our institution. Cases were deemed *true negatives* if there was at least one subsequent negative specimen or at least six months of negative clinical follow-up. Low-grade urothelial carcinomas were considered as negative follow-up. *False negatives* were defined as cases with either HGUC on surgical biopsy or a urine cytology specimen with diagnosis of suspicious for HGUC or positive for HGUC.

Results: The final cohort consisted of 2960 urine cytology specimens from 1894 patients. The majority of the clinical indications were for screening patients with a history of urothelial carcinoma (1478/2960, 50%), followed by hematuria (805/2960, 27%) and "other indication" (677/2960, 23%). The "other indication" category was primarily composed of nephrolithiasis, recurrent urinary tract infection and lower urinary tract symptoms. A total of 99 false negatives were identified generating a NPV of 96.7% (99/2960). Patients with a clinical indication of hematuria had an excellent NPV of 98.9% (9/805) while a history of urothelial carcinoma was statistically significant lower at 93.9% (90/1478) ($p<0.0001$). **Table 1**. Surprisingly, the "other indication" category (nephrolithiasis, infection, etc.) did not have a single event and, thus, generated a perfect NPV. When split by specimen type, voided urines had the highest NPV of 98.9% (4/364) followed by neobladder/ileal conduits at 97.2% (11/387), washings at 96.6% (73/2135), other 88.1% (5/42) and brushing 81.3% (6/32).

Clinical Indication	False Negative (n)	Total Cases (n)	Negative Predictive Value (%)
History of UC	90	1478	93.9
Hematuria	9	805	98.9
Other	0	677	100
Total	99	2960	96.7

Conclusions: Urinary cytology remains an excellent screening test for HGUC, generating an overall NPV of 96.7%. Additionally, clinical indication had a greater effect of NPV than specimen type. While TPS has reduced the rates of atypical diagnoses, as previously reported, the NPV has remained unchanged.

404 Genitourinary Pathologists Tend to Overcall High-Grade Urothelial Carcinomas in Surgical Biopsy Specimens as Compared to Genitourinary Pathologists with Cytopathology Training

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Disclosures: Patrick McIntire: None; Levent Trabzonlu: None; Eva Wojcik: None; Stefan Pambuccian: None; Guliz A. Barkan: None

Background: Traditionally, the gold-standard for diagnosing urothelial carcinoma is by surgical biopsy. The Paris System for Reporting Urinary Cytology (TPS) was created to standardize reporting of urine cytology (Ucyt) specimens. The purpose of this study was to compare the concordance rates of surgical biopsy specimens with Ucyt diagnoses of genitourinary pathologists who are also cytopathologists (GU/CY) with genitourinary pathologists (GU).

Design: Surgical biopsy specimens with diagnoses of papillary HGUC (with or without invasion), CIS and low-grade urothelial carcinomas (LGUC) from the urinary bladder were identified starting from 12/31/2017, going backwards in time. Consecutive cases from three GU/CY pathologists and two GU only pathologists were analyzed. All surgical specimens were required to have a Ucyt specimen within six months prior to the index biopsy. Cases with Ucyt diagnoses of "atypical" were excluded. Cases with cytology diagnoses of "negative for HGUC" or "low-grade urothelial neoplasm" were deemed concordant with surgical biopsy specimens of LGUC. Cases with cytology diagnoses of "positive for HGUC" or "suspicious for HGUC" with surgical biopsy specimens of HGUC or urothelial carcinoma in situ (UCIS) were deemed concordant. Concordance rates between cytology and surgical biopsies were calculated. A *p* value of <0.05 was deemed statistically significant.

Results: There were 289 cases analyzed for the GU/CY cohort and 289 for GU only cohort for a total of 578 cases. The overall concordance rate was 82.7% and 81.2% for GU/CY and GU only, respectively. When split by surgical diagnoses, papillary HGUC showed the greatest difference with the GU/CY cohort concordance rate of 90.0% (36/40) compared to the GU only rate of 71.0% (27/38), although the difference was not statistically significant ($p=0.06$). The combined papillary HGUC and UCIS rates were 82.5% (47/57) and 76.1% (35/46) for GU/CY and GU only, respectively. For LGUC, the GU/CY had concordance rate of 83.3% (20/24) and GU only was 87.2% (34/39). **Table 1**.

Concordance	GU/CY	GU only	p-value
LGUC	83.3% (20/24)	87.2% (34/39)	$p=0.95$
Papillary HGUC	90.0% (36/40)	71% (27/38)	$p=0.06$
Papillary HGUC and UCIS	82.5% (47/57)	76.1% (35/46)	$p=0.58$
Overall	82.7% (67/81)	81.2% (69/85)	$p=0.95$

Conclusions: When comparing the concordance rates of GU/CY pathologists and GU only pathologists, there was no statistical difference. However, for papillary HGUC, GU/CY tended towards higher concordance rates than GU only ($p=0.06$). Thus, with a larger sample size, it is possible that GU pathologists are over-calling HGUC on biopsy specimens as compared to their GU/CY colleagues.

405 PD-L1 expression and its association with molecular alterations in non-small cell lung carcinoma utilizing cytology specimens

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Background: PD-L1 expression by 22C3 pharmDx companion assay has been validated to support pembrolizumab treatment decisions in non-small cell lung carcinoma (NSCLC) in surgical specimens. The aims of this study were 1) to assess adequacy of cytological specimens for PD-L1 expression evaluation; and 2) to assess possible correlations of PD-L1 expression with clinicopathological and molecular variables.

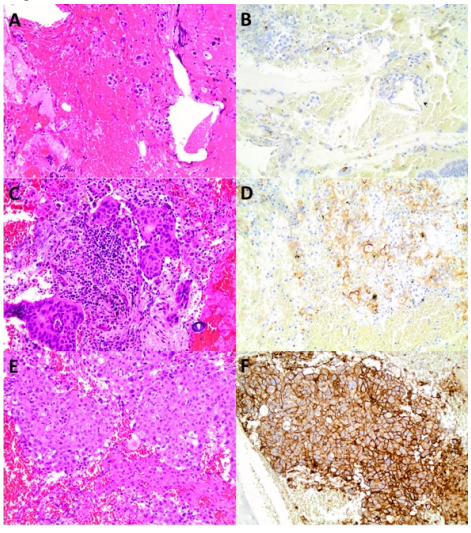
Design: The study cohort included 100 cytology [fluid (n=28) and fine needle aspiration (n=72)] and 165 surgical specimens [biopsy (n=138) and resection (n=27)]. PD-L1 IHC 22C3 assay and staining assessment were performed according to manufacturer's instruction (Figure 1: PD-L1 expression in representative cytology cases. A, B) One PD-L1 negative case; C, D) One case with PD-L1 expression ≥1%, but <50%; E, F) One case with PD-L1 expression ≥50%. A, C and E: H&E staining, 200x; B, D and F: PD-L1 immunostaining with 22C3 antibody, 200x). PD-L1 expression was correlated with patients' demographics, pathologic characteristics and molecular alterations.

Results: More than half of all specimens (53.6%) showed PD-L1 expression. No statistically significant difference in PD-L1 expression was identified between cytology (56.0%) and surgical (52.1%) specimens (Table 1). 178 cases had molecular testing including 73 mutated cases and 105 non-mutated cases. PD-L1-positivity (≥1%) was significantly more prevalent in mutated cases (69.9%, 51/73) than in non-mutated cases (48.6%, 51/105) (p=0.005). Furthermore, PD-L1 positivity was statistically associated with KRAS-mutations (p=0.013), but not with other molecular alterations (EGFR, CMET, ALK and RET). PD-L1 expression was not associated with any histologic phenotypes (data not shown).

Table 1. Overall demographic characteristics of 265 lung cancer cases with PD-L1 test.

		Total cases		Cytology		Surgical	
		265		100		165	
age		66	37-92	65	37-92	66	43-87
Gender	Male	153	57.7%	58	58.0%	95	57.6%
	Female	112	42.3%	42	42.0%	70	42.4%
Specimen types	Fluid	28	10.6%	28	28.0%		
	FNA	72	22.3%	72	72.0%		
	Surgical biopsy	138	52.1%			138	83.6%
	Surgical resection	27	10.2%			27	16.4%
PD-L1	Insufficient	4	1.5%	4	4.0%	0	0.0%
	negative	119	44.9%	40	40.0%	79	47.9%
	Positive (≥1%)	142	53.6%	56	56.0%	86	52.1%
	High Positive (≥50%)	71	26.8%	31	31.0%	40	24.2%
Diagnosis	Adenocarcinoma	148	55.8%	74	74.0%	74	44.8%
	Squamous cell carcinoma	83	31.3%	13	13.0%	70	42.4%
	NSLC	7	2.6%	6	6.0%	1	0.6%
	PDC	12	4.5%	4	4.0%	8	4.8%
	Adenosquamous	6	2.3%	0	0.0%	6	3.6%
	Other	9	3.4%	3	3.0%	6	3.6%
Molecular alterations	EGFR Exon19	6	2.3%	3	3.0%	3	1.8%
	EGFR Exon 21	1	0.4%	0	0.0%	1	0.6%
	RAS	57	21.5%	20	20.0%	37	22.4%
	CMET	4	1.5%	2	2.0%	2	1.2%
	ALK	6	2.3%	4	4.0%	2	1.2%
	RET	1	0.4%	0	0.0%	1	0.6%
	negative	115	43.4%	62	62.0%	53	32.1%
	Insufficient	3	1.1%	2	2.0%	1	0.6%
	NA	72	27.2%	7	7.0%	65	39.4%
	Total	265	100.0%	100	100.0%	165	100.0%

Figure 1 - 405



Conclusions: Our data indicate that cytologic specimens are comparable to surgical specimens in PD-L1 evaluation. Association between PD-L1 positivity and KRAS mutation may have clinical relevance in choosing immune therapy in NSCLC patients.

406 Dual stain of p16/Ki67 is useful to identify underlying high grade dysplastic cells in cytology specimens with ASCUS or LSIL

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Background: Approximately 5% of women with atypical squamous cells of undetermined significance (ASC-US) and 10-20% of low grade squamous intraepithelial lesion (LSIL) prove to have histologic CIN2+ during follow-up biopsies. We aimed to examine p16/Ki67 dual stain in identifying underlying high grade dysplastic cells in cytology specimens with ASCUS or LSIL.

Design: 177 ThinPrep cytology specimens including 95 ASC-US and 82 LSIL with histologic follow-up of CIN1 or CIN2+ were included. The cytology materials were preserved in -80℃ and dual stain (DS) with p16/Ki67 was performed on smear slides made from stored cytology materials. High risk HPV test using HC2 was also performed.

Results: Among 95 women with ASC-US, 38 showed CIN2+ and 57 showed CIN1 on histology. 36 ASC-US cases with CIN2+ on histology follow-up (36/38, 94.7%) were DS positive, and 7 ASC-US cases with CIN1 on histology (7/57, 12.3%) were DS positive. Among 82 women with LSIL, 32 showed CIN2+ and 50 showed CIN1 on histology. 30 LSIL cases with CIN2+ on histology (30/32, 93.8%) were DS positive, and 9 LSIL cases with CIN1 on histology (9/50, 18%) were DS positive. Together, 66 cases with CIN2+ on histology (66/70, 94.2%) were DS positive and 16 cases with CIN1 on histology (16/107, 15.0%) were DS positive. The sensitivity, specificity, positive predictive value(PPV) and negative predictive value(NPV) of p16/Ki67 dual stain identifying CIN2+ in ASCUS/LSIL cytology specimens were 94.2%、85.0%、80.5% and 95.8% respectively.HR-HPV was positive in 67 cases with CIN2+ on histology (67/70, 95.7%) and 83 cases with CIN1 on histology (83/107, 77.6%). Whereas the sensitivity, specificity, PPV and NPV of HC2 HPV testing were 95.7%、22.4%、44.7% and 88.9% respectively.

Table 1 p16/Ki67 dual stain in ASCUS, LSIL and ASCUS/LSIL follow-up with CIN1 and CIN2+

		CIN1	CIN2+
ASCUS	dual stain +	7(12.3%)	36(94.7%)
(n=95)	dual stain -	50	2
LSIL	dual stain +	9(18%)	30(93.8%)
(n=82)	dual stain -	41	2
ASCUS&LSIL	dual stain +	16(15.0%)	66(94.2%)
(n=177)	dual stain -	91	4

Conclusions: Our data demonstrated that P16/Ki-67 dual stain was able to identify underlying high grade dysplastic cells, suggested its potential utility in triaging ASCUS/LSIL cytology specimens.

407 Skip Metastasis in Lymph Node Staging of Lung Non-Small Carcinoma Using EBUS-FNA.

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Background: Metastasis to lymph nodes is often contiguous, with peribronchial and hilar nodes (N1) involved first, then ipsilateral mediastinal and sub-carinal second (N2) followed by contralateral, supraclavicular or scalene node (N3) involvement at the end. However, this pattern is often skipped in up 25% of metastasis (N1-N2+) significantly affecting the extent and sequence of N-staging. To what degree this occurs in EBUS-FNA staging has not been addressed adequately. The objective of this study is to assess skip metastasis in EBUS-FNA.

Design: This a retrospective correlational study in which we reviewed all cases of non-small cell carcinoma that were staged for N1, N2 and N3 node stations using EBUS-FNA in the period 2010-2018. Skip metastasis is defined as N1-N2+N3+ or N1+N2-N3+. Cases with or without metastasis and those with or without skip-metastasis were compared regarding age, gender, tumor location, tumor size and type using Student-t test, Chi squared or Fisher exact tests. Difference is considered significance at $p < .05$.

Results: During the study period, we identified 122 cases of non-small cell carcinoma that underwent EBU-FNA N-staging: 82 (67%) were N0 stage; 40 (33%) were NI, NII or NII stage. Age, gender ratio, primary lesion size and location were not significantly different for those with or without lymph node metastasis, Table. Cases with metastasis were less likely to be classified as adenocarcinoma. 18 (45%) of the metastasis were skip metastasis: 12 (30%) were N1-N2+N3+; 6 (15%) were N1-N2-N3+. Skip metastasis were more located in left lower and right upper lobes and tend to be smaller than non-skip metastasis.

Age, gender of subjects and tumor size and location of cases staged using EBUS-FNA cross-tabulated by presence of metastasis and its type.

	No Metastasis	Metastasis			*p Value
		No Skip Metastasis	Skip Metastasis	**P Value	
Age, mean (sd) yrs	68.5(10)	67.9 (9)	67.5 (11)	0.9	0.68
Female (%)	39 (47%)	8 (35%)	10 (56%)	0.37	0.94
Location				0.03	0.47
Left upper lobe	27 (33%)	5 (23%)	1 (6%)		
Left lower lobe	11 (13%)	3 (14%)	7 (39%		
Right upper lobe	23(28%)	3 (14%)	7 (39%)		
Right middle lobe	9 (11%)	3 (14%)	0 (0%)		
Right lower lobe	10 (12%)	8 (36%)	3 (17%)		
Multiple lobe	2 (2%)	NA	NA		
Size, mean (sd) cm	3.1 (1.8) cm	4.4 (2.5)	2.7 (1.5)	0.02	0.18
Type					
Adenocarcinoma	49 (60%)	8 (36%)	5 (28%)	0.72	0.001
Squamous cell carcinoma	25 (30%)	1 (5%)	1 (6%)		
Neuroendocrine	4 (5%)	7 (32%)	4 (22%)		
Non-small carcinoma (NOS)	4 (5%)	6 (27%)	8 (44%)		
Total	82	22	18		

* p Value for metastasis vs. non-metastasis

** p Value for non-skip vs. skip metastasis

Conclusions: Rate of N1-N2+ skip metastasis in EBU-FNA staging is similar to that reported for other procedures. N1-N-N3+ skip metastasis forms up to 1/3 of skip metastasis. This finding supports the current practice of sampling all nodes. Sampling N3 nodes first carries less risk of needle contamination than sampling N1or N2 nodes first, but the risk is still significant.

408 Correlation of Thyroid Imaging Reporting and Data System (TI-RADS) with Fine Needle Aspiration Cytology in the evaluation of thyroid nodules

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Disclosures: Lopa Modi: None; Wei Sun: None; Negin Shafizadeh: None; Raquel Negron: None; Melissa Yee-Chang: None; Aylin Simsir: None; Tamar Brandler: None

Background: Ultrasound (US) evaluation serves a key role in the management of thyroid nodules. The Thyroid Imaging Reporting and Data System (TI-RADS) was designed in 2017 to standardize thyroid US reports with risk stratification of thyroid nodules. TI-RADS uses a scoring system based on multiple US characteristics such as composition, margin, echogenicity, calcification, and shape. TI-RADS divides thyroid nodules into five categories (TR1 toTR5) to signify which nodules require fine needle aspiration (FNA) versus continued US surveillance. FNA is recommended for thyroid nodules with TR3 if ?2.5 cm, TR4 if ?1.5 cm and TR5 if ?1 cm. FNA cytology results are reported in The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) in which each category (BI-BVI) serves to risk-stratify nodules and is linked to a certain risk of malignancy. Our aim was to correlate the TI-RADS scores with the FNA diagnoses to determine if TI-RADS recommendations are justified in selection of nodules for cytologic evaluation.

Design: A retrospective review of cases with thyroid nodules from 1/1/2018-8/30/2018 was performed. Only patients with US reports including TI-RADS scores and FNA reports with TBSRTC classification were included in the study.

Results: 198 thyroid nodules were identified. 66/69 TR3 cases (95.7%) were reported as Bethesda (B) category II (BII, benign) the remaining 3 cases were B III (atypia of undetermined significance, AUS/FLUS). BII cases accounted for 80% and 69.7% of TR4 and TR5 cases; whereas BVI cases constituted 1.1% and 18.2% of TR4 and TR5 cases, respectively (Table 1).

Table 1:

TI-RADS	Age (mean, years)	Nodule Size (mean, cm)	BI n(%)	BII n(%)	BIII n(%)	BIV n(%)	BV n(%)	BVI n(%)	Total (n)
TR1			0	0	0	0	0	0	0
TR2	53.5	2.42	1 (16.7%)	4 (66.7%)	1 (16.7%)	0	0	0	6
TR3	56.9	2.83	0	66 (95.7%)	3 (4.3%)	0	0	0	69
TR4	59.1	2.28	0	72 (80.0%)	12 (13.3%)	3 (3.3%)	2 (2.2%)	1 (1.1%)	90
TR5	53.7	1.68	0	23 (69.7%)	4 (12.1%)	0	0	6 (18.2%)	33
Total			1	165	20	3	2	7	198

Conclusions: A decrease in benign TBSRTC diagnoses and increase in the indeterminate to malignant TBSRTC diagnoses were noted as TI-RADS scores increased. However, majority of the FNA diagnoses were benign regardless of the TI-RADS category even in the TR4 (moderately suspicious) and TR5 (highly suspicious) categories. These findings suggest that the TR4 and TR5 category levels may need to be renamed using less threatening language to prevent unnecessary patient anxiety associated with reading a "moderately or highly suspicious" radiology report.

409 Malignant Mesothelioma - NanoString PanCancer gene pathway signal transduction RNA analysis of routine clinical cytology effusion samples

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Disclosures: Cara Monroe: None; Joon-Yong Chung: None; Kris Ylaya: None; Armando Filie: None; Stephen Hewitt: None; Mark Roth: None

Background: NanoString is a high throughput RNA based platform and has emerged as a promising technology for multiplex RNA detection. This overcomes some limitations of RNA quality in clinical samples and is well suited to clinical cytology given its ability to measure even small fold changes of a single transcript present at low copy levels per cell. The aim of our study is to utilize NanoString's PanCancer gene panel to identify how RNA expression may differ between routine clinically benign and malignant mesothelial effusions to compliment morphologic assessment.

Design: Eleven (11) routine clinical cytology effusion samples representing benign, reactive mesothelial cells (n=5) and malignant mesothelioma (n=6) were examined via RNA extraction from formalin-fixed, paraffin-embedded (FFPE) unstained cell block sections. RNA quantity and quality were assessed using a NanoDrop spectrophotometer and the Agilent 2100 Bioanalyzer. Furthermore, we performed quantitative real-time reverse transcription polymerase chain reaction (RT-qPCR) using the TaqMan® Gene Expression reagent. The cycle threshold (Ct) values for protein tyrosine phosphatase, receptor type C (*PTPRC*/CD45) and beta-actin (*ACTB*) genes were examined prior to application of samples to the NanoString PanCancer Gene panel. Data analysis to determine genes represented within reactive and malignant mesothelial cell populations was performed with R-based NanoString nSolver.

Results: All samples used in the final analysis were amplified via RT-qPCR including a reference sample of Jurkat cells. The nCounter technology of the PanCancer Gene panel successfully and reproducibly detected RNA gene expression of low, medium and high abundance transcripts in all clinical samples, with FGF7 and ITGB4 expression over twenty-fold higher in malignant than benign effusions after normalization. Preliminary hierarchical agglomerative cluster analysis successfully distinguished benign from malignant effusions.

Conclusions: In summary, these efforts may provide diagnostic, prognostic and therapeutic information that was previously unobtainable for a variety of clinical cytology samples and may minimize the need for more invasive approaches. It enhances the diagnostic utility of routine cytology samples and potentially assists with the identification and therapeutic monitoring of biologic targets. This approach is a potentially cost-effective and minimally invasive methodology for future molecular diagnostics and therapeutics to facilitate clinical management.

410 Cytology Rapid On-Site Evaluation of Bone Lesions - an Institutional Study of 283 Cases Over a Two-year Period

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Disclosures: Paloma Monroig-Bosque: None; Paul Christensen: None; Haijun (Steve) Zhou: None; Dina Mody: None; Alberto Ayala: None

Background: Cytology rapid on-site evaluation of bone related lesions is challenging, especially for primary bone neoplasms.

Design: In this study, we retrospectively reviewed 283 bone cytology reports from January 2016 to June 2018. The reporting rates (RR) and risk of malignancies (ROM) for the procedures performed in our eight-hospital system were determined (Table 1). Using corresponding histology diagnoses we stratified samples into hematological malignancies, metastasis and primary bone tumors to determine our cytology false negative rate for neoplastic lesions (Table 2).

Results: The RR and ROM for each diagnostic category are summarized in Table 1. Samples determined negative for malignancy (NM) had a 1.4% ROM. Cases among the atypical (AT), suspicious for malignancy (SM) and positive for malignancy (PM) categories had an 85%, 55% and 96% ROMs, respectively. The sensitivity and specificity in detecting neoplastic lesions of the combined positive (AT, SM and PM) categories was 96% and 83%, respectively. The positive likelihood ratio (LR) of a patient having a neoplastic lesion within all positive categories was 5.7. Among 180 neoplastic cases with satisfactory cytology specimen, only 8 false negative cytology diagnoses were observed (4%). Within the subgroup of primary bone neoplasms, the cytology evaluation sensitivity and specificity were 85% and 83% (LR = 5.1), and the false negative rate was 5%.

	Cases	RR	ROM	Sensitivity	Specificity
Unsatisfactory (UN)	49	17%	24%	-	-
Negative for Malignancy (NM)	53	19%	8%	-	-
Atypical (AT)	13	5%	85%	58%	96%
Suspicious for Malignancy (SM)	31	11%	55%	78%	96%
Positive for Malignancy (PM)	137	48%	96%	94%	90%
Total	**283**	**100%**	**-**	**-**	**-**

Table 1. Number of Cases with Reporting Rate (RR), Risk of Malignancy (ROM), Sensitivity and Specificity.

Figure 1 - 410

	Neoplastic/Malignant
Hematological malignancies	**38**
AT	7
SM	8
PM	23
Metastasis	**116**
NG	4
AT	3
SM	5
PM	104
Primary bone lesions	**26**
NG	4
AT	1
SM	16
PM	5
Grand total	**180**

Table 2: Cytology specimens with neoplastic/malignant diagnoses in their corresponding surgical specimens.

Conclusions: Cytology rapid on-site evaluation is a cost-effective tool to triage bone lesions. In our institution, cytology rapid on-site evaluation for primary bone neoplasms achieved high diagnostic sensitivity and specificity.

411 Serial Fine Needle Aspiration (FNA) Allows Direct Sampling of Low-grade Lymphoma Tumor Nodules and Subsequent Analysis of the Tumor and Its Microenvironment in Clinical Trial Patients Receiving Immunotherapy

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Disclosures: Kelly Mooney: None; Steven Long: None; Brock Martin: None; Matthew Frank: None; Debra Czerwinski: None; Ronald Levy: None; Xiaojie Guo: None; Tanaya Shree: None; Rachel Greenstein: None

Background: Fine needle aspiration (FNA) is used in clinical practice to reliably sample lymph nodes for morphologic and flow cytometric analysis. Recent reports have also described the use of FNA to sample tumor immune microenvironments. This study describes our experience using FNA to directly and serially sample low-grade lymphoma tumors and the associated tumor immune microenvironment during immunotherapy clinical trials. To our knowledge, this is the largest study of FNAs performed on clinical trial patients profiling immune microenvironment changes over time.

Design: FNA samples were collected from patients during four IRB-approved low-grade B cell lymphoma immunotherapy clinical trials at our institution from 9/2013 to 9/2018. Biopsy was attempted at least three least three times sequentially for each tumor using 23-gauge needles. Cell yield, sample viability, and sample adequacy data were recorded. An “adequate” sample yielded sufficient cellularity for at least one 14-color flow cytometry panel (1*10^5 cells), which quantified as well as characterized malignant tumor cells, CD4+ effector T cells, CD4+ regulatory T cells, CD4+ T follicular helper cells, and CD8+ T cells. Categorical variables were compared using Fisher’s exact tests.

Results: Over five years, 224 FNAs were performed on 36 clinical trial patients (average number of FNAs per patient = 6, range 2-11). FNA samples were adequate in 192 cases (90%), and insufficient in 18 (10%). Mean cell yield was 11*10^6 cells, and median number of flow cytometry panels per sample was four (range 0-5). For all but one patient, FNA yielded adequate samples to measure cell population changes over time (Figure 1). Pre-therapy samples were more likely to be adequate compared to post-therapy samples (97% vs 88%, p=0.04). FNA samples yielded data showing differences in tumor and lymphocyte populations over time, and between FNA samples and matched peripheral blood samples (Figure 2). The research team experience with the FNA method was positive (Table 1).

Table 1. Advantages of fine-needle aspiration (FNA) using ultrasound-assisted adequacy assessment as a clinical trial methodology

Advantage	Details
Preservation of targeted lesion and cell number	-Compared to biopsy, does not compromise tumor integrity, allowing continued monitoring of tumor response via imaging -Does not waste any cells on smear preparations for on site evaluation
Convenience for doctor and patient	-Uses transportable FNA kits and ultrasound equipment -Does not waste time on smear preparation, staining, and adequacy evaluation on site -Relatively well-tolerated by patients with little to no recovery time
Efficacy	-Can be used for multiple ongoing trials -Facilitates serial sampling of the same target lesions -Allows sampling of directly treated and non-treated tumor nodules to evaluate systemic effects of therapy -Ultrasound allows visualization of lymph node hilum
Cost-effectiveness	-Less expensive compared to interventional radiology or surgical biopsy techniques

Figure 1 - 411

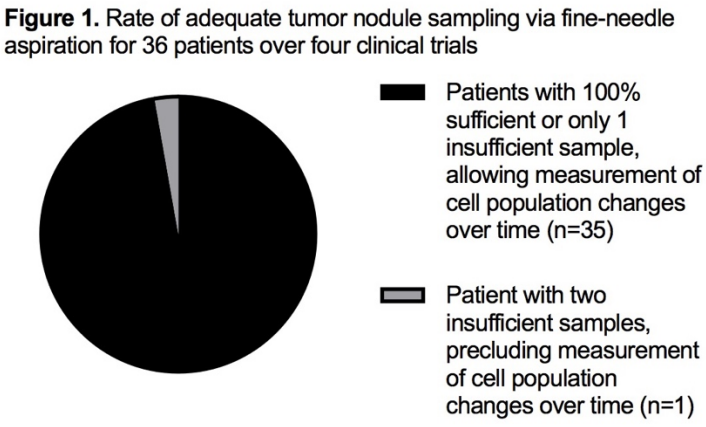
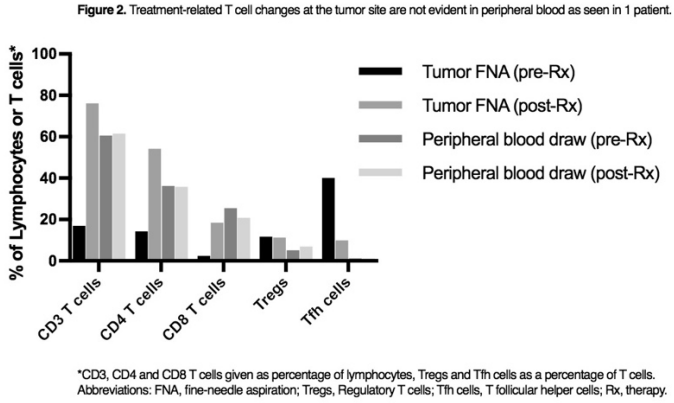


Figure 2 - 411



Conclusions: This is the first study using serial FNAs to evaluate changes in tumor cell and associated immune microenvironment cell populations over time in multiple clinical trials, including comparison with matched peripheral blood results. FNA is an easy, well-tolerated, and cost-effective way to sample tumors and their associated microenvironments directly from patients, and opens new opportunities for cellular and immunological analysis in the fields of cancer and immunotherapy.

