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ABSTRACTS

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1897 Formalin Wicking Permits Adequate Fixation of the Endometrium: A Comparative Study of Two Fixation Methods

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Disclosures: Heba Abdelal: None; Dengfeng Cao: None; Ian Hagemann: None

Background: Tissue fixation is an important preanalytic variable in pathology. Several methods can be used to open and fix hysterectomy specimens. In one method, the uterus is bivalved by the surgeon and a formalin-moistened gauze pad is placed in the cavity as a wick, before reapproximating the hemiuteri and tying a second gauze around the cervix. This method has the advantage of minimizing overall distortion of the uterus during fixation. In another method, the uterus is simply bivalved and immersed in formalin. This method permits more circulation of formalin, but allows for greater distortion as the tissue fixes. We performed a comparative analysis to determine whether one of these methods provides superior fixation of the endometrium.

Design: Hysterectomy cases were selected from the prior year at a single academic institution, without regard to pathologic diagnosis. For each case, two-three slides representing the endometrium were selected for analysis. These were scored for quality of fixation using a semiquantitative scale (Figure 1): 3, perfect fixation; 2, mild autolysis not hindering interpretation; 1, marked autolysis but still interpretable; 0, total autolysis, not adequate for diagnosis. Two pathologists performed scoring of each slide. When differences of >1 unit were present, reconciliation was performed in a consensus setting to reach a difference of <=1 unit.

Results: Power analysis showed that a set of 23 cases using each of the fixation methods would be sufficient to detect a difference in fixation quality of 0.5 semiquantitative units. A total of 53 cases were selected (25 for method 1 and 28 for method 2). Uterine mass ranged from 40 to 590 g (median 108 g) and did not differ between methods (Student t test). Prior to consensus, the two raters had significant agreement as to the degree of autolysis of each case (Spearman r = 0.567, p=0.000009). After consensus, there was no significant difference in autolysis between the methods (Mann-Whitney p=0.4295) (Figure 2).

Figure 1 - 1897

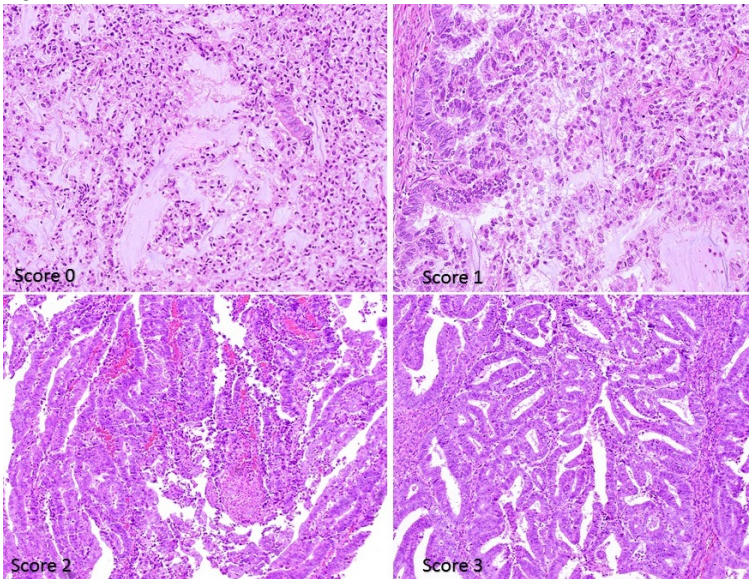
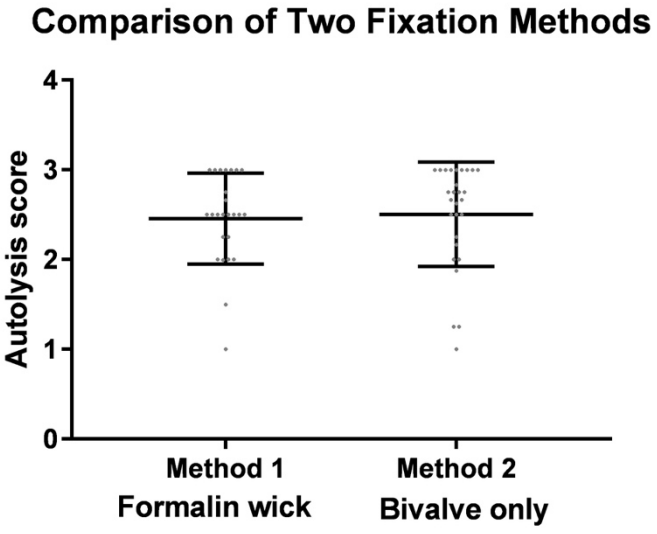


Figure 2 - 1897



Conclusions: The two methods studied for fixation of the endometrium in hysterectomy specimens were not significantly different in their ability to prevent autolysis. Method 1, in which a formalin wick is placed in the cavity and the uterus is reapproximated, has the additional advantage of minimizing anatomic distortion.

1898 PDL-2 Immunoreactivity in Human Tumors; What we See may not be What is True: Antibody/Clone Dependent Results and correlation with PD-L1 expression

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Disclosures: Lina Abdul Karim: None; DongHyang Kwon: None; Joeffrey Chahine: None; Bhaskar Kallakury: None

Background: PDL-1 negative tumors have shown clinical response to anti-PD1 therapy. This has prompted investigation into PDL-2, the other ligand of PD-1. PDL-2 has been shown to have a negative regulatory function on T-cells that is not compensated for by PDL-1. PDL-2 expression has been analyzed in a few studies mostly using a single antibody. Numerous PDL-2 clones are available; however, no single study evaluated the concordance of these clones. In our study, we investigated PDL-2 immunoreactivity with multiple antibodies in different human tumors and evaluated their concordance and correlation with PDL-1 expression.

Design: The studied tumors included 123 cases from 6 different primary sites (Table 1). Immunohistochemistry analysis was performed on the Autostainer Link 48 using FDA approved PDL-1 antibody (22C3 clone, Dako), polyclonal PDL-2 antibody (ab200377, Abcam) and two monoclonal PDL-2 antibodies (MM0511-10B6, Novus Biologicals and sc-80285, Santa Cruz Biotechnology). Immunoreactivity was semi-quantitatively scored for intensity and percentage positive distribution in tumor cells. Any case showing ? 1% expression was considered positive.

Results: Positivity rate for PDL2 expression with the polyclonal antibody (111/123, 90%) was significantly higher compared to PDL1 expression (14/123, 11%) (p value <0.01). However, 93% of PDL-1 positive cells were also positive for polyclonal PDL-2 expression. Similarly, both monoclonal PDL-2 antibodies, sc-80285 (62/123, 50%) and MM0511 (30/123, 24%), also showed higher expression compared to PDL1. Interestingly, PDL2 positivity rate was significantly higher with the polyclonal compared to both monoclonal antibodies ($p < 0.01$). PDL 2 expression across the three antibodies was most concordant in colorectal carcinomas only.

Table.1

Primary Carcinoma	Total Number of cases	Number of positive cases			
		PDL-1	PDL-2 Polyclonal	PDL-2 (sc-80285)	PDL-2 (MM0511-10B6)
Pulmonary	18	2	16	12	4
Colorectal	20	2	20	20	13
Biliary	20	1	20	11	4
Hepatic	13	1	13	7	2
Renal	23	5	21	4	2
Pancreatic	26	3	21	8	5
Total	120	14	111	62	30

Conclusions: The significantly higher positivity for PDL2 compared to PDL1 may explain the observed therapeutic response of anti-PD1 therapy in some PDL1 negative tumors and also support the current development of anti-PDL2 targeted therapy. Variability of PDL2 expression by antibody and tumor type should be recognized as a potential pitfall in experimental study design. Since no consensus has been reached as to which antibody should be utilized, larger studies are warranted to determine the optimal strategy for assessment of PDL2 immunoreactivity.

1899 Five Year Retrospective Review, Do We Still Need It? Should We Change It?

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Disclosures: Shahad Abdulameer: None; Grazina Chatt: None; Stefan Pambuccian: None; Swati Mehrotra: None; Guliz A. Barkan: None

Background: Federal regulations stipulate that all negative cervical cytology specimens obtained within the last five years must be reviewed when a new high-grade squamous intraepithelial lesion (HSIL) or above is detected in the same patient. If significant discrepancies are detected that would affect current patient care, the clinician must be notified and an amended report must be issued. This 5-year retrospective review (5YRR) serves as a quality monitor as well as an educational tool for laboratories. The aim of the study was to determine the value of the 5YRR in comparison to less stringent measures.

Design: We identified all cases diagnosed as HSIL from 2002 to 2017 though a search of our electronic database and institutional QA records. A 5YRR of all prior negative Pap tests of the patients with HSIL diagnoses was performed as per CLIA regulations. Disagreement on review was defined as minor (+1) (negative to ASCUS/LGSIL), or major (+2) (negative to HSIL).

Results: During the collection period, 2982 of 272,422 (1.1%) Pap tests had a diagnosis of HSIL or above, of which, 54.6% had prior Pap smears available for retrospective evaluation. The percentage of the false negative rate was 15% (11% minor and 4% major discrepancies) from the initial negative interpretation. None of the discrepant cases required an amended report. The false negative rate decreased significantly during this interval, starting in 2006. In our study we calculated 33/445 discrepancy cases (7.42%) between 2002-2005 (P1), and 38/1182 cases (3.41%) between 2006-2017 (P2). The data available from 2015-17 showed only 1/212 cases with a prior false negative Pap test (reinterpreted as HSIL on review). This discrepancy was discovered at one year interval highlighting that a shorter retrospective review period may suffice.

	Agree	Disagree	Total
P1 (2002-2005)	412	33	445
P2 (2006-2017)	1144	38	1182
Total	1556	71	1627

Conclusions: CLIA mandated 5YRR is supposed to be an effective tool for monitoring individual personnel competency; however it is a labor intensive and time consuming activity. In a laboratory where there is no or minimal personnel turn over, and the cytopathology personnel is experienced, a shorter retrospective period of screening may be adequate. In the present changed environment of gynecologic cytology, impacted by HPV vaccination (which lowers the prevalence of HSIL) and (co)testing (which reduces the false negative rate), and change in the Pap smear screening interval (which reduces the number of prior slides to be reviewed), this 5YRR mandate should be revisited.

1900 Challenges in interpreting early Barrett adenocarcinoma in endoscopic submucosal dissection specimens

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Disclosures: Ashwin Akki: None; Daniel Sanchez: None; Feng Yin: None; Jinping Lai: None; Xiuli Liu: None; Ashwini Esnakula: None

Background: Depth of submucosal invasion is a key prognostic factor for early stage Barrett's esophagus (BE) adenocarcinoma. Our systematic review of published data demonstrates a "rule of doubling" for the frequency of lymph node metastases: tumor invasion into each progressively deeper one third of submucosal layer corresponds with a twofold increase in the risk of nodal metastases (9.9% in superficial one third of submucosa (sm1) group, 22.0% in mid third of submucosa (sm2) group, and 40.7% in deep third of submucosa (sm3) group). Submucosal invasion can be evaluated with a "third" method or a microscopic measurement. Other important risk factors include lymphovascular invasion (LVI), tumor differentiation, deep margin status, desmoplasia, and tumor budding. However, interpretational challenges of these key prognostic features in endoscopic submucosal dissection (ESD) specimens have not been investigated.

Design: All slides from 22 early BE adenocarcinoma-containing ESD specimens from 2015-2017 were reviewed by 4 gastrointestinal pathologists to confirm the diagnosis, submucosal invasion, tumor differentiation, LVI, desmoplasia, tumor budding, and deep margin status. Submucosal invasion is further classified into superficial (<400 µm) and deep (>400 µm). A consensus interpretation of a diagnosis or feature was defined as an agreement by at least 3 pathologists.

Results: Four pathologists generated 88 readings including 36 submucosal invasive adenocarcinoma (SIAC), 48 intramucosal adenocarcinoma (IMC), and 4 high-grade dysplasia (HGD). Final interpretations included 20 cases with consensus (13 IMCs, 7 SIACs) and 2 cases with no consensus. The 4 reads of HGD were generated from cases with an IMC consensus. Interobserver agreement ranged from poor to perfect (kappa: -0.02 to 1.0). The "third" method of evaluating the submucosal invasion was not applicable to any cases as no muscular propria present in ESD specimens. Among 7 SIAC there was atleast 71% agreement on assessment of microscopic superficial and deep submucosal invasion, desmoplasia, deep margin status, tumor budding, LVI, and tumor differentiation [Table].

Prognostic Features (SIAC n=7)	Reading by 4 pathologists (total reads: 28)	Consensus
Depth of invasion	Superficial: 4 Deep: 24	Superficial: 0 Deep: 5 Non-consensus: 2
Desmoplasia	Absent: 6 Present: 22	Absent: 0 Positive: 5 Non-consensus: 2
Deep margin	Negative: 19 Positive: 9	Negative: 4 Positive: 1 Non-consensus: 2
Tumor budding	Low: 15 High: 13	Low: 4 High: 2 Non-consensus: 1
Lymphovascular invasion	Absent: 9 Present: 19	Positive: 5 Negative: 0 Non-consensus: 2
Differentiation	Poor: 10 Well-moderate: 18	Poor: 2 Well-moderate: 5

Conclusions: This pilot study reveals a spectrum of interobserver variability in diagnosing early BE adenocarcinoma in ESD specimens and the interpretational challenges in assessing key tumor prognostic features. Developing strict guidelines for each of the assessed parameter and educating pathologists will likely improve interpretational consistency and accuracy.

1901 Oncotype DX for Invasive Breast Carcinoma: Ordering of Test by Surgeon (Rather than Oncologist) can Reduce Turnaround Time

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Disclosures: Fatima Al-Baqali: None; Jordan Baum: None; Syed Hoda: None

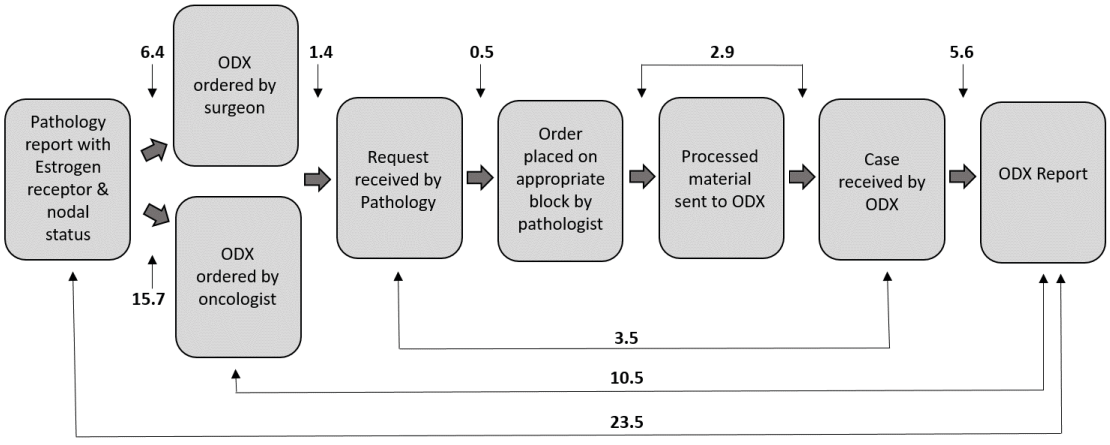
Background: Oncotype DX (ODX, Genomic Health, Redwood City, CA), a 21-gene expression assay, is integral to Prognostic Staging in the 2018 American Joint Committee on Cancer (AJCC) for estrogen receptor (ER): +, HER2: (-) and node: (-) invasive breast carcinoma (IBC). Also, TAILORx results (*NEJM* 2018;379:111) show ODX is helpful in guiding adjuvant therapy. Thus, ODX is crucial to render timely clinical decisions. We studied work flow to identify opportunities to reduce turnaround time (TAT) of ODX at a large academic medical center.

Design: IBC cases sent for ODX testing over a 13-month period (6/2017 to 7/2018) were investigated for TAT, and related factors, from issuance of pathology report (with node and ER status) to ODX report. TAT for each stage of the ODX ordering process **(Figure 1)** was measured in days (d, weekdays only). Cases were excluded if dates could not be confirmed in electronic medical record, or if there was insufficient tumor quantity for ODX testing, or multiple tumors (requiring stepwise processing by ODX) were present.

Results: TAT and related factors were studied in 127 IBCs in 125 patients. ODX was ordered more often on excisional biopsy (n=116/127, 91%) than on needle core biopsy (n=11/127, 9%). TAT ranged from 7 d to 92 d (mean 23.5 ±14.6 d). The longest, and most variable, portion of the workflow was the time between issuance of pathology report to ordering of ODX by clinician (mean 12.9 ±14.1 d). Surgeons (n=38, mean TAT= 6.4 d) ordered ODX significantly sooner than medical oncologists (n=89, mean TAT= 15.7 d) ($p<0.001$). Please see Figure 1 for additional results.

Figure 1 - 1901

Figure 1. Oncotype DX Workflow with Turn Around Times. Numbers denote mean workdays between various steps.



Conclusions: Surgeons (who see patients relatively earlier status-post pathology diagnosis of IBC) should order ODX, and not oncologists- since surgeon-initiated ODX results significantly reduces TAT. This finding is largely similar to that of reported earlier *J Onco Pract* 2017;13:e816-e820. Other steps that impede a streamlined ODX workflow should be evaluated.

1902 Potential Impacts of Instituting a Standard "Gross Only" Policy in the Examination of Surgical Pathology Specimens

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Disclosures: Karen Arispe Angulo: None; Ayesha Farooq: None; Hasan Samra: None; Wegahta Weldemichael: None; Julie Jorns: None

Background: CAP recommendations guide the development of institutional policy for determining which surgical specimens must be submitted to pathology for gross, but are exempt from routine microscopic, examination, or "gross only" specimens. At our institution we had not yet established such a policy. We sought to determine diagnostic, workflow and economic implications of instituting a standard gross only policy.

Design: Modeling after an established gross only policy from a neighboring academic institution, retrospective (2017) key word searches were performed to identify potential gross only cases for which microscopic evaluation was performed (N=448) and gross only cases per surgeon request (N=198). Cases were evaluated for specimen type(s), part(s), block volume (H&E +/- decalcification), turn-around-time (TAT), demographics and diagnosis. Laboratory cost vs reimbursement was evaluated.

Results: Microscopic evaluation was performed for 472 specimens: atherosclerotic plaques (33.5%), bariatric stomach/bowel (32.6%), hernia (15.7%), heart valves (12.7%) and other (5.9%) (Fig.1). 425 (94.9%) had 1, 22 (4.9%) 2 and 1 (0.2%) had 3 parts/case. Median blocks were highest for stomach/bowel (4/case). Decalcification was performed for plaque (149/158; 94.3%) and valve specimens (52/60; 86.7%).

4 (2.7%) cases for bariatric surgery had H. pylori, 3 of which constituted new diagnoses and were treated; these were the only cases with “significant” histologic findings.

Gross only specimens (N=225) were most frequently bone for surgical access (31.6%), devices (20%) and amputation for ischemia (20.4%) (Fig.2). 135/198 (68.2%) had 1 part and 63 (31.8%) had other parts for histology.

Table 1 shows TAT, with longer TAT for specimens requiring decalcification.

Table 2 shows estimated costs including labor for cutting/embedding blocks, staining, distribution, etc., reimbursement for these specimens based on average payments for billed CPT codes and costs that would be recouped via gross only reimbursement. % monetary loss would be most influenced by bariatric specimens (CPT 88307).

Table 1. TAT (days:hours:minutes) (mean, range).

	Potential Gross Only Specimens for which Microscopic Evaluation was Performed	Gross Only Specimens per Surgeon Request
Overall TAT	2:16:12 (0:18:39-4:16:28)	3:08:13 (0:01:12-4:02:15)
TAT if Other Parts for Histology	2:15:12 (0:18:39-4:16:28)	4:16:32 (1:02:53-4:02:15)
TAT if No Other Parts for Histology	3:00:56 (0:21:31-6:21:52)	2:17:28 (0:01:12-3:00:25)
TAT if Decalcification	3:12:58 (0:23:30-4:16:28)	N/A
TAT if No Decalcification	2:00:38 (0:18:39-6:21:52)	N/A

Table 2. Cost Analysis of Instituting a Standard Gross Only Policy.

	Reimbursed	Lab Costs	Gross Reimbursement	Net	% Loss
Plaque	9,578	905	1,567	-7,106	18.9%
Hernia	1,675	353	734	-587	1.6%
Stomach/bowel	28,051	2,555	1,528	-23,968	63.6%
Valves	6,496	338	595	-5,562	14.8%
Other	892	183	258	-451	1.2%
Total	46,691	4,334	4,682	-37,674	

*Costs of changes in physician time/work not analyzed

Figure 1 - 1902

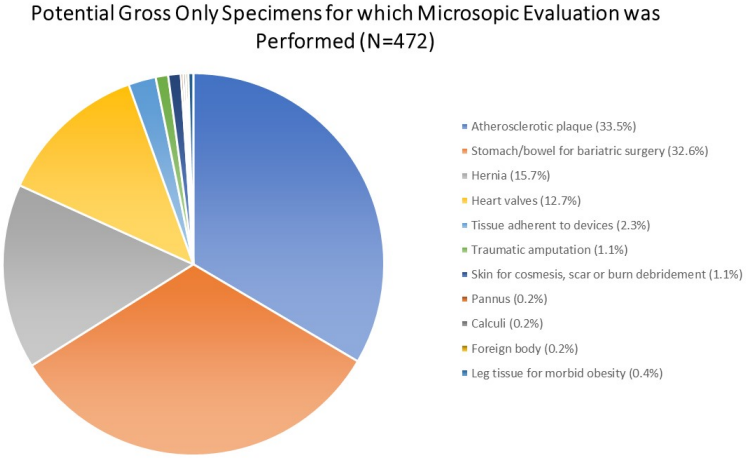
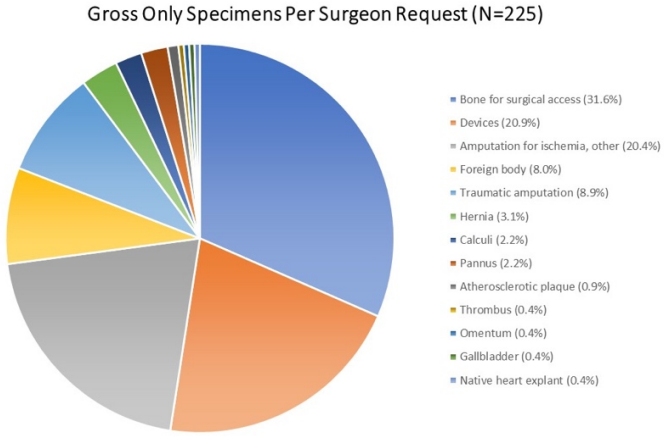


Figure 2 - 1902



Conclusions: It is reasonable to establish a gross only policy for most specimens currently undergoing histologic processing at our institution. This will improve efficiency and TAT without affecting patient care. The exception would be bariatric stomach specimens on which H. Pylori can only be diagnosed at the microscopic level; histologic evaluation of these specimens additionally was the greatest contributor to laboratory revenue.

1903 Analysis of Information Contained Within Barcode Labeling of Surgical Pathology Slides

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Disclosures: G. Thomas Brown: None; Paul Fontelo: None

Background: Modern barcoding systems, such as Data Matrix, and QR codes can contain a significant amount of important information useful for identification and tracking of pathology specimens. While barcode labeling of surgical pathology cases has only recently become commonplace, it has had a powerful impact on reducing errors. Although CAP and NSH provide general guidelines for labeling of specimens, we are unaware of recommendations or best practice guidelines on the type of information to embed into barcodes. To gain a better understanding of what information might be useful, we collected barcoding information from several laboratories for analysis.

Design: We collected 79 surgical pathology slides sent to our institution for consultation or for patient registration for clinical trials within the past 3 years. We photographed the slide labels to record the type of human readable information: accession number, slide number, date, patient name, MRN, and other information. We also decoded machine readable codes (e.g., QR, Data Matrix, etc.) to determine the information encoded within.

Results: Of the 79 slides collected, 60 had a barcode. By far, the most common barcoding system employed Data Matrix (51/60) to encode information. In accordance with CAP/NSH recommendations, all laboratories labeled their slides with accession numbers and the institution name. Fifty-seven laboratories also included patient name (or initials), and, 32 included a date (either the accession date or the date when the slide was cut). A few laboratories (8) included anatomic site. The data contained within barcodes almost uniformly encoded the accession number (44/60) and the slide number (31/60). MRN was included on 9 labels in human readable form but only one lab encoded it into their barcodes. Four laboratories encrypted or obscured the information before embedding it into the barcode. We were unable to decode seven barcodes because of faded or damaged labels.

Conclusions: This study reviewed the labeling and coding practices of several pathology laboratories nationwide. We discovered that the barcoding information varies widely between institutions as the human readable labels. Presumably, the functionality of the barcoding system meets the needs of the originating lab, however, guidelines or recommendations may be needed for interoperability and patient data protection in today's data driven environment and where a patient's data and pathology slides may travel with the patient.

1904 Factors Driving Tissue Contaminants in Paraffin-Embedded Tissue Blocks

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Disclosures: Timothy Carll: None; Peter Pytel: None; Tatjana Antic: None; Ricardo Lastra: None; Rachel Poon: None; Ryan McGary: None

Background: In anatomic pathology, tissue contaminants represent errant material that originates from one case but ends up on the histologic slides of another. Tissue contaminants can lead to serious diagnostic errors if not recognized. We define "floaters" as cut tissue sections that contaminate slides at any point subsequent to paraffin-embedding. Less well-described are factors that drive "carry-overs", tissue contaminants that become incorporated into the paraffin-embedded tissue block. The grossing bench and embedding station are often regarded as primary sources of such carry-overs. This study evaluates our institutional experience with cases in which the likely source of contamination was linked to the use of a pneumatic tube system for specimen transportation from the gross room to the histology laboratory.

Design: De-identified "donor" tissue composed of friable tumors as well as "recipient tissue" composed of spongy benign parenchymal tissues were obtained and submitted together in a series of parallel runs for routine histology, entailing submission via a pneumatic tube system in a sealed container with a small volume of formalin. The tissue was embedded according to standard histotechnology protocol and a single H&E-stained slide was cut from each block for histopathologic examination, while the residual formalin from each run was examined using cytospin techniques. Various combinations of packaging of the "donor" as well as the "recipient" tissues in plain cassettes or with either mash bags or filter paper were tested.

Results: Fluid movements during transport in the pneumatic tube system can dislodge fragments of tumor tissue even if these are packaged in mesh tissue bags or filter paper. These floating tissue fragments can be identified by the cytologic preparation on the formalin used for transport. The tissue fragments furthermore could be detected in the recipient tissue as carry-overs. Packaging in mesh bags or filter paper did not completely abate the risk of tissue contamination.

Conclusions: The use of pneumatic tube systems for transport of "wet" tissues can lead to tissue contamination. Safe use of a pneumatic tube system would therefore require careful validation of the conditions. Beyond the use of a pneumatic tube system, fluid movements during triage, transport and processing of tissue blocks may be associated with distinct but lower risk of tissue contamination.

1905 Intraoperative diagnosis of signet ring cell carcinoma: an 18-year experience and lesson of a single institution

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Disclosures: Fengming Chen: None; Kun Jiang: None; Bing Han: None

Background: Signet ring cell carcinoma (SRCC) is a rare form of poorly differentiated adenocarcinoma. It is difficult to be assessed on frozen diagnoses, with high false negative rates, which may have the potential to alter the operative maneuver and affect patient care. In this study, we aimed to 1) evaluate our institutional accuracy in the intraoperative diagnosis of SRCC; 2) investigate common factors

contributing to discrepancies between frozen section assessment and permanent diagnosis; 3) summarize our experience and lessons learned on how to avoid errors on frozen diagnosis of SRCC.

Design: We retrospectively reviewed our pathology database 05/25/2000 to 09/01/2018 in an effort to identify specimens diagnosed with SRCC on permanent sections, which also had previous intraoperative consultations. For all identified specimens frozen sections and permanent H&E slides were re-reviewed.

Results: The study included 81 specimens taken from 50 patients, comprised of metastasis assessment (61/81=75.3%), resection margin evaluation (12/81=14.8%), and correlation with the initial diagnosis (8/81=9.9%). A total of 7 discrepancies and 5 deferrals are identified with false negative rate of 14.8%. Common factors causing discrepancies in diagnosing SRCC between frozen and permanent sections include: 1) Clusters of SRCC mimic the appearance of myxoid background (n=4, 33.3%, Figure 1 and 2); 2) SRCC was mistakenly identified as adipocytes, histiocytes or large reactive lymphocytes because SRCC cells often demonstrate clear or depleted cytoplasmic mucin on frozen sections (n=2, 16.7%); 3) A small focus of SRCC, which was seen only on the permanent/deeper section and not on the frozen section (n=2, 16.7%); 4) Rare isolated cells with pools of extracellular mucin (n=1, 8.3%); 5) Marked thermal/frozen artifact (n=1, 8.3%); 6) Incomplete submission (n=1, 8.3%); 7) Personal threshold, specialty experiences and alertness (n=1, 8.3%).

Figure 1 - 1905

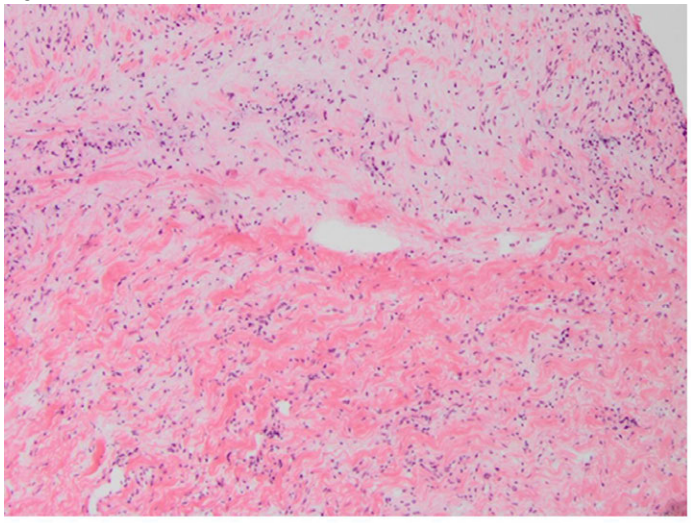

Figure 1. Signet ring cell carcinoma (SRCC) frequently hides in the myxoid background (top) on frozen sections, H&E x 100.

Figure 2 - 1905

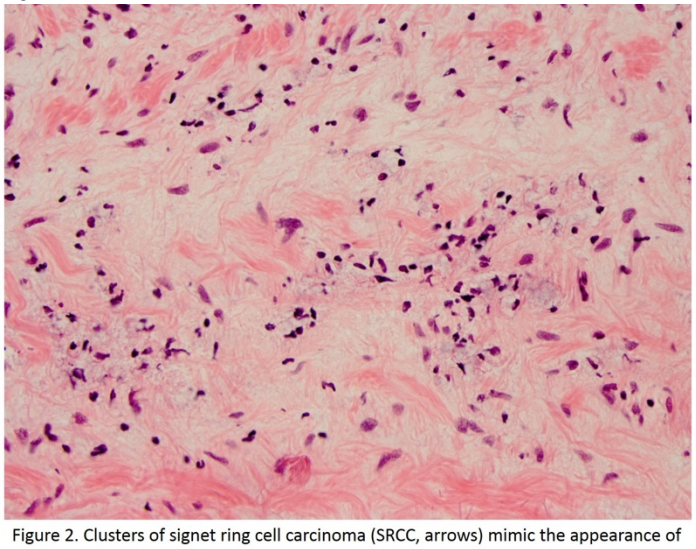

Figure 2. Clusters of signet ring cell carcinoma (SRCC, arrows) mimic the appearance of myxoid background on frozen sections, H&E x400.

Conclusions: Accurate diagnosis of SRCC during intraoperative consultations remains challenging. Based on our experience and lessons introduced above, the most important advices to reduce diagnostic errors are: 1) Understanding SRCC characteristics on frozen sections such as clear or depleted intracellular mucin, lack of desmoplastic changes and no adjacent pre-cancer changes; 2) Pay attention to abrupt transition from normal architecture (e.g. glandular or fibrous component) to myxoid and/or inflammatory-like appearance. SRCC frequently hides in the latter.

1906 Assessing Anatomic Pathologists' Productivity in The Value Based Era: Is it Time to Modernize Relative Value Units (RVU) Based Productivity and Compensation Model?

