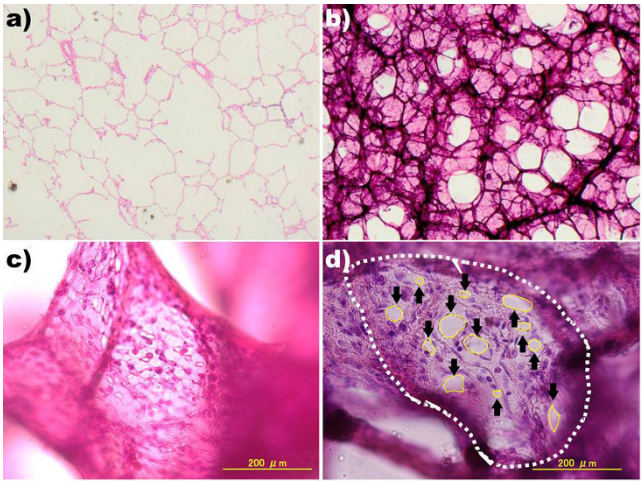
performed H&E staining (Figure a and b was from identical area). 5 areas of normal-looking lung parenchyma for each slide were randomly selected. The number of alveolar sac surrounded by string-like framework (FW) was counted.
Area ratios of Pores of Kohn to each alveolar sac membrane surrounded by framework (PK) were calculated with images from the spots of interest (Figure c). Image J was used for stack construction and measurement of images (Figure d). Clinical data including pulmonary function test of patients was collected. Comparison of clinical data was performed with t test. Multilevel linear mixed model was used to evaluate differences of FW and PK and associations with clinical data. P values <.05 were considered significant.



Results: Our approach revealed the structures that membrane-like alveolar sac is surrounded by thicker fibrous framework which spreads web-like structure throughout the lung parenchyma. Compared to lungs without emphysema, PK is higher (p=.04) and FW is lower (p=.02) in lungs with emphysema. Also, FW was influenced by %DLco (p=.04, r=.14), %FRC (p=.02, r=.11), FEV1% (p=.04, r=.28) and %DLco/VA (p<.01, r=.19), and PK was influenced by %DLco/VA (p<.01, r=-.011), CV (p=.04, r=.29) and %RV (p=.05, r=.01). Both did not show difference in %VC.
Conclusions: Histologically normal-looking lung from cases with emphysema had a higher area ratio of pores of Kohn/alveolar wall and a smaller number of alveolar sac. Presence of higher amount of pores of Kohn which associate with abnormal pulmonary function tests suggests that emphysema starts by increasing number of pores of Kohn.

1985 The Clinicopathological Characteristics of Lung Adenocarcinoma With Lgr5 Expression

Akihiko Yoshizawa. Kyoto University Hospital, Kyoto, Japan.
Background: The leucine-rich repeat-containing G-protein-coupled receptor 5 (Lgr5) has been identified as a promising gastrointestinal tract stem cell marker. There are only few published reports on the relationship between Lgr5 expression and clinicopathological features of patients with lung adenocarcinoma. RNAscope is a newly developed in situ RNA hybridization technique. The aim of this study was to detect expression of Lgr5 RNA in 349 consecutive surgically resected lung adenocarcinomas and to evaluate the relationship between expression of Lgr5 RNA and the clinicopathological parameters and prognosis of patients with lung cancer.
Design: In situ hybridization (ISH) for LGR5 was performed using the RNAscope Formalin-fixed, paraffin-embedded assay kit according to the manufacturer's instructions by using tissue microarray (TMA) slides. Based on the percentage of tumor cells that expressed LGR5, LGR5 staining was graded as: grade 0 (0%); grade 1 (1–5%); grade 2 (6–20%); grade 3 (21–100%). The results were grouped as positive (grade 3) or negative (grade 0 to 2). In addition, TTF-1, HNF4alpha, MUC2, Cdx2, MUC5AC, MUC5B, and MUC6 were immunohistochemically studied in the same TMAs. The associations between LGR5 expression and clinicopathological parameters/ other immunomarkers were evaluated. Kaplan-Meier survival analysis was used to estimate the effect of Lgr5 expression on survival.
Results: Lgr5 was detected in 20 tumors (5.7%). Lgr5 expression was significantly associated with vascular invasion (p = 0.015) and expression of Cdx2 (p = 0.017), MUC2 (p = 0.017), and HNF4alpha (p = 0.003), whereas it was not associated with age, sex, smoking history, tumor stage, tumor size, tumor grade, pleural invasion, lymphatic invasion, and expression of TTF-1, MUC5AC, MUC6, and MUC5B. Patients with Lgr5 expression showed significantly worse prognosis, with a 39.6% disease-free survival rate at 5 years compared to patients lacking expression of Lgr5 (5-year disease-free survival rate = 67.8%)(p = 0.008). However, the difference in overall survival rates between the two groups was not statistically significant.
Conclusions: The present study shows that tumors with Lgr5 RNA expression are a small subset of lung adenocarcinoma and are associated with expression of markers for colorectal cancer, HNF4alpha, and poorer prognosis. The results suggest that Lgr5-positive lung adenocarcinomas can be lineage of colorectal-type lung adenocarcinoma with poorer prognosis, although further studies are required to clarify the biological function of Lgr5 in lung adenocarcinoma.

1986 MASH1 Is Highly Specific for Neuroendocrine Carcinomas: An Immunohistochemical Evaluation in Normal and Various Neoplastic Tissues With Emphasis in Lung Cancer

Charlie Yu, David Tacha, Cristin Douglas, Faqian Li. Biocare Medical, Concord, CA; University of Rochester, Rochester, NY.
Background: Mammalian achaete-scute complex homolog-1 (MASH1) is a basic helix-loop-helix transcription factor crucial for neuroendocrine cell differentiation. High grade, poorly differentiated neuroendocrine carcinomas are classified by WHO (World Health Organization) as simply neuroendocrine carcinomas (NECs) and are distinguished from other neuroendocrine tumors (NETs). Neuroendocrine markers such as chromogranin and CD56 cannot distinguish NECs from NETs. Recent studies have shown MASH1 to stain a high percentage of small cell lung carcinomas (SCLCs) and large cell neuroendocrine carcinomas (LCNECs). Limited studies have shown MASH1 to be highly specific in various NECs versus other NETs. Our study will evaluate MASH1 on various normal and neoplastic tissues with emphasis on lung cancer.
Design: Formalin-fixed paraffin-embedded tissue microarrays (TMAs) were used consisting of normal tissues (n = 33), various neoplastic tissues (n = 751) and lung cancers (n = 250). MASH1 [24B72D11.1] titer was optimized at 1:200 and evaluated by IHC in all normal and neoplastic tissues. IHC of MASH1, chromogranin and CD56 was also compared in SCLC.
Results: In normal tissues, MASH1 was expressed (nuclear staining) in C-cells in thyroid and in neuroendocrine cells found in thymus. All other normal tissues were negative, including astrocytes and argentaffin cells found in the gastrointestinal tract. In lung cancers, MASH1 stained 1/91 squamous cells carcinomas and stained 1/87 lung adenocarcinoma, (Table 1). In SCLC, MASH1, chromogranin and CD56 stained 19/23, 18/23 and 21/23, respectively. In various cancers, MASH1 was expressed in thyroid medullary carcinomas (but not in thyroid papillary and follicular carcinomas), in thymic carcinomas, and in a small percentage of astrocytomas/glioblastomas and in pancreatic cancers. MASH1 was negative in all other cancer types.

Table 1: MASH1 Expression in Lung Cancer (n = 250)

Lung Cancers	MASH1	% Positive
Adenocarcinoma	1/87	1%
Squamous cell	1/91	1%
Classic large cell	0/30	0%
SCLC	19/23	83%
LCNEC	2/3	67%
Typical carcinoid	0/4	0%
A-typical carcinoid	5/11	42%

Conclusions: Although not organ specific, MASH1 is highly specific for NECs in lung cancers versus other lung phenotypes and may also be useful in discriminating NECs from other NETs in various types of cancers.

Quality Assurance

1987 Utility of Flow Cytometry in the Pathologic Evaluation of Tonsils and Adenoids

Omonigho Aisagbonhi, Amy Ly. Massachusetts General Hospital, Boston, MA.
Background: Tonsils and adenoids are often excised to treat infections and airway obstruction. In addition to histology, tonsils may be evaluated by flow cytometry, a study with significant financial cost. The added diagnostic value of flow cytometry in these specimens has not been addressed in literature. We examined our flow cytometry utilization pattern in tonsil/adenoid specimens and sought to identify clinical features where its application may be advantageous.
Design: Clinical, radiographic, and pathology findings were recorded for patients who underwent tonsil/adenoid excision or biopsy with concurrent flow cytometry analysis at Massachusetts General Hospital and Massachusetts Eye and Ear Institute from August 2011 to March 2014.
Results: The study included 154 patients (89 females, 65 males) averaging 27.4 years of age (range 2 to 87). 13 had malignancy histories: retinoblastoma (1), pediatric brain tumor NOS (1), Hodgkin lymphoma (1), pre B-ALL (2), lung adenocarcinoma (4), prostate adenocarcinoma (1), colon adenocarcinoma (1), breast carcinoma (1), melanoma (1) and lung small cell carcinoma (1).
Surgical removal/biopsy was prompted by adenotonsillar hypertrophy with tonsillitis and/or obstructive airway symptoms in 141 patients, discrete tonsillar masses in 10 patients, and PET-avid tonsillar lesions discovered during cancer staging scans in 3 patients.
In 148 cases, histology and flow cytometry findings were benign. Histology revealed malignancy in 6 of 154 (4%) patients: diffuse large B-cell lymphoma (2), small B-cell lymphoma (2), concomitant grade 3B follicular lymphoma and histocytic sarcoma (1), and extra-osseous plasmacytoma (1). Pre-operatively, 5 had unilateral tonsillar/neck masses, ranging from 1.5 to 7 cm in size. 1 had no definite mass, but had unilateral tonsillar fullness with cervical lymphadenopathy. All 6 patients were > 40 years old (range 42 – 87, mean 63.7). Only 1 patient had a history of malignancy (prostate adenocarcinoma).
Flow cytometry identified the 2 DLBCL and 2 small B-cell lymphomas; it failed to detect the follicular lymphoma/histiocytic sarcoma and plasmacytoma cases (67% sensitivity).
Conclusions: Flow cytometry is unnecessary for tonsil/adenoid specimens removed from patients without clinical/radiologic findings concerning for malignancy. Unilateral

discrete tonsillar masses, or fullness, particularly in patients > 40 years old with associated cervical lymphadenopathy, are features worrisome for tonsillar malignancy. Histology was more sensitive than flow cytometry for detection of tonsillar hematologic malignancies in this series.

1988 Time To Fixation: Does It Affect Frozen Section Diagnosis?

Mahmut Akgul, Mohamed El Hag, Marta Couce, Jay Wasman. Case Western Reserve University, Cleveland, OH.

Background: There is a general belief that prolonged exposure to room temperature (ERT) of frozen section slides before fixation and staining, significantly decreases quality due to air drying artifact. A literature search of PubMed did not identify any published study examining the effect of prolonged ERT on frozen section quality. We investigated the effect of air drying at room temperature on quality and interpretability of frozen sections.

Design: We selected 25 frozen section cases, representing a variety of tissue types during a 5 day time period.. Three consecutive, 5 microns thick sections were cut by one pathologist from each case,. The first section was immediately fixed in formalin (0ERT); the second was fixed after 1 minute ERT (1ERT); the third was fixed after 3 minutes ERT (3ERT). Slides from each case were stained together in one rack on a Leica ST4020 (Wetzlar, Germany) automated stainer. Slides from each case were blindly evaluated by three pathologists and the following characteristics were scored: nuclear detail (ND), architecture (A), and overall appearance (OA). Scores of 1=poor, 2=fair, and 3= good were assigned. Scores from each characteristic from the three pathologists were added together with 3 being the minimum score and 9 being the maximum for each characteristic. An all score (AS) was calculated for each slide by adding all characteristics scores (ND+A+OA) with a minimum score of 9 and a maximum score of 27. One way Anova test and Tukeys multiple comparison test were performed using GraphPad Prism (La Jolla, CA).

Results: The average scores for ND were as follows: 0ERT= 5.56, 1ERT= 5.96, and 3ERT=6.24; with no statistical significance between any of these groups. The average scores for A were: 0ERT=6.64, 1ERT=7.12, and 3ERT=7.8; the difference between 0ERT group and 3ERT group was statistically significant, with p=0.013. The average scores for OA were: 0ERT=6.56, 1ERT=6.96, and 3ERT=7.72; the difference between 0ERT and 3ERT groups was statistically significant, with p=0.006. The average AS were: 0ERT=18.76, 1ERT=20.04, and 3ERT=21.76; the difference between 0ERT and 3ERT groups was statistically significant, with p=0.0019.

Conclusions: Three minute ERT resulted in higher architectural quality and overall quality when compared with immediate fixation. Quality of nuclear detail appears not to be affected by duration of ERT. We conclude that rapid fixation does not result in higher quality frozen section slides.

1989 The Impact of Patients' Diagnoses on Their Decision To Participate in Research Biobanking

Amen Alam, Asaara Ali, Zahra Maamir, Nadia Amin, Dianne Chadwick, Michael Roehrl. University Health Network, Toronto, ON, Canada.

Background: The BioSpecimen Sciences Program (BSP) is a high volume biorepository dedicated to human specimens for research. This process depends on the acquisition and documentation of patient consent to research biobanking. We studied whether diagnosis played a contributing factor in patients' decisions to actively participate in research biobanking.

Design: The pre-admission charts for a full 12-month period were screened for consent status as well as pre-operative diagnosis documented by the surgical team. Charts without a consent, unavailable, or without a listed diagnosis were excluded. Next, diagnoses were divided into two groups: 'suspected or confirmed malignant' and 'likely or confirmed benign' patients. Each population was assessed for two outcomes: success and failure. Success was defined as any patient who agreed to research sample banking. Failure included patient charts with blank consents, refusals, withdrawn, and invalid consents.

Results: A total of 3856 patients were scheduled for a pre-admission visit. 3605 patients had a consent status and a documented diagnosis. 2735 (75.9%) patients were classified as having a 'suspected or confirmed malignant diagnosis' while 870 (24.1%) patients were categorized as 'likely or confirmed benign' cases. In the malignant group, 1999 (73.1%) patients agreed to biobanking while 736 (26.9%) patients failed to participate. Out of the 870 patients from the suspected benign group, 434 (49.9%) agreed to participate in tissue banking while 436 (50.11%) did not. The 'malignant diagnosis' group was significantly more likely to agree to research banking than the 'benign diagnosis' group (two tailed p-value <0.0001, Fisher's exact test).

Conclusions: Patients' diagnoses have significant impact on the decision to donate specimens for future research. A consent rate of over 73% in the suspected malignant group indicated that patients who were aware of the seriousness of their diagnosis were more willing to participate in research. This willingness could be due to their desire to help others as well as their eagerness to find a cure for their disease in the future. In contrast, the probable benign group had a consent rate of less than 50%. This could be a result of the patients' lack of interest in research or reduced physician research engagement. Low consent rates reduce specimen availability, and research involving non-cancerous specimens may be significantly impacted.

1990 The Contribution of Second Generation Fluorescence In Situ Hybridization (FISH) To histopathologic and Immunophenotypic Analyses in the Diagnosis of Ambiguous Melanocytic Tumors (AMT)

Rami Al-Rohil, Jonathan Curry, Carlos Torres-Cabala, Doina Ivan, Roland Bassett, Victor Prieto, Michael T Tetzlaff. University of Texas MD Anderson Cancer Center, Houston, TX.

Background: Diagnosing melanocytic proliferations as benign or malignant remains a diagnostic challenge with critical implications. Standard diagnostic algorithms integrate histopathologic and immunohistochemical (IHC) parameters. FISH has emerged as an informative ancillary tool, but most studies limit their assessment of FISH to unequivocal melanomas and nevi. The diagnostic utility of FISH in AMT remains controversial. Here, we correlate FISH results with morphologic, IHC and clinical parameters in a series of AMTs.

Design: 30 AMTs from our consultation service were reviewed. Histopathologic, IHC and FISH results (NeoGenomics; probes 6p25, 8q24, 11q13, 9p21 and Cen9) were correlated with the final consensus diagnosis and clinical follow-up using logistical regression and Fisher's exact test.

Results: Based on a synthesis of histopathologic and IHC findings, cases were designated as "favor benign" (FB; n=15) or "favor malignant" in (FM n=15) by a consensus group of 5 dermatopathologists. FISH testing was positive in 2/15 FB lesions and 6/15 FM lesions. For all cases, the final diagnosis reflected the histopathologic and IHC consensus impression. The sensitivity of FISH for the diagnosis of melanoma in this series was 40% and the specificity was 87%. Univariate logistic regression models for a final diagnosis of melanoma showed that only elevated Ki-67 (>5%) significantly correlated with the diagnosis of melanoma (p=0.02); no other clinical, histopathologic or IHC parameter was significant. No clinical or pathologic variable correlated with FISH positivity, and there was no relationship between the FISH result and the final diagnosis (melanoma or nevus; p=0.21). Follow-up (range: 79-572 d) was available for 29 cases (14 benign/15 melanoma). Sentinel lymph node metastases were detected in only 4 cases: 2 FISH-negative melanomas and 2 FISH-positive melanomas. The histopathologic diagnosis of melanoma (versus nevus) correlated with subsequent metastasis (p=0.04), but FISH positivity did not correlate with the development of metastases (p=0.30).

Conclusions: Diagnosing AMTs requires a systematic assessment of histopathologic and IHC parameters. FISH negativity in a FB lesion is reassuring, but given the apparent low sensitivity, in the setting of AMTs, the results of FISH testing must be integrated into the constellation of findings—especially in a FM setting.

1991 Recommendation for Pathologic Evaluation of Reduction Mammaplasty Specimens – A Prospective Study With Systematic Tissue Sampling

Abiy Ambaye, Andrew Goodwin, Susan MacLennan, Shelly Naud, Donald Weaver. University of Vermont, Burlington, VT.

Background: Reduction mammoplasty (RMP) is a common procedure and was performed in 103,775 US patients in 2013. The reported incidence of occult breast cancer in RMP ranges from 0.06% to 12.4%. No standard pathology assessment for RMP exists. This study's objectives were to report the incidence of significant pathologic findings (SPF) in RMP specimens; to identify clinical risk factors for SPF; and to propose standard sampling for microscopic evaluation of RMP specimens.

Design: All consecutive RMP specimens were prospectively examined to include a baseline gross examination and systematic microscopic sampling via rank-ordered tissue section sets (TSS). TSS-1 had 1 skin and 3 breast sections while TSS-2 and TSS-3 had 4 additional breast sections in each. The incidence of SPF was tabulated, as well as age, specimen weight, history of carcinoma, and preoperative mammogram results. Also examined were proliferative and non-proliferative changes as well as skin lesions.

Results: 595 cases were evaluated, and SPF was present in 9.8% of patients. 83% of SPF was identified in TSS-1 and TSS-2 (table 1). No SPF was identified in patients younger than 35 years. No carcinoma was identified in patients younger than 40 years. Patient age was a significant factor (p < .0001) (table 2). History of contralateral cancer, adjusting for age, was not significant (p=.48). Microscopic skin pathology was identified only in those with gross findings and not in randomly submitted skin sections.