412 Risk of High Grade Squamous Intraepithelial Lesions in 21-25 Year Old Women Before and After 2012 Changes in the USPSTF Recommendations for Cervical Cancer Screening

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Disclosures: Christopher Morris: None; Zahra Maleki: None; Sayanan Chowsilpa: None; Erika Rodriguez: None

Background: In 2012, the USPSTF changed the recommendations for cervical cancer screening, decreasing the frequency to once every 3 years from at least every 3 years. Additionally, the USPSTF recommended against testing women younger than 21 regardless of sexual history. As this significantly decreased the screening in the population, there was the question of whether this might lead to higher grade lesions at the time of diagnosis.

Design: We evaluated all of the cytopathologic cervical cancer screening (Pap smears) performed at the Johns Hopkins Hospital in 21-25 year old females in the years of 2011 and 2017. Odds ratios for high grade or at least potentially high grade lesions (HSIL, ASC-H and LSIL-H) were calculated to determine if there was a change in the rate of high grade lesions in 2017 compared to 2011. To evaluate potential differences in cytopathologic accuracy, the electronic medical record was searched for cervical surgical pathology specimens for each patient and results were correlated. Finally, all pap smears that had concurrent testing for high risk HPV (hrHPV) were correlated with cytopathologic diagnosis.

Results: There was a sizeable decrease in the number of pap smears performed at Johns Hopkins between 2011 (3,930) and 2017 (2,048). Additionally, there was a decrease in the number of High grade lesions (odds ratio of 0.36, confidence interval 0.15-0.86), or at least potentially high grade lesions (HSIL, ASC-H, LSIL-H) (odds ratio 0.46, confidence interval 0.3-0.7). Surgical pathologic diagnoses in these patients corroborated these findings with a 43% decrease in the number of high grade lesions and similar rates of correlation between cytopathologic and surgical pathologic diagnoses between the two years. Concurrent hrHPV was performed on 668 of the samples from 2011 with 51% positivity and 331 of the samples from 2017 with 52% positivity.

Pap Diagnosis	2011	2017
NILM	3341 (85%)	1725 (84%)
ASCUS	317 (8.1%)	180 (8.7%)
ASC-H	44 (1.2%)	14 (0.69%)
LSIL	156 (4.0%)	115 (5.6%)
LSIL-H	36 (0.9%)	7 (0.34%)
HSIL	32 (0.8%)	6 (0.29%)
AGC	4 (0.1%)	1 (0.05%)

Conclusions: Despite the decrease in the overall number of cytologic tests performed for cervical cancer screening, there was no increase in the number of high grade lesions from 2017 compared to 2011. Instead, we saw a decrease in the odds ratio of high grade or potentially

high grade lesions from 2017 compared to 2011. While cytopathologic screening has limitations, similar rates of correlation with surgical pathology between the two years are suggestive that the decrease accurately reflects a change in the rate of high grade lesions within the 21 to 25 year old female population treated at the Johns Hopkins Hospital.

413 Risk of High Grade Squamous Intraepithelial Lesions in 26-29 Year Old Women Before and After 2012 Changes in the USPSTF Recommendations for Cervical Cancer Screening

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Disclosures: Christopher Morris: None; Sayanan Chowsilpa: None; Zahra Maleki: None; Erika Rodriguez: None

Background: The 2012 update to the guidelines for cervical cancer screening decreased the recommended screening interval to once every 3 years from at least every 3 years. This change, along with the recommendation against screening women younger than 21 years of age regardless of sexual history reduced screening in the population. Decreasing the frequency of screening carries the inherent risk that patients may present with higher grade lesions.

Design: The electronic database was searched to determine all cytopathologic cervical cancer screening (Pap smears) performed on 26-29 year old women in 2011 and 2017 at the Johns Hopkins Hospital. The odds ratio for being diagnosed by pap-smear with a high grade or at least potentially high grade lesion in 2017 compared to 2011 was calculated. This was correlated with testing for high risk HPV (hrHPV) and follow up surgical pathology diagnoses. Slides from pap smears that were not called ASC-H, LSIL-H or HSIL but correlated with a high grade lesion on surgical pathology were reviewed.

Results: As expected, there was a decrease in the number of pap smears performed at Johns Hopkins between 2011 (3,676) and 2017 (2,013). Concurrent hrHPV was performed on 571 of the samples from 2011 with 37% positivity and 480 of the samples from 2017 with 34% positivity. While the total number of pap smears diagnosed as high grade or at least potentially high grade (HSIL, ASC-H, LSIL-H) was lower in 2017 (41) compared to 2011 (73), follow up Surgical pathologic diagnoses in these patients revealed that 32 pap smears in 2017 correlated with a high grade lesion on surgical pathology compared to 27 in 2011. A review of the pap-smear slides revealed that any underdiagnosis on pap-smear was likely due to sampling.

Pap Diagnosis	2011	2017
NILM	3312 (90%)	1763 (87.5%)
ASCUS	199 (5.4%)	134 (6.7%)
ASC-H	31 (0.84%)	15 (0.75%)
LSIL	89(2.4%)	74 (3.7%)
LSIL-H	17 (0.46%)	6(0.30%)
HSIL	25 (0.68%)	20 (0.99%)
AGC	3 (0.08%)	1 (.05%)

Conclusions: Despite similar odds of being diagnosed with at least a potentially high grade lesion between 2011 and 2017, there was a higher percentage of pap smears in 2017 that correlated with a high grade lesion on surgical pathology (1.6% compared to 0.7%). Total numbers of cases that were called HSIL on surgical pathology were similar between the two years.

414 Utility of ultrasound-guided fine needle aspiration for the initial evaluation of satellite lesions of index invasive mammary carcinoma

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Disclosures: Shima Mousavi: None; Tanya Moseley: None; Nour Sneige: None; Savitri Krishnamurthy: None

Background: The role of ultrasound-guided fine needle aspiration (US-FNA) for the investigation of satellite breast lesions, whose status affects treatment, is not well recognized. The primary objective of our study was to assess the utility of US-FNA for the initial categorization and marking of satellite lesions in patients with core needle biopsy (CNB) proven invasive carcinoma.

Design: Patients who underwent US-FNA for the evaluation of one or more satellite lesions during a one year period were identified from our institution's pathology files. Radiologists performed US-FNA, and cytopathologists immediately evaluated the Papanicolaou and Diff-Quik stained smears and categorized the lesions as benign, atypical, suspicious, or malignant. Lesions categorized as malignant, suspicious, and atypical were immediately clipped. The sensitivity, specificity, accuracy, positive and negative predictive values of US-FNA

for the evaluation of satellite lesions were determined based on the correlation of the results with histopathology findings in the surgical excision.

Results: We identified 112 US-FNA of satellite lesions ranging from 0.3 to 2.5 cm (mean, 0.8 cm) in 96 patients age 26-79 years (mean, 52 years). Index invasive carcinomas ranged from 0.7 to 7.5 cm (mean, 2.8 cm) including 85 (88%) ductal carcinoma and 11 (12%) lobular carcinoma belonging to luminal A (64), Luminal B(10), HER2(5)and triple negative (17)genomic types. Among the 112 satellite lesions, 24(21%) were categorized as benign, 11 (10%) as atypical, 8 (7%) as suspicious, and 69 (62%) as malignant. Marker clips were placed in the 87 satellite lesions. Of the 96 patients, 58 (60%) received neoadjuvant chemotherapy; 40 (42%) underwent segmental mastectomy, 48 (50%) underwent skin sparing mastectomy, and 8 (8%) underwent radical mastectomy. The sensitivity, specificity, accuracy, positive and negative predictive value of US-FNA for the evaluation of satellite lesions was 98.7%, 100%, 99%, 100%, and 97%, respectively.

Conclusions: US-FNA is a sensitive and specific test for the categorization of satellite lesions of index lesions of CNB-proven invasive mammary carcinoma. US-FNA with immediate assessment enables immediate clipping of malignant or suspicious lesions, thereby facilitating appropriate surgical management or monitoring of response to chemotherapy and the identification of the lesions in the surgical specimen.

415 The Efficacy of HPV16/18 Genotyping in Women with Pap-/HPV+ Co-testing Results in a Cervical Cancer Screening Population and a Cancer Surveillance Population

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Disclosures: Shima Mousavi: None; Uma Kundu: None; Ming Guo: None

Background: The aim of the study was to evaluate the efficacy of HPV16/18 genotyping in predicting high-grade cervical intraepithelial lesions in women with Pap-negative/HPV-positive co-testing results in a cervical cancer screening population and a cancer surveillance patient population in our institution.

Design: We retrospectively reviewed data from our institutional database to identify patients from either the Cancer Prevention Center (CPC) or the Gynecologic Oncology Clinic (GOC) who had a negative result for Pap cervical cytology (SurePath) and a positive result for high-risk HPV (hrHPV; Cervista HPV HR) on co-testing, with a reflex HPV16/18 genotyping result (Cervista HPV16/18), during the period 2012-2018. Each patient's follow-up data for up to 3 years after the index Pap/HPV co-testing were collected to compare the efficacy of the HPV16/18 testing in predicting high-grade cervical intraepithelial lesion (HSIL) in the two centers. The Fisher exact test was used to compare the efficacy of HPV16/18 genotyping in the two groups of patients.

Results: A total of 255 women in the CPC (age range 23-71 years, mean 52) and 194 women in the GOC (age range 24-75 years, mean 47) were included in the study. The HPV16/18 result was positive in 26.3% of women from the CPC and 28.9% of women from the GOC. The review of the follow-up Pap cytology/biopsy showed that a positive HPV16/18 result predicted more HSIL than a positive non-16/18 HPV result in both populations, although the difference was significant only in the women from the CPC (14.9% vs 4.8%, *P*=0.01) and not in the women from the GOC (9% vs. 3.6%, *P*=0.156). The distributions of the follow-up results stratified by HPV16/18 genotyping results are illustrated in Figures 1 and 2.

Figure 1 - 415

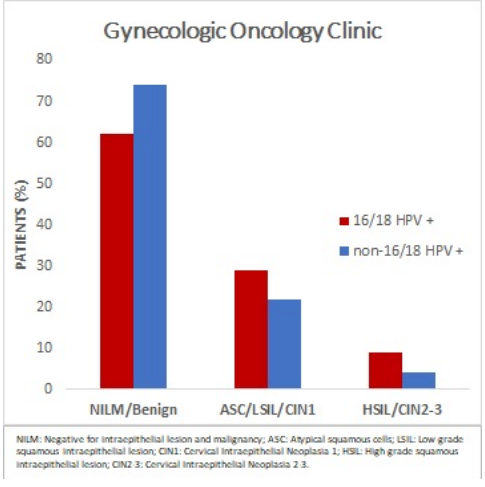
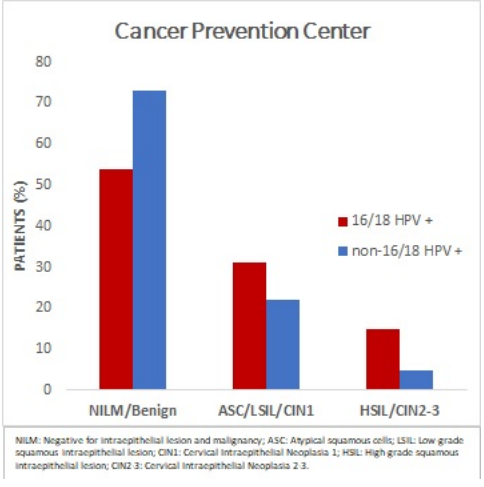


Figure 2 - 415



Conclusions: HPV16/18 genotyping for HSIL had a significantly greater efficacy in predicting HSIL in a low-risk screening population than in a high-risk cancer surveillance population in our institution. Women with a negative Pap result but a positive hrHPV result are still at risk of developing HSIL. Close follow-up monitoring with Pap/HPV co-testing is necessary for these patients.

416 Fine Needle Aspiration Cytology of Benign and Malignant Soft Tissue and Bone Tumors: an institutional experience over a 10-year period.

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Disclosures: Stephanie Muller: None; Sara Fasking: None; Dorota Rudomina: None; Narasimhan Agaram: None

Background: Soft tissue and bone tumors are rare tumors of mesenchymal origin. The rarity of these tumors leads to a relative lack of expertise among pathologists, thereby presenting a diagnostic challenge. The diversity and complexity of the classification also adds to the diagnostic difficulty. We have noticed an increase in the number of soft tissue and bone cytology specimens over the last few years. We hereby report our experience of fine needle aspiration (FNA) cytology in the diagnosis of benign and malignant soft tissue and bone tumors over a 10 year period in a large cancer center.

Design: A search of the cytology data base for soft tissue and bone lesions with a primary diagnosis of “Positive for sarcoma” and “Neoplastic cells present” over a 10 year period from January 2008 to July 2018 was performed. The cases included fine need aspiration cases and well as ‘touch preparations’ of core needle biopsies performed during rapid onsite evaluation (ROSE). Cytopathology reports, and corresponding surgical pathology reports, if available, were reviewed to determine the subtype of tumor. Cases with diagnosis of primary soft tissue and bone tumor entities were selected.

Results: 1453 cases were identified in all. The results are tabulated in the table. 856 (59%) of the cases were reported in the last 3 year period compared to 41% in the first 7 years. 923 (63%) of the cases had a primary diagnosis of 'Positive for Sarcoma' while 530 (37%) of the cases were reported as 'Neoplastic cells present'. Among the ‘Neoplastic cells present’ cases, gastrointestinal tumors (GIST) were the most common representing 19.6% of the cases followed by benign peripheral nerve sheath tumors (18.8%) and desmoid-type fibromatosis (9.4%). Miscellaneous group represented 27.7% of the cases. In the ‘Positive for Sarcoma’ group, Undifferentiated Pleomorphic Sarcoma (UPS) was the most common entity representing 19.3% of the cases followed by Dedifferentiated Liposarcoma (DDLS,18.6%) and Leiomyosarcoma (LMS,14.5%). Miscellaneous group represented 15.9% of the cases.

Case Type	Total (%)	Case Type	Total (%)
Positive for Sarcoma (total)	923	Neoplastic Cells Present (total)	530
Undifferentiated Pleomorphic Sarcoma	179 (19.3)	Gastrointestinal Stromal Tumor	104 (19.6)
Dedifferentiated Liposarcoma	172 (18.6)	Peripheral Nerve Sheath tumor (Schwannoma, Neurofibroma)	100 (18.8)
Leiomyosarcoma	134 (14.5)	Desmoid-type fibromatosis	50 (9.4)
Synovial sarcoma	66 (7.1)	Tenosynovial Giant Cell Tumor	39 (7.3)
Chondrosarcoma	58 (6.2)	Solitary Fibrous Tumor	25 (4.7)
Myxofibrosarcoma	53 (5.7)	Lipomatous Neoplasms	24 (4.5)
Myxoid Liposarcoma	50 (5.4)	Myxoma	22 (4.1)
Angiosarcoma	30 (3.3)	Cartilaginous Neoplasms	19 (3.5)
Epithelioid sarcoma	23 (2.5)	Miscellaneous	147 (27.7)
MPNST	11 (1.2)		
Miscellaneous	147 (15.9)		

Conclusions: Cytopathology is being increasingly used in the diagnosis of primary benign and malignant tumors of soft tissue and bone. UPS, DDLS, LMS, GIST and peripheral nerve sheath tumors were some the most common tumors biopsied in our institution. Awareness of soft tissue and bone tumor entities and their cytopathologic features is essential to the practicing cytopathologist, especially in large tertiary care centers.

417 Correlation of TIRADS Score with Cytologic and Histologic Findings: A One Year Single Institutional Retrospective Review of 275 Thyroid Nodules

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Disclosures: Mohamed Mustafa: None; Kristen Partyka: None; Harvey Cramer: None; Howard Wu: None

Background: Based on specific sonographic features, the American College of Radiology has proposed the Thyroid Imaging, Reporting and Data System (TIRADS) as a tool for risk stratification of thyroid lesions. Five categories can be assigned, ranging from TR1 (benign) to TR5 (highly suspicious). The TIRADS classifications are intended to guide clinicians who use thyroid ultrasound for the management of adult patients with thyroid nodules.

Design: A computerized search of our pathology data system was conducted for a one-year period (September 2017-August 2018) to identify all thyroid fine-needle aspiration (FNA) cases with a preceding thyroid ultrasound that was assigned a TIRADS score. FNA diagnoses based on the Bethesda System (TBS), follow-up histologic diagnoses, and any molecular testing were recorded for each case.

Results: 275 nodules were identified from 208 patients (age 19-89, mean=65), including 163 females and 45 males. 39 patients had 2 nodules aspirated, 10 patients had 3 nodules aspirated, and 1 patient had 4 nodules aspirated. The size of the nodules ranged from 0.4 to 9 cm (mean 2.4 cm). The findings are summarized in the table below. Molecular testing (7 Afirma and 1 Interpace) was performed on 8 indeterminate aspirates (7 FLUS and 1 FN). Of these, abnormal results were noted in 7 patients, and a benign result was noted in 1 patient. Three of 8 patients underwent thyroidectomy. Histology showed 1 papillary thyroid carcinoma, 1 nodular hyperplasia, and 1 noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP).

TIRADS score	Number (Histology)	TBS I ND	TBS II Benign	TBS III AUS/FLUS	TBS IV SFN/FN	TBS V Suspicious	TBS IV Malignant
1	1 (1)		1 (1 NH)				
2	5 (1)		5 (1 NH)				
3	76 (6)	2	59	9 (1 FA, 1 NIFTP)	5 (1 PTC, 1FA, 1 NH)		1 (1 PTC)
4	151 (11)	5	121 (1 NH)	13 (2 NH)	4 (1 HCA)	4 (3 PTC)	5 (4 PTC)
5	42 (7)	3	24	5	4 (1 HCA, 1 FC and 2 NH)		6 (3 PTC)
Total	275 (26)	10 (0)	209 (3)	27 (4)	13 (8)	4 (3)	12 (8)

FA: follicular adenoma; NIFTP: noninvasive follicular thyroid neoplasm with papillary-like features; NH: nodular hyperplasia; PTC: papillary thyroid carcinoma; HCA: Hürthle cell adenoma; FC: follicular carcinoma

Conclusions: TIRADS 4 is the most common category associated with patients referred to FNA (151/275, 55% of cases). The most common cytologic diagnosis was benign (209/275, 76%). TIRADS 3, 4, and 5 are associated with suspicious and malignant pathology in 3%, 6%, and 14% of cases, respectively. No cancers were identified in any of the cases diagnosed by FNA as ND, Benign, or AUS/FLUS irrespective of the TIRADS score.

418 Variants of Well Differentiated Neuroendocrine Tumors: A Cytomorphologic Analysis of 74 Cases with Clinical Correlation

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Disclosures: Shannon O'Brien: None; Alex Clavijo: None; Mohammad Mohammad: None; Kim HooKim: None; Yue Xue: None; Michelle Reid: None

Background: Well differentiated neuroendocrine tumors (WDNET) have classic cytomorphology including clusters and singly dispersed plasmacytoid cells with round nuclei, “salt and pepper” chromatin, inconspicuous nucleoli, scant cytoplasm and minimal pleomorphism. While the majority of WDNETs show these classical features, unusual histologic variants have been described. The extent of this variability and potential clinical implications has not been examined in cytologic specimens.

Design: Fine needle aspiration smears, cell blocks (and core biopsies, where available) of 74 WDNETs were blindly reviewed and assigned a variant classification (Table 1). The cytopathologist was blinded to tumors’ origin and clinical associations. Accompanying Ki67 immunohistochemical stains were also reviewed and cases were graded using the 2017 WHO guidelines as G1 or G2. Clinicopathologic data, grade, and extent of cytomorphologic variants were recorded. Variants were only assigned if >50% of tumor cells showed that morphology.

Results: There were 40 males and 34 females, of mean age 61 (range 26-87). Tumor locations included: 32 pancreas, 20 liver, 8 lung, 7 lymph nodes, and 7 other (mesentery, etc.). Of the 74 cases, 23 (31%) were classical, 14 (19%) oncocytic, 8 (11%) cohesive, 7 PTC-like, 6 lipid rich, 5 papillary/solid pseudopapillary neoplasm (SPN)-like, 4 lymphocyte-like, 3 pleomorphic, 2 rhabdoid, and 2 spindled (Figures 1 and 2). Oncocytic variant tended to be from pancreatic primaries (9/14, 64%), had higher Ki-67 (mean 5.2%) were more aggressive with T3/T4 stage on resection and regional and distant metastasis in 90%. "Cohesive" morphology was more frequently seen in luminal gastrointestinal (GI) primaries (63%) compared to pancreas (12%). Although not recorded as a variant, cytoplasmic granules were also more commonly seen in luminal GI primaries (40%) compared to pancreas (22%). Taken together, 67% of cohesive variant with cytoplasmic granules were associated with luminal GI primaries.

Variants	Cytomorphology	Misdiagnosis
Classical	Clusters and singly dispersed plasmacytoid cells with round nuclei, "salt and pepper" chromatin, inconspicuous nucleoli, and scant cytoplasm with minimal pleomorphism	
Oncocytic	Abundant oncocytic cytoplasm	HCC
Cohesive	Large cohesive clusters of cells	Basalioid SCC, small cell carcinoma
PTC-like	Cleared out chromatin with nuclear grooves and inclusions	Papillary thyroid carcinoma
Lipid rich	Numerous small lipid droplets within the cytoplasm	Renal cell carcinoma, adrenocortical carcinoma
Papillary/SPN-like	Papillary: Prominent papillary architecture with true fibrovascular cores SPN-like: Papillary architecture with monotonous ovoid cells containing nuclei with grooves	Solid pseudopapillary neoplasm
Lymphocyte-like	Discohesive cells with scant cytoplasm and naked nuclei	Benign lymphocytes, Small cell lymphoma
Pleomorphic	3 fold variation in nuclear size and shape	Carcinoma
Rhabdoid	Numerous rhabdoid-like cells with eccentrically placed nuclei and large red globule in the cytoplasm	Rhabdoid sarcoma
Spindled	Abundant spindle or ovoid cells with tapered ends	Schwannomas and gastrointestinal stromal tumors

Figure 1 - 418

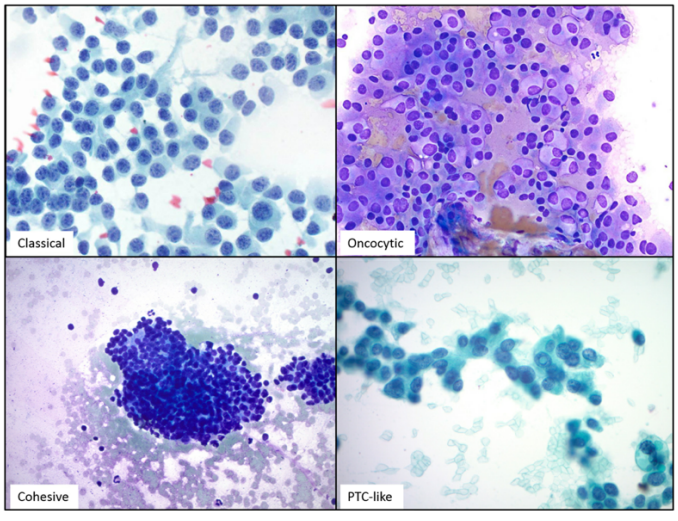
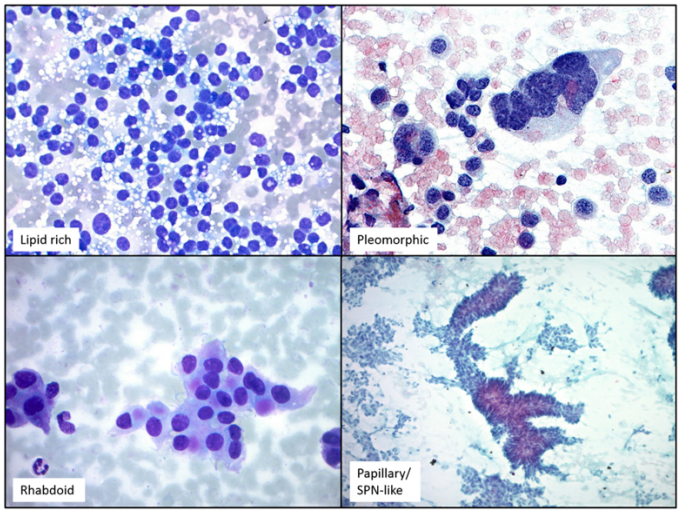


Figure 2 - 418



Conclusions: The cytomorphologic spectrum of WDNET is quite extensive. Recognition of variants is important as specific ones (particularly oncocytic) have strong association with aggressive behavior and higher rates of metastasis. Our results show that certain associations (oncocytic with pancreas and cohesive, granule-rich with luminal GI primaries) can be exploited in the assessment of metastatic WDNET with unknown primary sites. Cytopathologists should be aware of these variants so as not to misdiagnose these unusual cases.

419 Utility of SMAD4 and p53 Immunocytochemistry in Endoscopic Ultrasound-Guided Fine Needle Aspiration Diagnosis of Pancreatic Ductal Adenocarcinomas

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Disclosures: Maria Olave: None; Esther Yoon: None; Marie Robert: None; Adebowale Adeniran: None; Guoping Cai: None

Background: Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) is the method of choice for the diagnosis of pancreatic adenocarcinomas. However, up to 20% of EUS-FNA biopsies yield indeterminate diagnoses of either atypical or suspicious for malignancy. Application of ancillary tests, including immunocytochemistry and molecular testing may help improve diagnostic yield. In this retrospective study, we aimed to evaluate expression of SMAD4 and p53 in malignant and benign pancreatic FNA specimens and to explore the utility of these markers for risk stratification in cases with an indeterminate diagnosis.

Design: EUS-FNA cellblocks from 22 cases of pancreatic ductal adenocarcinoma (PDA), 11 cases with an indeterminate diagnosis and 5 cases with benign diagnoses were stained with p53 and SMAD4 antibodies. For p53, diffuse positivity or null expression pattern was considered positive while wild type pattern was interpreted as negative. A complete loss of SMAD4 staining was considered a positive result. In all indeterminate cases, *KRAS* mutation analysis was also performed.

Results: Sixteen of 22 PDA cases (72%) showed complete loss of SMAD4, and 21 out of 22 (95%) were p53 positive. All 5 benign cases showed preservation of SMAD4 expression and negative p53 result except for one case in which p53 was positive. In cases with an indeterminate diagnosis, positive p53 result, SMAD4 loss and *KRAS* mutation were seen in 8 (73%), 4 (36%), and 4 of 11 (36%) cases, respectively. Interestingly, 7 of 8 positive p53 cases, all 4 SMAD4 loss cases and all 4 *KRAS* mutated cases had confirmed malignancy on follow-up. SMAD4 loss and *KRAS* mutation were concurrent in only 2 of 4 cases. Overall, the calculated sensitivity and specificity for diagnosing PDA were 93% and 88% for p53 and 67% and 100% for SMAD4, repsectively.

Conclusions: Our results demonstrate that Immunocytochemical analysis of p53 and SMAD4 have high sensitivity and specificity for the diagnosis of PDA. In cases with an indeterminate cytological diagnosis, p53 and SMAD4 expression could have adjunctive value to *KRAS* mutation analysis, especially in those with negative *KRAS* mutation status.

