injury/fibrosis. Therefore, it is important that the diagnosis of "idiopathic" be reserved for cases in which such exposures have been excluded. We believe that public health would be enhanced by making pathologists and clinicians more aware of such cases.

2059 Aberrant and Overexpression of DNA Methyltransferase in KRAS Mutant Pulmonary Adenocarcinomas

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Background: Correlation between KRAS mutations and pulmonary adenocarcinomas (PA) has been well documented. We have previously shown that majority of the KRAS G12/G13 mutations is transversion (G>T and G>C) in PA compared to colorectal adenocarcinomas (p= 0.011). The aim of this study was to evaluate for possible relationships between transverse mutations and expressions of enzymes associated with DNA methylation and oxidative stress in KRAS mutant PA.

Design: A total of 109 PA patients without EGFR TKD mutations (Exon19 and 21) were enrolled in this study. Genomic DNA was used for KRAS G12/G13 codon mutation testing by direct sequencing. A tissue microarray consisting of 62 PA samples including 26 PA with KRAS mutation was evaluated for the expression of DNMT1, DNMT3a, and NQO1 by immunohistochemistry. The correlations between markers expression and clinicopathologic variables were examined by Kruskal-Wallis ranks test and Spearman Rank Order test.

Results: Among 26 mutant KRAS gene, 84.6% were transverse mutation. Moreover, 21 of 22 transverse mutation are G>T (>95%). No correlation was present between patients' KRAS mutation status and age or sex. The presence of KRAS mutations, however, was associated with increased expression of DNMT1 (r=0.582, p<0.0001), NQO1 (r=0.436, p=0.0004), and DNMT3A (r=0.35, p=0.0053) in the tumor cells. Nuclear expression of DNMT1 was seen in 25 of tumors (25/62), and majority (77.3%) of them had KRAS mutation (p=0.0054).

Conclusions: In this study, we further confirmed that most KRAS mutations in PA were C>T transverse mutation. The association between KRAS mutation and upregulation of nuclear DNA methyltransferase (DNMT1, DNMT3a) expressions in the tumor cells suggest aberrant activation of DNMT might involve in the KRAS G12/G13 mutation in PA.

2060 Comparison of Napsin A Expression in Tumors with Polyclonal and Monoclonal Antibodies

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Background: Napsin A is a useful marker in identifying adenocarcinoma of the lung in a tumor of unknown origin. Our preliminary data and literature using a polyclonal antibody to napsin A demonstrated that it was a highly sensitive marker for pulmonary adenocarcinomas. However, expression of napsin A was also observed in a significant percentage of other tumors, including renal cell carcinomas, thyroid papillary carcinomas and esophageal adenocarcinomas. With the availability of a monoclonal antibody to napsin A, we compared expression of the polyclonal and the monoclonal antibodies in tumors from various organs using a single immunostaining system (Dako).

Design: Immunohistochemical evaluation of napsin A (1. Cat No. 760-4446, rabbit polyclonal, prediluted, Ventana; 2. Cat No. CM 338CK, mouse monoclonal, BioCare Medical) expression was performed on 1058 cases of tumors on tissue microarray sections. The staining intensity and distribution were recorded.

Results: The immunostaining results are summarized in Table 1. The sensitivity and specificity for the polyclonal and monoclonal antibody were 83.3% and 95.6%, and 72.6% and 97.9%, respectively.

Table 1. Summary of Immunostaining Results

Tumor	Monoclonal antibody	Polyclonal antibody
Lung ADC	72.6% (61/84)	83.3% (70/84)
Papillary RCC	50% (8/16)	75% (12/16)
Papillary thyroid CA	15.2% (7/46)	22.7% (10/44)
Clear cell RCC	2.5% (1/40)	12.5% (5/40)
Esophageal ADC	0% (0/29)	11.5% (3/29)
Ovarian tumors	1.4% (1/72)	6.9% (5/72)
Endocervical CA	6.7% (1/15)	6.7% (1/15)
Pancreatic CA	0% (0/47)	6.4% (3/44)
Lung neuroendocrine tumors	7.3% (3/41)	4.9% (2/41)
Lung squamous cell CA	2% (1/49)	2% (1/49)
Breast lobular CA	0% (0/49)	2% (1/49)
Germ cell tumors	0% (0/79)	1.25% (1/80)
Pancreatic endocrine tumors	0% (0/16)	0% (0/16)
Thyroid follicular CA	0% (0/34)	0% (0/34)
Colon ADC	0% (0/36)	0% (0/29)
Cholangiocarcinoma	0% (0/11)	0% (0/11)
Hepatocellular CA	0% (0/18)	0% (0/18)
Prostatic ADC	0% (0/133)	0% (0/133)
Breast ductal ADC	0% (0/118)	0% (0/118)
Urothelial CA	0% (0/31)	0% (0/31)
Gastric ADC	0% (0/17)	0% (0/17)
Melanoma	0% (0/77)	0% (0/77)

