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ABSTRACTS

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953 ER-/PR+ Breast Cancer Cases Across Two FDA-Approved Platforms: Incidence and Clinicopathologic Correlates

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Background: Estrogen receptor (ER) and progesterone receptor (PR) are predictive/prognostic markers in breast cancer. While most hormone receptor-positive breast cancers are ER+/PR+ and ER+/PR-, rare cases of ER-/PR+ raise the possibility of technical or artifactual issues and can trigger re-testing and confusion. Commercially available antibodies target different ER/PR isoforms and have been reported to generate different results. Our goal is to compare the incidence and clinicopathologic features of ER-/PR+ cases using different two FDA-approved platforms.

Design: A retrospective review of 2089 breast cancer cases with ER and PR from 1/2019 and 7/2020, including 1639 cases tested on Ventana (ER SP1 and PR 1E2 antibodies) and 450 cases tested on Leica (ER 6F11 and PR 16 antibodies). Negative receptor results are defined as <1% of tumor cells with nuclear staining, low positive as 1-10%, and positive as >10%. Clinicopathologic data, including HER2 status, Ki-67 index, tumor histologic type, and tumor grade, were collected for correlation. Statistics performed using Fisher's exact test.

Results: ER results across the Ventana and Leica platforms were similar, while PR results were significantly different (p <0.001) (Table 1). The ER- rate was similar between Ventana SP1 (445/1639, 27.2%) and Leica 6F11 (119/450, 26.4%). Among the ER- cases, the overall PR+ rate was 14.0% (79/564), ten times higher in cases tested with Ventana PR 1E2 (77/445, 17.3%) than with Leica PR 16 (2/119, 1.7%) (Figure 1). The ER-/PR+ cases were predominantly invasive ductal carcinoma (IDC) (60/79, 75.9%) and Nottingham histologic grade 3 (49/79, 62.0%), HER2 negative by IHC (46/79, 58.2%), and with Ki-67 indices ranging from low (<17%) (7/79, 8.9%) to high (>35%) (26/79, 32.9%) (Table 1).

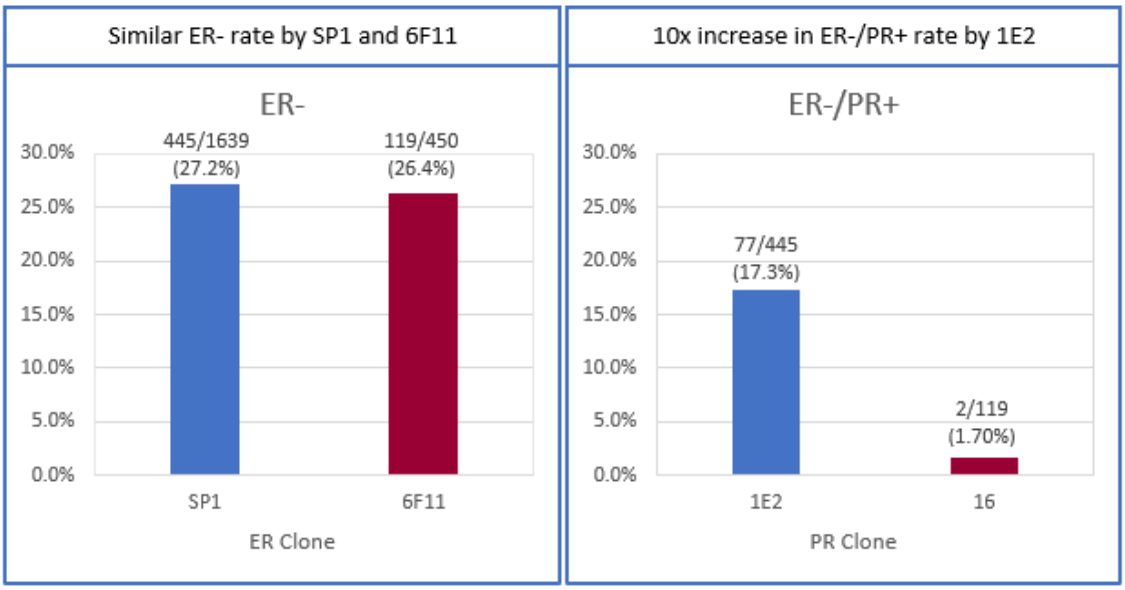
Table 1. Comparison of estrogen receptor and progesterone receptor testing by FDA approved platforms. (ER, estrogen receptor; PR: progesterone receptor; DCIS, ductal carcinoma in situ; IDC: invasive ductal carcinoma; IMC: invasive mammary carcinoma; MC, metaplastic carcinoma; MET: metastasis)

	Ventana (No = 1639)	Leica (No = 450)	P-Value
ER Negative Low Positive Positive	445 (27.2%) 64 (3.9%) 1130 (68.9%)	119 (26.4%) 16 (3.6%) 315 (70.0%)	0.891
PR Negative Low Positive Positive	491 (30.0%) 205 (12.5%) 943 (57.5%)	179 (39.8%) 36 (8.0%) 235 (52.2%)	< 0.001
ER+/PR+ ER+/PR- ER-/PR+ ER-/PR-	852 (61.3%) 153 (11.0%) 77 (5.5%) 308 (22.2%)	232 (58.1%) 53 (13.3%) 2 (0.5%) 112 (28.1%)	< 0.001
ER-PR+ Cases (79)			
Histology DCIS IDC IMC MC MET	2 (2.6%) 58 (75.3%) 4 (5.2%) 1 (1.3%) 12 (15.6%)	2 (100.0%)	N/A
Grade 1 2 3	1 (1.5%) 16 (24.6%) 48 (73.9%)	1 (50.0%) 1 (50.0%)	N/A
HER2	39 (50.6%)	1 (50.0%)	

0 1+ 2+ 3+ Not Tested	6 (7.8%) 10 (13.0%) 16 (20.8%) 6 (7.8%)	1 (50.0%)	N/A
Ki67 Low Moderate High	7 (11.7%) 29 (48.3%) 24 (40.0%)	2 (100%)	N/A

Figure 1 - 953

Figure 1. Higher PR+ interpretation by clone 1E2 than clone 16 in ER- breast cancer.



Conclusions: The significantly different PR results across the Ventana and Leica platforms are reflected in the higher rate of ER-/PR+ cases (17.3%) when using the Ventana system compared to the 1.7% of ER-/PR+ cases when using the Leica system. ER-/PR+ cases overall correlate with IDC histologic type, HER2-negative status, and high Ki-67. Caution is warranted when interpreting conflicting ER and PR results with these poor clinicopathologic characteristics due to the potential impact on treatment decisions.

(The first three authors contribute equally)

954 Discordance Between Intraoperative and Final Diagnoses of Sentinel Lymph Node Frozen Section in Patients with Breast Cancer: Causes and Improvements

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Disclosures: Ethar Al-Husseinawi: None; Rashna Madan: None; Fang Fan: None

Background: Intraoperative frozen section (FS) evaluation of sentinel lymph nodes (SLN) is an effective practice in many institutions for breast cancer patients undergoing mastectomy or lumpectomy/mastectomy after neoadjuvant systemic therapy (NAST). Cases with positive SLN FS diagnosis can proceed with axillary lymph node dissection (ALND) in the same operative procedure. This study aims to review our discordant cases in SLN FS evaluations, especially in the era of NAST. The causes of discordance, ways to improve, and clinical impact are discussed.

Design: Retrospective review was performed of all breast cancer surgeries with intraoperative SLN FS between July 2019 and June 2020. Discordant cases were identified by comparing the frozen section and final diagnoses of

SLN. Causes of discrepancy were categorized as technical and interpretive. Impact on clinical management was also assessed. False negative rate (FNR) was calculated as FN/True positive +False negative, and adjusted FNR (AFNR) was calculated as FN/total number of cases.

Results: A total of 337 cases with SLN FS were identified. Among them, 261 cases had concordant negative SLN diagnosis and 51 cases had concordant positive SLN diagnosis. Twenty-five cases had negative FS but positive final diagnoses (false negative cases). There was no case with false positive FS diagnosis. FNR was 32.9% and AFNR was 7.4%. Of the 25 FN cases, 21 were due to technical (84%) and 4 (16%) were due to interpretive causes. Of the 4 cases with interpretive discrepancy, 2 had lobular histology and 2 were due to tumor bed changes after NAST. Technical causes included superficial sectioning (tumor only present on deeper permanent sections), tissue folding, poor sectioning of fatty nodes and suboptimal staining. Micrometastasis accounted for 19 of the 25 FN cases (76%). Subsequent completion ALND was performed in 9 of the 25 FN cases (36%).

Conclusions: SLN FS remains an accurate method to guide axillary management in the same operative procedure. Our false negative rate is aligned with the reported range in the literature. Most cases are micrometastases and due to technical issues. Lobular morphology and tumor bed histology remain challenging in FS interpretation. Improvement of FS accuracy as the result of this quality improvement project could be achieved by careful gross examination, better sectioning practices and optimizing the staining protocol. Pathologists should be aware of the pitfalls of lobular and tumor bed morphology.

955 Root Cause Analysis in Anatomic Pathology: CAP ISO 15189 Laboratories Perspective

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Disclosures: Mohamed Alhamar: None; Gaurav Sharma: None; Caroline Maurer: None; Justin Caron: None; Ronald Paler: None; Brian Theisen: None; Jeremy Hart: None; Vipul Trivedi: None; Joe Rutledge: None

Background: Root cause analysis (RCA) is a powerful tool in any Quality Management System (QMS). The ISO 15189 standard is an international accreditation standard for medical laboratories. The ISO 15189 standard requires that laboratories perform RCA for the identification and control of non-conformances, and to deploy suitable corrective and preventive actions in all aspects of laboratory testing, including Anatomic Pathology (AP). The aim of this study was to ascertain the awareness, current conditions, and potential opportunities for AP RCA amongst CAP 15189 accredited laboratories in the United States.

Design: The CAP 15189 Committee drafted a survey of 16 questions pertaining to the awareness, barriers, encountered error-types, weaknesses, and follow-up corrective actions in a typical AP RCA. The online survey was distributed to 66 CAP 15189 accredited laboratories in the United States.

Results: Of 66 laboratories, 33 responded to the survey (50% response rate). Amongst the responders, the largest segment was academic medical centers (37%), followed by reference laboratories (31%). While 22 (67%) routinely performed AP RCA, 11 (33%) responders were either not aware of RCA or did not routinely perform it. Reasons for not performing RCA included a lack of knowledge (50%), lack of a formal process (25%), or lack of time (25%). The most common trigger of RCA was a singular AP error. The most common focus of AP RCA was on grossing/histology, followed by accessioning. The most common approach was formal interviews (87.67%) followed by Five Whys (73%) and Brainstorming (73%). The majority (60%) of responders had uncovered combined personnel and systemic/process issues, whereas 33% of responders identified systemic/process weaknesses only, and 6.67% of responders identified concerns with specific personnel issues only. Pathologists were part of the AP RCA team for both interpretive and non-interpretive errors.

Conclusions: The survey provides a good reflection of the current state of AP RCA amongst CAP 15189 accredited laboratories. While the practice of AP RCA is widely prevalent, lack of knowledge and/or formal process

may preclude its use in a subset of laboratories. There is a clear opportunity to improve educational QMS offerings in this area. AP RCA helps uncover systemic gaps in pre-analytics and manual steps, improving specimen safety and patient care.

956 Adequacy in Endocervical Curettage

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Disclosures: Roa Alqabbani: None; Joanna Chan: None; Allison Goldberg: None

Background: Specimen adequacy is the most important quality assurance component of a cervical Papanicolaou smear. We use cellularity of endocervical curettage (ECC) to evaluate specimen adequacy for accurate diagnosis of high-grade dysplasia (HGD).

Design: All patients with HGD diagnosed in an excisional biopsy (LEEP) from 1/1/2019 to 12/31/19 and an ECC in the preceding six months at our institution were included (n=41). ECCs prior to the LEEP were evaluated for cellularity of squamous cells using Aperio eSlide Manager. Biopsy results concurrent to the ECC were noted. Cellularity between positive and negative ECCs were compared using a student's T-test. Proportion of ECCs and concurrent biopsies undergoing immunohistochemical (IHC) staining for p16 were compared using chi-square test. P-value was <0.05.

Results: ECCs positive for HGD have increased cellularity compared to negative ECCs (mean cellularity 2866 vs 497, p<0.05). Further, IHC staining for p16 was more likely to be performed on an ECC positive for HGD than on a negative ECC (63% vs 3%, p<0.05). Biopsies performed concurrently with a negative ECC were more likely to undergo p16 IHC than biopsies performed concurrently with a positive ECC (52% vs 0%, p<0.05). Finally, there was no difference in proportion of biopsies undergoing IHC staining for p16 when comparing biopsies positive for HGD and negative biopsies (38% vs 56% p=0.33).

	ECC Negative (N=33)	ECC Positive (N=8)	P-value
Mean Cellularity (range)	497 (0-4482)	2866 (515-8839)	<0.05
P16 Performed on ECC (%)	1 (3%)	5 (63%)	<0.05
P16 Performed on Biopsy (%)	17 (52%)	0 (0%)	<0.05

Table 1. Mean cellularity and p16 IHC staining in biopsy and ECC specimens

Conclusions: We find a cellularity of approximately 3000 cells adequate to diagnose HGD in an ECC and a cellularity of approximately 500 cells to be inadequate. Further, we find p16 IHC commonly used as a "rule-in" test on ECCs at our institution. Biopsies accompanying a negative ECC are more likely to undergo p16 IHC than those accompanying an ECC positive for HGD, but there is no difference in proportion of biopsies undergoing p16 IHC when comparing positive and negative results in the biopsies themselves. These findings further support the need for adequate cellularity for diagnosis in ECC, especially when a biopsy is technically difficult. Further areas for exploration include increasing our sample size to more precisely define the exact minimum cellularity necessary to diagnose HGD in an ECC and investigating possible laboratory procedures to maximize cellularity of ECCs

957 Fine Needle Aspiration Versus Core Needle Biopsy as an Acquisition Method for Flow Cytometry Analysis: A 10 Year Institutional Experience

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Disclosures: Lame Balikani: None; Sharon Copley: None; Kossivi Dantey: None; Olukemi Esan: None

Background: The pathological diagnosis of hematologic neoplasms (HN) can be aided by the use of flow cytometry analysis (FCA). Acquisition methods include fine needle aspiration (FNA) and core needle biopsy (CNB). However, at our institution, when an HN is clinically suspected, there is no specific guideline in place regarding

which sample acquisition method is more likely to generate a high diagnostic yield (sufficient quantity of viable cells for analysis).

Design: We reviewed HN cases whose diagnoses were supported by FCA sampled by FNA or CNB, over a period of about ten years ranging from January 2010 to July 2020. The main inclusion criterion was all cases with a cytological diagnosis of a hematologic neoplasm along with FCA. Pertinent data including the cases with sufficient cellularity, insufficient cellularity and low cellularity/sample issues were collected. Statistical analysis was performed.

Results: Two-hundred and ten (210) FCA cases were selected. The acquisition method for 74 cases was FNA while 136 were acquired by CNB. FNA acquisition method resulted in a sufficient cellularity rate of 70 %(52 cases), an insufficient cellularity rate of 15 %(11 cases) and a low cellularity rate of 15 %(11 cases). The corresponding rates when the acquisition method was CNB were respectively: 33 % (45 cases), 47 % (64 cases) and 20 % (27 cases).

Conclusions: Specimens obtained by FNA showed a higher sufficient cellularity rate (70 % vs. 33 %), a lower insufficient cellularity rate (15 % vs 47 %) and a reduced low cellularity rate (15 % vs 20 %). Based on these results, FNA appears superior to CNB as an acquiring method for FCA.

958 CD138-/ CD38+ Plasma Cell Leukemia; A New Approach on Flow Cytometry

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Disclosures: Mohammad Barouqa: None; Xiaoling Guo: None; Yanhua Wang: None

Background: Plasma cell leukemia is an aggressive form of multiple myeloma characterized by high levels of malignant plasma cells circulating in the peripheral blood. Initially, it is assessed using bone marrow or peripheral blood specimens by flow cytometry. Certain antigens are tested as immunophenotypic markers in order to identify the malignant plasma cells. Plus, these markers are used as therapeutic targets.

CD38 is a common marker used to identify the plasma cells, however it is expressed in different cell types, such as activated B cells and monocytes. Normal and malignant plasma cells have a high-density CD38 expression (CD38++) on their surfaces in addition to CD138 which is another surface marker. The combination of CD38 and CD138 are commonly used to diagnose plasma cell neoplasm with additional clonality markers. However, the lack of CD138 expression by the malignant plasma cells can be challenging.Besides, aberrant loss of CD138 is associated with adverse outcomes.

Activated monocytes can express CD38, and they carry immunoglobulin Fc receptor (FcR) on their surfaces, which can bind to both Kappa and Lambda immunoglobulins. Hence, they add more challenge to precisely gate on the malignant plasma cells and detect their clonality.

Design: We retrospectively analyzed 289 bone marrow and blood specimens tested for plasma cell myeloma from January 1st to October 1st, 2020 in order to propose a method to accurately identify CD138 negative (CD138-) and CD38 positive (CD38+) malignant plasma cells. Our panel included the following antigens: cytoplasmic Kappa/Lambda (cKappa, cLambda), CD19, CD138, CD117, CD56, CD38, CD20 and CD45. The activated dim CD38+ monocytes express immunoglobulin FcR, both Kappa and lambda immunoglobulins bound homogeneously to the monocytic FcR receptors and served as internal control. Besides, they show diagonal distribution when they were gated on the Kappa vs Lambda plot (figure.1 A-B. Monocytes in lime green). The plasma cells were analyzed using both CD38 and CD138 in each sample by plotting CD38 versus CD138 cells and gating on the strongly (CD38++) plasma cells and dim CD38+ monocytes (figure.2 A) (CD38+ monocytes gated in purple and CD138-/ CD38++ gated in green).

Results: A total of 10 CD138- /CD38+ cases were found (10/289). Seven of them were bone marrow specimens, while the remaining three were blood specimens. The CD138-/ CD38+ population showed either kappa or lambda restriction (figure.2 B). The binding to Kappa and lambda immunoglobulins to the activated monocytic FcR helped

establishing an internal control to compare the CD138-/ CD38+ malignant plasma cells and confirmed their clonality as shown (figure.2 C-D).