420 Annual Surgical Removal Rate of Thyroid Lesions Before and After the Molecular Testing Era: Outcomes from the National Inpatient Sample Database (2009-2014)

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Disclosures: Diana Oramas: None; Odile David: None; Harry Fuentes: None

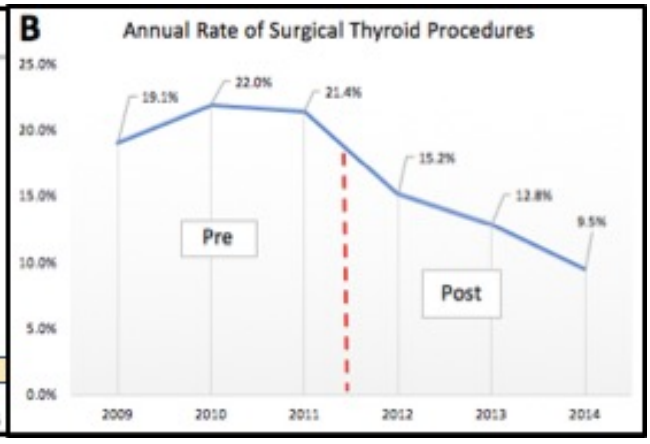
Background: Prior to the advent of ancillary molecular testing for cytologically indeterminate thyroid lesions there was a higher rate of surgical intervention for nodules that ultimately were benign. By 2012 ancillary molecular testing was widely used not only in academic but also in private practice, reducing unnecessary surgical interventions and resulting in better resource allocation in the care of these patients at the institutional level. However, at the national level the impact of ancillary molecular testing on the removal rate of thyroid lesion has not been established. The aim of this study is to assess the national trends of annual removal rate of thyroid lesions in the pre- and post-molecular testing era.

Design: Data were obtained from National Inpatient Sample (NIS) database files from 2009 to 2014. The NIS is part of the Healthcare Cost and Utilization Project, a family of healthcare databases and related software tools and products developed through a federal/state/industry partnership and sponsored by the Agency for Healthcare Research and Quality. Using ICD-9 diagnosis and procedures codes, we identified patients with thyroid disorders who underwent thyroid surgical intervention. We considered the pre-molecular testing era the years before 2012. We used descriptive-statistics to describe baseline characteristics, chi-squared-test to compare the proportions between groups and the Kendal-tau-test for trend analyses. All statistics were conducted in SPSS-25.

Results: We identified a total of 239,266 patients with thyroid lesions who underwent a surgical thyroid procedure. No major differences in baseline characteristics were found (Fig.1A). The overall removal rate in the pre-molecular testing group was 62.5% compared to 37.5% in the post-molecular testing group (Dif:25%, 95 CI: 24.6-25.4, p <0.01) (Fig.1B). Although we noted the median total charges were significantly higher in the post-molecular testing group (Pre: $22,299 vs Post: $28,167.5, p <0.01) we did not perform a formal cost effectiveness analysis as this was beyond our scope of work.

Figure 1 - 420

A Variables	All Cohort	Pre	Post
Age (median)	52.00	52.00	52.00
Female Gender (%)	78.3	78.5	77.8
Race (%)			
White	58.3	58.0	58.9
Black	13.6	13.0	14.5
Hispanic	9.8	9.3	10.8
Asian or Pacific Islander	4.0	3.9	4.2
Native American	0.4	0.3	0.5
Other	3.7	3.2	4.6
Removal Rate(%)	100	62.5%	37.5%
Mortality Rate (%)	0.1	0.1	0.1
Total Charges	24437.0	22299.0	28187.5



Conclusions: There was a significant decrease in the rate of surgical interventions from 2009 to 2014 at the national level. These findings are putatively secondary to the more accurate selection of patients in the presurgical stage, probably achieved by ancillary molecular testing that came to be widely used over that period of time.

421 Utility of Claudin – 4 in Diagnosing Metastatic Lung Adenocarcinoma in Pleural Fluids

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Disclosures: Ami Patel: None; Alain Borczuk: None; Momin Siddiqui: None

Background: Lung adenocarcinoma (LADC) is the most common occult primary in patients presenting with malignant pleural effusion. Of all causes of malignant effusions, however, distinguishing metastatic LADC from reactive mesothelial cells (RCM) and malignant mesothelioma (MM) based on morphology alone, has been a persistent diagnostic challenge in cytopathology. Claudin-4, a major functional constituent of tight junctions, has been shown to help distinguish LADC from RCM and MM in surgical specimens. Our goal was to further validate and assess the utility of claudin-4 in malignant effusions with a focus on metastatic LADC.

Design: We evaluated 60 pleural effusions (40 LADC, 10 RCM and 8 MM). Immunohistochemistry (IHC) was performed using claudin-4 monoclonal antibody (3E2C1) (Thermo Fisher Scientific, Rockford, IL) on cellblocks. Staining pattern and intensity (weak, moderate or strong) was assessed. Thyroid transcription factor 1 (TTF-1) immunostaining for LADC was also assessed when available.

Results: All cases of LADC were positive for claudin-4 with an overall sensitivity of 100% (40/40) and specificity of 100% (18/18). Of these, 66% (27/40) had strong membranous staining and 34% (13/40) had moderate membranous staining. All cases of RCM (10/10) and MM (8/8) were negative for claudin-4. However, 33% (4/12) of RCM and 36% (3/8) of MM showed dot-like cytoplasmic staining, which were interpreted as negative (**Figure 1**: **Dot like cytoplasmic staining with claudin-4 in MM** (1A:H&E, 1B:Claudin-4, 40x)). TTF-1 immunostaining was available in 70% (28/40), wherein 28% (8/28) showed strong nuclear staining, 52% (15/29) showed moderate nuclear staining and 18% (5/28) showed weak nuclear staining (**Figure 2**: **Claudin-4 and TTF-1 in metastatic LADC** (inset: H&E, 2A: Claudin-4, 2B: TTF-1,40x)).

Figure 1 - 421

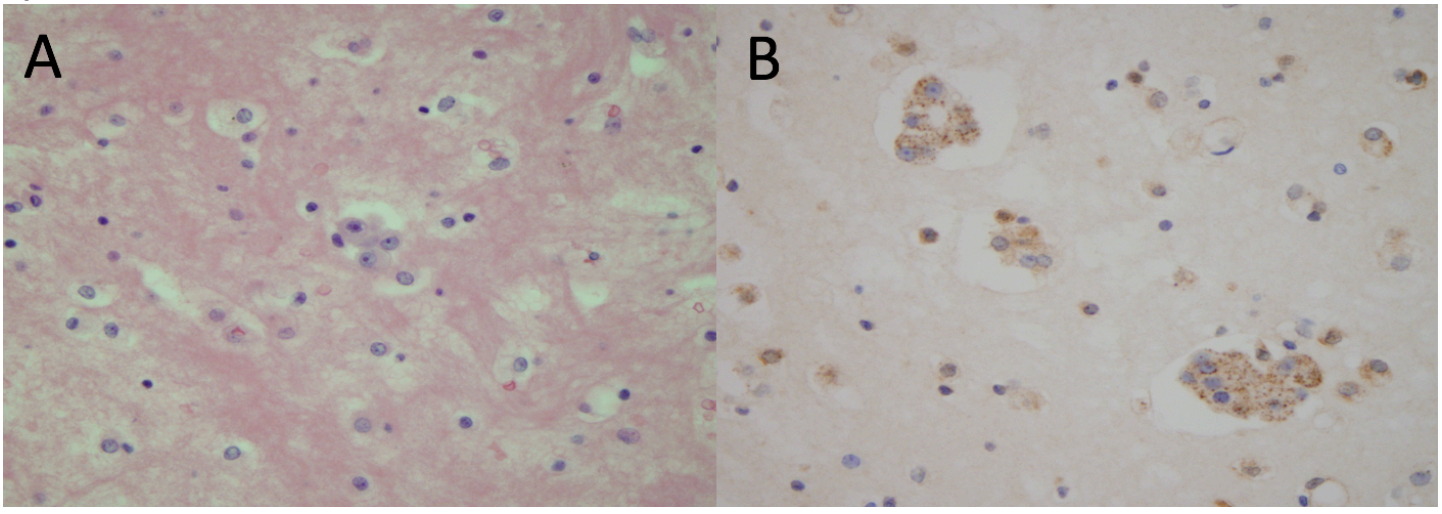
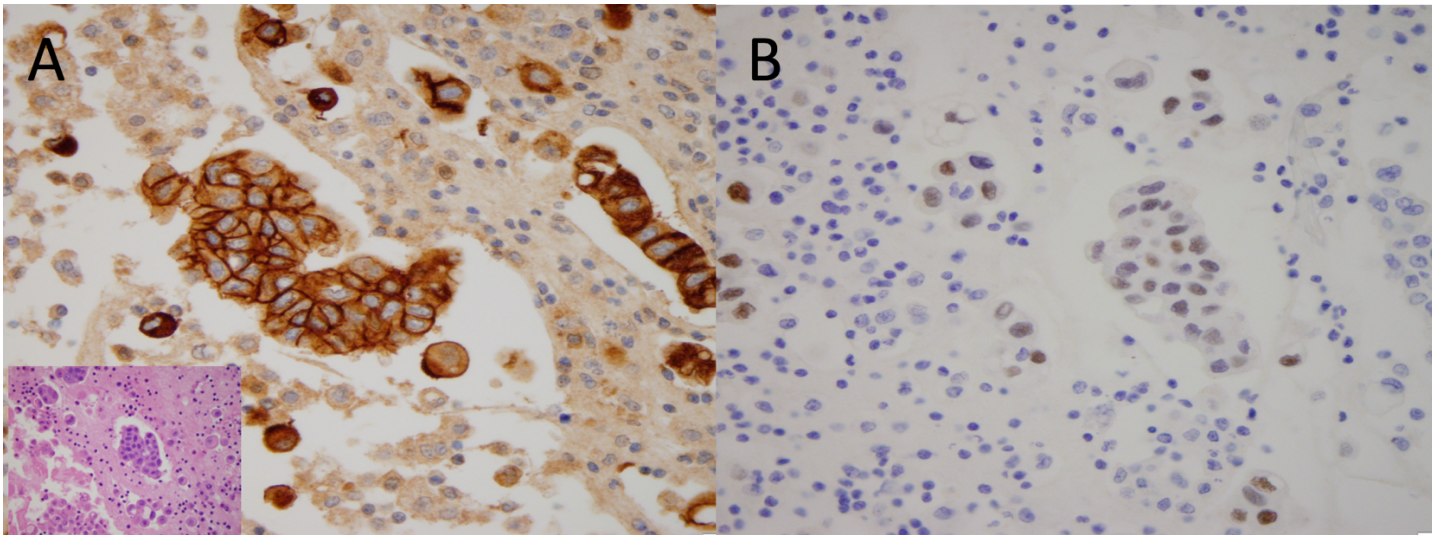


Figure 2 - 421



Conclusions: Claudin-4 IHC effectively distinguishes LADC from reactive/malignant mesothelium with high sensitivity and specificity. A dot-like cytoplasmic staining pattern can be identified in reactive/malignant mesothelial cells with claudin-4 and should be interpreted with caution. In addition, claudin-4 can be used in conjunction with TTF-1 in cases with weak nuclear staining, to support a diagnosis of metastatic LADC. Further studies with a larger cohort and concurrent surgical specimens could help support this approach.

422 The Utility of Lymphoid Enhancer Binding Factor 1 (LEF1) and Androgen Receptor (AR) in Diagnosing Solid Pseudopapillary Neoplasm (SPN) of Pancreas on Cytopathology

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Disclosures: Maria Luisa Policarpio-Nicolas: None; Edward Stelow: None; Grant Harrison: None; Kelsey McHugh: None

Background: Solid pseudopapillary neoplasm (SPN) is an uncommon tumor that is challenging to diagnose on cytopathology material due to morphologic overlap with other neoplasms. Recently, putative diagnostic markers in addition to beta-catenin have been reported in the surgical pathology literature, with nuclear positivity for lymphoid enhancer binding factor 1 (LEF1) and androgen receptor (AR) identified in >90% and > 80% of cases, respectively. We herein conduct a retrospective review of two institution's experience with SPNs, performing LEF1 (rabbit monoclonal, EPR2029Y, Abcam) and AR (mouse monoclonal, AR441, Agilent) immunohistochemistry (IHC) on cytopathology cell block material.

Design: Electronic record review of the cytopathology files at 2 institutions was conducted for all cases diagnosed as "solid pseudopapillary neoplasm". 14 cytopathology cases with retrievable cell blocks were identified. Thirteen (93%) of 14 cases had follow-up resection which showed SPN. Immunohistochemical stains for LEF1 and AR were performed and assessed for the presence of nuclear staining.

Results: Patients' age ranged from 16 to 79 years (mean 41.8, median 32). 86% (n=12) of patients were female; 14% were male (n =2). Pancreatic head was the most common location (6/14, 43%) followed by equal frequency in the body (4/14, 29%) and the tail (4/14, 29%). Tumor size ranged from 1.1 to 13.5 cm (mean 4.6, median 2.8). LEF1 was positive in 13 of 14 (92.9%) cases and AR was negative in 10 of 11 (90.9%) cases. Three (21%) of 14 cases stained for AR did not have remaining tumor cells on the cell block recut (Table 1).

Case	LEF1	AR
1	P	x
2	N	x
3	P	x
4	P	N
5	P	N
6	P	N
7	P	P
8	P	N
9	P	N
10	P	N
11	P	N
12	P	N
13	P	N
14	P	N

Table 1. LEF1 and AR IHC results for SPN cytology cell blocks.

P, positive; N, negative; x, no residual tumor on cell block.

Conclusions: The sensitivity of LEF1 for SPN on cytology material is 92.9%, similar to what has been reported in the surgical pathology literature. In contrast to the previously reported high AR sensitivity (>80%) in surgical SPN specimens, our result show a lower sensitivity (9.1%) on cytology cell block material. In summary, LEF1 appears to possess utility as a supporting marker in addition to beta-catenin on cytology cell block material for diagnosing SPN. The same does not hold true for AR on cytology cell block material.

423 Diagnostic Performance and Pitfalls of EUS-FNA of Gallbladder

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Disclosures: Morad Qarmali: None; Jessica Tracht: None; Isam-Eldin Eltoum: None

Background: Although gallbladder cancer is uncommon in the US, its incidence has more than doubled since 2000 mostly due to improved imaging and laparoscopic techniques. In a previous report, we demonstrated the efficiency of EUS-FNA in obtaining samples from the biliary tract including the gallbladder. In this study, we detail the diagnostic performance and pitfalls associated with EUS-FNA of gallbladder lesions.

Design: This is a retrospective clinicopathological correlation study in a large-volume EUS-FNA center (>300 EUS annually). Electronic medical records were searched for all patients who underwent EUS-FNA of the gallbladder. The cytologic findings were correlated with clinical, imaging, and histopathologic findings. Diagnostic category and associated risk of malignancy (ROM) were calculated based on the histological, radiographic and clinical follow-up.

Results: During the study period from 2000-2018, 38 gallbladder EUS-FNAs were performed (mean age 68 (SD 11), 70% female). The main patient presentation was either obstructive jaundice [18 (47%)] or pain [11, (29%)]. 30 cases had a defined lesion with an average maximum dimension of 16mm (SD 16) by EUS, while the remainder had ill-defined wall thickening. Cytology was positive for malignancy (POS) in 22 (58%), suspicious for malignancy (SUS) in 2 (5%), atypical (ATY) in 3 (8%) and negative (NEG) in 11 (29%). Median follow-up period was 50 days. 16 (73%) POS cases were confirmed either by histology [2 (9%)] or concurrent/subsequent metastasis [14 (64%)].

One SUS, one ATY and one NEG case were positive for carcinoma on histologic follow up. Six (16%) of the patients died of disease at follow up (6 POS). ROM is 100% for POS, 50% for SUS, 33% for atypical and 17% for NEG. The one false negative case was due to sampling error.

Conclusions: In this cohort of patients, the presence of a mass and/or wall thickening was highly suggestive of a neoplastic process. A positive EUS-FNA reliably confirms a malignant process. When clinical suspicion is very high an indeterminate or negative EUS-FNA result needs further investigation.

424 Fine Needle Aspiration Findings in Pancreatoblastoma (PBL): An Analysis of 10 Cases Reveals Helpful Cytologic Criteria in Their Distinction from Common Mimics

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Disclosures: Michelle Reid: None; Shristi Bhattarai: None; Rondell Graham: None; Burcin Pehlivanoglu: None; Carlie Sigel: None; Jiaqi Shi: None; Maryam Shirazi: None; Yue Xue: None; Olca Basturk: None; N. Volkan Adsay: None

Background: PBL is a rare malignant tumors that occur predominantly in childhood. It is diagnostically challenging because of its' polyphenotypic nature. While its' histologic features are well known its cytologic features are poorly characterized.

Design: Ten FNAs of PBL from 9 patients were analyzed.

Results: There were 5 men and 4 women, of median age 50 yrs (range 34– 60), median size 5cm (range 2.5-12), 6 (67%) in head and 3 (33%) tail; 3 were partly cystic and 4 were metastatic at diagnosis (Dx). Radiologic Dx included benign (pseudocyst, autoimmune pancreatitis) and malignant differentials. Median f/u was 39.8 mths (range 0.8-348) and 5 died of disease. [Table] One patient had Gardner syndrome and 1 FAP. FNAs were hypercellular with numerous 3-D clusters and singly dispersed mostly monotonous round blastema-like cells 1.5-2X an RBC, with high N/C, fine powdery chromatin and small distinct nucleoli somewhat resembling well-differentiated neuroendocrine tumor (NET) but without salt&pepper chromatin(S&P). Cytoplasm was scant with microvacuoles (n=4) on Diff Quik and/or red granules (n=5) on Pap similar to those in NET and acinar cell carcinoma (ACC). One tumor had prominent papillae and focally grooved nuclei resembling atypical solid-pseudopapillary neoplasm (SPN). Pleomorphism was seen in 4 (cells 5-20X RBC) and numerous mitoses (19/10HPFs) in 1. Squamoid morules (SMs) were seen in 70% (4 smears,5 cellblock) and consisted of cells with dense epithelioid cytoplasm and streaming elongated nuclei without keratinization [Figure]. IHC in 6 yielded (+) Synaptophysin (100%), trypsin (100%) and chromogranin (50%). Nuclear ß-catenin was (+) in 4/4 cases and highlighted even the subtle SMs. FNA Dx were: 2 (20%) PBL, 3 neuroendocrine neoplasm, 2 poorly differentiated carcinoma, 1 (+) for malignancy, 1 s/o ACC and 1 epithelioid neoplasm with endocrine and acinar differentiation.

Figure 1 - 424

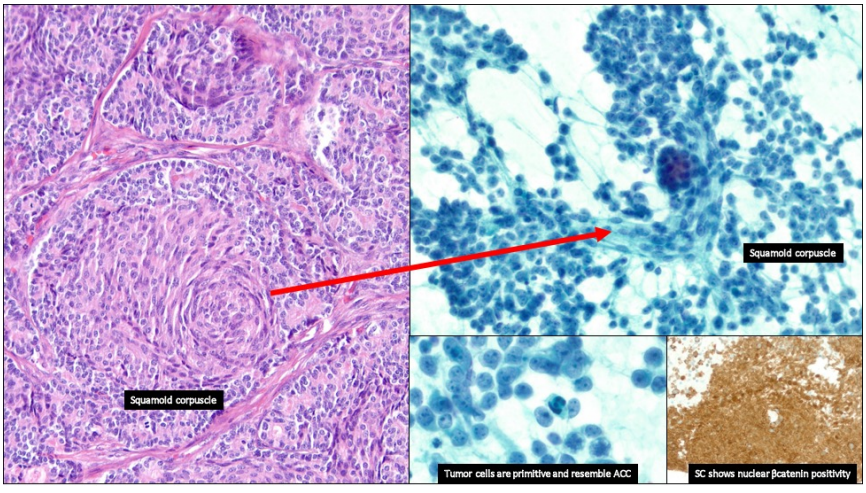

Figure 2 - 424

Clinicopathologic Features in 9 Patients

Feature	1	2	3	4	5	6	7	8	9	
Age	33	60	57	59	50	43	34	57	34	
Gender	Male	Male	Male	Male	Female	Female	Male	Female	Female	
Location	Head	Head	Tail	Head	Head	Tail	Tail	Head	Head	Liver
Size (cm)	2.8	2.5	5.0	8.7	7.5	3.4	2.5	10.5	12	2.0
Radiologic Diagnosis	Pancreatitis	N/A	Neoplasm	XX	XX	XX	Pseudocyst	NET vs ACC	Cystadenoma vs carcinoma	Liver met
Follow-up (mths)	72.5	17.9	3.6	85	143.7	13.6	0.8	6.5	348	
Status	Dead	Alive	Dead	Dead	Dead	Alive	Dead	Alive	Alive	
Assoc. Syndrome					FAP		Gardner's			

Cytologic Findings on Fine Needle Aspiration Specimens (n=10)

Finding	1	2	3	4	5	6	7	8	9	10
Hypercellularity	+	+	+	+	+	+	+	+	+	+
3-D Clusters	+	+	+	+	+	+	+	+	+	+
Nuclear molding		+	+	+	+	+	+	+	+	+
Single cells	+	+	+	+	+	+	+	+	+	+
Size (X RBC)	1.5 x	5 x	1.5 x	1.5 x	1.5 x	1.5 x	5-20X	1.5 x	1.5 x	1.5 x
Plasmacytoid cells							+			
Cytoplasmic:										
Microvacuoles	+			+		+	+	+		
Red granules	+	+	+	+		+				
Squamoid morules										
Smear	+	+	+				+			
Cell block	+					+	+	+	+	
2-cell population										
Pleomorphism	+	+					+	+		
Stromal Fragments	+	+	+				+	+	+	+

Results of immunocytochemical Stains

Pancytokeratin	+	+	+				+	+	+	
Synaptophysin	+	+	+	+	+	+	+	+		
Chromogranin	+	+	-		+	+		-	-	
CD56	+				+	+	+			
Trypsin			+		+	+	+	+		
Nuclear βcatenin		+				+	+	+		
NSE	+	+							-	
Ki67 index		50						11		
Cytologic Diagnosis	NEN	NET	Positive for Malignancy	NEN			c/w PBL	PBL	PDCA	PDCA

NEN, Neuroendocrine neoplasm; NET, Neuroendocrine tumor; c/w consistent with; PDCA, Poorly differentiated carcinoma.

Conclusions: PBL has subtle but distinctive cytologic characteristics that would help distinguish it from other solid cellular stroma-poor pancreatic neoplasms for which it is often mistaken but should be differentiated from due to its more aggressive behavior and association

with FAP related syndromes. These include, first and foremost, subtle SMs, hypercellularity and cohesive primitive blastema-like cells in a neuroendocrine like pattern but with powdery, not S&P chromatin, monotony, resemblance to higher grade SPN, and fewer mitoses than ACC.

425 Gender-Specific Rates of Malignancy Among Thyroid Cytology Specimens

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Disclosures: Stephanie Richards: None; Laura Malone: None; Paul Staats: None

Background: The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC), updated in 2017, is the widely-accepted classification scheme for reporting thyroid cytology. It has six categories: (I) Nondiagnostic or Unsatisfactory; (II) Benign; (III) Atypia of Undetermined Significance (AUS) or Follicular Lesion of Undetermined Significance; (IV) Follicular Neoplasm or Suspicious for a Follicular Neoplasm (FN); (V) Suspicious for Malignancy (SFM); and (VI) Malignant; an associated risk of malignancy (ROM) is provided for each category. There is a higher baseline ROM for thyroid nodules in males than females, but TBSRTC ROMs are not gender-stratified, and few studies have examined ROMs in males versus females. The goal of our study was to examine ROMs for TBSRTC categories by gender at our institution.

Design: A retrospective review of thyroid cytology cases was conducted at a tertiary care center over ten years (2008-2018). TBSRTC categories were recorded along with gender. All male cases (n=413) and an equal number of female cases were included. The cytology findings were correlated with follow-up diagnoses, when available. ROMs were calculated; cases with no follow-up were excluded.

Results: The distribution of diagnostic categories differed by gender (Table 1). ROM for AUS was 31.8% in males (7/22 with follow-up; 2 follicular carcinoma (FC), 5 papillary thyroid carcinoma (PTC)) and 21.4% in females (6/28; 2 FC, 3 PTC, 1 lymphoma), $p = 0.41$. ROM for FN was 46.7% for males (7/15; 6 FC, 1 PTC) and 14.3% in females (1/7, 1 FC), $p = 0.14$. ROM for SFM was 66.7% for males (2/3; 2 PTC) and 66.7% in females (2/3; 1 PTC, 1 anaplastic carcinoma), $p = 1.00$.

Table 1. TBSRTC Reporting Rates by Gender.

TBSRTC Cateory	Male	Female
I	**24** (5.8%)	**12** (2.9%)
II	**284** (68.8%)	**322** (78.0%)
III	**44** (10.7%)	**47** (11.4%)
IV	**16** (3.9%)	**9** (2.2%)
V	**6** (1.5%)	**4** (1.0%)
VI	**39** (9.4%)	**19** (4.6%)

Conclusions: The ROMs for the indeterminate TBSRTC categories differed between males and females, especially for FN, although the results were not statistically significant. ROMs for males for AUS and FN were also higher than reported TBSRTC ranges. The excess ROM in FN was due to more FCs, suggesting a higher likelihood of FC in males than females with FN cytology. Larger scale studies may be indicated to determine if different management guidelines are warranted based on gender.

426 Can The Paris System Criteria be used in all preparation types without alteration? A Split Sample Comparison of Urinary Cytology in ThinPrep and Cytospin Preparations

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Disclosures: Christopher Richardson: None; Guliz A. Barkan: None; Stefan Pambuccian: None

Background: The Paris System for Reporting Urinary Cytology (TPS), published in 2016, was introduced to provide clear diagnostic criteria and a standardized reporting method for urinary cytology specimens (Ucyt). According to TPS a nuclear cytoplasmic (N:C) ratio > 0.7, nuclear hyperchromasia, and irregular nuclear contours must be observed in order to render a diagnosis of high-grade urothelial carcinoma (HGUC). TPS criteria was based on evidence that was established using the liquid-based preparation methods ThinPrep and Surepath. However, approximately 45% of the laboratories in the US use the cytospin method for processing Ucyt. The aim of this study was to evaluate if the same diagnostic criteria for identifying HGUC could be applied to specimins prepared by both ThinPrep and cytospin methods.

Design: In this prospective study, the Ucyt from patients with a diagnosis of negative for HGUC (NHGUC) and HGUC were prepared using both the ThinPrep and cytospin methods. Pictures of cells were taken from both HGUC and NHGUC specimens prepared with both

methods. ImageJ Software was used to measure the N:C ratio and the nuclear pixel gray value of individual cells. Gray value assesses pixel darkness and is measured on a scale of 0 to 255, with 0 being black and 255 being white. Gray value was used to quantify hyperchromasia. N:C ratio and hyperchromasia were compared between both preparation methods for each patient via paired student t-test, with p-values <0.05 being significant.

Results: 10 HGUC and 9 NHGUC cases, represented by a total of 688 cells, were evaluated in this study. N:C ratio was not statistically different between ThinPrep and cytospin in any of the 10 HGUC cases. N:C ratio was statistically different in 2/9 NHGUC cases, showing larger N:C ratios in ThinPrep cells. Hyperchromasia was statistically different in 5 of 19 cases, four of which showed increased hyperchromasia in ThinPrep cells. An overall comparison of HGUC cells to NHGUC cells shows that HGUC cells have a higher average N:C ratio (0.5465 vs 0.2846, p<0.0001) and greater hyperchromasia as measured by average nuclear pixel gray value (100.8 vs 120.7, p<0.0001). [Table 1]

High Grade Urothelial Carcinoma					Negative for High Grade Urothelial Carcinoma				
Patient	Variable	ThinPrep	Cytospin	P-value	Patient	Variable	ThinPrep	Cytospin	P-value
1	N:C Ratio	0.5056	0.4772	0.4509	11	N:C Ratio	0.3018	0.2837	0.1294
	NPGV	65.23	112.3	<0.0001		NPGV	102.79	130	0.1233
2	N:C Ratio	0.5623	0.5621	0.9437	12	N:C Ratio	0.1106	0.122	0.8525
	NPGV	67.4	113.9	<0.0001		NPGV	144.3	152.3	0.273
3	N:C Ratio	0.499	0.5348	0.2319	13	N:C Ratio	0.3763	0.2222	0.0057
	NPGV	120.1	113.6	0.0323		NPGV	114.1	129.6	0.1650
4	N:C Ratio	0.4503	0.4451	0.8023	14	N:C Ratio	0.2412	0.2309	0.9607
	NPGV	94.67	109.9	0.0918		NPGV	97.83	119.1	0.0394
5	N:C Ratio	0.4601	0.4991	0.2688	15	N:C Ratio	0.3894	0.281	0.0252
	NPGV	81.38	100.6	0.0053		NPGV	139.9	122.7	0.1599
6	N:C Ratio	0.5213	0.5724	0.8814	16	N:C Ratio	0.2909	0.1961	<0.0001
	NPGV	89.49	85.21	0.1869		NPGV	127.6	125.3	0.5958
7	N:C Ratio	0.5615	0.5543	0.7432	17	N:C Ratio	0.3334	0.3513	0.5127
	NPGV	87.79	71.3	0.169		NPGV	129.9	117.1	0.1046
8	N:C Ratio	0.625	0.6429	0.2322	18	N:C Ratio	0.3489	0.2953	0.7406
	NPGV	94.64	93.69	0.8711		NPGV	85.25	86.11	0.9904
9	N:C Ratio	0.6258	0.5762	0.376	19	N:C Ratio	0.3797	0.2312	<0.0001
	NPGV	132.7	111.2	0.1071		NPGV	113.3	138.7	<0.0001
10	N:C Ratio	0.691	0.6709	0.2904					
	NPGV	120.1	124.4	0.9704					

Conclusions: Urothelial cell morphologies are not significantly different in Ucyt prepared with the ThinPrep compared to cytospin. TPS guidelines may be accurately applied in laboratories that employ both methods. Furthermore, this study confirms that HGUC cells have higher N:C ratio (>0.5) and a greater degree of hyperchromasia compared to normal cells.