Conclusions: Based on this prospective study, we recommend the following algorithm for RMP specimens:

- Patients younger than 35 years: gross examination only and microscopic evaluation reserved for grossly evident lesions.
- Patient 35 to 49 years old: 6-7 breast sections
- Patients 50 years or older: 10-11 breast sections
- Skin sections: only for grossly evident lesions

Diagnosis (n)	TSS-1a	TSS-2b	TSS-3c
ALH (32)	11	13	8*
LCIS (6)	5	1	0
ADH (12)	6	4	2@
DCIS (6)	3	3	0
Invasive (2)	0	2	0
Total (58)	25 (43.1%)	23 (39.7%0	10 (17.2%)

[a] Diagnosis made solely on TSS-1; [b] Diagnosis first made on TSS-2 (i.e., TSS-1 was negative); [c] Diagnosis first made on TSS-3

* 3 patients >50 years old

[@] Both >50 years old

Age Group	%	Mean Age	All SPF (%)	ALH	ADH	Invasive or in situ
	22.8	26.1	0	0	0	0
35-49 (n-224)	37.6	34.7	21(9.4)	12	5	4
>50 (n-236)	39.6	57.6	37(15.5)	20	7	10
All (595)	100	44.6	58(9.8)	32	12	14

1992 Clinical Impact of Routine Review of Thyroid Fine Needle Aspirations

Jordan Arkin, Tamar Giorgadze, Rana Hoda, Rema Rao, Theresa Scognamiglio. New York Presbyterian Hospital – Weill Cornell Medical Center, New York, NY.

Background: Patients are often referred to tertiary medical centers for surgical management based on fine needle aspiration (FNA) results. In many of these institutions, it is the standard of care to have all cases reviewed for second opinion diagnosis (SOD) by in-house cytopathologists. The aim of this study was to compare the outside diagnosis (OD) of thyroid FNAs with our SOD and determine impact on clinical management.

Design: We retrospectively reviewed the results of all thyroid FNAs referred from outside institutions to our laboratory for SOD over a two year period (9/2012 - 9/2014). Our SOD and the OD were compared. FNA diagnoses were categorized according to the Thyroid Bethesda System (TBS). Cases were categorized as follows: concordant (no change in TBS category), minor discordance (MiD; one degree change in TBS category), and major discordance (MaD; two or greater degree change in TBS category and/or a change in recommended management from surgery to no surgery or vice versa). SOD and the OD were compared with the final histology or repeat FNA results.

Results: One hundred forty-seven cases in 108 patients were identified. The concordance rate was 73% (108/147), with the highest concordance in lesions that were either called benign or malignant on OD (TBS II and TBS VI; 89% and 92%, respectively) and the lowest concordance in suspicious lesions (TBS V; 30%). 39 cases showed discordance (27%), of which 28 were MiDs (72%) and 11 were MaDs (28%). Of the 28 MiDs, the majority (14/28, 50%) were suspicious for malignancy on OD (TBS V), 12 (86%) of which were changed to malignant (TBS VI) on SOD. However in this group, there was no substantial change in surgical management decision. Of the 11 MaDs, 9 (82%) were indeterminate on OD (3 TBS III and 6 TBS IV) while 2 (18%) were malignant (TBS VI). In this group, management was changed in all 11 patients. Surgical follow up was available for 9 patients in this group, 3 (33%) of which received appropriate oncologic thyroid surgery and 3 (33%) of which avoided unnecessary surgery because of SOD.

Conclusions: SOD of thyroid FNA specimens should be a routine part of preoperative management of thyroid nodules as it can result in a change in surgical management for some patients. This is especially true in the indeterminate category, which accounted for the majority of MaDs (82%) in our study.

1993 Are Multilevel Recuts on Axillary Sentinel Lymph Nodes Truly Useful?

James Bauer, Lacy Normington, Josephine Harter, Agnes Loeffler, Aparna Mahajan. University of Wisconsin Hospital and Clinics, Madison, WI.

Background: The method of processing axillary sentinel lymph nodes (SLN) varies across institutions. Currently the CAP recommends that SLNs should be sectioned and examined at 2 mm intervals along the long axis and at least one H&E slide should be examined. However, it is common practice to examine multiple levels of SLNs. Although the value of such a practice has not been confirmed, it continues today driven primarily by the fear of missing a metastasis. However, the costs of such a practice can be significant, as it adds a large number of slides to the pathologists' work load. At our institution, we routinely examine three H&E levels per block but do not necessarily section at 2 mm. The goal of our pilot study was to determine whether the benefits of such a practice justify the costs.

Design: We performed a retrospective analysis of 100 consecutive breast lumpectomy and mastectomy cases with sentinel lymph node sampling and evaluated the practicality of examining multiple levels.

Results:

Cases Reviewed	Total Number of SLNs	Total SLN Cassettes Produced	Cases with Macro-metastases*	Cases with Micro-metastases**
100	275	376	8	8

*All detected by frozen section

**All except one was detected on first level H&E slide. The SLN on which a micrometastasis was detected on the deeper level was not sectioned at 2mm intervals at the time of grossing.

H&E slides produced including multilevel recuts: 878

Level 1 H&E slides produced: 376

Additional H&E slides generated from multilevel recuts (potential savings): 502

Cost per H&E stained slide: $2.50

Cost savings of H&E stained slides: $1255.00

Technician savings: $796.00

Total potential savings: $2051.00 per 100 breast cases containing sentinel node resections.

Conclusions: Multilevel recuts on SLNs did not help in the identification of macrometastasis. Additionally, all but 1 nodal micrometastasis, representing 0.36% of the 275 sentinel lymph nodes reviewed, were detected on the first H&E level. However the SLN in this case was not sectioned at 2mm. No additional slides would be required when the SLN is sectioned at 2 mm at grossing since such sampling would likely reveal the micrometastasis. Our pilot study does not support continuing to evaluate multilevel recuts on SLNs. The benefits did not outweigh the increased costs and resource requirements of the histopathology laboratory and pathologist's time. We anticipate that the benefits would be even greater when applied to daily workload in breast pathology in our institution.

1994 Anion Gap Underestimated By Point-of-Care Testing in Diabetics and End Stage Renal Disease Patients

Tiffany Caza, Kelly Costello, Jean Sgroi, Matthew Elkins. SUNY Upstate Medical University, Syracuse, NY.

Background: Point-of-care (POC) testing is a valuable resource, allowing rapid measurement of pH and electrolytes to assist clinical decision making for critically ill patients. In comparing POC and core lab measurements, we identified a discrepancy in 10.4% patients. As anion gap (AG) measurements provide important clues for determining the etiology of metabolic acidosis, we sought to identify whether a subset of patients is represented in the discrepancies to optimize use of POC testing in emergency departments.

Design: Concurrent measurement of >1500 samples of serum pH and electrolytes using iSTAT POC device CHEM8 and Roche P800 platform in the core laboratory from 1/2011 to 2/2014 was performed. Anion gap (AG)was calculated by AG = Na – (Cl +TCO_2). Full chart review was done with the 44 patients with discrepant Cl and AG measurements and 45 controls where the calculated AG measurements were within -1 to +1. Statistical analysis was completed utilizing t-tests and ANOVA to determine differences between groups. A p value of <0.05 was considered significant.

Results: Chloride levels in patients admitted with DKA or ESRD had a significant discrepancy between POC and core lab measurements (discrepant Cl difference +6 to +17 mmol/L, control Cl difference -5 to +4 mmol/L, $p = 6.2 \times 10^{-27}$). This resulted in normalization of a high AG, with an inverse relationship between AG and Cl discrepancy. iSTAT pH values (blood gas cartridge) are concordant with core lab measurements. Patients were younger in the discrepant group compared to controls (45.8 y compared to 57.6 y, p=0.01). The number of medications taken was not a significant variable (mean control 6.7, discrepant 8.2). Secondary diagnoses of atrial fibrillation, CAD, and CVA were more common in controls, while patients in the discrepant group had an increased frequency of metabolic acidosis, type I or II diabetes mellitus, diabetic complications (gastroparesis, retinopathy, neuropathy), and vomiting. Use of exogenous insulin (50% vs 2%), ondansetron (28% vs 0%), gabapentin (18% vs 8%), and nephrolite (14% vs 4%) were increased in the discrepant group, while furosemide use was increased in controls.

Conclusions: Chloride measurement by POC testing can be unreliable in a small cohort of patients, including those with DKA and ESRD. AG normalization by Cl discrepancy reduces identification of true AG metabolic acidosis and can result in delayed treatment. Therefore, caution should be taken in interpreting results of POC testing when the laboratory values do not seem to reflect the patient's condition.

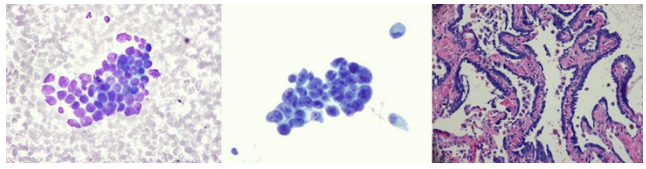
1995 Correlation of Atypical/Suspicious Rapid On-Site Fine Needle Aspiration Diagnoses With Final Diagnoses: An Institutional Experience With 154 Cases Over 3 Year Period

Michael Chaump, Navneet Narula, Rana Hoda, Tamar Giorgadze. Weill Cornell Medical College, New York, NY.

Background: Rapid on-site evaluation (ROSE) of lung lesions is useful for adequacy assessment of fine needle aspirations (FNA). Our academic center implemented an early lung cancer screening program utilizing FNA for even small lung lesions, < 5mm, with suspicious radiology findings. In all cases, ROSE is performed to ensure sample adequacy for diagnosis and ancillary studies (immunocytochemical and molecular), with a minimal number of passes. Atypical/suspicious (ATY/SUSP) ROSE diagnoses trigger additional FNA passes for diagnostic purposes and for allocation of material for ancillary studies. In this study we correlate ATY/SUSP ROSE diagnoses with final cytological and histological findings. This to our knowledge, has thus far, not been reported.

Design: All consecutive lung FNA with ATY/SUSP ROSE diagnoses over a 3-year period were retrospectively reviewed. Clinicopathological findings were documented. Two smears from each pass were prepared and stained with Diff-Quik (DQ) for ROSE and PAP stain for final. Residual material was submitted for cell block (CB). ROSE diagnosis was correlated with final cytological and histological diagnosis.

Results: A total of 154 lung FNAs from 148 patients (56 men and 92 women; age range, 25-95 years; mean, 69.8). Average number of passes was 2 (range 1-8). Final cytological diagnosis for ATY/SUSP ROSE was ATY, 30; SUSP, 18; malignant, 98 [adenocarcinoma (ACa), 68; squamous cell Ca, 12; neuroendocrine tumor, 6; non-small cell lung Ca, 5; Lymphoma, 1; Metastatic Ca, 6] and benign/reactive 8. Histology specimens were available in 106 (69%) cases. Cytohistological concordance rate was 96.2% (4 discordant cases, all seemingly attributable to sampling, rather than interpretaition issues).



Conclusions: The final cytological diagnoses in the majority of ATY/SUSP ROSE diagnoses were lung ACa. This may reflect difficulties in diagnosing well-differentiated ACa (lepidic growth pattern) on DQ during ROSE, due to morphologic overlap with reactive pneumocytes. Nevertheless, ATY/SUSP ROSE in our study did not seem to affect patient care as additional passes triggered by ROSE led to diagnostic yield of malignancy in 98% of cases with a cytohistological concordance rate of 96.2%.

1996 Developing ALK-1 Immunohistochemistry and In Situ Hybridization Proficiency Testing: Canadian Immunohistochemistry Quality Control (CIQC) Experience

Carol Cheung, John Garratt, C Blake Gilks, Jennifer Won, Jean-Claude Cutz, Ming-Sound Tsao, Emina Torlakovic. University Health Network, University of Toronto, Toronto, ON, Canada; Vancouver Coastal Health, Vancouver, BC, Canada; Vancouver General Hospital and University of British Columbia, Vancouver, BC, Canada; University of British Columbia, Vancouver, BC, Canada; McMaster University and St Joseph's Healthcare, Hamilton, ON, Canada.

Background: Intra-chromosomal rearrangements involving the ALK gene are found in 3-5% of non-small cell lung cancers (NSCLCs). Crizotinib is a tyrosine kinase inhibitor that has been shown to prolong progression free survival in patients with advanced NSCLC harbouring ALK gene rearrangements. In Canada, ALK-1 immunohistochemistry (IHC) is used as a screening test prior to confirmation by FISH.

Design: CIQC has performed two ALK (Lung Ca) runs to date. Proficiency testing (PT) samples included 32 previously characterized cases (IHC and FISH) from either Canadian ALK (CALK) project or samples from CIQC reference laboratories. The same design was used for both runs. 20 laboratories particpated in Run 1 and 22 in Run 2. Some laboratories participated in anticipation of future need and used the PT exercise as a part of test development and validation. The results of IHC testing were first self reported using the CIQC TMA Scorer and then evaluated by expert assessment. FISH results were self-reported only. Participants also reported details about IHC and FISH protocols. Percent correct results and kappa-values were calculated for which >90% and > 0.80 were used as acceptable results respectively. Pass rate between the two runs and between different primary antibodies were compared.

Results: Seven of 19 laboratories (37%) in Run 1 and 14 of 19 (74%) laboratories in Run 2 passed the CIQC PT criteria for IHC testing. The increase in pass rate for Run 2 was significant (p=0.012, Fisher's Exact Test). The pass rate was significantly higher for laboratories using 5A4 compared to other antibodies in both PT runs (p=0.004 in Run 1 and p=0.025 in Run 2, Chi-Square Test). All reported FISH results were correct.

Conclusions: PT for IHC for rare diseases such as ALK-positive lung cancer is feasible but challenging. The academic nature of the CIQC program and collaboration on a national level facilitated the development of appropriate PT samples. Participating laboratories made use of the PT exercise to either confirm that their testing was properly calibrated or to improve their protocols, which was confimed by achivement of significantly better results in Run 2. They also used CIQC's PT program for new test development and optimization.

1997 Quantifying Pre-Signout and Post-Signout Pathologist Quality Assurance Activities

Carol Cheung, Emina Torlakovic, Runjan Chetty, Bayardo Perez-Ordonez. University Health Network, University of Toronto, Toronto, ON, Canada.

Background: Although quality assurance (QA) activities in pathology are routine practice, the formal documentation of QA activities is largely focused on post-signout (postSO) correlations (eg. the interpretive accuracy of already issued reports). However, pre-signout (preSO) activities have more direct impact on the quality of reports and patient safety and may include reviewing patient charts, intradepartmental consultations, reviewing reports or slides from a previous procedure, etc. The growing requirement for documentation of "quality" has made it more important to quantify the work required for QA activities. Automatable Activity-Based Approach to Complexity Unity Scoring (AABACUS) is a recently published pathologist workload model, which may be well suited for translating laboratory information system (LIS)-documented QA activities into quantifiable workload. We present here results from the calendar year following the introduction preSO QA activities into our departmental LIS.

Design: All QA activities for clinical cases documented in the departmental LIS were analyzed. Workload was calculated in complexity units using AABACUS.

Results: A total of 121,259 clinical cases were assessed. QA activity was documented in 17% of cases; 13% of cases had preSO QA activities, and 4% had postSO QA activities. PreSO intradepartmental consultations were documented in 6% of cases, which represented 27% of all QA activities and 37% of all pre-SO QA activities. Review of the patient chart accounted for 3% of documented QA activities. Total documented QA activities accounted for 4.3% of overall departmental workload; specifically, preSO QA and postSO QA activities accounted for 3.7% and 0.6% of overall departmental workload. All documented QA activities accounted for 2.7 FTEs of work using relative benchmarking in AABACUS.

Conclusions: Peer case reviews and other professional QA activities in pathology can be quantified using the AABACUS workload model. The consistent documentation of QA activities by pathologists is a pre-requisite for the accuracy of results produced by AABACUS. PreSO QA activities, especially preSO intradepartmental consultations, represent a significant component of LIS-documented pathologist QA activities in our institution; facilitating the documentation of such activities is an important consideration if expansion of QA programs is undertaken.

1998 Reflexive Screening for Lynch Syndrome in the UK: An Audit and Cost-Effectiveness Analysis

Richard Colling, David Church, Juliet Carmichael, Lucinda Murphy, James East, Peter Risby, Rachel Kerr, Runjan Chetty, Lai Mun Wang. University of Oxford, Oxford, United Kingdom; University of Oxford, Oxford, United Kingdom; Oxford University Hospitals NHS Trust, Oxford, United Kingdom; University Health Network, Toronto, ON, Canada.

Background: Lynch Syndrome (LS) accounts for 0.3-2.4% of colorectal cancers and is caused by germline mutations in mismatch repair (MMR) proteins. Traditionally, patients thought to be at risk of LS were referred for Clinical Genetics assessment and genome testing where applicable. Recently, screening strategies to streamline referrals have become popular in the UK, however, uptake of screening has been inconsistent with the local cost of testing being a limiting factor for many institutions.

Design: We carried out a retrospective audit of all colorectal cancers which had undergone reflexive screening for LS in our institution in the year of 2013. All cancers meeting the modified Bethesda criteria had been screened with immunohistochemistry (IHC) for MLH1, PMS2, MSH2 and MSH6 and those with a loss of MLH1/PMS2 expression had been (where funding was available) followed up with mutational analysis of BRAF V600E. Patients with negative IHC/BRAF were followed up in Clinical Genetics for further genetic testing.

Results: 209 patients met the criteria for LS screening. 44 cases (21%) showed a loss in MLH1 expression and all but one of these cases showed concurrent loss of PMS2. BRAF V600E testing was carried out on 28 cases, only two of which were negative. IHC screening incurred a cost of $15,238 and BRAF testing incurred a cost of $5445. 18 patients were eligible for clinic referral at a cost of $15,758. Therefore, the total cost of LS screening was $36,452. Compared with traditional clinical follow up alone this gave a potential saving of $146,450. IHC screening alone reduced potential referrals from 209 to 45 at a saving of $143,509.

Conclusions: We have implemented LS screening within our institution at a significant potential financial benefit. In line with national and international recommendations, LS screening not only brings improved patient care but brings local financial savings and is increasingly recognised as a cost effective strategy for the National Health Service in the UK.

1999 Comparing Fetal Tissue Procurement Methods on Quality of Karyotype Analysis

Joanna Conant, Mary Tang, Brenda Waters. University of Vermont Medical Center, Burlington, VT.

Background: Chromosomal abnormalities are detected in up to 13% of all stillbirths and in over 20% of those with developmental anomalies. However, these estimates may be low since up to 50% of attempts to culture cells are unsuccessful due to microbial overgrowth or nonviability. Tissue for cytogenetics can be procured at bedside by the clinician or by the pathologist at autopsy. With clinical collection, tissue can be placed into culture media immediately, increasing chances of growth. However, tissue collection competes for attention with other activities, which may result in microbial overgrowth or selection of maternal rather than fetal tissue. Tissue obtained at autopsy is collected in a more controlled environment using sterile technique, but delay in procurement may decrease viability. The goal of this study was to determine which collection method yields better results.

Design: This retrospective study reviewed cases from 2007-2013 that had two separate samples submitted for cytogenetics, one from the clinician and one from the pathologist. Medical records and cytogenetic culture sheets were reviewed for specimen source, time of delivery, collection time, setup time, harvest date, cell growth, microbial overgrowth, maternal contamination, and final result.

Results: More clinical than autopsy cases had microbial overgrowth. There was no difference in the number of cases with maternal contamination or signed out as incomplete or as no growth.

Average Time from Delivery to Collection, Laboratory Setup, and Harvest

	Clinical	Autopsy	Paired T-Test
Delivery to Collect Time	2.0 hours	36.5 hours	p < 0.001
Delivery to Laboratory Setup	25.8 hours	48.4 hours	p = 0.003
Delivery to Harvest Date	18.4 days	17.5 days	p = 0.614

Paired Autopsy vs. Clinical Results

Signed Out As Complete

Autopsy \ Clinical	No	Yes	Total
No	3	6	9
Yes	9	23	32
Total	12	29	41

Fischer exact test (two-tailed): p=1.000

Signed Out As No Growth

Autopsy \ Clinical	No	Yes	Total
No	34	3	37
Yes	3	1	4
Total	37	4	41

Fischer exact test (two-tailed): p=0.348

No Result Due to Microbial Overgrowth

Autopsy \ Clinical	No	Yes	Total
No	33	6	39
Yes	0	2	2
Total	33	8	41

Fischer exact test (two-tailed): p=0.034

Evidence of Maternal Contamination

Autopsy \ Clinical	No	Yes	Total
No	18	3	21
Yes	1	1	2
Total	19	4	23

Fischer exact test (two-tailed): p=0.324

Conclusions: Our study demonstrated a significant increase in microbial overgrowth in clinician-procured samples. While there was a delay in the collection of tissue in pathologist-procured samples, there was no increase in the number of cases signed out as incomplete or as no growth. There was also no difference in the frequency of cases with maternal contamination between the two groups. These findings suggest that there may be benefit to collecting tissue for cytogenetics at time of autopsy rather than at bedside.