Figure 1 - 958

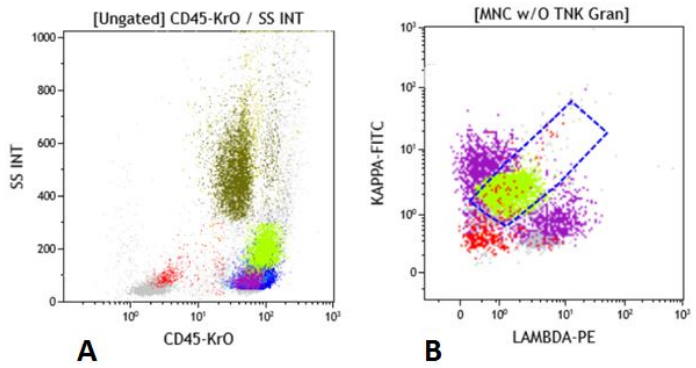

Figure 1. Flow cytometry plots; The monocytic population gated in lime green.

Figure 2 - 958

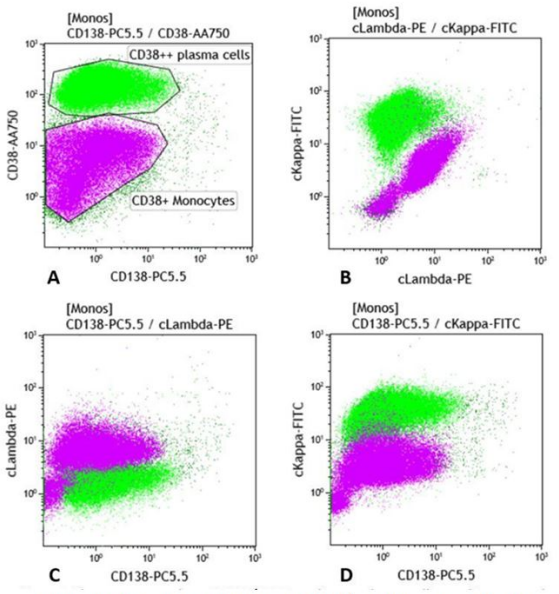

Figure 2. Flow cytometry plots; CD138-/ CD38+ malignant plasma cells gated in green, and activated CD38+ gated in purple.

Conclusions: This method enhances the accuracy of detecting CD138-/ CD38+ malignant plasma cells by flow cytometry, and it serves as an important quality assurance that has substantial implications in further patient treatment.

959 Evaluation of p16 Status on Cytology Specimens, Can It Be Done?

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Disclosures: Anne Bartels: None; Daniel Stefanko: None; Mariah Leivo: None; Somaye Zare: None; Farnaz Hasteh: None; Grace Lin: None; Vera Vavinskaya: None

Background: Human papilloma virus-associated oropharyngeal squamous cell carcinoma accounts for up to 25% of all head and neck carcinomas, commonly arising from the tonsil and base of the tongue. The clinical behavior of these tumors is distinct from HPV-negative squamous cell carcinoma. The tumor often presents as metastatic disease from an occult primary lesion, and the initial diagnosis is frequently made on cytology specimens. While p16 positivity in surgical specimens is defined as strong and diffuse nuclear staining in 70% of tumor cells, no such cutoff has been validated for cytology samples. Accurate interpretation of p16 immunostaining is crucial in guiding the management in these patients, and thus, establishing criteria for cytology specimens is important in the characterization of these neoplasms.

Design: We evaluated p16 staining in cytology specimens of metastatic squamous cell carcinoma and compared the staining results with that of their paired surgical biopsy or resection specimens. The anatomic pathology database was searched for cases of metastatic squamous cell carcinoma in patients with known HPV status. Only cases with at least 100 viable tumor cells were included in the study. We evaluated the percentage of p16 positive tumor cells in the cytology specimens of metastatic squamous cell carcinoma and compared the staining results with the p16 status of the paired surgical biopsy or resection specimens.

Results: We identified 17 cases whereby paired cytology samples and surgical pathology p16 immunostaining results were available. Of these, the majority of patients were male (88%) with an average age of 58 years. Using a cutoff of 10% expression in neoplastic cells obtained from cytology samples, p16 immunostaining showed the following results: 13 true positive cases, 3 true negative cases, and 1 false negative case. In our sample, a p16 staining expression threshold of at least 10% on the cytology material resulted in a sensitivity and specificity of 92.9% and 100%, respectively. The positive predictive value for this cutoff was 100% and the negative predictive value was 75%. However, when even minimal strong, nuclear expression of p16 on cytology was considered positive, the negative predictive value increased to 100%.

Conclusions: In our laboratory, p16 expression in more than 10% of neoplastic cells in cytology specimens should be considered a positive result. The strong concordance of p16 expression in cytological and surgical pathology specimens at a cutoff of 10% cell positivity suggests that this criteria can be used to classify metastatic squamous carcinoma as HPV-associated on cytology specimens. Below this 10% cutoff, p16 expression should be interpreted with caution.

960 Investigating Key Stakeholder Perspectives on Patient-Pathologist Interactions: A Qualitative Study of Clinician's Attitudes

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Disclosures: Sarah Bergholtz: None; Sophia Kurnot: None; Melissa DeJonckheere: None; Cathryn Lapedis: None

Background: In order to make high quality medical decisions, it is necessary for patients to have correct and comprehensible information concerning not only the treatment options but their diagnosis as well. Recent literature shows cancer patients and pathologists are interested in meeting to review diagnostic materials. The attitudes of clinicians, key-stakeholders in this interaction, have not yet been assessed.

Design: Using a snowball recruitment strategy, 59 clinicians from specialties including surgery, internal medicine, and hematology oncology were recruited from a tertiary care academic medical center. Clinicians were asked, "How interested would you be in having your patient meet with a pathologist to discuss their pathology report and see their tissue under the microscope?". Clinicians ranked their interest on a six-point Likert scale, then expanded on specific challenges and benefits they anticipated in a semi-structured interview. Demographic information such as age, gender, rank (resident/fellow, junior, mid-career, or senior attending), and specialty was also collected. Audio recordings of interviews were transcribed. Using the software NVivo, qualitative thematic analysis identifying codes and themes was completed by three members of the study team. Independent coding with group resolution was used to develop a codebook, apply codes to all transcripts, and develop themes that represented the perceived challenges and benefits.

Results: A total of 35 clinicians were interviewed with 57% reporting they were either definitely interested or interested in having their patients meet with pathologists. Clinicians identified an impact of including patient-pathologist interactions on patients and the care team, and noted that a subset of patients may gain cognitive and emotional benefits from meeting with a pathologist, but also expressed concerns that some patients may find the added information emotionally taxing and incomprehensible. Clinicians noted that pathologists may be helpful to the care team by adding their unique knowledge, but worried about pathologists' communication skills and fragmentation in patient care.

Conclusions: Overall, clinicians had a mixed level of interest in their patients meeting with pathologists to review their diagnostic material. Clinicians approve of this interaction in only certain situations where patients are highly motivated to interact with the pathologist and the pathologist can provide unique value. Clinicians are particularly concerned about pathologist communication skills, overwhelming patients, and fragmentation of care. These findings and direct clinician collaboration must be incorporated into program development and future research to ensure maximal patient benefit.

961 How Do You Count? An Observational Study of Lymph Node Counting in 1,497 Colorectal Cancer Resections

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Disclosures: Michael Bonert: None; Charles Jian: None; Ipshita Kak: None; Gary Foster: None; Pierre Major: None

Background: Lymph node status and lymph node count (LNC) are predictors of colorectal cancer outcome. Under-sampling of lymph nodes may lead to clinically relevant stage migration.

Design: Colorectal cancer cases with a synoptic report, accessioned 2011-2017 at a regional laboratory, were extracted. LNC, number of positive lymph nodes (PLNC) and 'y' (staging) prefix (YS) were tabulated by pathologist using custom software. Statistical analyses were done with LibreCalc, R and SAS.

Results: The cohort had 1,694 CRC resections. Twenty-two pathologists interpreted >25 cases (range: 29-253) each and collectively saw 1,519 cases. After cases with zero lymph nodes/unavailable data were purged, 1,497 cases remained; these had a total of 32,908 lymph nodes of which 1,883 were positive. 281 of 1,497 cases had a 'y' prefix. The group of 22 pathologists' median LNC/case was 19.5 (range: 13.5-27.0), and the mean PLNC per case was 1.3 (range: 0.7-3.1). Kruskal-Wallis rank sum tests showed that there were differences in LNC ($p<0.001$) and PLNC ($p=0.033$) among pathologists. T-tests showed that mean LNC ($p<0.001$) differed between YS groups; however, mean PLNC ($p=0.084$) did not show this association. 106 of 1497 cases had less than the 12 LNC target; logistic regression analysis revealed that there was a strong association between LNC target category and pathologist ($p<0.005$).

Conclusions: Positive lymph node call rate has a fair consistency in the laboratory. Standardized criteria for lymph node counting should be developed, and synoptic report data could be used, in the context of a next generation quality process, to facilitate adoption.

962 Machine Learning for Predicting Survival in Poorly Differentiated Neuroendocrine Carcinoma: Pooled Analysis of Four Retrospective Studies

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Background: Lung and Digestive system represent the most frequent occurrence sites for neuroendocrine neoplasms (NENs). NEN clinical outcome can be predicted by the integrated evaluation of morphology and proliferation index, allowing NENs distinction into well differentiated neuroendocrine tumors (WD-NET) and poorly differentiated neuroendocrine carcinoma (PD-NEC). We recently published four studies addressed to PD-NECs in order to identify PD-NECs subgroups with better prognosis and/or to predict their therapy outcome.

Design: A pooled analysis of our four retrospective studies (3 on digestive [PMID: 26943788; 29592868; 31557757] and 1 on lung NENs [PMID: 32365350]) was performed to evaluate for PD-NEC: i) Best Ki-67 cut-off in predicting Overall Survival (OS); ii) OS according to cancer primary site iii) best common predictive model using

different variable selection methods in Cox proportional hazards model (Cox) and machine learning Random Survival Forest (RSF).

Results: Overall, 422 PDNECs were analyzed distributed in colorectal (n = 156, 37%), lung (n = 111, 26.3%), gastroesophageal (n = 83, 19.7%), pancreas (n = 42, 10%), ileum-cecum-duodenum (n = 18, 4.2%) and gallbladder/biliary (n = 12, 2.8%). Pure neuroendocrine morphology (n = 227, 53.8%) was slightly more represented than combined (n = 195, 46.2%) although is more frequent in colorectal (59%), gastroesophageal (53%) and gallbladder/biliary (83.3%) compared to lung (31.5%) and pancreas (33.3%). Interestingly, all PDNEC in ileum-cecum-duodenum had pure morphology. Ki-67 at 55% was confirmed as the best value in predicting OS. Colorectal and gastroesophageal PD-NEC showed worse OS than pancreatic and lung. The most predictive Cox model included Ki67 (HR 1.03 - CI95% 1.03-1.04), Morphology (Pure vs Combined - HR 1.44 - CI95% 1.16-1.78), Stage III-IV (HR 1.47 - CI 95% 1.06-2.04) and Age (HR 1.01 - CI 95% 1.00-1.02). In Pancreas PD-NEC HR decreased by 0.58 (CI 95% 0.40-0.83) if compared to colorectal PD-NEC. RSF, which is dependent on the complete combination of all risk factors, confirmed that Ki-67 was the most relevant predictor followed by morphology, stage and site. The predicted response for survival at 1 or 3 years of the forest showed decreasing survival with increasing Ki-67, pure morphology, stage III-IV, and colorectal and gastroesophageal NEC disease. Furthermore, patients with Ki-67<55% and combined morphology had better survival than those with pure morphology. Morphology became irrelevant in NENs when Ki-67 resulted ≥ 55%. RSF had the best predictive accuracy (AUC > 80) compare to other models computed at 6, 12, 24 and 36 months specific time points.

Conclusions: The present pooled analysis showed that most predictive parameters to predict OS for PD-NEC patients included Ki67, Morphology, Stage and Site. RSF outperformed all other models in OS prediction performance.

963 Application and Adherence to Z0011 in the Surgical Management of Axillary Lymph Nodes in Breast Conserving Surgery: A Single Institution's Experience

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Disclosures: Lauren Duckworth: None; Celeste Santos Martins: None; Zahraa Al-Hilli: None; Erinn Downs-Kelly: None; Miglena Komforti: None

Background: The ACOSOG Z0011 (Z0011) trial demonstrated omission of axillary lymph node dissection (ALND) was non-inferior to sentinel lymph node dissection (SLND) in breast conserving surgery (BCS) with cT1-2 invasive breast carcinoma (IBC), no palpable adenopathy, and 1-2 sentinel lymph nodes (SLN) with metastasis. A decade after, we evaluate our institution's intraoperative consultation (IOF) and ALND practices.

Design: Patients (pts) treated in our hospital system in 2019 meeting Z0011 inclusion (cT1-2N0M0, undergoing BCS) and exclusion criteria (neoadjuvant therapy, cT3/4, cTis) were identified.

Results: Data were recorded in Table 1: 455 pts were included in the study (median age 66 years). Subtypes included 90% ER/PR-positive, 0.7% HER2-positive and 8.2%-triple negative IBC. Overall, ALND was performed in 14/376 with SNLD. 8/14 pts had SLND IOF while 4/14 had disease identified on PS; 2/14 pts underwent ALND without prior pathologic evaluation PS/IOF of lymph nodes (LN). Of the 14 pts with ALND, 4 had ≥3 positive LN, 3/4 had ≥3 positive SLND IOF, 3/4 had additional positive LN within the ALND and 2/4 upstaged the pN from pN1 to pN2. 10 pts with ALND had <3 positive LN. In 6/10, macrometastatic disease was identified on SLND IOF. While additional metastatic disease was identified in 5/10, the pN assignment was not affected. 7/10 ALND were performed by breast surgeons, and 2 surgeons were overrepresented. Overall, only 2/14 pts had an upstaged pN assignment, all with ≥3 positive SNLD on IOF. All pts with ALND had ER-positive IBC, while 21% were HER2-amplified, 79% ductal, 14% mixed ductal/lobular, and 7% lobular.

Statistically significant associations with ALND ($p<0.05$) were identified with ENE, age >70, and pT1 vs pT2 but not with cT1 vs cT2, morphologic type, Nottingham grade, or receptor expression.

In the 441 pts who did not undergo ALND, 3 had ≥3 positive SLND. One of these pts had only isolated tumor cells while the other opted for axillary radiation. No reason to omit ALND was disclosed for the third pt.

Table 1: Clinicopathologic characteristics of all patients with breast conserving surgeries in 2019			
	ALND (N=14)	**No ALND (N=441)**	***p***
Median Age (year)	70 (49-80)	64 (36-92)	
Median clinical tumor size (cm)	1.6 (0.5-3.2)	1.2 (range 0.1-4.7)	
Patient age (years)			
<50	1 (7%)	52 (12%)	
50-70	3 (21%)	239 (54%)	
>70	10 (72%)	150 (34%)	
Clinical T stage			
T1	9 (64%)	369 (83%)	0.06
T2	4 (29%)	49 (11%)	
Missing	1 (7%)	24 (6%)	
Median pathologic tumor size (cm)	1.7	1.3	
Pathologic T stage			
T1	8 (57%)	378 (86%)	0.03
T2	5 (36%)	63 (14%)	
T3	1 (7%)	0	
Histology			
Ductal	11 (79%)	314 (71%)	
Lobular	1 (7%)	49 (11%)	
Mixed	2 (14%)	56 (13%)	
Other	0	22 (5%)	
Nuclear grade			
Low	2 (14%)	148 (34%)	
Intermediate	8 (57%)	203 (46%)	
High	4 (29%)	90 (20%)	
Hormone receptor status			
ER/PR positive	13 (93%)	396 (90%)	1.00
ER/PR negative	1 (7%)	41 (10%)	
HER2 receptor status			
HER2 positive	3 (21%)	27 (6%)	0.6
HER2 negative	11 (79%)	409 (93%)	
Lymphovascular invasion			
Present	5 (36%)	70 (16%)	0.05
Absent/missing	8 (57%)	364 (83%)	
Median No. SLN	3 (0-11)	2 (0-9)	
No. positive SLN			
0	1 (7%)	357 (81%)	
1	8 (57%)	43 (10%)	
2	1 (7%)	4 (1%)	
≥3	3 (21%)	3 (0.7%)	
No SLN submitted	1 (7%)	34 (6.3%)	
Extranodal extension			
Yes	5 (36%)	10 (2%)	0.03
No	9 (64%)	76 (17%)	
Micrometastasis			
Yes	1 (7%)	18 (4%)	
No	13 (93%)		
Isolated tumor cells			
Yes	1 (7%)	9 (2%)	
No	13 (93%)		

Legend: ALND axillary lymph node dissection, ER estrogen receptor, PR progesterone receptor, SLN sentinel lymph node

Conclusions: Our data shows the necessity for ALND is low (3.7%) in the setting of BCS with cT1-T2N0M0 disease, and supports the need for ALND only in cT1-2N0M0 invasive mammary carcinomas with ≥3 positive SLND, as seen with Z0011 outcomes. Most importantly, it also shows SLND IOF does not guide management and can be completely abandoned in this cohort, saving time, resources, improving workflow, and ultimately providing better care for our patients.

964 How Reproducible Must a Test Be to Maintain Clinical Accuracy? Application to Oncology Biomarkers Such as PD-L1

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Background: Oncology tests with established clinical accuracy such as those for detecting PD-L1 have receiver operating characteristic (ROC) curves with areas under the curves (AUCs) of 0.62-0.74. ROC curves can reflect analytical error, including reproducibility, as well as biologic factors, but standards for qualitative reproducibility have not been justified based on the need for clinical accuracy. This creates angst among some practicing pathologists, who may believe that some tests, such as those for PD-L1, can be performed only by a few experts proficient at scoring such tests. Herein, we describe a stochastic model which relates analytical error and reproducibility to clinical accuracy.

Design: The symmetric case of the well-known binormal distribution was the starting point of the model. The novel aspect is partitioning error into analytical and biological components based on assumptions derived from the Cotlove criterion that analytical error should be at most half of biological error. The model assumed the following: (1) a normal distribution of true biomarker values in the “disease” group had a mean of +1; (2) a normal distribution of true biomarker values in the “no disease” group had a mean of –1; (3) both distributions had the same standard deviation; (4) normal distribution of assay error; and (5) assay cutoff was correctly set at 0. Explicit mathematical solutions were derived, then verified by Monte Carlo analyses. Disease prevalence did not affect calculations.

Results: ROC curves for various values of total error are shown in the **Figure**. Reproducibility is presented in the **Table**. The model demonstrated that tests with analytical error that conform to the classic Cotlove criterion achieved ROC curves with AUCs of 0.68-0.76 and Youden Indices of 0.26-0.38 yet had overall agreement for duplicate measurements of only 80%-82%. Analytically accurate agreement was only 75%-78% and clinically accurate agreement only 50%-60%. Monte Carlo analyses verify these explicit calculations.