RCC-renal cell carcinoma; ADC-adenocarcinoma; CA-carcinoma

Conclusions: The polyclonal antibody to napsin A is more sensitive but less specific than the monoclonal antibody in identifying lung adenocarcinoma. A monoclonal antibody is the better choice for a tumor of unknown origin; whereas a polyclonal antibody is preferred for the distinction of primary lung ADC from squamous cell CA.

Quality Assurance

2061 Impact of General Versus Sub-Specialization Pathology Practice Models on Immunohistochemistry Utilization

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Background: Immunohistochemistry (IHC) plays an important role in pathology practice, particularly in the sub-specialties of oncologic pathology, neuropathology, and hematopathology. There is a limited knowledge on the impact of various pathology practice models (i.e., general vs. specialty) on IHC utilization rate.

Design: We performed a cross-sectional analysis of aggregate surgical pathology specimen case data collected during a 7-month period (January to July 2011) encompassing pre- and post-general versus specialization sign-out practice models. In the general practice model 16 pathologists signed out the majority of all cases and in the subspecialty model, 2-4 pathologists signed out each major subspecialty. We compared IHC utilization metrics (e.g., slides and antibodies per month) for the two models. We specifically evaluated the use of specific IHC protocols (e.g., melanoma protocol in patients who had pigmented skin lesions) and individual IHC stains.

Results: During the study period, 707,736 glass slides were produced (mean number of 228 slides per day and 10,105 slides per month) and 24,097 IHC slides were produced (mean number of 115 IHC slides per day and 3,442 slides per month). The IHC utilization rate was higher in general practice (29.5%) compared to subspecialty practice (25.0%) (P < .0001). The use of IHC protocols differed in the two practice models; for example, the IHC melanoma protocol was utilized more in the general practice model compared to sub-specialty practice model (P = .001). Individual stain utilization differed in the two practice models; for example, a pan-keratin stain was the most common IHC stain utilized in subspecialty practice (P < .001), while 34βE12 stain was the most frequent stain used in the general model.

Conclusions: In our institution, subspecialty practice had a lower IHC utilization frequency compared to general practice. We hypothesize that subspecialty practice results in a higher level of standardization in IHC ordering, which may be secondary to diagnostic certainty, knowledge of established IHC protocols, and experience with common and uncommon subspecialty diagnostic dilemmas.

2062 Improving Quality in the Laboratory by Implementing a Novel System of Ownership, Chain of Custody and Verification of Process and Patient

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Background: Approximately 250,000 new cases of prostate cancer are diagnosed annually in USA. This number translates into over one million biopsies and each biopsy encompasses multiple sites. The process of collecting, handling, analyzing, diagnosing, reporting and acting upon tissue biopsies is complex and involves many steps. Despite the utilization of labeling systems, the opportunity for diagnostic mistakes due to occult specimen provenance complications persists. Our aim is to evaluate our novel system in order to identify the number of errors and minimize specimen provenance complications.

Design: Our unique process of specimen ownership involves the following steps: The Patient participates in self-identification via introduction to the Know Error identification process and DNA buccal swab. The Urologist participates via actively placing prostate cores directly into a pre-bar-coded, site-specific cassette after ordering the test electronically in the EMR. The courier participates by scanning each specimen both at the urology office and upon delivery to the pathology lab. The Pathology lab personnel participate by positively identifying each specimen via 2D barcode, verification of the office-based order and registration into the Pathology LIS. Each specimen is handled one at a time using the Ventana Vantage protocol. The Pathologist participates by scanning each case before reading it. Quality of reads is ensured by a second read of all abnormal findings, and 50% of random blind reads. The ultimate step of the chain of custody designed in this lab occurs when the positive cores are verified against the patient's self-identified buccal DNA sample.

Results: In a nine month period, 89 Urologists swabbed 3,754 patients. Of those, 1,282 patients had adenocarcinoma involving 5,198 cores collectively. Although initially there were 8 cores reported as 'mis-match', these were resolved with re-submission of adequate samples. In addition, 2 patient name errors and 8 DOB errors were identified prior to testing. There were no provenance errors in any of the 5,198 positive tissue cores processed.