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Disclosures: Dhananjay Chitale: None

Background: Increasingly, hospital and group practice administrators mainly use RVU to measure physician's productivity and compensation including anatomic pathologists. The correlation between RVUs and actual pathologists' efforts are not well characterized, especially in the subspecialty practice or a hybrid general and subspecialty anatomic pathology practice. In addition, the current procedural terminology (CPT) code and RVU values have remained static and pathologists work has gotten further complex with increased reporting demands on tissue-derived parameters, checklists, biomarkers etc. Aim of this study was to assess discrepancies and imbalances between RVUs and quantifiable metrics of pathologists' sign out effort within multiple specialties in pathology department at a large metropolitan health care system and improve equitable work distribution.

Design: Using institutional pathology database, total number of surgical pathology specimens (part types) with associated CPT codes and work RVU (wRVU) over a period of 10 years were analyzed. Top high volume current procedural terminology (CPT) codes that covered

90% of our anatomic pathology service were selected for analysis. We then identified all the part types associated with the top two procedural CPT codes within different major subspecialties. To assess degree of difficulty and time spent on individual specimens, points were recorded for each part type (1 point = 5 minutes) that also included number of blocks, slides, special stains.

Results: The two highest CPT codes covering close to 90% of our practise remained the same over a decade with an increasing volume trend in both. In 2016 (table 1), they were 88305 [100,244/129,672 (77%)], 88307 [13,708/129,672 (11%)]. The top four subspecialities with higher complexity and effort and lower wRVU included hematopathology, breast, musculoskeletal and thoracic services.

	Total wRVU	Total Points	Ratio of points/wRVU
Hematology-Liquid	4000	20081	5.0
Hematology-Solid	1290	5462	4.2
Thoracic	2003	8269	4.1
Musculoskeletal	4055	16729	4.1
Breast	7738	30301	3.9
Neuropathology	1991	6886	3.5
Genitourinary	13364	41122	3.1
Head & Neck	2540	7739	3.0
Cardiovascular	1050	3161	3.0
Dermatology-plastic	2660	6104	2.3
Gynecology	14956	30053	2.0
Endocrine	164	323	2.0
Gastrointestinal	50734	89712	1.8
Medical Kidney	2778	4890	1.8
Dermatology	9386	13899	1.5

Conclusions: The correlation of wRVU vs effort of pathologists' in many subspecialities of anatomic pathology is poor and skewed. Given the increasing emphasis on measuring pathologists' productivity, more objective and standardized measures of work productivity need to be developed to prevent / reduce errors, maintain turnaround time, decrease physician burnout and improve retention.

1907 The Utility of Low-Grade Squamous Intraepithelial Lesion Cannot Rule High-Grade in Anal Cytology and Comparison with Other Categories in HIV Positive Patient Population

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

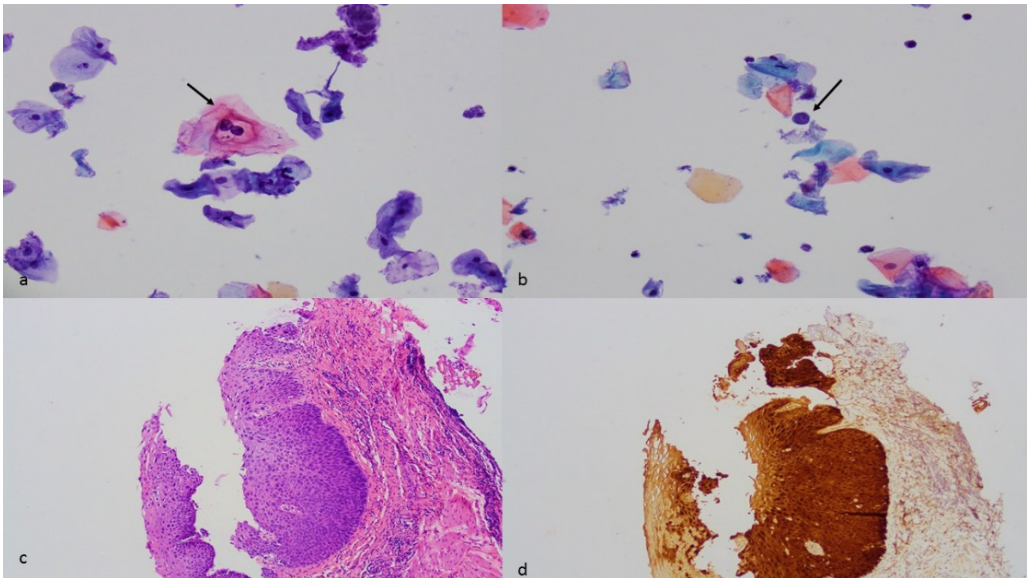
Background: Low-grade squamous epithelial lesion cannot rule out high-grade (LSIL-H) is a category used by some institutions in cytology specimens when the lesion does not fulfill the criteria for a high-grade lesion (Figure 1: a- low-grade dysplasia; b-rare small cells suspicious for high-grade; c. CIN2 on follow-up biopsy; d. positive p16 immunostaining). The 2014 Pap Bethesda System does not recognize this category. The purpose of this study is to investigate the utility of the category in anal cytology and compare it with other Bethesda categories.

Design: We retrospectively searched the database from 01/2013-12/2017 for all anal pap tests and we identified 5982 specimens. Of those, we retrieved 1754 patients with a follow-up biopsy within 6 months. If multiple biopsies are available, for the purposes of this study the most severe dysplasia was recorded. All patients are HIV positive with unknown HRHPV status. Unsatisfactory specimens were excluded from the study.

Results: Of 1754 patient with histopathologic follow-up 37.7% were women and 62.3% were men. The cytologic results included NILM: 9.6%, ASCUS: 43.9%, ASC-H: 6.1%, LSIL-H: 11.4%, LSIL: 18.7%, HSIL: 10.1%. Cytologic diagnoses and histologic follow-up are summarized in Table 1.

Biopsy follow-up	Cytology				
	ASC-US	ASC-H	LSIL-H	LSIL	HSIL
Negative for dysplasia	357 (46.3%)	44 (41.1%)	22 (12.4%)	98 (29.8%)	35 (19.7%)
AIN 1	120 (15.5%)	20 (18.6%)	44 (24.8%)	33 (10%)	24 (13.5%)
AIN 2/3	333 (43.1)	43 (40.2%)	135 (76.2%)	198 (60.2%)	118 (66.6%)

Figure 1 - 1907



Conclusions: Anal Pap tests, if ASC-US diagnosis is included, have high sensitivity but low specificity in predicting high-grade lesions. High ASC-US rate with positive follow-up biopsy, highlight the need for HR-HPV testing to improve specificity even in HIV positive population. In our study LSIL-H interpretation correlates better with high-grade histologic follow-up when compared with ASC-H and LSIL diagnosis alone ($p<0.0001$ and $p<0.0005$ respectively). In this setting, the finding of a low-grade lesion serves as a surrogate for HPV test. Our results indicate that this category is useful, however in order to comply with the 2014 Bethesda reporting system, we suggest using this category with ASC-H as the main diagnosis, and additional finding of LSIL as a comment.

1908 Patterns of Frozen Section Interpretation Error: An in Depth Analysis from a Complex Academic Surgical Pathology Practice

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Disclosures: Lauren Dehan: None; James Lewis: None; Mitra Mehrad: None; Kim Ely: None

Background: Discrepancies between intraoperative frozen section (FS) and final diagnoses have the potential to alter clinical decision-making and to cause serious harm. Monitoring these discrepancies for patterns and targeting high risk scenarios are important for high reliability in surgical pathology. The goal of this study was to establish baseline data on error rates and to identify specific scenarios in which discrepancies are most frequent so they could be specifically targeted for improvement.

Design: All FS diagnoses from a complex service where FS us covered in a general manner by all surgical pathology faculty, between 7/1/2016 and 6/30/2018, had been reviewed as part of long term, ongoing quality assurance. Interpretation errors, where the diagnosis rendered at the time of surgery was incorrect, were studied in detail and classified as major or minor based upon the degree of error and on their potential for (and actual) impact on surgical management.

Results: Of the 4,449 total FS over the time period, 1.3% had interpretation error (58/4449), 0.52% (23/4449) which were major. Those with major clinical impact were 0.045% (2/4449) and minor 0.79% (35/4449). Cases were evenly spread across subspecialty areas without any clear concentration by site/subspecialty. The fraction of major interpretation errors out of total interpretation errors was highest for the thoracic (3/3, 100%) and gastrointestinal/liver (4/6, 66%) services. Seventy-four percent (35/47) of interpretation errors were made in subspecialty areas that were not those of the attending involved. Recurrent scenarios in which interpretation errors were made included post-treatment cancer cases (6 cases), tracheal margins with immature squamous metaplasia being called severe dysplasia (3 cases), and diagnostic lung cases with reactive mesothelial cells overcalled as carcinoma (3 cases).

Conclusions: Overall, interpretation errors in FS diagnosis are rare and even more rarely have major clinical impact. Dedicated subspecialty FS sign out (or at least having a lower threshold to show a pathologist in the area of subspecialty for the FS) might decrease errors, particularly for high risk sites/scenarios such as pleura, head and neck margins, and post chemo-rads cancer surgeries.

1909 Impact of 2018 American Society of Clinical Oncology/College of American Pathologists Clinical Guidelines Update on HER-2 Oncogene Testing in Breast Cancer Cases

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Disclosures: Lorena Di Pasquale Guadalupe: None; Laila Khazai: None; Yin Xiong: None; Emmanuel Agosto-Arroyo: None

Background: Human Epidermal Growth Factor Receptor 2 (HER2) is overexpressed in 15–20 % of invasive breast carcinomas, which is associated with increased rates of recurrence, metastasis and mortality. Accurate determination of HER2 status is exceptionally important due to increased survival benefit of anti-HER2 therapy in HER2 positive patients and the potential avoidance of drug-related costs and risks in HER2 negative patients. The aim of this project is to assess the impact of the new 2018 American Society of Clinical Oncology (ASCO)/College of American Pathologists (CAP) ASCO/CAP HER2 interpretation guidelines on breast cancer cases previously interpreted based on the 2013 guidelines.

Design: The laboratory information system was retrospectively reviewed for HER2 assays with both immunohistochemistry (IHC) and in situ hybridization (ISH) performed in our institution from July 1, 2017 to June 30, 2018. The frequency of HER2 positive, negative and equivocal cases by IHC and ISH assays diagnosed using the 2013 guidelines was determined. ISH cases were reclassified according to the 2018 guidelines. The rate of concordance between 2013 and 2018 guidelines results was determined using one-sample proportion test.

Results: A total of 821 cases were included in the study. Two hundred and thirty seven (28.9%), 313 (38.1%), 165 (20.1%) and 106 (12.9%) cases were classified by IHC as 0, 1, 2 and 3, respectively. Table 1 summarizes HER2 IHC and ISH results following ASCO/CAP 2013 guidelines and their corresponding classification based on 2018 guidelines. Four out of 5 IHC 1+ and 3 IHC 2+ cases initially classified as ISH positive based on 2013 guidelines were reclassified as negative under 2018 guidelines (0.85%). Eleven IHC 2+ cases classified as ISH equivocal were reclassified as negative (1.34%) and 2 IHC 3+ cases classified as ISH equivocal were reclassified as positive (0.24%). The overall discordance rate of HER2 ISH results by the 2013 and 2018 was 2.43% (p=0.0008), which is significantly lower than the generally accepted significance level of 5%.

	ISH Results 2013 Guidelines			**ISH Results 2018 Guidelines**	
IHC Result	Negative	Equivocal	Positive	Negative	Positive
0	237	0	0	237	0
1	308	0	5	312	1
2	118	11	36	132	33
3	1	2	103	1	105
Total	**664 (80.9%)**	**13 (1.6%)**	**144 (17.5%)**	**682 (83%)**	**139 (17%)**

Conclusions: HER2 ISH results interpreted by the 2013 and 2018 are highly concordant. The new guidelines allow for classification of ISH equivocal cases into positive or negative, with more correlation with the IHC results.

1910 Frozen Section for Margin Assessment during Radical Prostatectomies – An Institutional Experience

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Disclosures: Nikolina Dioufa: None; Richard Morris: None; Aileen Grace Arriola: None

Background: The utility of intraoperative frozen section (FS) for margin assessment during radical prostatectomies (RP) remains controversial. We have noticed increased usage of FS for RP margin assessment at our institution, especially with regards to seminal vesicle (SV). Hence, this study aims to evaluate our institutional experience with this practice.

Design: The pathology LIS was used to identify RP with FS of margins (1/1/08-8/13/18). FS of lymph nodes (LN) were excluded. Clinicopathologic data was collected (FS specimen, number of FS parts, FS diagnosis (Dx), permanent Dx (PDx), Gleason score, tumor

volume, margin status, extraprostatic extension (EPE), LN status, and SV invasion). Differences between categorical values were assessed by Fisher exact test and continuous values by student T-test.

Results: 212 RP with FS for margin assessment were identified (390 individual FS). The most common FS specimen were SV (n=204, 52.3%). FS Dx included negative for carcinoma (n=352), positive for carcinoma (n=22), and atypical/indeterminate (ATYP) (n=16). FS SN, SP, PPV, and NPV are 87.5%, 99.7%, 95.5%, and 99.1%, respectively if ATYP cases are excluded and 87.1%, 98.3%, 81.8%, and 98.9%, respectively if ATYP cases are included. 10 FS Dx were discordant with PDx, for a FS accuracy rate of 97.4%. Majority of SV FS Dx were negative (98.5%,n=201/204) and SVs also accounted for the majority of FS discordances (30%,n=3) with 2 false negatives likely due to sampling. 56.3% (n=9/16) of ATYP FS Dx resulted in a negative PDx, more so in cases called “atypical, favor benign” (n=4/5). ATYP FS Dx led to additional margin excision in only 2 cases (n=2/16,12.5%) as compared to a positive Dx (n=10/22,45.5%). Cautery artifact was noted in 10 FS (2.6%) and found in 30% (n=3/10) of discordances. Finally, cases with positive FS Dx were significantly associated with adverse RP pathology but 31.9% (n=59/185) of negative FS Dx showed positive final RP margins (Table 1).

Table 1. Pathologic features of radical prostatectomies with frozen section assessment of margins.

	FS positive (n=17)	**FS negative (n=185)**	**P-value**
Positive RP margins	11	59	**0.014**
Negative RP margins	6	125	
Not documented	0	1	
EPE present	13	31	**<0.00001**
EPE absent	4	153	
Not documented	0	1	
SV invasion	7	16	**0.0009**
No SV invasion	10	169	
LN positive	4	13	**0.0383**
LN negative	12	165	
LN not excised	1	7	
Gleason score, mean	7.82 (range 6-10)	6.92 (range 6-10)	**<0.00001**
Tumor volume, mean	38.25% (range 10-85%)	23.37% (range 1-90%)	**0.0016**

Conclusions: Our experience highlights the acceptable performance of FS and shows that positive FS correlates with adverse RP pathology. However, the practice has limitations which include questionable clinical utility, as less than half of positive FS Dx resulted in additional margin excision, and negative FS not necessarily predictive of negative final RP margins. Other limitations include discordances in SV FS and cautery artifact. Additional studies to determine the exact value of FS in RP, potentially considering impact on patient outcomes is warranted.

1911 Inter- and Intra-observer Agreement of PD-L1 Scoring in Hypopharyngeal Squamous Cell Carcinoma (HSCC), Urothelial Carcinoma (UC), and Breast Carcinoma (BC)

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Disclosures: Michelle Downes: None; Elzbieta Slodkowska: None; Nora Katabi: None; Achim Jungbluth: None; Bin Xu: None

Background: Programmed death-ligand 1 (PD-L1) expression by tumor cells (TC) is a mechanism for tumor immune escape and is a target for immunotherapy in various cancers. PD-L1 status as a predictor of treatment response has led to the development of multiple

biomarkers with different reference cut-offs. We assessed the consistency of pathologists in determining PD-L1 status by evaluating both inter- and intra-observer agreement using various antibody clones and cancer types.

Design: PD-L1 expression in TC and immune cells (IC) were manually scored in 27 HSCC, 30 UC, and 30 BC using three commercial clones (SP263, SP142, 22C3) and one platform-independent test (E1L3N). For inter-observer agreement, PD-L1 status was evaluated blindly by three fellowship-trained pathologists. For intra-observer agreement, PD-L1 reading was re-evaluated following a wash-out period of > 1 month. Intraclass correlation coefficient (ICC), overall percentage agreement (OPA) and values were calculated.

Results: Using clinical algorithms established for UC and non-small cell lung carcinoma, the percentage of PD-L1 positive cases in HSCC, BC, and UC were 7-26%, 0-53%, and 7-43% respectively. Such variation in positivity was largely due to different cut-off values established for different antibody clones. Near perfect inter-observer and intra-observer agreement was achieved when only TC scoring was used in determining positivity (inter-observer: κ 0.836-1.000, OPA 96%-100%; intra-observer: κ 0.705-1.000, OPA 96%-100%), whereas a range of moderate to substantial agreement was observed when IC score was factored in (inter-observer: κ 0.474-0.808, OPA 80%-96%; intra-observer: κ 0.423-0.867, OPA 81%-96%). When evaluating the ICC of the raw percentage scoring of TC and ICs, excellent reliability was achieved in TCs using 22C3, SP263 and E1L3N clones (ICC = 0.922, 0.983, and 0.983 respectively). There was also good correlation in IC score using these three clones (ICC = 0.836, 0.851, and 0.892). The SP142 clone showed moderate correlation (ICC=0.694 and 0.689 for TC and IC).

Conclusions: The percentage of PD-L1 positive cases relies heavily on the algorithm used. Excellent inter- and intra-observer agreement can be achieved on TC scoring, whereas IC scoring appears to be associated with a higher level of subjectivity. Moreover, congruency of immunoreactivity of platform-dependent and independent anti-PD-L1 reagents is demonstrated.

1912 Utility of Flow Cytometric Ogata Score in Myelodysplastic Syndrome Diagnosis

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Disclosures: Ghazaleh Eskandari: None; Christine Roth: None

Background: Diagnosis of myelodysplastic syndrome (MDS) is challenging due to the lack of specific diagnostic markers & overlap with non-neoplastic processes. Flow cytometry has been proposed as a potential diagnostic tool and various scoring systems have been developed including the Ogata score which incorporates data that can be drawn from flow cytometric analysis using a basic screening tube. However, this scoring system has not been widely implemented and it is also unknown if some of the Ogata parameters would distinguish MDS in peripheral blood (PB) samples.The aim of this study is to evaluate the utility of the Ogata score to enable cost-effective diagnosis of MDS for our patient population in both BM and PB samples.

Design: 60 cases were evaluated by flow cytometry with a "basic blast" tube with CD34, CD19, CD13/33, and CD45. Cases included 52 bone marrow (BM) and 8 peripheral blood (PB) with following diagnoses: 7 MDS+MDS/MPN,4 non-AML myeloid neoplasm,4 lymphoid neoplasm,8 plasma cell neoplasm & 38 non-neoplastic cases.The Ogata score was calculated for BM cases using the 4 cardinal parameters: percentage of CD34+,CD13/33+ myeloblasts, percentage of CD19+ B-cell progenitors within the CD34+ compartment, CD45 expression on the myeloid progenitors relative to CD45 expression on lymphocytes, and side scatter of granulocytes relative to lymphocytes. For PB cases, the B cell progenitor parameter was not included, since B cell progenitor cells are not normally found in this type of sample. Student's t test and Chi-square analysis were used for numerical and categorical comparisons between groups, respectively.

Results: The Ogata scores for the various categories are shown in Table 1.

For BM, Ogata scores did not differ when comparing MDS+MDS/MPN (range 0-3) with non-neoplastic (range 0-3), P= 0.167; MDS+MDS/MPN with other non-AML myeloid neoplasm (range 0-2), P=0.445; MDS+ MDS/MPN with non-myeloid neoplasm (range 0-2), P=0.46. For PB, the one MDS patient showed an Ogata score of 2, as compared to an average of 0.6 for non-neoplastic (range 0-1).

For BM,there was a trend towards significance with 33% (2/6) MDS showing a high Ogata score (3 or 4) as compared to 3% (1/32) non-neoplastic cases (P=0.059).

Subgroup	Average Ogata Score BM (n) (score1-4)	Average Ogata Score PB (n) (score 1-3)
MDS+ MDS/MPN	1.66 (n=7)	2 (n=1)
Non-Neoplastic	1.12 (n=32)	0.5 (n=6)
Other Non-AML myeloid neoplasm	1 (n=3)	N/A (n=0)
Non-myeloid neoplasm	0.81 (n=11)	1 (n=1)

Conclusions: The BM Ogata score, although simple and cost-effective, does not reliably distinguish MDS from non-neoplastic cases or other non-AML myeloid neoplasms; more studies are required to further evaluate its efficacy in PB samples.

1913 Heat Artifact Simulating Tubal Intraepithelial Carcinoma: Systemic Histological Analysis of Prophylactic Fallopian Tube Resection Specimens

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Disclosures: Masaharu Fukunaga: None

Background: Prophylactic fallopian tube resection has been prevailing because the tubal fimbria is a possible primary site of extra-uterine high grade serous carcinoma in a substantial number of cases. Among pathological changes in tubular resection specimens, serous tubal intraepithelial carcinoma (STIC) is most important for patient management, and heat artifacts simulating tubular neoplasms, including STIC, should be acknowledged in order to avoid histological misdiagnosis.

Design: Eight hundred consecutive cases of prophylactic fallopian tube resection by laparoscopic excision using an electronic knife in this hospital in 2015, 2016 and 2017 were histologically examined, and the characteristic morphology and incidence of heat artifacts were analyzed. Two blocks of the distal fallopian tube were prepared for histological examination in each case.

Results: The examined cases were from patients with benign uterine and ovarian disorders, and low grade endometrial or cervical carcinomas. No gross abnormalities were noted in fallopian tubes at surgery or cutting. Heat artifacts were observed in 441 of 800 cases (55%). Marked changes were found in 98 cases (12.2%), moderate changes in 84 (10.5%) and minor changes in 258 cases (32.3%). Seven cases were initially diagnosed as STIC. No patient had STIC. Histological findings of heat artifacts included cellular pseudo-stratification, a pronounced papillary arrangement (Fig. 1) and detachment of the epithelium from the connective tissue, mainly in the fimbria. The changes measured up to 9 mm. Cytological changes included marked nuclear elongation and smudging, eosinophilic cytoplasm and obliteration of cell boundaries (Fig. 2) and lack of mitotic figures in the epithelial lining. No invasion lesion was noted. These findings mimicked adenocarcinoma in situ of the tube. Immunostaining of p53, WT1 and Ki67 was performed for 30 representative cases and there were no significant results indicating STIC. Patients with benign disorders remained asymptomatic after

Figure 1 - 1913

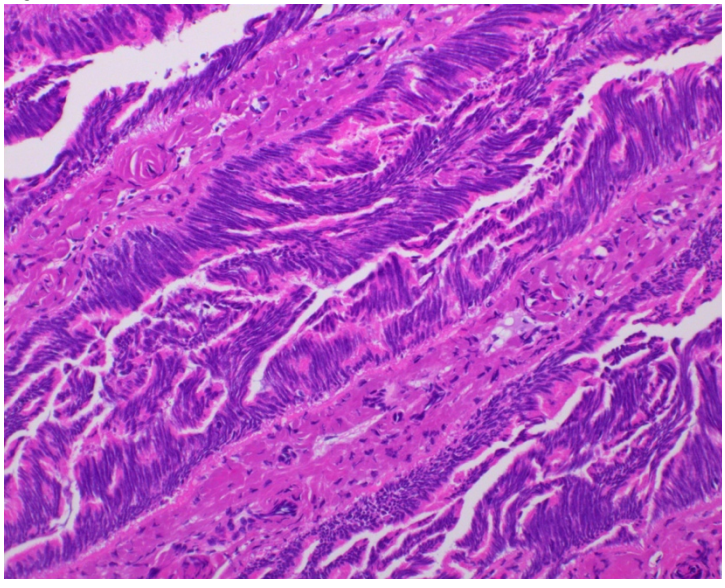
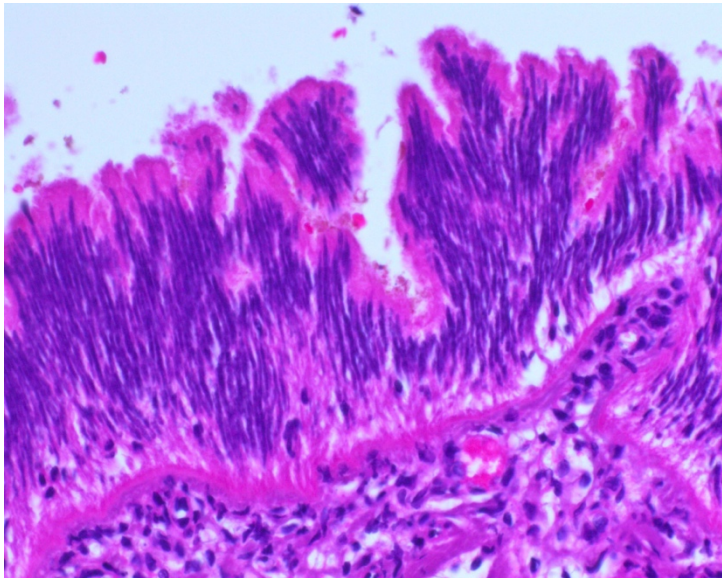


Figure 2 - 1913



Conclusions: Heat artifacts from electronic knife usage are not uncommon. The marked papillary pattern of the epithelium was the principal histological characteristic leading to confusion with STIC, likely resulting from the structural characteristics of the tubal fimbria. Heat applied to tissue can produce nuclear elongation, hyperchromatism, smudging of nuclei, eosinophilic cytoplasm, and obliteration of cell boundaries. Awareness of this potential source of diagnostic error leads to its complete avoidance.

1914 Impact of Specimen Utilization in Lung Adenocarcinomas on Adequacy for Molecular Testing: A Retrospective Study with ALK and EGFR

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Background: Molecular testing is part of the standard of care for patients diagnosed with advanced lung cancer. The majority of diagnoses are based on small specimens, which stresses the importance of careful utilization of tissue in order to preserve material for molecular testing. The 2015 World Health Organization (WHO) classification proposed guidelines to encourage appropriate use of immunohistochemistry (IHC) stains for diagnosis of lung cancer on small specimens. In this study, we assessed whether following WHO recommendations impacts the inadequacy rate of ALK and EGFR testing. We also evaluated if other parameters were associated with the rate of inadequate specimens.

Design: This retrospective cohort included 2524 patients tested for ALK by IHC and EGFR on a PCR platform in our center from 2014 to 2017. Patients had a diagnosis of lung adenocarcinoma (ADK), non-small cell lung cancer (NSCLC) favoring an ADK or NSCLC not otherwise specified. The following data were collected from medical files: age and sex, site (lung, lymph node or distance metastasis), type (cytology, biopsy or surgery) and size of specimens, medical center (community or reference hospital), number of IHC stains and specimen age. The associations between these parameters and adequacy for molecular testing were evaluated with chi square tests and multivariate logistic regression.

Results: 215 (8.5%) patients had an inadequate specimen for ALK and EGFR testing. After 2015, among TTF1 positive ADK, p40 was ordered in 29.4% of cases and additional unnecessary IHC for 69.6% of specimens. However, the number of IHC stains was not significantly associated with inadequate specimens (p=0.49), but community hospitals significantly ordered more IHC than the reference center (p<0.001). Cytology and biopsy (p<0.001) as well as small size specimens (p<0.001) were significantly associated with a higher rate of inadequate specimens. In both univariate and multivariate analysis, community hospitals (OR 2.4, p=0.036) and specimens from the primary lung tumor (OR 2.6, p=0.029) were significantly associated with an increased rate of inadequate specimens.

Conclusions: Our study showed that adequate management of small specimens for lung cancer diagnosis is deficient in a high number of cases. We found that factors such as size of specimen, cytology and biopsy specimens and pathologist experience in community hospitals have an impact on the capacity to perform EGFR and ALK testing, emphasizing the importance of education in pulmonary pathology.

1915 Should Colorectal Surgeons be Penalized for Lower Lymph Node Counts in Resection Specimens for Adenomas?

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Disclosures: Samuel Gamsky: None; Craig Cousineau: None; Mitual Amin: None

Background: The risk of colorectal adenomas harbouring an invasive carcinoma (CRC) is relatively low for lesions measuring ?9 mm in diameter but high for those measuring ?20 mm in diameter. Many clinicians consider a surgical option, especially laparoscopic colectomy for endoscopically unresectable polyps. National guidelines necessitate evaluating a minimum of 12 lymph nodes (LN) for adequate tumor staging; this is also a quality metric for annual evaluation of the surgeon. We hypothesize that colectomy for adenomas may not always yield the expected nodal counts.

Design: We selected 124 cases of colectomies for adenoma and compared findings against 475 colectomies for CRC between the years of 2012-15. We excluded cases of familial cancer syndromes, and those with greater than 4 polyps that may be suspicious for a familial cancer syndrome. We studied patient demographics, size and location of adenoma, type of surgery, and lymph node counts.

Results: The total LN count for open colectomy was 26 $\pm$ 16, whereas for laparoscopic colectomy the count was 23 $\pm$ 12; this difference was statistically significant (p=0.007). In general, the pathology assistants (PAs) retrieved a higher number of LNs (25$\pm$14) as compared to residents (19$\pm$9); this difference was statistically significant (p=<0.001).

Lesion	Adenoma	Carcinoma
No. of cases	124	475
Lymph nodes	17 (0-73)	26 (0-100)
<12 LN found	28%	4%
Colectomy size in cm	18.4 (2.3-83)	25.2 (4.5-150)
Size of tumor	3.2 (0.5-12.5)	4.79 (0.1-15.5)
Laparoscopic surgery	77%	57%
Resident Grossing	22.6%	24.4%

Conclusions: In general, at least one fourth of resections for adenomas in our series had less than 12 LNs. Colectomies for adenomas tend to yield a slightly lower average number of LNs retrieved, the cause of which is likely multifactorial with choice of laparoscopic surgery and smaller size of resected specimen being prime culprits. Although grossing performed by residents is a factor, this was likely not a major contributing factor here. Adenomas may not provide sufficient antigenic challenge for stimulation of LNs, leading to smaller size and inability to detect them as compared to CRC. These fndings indicate that lower LN counts may be inherent to the nature of the lesion, i.e. adenoma, and should not be counted as a quality metric for the surgeon. The pressure for pathologists to produce 12 lymph nodes in small size, laparoscopic specimens needs to be reassesed.

1916 Pathologist Diagnostic Rate Variation in 1,334 Transurethral Resection of Prostate Specimens Assessed Using Funnel Plots, Control Charts and an in silico Kappa

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Disclosures: Alice Graham: None; Ihab El-Shinnawy: None; Anil Kapoor: None; Michael Bonert: *Speaker*, Roche; *Major Shareholder*, Libre Pathology Ltd.

Background: Interrater variation can be assessed via the pathologist diagnostic rate (PDR) obtained from pathology reports.

Design: All in house transurethral resection of prostate specimens (TURPS) at two teaching institutions were retrieved for a seven year period (2011-17). Using custom computer code, specimens were categorized using a hierarchical free text string matching algorithm (HFTSMA), and PDRs calculated and normed by the highest volume pathologist. Gleason scores were converted to the World Health Organization grade groups (WHO1-5). PDRs and normed PDRs were plotted on funnel plots and control charts centered on the group median diagnostic rate (GMDR). In silico kappas were generated using the PDRs and either a maximal diagnostic overlap assumption (MDOA) or an ordered mutually exclusive diagnosis assumption (OMEDA). The MDOA presumed all cases for given a diagnosis (e.g. “urothelial carcinoma present”) by a pathologist will be diagnosed by all pathologists with a higher PDR.

Results: Data could be extracted for 1,781 TURPS and the HFTSMA could classify ~99% of them. A random audit of 500 specimens showed the categorized cases had approximately a 1-2% error. Fourteen pathologists read at least 40 cases and together interpreted 1,334. The median call rates/normed ranges were 3%/1-5% for WHO1, 2%/1-6% for WHO2, 1%/0-3% for WHO3, 1%/0-3% for WHO4, 3%/1-7% for WHO5, 2/0-4% for granulomas, 6/4-9% for WHO1-2, 5/4-8% for WHO3-4-5, 14/9-19% for WHO1-5, 7/1-13% for urothelial carcinoma (UCC) and 19/14-26% for all cancer. The number of statistical outliers ($p<0.05$/$p<0.001$) in relation to the GMCR were 0 ($p<0.05$) / 0 ($p<0.001$) of 14 for WHO1, 5 ($p<0.05$) / 3 ($p<0.001$) of 14 for WHO2, 2/1 of 14 for WHO3, 0/0 of 14 for WHO4, 2/0 of 14 for WHO5, 0/0 of 14 for WHO1-2, WHO3-5, WHO1-5, 2/2 of 14 for UCC, and 2/0 of 14 for all cancer. The simulated kappas for presence of prostate cancer, UCC, and all cancer, and WHO grade group were: 0.78, 0.71, 0.81, 0.55.