Figure 1 - 964

Figure. Receiver operating characteristic (ROC) curves based on the binormal distribution at various standard deviations. The curve is virtually perfect for S_{tot}=0.1. The curve is a virtual diagonal line for S_{tot}=100. Intermediate models (S_{tot}=1, 2, 3, 4, or 5) demonstrate various levels of clinical performance.

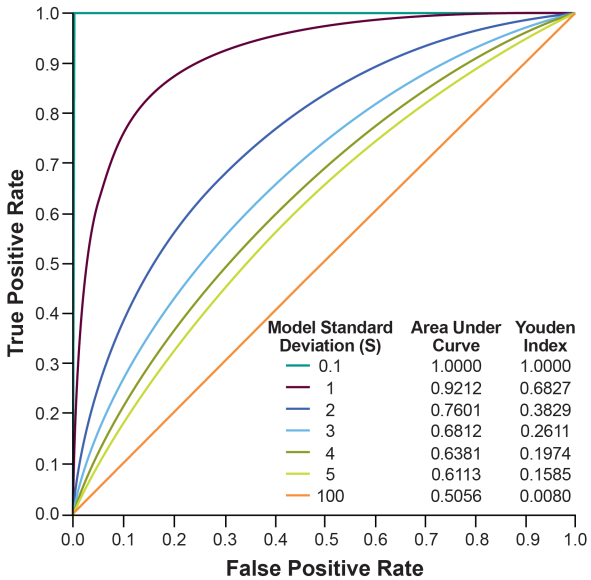

Figure 2 - 964

Table. Dichotomized Agreement Between Two Successive Assays Based on the Partitioned Binormal Distribution[a]

Model Standard Deviation (*S*)	Low Error[b] Overall Agreement (%)	Low Error[b] Analytically Accurate Agreement (%)	Low Error[b] Clinically Accurate Agreement (%)	High Error[c] Overall Agreement (%)	High Error[c] Analytically Accurate Agreement (%)	High Error[c] Clinically Accurate Agreement (%)
0.1	100.00	100.00	100.00	100.00	100.00	100.00
1	87.80	85.29	78.03	80.77	77.04	74.52
2	82.00	78.10	60.15	70.96	64.14	54.62
3	80.66	76.43	53.39	68.65	61.03	47.38
4	80.17	75.81	49.96	67.80	59.87	43.77
5	79.94	75.53	47.89	67.39	59.33	41.62
100	79.52	75.00	40.16	66.67	58.34	33.73

[a]The table shows agreements calculated from explicit formulas.

[b]Analytical error is half the biological error (S_{err}=½S_{bio}); at threshold of Cotlove criterion.

[c]Analytical error equals the biological error (S_{err}=S_{bio}); well beyond threshold of Cotlove criterion.

Conclusions: Tests may have reasonable clinical accuracy despite having reproducibility of <85%. Imperfect assays can substantially improve medical decision making. The findings must be interpreted with caution due to the binormal assumptions, but such assumptions are often useful as a first approximation. Practicing pathologists should feel comfortable performing semi-quantitative assays shown to have a strong biological association with clinical outcome.

965 Tissue Loss During Immunohistochemistry Varies by Slide Brand and IHC Assay Conditions

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Background: Tissue loss on immunohistochemically stained slides is frustrating and may lead to diagnostic uncertainty and/or unresolved predictive biomarker status. Special positively charged or adhesive slides are marketed specifically for use with IHC. We hypothesized that tissue loss would vary among these slide brands. We also hypothesized that total assay conditions (including antigen retrieval) would influence results. We used digital image analysis of whole slide images of immunohistochemically stained slides to quantify cell loss among slide brands and laboratories.

Design: A cell culture microarray block was constructed from 39 well-fixed T-47D cell culture pellets. The microarray was sectioned onto 15 adhesive slide brands, with 9 laboratories performing their own estrogen receptor assay on each of these 15 slides. Slides were returned to a central laboratory for whole slide imaging with an Aperio AT2 scanner at 20x and QuPath quantitation. Counts were normalized to the average number of cells present in bracketing H&E sections. In a second round, an additional 5 breast cancer cores selected based on the H&E impression of delayed or incomplete fixation were arrayed, with laboratories performing Ki-67 IHC on 5 of the slide brands (selected from the initial 15).

Results: In round 1, marked differences in cell culture pellet retention were observed between laboratories (range: 59%-85% of cells), while no slide brand showed superior retention (Figure 1). In round 2, though, there were dramatic retention differences between slide brands for the breast cancer tissue cores (range: 13%-62%) (Figure 2).

Figure 1 - 965

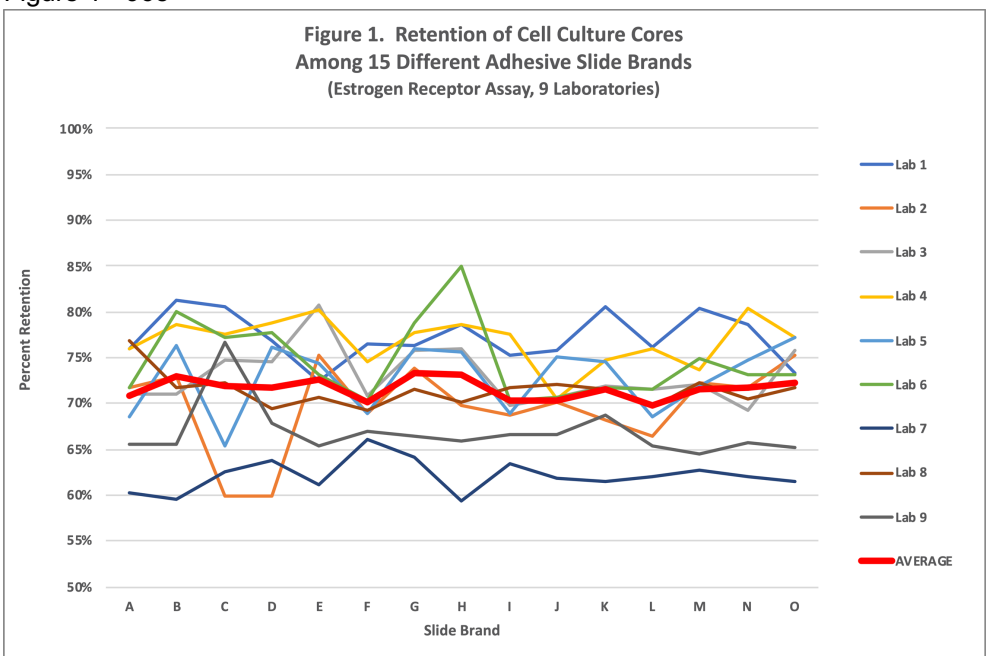
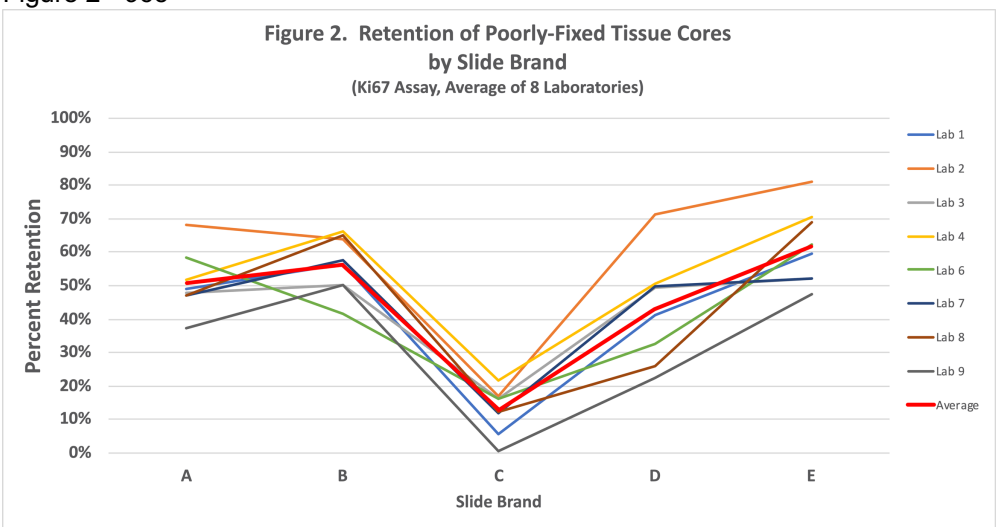


Figure 2 - 965



Conclusions: A wide selection of instruments and assay conditions were represented in this study. The inclusion of cell culture material allowed precise measurements of large numbers of individual cells. Somewhat surprisingly, there was no significant difference in cell culture pellet adhesion across the 15 slide brands examined. However, retention did vary significantly among laboratories, consistent with differences in “harshness” among assays. In contrast, in round 2, 5 slides brands showed marked and consistent differences in adhesive performance in breast cancer tissues selected based on the impression of poor fixation. These findings suggest that the choice of slide brand may be an important consideration for tissue adhesion in some situations. We are planning a follow up study to specifically address the impact of delayed, under-, and overfixed tissues on IHC slide adhesion.

966 Analysis of Quality Issues in the Histology Laboratory

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Disclosures: Li Ge: None; Schaundra Walton: None; Jennifer Gordetsky: None; Florencia Jalikis: None

Background: Consistent, high quality histology is critical for the evaluation of surgical pathology specimens and ensuring an accurate diagnosis. Our quality assurance (QA) program monitors the characteristics of histologic slides. Issues that arise are documented and addressed on a weekly basis according to the highest standards. We present our experience with commonly encountered issues in histology quality and ways to prevent them.

Design: We reviewed the data from our histology QA program from June to December 2019 including total number of blocks per month, average number of blocks per work day, total number of slides prepared, and number of slides with quality issues. Histologic quality markers included incomplete sections, inappropriate hematoxylin and eosin staining, Loss of nuclear detail (nuclear meltdown), and tissue broken up during cutting (chatter).

Results: The number of blocks processed per month by the histology lab ranged from 21,906 to 25,480 (mean: 24,215). The number of total slides prepared per month ranged from 41,889 to 49,162 (mean: 46,521). The most common quality issue was incomplete sections, with a monthly average of 127 slides requiring a recut for diagnosis, comprising 0.3% of the total number of slides per month and 11% of the total number of blocks per workday (Table 1). Other histologic quality issues included chatter (monthly average: 12), nuclear meltdown (monthly average: 4), and overstaining (monthly average: 1).

Incomplete sectioning can be caused by improper embedding, cutting too shallow, or rough and rapid course facing, which leads to chunks of tissue popping out of block.

Common causes of chatter include poor fixation, loose or dull microtomy blades, and improper blade clearance angles in microtomy. We have found cold blocks and dehydrated tissue are also associated with chatter. In our experience, gastrointestinal biopsies were most susceptible to this artifact.

Nuclear meltdown is an overall rare problem but can have disastrous results for histologic quality. Inappropriate fixation is a major cause of nuclear meltdown and can be seen in specimens with less than 6 hours of fixation prior to processing or in sections of tissue that are very thick. Inappropriately mixing of reagents in the processor can also lead to this phenomenon.

We found that dark/over-staining was often caused by thick sections. Reducing the thickness of sections to 3 microns for GI biopsies and ensuring complete draining of water from the slides prior to staining was helpful in resolving this issue (Table 2).

Table 1. Numbers of blocks, slides, and slides with quality issues from June 2019 to December 2019.

Month	Total number of blocks	Average number of blocks per work day	Total number of slides	Number of slides with incomplete section	Number of slides with chatter	Number of slides with nuclear meltdown	Number of slides with overstaining
Jun	21,906	1,095	41,889	143	5	0	1
Jul	23,846	1,084	46,752	109	23	0	0
Aug	25,584	1,163	48,465	146	5	1	4
Sep	23,906	1,195	44,074	46	15	0	0
Oct	25,480	1,108	49,162	90	26	7	0
Nov	24,170	1,209	47,451	236	11	22	0
Dec	24,611	1,231	47,855	118	0	1	0
Average	24,215	1,155	46,521	126.9	12.1	4.4	0.7

Table 2. Causes and cures of the issues in histology quality.

Issues	Causes	Cures
Incomplete sections requiring recuts	• Didn't cut deep enough • Embedded improperly • Poor fixation/processing	• Blocks given back to original cutters for feedback • Education of grossers (tissue in cassettes no thicker than a nickel) • Reprocess blocks
Chatter	• Blocks may be getting too cold • Blocks may need to be rehydrated prior to cutting • Cutting speed too fast	• Don't let water build up in the ice bath that the blocks rest on • Soak block for a couple of minutes in ammonium water to rehydrate • Education of techs to slow cutting speed
Nuclear meltdown	• Tissue too big in a processing run that is too short • Reagents are mixing inappropriately in the processor • Excessive time in heat	• Larger GI polyps do not go on a short run; do not over fill cassettes at grossing • Make sure the processor is not failing (e.g. valves)-processors replaced with newer model and fail-safe features • Remove heat from all processing steps where not necessary, reduce wax temperatures to 2-4 degrees Celsius above melting point, and ensure tissues are not left in hot wax, ovens, or warming chambers of embedding centers for extended periods of time
Overstaining	• Sections are being cut too thick, especially noticed on GI biopsies	• Change thickness to 3 microns for GI biopsies • Ensure that all water is drained from sections prior to drying in the oven and staining

Conclusions: Histologic quality is a crucial part of patient care. There are common issues affecting histologic characteristics that can be tracked, corrected, and prevented. A team approach, including input from pathologists, histology technicians, and gross room managers, should be taken to ensure excellent histologic quality in anatomic pathology.

967 Patients with Immediate Access to the Pathology Report are More Active in Their Care: The Ottawa Hospital Experience So Far

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Disclosures: Zuzanna Gorski: None; Anthea Lafreniere: None; Bibianna Purgina: None; Virginia Roth: None; Kathleen Gartke: None; Debra Bournes: None; Jason Wasserman: None

Background: Patients now have access to their medical records via online patient portals. However, many institutions have opted to delay access to pathology reports by up to two weeks due to their sensitive and highly technical nature. In July 2020, The Ottawa Hospital (TOH) started to provide patients with immediate access to

their pathology report via the MyChart online portal. This decision was made after extensive consultation with focus groups and the hospital's Patient and Family Advisory Council. Patients were also provided with a link to MyPathologyReport (www.MyPathologyReport.ca), an online patient-centered pathology education resource. The purpose of this study was to compare the number of patients arriving at MyPathologyReport directly from MyChart before and after the initiation of immediate access.

Design: We compared the number of patients arriving at MyPathologyReport directly from MyChart for three months leading up to (April 20 – July 21, 2020) and three months following (July 22 – October 25, 2020) the initiation of immediate access. Anonymous user information was collected by Google Analytics. No personal identifying information was collected at any time nor did MyPathologyReport have access to the patient's electronic medical record.

Results: The number of patients arriving at MyPathologyReport directly from MyChart increased from 5,487 for the three months leading up to the initiation of immediate access to 8,383 after the change (an increase of 53%). The most commonly accessed articles were similar in both groups. Specifically, introductory articles describing the interpretation of COVID-19 test results, pap smears, and bone marrow biopsies were the top three most read articles in both groups. Articles describing invasive ductal carcinoma, prostatic adenocarcinoma, lung adenocarcinoma, and ductal carcinoma in situ were also in the top ten most read articles for both groups. There was no difference between the two groups in the overall time spent on the site.

Conclusions: Patients given immediate access to their pathology reports were more likely to visit a patient-centered pathology education resource to learn more about their report. Providing a direct link from online patient portals to such resources allows patients to obtain reliable and trusted information about their results. Whether this change leads to improved patient experience has yet to be determined.

968 In Tune with the Target Audience: A Quality Improvement Initiative to Enhance Communication Between Gastrointestinal (GI) Pathologists and the Clinical Care Team

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Disclosures: Maria Gubbiotti: None; Jogarao Vedula: None; Ciera Mangone: None; Rashmi Tondon: None

Background: The primary means of pathologist-clinician crosstalk is the pathology report. However, report formatting varies among pathologists and often includes esoteric histologic descriptions, making it difficult for clinicians to extract pertinent information to help guide treatment. Therefore, there is a need to optimize pathology reporting to include relevant and concise microscopic descriptions and immunohistochemical (IHC) profiles while also maintaining readability.

Design: To address clarity of communication of pathology reports with clinicians as part of a quality improvement project, a 10 question survey was provided to members of GI clinical care teams throughout the university's health system. Questions assessed level of experience, time spent reading a pathology report, and the importance of report components including gross, microscopic, and IHC descriptions as well as verbiage. An open response question was also included.

Results: 49 clinical team members responded to the survey (see table 1). The free response question yielded 44% comments about Cerner/EPIC interface formatting issues including unusual characters, unusual formatting of sentences, and text taking up many more rows than they should. Additional suggestions included keeping pertinent information in the diagnostic line, such as Metavir and NAFLD activity scores, and improving clarity about follow-up addendum reports (such as for reflex testing in cancer diagnosis).

	Responses
Level of experience	Attending physician >10 years: 12 Attending physician 5-10 years: 9 Attending physician <5 years: 12 Fellow physician: 7 Resident physician: 3 Advanced practice provider: 6
Time spent reading report	<5 minutes: 32 5-15 minutes: 16 15-30 minutes: 1
How often gross description is read	Always: 9 Usually: 10 Sometimes: 21 Rarely: 9 Never: 0
How often is the note important to clinical care	Always: 4 Usually: 16 Sometimes: 26 Rarely: 2 Never: 0
How often is the microscopic description important to clinical care	Always: 16 Usually: 16 Sometimes: 15 Rarely: 1 Never: 0
How often is immunohistochemistry important to clinical care	Always: 7 Usually: 25 Sometimes: 15 Rarely: 1 Never: 0
Is direct communication from pathologist to clinician beneficial?	Yes: 48 No: 0
Are the phrases "compatible with," "suggestive of," "consistent with," and "cannot rule out" helpful when analyzing the report?	Yes: 35 No: 9 Does not matter: 5
Does the mention of clinical correlation, negative findings, and suggestions of future studies such as re-biopsy or imaging help to clarify the report?	Yes: 43 No: 3 Does not matter: 2

Conclusions: Our survey results demonstrate that the clinical team values each component of the pathology report (gross, microscopic descriptions, and IHC data) for best patient care. Verbiage used in the final diagnostic line is of paramount importance. Clinicians unanimously value verbal communication about pathology reports, especially in complex cases. Based on these survey results, we are attempting to make several changes to our current reporting system as follows:

1. To prevent CERNER/EPIC formatting errors, reduce the font size of IHC disclaimer and provide a separate disclaimer section instead of embedding in the main body of the report

2. Separately uploading reports to the EPIC media tab as PDFs for better readability

3. Avoid unnecessary addendums and notes, if possible

4. Design expedites, which create auto-populated notes stating that an addendum is pending which should be mentioned in the final diagnosis

5. Future plan to move to EPIC beaker

We conclude that clear verbiage and communication are the bridge between the pathologist and the target audience and we can adjust our reporting style to enhance this symbiosis.