2000 Positive PAX8 Staining In Lymphoid Neoplasms Depends on Target of Antibody

Joanna Conant, Michael DeSarno, Abiy Ambaye, Ronald Bryant, Maryam Zenali. University of Vermont Medical Center, Burlington, VT; University of Vermont, Burlington, VT.

Background: Paired-box (PAX) genes are a family of transcription factors involved in embryonic development and differentiation. PAX5 is expressed in neoplastic and non-neoplastic B-cells; PAX8 is expressed in normal kidney and in thyroid, renal, and Müllerian malignancies. PAX8 expression in lymphoid neoplasms is not well known. Rare studies report expression of polyclonal PAX8 in lymphoid proliferations due to high sequence homology between the N-terminus of PAX8 and PAX5. It is suspected that in B-cell neoplasms, antibodies with activity against the N-terminus of PAX8 will show positive staining due to cross reactivity. The goals of this study include evaluating the status of monoclonal PAX8 staining directed at the N-terminus (PAX8N), monoclonal PAX8 staining directed at the C-terminus (PAX8C), and to compare the results with PAX5 staining in the same lymphoid neoplasms.

Design: PAX5 (Thermo Scientific, SP34), PAX8N (Ventana, MRQ-50), and PAX8C (Abcam, PAX8R1) expression was analyzed by immunohistochemistry on follicular lymphoma grades 1-3 (FL1, FL2, FL3), diffuse large B-cell lymphoma (DLBCL), small lymphocytic lymphoma (SLL), plasmacytoma, and anaplastic large cell lymphoma (ALCL). Expression was scored based on percentage of moderate to strong nuclear staining in neoplastic cells: 0=<5%, 1=5-25%, 2=26-50%, 3=51-75%, and 4=>75%.

Results: In all neoplasms examined, PAX8N staining correlated with PAX5 and was strongly positive in all FL, DLBCL, and SLL. PAX8C was negative in all neoplasms examined. All PAX stains were negative in ALCL.

PAX Staining and Comparison of PAX5 vs PAX8Nand PAX8C

	Staining (Mean Score)			Signed Rank Test, P-Value	
	PAX5	PAX8N	PAX8C	PAX5 vs PAX8N	PAX5 vs PAX8C
FL1 (n=20)	3.95	3.85	0	0.63	
FL2 (n=13)	4.00	3.92	0	1.00	0.0002
FL3 (n=10)	4.00	4.00	0	1.00	
DLBCL (n=23)	4.00	3.87	0	0.50	
SLL (n=23)	3.70	3.87	0	0.29	
Plasmacytoma (n=14)	0.64	0.57	0	1.00	0.25
ALCL (n=8)	0	0	0	1.00	1.00

Conclusions: PAX8N stains FL, DLBCL, and SLL and its positivity parallels that of PAX5. PAX8C, however, does not stain any of the aforementioned. Regarding discriminatory staining between lymphoid and epithelial malignancies, while PAX8C has a role, neither monoclonal PAX8N nor polyclonal PAX8 is helpful. This study illustrates the importance of knowing specific immunostaining targets to avoid misdiagnosis.

2001 The Impact of Second-Opinion Dermatopathology Review on Melanoma Management and Stage at a Tertiary Cancer Referral Center

Richard Danialan, Kudakwashe Mutyambizi, Jonathan Curry, Carlos Torres-Cabala, Doina Ivan, Priya Nagarajan, Phyu Aung, Victor Prieto, Michael T Tetzlaff. University of Texas MD Anderson Cancer Center, Houston, TX.

Background: Given the increasing attention to cost control in health care, whether second-opinion pathology review objectively impacts patient care and treatment decisions remains controversial. We chose primary cutaneous melanoma as a model to address this question since surgical management and AJCC cancer staging of primary cutaneous melanoma is directed by the histopathologic parameters (e.g. Breslow thickness, ulceration, mitotic rate, satellitosis) of the lesion. We thus examined the relative rate of diagnostic changes that resulted in a change of stage and/or management of patients treated for primary cutaneous melanoma at our tertiary cancer referral center.

Design: We performed a retrospective review of primary cutaneous melanoma diagnoses for 50 patients seeking surgical or medical consultation at our institution for the month of June, 2014. Major discrepancies were defined as a difference in diagnosis that would change patient stage and/or clinical management and were tabulated. Each case for which there was a discrepancy was reviewed by up to 5 dermatopathologists to achieve consensus.

Results: We identified the rate of major discrepancies at 20% (10/50 cases) in this pilot study. The most common discrepancy (n=6 cases) was the identification of a dermal mitotic figure in a thin (≤ 1.00 mm) melanoma, resulting in a change of stage from pT1a to pT1b. At our institution, most patients with pT1b primary cutaneous melanoma are offered sentinel lymph node biopsy, whereas patients with pT1a lesions are typically not. In two of these cases, the patients presented to our institution with metastases. In addition, two discrepant cases originally diagnosed as melanoma in situ demonstrated dermal invasion upon re-review at our institution. Finally, second review of one case demonstrated multiple dermal satellite lesions in the excision specimen that were interpreted as part of the primary lesion by the referring pathologist. Based on the 2010 AJCC criteria, the presence of satellitosis dictates a pN2c (at least Stage IIIb), and the patient presented to our clinic with additional cutaneous metastases. The reasons underlying these discrepant opinions included both interpretation and tissue sampling.

Conclusions: Second-opinion dermatopathology review (including consensus review for discrepant cases) changed the stage and/or management of 20% of patients with primary cutaneous melanoma at our institution and thus improves diagnostic accuracy to direct the most appropriate patient management.

2002 Rapid Improvement of Prostate Needle Core Biopsy Fixation Via an Interdepartmental Collaboration

Paul DiMaggio, Ashley Winter, Brian Robinson. New York Presbyterian Hospital – Weill Cornell Medical Center, New York, NY.

Background: Adequate tissue fixation is a basic quality measure impacting diagnosis, cost, and patient safety. Poorly fixed prostate needle core biopsy specimens (PNCBS) suffer artifactual changes having the potential to negatively impact patient care. To fix a situation in which poorly fixed PNCBS were being received, a collaborative root cause analysis and quality improvement initiative was undertaken by the Departments of Pathology and Urology via our institution's resident-led Housestaff Quality Council (HQC).

Design: H&E slides of all PNCBS received in a one month period were reviewed by two pathologists, with one blinded to the originating urology practice. Biopsies were assessed for histologic artifacts of poor preservation including: nuclear smudging and "halo" formation, especially of lymphocytes; cytoplasmic vacuoles; stromal cracking and retraction; and lack of hyperchromasia and nucleoli in prostatic carcinoma. PNCBS demonstrating at least one artifact were categorized as poorly fixed, and PNCBS lacking artifacts were categorized as adequately fixed. The source practice of each biopsy was then reviewed. One practice was identified as the source of poorly fixed PNCBS, and the Department of Urology was contacted via the HQC. Standard operating procedures (SOP) in all practices were reviewed to identify differences between the adequately and poorly fixed practices.

Results: Forty-two PNCBS were reviewed prior to intervention. Eighteen (43%) were poorly fixed, all from one referring practice. Consultation and investigation through the HQC revealed that PNCBS were placed on sterile water soaked sponges prior to formalin fixation, while the other practices used normal saline. No other differences were identified. The SOP in the practice with poor fixation was immediately changed to utilize normal saline instead of sterile water. To assess efficacy of the change, thirty-one consecutive biopsies sent following the change were reviewed in a blinded fashion. All biopsies were adequately fixed following intervention, including all 16 submitted from the practice with a history of poor fixation.

Conclusions: The HQC facilitated a root cause analysis of a significant problem which led to a rapid improvement in PNCBS fixation. Resident-led quality assurance committees within hospitals can serve as a model for interdepartmental collaboration in resolving QA/QC problems while facilitating resident education.

2003 Paraneoplastic Autoantibody Panel Ordering as a Model for Laboratory Test Utilization Analysis and Intervention

Anna Dolezal, Matthew Krasowski. University of Iowa Hospitals and Clinics, Iowa City, IA.

Background: Proper laboratory test utilization is a continuing challenge in medicine, with significant downstream clinical and financial effects of test misutilization. Pathology is in a unique position to analyze test ordering patterns and to institute interventions to promote appropriate test utilization. One intervention for high cost laboratory tests is to put a hard stop in the electronic medical record (EMR) that requires the ordering physician to have preapproval by pathologist. We focused on a low volume but high cost testing panel for serum paraneoplastic autoantibodies at University of Iowa Hospitals and Clinics, a 711 bed academic medical center.

Design: A search of the EMR for orders of the serum paraneoplastic panel was performed for dates between January 2009 and September 2013. Ordering of this panel had a hard stop requiring pathologist approval as of May 30th, 2012 (the "intervention"). A manual chart review was performed for patients with any positive results to see if the result was acknowledged in the medical chart. This study had Institutional Review Board approval as a retrospective study.

Results: The serum paraneoplastic panel was ordered 279 times before the intervention (average: 6.8 panels/month) to 22 orders after the intervention (average: 1.47 panels/month). There were multiple cases pre-intervention of duplicate testing for the same patient and of cases where results became available only after patients had expired or had been transitioned to hospice care. Before intervention, there were 65 panels with positive results (23% of total panels ordered) which were acknowledged in the medical record in only 38 of these patients (58% of positive results). After the intervention, there were 4 panels with positive results (18% of total panels ordered) which were acknowledged in the medical records in all 4 of these patients (100%).

Conclusions: The EMR can be a useful tool for limiting ordering of specialized and expensive laboratory testing. Based on our experience with one such test, the serum paraneoplastic autoantibody panel, such an intervention decreased the average number of tests ordered significantly, but without significantly changing the proportion of patients with a positive result. Furthermore, in a small sample size, the percentage of the time these results were acknowledged in the medical chart was increased. This would suggest that interventions of this type may help restrict the ordering of unnecessary tests, resulting in both cost savings to the hospital and the patient.

2004 Validation of Digital Whole Slide Imaging According To the College of American Pathologists Guidelines in the Evaluation of Pre-Implant Kidney Biopsies

Albino Eccher, Anna Calio', Romano Colombari, Luigino Boschiero, Marilena Liviero Casartelli, Laura Zampicinini, Marco Chilosi, Claudio Ghimenton, Guido Martignoni, Matteo Brunelli. University and Hospital Trust, Verona, Italy; Ulss 20 Fracastoro Hospital, San Bonifacio, Italy.

Background: We sought to validate the accuracy and quality of the digital medical devices for kidney biopsies during transplantation according to the College of American Pathologists guidelines.

Design: Sixty-two histopathological cases from pre-implantation kidney biopsies were scanned by ScanScope Digital Slides Scanner (Aperio, Vista, CA) along 2013-2014 yrs. The diagnosis was performed by two pathologists of the call rota system during transplantation, on routine light microscopy, in order to quantify glomerulosclerosis, tubular atrophia, fibrosis and arteriosclerosis in accordance to the Remuzzi criteria. Both pathologists have a remote access to virtual slides from all the computers of the hospital via the viewer Web pocket with an user id. After two weeks, as wash out period, all slides were re-evaluated on computer devices. An overall assessment was obtained in a dedicated board room area to achieve concordance.

Results: 124 whole glass slides were reviewed. Scan time averaged two minutes and 10 seconds per slide. The diagnostic score ranged from 2 to 8. After two weeks, side by side comparisons, between diagnosis performed on tissue glass slides versus pc widescreen were almost perfect (0,96 concordance) of intra-observer variability. All scores were confirmed by the same observer except for 5 slides (3 cases) which were upgraded at digitals for fibrosis and tubular atrophy, without changing the suitability for transplants. The inter-observer concordance between evaluation at glass slides and whole slide imaging was almost perfect (0,92) by the two pathologists. Other minor discrepancies were in the report of tubular acute necrosis features. The mean turnaround diagnostic time was respectively 15 min for glass slides and 18 min for digital slides.

Conclusions: We validated the mode of digital score for pre-implantation kidney biopsies according to the College of American Pathologists guidelines. Digital pathology is adequate for primary diagnosis without delaying diagnosis to bridge temporal and geographic gaps between distant located pathologists involved in transplantation process. Furthermore the simple possibility of gathering a second opinion on a difficult case via digital device enhances the quality and safety of patient care.

2005 Improving Next-Generation Sequencing (NGS) Success in Solid Tumors

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Background: Next generation sequencing (NGS) is important in the workup of solid tumors as genomic information becomes integrated into clinical practice. Performing NGS on solid tumors can be challenging due to the small size of biopsy specimens. Currently, there is little in the literature to indicate if manufacturer recommended NGS protocols can be improved to maximize the use of low DNA-yield specimens. The aim of this study was to determine if the manufacturer's DNA requirements (>0.85ng/uL) for the Ampliseq Cancer Hotspot v2 panel could be reduced, and still yield clinically useful results.

Design: In a retrospective study of 614 consecutive solid tumor cases allocated to NGS, 67 (11%) cases were removed from the pipeline due to DNA yield <0.85ng/uL. We tested 25 available cases with DNA <0.85ng/uL to determine if they could be successfully sequenced using the Ampliseq Cancer Hotspot v2 panel on the Ion Torrent PGM. Single gene confirmatory testing via Sanger or pyrosequencing was performed to confirm mutations discovered. In addition, a prospective study was performed on 408 consecutive cases collected from February 14-March 21, 2014. Cases were subjected to NGS analysis regardless of DNA concentration. We examined the NGS outcomes using previously identified characteristics such as selected tumor size and procedure types.

Results: We demonstrated that NGS can be carried out on samples with DNA concentrations <0.85ng/uL. Of 25 cases, 17 (68%) were successfully sequenced (>300,000 reads with an AQ20 quality score). Of these, 13 cases showed mutations that could be tested using orthogonal methods, 8 of which were confirmed independently. The remaining cases could not be confirmed due to lack of DNA, poor PCR amplification/Sanger sequencing quality, lack of primer coverage at the mutation site, and lower sensitivity of the orthogonal assay.

For the prospective phase of this study, NGS success rates increased from 88% (the success rate in the retrospective phase with exclusion of cases <0.85ng/uL) to 95% (387/408). The gains were most pronounced among tiny (<10 mm2) biopsy samples (success rate from 76% to 94%) as well as cytology smears and cell blocks (success rate from 58% to 87%) (p<0.01).

Conclusions: NGS can be successfully performed on cases using DNA concentrations less than the manufacturer's recommendations. This will expand the use of NGS in cases yielding minimal quantities of DNA including fine needle aspirates and tiny biopsies, allowing for the detection of clinically targetable mutations for patients with minute biopsies.

2006 Insufficient Endometrial Sampling: Clinico-Pathologic Quality Assurance

Grzegorz Gurda, Esther Elishaev, Gloria Carter. University of Pittsburgh Medical Center, Pittsburgh, PA.

Background: Endometrial sampling either a biopsy or curettage, are the first step procedure utilized for evaluation of endometrial status in order and to establish a definitive, tissue-based diagnosis of gynecologic disease. Unfortunately at times the tissue obtained may be insufficient or inadequate (InS/InA) for assessment. The management and clinical outcomes of these patients and the factors that influence the initial and subsequent endometrial sampling have not been well-studied.

Design: A search of all patient records for 2003-2013 at University of Pittsburgh Medical Center was conducted via automated, de-identified TIES database tool. Sample data, general patient characteristics and pathology reports were retrieved in a blinded, automated fashion, then manually verified and analyzed. All-time and 1-year followup (F/U) procedure rates and clinical outcomes were tracked for all InS/InA samples.

Results: A total of 1011 endometrial sampling procedures were identified over 10 years, comprising 2.0% of all such cases (total 52,137). InS/InA rate was similar on an annual basis (range 1.5-3.2%), but more frequent in July and August (beginning of the academic year, comprising 20% of total). InS/InA samples were more common among older patients (avg age 55.9 vs 49.5). Within 1 year, 41% of patients with InS/InA had follow-up and 13% were again InS/InA and again more commonly among older patients (avg age 57.6). Among remaining 87% of patients: 89% showed benign F/U and 11% showed hyperplasia or neoplasia. For benign F/U cases a larger than expected 24% showed polyp(s) and a substantial 43% of cases with hyperplasia/neoplasia showed a carcinoma.

Conclusions: InS/InA diagnosis in endometrial sampling procedures is not uncommon, particularly among older population. Though on F/U most result in a benign diagnosis (often an endometrial polyp), a more advanced hyperplastic or neoplastic lesion occur in approximately 10% of the cases. The study also shows feasibility of de-identified database search tool to expeditiously create a large-scale quality assurance study, while offering best protection of patient heath information.

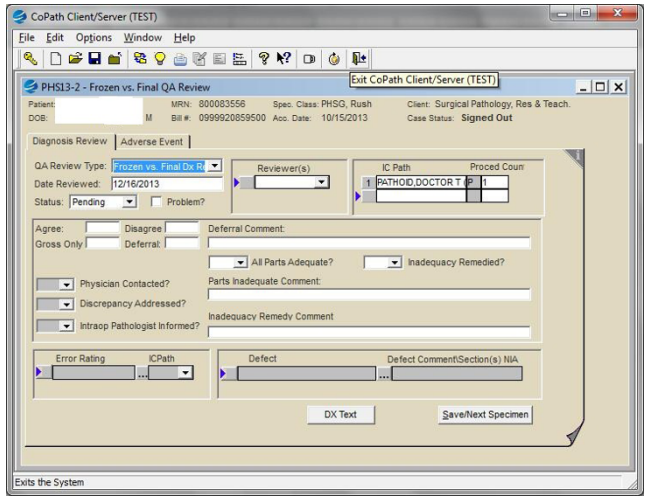
Sufficient on F/U – **87%**		InS/InA again on F/U = **13%**
Benign – 89%	**Hyperplasia/Neoplasia – 11%**	
- Secretory/Proliferative/Disordered = **65%**	- Simple/Complex HyperP w/o atypia = **24%**	
- Polyp = **24%**	- Complex HyperP w/ atypia = **33%**	
- US/Hysteroscopic only (benign) – **10%**	- Carcinoma – **43%**	

2007 Novel Tool To Streamline Frozen Section Versus Final Diagnosis Evaluation By Pathologists

Douglas J Hartman, Liron Pantanowitz, Samuel Yousem, Anil Parwani, Rick Nestler, Luke Wiehagen, Anthony Piccoli, Lindsey Seigh. University of Pittsburgh Medical Center, Pittsburgh, PA.

Background: Currently pathology departments are mandated to perform review of frozen section diagnoses for discrepancies with the final diagnosis. Historically, this has been performed by manually collating printed reports and distributing them to faculty not involved in the final report of the intraoperative evaluation. The review was performed on a sheet of paper attached to the printed reports. We report our experience with developing an automated frozen versus final review activity.

Design: A new activity was developed for our existing Laboratory Information Systems (LIS) CoPathPlus (Cerner, Kansas City, MO) that incorporated an electronic process instead of a paper form for completing frozen versus final diagnosis evaluation. The paper form included a signature line, date field, critical value assessment, number of frozen sections performed, number in agreement, diagnoses deferred, diagnostic discrepancies, and assessment for the adequacy of tissue submitted. Given the manual effort required to print and distribute packages for review as well as capture and organize the data, this process was automated to streamline the workflow. The LIS tool allowed cases to be assigned to designated pathologist worklists, the reviewing pathologist to electronically review the intraoperative diagnosis in direct relation to the final diagnosis, and have them complete their review using limited data fields with drop down menus.