Conclusions: There is minimal PDR variation for prostate cancer presence on TURPS, and low (WHO1-2) and high (WHO3-5) grade cancer are likely classified reproducibly. The PDRs for UCC show moderate variation. The in silico kappas suggest good agreement; however, MDOA and OMEDA likely represent the best case scenarios for the PDRs herein. Observational data can be used to confirm good reproducibility and can identify areas for improvement.

1917 Progesterone receptor in Luminal breast cancers, which clone should be used and does it really matter?

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Disclosures: Michael Hana: None; Teddy Nagaria: None; Catherine Streutker: None; Kiran Jakate: None; Hala Faragalla: None

Background: Hormone receptor (HR) positive breast cancers (BC) are divided by gene expression analysis into two major subgroups: Luminal A (ER+ve and /or PR +ve and low proliferation) and Luminal B (ER+ve and /or PR +ve and higher proliferation). These subgroups have different prognosis and treatment implications. Luminal As have better prognosis and usually treated with endocrine therapy compared to Luminal Bs which have poorer prognosis and usually treated with endocine therapy plus adjuvant chemotherapy. Oncotype

Dx assay provides risk stratification for HR positive BC. PR is conisdered an independent prognostic factor in ER +ve BC for evaluating long term prognosis with 20% cut off suggested in some studies for predicting survival differences. The aim of this study is to evaluate PR using two clones, clone16 and 1E2 and compare them to Oncotype Dx recurrence score (RS).

Design: Formalin fixed paraffin embed tissue sections from 93 ER+ve invasive BC with Oncotype Dx results from our files are retrieved and immunostained with mouse monoclonal antibody (clone 16) and rabbit monoclonal antibody(1E2). Progesterone was read using the H-score combining the staining intensity x the percentage of the positive nuclei staining in each intensity level. Oncotype RS categories were defined as follows: low-risk (RS <18), intermediate-risk (RS =19-30) and high-risk (RS>31).

Results: The study cohort included 93 patients, stratified according to the Oncotype Dx RS into low risk (n= 56), intermediate risk (n=32) and high risk (n=9).

Lower PR values were associated with higher risk Oncotype and higher Nottingham grades with both PR clones (clone 16 and 1E2). A statistically significant difference in PR level was seen when PR in low risk and high risk categories were compared by clone (p value < 0.0001) and when PR in Nottingham grade I and Nottingham grade III were compared (p value 0.01 and 0.04 respectively), Figure 1.

A trend of lower PR value using clone 16 compared to 1E2 is seen in all cases included in the study; however this difference didn't reach statistical significance.

When Oncotype PR score was compared to clone 16 and 1E2, the r value is 0.78 for clone 16 and 0.69 for clone 1E2.

Figure 1 - 1917

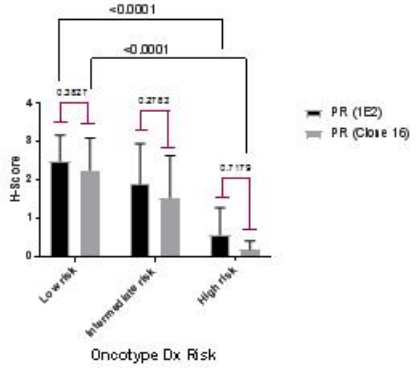
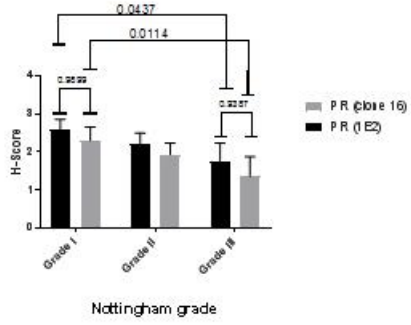


Figure 2 - 1917



Conclusions: Our results show that there is tendency with higher PR results with clone 1E2 compared to clone 16; however this difference didnt reach statistical significane and both clones show good correlation with Oncotype Dx RS. It also highlights the inverse relation between PR and Oncotype Dx RS.

1918 How our Bias of high-risk Human Papilloma Virus (hrHPV) Result Affect Pap Test (PT) Outcomes

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Disclosures: Stephanie Holdener: None; Hongxia Sun: None; Vijayalakshmi Padmanabhan: None

Background: In medicine and research, we try to be objective and avoid bias. However, as humans we can be prejudiced and change practice based on beliefs and knowledge of certain test results. This aspect of human behavior as it relates to hrHPV testing and results of the PT is not well studied in the literature. There are reports assessing PT with Negative for Intraepithelial Lesion or Malignancy (NILM) diagnosis with and without knowledge of hrHPV status. However, there is no study that has directly asked for behavior patterns of cytotechnologists and cytopathologists as it relates to bias with hrHPV test result and High Grade Squamous Intraepithelial Lesion (HSIL) PT. In this voluntary questionnaire we asked cytotechnologists and cytopathologists how they react when they are faced with certain PT diagnosis like Atypical Squamous Cells of Undetermined Significance (ASCUS) and HSIL with regards to the hrHPV test result.

Design: A voluntary survey composed of 9 questions using Survey Monkey Software was submitted to multiple institutions and cytopathology listservs. Demographic data, PT volume, HPV platforms and direct questions were asked regarding behavior with certain scenarios, i.e. final diagnosis in PT submitted as ASCUS but looks like NILM based on HPV status, diagnosis of HSIL if HPV test result is negative, etc.

Results: Of 70 respondents, the majority were in academic setting (58%; 40/ 70) and PT volumes ranged from 100-385,000. Various HPV testing platforms were used. Almost equal number of respondents did (48%) and did not (44%) look at HPV results prior to signing out the PT. Table 1 shows hypothetical scenarios of potential bias with hr HPV results.

Table 1:

If the Pap test looks like HSIL, but the HR-HPV is negative, which of the following are you likely to do? (Please select all that apply)		
Answer Choices	Responses	
Sign the Pap as HSIL and not worry about the negative HR-HPV test result	53.13%	34
Sign the Pap as HSIL after reviewing it again "just in case" you are overcalling the Pap.	40.63%	26
Call it HSIL only after showing the slide to another Pathologist and he/she agrees.	28.13%	18
Look at the history to check if there has ever been a positive HR-HPV result and sign it out has HSIL if there has been	14.06%	9
Sign the Pap as ASC-H if there are only a few HSIL/HSIL-like cells because you know the HR-HPV is negative and you don't want to take the chance	12.50%	8
Sign the Pap as ASC-H even if it obviously looks like HSIL because the negative HR-HPV bothers you	6.25%	4
Change HSIL to ASC-H if the genotype is something other than 16, 18, or 45	1.56%	1
Sign the Pap as ASC-H instead of HSIL if the patient is pregnant regardless of HR-HPV status	3.13%	2
Sign the Pap as ASC-H instead of HSIL if the patient is postmenopausal regardless of HR-HPV status	3.13%	2

Conclusions: Positive or negative hrHPV results appear to play a role in up or downgrading a PT to ASCUS or NILM, respectively. Practice varies when hrHPV is negative and the PT looks like HSIL; because of test bias, the PT may be signed out as ASC-H. The significance of bias is appreciably increasing as HPV testing is being considered as the sole or primary screening for cervical lesions. Furthermore, each institution needs to evaluate the outcomes of bias like this in terms of how it affects patient care and follow up.

1919 Synthetic Antigen Gels as Practical Controls for Standardized and Quantitative Immunohistochemistry

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Disclosures: Kathy Hotzel: None; Charles Havnar: None; Hai Ngu: *Employee*, Genentech, Inc.; *Employee*, Roche; Scot Liu: None; Frank Peale: *Employee*, Genentech; *Employee*, Roche

Background: Optimization and standardization of immunohistochemistry (IHC) protocols within and between laboratories requires reproducible positive and negative control samples. In many situations, suitable tissue or cell line controls are not available. To address this limitation, we developed a general method to incorporate peptide antigens into synthetic gels of defined composition that can serve as on-slide IHC controls.

Design: Solutions of 25% BSA in PBS containing serial dilutions of synthetic peptides encoding BCL2 aa 41-54 and MYC aa 9-24 were mixed with equal volumes of 37% formaldehyde, heated for 10 minutes at 85C, fixed overnight at room temperature and processed into paraffin blocks. Tissue microarrays (TMAs) were constructed containing duplicate 1 mm diameter cores. Four-micron TMA sections were stained with antibodies specific to the incorporated antigen (BCL2, clone 124; MYC, clone Y69) and detected with chromogenic or fluorescent assays. After digital slide scanning and quantification, parameters relevant to IHC assay performance- non-specific background, limit of detection, dynamic range, antigen concentration at half-maximum signal (ACHM) and Hill Slope - were objectively assessed.

Results: Synthetic gels containing BCL2 or MYC epitopes at concentrations from 2.5E-8M to 2.5E-4M show IHC signal intensity correlated with antigen abundance. The MYC assay shows higher sensitivity than the BCL2 assay, reflected in a 4-fold lower ACHM (MYC, 8.41E-7M vs. BCL2, 3.57E-6M) (Fig. 1). Comparison of chromogenic and fluorescent BCL2 detection methods (Fig. 2) shows: 1) higher sensitivity of DAB detection reflected by a lower ACHM (BCL2 DAB: 3.3E-6M vs. BCL2-IF: 2.2E-5M); 2) greater than 1000-fold lower non-specific signal in the IF assay (0.002% of maximum signal for BCL2-IF vs. 2.8% BCL2-DAB); 3) steeper Hill slope in the IF assay (BCL2-IF: 1.78 vs 1.12 BCL2-DAB). Negative controls containing irrelevant epitopes show negligible staining (Figs. 1 and 2).

Figure 1 - 1919

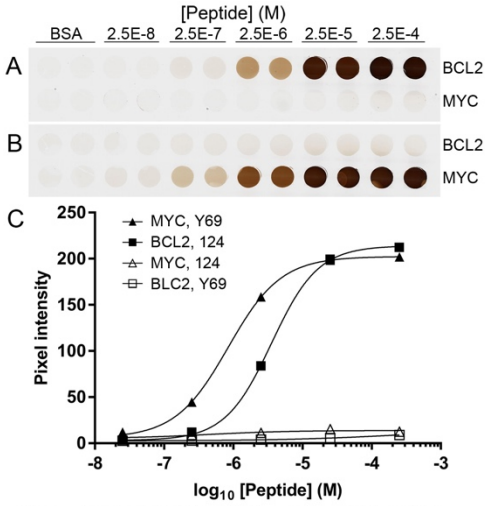

Figure 1. BCL2 and MYC IHC on TMAs containing BLC2 and MYC peptides. A) Chromogenic detection with anti-BCL2 clone 124. B) Chromogenic detection with anti-MYC clone Y69. C) Quantification of results from panel A and B.

Figure 2 - 1919

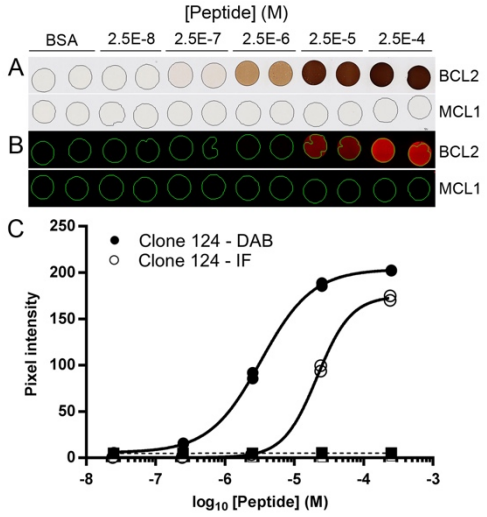

Figure 2. BCL2 IHC. A) Chromogenic detection. B) Fluorescent detection. C) Quantification of results from panel A and B. Circles: BCL2 peptide; squares: irrelevant MCL1 peptide.

Conclusions: Antigen-containing gels created using materials and methods available in any histology laboratory can be embedded and sectioned to produce uniformly stained samples. Tissue microarrays with a range of antigen concentrations can be used to objectively quantify and calibrate chromogenic and fluorescent IHC protocols. The method offers an opportunity to objectively quantify IHC staining results, and to optimize and standardize IHC protocols within and between laboratories.

1920 Simple Laboratory Utility Interventions to Reduce Inappropriate Coagulation Testing

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Disclosures: Huiya Huang: None; Ashley Cunningham: None; Alexandra Harrington: None

Background: Coagulation factor assays are commonly ordered lab tests. The naming convention in coagulation though (eg. use of Roman numerals) may cause confusion in electronic ordering systems and lead to inappropriate test orders, which can result in delayed diagnosis, additional testing and unnecessary costs. In April 2017, our lab found several inappropriate orders, when clinicians confused Factor V and X activites for Factor V Leiden and anti-Xa assay (heparin monitoring), respectively. We developed several interventions and studied pre- and post-lab utilization.

Design: Two interventions were implemented: 1) The EPIC test name was changed to Factor V and X *activity* instead of *assay* and 2) residents reviewed all Factor V and X requests. A retrospective review of orders was performed, 1-year before and after the interventions (5/2016-5/2018), to include activity assays for Factors V, X, and Factor V Leiden gene mutation test. The number of tests ordered/resulted, number of patients tested/resulted, and providers by location were summarized for each test.

Results: After the interventions, there was a 32.9% decrease in the number of orders for Factor V activity (158 to 106 orders per year, Fig. 1). The resulted tests decreased by 47.5% (139 to 73), corresponding to a $1935.78/year reduction in laboratory charges. The percentage of abnormal results increased from 43% (60/139) to 59% (43/73), indicating a better test utilization. There was a considerable decrease in orders placed from outpatient clinics after the name change (41.1% to 15.2%), while the ICU orders increased (34.2% to 63.8%, Fig. 2). For Factor V Leiden gene mutation tests, although there was a decrease in total order numbers (688 to 623), the number of abnormal results increased (82 to 89). Both Factor V activity and Factor V Leiden tests were ordered concomittantly for a small number of patients, mostly from outpatient clinics. Post-name change, these orders decreased (29 to 19). Post-resident review, the resulted double-orders decreased to 5. In addition, Factor X activity orders also decreased by 37.7% (106 to 60) after the interventions.

Figure 1 - 1920

Figure 1. Summary of Factor V Activity order numbers before and after the interventions. Left: total order numbers, total resulted orders and normal results. Right: number of patients with the order placed, numb of patients with results and patients with normal results.

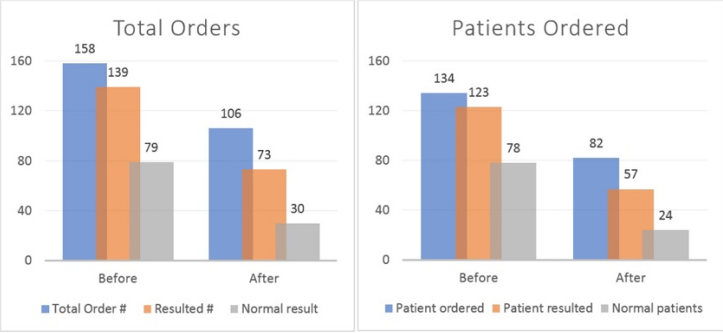
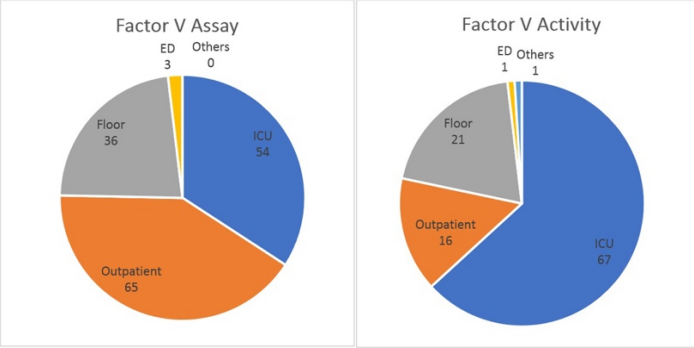


Figure 2 - 1920

Figure 2. Summary of providers for total numbers of orders before (Factor V Assay) and after (Factor V Activity) the interventions.



Conclusions: Simple interventions, such as name changes in the electronic ordering system and pathology utilization review, can reduce inappropriate coagulation test ordering and unneccessary costs and improve patient care.

1921 Pap Smear with Diagnosis of ASCUS, ASC-H, or LSIL, HPV Testing and Follow Up Biopsy in Perimenopausal and Postmenopausal Women: A Comparative Retrospective Analysis

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Disclosures: Ling Hui: None; Vijayalakshmi Padmanabhan: None; Ya Xu: None

Background: The hormone change in perimenopausal and postmenopausal patients may create cytologic atrophic atypia, which could increase the false positive diagnosis of atypical squamous cells of undetermined significance (ASCUS), atypical squamous cells, cannot exclude HSIL (high grade squamous intraepithelial lesion) (ASC-H) or low grade epithelial lesions (LSIL) in Pap smear.

Design: Cervicovaginal smear specimens in the past year with diagnosis under the category of epithelial cell abnormality including ASCUS, ASC-H, LSIL along with HPV status and subsequent cervical biopsy in women of age 50 years or older are collected for review.

Results: There are total 914 Pap cases with the diagnosis under the category of epithelial cell abnormality: 546 cases of ASCUS (59.7%; 8 cases also with atypical glandular cell, AGS), 53 cases of ASC-H (5.7%), 232 cases of LSIL (25.5%, one case also with AGS).

Among the 546 patients with Pap diagnosis of ASCUS, 88 (16.1%) patients had follow up biopsy. The patients' ages were ranging from 50 to 69 years old (average 57.9 years). The biopsies (Table 1) showed: 25 (28.4%) cases with negative findings, 12 (13.6%) cases with koilocytic changes, 33 (37.5%) cases with LSIL, 17 with HSIL (19.3%), one (1.1%) with invasive SCC. There were 78 patients positive for high risk (HR) HPV (Table 1).

Among the 52 patients with Pap diagnosis of ASC-H, 38 (73.1%) patients had follow up biopsy. The patients' ages were ranging from 50 to 72 years old (average 56.8 years). The biopsies (Table 1) showed: 12 (30.8%) cases with negative findings, 3 (7.7%) cases with koilocytic changes, 9 (23.1%) cases with LSIL, 14 (48.7%) cases with HSIL, one (2.6%) patient with invasive SCC. There were 30 patients positive for HRHPV (Table 1).

Among the 232 patients with Pap diagnosis LSIL, 111 (47.8 %) patients had follow up biopsy. The patients' ages were ranging from 50 to 69 years old (average 57.9 years). The biopsies (Table 1) showed: 21 (18.9%) cases with negative findings, 14 (12.6%) cases with koilocytic changes, 61(55%) cases with LSIL, 15 cases with HSIL (13.5%). There were 79 patients positive for HRHPV (Table 1).

Table 1. Follow up cervicovaginal biopsy diagnoses and HPV status in patients with ASCUS, ASC-H or LSIL by Pap smear

Follow up cervicovaginal biopsy diagnosis and HPV status		ASCUS	ASC-H	LSIL
Negative		25	12	21
Koilocytosis		12	3	14
LSIL		33	9	61
HSIL		17	14	15
Invasive SCC		1	1	0
HPV not tested		0	1	5
HPV negative		10	8	27
High risk HPV positive	HPV Non 16 or 18/45	59	17	59
	HPV 16	8	7	8
	HPV 18	11	6	12

Conclusions: Pap diagnosis of ASCUS, ASC-H, and LSIL has 28.4%, 30.8% and 18.9% false positive rate in perimenopausal and postmenopausal women, respectively. Atrophic atypia may contribute to these diagnosis errors. HPV types of Non 16 or 18/45 are more prevalent than HPV 16 and HPV 18 in these patients.

1922 Diagnostic Improvement and Challenges in a Cohort of Gastric Well Differentiated Neuroendocrine Tumors

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Disclosures: Zhongbo Jin: None; Xiuli Liu: None; Jinping Lai: None

Background: Gastric well differentiated neuroendocrine tumor (GWDNET) is classified on the basis of criteria that are common to all gastrointestinal and pancreatic NET. The AJCC7th published in year 2010 first introduced a system to grade the tumor based on mitotic activity and ki67 laebling index and to stage the tumor based on the size and depth of invastion. This study aims to examine the diagnostic improvement in gastric NET since the introduction of grading and staging system in year 2010.

Design: A consecutive cohort of GWDNETs were included. Time of diagnosis, ki67 testing status, and tumor size were extracted from pathology reports. Data were stratified according to the time of diagnosis (year 2000-2009 vs year 2000 or after). Medical charts of patients with ki67 tested tumors were reviewed.

Results: 118 tumors from 88 patients (52 females, 36 males, mean age of 64 (range: 36-92)) from year 2000 to 2016 were included. Ki67 testing status and tumor size recording rate were summarized in Table 1. Briefly, 45 tumors were diagnosed between year 2000-2009 and none of them was tested for Ki67. in contract, 61 of 73 tumors diagnosed in year 2010 and after were tested for Ki67($p<0.0001$). During these two periods, tumor size recording rate was 11% and 75.3% ($p<0.0001$). 34 and 24 tumors had Ki67 of <=2% and 3-20% respectively, 3 tumors had Ki67 of >20%. Tumor size was comparable between tumors with Ki67 <=2% and those with Ki67 of 3-20% (4.8±10.3 vs. 4.1±4.3 mm, $p=0.8$). 25 patients with Ki67 <20% tested tumors had adequate follow-up and none of them died of NET. 2 of 3 patients with Ki67 >20% had limited follow-up. One patient was a 58 years old woman, tumor was 10mm, body-located, and removed by endoscopic mucosal resection with negative margin. She had chronic atrophic gastritis and enterochromaffin-like (ECL) hyperplasia. The other patient was a 69 years old woman. Her tumor was 20mm, foundus-located, and removed by wedge resection. There was no evidence of atrophic gastritis or endocrine cell hyperplasia in the uninvolved fragments of gastric mucosa was present. They did well at 2 and 3 months post local resection but lost to clinical follow-up.

Table 1: Ki67 testing and tumor size recording in a cohort of 118 gastric well differentiated neuroendocrine tumors

		Diagnosed between year 2000-2009 N=45	Diagnosed between 2010 and after (N=73)	P value
Ki67	Tested, N (%)	0 (0)	61 (83.5)	<0.0001
	Not tested, N(%)	45 (100)	12 (16.5)	
Tumor size	Recorded, N (%)	5 (11)	55 (75.3)	<0.0001
	Not recorded, N (%)	40 (89)	18 (24.7)	
Ki67 distribution	<= 2%, N (%)	N/A	34 (56)	N/A
	3-20%, N (%)	N/A	24 (39)	
	>20%, N (%)	N/A	3 (5)	

Conclusions: There has been significant diagnostic improvement in gastric WDNETs since the introduction of a grading and staging system in year 2010 with increasing rates of Ki67 testing and tumor size recording. While most GWDNETs have indolent clinical course, about 5% gastric WDNETs have high ki67 and may pose diagnostic and therapeutic challenges.

1923 The Utility of Regional Affiliate Surgical Pathology Case Review: Ensuring Efficiency and Quality in the Age of Practice Expansion

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Disclosures: Steven Johnson: None; Teresa Samulski: None; Siobhan O'Connor: None; William Funkhouser: None; Scott Smith: None; Benjamin Calhoun: None

Background: Review of referral material may result in changes in diagnosis for patients; however, low rates of disagreement have been reported, often less than 10%, with even lower rates of management-altering discrepancies. As practices expand, regional affiliates are incorporated into one hospital system under a “hub and spoke” model, with review of affiliate referral material as patients are referred to the “hub.” To date, no study has analyzed the utility of pathology review specifically within a single regional health care system. We sought to characterize diagnostic discrepancies among our main campus and 9 regional affiliate hospitals.

Design: Main campus reviewed 869 cases from regional affiliates from 04/2016 to 08/2018 (excluding skin, medical renal, and hematopathology cases), of which 740 were included for review. Organ system, number of slides reviewed, and main campus ancillary studies were documented for each case. Reports were reviewed to identify discrepancies from referring diagnoses. Charts from patients with discrepancies were reviewed to determine outcomes and changes in clinical management.

Results: Cases from affiliate hospitals comprised 13% of all referral material during the study period. Gynecologic, genitourinary, and breast were the most commonly reviewed organ systems, collectively accounting for 72% and 78% of affiliate case and slide volume, respectively. Additional stains or molecular studies were performed in 10% of cases. There were 104 cases (14%) with discrepancies, all of which involved atypical or neoplastic diagnoses. Clinicians documented revised diagnoses in patient charts in 75 (72%) discrepant cases. Median time interval for case review was 2 weeks from original diagnosis, and 8 patients (8%) had already received definitive therapy based on the original diagnoses prior to referral. In total, 27 (3.6%) patients had a documented change in management based on a revised diagnosis, most frequently in gynecologic cases. Potential harm was identified in only 4 (0.5%) cases related to additional performed procedures.

Conclusions: Health care systems are under increasing pressure to deliver value to patients while using resources, including physician time, efficiently. The data from our system and others suggest that very few patients benefit from reviewing all affiliate referral material. Individual health care systems may benefit from similar analyses to determine the value of outside review for specific types of cases.

1924 Is the Incidence of High Grade Cervical Dysplasia Rising in Women, Especially in The Older Age Group? Trends in Cervical Dysplasia Over a Span of 10 Years (2001-2010). Analysis of 6819 Patients

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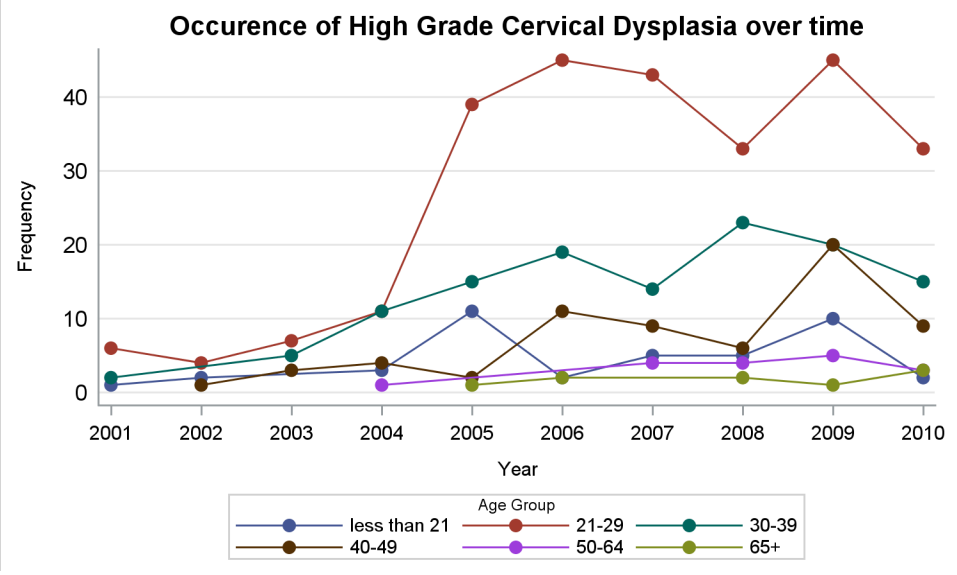
Disclosures: Guneet Kaleka: None; Victoria Lucia: None; Mitual Amin: None

Background: The U.S. Preventive Services Task Force (USPSTF) recommends against screening for cervical cancer in women older than age 65 years who have had adequate prior screening and are not otherwise at high risk for cervical cancer. The primary aim of this study is to study the temporal trends in high grade dysplasia among different age groups during the years 2001-2010.

Design: Pathology electronic records of our institute was used to conduct a retrospective chart review of biopsy results showing cervical dysplasias over a 10 year period (from 2001-2010). Biopsy confirmed cervical dysplasia was used as a surrogate marker for patients with positive PAP smears, due to the sheer magnitude of patient cases and complexity from repeat PAP smears on the same patients. Further analysis was performed for age groups by decade. We also analyzed the trends based on the incidence in each calendar year in this period.

Results: 649,316 PAP smears were examined over the same year period. A total of 6819 patients with first time diagnosis of cervical dysplasia by biopsy were identified. 6295 (92%) of these patients had LSIL and 524 (8%) had HSIL. The results demonstrate an increasing trend in biopsy diagnosed cervical dysplasias in all age groups starting 2005, with a reducing trend after 2009. The greatest incidence of biopsy diagnosed cervical dysplasia, as expected, occurs in the 21-30 age group (45%) followed by the 31-40 years (22%), 41-50 years (13%), 51-60 years (4%), 61-70 years (1%) and 71+ years (0.2%). Importantly, analysis indicates that presence of cervical dysplasia, specifically HSIL is noted for the very first time in our cohort for the women older than 65 years in 2005 and subsequently shows a slow but increasing trend. Furthermore, biopsy diagnosed cervical dysplasia is also shown to occur in the 71+ age group for the first time after 2008.

Figure 1 - 1924



Conclusions: While there were some expected findings, we were able to confirm an increasing trend starting in 2005, of a first-time, diagnoses of HSIL in the 50+ year age group in our patient population. Curiously, there was increase in HSIL diagnosis in all age groups between 2005-9, begging an epidemiologic investigation for its cause. This highlights the need to further reconsider national guidelines for cervical cancer surveillance based on regional epidemiological considerations.

1925 Clinical Relevance of Specialist Gynecologic Pathologist Second Review of Endometrial Biopsies from Referring Hospitals

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Disclosures: Elizabeth Kalife: None; Jenna Emerson: None; Cherie Paquette: None

Background: Initial diagnosis of endometrial pathology is often at community hospitals by general pathologists. As fellowship-trained gynecologic pathologists are uncommon, review by specialists mainly occurs at tertiary care settings. Endometrial biopsies are a frequent source of diagnostic disagreement, partly due to changes in diagnostic criteria (replacement of atypical hyperplasia [AH] nomenclature with endometrial intraepithelial neoplasia [EIN]), interpretation of metaplasia and fragmentation. In this study, we aim to quantify diagnostic changes and estimate clinical impact of discrepancy after specialist review of endometrial specimens.

Design: Retrospective review identified external cases containing “endometrium” or “endometrial” accessioned 10/1/2015-7/20/2017 in women >18 years. True consults were excluded. The included cases were evaluated by specialist gynecologic pathologists per standard patient referral for gynecologic oncology tumor board. A dataset compiled patient age, specimen type, original diagnosis, specialist diagnosis and follow-up pathology when available. The cases were classified by a gynecologic oncology fellow (only provided original vs. specialist diagnosis) as follows: 1) No discrepancy; 2) minor discrepancy - lacking significant clinical impact or 3) major discrepancy - likely significant impact on surgical/medical management.

Results: Of 406 cases, 190 met criteria for inclusion. 73 cases were classified as discrepant: 42 (22%) minor and 31 (16%) major. The most frequent source of major discrepancy was AH/EIN vs. endometrioid carcinoma (n=8), and changes between endometrioid carcinoma FIGO grades 2 and 3 (n=6). A less common, but notable major diagnostic change was made in 3 cases of outside FIGO 1 or FIGO1/2 endometrioid carcinoma reclassified as gland-forming high-grade serous carcinoma, all of which were confirmed on follow-up hysterectomy. The most frequent source of minor discrepancy was different histologic subtype designation of high-grade carcinoma (n=12) and changes between FIGO grades 1 and 2 (n=10).

Conclusions: Endometrial specimens can be a diagnostic challenge for any pathologist. In selected review of cases diagnosed initially by a referral hospital, 37% of diagnoses were changed upon specialist review; in 16% of cases, the change in diagnosis would likely significantly alter treatment per the opinion of a gynecologic oncologist. These results suggest meaningful clinical benefit of specialty pathologist review prior to definitive surgery.

1926 A Diagnostic Dilemma: Synchronous Vs Intrapulmonary Metastasis of Lung Adenocarcinomas

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Disclosures: Amandeep Kaur: None; Lin Liu: None; Linda M. Sabatini: None

Background: The incidence of patients with multiple lung nodules varies from 0.2% to 20% and it is increasing with advanced imaging modalities. To distinguish synchronous tumors from intrapulmonary metastasis in these patients is challenging. According to the current AJCC 8th edition, tumor staging varies between multiple synchronous lung cancers and intrapulmonary metastasis which may result in different treatment.