969 Adoption of an Alternate Innovative Performance Improvement Filter in the Management of Adverse Events in Anatomic Pathology Practice at an Academic Medical Center

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Disclosures: Zainab Harb: None; John Hunt: None; David Gang: None; Vandita Johari: None; Ashraf Khan: None; Rahul Jawale: None

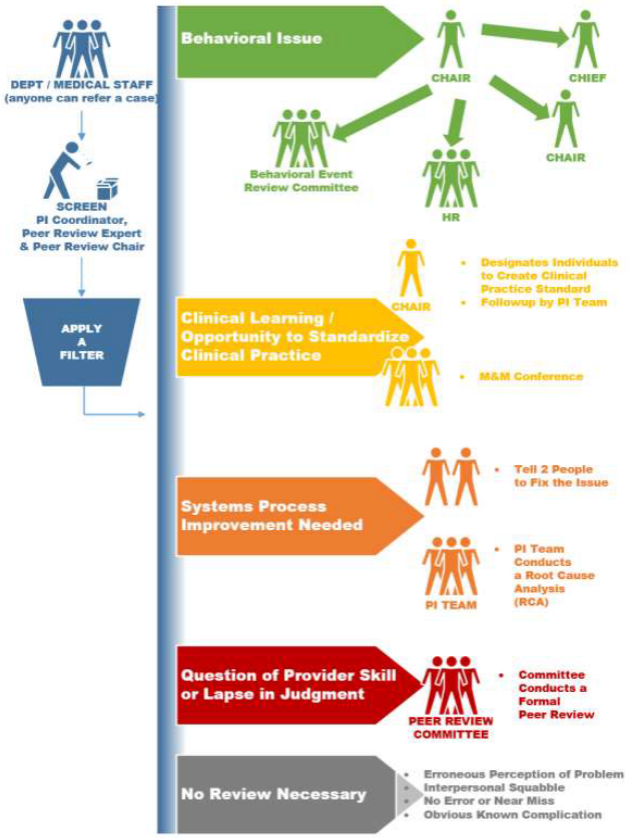
Background: The role of quality improvement and analysis of errors in anatomic pathology is well established, and there is a variation in assessing these incidents. Majority efforts are focused on categorizing these incidents; however, little data exists on appropriate actions and management of these events. We share our experience of adopting an alternate innovative Performance Improvement (PI) Filter guiding us to manage occurring adverse events in our anatomic pathology laboratory.

Design: Our pathology department recently adopted a PI Filter (see figure), in congruent with a standardized approach followed by Risk Management of our Health System. All adverse events (2018 onwards) were submitted to the pathology PI Coordinator by providers (including pathologists). An in-depth analysis of these cases was performed by the Peer Review Screen Team (Peer Review Chair and Experts, PI Coordinator and Risk Management), and using the Filter, cases were characterized in 1 or more of the 5 established categories.

Results: 122 adverse events were scrutinized, 34 events self-referred, 61 events referred by another pathologist, and 26 events were referred by providers. 41 were pre-sign-out events, 56 were events at sign-out and 23 were post-sign-out events. Notably, a subset of adverse events qualified for more than one category. There were 8 instances of categorization as Behavioral Issue, 31 instances of Clinical Learning Opportunity, 26 instances of System Process Improvement Needed, 9 instances of Question of Provider Skill or Lapse in Judgement and 61 instances of No Review Necessary (see table). In response to these findings, 9 cases were referred to formal Peer Review, 16 Mortality and Morbidity Conferences were organized, there were 26 alerts to improve processes, and opportunities to address and promote a targeted culture of safety and communication were present.

Category	Sub-category	Instances	Percentage	Example of action taken
Behavioral Issue		8	6.5	Culture of Safety
Clinical Learning Opportunity	Opportunity to Standardize Practice	5	4.09	Standardization
	M&M Conference	16	13	Education
System Process Improvement		26	21.3	Process Improvement strategies
Question of Provider Skill or Lapse in Judgement		9	7.38	Formal Peer review
No Further Review Necessary	Outside Hospital Issue	9	7.38	Communication
	Provider Issue	8	6.5	Communication
	Erroneous Perception of Problem	9	7.38	Communication, Education, Standardization
	No Error/Near Miss	11	9.02	Communication, Education
	Obvious Known Complication	15	12.29	Education

Figure 1 - 969



Conclusions: The PI Filter adopted has proven to be effective in dissecting and objectively assessing adverse events in anatomic pathology. In addition to identifying cases with potential harm for peer-review; cases with no potential harm provided ample opportunities for clinical learning, clinical practice standardization, systems process improvement, conferences, and trainee education as well as addressing behavioral issues in a safe environment. We highly recommend pathology practices to implement this PI Tool in their practice.

970 Success Could Be Automated or Through Doing Less: Our Experience on Nucleic Acid Extraction For COVID-19 Tests

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Disclosures: Krishna Iyer: None; Monica Talmor: None; Chen Liu: None; Pei Hui: None; Minghao Zhong: None

Background: The molecular diagnostics are currently highly complex. One of contributors to this complexity include the numerous steps involved in material preparation. At the beginning of COVID19 pandemic, we were forced to use labor-intensive manual processing for nucleic acid (NA) extraction, because of national wide supply chain disruption. Additionally, we were suffering from staff shortage and fatigue. Later on, we solved these problems by implementation of a KingFisher automated NA extraction instrument. We also took advantage of SalivaDirect™, a rapid testing method, developed in house for emergency use authorization. This method is intended to replace our current NA extraction methods, using simpler proteinase K preparation and heat treatment methods. In this study, we analyzed the failure rate of NA extraction from different these various approaches.

Design: The NA extraction failure was determined by invalid MS2 reporter gene values, a processing control used by the ThermoFisher TaqPath COVID-19 test. We compared failure rates before and after implementation of KingFisher. SalivaDirect does not use a processing control; rather it uses a primer/probe set for RNaseP, an

internal control to determine if enough sample was collected. The internal control failure indicates either problems with NA extraction and/or sampling. A test is repeated when a sample fails the internal control. If 2nd test still fail, this indicates a sampling error.

Results: The failure rates (i.e invalid MS2 reporting) due to manual NA extraction were collected for a period of time before and after implementation of the KingFisher automatic method. The average NA extraction failure rate was ~5.9% for the manual method vs 1.0% for the Kingfisher extraction method . We also experienced significant between and within personnel variation in NA extraction , whereas KingFisher was more consistent. The most failure rates occurred at early phase implementation and most likely was due to technical and specimen handling errors. For SalivaDirect, the failed tests were attributed to inadequate sample and not NA extraction failure.

Conclusions: Our data demonstrated that implementation of automation or simplification of labor-intensive process resulted in improvements in extraction failure and more consistent test results, which translated to improved turn-around time, reduced reagent cost and increased efficiency without compromising test quality.

971 Patient Use of Pathology Reports: An Institutional Survey of Breast Clinic Patients

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Disclosures: Kimberly Johnson: None; Julie Jorns: None

Background: Patients now have access to their medical record through online patient portals. However, most pathology reports are designed to communicate to clinical providers, not patients. We sought to understand how patients utilize pathology reports, while raising awareness to the availability of pathology reports and other results via the online patient portal.

Design: Surveys were administered exclusively in breast clinics and any patient that had a pathology report generated after 03/2018 (the first month reports were made available to patients online) and scheduled for an appointment on days of administration was eligible. However, patients could decline to participate and were asked to complete the survey only once. Ideally, nursing staff filled in four (4) administrative data points (age, benign vs malignant diagnosis, 1st vs later visit and Distress Tool Score). Patients answered all other questions. Surveys contained no identifying information, and all (partially or fully) completed surveys were collected and stored in a secure location for later batch pick-up and analysis (Figure 1).

Results: 149 surveys were received. All patients answered main questions 1 and 2; however, only 56 (37.6%) had administrative data. Patient responses were stratified by their answers to the first question (Figure 2).

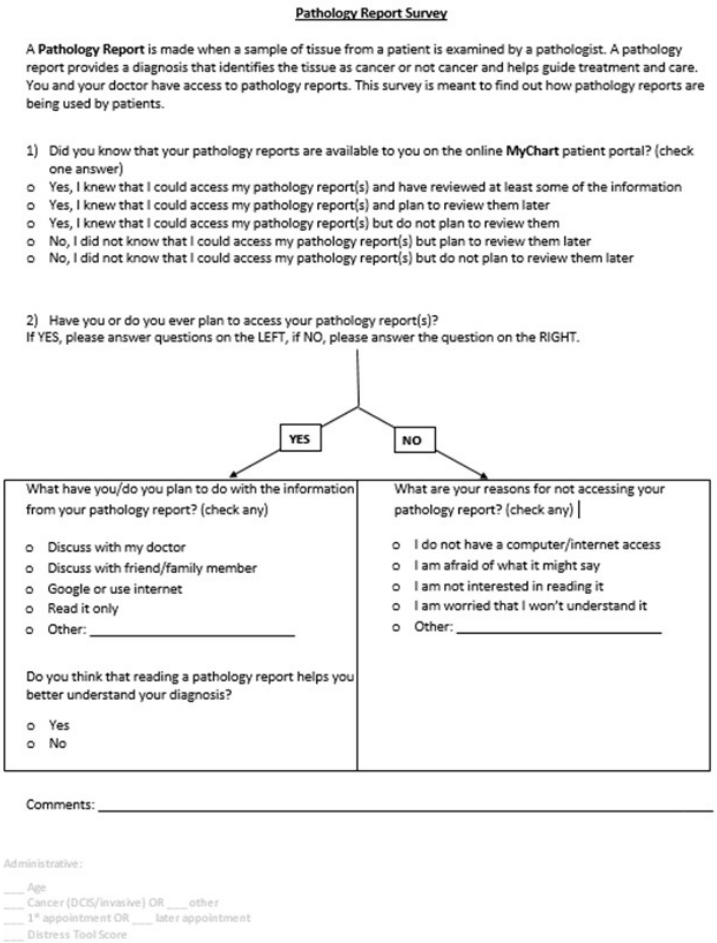
Question 2 responses showed most participants (123/149; 82.5%) selected “Yes they have or plan to review their pathology reports,” with 26 (17.4%) selecting “No I do not plan to review report.” Answering “Yes” to this question was significantly associated with younger patient age (mean 54.5 vs 61.8 years) (p=.035). Reasons for use and lack of use were varied (Table 1).

Most (118/149; 79.2%) respondents indicated that they believe that their pathology report allows them to better understand their diagnosis.

Table 1. Follow-up of Question 2: “Have you or do you ever plan to access your pathology report(s)?” Patient reasons for use and for not accessing their pathology reports

Yes (N,%) (N=123)		No (N,%) (N=26)	
Discuss with MD	98 (79.7)	Other	17 (65.4)
Discuss with friend/family member	76 (61.8)	Afraid of what it might say	7 (2.7)
Look up on internet	42 (31.4)	Worried won’t understand	6 (2.3)
Read only	27 (22.0)	Lack of computer/internet	2 (0.8)
Other	11 (8.9)		

Figure 1 - 971



Pathology Report Survey

A **Pathology Report** is made when a sample of tissue from a patient is examined by a pathologist. A pathology report provides a diagnosis that identifies the tissue as cancer or not cancer and helps guide treatment and care. You and your doctor have access to pathology reports. This survey is meant to find out how pathology reports are being used by patients.

1) Did you know that your pathology reports are available to you on the online **MyChart** patient portal? (check one answer)
- o Yes, I knew that I could access my pathology report(s) and have reviewed at least some of the information
- o Yes, I knew that I could access my pathology report(s) and plan to review them later
- o Yes, I knew that I could access my pathology report(s) but do not plan to review them
- o No, I did not know that I could access my pathology report(s) but plan to review them later
- o No, I did not know that I could access my pathology report(s) but do not plan to review them later

2) Have you or do you ever plan to access your pathology report(s)?
If YES, please answer questions on the LEFT, if NO, please answer the question on the RIGHT.

YES

What have you/do you plan to do with the information from your pathology report? (check any)
- o Discuss with my doctor
- o Discuss with friend/family member
- o Google or use internet
- o Read it only
- o Other: _____

Do you think that reading a pathology report helps you better understand your diagnosis?
- o Yes
- o No

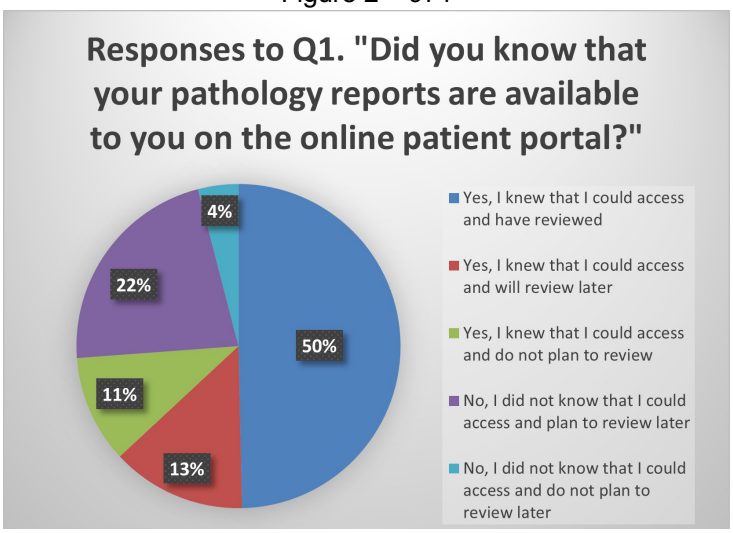
NO

What are your reasons for not accessing your pathology report? (check any)
- o I do not have a computer/internet access
- o I am afraid of what it might say
- o I am not interested in reading it
- o I am worried that I won't understand it
- o Other: _____

Comments: _____

Administrative:
___ Age
___ Cancer (DCIS/invasive) OR ___ other
___ 1st appointment OR ___ later appointment
___ Distress Tool Score

Figure 2 – 971



Conclusions: Although responses varied, many patients felt that having access to their pathology reports was beneficial, which showed an association with younger age. For some patients, this benefit may extend to development of pathology consultation services where patients can discuss their pathology reports and/or view slides with a pathologist.

972 Use of Pathology Data to Evaluate Impact of COVID on Stage at Presentation for Genitourinary Malignancies

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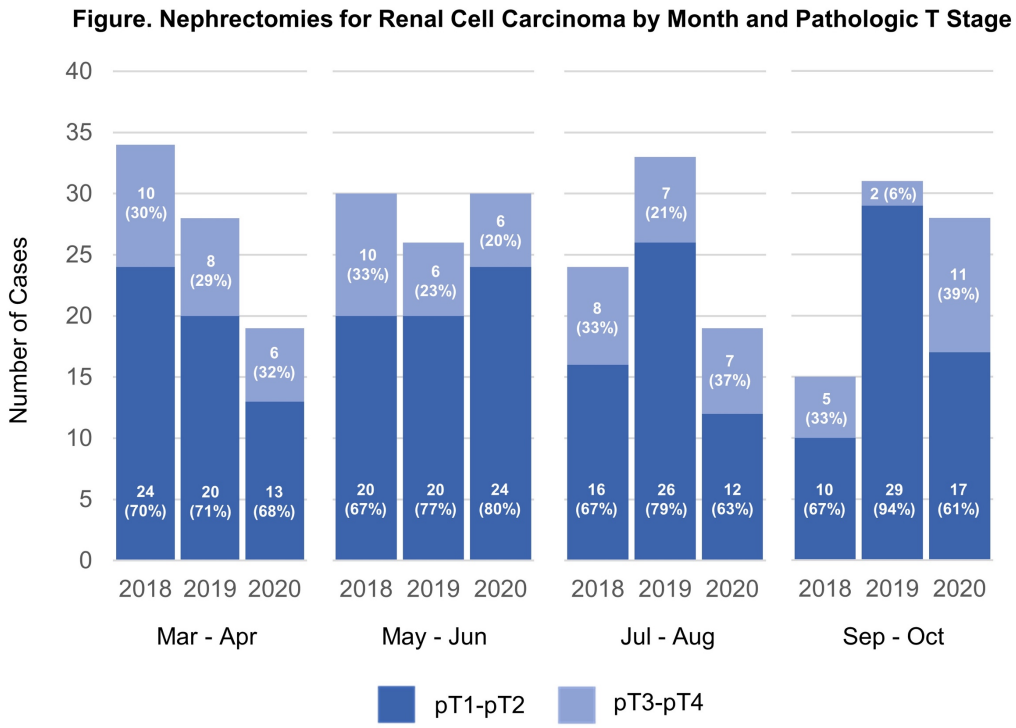
Disclosures : Steven Johnson: None; Hung-Jui Tan: None; Sara Wobker: None

Background: According to the Centers for Disease Control and Prevention, it is estimated that nearly one-third of Americans have delayed routine medical care and 12% have delayed urgent or emergent care during the COVID pandemic. The COVID and Cancer Research Network (CCRN) has shown significant decreases in cancer-specific care during this time. Additionally, many hospital systems halted elective surgeries and procedures, further limiting access to screening and early interventions for cancer. AJCC pathologic T stage may provide early insight into COVID-related trends in surgical utilization and stage at presentation.

Design: In this retrospective review of cancer cases, we sought to characterize trends in stage at presentation between similar time periods relevant to the COVID pandemic (Mar 1 - Oct 28) in 2018, 2019 and 2020. We performed a search of our laboratory information system for nephrectomies performed with a final diagnosis of renal cell carcinoma. We chose renal cell carcinoma due to the fact that surgery is the primary treatment and neoadjuvant treatment is not commonly used in this setting. The following data were abstracted for the cases: date of surgery, patient sex, age, specimen type (partial versus total/radical nephrectomy), histologic diagnosis, tumor size, margin status, and final pathologic stage. Ongoing data collection will extend the time period evaluated and include other GU malignancies.

Results: 511 nephrectomies were performed over the search period, 328 of which had an RCC diagnosis (2018 n=104, 2019 n=121, 2020 n=103). There was no significant difference in total case volume during these time periods each year. In addition, no significant differences were seen in total rates of pT1-2 for 2018, 2019, and 2020, respectively (67.3%, 78.5%, 72.8%) and pT3-4 cancers (32.7%, 21.5%, 27.2%). However, when analyzed by individual months (Figure 1), there was a significant increase in the proportion of pT3-4 cancers seen in Sep-Oct 2020 (11/28, 39%) when compared to those months in 2018 and 2019, collectively (7/39, 18%; p = 0.026 by Fisher's exact test).