Conclusions: Implementation of the "IMP Pathology Laboratory Quality System" led to no provenance errors, verifying the effectiveness of the system. The system is LEAN, removing any superfluous steps, it provides an absolute chain of custody of patient tissue samples from the time of biopsy to the verification of positive patient cores.

2063 Analysis of Addendum Reports in Anatomic Pathology as a Quality Improvement Initiative

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Background: An addendum report is commonly defined as a report that provides supplementary information to the original report. On the other hand, an amended report replaces the original report in cases where the initially contained information needs to be significantly changed. There are key differences in how these reports are issued and presented in the electronic record which have implications for patient safety. The purpose of our study was to audit addendum reports and identify opportunities for quality improvement.

Design: All Anatomic Pathology addendum reports in a subspecialized academic department that were issued over a 30 month period were retrieved. These were classified

by accession class, pathologist/site group, indication for addendum, and whether or not the addendum constituted a significant change from the original report, suggesting that an amendment may have been more appropriate.
Results: A total of 6992 addendum reports were identified (35 autopsy, 2301 cytology, and 4556 surgical pathology). All autopsy and cytology addenda contained information which was deemed supplemental to the original report without conflicting with it. In surgical pathology, 31 addenda (0.6%) represented either a change in information from the original report or a significant omission. Of these 31 addenda, 7 were deemed to be contradictory to the original diagnosis; 30 contained information that potentially changed patient management and 29 altered prognostic information. Reasons for issuing the addenda included immunohistochemical studies, omitted key information in the original surgical pathology report, findings on deeper H&E sections, findings on decalcified sections, and histochemical special stains. 8 out of the 31 reports were issued by a single pathologist (in a department of 18).
Conclusions: While the vast majority of addendum reports are truly supplemental in nature, there is a subset which contains important information that needs to replace some components of the original surgical pathology report. It is noteworthy that many of these reports were necessary because Pathologists signed out reports before receiving all slides/special stains associated with the case. Educational efforts should focus on 1) reviewing all sections/stains prior to issuing the final report, and 2) defining when an amendment is necessary to provide clarity and ensure patient safety.

2064 Determining the Prevalence of Pre-Operative Anemia in Elective Orthopedic Surgery Patients: A Quality Improvement Initiative

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Background: Patients undergoing elective total knee arthroplasty (TKA) or total hip arthroplasties (THA) are often highly transfused. In our hospital patients undergoing either TKA or THA are routinely crossmatched for 2 RBC units. Pre-operative anemia is a risk factor for allogeneic red blood cell (RBC) transfusion, although the prevalence of anemia in pre-operative orthopedic surgery patients is unknown. As part of a quality improvement project under the auspice of the hospital's blood management program we determined the prevalence of pre-operative anemia in elective TKA and THA patients.
Design: The OR schedules were reviewed over a 6 week period to identify elective TKA and THA patients. Elective surgery was defined as non-traumatic cases where the patients had been admitted to the hospital <24 hours before the procedure. Basic patient demographics were obtained from the hospital's electronic medical records. Anemia was defined using the WHO's criteria of <13 g/dl in adult men and <12 g/dl in non-pregnant adult women.
Results: There were 62 patients who underwent elective surgery performed by 6 different surgeons; 37 (60%) had first time or redo TKR, while 25 (40%) had first time or redo THR. The average age of the 62 patients was 64.6 (±9.6) and 33/62 (53%) were female. Overall there were 6/62 (9.7%) patients who were anemic before their surgery. The anemic patients had an average pre-operative Hb level of 10.6 (±1.2) g/dl compared to 14.2 (±1.1) g/dl amongst the non-anemic patients ($p<0.0001$). Of the anemic patients 4/6 (67%) received at least 1 RBC unit in the peri-operative period, compared to 8/56 (14%) of the non-anemic patients ($p=0.01$). The relative risk of requiring a peri-operative RBC transfusion was 8.3x (95% CI: 1.7 – 40.3), higher in the anemic patients compared to the non-anemic patients. One THA patient who was not anemic before surgery was transfused with an autologous RBC unit on the day of surgery. There was also a trend towards longer hospital length of stays (LOS) in the anemic compared to the non-anemic patients: (4.2 (1.6) days vs. 3.2 (0.99) days, respectively ($p=0.12$)).
Conclusions: In this small cohort, the patients who were anemic before surgery had a higher incidence of receiving a peri-operative allogeneic RBC transfusions and a trend towards longer hospital LOS. Interventions that reduce pre-operative anemia would be expected to improve patient safety by reducing the need for transfusions and decreasing LOS.