Design: We describe 10 patients with multiple lung adenocarcinomas with similar histology over a period of two years. Comparison by Next generation sequencing (NGS) was done for six cases.

Results: Four out of six patients had different gene mutations between their lung tumors as shown in table 1. These patients were diagnosed to have synchronous lung adenocarcinomas. Three out of these four patients were down-staged to avoid further adjuvant therapy. The fourth patient already had stage IIa tumor. The other two patients had the same gene mutations and were considered as intrapulmonary metastasis. Adjuvant therapy was given to these patients.

Table 1:

	Age/Sex	Smoker	Number of tumors	Clinical Stage	NGS result	Adjuvant therapy	Comments
1.	81/M	Yes	4	IIb	BRAF V600E in all tumors	Yes	
2.	72/M	Yes	2	IIb	KRAS G12C in both tumors	Yes	Intrapulmonary metastasis based on NGS result
3.	82/F	Yes	2	Ia	KRAS G12S and KRAS G12A	No	
4.	77/M	No	2	IIIb	EML4-ALK translocation	Yes	NGS was done on only one tumor
5.	75/F	Yes	2	Ia	TP53 R248Q and TP53 T155I	No	
6.	74/F	Yes	2	Ia	KRAS G12V and BRAF K601E	No	
7.	66/F	Yes	3	IIa	Three different KRAS G12 mutations	Yes	Adjuvant therapy for largest tumor
8.	77/M	Yes	2	IIb	Not done	No	patient has Interstitial lung disease
9.	81/M	Yes	2	IV	KRAS G12D	Yes	NGS was done on only one tumor. Positive pleural fluid
10.	86/F	Yes	3	IV	No somatic variants	Yes	Bilateral pulmonary nodules, NGS was done on only one

Conclusions: Multiple morphologically similar lung adenocarcinomas can be misdiagnosed as intrapulmonary metastasis by histology alone. NGS should be applied in these tumors to guide the right clinical management.

1927 Discordance between Intraoperative and Final Pathologic Diagnoses of Ovarian Tumors and Lessons Learned

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Disclosures: Sarah Kelting: None; Wei Cui: None; Fang Fan: None

Background: Frozen section (FS) evaluation of adnexal tumors plays an important role in patient management. Malignant and borderline epithelial tumors require staging procedures in the form of more extensive tissue sampling, whereas benign tumors do not. Therefore, false positive diagnoses may subject patients to unnecessary surgery and false negative diagnosis may cause delay in appropriate surgical staging and subject patients to more than one procedure. The goal of this study is to assess accuracy of our FS diagnosis of ovarian tumors, the cause of discordance and its impact on management.

Design: Retrospective review was performed on all salpingo-oophorectomy specimens submitted for FS between January and June 2017. Discordance rates between FS and final diagnoses (FD) were quantified, causes documented and impact on surgical management assessed. The discordance is considered major if benign (FS) versus borderline/malignant (FD) and borderline/malignant (FS) versus benign (FD), with all other discordances considered minor.

Results: A total of 87 cases were reviewed (age range: 21-82). Ten cases (11%) had discordance between FS and FD, with 2 (2%) cases having major and 8 (9%) cases having minor discordance. Seven cases were due to sampling and 3 cases were due to interpretation. Results are summarized in Table 1.

Table 1. Discordance between FS and FD of ovarian tumors

	minor discrepancy	major discrepancy	Due to sampling	due to interpretation	Impact on management
Serous tumors (n= 33)	3 (9%)	2 (6%)	4 (12%)	1 (3%)	None
Mucinous tumors (n= 15)	4 (27%)	0 (0%)	2 (13%)	2 (13%)	None
Other (n=39)	1 (3%)	0 (0%)	1 (3%)	0 (0%)	None

Conclusions: The discordance rate between FS and FD of ovarian tumors is low, with sampling accounting for the majority of discordant cases and interpretive errors a minority of cases. Regular retrospective review of discordant cases and identification of cause of discrepancy as part of the quality improvement program is critical to improve FS accuracy.

1928 Improved RNA Extraction and Sequencing from Clinical FFPE Specimens Using Mineral Oil

J. Keith Killian[1], Jeffrey Ross[1], Julia Elvin[1], Lee Albacker[1], Jo-Anne Vergilio[1], Nhu Ngo[1], Shakti Ramkissoon[2], Eric Severson[2], Amanda Hemmerich[2], Siraj Ali[3], David Fabrizio[1], Laurie Gay[3], Geneva Young[4], Dean Pavlick[1], Susan Smith[4], Jessica Mazzone[4], Eugene Stirchak[4], Christine Malboeuf[4], Mark Kennedy[4], Andrej Savol[4], Eliana Polisecki[4], Je Hie[4], Chris Wright[4], Tony Perez[4], Tim Brennan[4], Lazaro Garcia[4], Vera Banning[4], Michelle Nahas[4], Geoff Otto[4], Charlotte Brown[4]
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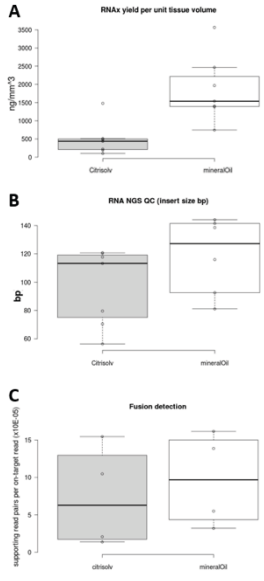
Disclosures: J. Keith Killian: *Employee*, Foundation Medicine; Julia Elvin: *Employee*, Foundation Medicine, Inc.; Nhu Ngo: *Employee*, Foundation Medicine, Inc.; Laurie Gay: *Employee*, Foundation Medicine, Inc.; Dean Pavlick: *Employee*, Foundation Medicine, Inc.; Eugene Stirchak: *Employee*, Foundation Medicine, Inc.; *Employee*, Foundation Medicine, Inc.; Andrej Savol: None; Vera Banning: *Employee*, FMI

Background: RNA extracted from FFPE specimens must satisfy yield and quality specifications for detecting and reporting gene expression profiles and fusions in NGS cancer assays. Manual steps during RNA extraction (RNAx) place specimens at risk and prevent high-throughput. Paraffin removal prior to tissue lysis using either xylene or xylene-substitutes is common, but the effects of such efforts on yield, quality and sequencing QC metrics are not well established. Herein we compare a citrisolv-based dewaxing process to direct lysis of FFPE tissue curls in the presence of mineral oil.

Design: Eight different FFPE tumor cases were used for the comparison. For citrisolv dewaxing, block sections (40 microns total) were floated on a waterbath, captured onto glass slides, oven-baked, dewaxed in citrisolv (one case/coplin jar), washed in ethanol, dried, and scraped into a tissue lysis tube. Alternatively, in the direct method, a single 20-micron FFPE curl was placed directly into a lysis tube. Lysis and RNAx were performed similarly, except that mineral oil was added to the tubes with curls to liquify the paraffin wax to enable RNAx automation. Purified RNAs were interrogated for yield, sequence QC, and presence and quality of gene fusions in 265 commonly rearranged genes.

Results: RNA yields were 3.5-fold higher with direct lysis (Figure 1a). These RNAs manifested substantially larger insert sizes in the cDNA libraries (Figure 1b), whereas one de-waxed sample failed the insert size criterion. Larger numbers of supporting read pairs for reportable gene fusion events were detected in the mineral oil method (Figure 1c). One citrisolv sample failed sequence QC for low total aligned reads, while the matched mineral oil specimen passed. There were two false-positive and two missed fusion calls in the citrisolv group, versus one false-positive and zero missed fusion calls with mineral oil.

Figure 1 - 1928



Method Requirement	mineral Oil	citrisolv
Max RNA yield	✓	
scalable	✓	
min tech time	✓	
automatable	✓	
min TAT	✓	
min lab space	✓	
no fume hood	✓	
min hazardous exposure	✓	
min hazardous waste disposal	✓	
part of kit	✓	
lower RNAse risk	✓	
RNA NGS QC	✓	
lower input tissue req.	✓	
fusion counts	✓	
sensitivity and specificity	✓	
pass/non-qualified reports	✓	

Conclusions: We identified 16 laboratory operations and sequence quality metrics that are improved by eliminating the dewaxing process, and directly lysing tissue with the addition of mineral oil (Table 1). Thus resource-intensive steps that aim to completely dewax FFPE specimens are unnecessary, and may inhibit successful RNA sequencing. De-waxing steps including oven-baking, solvent exposures, and RNAse exposures from water baths and glass- and plastic-wares are avoided with direct lysis. Going beyond RNAx yield comparisons, sequencing QC metrics provide insights into the potential mechanisms of differential performance.

1929 Is EUS-guided Fine Needle Biopsy (FNB) Independent of Fine Needle Aspiration Cytology (FNAC), Adequate for Diagnosis of Cystic Pancreatic Lesions?

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Disclosures: Do Hwan Kim: None; Liye Suo: None

Background: Due to availability new advanced needles, EUS-guided fine needle biopsy (FNB) can provide good diagnostic yield for pancreatic tumors without FNAC with or without rapid on-site evaluation (ROSE). At our institution, EUS-guided FNB are performed occasionally by gastroenterologists without ROSE and submitted in formalin for diagnostic evaluation. Occasionally, there is concurrent cytology specimen available for independent evaluation by cytopathologist. The aim of this study is to investigate the diagnostic accuracy of FNB without ROSE in pancreatic cystic lesions.

Design: Pathology database at our hospital was searched to detect surgical biopsy samples from cystic pancreatic lesions from January 2016 to August 2018. A total of 21 patients were identified. Database was further searched to see if concurrent cytology specimens were submitted independently for patients. A retrospective chart review was performed to gather information including patient's age, gender, clinical history, types of needle, gauge of needle, number of passes and final pathologic diagnoses. Diagnostic accuracy was compared between biopsy specimen and concurrent cytology specimen.

Results: Twenty patients were selected for study and had a mean age of 60 (age-range of 23-84, M:F 10:11. The final diagnosis rendered on biopsy specimens is shown in figure. Nineteen of 21 patients had concurrent cytology specimens (cytospin and cell block); while 2 patients had only biopsy specimens. Diagnostic accuracy by EUS-FNB was 95.2% (20/21). The only one false negative case was negative for malignancy, both on biopsy as well as cytology specimen, however biopsy of liver nodule showed metastatic pancreatic adenocarcinoma. Diagnostic accuracy of biopsy specimen was 85.7% (18/21) and was significantly higher (P=0.2) than that of cytology specimen (68.4%=13/19). Three types of needles were used: Cook Procore 20G, Expect Slimline 19G with Moray forceps, and Acquire 22G. Among these three types, there were no significant difference in number of passes and accuracy of diagnosis. In all 21 patients, no major complications were reported after FNB procedures.

Figure 1 - 1929

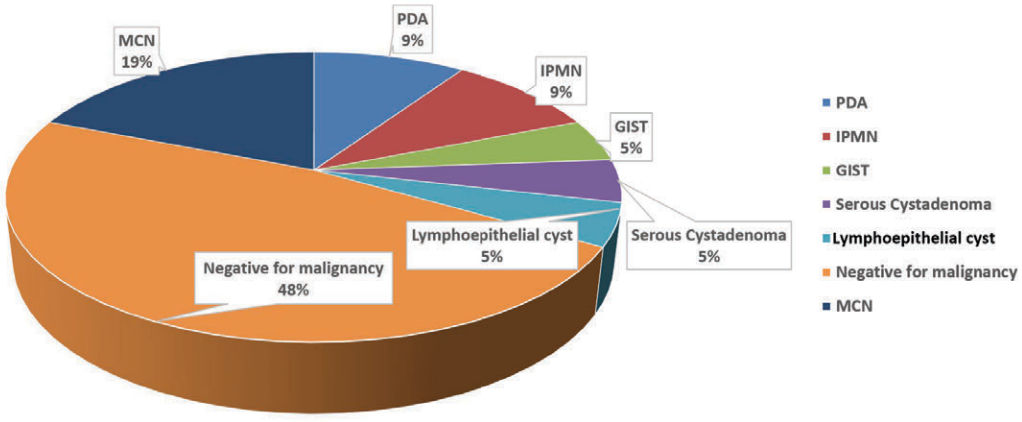

Figure. Distribution of final diagnosis in all pancreatic cystic lesions (N=21)

Conclusions: To our knowledge, this is the first study to evaluate the diagnostic accuracy of EUS-guided FNB without ROSE in cystic pancreatic lesions. EUS-guided FNB is safe and effective; and it has similar good diagnostic accuracy as cytology for pancreatic cystic lesions.

1930 Inadequate Clinical Information Supplied by Clinicians on Histopathology Request Forms: How Big and How to Improve

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Disclosures: Abdulkarim Kohail: None

Background: The importance of adequate completion of the histopathology request forms is usually underestimated by physicians which may result in diagnostic errors or delay in instituting appropriate treatment. We aimed to study the aequacy of the required information on some request forms and make a recommendation to shorten the delay, reduce errors and prevent unnecessary tests.

Design: One thousand sequential histopathology request forms were scrutinized for the completion of specific parameters that should be fulfilled in each form (1-Patient's name. 2- Other Patient's identification. 3- Patient's location (ward).4- Patient's Age. 5- Gender. 6- Source of the specimen. 7- Procedure. 8- Labeling of multiple containers. 9- Date of collection. 10- Time of collection. 11- Relevant Clinical data. 12- Previous relevant investigations. 13- Clinician's name. 14- Clinician's signature. 15- Clinician's contact details).

Hard copies of request forms received for routine histopathology laboratory investigations were manually retrieved and evaluated for the purposes of this study. Extracted data were entered into a Microsoft Excel sheet then analyzed.

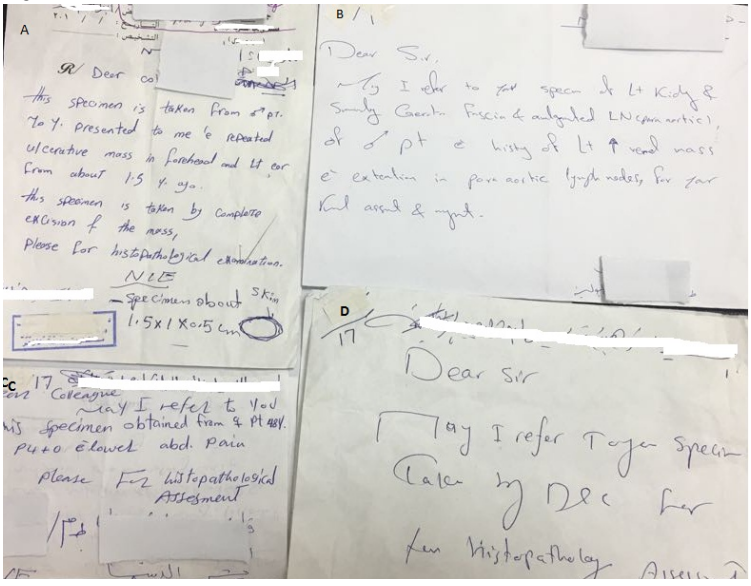
Permission was obtained from the head of histopathology department and head of scientific research ethical committee of our institute.

We keep retaining patient confidentiality where the patient names and hospital identification numbers were not collected as part of the data record sheet.

Results: Only 1.1% of forms were completely filled. 21.7% forms were not containing the patient name, whereas 16.4% forms did not show any clinical data for the patient. Completeness of the studied items on the collected RFs is shown in the table below.

Required Information	Completed	%	Not completed	%
Patient's name	567	56.7%	433 (217 not completed, 216 partially	43.3 (2.17 not completed, 21.6 partially completed)
Other Patient's identification	187	18.7%	813	81.3%
Patient's location (ward)	630	63%	370	37%
Patient's Age	873	87.3%	127	12.7%
Gender	906	90.6%	94	9.4%
Source of specimen	842	84.2%	158	15.8%
Procedure	828	82.8%	172	17.2%
Labeling of containers	832	83.2%	168	16.8%
Date of collection	303	30.3%	697	69.7%
Time of collection	13	1.3%	987	98.7%
Relevant Clinical data	836	83.6%	164	16.4%
Previous relevant investigations	470	47%	530	53%
Name of requestor	734	73.4%	266	26.6%
Signature of requestor	509	50.9%	491	49.1%
Clinician's contact details	188	18.8%	812	81.2%

Figure 1 - 1930



Conclusions: Failure to get the requisite information prevents the histopathologist to render a complete and correct diagnosis to the correct patient in the expected time. This study shows that the majority of the pathology requests sent by clinicians are inadequately completed, less than 20% of requests include a requestor contact details so that getting more information needs more time and effort. We recommend using only the designed forms by all clinicians, implementation of strict rejection criteria of specimens by pathologists and making a closer interaction between pathologists and clinicians through enforcement of medical education programs. Clinicians of all grades and specialties have to make aware of their responsibility to write down the request forms in a correct and complete manner.

1931 Efficiency of PD-L1 Testing on Non-Small Cell Lung Cancer Cytology Specimens: An Institutional Experience

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Disclosures: Oleksandr Kravtsov: None; Yuri Sheinin: None; Christopher Hartley: None; Bryan Hunt: None; Juan Felix: None; Tamar Giorgadze: None

Background: Programmed death ligand 1 (PD-L1) blockade is emerging as an effective type of lung cancer immunotherapy. Immunohistochemical assessment of PD-L1 status is necessary in metastatic non-small cell lung cancers (NSCLCs). Although cytology preparations provide valuable material for PD-L1 assessment in lung cancer, the literature on this topic is limited. Our aim was to review PD-L1 performed on cytology specimens to evaluate adequacy.

Design: A database search was performed for all cases of NSCLC that had PD-L1 immunohistochemical stain performed on cytological preparations from January 2015 to August 2018. The 22C3 clone of anti-PD-L1 antibody was used on Dako Link 48 platform by our laboratory throughout the entire testing period. 10 cytology cases were randomly selected and re-evaluated by 2 additional cytopathologists to study interobserver reproducibility. Interobserver variation was compared across tumor proportion score (TPS) categories via the Fleiss kappa statistic. The cases with <100 tumor cells were considered insufficient for PD-L1 evaluation. <1%, 1-50%, and >50% TPS cutoffs were used corresponding to negative, low positive, and high positive results respectively.

Results: 75 NSCLC cytology cases, including 47 adenocarcinomas and 29 squamous cell carcinomas were identified (see Table 1). Upon review of clinical data 27 patients were found to be deceased at the time of database search. PD-L1 stains performed on cytology preparations were adequate for evaluation in 84% of all cases. A 1% to 25% (median, 2%; mean, 4.4%) interobserver discrepancy in evaluation of percentage of PD-L1 positive cells was present in 8 of 10 cases. The interpretation of positive versus negative versus insufficient did not change in any case. The interpretation changed to low positive from high positive in one case with the reported TPS of 50% due to interobserver discrepancy of 10%. The Fleiss kappa statistic was 0.89 (almost perfect agreement), p<0.001) for all categories among the three observers. Finally, the distribution of PD-L1 results in deceased patients showed no significant differences with the overall distribution (Fisher's exact test, p=0.63).

Diagnosis	Negative, n (%)	Low positive, n (%)	High positive, n (%)	Insufficient, n (%)
Adenocarcinoma	12 (16)	7 (9)	19 (25)	9 (12)
Squamous cell carcinoma	6 (8)	8 (11)	11 (15)	3 (4)
Total	18 (24)	15 (20)	30 (40)	12 (16)

Conclusions: Our study demonstrates that cytology specimens are adequate source for PD-L1 testing, that are occasionally (16% of cases) insufficient due to low number of tumor cells. Cytology PD-L1 results showed almost perfect interobserver interpretation agreement, except for one case with PD-L1 expression close to 50% TPS cutoff.

1932 Implementation of a data-driven approach to continuous quality improvement in the grossing laboratory.

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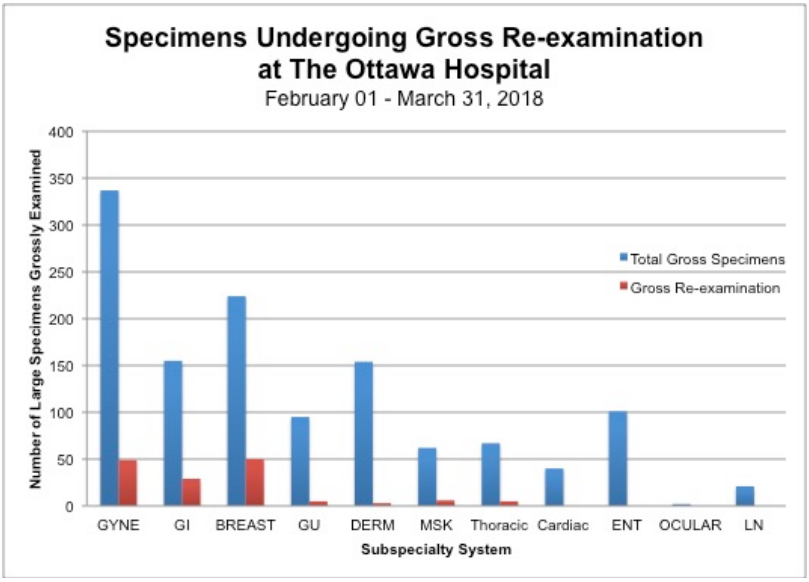
Disclosures: Anthea Lafreniere: None; Sergey Pyatibrat: None; Bibianna Purgina: None; William Parks: None; Joanne Swift: None; Janet Stinson: None; Iris Teo: None

Background: The quality of work performed in the grossing laboratory impacts pathologists' ability to formulate complete, accurate, and timely reports. Published metrics to quantify grossing quality by pathology assistants (PAs) focus largely on lymph node retrieval rates. Tissue re-submission rates have been proposed as a metric. Thus, the definition of quality strictly related to the delegated medical act of gross examination and dissection by pathology assistants is difficult to identify. A previous attempt to perform retrospective analysis of the gross specimen re-examination (GRE) at our institution revealed gaps in our ability to analyze this data. A prospective data-driven system was developed and implemented.

Design: In collaboration with LIS administrators, two pathologists and senior/charge PAs developed a new workflow and computerized order system for GREs. Within the LIS, all cases for which GRE was ordered include an area for instructions by the ordering physician. Between February 1 and March 31, 2018, a list of all GRE cases grossed by PAs originating from The Ottawa Hospital was retrieved. We reviewed the final pathology report and the entered instructions. Clinical/pathologic impact and root cause analysis codes were assigned to each case using an internal classification system, as assessed by one pathologist (IT).

Results: For this time period, out of 1258 large specimens, 140 cases fulfilled the above criteria (GRE rate of 11%). The majority of GRE specimens were breast (N=50; 36%), gynecologic (N=49; 35%), and gastrointestinal (N=29; 21%). The rate of GRE per total number of large subspecialty specimens was: gastrointestinal, 15%; breast, 22%; gynecologic, 15%; MSK, 10%, dermatologic, 2%; and thoracic, 7% (Fig. 1). Of the cases undergoing GRE, pre-analytic issues accounted for 3% (N=4) and nature of the lesion accounted for 60% (N=84). The remaining (N=44; 31%) were considered analytic phase issues, which could be further categorized into grossing error (N=2; 5%), typographical errors (N=6; 14%), insufficient gross description (N=9; 21%), and suboptimal sampling (N=26; 59%).

Figure 1 - 1932



Conclusions: Using a computerized entry system, it is possible to obtain a baseline of cases that undergo GRE. While our rate of GRE is approximately two-fold higher than literature rates, our subspecialty-specific rates were comparable. Classifying cases by clinical impact and possible causes adds value to quality improvement assessments. The utility of these findings should be studied further.

1933 Pathology Report Interpretation by Clinicians - What Do They Actually Read?

Anthea Lafreniere[1], Horia Marginean[2], Bibianna Purgina[3], Esmeralda Marginean[4], Jason Wasserman[5]
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Disclosures: Anthea Lafreniere: None; Horia Marginean: None; Bibianna Purgina: None; Esmeralda Marginean: None; Jason Wasserman: None

Background: The pathology report (PR) conveys critical information between the pathologist and clinician. Although there are mandatory fields in a PR, there is limited standardization of reporting key pathologic findings. In addition, pathologists incorporate components varyingly with uncertain utility for the clinicians. We obtained feedback regarding the clinicians' use and understanding of the PR in a tertiary center.

Design: An online survey with a link to www.mypathologyreport.ca - a pathology education resource for patients created by Canadian pathologists - was distributed to attendings and fellows/residents at The Ottawa Hospital via TOH REDCap software.

Results: 348 clinicians (82% staff; 18% trainees) from surgical, oncologic, and medical specialties were polled; 22% completed the survey. They ranked as most important PR components: diagnosis (73%), synoptic report (42%) and comments (27%), with 14% equally distributed amongst other PR components. Clinicians always/often read the synoptic report (90%), comments (88%), microscopic description (81%) and references (34%).

If the PR is unclear, 75% of clinicians contact the reporting pathologist, 51% a pathologist they know, and 48% contact the subspecialty head. Preferred methods of communication with pathologists are email (43%) and telephone (37%).

68% staff stated they provided direct training in interpretation of PRs to their trainees, but only 7% of surveyed trainees stated they received this training. 38% of staff and 21% of trainees stated that trainees complete a pathology elective rotation.

PRs are always/often explained to patients (90% staff; 71% trainees) and some patients require a copy of their PR (32% staff; 14% trainees). If a website was available to provide patients information regarding their PR, 76% of staff and 71% of trainees would recommend it.

Table 1. Summary of Survey Responses from Attendings and Trainees (N=77)

Characteristics of Survey Respondents			
Specialty	**n (%)**		
Radiation Oncology	11 (14)		
Medical Oncology	12 (16)		
Surgery	29 (38)		
Medicine	18 (23)		
Other	7 (9)		
Interpretation of the PR			
Components of PR considered relevant to clinical practice*	**Total**	**Attendings (n=63)**	**Trainees (n=14)**
Diagnosis	56 (73)	48 (76)	8 (57)
Comment	21 (27)	16 (25)	5 (36)
Microscopic description	12 (16)	8 (13)	4 (29)
Synoptic report (cancer)	32 (42)	30 (48)	2 (14)
Molecular result	11 (14)	8 (13)	3 (21)
Immunohistochemistry	11 (14)	8 (13)	3 (21)
Gross description	11 (14)	8 (13)	3 (21)
PR components read always/often			
Microscopic description	62 (81)	55 (87)	7 (50)
Comment	68 (88)	59 (94)	9 (64)
Synoptic report (cancer)	69 (90)	57 (90)	12 (86)
References	26 (34)	24 (38)	2 (14)
Management by clinicians of an unclear PR*			
Contact the reporting pathologist		47 (75)	
Contact pathologist they know		32 (51)	
Contact subspecialty lead		39 (48)	
Contact QA lead		8 (13)	
Add patient to tumor boards		19 (30)	
Request a second review		5 (8)	
None of the above/other		7 (11)	
Preferred method of communication with pathologists			
E-mail		27 (43)	
Telephone		23 (37)	
In-person meeting		9 (14)	
Tumor boards		4 (6)	
Education of Clinical Trainees in PR Interpretation			
Residents in my program/I rotate through pathology during training.		24 (38)	3 (21)
I provide to residents/I receive as a resident training on the interpretation of PRs.		43 (68)	1 (7)
Patients and PRs in the Clinical Setting			
PR report is discussed with patient	67 (87)	57 (90)	10 (71)
Patient requests PR to be explained	48 (62)	43 (68)	5 (36)
Patient requests a copy of PR	22 (29)	19 (32)	2 (14)
Would recommend a pathology education website to patients	58 (75)	48 (76)	8 (71)

*Given rank 1 or 2 out of a total of 7 by respondents, leading to a total >100%

Conclusions: Clinician responses demonstrate the practical relevance of diagnosis and synoptic report sections in PRs. Clinicians prefer to communicate with a reporting pathologist or a pathologist they know personally via email. Interestingly, while clinicians believe they provide PR interpretation teaching to trainees, most trainees do not believe they receive this training, despite a majority discussing PRs with patients. Creating more practical PRs and providing tools for their interpretation by clinicians, residents, and patients, such as www.mypathologyreport.ca, have the potential to create a meaningful clinical impact.

1934 Anti-CD38 Treated Plasma Cell Myeloma Causing Laboratory Interferences: A Quality Assurance Study Identifying Pitfalls for the Pathologist

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Disclosures: Erin Langford: None; Danyel Tacker: None; Aaron Shmookler: None; Jeffrey Vos: None

Background: The use of anti-CD38 therapy to treat refractory plasma cell myeloma (PCM) has dramatically increased over time. These drugs are IgG1-kappa monoclonal antibodies targeting CD38 antigens overexpressed on plasma cells. Assessing for residual disease in patients on these therapies poses unique challenges in the laboratory due to drug interference. In our study, we identified interfering effects of anti-CD38 therapy in a number of routine tests used to monitor refractory PCM.

Design: A single institutional retrospective review was performed. The electronic medical record was searched for refractory PCM patients on anti-CD38 therapy who had available clinicopathologic materials between January 2017 to August 2018. Clinical history and lab findings were reviewed, including flow cytometry (FC), serum electrophoresis (ELP), and blood type/screen (TS) results. Specifically, FC studies (Becton Dickinson) used to detect residual monoclonal plasma cells in bone marrow, ELP (Sebia, Capillarys) used to monitor M-protein levels in the serum, and TS (NEO, Immucor) for transfusion requirements, were analyzed for interferences.

Results: Of 36 patients who met inclusion criteria, 7 had bone marrow biopsies with residual disease but FC showed aberrant absent CD38 expression in 43% (3/7); average length of therapy (LOT) prior to artifact detection was 7 months. Erroneous ELP results were intermittently seen in 92% (33/36) showing a small IgG-kappa monoclonal immunoglobulin in the gamma region; average LOT prior to detection was 2 months. ELP interpretation proved difficult in 42% (15/36) due to co-migration of the therapy-related clone and the patient's endogenous M-spike. TS performed on 20 patients showed 55% (11/20) had positive antibody screening due to panagglutinins; average LOT prior to detection was 3 months.

Refractory Plasma Cell Myeloma Patients Treated with Anti-CD38 Therapy			
Lab tests performed in refractory PCM patients	**FC**	**ELP**	**TS**
Total number of study patients tested	7	36	20
Erroneous results due to drug artifact	3 (43%)	33 (92%)	11 (55%)
Average LOT prior to artifact detection (months)	7	2	3

Conclusions: Anti-CD38 therapy frequently interferes with lab tests used in monitoring PCM. FC detection of plasma cells may result in a false negative study in refractory PCM. ELP interpretation may be difficult due to a therapy-related clone precluding recognition of the endogenous M-spike. Finally, underlying alloantibodies must be detected with panagglutination, causing delays in issuing blood. Interestingly, spurious FC results appear to require slightly longer duration of therapy as compared to effects seen in ELP and TS. Pathologists diagnosing refractory PCM in patients treated with anti-CD38 therapy need to be aware of potential erroneous results secondary to drug interference.

1935 Concordance Between Immunohistochemistry and Next Generation Sequencing in Testing Patients for Hereditary Nonpolyposis Colorectal Cancer

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Disclosures: Lauren Lawrence: None; Teri Longacre: None; Atif Saleem: None; Christian Kunder: None

Background: Lynch syndrome is an autosomal dominant disorder which is the most common cause of inherited colorectal cancer and also portends an increased risk for endometrial, ovarian, stomach, small bowel and other malignancies. Universal testing of colorectal cancers has been shown to improve sensitivity for the identification of Lynch syndrome with the most prevalent methods for the evaluation of microsatellite instability by polymerase chain reaction (PCR) and/or immunohistochemistry. Next generation sequencing of tumors has become a novel advancement in genetic testing and we investigated it's concordance with immunohistochemistry in the evaluation for Lynch syndrome.

Design: Patients diagnosed with colorectal carcinomas for which immunohistochemistry for the evaluation of mismatch protein expression had been performed and who had next generation sequencing completed on the same tumor tissue were retrospectively analyzed from July 2016 to December 2017. Correlation was assessed between immunohistochemistry and next generation sequencing with definitions including concordance, discordance or indeterminate.