Figure 1 - 972



Conclusions: While surgical volumes remained stable over the 3 year period, an increase in the proportion of high stage cancers during Sep-Oct 2020 was seen when compared to similar periods in 2018 and 2019. This may indicate a lagging indicator of more advanced disease presentation that will become more pronounced over time. The potential negative consequences of detection and treatment delays in cancer due to COVID will become evident over time, with likely impacts on recurrence and mortality rates. Secondary databases may be delayed in their ability to detect deleterious effects of decreased cancer care during COVID, and pathology data provide real-time indicators of these emerging trends.

973 Does Rapid On-Site Evaluation (ROSE) or Thyroid Imaging Reporting and Data System (TI-RADS) Score Correlate with Adequacy Rate for Ultrasound Guided Fine Needle Aspiration (FNA) Biopsy of the Thyroid?

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Disclosures: David Kim: None; Glorimar Rivera Colon: None; Elena Lucas: None; Devin Sanders: None

Background: An adequate specimen is imperative for an accurate diagnosis of thyroid nodules sampled by FNA. However, a wide range of adequacy rates (3-34%) have been reported across various institutions. Although ROSE had historically been employed for all ultrasound guided thyroid FNAs at our 870 bed tertiary care hospital, limited resources and increasing time constraints prompted a decision to forego ROSE for first time evaluation. We sought to determine how replacement of ROSE with a standard “three passes, no check” procedure affects specimen adequacy rate. We also attempted to determine if TI-RADS score affects specimen adequacy rate.

Design: A search of ultrasound guided thyroid FNAs performed from March to December 2019 yielded 377 nodules. 190 thyroid nodules were sampled with ROSE. 187 nodules were sampled without ROSE. Adequacy was defined by The Bethesda System for Reporting Thyroid Cytopathology. We compared adequacy rates of FNAs performed with ROSE to FNAs performed without ROSE. We also compared adequacy rates of thyroid nodules, grouped by TI-RADS scores. All rates were compared using the chi-square test.

Results: Of the 190 nodules evaluated with ROSE, the FNA was inadequate in 27 cases (adequacy rate 85.8%). The average number of passes with ROSE was 3.7 passes. Of the 187 nodules evaluated without ROSE, the FNA was inadequate in 31 nodules (adequacy rate 83.4%). The average number of passes without ROSE was 3.2 passes. The difference in adequacy with ROSE and without ROSE was not statistically significant (p-value: 0.52). TI-RADS scores (3: mildly suspicious, 4: moderately suspicious, and 5: highly suspicious) did not have a bearing on adequacy regardless of whether or not ROSE was employed (p-value: 0.55), see table 1. Higher TI-RADS scores correlated with higher risk of malignancy and with higher Bethesda categories. Every surgical excision (n=25) of the 32 thyroid nodules diagnosed as Bethesda category V (suspicious for malignancy) and VI (malignant) revealed a thyroid malignancy.

Table 1. Number of Nodules by Adequacy and TI-RADS Scores

	TI-RADS 3	TI-RADS 4	TI-RADS 5	Total
Inadequate	13 (15.7%)	27 (13.4%)	14 (18.7%)	54
Adequate	70 (84.3%)	174 (86.6%)	61 (81.3%)	305
Total	83	201	75	359
Adequacy Rate	84%	87%	81%	85%
P-value (chi-square)	0.55			

Conclusions: In a busy setting with limited resources, it is reasonable to forego ROSE if adequacy rates are high. Three passes with proper technique appears to provide acceptable adequacy rates. Higher TI-RADS scores should not necessarily prompt the radiologist to take additional passes. Reassessment of rates should regularly take place to ensure proper patient care.

974 A College of American Pathologists (CAP) Immunohistochemistry Survey Identifies Lack of Interchangeability of Ki-67 Immunohistochemistry Assays

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Disclosures: Dylan Miller: None; Rhona Souers: None; Andrew Bellizzi: None

Background: Ki-67 immunohistochemistry (IHC) is widely utilized in surgical pathology for the purpose of grading (e.g., neuroendocrine tumors) and as a prognostic marker (in many tumor types). Recent breast cancer clinical trials have used the Ki-67 proliferation index (PI) to assign patients to different treatment arms. While the MIB-1 clone has a long track record, alternative clones are increasingly utilized. Given Ki-67's emerging role as a predictive marker, interassay comparisons and a proficiency testing program are sorely needed.

Design: Ki-67 was challenged as part of the 2020 CAP PM5 (rotating markers) IHC survey--distributed to participants as a 10 core tissue microarray (TMA) consisting of 5 breast cancers and 5 neuroendocrine epithelial neoplasms selected to challenge various diagnostic and clinically relevant thresholds (i.e., 15% for breast; 3%, 20%, and 55% for neuroendocrine). Laboratories were asked to report a Ki-67 PI for each core. In addition, data were collected on antibody formulation, clone, staining method, testing platform, antigen retrieval pH, primary antibody incubation time, detection system, and use of image analysis.

Ki-67 PI distribution differences for these testing parameters (minimum group size=8 laboratories) were assessed with Kruskal-Wallis or Wilcoxon rank sum tests on a core-by-core basis. The relationship between clone and platform was assessed with a phi coefficient. Given the inherent repeated measures structure of the 10-core TMA, subsequent to univariate testing, a generalized linear mixed effects repeated measures analysis (GLM) was fit for clone 30-9 vs MIB-1 and the interaction between core and clone. Analyses were performed with SAS 9.4 and assessed at a significance level of 0.05.

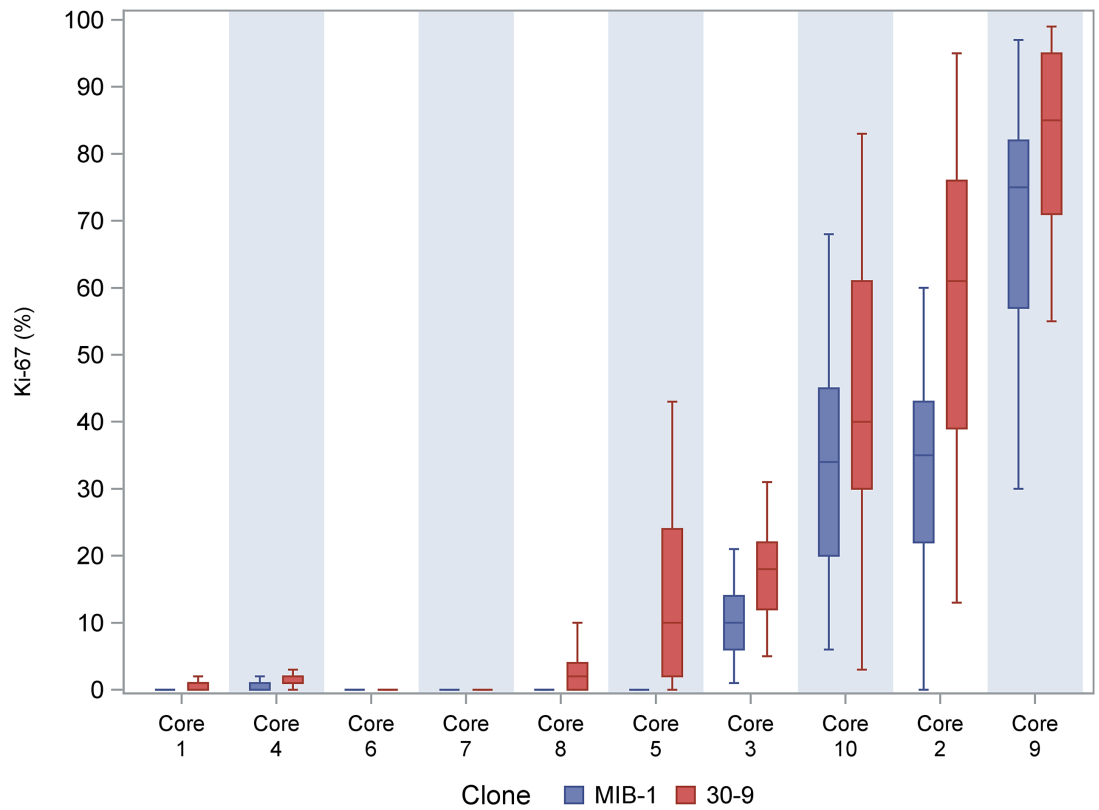
Results: Data from 85 laboratories showed significant KI-67 PI differences for clone and platform on univariate analyses, though these parameters were highly correlated (Φ=0.97). All other parameters were not significant ($p>0.05$), with the exception of antigen retrieval pH in 3 cores. For the GLM, 718 Ki-67 PIs from 72 laboratories, including 39 using clone 30-9 and 33 using MIB-1, were analyzed; the interaction term F statistic is 7.07 ($p<0.01$), indicating significant clone-specific differences within different cores (with the difference varying core-by-core). Ki-67 PI distributions by core and clone and detailed testing practice data are presented in the Figure and Table.

Table: Ki-67 Testing Practices Summary

Testing practice		**No. of labs**	
Antibody formulation	Pre-diluted	59	
	Concentrated	22	
Clone	30-9	39	
	MIB-1	33	
	MM1	7	
	SP6	4	
	K2	2	
Staining method	Automated	83	
	Manual	1	
	Do not perform staining	1	**Platform-specfic clone usage**
Testing platform	Ventana	44	30-9 (n=38) MIB-1 (n=4) MM1 (n=2)

	Leica	22	MIB-1 (n=12) MM1 (n=5) SP6 (n=3) K2 (n=2)
	Dako	15	MIB-1 (n=15)
	Biocare	1	
	Manual	1	
	Other	1	
Antigen retrieval	High pH	72	
	Low pH	12	
Primary antibody incubation	<15 minutes	21	
	15-30 minutes	52	
	>30-60 minutes	10	
	>120 minutes	1	
Detection system	Ventana UltraView DAB	33	
	Leica Bond Polymer Refine	22	
	Dako EnVision FLEX	10	
	Ventana OptiView	8	
	Dako EnVision+ HRP	5	
	Ventana iView	3	
	Other	3	
Digital image analysis	Yes	13	
	No	69	

Figure 1 - 974



Conclusions: Ki-67 assays are not interchangeable, with clone and platform (which is highly correlated with clone) significantly influencing the PI. In 2021 the CAP IHC Committee will launch a standalone Ki-67 survey with two mailings a year. The 10-core TMA will be composed of calibrated cell line mixtures representing a range of PIs. Apparent lack of interchangeability of Ki-67 assays is distressing given the marker's emerging use as a predictive marker and demands industry and regulatory body attention.

975 Impact of the COVID-19 Pandemic in an Academic Hospital-Based Tertiary Cytopathology Practice: A V-Shaped Recovery

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Disclosures: Kanish Mirchia: None; Kamal Khurana: None

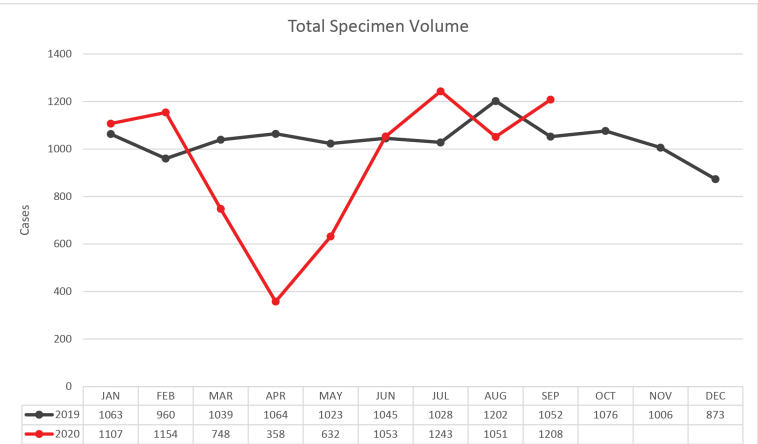
Background: The ongoing COVID-19 pandemic has led to a dramatic shift in volumes and practice patterns for hospitals around the globe. Using granular data, we analyzed its effect on the cytopathology subspecialty practice in a tertiary academic hospital-based setting.

Design: Overall specimen volume was analyzed for the cytology practice for 2019 and year-to-date (YTD) for 2020. Variables such as patient population, intake area, and financial accounts were included in the analysis when comparing years 2019 and 2020. The data was further subdivided into gynecological specimens, non-gynecological cytology, and fine-needle aspirate (FNA) specimens. Institutional and state/national guidelines as well as stimulus strategies to ease the effect of the pandemic were also taken into account.

Results: The overall specimens (Figure 1) decreased by 28% in March 2020 ($p < 0.00001$, chi-square), with a continuing decline in April (66% decrease YoY, $p < 0.00001$, chi-square), beginning of recovery in May and return to baseline within the month of June 2020. The year-to-date total specimen intake (January – September 2020) is 9.72% lower than in 2019, with a final projected volume deficit of 22.79% assuming a steady state during October – December 2020.

The subdivided specimen populations showed a similar trend with a few notable differences. The gynecologic specimen (Figure 2A) average for 2020 despite the effect of the COVID-19 pandemic is higher than 2019 with a final projected volume of +4.97%. This could in part be represented by addition of a new intake account in January 2020; also reflected in the higher volume of specimens in February 2020 compared to February 2019 ($p = 0.001321$, chi-square). The non-gynecologic specimens (Figure 2B) showed a similar recovery trend, however, demonstrating consistently lower volumes from June through September 2020, compared to similar duration in 2019. FNA specimens (Figure 2C) showed a marginally delayed recovery with return to baseline in July 2020 compared to June 2020 for the remaining services.

Figure 1 - 975



	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC
2019	1063	960	1039	1064	1023	1045	1028	1202	1052	1076	1006	873
2020	1107	1154	748	358	632	1053	1243	1051	1208			

Figure 1. Overall specimen volume for financial year (FY) 2019 (black) and 2020 (red)

Figure 2 - 975

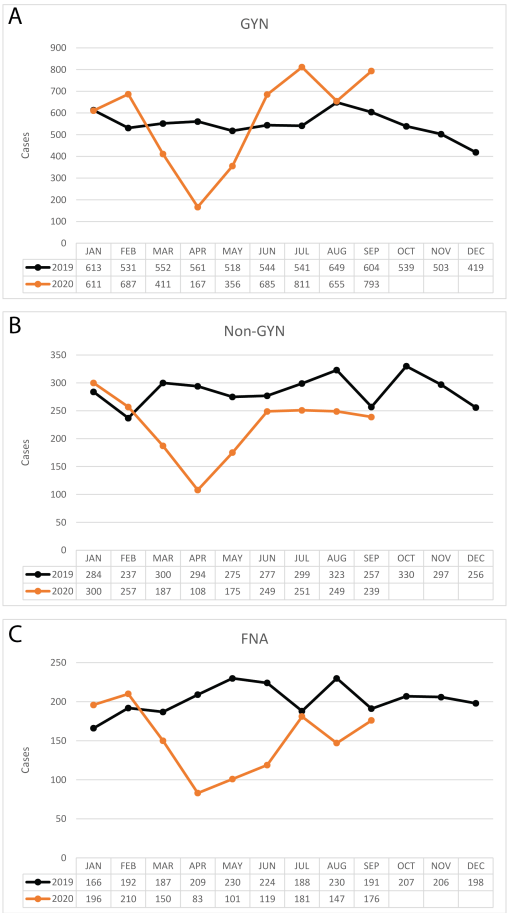


Figure 2. Gynecologic cytology (A), non-gynecologic cytology (B), and fine-needle aspirate (C) specimen volume for financial year (FY) 2019 (black) and 2020 (orange)

Conclusions: Overall, our study informs policy-making. Our data shows a sharp and significant decrease in patient volume, mostly due to stringent guidelines set by the state and national governments and our institution in response to the pandemic. The recovery curve was V-shaped; essentially the most ideal economic response to a downturn. The recovery efforts were also helped by stimulus measures such as the HSS provider relief CARES act, avoiding any potential loss of employees and a quick return to full workload and workforce.

976 Effects of SARS-CoV-2 on Placental Pathology and the Implications for Testing Pregnant Women

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Disclosures: Zunaira Naeem: None; Zimeng Gao: None; Emily Oliver: None; Rupsa Boelig: None; Joanna Chan: None; Allison Goldberg: None

Background: SARS-CoV-2 (SC2) infection is thought to be pro-thrombotic, but limited data exists on its effect on placental pathology. There is also limited data on best practices for SC2 screening in pregnant women. This study sought to further elucidate placental features seen with SC2 infection and support a SC2 testing strategy.

Design: A retrospective review of all placentas with pathology evaluation from 1/2020 to 7/2020 was performed, using placentas evaluated from 1/2019-7/2019 as a control group. Placentas from 2020 were divided into a positive cohort of patients with a positive SC2 test during pregnancy and an untested cohort consisting of placentas delivered to women not tested for SC2. Diagnoses of decidual vasculopathy (DV), intervillous thrombi

(IT), chorangiosis/chorangioma (CG), massive perivillous fibrin deposition (MPVFD), avascular villi (AV) and infarction (IF) were noted, as well as clinical diagnoses of pre-eclampsia (PE) or hypertension (HTN). Personnel performing and indications for placental pathology evaluation were static. Chi-squared test was used to compare patient populations and p-value was set at <0.05.

Results: There was no difference in proportion of patients with PE from 2019 (n=370) to 2020 (n=453) (17% vs 21%, p=0.11) and more patients had HTN in 2019 than 2020 (29% vs 21%, p=0.01). Of placentas from the positive cohort (n=32), 28% had DV, 6% had IT, 0% had MPVFD, 0% had CG, 0% had AV, and 9% had IF. The untested cohort of placentas (n=217) had a higher rate of DV (26% vs 13%, p<0.05) and MPFVD (2% vs 0%, p=0.003) than the 2019 group and the same rate of DV (26% vs 28%, p=0.82) and MPVFD (2% vs 0%, p=0.70) as the positive group. The 2020 untested cohort had the same rate of IT, CG, AV and IF compared to the control group (12% vs 11%, p=0.37), (1% vs 1%, p=0.59), (0% vs 3%, p=0.05), (14% vs 16%, p=0.39) and compared to the positive group (12% vs 6%, p=0.37), (0% vs 0%, p=0.70), (1% vs 0%, p=0.59), (14% vs 9%, p=0.49).

Conclusions: Increases in DV and MPVFD seen without increases in PE or HTN support the possibility that SC2 infections were missed when limited testing was performed and supports universal testing of pregnant women. Other features evaluated are either seen rarely or are non-specific which may explain lack of statistical significance in our study. Further study, including optimal timing for universal SC2 testing and if clinical sequelae of DV seen with SC2 recur in future pregnancies as they do when DV is associated with PE, should be considered.