2065 The Impact of Immunohistochemistry on Turn-around-Times in Surgical Pathology Reporting

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Background: Rapid turn-around-times (TAT) in surgical pathology are important for optimal patient management. The College of American Pathologists mandates a two-day TAT in over 80% of routine cases. However, immunohistochemistry (IHC) that is often required prior to rendering a diagnosis may potentially increase TAT. To our knowledge, there has not been any systematic analysis of the impact of IHC on TAT. We analyzed the effect of performing IHC on TAT in cases with a diagnosis of dysplasia or carcinoma.
Design: We searched the pathology database of a tertiary care teaching hospital to identify all cases with a diagnosis of dysplasia or carcinoma in a one-year period. TATs were noted for each case and then cases were classified based on whether or not IHC had been performed. Cases were also analyzed by type of specimen (resection vs. biopsy) and by organ system/site. Data was tabulated and analyzed.
Results: A total of 940 cases with a diagnosis of dysplasia or carcinoma were included for study. Most cases were from the genitourinary tract (GU) (308 cases), followed by lower gastrointestinal tract (GIT) (306 cases), lung (192 cases) and upper GIT (134 cases). IHC was performed in 249 (26%) cases. IHCs were performed more frequently in lung (87/192, 45.3%) and upper GIT (59/134, 44%) specimens than in lower GIT (70/306, 22.9%) and GU (33/308, 10.7%) specimens. The average TAT for all cases was 3.12 days, with TAT being significantly higher in cases with IHC (4.11 days) than in those without IHC (2.76 days). IHC increased TAT in both surgical resections (5.17 days with vs. 3.49 days without IHC) and in biopsy specimens (3.05 days with vs. 1.85 days without IHC). TATs with and without the use of IHC by organ system were GU 4.24/2.95, lung 4.25/2.87, lower GIT 4.34/2.56 and upper GIT 3.56/2.53. All the pairs analyzed showed statistically significant increases in TAT following use of IHC ($p<0.05$). When IHC was used, 80% of samples had a TAT of 3.15 days (2.29 days for biopsy specimens and 4.11 days for surgical resections).
Conclusions: The use of IHC significantly increases TAT in both surgical resection and biopsy specimens with a diagnosis of dysplasia or carcinoma. Our data potentially provides a useful benchmark for additional time required for IHC. Since many specimens require IHC prior to issuing a surgical pathology report, similar studies from other institutions will help evolve TAT recommendations for specimens requiring IHC.

2066 Cytohistologic Correlation of Thyroid Lesions: The Effect of the Bethesda System for Reporting Thyroid Cytopathology

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Background: Fine needle aspiration (FNA) is commonly used in the evaluation of thyroid pathology. This study correlates thyroid FNA cytology results with subsequent histopathologic diagnoses and compares correlation rates pre- and post- implementation of the *Bethesda System for Reporting Thyroid Cytopathology.*
Design: We reviewed all thyroid FNAs performed at a large academic medical center between 01/2006 and 09/2011 and identified patients that underwent subsequent surgical resection. The *Besthesda System for Reporting Thyroid Cytopathology* was implemented in 2010.
Results: Over a 5.75 year period, 156 patients underwent thyroid FNA and subsequent resection. Overall, cytohistologic correlation was achieved in **73%** (114/156) of patients. Of the 42 cases with cytohistologic disparity: 15 follicular adenomas were called benign(7), suspicious for papillary thyroid carcinoma (PTC)(4), or unsatisfactory(4) on preceding FNA; 10 PTCs were called benign(2), AUS/FLUS(2), follicular neoplasm(3), or unsatisfactory(3); 13 benign lesions were called FLUS(1), suspicious for follicular neoplasm(1), follicular neoplasm(1), suspicious for PTC(3), or unsatisfactory(7); 2 follicular carcinomas were called either FLUS or benign; 1 poorly-differentiated carcinoma was called medullary carcinoma; and 1 leiomyosarcoma was unsatisfactory on FNA.
Cytohistologic correlation pre- and post-Bethesda implementation was **71%** (77/109) and **79%** (37/47), respectively. Pre-implementation, 32 cases showed cytohistologic disparity: 8 cases called benign on FNA showed follicular adenoma(6), follicular carcinoma(1), or PTC(1) on subsequent resection; 12 unsatisfactory FNAs were benign(5), follicular adenoma(4), or PTC(3); 4 cases called follicular neoplasm were PTC(3) or benign(1); 1 case called suspicious for follicular neoplasm was benign; and 7 cases called suspicious for PTC were follicular adenoma(4) or benign(3). Post-Bethesda implementation, 10 cases showed disparity: 2 cases called benign on FNA showed either follicular adenoma or PTC on subsequent resection; 3 unsatisfactory FNAs were benign(2) or leiomyosarcoma(1); 4 AUS/FLUS on FNA were follicular carcinoma(1), PTC(2), or benign(1); and 1 case called medullary carcinoma on FNA showed poorly-differentiated carcinoma histologically.
Conclusions: Thyroid FNA cytology and subsequent histopathologic diagnoses correlate well overall, with modest improvement post-Bethesda implementation. In our setting, the high prevalence of thyroid pathology and the well-defined Bethesda criteria thereof will likely further improve cytohistologic correlation rates over time.