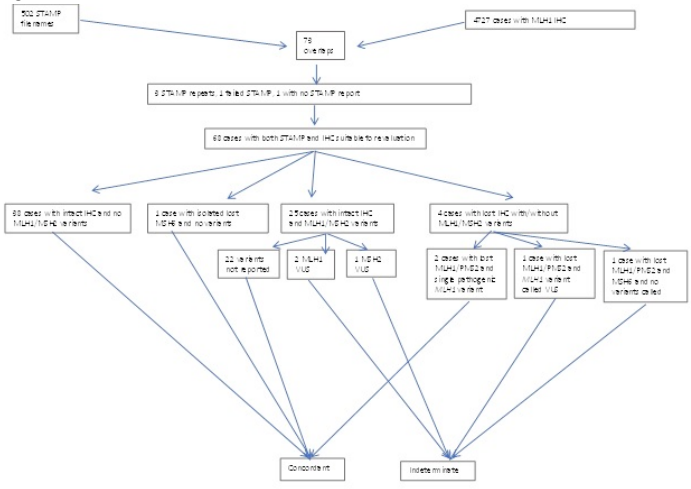
Results: Excluding indeterminate cases, 100% of cases (63/63) showed concordance in comparing immunohistochemistry to next generation sequencing results for mismatch repair protein evaluation. By including indeterminate cases (7.3% of all cases (5/68)), 92.6% of cases (63/68) showed concordance. Of the indeterminate cases, one case with loss of MLH1, PMS2 and MSH6 expression exhibited MLH1 promoter hypermethylation. The remaining indeterminate cases showed variants of unknown significance in MLH1 or MSH2 by next generation sequencing.

Table 1: Criteria that define concordant, discordant or indeterminate status by IHC and STAMP

Concordant	Discordant	Indeterminate
1. Intact expression of MMR by IHC and no variants in *MLH1/MSH2* by STAMP or 2. Loss of expression of MMR by IHC (MLH1/ PMS2) and mono- or bi-allelic *MLH1* pathogenic variants or 3. Loss of expression of MMR by IHC (MSH2/ MSH6) and bi-allelic *MSH2* pathogenic variants	1. Intact expression of MMR by IHC with biallelic *MLH1* or *MSH2* pathogenic variants on STAMP or 2. Intact expression of MMR by IHC with single allele *MLH1* or *MSH2* pathogenic variants on STAMP plus additional evidence of MMR-D	1. Intact expression of MMR by IHC and VUS on STAMP or 1. Loss of expression of MMR by IHC (MLH1/PMS2) and no *MLH1* variants (putative biallelic promoter methylation)

MMR: mismatch repair, IHC: immunohistochemistry, MLH1: MutL Homolog 1

Figure 1 - 1935



Conclusions: We evaluated the concordance between immunohistochemistry and next generation sequencing in the evaluation of mismatch repair protein status for Lynch syndrome testing to be 93%. Given this high concordance, we recommend immunohistochemistry as an initial screening test in colorectal tumors to screen for Lynch syndrome.

1936 Misdiagnosis of Metastatic Hormone Receptor Positive Breast Cancer: Clinical Consequences and Root Cause Analysis of the Source of Errors

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Disclosures: Susan Lester: None; Lei Li: None; Xiaohua Qian: None; Lynette Sholl: *Consultant*, Foghorn Therapeutics; *Speaker*, Astra Zeneca Pharmaceuticals; *Advisory Board Member*, Loxo Oncology

Background: It is important to correctly identify metastatic hormone receptor (HR) positive breast cancer as palliative endocrine therapy can lead to long-term survival. Failure to recognize these cancers could lead to inappropriate management and significant clinical consequences. Information concerning this type of error is very limited, as only 5 patients have been reported in a single study. Root cause analysis of the reasons for misdiagnosis in this setting could identify methods to improve patient care.

Design: Cases were collected over a 16-year period. Clinical records, pathology reports, and slides were reviewed to determine contributory factors, mechanism of discovery, and clinical consequences.

Results: Seven women with HR positive breast cancer underwent biopsies of metastases to bone (n=4), lung, cervical lymph node, and mediastinum. A history of breast cancer was provided in only 2 of 4 cases; in 3 cases the cancer was clinically occult. Incorrect diagnoses were neuroendocrine or small cell cancer (NEC; n=5), gastric signet ring cell cancer, and thymic cancer. In 4 cases, immunohistochemical studies (IHC) for chromogranin and/or synaptophysin were positive. No breast markers were performed in 5 cases, were misinterpreted in

1 case, and were negative in 1 case due to both HR positive and negative metastases. The pathologists, all from academic medical centers, had 5 to 34 years of experience. The errors were discovered when the cases were reviewed at another institution (n=4) or when a subsequent biopsy showed metastatic breast cancer (n=3). The interval to correct diagnosis ranged from 49 days to 2 years. Five patients underwent unnecessary biopsies, 5 inappropriate chemotherapy with significant side effects, and 4 had a prolonged delay in the initiation of endocrine therapy.

Figure 1 - 1936

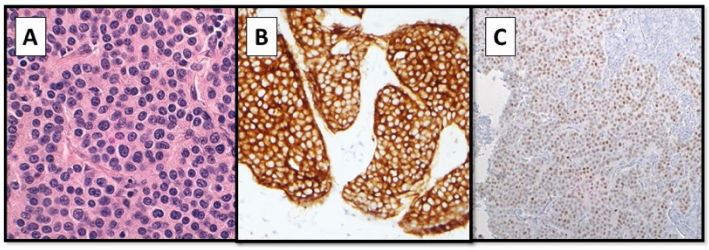

Figure 1. A. This cervical lymph node metastasis was diagnosed as neuroendocrine cancer due to the nested pattern with uniform round nuclei. The patient had a history of breast cancer. B. The cancer was immunoreactive for synaptophysin (shown) and chromogranin. She was treated with chemotherapy. C. Two years later the patient was diagnosed with recurrent breast cancer. Additional studies on the cervical node metastasis showed immunoreactivity for estrogen receptor (shown), progesterone receptor, GATA3, GCDFP-15, and mammaglobin, demonstrating that the patient only had breast cancer and not neuroendocrine cancer.

Conclusions: The majority of errors occurred due to metastatic breast cancer being mistaken for NEC. Strikingly, the 5 previously reported cases were also misdiagnosed as NEC. Other contributing factors were metastasis occurring in the setting of an occult primary and failure of clinicians to provide a history of breast cancer. Patients experienced considerable morbidity and delay in appropriate treatment. Breast cancer should always be included in the differential diagnosis of metastatic carcinoma in women, regardless of whether or not there is a prior history of breast cancer. Pathologists need to be aware that resemblance to NEC and/or expression of neuroendocrine markers does not exclude this diagnosis.

1937 Sectioning Automation to Improve Quality and Decrease Costs for a High-Throughput Slide Scanning Facility

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Disclosures: Mark Lloyd: *Employee*, Inspirata, Inc; Tina Shulgay: None; Carla Curtiss: None; Greg Krueger: *Employee*, Aquaro Histology Tarren Gill: *Employee*, Inspirata; Anil Parwani: None

Background: The sectioning process has a great impact on the digitization process. By improving the consistency of histology, the quality of whole slide imaging increases while costs of such projects decrease. The Aquaro ASM automated section mounting system standardizes the sectioning process. This process was studied in the context of the world's largest throughput slide scanning facility to understand the impacts of sectioning standardization over hundreds of thousands of digital pathology images.

Design: Our group studied the impact of slide contaminants on the digitization process and extrapolated our findings to calculate the expected impact on a facility creating over 750,000 images each calendar year.

Results: 65 slides were prepared with one or two sections per slide utilizing manual section transfer and mounting and the Aquaro ASM. Slides were scanned, and file size and scan time were noted. Utilizing the Aquaro ASM yielded a reduction in file size of 5.92% for slides that were mounted in water spiked with floaters, though results were not statistically significant.

Overall, the file sizes for slides generated by the ASM were reduced by 5.92%. When scaled up to the volume of slides that can be scanned and stored in a laboratory, this reduction in file size can mean significant cost savings.

In our facility, we scan and store up to 1 PB of WSI data annually. Therefore, a 5.92% file size savings represents nearly 60TB. At a fully loaded rate of $2.95 per GB, a laboratory could save $175,000 each year that it continues to grow its digital repository.

Conclusions: The experiments described here demonstrated a potential for utilizing the Aquaro ASM to prepare slides that yield a smaller file size when scanned for whole slide imaging, yielding lower file storage costs. Larger sample sizes need to be collected to determine whether this trend is statistically significant.

The Aquaro ASM also improves the consistency of slides by providing more consistent section placement and reducing the occurrence of contaminants like floaters ending up on slides. Both of these features are important for producing high-quality slides but become more important when digitally scanning slides where tissue must be placed within specific boundaries, and contaminants hold the potential for increasing file size and scan times.

1938 Establishment of Normal Weights for Products of Conception

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Disclosures: David Loeffler: None; Manmeet Singh: None; John Groth: None

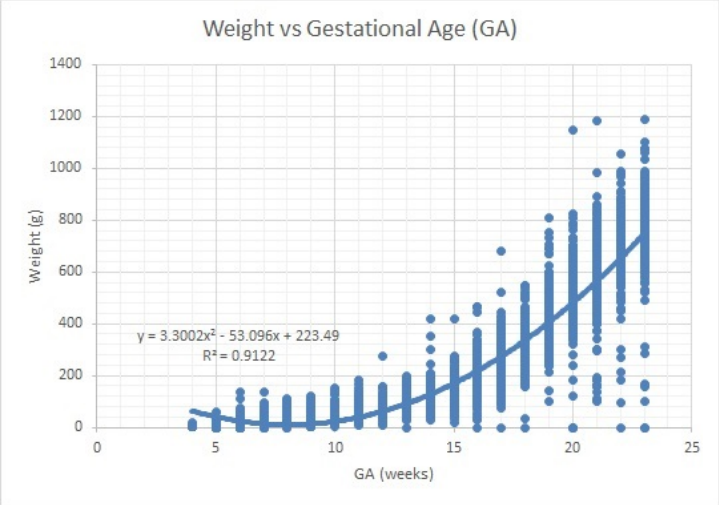
Background: Our institution has recently taken on a contract to receive and process products of conception (POC) specimens. One of the most common initial clarification requests we have received from our clients is to double-check the weight of the specimen. The client was worried that some POC material had be retained and therefore posed a risk to the patient for infection, sepsis, and death. To our knowledge there is limited analysis of normal weights of POC specimens published in the literature and therefore, we aim to establish a mean, 10th percentile, and 90th percentile weight for normal POC specimens based on gestational age.

Design: Using Cerner PathNet® Pathology Case Retrieval we retrieved information from all of the induced abortion cases from the clients during October 1, 2016 until June 30, 2018 (n=13892). Then using Microsoft Excel® we searched the clinical information and gross descriptions to find the gestational age and weight of specimen. We extracted that data and categorized it into gestational age, rounding down to nearest week. Then we found the count, minimum, maximum, average weight, standard deviation, 10th percentile weight, 90th percentile weight, and coefficient of variation for each week gestational age. We omitted twin gestation, gestational sacs without fetuses, unknown gestational ages, missing data, or obviously incorrect gestational ages totaling 750 cases (5% of total cases).

Results: Overall we were able to retrieve and analyze the gestational age and weight of 13142 POC specimens over the span of 44 months at our institution. The gestational ages ranged from 4 week to 23 weeks with specimens of 7 weeks gestational age being most numerous (n=2070). Due to low numbers of specimens with gestational age lower than 4 weeks, we excluded them from the table. The table below shows the results for specimens with gestational ages from 4 weeks to 23 weeks with weights that increase in an exponential fashion, as seen in the figure.

GA (weeks)	N	SD	CV (%)	10th Percentile Weight (g)	Mean Weight (g)	90th Percentile Weight (g)
4	11	5	100	3	5	17
5	568	6	76	7	8	52
6	1939	9	69	14	14	121
7	2070	11	59	15	19	123
8	1414	13	56	13	23	100
9	1184	15	48	17	32	111
10	826	18	43	18	41	139
11	781	22	41	23	52	163
12	690	24	39	37	63	250
13	693	26	34	43	77	183
14	399	39	37	65	107	379
15	519	38	29	58	132	379
16	276	66	36	71	186	423
17	299	73	29	137	249	619
18	268	82	26	87	313	498
19	279	95	23	173	423	737
20	279	106	21	224	514	1044
21	249	143	25	208	576	1076
22	226	129	19	191	684	962
23	172	155	20	207	758	1079
Total	13142					

Figure 1 - 1938



Conclusions: We have used 13142 specimens to establish normal weights for POC specimens based on gestational age from 4 weeks to 23 weeks. This data can be used to assess POC specimens in the future for other relationships or clinical outcomes.

1939 Impact of Electronic Synoptic Reporting Implementation on Turnaround Time of Surgical Pathology Reports

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Disclosures: Emilio Madrigal: None; Vania Nose: None; Veronica Klepeis: None

Background: Turnaround time (TAT) of surgical pathology reports is considered an important quality indicator in anatomic pathology (AP). Although the benefits of standardized synoptic reporting are well documented, the impact on TAT remains unsettled. We set out to compare variations in TAT across multiple AP subspecialties, focusing on a transition period between the use of an in-house solution for synoptic reporting involving hand-annotated printed sheets processed by a transcriptionist and the commercially available mTuitive xPert electronic synoptic reporting software.

Design: The AP laboratory information systems (LIS), Sunquest CoPath Plus, was queried for synoptic reports encompassing six malignant specimen types (breast, endometrium, kidney, skin, soft tissue, and thyroid) signed out by 15 subspecialty pathologists. To control for laboratory variables, non-synoptic reports for bone marrow, medical renal, and valve specimens were also analyzed. The study period spanned six years (2012 – 2017, inclusive), divided into *pre-* (2.5 years), *transition* (1 year; standalone xPert), and *post-* implementation (2.5 years; xPert interfaced with the AP-LIS) of electronic synoptic reporting. A one-way analysis of variance with the Tukey honest significant difference test was used for comparisons, with $P \leq .05$ considered significant.

Results: A total of 10,009 reports were analyzed. Surgical pathology synoptic reporting in the transition and post-implementation periods demonstrated non-significant decreases and increases in TAT ranging from 8.7% to 10.8%, respectively (Table). Cases without synoptic reports signed out during the same time period did not show any significant change in TAT.

Report	Specimen type (N=pathologists)	TAT (days) (N=reports)		
		Pre (Jan 2012 – May 2014)	Transition (Jun 2014 – May 2015)	Post (Jun 2015 – Dec 2017)
Synoptic	Breast (N=5)	6.75 ±3.3 (N=1264)	6.35 ±3.5 (N=502)	6.84 ±3.7 (N=1316)
	Endometrium* (N=2)	6.15 ±2.1 (N=104)	-	6.77 ±1.6 (N=96)
	Kidney* (N=3)	5.7 ±2.1 (N=103)	-	5.21 ±1.6 (N=156)
	Skin (N=2)	6.29 ±3.1 (N=230)	6.01 ±2.5 (N=103)	6.21 ±2.9 (N=271)
	Soft tissue (N=2)	9.4 ±4.7 (N=210)	10.17 ±4.8 (N=78)	9.31 ±5.3 (N=209)
	Thyroid (N=3)	4.76 ±2.1 (N=467)	4.68 ±1.8 (N=161)	5.27 ±2.0 (N=295)
Non-synoptic	Bone marrow (N=1)	4.44 ±2.0 (N=721)	4.54 ±1.8 (N=395)	4.65 ±1.8 (N=973)
	Medical renal (N=1)	5.01 ±2.5 (N=205)	4.84 ±1.8 (N113)	5.21 ±2.1 (N=308)
	Valve (N=1)	5.17 ±2.4 (N=714)	4.59 ±2.1 (N=236)	5.20 ±2.2 (N=779)

*Malignant endometrial and kidney synoptic reporting began in quarter 3 of 2013.

Conclusions: As pathology reporting evolves from traditional narrative reports to structured synoptic records, benefits such as improved consistency of data fields, reduction in cost and errors associated with transcription, compliance with reporting standards, and strong physician satisfaction are well recognized. In addition, electronic synoptic reporting provides the added benefit of structured data capture. This study demonstrates evidence to suggest that the AP laboratory can leverage the advantages of synoptic reporting and structured data capture at no significant cost to TAT.

1940 Risk Stratification of HIV Infection for Patients Needing Molecular Confirmation with the Abbott 4th Generation Architect System

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Disclosures: Renuka Malenie: None; Richard Baltaro: None; Heather Melbourne: None; Francisco Garcia: None; Edwin Gould: None; Andrew Renshaw: None

Background: Some patients need their 4th generation Human Immunodeficiency Virus (HIV) testing results confirmed with molecular testing which may not be immediately available. Further risk stratification of these patients pending the results of molecular testing may be of value not only for patient counseling but also for treatment of women in labor.

Design: To improve risk stratification using additional laboratory data, we sought to determine if more accurate risk stratification could be achieved in patients needing confirmation of their HIV result using both the signal cut off ratio (S/CO) from the Architect machine and additional laboratory information, such as the patient's white blood cell (WBC) count. The risk of a positive molecular test result for patients with a result needing molecular confirmation on a 4th generation HIV testing algorithm (Abbott Architect, Multispot/Geenius confirmatory

test) was stratified based on the patient's WBC count and the magnitude of Architect result, S/CO. Statistical analysis was performed using a Chi square test.

Results: A total of 61,666 patients were tested, in two large medical centers, with 658 (1.1%) positive results and 76 (0.12%) patients needing molecular confirmation. Patients with an S/CO of <5 or an S/CO of 5-100 with a WBC ≥ 6.5 cells/l had a significantly lower risk of a positive molecular HIV test (0/48, 0%) than patients with an S/CO 5-100 with a WBC < 6.0 cells/l (5/9, 56%, p <.001) or an S/CO >100 (2/2, 100%, p <.001). Pregnant women had a significantly lower rate of positive test results (24/6924, 0.4%) than non-pregnant patients (634/55856, 1.1%, p < 0.001). All 12 pregnant women needing molecular confirmation had negative Nucleic Acid Test (NAT) results.

Conclusions: Patients who need their HIV results confirmed with molecular testing using a 4th generation algorithm that includes the Abbott Architect System can be further stratified into low, intermediate, and high risk groups based on additional laboratory information pending the results of molecular testing. This information may be of value for patient counseling and treatment of women in labor.

1941 Impact of Timing on Nucleic Acid Integrity and Tumor Organoid Development in a Next-Generation Rapid Autopsy Program

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Disclosures: Maria Mastropaolo: None; Erika Hissong: None; Kevin Delfino: None; Shaham Beg: None; Aram Vosoughi: None; Terra McNary: None; Rohan Bareja: None; Anastasia Tsomides: None; Cynthia Cheung: None; Yelena Churakova: None; Rema Rao: None; Brian Robinson: None; Andrea Sboner: None; Steven Salvatore: None; Olivier Elemento: None; Juan Miguel Mosquera: None; David Pisapia: None

Background: Our rapid autopsy program offers a full complement of platforms regardless of tumor type, age, and time of death, that includes whole exome sequencing, RNA-seq, tumor organoid development, and xenograft modeling. Performing autopsies within a short time interval is thought to reduce nucleic acid degradation and increase the likelihood of obtaining viable tumor cultures for *ex vivo* assays. The aim of this study was to correlate quality control (QC) analysis of DNA and RNA integrity and success of organoid development with post mortem interval (PMI).

Design: We analyzed data on 20 rapid autopsies including carcinomas from prostate (n=6), bladder (n=3), kidney (n=3), ovary (n=1) colon (n=1), lung (n=1), brain tumors (n=4) and melanoma (n=1). After H&E evaluation of frozen samples, DNA and RNA were extracted for QC analysis and sequencing. Samples were also harvested for tumor organoids; QC included Diff-Quick smear of submitted tissues. PMI was compared with QC metrics of nucleic acids as well as organoid growth evaluation.

Results: PMI ranged from 0.5 hours to 18 hours (mean = 5.6 hours). WES data was available in 19/20 cases and RNA-seq data in 18/20 cases. Mean RNA integrity number (RIN) was 4.7 (range 2.7 to 6.9) (n=20); mean DNA integrity number (DIN) was 7.8 (range 6.7 to 8.9) (n=15). Linear regression analysis was performed to compare PMI to these QC metrics (**Figure 1**) and no correlation was identified. Expression analysis and gene fusion detection were successful with RIN values ≥4. Organoid growth was successful in 5 of 8 attempted cases demonstrated with no correlation detected between growth success and PMI.

Figure 1 - 1941

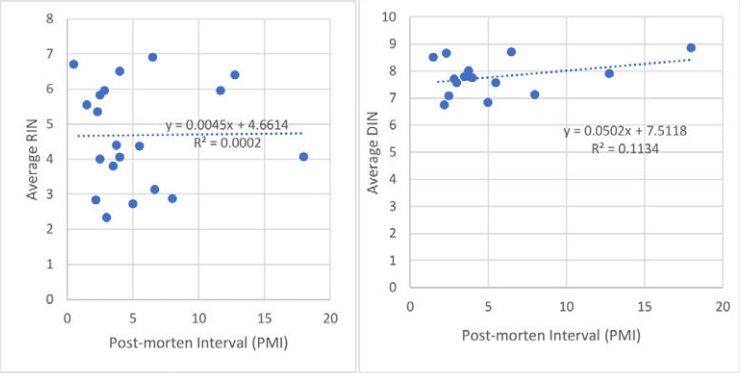

Figure 1: Linear regression analysis comparing post-mortem interval (PMI) (hours) to (left) RNA integrity number (RIN) (p=0.53) and (right) DNA integrity number (DIN) (p=0.0548).

Conclusions: PMI did not correlate with DNA and RNA integrity values. Interpretable WES and RNA-seq data was obtained with PMI up to 18 hours (max in this cohort) and organoid development was successful with a PMI of 10 hours. This study demonstrates that factors other than PMI should be investigated as critical drivers of autopsy tissue QC metric variance, such as pre-mortem comorbidities, the anatomic origin of tissue samples, and specimen handling. Moreover, the resources necessary to facilitate short PMI may not necessarily provide a justifiable cost to benefit ratio in a programmatic setting.

1942 Comparison of Cytological and Histological Specimens for PDL1 Testing in Non-Small Cell Lung Cancers

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Disclosures: Laura McKenna: None; Sean Hynes: *Consultant*, Merck MSD Ireland; *Consultant*, Roche, Ireland; Silvie Blazkova: None; Sine Phelan: None

Background: Lung cancer remains a leading cause of mortality worldwide. Despite diagnostic improvements it continues to present at an advanced stage. Immunotherapy targeting the PDL1/PD1 pathway has emerged recently as a treatment for advanced non small cell lung carcinomas. PDL1 expression, as evaluated by immunohistochemistry(IHC) in tumour cells can predict the response of disease to PDL1/PD 1 inhibitors. Although variation in PDL1 expression in primary and metastatic disease has been reported, testing by IHC has been shown to be effective in both histological specimens and on formalin fixed cytology cell blocks. In some cases where a delay occurs patients may be started on chemotherapy affecting subsequent immunotherapy. In our institution, a tertiary referral centre in Ireland, testing for PDL1 expression by IHC has recently been introduced. A significant proportion of this testing involves cytology specimens. Given the potential for rapid disease progression and the lower turnaround time with cytology we aimed to confirm that our testing on cytological specimens was robust and comparable to histological testing.

Design: A database search of all PDL1 IHC tests was undertaken with a subsequent review of the reports of PDL1 testing in lung carcinomas. Cases were dichotomised into two groups; over-expressors had at ?50% tumour cell positivity for PDL1 and low/non-expressors had <50% tumour cell positivity.

Results: In 4 months of PDL1 testing, 67 cases were successfully tested. Testing was successful on 26 cytology samples and 32 histology samples, with 9 cases from affiliated hospitals. Of the successful tests, 46% of the cytology group and 41% of the histology group were over-expressors. For adenocarcinomas, 47% of both the cytology and histology groups were found to be over-expressors. For squamous cell carcinomas similar results were seen with overexpression in 29% of the cytology group and 33% of the histology group. Interestingly in one case there was a change in PDL1 status when cytology from the metastasis was tested compared to the primary.

Conclusions: In our institution, we demonstrated comparable results between histology and cytology samples, suggesting robust results in the cytology samples. Given that cytological samples can be more easily obtained from metastatic sites and given the more rapid turnaround time, we favour testing formalin-fixed cytology samples when available to facilitate effective and rapid treatment of patients.

1943 Evaluation of the Impact of the Updated ASCO/CAP 2018 HER2 Guidelines in Invasive Breast Carcinoma

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Disclosures: Chelsea Mehr: None; Laura Collins: None; Liza Quintana: None

Background: In 2018, the ASCO/CAP guidelines for HER2 testing in invasive breast carcinoma were updated following review by an expert panel. A notable area of change involved HER2 FISH cases with contradicting HER2 ratio and copy number results (non-classical cases). These cases have been designated Group 2 (HER2/CEP17 ratio >/= 2.0, Average HER2 copy number <4.0), Group 3 (HER2/CEP17 ratio < 2.0, Average HER2 copy number >/= 6.0) and Group 4 (HER2/CEP17 ratio < 2.0, Average HER2 copy number >/= 4.0 and < 6.0). Our institutional practice of performing HER2 IHC and FISH on all new invasive breast cancers offers a unique opportunity to evaluate the impact of the guideline updates to determine the potential clinical ramifications of these new group designations.

Design: Data from cases of invasive breast carcinoma from 11/16-6/18 were collected. HER2 IHC and FISH copy number and ratios were recorded and cases in groups 2, 3 and 4 were identified. Under the 2013 guidelines, FISH results falling in groups 2 and 3 were classified as positive. For group 4, the former FISH equivocal group, alternative chromosome 17 probe testing was performed to determine HER2 status. The new guidelines were applied to these cases using the HER2 IHC result. HER2 IHC slides were available for re-review in 38 of 44 cases.

Results: 742 cases were identified. Of these cases, 44 (5.9% of total) had FISH results in groups 2, 3 and 4. Under the new guidelines, 28 cases would be changed from positive to negative (table). This represents 3.7% of the total cases and 63.6% of the non-classical cases. One group 4 3+ case, which was discordant in 2013 as FISH was negative by alternative probe testing, would be classified as positive by 2018 guidelines.

HER2 FISH Reporting	Group 2	Group 3	Group 4	Total
2013 Positive -> 2018 Positive	0	4	6	10
2013 Positive -> 2018 Negative	8	1	19	28
2013 Negative -> 2018 Negative	N/A	N/A	5	5
2013 Negative -> 2018 Positive	N/A	N/A	1	1
Total	8	5	31	44

Conclusions: The updated ASCO/CAP guidelines led to a change in HER2 FISH status from positive to negative in 63.6% of non-classical cases when compared to the 2013 results. This represents a significant subset of cases (3.7%) impacted by the guideline changes. Though rare, the response to anti-HER2 therapy of this group of patients remains unclear and more studies are needed into the clinical outcomes of this small but challenging patient population.

1944 Complete vs Partial Submission of Pelvic Lymphadenectomy Specimens Following Radical Prostatectomy: Impact on Lymph Node Yield and Detection of Metastases for Accurate Nodal Staging

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Disclosures: Sarah Ni Mhaolcatha: None; Elaine Power: None; Nick Mayer: None; Susan Prendeville: None

Background: Lymph node (LN) status is an important prognostic parameter in men undergoing radical prostatectomy (RP) for clinically localised prostate cancer (PCa). Pathologic evaluation of pelvic lymphadenectomy specimens (PLND) plays a critical role in accurate LN staging, yet there is currently no consensus regarding the optimal extent of PLND sampling in PCa. This study evaluated the impact of complete PLND submission on LN yield, detection of LN metastases and laboratory workload.

Design: RPs with concomitant PLND for PCa performed at a single institution (2015-2017) were included. PLND specimens were embedded in toto as follows: all palpable/visible LNs and potential LNs were blocked separately followed by complete submission of the remaining fatty tissue. LNs identified microscopically in the blocks of fatty tissue were considered non-palpable. RP pathologic tumour variables; number of palpable/non-palpable LNs identified; location, number and size of any metastatic deposits and the number of tissue blocks required were recorded for each case.

Results: 135 cases were included in the study. Grade Group (GG) at RP was: GG1 in 8%, GG2 in 50%, GG3 in 33%, GG4 in 3% and GG5 in 6%. T-stage at RP was: pT2 in 53%, pT3a in 31% and pT3b in 16%.

Median LN yield at PLND was 17(1-57) with a median of 9 palpable LNs (1-42) and 6 non-palpable LNs (0-55). Metastatic PCa (pN1) was identified in 22 cases (16%) with a median of 1.5 (1-9) positive LNs. The metastatic deposits were identified in palpable LNs only in 3% (4/22); in both palpable and non-palpable LNs in 10% (14/22) and in non-palpable LNs only in 3% (4/22).

The median diameter of palpable and non-palpable LNs containing metastatic deposits was 6mm (2-20mm) and 3mm (1-5mm) respectively. The median diameter of the metastatic deposit in palpable and non-palpable LNs was 2mm (0.25-20mm) and 1mm (0.1-3mm) respectively.

Overall, 929 blocks of palpable LNs and 1054 blocks of non-palpable LNs were submitted. The median number of blocks of palpable LNs was 6 (1-17) and of fatty tissue was 7 (1-28).

Conclusions: In this series, complete PLND submission increased LN yield and detection of metastases, resulting in 3% of cases (4/135) being upstaged from pN0 to pN1 due to metastases in small non-palpable LNs. This, however, had a significant impact on workload, with 133% increase in the number of blocks submitted. Further study and correlation with clinical outcome is required to determine if complete PLND submission is routinely justified in all cases.

1945 Do Multiple Levels of Gomori Methenamine Silver (GMS) Stains Improve Diagnostic Yield in Esophageal Biopsies?: A Quality Improvement Pilot Study

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Disclosures: Michael Occidental: None; Andrew Dunn: None; Mark Ettel: None; Jennifer Findeis-Hosey: None; Aaron Huber: None

Background: Lab efficiency is important to consider in a high-volume laboratory as it decreases costs, time, and resources for both technologists and pathologists. Our institutional standard operating procedure (SOP) states that there should be two levels cut on all special stains, although in practice it was observed that a variable number of levels were obtained on special stains. In an attempt to establish standardization and provide rationale and potential re-assessment for the historically defined SOP, we investigated if the number of levels changed diagnostic yield for fungal organisms in esophageal biopsies assessed with Gomori Methenamine Silver (GMS) stain.

Design: We retrospectively identified 127 esophageal biopsy specimens with previously performed GMS staining from 2017-2018 in our surgical pathology archives. Cases were selected such that they were roughly equivalent for presence or absence of fungal organisms, and many cases had at least two GMS-stained levels. Two gastrointestinal pathologists blindly re-reviewed the GMS-stained slides, noting for each case the presence or absence of fungal organisms, the number of levels and which level(s) included fungal elements, and the total time of slide review.

Results: One hundred twenty-seven esophageal biopsy cases were reviewed with 62 demonstrating GMS-positive fungal elements and 65 lacking fungal elements on GMS stain. Sixty-one (98%) of the GMS-positive cases had fungal elements on all levels; one case demonstrated GMS-positive fungal elements on only the first of two levels. No statistical difference was found between the proportion of positive GMS stains with 1 level versus cases with greater than 1 level ($p = 0.268$). Average viewing time of cases with 1 level (37.77 s) was not statistically different than time to view those with greater than 1 level (45.71 s; p value = 0.061).

Conclusions: Quality improvement of pathology labs requires the constant evaluation of laboratory practices in order to deliver efficient, quality care. This study demonstrates that one GMS-stained level is sufficient for rendering a consistent diagnosis for fungal organisms on esophageal biopsies, with extra levels having no statistical difference in providing diagnostic value. By standardizing a protocol to one level for GMS stains, time and resources may be conserved in the pathology laboratory.

1946 Push Pin Induced Artifact in Gastrointestinal Specimens: A potential mimicker of iron pill induced mucosal injury

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Disclosures: Maria Olave: None; Padmini Manrai: None; Ilke Nalbantoglu: None; Dhanpat Jain: None; Andrea Barbieri: None

Background: Metallic push pins are commonly used in pathology laboratories to secure luminal gastrointestinal (GI) resections during formalin fixation. In addition to imparting gross tissue defects, iron can diffuse from the pin into tissue and create deposits that resemble iron pill (IP) induced mucosal injury. The histologic patterns of pin induced iron deposition were investigated.