427 Clinical Significance of Testing Negative for HPV in Cervical Cytology with High-Grade Squamous Intraepithelial Lesion (HSIL)

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Disclosures: Ariane Robison: None; Ghassan Allo: None

Background: As human papillomavirus (HPV) testing is being introduced together with routine cervical cytology, or as a standalone testing, the clinical significance of unusual subsets remains undetermined. We aim in this study to characterize cases that test negative for HPV (HPV-) while the cervical cytology shows high-grade squamous intraepithelial lesion (HSIL+)

Design: We retrospectively analysed patients who underwent cervical cytology and HPV co-testing at our institution in 2013-2014. High-risk HPV testing was conducted using FDA-approved Cobas HPV Test (Roche Diagnostics). Cases were classified based on the presence of HSIL (HSIL+ vs HSIL-) and the presence of high-risk HPV (HPV+ vs HPV-). Results of previous and subsequent pathology are recorded, specifically the presence of HSIL or carcinoma (categorized in this study under HSIL) and HPV. Descriptive analysis and Pearson Chi-square test were conducted.

Results: A total of 11986 cases were analyzed, of which 196 (2%) were HSIL+/HPV-, with median age of 44(19-90) years, and median follow-up of 782(14-1580) days. History of HSIL was found in 93 of 139 (67%), and HPV was previously negative in 129 of 139 (93%) cases. On follow-up, 14 of 167 (8%) demonstrated HSIL on cytology or surgical pathology specimens.

HSIL+/HPV- cases are more likely to have previous HPV positivity than HSIL-/HPV- cases (10 of 139, 7% vs 138 of 5259, 3%; p=0.005), and more likely to have subsequent HSIL (14 of 167, 8% vs 38 of 51555, 0.7%; OR, 12.3; p<0.0001) but without different subsequent HPV status (9 of 54, 17% vs 201 of 1798, 11%; p=0.195).

HSIL+/HPV- are less likely to have previous history of HSIL than HSIL+/HPV+ (93 of 139, 67% vs 55 of 55, 91%; p<0.0001), and less likely to have previous HPV positivity (10 of 139, 7% vs 55 of 55, 100%; p<0.0001). In addition, HSIL+/HPV- are less likely to have subsequent HSIL than HSIL+/HPV+ (14 of 167, 8% vs 53 of 111, 48%; p<0.0001), and less likely to test positive for HPV (9 of 54, 17% vs 20 of 40, 50%; p=0.001).

Conclusions: HSIL+/HPV- cases constitute a minor subset of co-tested cervical cytology samples, but with a substantially higher risk of developing subsequent HSIL. If using HPV testing solely for screening, clinical history of previous HPV positivity may aid finding these cases. The lack of significant difference in subsequent HPV detection rate raises the possibility of underlying HPV subsets that are not covered by the current test.

428 Performance of Novel Non-Invasive Assay UroSEEK in Atypical Urine Cytology Obtained for Early Detection of Bladder Cancer

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Disclosures: Maria Del Carmen Rodriguez Pena: None; Diana Taheri: None; Marie-Lisa Eich: None; Aline Tregnago: None Christopher VandenBussche: *Grant or Research Support*, PapGene; Isam-Eldin Eltoum: None; Bert Vogelstein: *Advisory Board Member*, PapGene, Inc.; *Advisory Board Member*, Personal Genome Diagnostics; *Advisory Board Member*, Morphotek Inc.; *Advisory Board Member*, Sysmex Inostics, Inc.; *Advisory Board Member*, Exelixis GP; George Netto: None

Background: The Paris system for urine cytology is a standardized reporting system aiming to accurately diagnose high grade urothelial cancer. A significant proportion of cases remain indeterminate and are placed in the “atypical” or “suspicious” category, posing difficulty in patient management. We aim to report the performance of our recently described assay "UroSEEK" in a cohort of patients who underwent cytology screening for early detection (ED) of bladder cancer (BC).

Design: Urine samples were prospectively collected in one institution. Patients with hematuria or lower urinary tract symptoms underwent urine cytology examination to rule out BC. Atypical and suspicious cytology categories were combined (ATYP). Urine samples were analyzed for mutations by three components: a multiplex PCR was used to detect mutations in regions of *CDKN2A, ERBB2, FGFR3, HRAS, KRAS, MET, MLL, PIK3CA, TP53*, and *VHL* (UroSeqS). An amplification primer was used to amplify a 73-bp segment containing the region of the *TERT* promoter (TERTSeqS). Aneuploidy was assessed with FastSeqS, which uses a single primer pair to amplify ~38,000 loci scattered throughout the genome. FastSeqS was performed on a subset of samples. Follow up data was obtained.

Results: We collected 375 urine samples from 348 patients. On cytology, 25/375 (7%) samples were positive for malignancy, 236/375 (63%) negative and 114/375 (30%) ATYP. Among samples categorized as ATYP, 24/114 (21%) developed tumor upon follow up. UroSEEK was positive in 21 (88%) of these 24 samples. TERTSeqS detected mutations in 15/24 (63%), UroSeqS detected mutations in 18/24 (75%) and FastSeqS detected aneuploidy in 10/24 (48%) samples. Performance characteristics of the assay and its components are highlighted in Table 1. Out of 30 samples positive for UroSEEK, 21 developed tumor (70%) while 9 (30%) did not. UroSEEK positivity preceded tumor diagnosis in average by one month with a range between 0 to 18 months. Seven cases had a lead time of over 6 months. UroSEEK was positive in 3/3 urines subsequently diagnosed with low grade urothelial tumors, and 18/21 (86%) diagnosed with high grade urothelial tumors.

Table 1. Performance features of UroSEEK and each of the components.

	UroSEEK	TERTSeqS	UROSeqS	FastSeqS
Sensitivity	88%	63%	75%	48%
Specificity	90%	92%	97%	100%
NPV	96%	90%	94%	82%
PPV	70%	68%	86%	100%

Conclusions: UroSEEK demonstrates a strong negative predictive value of 96% and a sensitivity of 88%. In ED setting, UroSEEK has the potential for predicting outcome in difficult cytology cases, namely those classified as “atypical/suspicious”. Prospective trials are needed to demonstrate the ability of UroSEEK to improve management and outcome of bladder cancer.

429 Performance of Novel Non-Invasive Method UroSEEK in Atypical Urine Cytology Obtained for Surveillance of Bladder Cancer

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Disclosures: Maria Del Carmen Rodriguez Pena: None; Diana Taheri: None; Marie-Lisa Eich: None; Aline Tregnago: None; Christopher VandenBussche: *Grant or Research Support*, PapGene; Isam-Eldin Eltoum: None; Bert Vogelstein: *Advisory Board Member*, PapGene, Inc.; *Advisory Board Member*, Personal Genome Diagnostics, Inc.; *Advisory Board Member*, Morphotek, Inc.; *Advisory Board Member*, Exelixis GP; *Advisory Board Member*, Sysmex Inostics, Inc.; George Netto: None

Background: The Paris system for urine cytology is a standardized reporting system aiming to accurately diagnose high grade urothelial cancer. A significant proportion of cases remains indeterminate and placed in the “atypical” or "suspicious" category, posing difficulty in patient management. We aim to report the performance of UroSEEK assay in a cohort of patients who underwent cytology for surveillance of bladder cancer (BC).

Design: Urine samples were collected prospectively from one institution. The patients selected were under standard surveillance with cystoscopy and urine cytology following a diagnosis of BC. Atypical and suspicious cytology categories were combined (ATYP). Urine samples were analyzed for mutations by three components: a multiplex PCR to detect mutations in regions of *CDKN2A, ERBB2, FGFR3, HRAS, KRAS, MET, MLL, PIK3CA, TP53*, and *VHL* (UroSeqS). An amplification primer to amplify a 73-bp segment containing the region of the *TERT* promoter (TERTSeqS). Aneuploidy was assessed with FastSeqS, which uses a single primer pair to amplify ~38,000 loci scattered throughout the genome. FastSeqS was performed on a subset of samples. Follow up data was obtained.

Results: A total of 717 urine samples were collected from 496 patients. On cytology, 84/717 (12%) samples were categorized as positive for malignancy, 301/717 (42%) as negative and 332/717 (46%) as ATYP.

Upon follow up, tumor recurrence was detected in 235 samples categorized as ATYP. UroSEEK was positive in 164/235 (70%) of ATYP urines with positive outcome. TERTSeqS detected mutations in 140/235 (60%), UroSeqS detected mutations in 109/235 (46%) and FastSeqS detected aneuploidy in 31/235 (13%) of ATYP samples. Performance characteristics are highlighted in Table 1. Out of the 188 ATYP samples that are positive for UroSEEK, 164 developed tumor (87%) while 24 (13%) did not. UroSEEK positivity preceded tumor diagnosis on average by 4 months with a range between 0 to 26 months.

Table 1. Performance Characteristics of UroSEEK

	UroSEEK	TERTSeqS	UROSeqS	FastSeqS
Sensitivity	70%	60%	46%	18%
Specificity	75%	79%	92%	98%
NPV	**87%**	45%	41%	28%
PPV	51%	88%	93%	97%

Conclusions: In ATYP urine cytology samples, UroSEEK demonstrated a high negative predictive value of 87% for likelihood of BC recurrence.The UroSEEK assay has the potential for predicting outcome in difficult urine cytology cases, namely those classified as atypical or suspicious. UroSEEK positivity preceded clinical diagnosis by months to years. Prospective trials are needed to demonstrate the ability of UroSEEK to improve outcome and management in surveillance of bladder cancer.

430 Cytopathology of Rosai-Dorfman Disease of the Pancreas: An Analysis of 5 Cases presenting as A Pancreatic Mass

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Disclosures: Catherine Roe: None; Jessica Tracht: None; Emilio Madrigal: None; Alyssa Krasinskas: None; Yue Xue: None; Michelle Reid: None

Background: Rosai-Dorfman Disease (RDD), or sinus histiocytosis with massive lymphadenopathy, is a benign histiocytic proliferation with characteristic cytologic features of enlarged histiocytes with emperipolesis. RDD is most commonly found in lymph nodes with extranodal involvement usually occurring in the head and neck region. Gastrointestinal involvement, particularly pancreatic, is extremely rare. We reviewed the clinicopathologic and cytologic features of 5 cases of pancreatic RDD.

Design: Clinicopathologic features, cytology slides, immunohistochemical stains (IHC) and surgical resections from 5 FNAs in 3 patients diagnosed as pancreatic RDD were reviewed.

Results: There were 3 female patients, aged 65, 69 and 75, with involvement of the tail (n=2) and head (n=1). Median size was 2.3 cm (range 2.1-4.5) and radiologic diagnoses of masses with benign and malignant differentials in all 3 (Table 1). Notable cytologic features on smears were multiple histiocyte clusters reminiscent of epithelioid granulomas. Histiocytes had abundant granular cytoplasm containing red granules and engulfed red blood cells, neutrophils, and lymphocytes (emperipolesis). Singly dispersed histiocytes with moderate to marked nuclear atypia, including large peripheral nuclei (significantly larger than that of an ordinary histiocyte) with distinctive vesicular chromatin, irregular contours, and prominent nucleoli, an unusual finding in ordinary histiocytes. Emperipolesis were seen in variable numbers (Figure). Background neutrophils, plasma cells and granular debris suggestive of necrosis were also seen. Densely fibrotic, hyalinized stromal fragments with keloid-like zones of fibrosis were also seen on cell block. These contained sheets and clusters of atypical histiocytes which stained positively for S100, CD68 and CD163 and were negative for CD1a, and IgG4. (Table 2). Two of 3 were resected and the diagnosis confirmed.

Figure 1 - 430

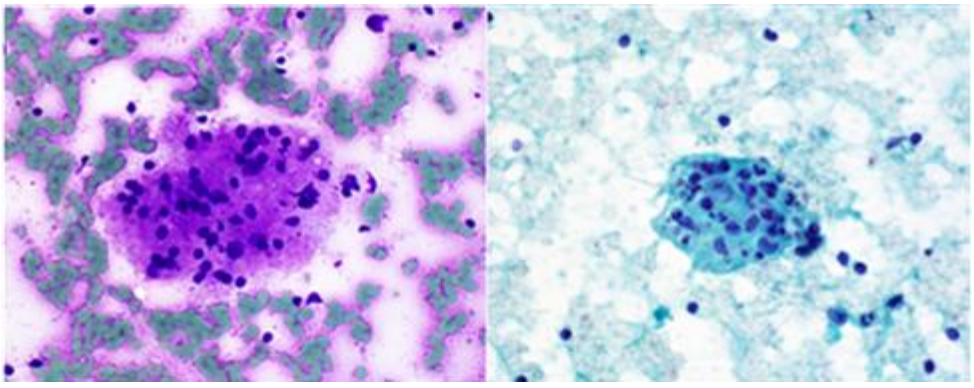
Table 1. Patient clinicopathologic features

Patient	Age	Sex	Clinical presentation	Location	Size (cm)	Radiologic diagnosis	Cytologic diagnosis	Follow -up
1 FNA#1	75	F	Weight loss	Pancreatic head	4.5	Focal pancreatitis vs. pancreatic adenocarcinoma	Consistent with RDD	RDD confirmed on core biopsy
FNA#2							Rare strips of fibrous tissue	
FNA#3							Predominately benign spindle cells-suggestive of fibrosis	
2	69	F	Abdominal pain	Pancreatic tail	2.3	Pancreatic adenocarcinoma vs. pancreatic islet cell tumor	Highly suggestive of RDD	RDD confirmed on surgical resection
3	65	F	Incidental	Pancreatic tail	2.1	Pancreatic adenocarcinoma	Fibrous tissue with chronic inflammation	RDD on surgical resection

Table 2. Cytologic features

	1	2	3	4	5
Cellularity	Paucicellular	Paucicellular	Hypercellular	Hypercellular	Hypercellular
Emperipolesis (+ few, ++ moderate, +++ many)	+	+	++	+++	+
Histiocyte clusters (Y or N)	Y	Y	Y	Y	Y
Cytoplasmic granules (Y or N)	Y	Y	Y	Y	Y
Background "Necrosis" (Y or N)	Y	Y	N	Y	Y
Background inflammation	Chronic	Chronic	Chronic	Chronic	Acute and chronic
Stromal fragments (Y or N)	N	Y	Y	Y	Y
IHC Results CD68/CD163, S100 (+ or -)	N/A	N/A	+S100, CD163	+S100, CD68, CD163	N/A

Figure 2 - 430



Conclusions: Pancreatic RDD is a rare benign inflammatory process that is diagnostically challenging on radiology and cytology. Marked nuclear atypia and histiocytic clusters may result in misdiagnosis as carcinoma, granulomatous inflammation/infection, autoimmune pancreatitis and low-grade soft tissue tumors (solitary fibrous tumor, inflammatory myofibroblastic tumor). Identification of histiocytes with emperipolesis and matching IHC profile can ensure accurate cytologic diagnosis. Failure to identify these characteristic features may lead to delays in diagnosis or mis-diagnosis of this rare entity.

431 Next Generation Sequencing Improves Detection of Mucinous and High-Risk Pancreatic Cysts

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Disclosures: Matthew Rosenbaum: None; Raza Hoda: None; Elizabeth Finer: None; Ronald Arpin: None; Long Le: *Consultant*, ArcherDx; *Major Shareholder*, ArcherDx; John Iafrate: *Major Shareholder*, ArcherDx; Martha Pitman: None

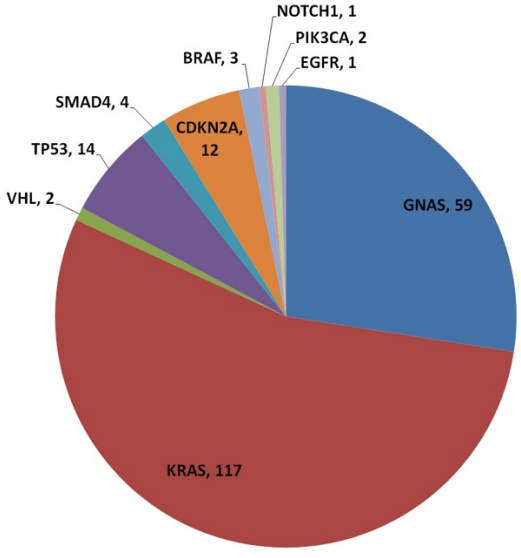
Background: Genetic analysis of pancreatic cyst fluid (PCF) provides valuable pre-treatment information to enhance the diagnostic value of cytology. Here we report on our expanded experience using genetic analysis in the evaluation of pancreatic cysts.

Design: We reviewed all patients with molecular analysis of PCF prospectively performed between 03/2013-04/2018. Testing was performed using nested PCR in 2013; next generation sequencing (NGS) was used 2014 onward. Cysts were classified as mucinous based on the presence of thick, extracellular mucin or mucinous epithelium, a CEA >192ng/mL, or a *KRAS* or *GNAS* mutation. Late mutations were defined as *TP53, SMAD4, CDKN2A, and NOTCH1*. Gold standard diagnosis was established via clinicopathologic follow-up. High-risk (HR) lesions were defined as high-grade dysplasia in a mucinous cyst, neuroendocrine tumor and adenocarcinoma, all of which could produce high-grade atypia (HGA) on cytology.

Results: Mutations were detected in 134 of 333 PCF (41.7%) (Figure 1). A mucinous etiology was established by mucinous cytology (mucinous epithelium or thick, extracellular mucin) in 123 PCF (36.9%), and/or an elevated CEA in 154 (46.2%) and/or the presence of a *KRAS* or *GNAS* mutation in 190 (57.1%). Genetic analysis increased the diagnosis of a mucinous cyst by 53% over cytology alone ($p<0.001$) and 23% over cytology and/or elevated CEA ($p=0.003$). Late mutations were present in 26 (8%) PCF from 23 patients, 78% (18/23) of which were HR on follow-up. Of these 18 PCF, 15 (83%) had HGA on cytology. Of the 5 patients with late mutations and no HR lesion on follow-up, none had HGA on cytology, although only one of these patients had subsequent resection.

Clinical Characteristic	
Median age (y)	68
Age range (y)	12-91
Female, *n* (%)	163 (50.6)
Specimen Adequacy	***n* (%)**
Satisfactory for evaluation	227 (68.2)
Evaluation limited	105 (31.5)
Unsatisfactory for evaluation	1 (0.3)
Cytology Diagnosis	***n* (%)**
Benign	145(43.5)
Atypical	20(6)
Suspicious	7(2.1)
Positive	24(7.2)
Nondiagnostic	56(16.8)
Neuroendocrine Tumor	4(1.2)
Neoplastic: Other	76(22.8)
Neoplastic: Benign	1(0.3)
Cytologic Characteristics	***n* (%)**
Negative/Not mentioned	235(70.6)
Low-Grade Atypia	48(14.4)
Intermediate-Grade Atypia	18(5.4)
High-Grade Atypia or Worse	32(9.6)
Mucinous Criteria	**n (%)**
Extracellular mucin	59 (21.3)
Mucinous Epithelium	74 (21.3)
Mucinous Cytology	123 (36.9)
Mucinous Cytology + CEA	154 (46.2)
Mucinous Cytology + CEA + NGS	190 (57.1)

Figure 1 - 431



Conclusions: The addition of NGS significantly improved the pre-operative diagnosis of mucinous and HR cysts and is a valuable pre-operative ancillary test for patient management.

432 Utility of UroVysion Florescence In Situ Hybridization (FISH) for Urinary Tract Cytology Specimens With Rare Atypical Cells

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Disclosures: Erin Weeden: None; Jacquelyn Knapik: None; Faisal Mukhtar: None; Peter Drew: None; Marino Leon: None

Background: UroVysion florescence in situ hybridization (FISH) is an FDA approved ancillary test to aid in the diagnosis of urothelial carcinoma in urine cytology specimens. Currently, in our institution, when specified by the submitting clinician, urinary tract (UT) cytology specimens diagnosed as atypical urothelial cells (AUC) or suspicious for urothelial carcinoma (SUC) are reflexed for UroVysion FISH testing. Occasionally, UT cytology specimens only contain "rare" atypical cells. Given that UroVysion FISH testing requires at least 4 abnormal cells to be resulted as positive, we hypothesized that reflex testing of UT specimens containing less than 4 atypical cells (i.e. rare) may result in false negative tests.

Design: Our pathology archives were searched for UT cytology specimens diagnosed as AUC or SUC with a note of “rare atypical urothelial cells” present which also had UroVysion FISH testing performed during a year-period (April 2017-April 2018). Cases with an adequate specimen were included; cases insufficient for UroVysion were excluded. Collection types included voided, instrumented and selective sampling. 51 cases were identified; six cases were excluded due to insufficient material for UroVysion FISH. The number of positive UroVysion FISH results was compared to all UT cytology specimens diagnosed with rare atypical cells and expressed as a percentage risk.

Results: Forty six cases of UT cytology specimens with “rare” atypical urothelial cells and concurrent UroVysion testing were identified; 35 cases were AUC and 11 were SUC. The patients included 43 (93.5%) males and 3 females (6.5%) with an average age of 71.7 years (range: 50-96). 25 specimens were voided urine and 21 were instrumented/selective sampling. Of these, 14 cases had a positive UroVysion FISH result (31%); 13 cases were identified as positive based on gains of multiple chromosomes and homozygous loss of 9p21 and 1 case based on homozygous loss of 9p21 only.

Conclusions: Despite the rarity of atypical urothelial cells found in some UT cytology specimens, UroVysion FISH was positive 31% of the time when only rare atypical cells were present, supporting a diagnosis of urothelial carcinoma. These findings suggest that genetic changes of the disease might be detected when the characteristic cytomorphologic features associated with high-grade urothelial carcinoma are not well established. This study argues for continued UroVysion FISH testing of UT cytology specimens when only rare atypical urothelial cells are identified.

433 Low Grade Squamous Intraepithelial Lesion on Pap Test – Impact of hrHPV Test Results on Clinical Decision Making and Outcomes

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Disclosures: Miguel Rufail: None; Madelyn Lew: None; Richard Cantley: None

Background: Low grade squamous intraepithelial lesion (LSIL) on Pap test is associated with ~15-25% rate of high grade squamous intraepithelial (HSIL) on follow-up biopsy, and those with positive concurrent high risk human papillomavirus (hrHPV) test have an increased risk for HSIL on biopsy. American Society of Colposcopy and Cervical Pathology (ASCCP) guidelines recommend colposcopy in women ages 25-29 for LSIL Pap tests regardless of hrHPV status. For ages 30-65, colposcopy is recommended for those hrHPV+ and without hrHPV testing, while repeat co-testing at 1 year or immediate colposcopy is recommended when hrHPV-. LSIL/HPV- co-test result has been reported to have a low risk of HSIL at biopsy. The goal of our study was to assess differences in clinical follow-up and HSIL rates based on hrHPV status in patients with LSIL Pap test.

Design: We searched our anatomic pathology archives for LSIL Pap tests in patients aged 25-65 from 1/1/2015-12/31/2016. Age, Roche cobas hrHPV result, and follow-up rates and findings were recorded, including biopsies and/or one-year co-testing results.

Results: 526 Pap tests fit our parameters. 376 (72%) patients had follow-up colposcopic biopsy. 68/376 (18%) had HSIL on biopsy, including 46/226 (20%) hrHPV+, 17/101 (17%) hrHPV not performed (NP), and 5/49 (10%) hrHPV-. 20/62 (32%) with HPV16 and/or HPV18 had HSIL at biopsy, including 11/24 (46%) with ?2 hrHPV subtypes, compared to 26/164 (16%) with HPVother alone.

Among patients who were hrHPV-, ASCCP-approved follow-up (Co-test and/or biopsy) occurred in 62/115 (54%), compared to biopsy follow-up in 101/136 (74%) hrHPV NP and 226/275 (82%) hrHPV+. Among hrHPV+ patients, biopsy rates were similar regardless of hrHPV subtype (85% HPV 16/18 or multiple subtypes vs 81% HPV other alone).

Among co-tested patients with LSIL Pap test, hrHPV+ rates were higher in patients 25-29 (76/90, 84%) compared to patients 30-65 (199/300, 67%). Biopsy rates were similar between the two age groups when HPV+ (59/76 [78%] vs 167/199 [84%]). ASCCP-approved follow-up in HPV- patients was lower in patients 25-29 (3/14 [21%]) compared to 30-65 (59/101 [58%]).

Conclusions: ASCCP-approved follow-up management after co-testing was significantly more common for LSIL/HPV+ compared to LSIL/HPV- (82% vs 54%). Nonetheless, LSIL/HPV- was associated with a significant risk of HSIL on biopsy (10%), comparable to that seen with HPVother+ (16%). The presence of HPV16 and/or HPV18 was associated with the highest rates of HSIL on biopsy (32%).

434 A Comparison of Diagnostic Rates and Concordance in Different Preparations for Thyroid Fine Needle Aspirations (T-FNA).

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Disclosures: Miguel Rufail: None; Brian Smola: None; Xin Jing: None; Amer Heider: None; Robertson Davenport: None; Richard Cantley: None; Judy Pang: None; Madelyn Lew: None

Background: Fine needle aspiration (FNA) cytology is commonly utilized to guide clinical management of patients with thyroid nodules. Although many institutions elect to utilize either a liquid-based monolayer preparation and/or conventional smear preparations, there are few studies that directly compare the diagnostic rates of categories listed by The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) between different preparations. This study evaluates the comparative diagnostic rates of TBSRTC categories in T-FNA prepared by ThinPrep (TP) only with T-FNA prepared by both conventional smear preparations (CS) and TP and correlates these cytologic diagnoses with subsequent resections to evaluate potential differences in rates of neoplasia (RON) and malignancy (ROM).

Design: A total of 200 consecutive thyroid FNA specimens were collected from the same period and were stratified by preparation type (TP vs. CS & TP). For T-FNAs with CS, each pass resulted in one air-dried Diff-Quik CS and one alcohol-fixed Papanicolaou stained CS and the needle was then rinsed in Cytolyt to produce a TP slide. Diagnostic rates for each TBSRTC diagnostic category were calculated. The EMR was searched for histologic diagnoses of previously sampled thyroid nodules to evaluate RON and ROM for each cohort.

Results: Of 200 thyroid FNA specimens, 37 (18.5%) were evaluated by TP only and 163 (81.5%) were evaluated by CS&TP, reflecting the predominance of on-site evaluation with CS for T-FNAs at our institution. Of the TP only and CS&TP cohorts, 14 (37.8%) and 22 (13.5%) had subsequent resections, respectively. The diagnostic rates and comparative rates of neoplasia (RON) and malignancy (ROM) from subsequent resections are summarized in Table 1.