Results: The tool was deployed at one site; 54 cases with 73 reviews were completed in the first two months. The automated activity was well-received by faculty and the new activity was felt to be an improvement. The benefits realized by department and QA staff include automatic mechanism to assign cases to pathologists for review, less expensive process, and easier to perform statistics about frozen versus final diagnosis discrepancies.
Conclusions: Pathology departments are required to review frozen section diagnoses for discrepancies. We developed and implemented an LIS-based tool to replace the manual paper-centric task of reviewing the frozen section diagnoses. The tool was well-received by pathologists and represents an improvement on our prior manual workflow for frozen section versus final diagnosis review.

2008 An Assessment of the Reliability of Platelet-Associated Flags Generated By the Sysmex XE-5000 Automated Hematology Analyzer

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Background: XE-5000 is an automated hematology analyzer utilized by clinical laboratories worldwide to perform CBC and differential leukocyte counts. The CBC results generated on some of the blood specimens are flagged by the analyzer for verification of the result of the flagged parameter. One such parameter of clinical significance is the automated platelet count, which is often unreliable if the blood specimen contains platelet clumps. We have determined the sensitivity and specificity of each of the three platelet-associated flags generated by this analyzer, with emphasis on its ability to flag for the presence of platelet clumps.
Design: The CBC results of 200 selected blood specimens were retrospectively reviewed for the presence of analyzer-generated platelet-associated flags, which included the abnormal platelet size distribution or PAD flag, platelet clumps or CLP flag, and the large/giant platelets or LGP flag. One-half of the selected specimens were positive for platelet clumps by microscopic review and the remaining 100 were negative. The sensitivity was defined as the percentage of specimens revealing analyzer-generated flag among the morphologically positive cases. The specificity was defined as the percentage of specimens revealing no flag in the morphologically negative cases.
Results: Among the morphologically positive specimens, 42 were flagged for the PAD, 57 for the CLP and none for the LGP, giving us the respective sensitivities of 42%, 57% and 0%. Among the morphologically negative specimens, 17 were flagged for the PAD, 1 for the CLP and none for the LGP, giving us the respective specificities of 83%, 99%, and 100%. The sensitivity did increase to 72% when a specimen was considered flagged for platelet clumps when either the PAD and/or the CLP flag was generated by the analyzer.
Conclusions: The CLP has the highest sensitivity and the highest specificity, however, its sensitivity is below the desired level of 100%. Both, the sensitivity and specificity of the PAD flag are undesirably low. The LGP flag is expectedly insensitive to the detection of platelet clumps. To maximize the sensitivity to detect platelet clumps while maintaining the specificity, it is highly desirable for users of the XE-5000 analyzer to utilize the CLP flag along with an additional criteria of reviewing a blood smear on all new patients with a decreased platelet count and/or for the manufacturer of the analyzer to find ways to enhance the automatic detectability of platelet clumps.

2009 Cost-Benefit Analysis of Routine Staining of All Lung Transplant Biopsies for CMV and Fungus in Anatomic Pathology

Ian Hughes, Stefan Pambuccian, Vijayalakshmi Ananthanarayanan, Swati Mehrotra. Loyola University Medical Center, Maywood, IL.
Background: Lung transplant patients are at high risk of opportunistic infections. While the post-transplant infection rates have dropped dramatically with routine prophylaxis for CMV in seronegative patients and pan-prophylaxis for community-acquired infections, these patients must be judiciously monitored for infections and organ rejection. At our institution this involves transbronchial biopsy in conjunction with bronchialveolar lavage (BAL). Biopsies are processed with three H&E levels, Grocott methenamine silver (GMS) stain, and cytomegalovirus immunohistochemistry (CMV IHC). BAL specimens are subjected to a thorough laboratory work-up including fluid count, fungal smear, Pneumocystis carinii smear, fungal culture, quantitative bacterial culture, acid-fast bacilli (AFB) culture, 12-virus respiratory PCR panel, and 48-hour CMV PCR. When the economy necessitates review of current practices to stem the rising tide of healthcare costs, the utility of dual testing with CMV IHC and GMS stains on lung transplant biopsies seems increasingly questionable. In this study, our aim is to determine the frequency and clinical impact of positive CMV IHC/GMS cases and calculate the total cost of performing these tests.
Design: Cases of transbronchial lung transplant biopsies were identified using a retrospective review of our database over the period from January 1, 2012 to June 17, 2014. A total of 463 cases were identified and evaluated in regards to GMS/CMV stain positivity and clinical significance.
Results: Of the 463 total cases, 461 (99.56%) had CMV IHC and 462 (99.78%) had GMS stain performed. Results and calculated costs are shown in Table 1. The combined amount billed for all tests was $201,827.

	Number of Stains Performed	Number of Positive Results	Total Amount Billed
CMV IHC	461	0 (0%)	$158,399
GMS	462	1 (0.22%)	$43,428

Conclusions: No cases were positive by CMV IHC. A single case showed fungal organisms by GMS stain, but review of this patient's biopsy specimen and clinical picture revealed the fungal elements to most likely be contaminant. Routine CMV IHC and staining for GMS on transbronchial transplant lung biopsies do not appear to offer any clinically significant information that isn't already derived from culture results or microbiologic studies. The cost incurred by our laboratories and charged to Medicare/insurance companies over the period studied amounts to $201,827 or approximately $82,034 per year. Dual testing for these infectious agents by less sensitive methods seems to be a waste of health care dollars.

2010 Are Additional Deeper Levels in Bladder Biopsies Crucial?

Gena Ibrahim, Manal Gabril, Jose Gomez, Madeleine Moussa. London Health Sciences Centre, Western University, London, ON, Canada.
Background: Microscopic examination of the routine three levels from bladder biopsies obtained from flat or papillary lesions identified in cystoscopy occasionally fails to identify a pathological lesion. However abnormalities may be found on additional deeper levels. The objective of this study is to assess the significance of deeper levels in bladder biopsies performed to diagnose papillary or flat lesions after routine levels are non-diagnostic as well as to revise the ideal number of levels which should be routinely examined in bladder biopsies in order to diagnose flat or papillary lesions encountered at cystoscopy.
Design: 82 bladder biopsies performed at our institution (2012-2013) were included in this study. The total number of levels in each case was recorded. The number of additional levels ranged from 3 to 9. The pathological diagnoses from all cases including papillary low grade urothelial carcinoma (PLGUC) or papillary high grade urothelial carcinoma (PHGUC) and urothelial carcinoma in situ (CIS) were correlated with the cystoscopic findings and with the additional deeper levels in order to reach a definite diagnosis. Each case had three standard levels (4 µm in thickness); according to our Laboratory Protocols (50 microns trimmed off the block before the next level).
Results: 31/82 (37.8%) cases required additional tissue levels (the number of additional levels ranged from 3 to 9). 21/31 (67.74%) of these cases were positive for malignancy including low or high grade papillary urothelial carcinoma. 85% of the cases required additional levels were noninvasive papillary UC (mainly low grade UC type) while 14% of the cases were invasive papillary carcinoma into lamina propria only and one case of carcinoma in situ. All of the 21 malignant cases had positive or suspicious cystoscopic findings. 10/31 (32.26%) cases were negative for malignancy and had negative or suspicious cystoscopic findings.
Conclusions: In our study the initial three levels were non-diagnostic of approximately 37.8% (31/82) of the cases. 67.74% (21/31) of these cases had urothelial carcinoma which correlated with positive or suspicious cystoscopic findings. Based on these data, we realize that additional deeper levels are often essential in establishing an accurate diagnosis and therefore we suggest that the recommendation for the appropriate number of levels in bladder biopsies should be revised. Also an increase in the number of the initial levels should be reconsidered not only for accurate diagnosis but also to avoid tissue loss on re-cutting extra levels.

2011 Quality Assessment Policy for HER2 Testing in Breast Cancer By Monitoring of Positivity Rates: From Quality Control To Epidemiologic Data in Spanish Centers

Mar Iglesias, Josep Maria Corominas, Federico Rojo, Lydia Sanchez, Juan Francisco Garcia, Antonio Martinez, Jesus Sola. Hospital del Mar, Barcelona, Spain; Fundacion Jimenez Diaz, Madrid, Spain; Spanish Society of Pathology, Madrid, Spain; Roche, Madrid, Spain; Hospital Clínic i Provincial, Barcelona, Spain; Hospital de San Pedro, Logroño, Spain.
Background: The human epidermal growth factor receptor 2 (*HER2*) is amplified and/or overexpressed in 15% to 20% of primary breast cancers. Interlaboratory variability in HER2 testing is a challenge for targeted therapy in these patients. Assessment of positivity rates among laboratories, combined with regular external quality control strategies, provides a powerful tool to monitor their performance and define reference values for positivity rates in a geographic region.
Design: From January 2013 to September 2014, pathologists that determine HER2 are enrolled in a National Confirma HER2 central website. HER2 status is assessed by immunohistochemistry and/or *in situ* hybridization methods in breast cancer patients. Type of assays, HER2 evaluation criteria and HER2 status data are collected from each participant. Clinical data, including age, primary or metastatic disease and HER2 results are registered in a weekly or monthly basis. The overall positivity rate of each individual participant was calculated and compared with the average rates of all other institutions. Differences between institutions were analyzed by using the **c**2 test.
Results: A total of 19,524 breast cancer cases from 98 institutions were registered. The global mean proportion of positive cases was 17.16% (range: 9.5 to 32.5%). In metastatic cases, the HER2 average was 21.2%, while in non-metastatic cases was 16.9%.
A total of 14 institutions (14.3%) were significantly out of range ($p<0.05$). These outlier institutions were related to poor results in external quality control program or to be referring hospitals in oncology with a large number of advance disease breast cancer patients.
Conclusions: Although regular participation in proficiency testing and the existence of recommendations for HER2 testing significantly improved its performance in individual centers, quality assurance programs might be not sufficient to reduce interlaboratory variation, which became obvious using Confirma HER2 registry. This application allows to define the national rate of HER2 positivity in breast cancer and helps pathologists to be alerted about potential errors in laboratory assays, causative for over- or underestimation of cases suited for anti-HER2 therapy.

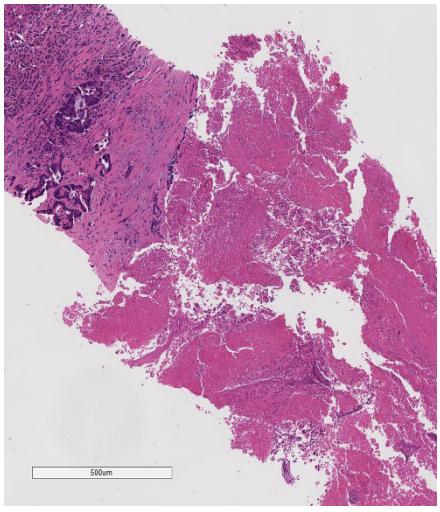
2012 Impact of Tumor Necrosis on Success of Clinical Next Generation Sequencing

Kausar Jabbar, Mark Routbort, Charanjeet Singh, Asif Rashid, Russell Broaddus. University of Texas MD Anderson Cancer Center, Houston, TX.

Background: Analysis of degraded DNA is a challenge in clinical molecular diagnostics laboratories. New methods such as next generation sequencing (NGS), which has the capability of analyzing multiple genes at the same time with little input material, requires a need for high quality formalin fixed paraffin embedded (FFPE) DNA extracts. Before molecular analysis, for all cases we routinely confirm and map presence of tumor, estimate % tumor, and exclude cases with too much necrosis. For many patients, the only sample available for testing is necrotic. The objective of this study was to examine the impact of tumor necrosis on success of clinical NGS testing.

Design: Colonic adenocarcinoma cases from January –August 2014 for which clinical NGS had been performed were analyzed. The NGS platform employed was a 50 gene hotspot panel. Tumor necrosis was estimated via microscopic examination of an H&E stained slide from the analyzed paraffin block. Tumor necrosis was divided into 3 categories: mild (1-5%; n=64), moderate (>5-20%; n=40) and severe (>20%; n=29).

Results: A total of 139 cases were identified. Six cases were excluded from further analysis because they lacked somatic mutations (3 excluded from mild category; 2 from moderate; 1 from severe), leaving 133 cases (33 biopsies, 100 resections). Tumor percentage ranged from 20-80%, while tumor necrosis varied from 1%-80%. One or more somatic mutations in *KRAS, NRAS, BRAF, APC, TP53, PIK3CA, GNAS, SMAD4, PTEN, FBXW7, CTNNB1, AKT1* or *ERBB4* were identified. The median number of somatic mutations detected (2) was equivalent amongst the 3 different necrosis categories. The number of individual cases with 3 or more mutations was similar comparing the mild necrosis group (45%) to the severe group (41%).



The figure is a representative case in the severe necrosis category (70%) that had more than 2 somatic mutations.

Conclusions: Clinical NGS testing was able to detect somatic mutations independent of % necrosis, up to a maximum of 80% tumor necrosis. This suggests that clinical analysis of tumors with more extensive necrosis may be feasible. This is especially relevant for colorectal adenocarcinoma, as the metastases are frequently associated with extensive necrosis.

2013 Contamination of Immunohistochemical Stains By On-Slide Positive Controls: A Potential Diagnostic Pitfall

Florencia Jalikis, Paul Swanson. University of Washington, Seattle, WA; University of Calgary, Calgary, AB, Canada.

Background: The use of on-slide positive controls in immunohistochemistry (IHC) provides the pathologist immediate and relevant information regarding the quality of the stain. This approach, recommended by the College of American Pathologists Laboratory Accreditation Program (ANP 22550), is an increasingly important part of IHC quality management programs. However, placement of tissue from more than one source on a given slide potentially facilitates the contamination of patient material by small portions of control tissue. Based on anecdotal observations, we postulated that when an actionable IHC result can be based on reactivity in single cells or small cell clusters, the presence of immunoreactive contaminants in or overlaying patient material might be misinterpreted as a true positive result. IHC for cytomegalovirus (CMV) is one such example.

Design: 3 cases were captured prospectively in which CMV IHC stains were contaminated by single immunoreactive cells or small CMV positive clusters, presumably from the morphologically identical on-slide positive control. 2 were from patients with refractory inflammatory bowel disease on immunosuppressive treatment; CMV infection was clinically suspected in each. 1 was from an immunocompetent patient with chronic eosinophilia and dysphagia, and a biopsy with histological changes concerning for viral cytopathic effect. CMV IHC was performed on representative slides that contained both patient tissue and a positive control, using a cocktail of anti-CMV clones (CCH2/DDG9, 1:20; 8B1.2, 1:2000) and polymer-based detection after antigen retrieval.

Results: All cases contained detached CMV immunoreactive cells either on the patient tissue sample (above the plane of section) or loosely admixed with patient material. Detached positive elements were also seen on the slide around or between separately mounted sections of the tissue ribbon. CMV positive elements were not present in or near patient material when IHC was repeated on additional tissue levels.

Conclusions: The contamination of patient material by detached CMV positive cells is uncommon, but raises concerns that the use of on-slide positive controls may eventually result in a false-positive result in a patient suspected of having clinically-relevant CMV infection. However, our cases also emphasize that careful evaluation of the patient material and areas adjacent to tissue, as well as assessment of the apparent plane of focus of IHC positive material, may mitigate this risk.

2014 Successful Implementation of Six Sigma Methodology in Gastrointestinal Pathology Service

Merce Jorda, Brianne Neuburger, Maritza Polania, Richard Melnick, Howard Gitlow, Maria Abreu, Richard Cote, Monica Garcia. University of Miami Miller School of Medicine, Miami, FL; University of Miami, Miami, FL.

Background: Six Sigma management can be defined as the relentless and rigorous pursuit of the reduction of variation in all critical processes to achieve continuous and breakthrough improvements that impact the bottom-line and/or top-line of the organization and increase customer satisfaction. According to The College of American Pathologists (CAP) "report signoffs on routine biopsy cases should be provided in a timely manner". Benchmark data defines "timely matter" to be a turnaround time (TAT) of not more than 2 working days. The current TAT of gastrointestinal (GI) small biopsies originating at the University of Miami Hospital Gastroenterology Clinic is 2.7 working days, which is higher than the industry standard. The aim of this project was to decrease the overall TAT while also improving patient, pathologist and clinician satisfaction.

Design: The project was conducted by a multidisciplinary team including process improvement professionals, utilizing the Six Sigma DMAIC model (Define, Measure, Analyze, Improve and Control). First, the team studied the current state by mapping out processes, interviewing stakeholders, and collecting baseline data. Next, the team identified factors which caused the TAT to be problematic. The team then came up with solutions to mitigate the problematic factors and conducted several pilot tests to optimize the solutions. Finally the team implemented the new process full scale and sustained the changes via documentation and training.

Results: By applying interventions that included modification of the courier shifts, implementation of a third histotechnologist shift, the creation of quick texts for standardized diagnoses and Pathologist sign-out modifications, the TAT improved from a baseline of 2.7 working days to an average of 1.7 working days.

Conclusions: The application of process improvement methodologies, specifically the Six Sigma DMAIC model, to the Histology Laboratory setting helped to decrease the TAT of GI small biopsies from 2.7 working days to 1.7 working days, a 62% TAT reduction. In the opinion of the authors, the structured nature of the Six Sigma DMAIC methodology provides the rigor and discipline needed to create breakthrough process improvements in academic pathology settings.

2015 Screening for Lynch Syndrome in Women With Endometrial Carcinoma Less Than 60: An Informatics-Based Approach

Mark Kilgore, Carrie McIlwain, Rodney Schmidt, Barbara Norquist, Elizabeth Swisher, Rochelle Garcia, Mara Rendi. University of Washington, Seattle, WA.

Background: Endometrial carcinoma (EC) is the most common extracolonic malignant neoplasm associated with Lynch syndrome. Lynch is caused by autosomal dominant germ-line mutations in DNA mismatch repair genes. Screening for Lynch in EC is often evaluated by loss of immunohistochemical (IHC) expression of DNA mismatch repair enzymes MLH1, MSH2, MSH6, and PMS2. In July 2013, our clinicians asked that we screen all EC in patients (pts) ≤60. Despite this policy, several cases were not screened, or screening was delayed. We implemented an informatics-based approach to ensure that all women who met criteria would have timely screening.

Design: Reports are created in PowerPath (Sunquest Information Systems, Tucson, AZ) with custom synoptic templates. We implemented an algorithm 3/6/14 requiring pathologists to address Lynch IHC in pts ≤60 with EC prior to sign out (S/O). Pathologists must answer these questions: Is pt ≤60 (yes/no), if yes, follow-up questions (IHC done previously, ordered with addendum to follow, results included in report, N/A, or not ordered), if not ordered, one must explain. We analyzed cases from 7/18/13-9/16/14 pre-implementation (PreImp) and post-implementation (PostImp) that met criteria.

Results: There were 56 pts who met criteria (30 PreImp and 26 PostImp). IHC was ordered in a more complete and timely fashion PostImp than PreImp. PreImp, 4/30 (13.3%) cases did not get any IHC, but PostImp, no cases were missed. Of cases with IHC ordered, 61.5% (16/26) were ordered before or at S/O PreImp vs. 92.3% (24/26) PostImp (p=0.019). Relative to day of S/O, the mean days of order delay was longer PreImp vs. PostImp (12.4±39.9 vs. -0.654±1.26; p=0.074), with the average being before S/O PostImp.

Conclusions: This algorithm ensures Lynch IHC ordering in women ≤60 with EC, and can be applied to similar scenarios. Ancillary tests for management are increasing, especially genetic and molecular-based methods. The burden of managing orders and results remains with the pathologist, and relying on human intervention alone is ineffective. Ordering IHC before or at S/O prevents oversight and the additional work of retrospective ordering and reporting.

2016 Intraoperative Frozen Section of Margins in Head and Neck Cancer: The Surgeon Factor

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Background: Intraoperative frozen section (FS) analysis of surgical margins is a common practice in head and neck (H&N) cancer surgery. Although much is written about the accuracy of the technique, there is still no consensus about its impact on the outcome of H&N cancer. Similarly, there are no standard surgical protocols for submission of tissue for FS evaluation of margins. *(Black C, et al. Cancer. 2006)*. In addition to the effect on length of anesthesia and OR time, multiple FSs are associated with increased cost as well as with a high cost-benefit ratio *(DiNardo L J, et al. Laryngoscope. 2000)*. In this study we reviewed the number of frozen sections requested by our H&N surgeons in relation to the stage of tumors and the clinical outcomes.