Design: Twenty GI resections (11 colon, 5 small bowel, 3 stomach, 1 esophagus) were studied. Sections were obtained from areas where pins were applied after 24 (n=15) and 48 (n=5) hours of fixation. As a control group, sections of non-pinned areas were taken. Prussian blue iron stain was performed on all cases. The pattern of iron deposition, the diameter of iron diffusion, and any associated histologic changes were recorded. The clinical history of iron medication was obtained in all cases.

Results: In 14 of 20 (70%) cases, the sections taken from the areas of pin application showed iron deposition. The maximum diameter of iron diffusion was 6.5 mm, with a median of 1.5 mm (IQR= 0-5). The median iron diameter after 24 and 48 hours of fixation were 1 mm (IQR= 0- 4.5) and 5 mm (IQR=1-6), respectively. The difference between the diameter of diffusion at 24 and 48 hours was not statistically significant (p = 0.2099, Mann-Whitney U). In 7 cases, the quality of iron deposition was green to black, crystalline and deposited along the mucosal surface and/or within the lamina propria; this was highlighted on Prussian blue (Figures 1&2). In the remaining 7 cases, Prussian blue showed a fine and diffuse pattern throughout the bowel wall. There was no evidence of mucosal injury in any of the cases. The control group lacked iron deposition on H&E and Prussian blue stains.

Figure 1 - 1946

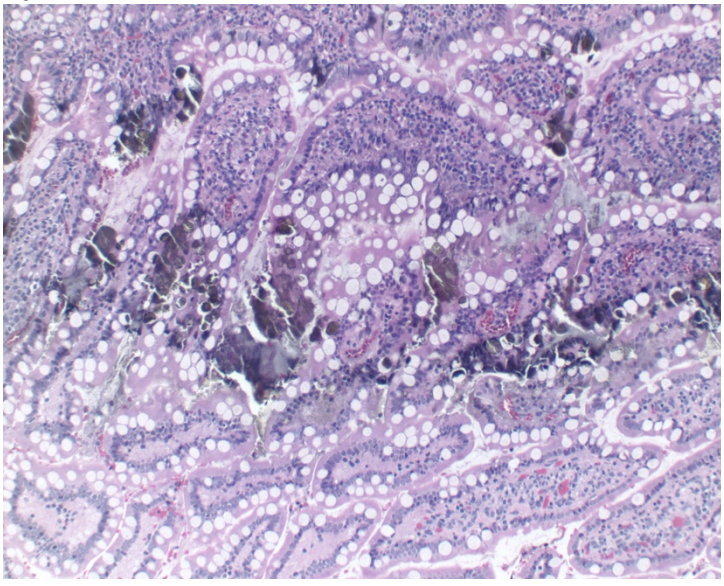
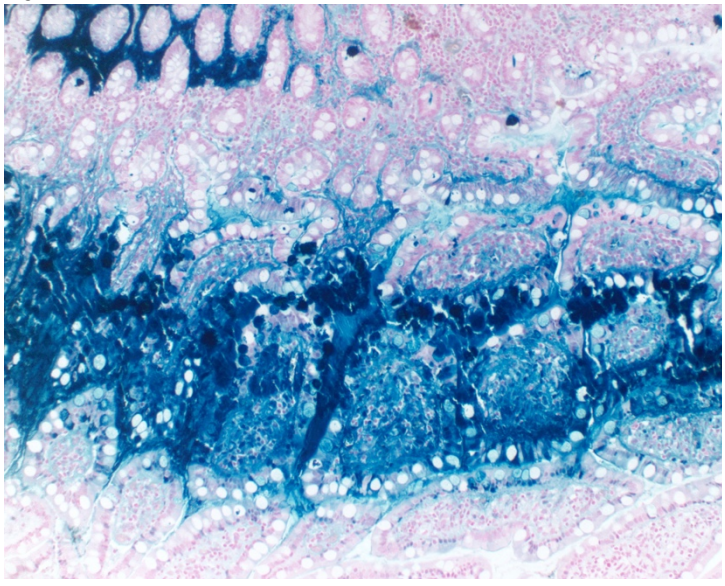


Figure 2 - 1946



Conclusions: IP induced mucosal injury due to iron medication use is seen primarily in the upper GI tract. Crystalline extracellular deposits along the mucosal surface and within the stroma are common patterns of iron deposition in this setting. A similar pattern was seen in half of our cases of pin associated iron deposition, which can closely mimic IP induced mucosal injury. The absence of mucosal injury and clinical history helps distinguish this from a true IP induced injury. Pathologists need to be aware of pin induced iron deposition to distinguish it from other causes with clinical relevance. Documentation of sections taken near pins at the time of gross evaluation, absence of mucosal injury, and absence of IP use may be of value to avoid misinterpretation.

1947 Avoiding the Over-and Under-Diagnosis of Perianal Extra-Mammary Paget Diseases by Adopting Essential Ancillary Methods

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Disclosures: Christina Ombres: None; Meghan Kubala: None; Lei Lou: None; Brian Martens: None; Kun Jiang: None

Background: Perianal Extra-mammary Paget disease (PEMPD) arises from skin adnexa, viscera, or anal canal neoplasms and is composed of mucin-containing cells that mimic intradermal Toker/Toker-like keratinocytes. Diagnosing PEMPD is challenging due to overlapping histomorphology and suboptimal immunoprofiling, even when viewed by experienced pathologists. The under- and over-diagnosis of PEMPD frequently occurs, leading to incomplete or over-aggressive resection. Our institutional review has illustrated key histochemical and immunohistochemical criteria that may improve PEMPD diagnosis.

Design: A total of twenty-four PEMPD cases were reviewed retrospectively and no visceral malignancies were known for any of the patients. Clinical, histochemical, and immunohistochemical findings were summarized and compared to those published in the literature.

Results: Microscopically PEMPD shows mucin-congested, signet-ring-like cells involving squamous mucosa and epithelium. This peculiar cytology mimics Toker/Toker-like cells, posing a diagnostic challenge. Contrary to popular belief, immunohistochemistry offers limited help due to overlapping CK7 and GATA3 immunoprofile. Twenty-one biopsies showed skin-primary PEMPD (mucicarmine+/CK7+/GCDFP+/GATA3+/CK20-/CDX2-/P40-) profile. The remaining 3 showed a distinct (mucicarmine+/CK7+/GCDFP-/GATA3-/CK20+/CDX2+/P40-) profile and were confirmed to arise from anal canal adenocarcinomas in subsequent resections. Interestingly, the Toker/Toker-like mimickers in each case were also labeled by CK7 and some other markers, but never by mucicarmine. Additionally PEMPD mimickers demonstrate central/round nuclei, intercellular bridges and are mucicarmine-negative. Hence, this investigation highlighted key criteria in diagnosing PEMPD: mucicarmine-positivity, compressed/crescent-shaped nuclei and an absence of intercellular bridges.

Conclusions: PEMPD is an insidious and persistent process that is frequently associated with an underlying adenocarcinoma. An accurate diagnosis/classification of PEMPD will lead to more appropriate clinical management and subsequently improve the overall prognosis of the patient.

1948 Intraoperative Evaluation of Poorly Differentiated Gastrointestinal and Pancreato-Biliary Carcinomas, Diagnostic Challenges and Pitfalls: Review of 435 Cases

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Disclosures: Christina Ombres: None; Shohreh Eliaszadeh: None; Reima El Naili: None; Kun Jiang: None

Background: Poorly cohesive carcinomas of the gastrointestinal and poorly differentiated adenocarcinomas of pancreato-biliary tracts are notorious for causing intraoperative consultation difficulties, especially following chemoradiation therapies prior to surgeries. Under- and over-diagnoses of these processes remain clinical challenges. Currently, there is no consensus or delineated guideline found in the literature to accurately recognize these malignancies intraoperatively. The aim of this study is to determine the most likely contributing factors that lead to these discrepancies and to improve intraoperative judgment of these entities for optimizing patient management.

Design: Four hundred and thirty five intraoperative consultation cases of biopsy-proven poorly differentiated/cohesive adenocarcinomas were reviewed. The pitfalls and contributing factors of the erroneous diagnoses were investigated.

Results: Among the 435 intraoperative cases, 19 (4.4%) discrepancies with clinical impact were identified, including 13 false-negative and 6 false-positive frozen diagnoses. The top three contributing factors of false-negative diagnoses were superficial (not deep enough) sectioning (46%), unfamiliarity with challenging histomorphology (31%), and frozen artifact (23%). The top three reasons for overcalling reactive cells were frozen artifact (50%), unfamiliarity with diagnostic features (33%), and chemoradiation-related atypia (17%).

Conclusions: Our study highlights the importance of establishing a consensus on how to recognize the contributing factors that commonly lead to the inaccurate intraoperative consultation of poorly cohesive carcinomas of the gastrointestinal and poorly differentiated adenocarcinoma of the pancreato-biliary tract. The leading identified causes that contribute to these errors are tumor sampling, unfamiliarity of diagnostic features and treatment effect, marked frozen artifacts, and lack of subspecialty training. In order to improve clinical management and patient outcome, it is imperative to delineate and eliminate such avoidable frozen diagnosis errors.

1949 Analysis of Histology Processing Quality - A Regional System Perspective

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Disclosures: Tamera Paczos: None; Phoenix Bell: None

Background: In the current healthcare environment hospital laboratories are struggling with decreased reimbursement and an aging workforce composed of a dwindling technical staff resulting in a push towards testing centralization to help mitigate these factors. The University of Rochester Medical Center (URMC) - Strong Memorial Hospital (SMH) has an expanding regional hospital network with affiliations and relationships to several Hospitals in the Central N.Y. area: FF Thompson Hospital (FFTH) in Canandaigua, Noyes Memorial Hospital (Noyes) in Dansville, Jones Memorial Hospital (Jones) in Wellsville, St. James Hospital in Hornell (SJMH), Highland Hospital (HH) in Rochester, and Wyoming County Community Hospital (WCCH) in Warsaw. At the time of data collection each of these sites performed varying degrees of onsite histology processing. In this study we examine quality scores from each of the sites and compare them to the quality score at the central laboratory (SMH) to determine whether there is any potential quality benefit to centralized histology services.

Design: Histology processing quality was assessed by examining the slides from 20 random 2016 cases pulled from each site. The slides were blinded as to site of origin and assessed for quality using the College of American Pathology histology quality improvement program (HistoQIP) and Q-Probes studies as guidelines for development of a scorecard and the subsequent analysis. The slides were examined

and scored, with a higher score translating to better quality. The average scores from each site were compared to the average score from the central lab using a T-test analysis to determine if any statistically significant differences were present.

Results: Analysis of the data demonstrates that sites currently processing histology at the central lab (SMH) have higher overall quality scores than those sites that perform their own histology. Furthermore, one site demonstrates a statistically significant decreased average quality score when compared with the central lab (p-value = 0.00005). Please refer to Table 1 for details.

				Table 1			
3	HH		3	Jones		1	Noyes
3	HH		2	Jones		2	Noyes
3	HH		2	Jones		2	Noyes
2	HH		2	Jones		2	Noyes
3	HH		3	Jones		0	Noyes
3	HH		3	Jones		3	Noyes
3	HH		2	Jones		3	Noyes
3	HH		3	Jones		2	Noyes
1	HH		3	Jones		3	Noyes
3	HH		3	Jones		1	Noyes
3	HH		3	Jones		2	Noyes
3	HH		1	Jones		2	Noyes
3	HH		3	Jones		3	Noyes
2	HH		3	Jones		1	Noyes
3	HH		3	Jones		1	Noyes
3	HH		3	Jones		0	Noyes
3	HH		2	Jones		1	Noyes
3	HH		2	Jones		2	Noyes
3	HH		3	Jones		0	Noyes
3	HH		3	Jones		2	Noyes
2.8			2.6			1.65	
T-test --average			T-Test average			T-Test average	
Strong vs. HH			Strong vs. Jones			Strong vs. Noyes	
0.746363488			0.374			0.0000551	
3	WCCH/SJMH		3	SMH		2	FFTH
3	WCCH/SJMH		3	SMH		3	FFTH
2	WCCH/SJMH		3	SMH		2	FFTH
3	WCCH/SJMH		3	SMH		3	FFTH
2	WCCH/SJMH		3	SMH		2	FFTH
3	WCCH/SJMH		3	SMH		2	FFTH
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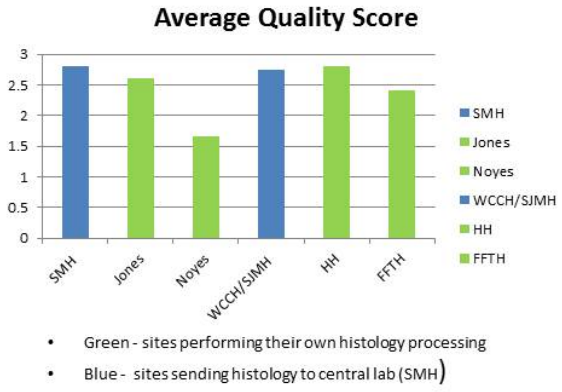
2	WCCH/SJMH		3	SMH		1	FFTH
3	WCCH/SJMH		2	SMH		3	FFTH
3	WCCH/SJMH		3	SMH		1	FFTH
3	WCCH/SJMH		3	SMH		3	FFTH
2.75			2.75			2.4	
T-Test average						T-Test average	
Strong vs. WCCH/SJM						Strong vs. FFTH	
1						0.061620529	

Figure 1 - 1949



Conclusions: In summary, our analysis shows that slide quality would be maintained, if not improved, when processing is performed at the central lab (SMH) with the potential for significant quality improvement. This supports the Regional Systems strategic initiative to centralize laboratory testing in order to realize increased efficiencies and mitigate staffing shortages.

1950 PCR Testing for Determination of Vector-Borne Parasite and Bacterial Organisms, is an Order Best Added After Initial Peripheral Blood Smear Evaluation and Pathologist Consultation- Study from an Endemic Area

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Disclosures: Pallavi Patil: None; Diana Treaba: None; Mark Legolvan: None; Dariusz Stachurski: None; April Bobenchik: None; Kimberle Chapin: None

Background: Send-out PCR testing for vector borne organisms (VBO), in our study namely- Babesia (Bb), Plasmodium (Pm), Ehrlichia (Er), and Anaplasma (Ap) entails a large non-reimbursed expenditure for the hospital in endemic regions. These are detectable on peripheral blood smear examination. Guidelines on work-up for these VBO are limited. We sought to study the ordering practices of PCR requests for Bb, Pm, Er, and Ap, determine their value in diagnosis and if reduced testing for these organisms by PCR was appropriate. For patients with a clinical suspicion of these VBO, in our institute, a “blood smear for parasite” order (PBSO) is used that entails careful smear screening for organisms. We intended to use our findings to guide PBSO orders and test requests by clinical colleagues to reduce unnecessary, non-reimbursed expenditures, and inappropriate PCR use.

Design: Laboratory records were queried for orders of PBSO and serology performed in-house, sendout PCR requests for VBO (Bb, Pm, Er, and Ap) during peak months of detection in our region (June - Sept 2015). An IRB approved database was used to record results of PBSO, serology and PCR.

Results: We found 870 cases with PBSO requests, 65 cases with PCR requests, and 98 cases with serology orders. The number of cases with PBSO, PCR and serology test requests with detection results as positive and negative are shown in Table 1. Characteristic morphology of VBO is shown in Figure 1. PCR requests without PBSO were all negative. PBSO correlated 100% with PCR results. No co-infection was noted in cases diagnosed for a single organism by PBSO. Serology was difficult to interpret in past or current infection in this endemic area, but for Bb was not as sensitive as smear.

Table 1: Vector-borne parasite and bacterial disease (Bb, Pm, Er, Ap) test orders and results June-Sept 2015

Tests requests	Smear n (%total)	PCR n (%total)	PCR Result and Interpretation	Serology n (%total)	Positive Serology n(%total)
Total	870	65		98	30
Smear positive (any pathogen)	68 (8%)	16 (24%)	9 agreed with smear interpretation 7 negative for pathogen requested	56 (82%)	20 (35.7%)
Smear negative	802 (92%)	33 (4%)	All negative	29 (3.6%)	7 (0.8%)
Molecular only	NA	16	All negative	13	3 (23.1%)

Figure 1 - 1950

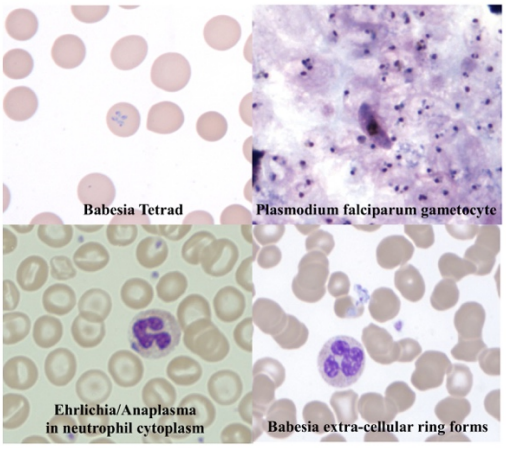
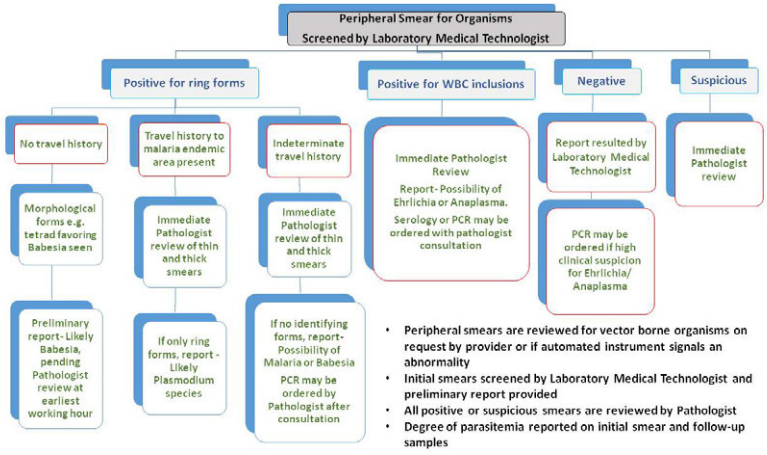


Figure 2 - 1950



Conclusions: PBSO is sensitive and specific for Bb and Pm with definitive morphology and travel history in acute disease. PCR can be used for Bb or Pm in indeterminate travel history and lack of definitive morphology. In cases with Er/Ap, PCR or serology may be used to distinguish. Serology or PCR considered in PBSO negative cases with strong clinical suspicion for Er/Ap, due to low sensitivity of PBSO. In our setting, PCR orders at the outset did not add higher quality of care but increased expenditure. Subsequent to this review, an in-house flowchart (Figure 2) was developed to guide work-ups. PCR for these VBO should only be considered after PBSO, and consultation with a pathologist for appropriate test utilization, reducing non-reimbursed expenditures.

1951 Quantification of Diagnostic Error in Histopathology - 5 year Experience from a National Quality Improvement Programme

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Background: There is little evidence based information available on the frequency of interpretive error in diagnostic histopathology. Information on interpretative error rates is largely gleaned from review of report amendments, which record identified interpretive errors and form a good surrogate marker for error. A national Histopathology Quality Improvement (HQI) Programme was launched by the Faculty of Pathology, Royal College of Physicians in Ireland (RCPI) in 2009, with the aim of enhancing patient safety. Thirty-two laboratories participate in this programme, recording key quality indicators (KQIs). Laboratories are categorised as either cancer centres (CC) (medium-large regional centres), or general centres (GC).

Design: The QI programme sub-classifies addendum reports into three subgroups;- supplementary, amended and corrected reports and all are recorded using a quality code (Q-code). A supplementary report is issued when new information becomes available after the final report has been submitted. A corrected report is issued when transcription, patient identification or other error is identified, which does not change the original diagnosis. An amended report is issued when the final report diagnosis changes due to an interpretive error. Laboratories (n=32) apply QI codes to all supplementary, amended and corrected reports issued and are advised to carry out regular audit

to ensure the accuracy of the data collected. The QI codes are extracted from local LIS systems and uploaded to a national data collection system (Health Atlas Ireland). Total number of specimens, tissue blocks and slides are also available. Data for a five year period (2013-2017) i

Results: The number of amended reports recorded nationally was relatively stable over the five year period. For histology this averaged 444 per year (0.1%). The number of corrected reports recorded was also stable and averaged 776 per year (0.2%). Combining the two parameters gives a rate of 0.3%, which represents a surrogate marker for overall recorded rate of error in histology (Table 1). Similarly, for cytology this rate ranged from 81-101 (0.24%-0.29%)(Table 2). The recorded rates of error did not differ significantly between Cancer centres and General Centres.

Table 1. Combined amended and corrected report rates, Histology, 2013-2017

year	2013	2014	2015	2016	2017	Average
CC sites	640(0.34%)	673(0.35%)	767(0.38%)	902(0.43%)	782(0.36%)	753 (0.37%)
GC sites	401(0.21%)	427(0.23%)	615(0.32%)	439(0.22%)	407(0.20%)	458 (0.24%)
All sites	1041(0.28%)	1100(0.29%)	1382(0.35%)	1341(0.33%)	1189(0.28%)	1211(0.30%)

Table 2. Combined amended and corrected report rates, Cytology, 2013-2017

year	2013	2014	2015	2016	2017	Average
CC sites	57(0.25%)	77(0.33%)	45(0.20%)	60(0.27%)	58(0.27%)	59(0.26%)
GC sites	24(0.21%)	24(0.22%)	42(0.37%)	35(0.30%)	23(0.19%)	30(0.29%)
All sites	81(0.24%)	101(0.29%)	87(0.26%)	95(0.28%)	81(0.24%)	89 (0.26%)

Conclusions: The recorded rates of amended and corrected reports are a surrogate marker for diagnostic error in Histopathology. Although error is likely to be underreported, based on this data it is reasonable to expect overall recorded error rates in Histopathology to fall below 0.5%.

1952 Clinical, Educational, and Financial Impact of a Standardized Workflow for Salvaging Quality and Quantity Not Sufficient (QNS) Samples in an Academic NGS Laboratory

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Background: Quality/quantity not sufficient (QNS) samples result from a variety of factors including, but not limited to, effects of pre-processing and specimen viability. Lack of results precludes identification of genetic aberrations which may be of diagnostic, prognostic, or therapeutic utility. We evaluate the performance of a new QNS workflow over the six months following implementation in our academic NGS laboratory and discuss the resulting clinical, educational, and financial implications.

Design: Data was prospectively collected following the implementation of the QNS workflow to determine the fate of each case that was initially classified as QNS. QNS case disposition results in two major outcomes for the patient: A clinically relevant assay was performed and reported or testing was not performed/successful. Based on the number of salvaged cases we were able to estimate how much additional revenue was generated following implementation of the workflow. Pathology trainees involved in assessing QNS samples were surveyed to determine the educational impact and areas of improvement for the workflow.

Results: Since implementation, 60% of QNS cases had more material that could be submitted for NGS testing. An additional 9% were referred to another laboratory for testing (ex. targeted EGFR analysis for lung adenocarcinoma). 30% of cases were either not appropriate for referred testing or had no other available material. Approximately 71% of cases that underwent a second attempt at NGS testing generated data for analysis, and a clinical report of the findings. Based on the number of cases ultimately salvaged from QNS status, we estimated the recovered revenue based on the operating costs of our laboratory. A summary of the survey responses from residents is presented along with a discussion about how the QNS workflow reinforces important educational concepts in Molecular Anatomic Pathology.

Conclusions: A dedicated, proactive, laboratory-driven workflow is an effective tool for salvaging QNS cases and integrating Molecular Anatomic Pathology concepts into a residency training program. In our experience approximately 52% of cases can be salvaged to produce either an NGS result or a targeted analysis of a disease relevant gene(s). The modest time investment (1-2 hours a week based on our case load) produces clinically relevant results in a majority of cases and captures additional laboratory revenue that otherwise would have been lost.

1953 Gross-Only Examination and its Effect on Patient Safety and Efficiency

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Background: Gross-only examination (GOE) in surgical pathology is typically reserved for specimens with a low probability of significant microscopic findings. However, there remains great inter-institutional variability in GOE policy, perhaps due to a general lack of agreement between pathologists and treating clinicians on which specimen types qualify for GOE. We considered the impact of a change in GOE policy on patient safety and laboratory resource utilization.

Design: Our GOE policy was compared with the policies of 4 departments of various sizes in the Eastern and Midwestern United States. Based on non-uniform GOE policies, we identified 31 of 63 candidate specimen types submitted for histologic analysis at our institution but GOE for at least one other institution. From this list, 12 specimen types were selected for in-depth review based on local subspecialty consensus and specimen frequency. We reviewed the initial clinical and final histopathologic diagnosis for all cases over the prior one-to-three-year period (depending on specimen volume) for significant clinically actionable information.

Results: Six specimen types were ultimately identified for which histologic examination had provided no significant diagnostic benefit over GOE: femoral heads and knee joints removed for osteoarthritis, hernia sacs, incidentally removed vaginal mucosa, spermatic cord lipomas, middle ear ossicles, and non-brain thrombi. The former three specimen types each had 98-200 cases processed over the prior year, and the latter three specimen types each had 33-39 cases processed over the prior three years, all without clinically significant findings identified on histology. Including these new specimen types in our GOE policy would improve histology laboratory efficiency by a projected reduction of over 600 specimens (approximately 645 blocks) per year without impacting patient safety.

Conclusions: In the age of cost and labor constraints, accumulated small reductions in cost and workload can lead to improved efficiency and better allocation of scarce resources. When making these changes, impact on patient safety should be considered and included in cost-benefit analyses. Gaining consensus from clinical partners is a key part of change efforts. Based on this study, we recommend a periodic review of GOE policy with transitioning to GOE alone when impact on patient safety is negligible.

1954 Pathology Team and Community Engagement Using Social Movement Methods to Improve the Equity of Cervical and Breast Cancer Screening

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Background: The Mississippi incidence and mortality rates of cervical and breast cancer are high compared to other states and are largely secondary to lower levels of screening in rural communities. We investigated if methods of pathologist-led community social movement activism could increase attendance at screening events compared to traditional, more passive recruitment methods and could change the role of the pathologist in the community.

Design: We performed two College of American Pathologists (CAP) See, Test & Treat (STT) screening events, a program that provides same day diagnoses for cervical and breast cancer screening for underserved women. One program used traditional methods of recruitment (STT-T) and the second program used traditional and social movement methods (STT-SM). Using pre-event discussion, event observations, and post-event wrap sessions we qualitatively assessed the STT recruitment processes for the two events, held in consecutive years. We compared the quality metrics of attendance and no-show rate for both STT events. We developed a process chart of activities, pathways, and connections for STT recruitment work and assessed latent factors (e.g., cultural variables) that affected the quality metrics.

Results: The attendance and no-show rates at the STT-T and STT+SM were 41 women and 49% and 118 women and 19%, respectively. The STT-T and STT-SM recruitment methods included mixed media (radio, television, print), faith based pathways (congregational connections), person-to-person engagement, follow-up phone calls, and supportive services (e.g., transportation). The STT+SM methods also involved pathologist activist teams that engaged community business, governmental, healthcare, and social leaders to drive the recruitment and shepherding of underserved women. Improvement in attendance occurred as community leaders began to own a portion of the work pathway in the recruitment process. The pathology teams partnered with activists to empower the lab personnel including pathologists to work differently with the community and jointly identify and eliminate cultural barriers.

Conclusions: We conclude that pathology teams 1) may increase cervical and breast cancer screening through community engagement activities such as the CAP STT, and 2) may lead social movement activism in communities to build stronger lab-community ties to improve preventative care and maintenance care for underserved populations. This role changes the paradigm of pathologist work.

1955 Implementation of Synoptic Reporting for Early Carcinomas of the Gastrointestinal Tract, removed by Endoscopic Submucosal Dissection, Significantly Improves the Completeness of Pathology Report in Six Parameters

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Background: Endoscopic submucosal dissection (ESD) is an advanced technique for resection of endoscopic mucosal and submucosal lesions pioneered in Japan in the 1990s. The data in the pathology reports is used to further manage the patient either conservatively, or with complete resection. Traditionally, anatomic pathology reports have used a narrative style of reporting. Narrative reporting lacks structure and sometimes results in an incomplete report due to missing information. In the early 2000s, the College of American Pathologists (CAP) introduced synoptic reporting for oncological cases. Although "CAP Cancer Checklists" or "Cancer Protocols" have been around since 1986, they were only available on paper, and only for a few common cancers. By 2010, the CAP cancer checklists had expanded to 65 cancers, and synoptic reporting was made available electronically to interface with pathology information systems. In 2014, standardization of pathology reports in the form of Synoptic Reporting (SR) was introduced at NYU Winthrop hospital for early cancers (EC)(pT1 lesions) of the gastrointestinal tract (GIT).

Design: The study received IRB approval. The pathology database was searched for early carcinoma of GIT diagnosed on endoscopic resections between 1/1/2010 and 10/06/2017. Pathology reports were audited for the following data: organ, exact site in the organ, tumor size, histology of tumor, differentiation grade of tumor, presence of ulcer overlying tumor, depth of invasion, lympho-vascular invasion (LVI), immunohistochemical stains (IHC) to detect LVI, margins, pT and Her2/MSI. The data were analyzed using chi-square test and p.value <0.05 was considered as significant difference.

Results: 108 cases in 106 patients with EC of the GIT were identified between 2010 and 2017. Twenty-six cases were prior to the standardization and 82 cases after. There was significant improvement in 6 of 12 metrics: IHC for LVI (P<0.0001), tumor size (P<0.0001), ulcer (P=0.0007), pT (P<0.0001), Her2/MSI (P=0.001), LVI (P=0.046).

Variable	Pre-standardization		Post-standardization		Absolute change	P.value
	Number of cases	Percent reported	Number of cases	Percent reported		
IHC LVI	26	11.5%	73	82.2%	70.7%	p<0.0001
Size	26	38.5%	82	90.2%	51.7%	p<0.0001
Ulcer	26	30.8%	82	70.7%	39.9%	p=0.0007
pT	26	57.7%	82	95.1%	37.4%	p<0.0001
Her2/MSI	25	8%	75	45.3%	37.3%	p=0.001
LVI	26	69.2%	78	93.6%	24.4%	p=0.046

Conclusions: This audit of 108 pathology reports of Early Cancers of gastrointestinal tract, resected endoscopically reiterates that synoptic reporting increases the completeness of pathology report as compared to a traditional narrative report and is therefore, a significant quality improvement tool.

1956 Paired Analysis of PDL-1 IHC Performance in Cytologic and Formalin-Fixed Paraffin Embedded Tissue Samples

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Background: The increased use of Fine Needle Aspiration (FNA) to obtain biopsy specimens has led increasing use of both diagnostic and therapeutic immunohistochemical (IHC) stains on cell blocks. IHC methods are typically validated against formalin-fixed paraffin embedded tissues (FFPE) not against cytologic preparations, where differences in fixatives and processing may impact antigen recovery. We describe our effort to determine what effect, if any, can be ascribed to fixation and processing utilized in cytologic preparations vs FFPE subjected to IHC.

Design: Eight specimens including three placentas and five solid tumors were included in this study. Six specimens were sampled fresh with FNA at the grossing bench, immediately placed into a methanol based buffered preservative and processed into cell blocks using plasmin-thrombin preparation techniques. The same area subjected to FNA was then sectioned, placed into formalin, and processed using standard histological preparation techniques. Two cases with paired specimens were obtained by archival search. Each paired specimen block was stained with PDL-1 (SP2630), and Pancytokeratin (AE1/AE3) and evaluated for staining consistency by two blinded pathologists.

Results: PDL-1 showed inconsistent results in 60% (3/5) of tumor cases with all of the cases showing variability in the percentage of cells staining when comparing cytologic vs. FFPE tissue samples. Two tumor samples showed increased percentage of positive staining cells and one sample showed decreased percentage on cytologic preparation while two samples of tumor tissue stained identically compared with the result of IHC on the corresponding FFPE sample. Pancytokeratin showed consistent staining percentage in all samples (8/8). All placentas show 100% (3/3) congruent results between FFPE and FNA specimens for both stains tested. All results are summarized in Table 1.

Table 1: Paired FNA and FFPE Staining Patterns in Tumor and Placental Tissues.