977 Cytology-Histology Correlation of Cervical Pap Smears and Biopsies Performed at a Single Institution Compared to those Performed at Different Institutions

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Disclosures: Yanina Nikolaus: None; Allison Goldberg: None

Background: Cytology-histology correlation (CHC) is the gold standard for quality assurance in cytology laboratories. CHC can prevent under or over treatment of patients and serves as an educational tool for the personnel in cytology laboratories. If cervical pap smears (CP) and cervical biopsies (CB) are performed at different institutions, these benefits may be lost.

Design: All CB performed at our institution from 1/1/2019 to 12/31/2019 with an adequate CP performed in the six months prior to the CB were included in this retrospective review. We compared CHC for CP and CB performed at a single institution compared to CHC for CP and CB performed at different institutions, with a focus on proportion of overcalls on CP, as those are the most challenging discrepant CHC to manage clinically. We used the America Society of Cytology guidelines for our discrepancy assessment grid. Chi-squared test was used to compare proportions of populations. P-value was set at <0.05.

Results: Of the 305 CB in our study population, 69 had CP performed at our institution and 236 had CP performed at an outside institution. CHC for CB and CP performed at a single institution had statistically significantly less disagreement than for those performed at different institutions (p<0.05). Further, CB and CP performed at as single institution had statistically significantly fewer overcalls than CB and CP performed at different institutions (p<0.05) (table 1).

	Agree	Minor Variance	Minor Undercall	Major Undercall	Minor Overcall	Major Overcall	Totals
Same Institution N (%)	27 (39%)	23 (33%)	3 (4%)	9 (13%)	7 (10%)	0 (0%)	69
Different Institutions N (%)	110 (47%)	41 (17%)	18 (8%)	39 (17%)	4 (2%)	24 (10%)	236
Totals	137	64	21	48	11	24	305

Conclusions: This study further supports the use of CHC and encourages performance of CP and CB as the same institution. If performing CP and CB at the same institution is not feasible, prospective consultation review of CP by institution performing CB should be strongly considered. Further study, including evaluation of reason for

discrepancy in discordant cases may be considered to better elucidate reasons for better CHC agreement when CP and CB are performed at the same institution.

978 Do Gross and Microscopic Pathology Findings Support the Existence of a Subconscious Bias in Recommending Hip Arthroplasty for Patients with Osteoarthritis?

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Disclosures: Farres Obeidin: None; Sarah Dry: None

Background: Recent studies show primary care doctors and orthopedic surgeons are more likely to recommend surgery (arthroplasty) for osteoarthritis (OA) to men. As women disproportionately are affected by OA, this highlights a gender disparity in the management of OA and is worrisome, given broader subconscious gender and racial biases in the medical management of a number of health conditions. To our knowledge, no prior studies have assessed the pathologic severity of OA in men and women at joint arthroplasty surgery, which could help us understand if differences in management are or are not appropriately associated with objective indicators of disease severity.

Design: A retrospective review of EPIC/Beaker was performed for all hip arthroplasty (HA) specimens performed at our institution for primary osteoarthritis between January 1, 2019 and October 15, 2020. Excluded from study were cases of OA secondary to congenital hip dysplasia or autoimmune disease, primary avascular necrosis and arthroplasy for hip fracture. Gross (percentage of eburnation, presence of osteophytes, gross subchondral cyst formation) and microscopic (complete effacement of articular cartilage, thickened subchondral bone, subchondral cysts/fibrosis) criteria for osteoarthritis,and severity, were established prior to slide review (Table 1). Two pathologists with bone pathology expertise reviewed all slides and reports. Data was analyzed by Fisher's exact test.

Results: 517 cases met initial criteria. Following histologic review, 16 were excluded due to poor slide quality (inability to evaluate full articular surface), leaving a study group of 501 cases. This consisted of 284 women (57%) and 217 (43%) men, with a mean age of 67. Statistically significant differences (Table 1) were noted in age, gross percentage of eburnation and microscopic presence of subchondral cysts/fibrosis. For gross eburnation, 65 (23%) of women showed at least 50% eburnation of the femoral head compared to 33 (15%) of men, and 160 (56%) of women showed subchondral cysts/fibrosis compared to 100 (46%) of men. No statistically significant differences were seen in presence of osteophytes, gross evidence of cyst formation, histologic presence of complete cartilage effacement or thickened subchondral bone.

Table 1: Patient Characteristic Differences between Sex

Characteristic	Women	Men	[1]P
Age (*years*), (N) mean ± SD	(284) 69 ± 10	(217) 66 ± 11	0.002
Gross Eburnation, (N) %			0.030
None	(31) 11%	(17) 8%	
<50%	(188) 66%	(167) 77%	
≥50%	(65) 23%	(33) 15%	
Osteophytes, (N) %			0.783
Absent	(168) 59%	(125) 58%	
Present	(116) 41%	(92) 42%	
Gross Cyst Formation, (N) %			0.756
Absent	(258) 91%	(195) 90%	
Present	(25) 9%	(21) 10%	
Microscopic Complete Effacement of Cartilage, (N) %			0.646
Absent	(52) 18%	(44) 20%	
Present	(232) 82%	(173) 80%	

Microscopic Thickened Subchondral Bone, (N) %			0.644
Absent	(51) 18%	(43) 20%	
Present	(233) 82%	(174) 80%	
Microscopic Subchondral Cyst/Fibrosis, (N) %			0.024
Absent	(124) 44%	(117) 54%	
Present	(160) 56%	(100) 46%	
[1]Welch's t-test or Fisher's exact test			

Conclusions: Our data show women had more severe OA compared to men at the time of HA, measured by gross eburnation ≥50% and the presence of microscopic subchondral cysts/fibrosis. This supports prior data showing women are more symptomatic than men at the time of arthroplasty, and suggests possible subconscious gender bias in managing OA. We will review more cases, collaborate with Radiology to assess the radiologic severity of OA in our study group, and perform a medical records review to identify possible medical reasons for surgical delays in our study group, to understand if subtle medical factors can explain the differences identified.

979 Patterns of Error in Interpretive Pathology – A Review of 23 PowerPoint Presentations of Discordances

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Disclosures: Matthew Packer: None; Esther Ravinsky: None; Nazila Azordegan: None

Background: Quality assurance initiatives and analyses in Anatomical Pathology have until recently focused largely on the technical and administrative aspects of laboratory practice. The interpretive component of quality is less well studied. Targeted review of cases with discrepant interpretive findings between pathologists can raise awareness for specific diagnostic errors through identification of common overarching patterns of error in Interpretive Pathology. Between 2010 and 2017, our institution regularly performed PowerPoint presentations of discordances for quality assurance and educational purposes.

Design: We performed a review of 134 Surgical Pathology and Cytopathology cases of discordances from 23 PowerPoint presentations presented between 2010 and 2017. The discordant initial interpretations were classified into three categories according to a system proposed by The Royal College of Pathologists: UK1 (a diagnosis which one is surprised to see from any pathologist), UK2 (a diagnosis which is fairly clearly incorrect, but which one is not surprised to see a small percentage of pathologists suggesting), and UK3 (a diagnosis where inter-observer variation is known to be large). Pathologists and pathology residents, blinded from the official interpretations, were presented each case and surveyed for their own diagnostic assessments. Survey results were compared with the initial and final interpretations of the official signing pathologists.

Results: Based on The Royal College of Pathologists categorization system, 44% of the initial official diagnostic interpretations were classified as UK3 discrepancies, 54% as UK2, and 1% as UK1. Of the 134 reviewed cases, there were 87 (65%) for which most survey respondents proposed a diagnostic interpretation concordant with the final official diagnosis. There were 37 cases (28%) for which most survey responses were either wholly or partially discordant with the final diagnosis. For 10 cases (7%), there were equal numbers of concordant and discordant survey responses.

Conclusions: While the majority of survey respondents correctly identified the final official diagnosis for most of the cases, a large minority did not. Our analyses of the cases with frequent erroneous diagnoses reveal common patterns of error that are widely applicable and outline specific error-prone interpretive tendencies. Greater awareness for these tendencies, highlighted by presentation of discordant cases, can improve the quality of diagnostic pathology services.

980 Trend Analysis Insights from Reflex Mismatch Repair-Deficiency Screening of Endometrial Cancers: A Single Centre Experience

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Disclosures: Anna Plotkin: None; Ekaterina Olkhov-Mitsel: None; Liying Zhang: None; Sharon Nofech-Mozes: None; Bojana Djordjevic: None

Background: Monitoring positive receptors results over time (trend analysis) is an established quality measurement in breast carcinoma. Reflex testing using mismatch repair (MMR) immunohistochemistry (IHC) is the clinical standard of care for endometrial cancers (EC) patients for Lynch Syndrome (LS) screening and treatment decisions, and is performed in many hospitals. In this study, we sought to define the rates of MMR IHC loss in EC during the first 3 years of implementation of reflex LS screening, in order to identify the trends for establishing benchmarks for future IHC laboratory practices. Our hypothesis was that the proportion of cases with MMR deficiency is constant over time.

Design: Biomarker reports generated as part of our reflex MMR IHC testing program (with antibodies against MLH1, PMS2, MSH2 and MSH6) were retrieved. This encompassed all patients ≤60 years old from 06/2017 to12/2018 and patients ≤70 years old from 01/2019 to 08/2020. We assumed a 5-6% and 2-3% difference for MLH1 and MSH2 loss will be detected between follow-up time intervals, respectively. Two-sided binominal test was used for sample size analysis.

Results: For semiannual analysis over 3 years, sample size analysis identified a total case volume to establish benchmarks for testing proficiency to be 64 patients for MLH1 and 53 patients for MSH2/MSH6/PMS2, with a 0.048 significance level, 80% power. Our cohort contained 534 EC cases (110 biopsies and 424 resections) thus meeting this requirement. There were 409 endometrioid, 25 serous, 15 carcinosarcomas, 7 mixed, 6 clear cell, 4 de-differentiated, and 68 carcinomas with mixed epithelial histotypes. Mean rate of MLH1/PMS2 loss was 19%, MSH2/MSH6 3%, MSH6 4% and PMS2 2% (Figure 1). The proportion of MMR deficient cases was steady over time (Figure 2).

Figure 1 - 980

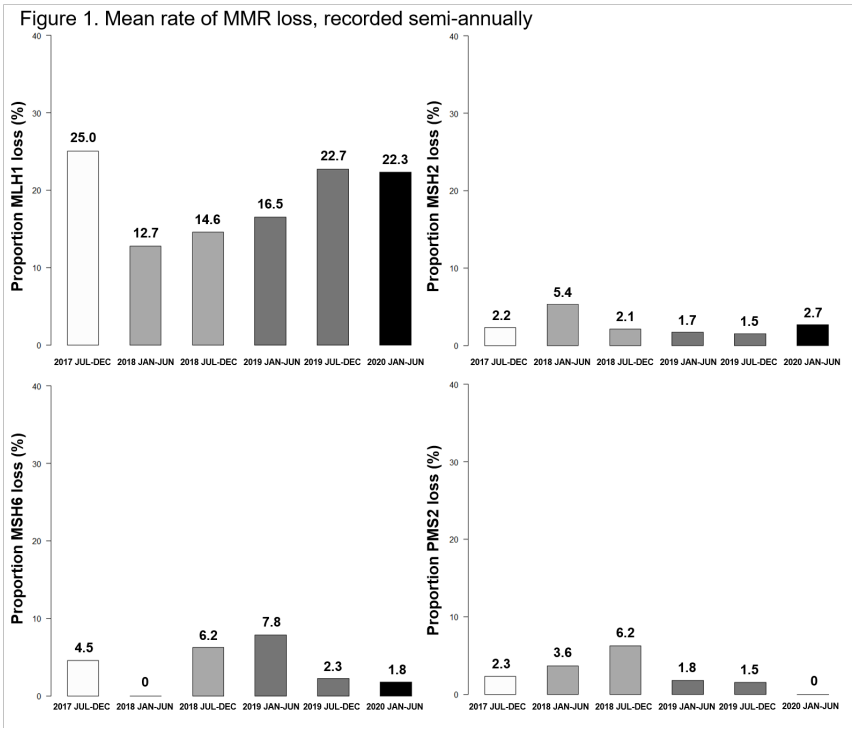

Figure 2 - 980

Figure 2. Pair-wise comparison of semi-annual time points using generalized estimating equations (GEEs) methodology, showing p-value Odds ratio (OR) and 95% CI of OR for each protein biomarker

	p-value	OR		95% CI of OR
Outcome: MLH1 Loss				
Semi-annual Time (6 categories)	0.3648			
2018 Jan-Jun vs. 2017 Jul-Dec	0.1214	0.438	0.154	1.245
2018 Jul-Dec vs. 2018 Jan-Jun	0.7841	1.171	0.379	3.615
2019 Jan-Jun vs. 2018 Jul-Dec	0.7582	1.159	0.453	2.969
2019 Jul-Dec vs. 2019 Jan-Jun	0.2241	1.486	0.785	2.815
2020 Jan-Jun vs. 2019 Jul-Dec	0.9397	0.977	0.535	1.786
Outcome: MSH2 Loss				
Semi-annual Time (6 categories)	0.7982			
2018 Jan-Jun vs. 2017 Jul-Dec	0.4482	2.434	0.244	24.244
2018 Jul-Dec vs. 2018 Jan-Jun	0.4143	0.384	0.039	3.821
2019 Jan-Jun vs. 2018 Jul-Dec	0.8624	0.807	0.071	9.119
2019 Jul-Dec vs. 2019 Jan-Jun	0.9024	0.884	0.123	6.376
2020 Jan-Jun vs. 2019 Jul-Dec	0.5271	1.792	0.294	10.919
Outcome: MSH6 Loss				
Semi-annual Time (6 categories) *	0.1373			
2018 Jul-Dec vs. 2017 Jul-Dec	0.7197	1.400	0.223	8.797
2019 Jan-Jun vs. 2018 Jul-Dec	0.7260	1.274	0.329	4.924
2019 Jul-Dec vs. 2019 Jan-Jun	0.0552	0.272	0.072	1.029
2020 Jan-Jun vs. 2019 Jul-Dec	0.8036	0.795	0.131	4.845
Outcome: PMS2 Loss				
Semi-annual Time (6 categories) *	0.5939			
2018 Jan-Jun vs. 2017 Jul-Dec	0.6967	1.623	0.142	18.504
2018 Jul-Dec vs. 2018 Jan-Jun	0.5428	1.767	0.283	11.044
2019 Jan-Jun vs. 2018 Jul-Dec	0.1565	0.268	0.043	1.657
2019 Jul-Dec vs. 2019 Jan-Jun	0.8885	0.868	0.120	6.265

Conclusions: Successful IHC trend analysis is contingent not only on volume of testing but frequency of the event being tested. It is required to establish benchmarks for risk mitigation. While our laboratory, which is affiliated with a large cancer center and accepts regional cancer patient referrals, showed that we do have the minimum volume for establishing the benchmarks to for internal MMR IHC quality control, this volume is not attainable for smaller laboratories. This study underscores the necessity for such laboratories to participate in external quality control programs and/or lab consortiums. Alternatively, there should be regional centralization of MMR IHC testing.

981 The Utility of Postmortem Blood Cultures: A Two-Year Institutional Assessment

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Disclosures: Stephanie Riviere: None; Abigail Alexander: None; Lee Cross: None; Katelyn Dannheim: *Consultant*, K.D. has received consulting fees from PathAI for work unrelated to this manuscript; April Bobenchik: None

Background: There has been a general lack of consensus as to whether obtaining postmortem cultures at autopsy is of clinical utility. Much of this is due to difficulty with interpretation of results and frequent gross contamination. Though our institution adopts a standard procedure for how to collect postmortem blood cultures, there are no explicit guidelines or indications for doing so. In this retrospective study, we sought to review autopsy cases and determine whether obtaining postmortem cultures is of clinical benefit and if they add value to the final autopsy report.

Design: From January 2017 to January 2019, 205 autopsies were identified at one institution. Clinical, autopsy, and postmortem blood culture data were reviewed including antemortem blood culture findings, clinical cause of

death, time between patient expiration and autopsy (postmortem interval) and autopsy diagnosis/cause of death. Postmortem blood culture contamination was identified by using the criteria of having >1 species growing in the blood culture.

Results: Of the 205 autopsies performed, postmortem blood cultures were obtained in 66% (135/205) of autopsies. The postmortem blood cultures were deemed contaminants in 65% (88/135) of cases, 23% (31/135) of cases grew only one species, and 12% (16/135) of cases showed no growth. The average postmortem interval was 25 hours for cases with no growth and 34 hours for contaminated cases and for cases where only a single organism grew. Additionally, in cases with postmortem cultures taken, only 53% (71/135) had the postmortem culture results included in the autopsy report while 47% (64/135) had no mention of the results at all. In 3% (4/135) of cases, the autopsy diagnosis of sepsis confirmed the antemortem findings and in 5% (6/135) of cases, an autopsy diagnosis of sepsis was made where clinically it was not identified.

Conclusions: Overall, postmortem blood cultures have a limited utility and significance mainly due to the high rate of contamination and lack of reporting. To enhance efficiency by reducing time, effort and cost, our institution would benefit by adopting standard autopsy guidelines which detail how and when blood cultures should be taken. The guidelines should include the following: (1) taking postmortem cultures only when clinically warranted, (2) the review of proper sample collection technique, (3) considering the impact that the postmortem interval has on culture results, and (4) ensuring the results of the cultures are clearly communicated in the autopsy reports.

982 A Method for Assessing Performance of Automated Immunohistochemical Staining Platforms Using Digital Image Analysis

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Disclosures: Rebecca Rojansky: None; Sebastian Fernandez-Pol: None; Ellen Gomulia: None; Yasodha Natkunam: None; Megan Troxell: None

Background: Assessment of immunohistochemical staining platform performance is largely limited to subjective evaluation by trained personnel. Rigorous, routine, and/or semi-quantitative assessment of stain intensity is not typically performed. In this study we have developed a semi-automated method using whole slide images (WSIs) to assess stain intensity. This method substantiated staining variability that was suspected by visual evaluation, identified outlier instruments for further troubleshooting, and confirmed successful intervention.

Design: We assessed performance for five stainers by staining three positive control sections with anti-Anaplastic Lymphoma Kinase (ALK) on each. After slide scanning, 5x images were exported. Cell boundaries were detected using watershed cell detection in QuPath and mean DAB intensity per cell was calculated. Data was analyzed in R. We then focused analysis on three stainers, running a total of 48 positive and 48 negative control sections with or without uninterruptible power managers (UPMs). We replaced one instrument and installed UPMs on all five. 1,036 on-slide controls from clinical cases stained with either ALK (144 sections) or estrogen receptor (892 sections) over six months were retrospectively analyzed to confirm improved performance.