Diagnosis	TP only n (%)	CS & TP n (%)
Non-diagnostic	5 (13.5)	25 (15.3)
# of subsequent resections	2 (40)	4 (16)
-RON	0%	25%
-ROM	0%	25%
Benign	23 (62.2)	109 (67.5)
# of subsequent resections	4 (17.4)	2 (1.8)
-RON	0%	50%
-ROM	0%	50%
Atypical cells present	-	1 (0.6)
# of subsequent resections	-	1 (100)
-RON	-	100%
-ROM	-	100%
Follicular lesion of undetermined significance (FLUS)	6 (16.2)	22 (13.5)
# of subsequent resections	6 (100)	9 (40.9)
-RON	33.3%	33.3%
-ROM	16.7%	11.1%
Hurthle cell lesion of undetermined significance (HLUS)	1 (2.7)	1 (0.6)
# of subsequent resections	1 (100)	1 (100)
-RON	0%	100%
-ROM	0%	0%
Suspicious for follicular neoplasm	-	2 (1.2)
# of subsequent resections	-	2 (100)
-RON	-	50%
-ROM	-	50%
Suspicious for papillary thyroid carcinoma	-	1 (0.6)
# of subsequent resections	-	0 (0)
-RON	-	-
-ROM	-	-
Positive for papillary thyroid carcinoma	1 (2.7)	2 (1.2)
# of subsequent resections	1 (100)	2 (100)
-RON	100%	100%
-ROM	100%	100%
Positive for poorly differentiated carcinoma	1 (2.7)	-
# of subsequent resections	0 (0)	-
-RON	0	-
-ROM	0	-

Conclusions: The diagnostic rates of TBSRTC do not vary significantly between T-FNAs prepared by either TP only or CS & TP, particularly in the non-diagnostic, benign, and FLUS/HLUS diagnostic categories. The rate of resection for FLUS diagnoses is higher in the TP only cohort, but respective RON/ROM are still comparable to T-FNAs evaluated by CS & TP. The RON/ROM within each diagnostic category for both cohorts are relatively similar, suggesting institutions can use either preparation for T-FNAs with similar reliability.

435 Evaluating ASC-H:HSIL Ratio as a Means to Establish a Benchmark for the Frequency of the Worrisome Yet Indeterminate Category of ASC-H

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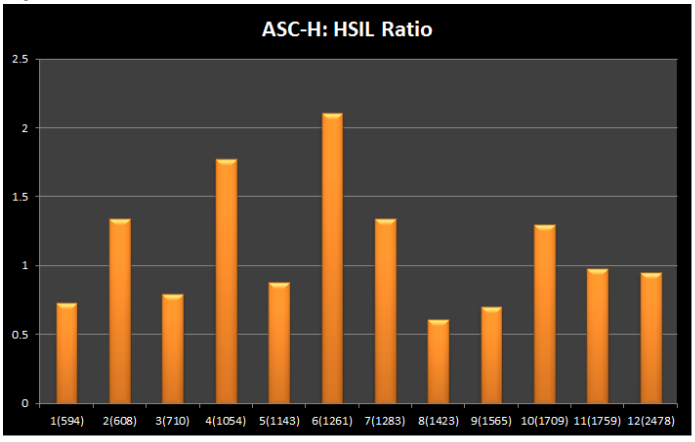
Disclosures: Siavash Samimi: None; Ashwyna Sunassee: None; Dina Mody: None; Michael Thrall: None

Background: Pap test results reflect the diagnostic certainty of the nature of the disease process on the part of the cytopathologist (CP). Established quality assurance methods use rates of atypical squamous cells to squamous intraepithelial lesion (ASC: SIL ratio) as a benchmark for CP performance. We have evaluated the possibility of using ASC-H: HSIL ratio as a benchmark in a high volume practice with large numbers of both interpretations.

Design: We retrospectively reviewed Pap test interpretations during a 5 year period from 12 CPs. There were 15587 cases signed out by pathologists. These are screening population Pap tests. Chi square statistical analysis was utilized.

Results: There were 641 cases of ASC-H with follow up biopsy results, of which 390 had Squamous intraepithelial lesion (SIL) on follow-up biopsy and 662 cases of HSIL Pap tests with follow up biopsy results, of which 481 had SIL on biopsy. Among the ASC-H cases, 61% showed SIL on the follow up biopsy while the rate was 72% for HSIL Pap test results (p <0.01). These results are expected as the diagnostic certainty is higher in the HSIL category in comparison to ASC-H. The ASC-H: HSIL ratios among CPs ranged from 0.61-2.11 (mean, 1.02). Figure 1 shows the ASC-H: HSIL ratios for each pathologist, organized by number of Pap tests signed out, from highest to lowest.

Figure 1 - 435



Conclusions: ASC-H is defined by being insufficient quantitatively or qualitatively for HSIL. Pathologists with a high number of ASC-H cases have the option of interpreting the less worrisome ones as atypical squamous cells of undetermined significance (ASC-US) and sending them to HPV triage rather than directly to colposcopy. As a quality assurance benchmark, therefore, the use of an ASC-H: HSIL ratio may be useful. We have found that ASC-H: HSIL ratios among CPs are on average about 1. The CPs with the highest ASC-H: HSIL ratios were around 1.5-2, similar to already widely-used ASC: SIL ratios. CPs who view substantial numbers of ASC-H and HSIL Pap tests can therefore mentally track their ratio and detect the possibility that ASC-H is being used too often if they are well above 2. Awareness of ASC-H: HSIL ratio during sign-out may help CPs to avoid over-use of ASC-H and potentially reduce the colposcopy rate.

436 Role of Programmed Death-ligand 1 Overexpression on Thyroid Fine Needle Aspiration. Diagnostic Marker for NIFTP, I-FVPC and PTC.

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[1]Catholic University of Sacred Heart, Barletta, Italy, [2]Catholic University of Sacred Heart, Rome, Italy, [3]Roma, Italy, [4]University Cattolica Sacro Cuore, Rome, Italy, [5]Fondazione Policlinico Universitario A. Gemelli, Rome, Italy, [6]Catholic University, Rome, Italy, Italy

Disclosures: Stefania Sfregola: None; Marco Dell'Aquila: None; Teresa Musarra: None; Vincenzo Fiorentino: None; Guido Fadda: None; Maurizio Martini: None; Luigi Maria Larocca: None; Esther Rossi: None

Background: Programmed death-ligand 1 (PD-L1) expression on tumor cells is emerging as a predictive biomarker in anti-PD-L1 directed cancer immunotherapy. Its role has been clearly defined in a variety of human cancers and linked to poor prognosis and resistance to anticancer therapies. However the specific role of PD-L1 expression in thyroid cancers has not been well described. This preliminary study was designed to investigate the alterations in expression and specific localization of PD-L1 in different thyroid lesions. We sought to define if PD-L1 expression may be used to discriminate encapsulated non-invasive follicular variant of papillary thyroid carcinoma (E-FVPC) reclassified as Noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) from the invasive FVPC (I-FVPC) also on fine needle aspiration cytology (FNAC)

Design: From January to July 2018 we enrolled all the cases (66) with a cytological diagnosis of indeterminate and malignant lesions on FNAC. Immunocytochemistry- ICC for PD-L1 was carried out on liquid based cytology (LBC)

Results: The retrospective FNAC cohort included 11 atypia of undetermined significance (AUS/FLUS), 16 follicular neoplasm (FN), 7 suspicious for malignancy (SM) and 32 positive for malignancy (PM). Histologically, AUS/FLUS resulted in nine follicular adenomas (FA), one NIFTP and one follicular carcinoma (FC) whereas FN/SFN included seven FAs and 9 malignancies (5 I-FVPC, 1NIFTP and 3PTC). The 7SM were diagnosed as one FA, two I-FVPC and 4PTC whilst the 32 PMs included 6 NIFTP, 5 I-FVPCs, 15 PTCs, 4 tall cell PTC-TCV, 2MTC. The clinical-pathological factors were correlated with the PD-L1 expression. Increased plasma membrane and cytoplasm PD-L1 expression was found in 23 out of 42 (54.7%) malignant cases including 40.5% PTC. Controversial expression was found in the TCV

(only few cells-2%). The PD-L1 expression was present in 50% of I-FVPC and negative in all NIFTP. Negative PD-L1 expression was found also in all FA on both cytological and histological samples demonstrating the similarities between FA and NIFTP

Conclusions: Our preliminary data showed that PD-L1 expression in PTC correlates with a BRAF mutation. The different expression of PD-L1 in FVPC seems to support the concept that NIFTP is a non-malignant neoplasm. PD-L1 expression might be used on thyroid FNAC as an additional diagnostic biomarker. However, larger series with surgical follow-up need to be studied in order to permit a clearer statement about a correlation

437 Tiny but Mighty: A Successful Clinical Experience Repurposing Diagnostic Cytology Slides for Lung Cancer Targeted Next-Generation Sequencing

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Disclosures: Rosalind Sharain: None; Shannon Knight: None; Jesse Voss: None; Benjamin Kipp: None; Sarah Kerr: None

Background: Rapidly expanding targeted therapies have made molecular testing the standard of care for lung cancer. Formalin-fixed, paraffin-embedded (FFPE) biopsies are most commonly used, however, cytology smears may offer superior quality and the benefit of on-site adequacy assessment. We report our experience using a lung targeted next-generation sequencing (NGS) assay specifically validated for cytology slides.

Design: Cytology slides (direct smears or liquid-based) were decoverslipped and scraped for total nucleic acid extraction and NGS covering mutations in *EGFR*, *BRAF*, *KRAS*, *HRAS*, *NRAS*, *ALK*, *ERBB2*, and *MET*, and gene fusions involving *ALK*, *ROS1*, *RET*, and *NTRK1*. Libraries prepared using targeted multiplex PCR were sequenced on an Illumina platform. Target specimen adequacy was 5000 total nucleated cells, with a required tumor cellularity of 20%.

Results: We received 280 cytology specimens for testing over 20 months, including 218 in-house and 62 reference laboratory cases. Provided diagnoses included 215 adenocarcinomas, 35 non-small cell carcinomas, 19 squamous cell carcinomas, 8 small cell/combined small cell carcinomas, and 3 others. Nearly 100% (279) of cases passed mutation analysis, and 89% (249) passed fusion analysis. Of cases failing fusion analysis, 18 had a pathogenic mutation that would make a targetable fusion very unlikely. Excluding variants of uncertain significance, 166 pathogenic alterations were reported for 150 specimens, including mutations in *KRAS* (75), *EGFR* (50), *BRAF* (9), *ERBB2* (7), *MET* (6), *NRAS* (4), and *ALK* (1), and fusions in *ALK* (10), RET (2), and ROS1 (2). Therefore, excluding KRAS mutations (26%) and cases without a detected alteration (46%), the percentage of specimens with a potentially targetable mutation was 28%.

Conclusions: Our clinical experience demonstrates a high success rate repurposing cytology slides for targeted NGS. This approach extends limited specimens and reserves FFPE tissue for diagnostic and theranostic immunostains. Moreover, on-site evaluation can ensure specimen adequacy, potentially sparing patients multiple procedures. Due to the success of this strategy, we have implemented a system to prioritize cytology slides for NGS when adequate. We are investigating and troubleshooting the lower success rate for the RNA fusion portion of the test. Validation of all molecular oncology tests should include cytology slides to most efficiently use these increasingly common and precious specimens.

438 Comparison of Cobas 4800 HPV and Cervista HPV HR Assays for Detecting High-risk HPV in SurePath Pap Specimens

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Background: The Cobas 4800 HPV assay was approved by the U.S. Food and Drug Administration for HPV testing for cervical cancer prevention in SurePath Pap specimens. To validate the Cobas 4800 HPV assay in our institution, we compared the Cobas 4800 HPV assay to the Cervista HPV HR assay in detecting high-risk HPV (hrHPV) in SurePath Pap cytology specimens.

Design: A total of 138 SurePath Pap cytology specimens collected in our institution for Pap/HPV co-testing in 2018 were used for the study. After Pap cytology testing, the residual Pap specimens were split for testing by the Cobas 4800 HPV and Cervista HPV HR assays. The patient ages ranged from 25-77 years (mean, 48 years). PCR-based HPV testing (GP5+/GP6+) was performed in the Pap specimens whose Cobas 4800 and Cervista HR assay results were discrepant. Clinical data for patients with discrepant HPV testing results were reviewed. Descriptive statistical analysis was performed to compare the agreement and the testing efficacy between the two HPV testing assays.

Results: In the 138 Pap specimens, the Cobas 4800 HPV and Cervista HPV HR showed 54 positive and 69 negative results, a good testing concordance (89.1%) with a kappa value of 0.78 (95% CI: 0.675-0.885). Fifteen of the specimens showed discrepant results between the two assays. Of the 7 cases with Cervista-/Cobas+ results, 5 (71%) were confirmed as positive by PCR. Of the 8 cases with Cervista+/Cobas- results, 4 (50%) were confirmed as positive by PCR (Table 1). The sensitivities and the specificities for detecting hrHPV between Cobas HPV (93.7%, 97.3%) and Cervista HPV HR (92.1%, 94.7%) were comparable. All 7 patients with Cervista-/Cobas+ results had a history of cervical dysplasia, with 6 having previous positive HPV testing results. In the 8 patients with Cervista+/Cobas- results, 2 had a history of cervical dysplasia and 3 had previous positive HPV testing results (Table 1). Reflex HPV16/18 testing was negative in 6 of the 8 cases with Cervista+/Cobas- results.

Table 1. Clinical characteristics of cases with discrepant HPV results between Cervista HPV HR and Cobas HPV assays (N=15)

Case No.	Age	Pap results	Cervista HPV HR	Cobas HPV	PCR HPV	History of dysplasia	Past HPV results
1	61	NILM	-	HPV16	+	HSIL, CIN2-3, adenocarcinoma	HPVHR +
2	41	ASC-US	-	HPV16	+	HSIL	HPVHR+ HPV16+ HPV18-
3	30	NILM	-	HPV16	+	No	No
4	25	ASC-US	-	HR	+	LSIL, ASC-US	HPVHR + HPV16- HPV18-
5	53	ASC-US	-	HR	-	LSIL, CIN1	HPVHR+ HPV16+ HPV18-
6	33	ASC-US	-	HR	+	CIN1	HPVHR+ HPV16- HPV18-
7	46	ASC-US	-	HR	-	HSIL, VAIN3, CIN2	HPVHR+ HPV16- HPV18-
8	60	ASC-US	+	-	+	HSIL	HPVHR+
9	63	NILM	+	-	-	ASC-US	HPV16- HPV18-
10	60	NILM	+	-	+	No	HPV16- HPV18-
11	38	NILM	+	-	-	No	HPVHR+ HPV16- HPV18-
12	34	NILM	+	-	-	No	HPV16- HPV18-
13	33	NILM	+	-	+	No	HPV16- HPV18-
14	34	NILM	+	-	-	No	HPV16- HPV18-
15	56	ASC-US	+	-	+	ASC-H, CIN2	HPVHR+

Conclusions: The Cobas 4800 HPV assay is a valid testing assay for hrHPV in SurePath Pap cytology specimens in our institution, with slightly higher sensitivity and specificity than Cervista HPV HR for detection of hrHPV. The Cobas 4800 HPV assay appears to be more clinically relevant than the Cervista HPV assay. Further study with large clinical datasets is required to confirm its clinical efficacy.

439 Non-16/18 High-Risk HPV Types in African–American Women With Biopsy-Proven HSIL: An analysis of 131 Cases

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Background: The incidence and mortality rates of invasive cervical cancer are higher in African-American women. The consensus is that up to 50% of high-grade squamous intraepithelial lesions of the cervix (HSIL) and 70% of invasive cervical carcinoma are caused by high risk-human papillomavirus 16/18 (HR-HPV 16/18). However some studies have suggested variability in the prevalence of HPV genotypes associated with cervical lesions by race/ethnicity and geographic region. Non-16/18 HR-HPV types such as HPV 31, 33, 35, 39, 45, 51, 52, 58 and 59 have been reported to cause cervical intraepithelial lesions and invasive cervical carcinoma. The FDA-approved HPV Cobas test simultaneously provide pooled results on high risk HPV genotypes 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68 and individual results for HPV 16 and 18 (the highest- risk genotypes). The objective of this study was to determine the pattern of distribution of HR-HPV in an African-American (AA) cohort from the Detroit area, with biopsy-proven HSIL.

Design: A search of the electronic medical records was conducted with the search terms “HSIL” and “HPV” from 2015-2017. Exclusion criteria included negative HPV test results and prior HPV vaccination. AA patients with positive cytology and positive HPV test results were identified. Results of histopathology follow-up after cytology were documented. HPV testing was performed with the Cobas 4800 system; pap smears were prepared using the ThinPrep Pap test.

Results: 131 cases selected for the study included 52 cases of atypical squamous cells-cannot exclude HSIL (ASC-H), 42 cases of low-grade squamous intraepithelial lesion-cannot exclude high grade (LSIL-H) and 37 cases of HSIL. None of the patients received the HPV vaccine prior to their pap smears. Histopathology follow-up was available for 59 cases (45%), 41 of these (69%) had biopsy-proven CIN2/3 (cervical intraepithelial neoplasia). Out of these 41, 24 cases (59%) were positive for non-16/18 HR-HPV only while 12 (29%) were positive for HPV 16/18 only. Coinfection with HPV16/18 and other HR-HPV was found in 5 cases (12%).

Conclusions: This study suggests that AA women from the Detroit area with biopsy-proven HSIL are more likely to be positive for non-16/18 HR-HPV types. Future HPV vaccination strategies may need to include several more non-16/18 HR-HPV types.

440 Cytomorphologic Study of Urine after Bacillus Calmette-Guérin Intravesical Therapy

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Background: Urinary cytology plays a key role in management of patients with urothelial carcinoma. Intravesical Bacillus Calmette-Guérin (BCG) immunotherapy is standard first-line treatment for bladder carcinoma in situ (CIS), as well as standard adjuvant therapy for intermediate to high grade non-muscle-invasive bladder cancer. >30% of patients who receive BCG have been reported to experience progression or recurrence; failure to respond to BCG has been suggested to be a poor prognostic sign. European Association of Urology (EAU) guidelines mandate surveillance cystoscopy, often combined with urine cytology, during treatment because of the high progression/recurrence rate.

BCG instillation may lead to severe bladder inflammation and reactive epithelial changes; both impede accurate urine cytological assessment. While studies have commented specifically on the cytologic changes found in urothelial cells, the greater cytomorphologic spectrum of findings in urine after BCG has not been well-defined.

Design: We performed a retrospective cytomorphologic study of 146 post-BCG urine specimens. All cytologic preparations were stained with Papanicolau and examined for cytological characteristics. Pertinent clinical findings were reviewed.

Results: 70 (48%) urine specimens were negative for atypia/malignancy, 40 (27%) had cells of uncertain significance, 10 (7%) were suspicious for high grade urothelial carcinoma (HGUC), 25 (17%) were positive for HGUC, and 1 (1%) was unsatisfactory. The specimens were collected at a mean of 50.4 $\pm$ 22 days after BCG treatment. 129 (88%) specimens demonstrated an inflammatory background. Macrophages (48%), degenerative changes (47%), and columnar cells (43%) were common findings. Multinucleated/umbrella cells were present in 41 (28%) of cases without atypia, and in 16 (11%) with atypia. We also identified

the presence of extremely large cells with enlarged but bland nuclear features and abundant cytoplasm in 11 (8%) of cases. To our knowledge, these cells have not been reported in any studies.

Figure 1 - 440

	NUAM	AUCUS	AUC-H	HGUC	UNSAT	Total
Demographics						
# Cases	70 (48%)	40 (27%)	10 (7%)	25 (17%)	1 (1%)	146 (100%)
Avg Days after BCG	49.5 ± 14	53.7 ± 37	55.9 ± 17	46.4 ± 12	37.0 ± 0	50.4 ± 22
Cytomorphology						
Granular Debris	14 (20%)	12 (30%)	2 (20%)	13 (52%)	0 (0%)	41 (28%)
Macrophages	26 (37%)	23 (58%)	4 (40%)	17 (68%)	0 (0%)	70 (48%)
Giant Cells	6 (9%)	3 (8%)	1 (10%)	2 (8%)	0 (0%)	12 (8%)
Granulomatous inflammation	2 (3%)	1 (3%)	0 (0%)	0 (0%)	0 (0%)	3 (2%)
Inflammation						
Total	55	36	6	32	0	129 (88%)
Acute	31	18	3	18	0	70 (48%)
Chronic	24	18	3	14	0	59 (40%)
Degenerative Changes	20 (29%)	20 (50%)	10 (100%)	19 (76%)	0 (0%)	69 (47%)
Multinucleated/ Umbrella Cells	19 (27%)	15 (38%)	1 (10%)	6 (24%)	0 (0%)	41 (28%)
Multinucleated Cells w/Atypia	2 (3%)	2 (5%)	0 (0%)	12 (48%)	0 (0%)	16 (11%)
Large Cells	4 (6%)	5 (13%)	1 (10%)	1 (4%)	0 (0%)	11 (8%)
Calcifications/Crystals	2 (3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (1%)
Vacuolization	10 (14%)	8 (20%)	3 (30%)	8 (32%)	0 (0%)	29 (20%)
Columnar Cells	28 (40%)	22 (55%)	5 (50%)	8 (32%)	0 (0%)	63 (43%)
Cystitis Glandularis	12 (17%)	5 (13%)	1 (10%)	2 (8%)	0 (0%)	20 (14%)

Conclusions: Inflammation, macrophages, degenerative changes, and columnar cells are common findings in urine cytology specimens after BCG treatment. Atypical and large multinucleated cells can also be seen. Granulomas, a common finding in post-BCG histology samples associated with therapeutic response, are rare. Awareness of the range of cytomorphologic findings in these specimens may lead to more accurate interpretation of post-BCG urine samples.

441 PAX8 Expression in Benign Mesothelial Cells in Effusion Cytology

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Background: Immunohistochemistry for PAX8 has frequently been utilized in cytology and surgical resection specimens to differentiate between organ-specific neoplastic processes. Several studies have noted the utility of PAX8 in detecting malignancies derived from the kidney, thyroid, and Müllerian tract, and more recently pancreatic neuroendocrine tumors and a subset of urothelial carcinomas. However, PAX8 expression has recently been reported in benign and malignant mesothelial cells (msc) on surgical resection specimens. As such, this study aims to investigate the incidence of PAX8 expression in benign msc in effusion cytology specimens, evaluate the extent and intensity of staining in cases with PAX8 positive msc, and to correlate cases of PAX8 positive msc with concurrent clinical diagnoses.

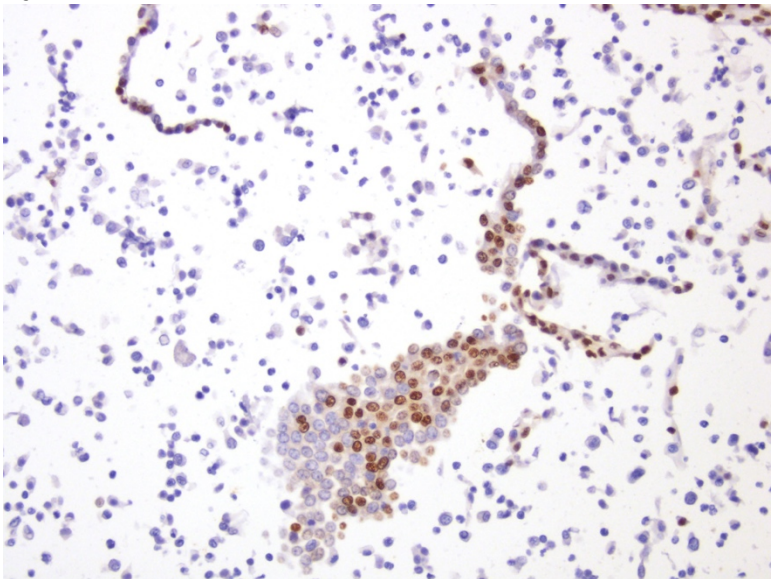
Design: A search in the electronic medical record (EMR) system (from 1/1/15 to 12/31/16) of a large, tertiary care academic institution yielded 122 pelvic washing, pleural, and ascetic fluid cytology specimens with cell block material containing adequate cellularity (defined as >100 msc) for subsequent evaluation by PAX8 immunohistochemistry. The intensity and extent of PAX8 staining in msc is scored as follows: Intensity of staining: 0, none; 1+, weak; 2+, moderate; 3+, strong; Extent of staining: 0, none; 1+, <10% msc; 2+, 11-50% msc; 3+, >50% msc; The EMR was searched for clinical diagnoses associated with all 122 cases.

Results: The 122 cases consisted of 117 pelvic washes, 4 pleural fluids, 1 ascitic fluid collected from 118 women and 3 men. 44 (36%) cases showed variable immunoreactivity in benign msc for PAX8 (Figure 1). Of these, 43 were pelvic washes and 1 was ascitic fluid, all collected from women ranging from 23 to 80 years of age. Results of PAX8 staining in msc were associated with clinical diagnoses and summarized in Table 1.

Table 1: Results of PAX8 staining associated with clinical Diagnoses

Diagnosis	n (%)	PAX8+ msc n (%)	Staining in PAX8+ msc n (intensity,extent)	% of all cases with PAX8+ msc
Neoplastic: malignant				
Adenocarcinoma				
Ampullary	1 (0.8)	0 (0)		0.0
Breast	1 (0.8)	0 (0)		0.0
Biliary	2 (1.6)	0 (0)		0.0
Cervical	1 (0.8)	1 (100)	(3+,1+)	2.3
Endometrial				
-Endometrioid	20 (16.5)	6 (30.0)	2 (1+,1+) 1 (2+,1+) 2 (2+,2+) 1 (2+,3+)	13.6
-Serous	1 (0.8)	0 (0)		0.0
-Mixed	1 (0.8)	1 (100)	(1+,1+)	2.3
-Malignant mixed Mullerian tumor	1 (0.8)	1 (100)	(2+,1+)	2.3
Esophageal	1 (0.8)	0 (0)		0.0
Gastric	2 (1.6)	0 (0)		0.0
Ovarian				
-Clear cell	3 (2.6)	2 (66.7)	1 (1+,1+) 1 (3+,1+)	4.5
-Endometrioid	1 (0.8)	0 (0)		0.0
-Serous (high-grade)	8 (6.7)	2 (25)	1 (2+,1+) 1 (2+,2+)	4.7
-Mixed	1 (0.8)	1 (100)	(2+,2+)	2.3
-Unclassified	2 (1.6)	1 (50)	(2+,2+)	2.3
Pancreatic	1 (0.8)	0 (0)		0.0
Clear cell sarcoma	1 (0.8)	0 (0)		0.0
Endometrial stromal sarcoma	2 (1.6)	0 (0)		0.0
Epithelioid hemangioendothelioma	1 (0.8)	0 (0)		0.0
Neuroendocrine carcinoma	1 (0.8)	0 (0)		0.0
Lymphoma	2 (1.7)	0 (0)		0.0
Mesothelioma	1 (0.8)	0 (0)		0.0
Neoplastic: Benign				
Leiomyoma	3 (2.6)	1 (33.3)	(1+, 1+)	2.3
Ovarian				
-Mucinous borderline tumor	1 (0.8)	0 (0)		0.0
-Fibroma	2 (1.6)	2 (100)	1 (2+,3+) 1 (3+,2+)	5.0
-Mucinous cystadenoma	9 (7.5)	5 (55.6)	2 (1+,1+) 2 (2+,1+) 1 (3+,3+)	11.4
-Seromucinous cystadenoma	1 (0.8)	1 (100)	(2+,1+)	2.3
-Serous cystadenoma	7 (5.8)	2 (28.6)	1 (1+,1+) 1 (3+,3+)	5.0
-Teratoma	7 (5.8)	3 (42.9)	3 (1+,1+)	6.8
-Fibrothecoma	1 (0.8)	0 (0)		0.0
-Adult granulosa cell tumor	2 (1.6)	2 (100)	1 (2+,1+) 1 (1+,1+)	5.0
Non-neoplastic				
Benign hemorrhagic cyst of the ovary	1 (0.8)	0 (0)		0.0
Cirrhosis	2 (1.6)	0 (0)		0.0
Congestive heart failure	2 (1.6)	0 (0)		0.0
Uterine				
-No diagnostic abnormality	1 (0.8)	0 (0)		0.0
-Endometrial polyp	1 (0.8)	1 (100)	(2+,1+)	2.3
-Endometriosis	13 (10.8)	9 (69.2)	1 (2+,1+) 3 (2+,2+) 1 (2+,3+) 3 (3+,2+) 1 (3+,3+)	21.0
-Complex atypical hyperplasia	2 (1.6)	1 (50)	(3+,3+)	2.3
Fibrosis of fallopian tube	1 (0.8)	0 (0)		0.0
Granulomatous inflammation	2 (1.6)	0 (0)		0.0
Ischemic bowel with necrosis	1 (0.8)	0 (0)		0.0
Ovarian torsion with necrosis	1 (0.8)	1 (100)	(1+,2+)	2.3
Ovary with simple cyst	2 (1.6)	0 (0)		0.0
Paratubal cyst	2 (1.6)	1 (50)	(2+,1+)	0.0
Pericarditis	1 (0.8)	0 (0)		0.0
Pleuritis	1 (0.8)	0 (0)		0.0
Salpingitis	1 (0.8)	0 (0)		0.0
Total	122	44		

Figure 1 - 441



Conclusions: Our results show a significant subset (36.8%) of pelvic washes show variable PAX8 expression in benign msc. PAX8 expression in msc is most commonly associated with endometrioid adenocarcinoma (14%), benign cystadeno(fibro)ma (18%), and endometriosis (20.5%), highlighting the importance of careful interpretation of PAX8 positivity and use of immunohistochemical panels rather than single stains in effusion cytology.