Specimen	Cytology Sample	FFPE Sample	Cytology Sample	FFPE Sample
	% of cells staining positive for PDL-1 IHC.	% of cells staining positive for PDL-1 IHC.	% of cells staining positive for AE1/AE3 IHC.	% of cells staining positive for AE1/AE3 IHC.
Endometrial adenocarcinoma, endometrioid type	>50	<10	100	100
Endometrial adenocarcinoma, endometrioid type	>50	>50	100	100
High grade Serous Carcinoma of the Ovary	<10	<10	100	100
Pancreatic adenocarcinoma, ductal type	<50	100	100	100
Mucinous borderline tumor of Ovary	>50	<10	100	100
Placenta 1	100	100	100	100
Placenta 2	100	100	100	100
Placenta 3	100	100	100	100

Conclusions: Stains on placenta perform identically in cytologic and tissue section comparison. Thus, differences observed in PDL-1 IHC are attributable to tumor heterogeneity. Staining upon resection is warranted in neoplastic cases where FNA fails to demonstrate PDL-1 staining IHC. Expanded studies including various tissue types are needed to validate antigen retrieval protocols across tissue preparation platforms. Repeat PDL-1 testing following negative results on FNA specimens is compulsory and should be reported as a disclaimer on all FNAs subjected to IHC for PDL-1.

1957 Placental Grossing: Can We Do Better?

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Background: Placental weight (PW) is a standard measure obtained during placental gross examination. PW is considered a surrogate for placental function, with values at the extremes suggesting underlying pathology. Consensus guidelines for placental grossing establish trimming of membranes and cord prior to weighing as the preferred practice. Reference charts categorizing PW are based on trimmed placental discs (TPW). Our tertiary care hospital processes >2000 placentas annually. Prior to this study, our institution traditionally measured PW with the cord and membranes attached (UPW). We set out to establish the need for pre-weight trimming to align our practice with consensus guidelines and to validate the clinical benefit of reporting TPW for both clinical practice and future research.

Design: For 1 month, all singleton placentas ≥35 weeks gestational age (GA) received by pathology were weighed both before and after trimming, with the TPW measured before and after formalin fixation. A grossing sheet was constructed to record all critical data. Each weight was then assigned a weight percentile category (WPC) (<10th, 11-25th, 26-50th, 51st-75th, 76th-89th, >90th) for GA based on published reference values. WPC were then compared for the same placentas (UPW vs TPW unfixed vs TPW fixed) and trends examined. The reported UPW for a similar cohort processed in the two months prior to study were reviewed, analyzed and compared.

Results: 56 placentas were assigned a WPC for UPW, TPW unfixed and TPW fixed based on gestational age. Statistical analysis with Wilcoxon signed-rank test was performed. The UPW was ~27% higher than the TPW unfixed, with a high variance. Additionally, WPC by gestational age was statistically higher for UPW ($p<0.001$) when compared with TPW (Fig 1), with 82% of placentas re-classified into a different WPC after trimming, 46% of which were misclassified into or out of a clinically relevant extreme category. Fixation did not significantly affect WPC.

Figure 1 - 1957

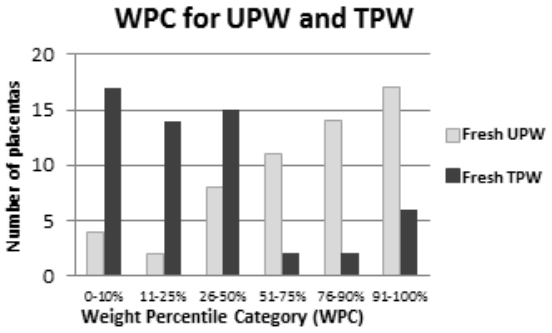

Figure 1. Number of placentas in each weight percentile category (WPC) for untrimmed placental weight (UPW) versus trimmed placental weight (TPW).

Conclusions: Our findings illustrate the misclassification of WPC from UPW and stress the importance of trimming. Categorization by UPW resulted in clinically relevant misclassification of WPC in over one third of placentas. These results were presented to leaders in the division of anatomic pathology and the grossing protocol and practices were changed at our institution as a result of this intervention. The post-intervention TPWs and WPCs were collected for 1 month and the distributions were found to be compatible with those in our study.

1958 The Idylla Molecular Testing System Is a Useful Option for the Detection of Clinically Actionable Variants in Challenging FFPE Samples Not Suitable for Conventional Sanger and NGS Testing

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Background: Optimal care of cancer patients often requires precise pairing of chemotherapeutics with the specific underlying genetic variants present in their tumors. To achieve this, DNA is isolated from tumor cells and molecular analysis is used to identify clinically actionable genetic variants. Next generation sequencing (NGS), and to a lesser extent, Sanger sequencing are broadly used for this analysis. Often, FFPE specimens submitted for testing are suboptimal and rejected due to insufficient quantity (QNS). Examples include small biopsies with scanty tissue, decalcified bone specimens, and samples with a low percent of tumor. To address this common problem, we evaluated the Idylla Molecular Testing System on 46 patient FFPE samples that were suboptimal for clinical NGS or Sanger testing.

Design: The study cohort consists of 46 FFPE cancer specimens (9 decalcified bone, 37 FNA) previously evaluated and assessed by pathologist as QNS for conventional NGS or Sanger testing. Of the bone specimens, 8 had previous NGS results with the remaining case having unsuccessful library preparation. Of the QNS specimens, none were previously analyzed due to either paucicellularity or malignant cells representing <5% of the total cellularity. We utilized the Idylla™ (Biocartis) System to test these specimens. FFPE tissue sections were directly loaded onto Idylla™ cartridges (KRAS, BRAF or EGFR assay). DNA was isolated and fluorescence-based real-time PCR was performed. Results were evaluated with the Idylla Explore Software.

Results: The indication for testing was BRAF (4 cases) and EGFR (42 cases). Amplification was observed in all cases. The three bone cases with previously known KRAS mutations were also identified with the Idylla assay. The previously untested bone case demonstrated amplification with Idylla, and an actionable variant was not identified. Of the QNS samples that were previously rejected for NGS testing, clinically actionable variants were identified in 12% of these cases.

Conclusions: The Idylla Molecular Testing System is an accessible, rapid, and effective testing option for challenging FFPE specimens that are suboptimal for NGS or other conventional methods. A limitation of this system is the inability to discern true negative results from false negative results. In addition, true positive results are difficult to confirm by alternative methods or by repeat testing due to lack of sensitivity and the potential lack of residual tissue, respectively.

1959 STAT Liver: A Workflow Model for Processing Same-Day Outpatient Biopsies of Liver Transplant Patients with Elevated Liver Enzymes

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Background: Post liver transplant, patients are monitored by blood draws for liver enzyme abnormalities (LEA). Asymptomatic liver transplant patients (ALTPs) with LEA often need a substantial workup including liver biopsy, to assess the cause and initiate appropriate management. Tissue biopsies require adequate processing time. If patients were potentially unreliable or traveled a long distance, they are often admitted overnight until pathology results were available, which consumed substantial healthcare resources. We had implemented successful same-day, outpatient workup (SDOW) for renal transplant biopsies. Here we report our workflow for the anatomic pathology laboratory's (APL) SDOW for ALTPs with LEA.

Design: Our major academic transplant center (approximately 160 liver transplants per year) implemented a coordinated, multidisciplinary protocol for ALTPs with LEA. When LEA are detected, the transplant coordinator notifies affiliate departments, including radiology and pathology, and schedules a SDOW. This includes ultrasound studies and image-guided liver biopsy. The tissue is then received into the APL where it is rush processed for permanent section in order to provide a preliminary diagnosis by the late afternoon. During this time, the patient waits in an outpatient lounge prior to being admitted or discharged based on the preliminary pathology.

Results: Between July 2017 and September 2018, 11 patients were enrolled in SDOW. Ultrasound exam excluded large bile duct obstruction and vascular compromise in all patients. The mean turnaround time was 6.25 hours for a preliminary pathology diagnosis to be discussed with the transplant coordinator. Other quality parameters, biopsy characteristics, and clinical outcomes are summarized in Table 1. 8 of the 11 patients (73%) were discharged home immediately after preliminary biopsy results to be followed up as an outpatient. Based on the average length of stay and inpatient costs, SDOW saved an estimated $210,000-250,000 and 60-100 bed days.

Mean Turnaround Time (Hr:Min)			Clinical Outcomes	Pathology Diagnosis	Clinical Outcomes
Radiology Suite Collection to APL	Received in APL to Histology	Received in APL to Preliminary Diagnosis			
0:33	1:02	6:16	Discharged Home (n=8)	Acute Rejection (n=3) No Etiology to LEs (n=2) Recurrent Disease (n=1) Drug Toxicity (n=1) Features of Biliary Obstruction (n=1)	Given Oral Steroids (n=2) Immunosuppression Changes (n=2) No Changes (n=4)
			Admitted to Inpatient (n=3)	Acute Rejection (n=2) Indeterminate Rejection (n=1)	Given Intravenous Steroids (n=2) No Changes (n=1)

Table 1: Quality parameters, biopsy findings, and clinical outcomes for the 11 post liver transplant patients who underwent same-day outpatient workup for elevated liver enzymes.

Conclusions: Following enactment of this same-day coordinated, multidisciplinary effort at our transplant center, 8 of 11 patients were discharged home, improving quality and saving substantial costs and resources through averted admissions and inpatient workups. Our model demonstrates that the APL at major transplant centers can successfully employ a same-day outpatient workflow for liver transplant biopsies in order to provide quality, rapid tissue evaluation in asymptomatic patients with LEA.

1960 Improving ROSE: Discrepant Touch Preparation and Histology Findings in Cytology of Renal Masses: A 10 Year Retrospective Review

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Background: The number of renal incidentalomas is on the rise due to increasing use of radiologic studies. Image-guided core needle biopsies (CNB) with touch preparations are performed in high risk patients to guide specimen collection and triage of sample for additional studies. This allows the clinical team to perform ablative techniques, begin chemotherapy, do surgical resection or continue to monitor the patient.

Design: As part of our departmental quality control process, we searched our electronic database from January 2008-June 2018 to identify 180 CT-guided biopsies of renal masses with rapid on-site evaluation (ROSE). Diff-Quik and rapid modified Pap stained touch preparation smears of discrepant cases were examined by cytopathologists blinded to the original interpretation or results of permanent sections, and correlated to final biopsy diagnosis to highlight the main interpretation pitfalls.

Results: The study included 143 primary malignant renal neoplasms, 5 angiomyolipomas, 4 metastases, 2 lymphoproliferative disorders, and 26 benign inflammatory processes. Intraoperative touch preps correctly identified the lesion as neoplastic or not in 137 of 180 cases (76.1%). 8 cases were interpreted as neoplastic on touch preps, whereas the core biopsy findings were benign (false positive rate of 4.4%) and 35 cases were non-neoplastic on touch preps, with malignant neoplasm demonstrated on follow-up (false negative rate 19.4%). Angiomyolipoma and oncocytic change in renal tubular epithelium were the most frequent causes of false positive interpretation (7 out of 8 cases, or 87.5%), whereas sparse cellularity, (either from slide preparation or sampling), and predominately bloody smears were the main reasons for false negative results (32 out of 35 cases, or 91.5%).

Conclusions: Touch preparation smears are vital, but imperfect tools in evaluation for renal neoplasms. In the majority of cases, the distinction between a neoplastic and non-neoplastic sample can be done with certainty, but there are limitations. Increased awareness of the interpretation pitfalls for these samples allows the pathologist and radiologist to make a more informed decision regarding specimen collection and patient management.

1961 Detection of Low-Grade Squamous Intraepithelial Lesions: Predictive Value of Molecular, Cytologic, Colposcopic, and Histologic Evaluation

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Disclosures: Stephanie Skala: None; Emily Mcmullen: None; Girume Degu: None; Heather Walline: None; Richard Lieberman: None

Background: Over the past 30 years, management protocols for patients with abnormal cervical cytology and/or high-risk HPV (hrHPV) have been refined based on long term follow-up data and risk stratification. Colposcopic evaluation with directed biopsies aids in determination of the next steps in management. While high-grade squamous intraepithelial lesion (HSIL) can be confirmed with p16, diagnostic reproducibility in the biopsy diagnosis of low-grade squamous intraepithelial lesions (LSIL) is poor (reported kappa < 0.5 in numerous studies). LSIL may not require immediate treatment as over half of these lesions may regress spontaneously. Proper biopsy classification provides important clinical feedback regarding the colposcopic findings as well as risk stratification.

Design: Patients referred to a large academic institution for evaluation underwent colposcopically-directed cervical biopsies (2013-2017) and were diagnosed with benign changes or low-grade squamous intraepithelial lesion (LSIL). Cases with concurrent HSIL were excluded. Colposcopic appearance, referral cytology diagnoses, hrHPV screening, biopsy diagnoses, and clinical follow-up were recorded for 66 patients. HPV multiplex PCR-MassArray and L1 consensus PCR and sequencing were used to identify high and low risk HPV in the biopsy tissue.

Results: For this study, detection of HPV by multiplex PCR-MassArray in cervical biopsy specimens was considered the “ground truth.” Clinical hrHPV testing showed high sensitivity but poor specificity for presence of LSIL. Referral cervical cytology screening diagnoses of SIL showed the highest specificity and positive predictive value (PPV).

In patients who subsequently progressed to HSIL, hrHPV screening and abnormal cytology showed 100% sensitivity and 100% NPV. SIL cytology and SIL biopsy showed 71.4% sensitivity for detection of these high-risk patients, with respective specificities of 65.3% and 46.9%. SIL cytology had the highest PPV (22.7%) for this group.

	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)
hrHPV screening	**91.4**	33.3	72.7	**66.7**
Abnormal cytology	82.2	38.0	74.0	50.0
SIL cytology	48.9	**71.4**	**78.6**	39.5
SIL biopsy	57.8	52.4	72.2	36.7
Colposcopic SIL	75.6	38.0	72.3	42.1

Conclusions: These data suggest that while hrHPV screening is quite sensitive, cytology is a useful tool for diagnosis and stratification of SIL. Biopsy diagnosis of SIL has poor sensitivity and specificity for tissue with detectable HPV infection. Further studies may elucidate why cytology is superior to biopsy for prediction of HPV infection and progression to HSIL. In this regard, morphometric analysis and comparison to subjective scoring of the morphologic features of LSIL in these biopsies are ongoing.

1962 Bone marrow adequacy: Comparison of assisted versus unassisted bedside collections by a laboratory technologist

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Disclosures: Joo Song: None; Adam Cloe: None; Saba Ali: None; Parwiz Siaghani: None; Evan Himchak: None; David Cantu Duran: None; Wanda Chan: None; Elizabeth Quirk: None; Patricia Aoun: None

Background: In the past, bone marrow collections at the City of Hope were performed by a sole provider or operator (e.g. attending physician/fellow or physician assistant/nurse practitioner) without any bedside technical assistance. This left the operator to perform the core biopsy as well as perform aspirate smears and create clot/particle and touch imprints of the core biopsy during the procedure. At other institutions, there is typically a laboratory technologist there to assist in making the smears and touch imprints, as well as the clot/particle specimens and checking for adequacy of the specimen, which is important for morphologic evaluation by the hematopathologist. We hypothesized that having a technologists at the bedside will improve the quality of these specimens as well as improve clinical environment of this somewhat challenging and stressful procedure.

Design: We collected data from our hematopathology bone marrow reports comparing sequential cases that were unassisted (November 2016-December 2016) to cases that were assisted (November 2017-January 2018) by a laboratory technologist. We recorded the bone marrow parts (aspirate smears, touch imprints, core biopsy, and clot/particle sections) as adequate (score 2), suboptimal (score 1), or inadequate (0). Student T-test statistical analysis was performed between the parts of the two groups and p value of ≤ 0.05 was considered statistically significant.

Results: An equal number of bone marrow cases were compared between unassisted and assisted collections (211 for both groups, total 422 bone marrow cases). The quality of the assisted bone marrow cases was significantly better compared to unassisted cases for most specimen types (aspirate smears, touch imprints, and core biopsy) with the exception of the clot sections (see Table 1).

Table 1. Comparison of unassisted and assisted bone marrow collections

	Average Score		
Specimen type	**Unassisted (N=211)**	**Assisted (N=211)**	**P value**
Aspirate smears	1.4	1.7	<0.0001
Touch imprints	1.2	1.7	<0.0001
Core biopsy	1.6	1.8	0.0038
Clot/particle sections	1.5	1.3	0.0015
Score 2= adequate, 1= suboptimal, 0=inadequate			

Conclusions: Bone marrow collections that are assisted by a laboratory technologist are of better quality with the exception of clot/particle sections. For this study, there was a modification of the collection procedure which may have impacted the number of particles in the clot section, thus lowering the quality of this particular part type. However, the aspirate smears are one of the most important parts of the bone marrow specimen for the best morphologic assessment for disease. We conclude that a bone marrow technologist is necessary for high quality bone marrow collections and should be made available for all collections.

1963 The Continual Impact of the Paris System on Urine Cytology, a Three Year Experience

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Disclosures: Nicholas Stanzione: None; Tagreed Ahmed: None; Po Chu Fung: None; David Lu: None; Neda Moatamed: None

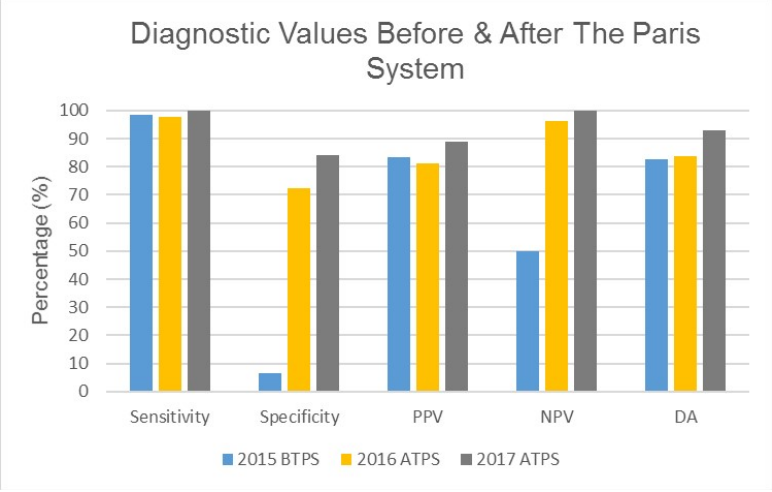
Background: The evaluation of urine cytology remains an important diagnostic tool in the diagnosis of urothelial carcinoma. The development of the Paris System (TPS) has provided a standard, reproducible, and accepted system for reporting urine cytopathology with a qualitative as well as semi-quantitative approach. Our goal was to study the impact of TPS on the diagnostic accuracy of urine cytology since we began using it in 2016.

Design: We performed a retrospective study of all urine cytology specimens received from January 2015 through July 2017. Cases were included in the study if they had a follow up biopsy to serve as the gold standard performed within 0-6 months of the cytology case. A total of 3829 cases were identified over this time period, with 381 cases meeting inclusion criteria, 87 cases from 2015, 166 from 2016 and 128 from 2017. Using the histopathology diagnoses as the gold standard, true positive, true negative, false positive, or false negative was assigned to each case, from which sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and diagnostic accuracy (DA) were calculated (Table 1).

Results: Before TPS (BTPS) urine cytology had a sensitivity of 98.6%, specificity of 6.7%, PPV of 83.5%, NPV of 50.0%, and DA of 82.8%. After The Paris System (ATPS), for the year 2016, the sensitivity was 97.7%, specificity of 72.2%, PPV of 81.3%, NPV of 96.3%, and the DA was 83.7%. For the year 2017 ATPS, the sensitivity was 100%, specificity of 84.21%, PPV of 88.75%, NPV of 100%, and the DA was 92.9%.

Table 1. Diagnostic Values of Urine Cytology Before & After The Paris System			
	2015	**2016**	**2017**
Sensitivity	98.61	97.75	100
Specificity	6.67	72.22	84.21
PPV	83.53	81.31	88.75
NPV	50.00	96.30	100.00
DA	82.76	83.73	92.97
All values reported as a percentage (%).			

Figure 1 - 1963



Conclusions: After switching to TPS, we observed a marked increase in the specificity and NPV, both of which have continued to gradually increase from 2016 to 2017. The DA also improved after switching to TPS, and demonstrated interval improvement from 2016 to 2017. These findings may be attributed to the more defined qualitative and quantitative diagnostic criteria set forth by TPS. The trend of improved results from 2016 to 2017 may reflect the pathologists continued adjustment to TPS over time due to increasing comfort with the system. Of note, there were only a few cases with negative urine cytology followed up with a biopsy in the year 2015; therefore, the low specificity may not be representative due to a small sample size. These results are supportive of TPS's ability to improve reliability and accuracy of the interpretation of urine cytology. Our study illustrate that TPS has continually improved the quality and DA of the reporting of urine cytology.

1964 Effects of Different Decalcification Agents of Variable Duration on PD-L1 Expression by Immunohistochemistry

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Disclosures: Amanda Strickland: None; Sara Blacketer: None; Kyle Molberg: None; John Markantonis: None; Elena Lucas: None

Background: Cancers may present as bone metastases requiring decalcification prior to testing for PD-L1 (programmed cell death ligand 1) expression by immunohistochemistry (IHC). However, data on PD-L1 expression on decalcified specimens is lacking. We evaluated the effects of various decalcifying agents on PD-L1 IHC 22C3 pharmDx (Dako).

Design: Fragments of 10 placentas (high PD-L1 expressor with membranous circumferential trophoblastic staining) fixed in 10% formalin for 24-48 hrs were subjected to 4 decalcifying solutions: EDTA (ACID FREE)™, formic acid-based decalcifier MasterCal™IM Plus (FA/MC), 12% hydrochloric acid (HCl) and Decal STAT (23% HCl) for 1, 2, 6, or 24 hrs. Tissue microarrays (TMA) using 3.5 mm tissue cores were made. For each case, cores from 17 sections were included (1 reference non-treated section and 16 sections from tissues decalcified for 4 different lengths of time with 4 different decal agents). H&E sections were performed on each microarray. The percentage of cells expressing PD-L1 was visually estimated. Staining intensity was reported from 0 to 4+ (absent to strong).

Results: No change in staining with EDTA or FA/MC was seen at 1, 2, 6, or 24 hrs by intensity or proportion of positively staining cells (PPSC). Of tissues decalcified with HCl, no change was observed in intensity or PPSC at 1 hr; 3/10 cases had intensity decrease (ID) from 4+ to 3+ and no drop in PPSC at 2 hrs; 5/10 had ID from 4+ to 2-3+ and no drop in PPSC at 6 hrs; 2/10 had ID from 4+ to 1-2+ and approximately 20% reduction in PPSC at 24 hrs. Of tissues decalcified with Decal STAT, 9/10 cases had ID from 4+ to 3+ and no drop in PPSC at 1 hr; all cases had ID from 4+ to 2-3+ and 2/10 had 10% decrease in PPSC at 2 hrs; all cases had ID from 4+ to 1-3+ and 2/10 cases had 5-30% drop in PPSC at 6 hrs; all cases had ID from 4+ to 0-1+ and 90% reduction in PPSC at 24 hrs.

Conclusions: EDTA and FA/MC do not affect PD-L1 expression in tissue with normally highPD-L1 expression while HCl reduces the intensity of staining at 2, 6 and 24 hrs with a drop in number of positive staining cells at 24 hrs. Decal STAT affects PD-L1 expression by both progressively reducing the proportion of positive cells and decreasing the intensity of staining at all time points, most notable at 24 hrs.

1965 Manual Estimation of Tumor Purity is Poor Compared to Sequencing Based Estimates, Especially with Low Tumor Fraction

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Disclosures: Sherry Tang: None; Mahmut Akgul: None; Taebeom Kim: None; Ken Chen: None; Fang Wang: None; Kanishka Sircar: None

Background: In clinical practice, targeted next generation sequencing usually requires a minimum of 20% viable tumor fraction in the samples. Prior to sequencing, the qualitative and quantitative assessment of the sample is manually performed by the pathologist who selects the viable tumor-rich regions (TRRs) in H&E stained slides and estimates the tumor percentage in the annotated area. Inaccurate manual estimation may increase the risk of unnecessary sequencing, particularly due to over-estimation of low-level tumor fraction. The aim of this study is to evaluate the concordance between manual interpretation and a sequencing-based indicator of tumor fraction in advanced therapy resistant renal cell carcinoma (RCC) cases.

Design: Thirty-seven cases of aggressive RCC (clear cell, n=22; chromophobe, n=10; papillary, n=4; unclassified, n=1, including n=31 cases with sarcomatoid features) were selected. Representative sections of each tumor were selected and TRRs were annotated and digitized (Aperio AT2, Leica Biosystems Imaging Inc, Buffalo, IL). Three pathologists (ST, MA, KS) individually and blindly estimated tumor-fractions on TRRs of each case using whole slide images. TRRs were used for DNA extraction prior to whole exome and targeted sequencing (HiSeq2000/3000, Illumina, San Diego, CA). Subsequently, sequencing data of each case were migrated to a pipeline (Texomer) that reports sequence-based tumor estimate (SBTE).

SBTE was considered the reference or gold standard and cases were separated into three groups in terms of SBTE (0-24%; 25%-49%; 50%-75%). The correlation between pathologist tumor purity estimate and the SBTE was compared using the concordance coefficient (CC). Comparison of CC between manual estimations and SBTE between three groups were performed using student t-test.

Results: The concordance between pathologist tumor purity estimate and SBTE was low in all groups (CC range, 0.14 – 0.23 overall (n=37); see Table-1 for details). However, there was significantly greater discordance on the low SBTE (0-24%) group compared to the remaining cases (25-75%, p=0.01) (Figure 1.1 and 1.2).

Tumor purity (number of cases)	Manual estimation by pathologists			SBTE (Reference)
	MA	ST	KS	
0-24% (18)	0.01	0.01	0.02	1
25-49% (8)	0.23	0.01	0.3	1
50-75% (11)	0.18	0.39	0.4	1
Overall	0.23	0.14	0.15	1

Table 1: Concordance coefficients between manual estimation of tumor purity and sequence based tumor estimation (SBTE)

Figure 1 - 1965

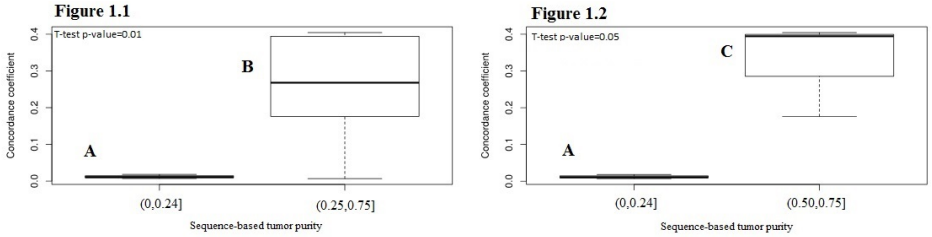

Figure 1.1 and Figure 1.2: Boxplots showing concordance coefficient comparison between manual and sequence-based estimation between different levels of sequence-based tumor purity. A= concordance coefficients in group with 0-24% tumor purity; B= concordance coefficients in group with 25-75% tumor purity; C= concordance coefficients in group with 50-75% tumor purity.

Conclusions: Our results suggest that manual estimation of tumor fraction performs particularly poorly in low tumor purity samples which may lead to suboptimal and cost ineffective sequencing in a clinical setting.

1966 Real-Time Intraoperative Consultation (IOC) Reporting in the Electronic Health Records (EHR) Reduces, But Does Not Eliminate Miscommunication

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Disclosures: Maryna Tarbunova: None; Mahmoud Khalifa: None

Background: An earlier review at our institution uncovered significant discrepancies between the pathologist's IOC as communicated by telephone or in person, and the surgeon's documentation in the operative note. Published reviews from other institutions have shown similar discrepancies. Accordingly, we elected to implement real-time IOC reporting in the EHR. In October 2016, we began reporting IOC results in the EHR so that they would be immediately accessible to the clinical team, in addition to standard verbal reports directly to the surgeon. We then performed an audit of charts before and after implementation, to show the effects and benefits of this newly-adopted workflow.

Design: We extracted 150 consecutive cases each from the first year pre-implementation, the first year post-implementation (post-yr1) and the second year post-implementation (post-yr2). We compared the IOC as recorded by the pathologist in the EHR to the surgeon or house staff's dictated operative note and categorized discrepancies when present. We excluded cases which did not have surgeon's interpretation of the IOC in operative notes.

Results: As shown in Table 1, the total number of discrepancies dropped from 12/150 in the pre-implementation era to 6/150 and 7/150 in post-yr1 and post-yr2 respectively. Discrepancies attributed to vague diagnostic language in the pathologist's IOC decreased as a proportion of identified discrepancies post- implementation (from 50% to 17% post-yr1 and 14% post-yr2). We identified a similar trend for discrepancies attributable to evidently erroneous surgeon's operative note (from 25% to 17% post-yr1 and 19% post-yr2). Interestingly, we noted a relative increase in discrepancies due to the inclusion of additional pathology-specific terminology in the surgeon's note but not documented in the IOC report (from 25% to 67% post-yr1 and 57% post-yr2). Nearly all identified discrepancies (24/25) resulted in only minor clinical impact.

Table 1. Type of Discrepancy between IOC diagnosis and Operative Note

	Vague IOC Diagnosis	Evidently erroneous Operative Note	Terminology included in Operative Note but not IOC	TOTAL
Pre-implementation (n=150)	6 (50%)	3 (25%)	3 (25%)	12 (100%)
Post-yr1 (n=150)	1 (17%)	1 (17%)	4 (67%)	6 (100%)
Post-yr2 (n=150)	1 (14%)	2 (19%)	4 (57%)	7 (100%)
TOTAL	8	6	11	25

Conclusions: Real-time documentation of IOC results in the EHR reduces intraoperative miscommunication due to pathologists' use of vague diagnoses and improves the documentation by the surgeon in the operative note. However, we noted persistent and even increased discrepancies seemingly related to less formal, back and forth intraoperative discussion between the pathologist and surgeon but not documented in pathologist's IOC. These lessons learned will help us to most effectively communicate our frozen section diagnoses, with the ultimate goal of optimizing patient care.

1967 The Morphology of Fixation Artefacts

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Disclosures: Dominique Trudel: None; Nazim Benzerdjeb: None; Francis Rodier: None

Background: Based on empirical experience, pathologists can usually identify the artifacts associated with pre-analytic issues. However, the effects of the different phases of the pre-analytic process have not been systematically evaluated. We here tested the effect of fixation on the histological appearance of tissue.

Design: Tissues from xenografts of the ovarian cancer cell line TOV112D were processed in several fixation conditions (fixative, duration of formalin fixation, delayed time to formalin fixation, with or without saline solution at room temperature or at 4°C). Each condition was tested in six pieces of xenograft tumor before circulation and paraffin-embedding. Three cores per specimen were then included in a tissue microarray (TMA). Cores were evaluated independently by two pathologists without knowledge of fixation conditions, according to the following scale: 0 = standard, 1 = inconspicuous changes, 2 = cell retraction, 3 = ballooning changes, 4 = necrosis (Figure 1). Descriptive statistics were performed.

Results: Interobserver agreement was found to be strong (k=0.611). The three tested fixative did not significantly impact cell morphology. A score of 0 or 1 were observed with up to 2 hours of delayed fixation (room temperature) and with 6h to 1 week of fixation in paraformaldehyde (Figure 2). A score 2 was observed when the fixation was delayed for 24 hours, whether at room temperature but in a physiological saline solution or at 4C without the saline solution. Scores 3 and 4 were observed only when fixation was delayed at room temperature, even if only for two hours.

Figure 1 - 1967

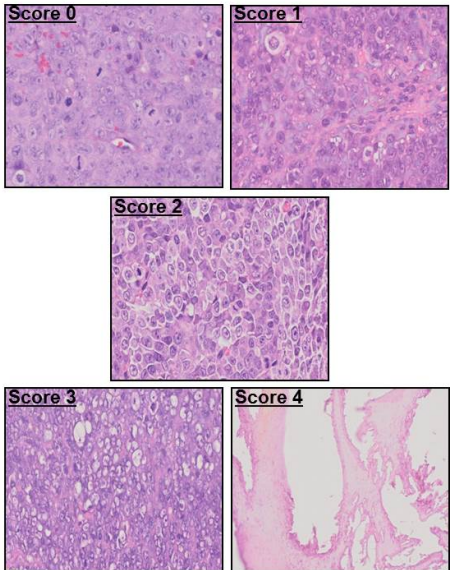
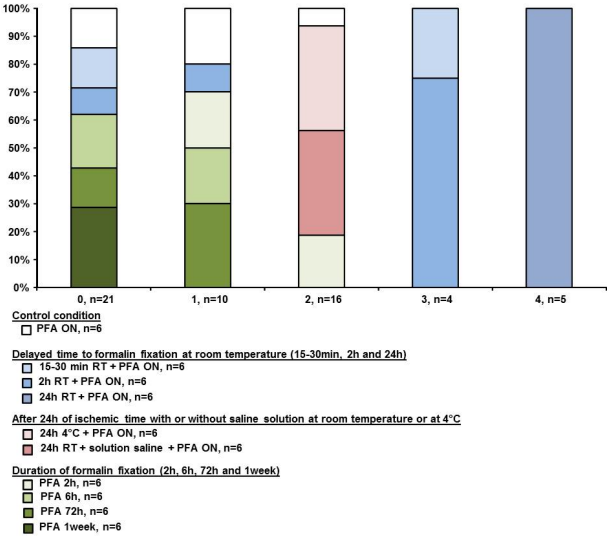


Figure 2 - 1967



Conclusions: As the significance of our results needs to be validated in other tissue types, we here show that the observation of morphology can provide insight on fixation variables for a given tissue. Delayed fixation can be associated with minimal or drastic morphological changes. If delayed fixation cannot be avoided, the morphology will be of better quality if performed indifferently at 4C or in a saline solution at room temperature.