Results: This method revealed two technical variables impacting quality. The addition of UPMs resulted in a statistically significant increase in average DAB intensity per cell of over two-fold. This finding was independently corroborated on visual inspection. Digital analysis also highlighted one outlier instrument with over two-fold lower stain intensity than other instruments. This quantitation facilitated instrument replacement by the manufacturer. The replacement showed comparable stain intensity to the other instruments in our lab. Analysis of clinical cases confirmed sustained improvement in staining quality after our interventions.

Figure 1 - 982

Distribution of Average Max Intensity With and Without UPM

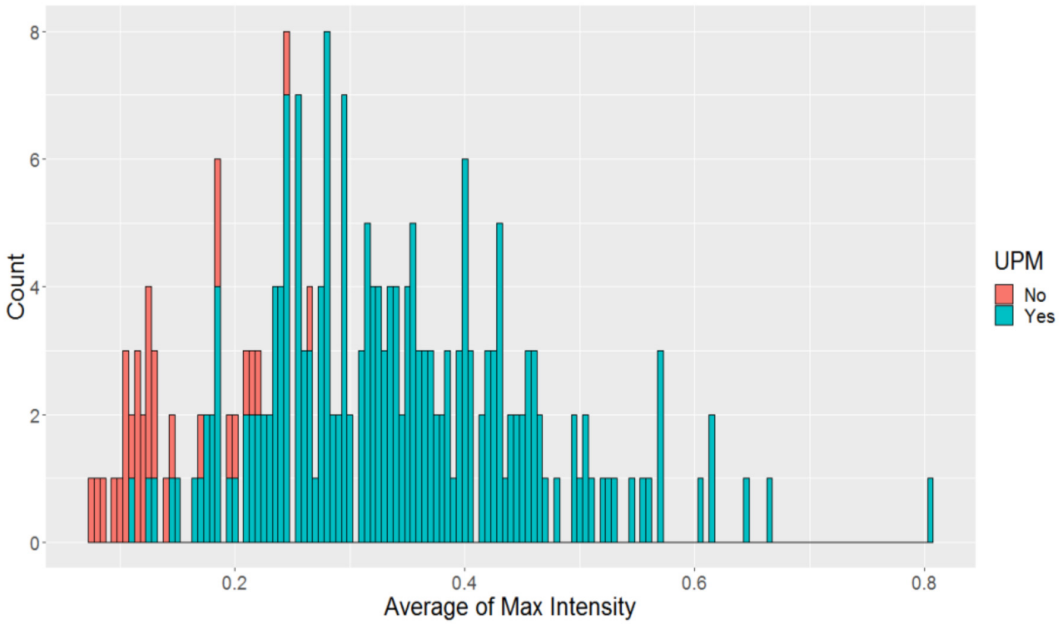
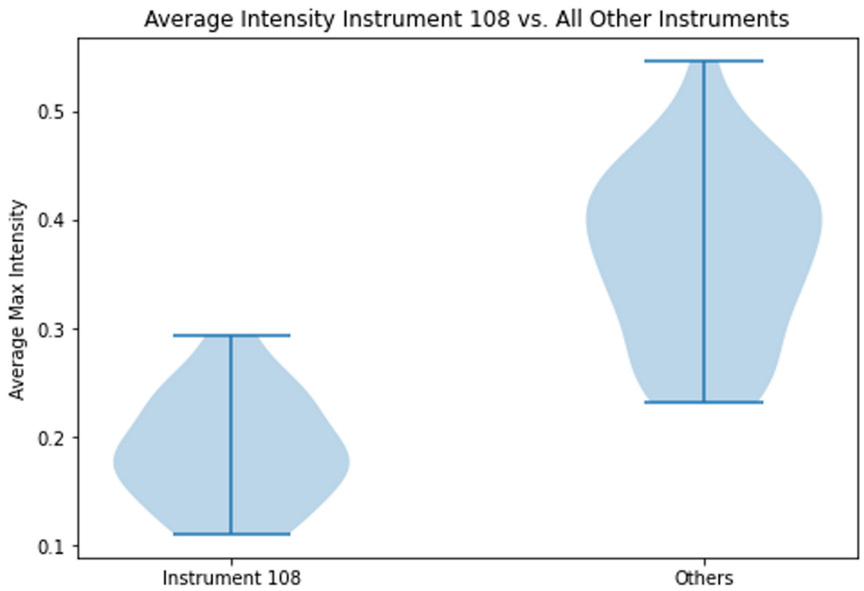


Figure 2 - 982



Conclusions: We show that routine evaluation of WSIs can be used to rigorously test immunohistochemical staining performance. Our approach requires minimal active time and utilizes freely available image processing and data analysis tools. On-slide controls can be analyzed without additional reagent costs, while the costs for dedicated or batch controls include only control tissue, slides, and reagents. In the future, a seamless data pipeline could be developed based on this method to utilize on slide control tissue to monitor stain quality in in a real time or nearly real time manner.

983 Deeper Sections Increase Detection Rate of Adenomas In Colorectal Polyp Biopsies

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Disclosures: Dongpo Salas: None; Changzhao Li: None; Dali Huang: None; Nicholas Dietz: None

Background: Colorectal cancer is the third most common cancer in the United States estimated to cause about 53,200 deaths during 2020. Thanks to surveillance colonoscopy, the death rate of colorectal cancer has been declining for several decades. Accurate pathology diagnosis on colonic polyp biopsies is critical for patient care as it determines surveillance interval. Occasionally, a histologic explanation of the polyp formation is not made while initial sections featuring normal histology. However, there are no guidelines on what to do in this situation. Recent studies have suggested the need for deeper sections since occult adenomas were noted in 1.3 %–19.7% of cases. Therefore, this study aims to investigate whether deeper sections can help to improve the diagnostic accuracy in specimens with initial normal histology.

Design: Since July 2018, the recommendation for deeper sections on all colorectal polyps with an initial normal histology has been implemented in our institution. Pre and post-implementation data from July 2017 to June 2019 were collected on all colorectal polyps with initial diagnosis of normal histology. Specimens from polyposis genetic syndrome, inflammatory bowel diseases, initial diagnosis of carcinomas and multiple polyps with initial diagnosis of adenoma in at least one polyp were excluded. The detection rate and overall rate of occult adenomas were analyzed and compared between pre and post-implementation.

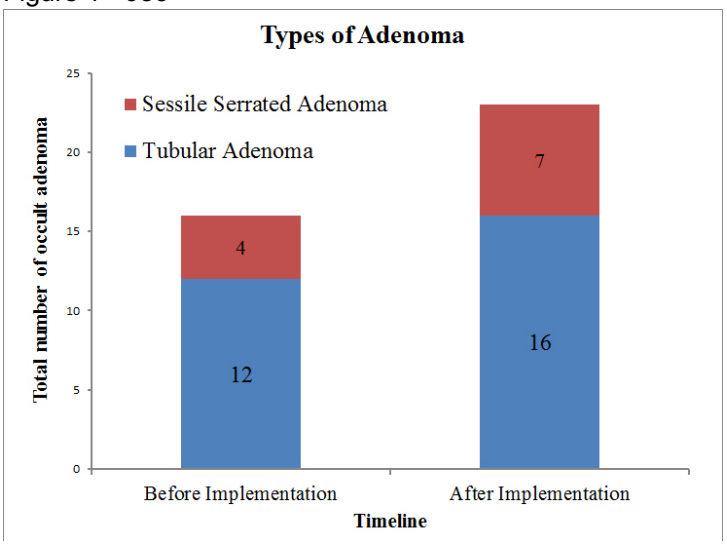
Results: The rate of deeper sections was increased significantly from 23.5% (103/429) to 40.0% (131/327) after implementation of the protocol. The pre-implementation detection rate of occult adenomas in deeper sections was 15.5%, which was slightly increased to 17.5% post-implementation ($p>0.05$). The overall rate of occult adenoma detection was improved significantly from 3.7% (16/429) to 7.0% (23/327) in the studied cohort when comparing pre and post-implementation data ($p<0.05$) (Table 1). The occult adenomas consist of predominantly tubular adenoma and to a less extent of sessile serrated adenoma (Figure 1).

Table 1

Title	Year	Initial Negative Specimen	Deeper	Deeper Rate	Occult Adenoma	% of Occult Adenoma / Deeper	% of Overall Occult Adenoma
Pre-implementation	7/1/2017-6/30/2018	429	103	23.5% (103/429)	16	15.5% (16/103)	3.7% (16/429)
Post-implementation	7/1/2018-6/30/2019	327	131	40.0%** (131/327)	23	17.5% (23/131)	7.0%* (23/327)

* $p<0.05$; ** $p<0.001$

Figure 1 - 983



Conclusions: The detection rate of occult adenomas on deeper sections of initial normal colonic polyp biopsies was compatible with that reported in the literature (1.3%-19.7%). The significant increase in rate of adenoma detection in patients with otherwise normal histology suggested deeper sections can increase the diagnostic accuracy in colorectal biopsies and improve the patient care.

984 Value Proposition Canvas: A Roadmap for Engaging Clinicians and Understanding Clinical Requirements

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Disclosures: Gaurav Sharma: None; Brian Castle: None; Dhananjay Chitale: None; David Willens: None

Background: In business parlance, the Value Proposition (VP) of any service refers to the perception of the service as promised, communicated, delivered, and acknowledged by both the producer and the consumer of the service. Value Proposition Canvas (VPC) is a unique business exercise that helps organizations understand their VP. To our knowledge, VPC has never been utilized in Pathology. Herein, we describe the outcomes of two Pathology VPC workshops.

Design: Since 2019, annual VPC workshops were performed using the methodology described by *Osterwalder, A. Value Proposition Design: How to Create Products and Services Customers Want. John Wiley & Sons (2014)*. Each VPC workshop captured the VP of a pathology laboratory in two distinct segments: Customer Profile, and Value Map. To create a comprehensive Customer Profile, we invited a group of four internists (one hospitalist, two outpatient physicians, one chief resident), one nurse, and one surgical pathologist (representing surgeons) to conduct individual didactic and Q&A sessions (45-60 minutes each). Each presenter described their daily tasks, requirements from the pathology laboratory, and challenges. This information was collated into a comprehensive Customer Profile. Thereafter, the VPC workshop attendees (technologists, laboratory administrators, and pathologists) created a corresponding Value Map for the pathology laboratory services.

Results: The 2019 in-person workshop included 20 attendees, and the 2020 virtual workshop included 30 attendees. The collated Customer Profile captured unmet needs (i.e. clinician Pain-points) that included limited integration with mobile devices, limited knowledge of appropriate test utilization, and routing of time-sensitive diagnoses to one individual rather than the entire clinical team. The envisioned Pain-relievers included integration with mobile reporting, modules towards appropriate laboratory utilization for clinical trainees, and streamlined result routing to the entire clinical team. The clinician's Gain-points included consistent turnaround times, A1c point-of-care testing, interpretive comments, and a responsive customer center. The envisioned Gain-creators included

information on referred testing turnaround time, expanding A1c point-of-care testing, and streamlining means of contacting pathologists.

Figure 1 - 984

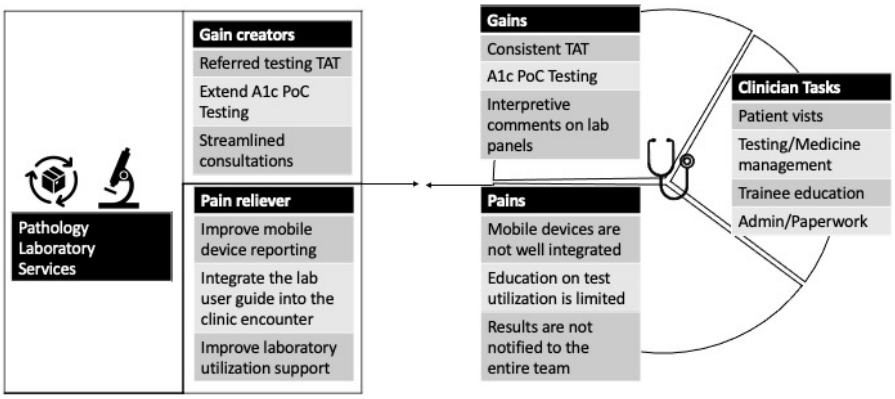

Figure: Value Proposition Canvas of Pathology Laboratory Services

Conclusions: The VPC workshops allowed us to systematically identify our local customer needs. While the majority of the identified opportunities require complex interventions, we feel that a formal and documented VPC workshop provides a framework that allows pathologists, clinicians, and other stakeholders to understand service requirements and envision practical solutions. This proactive approach is a definite improvement compared to reactive problem-solving. Based on our experience, we recommend that pathologists should explore and adopt VPC in their practice.

985 Peribronchial Lymph Nodes in Anatomic Lung Cancer Resections: Measures to Improve Nodal Staging

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Disclosures: Robert Ta: None; Gracijela Bozovic: None; Alexander Bankier: *Consultant*, Daiichi Pharmaceuticals, Olympus Medical; Paul VanderLaan: *Consultant*, Gala Therapeutics; *Advisory Board Member*, Caris Life Sciences; *Consultant*, Intuitive Surgical; *Consultant*, Flatiron Health

Background: Accurate assessment of lymph node (LN) status is essential for proper staging of resected lung cancer specimens, with the pathologist responsible for identifying LNs within the resection specimen, including the lobar (level 12), segmental (level 13), and subsegmental (level 14) stations. A growing body of literature suggests that suboptimal sampling of these LNs leads to tumor understaging. Here, we assessed interventions taken by our department to optimize evaluation of peribronchial LNs in lung cancer resection specimens as part of a Plan-Do-Study-Act quality improvement cycle.

Design: All lung cancer anatomic resection specimens from 2017 to 2020 at our institution were evaluated, including specimens from two years pre-intervention and one year post-intervention. The measures to increase peribronchial LN yield included: educational grossing sessions for pathology assistants and residents, instructions to submit two cassettes of peribronchial tissue if no LNs were identified grossly, and a hard-stop prior to sign-out by the attending pathologist if no peribronchial LNs were identified. Statistical significance was established using the rank correlation.

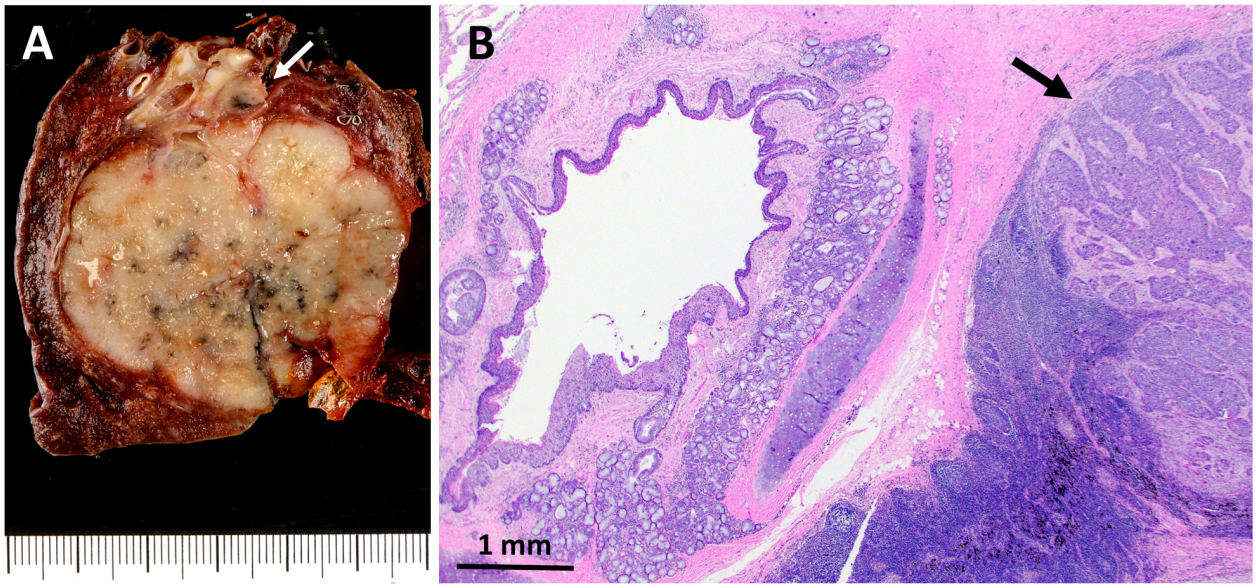
Results: Over the 3 year study period, there were a total of 227 resection specimens for non-small cell lung cancer, further subdivided into 184 (81%) adenocarcinomas and 43 (19%) squamous cell carcinomas (Table). Prior

to the intervention, 91/151 (60.3%) specimens had peribronchial LNs identified during grossing (Figure panel A), with an additional 16/151 (10.6%) specimens with peribronchial LNs identified by microscopic examination only (Figure panel B). After the intervention, significantly more (58/76, 76.3%, p=0.016) specimens had peribronchial LNs identified during grossing, with a similar proportion of specimens (8/76, 10.5%) specimens with peribronchial LNs identified by microscopic examination only. The mean number of peribronchial LNs significantly increased from 2.68±3.31 pre-intervention to 4.32±3.98 post-intervention (p<0.001). Despite identifying more peribronchial LNs, there was no significant difference in peribronchial LN metastases pre-intervention (19/151, 12.6%) compared to post-intervention (8/76, 10.5%, p=0.326). Further analysis revealed a strong correlation between peribronchial LN metastases with both overall tumor size and invasive component size (for adenocarcinomas), correlation coefficient 0.974, p<0.0001.