2067 Intraoperative Thyroid Frozen Section Consultation: A Continued Quality Dilemma and Monitoring Need

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Background: The use of frozen sections (FS) on the thyroid is controversial. Most of the FS on thyroid are non-contributory since fine needle aspiration biopsy usually guides surgical procedures. However, many surgeons continue to request thyroid intraoperative consultation. Our goal was to investigate the prevalence and value of FS on resected thyroids within our institution in patients who had already undergone fine needle aspiration (FNA) and to determine whether or not the use of FS provided any diagnostic or therapeutic value.
Design: We gathered the reports of all patients with thyroid FNA and subsequently resected thyroid over a 24 month period within two institutions of our service. Patients were separated into two groups; those whose surgeons requested FS and those who did not. Among these groups, patients were categorized by age, gender, cytology diagnosis, final diagnosis, and specialty of surgeon. Those receiving FS were assessed for major discordances. Major discordance was defined as an intraoperative diagnosis of a benign lesion with a final diagnosis of malignancy, or vice versa.
Results: 211 patients over a 24 month period received thyroid FNA and subsequent resections (171 female and 40 male patients). Mean age for both genders was 49 (range 16 to 84). Three types of surgeons were identified in the study; endocrine, otolaryngology, and general. There were 78 resected thyroid for which FS were performed; 16 had major FS discordances (20.5%). 16 of 16 discordances were diagnosed as benign on frozen section and were found to be malignant on permanent sections (14 papillary carcinoma; 2 follicular carcinoma). Of the cases with discordance, the cytology diagnosis were as follows: 8 benign, 5 suspicious, 2 malignant, and 1 indeterminate. All FS for which the pathologist made a diagnosis of malignancy maintained concordance on permanent sections. 92% of surgeons requesting FS were otolaryngologists, 4% were endocrine, and 4 % were general. Of the surgeons who did not request FS 35% were otolaryngologists, 28% were general, and 37% were endocrine.
Conclusions: Otolaryngologists were far more likely to request FS on thyroid specimens than other surgeons. FS on thyroid glands had an extremely high rate of discordance (20.5%). In all cases of discordance, the FS did not contribute to the final diagnosis or give any additional information as compared to the FNA. Our study serves as a reminder of the ineffectiveness of FS on thyroid. Ineffective FS leads to unnecessary allocation of valuable time and resources as well as increases operative time.

2068 Eye-Tracking Experiments Underscore the Bias That Architecture Exerts on Nuclear Grading in Prostate Cancer

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Background: We recently described that nuclear grade assignment of prostate carcinomas is subject to a cognitive bias induced by the architectural organization of the tumor.

Design: Here, we asked whether this bias is mediated by the unconscious selection of nuclei that "match the expectation". 20 pathologists were asked to grade nuclei in high power fields of prostate carcinomas on a computer screen, superimposed over a low power image of the tumor architecture. Unknown to the subjects, each carcinoma was shown twice, once before a background of a well-differentiated, tubule-rich carcinoma and once before the background of an undifferentiated, solid carcinoma. Eye tracking allowed to identify which nuclei the pathologists fixated on during the 8 second projection period.

Results: Nuclear grade assignment was significantly biased by the architectural differentiation of the tumors. "Gravitation" of nuclear grades towards the architectural grade depended on the magnitude of the architectural grade difference of the background images, but not on the experience of the pathologists. Most pathologists tended to fixate on bigger or darker nuclei when high power fields were projected before background images of undifferentiated, solid carcinomas *and vice versa.* However, the morphological differences of the thus selected nuclei accounted only for about 11% of the total bias induced by the tumor architecture.

Conclusions: We conclude that the selection of " matching nuclei " represents nothing but an unconscious effort to vindicate the bias induced by the architectural growth pattern.