1968 Evaluation of Cytologic-Histologic Discordance Rates in Anal Dysplasia and Cancer Screening

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Disclosures: Kent Truong: None; Rita Ung: None; Poonam Vohra: None; Joshua Menke: None; Dianna Ng: None

Background: While data regarding the cytologic-histologic correlations in cervical cancer screening are well-established, these data for anal squamous intraepithelial lesion screening are not as thoroughly evaluated. The purpose of this study is to investigate the rate of

discordant diagnoses between concurrently obtained anal Papanicolaou (Pap) tests and anal biopsies and additionally to identify any cytomorphologic features that may improve classification.

Design: We retrospectively reviewed all reports of anal Pap tests and biopsies that were concurrently collected at our institution from 1/2016 to 12/2017. Discordant cases were defined by a diagnosis of negative for intraepithelial lesion/malignancy (NILM) on Pap but with low grade squamous intraepithelial lesion (LSIL) or high grade squamous intraepithelial lesion (HSIL) on biopsy or vice versa. To confirm the cytologic diagnoses, 2 cytopathologists reviewed slides from all discordant cases and additionally from cases with cytologic diagnoses of atypical squamous cells of undetermined significance (ASCUS) and corresponding biopsy diagnoses of HSIL, while blinded. The cytomorphologic features of the Pap tests from these 2 groups were reviewed and compared.

Results: A total of 51 concurrently collected anal Pap tests and biopsies were identified. Five cases had discordant diagnoses (10% discordance rate). Four of the discordant cases were reported as ASCUS on Pap and benign on anal biopsy. The remaining discordant case was reported as NILM on Pap, but HSIL on biopsy. Slides from 4 discordant cases reported as ASCUS with benign biopsy results were compared against 7 ASCUS cases with HSIL diagnosis on biopsy. We found no significant difference in the cytomorphologic features in these groups (Table 1).

Figure 1 - 1968

Table 1: Comparison of cytomorphologic features of ASCUS anal Pap tests with benign biopsy results versus ASCUS anal Pap tests with HSIL biopsy results.

	Pap Diagnosis	ASCUS	
	Biopsy Diagnosis	Benign	HSIL
Cytomorphologic Features	Parakeratosis	1/4 (25%)	1/7 (14%)
	Nuclear enlargement	3/4 (75%)	7/7 (100%)
	Hyperchromasia	3/4 (75%)	6/7 (86%)
	Binucleation	1/4 (25%)	4/7 (57%)
	Koilocytic change	1/4 (25%)	1/7 (14%)
	Basaloid cells	0/4 (0%)	3/7 (43%)
	Rectal columnar cells	3/4 (75%)	7/7 (100%)
	Poor preservation	1/4 (25%)	1/7 (14%)

Conclusions: We found a 10% discordance rate in concurrently obtained anal Pap tests and anal biopsies over a 2-year period. We did not identify any distinguishing cytomorphologic features between ASCUS diagnoses with concurrent benign versus HSIL biopsy results. Additional studies are needed to identify specific cytomorphologic features and to evaluate the role of human papilloma virus testing to improve the sensitivity and specificity of anal cytology screening.

1969 Is Immunohistochemistry Over-Utilized in Detection of CMV in Cases Suspected of CMV Colitis? A Retrospective Correlational Study

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Disclosures: Kai Wang: None; Jessica Tracht: None; Upender Manne: None; Isam-Eldin Eltoum: None; Rongjun Guo: None

Background: Confirming CMV presence in colon of patients suspected of having CMV colitis is important for guiding appropriate available treatment. However, there is a concern of overutilization of CMV immunohistochemistry (IHC). This project aims to assess if there is overutilization of IHC for detection of CMV-related colitis.

Design: Our database was retrospectively searched for all reports of CMV IHC performed in cases suspected of CMV colitis in the period 01/01/2014 to 06/30/2018. In our practice, we order CMV IHC when clinicians requested it. The surgical pathology report was reviewed and the presence of CMV was confirmed independently by two pathologists on H&E and IHC slides. Correlation with viral load was performed.

Results: IHC for CMV were performed on 175 cases, 18 (10.3%) cases were positive. Of these, 17 (94.4%) had active colitis. None of these 18 cases were diagnosed on the original H&E with certainty. On re-review of the H&E, CMV infection cytopathic features were identified in 9/18 (50%) cases, equivocal in four cases (22%), and not identified in five cases (28%). CMV viral load was performed in eight of the eighteen CMV IHC positive cases. Six (75%) were detected as positive in the serum and two were negative; one of these negative cases showed colitis and CMV changes on H&E. The other case showed patchy active cryptitis, but no CMV cytopathic features. On H&E, CMV changes were identified in all cases with high viral load. Among the 157 CMV IHC negative cases (89.7%), CMV viral load was performed in 34 cases, 32 (91.4%) were negative and the remaining, 2, had high viral load (Table). The sensitivity and specificity of serum viral load of detection of CMV colitis is 75% and 94%, respectively. Overall, two cases would have been missed by both histology and viral load, and 9 cases would have been missed by histology.

Table 1: Agreement between serum viral load for detection of CMV colitis and immunostain for detection of CMV infection in colon

Viral Load	Immunostains		
	Positive	Negative	Total
Positive	6 (75%)	2 (25%)	8
Negative	2 (6%)	32 (94%)	34
Total	8 (100%)	34(100%)	42

Conclusions: Significant number, ~10%, of CMV colitis is missed if CMV IHC is not performed. 90% of cases positive for IHC show evidence of active colitis [~5% unconfirmed on H&E and 5% true negative]. CMV viral load is not substitute for CMV IHC. This data supports the use of routine IHC for CMV when CMV colitis is expected.

1970 Comparison of Core Biopsy and Resection Specimen Diagnoses of Bone Lesions at a Musculoskeletal Tumor Center

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Disclosures: Laura Warmke: None; Jeanne Meis: None

Background: The initial evaluation of bone lesions usually entails core biopsy. We analyzed the histologic diagnoses of bone resection specimens from a major musculoskeletal tumor center and compared them with the prior core biopsy diagnoses. The intent was to determine how often there was a clinically significant discrepancy between the resection and the core biopsy diagnoses of primary bone tumors.

Design: The pathology database was searched for all bone resection specimens within the last academic year. A total of 315 bone resection specimens were identified, including 113 (36%) primary bone lesions, 126 (40%) metastases and 76 (24%) non-neoplastic lesions. All corresponding core needle biopsy diagnoses were tabulated.

Results: Among primary bone tumors, the most common diagnoses were osteosarcoma (14), plasma cell neoplasm (12), chordoma (12), chondrosarcoma (12), enchondroma (8), osteochondroma (8), giant cell tumor (7), and Ewing sarcoma (7). Of these 113, 41 (36%) did not have a prior core biopsy; 59 (52%) had one prior biopsy; and 13 (12%) had two prior biopsies. A final diagnosis was rendered in 81% of core biopsies, and the remainder were diagnosed on resection. On resection, 3 chondrosarcomas were upgraded, and a high grade spindle cell sarcoma was revised to high grade osteosarcoma. There were 3 significant discrepancies (5%) between the core biopsy and resection diagnoses, including a change from atypical cartilaginous lesion to chondroblastic osteosarcoma; high grade chondroblastic osteosarcoma to high grade chondrosarcoma (confirmed *IDH2* mutation); and an unclassified chondromyxoid lesion to chondrosarcoma (confirmed *IDH1* mutation). Among the 126 metastases to bone, the most common primary sites (>75%) were renal (29%), lung (21%), breast (17%), and sarcoma (9%).

Conclusions: (1) Metastases accounted for the largest proportion of tumors involving bone resections at our center. (2) Core biopsies were adequate to establish a definitive diagnosis in 80% of primary bone tumors. (3) A clinically significant discrepancy between biopsy and resection diagnoses occurred in 5% of primary bone tumors. (4) The distinction between chondroblastic osteosarcoma and high-grade chondrosarcoma may be problematic on core biopsies. (5) Mutation testing is very useful in selected cases. (6) Due to limited biopsy sampling, high-grade tumor and osteoid may not be represented.

1971 Significant Improvement of Diagnosis by Remote Digital Consultation in Japan

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Background: Consultation by subspecialty experts is the most common mode of rendering challenging diagnostic cases in pathology practice. However, there is no insurance coverage of remote consultation inside Japan mostly due to lack of evidence to prove the diagnostic efficiency. Recent development of the whole-slide imaging (WSI) has facilitated remote consultation. The aim of our study is to clarify the diagnostic benefits of WSI-based remote consultation in the local settings.

Design: We enrolled diagnostically challenging cases from the database of two institutions during the last two years. Cases with the final histological diagnoses contained keywords “probable”, “suggestive”, “suspicious”, or “difficult” were retrieved from the medical records. Out of eligible 1018 cases, 270 were selected (30 cases in each of 9 subspecialty categories). All selected WSI images along with clinical data were distributed to 12 subspecialty experts in DMZ server. When the original and consultation diagnoses were discordant, additional opinion was sorted from other 12 subspecialty experts. For cases where definite diagnosis was not rendered after that, the consensus diagnosis was given by six senior pathologists.

Results: The first consultation for challenging cases yielded 43% concordance, and a change of diagnosis was done in majority of cases. The most frequent change was making a definite diagnosis and removal of uncertainty from the diagnostic line (30%). Major discordance, which would require changes in treatment strategy, was found in 15% of cases, while a minor discordance not altering treatment was recorded in 12% of cases. (Fig.1A)

Cases with discordant diagnosis were further submitted to the second consultation, and the experts changed a diagnosis in 53% of cases. Finally, consensus diagnosis on discordant cases was entertained, and 83% of 1st consultants’ diagnosis, 3% of second consultants’ diagnosis, and 11% of original uncertain diagnosis were considered as favorable diagnosis, respectively. Nevertheless, 3% of cases have not met consensus diagnosis even after the discussion. (Fig.1B) Eventually, 89% of diagnoses in discordant cases, that is 27% of all, were changed from the original diagnosis.

Figure 1 - 1971

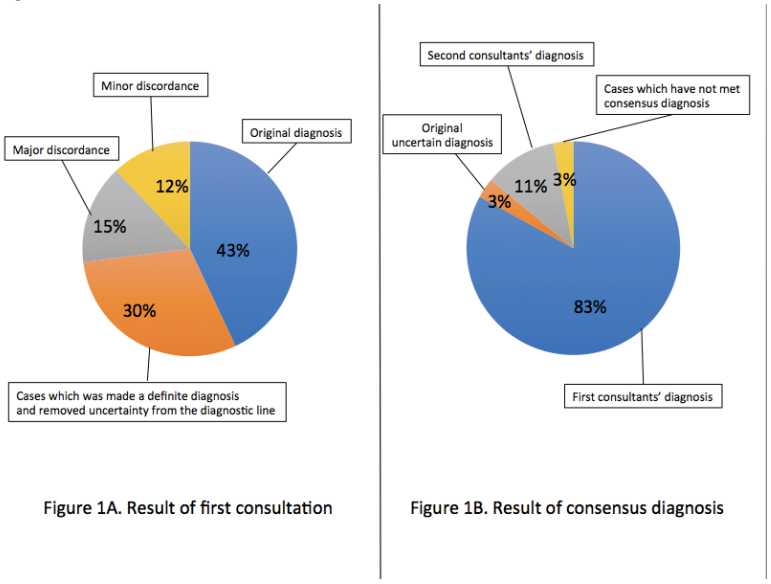

Figure 1A. Result of first consultation

Figure 1B. Result of consensus diagnosis

Conclusions: This is a first study to clarify the diagnostic improvement by remote digital consultation in collaboration with a number of experts. WSI-based digital consultation is useful and critical as it changed the majority of histopathological diagnoses in challenging cases.

1972 Role of Cytokeratin Immunostains in Assessing Sentinel Lymph Node Metastasis in Lobular Breast Carcinoma

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Background: The assessment of metastatic lobular carcinoma in lymph nodes can be difficult on H&E stained slides prompting many to use cytokeratin (CK) immunohistochemistry (IHC), particularly to find minimal disease. Many clinical trials have demonstrated that minimal lymph node involvement (isolated tumor cells (ITC) and micrometastases) does not affect clinical outcomes. In the context of evolving national consensus, we reviewed our sentinel lymph node (SLN) data to assess the role of CK IHC in evaluating SLNs in invasive lobular carcinoma (ILC) of the breast and its effect on patient clinical management and outcomes at our institution.

Design: Initial retrospective review was performed using PowerPath case query for ILC with accompanying SLN excisions from 2008-2018. Clinical information including stage (T and N categories), total number of lymph nodes, size of metastatic deposit, status of CK IHC, and the results of subsequent axillary dissections was also collected. The proportion of ILC cases which were upstaged or for which clinical management was changed due to CK SLN IHC results was determined.

Results: A total of 313 cases of ILC with SLN excisions were reviewed. 264 (84%) of those had SLN CK IHC performed. 81 (30.6%) CK stained SLNs were positive as follows: isolated tumor cells in 47 (18%), micrometastases in 20 (7.6%), and macrometastases in 14 (5.3%). Only one case (0.2%) had macrometastatic involvement not visualized on H&E. 14 of the 81 (17.3%) CK-positive cases underwent subsequent axillary dissection. 4 of the axillary dissections demonstrated additional positive nodes (> ITC involvement). All cases with positive nodes within the axillary dissection had previous SLNs with macrometastases. 27 cases (10%) had CK performed on additional SLNs despite already having visualized involvement by H&E.

Conclusions: While the majority of cases with positive CK IHC revealed only ITC involvement (18%), 13% of cases were upstaged by CK IHC in SLNs. A majority of upstaged cases revealed micrometastatic involvement and subsequent axillary dissection was not performed. Of cases with macrometastases, only a single case was not visualized on H&E. Additionally, 10% of cases had CK performed despite visualized involvement by H&E, resulting in no change in staging or management. At our institution CK IHC contributes primarily to detecting minimal lymph node involvement for which axillary dissection is not indicated.

1973 The Clinical Benefit of Pathologic Review of Genomic-Directed Specimens and Lessons Learned from Discrepant Cases

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Disclosures: Rumeal Whaley: None; Rachel Rominger: None; Milan Radovich: None; Patrick Kiel: None; Bryan Schneider: None; Liang Cheng: None

Background: Pathologic review of genomic-directed specimens is an integral component of any precision genomics program. The evaluation of tumors is increasingly becoming an integrated diagnosis based on the histologic and molecular characteristics. Thus, genomic-directed specimens are becoming increasingly commonplace. This increase has revealed occasional discrepant cases. We aim to assess the incidence and frequency of discrepant diagnoses in genomic-directed specimens.

Design: Discrepancies were identified as a new primary malignancy, a modification of tumor sub-classification, or determining the origin of cancers in patients with unknown primaries. We sought to assess the rate of these occurrences since the inception of the Indiana University Health Precision Genomics Program. Patients with metastatic refractory solid tumors, progression on at least one line of standard therapy, or rare solid tumors were referred to Indiana University Health Precision Genomics Program. Next-generation sequencing data, clinical histories, and tumor samples for these patients were compiled and retrospectively analyzed.

Results: Of the 393 patients referred, 381 patients had their tumors sequenced. The tumor types spanned a wide range. The most common tumors were pancreatic carcinomas (11.3%), soft tissue sarcomas (10.8%), breast carcinomas (10.3%), and colorectal carcinomas (10.1%). Fifteen (3.9%) diagnoses were discrepant from the historical diagnosis. Five of these discrepancies were revealed as part of routine pathologic review prior to molecular processing. Ten discrepancies were revealed after molecular aberrations were identified by NGS. These diagnostic revisions were due to either specific mutations that were identified in the tumor or ambiguous cases that were resolved with additional molecular information.

Conclusions: Our study emphasizes the impact of pathologic review of genomic-directed specimens in a variety of tumor types. Diagnostic discrepancies occur at a surprisingly high frequency in genomic-directed samples (3.9%).

1974 Is Use of Cancer Protocol Templates (CAP Synoptics Reports) Associated with Improved Cancer Patient Survival? An Exploratory Ecological Study Using Data from the Surveillance, Epidemiology, and End Results (SEER) Program and Public Searching Engines

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Background: College of American Pathologists (CAP) developed structured checklists for cancer reporting (Cancer Protocol Templates, CAP synoptics), which were mandated in 2004. The effectiveness of CAP synoptic in ensuring pathology reports accurate and complete has been proved. However, their impact on patient survival has not been examined.

Design: Our aim was to investigate the correlation between CAP synoptic reporting compliance and patient outcomes. Since no compliance rate data are available at an individual patient level, ecological study was the best design (Rothman:Modern Epidemiology,chap25). Study unit was annual diagnosed patients with solid malignancy from SEER database between 2001-2011. Exposure was CAP synoptic reporting compliance rate. Annual ACS CoC commendation rate was used as proxy of exposure, which required:1)scientifically validated data elements(*SVDE*) included in 90% of pathology reports; 2)SVDE in CAP synoptic format. We obtained 2004–2008 ACS CoC commendation rate from the 2010 CoC survey. A CAP Q-Probe study reported that standard pathology report was used in 20.8% resected primary lung carcinomas in 1996(Idowu, 2010). This number denoted synoptic usage in 2003. Outcome was measured by Kaplan-Meier survival curve. Conditional multivariate adjustment of age, sex, race, tumor location, histology type, grade and stage on survival curve was performed to control background risk (Therneau,2015). Linear correlation was used. Bias of chronological survival improvement was analyzed with solid cancer patients unexposed to CAP synoptics (no standard pathology diagnosis). R3.2.2 was used.

Results: 1718533 patients exposed to CAP synoptics. CAP synoptic compliance rate was 20.8%, 21%, 42%, 35%, 36% and 59% in 2003-2008(Tab1). Improvement was observed in unadjusted and adjusted survival curves with the increase of compliance rate (Fig1A). Annual survival rate was showed in Tab1. Strong correlations between survival rate at 10^{th} and 50^{th} month vs. CAP synoptic compliance rate were observed (correlation coefficients:0.84 and 0.79; R^2:0.70 and 0.62, respectively.Fig2). 4861 patients did not have standard pathological diagnosis (unexposed to CAP synoptics). No chronological improvement was observed (Fig1B,Tab1).

Table 1: Proxy of annual CAP synoptic compliance rate and survival rates at 10th and 50th months of solid cancer patient who had or had not standard pathology reports diagnosed in each year.

Year of diagnosis	Proxy of CAP synoptics compliance rate	Patients exposed to CAP synoptics report		Patients unexposed to CAP synoptics report	
		10th month Survival Rate	50th month Survival Rate	10th month Survival Rate	50thmonth Survival Rate
2003	20.80%	92.81%	75.21%	88.46%	53.85%
2004	21.00%	93.03%	75.71%	86.67%	46.67%
2005	42.00%	93.27%	76.14%	N.A.*	N.A.*
2006	35.00%	93.30%	76.31%	90.91%	54.55%
2007	36.00%	93.55%	76.92%	91.67%	68.75%
2008	59.00%	93.60%	76.89%	77.14%	61.43%

*Data not available because conditional multivariate adjustment requires baseline characteristics must be identical to the reference group. In this group, no reference group data with identical baseline characteristics was available.

Figure 1 - 1974

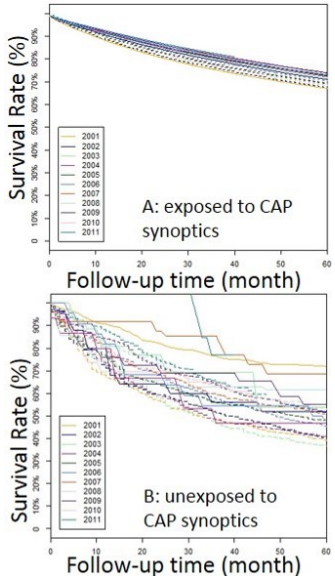
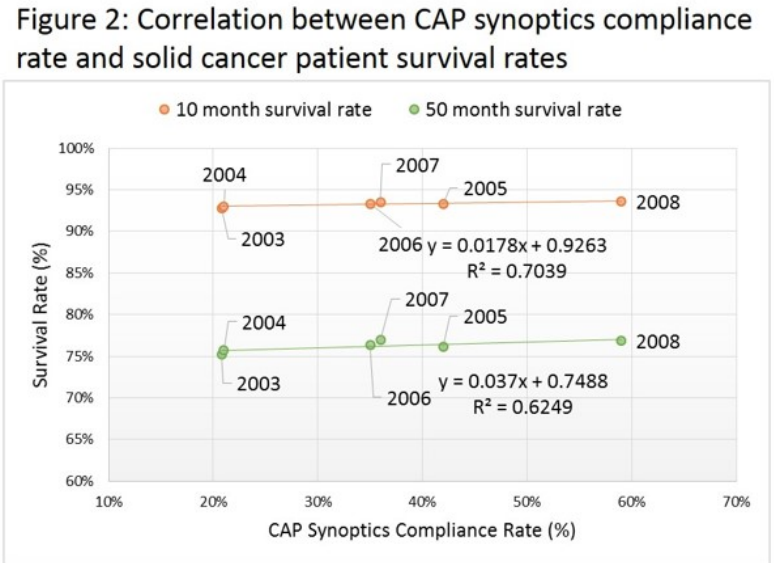


Figure 1: Unadjusted and adjusted Kaplan-Meier survival curves of patients diagnosed in different years. Dotted line: unadjusted survival curve; Solid line: adjusted survival curve.

Figure 2 - 1974



Conclusions: With the increase of CAP synoptic compliance, solid cancer patient survival improved. Patient survival rate showed strong correlation with CAP synoptic compliance rate. This ecological study demonstrated CAP synoptics had positive impact on solid cancer patient survival.

1975 Conditions associated with the need of more needle passes in thyroid fine needle aspiration

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Disclosures: Ramin Zargham: None; Allison Ciolino: None; Scott Anderson: None

Background: Assessment of specimen adequacy is considered the most important part of the rapid on site evaluation of thyroid nodules. The dilemma of having an inadequate specimen leads to the request of more needle passes. However, each pass can induce significant pain and increased risk of hematoma. In order to minimize the number of required passes while not compromising the adequacy of the specimen we aimed to identify conditions in which there is an increased number of needle passes.

Design: A retrospective quality review of ultrasound guided thyroid FNAs was performed between June 2018- till September 2018 at the University of Vermont Medical Center. Patient demographics, nodule characteristics, procedural technique, cytologic diagnosis, number of passes and size of the needles were recorded. The minimal numbers of passes performed by radiologists at our institution are 3 passes. Age and sex-matched patients were divided into two groups of less than 3 passes and more than 3 passes.

Results: Our study controlled for level of expertise and procedural technique so that we were able to investigate other variables. All procedures were performed by a board-certified radiologist and all rapid on-site evaluations were completed by a cytopathologists. The sizes of the needles were the same for all cases. Diagnostic results were obtained from rapid on –site evaluation reports. In cases with only

3 passes, 86% had a benign diagnosis while 14% were atypical/suspicious or malignant. In cases with more than 3 passes, 40% were benign versus 60% atypical/suspicious or malignant. In addition, just 43 % of the 3 pass group had a nodule size of more than 2 cm while 80% of the other group had nodules of more than 2 cm. Statistical analysis showed the obtained data on nodule size and diagnosis were both significant with a p-value of <0.05.

Conclusions: Our data shows that in situations where the operators and pathologists have equal level of experience, the request for additional passes is seen more frequently when the size of the nodule is bigger and the nodules have a cytologic diagnosis of atypical/suspicious or malignant. While the exact cause and effect relationship of these two factors is currently not understood, our speculation is that the larger nodules might have more cystic areas requiring more passes to meet adequacy. We are currently in the process of increasing our data set to verify the aforementioned factors and help improve patient care and overall satisfaction with ultrasound guided thyroid FNAs.

1976 The Reduction of Atypia of Undetermined Significance (AUS)/Follicular Lesion of Undetermined Significance (FLUS) Rate by Quality Assurance Measures and Their Financial Impact

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Disclosures: Bin Zhang: None; Fan Lin: None; Renee Frank: None; Haiyan Liu: None

Background: The "indeterminate" category of AUS/FLUS is reserved for cases with a lesser degree of cytological and/or architectural atypia that is insufficient to qualify for suspicious or neoplasm categories. The rate of AUS/FLUS is recommended at 7-10% by the Bethesda System for Reporting Thyroid Cytopathology. A higher rate of 14.42% in 2017 was noticed in our laboratory. The aim of the study is to evaluate the effectiveness of quality assurance measures in reducing the rate of AUS/FLUS, and in savings economically.

Design: When noticing a higher rate of 14.42% (228/1581) for AUS/FLUS in 2017, quality assurance measures were immediately implemented starting January 2018 to include: 1. Monitoring the AUS/FLUS rate for each cytopathologist; 2. Mandatory peer review for AUS/FLUS cases before signing out; 3. Discussing progress at monthly cytology best practice meeting. The AUS/FLUS rate for 2018 (8 months) was evaluated. To assess the financial impact, all thyroid AUS/FLUS cases and their follow ups for 2017 were retrieved from CoPath data base, analyzed and calculated.

Results: All thyroid FNA cases in 2017 and 1st 8 months of 2018 are summarized in Table 1. The AUS/FLUS rates are 14.42% (228/1581) in 2017 and 9.59% (110/1147) in 1st 8 months of 2018. Since the implementation of quality assurance measures, the AUS/FLUS rate has decreased by 33.5% (14.42%-9.59%/14.42% in 2017), with a AUS/FLUS: malignant ratio of 2.75 (110/40, 2018), along with a 10.7% increase of benign rate (70.88%-64.01%/64.01% in 2017). All other categories were relatively unchanged. All 228 AUS/FLUS cases in 2017 were sent for molecular test ($1,250/each). A total of 109 follow-ups in 96 patients in 2017 include 19 repeat FNA ($5,250/each), 47 lobectomy ($65,900/each), 41 thyroidectomy ($70,500/each) and 2 parathyroidectomy ($88,400/each). The overall expense for AUS/FLUS cases in 2017 was $6,549,350. The 33.5% reduction of AUS/FLUS rate is projected to save healthcare expense of $2,193,714 annually.

Table 1. Summary of Thyroid FNA Cases in 2017 and 1st 8 Months of 2018

Year/Category	Non-Diag. (%)	Benign (%)	AUS/FLUS (%)	Other Indeterminate (%)	Suspicious (%)	Malignant (%)
2017 (Jan –Dec) (n=1581)	201 (12.71)	1012 (64.01)	228 (14.42)	63 (3.98)	23 (1.45)	54 (3.42)
2018 (Jan – Aug) (n=1147)	131 (11.42)	813 (70.88)	110 (9.59)	31 (2.70)	22 (1.92)	40 (3.49)

Conclusions: Our data indicate that quality assurance measures are effective in reducing the rate of AUS/FLUS category (33.5% in our study), meanwhile, increasing the rate of benign category (10.7% in our study). The lower rate of AUS/FLUS category resulted in better patient care by eliminating unnecessaary procedures and saving millions of healthcare expense.

1977 Variations of Atypical Cytologic Diagnostic Category of EUS-FNA of the Pancreas: Trends overtime and the Impact of Change in Staff

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Disclosures: Yiqin Zuo: None; Jessica Tracht: None; Isam-Eldin Eltoum: None

Background: In a previous meta-analysis, we reported inter-institutional variations of Atypical Cytologic Diagnostic Category (ACDC) of pancreatic EUS-FNAs of 1-14% with an associated risk of malignancy (ROM) of 25-100%. The objective of this study is to assess the intra-institutional variations of these rates with changing staff over an 18 year period in a high volume EUS-FNA center.

Design: 18 years of pancreatic EUS-FNAs were retrospectively analyzed and divided into diagnostic categories (unsatisfactory (UN), negative for neoplasm (NEG), ACDC, suspicious (SUS) and positive for neoplasm (POS)). With a focus on ACDC, these cases were stratified according to the performing endoscopist and reviewing pathologist. Trend of annual rates was assessed using quality control chart (QCC) and variations between pathologists and endoscopists were compared using coefficient of variation (CV) modified signed-likelihood ratio. Spearman correlation coefficient (R) was used to assess relation between atypical rates and the other diagnostic categories. Results were considered significant at $p < .05$.

Results: During the study period a total of 5339 (304 per year) pancreatic EUS-FNAs were performed with an average rate of 8.1% ACDC, 1% UN, 2.6% SUS and 62% POS. ACDC varied from 3.6-13.7% with a significant trend upwards in the last two years, Figure 1. There were six endoscopists (average employment 7.1 (3.1 SD) years) and 11 pathologists (average employment 8.2 (5.7 SD) years) over the study period. Among endoscopists, ACDC varied from 5.9-13% with CV of 0.26; Pathologists varied from 3.7-13.6% with CV of 0.39. Among endoscopists, ACDC rate correlated negatively with POS rates. For pathologists it correlated positively with SUS rates and negatively with POS rates ($p<.05$), Figure 2. Of 103 with histologic follow-up, ROM varied from 0-100% with an average of 31% (29 SD) among pathologists and 0-64% with an average of 31% among endoscopists. There was no correlation between ROM and ACDC.

Figure 1 - 1977

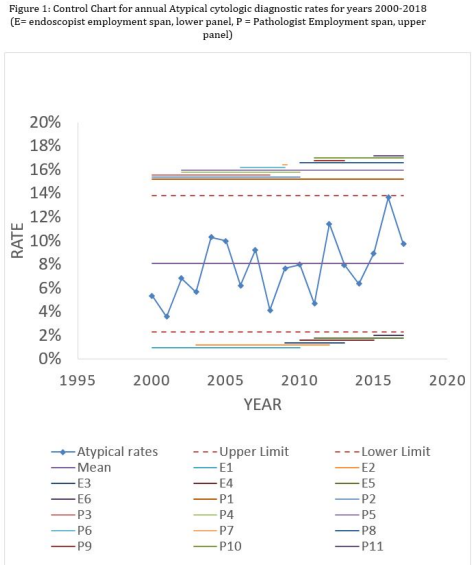
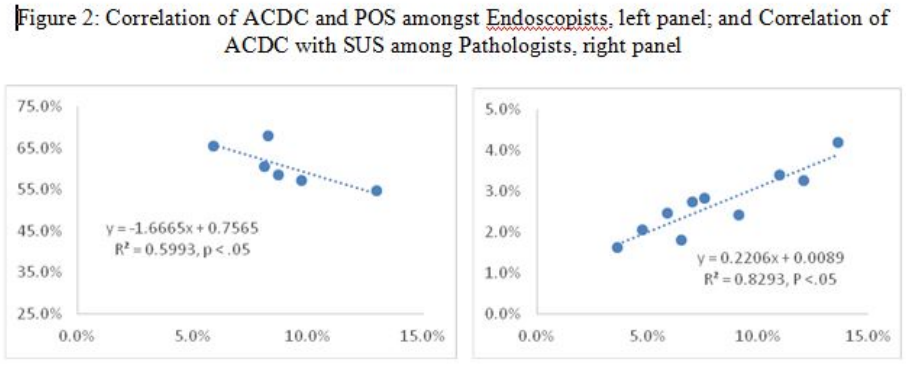


Figure 2 - 1977



Conclusions: Intra-institutional variation of ACDC rates is different than that of inter-institutional variations. The annual variation of ACDC is likely related to change in staff (Figure 1). Among pathologists, variation is related to threshold as those who make more diagnoses of ACDC also diagnose more SUS rather than POS. Among endoscopists, ACDC is likely related to patient selection, nature of the lesion and endoscopist skill. ROM varies more within than between institutions and doesn't correlate with ACDC rate.