442 An Institutional Experience: Does AUS with Subclassified Atypia for Thyroid Fine Needle Aspirations (FNA) Improve the Rates of Neoplasia and Malignancy?

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Background: The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) uses the diagnostic category of atypia of undetermined significance (AUS)/follicular lesion of undetermined significance (FLUS) in cases with architectural and/or cytologic atypia insufficient for a more definitive diagnosis, but surpassing that expected in benign cases. Historically, our institution used FLUS for indeterminate lesions with architectural and/or cytologic atypia or Hurthle cell lesion of undetermined significance (HLUS) for lesions comprised exclusively of Hurthle cells (HC). In 2018, we implemented the new preferred TBSRTC which uses AUS with subclassified atypia - architectural, cytologic, architectural and cytologic, and predominantly HC. We sought to determine whether this preferred reporting system for atypical thyroid FNAs would improve the rates of neoplasia (RON) and malignancy (ROM) when compared to the original FLUS/HLUS categories.

Design: A search in our electronic medical record system for thyroid FNA cases diagnosed as FLUS or HLUS in a 2-year period with subsequent surgical resections yielded 100 cases with cytologic slides available for review. 5 resections had no correlating sampling from pre-operative FNA sites and were excluded, leaving 95 cases. Two cytopathologists (CP) (ML, XJ) reclassified pre-operative FLUS and HLUS cases using TBSRTC AUS subclassification. RON and ROM were then calculated for each subcategory.

Results: 86 (90.5%) and 9 (9.5%) cases were originally classified as FLUS and HLUS, respectively. RON and ROM for FLUS were 31.4% and 15.1% and 77.8% and 22.2% for HLUS. Diagnostic rates after using TBSRTC AUS subclassification with respective RON and ROM are shown in Table 1. Of the AUS subcategories, architectural atypia (AA) was the most commonly used subclassification. RON and ROM for AUS, AA was similar to those from the original FLUS category. The highest RON and ROM for an AUS subcategory were seen in AUS, predominantly HC, which was relatively similar to those from the original HLUS category. The other AUS subcategories were utilized inconsistently between the two CP.

Table 1: Comparative Diagnostic Rates and respective rates of neoplasia (RON) and malignancy (ROM) after subcategorizing AUS thyroid FNAs

Diagnostic Category	CP 1	CP 2
Non-diagnostic	3 (3.2%)	1 (1%)
-RON	66.7%	0%
-ROM	66.7%	0%
Benign	36 (37.9%)	5 (5.3%)
-RON	27.8%	0%
-ROM	11.1%	0%
AUS (architectural atypia)	25 (26.3%)	73 (76.8%)
-RON	32%	30.1%
-ROM	16%	13.7%
AUS (cytologic atypia)	0	3 (3.2%)
-RON	-	33.3%
-ROM	-	33.3%
AUS (architectural & cytologic atypia)	17 (17.9%)	3 (3.2%)
-RON	35.3%	66.7%
-ROM	5.9%	0%
AUS (predominantly Hurthle cells)	7 (7.4%)	8 (8.4%)
-RON	57.1%	87.5%
-ROM	14.3%	25%
Suspicious for follicular neoplasm	3 (3.1%)	0
-RON	0%	-
-ROM	0%	-
Suspicious for papillary thyroid carcinoma	4 (4.2%)	2 (2.1%)
-RON	100%	100%
-ROM	75%	100%

Conclusions: Based on our preliminary data, the utilization of AUS with subclassified atypia in thyroid FNA specimens increases interobserver variability without significant and consistent differences in RON or ROM.

443 Artifacts Noted on New Endoscopic Ultrasound Guided Tissue Acquisition Needles.

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Background: Tissue acquisition using endoscopic ultrasound (EUS) guided fine needle aspiration (FNA) and biopsy (FNB) is commonly utilized for sampling pancreatic masses. Innovations in biomaterial and design in FNA and FNB needles were undertaken to ease sample acquisition, enrich adequacy and improve diagnostic accuracy. Shedding of biomaterials from needles in tissues during sampling may have patient implications. The frequency and types of artifacts from biomaterial shedding noted on cytology preparations from FNA and FNB needles has not been investigated to date. These may be observed as a result of multiple factors including friction with tissues or bending of needle. This report analyzes the frequency and types of artifacts noted on cytology sample preparations from biomaterial shedding from EUS-FNA and FNB needles.

Design: A review of EUS guided tissue acquisitions from 99 pancreatic lesions was performed. Diff Quik and Papanicolaou stained smears as well as cell block preparations were reviewed. We analyzed artifacts from needle alloy (brown-black particulate matter) and sheath material (polygonal shape) shed from EUS-FNA and FNB needles. Analysis on the frequency of type of biomaterial shedding, and association with needle gauge was performed. Association of artifacts with type of needle design was performed where available.

Results: Artifacts from needle alloy or sheath material are frequently noted in sample preparations (95/99; 96%; Table 1). Particulate material was more frequent in comparison to sheath material (96% vs. 67%). Sheath material was significantly more frequently noted with use of either 22-G or 25-G needle in comparison to 19-G ($p<0.05$). This data held true regardless of the needle design (Shark core versus Cook).

Artifacts from needle alloy or sheath material		
Size of needle	**Presence of artifact**	**Absence of artifact**
19-G	4	1
22-G	73	3
25-G	12	0
22-G and 25-G	6	0

Conclusions: It is common to find artifacts from needle bending or shearing from tissues on samples acquired under EUS guidance. Scrapping of sheath material by needle tip is observed significantly more frequently with 22-G or 25-G needles. This study highlights the importance of studying biomaterial and needle construction effects on adverse events when designing novel EUS guided tissue acquisition needles.

444 Cytomorphology and morphometry of gastric-type endocervical adenocarcinoma in liquid-based preparations

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Background: Gastric-type endocervical adenocarcinoma (GAS) is a recently described, uncommon and aggressive tumor with subtle morphological features and HPV-independent etiology. Prior studies examined GAS in histology and Papanicolaou test (Pap) cytology (mainly direct smear preparations), but data on GAS cytomorphology in liquid-based cytology (LBC) and a North American setting are scant. We aimed to investigate whether previously described cytomorphologic features can be detected in LBC. We hypothesized that nuclear enlargement as a readily assessable morphometric feature may aid in GAS detection.

Design: GAS surgical diagnoses were retrieved from the laboratory information systems. Pap slides preceding the surgical sample were retrieved or requested from outside laboratories. 2 cytopathologists and 1 trainee reviewed the LBC slides for 15 predetermined cytomorphological features and compared them to usual-type endocervical adenocarcinoma (UEA). Morphometry of the glandular cell nuclear area (GAS, UEA, CTRL [control: benign endocervical cells]) was performed using Aperio ImageScope (Sausalito, CA). Measurement of 3 neutrophils per slide was used to generate a normalized nuclear/neutrophil area ratio. Statistical analysis was performed (GrapPad Prism). $P<0.05$ was considered statistically significant.

Results: We identified 16 patients with confirmed histopathological GAS diagnosis. For 14 patients ≥1 Pap were available (1 patient: 2, 1 patient: 3); 16 LBC slides (5 ThinPrep, 11 SurePath), 1 direct smear. Initial diagnoses rendered in LBC were adenocarcinoma/carcinoma (6/16), atypical glandular cells (2), adenocarcinoma in-situ (1), and NILM (7). Review revealed abnormal glandular cells in 6/7 NILM cases. Flat/honeycomb-like sheets, microvesicular cytoplasm, prominent nucleoli and abrupt anisonucleosis (87 vs. 8.3%, 100 vs. 17%, 93 vs. 25%, 92 vs. 50%) were most discriminatory for GAS vs. UEA, respectively. Yellow mucin (20%), intranuclear cytoplasmic pseudoinclusions (20%), and Paneth/goblet cells (20%) were GAS-unique. Normalized GAS nuclear areas were found to be increased compared to CTRL ($p<0.05$).

Conclusions: GAS is under-recognized and may mimic reactive endocervical cells. Focus on glandular cells with abnormal nuclear enlargement in conjunction with any of the described cytological features may avoid false-negative Pap results. Using neutrophils as internal size reference may be useful as visual aid in LBC. Morphology is critical for the early detection of this HPV-unrelated entity.

445 Cytologic Features within Hyperchromatic Crowded Groups on Pap tests from Women 50 Years of Age or Older to Distinguish Atrophy-Related Changes from High Grade Dysplasia.

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Disclosures: Melissa Sweeney: None; Sharlin Varghese: None; Sierra Kovar: None; Emily Almeter: None; John Plavnicky: None; Hasan Khatib: None; Luis De Las Casas: None

Background: Pap tests from women 50 years of age or older often display atrophic changes (AC) including hyperchromatic crowded groups (HCG) of squamous cells that could mimic high grade squamous intraepithelial lesions (HSIL). In addition, HCG could be the only evidence of HSIL on Pap tests.

The aim to this study is to identify cytologic features within HCG that could help in distinguishing HSIL from AC.

Design: An IRB approved 7-year retrospective review of cervical ThinPrep Pap tests (TP) from women age 50 years and older who underwent high risk Human Papilloma virus (hrHPV) testing and had a cervical biopsy with p16 immunostaining at our institution was performed. Glandular lesions were excluded. TP slides were randomly distributed and blindly reviewed for hyperchromatic crowded groups by two experienced board certified cytopathologists who also practice gynecologic pathology as their subspecialty. HCG as defined by Dr. Richard DeMay are “3-dimensional aggregates of crowded cells with hyperchromatic nuclei.”[1]

HCG were assessed for unequivocal lack of cell polarity, atypical or parakeratotic cells at HCG edges, irregular nuclear membranes, uneven chromatin distribution, irregular enlarged nucleoli, mitosis, and apoptotic bodies.

Results: HCG from twenty seven Thin Prep (TP) slides including eighteen (18/27; 66.67%) cases from HSIL and nine (9/27; 33.33%) from atrophic changes were analyzed.

Lack of cell polarity was identified in 0% (0/9) AC and 100% (18/18) HSIL, atypical cells at HCG edges in 11% (1/9) AC and 5% (1/18) HSIL, parakeratotic cells at HCG edges 67% (6/9) AC and 89% (16/18) HGD, irregular nuclear membranes in 0% (0/9) AC and 11% (2/18) HSIL, uneven chromatin distribution in 0% (0/9) AC and 11% (2/18) HSIL, irregular enlarged nucleoli in 0% (0/9) AC and 11% (2/18) HSIL, mitosis in 0% (0/9) AC and 0% (0/18) HSIL, and apoptotic bodies in 0% (0/9) AC and 0% (0/18) HSIL.

Results were analyzed using two-sided Fisher exact test.

Conclusions: Although our study sample size is relatively small, our results revealed that unequivocal lack of polarity within hyperchromatic crowded groups in TP from women 50 years of age and older, could be a reliable predictor for the presence of HSIL ($p<0.0001$). Other HCG cytologic features studied overlap between atrophy and high grade dysplasia.

446 Endoscopic Ultrasound-guided Tissue Acquisition of Solid Mass Lesions of Pancreas: A Retrospective Comparison Study of Fine Needle Aspiration and Fine Needle Biopsy

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Disclosures: Jacob Sweeney: None; Lauren Soong: None; Abha Goyal: None

Background: Endoscopic ultrasound (EUS) guided fine needle aspiration (FNA) with rapid on site evaluation (ROSE) has allowed for safe and effective sampling of pancreatic solid mass lesions. In recent years, fine needle biopsy (FNB) has emerged as an alternative that may require fewer needle passes, be efficacious in absence of ROSE and provide adequate tissue for ancillary studies. Still, it remains unclear which method is more effective. Also, literature examining the relative efficacy of combined FNA/FNB sampling is limited. In this study, we compared the diagnostic yields of FNA, FNB, and combined FNA/FNB at a tertiary care institution.

Design: EUS-FNA (04/2014-08/2017) and EUS-FNB (10/2015-08/2017) specimens of pancreatic solid mass lesions were retrieved. Only FNB specimens procured using SharkCore needle were included. Clinico-radiologic data and pathology findings were recorded. Pathology results of “positive”, “suspicious” and “neoplasm” were considered true positive. The only “negative” cases included were with at least 6 months of follow up. Non-diagnostic cases showed unremarkable pancreatic tissue, non-pancreatic elements, or atypia insufficient for suspicious diagnosis. Diagnostic yield of the procedure was defined as percentage of lesions sampled in which a tissue diagnosis was obtained. A Chi-square test was used for comparisons.

Results: The study cohort included 88 FNA only cases, 39 combined FNA/FNB cases, and 89 FNB only cases. Average lesion size was 2.9 cm (range: 0.8-8.5). Average number of passes was 2.8 (FNA), 2.7 (FNB), 4.5 (FNA/FNB). The 22 gauge needle was used in most patients: 103 (FNB), 66 (FNA). ROSE was performed in 58% cases. The diagnostic yields were 76% (FNA), 74% (FNB), 82% (FNA/FNB). With respect to different parameters, they are depicted in Table 1. The diagnostic yields of FNA and FNB in comparison to one another and to that of FNA/FNB were not statistically different with respect to lesion size or presence/absence of ROSE or with more than 3 passes. The diagnostic yield of FNA/FNB was significantly higher than that of FNA ($p=0.007$) or FNB ($p=0.001$) alone when number of passes was up to three.

Table 1

Parameter	Diagnostic Yield FNA (%)	Diagnostic Yield FNB (%)	Diagnostic Yield FNA/FNB (%)
Overall	76	74	82
Lesion Size <3 cm	70	74	75
Lesion Size > or = to 3 cm	91	86	90
No. of passes < or = to 3	76	73	91
No. of passes >3	81	88	81
With ROSE	85	94	86
Without ROSE	56	63	73

Conclusions: Our results demonstrate that for solid pancreatic lesions, the diagnostic yields of FNA, FNB and combined FNA and FNB are comparable. The combination appears to increment the diagnostic yield over that of either procedure alone when the number of passes is limited. The impact of ROSE on the different procedures is similar.

447 ASC-US Cytology Reporting Rate, HPV Testing, and Histological Results in China's Largest Women Hospital

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Disclosures: Xiang Tao: None; Chengquan Zhao: None

Background: ASC-US report rate as well as HPV positivity of ASC-US patients remain as good quality controls of cervical cytology. This study investigates histopathologic outcomes of ASC-US cervical cytology stratified by HPV testing results in China's largest women hospital.ASC-US report rate as well as HPV positivity of ASC-US patients remain as good quality controls of cervical cytology. This study investigates histopathologic outcomes of ASC-US cervical cytology stratified by HPV testing results in China's largest women hospital.

Design: A total of 1,424,182 cases with Pap cytology test (336,631 ThinPrep, 959,326 SurePath and 128,225 conventional Pap test, CPT) were performed from January, 2011-June, 2018. ASC-US reporting rate, the cases with HR-HPV tests and histopathological findings were analyzed. HPV testing was performed on one of the following platforms randomly chosen: HC2, Cervista, Cobas 4800 and Bioperfectus (Taizhou, China).

Results: Overall ASC-US reporting rate was 3.7%, with highest in 60~69 years age group (6.5%) followed by age less than 20 group (5.5%). ASC-US rate was 3.1%, 4.3%, and 1.2% in ThinPrep, SurePath, and CPT, respectively. Of 15575 women with ASC-US Pap and HPV testing, the HR-HPV positive rate was 47.3% with the highest in women younger than 30 years (52.6%). 20,440 ASC-US cases had histopathology follow-up findings within 6 months. CIN2 and above (CIN2+) lesion was identified in 7.5% of ASC-US women. 7142 women with ASC-US and HPV testing had histological findings within 6 months. CIN2+ lesion was found in 12.1% (468/3880) of women with HPV positive testing, significantly higher than 1.7% (54/3262) for women with negative HPV testing. Of 5768 women with ASC-US and Cobas4800 test, CIN2+ lesion was found in 29.4% (HPV16+), 8.1% (HPV18+), 27.6% (HPV16/18+), 7.5% (other 12 HPV types), 1.5% (HPV negative), respectively.

Table 1. Histopathologic follow-up results for women with ASC-US/HPV testing results, by different ages

Age	HPV positive cases			HPV negative cases		
	Total F/U	CIN1	CIN2+	Total F/U	CIN1	CIN2+
<30	918	437 (47.6%)	89 (9.7%)	536	73 (13.6%)	5 (0.9%)
30-39	1162	455 (39.2%)	147 (12.7%)	872	79 (9.1%)	14 (1.6%)
40-49	828	286 (34.5%)	107 (12.9%)	882	97 (11.0%)	21 (2.4%)
50-59	632	194 (30.7%)	80 (12.7%)	658	65 (9.9%)	7 (1.1%)
>=60	340	90 (26.5%)	45 (13.2%)	314	38 (12.1%)	7 (2.2%)
Total	3880	1462 (37.7%)	468 (12.1%)	3262	352 (10.8%)	54 (1.7%)

Conclusions: This is the largest cohort study about women with ASC-US Pap, HPV test and histopathological finding in China. ASC-US reporting rate, HPV positive rate, and histological findings were within the currently recognized benchmark range. These findings may contribute to stablishing a baseline for better understanding of the status of cervical cancer screening in China.

448 Comparison of Fine-Needle Aspirates with Core Needle Biopsy in Diagnosing Malignancy in Pancreatic Masses: A Single Institutional Experience

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Disclosures: Meryem Terzioglu: None; Kelly Hanley: None; Kelsey McHugh: None; Scott Robertson: None; Jordan Reynolds: None; Maria Luisa Policarpio-Nicolas: None

Background: Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) is a widely used minimally-invasive procedure in diagnosing pancreatic masses. One study showed that the diagnostic yield of US-guided core needle biopsy (CNB) for solid pancreatic lesions is superior to that of EUS-guided FNA. However, another study showed that EUS FNA has a better diagnostic yield and higher sensitivity than core needle biopsy. Given the divergent results, our goal was to investigate our diagnostic yield in EUS-FNA versus concurrent CNB.

Design: A retrospective review of the pathology files was performed to identify patients who underwent both FNA and CNB during the same EUS procedure for a pancreatic mass. Variable data were collected from CoPath (CoPathPlus, Cerner Corp.) & EPIC (Epic, Epic Systems Corp.). The diagnostic yield (defined as percentage of definitive diagnosis), sensitivity, and specificity for malignancy were compared between FNA and CNB.

Results: We had a total of 134 FNA cases with corresponding CNB. The diagnostic classifications were as follows: Nondiagnostic 14, Negative for malignancy 47, Atypical 12, Neoplastic 12, Suspicious 0, Malignant 49. Of the 49 malignant cases, the diagnostic yield for FNA was 97.4% and 75.5% for CNB, p value <0.001. The sensitivity for diagnosing malignancy on FNA was 97.3% and CNB was 69%, p value <0.001. The specificity for diagnosing malignancy was 100% for both FNA and CNB.

Conclusions: Our results show that FNA has a higher sensitivity and diagnostic yield compared to CNB in assessing malignancy in pancreatic masses.

449 Evaluating the Sensitivity of Cytology in Diagnosing Malignant Pericardial Effusions Compared to Pericardial Window Biopsy

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Disclosures: Matthew Thomas: None; Josephine Dermawan: None; Maria Luisa Policarpio-Nicolas: None

Background: Malignant pericardial effusion occurs in a relatively small subset of patients diagnosed with cancer and are predominantly secondary to metastatic disease, as opposed to a primary process of the pericardium. We investigated our cases of malignant pericardial effusions interpreted as positive on cytology, and compared them to the corresponding pericardial window biopsy.

Design: The specimens were limited to cytology cases from pericardial fluid from 2000-2016. The cases were identified through a natural language search using CoPath (pathology information system), and included cytopathology case number, age, gender, and cytological diagnosis. The corresponding pericardial biopsies were also evaluated.

Results: Out of a total of 1287 cases of pericardial effusions, 154 (12%) cases were positive for malignancy. Only 94 malignant pericardial effusion had a corresponding pericardial biopsy. Of these, 53 (60%) pericardial biopsies showed the presence of malignancy and 41 (40%) were diagnosed as benign or showed non-specific changes. Of the 53 cases, 36 (67%) were females, and 17 (33%) were males. Overall the predominant type of malignancy was adenocarcinoma (42 cases, 79%). Most of them were metastasis from the lung, breast, ovary, endometrium, colon, or upper gastrointestinal tract. Seven cases (13%) were of unknown primary. The most common malignancy for females was of breast (36%) origin and lung (47%) in males (Table 1).

Table 1: Distribution of cases by Neoplasm Type on Pericardial Window Biopsy

Neoplasm Type	Positive for Malignancy (All cases)	Positive for Malignancy (Male)	Positive for Malignancy (Female)
Lung (A)	20 (38%)	8 (47%)	12 (33%)
Breast (A)	13 (25%)	0 (0%)	13 (36%)
Ovarian (A)	4 (8%)	0 (0%)	4 (11%)
Endometrial (A)	2 (4%)	0 (0%)	2 (6%)
Colon (A)	2 (4%)	2 (12%)	0 (0%)
Gastroesophageal (A)	1 (2%)	1 (6%)	0 (0%)
Unknown (A)	7 (13%)	4 (24%)	3 (8%)
Small cell carcinoma	1 (2%)	1 (6%)	0 (0%)
Lymphoma	2 (4%)	0 (0%)	2 (6%)
Mesothelioma	1 (2%)	1 (6%)	0 (0%)
Total	53	17	36

***A= Adenocarcinoma**

Conclusions: Pericardial fluid cytology is more sensitive in detecting malignancy compared to pericardial window biopsy. The predominant tumor type is adenocarcinoma.

450 Utility of p53 and mCEA Immunostaining In Biliary Cytology Specimens

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Disclosures: Beena Umar: None; Ariane Robison: None; Mehrnoosh Tashakori: None; Daniel Schultz: None; Chad Stone: None; Kyle Perry: None; Adjoa Denyo Zakhia: None; Lauren Gagnon: None; Love Tsai: None; Ziying Zhang: None

Background: Evaluating biliary strictures by ERCP brushing with cytopathologic exam has a low diagnostic yield due to poor specimen quality and quantity. In addition, ulceration, inflammation, or stent-related atypia make distinguishing benign from malignancy particularly challenging. Literature suggests that p53 and mCEA immunostaining might improve the diagnostic yield in these specimens. We conducted this study to evaluate the utility of p53 and mCEA immunostaining of biliary cytology specimens

Design: 35 cases of biliary cytology specimens with sufficient cell block material for immunohistochemistry from 2015 – 2018 were identified. Of these 35 cases, 12 were diagnosed as malignant, 14 were atypical/suspicious, and 9 were benign. Staining pattern of p53 were evaluated according to the intensity and percentage of positive nuclei and categorized as (1) diffuse overexpression with strong dark nuclear staining (>80%); (2) focal overexpression with strong dark nuclear staining (< 80%); (3) wild type with pale nuclear staining; or (4) negative. mCEA staining was classified as (1) diffuse strong cytoplasmic staining; (2) focal moderate to weak cytoplasmic staining; or (3) negative. Follow up data was collected including cyto-histo correlation and clinical follow up.

Results: Of the 12 diagnosed malignant cases, 9 showed p53 overexpression (diffuse or focal, see figure 1); 5 showed diffuse strong cytoplasmic mCEA positivity and 4 showed focal moderate to weak cytoplasmic mCEA staining (see figure 2). Of the 14 atypical / suspicious cases, two were malignant at clinical follow-up; both showed focal positivity for mCEA while negative for p53, and cytologically lacked unequivocal malignant features (see table 1).

Patterns of staining	Malignant cases, all were malignant on follow up (n=12)	Atypical/suspicious cases, turned out to be malignant on follow-up (n=2)	Atypical/suspicious cases, remained benign on follow up (n=12)	Negative cases, all remained benign on follow up (n=9)
p53 staining patterns				
Diffuse overexpression	5	0	0	0
Focal overexpression	4	0	0	0
Wild type	1	1	7	7
Negative	2	1	5	2
mCEA staining patterns				
Diffuse strong cytoplasmic positivity	5	0	0	0
Focal moderate to weak cytoplasmic positivity	4	2	5	0
Negative	3	0	7	9

Figure 1 - 450

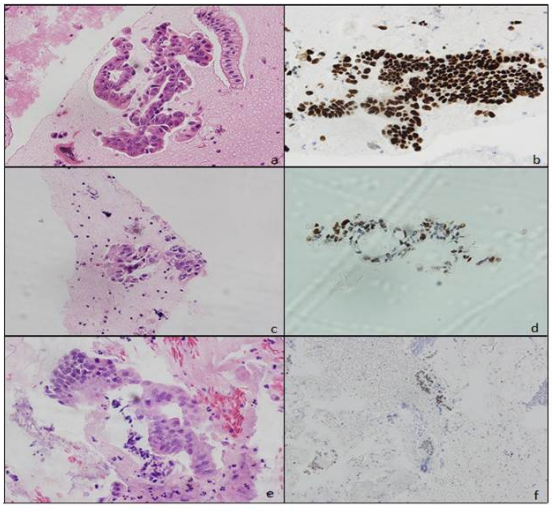

Figure 1: Positive case with diffuse (>80%) p53 expression(a,b); positive case with focal (<80%) p53 expression(c,d); atypical/suspicious case with wild type staining (e,f)

Figure 2 - 450

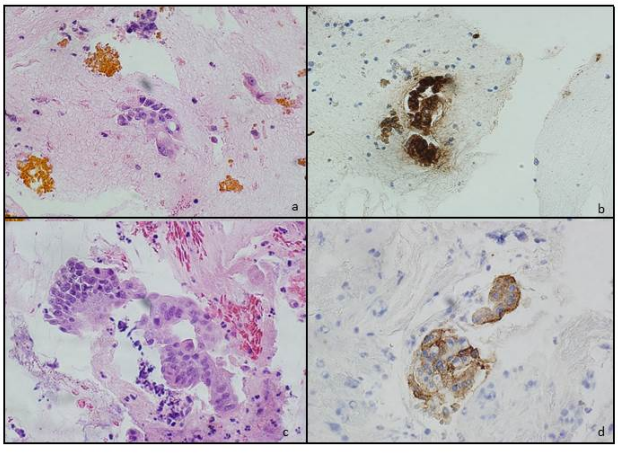

Figure 2: Positive case with diffuse strong mCEA staining(a,b); atypical/suspicious case with focal moderate to weak mCEA staining(c,d)

Conclusions: Our study supports that mCEA is sensitive (78%) while p53 overexpression is specific (100%) in assessment of billary cytology specimens. When encountering equivocal (atypical/suspicious) biliary cytology cases, p53 and mCEA can be utilized but should be cautiously interpreted. Only p53 overexpression (diffuse or focal) and diffuse strong cytoplasmic mCEA staining can be used to increase the diagnostic suspicion for malignancy. Focal mCEA staining is non-specific and cannot be used reliably.

451 Detection of Non-Hematolymphoid Malignancies in Bronchoalveolar Lavages - A Cancer Center's Ten-Year Experience

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Disclosures: Anneliese Velez Perez: None; Gene Landon: None

Background: Flexible bronchoscopy with bronchoalveolar lavage (FB-BAL) is often performed in immunocompromised and cancer patients to investigate possible infectious and non-infectious causes of acute respiratory failure, non-resolving pneumonia, progression of disease, and other respiratory abnormalities. Knowledge of the incidence and distribution of non-hematolymphoid malignancies (NHLM) detected by FB-BAL in this population is limited. Herein, we present the incidence, distribution of cancer types, and patient demographics of BAL specimens diagnosed with NHLM in our cancer specialty hospital over a ten-year time period.