2069 A Comparative Study of Tissue Microarray (TMA) Versus Conventional Immunohistochemistry (IHC) for Evaluation of Mismatch Repair (MMR) Systems in Colorectal Cancers (CRCs)

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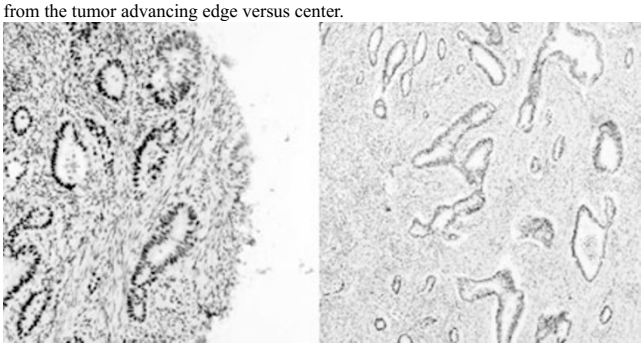
Background: 15–20% of CRCs show microsatellite instability (MSI), a subset associated with better outcomes, poor response to 5-FU and includes Lynch Syndrome. Whole slide (WS) IHC for MMR proteins (MLH1, MSH2, PMS2, MSH6*)* is popular, however TMA is a cost effective option which allows for high throughput analysis and may be a viable option as institutions adopt universal screening. Little is known about optimal sampling when constructing a TMA. We evaluated concordance rates between WS IHC and TMA and explored the effect of TMA core sites (center versus advancing edge) on concordance.

Design: MMR protein expression was analyzed in 52 unselected cases of primary CRC, first by WS IHC and then by TMA on the same block. TMA included four (1 mm) cores per case, two from the center and two from the advancing edge. Staining was graded as positive, negative (absence of tumor nuclear staining with concurrent positive labeling of surrounding normal tissue) or equivocal (indeterminate staining pattern, insufficient tumor for evaluation).

Results: Of the 52 cases, 36 (69%) stained positive for all proteins, 14 (27%) had concurrent loss of MLH1 and PMS 2 and 2 (4%) had concurrent loss of MSH2 and MSH6 by WS examination. Comparison of WS versus TMA showed an overall concordance of 96%, 98%, 96% and 98% for MLH1 (see figure with TMA on left and WS on right), MSH2, MSH6 and PMS2 respectively, with only 4 discordant cases. Features associated with discordance included weak patchy staining of MSH6 and MSH2, background lymphocytes obscuring interpretation, and inadvertent coring outside the tumor area. No improvement in staining was found between cores taken from the tumor advancing edge versus center.



Conclusions: MMR protein expression by TMA yields comparable results to that of WS IHC and thus may be feasible for diagnostic purposes in a clinical practice setting. While studies have suggested the advancing tumor margin may be more consistently immunoreactive compared to the tumor center, we found no difference in concordance between these locations. In fact, cores taken from the tumor periphery were more likely to miss the tumor and better results may be obtained from the tumor center or combining center and advancing edge.

2070 Diagnoses Rendered by Whole Slide Imaging (WSI) Alone Are Accurate for Use in a General Surgical Pathology Practice

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Background: Whole Slide Imaging (WSI) holds promise for supporting many of the functional requirements of a general surgical pathology service. Multiple recent studies have described applications for pathology education and training, distant consultation and general diagnostic use. Several validation studies have been conducted to date. However, their data sets have either been limited or highly focused on single organ/tissue types and have not established equivalence between WSI and light microscopy (LM) for general diagnostic purposes. The purpose of this study was to determine the diagnostic concordance between pathologic interpretations using WSI and LM in routine surgical pathology practice with a broad array of tissue types and cases.

Design: 215 consecutive previously signed out surgical pathology cases were included in the study. A broad array of case types and tissue sources was represented. All slides from each case were scanned (digitized at 20x) and presented to two senior pathologists (who had not seen any of the cases previously in any format) for diagnosis using WSI as the sole diagnostic tool. Diagnoses rendered by WSI were compared to the original LM diagnoses (recorded in archival surgical pathology reports) and concordance determined by a third senior pathologist.

Results: Concordance between WSI and LM was 98% and concordance between the two WSI pathologists was 99%. Five (5) cases were determined to have discordant diagnoses, two of which were clinically significant, between those recorded using WSI and archived LM diagnoses. Discordant cases resulted from interpretive criteria or diagnostic error whereas the WSI modality did not contribute to these diagnostic differences. Problems encountered by the pathologists were primarily related to the inability to clearly visualize microscopic details at higher power due to poor digital magnification of the 20x slide scans and difficulty in digital image navigation. Advantages of WSI noted include the ability to visualize a very low power image (lower than that provided by LM), ease of measurement using the built in scale and the comfort of viewing slides from any place.

Conclusions: This study supports the use of WSI in general surgical pathology. Improvements in image navigational ability and clarity in visualization of microscopic detail at higher power would help in further advancing the adaptability of this method to a general surgical pathology practice.