Design: The pathology report and clinical information of all patients who underwent surgery for squamous cell carcinoma (SCC) of H&N were reviewed. The total and average number of frozen sections per surgeon in relation to tumor stage and clinical outcomes were recorded. Statistical analysis was used to compare the average number of FS requests per surgeon (Kruskal-Wallis) and to assess the relationship of FS with clinical outcome (Wilcox).

Results: The patient cohort consisted of 255 patients with SCC of H&N, of which 183 had complete clinical follow-ups, with an average of 39 months. The number of frozen sections of margins requested by our group of H&N surgeons ranged between 2 and 35 (mean 12.0; median 12.8). The mean FS requests however, varied considerably among surgeons and ranged from 6.9 to 15.8 per case ($p<0.0001$). This average did not change with tumor stage or nodal status ($p=0.08$). Similarly, the mean FS requests per surgeon did not differ significantly in cases with locoregional recurrence and those without it (13.6 vs 12.6 FS; $p=0.412$), as well as with "death with disease" and "alive without disease" groups (13.6 vs 12.1; $p=0.098$).

Conclusions: The total and average number of FS requests for SCC of the H&N in our institution was highly associated with the performing surgeon. The preference in number of FS was not related to tumor stage, nodal status or patients' clinical outcome. In the current era of decreasing health care expenditure along with efforts to improve the quality of patient care, the results of this study call for a revisit of surgical protocols for FS of margins in H&N cancer, hopefully with active participation of pathologists.

2017 Liver Specimens Containing Yttrium-90 Microspheres: Is Radioactive Contamination Preventable?

Murli Krishna, Khela Pursell, Kevin Nelson. Mayo Clinic Florida, Jacksonville, FL.

Background: Transarterial radioembolization (RE) with Yttrium-90 microspheres ((90)Y) is selectively used for treatment of primary and metastatic hepatic malignancies. Treatment response may lead to transplantation or partial hepatectomy. TheraSphere and SIR-sphere are 2 available delivery systems. Stringent monitoring of resected livers containing (90)Y is essential in preventing contamination.

Design: This study reviewed the effectiveness of a Radiation Safety Protocol (RSP) for processing of resected liver specimens containing (90)Y. Study population was patients treated with (90)Y who had subsequent liver resection. Patients were identified from clinical, pathologic and radiation safety databases at our institution. Records were reviewed for radioactivity at each stage of tissue processing from specimen receipt to production of H&E slides. All radioactive tissues were processed in a contained environment. 2 radiation detectors were used: Model 44-3 for initial screening and Model 44-9 for detection of contamination (Ludlum Measurements, Inc., Sweetwater TX).

Results: 15 patients received (90)Y RE between 1/2008 and 9/2014 with subsequent resection of liver (11M, 4F, ages 17-81yrs). Tumors included HCC (9), cholangioca (1), met. NE ca (3), met. colon ca (1) and donor-derived small cell ca (1). Delivery system was known for 14 patients (7 TheraSphere; 7 SIR-Sphere). 4 patients received more than one (90)Y treatments. Resections were performed 3.8 - 27mo after treatment (Therasphere 6.2-11.1mo; SIR-sphere 3.8-27mo), and included 8 explanted livers (7 native, 1 allograft), and 7 partial hepatectomies. All Therasphere-treated livers were radioactive upon receipt in lab; after RSP processing (upto 1wk) sections from 4 of these were radioactive in the histology lab. All 4 were treated 6.2 -7.6mo prior to surgery. No contamination was detected in the lab after processing was completed. All SIR-sphere treated livers were non-radioactive upon receipt in the lab.

Conclusions: 1) Resected livers previously embolized with (90)Y may show detectable radioactivity. 2) Radioactivity is associated with TheraSphere treatment and a shorter duration between treatment and surgery. 3) Processing of (90)Y treated liver specimens under stringent RSP prevents contamination. 4) To our knowledge, this is the first report of protocol-based monitoring for liver specimens treated with (90)Y RE.

2018 Pap Test Utilization Trends in the Era of Changing Cervical Cancer Screening Guidelines: A Community Outreach Laboratory Experience

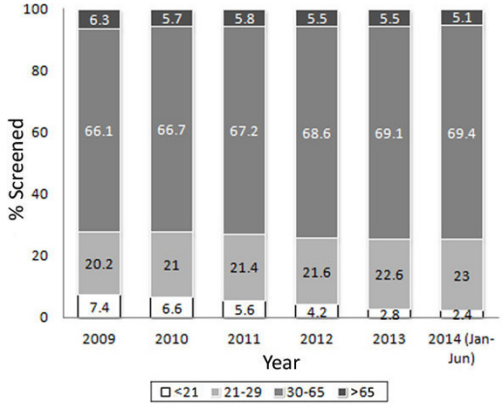
Asangi Kumarapeli, Rachel Gullatta, Cherie Hart-Spicer. Summa Barberton Hospital, Barberton, OH.

Background: Cervical cancer screening guidelines in the US have evolved steadily over the past decade owing to better understanding of the pathobiology of disease as well as the introduction of high-risk human papilloma virus (HR-HPV) "cotesting" and HPV vaccination. Adherence to 2012 American Society for Colposcopy and Cervical Pathology (ASCCP) recommendations, especially among community practitioners, is not well evaluated.

Design: We reviewed the cervical cytology data from January 1, 2009 to June 30, 2014, and age-specific screening coverage trends were examined. To minimize the impact of Pap test volume fluctuations due to such variables like competing laboratories and addition/withdrawal of clients, we also separately analyzed the screening trends in 3 stable clinical practice groups. Pap test results for 2013 were also studied in the <21 year old and >65 year old populations based on the 2001 Bethesda System classification.

Results: Our laboratory processed 196,060 Pap tests during the study period with the highest volume (45,284) in 2009 and a 36% decline in volume by end of 2013. The most significant Pap test utilization change was observed in women <21 years with a 60% reduction in screening from 2009-2014. Modest screening increases (13% and 5%, respectively) were seen in 21-29 and 30-65 age groups and 19% decrease was seen in >65 group.

Figure 1. Pap Test Utilization by Age Group



These trends were comparable in the 3 separately studied clinical practices with one group showing nearly 90% reduction in their screening of women <21 years. While the majority (85%) of Pap test results were negative, most abnormalities were observed in younger women; in 2013, low-grade cytological abnormalities (ASC-US + LSIL) were reported in 20% of women <21 years screened compared to 4.5% of women >65 years.

Conclusions: Our study demonstrates the awareness among community health providers of the 2012 ASCCP cervical cancer screening recommendations. The adherence to guidelines was best reflected in the <21 age group with significant reduction in the use of Pap tests.

2019 Evaluation of Intraoperative Frozen Section Discrepancies for Pancreatic Resections

Katherine Levinson, Stuti Shroff. University of Pennsylvania, Philadelphia, PA.

Background: Positive resection margins in pancreatic adenocarcinoma (PA) and intraductal papillary mucinous neoplasms of the pancreas (IPMN) are associated with increased morbidity and mortality. Consequently, evaluation of pancreatic neck margins and bile duct margins for pancreaticoduodenectomy specimens and proximal pancreatic margin for distal pancreatectomy specimens are routinely performed as intraoperative consultation (IOC) to determine extent of surgery. With the advent of neoadjuvant therapy, IOC of these specimens is becoming increasingly difficult. Additionally, there are several confounding factors such as preoperative biliary stent placement that may make intraoperative interpretation of these specimens challenging. We evaluated pancreatectomy specimens to determine the variables associated with erroneus interpretation and identify methods to decrease discrepancies for margin assessment during IOC.

Design: 112 consecutive pancreatectomy specimens received at the Hospital of the University of Pennsylvania over the course of one year (2013-2014) were reviewed. The following variables were studied: patient age/gender, histologic diagnosis and location of tumor, presence of pre-operative biliary stent placement, neoadjuvant therapy, and evaluation of margins by general surgical pathologists versus gastrointestinal pathologists.

Results: Our study group consisted of 76 patients who underwent a pancreaticoduodenectomy and 36 patients who underwent a distal pancreatic resection. The most frequent diagnoses were 42-pancreatic adenocarcinoma (38%), 15-pancreatic endocrine neoplasms (14%), 13-pancreatic intraductal papillary mucinous neoplasms (12%) and 14-ampullary and duodenal neoplasia (13%). Intraoperative frozen section consultation was performed for 80 cases. Thirteen (11.6%) of these cases had discrepant IOC reporting at one margin (eight at pancreatic resection margin and five at bile duct margin). Of these, nine cases had interpretive errors and four were due to confounding factors (such as neoadjuvant therapy, 1, and evaluation of the bile duct margin post stent placement, 3). Ten (8.9%) discrepant cases were evaluated by general surgical pathologists at IOC and three (2.7%) evaluated by gastrointestinal pathologists.

Conclusions: Our analysis suggests errors in IOC for pancreatectomy specimens can be avoided by obtaining history regarding neoadjuvant therapy and biliary stent placement. Errors in interpretation may also be decreased by consulting a gastrointestinal pathologist for challenging cases.

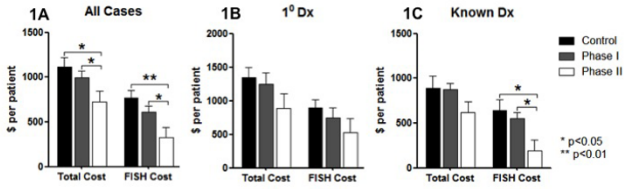
2020 Improving the Cost-Effectiveness of Specialized Testing for Bone Marrow Biopsies Using a Collaborative Algorithm-Based Approach

Wei Liu, Jennifer Ford, Julianne Qualtieri. University of Cincinnati College of Medicine, Cincinnati, OH.

Background: We have noticed a trend of inappropriate uses of specialized testing for hematological disorders although the clinicians are typically responsible for the ordering at the time of bone marrow biopsies. Hematopathologists have an opportunity to minimize inappropriate tests from being ordered by previewing available smears. It is warranted to establish a testing algorithm in conjunction with hematologists/oncologists with a goal of improving the cost-effectiveness.

Design: This project was divided into two phases. In phase I hematopathologists reviewed preliminary data and revised the specialized testing requests placed by clinicians. This phase lasted 7 months from November 2013 to May 2014 with a goal of establishing potential cost benefit and drafting a working algorithm. Phase II started in June 2014 with hematopathologists ordering specialized tests based on review of available blood and marrow films and clinical information. The month of June 2013 is used as pre-phase control for statistical analysis (t test), $p<0.05$ considered significant.

Results:



The average total costs per case, including molecular testing, FISH and chromosomal analysis, significantly decreased from $1112 of the pre-phase month to $1000 of the phase I and $727 of the phase II (Fig. 1A). More dramatic cost savings were observed in the FISH tests with more than 50% reduction from pre-phase ($728) to phase II ($326). Between patients with unknown (Fig. 1B) and known (Fig. 1C) diagnoses, there were more prominent decreases in the latter-mentioned patient population with $621 for total and $189 for FISH costs in phase II in comparison to $893 and $641 respectively in the pre-phase month. Given an estimated annual bone marrow volume of 400, the annual savings are estimated at $ 160,000.

Conclusions: Hematopathologist-driven specialized test ordering with an algorithm-based system is a practical approach to optimize cost-effectiveness. Further assessment of quality and clinical satisfaction is necessitated to validate our approach.

2021 Application of the Clinical and Laboratory Standards Institute EP23-A To Anatomic Pathology

Megan Lockyer, Daniel Grimmer. Baylor College of Medicine, Houston, TX.

Background: As laboratory technology has become increasingly automated with system programs capable of assessing the results of a particular analyte for deviations from the mean and alarming when an outlying result is obtained, so too has quality control developed from a procedure for monitoring measuring system stability to a program of risk management. In the Clinical and Laboratory Standards Institute document EP23-A, the development of a risk management-based quality control program is outlined based on risk management procedures used and proven in industries for years. We applied the model described in EP23-A to create a risk-based quality control program for anatomic pathology.

Design: We began by gathering information to create a process flow chart beginning with the acquisition of the specimen and ending with the final report being signed out. Once a complete process chart was established, we analyzed every step for possible failure modes. For each failure mode, we determined what possible impact it may have on the ultimate goal of correct specimen, correct patient and correct diagnosis. We then stratified the failure modes into low risk, intermediate risk and high risk depending on their impact. Once we identified all possible failure modes, we developed mitigations for the respective risks. The mitigations varied from education of housestaff to procurement of an automated barcode scanner system. We also outlined actions to be taken should a particular failure mode take place. Finally, we designed a dashboard for following errors with each error categorized based on the main components of our process. These included, but are not limited to, patient and/or specimen mislabeling, slide processing and turnaround time.

Results: The comprehensive dashboard now serves as quality review at weekly departmental meetings and monthly interdepartmental meetings. It has allowed us to better evaluate when errors occur, why an error occurred and how we may decrease the liklihood of an error occurring again. Furthermore, the mitigations we developed have served to decrease errors in our laboratory.

Conclusions: Risk-based quality control programs have been used in industries for years, and have been shown to be extremely effective. Following the same principles, EP23-A outlines how to create a laboratory quality control program based on risk management. We applied EP23-A to anatomic pathology, and created a quality control plan specific to our department allowing for continued identification, evaluation and mitigation of errors.

2022 Cytologic Diagnosis By Fine Needle Aspiration: A Retrospective Quality Assurance Study Comparing Diagnoses of Cytotechnologists VersusPathologists

Brett Lowenthal, Xiaoyan Liao, Crystal Teschendorf, Farnaz Hasteh. University of California San Diego Medical Center, San Diego, CA.

Background: Fine needle aspiration (FNA) is a diagnostic procedure used to investigate mass lesions either superficially or deep with the aid of endoscopy, ultrasound, or CT scan. Cytotechnologists screen all FNA cases and render a preliminary diagnosis. This study retrospectively compares the diagnoses made by cytotechnologist and pathologist, as well as any available concurrent or follow-up biopsy or excision diagnosis.

Design: All organ-specific FNAs performed at our institution from January 1, 2013 to March 31, 2013 were reviewed for diagnosis from cytotechnologist, cytopathologist and the available follow-up histologic diagnosis. A total of 232 FNA cytology cases were collected, among which 90 cases were satisfactory with follow-up histology. Each case was categorized as a benign, malignant, or inflammatory process for statistical analysis.

Results: Of the 90 cases, cytotechnologists misdiagnosed 25 cases (28%), while pathologists misdiagnosed 16 cases (18%). Among all the missed cases, the lung/trachea organ was the most frequently misdiagnosed organ system by cytotechnologists (5 cases changed to inflammatory process, 2 cases changed to malignancy, and 1 changed to benign/reactive changes. This was followed by pancreas, thyroid, and head/neck. In contrast, thyroid is the most frequently misdiagnosed organ by pathologists with 7 under-called malignancy. This was followed by lung and head/neck. It appears that malignancy was the most common and equally under-called category by pathologists and cytotechnologists. Furthermore, cytotechnologists more frequently over-called or did not recognize granulomatous inflammation as compared to pathologists (p=0.0406). These were missed in 7 of 8 cases (88%) by cytotechnologists, where the pathologist missed 2 of 8 cases (25%).

	Number of Cases	Misdiagnosed by Cytotechnologist	Misdiagnosed by Pathologist	p-value
Benign	9	3	1	not significant
Inflammatory	8	7	2	0.0406
Malignant	73	15	13	not significant
Total Cases	90	25	16	----------

Conclusions: Overall, our institution demonstrates accurate FNA diagnoses with both pathologists and cytotechnologists. However, inflammatory processes, especially in the lung, remain a challenge for cytotechnologists. Inflammatory processes tend to be over-called as neoplasm or not recognized as granulomatous inflammation. Continued education and regular quality assurance conferences is important to maintain diagnostic precision.

2023 Retrospective Review of Cervical Excision at a Single Institution: A Quality Assurance Study

Zheng Ma, Eric Huang. UC Davis Medical Center, Sacramento, CA.

Background: Patients with high grade squamous intraepithelial lesion (HSIL) or cervical intraepithelial neoplasia (CIN) 2 or 3 are often treated with loop electrosurgical excision procedure (LEEP). However, a small number of LEEP fails to confirm the HSIL diagnosis. This study aims to re-review the non-HSIL LEEP specimens and determine if additional means can reduce the number of non-HSIL LEEP.

Design: An institutional retrospective review of all LEEP specimens from 2011-2012 by Pathology Laboratory Information System identified 166 cases. The clinical information and pathology material were gathered. Pathology slides for cases with non-HSIL LEEP follow by HSIL diagnosis were re-reviewed by a subspecialty trained gynecologic pathologist.

Results: Of the 166 identified LEEP cases, 102 cases with HSIL diagnosis preceded LEEP were included in the study. Of these, LEEP confirmed 73 cases (71.6%) of HSIL while low grade or no SIL was found in 29 cases (28.4%). Re-review of the pathology material from the discrepant cases revealed that HSIL is reconfirmed in 18 cases (62.1%) while 11 cases (37.9%) were reclassified as non-HSIL. In the 11 reclassified cases, the original diagnoses included CIN2 (9 cases; 81.8%) and CIN3 (2 cases; 18.2%).

Conclusions: Correlation between pre-LEEP and LEEP specimens is an important quality assurance exercise for cervical excisions, similar to cytologic-histologic correlation required by CLIA 88. In the present study, majority of the discrepant cases had an initial diagnosis of CIN2, confirming the poorly reproducibility of this diagnosis. Given the complications associated with LEEP, particularly cervical incompetence in future pregnancy, supporting immunohistochemistry or concurrence by another pathologist should be considered prior to a diagnosis of CIN2.

2024 Intratumoural HER2/neu Heterogeneity in Invasive Breast Carcinoma: A Needle in the Haystack?

Sarah Mahon, Akke Vellinga, Margaret Sheehan. Galway University Hospital, Galway, Ireland; National University of Ireland, Galway, Ireland.

Background: Intratumoural HER2 heterogeneity has differing frequencies amongst the subtypes of breast cancer. The new ASCO/CAP recommendations for HER 2 reporting allow for greater heterogeneity. Local constrainsts at our institution required that needle core biopsies (NCB) had 48 hours formulin fixation. Our study assessed whether prolonged fixation can compromise NCB HER2 assessment and whether the results are impacted by tumoural heterogeneity.

Design: We prospectively analysed HER 2 expresssion in 163 invasive breast carcinomas, both the NCB and the paired excision specimen. Each was scored

independently by two pathologists and scoring of the excision was blinded to the NCB result(SM, MS). A 2+ score from either pathologist initiated a FISH test. Kappa values were calculated to determine the concordance between these results.

Results: Her2 immunohistochemistry(IHC) scoring categories using the original guidelines showed moderate agreement k=0.561(95% CI 0.383-0.649, P<0.001). When FISH analysis was added and final outcome was either positive (3+ IHC and/or FISH amplified) or negative the discordant cases fell to 5 (3.1% of all cases).[SeeTable 1]

Case	NCB			Resection			Comment
	IHC	FISH (Ratio)	FISH (Copy number)	IHC	FISH (Ratio)	FISH (Copy number)	
1	1+			Focal 3+			True hetero-geneity
2	3+			1+			True hetero-geneity
3	2+	2.28 (Amplified)	5.8	1+	2.61 (Amplified)	7.6	Low copy number
4	2+	2.99 (Amplified)	4.4	1+	2.45 (Amplified)	3.7	Low copy number
5	2+	2.07 (Amplified)	5	1+	1.36 (non-amplified)	2.73	Low copy number

[Table 1] FISH *HER2:CEP17 RATIO*, 60 cells counted

Of the 5 discordant cases 2 of these represent true HER2 heterogeneity. The other 3 discordant cases demonstrated gene amplification in the low/equivocal range and raise questions about polysomy. Interestingly when the new ASCO recommendations were applied to case 4 and 5 it was found that the biospy would now score as positive.