Design: Our 7/01/2008 to 6/30/2018 pathology electronic database was searched for BAL specimens with diagnoses categorized as "malignant". For such cases, a review of the pathology report and electronic medical record was performed to document the specific cancer type and patient demographics. Those cases with hematolymphoid diagnoses were excluded from this study in order to avoid malignant diagnoses based on cells that might have come from leukemic cells in contaminant blood. Statistical analyses were performed to determine the incidence, distribution of NHLM, and demographics of patients in these selected BALs.

Results: In the ten year period, a total of 209 (1.92%) out of 11,035 BAL cases were reported in the "malignant" category. After exclusion of 22 cases with hematolymphoid malignancies, 187 cases were included in this study. The average patient age was 58 years (ranging from 9 to 83 years) with a male to female ratio of 0.9 (male=83; female=95). The most common NHLM identified were from lung primaries (n=103; 55.1%) with adenocarcinoma being the most common type of lung primary (n=91; 88%). Breast carcinomas were the second most common malignancies detected (n=34; 18.2%). Other tumors detected included carcinomas from gastrointestinal tract (n=17; 9.1%), genitourinary tract (n=13; 7%), Müllerian origin (n=8; 4.3%), and head and neck (n=6; 3.2%). Rarer NHLM, included pancreatic carcinoma, melanoma, osteosarcoma, and metastatic squamous cell carcinoma of unknown primary, which encompassed 3.2% of BALs (n=6).

Conclusions: FB-BAL is a useful tool in the evaluation of various pulmonary abnormalities in our cancer institute's patient population and is a valuable method to detect NHLM, which is critical to guide appropriate subsequent therapies.

452 Concordance of Ki-67 Proliferative Index in B-Cell Non-Hodgkin Lymphomas between Fine Needle Aspiration and Corresponding Tissue Biopsy Samples

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Disclosures: Minhua Wang: None; Yun Gong: None

Background: Ki-67 proliferative index (PI), evaluated by immunostaining, is a useful parameter for grading B-cell non-Hodgkin lymphomas and predicting prognosis in histologic samples. However, its utility in fine needle aspiration (FNA) samples has been rarely studied and thus its value is disputable. The purpose of this study is to evaluate the concordance of Ki-67 PI between FNA samples and the corresponding tissue biopsies of the lymphomas obtained at the same sites.

Design: FNA cases diagnosed with B-cell lymphoma (excluding large cell lymphoma) during January 2016 and July 2018 at our institution that had corresponding tissue biopsies with Ki-67 PI available in the paired samples were searched. Ki-67 staining in FNA samples was routinely performed on cytospin preparation containing Ficoll-Hypaque enriched mononuclear cells or cell block section. The concordance rates of Ki-67 in the paired samples were evaluated with 45% as a cutoff for Ki-67 PI being low or high. Final diagnoses and/or subtyping of lymphoma were based on tissue biopsies.

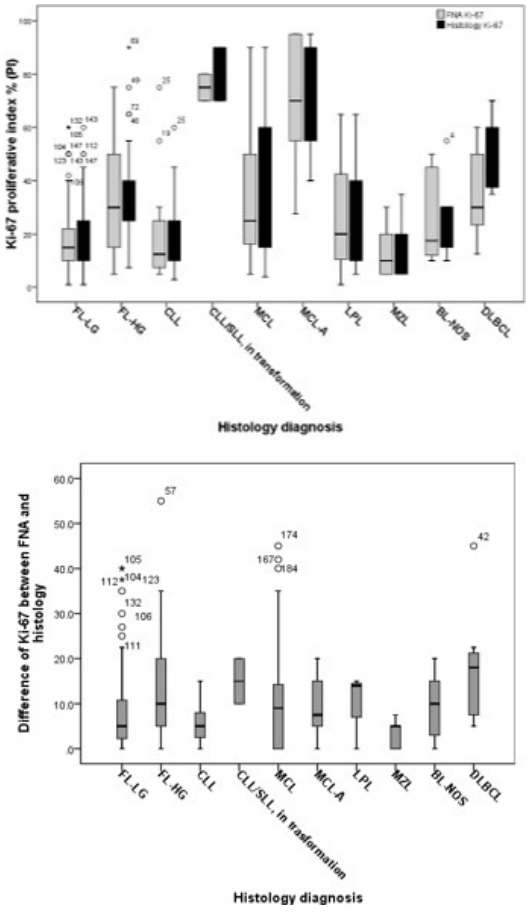
Results: A total 216 cases from 216 patients (133 males and 83 females) were identified; 173 were from lymph nodes and 43 were from extranodal sites. The mean Ki-67 PI and difference between FNA and tissue biopsies varied in different types of lymphoma (Figure 1 and Table 1). Ki-67 PI estimated on FNA showed an overall good concordance rate of 0.90 with tissue biopsy samples. For CLL/SLL, CLL/SLL in transformation, LPL and MZL, the concordance rate of Ki-67 PI was 1.0 each and for FL-LG, FL-HG, MCL, MCL-A, BL-NOS and DLBCL, it was 0.92, 0.8, 0.84, 0.93, 0.83 and 0.86 respectively (Table 1).

Table 1 Ki-67 PI difference between FNA and histology and concordance evaluation

Final Diagnosis	Case #	Ki-67 difference between FNA and histology		Concordance rate (%)
		Mean	Range (%)	
FL-LG	83	8.04±9.57	0-40	0.92
FL-HG	30	12.95±12.58	0-55	0.8
CLL/SLL	30	5.37±4.22	0-15	1
CLL/SLL, in transformation	2	15±7.39	10-20	1
MCL	32	10.5±12.84	0-45	0.84
MCL-A	14	9.82±6.68	0-20	0.93
LPL	3	9.67±8.39	0-15	1
MZL	9	3.33±2.8	0-7.5	1
BL-NOS	6	9.67±7.39	0-20	0.83
DLBCL	7	17.9±13.88	5-45	0.86
Total	216			0.90

Abbreviation: FL-LG, follicular lymphoma low grade; FL-HG, follicular lymphoma high grade; CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; MCL, mantle cell lymphoma; MCL-A, mantle cell lymphoma aggressive variants; LPL, lymphoplasmacytic lymphoma; MZL, marginal zone lymphoma; BL-NOS, B-cell lymphoma NOS; DLBCL, diffuse large B-cell lymphoma

Figure 1 - 452



Conclusions: A generally high concordance rate of Ki-67 PI between FNA and corresponding tissue biopsy samples is found in different types of B-cell lymphoma, indicating that Ki-67 PI performed on FNA samples can be used to guide clinical management.

453 The Diagnostic Accuracy of Fine-Needle Aspiration (FNA) on Thymic Lesions: A Review of Cytologic Features in Conjunction with Histologic Findings

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Disclosures: Minhua Wang: None; Uma Kundu: None; Yun Gong: None

Background: Fine needle aspiration (FNA) is minimally invasive and often the initial sampling method for lesions of mediastinal sites. Diagnosis of thymic lesions by FNA can be challenging due to varying morphologic presentations and rarity of thymic tumors. We examined the diagnostic accuracy of FNA diagnoses in such lesions by comparing with their final surgical diagnoses.

Design: FNA cases with a cytologic diagnosis of thymoma, suspicious for thymoma, atypical thymoma, and thymic lesion/neoplasm/carcinoma of the mediastinum rendered from 2002 to 2018 were searched. The cytologic findings were correlated with final diagnoses of corresponding core biopsy/resection samples. Diagnostic pitfalls were evaluated.

Results: A total of 110 cases from 108 patients (average age 57.5 years) with FNA of thymic lesions were included. Ancillary studies including immunostaining and flow cytometric analysis were performed in 66 FNA cases (60%). Cytologic diagnoses were concordant with histologic diagnoses in 98/110 cases (89.0%). The most common cytology diagnosis was thymoma (n=103), of which 96 (93.2%) were confirmed by surgical diagnoses and seven (6.8%) showed major discrepancy (Table 1 cases 1-7). Four FNA cases were interpreted as malignancy. Of them, three were confirmed by final diagnosis and one showed major discrepancy (Table 1 case 8). Common reasons for misinterpretation are due to intrinsic limitation of FNA diagnosis such as sampling error, sparse cellularity, and lack of architecture/invasion assessment. Lymphoma is a differential diagnosis that often needs to be carefully considered in thymic lesions.

Table 1 Cases with cytology-histology discordance

Table 1 Cases with cytology-histology discordance

Case number	Cytologic diagnosis	Histologic diagnosis	Potential reasons for misinterpretation
1	Thymoma	Thymic carcinoma	Lack of cytologic atypia and invasion assessment
2	Thymoma	Thymic carcinoma	Lack of cytologic atypia and invasion assessment
3	Thymoma	Thymic carcinoma	Lack of cytologic atypia and invasion assessment
4	Thymoma	Diffuse large B-cell lymphoma with sclerosis	Sclerosing large B-cell lymphoma can show spindle cell morphology addition to polymorphic lymphocytes
5	Thymoma	Hodgkin's lymphoma	Epithelioid cells and lymphocytes can be seen in both entities
6	Thymoma	Thymic mucosa-associated lymphoid tissue (malt) lymphoma	Malt lymphoma developed in thymic tissue
7	Thymoma	spindle cell sarcoma	Lack of immunostaining workup
8	T lymphoblastic Leukemia/lymphoma	Thymoma	Misinterpretation of flow result as lymphocytes in thymoma have similar phenotype to that of T lymphoblastic Leukemia/lymphoma
9	Sparse polymorphous lymphocytes	Thymoma	Sampling error
10	Biphasic lymphoid/epithelioid cell proliferation	Invasive thymoma	Lack of invasion assessment
11	Non-diagnostic	Invasive atypical thymoma	Sampling error

Conclusions: The diagnostic accuracy of FNA on thymic lesions is admirable (99/110, 90.0%) despite intrinsic limitations of FNA samples. Lymphoma should be considered carefully in the differential diagnosis and knowledge of immunophenotype of lymphocytes in thymoma is important to avoid misinterpretation.

454 Risk Stratification and the Clinical Outcome in the Atypia of Undetermined Significance Category in the Milan System for Reporting Salivary Gland Cytopathology

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Disclosures: Sintawat Wangsiricharoen: None; Zahra Maleki: None

Background: The main goal of salivary gland fine needle aspiration (FNA) is to determine if an aspirated lesion is neoplastic or non-neoplastic and if it requires surgical management. Atypia of undetermined significance (AUS) is one out of six categories of the Milan System for Reporting Salivary Gland Cytopathology (TMSRSGC). AUS applies to salivary gland FNAs that quantitatively or qualitatively fall short to be definitively diagnosed as neoplastic or non-neoplastic. The risk of malignancy (ROM) in AUS category is estimated 20%. Herein, we evaluate the risk of neoplasm (RON), ROM, and the clinical outcome for the different scenarios in the AUS.

Design: The electronic pathology archive in a large academic institution was searched for salivary gland FNAs diagnosed atypical in a 5 year period (2013 - 2018). Then the cases were divided into six main AUS subgroups. Patients' demographic, cytology, histopathology and clinical outcome were recorded. ROM and RON for each subgroup were calculated.

Results: A total of 88 cases were found: 54 males and 34 females. The mean age was 62 years (range 10-87 years). Parotid gland was the most common FNA site (n=73), followed by submandibular gland (n=8). 22 cases were excluded from calculating RON and ROM due to no follow-ups in our institution. The overall RON and ROM were 54.5% and 50%, respectively. Among subgroups, "salivary gland lymph nodes or lymphoid lesions that were indefinite for a lymphoproliferative disorder" was the most common diagnosis (37.8%), while "Mucinous cystic lesions with an absent or very scant epithelial component" was the least common (3%). "Salivary gland lymph nodes or lymphoid lesions that were indefinite for a lymphoproliferative disorder" had the highest RON (76%) and ROM (76%), whereas "reactive and reparative atypia indefinite for a neoplasm" had the lowest RON (7.1%) and ROM (7.1%) (Table 1).

Atypia of Undetermined Significance subgroup	Histology Diagnosis	Risk of neoplasm	Risk of malignancy	Total
Reactive and reparative atypia indefinite for a neoplasm	• Dense fibrosis (2) • Benign cyst (2) • Chronic sialadenitis (1) • Metastatic melanoma (1)	1/14 (7.1%)	1/14 (7.1%)	14
Squamous, oncocytic, or other metaplastic changes indefinite for a neoplasm	• Cyst with squamous metaplasia (1) • Chronic sialadenitis with squamous metaplasia (1) • Warthin's tumor with squamous metaplasia (1) • Metastatic squamous cell carcinoma (2)	3/7 (42.8%)	2/7 (28.5%)	7
Low cellularity specimens suggestive of, but not diagnostic of a neoplasm **Or** **Specimens with preparation artifacts hampering distinction between a non-neoplastic and neoplastic process**	• Chronic sialadenitis (2) • Reactive lymph node (2) • Pleomorphic adenoma (1) • Myoepithelioma (1) • Cribriform adenocarcinoma of the tongue and minor salivary gland (1) • Salivary duct carcinoma (1) • Metastatic squamous cell carcinoma (4) • Metastatic chondroblastic osteosarcoma (1) • Metastatic Ewing sarcoma/primitive neuroectodermal tumor, adamantinoma-like variant (1) • Metastatic transitional cell carcinoma of the lacrimal duct (1) • Metastatic angiosarcoma (1) • Carcinoma, uncertain subtype (1)	13/17 (76.4%)	11/17 (64.7%)	18
Mucinous cystic lesions with an absent **or very scant epithelial component**	• Acute and chronic sialadenitis with fibrous obliteration of a duct (1) • Low-grade mucoepidermoid carcinoma (1)	1/2 (50%)	1/2 (50%)	2
Salivary gland lymph nodes or lymphoid lesions that are indefinite for a lymphoproliferative disorder	• Reactive lymph node (2) • Follicular lymphoma (7) • Marginal zone lymphoma (1) • Diffuse large B-cell lymphoma (4) • Mantle cell lymphoma (2) • Low-grade B-cell lymphoma (1) • B-cell lymphoma, unclassifiable (3) • Lymphoepithelioma-like carcinoma (1)	19/25 (76%)	19/25 (76%)	25
Overall		36/66 (54.5%)	33/66 (50%)	66

Conclusions: The overall RON and ROM for the AUS category in TMSRSGC are 54.5% and 50%, respectively in our study. The RON and ROM vary among different subgroups with highest in "Salivary gland lymph nodes or lymphoid lesions that are indefinite for a lymphoproliferative disorder" and lowest in "reactive and reparative atypia indefinite for a neoplasm". This study reflects the importance of subgrouping in the AUS category.

455 The Fine-Needle Aspiration of Cystic Renal Lesions

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Disclosures: Sintawat Wangsiricharoen: None; Christopher VandenBussche: None

Background: Cystic renal lesions comprise a spectrum of lesions. Although the majority are benign simple cysts, renal neoplasms occasionally have cystic components or cystic degeneration. Fine-needle aspiration (FNA) is one method of evaluating cystic lesions and may be employed to sample renal lesions, especially those with an indeterminate radiologic appearance. However, few studies have been conducted to examine the utility and performance of FNA in this setting. We reviewed the FNA of cystic renal lesions at our institution over the last three decades.

Design: We identified surgical resection specimens containing cystic renal lesions with corresponding preceding FNA specimens from January 1990 to July 2018. In addition, we identified specimens in which cystic renal lesions underwent FNA. For the purposes of cytologic-histologic correlation, cytologic diagnoses were classified in 6 groups: non-diagnostic, benign, atypical, suspicious for neoplasm, suspicious for malignancy and malignant. The histopathologic diagnoses were classified as non-neoplastic, benign, borderline or malignant.

Results: A total of 164 cases were identified. Most FNAs were given a benign diagnosis (n=102, 62%). 20 (12%) cases were atypical, 5 (3%) were suspicious for neoplasm, 5 (3%) were suspicious for malignancy, 5 (3%) were malignant, and 27 (16%) were non-diagnostic. Excluding the non-diagnostic aspirates, there was concordance in 104 cases (76%) (Table 1). The most common surgical diagnosis was simple cyst (n=108, 65%), while the two most common malignant diagnoses were clear cell renal cell carcinoma (RCC) (n=10, 37%) and papillary RCC (n= 5, 18%). The risk of malignancy (ROM) of FNA was 100% for a malignant diagnosis, 60% for a suspicious for malignancy diagnosis and 40% for a suspicious for neoplasm diagnosis. Despite the high ROM for malignancy, FNA had a low sensitivity (22%). Diagnostic pitfalls identified included the identification of benign tubular cells as “atypical”, poor sampling of cystic renal cell carcinomas, and the misclassification of cystic nephroma and mixed epithelial and stromal tumor.

Cytologic diagnosis	Histopathologic diagnosis				
	Non-neoplastic	Benign neoplasm	Borderline	Malignant neoplasm	Total
Benign	84 (82%)	3 (3%)	7 (7%)	8 (8%)	102
Atypical	11 (55%)	2 (10%)	2 (10%)	5 (25%)	20
Suspicious for neoplasm	3 (60%)	0 (0%)	0 (0%)	2 (40%)	5
Suspicious for malignancy	1 (20%)	1 (20%)	0 (0%)	3 (60%)	5
Malignant	0 (0%)	0 (0%)	0 (0%)	5 (100%)	5
Non-diagnostic	21 (78%)	0 (0%)	2 (7%)	4 (15%)	27
Total	120 (73%)	6 (3%)	11 (7%)	27 (17%)	164

Conclusions: Despite challenges, the FNA of cystic renal lesions correlates well with findings on follow up resection. It is especially of value when positive findings are found. Common pitfalls include negative or non-diagnostic aspirates in cystic RCCs and cytomorphologically atypical cells in otherwise benign cysts.

456 Validation of HPV E6 E7 mRNA Detection via RNAscope ISH on FNA Cell Block Material with p16 Correlation

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Disclosures: Bennett Wilson: None; Anna-Karoline Israel: None; Abberly Lott Limbach: None

Background: Oropharyngeal squamous cell carcinoma (OPSCC), driven by high-risk HPV, is a clinically and pathologically distinct entity from non-HPV positive head and neck (H&N) SCC. HPV related OPSCC has a better prognosis and response to therapy, therefore, early determination of the HPV status guides treatment decisions.

Recently published guidelines by the College of American Pathologists recommend that fine needle aspiration (FNA) specimens from patients with OPSCC and head and neck SCC of unknown primary undergo HPV evaluation, however, there is insufficient evidence regarding optimal testing strategies on FNA specimens. Recent studies have evaluated p16 IHC on FNA cell blocks and have suggested positive thresholds of 10-15% (as opposed to the 70% threshold recommended for tissue). In our study we are examining the utility of high risk (HR) HPV E6 E7 mRNA ISH via RNAscope (HPV ISH) for HPV detection on cell block as compared with p16 IHC of FNA of H&N SCC.

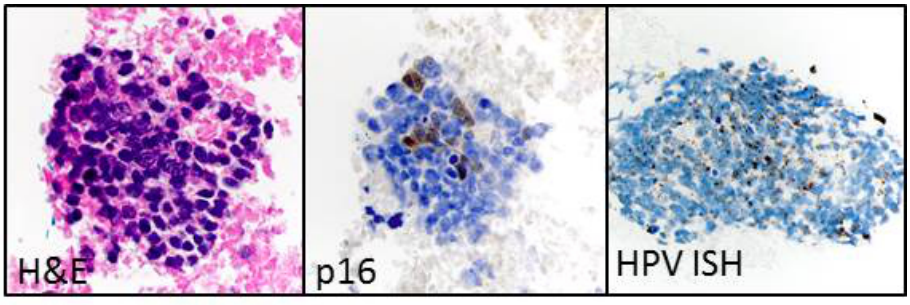
Design: The pathology LIS was searched for all head and neck cytology cases that had been evaluated with p16 immunohistochemistry between 1/1/2015 and 2/1/2018. If a resection or biopsy had been performed, the corresponding surgical specimen was also included. High

risk HPV ISH was performed on FNA cell block, as well as representative blocks of surgical specimen. HPV ISH and p16 IHC were compared and correlation was determined.

Results: Available cases included 9 cytology, and 3 corresponding surgical resections from 8 males and 1 female with an average age of 66 years. On evaluation: 5 HPV ISH stains agreed with the original p16; 4 disagreed including 2 with an indeterminate p16 and positive HPV ISH, 1 with negative p16 and positive ISH, and one with insufficient cellularity for p16 staining and positive HPV ISH; 2 surgical specimens had HPV that agreed with p16, and 1 had insufficient tumor cells for HPV ISH staining, table 1. Most notable were the 3 cases with indeterminate or insufficient p16 staining that were clearly HPV positive with the HPV RNA ISH, figure 1.

Cell block p16 Results	Cell Block HPV ISH	Surgical resection
p16 positive (5)	Positive (5)	P16+/HPV ISH + (1)
P16 indeterminate (2)	Positive (2)	
P16 negative (1)	Positive (1)	
P16 insufficent tissue (1)	Positive (1)	P16+/HPV ISH+ (1)

Figure 1 - 456



Conclusions: HR HPV ISH is especially useful in cell blocks with scant tissue where interpretation of the p16 IHC is challenging. Staining with HPV ISH is consistent, dark, and localized to the tumor cells, making it easier to interpret than p16 on FNA cell blocks. Since the stain is sold as a kit, it adds no additional burden to the IHC lab workload. High risk HPV E6 E7 mRNA ISH via RNAscope is a valid method for HPV detection in cell block preparations of head and neck FNAs.

457 Heterogeneity of p16 Immunohistochemistry in Cytology Specimens of HPV-Related Head and Neck Squamous Cell Carcinoma

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Disclosures: Kristine Wong: None; Jeffrey Krane: None; Vickie Jo: None

Background: HPV-related head and neck squamous cell carcinoma (HPV-HNSCC) is associated with distinct clinical and biologic features. While there is no single "gold-standard" for assessing HPV-HNSCC, p16 immunohistochemistry (IHC) is most commonly used as a surrogate marker for HPV status. The College of American Pathologists recommends a cutoff of moderate to strong staining in ≥70% of tumor cells in surgical specimens. However, criteria for a p16 positive result in cytologic material are not well-established. The goal of this study was to better characterize p16 IHC in cytology samples of HPV-HNSCC.

Design: Cytology specimens of HPV-HNSCC obtained from 2013-2018 were identified. HPV status was previously confirmed by *in situ* hybridization (ISH) or polymerase chain reaction (PCR) in all cases. A cohort of 12 non-HPV-related SCC was used as a control. Tumor cellularity (<100, 100-500, >500 cells) and quality (presence of cell clusters and necrosis) were recorded. P16 IHC was performed on all cases unless previously done, and staining intensity (weak, moderate, strong) and percentage (<10%, 10-69%, ≥70%) were scored.

Results: 77 cases of HPV-HNSCC were identified from 75 (97%) fine needle aspirations and 2 (3%) bronchoalveolar lavages. There were 63 (82%) local and 14 (18%) distant metastases. Primary sites included 64 (83%) oropharyngeal, 2 (3%) nasopharyngeal, and 11 (14%) unknown. HPV status was determined by PCR in 46 (60%) cases, DNA or RNA ISH in 30 (39%) cases, and both PCR and ISH in 1 (1%) case. P16 IHC was moderate-strong in 57 cases, with 28 (36%) cases positive in ≥70% of tumor cells, 24 (31%) cases in 10-69% cells, and 5 (6%) cases in <10% cells. 15 (19%) cases demonstrated only weak staining, while 5 (6%) cases were negative. Of the 49 cases with either weak/absent expression or staining in <70% of cells, 24 (49%) cases had <100 tumor cells, 11 (22%) did not have tumor clusters, and 16 (33%) had a necrotic background.

Among the control group, 11 (92%) cases were negative for p16, while 1 (8%) case had moderate staining in <10% of cells. The positive case was a lymph node metastasis from an oral tongue SCC.

Conclusions: P16 IHC is highly variable in cytology specimens of HPV-HNSCC, with a lower sensitivity compared to that reported in surgical specimens. These results suggest that any p16 positivity should prompt HPV confirmatory studies and that repeat p16 testing should be performed on subsequent surgical specimens if p16 and other HPV tests are negative on cytologic material.

458 Malignancy Risk for Solitary and Multiple Nodules in Hürthle Cell-Predominant Thyroid Fine Needle Aspirations: A Multi-Institutional Study

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Disclosures: Kristine Wong: None; Vickie Jo: None; Alarice Lowe: None; Akeesha Shah: None; Michael Roh: None; Edward Stelow: None; Andrew Renshaw: None; William Faquin: None; Jeffrey Krane: None

Background: Hürthle cell metaplasia is common in hyperplastic nodules, particularly in the setting of lymphocytic thyroiditis (LT). The Bethesda System (TBS) indicates that it is acceptable to classify Hürthle cell-predominant fine needle aspirations (HC FNA) as “Atypia of Undetermined Significance” (AUS) rather than "Suspicious for a Hürthle Cell Neoplasm" (HUR) in the setting of multiple nodules or known LT. The goal of this study is to address whether this approach was justified.

Design: HC FNAs were identified and correlated with ultrasound (US) and surgical pathology reports. Multinodularity was determined by findings on gross examination if US results were unavailable. As cases pre-dated the introduction of non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP), follicular variant with unclear invasion status or un-subtyped PTCs (PTCNOS) which were unavailable for review were excluded from the analysis.

Results: Overall, 468 HC FNAs from 447 nodules were identified. The FNA diagnosis was Benign in 12 (3%) cases, AUS in 186 (40%) cases, HUR in 266 (57%) cases, Suspicious for Malignancy in 3 (1%) cases, and Malignant in 1 (<1%) case. Excluding 12 cases of PTCNOS, there were 334 resected nodules, of which 272 (81%) were benign and 62 (19%) malignant.

The mean size of benign nodules was 2.3 cm by US and 2.1 cm on resection, with multiple nodules in 172 (63%) cases. The nodules consisted of 163 (60%) follicular adenomas or adenomatous nodules, 91 (33%) hyperplastic nodules, 7 (3%) tumors retrospectively classified as NIFTP, 2 (1%) infarcted nodules, and 1 (<1%) hyalinizing trabecular tumor. The remaining 8 (3%) cases demonstrated LT without a dominant nodule, although 70 (26%) cases overall had histologic LT.

Of malignant nodules, the mean size was 3.0 cm on both US and resection, with multiple nodules in 40 (65%) cases. There were 42 (68%) follicular carcinomas (including Hürthle cell carcinomas), 12 (19%) PTCs, 5 (8%) poorly differentiated carcinomas, 2 (3%) medullary carcinomas, and 1 (2%) undifferentiated carcinoma. Nine (15%) cases demonstrated histologic LT.

Malignancy rate did not differ between solitary or multiple nodules (p=0.88) or in the presence or absence of LT (p=0.069). However, size did significantly differ between malignant and benign nodules (p<0.001).

Conclusions: The malignancy rate did not significantly differ in the presence of multiple nodules or LT, suggesting that a diagnosis of AUS over HUR may not be warranted in these situations.

459 Cytologic and clinical features of NIFTP: Can we diagnose based on pre-operative FNA?

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Disclosures: Lei Yan: None

Background: Noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) is considered an indolent neoplasm of thyroid. This retrospective study was conducted to assess the clinical features and cytologic characteristics of NIFTP, including analysis of previous FNA diagnoses.

Design: Cases of NIFTP and encapsulated follicular variant of papillary thyroid carcinoma (EFVPTC) from January 1994 to August 2018 were retrieved from our institution’s pathology databases, and their diagnoses, clinical, and cytopathologic features were reviewed.

Results: There were a total of 30 cases of NIFTP and EFVPTC, 22 women (73.3%) and 8 men (26.7%). The mean age of patients was 50 years (range 18-91). The average size of tumor was 26.7 ± 4.3 mm (range 1-105 mm). 25 of 30 cases involved single lobes, 5 cases were

bilateral and 10 cases showed multifocal tumors. 27 of 30 patients had presurgery thyroid FNAs, 19 of which showed abnormal cytology (19/27). 8 thyroid FNAs showed goiter only and patients received surgery due to compressive symptoms (8/27). 3 of 30 patients received thyroidectomy for Grave's disease or hyperthyroidism. NIFTPs were most often classified in the indeterminate diagnostic categories including suspicious for follicular neoplasm (8/19), suspicious for malignancy (3/19) and atypical (3/19). 5 patients had a cytologic diagnosis of papillary thyroid carcinoma (5/19). 12 of 19 cases with abnormal FNAs had in-house cytology preparations for review. The most frequent cytology features observed in NIFTPs include architectural abnormalities, such as crowded clusters (12/12), moderate to high cellularity (11/12), nuclear overlapping (11/12), individual microfollicles (10/12), and isolated cells (9/12). The papillary nuclear features observed include nuclear enlargement (12/12), eccentric nucleoli (11/12), nuclear membrane irregularity (10/12), nuclear clearing (10/12), and nuclear grooves (8/12). Dense colloid and giant cells were observed in 10/12 and 2/12 cases respectively. The only FNAs diagnosed as outright papillary thyroid carcinoma showed pseudo-papillary architecture and intranuclear inclusions.