2071 Genetic Markers of Cancer – A Molecular Oncology Laboratory Adjusts to Changing Demands of Integrated Hospitals, Medical Centers and Outreach Services

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Background: Molecular oncology testing is exponentially increasing to aid in diagnosis and targeted therapy. In complex, budget limited health systems molecular labs are under pressure to cut costs. To align with our system's goal of integration and consolidation we aimed to re-examine and streamline already existing work processes and pathways to reduce waste due to lack of understanding, miscommunication, missing information, and miss delivered specimens. The ultimate goal is to provide timely and seamless service to our customers with zero defects.

Design: Following the specimen trail we focussed efforts on 1) Increasing clinician awareness of test availability and specimen requirements (lectures, consultation, information brochures, internet resources); 2) Educating nursing, laboratory, administrative personnel by a) clearly defined standard processes (value stream maps, written instructions, internet links); b) monitoring different sites for test requisition completeness and specimen acceptability; 3) Establishing contact with leadership at off site locations; 4) Expanding already existing processes to include remote locations (TAT monitoring; provision of special blood collection tubes); 5) Reinforcing lab's commitment to superior customer service and LEAN practices (refresher training).

Results: Clinician awareness was shown by increased utilization of our test menu with appropriate test selection (e.g. vIII EGFR vs EGFR exon 19/21 mutation), and reduced phone call/E-mail questions. There was 80% decrease in missing information (ICD9 codes, clinical information). Process flow maps facilitated tissue selection (tumor in block, little/no necrosis) making >90% of specimens acceptable for testing. LEAN practices reduced delay in processing from 31% to 5% in the past 2.5 years even when specimens needed to arrive from different sites and through different pathways. Although volumes increased by about 20% per year our TATs remained constant at 2 to 3 business days (vs the industry standard of 7-14 days).

Conclusions: Correct test ordering and timely specimen delivery often necessitate collaboration with individuals separated by geography, leadership structure, and educational levels. By taking initiative, our laboratory has ensured that latest developments in molecular oncologic testing quickly translate into benefits to cancer patients. By eliminating non-value added waste we have been able to maintain record short turn around times even with increasing testing volumes and new hospitals and medical centers being integrated into our health system.

2072 Standardized Prosection Protocol Increases Detection Rate of Positive Circumferential Margins in Whipple Specimens

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Background: Adenocarcinoma of the pancreas has a dismal prognosis, with high recurrence rates even when surgical margins, including circumferential resection margins (CRM), are reported negative (R0). In the literature, reported rates of microscopically positive margins (R1) vary widely and are often lower than recurrence rates, raising the question of R1 disease being classified as R0 due to sampling error. The traditional protocol (TP) for prosection of pancreatoduodenectomy (Whipple) specimens included

an *X* section through the duodenum, pancreatic duct, and common bile duct for tumor visualization, gross assessment of the margin status, and radial or en face *sampling* of the CRM based on prosector judgment. A newer standardized protocol (SP) is performed by serially sectioning the entire pancreatic head and peripancreatic fat perpendicular to the opened duodenal segment and completely embedding the sectioned tissue surrounding the tumor for complete radial assessment of the CRM. The aim of this study is to evaluate whether the new SP increases detection of R1 disease.

Design: Whipple cases diagnosed as adenocarcinoma arising in the pancreatic head or ampulla were evaluated; 115 consecutive cases (predominantly since divisional protocol change Oct 2009) were included in the SP group; consecutive Whipple specimens following the TP from the prior year were the comparator group (n=70). Cases with surgically evident positive margins (R2), non-adenocarcinoma cases, and primary common bile duct or small bowel (excluding ampulla) were excluded from both groups. The surgeons for both groups were the same. Positive circumferential margins, defined as carcinoma ≤1mm from inked margins, were tallied by site (posterior, portal vein groove, uncinate) and compared using Fischer's exact test. The total number of blocks submitted for each Whipple specimen was also recorded and the mean number of blocks for SP and TP was calculated and compared using student's t test.

Results: The TP group had 22 cases with at least one CRM positive for tumor (31.4%) while the SP group had 57 cases with at least one CRM positive (49.6%) (p=0.02). On average in the TP group, 23.4 blocks were submitted per Whipple and, in the SP group, 42.8 blocks were submitted (p=0.0001).

Conclusions: Evaluation of entire circumferential resection margins CRM in radial sections increases detection rate of R1 disease in a statistically significant fashion. The radial assessment of all margins increases the number of blocks submitted by nearly two-fold.