Conclusions: Our study demonstrates good concordance rates for HER2 positivity for resection specimens and NCBs with up to 48 hour fixation. Our findings also demonstrate that tumoural heterogeneity can impact on accurate HER 2 assessment. However, the new ASCO/CAP recommendations allow for this and may prevent unnecessary FISH analysis. In addition prolonged fixation as allowed for in the new guidelines demonstrates good concordance.

2025 The Use of a National Quality Assurance Intelligence System (NQAIS) To Audit Addendum Reports

Sarah Mahon, Brianan McGovern, Niall Swan. St. Vincent's University Hospital, Dublin, Ireland.

Background: Quality Assurance (QA) in Histopathology aims to continuously assure and enhance patient safety. The Irish National Quality Assurance Programme was launched in 2010 with the development of the National Quality Assurance Intelligence System (NQAIS), for storage, analysis and QA report generation. Continuous review of addendum reports is one of the eleven monitors recommended by the National QA Programme Guidelines.

Design: This study was designed to:

1. Evaluate the categorisation of addendum reports over a one year (2013) period.
2. Compare the addendum report rates to the prior year (re-audit).
3. Calculate the percentage of amended reports arising from Multi-disciplinary Team (MDT) meeting discussion.
4. Estimate the departmental defect rate.

All cases coded as corrected, amended and supplementary were extracted from the NQAIS system for 2013. All corrected and amended reports and 571 consecutive supplementary reports (27% of total) were reviewed and the results were compared with the prior 2012 audit performed.

Results: The addendum report rate for 2013 was 7.3% (24 amended, 116 corrected, 1895 supplementary reports). 20.7% (24/116) of corrected reports were re-categorised as amended and 2.8% (16/571) of supplementary reports were re-categorised as amended with 1.7% (10/571) re-categorised as corrected. This translates to a predicted departmental defect rate of 8.6/1000 cases and compares to a defect rate of 5.1/1000 cases for the previous year. The major defect rate (amended reports) was 4.1/1000 cases and the minor defect rate (corrected reports) 4.5/1000 cases. MDT discussion was the initiating factor in 66% (46/70) of amended reports issued (figure calculated post review of addendum reports).

Conclusions: Continuous review of addendum reports is an important quality improvement monitor and should include review of all supplementary, corrected and amended reports to improve accurate categorisation and estimation of a departmental defect rate. The importance of peer review related to MDT discussion is also highlighted.

2026 Cost-Effective Approach To the Diagnostic Workup of Lymphoproliferative Disorders Via Optimal Integration of Flow Cytometric Data

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Background: The diagnostic workup of lymphoproliferative disorders (LPDs) involves the combined use of flow cytometry (FC) and immunohistochemistry (IHC). This approach often results in duplicate testing, particularly in the academic setting, where trainees may independently order IHC, and adds costs that may not be eligible for reimbursement based on the Medicare National Correct Coding Initiative. We aimed to establish a cost-effective diagnostic algorithm based on initial FC categorization to eliminate duplicate IHC marker usage.

Design: We retrospectively reviewed 242 cases of suspected LPDs with concurrent FC and IHC testing over a 12-month period. We correlated FC with surgical diagnoses and evaluated the frequency of repeat IHC testing on concordant cases.

Results: The most frequently repeated markers were CD3, CD5, CD10 and CD20 (Table 1). Of concordant B-cell malignancies, 60% represented recurrent disease; however, this resulted in significantly fewer IHC stains only for cases of CLL (3.1 *vs.* 7 stains; p=0.04) despite accurate FC classification. FC did not reliably diagnose diffuse large B-cell lymphoma (n=50; 48% concordant).

Table 1. Correlation between FC and surgical diagnoses and duplicate marker usage.

		Concordant cases				
Tissue Diagnosis (n)	Concordant by FC (%)	Average number of IHC stains	Cases with stains repeated on IHC (%)			
			CD5	CD10	CD20	CD3
Benign (85)	84 (99)	4	14 (17)	10 (12)	49 (58)	50 (60)
Atypical (8)	8 (100)	12	7 (88)	8 (100)	7 (88)	7 (88)
Chronic lymphocytic leukemia (14)	13 (93)	4	9 (70)	n/a	5 (38)	9 (69)
Mantle cell lymphoma (2)	2 (100)	7	2 (100)	n/a	1 (50)	2 (100)
Follicular lymphoma (35)	30 (86)	8	n/a	27 (90)	25 (83)	27 (90)
Low-grade B-cell LPD (13)	11 (85)	8	4 (36)	3 (27)	11 (100)	7 (64)
Large B-cell (53)	25 (47)	9	15 (60)	18 (72)	20 (80)	21 (84)
T-cell LPD (12)	7 (58)	11	6 (86)	n/a	6 (86)	7 (100)

Conclusions: We propose that, in de novo concordant cases, CD5 and CD10 should not be repeated by IHC; this would decrease use of these two commonly repeated IHC markers by an average of 79%. Furthermore, in recurrent cases, elimination of duplicate usage of CD3 and CD20 in addition to CD5 and CD10 would reduce IHC-associated costs by an average of 61%. Finally, we show that FC reliably characterizes benign entities and, when considered along with morphology, may constitute a sufficient immunophenotypic work-up for such cases.

2027 Reprioritizing the Surgical Pathology Workflow of Cases: Decreasing Large Surgical Pathology Specimen Turnaround Time in an Academic Medical Center

Gagan Mathur, Michael Gailey, Melissa Jans, Kent Becker, Emily Fuller, Patricia Kirby, Nitin Karandikar, Robert Robinson. University of Iowa, Iowa City, IA.

Background: Turnaround time (TAT) is an important metric for pathology laboratories as it pushes the system to provide services in a time that is as optimal as possible for patient care. In our institution, the time of signout of complex surgical cases of malignant neoplasms historically was relegated to the last cases processed by the histology laboratory. In recent years, the emergence of multidisciplinary tumor boards where oncologic patient management is decided is commonplace and pathology evaluation of the patient's specimen is a cornerstone. Making the pathology report of these large and complex cases available as soon as possible speeds management decisions.

Design: In an effort to improve TAT for large cases that would be presented in weekly multidisciplinary oncology planning conference tumor boards. We re-prioritized the order of cases coming out of the histology laboratory. We maintained as first priority biopsy specimens that were requested to be emergent by the clinician or cases in which a tumor was biopsied. Subsequently, surgical oncologic cases were available. Following these cases, biopsies judged less urgent were cut and stained. To evaluate the change in TAT (time from specimen accessioning to reporting of results), we compared the TAT data based on CPT codes of 88307 and/or 88309 extracted from laboratory information system (Cerner, Kansas City, MO) for the 6 months period (Jan-June 2014) after implementation of changes with TAT data from 11 months prior to changes (Jan-Nov 2013). The analysis was performed in Microsoft Access and Excel 2013 (Microsoft, Redmond, WA).

Results: The average TAT for 2388 large cases from first half of 2014 (Jan-June) improved to 3.40 days (95% CI 3.30-3.50 days) as compared to a TAT of 3.98 days (95% CI 3.86-4.11 days) for 4748 large specimens in 2013 (Jan-Nov). The absolute TAT for large specimens decreased by 15% (p-value <0.01). Counting days, the decrease was 0.58 days. Cases requiring immunohistochemical staining or additional submission of histology blocks was much more easily accomplished on all large cases as these activities were performed much earlier in the work day. Handling complex cases earlier also resulted in increased resident and faculty satisfaction.

Conclusions: Rearranging the priority of surgical cases such that large tumor resection cases are entered into the workflow earlier has resulted in decreased TAT for these cases, allowing more cases to be presented at weekly tumor boards and has increased satisfaction amongst pathologists.

2028 Expectation-Interpretation Mismatch: Lack of Standard Definitions for Histology Lab Terms and Resulting Implications for Workflow and Patient Care

Whitney McCarthy, Jason Moss. Baylor College of Medicine, Houston, TX.

Background: Pathologists (PTs) requesting additional H&E-stained slides often use terms such as *recut*, *level*, and *deeper*, which must be interpreted by histotechnologists (HTs). Our prior single institution survey regarding usage of these terms showed marked disagreement between and among PTs and HTs, potentially increasing PT turn-around time and HT workload, and raising the possibility of unsampled lesions in the block. To gain further insight into this issue, a survey was distributed to PTs and HTs at several of our affiliated institutions.

Design: A survey with twelve open-ended questions (e.g., tissue section thickness, number of sections discarded between slides, definitions for *recut*, *level*, and *deeper*) was distributed to 50 PTs and 32 HTs at five affiliated institutions.

Results: 1. Survey response rate: 78% PTs, 69% HTs

2. Average section thickness (by institution #s 1-5):
PTs: 3.9 mm, 4.1 mm, 5.2 mm, 4.3 mm, 4.5 mm
HTs: 3.2 mm, 5.0 mm, 3.7 mm, 3.7 mm, 3.8 mm

3. Average number of sections discarded between *levels* (by institution #s 1-5):
PTs: 3.4, 2.0, 4.6, 7.7, 5.5
HTs: 3.7, 6.0, 2.0, 1.3, 4.2

4. Average number of sections discarded between *deepers* (by institution #s 1-5):
PTs: 6.0, 7.5, 8.3, 11.7, 6.5
HTs: 7.3, 15.0, 4.0, 2.5, 9.7.

Conclusions: 1. This multi-institution study reinforces the findings of our prior single institution study, which found PTs and HTs have a marked disagreement in their definitions of *recut*, *level*, and *deeper*.

2. Non-standardized definitions for these terms may lead to an expectation-interpretation mismatch between PTs and HTs, resulting in:

a. Repeat requests for additional sections and increased HT workload/PT turn-around time.

b. Tissue sampling that is inadequate or inappropriately deep (Fig. 1).

3. Rather than using qualitative, subjective definitions for these terms, quantitative standards should be developed. Further investigation and communication between PT and HT professional organizations will be needed to reach a consensus.

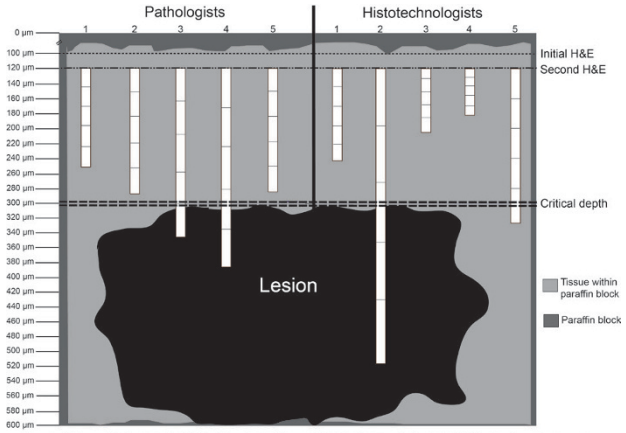


Figure 1. Theoretical scenario: Initial slides from this paraffin block suggested an underlying malignant process; five deeper sections were ordered. The horizontal black bars within the vertical white bars represent the depths at which deeper sections would be cut, per institution (avg. # sections discarded x avg. section thickness). Lesional tissue would only be obtained a fraction of the time (2/5 for PTs, 2/5 for HTs).

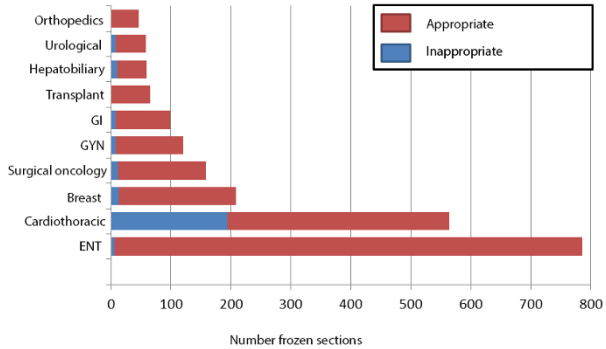
2029 Frozen Section: Guiding the Hands of Surgeons?

Eleanor McIntosh, Joseph Drwiega, Margaret Brandwein-Gensler, Shuko Harada, Jennifer Gordetsky. University of Alabama, Birmingham, AL.

Background: Intraoperative frozen section (FS) analysis is a powerful tool that can provide a rapid diagnosis, thereby directing operative management. However, FS can also be misused. We consider a FS to be "inappropriate" when it does not influence operative management. One example is sending a FS to allow the surgeon to provide reassurance, or convey an early diagnosis to the patient or family. Inherent in this action is a failure to acknowledge the limitations of a "preliminary diagnoses". Not only can inappropriate FS compromise limited diagnostic material, they can impact turn-around-time of other appropriate FS submitted simultaneously. The objective of our study was to evaluate the utilization of FS at our institution and assess influence on operative management.

Design: Our pathology database was searched from December - June of 2013 for FS cases, which were then stratified by surgical subspecialty. Operative, clinical, and pathology notes were reviewed to determine the rationale for sending each FS and to determine its impact on operative management. Cases lacking operative notes were excluded from this study.

Results: 2165 FS were performed in 1057 surgical cases; the average number of FS per case was 2. Surgical subspecialties that utilized FS included cardiothoracic, otolaryngology, breast, surgical oncology, gynecology, gastrointestinal, hepatobiliary, urological, transplant, and orthopedics. 41% of FS evaluated margin status, 35% confirmed or excluded malignancy, 11% were for tumor classification, 6% assessed adequacy for diagnosis, 3% were to confirm or exclude infection, 3% were for transplant, and 2% were for lymphoma workup. We found that 12% (259/2165) of FS did not influence operative management. This was most common among cardiothoracic surgeries (34%). No "inappropriate" FS were sent for any transplant or orthopedic surgeries. ENT utilized the most FS and had <1% that were "inappropriate".



Conclusions: At our institution, the majority of FS influence operative management, with margin assessment being the most common scenario. The rationale for sending a FS and its influence on operative management was highly subspecialty dependent. Interdepartmental discussions on FS utilization might be helpful in the elimination of unnecessary FS.

2030 Delayed Autopsy Reporting – A Self Study and Root Cause Analysis

Stephanie Moss, Caroline Alquist, Robin McGoey. Louisiana State University Health Sciences Center, New Orleans, LA.

Background: The medical autopsy at our teaching institution is a multi-step procedural process aimed at understanding disease processes that contribute to a patient's death. Correlation with ante mortem lab and clinical data is required both prior to and following the procedure. Both gross and microscopic analyses of every organ system are conducted and lab studies such as cultures and toxicology are frequently ordered. The final autopsy protocol averages 7-10 pages and includes documentation of findings from every step in the process. Approximately 180-240 cases are performed per year by the service.

Design: In response to a citation issued by the College of American Pathologists (CAP) regarding delayed autopsy reporting, the autospy service launched a resident-initiated root cause analysis (RCA) and self-study in order to identify the contributing causes for delayed reports and to design workflow efficiencies and process improvements such that turnaround time was monitored, tracked and improved. Focused interviews were conducted with all of the residents, staff and faculty involved with the service. Data on all case turnaround time from 2011-2013 (n=656) was calculated.

Results: The average turnaround time was 80 (2011), 85 (2012), and 89 (2013). The CAP standard requires 90% of cases finalized within 60 working days. Our service completed 22-42% of cases within 60 working days. The focused interviews with residents and faculty clearly identified areas of significant delay. Objective review of data including log books and histology tracking records substantiated some of the perceived areas of delay while clearly refuting others. The incorporation of a monitoring system and elimination of redundancy in workflow processes significantly improved turnaround time of reports. To date, the average turnaround time in 2014 is 36.3 days with 93.3% of cases finalized within 60 working days.

Conclusions: RCA and self-study analyses are effective methods for elucidating both real and perceived barriers to efficiency in the workplace yielding a better understanding of the organizational culture and its openness to change. As a result of the RCA on delayed autopsy reporting, corrective actions were proposed to the CAP and implemented into the autopsy service. The measurable outcome has been better compliance with the autopsy reporting standard and a system in place for tracking turnaround time compliance. Moreover, an added outcome of earlier reporting of autopsy findings will undoubtedly be better quality of care and communication of post mortem findings to the clinical care team.

2031 CAP/ASCO Low HER2 Guidelines 2013 – Immunohistochemistry Quantitation Visually and By Image Cytometry (ACIS) Versus FISH

Charles Myers, Godfrey Guerzon, Diane Lawson, Debra Saxe, Cynthia Cohen. Emory University, Atlanta, GA.

Background: In 2013, a College of American Pathology/American Society of Clinical Oncology (CAP/ASCO) guidelines update was released with respect to interpretation of Human Epidermal Growth Factor Receptor 2 (HER2). Immunohistochemistry (IHC) criteria for determination of an equivocal test were altered from the 2007 guidelines. Previously a 2+ staining pattern on IHC, indicating an equivocal test, was described as complete membrane staining in >10% but <30% of cells. The updated guidelines define a 2+ as incomplete or weak membrane staining in >10% of tumor cells (low 2+) or complete membrane staining in < 10% of cells. These guidelines, however, did not discuss the utility of ACIS, and recommend the utility of FISH in these low 2+ HER2 breast carcinomas. Our goal was to identify the necessity for FISH in those cases with the low 2+ pattern and those stratified by ACIS IHC results.

Design: All breast carcinomas that were rated by visual IHC as incomplete staining in >10% of tumor cells (low 2+ pattern) were collected from February to September 2014. These were analyzed by Automated Cellular Imaging System III (ACIS) (DAKO) and scored as the mean of 6 areas with a 40x objective. Scores of 0.4-1.7 were graded as 0-1+ (not expressed), 1.8-2.6 as 2+ (equivocal), and above 2.6 as 3+ (overexpressed).

FISH for HER2 amplification used the PathVysion HER2 DNA probe kit (Abbott Molecular). Interpretation of the HER2/centromere 17 ratios for the FISH were per the CAP/ASCO guidelines.

Results: A total of 28 cases of low 2+ HER2 were included. Tables 1 and 2 demonstrate the visual and image cytometric scores compared to HER2 FISH, respectively. In 24 (85.7%), visual IHC and FISH results were concordant (negative, non amplified). In 20, ACIS IHC <1.8 and FISH results were 100 % concordant (negative, non amplified). None of the HER2 FISH on the 28 cases was amplified.

Table 1: HER2 Concordance with Visual IHC

Visual IHC	2+ Staining (low 2+) (n=28)
FISH Negative	24
FISH Equivocal	4
Concordance	85.7%

Table 2: HER2 Concordance with ACIS IHC.

ACIS IHC	1.8-2.6 (Equivocal) (n=8)	
FISH Negative	4	20
FISH Equivocal	4	0
Concordance	50%	100%

Conclusions: There is improved concordance between the image cytometric analysis scores <1.8 (negative) and HER2 FISH compared to visual IHC of low 2+ (equivocal) and HER2 FISH, 100% to 85.7%, respectively. The guideline of utilization of HER2 FISH on the low 2+, ACIS negative pattern is questioned as all were FISH non-amplified.

2032 Validation of Breast Biomarker Assays for an Automated Microwave-Assisted Rapid Tissue Processing Method

Houman Nafisi, Corwyn Rowsell, Patrice Boulianne, Guangming Han, Fang-I Lu, Elzbieta Slodkowska, Wedad Hanna, Sharon Nofech-Mozes. Sunnybrook Health Sciences Centre, Toronto, ON, Canada; University of Toronto, Toronto, ON, Canada.

Background: Recommendations to validate any modification in receptor testing in breast cancer have been endorsed by CAP and other regulatory bodies to ensure accurate testing (Fitzgibbon et al 2010). Accordingly, any proposed modification has to be tested against a previously validated technique. For modifications in preanalytical variables this entails creating a validation set of paired samples, consisting of a combination of positive (P), low positive (LP, <10%) and negative (N) cases that have been prepared under the same conditions and differing only with respect to the modified variable. Microwave-assisted rapid tissue processing (MWARTP) significantly reduces tissue processing time. Herein, we report our experience in validation of breast biomarkers using MWARTP with emphasis on challenges to comply with current recomendations.