	Total	Pre-Intervention	Post-Intervention	p-value
Resection specimens	227	151 (66.5%)	76 (33.5%)	
Gender Male Female	85 (37.4%) 142 (62.6%)	58 (38.4%) 93 (61.6%)	27 (35.5%) 49 (64.5%)	n.s.
Age (mean)	65.58 ± 9.07	68.43 ± 9.73	68.86 ± 7.66	n.s.
Specimen Type Lobectomy Bilobectomy Segmentectomy Bisegmentectomy Pneumonectomy	181 (79.7%) 4 (1.8%) 30 (13.2%) 9 (4.0%) 3 (1.3%)	117 (77.5%) 2 (1.3%) 23 (15.2%) 7 (4.6%) 2 (1.3%)	64 (84.2%) 2 (2.6%) 7 (9.2%) 2 (2.6%) 1 (1.3%)	n.s.
Location Right upper lobe Right middle lobe Right lower lobe Left upper lobe Left lower lobe	77 (33.9%) 16 (7.0%) 39 (17.2%) 58 (25.6%) 30 (13.2%)	44 (29.1%) 13 (8.6%) 28 (18.5%) 36 (23.8%) 26 (17.2%)	33 (43.4%) 3 (3.9%) 11 (14.5%) 22 (28.9%) 4 (5.3%)	n.s.
Histologic type Adenocarcinoma Squamous Cell Carcinoma	184 (81.1%) 43 (18.9%)	118 (78.1%) 33 (21.9%)	66 (86.8%) 11 (14.5%)	n.s.
Mean maximal tumor size (mm)	24	27	22	n.s.
Mean invasive tumor size (mm)	19	21	18	n.s.
LVI Yes No Indeterminate	59 (26.0%) 159 (70.0%) 9 (4.0%)	43 (28.5%) 101 (66.9%) 7 (4.6%)	14 (18.4%) 60 (78.9%) 2 (2.6%)	n.s.
STAS Yes No Indeterminate	105 (46.3%) 121 (53.3%) 1 (0.4%)	69 (45.7%) 81 (53.6%) 1 (0.7%)	36 (47.4%) 40 (52.6%) 0 (0%)	n.s.
Pleural Invasion Yes No Indeterminate	26 (11.5%) 198 (87.2%) 3 (1.3%)	21 (13.9%) 127 (84.1%) 3 (2.0%)	5 (6.6%) 71 (93.4%) 0 (0%)	n.s.
Lymph nodes Specimens with peribronchial lymph nodes identified Specimens with peribronchial lymph nodes identified during grossing Mean number of peribronchial lymph nodes per specimen Peribronchial lymph nodes with metastases	173 (76.2%) 149 (65.6%) 3.22 ± 3.62 27 (11.9%)	107 (70.9%) 91 (60.3%) 2.68 ± 3.31 19 (12.6%)	66 (86.8%) 58 (76.3%) 4.32 ± 3.98 8 (10.5%)	0.008 0.016 0.001 n.s.
pT staging In situ 1a(mi) 1a 1b 1c	1 (0.4%) 13 (5.7%) 21 (9.3%) 76 (33.5%) 29 (12.8%) 7 (3.1%)	0 (0%) 8 (5.3%) 14 (9.3%) 47 (31.1%) 20 (13.2%) 4 (2.6%)	1 (1.3%) 5 (6.6%) 7 (9.2%) 29 (38.2%) 9 (11.8%) 3 (3.9%)	n.s.

2 2a 2b 3 4	32 (14.1%) 14 (6.2%) 19 (8.4%) 15 (6.6%)	21 (13.9%) 9 (6.0%) 16 (10.6%) 12 (7.9%)	11 (14.5%) 5 (6.6%) 3 (3.9%) 3 (3.9%)	
pN staging pNx 0 1 1a 1b 2 2a1 2a2 2b	1 (0.4%) 180 (79.3%) 6 (2.6%) 17 (7.5%) 8 (3.5%) 3 (1.3%) 3 (1.3%) 8 (3.5%) 1 (0.4%)	1 (0.7%) 115 (76.2%) 5 (3.3%) 11 (7.3%) 8 (5.3%) 3 (2.0%) 2 (1.3%) 6 (4.0%) 0 (0%)	0 (0%) 65 (85.5%) 1 (1.3%) 6 (7.9%) 0 (0%) 0 (0%) 1 (1.3%) 2 (2.6%) 1 (1.3%)	n.s.

Figure 1 - 985



Conclusions: The intervention led to a significant increase in the number of peribronchial LNs identified and assessed during histopathologic evaluation of anatomic lung cancer resection specimens, although this did not lead to an increase in nodal up-staging. Larger tumors are more likely to have occult peribronchial LN metastases, which may warrant a more aggressive peribronchial LN search for larger resected tumors.

986 Use of an Analytical Software Application linked to the Pathology Laboratory Information System to Obtain Cytopathology Lab Performance Data, Quality Data, and Staff Competency Metrics

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Disclosures: Stephen Wall: None; Adam Brown: None; Steven Meschter: None; Michele Zelonis: None; Sandy Mullay: None; Jeff Prichard: None; Sara Monaco: None

Background: Cytology laboratories are required to establish quality assurance (QA) programs to evaluate laboratory performance and the competency of staff using various metrics. Given the high volume of data generated by the laboratory information system (LIS) and our large integrated health system, our laboratory established an analytical software solution to extract and summarize important data to look at quality metrics. The aim of this study was to review our experience with this novel tool for performance review and quality improvement in gynecological (GYN) and non-GYN cytopathology.

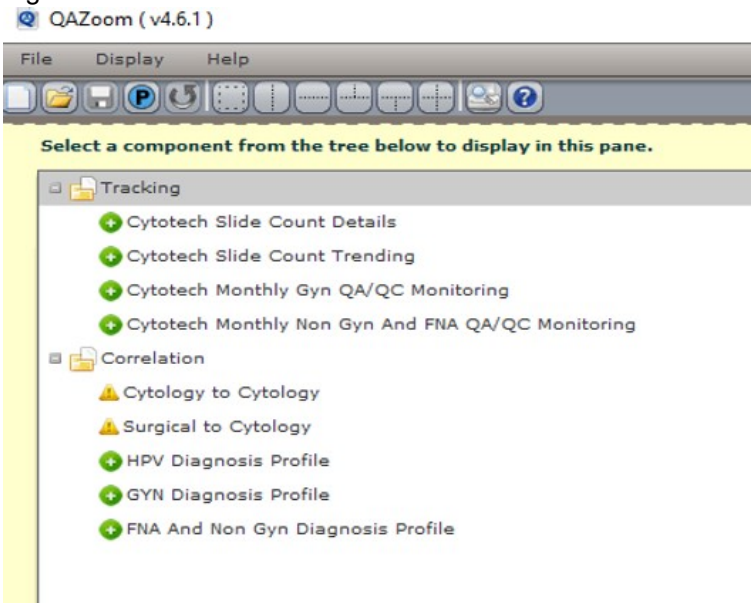
Design: Our laboratory created an analytical database software tool (QA zoom, version 4.6, created 2008) that extracts daily data from the pathology LIS (CoPathPlus, Cerner, version 2017.01.1.124) and a time entry tool for cytotechnologists. Data is accessible to staff with a secure login. Quality metrics are analyzed on an ongoing monthly basis for the laboratory and cytotechnologists, and an annual basis for cytopathologists.

Results: An average of 51,236 cases per year have been analyzed by QA zoom over the past 3 years. Various metrics have been examined for the laboratory and individuals, including volume of cases, ASCUS/SIL ratio, and nondiagnostic/indeterminate rates. Cytotechnologists can track daily slide workload and discrepancies, and then sign off when they review their discrepancies, which provides ongoing feedback. The laboratory also uses this tool for quintile analysis/verification for the GYN cytology automated screener and stainer, and has detected quality control issues with the staining based on drift of the high-grade GYN cytology results out of the expected quintiles. This has also provided important information on staff and laboratory performance that has enhanced our regulatory compliance documentation, in addition to initiating and tracking different quality improvement projects, including second review to reduce indeterminate thyroid diagnoses. An example of the QA Zoom interface (Figure 1) and quality measures extracted (Table 1) are shown.

Table 1. Mapping QA Zoom Analytics to Quality Measures and Performance Data for the Cytopathology Lab & Staff

QA Zoom Analytic	Lab Performance	Staff Performance	Technical Quality
Case volume by specimen type with trend over time	X		
Specimen counts by cytotechnologist or cytopathologist, separated by specimen type and final diagnosis		X	
ASCUS/SIL ratio for laboratory with trend over time	X		
ASCUS/SIL ratio for cytotechnologist or cytopathologist		X	
Monitoring of HPV positive results by GYN cytology diagnostic category	X	X	X
Monitoring correlation of GYN cytology data with the quintile assigned on the GYN cytology automated screening imager	X		X
Non-diagnostic rate for cytopathologist performed FNA		X	
Non-diagnostic and Indeterminate rates for GYN and Non-Gyn specimens	X		X
Slide Workload & hours of screening	X	X	
Cytotechnologist discrepancies with discrepant case numbers and mandated sign-off after review	X	X	

Figure 1 - 986



Conclusions: The implementation of an analytical database tool has provided our cytopathology laboratory with important quality data that has allowed us to track performance of the laboratory, in addition to providing personalized feedback and obtaining individualized competency data on staff. This LIS-driven tool allows us to readily obtain important QA data to monitor important trends in data, provide educational feedback for staff, determine staffing needs, verify performance of lab equipment, and overall, improve patient care by looking into ways to improve indeterminate rates. In the future, expanding the application to include more rapid on-site evaluation data and cytology-histology correlation data, in addition to linking to our new LIS, will be explored.

987 Paired Comparison of Molecular Tests for Cytologically Indeterminate Thyroid Nodules

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Disclosures: Rong Xia: None; Fang Zhou: None; Wei Sun: None; Cheng Liu: None; Aylin Simsir: None; Joan Cangiarella: None; Tamar Brandler: None

Background: Thyroseq next-generation sequencing assay and Afirma gene expression classifier (GEC) are used to risk-stratify thyroid nodules with indeterminate cytology: Bethesda III (atypia of undetermined significance, AUS/FLUS) and IV (suspicious for follicular neoplasm, SFN). In this study, we performed a paired comparison of both tests on the same group of indeterminate thyroid nodules with surgical followup.

Design: Of 645 AUS/FLUS/SFN cases with both molecular testing and surgical resection in 2014-2017, 40 cases had both Thyroseq (v2) and Afirma GEC performed on the same specimen. Cross-tabulations and ROC curves were created. McNemar tests were done to compare the performance of Thyroseq versus Afirma. The diagnostic performance of combined results were also examined: the combined result was called positive only if both Thyroseq and Afirma were positive/suspicious. Non-invasive follicular thyroid with papillary like nuclear features (NIFTP) on surgical resections was defined as “positive.”

Results: 20/40 (50%) cases were “positive” on surgical pathology: 8 papillary thyroid carcinoma (PTC), 11 NIFTP, and 1 follicular carcinoma. Thyroseq and Afirma both showed high sensitivity and low specificity in diagnosing malignancy in indeterminate thyroid nodules.

Next, the results of both tests were combined. The overall accuracy of combined testing was higher than either test alone (Figure 1). Compared to Afirma alone, the combined test had significantly higher specificity (30% vs 70%,

p<0.05, Table 1), while the sensitivity declined from 90% to 75% (p=0.25, Table 1). Compared to Thyroseq alone, there was no significant difference in specificity (45% vs 70% p=0.06) or sensitivity (80% vs 75%, p=1.00, Table 1). Positive predictive value (PPV) improved compared to either test alone. Negative predictive value (NPV) improved compared to Thyroseq alone, and declined only slightly compared to Afirma alone.

Table 1. Performance of Thyroseq, Afirma and Combined Results

	Thyroseq	Afirma	Combined RESULTS
Sensitivity (95% CI)	80.00% (56.3% to 94.3%)	90.00% (68.3% to 98.8%)	75.00% (50.9% to 91.3%)
Specificity (95% CI)	45.00% (23.1% to 68.5%)	***30.00%** (11.9% to 54.3%)	***70.00%** (45.7% to 88.1%)
PPV	59.26%	56.25%	71.43%
NPV	69.23%	75.00%	73.68%
Accuracy (95% CI)	62.50% (45.8% to 77.3%)	60.00% (43.3% to 75.1%)	72.50% (56.1% to 85.4%)

***McNemar's test, two-tailed p<0.05 when comparing the specificity of Afirma alone vs Combined Results**
Abbreviations: CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value

Figure 1 - 987

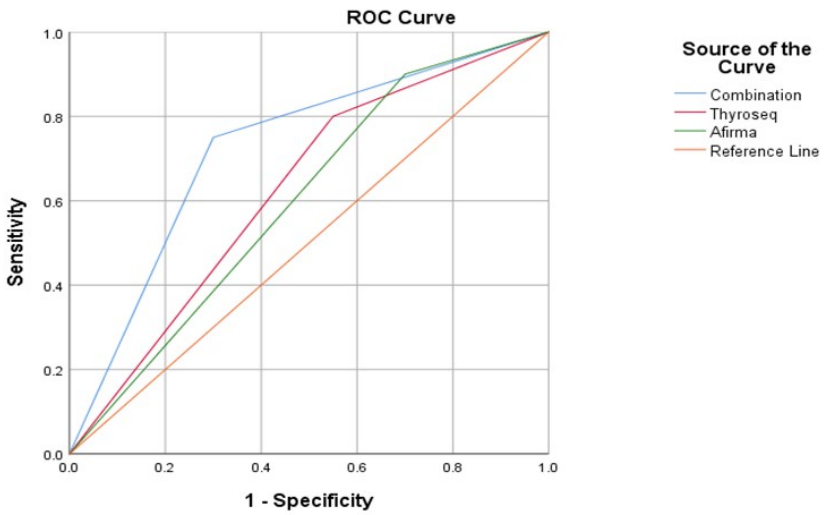

Figure 1. Receiver operating curves for Thyroseq, Afirma, and Combined results

Conclusions: Molecular testing of cytologically indeterminate thyroid nodules helps determine the extent of surgery. Low diagnostic performance metrics may limit the utility of molecular studies in distinguishing benign from malignant thyroid lesions. Our results show that the combined results of Thyroseq and Afirma improved the specificity and overall accuracy of molecular testing, and provided additional value in the surgical management of patients with indeterminate thyroid nodules. To the best of our knowledge, this is the first study that compares the performance of these two molecular tests on the same thyroid nodules.

988 Rapid Diagnostics of Sepsis in Patients with Positive Blood Culture by BCID Multiple PCR

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Disclosures: Kemin Xu: None; Guiqing Wang: None

Background: The FilmArray BCID assay is an FDA-cleared multiple real-time PCR test that detects 20 common microorganisms causing bloodstream infections and three resistance genes. The performance of BCID PCR and the turnaround times from the flagged positive on the BACTEC Blood Culture System to reporting of gram stain and BCID multiplex PCR results remain variable and depend on many factors. Therefore, the accuracy and turnaround time of reporting blood culture results by BCID Multiple PCR will be analyzed.

Design: All BCID multiplex PCR performed from Jan 2019 to Dec 2019 at WMC Microbiology Laboratory were retrospectively retrieved. The time of BACTEC flag positive, gram stain result and BCID multiplex PCR results of BCID test were obtained by reviewing the workcard of each positive blood culture.

Results: From January 2019 to December 2019, a total of 2,540 positive blood cultures were identified at the WMC Clinical Microbiology Laboratory with an average monthly positive of 212 blood cultures. 792 BCID multiplex PCR were performed, which account for 32.5% of positive blood cultures. The sensitivity of BCID is 90.2% with 9.8% of false negative rate. However, for 4.5% of those negatives, the microorganism detected by conventional method was not included in BCID panel list.

The turnaround time of reporting blood culture results is critical for patient management. From the instrument flagged positive to gram stain results, 27.1% of cases were reported within 30 minutes, 70.8% of cases were reported within 60 minutes and 91% of cases were reported within 2 hours with median time of 44 minutes. From gram stain results to BCID multiplex PCR results, 46.1 % of cases were reported within 2 hours, while 87.3% of cases were reported within 8 hours with median time of 128 minutes (Table 1).

The most common microorganisms detected by BCID multiplex PCR were *Staphylococcus epidermidis* and *Escherichia coli*, which account for 24.2% and 17.7% of all isolates respectively, followed by *Staphylococcus aureus*, which account for 11.1% of all isolates. *Candida* sp, *Streptococcus* species, *Klebsiella pneumonia* and *Enterococcus* had similar detection rate by BCID with 8-9% of all isolates.

Approximately 38.6% of *S. aureus* isolates were methicillin-resistant S. aureus (MRSA), which accounts for 17.6% of total isolates with resistance gene. 26 out of 59 enterococcus (44.1%) have vancomycin-resistance gene and 3 strains of *Klebsiella pneumonia* (4.8%) have carbapenem-resistance gene.

Table 1. Gram stain results to BCID multiplex PCR results

Time	Case Number	Percentage	Accumulated percentage
<2 hours	365	46.1%	46.1%
2-8 hours	326	41.2%	87.3%
>8 hours	101	12.7%	100%
Total	792	100%	
Median time	128		

Conclusions: BCID multiplex PCR is able to provide accurate and rapid results with potential clinical added value and can serve as a complementary tool to current routine microbiology techniques, although it remains necessary to obtain complete susceptibility results for definitive therapy.

989 Impact of Adherence to Guideline-Recommended Diagnostic Testing on Treatment Selection and Survival in Patients with Diffuse Large B-Cell Lymphoma in the US

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Disclosures: Fei Yang: *Employee*, Roche; Anup Abraham: None; Richard Hammer: *Speaker*, Roche; *Grant or Research Support*, Roche; *Stock Ownership*, PathEdex; *Advisory Board Member*, Caris; Matthew Prime: *Employee*, Roche Diagnostics; *Stock Ownership*, Open Medical Holdings Ltd

Background: Adequate immunophenotyping and molecular testing are important for the diagnosis and prognosis in patients with diffuse large B-cell lymphoma (DLBCL) and may guide treatment selection to achieve better outcomes. This study aims to assess the impact of adherence to guideline-recommended diagnostic testing on treatment selection and overall survival (OS) in patients with DLBCL who initiated rituximab-based first line of therapy (1-LOT).

Design: This is a retrospective cohort study leveraging data from the Flatiron Health electronic health record-derived de-identified database, including diagnostic testing information on immunohistochemistry (IHC), fluorescence in situ hybridization (FISH) and karyotype analysis that were abstracted from pathology reports or clinical visit notes, where available. This study includes patients above 18 years old who were diagnosed with DLBCL between Jan-2011 and Dec-2019 and initiated rituximab-based 1-LOT. Patients were classified into 'non-adherence', 'partial-adherence', and 'complete-adherence' groups according to the evidence/documentation of a confirmed known result for IHC and molecular testing (FISH and Karyotype) on a selection of the markers prior to the initiation of 1-LOT. Logistic regression was used to evaluate associations of adherence to diagnostic testing with 1-LOT between R-CHOP and other rituximab-based regimens. Median OS after the start of rituximab-based 1-LOT was calculated using the Kaplan-Meier method. Multivariable-adjusted Cox proportional hazards regression was used to assess the risk of mortality after initiation of 1-LOT by the degree of adherence to diagnostic testing.

Results: In total 3830 patients with DLBCL who initiated rituximab-based 1-LOT were included. No association was found between adherence to guideline-recommended diagnostic testing and treatment selection of 1-LOT. Patients with a higher degree of adherence to diagnostic testing survived longer (median OS at 61.1, 83.0 and 84.9 months for 'non-adherence', 'partial-adherence', and 'complete-adherence' groups, respectively [log-rank $p<0.001$]) and had a decreased mortality risk (adjusted hazard ratio with 95% confidence intervals at 0.83 [0.70-0.98] for 'partial-adherence' and 0.77 [0.65-0.91] for 'complete-adherence' groups, respectively).

Conclusions: Patients adherence to guideline-recommended diagnostic testing were associated with better survival benefit, reinforcing the need for adoption of diagnostic testing guidelines in routine clinical care.