Conclusions: Most NIFTPs were not diagnosed as papillary thyroid carcinoma on thyroid FNAs. The NIFTPs were most frequently categorized as suspicious for follicular neoplasm on cytology. Recognition of the architectural and nuclear features of NIFTP can be helpful in distinguishing NIFTPs from other entities, such as papillary thyroid carcinoma and follicular neoplasms.

460 Targeted deep sequencing of cell-free DNA from body cavity fluids with malignant, suspicious, and benign cytology

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Disclosures: Soo-Ryum Yang: None; Paolo Libiran: None; Carol Jones: None; Rohan Joshi: None; Hubert Lau: None; Henning Stehr: None; Teri Longacre: None; Kimberly Allison: None; James Zehnder: None; Steven Long: None; Gerald Berry: None; Christian Kunder: None

Background: Liquid biopsy using cell-free DNA (cfDNA) presents new opportunities and challenges for solid tumor genotyping. While studies have demonstrated the utility of cfDNA from plasma, cfDNA derived from other body fluids remains largely unexplored. In this study, we evaluated the molecular and clinicopathologic correlates of cfDNA from serosal body cavity fluids by performing targeted next-generation sequencing (NGS) on residual supernatants from pleural, peritoneal, and pericardial effusions.

Design: Postcentrifuged supernantants from 21 body cavity fluids (13 malignant, 2 suspicious, and 6 benign) were saved and frozen at -80°C. cfDNA was purified from 5-10 ml of thawed supernatant material and sequenced using a hybrid capture-based NGS assay validated for targeted deep sequencing of 130 cancer-related genes.

Results: The supernatants yielded a mean cfDNA concentration of 22.1 ng/µL (range: 0.3 - 96.7 ng/µL) (Table 1). Notably, all samples were sequenced successfully with an average median depth of 1871x (1289 – 3450x) and revealed a variety of genetic alterations including sequence mutations, amplifications, and fusions. In our cohort, pathogenic alterations were identified in all malignant fluids (13/13), all fluids suspicious for malignancy (2/2), and one benign fluid (1/6) (Figure 1). Furthermore, 11/21 patients (52%) had additional molecular testing performed on formalin-fixed, paraffin-embedded (FFPE) tissues and cell blocks (Figure 2). In seven patients, the paired results between FFPE and supernatant samples were entirely concordant, whereas in the remaining four patients, supernatant analysis identified additional variants associated with resistance to targeted therapies. Comparison between FFPE and supernatant samples showed no difference in the mean DNA concentration (30.1 and 18.1 ng/µL, P= 0.6), median depth of coverage (1563 and 1744x, P= 0.4), and variant allele fraction of shared pathogenic mutations (0.21 and 0.24, P= 0.8).

Patient characteristics (n = 21)	**Data (range or %)**
Age, mean (years)	60 (43 - 80)
Sex	
Male	10 (47.6)
Female	11 (52.4)
Cancer history	
Lung	7 (33.3)
GI and pancreas	5 (23.8)
Breast	4 (19.0)
Peritoneum	1 (4.8)
None	4 (19.0)
Fluid type	
Pleural	15 (71.4)
Peritoneal	5 (23.8)
Pericardial	1 (4.8)
Cytology	
Malignant	13 (61.9)
Suspicious	2 (9.5)
Benign	6 (28.6)
Preanalytical variables	**Mean (range)**
Total volume (ml)	177 (5 - 1000)
Nucleated cell count (cells/µL)	1317 (8 - 4020)
Tumor cellularity (%)	22 (0 - 90)
cfDNA yield (ng/µL)	22.1 (0.3 - 96.7)
Quality control statistics	**Mean (range)**
On-target rate (%)	68.6 (47.8 - 80.5)
Median depth (unique reads)	1871 (1289 - 3450)
Median fragment length (base pairs)	199.4 (160 - 256)
Positions over 200x (%)	96.4 (95.0 - 97.7)
Positions over 500x (%)	92.1 (86.6 - 96.3)
Variant annotation	**Data (%)**
Pathogenic alterations	n = 51
Missense	18 (35.3)
Amplification	16 (31.4)
Nonsense	7 (13.7)
In-frame indel	4 (7.8)
Frameshift	4 (7.8)
Fusion	2 (3.9)
Actionable alterations	12 (23.5)

Figure 1 - 460

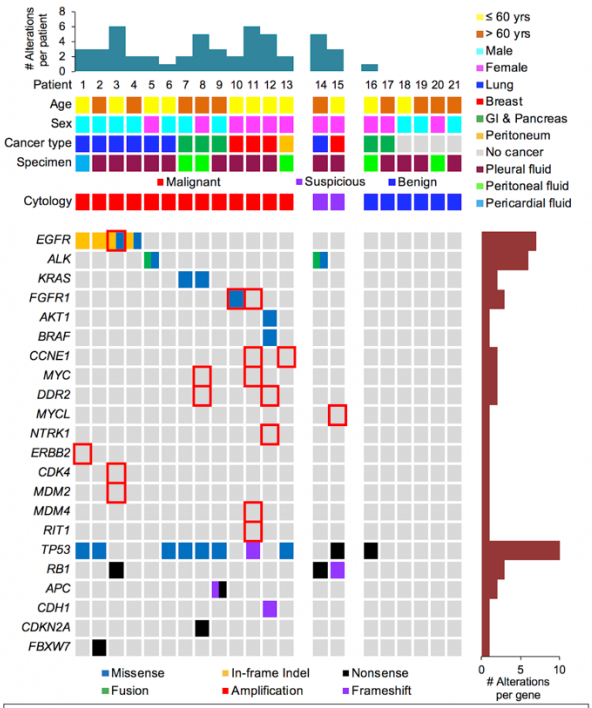
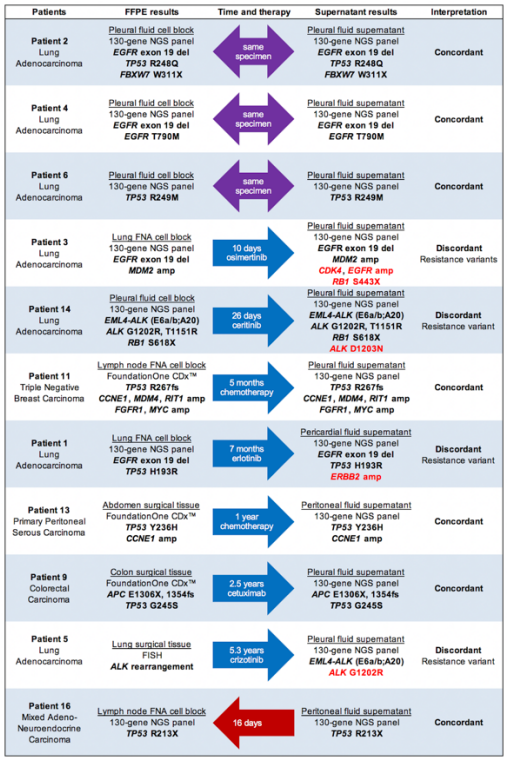


Figure 1: Co-mutation plot of 21 patient samples with clinicopathologic annotation. GI: gastrointestinal tract, indel: insertion and deletion

Figure 2 - 460



Conclusions: cfDNA isolated from serosal body cavity fluids is a clinically valid source of genomic input for targeted NGS. By applying cfDNA testing to effusion samples, our custom liquid biopsy approach enables robust detection of clinically actionable variants from routinely discarded material and provides a viable alternative to tissue and plasma-based testing in select patients.

461 Chronic Pancreatitis: A Potential Pitfall in Pancreatic Fine Needle Aspiration

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Disclosures: Jack Yang: None; Daniel Skipper: None; Kathryn Lindsey: None; Denise Lambrou: None

Background: The diagnosis of chronic pancreatitis is generally made based on clinical and radiologic findings. However, a subset of cases of chronic pancreatitis can form mass lesions that mimic pancreatic cancers both clinically and on imaging studies. This often requires fine needle aspiration (FNA) to aid in diagnosis. The present study explored the challenges and potential pitfalls in the diagnosis of chronic pancreatitis on FNA cytology.

Design: Surgical resection specimens (Whipple or partial pancreatectomy) with a diagnosis of pancreatitis without concurrent pancreatic neoplasms from 2007 - 2018 were identified from the department of pathology database. Histologic-cytologic correlation was made in the cases that had preceding pancreatic FNA. The cases with histologic- cytologic descrepancies were revired and the potential sources of error were analyzed.

Results: A total of 555 surgical resection specimens which met criteria were identified and 101 of them had preceding pancreatic FNA. The diagnoses of FNA cytology included 7 Unsatisfactory, 19 Atypical Cells, 11 Neoplasm, 2 Suspicious for Malignant Cells, and 3 Adenocarcinoma. Pancreatic intraepithelial neoplasm (PanIN) which occurred in at least 26.5% of pancreatitis may have contributed to the errors in the cytologic diagnosis in most of the cases (Table 1, Figure 1). Additional sources of error included islet cell hyperplasia and squamous metaplasia in the settings of chronic pancreatitis (Figure 2).

Cytologic Diagnosis	Number of Cases	Chronic Pancreatitis			
		No PanIN	PanIN 1	PanIN 2	PanIN 3
Pancreatitis	59	45	11	2	1
Atypical Cells	19	11	1	5	2
Mucinous Neoplasm	7	3	4	0	0
Neuroendocrine Tumor	3	1	2	0	0
Solid Pseudopapillary Tumor	1	1	0	0	0
Suspicious	2	1	0	0	1
Adenocarcinoma	3	0	0	1	2
Unsatisfactory	7	7	0	0	0

Figure 1 - 461

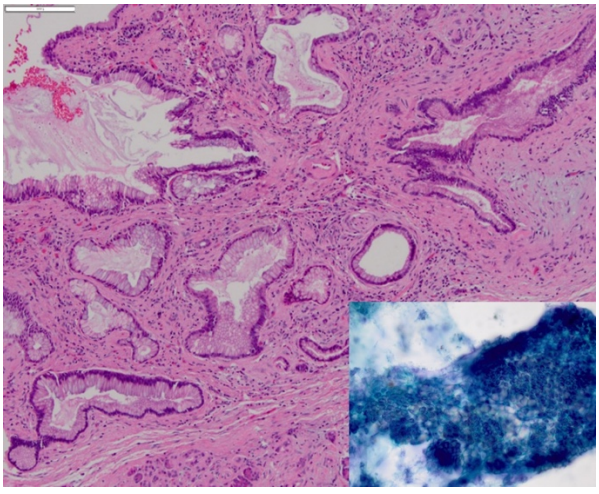
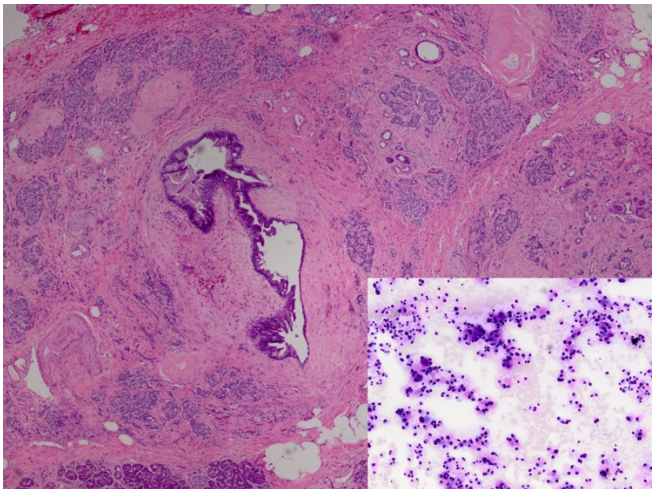


Figure 2 - 461



Conclusions: Most patients with chronic pancreatitis can be managed conservatively. Inaccurate cytologic diagnosis may lead to significant changes in clinical management of patients with serious consequences. Cytologists should be familiar with the potential pitfalls in evaluating cytology samples in the setting of chronic pancreatitis. Both the cytologic and quantitative features of concerning cells are important in the cytologic diagnosis of pancreatic neoplasms.

462 Cotest Results Preceding Biopsy Proven Cervical High Grade Lesions and Carcinoma: Analysis from an Academic Medical Center

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Disclosures: Lindsay Yassan: None; Kruti Maniar: None; Nazneen Fatima: None; Joseph Peevey: None; Julia Samolczyk: None; Holly Lose: None; Ritu Nayar: None

Background: In August 2018, the USPSTF updated guidelines for cervical cancer screening and retained cotesting as an option for women aged 30-65 years. Based on educational endeavors and EMR ordering support, we have excellent compliance with age appropriate cotesting. Based on monitoring compliance with screening and management guidelines, we implemented additional pathologist review of NIL HPV 16/18+ Paps in 2013. We have previously observed that (1) clinicians tend not to follow guidelines related to 'other' (non-16/18) HPV+ genotyping results and do send these women to colposcopy and (2) a significant number of histologic HSIL/AIS+ following NIL/HPV+ cotests have non-16/18 genotypes. Our goal for this study was to correlate histologically proven cervical high grade (HG) lesions and carcinoma with preceding cytology and HPV results.

Design: We retrieved all biopsies (bx), excisions, and endocervical curettings from June 2014-June 2017 diagnosed as HSIL(CIN2/3) or carcinoma (including AIS) that had preceding cervical cytology at our institution within a year of biopsy. Pertinent information, including cytology Bethesda interpretation, HPV status, surgical pathology diagnosis, p16 results, and follow up dates, was collected.

Results: 443 HSIL/carcinoma bx from 443 patients qualified for the study. The Bethesda interpretation for the HPV+ cases showed 249 ASCUS+, 75 NIL, and 2 unsatisfactory (unsat) Paps. HPV testing was not done in 108 cases (10 NIL/unsat, 98 LSIL+); the remaining 9 were HPV negative (1NIL, 1 ASCUS, 3 LSIL, 1 ASC-H, and 3 HSIL) (see Figure 1).

70 HSIL, 5 AIS and 3 endocervical adenocarcinoma were preceded by NIL (76) or unsat (2) Paps. Concurrent HR-HPV testing was performed in 77 of 78 bx with NIL/unsat Paps (see Figure 2). For these 78, the average interval between Pap and bx was 55 days and did not differ significantly based on HPV genotype.

Figure 1 - 462

Figure 1. HR-HPV Partial Genotype Breakdown for Cases of HSIL/carcinoma (n= 243, July 2015 to June 2017)

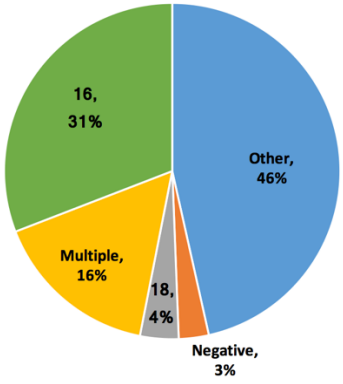

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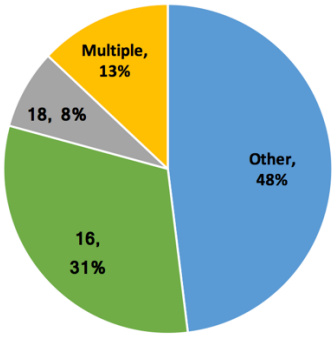
Figure 2. HR-HPV Partial Genotype for HSIL/carcinoma preceded by NIL/unsat Paps (n=77, June 2014 to June 2017)



Conclusions: 78 out of 443 cases (17%) of biopsy proven HSIL/AIS or higher were preceded by NIL (n=76) or unsat (n=2) Paps. 'Other' HR-HPV genotypes were most prevalent in the NIL/ HPV+ cases preceding histologic HG lesions/carcinoma (48% 'other' HPV types; 13% multiple HPV types). Clinicians tend to manage all HR-HPV+ cases similarly, and send NIL/'other' HR-HPV+ women to colposcopy. This practice does lead to earlier detection of HG lesions. HPV genotypic variations in US women with HG cervical lesions should be considered as ASCCP proceeds with the development of a "risk-based" management guidelines update.

463 HPV Genotyping Analysis and Follow-up Biopsy Results for Abnormal Pap Smears: HR-HPV16 is a Better Predictor than HR-HPV18 for High-grade Squamous Lesion (HGSIL) on Follow-up Biopsy

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Disclosures: Esther Yoon: None; Padmini Manrai: None; Angelique Levi: None; Rita Abi-Raad: None; Kara Duch: None; Malini Harigopal: None

Background: The causal relationship between HPV and cervical carcinoma and its precursor lesions is well established. The increased sensitivity for detection of high-grade CIN conferred by high-risk HPV DNA (HR-HPV) testing has led the American Society for Colposcopy and Cytopathology to include genotyping for HPV16/18. The current guidelines require that the pap test and a HPV DNA test be performed every 5 years in women between ages of 30 and 65 years. In this retrospective study, we investigated the relationship of the abnormal Pap tests and the follow up biopsy diagnosis in HPV16+ or 18+ patients.

Design: A database search was performed for specimens with an abnormal Pap diagnosis (ASC-US, LSIL, ASC-H and HSIL) on all liquid-based Pap tests (ThinPrep and SurePap) specimens between January 2016 to December 2017 following IRB approval using Roche cobas HPV test. All patients with positive HR-HPV (16/18) DNA were identified. Follow up biopsy reports were obtained and reviewed. Basic statistical analysis was performed to analyze the data.

Results: A total of 160 abnormal Pap tests were studied (128 cases HPV16+ (80%) and 32 cases HPV18+ (20%)). There were 127 follow-up biopsies (79.4%) including all HSIL diagnosis. The most common Pap test diagnosis was ASCUS (75 cases; 59.1%) followed by LSIL (31 cases; 24.4%). The most common histologic diagnosis was CIN I (51 cases; 40.2%) followed by no pathology (40 cases; 31.5%) in both HPV16+ or HPV18+. Eighty biopsy cases were associated with squamous lesions (63.0%) including 1 case invasive squamous cell carcinoma (0.8%). ASCUS and CIN I were the most common diagnosis on Pap test and biopsy in HPV16+ or HPV18+ patients. One case of endocervical adenocarcinoma (0.8%) was associated with HPV16+. CIN I was diagnosed on biopsy more frequently in HPV16+ ASCUS Pap test (28 cases; 27.2%). However, equal percentage of benign and CIN I was diagnosis on biopsy in HPV18+ ASCUS on Pap test (7 cases; 29.2%). Please refer to tables for detailed analysis.

HPV16 OR HPV18		Dx	ASCUS	LSIL	ASC-H	HSIL	Total
		Benign	29 (22.8)	7 (5.5)	3 (2.4)	1 (0.8)	40 (31.5)
		HPV Change	3 (2.4)	3 (2.4)	0 (0)	0 (0)	6 (4.7)
Total Pap test (n)	160	CIN I	35 (27.6)	13 (10.2)	3 (2.4)	0 (0)	51 (40.2)
Follow up Bx n (%)	127 (79.4)	CIN II	1 (0.8)	5 (3.9)	1 (0.8)	2 (1.6)	9 (7.1)
Age (avg)	44.3	CIN III	4 (3.1)	2 (1.6)	4 (3.1)	5 (3.9)	15 (11.8)
		Invasive CA	0 (0)	0 (0)	2 (1.6)	0 (0)	2 (1.6)
		HG-lesion	5 (3.9)	7 (5.5)	7 (5.5)	7 (5.5)	26 (20.5)
		VAIN lesion	3 (2.4)	1 (0.8)	0 (0)	0 (0)	4 (3.1)
			75 (59.1)	31 (24.4)	13 (10.2)	8 (6.3)	127 (100)

Table 1. Patients with either genotype HPV16 or HPV18

HPV 16 only		Diagnosis	ASCUS	LSIL	ASC-H	HSIL	Total
		Benign	22 (21.4)	6 (5.8)	3 (2.9)	1 (1.0)	32 (31.1)
		HPV Change	3 (2.9)	2 (1.9)	0 (0)	0 (0)	5 (4.9)
Total Pap test (n)	128	CIN I	28 (27.2)	8 (7.8)	2 (1.9)	0 (0)	38 (36.9)
Follow up Bx n (%)	103 (80.5%)	CIN II	1 (1.0)	4 (3.9)	1 (1.0)	2 (1.9)	8 (7.8)
Age (avg)	44.5	CIN III	4 (3.9)	2 (1.9)	4 (3.9)	4 (3.9)	14 (13.6)
		Invasive CA	0 (0)	0 (0)	0 (0)	0 (0)	2 (1.9)
		HG-lesion	5 (4.9)	6 (5.8)	4 (3.9)	6 (5.8)	24 (23.3)
		VAIN lesion	3 (2.9)	1 (1.0)	0 (0)	0 (0)	4 (3.9)
			61 (59.2)	23 (22.3)	12 (11.7)	7 (6.8)	103 (100)
HPV 18 only		Diagnosis	ASCUS	LSIL	ASC-H	HSIL	Total
		Benign	7 (29.2)	1 (4.2)	0 (0)	0 (0)	8 (33.3)
		HPV Change	0 (0)	1 (4.2)	0 (0)	0 (0)	1 (4.2)
Total Pap test (n)	32	CIN I	7 (29.2)	5 (20.8)	1 (4.2)	0 (0)	13 (54.2)
Follow up Bx n (%)	24 (75.0%)	CIN II	0 (0)	1 (4.2)	0 (0)	0 (0)	1 (4.2)
Age (avg)	43.6	CIN III	0 (0)	0 (0)	0 (0)	1 (4.2)	1 (4.2)
		Invasive CA	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
		HG-lesion	0 (0)	1 (4.2)	0 (0)	1 (4.2)	2 (8.3)
		VAIN lesion	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
			14 (58.3)	8 (33.3)	1 (4.2)	1 (4.2)	24 (100)

Table 2. Patients with genotype HPV16. Patients with genotype HPV18.

Conclusions: In our Pap test diagnosis of ASCUS, LSIL, ASC-H and HSIL, HPV16 was more prevalent than HPV18. Both genotypes were highly associated with squamous lesions. HPV16+ patients had higher number of HGSIL on follow up biopsy than HPV18+ patients. Our data indicates in HPV16/HPV18 positive patients with ASC-H or HSIL diagnosis on Pap test, the most common histologic diagnosis is HGSIL.

464 An Indeterminate Diagnosis in Endoscopic Ultrasound-Guided Fine Needle Aspiration of Pancreatic Lesions: The Roles of Repeat Biopsy and KRAS Mutation Analysis

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Disclosures: Esther Yoon: None; Rita Abi-Raad: None; Harry Aslanian: None; Adebowale Adeniran: None; Guoping Cai: None

Background: Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) is often the choice of diagnostic test for solid pancreatic lesions. However, not infrequently, the lesion is diagnosed as “atypical” or “suspicious” and this indeterminate category creates a dilemma for clinical management. In this retrospective study, we aimed to assess the risk of malignancy in cases with atypical and suspicious diagnosis and evaluated the values of repeat biopsy and *KRAS* mutation analysis in improving clinical management.

Design: We retrieved all pancreatic cases with EUS-FNA diagnosis of atypical or suspicious for malignancy from January 2016 to June 2018. The results of *KRAS* mutational analysis, if available, were collected. The histologic diagnosis on subsequent biopsy or surgical resection was correlated. The cases with no histologic diagnosis, patient’s electronic medical records including imaging studies, gastroenterology and oncology consult notes and treatment plans were reviewed as clinical follow-up.

Results: A total of 63 cases were diagnosed with atypical (n=43) or suspicious (n=20) cytology. Twenty-eight cases had repeat FNAs (44.4%), among which 11 cases (39%) were upgraded to either suspicious or malignant diagnosis and 8 cases (29%) were downgraded to benign diagnosis. *KRAS* mutation analysis was performed in 61 cases (97%) with a positive mutation status seen in 11 cases (18%) including 5 atypical and 7 suspicious cases. Based on the histological diagnosis (42 cases) or clinical follow-up (21 cases), 37 cases (59%) were malignant while the remaining 26 (41%) cases were benign. Interestingly, all 11 cases with positive *KRAS* mutation were malignant in the follow-up. In this cohort, the calculated risk of malignancy was 40% in cases with atypical diagnosis and 100% in suspicious group.

Conclusions: Our results demonstrate that repeat biopsy can further stratify the cases with initial atypical or suspicious diagnosis in the EUS-FNA of pancreatic lesions. Reflex KRAS mutation test, although sensitivity is relatively low, may add additional value in triaging an intermediate cytological diagnosis.

465 HPV Genotype Distribution of Human Papillomavirus in 16054 Chinese Women with Abnormal and Normal Cervical Pap Tests

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Disclosures: Baowen Zheng: None; Juan Li: None; Chengquan Zhao: None

Background: Cervical cancer is one of the most common cancers in Chinese women. The data for HPV genotype distribution in women with normal and abnormal cervical Pap tests is very limited in China.

Design: HPV genotyping results in women with Pap tests in 2015 and 2016 at KingMed Laboratory were retrospectively analyzed. HPV genotypes were performed using 26 HPV Genotyping Panel Kit from Tellgenplex (TELLGEN Shanghai, China).

Results: 16054 women with HPV genotyping results (18 HR and 8 LR types) were identified including 219 HSIL, 683 LSIL, 163 ASC-H, 1458 ASC-US, and 13531 NILM cases. The average of these women was 38 years (16-91years). The overall HR-HPV positive rate was 20.8% with the most common type HPV 52 (4.3%), 16 (2.8%), 58 (2%). The prevalence of HR-HPV was 83.6%, 75.4%, 71.8%, 35.0%, 14.9% in women with HSIL, LSIL, ASC-H, ASC-US, and normal Pap cytology, respectively. HPV16 is the most common type in women with HSIL (39.2%) and ASC-H (27.6%), and the second most common type in ASCUS (4.3%), NILM (1.5%), while HPV52 is the most common type in LSIL (19.1%), ASCUS (7.8%) and NILM (2.8%), the second most common In HSIL (16.9%), ASC-H (16%) Paps. HPV58 is the second most common type in LSIL (8.9%), third most common type in HSIL (11.4%), ASC-H (13.5%), and ASCUS (3.7%) Paps, and the fifth cost common type in NILM. HPV18 counts less percentage in all categories. Multiple HRHPV infection accounted for 21% and 14% HRHPV positive cases in women with abnormal Pap and normal Pap tests, respectively ($p<0.05\%$). LR-HPV only infection was found in 8.9% women with LSIL Pap, 5.0% women with ASC-US Pap, and 3.5% women with NILM Pap.

Table 1. Six most common HRHPV genotypes in women with various Paps

HSIL	HPV16	HPV52	HPV58	HPV33	HPV18	HPV31
219 (%)	86 (39.2)	37 (16.9)	25 (11.4)	21 (9.6)	10 (4.6)	9 (4.1)
ASC-H	HPV16	HPV52	HPV58	HPV18	HPV33	HPV31
163 (%)	45 (27.6)	26 (16.0)	22 (13.5)	12 (7.4)	8 (4.9)	6 (3.7)
LSIL	HPV52	HPV58	HPV16	HPV53	HPV51	HPV39
683 (%)	136 (19.1)	61 (8.9)	56 (8.2)	54 (7.9)	50 (7.3)	40 (5.9)
ASC-US	HPV52	HPV16	HPV58	HPV51	HPV53	HPV39
1458 (%)	114 (7.8)	62 (4.3)	54 (3.7)	47 (3.2)	46 (3.2)	41 (2.8)
NILM	HPV52	HPV16	HPV53	HPV39	HPV58	HPV51
13531 (%)	377 (2.8)	206 (1.5)	175 (1.3)	156 (1.2)	153 (1.1)	124 (0.9)

Conclusions: This is one of the largest study about HPV genotypes in Chinese women with Pap cytology. The prevalence of HR-HPV infection among Chinese women is high. Overall, the most prevalent genotypes were HPV52, HPV16, 58, and 53. HPV16 is the most common type in women with the high grade Pap cytology (HSIL, ASC-H) and HPV52 is the most common types in women with the low grade Pap cytology (LSIL, ASC-US), and NILM cytology. These data can provide the value to understand the HPV epidemiology and to guide for vaccine selection for Chinese women.