Design: Over a period of 2 years, 158 breast cancer resection specimens with a grossly identified mass and a diagnosis of invasive breast carcinoma were prospectively selected. At the time of grossing, a tissue core was created and processed by MWARTP(Pathos Delta, Milestone). The remaining blocks from each case were processed by conventional overnight tissue processing (CTP). Ischemic and fixation times were similar. Parallel blocks from each case were placed on the same run on the immunostainer and read by the same pathologist.The set was specifically enriched in HER2 positive cases.

Results: Table 1

Biomarker	Status, CTP	Concordant	Overall agreement(%)
ER (SP1)	P(LP)	130(3)/131(4)	99.2
	N	27/27	100
PgR (1E2)	P(LP)	110(13)/115(17)	95.6
	N	41/42	97.6
HER2 IHC(4B5)	P	24/24	100
	N	972/97	100
HER2 SISH1	Amplified	263/27	96.2
	Non-amplified	34/34	100

[1]silver-enhanced in situ hybridization (SISH INFORM HER2; Ventana)
[2]3 CTP HER2 IHC 1+ were 2+ by MWATP but were not amplified.
[3]Discordant due to intratumoral heterogeneity

Conclusions: The overall concordance between MWATP and CTP is excellent and the former can be safely used for processing of breast specimens. Archival material cannot be used to validate modified preanalytical variables therefore prospective collection of paired samples of grossly identified tumors is required. Our experience illustrates that this can only be achieved by continuous, collaborative effort from pathologist assistants, technologists and pathologists, making it a time consuming, expensive and labor intensive process.

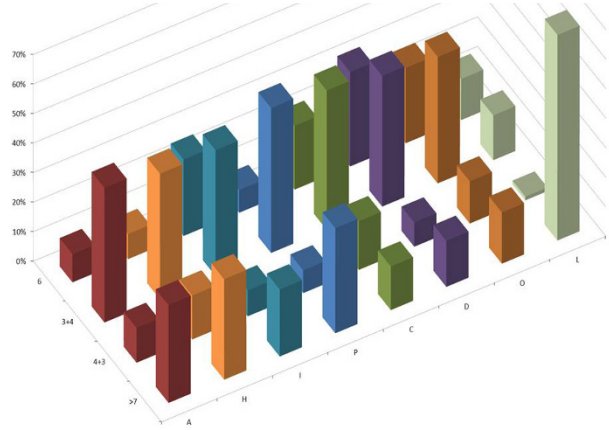
2033 Use of Synoptic Pathology Reports To Efficiently Assess Variance of Pathologists in Grading Prostate Cancer

Colin Newbill, Chris Magnusson, Rodney Schmidt, Lawrence True. University of Washington, Seattle, WA.

Background: Consistent characterization of the clinically actionable pathologic features of cancers is fundamental to high quality patient care. Grading prostate cancer in needle biopsies stratifies patients into specific management regimens (i.e. active surveillance, intent to cure therapy, neoadjuvant therapy) that have distinct therapeutic implications and complication rates. It follows that deviation from consensus Gleason grades (ISUP/WHO 2005) might classify some patients as having higher risk than is appropriate for their cancer. Conversely, under-grading might lead to therapy inadequate for their cancer. Structured data in pathology report templates provide a way to assess in near real time variance in grading.

Design: Data in our synoptic reports are saved as discrete elements which can be searched and collated in real time. Reviewing records of 2,664 biopsies and of 1,411 prostatectomies that spanned a 9 year period, we tabulated the frequency with which individual pathologists assigned Gleason scores 6, 3+4, 4+3, and 8-10. Differences in frequency were assessed by chi square analysis, using $p < 0.005$ as the threshold value for significance. More than 90% of cases were graded by a randomly assigned pathologist, minimizing the potential for selection bias in case assignment to a GU pathologist.

Results: One of eight pathologists who reported at least 75 cancers in RPs significantly ($p<0.05$) over-graded the cancers (pale green) compared with all other pathologists.



There was no significant difference among the 19 pathologists (average 134 cases per pathologist) in grading cancer in needle core biopsies.

Conclusions: Synoptic reports with discrete, searchable data elements can be used in real time (daily, weekly, monthly, or ad hoc) as a QA metric to identify pathologist(s) who tend to under- or over-grade prostate carcinoma in needle biopsies and radical prostatectomies. Since inaccurate grading has clinical consequences, both for patient management and for prognosis, it is important to determine as efficiently and quickly as possible whether a pathologist varies from standard of practice. Synoptic reports with data elements that can be searched any time provide such a QA tool.

2034 Real World Molecular Pathology Reporting: A Survey-Based Review of Guideline Adherence

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Background: While guidelines exist regarding key elements of molecular pathology reports, there is little data available assessing real world compliance. In this study we investigate how laboratories report molecular tests using the BRAF College of American Pathologists (CAP) proficiency testing as a mock patient sample report.

Design: Laboratories subscribing to the CAP BRAF proficiency test were asked to submit a full mock patient report based on the sample. The reports were de-identified at CAP and the data were abstracted by two members of the CAP Molecular Oncology Committee. Variables recorded included basic elements (methodology, specimen source, etc) and elements specific to molecular diagnostics (gene nomenclature, specific assay target, etc) derived from CAP checklists and published guidelines on molecular reporting (Gulley et al. Arch Pathol Lab Med 2007;131:852-863).

Results: 62 laboratories participated. The CAP checklists require correct gene nomenclature: none of the surveyed used the full HUGO gene name but all provided the correct gene symbol. 100% listed a test methodology, while 53 (85.6%) also specified the method target. 34 (54%) included an interpretive comment. None of the reports listed the required percentage of malignant cells. Limit of detection (LOD) and performance of dissection are not specifically required in current guidelines, but were tracked in this study. 44 (71%) reports included LOD with majority (73%) claiming between 1-5% LOD. 8 (13%) reports specified performance of dissection.

Conclusions: Molecular tests have specific reporting necessary elements to ensure appropriate interpretation. The results of the present study indicate that the majority of laboratories include required elements including specific target and methodology, while only half include an interpretive comment. Some report components are not yet required (LOD and dissection) and are currently provided by a subset of laboratories. Limitations of the study include difficulty in generalizing BRAF data to other molecular tests, as well as responder bias to this voluntary survey. These preliminary data suggest that updated guidance should be provided regarding an adequate molecular pathology report, including possibly requiring relevant data elements such as LOD and dissection in future guidelines.

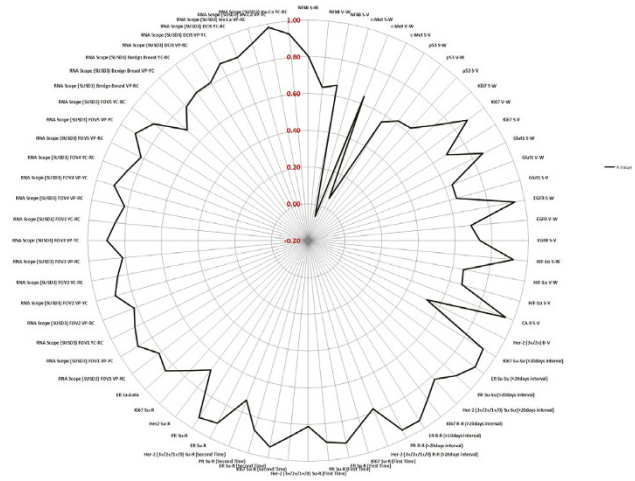
2035 Inter and Intra Observer Concordance of Tissue Based Biomarkers in Pathology

Vamsi Parimi, Julianne Ubago, Yelda Orhan, Megan Sullivan, Stephen Rohan, Michael Balco, Robert Chatterton, Piotr Kulesza, Demirkan Gursel, Jian-Jun Wei. Northwestern University, Chicago, IL.

Background: Independent inter and intra observer review and single field of view (FOV) with multi-reviewer evaluation methodologies are not studied well in context to reviewer concordance. We conducted assessment study of inter and intra observer variation among tissue based biomarker evaluation by immunohistochemistry and insitu mRNA. Various variables like scoring criteria, simplicity of criteria, number of classification tiers, heterogeneous biomarker expression and sampling regions that may influence the inconsistencies among observers are evaluated in this study.

Design: To examine observer agreement, twelve biomarkers as part of 50 studies with nuclear, cytoplasmic and membranous localization stained on whole slide and tissue microarray were evaluated independently by multiple pathologists and pathologists in training. Nuclear biomarkers Ki67, p53, ER and PR were evaluated by percentage of positively stained nuclei in tumor cells of interest. Similarly biomarkers expressing cytoplasmic staining are evaluated by 4 tier system and H-Score (composite) which accounts for percentage of cell stained at low, moderate to high intensity. Membranous staining for Her-2 neu expression is performed by ASCO/CAP guidelines. Insitu mRNA transcript density review was also conducted. The intra observer evaluation was performed with 20 day washout period to reduce recall bias. Pearson's concordance correlation was calculated among respective observers.

Results: The results of our study show wide range (-0.06 to 0.95) of concordance among observers with glass slide evaluation. Biomarkers localized to nucleus had the highest concordance among inter and intra observer evaluation compared to membranous and cytoplasmic stains.



Conclusions: Nuclear biomarker evaluation has the highest concordance rate among independent reviewers. Simplified scoring criteria with low tier system showed higher concordance.

2036 Analyzing the Attrition Rate of Sample Flow in High-Volume Personalized Cancer Genomic Profiling

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Background: Molecular Profiling is increasingly being used to provide personalize cancer care for oncology patients. At our center, close to 2000 patients have to date been enrolled in Cancer Molecular Profiling in which next generation sequencing of FFPE tumors is performed. The purpose of this study was to determine the sample-limiting factors that preclude a subset of patients from having their tumor profiled.

Design: Enrollment in molecular trials requires that patients have diagnostic archival tissue on file from a previous surgery or biopsy. Data tracking includes: number of patients enrolled in the trial, the tumor site, whether the tumor sample was considered suitable following pathology review (at least 10% tumor nuclei), and whether a successful molecular profiling result was reported in the patient's electronic medical record.

Results: Of 1975 patients enrolled over 2.5 years, 1661 (84.1%) had successful molecular profiling results reported. Of the 314 patients that were not successfully profiled, 160 failed pathology review (i.e., the available material was deemed inadequate) and 154 patients passed pathology review but had material that subsequently yielded insufficient or degraded DNA not suitable for sequencing. The molecular profiling success rate was 94.2% for gynecologic (n=512 samples), 90.7% for breast (n=398), 83.3% for gastrointestinal (n=401), and 70.5% for lung tumors (n=393 samples). 11.7% (n=46) of lung tumors failed pathology review, and 20.2% (n=70) of those that passed pathology review were not suitable for sequencing.

Conclusions: The majority (84.1%) of patient samples submitted for molecular cancer genomic profiling have successful results reported. The overall attrition rate at the level of pathology slide review was 8.1%, at the level of subsequent suitability for DNA sequencing the attrition rate was 8.5%. Interestingly, there was significant variability as a function of tumor site, possibly related to size and quality of obtainable tissue (resection/excision vs. small biopsy). A closer interrogation of archival samples that are not successfully profiled may help identify ways of improving the success rate of targeted sequencing (increased specimen banking, special handling of small biopsies, improved preservation of DNA).

2037 Whole-Slide Digital Imaging for Frozen Section Diagnosis: Phase 1 of a Validation Study, With a Focus on Image Flaws

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Background: With an active multisite frozen section (FS) operation, we have a practical interest in the utilization of whole-slide digital imaging (WSDI) for FS telepathology services. We aim to validate WSDI technology for routine FS diagnosis on a representative cohort of FSs, hypothesizing that the diagnostic value of digital slides is comparable to that of physical FS glass slides. Herein, we describe Phase 1 of our validation study, in which we assess whole-slide FS digital image quality, rate of image flaws, and root causes of flaws. To our knowledge, our study is the largest to examine WSDI for FS diagnosis to date.

Design: Whole-slide digital images generated from 541 randomly selected cases from the UCSF archives from years 2012-2013 using a Philips platform, with a total of 2158 FSs, were evaluated by a single pathologist (ZGL) for diagnostic image quality. The characteristics and root causes of image flaws were recorded and classified. Suboptimal images with a potential to impede the diagnosis were rescanned and then reevaluated. Prior to rescanning, FSs with air bubbles were recoverslipped.

Results: Of 541 cases and 2158 FSs, 199 cases (37%) and 271 slides (13%) were affected by an image flaw upon initial scanning. The vast majority of these flaws were out-of-focus areas (95% of flawed slides). Other flaws included truncated images (3% of flawed slides) and absent images (0.4% of flawed slides). Of the out-of-focus images, most (66%) had no apparent underlying root cause, but in the remainder (34%), the problem was due to artifacts or poor FS quality, including air bubbles (23%), thick/uneven sections (6%), tissue fragmentation (2%), and folded sections (2%). Of the 224 rescanned slides, flaws were completely corrected in 97 slides (43%) and partially corrected in 23 slides (10%). For 92 slides (41%), the problem remained the same, and in 12 slides (5%) the problem worsened. However, in only one case (0.18% of all cases) did the severity of the image flaw render the case non-diagnostic.

Conclusions: Whole-slide digital imaging of FSs with a Philips platform yields diagnostic-quality images in the overwhelming majority of cases. In a significant proportion of flawed images, artifacts introduced during FS preparation were the root cause, emphasizing the need for high-quality FSs intended for WSDI.

2038 HER2 Status in Gastroesophageal Adenocarcinomas: Correlation Between Herceptest and FISH Methodologies

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Background: Semiquantitative immunohistochemistry (IHC) and fluorescent *in situ* hybridization (FISH) are commonly used in combination to detect HER2 amplification in gastroesophageal adenocarcinomas. While published guidelines do exist, there is some variation in how IHC and FISH are applied between laboratories. At our institution, IHC is used as a frontline test while FISH is performed on cases with IHC (HercepTest) scores 0, 1+ and 2+. In this study we correlate HercepTest with FISH results with the goal of optimizing our testing algorithm.

Design: We identified all gastroesophageal adenocarcinomas at our institution analyzed with HercepTest (Dako). We recorded the HercepTest score in addition to the HER2/D17Z1 ratio obtained by FISH (PathVysion, Abbott). We also recorded tumor site, tumor grade , treatment status and specimen type.

Results: We identified 123 gastroesophageal adenocarcinomas from June 2009 to August 2014 analyzed with HercepTest. Matched HER2 FISH results were available for most cases, 116/123 (94%). For cases with matched IHC and FISH results, the tumor site, specimen type and tumor differentiation were examined.

Tumor Site	N = (%)
Esophagus	25 (22)
GE Junction	28 (24)
Stomach	49 (42)
Other Site	14 (12)
Specimen Type	
Biopsy	81 (70)
Resection	25 (30)
Tumor Differentiation	
Well	0 (0)
Moderate	19 (16)
Poor	75 (65)
Not Specified	22 (19)

For each IHC score category, the HER2/D17Z1 ratio range, mean and number of cases with a ratio of > 2.2 (considered HER2 amplified) were determined.

HercepTest Score	N (%)	Range	Mean	N >2.2 (%)
0	61 (53)	0.70 - 1.9	1.2	0 (0)
1+	29 (25)	0.8 - 5.3	1.6	3 (10)
2+	20 (17)	0.6 - 10.8	2.4	4 (20)
3+	6 (5)	2.5 - 16.2	7.7	6 (100)

For cases with equivocal IHC scores 1+ and 2+, there were no differences in tumor site, grade or treatment status between HER2 amplified and non-amplified cases (by FISH). Overall, 13 of 116 cases (11%) were HER2 amplified.

Conclusions: No cases with IHC score of 0 were shown to have HER2 amplification by FISH while all cases with IHC score 3+ were amplified. These cases made up 51% (score 0) and 6.5% (score 3+) of all cases tested with HercepTest and suggest that a large proportion of FISH tests could be eliminated with no decrease in sensitivity for detecting HER2 amplified tumors.

2039 Is the Anti-Nuclear Antibody (ANA) Indirect Immunofluorescent Assay (IFA) at 1:40 Titer a Useful Clinical Test for Diagnosis of Autoimmune Connective Tissue Diseases (AICTD)?

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Background: The ANA IFA technique is considered the gold standard for ANA testing according to the American College of Rheumatology. Commercially available ANA screening kits recommend a 1:40 cutoff titer, but there is a high fraction of false positives at this dilution. Recently, the European Autoimmunity Standardization Initiative recommended a 1:160 cutoff titer. We analyzed patient data with positive ANA at 1:40 only to determine the test's utility in diagnosis of AICTD.

Design: Data was collected using our laboratory information system (SunQuest) to identify patients positive for ANA at 1:40 (Fluorescent HEp-2, Immuno Concepts, Sacramento, CA) but negative at 1:80 in the period 07/2013 – 07/2014. Medical Records (EMR, EPIC) of all positive patients were reviewed for demographic data, levels of auto-antibodies to Extractable nuclear antigens (ENA), Cardiolipin, double-stranded DNA, Rheumatoid Factor, Cyclic Citrullinated Peptide and final diagnosis rendered by treating clinicians.

Results: 341 patients positive for ANA at 1:40 only were found; 182 had available EMR records and were included in the study. Median age was 48 (5-90) and the F:M ratio was 3.7:1. Only 7 (3.8%) new diagnosis of AICTD were made (2-SLE, 2-Sjögren's syndrome, 2-Unspecified, 1- Polymyalgia Rheumatica). 22 patients (12.1%) had a previous diagnosis of AICTD. Non-autoimmune diseases were diagnosed in 116 cases (63.7%) including skeletal-muscular (66), Neurological-psychiatric (11), viral-related (7), renal (5) and dermatological (4). In 6 cases the ANA result by itself prompted an unnecessary referral to rheumatology. Of the 7 new cases of AICTD abnormal additional testing was identified in 5 cases.

Conclusions: In the present study, ANA at 1:40 was found useful in only 7 cases (new diagnoses of AICTD) with a significant proportion of patients having false positives (116/145) results. A case for increasing the cut-off titer for a screening ANA can be made considering the wasted resources and additional anxiety caused in patients. In 83 cases unnecessary reflex ENA ($17 each) was ordered. On the other hand, with the proposed higher cutoff value 7 true cases of AICTD might have been missed with potential harm to patients.

Further studies are required to help define better cutoff titers that could perhaps be different according to the demographic characteristics of the patients as some studies have suggested.

2040 Specimen Contamination in Clinical NGS Data

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Background: Specimen provenance errors (SPE) are known to occur in laboratory testing and are a potential source of misdiagnosis and suboptimal patient management. Due to complex workflows involved with clinical next-generation sequencing (NGS) assays, it is likely that SPE are also an issue in NGS testing. Because NGS methods are used to identify and report variants present at variant allele frequency (VAF) of 10% or lower in clinical testing of cancer samples for tumor genetic profiling, it is critical to quantitate the degree of specimen contamination in NGS data, particularly since reported variants can be used as a basis for patient management decisions. CAP and ACMG guidelines for molecular testing stipulate the need to assure that patient specimens are not contaminated during laboratory testing, but the means for doing so are not yet established for NGS assays.

Design: Using a haplotyping approach for identity determination with orthogonal validation by short tandem repeat (STR) analysis, we sought to determine the rate of clinically significant (≥5%) DNA contamination in clinical NGS data from 296 consecutive cases. Haplotype analysis was performed by identifying the number of HapMap-derived haplotypes that were present at closely spaced (within a single sequenced DNA fragment) SNP pairs that were present in the genomic regions targeted by the clinical assay. Percent admixture was estimated based on the VAF of minor haplotypes across multiple loci.

Results: We identified 9 cases (3%) with >5% admixture of the sequenced DNA as determined by haplotype and STR analyses. Three cases were from bone marrow transplant patients who were known to be chimeric. DNA yields for 5 cases were suboptimal (110-450 ng, where 1,000 ng is the preferred amount for clinical sequencing). One case yielded 1,340 ng of DNA but was contaminated during tissue collection from the block or DNA extraction, based on stepwise STR testing. In all, 10.9% of cases with DNA yield <500 ng and 21.4% of cases with DNA yield <200 ng were contaminated by the criteria used in this study (p=0.01 and p=0.003, respectively).

Conclusions: Specimen contamination with foreign human DNA occurs in clinical NGS testing. Tools for detecting contamination in NGS sequence data must be integrated into clinical bioinformatics pipelines to prevent reporting of potentially actionable variants in patients whose tumors do not actually harbor those variants, especially as laboratories tend toward using smaller amounts of input DNA and reporting lower frequency variants.

2041 Utility of Histochemical Stains for Infectious Organisms in Fine Needle Aspiration Cytology Specimens of Patients With Clinical Suspicion of Sarcoidosis ndash] A Single Institution Study

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Background: Histochemical staining with Ziehl Neelson (ZN) and Gomori Methenamine Silver (GMS) to exclude infection is the current standard practice for granulomas found on cytology specimens. However, in institutions with a high prevalence of patients with sarcoidosis this practice may be a waste of resources and negatively impact turnaround time. The aim of this study is to determine the need to reflexively order histochemical stains on granulomas identified in fine needle aspiration (FNA) specimens of patients with clinical suspicion or previous history of sarcoidosis.

Design: Using the Pathology Department database all CT- or EBUS(endobronchial ultrasound)-guided FNA of lung and mediastinal lymph nodes performed between Jan 2011 and Jan 2012 were selected that had any of these features: granulomas on cytology, imaging suggestive of sarcoidosis, clinically suspicious or previous diagnosis of sarcoidosis. Patient demographics, location of procedure, imaging results, culture results, concurrent tissue biopsy results, histochemical stain results, and clinical context were recorded.

Results: A total of 179 patients were identified that fulfilled the above conditions. Granulomas were identified in 47 patients: 79% had non-necrotizing granulomas, 11% had necrotizing granulomas, 10% had nonspecific granulomatous inflammation. Of the patients with clinical suspicion of sarcoidosis and non-necrotizing granulomas, 62% had ZN and GMS stains performed on the cell block material; 100% of these were negative for infectious organisms. Only 3% of concurrent cultures were positive.

Findings on FNA	Patients with clinical/ radiographic suspicion of Sarcoidosis	Patient known history of Sarcoidosis	Histo-chemical stains ordered	Positive stain results	Cultures ordered	Positive culture results
Non-necrotizing granulomas (n=37)	21	4	23	0	19	1

Conclusions: Though histochemical stains were performed in the majority of patients with clinical/imaging suspicion or confirmed history of sarcoidosis, lack of positive histochemical stain results suggests that these tests may have been unnecessary. In addition, concurrent cultures were largely negative. The results suggest that histochemical organism stains in this patient population may be unnecessary when non-necrotizing granulomas are identified in the cell block material.

2042 Errors in Gynecological Frozen Section Consultations

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Background: Intraoperative consultations play an important role in management during gynecological surgeries. Pathologists must make appropriate judgments regarding what tissue to sample, make an accurate interpretation of the selected frozen section and effectively communicate those findings in order to guide decisions regarding the extent of surgery. Error during any part of this process may result in significant adverse outcomes for the patient. Correlation of frozen section diagnosis with permanent sections is an integral component of laboratories' quality assurance (QA) programs and provides an opportunity to reduce future adverse outcomes. The aim of our study was to identify specific sources of error leading to discordant frozen section diagnoses of gynecologic lesions.

Design: All gynecological frozen sections performed between 2009 and 2013, excluding metastases from non-gynecological primary sites, were selected and the pathology reports were reviewed for concordance between frozen section and final diagnoses. Cases were reviewed for histologic classification, grade and whether subsequent staging surgery was performed. The slides for discordant cases were further reviewed at QA meetings and a consensus root cause of error was determined.

Results: Discordant findings between frozen section and final reports were identified in 118 of 1419 cases (8.3%). The cause of discordance was attributed to sampling error in 84% of the cases and interpretive error in the remaining 16%. The two most common scenarios for sampling error were 1) cases where the endometrium was interpreted as negative or atypical hyperplasia on frozen section and found to be endometrial adenocarcinoma (generally microscopic and low grade) on final sections (48 cases) and 2) grading of endometrial adenocarcinoma (25 cases). Discordance was not associated with subsequent staging ($p = 0.18$) however, it was associated with tumor category (i.e. benign vs. malignant) as a greater proportion of discordant cases were malignant compared to concordant cases ($p < 0.0001$).

Conclusions: The majority of discordant frozen section diagnoses indentified in our analysis resulted in little or no significant clinical consequence; however, rare cases were identified in which operative management was not optimal due to either sampling or interpretive error. Careful gross examination of specimens to optimize sampling is of paramount importance. Nevertheless, pathologists and surgeons should have a mutual understanding of the limitations of the frozen section. Consensus review of cases as part of a QA program serves as an effective means of learning from past errors.

2043 ICSH Guidelines for the Standardization of Bone Marrow Immunohistochemistry

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Background: Bone marrow (BM) tissue biopsy evaluation is an integral part of BM investigation and is often followed by ancillary studies, in particular immunohistochemistry (IHC). The aim of these guidelines is to define BM IHC parameters relevant to standardization, set the stage for development of BM IHC EQA/PT, and to develop a relevant framework for BM IHC performance characteristics.

Design: An international Working Party for the Standardization of Bone Marrow IHC was formed by the International Council for Standardization in Hematology (ICSH) in order to prepare a set of guidelines for the standardization of BM IHC based on currently available published evidence and modern understanding of quality assurance principles as applied to IHC. The guidelines were discussed at the ICSH General Assemblies and reviewed by an international panel of experts to achieve further consensus and represent follow up to the previously published ICSH guidelines for the standardization of BM specimens handling and reports.

Results: These guidelines focus on technical and other general issues related to BM IHC. Recommended pre-analytical standards (including ischemic time, technique for preparation of clot samples, fixative and fixation time, decalcification, embedding, and cutting), analytical standards (including protocol validation, monitoring of performance characteristics, and documentation), post-analytical standards (interpretation of results of controls and patient samples), and quality assurance standards (design and use of appropriate positive and negative controls, feasibility of proficiency testing, potential for use of flow cytometry for QA, and education). Recommended tissue processing is tailored based on turn-around-times as per institutional requirements. Feasibility of short protocols is defined based on the type of samples available to (hemato)pathologists.

Conclusions: Although standardization of BM IHC is not fully achievable at this time, these guidelines define which components can be standardized at present and which components can be harmonized now and possibly standardized in the future.

2044 Immunohistochemistry Critical Assay Performance Controls (iCAPCs) – A Novel Tool in Diagnostic Immunohistochemistry (dIHC)

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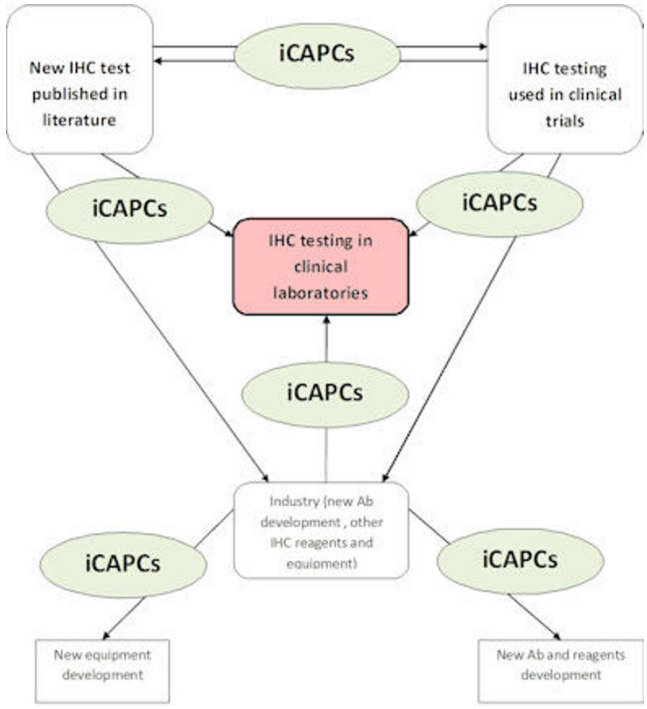
Background: The main purpose of positive and negative controls is to monitor the analytical component of previously validated IHC protocols. However, defined control tissues are also necessary for other purposes (methodology transfer, protocol development, proficiency testing, new antibody development, etc.). A concept of IHC critical assay performance controls (iCAPCs) was developed as a tool for these additional applications.

Design: iCAPCs are human tissues that are well characterized and demonstrate predictable levels and patterns of expression and cellular localization. iCAPCs are developed by expert consensus. For any useful standardization to occur, it is necessary to reach expert agreement on the choice of tissue(s) that will serve as iCAPCs for each IHC test. As a first step the International Ad Hoc Expert Committee for standardization of IHC controls developed iCAPCs for 10 frequently used IHC tests (pan-CK, LMWCK,HMWCK, CK20, CK7, S-100, TTF-1, CDX-2, vimentin, synaptophysin). The carefully characterized controls (iCAPCs) were designed to provide biologically relevant information that cannot be directly obtained from cell lines, xenografts, histoids, or peptides, or even other patients' samples.

Results: Recommended uses of iCAPCs include: i) serving as the the component of the TMA design for protocol development, as daily tissue controls, and EQA PT sample design; ii) validation of secondary external controls (cell line preparations, xenografts, peptides, or histoids); iii) methodology transfer (clinical trial and other research protocols to the clinical laboratory, or from one laboratory to another, etc.); iv) for manufacturers and laboratories using "closed dIHC tests" based on Ready-To-Use analytes, for which iCAPCs provide standard information on the analytical precision of these.



Conclusions: Optimal identification and use of iCAPCs is expected to improve standardization of results of IHC testing, improve monitoring of "closed dIHC tests", facilitate methodology transfer, and represents a first step towards harmonization of diagnostic IHC.

2045 Standardization of Positive Controls in Diagnostic Immunohistochemistry: Recommendations From the International Ad Hoc Expert Committee

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Background: Diagnostic immunohistochemistry (dIHC) has been in use for several decades, but its standardization has not yet been achieved despite significant advances in its methodology and expanding applications for both diagnostic uses as well as for prognostic and predictive markers.

Design: The Committe developed consensus recommendations for best laboratory practices in dIHC for positive controls. The Committee also developed a concept of IHC critical assay performance controls (iCAPCs) in order to facilitate methodology transfer and harmonization in dIHC. Furthermore, the Committee clarified definitions of IHC assay sensitivity and specificity with special emphasis on how these definitions apply to positive controls. The recommendations are based on: i) published literature; ii) evidence generated in various EQA programs, and iii) current expert opinion.

Results: Standardization of terminology and definitions (primary vs. secondary positive controls, quantitative vs. qualitative controls, internal vs. external controls, technical vs. diagnostic vs. clinical sensitivity and specificity) is proposed. Standardization of tissue processing, building of quality control tissue archives, design of tissue microarrays for protocol optimization, on-slide controls, processing of unstained slides with controls, and development of adequate SOPs for standardized positive controls are recommended.

Conclusions: The Ad Hoc Expert Committee proposes standardization of controls for immunohistochemistry, which is a missing link in demonstrating and assuring standardization of various components of dIHC and is the basis for methodology transfer between published literature, clinical trials and dIHC laboratories.

2046 Molecular Testing in Anatomic Pathology and Adherence To Guidelines: A College of American Pathologists Q-PROBESTM Study of 2230 Testing Events Reported By 26 Institutions

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Background: Appropriate and timely performance of molecular testing in anatomic pathology is an indicator of quality. The National Comprehensive Cancer Care Network® (NCCN) guideline includes recommendations for ancillary testing. This multi-institutional study aimed to establish benchmarks for rates of adherence to NCCN guidelines.

Design: Participants reported data from molecular testing on anatomic pathology specimens, excluding hematolymphoid neoplasms, breast primary carcinomas and gynecological cytology. Each test was evaluated in its clinical and pathological context and compared against NCCN guidelines as were current during the study period (early 2013).

Results: 26 institutions reported data from 2230 testing events. In a retrospective data collection limited to colon, lung and melanoma, the most common tests performed were EGFR, ALK and KRAS; there was strict adherence to guidelines in a median 71%, with at least loose adherence in a median 95% (see table). There was adequate tissue to complete testing in a median 98% (10^{th} to 90^{th} percentile range 86-100%), though the adequacy rate for cell blocks was lower (84%, $P<.001$). Median test turnaround time was 8 days (10^{th} to 90^{th} percentile range 4-13). In a separate prospective data collection of all organ sites, the most common tests requested were EGFR, KRAS, ALK, Lynch syndrome screening and BRAF; there was strict adherence to guidelines in a median 53%, with at least loose adherence in a median 94% (see table). Adherence to guidelines was higher for lung specimens and in institutions with a higher number of multidisciplinary conferences. Pathology approval for molecular tests was required in 52% of institutions and pathologist-initiated reflex testing was offered in 57% of institutions.

Institution Percentiles	10th	25th	50th	75th	90th
Retrospective Data					
Strict adherence	33	65	71	83	90
At least loose adherence	57	91	95	99	100
Prospective Data					
Strict adherence	20	31	53	67	71
At least loose adherence	75	87	94	100	100

Conclusions: This multi-institutional study provides benchmarking data on appropriateness and timeliness of molecular testing in anatomic pathology.

2047 Whole Slide Digital Imaging Is Applicable for Routine Frozen Section Diagnosis

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Background: Whole slide digital imaging (WSDI) is a rapidly evolving technology with broad applications including medical education and telepathology. However, limited data exist on the use of WSDI for rendering frozen section diagnosis. We aim to validate a Philips WSDI platform for routine diagnosis in frozen sections. Here we hypothesize that diagnostic interpretation of whole slide digital images of frozen sections is not hampered to a significant extent by image quality faults and that the diagnostic potential of such digital images is comparable to that of conventional glass slide frozen section interpretation. We test our hypothesis by studying the image quality of whole slide digital images on an unbiased representative cohort of frozen sections and by assessing the spectrum of diagnostic limitations related to whole slide digital image quality deficiencies.

Design: Whole slide digital images of frozen sections from the UCSF surgical pathology archives from years 2012-2013, comprising 541 randomly selected cases with 2158 slides across all subspecialties, were evaluated for image quality and diagnostic utility. Touch preps routinely used for neuropathology cases were included. Defects identified on digital images upon initial scanning were documented and classified. For flaws on the digital images that could potentially impede the diagnosis, the slides were rescanned and reevaluated. The flaw characteristics of the images from the initial scan and rescan were recorded and analyzed for potential impact on diagnosis.

Results: Out of a total of 547 cases, only one case was deemed non-diagnostic due to image quality problems on a touch prep specimen (0.18%), corresponding to one part out of 890 parts (0.1% total parts). Although 22 additional digital images of a total of 2167 frozen sections were also classified as non-diagnostic (1.0% of total slides), a diagnosis could still be rendered on all of these cases since images of level sections were of diagnostic quality.

Conclusions: WSDI technology is applicable for frozen section diagnosis as digital images of 99.8% of cases out of a cohort of 547 unbiased randomly selected cases were interpreted as being diagnostic. We are further investigating the potential pitfalls of WSDI technology for frozen section diagnosis via in depth analysis of intra-observer diagnostic concordance in our group of pathologists.

2048 Effect of Needle Rinse Solution on Cellularity of Cellblock Preparations in Fine Needle Aspiration Biopsies

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Background: Cellblock (CB) preparations are vital in current cytology practice. As personalized medicine requires more immunocytochemistry and molecular testing, there is increasing for highly cellular CBs. Studies have compared various protocols of CB processing; however, only limited data is available regarding effects of needle rinse solution (NRS) on cellularity. The aim of our study is to evaluate potential effects of NRSs on the cellularity of CB preparations and to assess the cost-effectiveness.

Design: 8 surgical specimens were selected, on which 4 paired fine needle aspiration biopsies (FNABs) were performed with needle rinses into 10mls of either RPMI or Cytolyt, generating 32 paired FNABs. For each FNAB, 3 passes were performed; the first yields a single air dried smear, DiffQuick stained, to evaluate adequacy, with subsequent 2 directly rinsed in either solution. The NRSs were processed via thrombin clot method to yield CBs. The H&E sections were evaluated for cellularity, measured in terms of cell clusters (>6cells in a group) and background cellularity (cells <6/cluster or single cells per average 40x field). The cellularity was compared for each paired FNAB, specimen average, and overall for RPMI vs Cytolyt. P-values were calculated using student T-test. In addition, the cost for each 10 ml aliquot (RPMI or Cytolyt) was calculated.

Results: Both CBs using RPMI or Cytolyt yield adequate cellularity. The cellularity in CBs using RPMI ranges from 11-923 cell clusters and 1-167 background cellularity. Cellularity in CBs using Cytolyt ranges from 3-1122 cell clusters and 6-188 background cellularity. The average cell clusters per specimen show a trend of higher cellularity with Cytolyt; however, only one specimen showed statistical significance (p-value of 0.039). The same is true for background cellularity, with one specimen having a p-value of 0.007. When comparing all FNABs using RPMI vs Cytolyt, cluster cellularity is not statistically significant with a p-value of 0.356, while background cellularity is statistically different with a p-value of 0.006. The cost of 10 ml aliquot is $0.88 for RPMI and $0.50 for Cytolyt.

Conclusions: Our data shows CBs using RPMI or Cytolyt yield adequate cellularity with Cytolyt trending higher than RPMI; however, the difference is not statistically significant. The cost of Cytolyt is marginally less than RPMI. With little difference in the cellularity using RPMI or Cytolyt, other factors such as specimen versatility and cost should be evaluated based on overall needs of individual laboratory when selecting an NSR.

2049 Achieving Reliability in Histology

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Background: Specimen misidentification in the histology laboratory can result in serious patient harm. Despite efforts to abate labeling errors, incidence specifics have not been rigorously studied and standardized improvement efforts have not been reported. By utilizing tools such as root cause analysis, process mapping, quality metric assessment, and Lean methodology, we identified vulnerable steps in the histology laboratory and designed targeted improvement efforts.

Design: The study was conducted within the histology laboratory of a major academic institution with an annual specimen volume of approximately 60,000. A novel numerical step-key mapped histology workflow, facilitated error data collection, and identified the most vulnerable steps to labeling error (the root causes). Two most prevalent root causes were targeted for Lean workflow redesign: manual slide printing and microtome cutting. The initial plan-do-study-act (PDSA) cycle introduced bar-coding technology at the slide-printing step with the aim of decreasing specimen mixups by obviating the need for manual entry of accession numbers. The second PDSA cycle utilized the Lean concept of Single Piece Workflow (SPW) in the form of an innovative compartmentalized crushed ice design entitled the 'Framework to Engage and Effect Zero Errors' (iFREEZE). iFREEZE hermetically cooled, separated, and sequestered matching blocks and slides, further decreasing the incidence of specimen labeling errors.

Results: 152,952 cases were analyzed over a 31 month study period. A baseline error rate of 1% (793 errors/76,958 cases) was established prior to any systematic workflow changes over the first 15 months. Following implementation of slide printer bar coding (PDSA cycle 1), the error rate decreased to 0.3% (92 errors/32,534 cases) over the next 7 months. Following iFREEZE implementation (PDSA cycle 2), the rate was 0.2% (86 errors/43,460 cases) over the last 9 months. Overall, a 90% reduction in labeling errors has been observed since the initiation of our study.

Conclusions: Histology labeling errors can be captured in real time, attributed to a root cause, and subjected to targeted quality improvement efforts. Using relatively simple quality improvement tools, we were able to characterize and drastically reduce our institution's labeling error rate in a quantifiable manner. Our generalizable process redesign efforts have the potential to greatly improve reliability in histology as part of national and institutional patient safety goals.

Techniques

2050 Molecular Profiling of Common Melanoma Mutations – A Large Cohort Study

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Background: Melanoma is one of the deadliest skin cancers. It is predicted that in 2014 alone, 6500 Canadians will be diagnosed with melanoma, of which 1050 will die. Historically, melanoma classification has been based on pathological criteria and