2073 Retrospective Blinded Review of Major Errors in Anatomic Pathology: Experience of a Tertiary Care Facility

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Background: Quality control and quality assurance are integral to the practice of Anatomic Pathology, a discipline in which it is difficult to define criteria's for evaluating these parameters. This study is focused on pathologist's interpretational diagnostic errors. We present a unique model of quality assurance in which the pathologists in the department perform a blinded review of major discrepancies which served to heightened awareness of patient consequences and reduce the number of errors.

Design: All types of errors including false positive/false negative and any error which was of clinical consequences were included in the study. The cases were blinded and given numeric designation. All pathologists were required to review the pertinent slides with the same information that was available to sign out pathologist. Based on the pathologist's consensus opinions, a final performance improvement report was generated. Impact on patient management was considered significant if error necessitated second surgery or an inappropriate surgery was performed because of incorrect diagnosis. Also, delayed treatment resulting from inappropriate diagnosis was considered as significant. If the diagnosis was corrected within short time frame and there was no change in management, the error was considered to be clinically insignificant.

Results: There were a total of 303 cases over the past 18 years. The cases were divided into various subspecialties and source of error (frozen section or permanent section) was noted.

Comparison of key features between two time periods

	1993-2001	2002-2010
Total errors	230/ 189515 (0.12%)	73/221112 (<0.01%)
Frozen interpretative errors	129	48
Errors on non frozen section cases	101	25
Significant patient consequences	31	15

Distribution of cases divided as per subspecialities

Subspeciality	cases no (%) [1993-2001]	cases no (%) [2002-2010]
Bone and Soft tissue	33 (14.4)	8 (10.9)
Neuropathology	19 (8.3)	4 (5.5)
Breast	36 (15.6)	14 (19.2)
GI	19 (8.3)	10 (13.7)
GU	20 (8.7)	5 (6.8)
GYN	38 (16.5)	11 (15.1)
Head & Neck	50 (21.7)	10 (13.7)
Thoracic and Pulm	15 (6.5)	11 (15.1)
Total	230	73

Conclusions: This study highlights the positive impact of systematic review in reducing pathologist's interpretational error and in identifying potential sources of error. Anonymous review process encourages active participation. To conclude, besides the routine quality control and assurance parameters, these cases can be used as an objective tool for monitoring professional competency and provides objective criteria for performance improvement for pathologists.

2074 Academic and Non-Academic Laboratories Perform Equally on CIQC Immunohistochemistry External Quality Assessment

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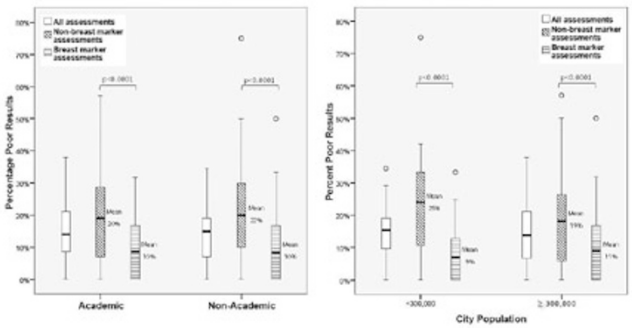
Background: Expertise in medicine tends to concentrate in academic institutions in larger cities. Quality of laboratory testing may be expected to follow this trend. We hypothesize that academic centers (AC) are more successful than non-academic centers (NAC) in immunohistochemistry (IHC) external quality assessment (EQA) challenges in the Canadian IHC Quality Control (CIQC) program, an EQA program supported by the Canadian Partnership Against Cancer.

Design: Results of 9 CIQC challenges for ER, PR, Her2, CD45, CD20, CD3, cyclin D1, Bcl-2, Bcl-6, Ki-67, pankeratin, LMWK, HMWK, CK7, CK20 and CK5 were examined. Performance on breast marker tests (BT) was assessed based on concordance to reference values. Performance on other tests was assigned a 3 or 4-tier score ranging from optimal to poor by expert assessors based on preestablished criteria for each test. For this study, these results were converted to a binary result (poor/good) as follows: for BT, <90% concordance=poor, ≥90%=good; for non-BT, lowest tier score=poor, all other scores=good. AC were compared to NAC, and labs located in a small city (pop. <300,000) were compared to those located in a large city (pop. ≥300,000).

Results: A total of 66 Canadian and 8 foreign labs, of which 33 (45%) were AC and 48 (65%) in large cities, participated in at least one CIQC test. The number of participants in each test ranged from 17 to 53. There was no difference in performance on any test compared to AC/NAC nature or city size. However, overall performance on BT was significantly better (p<0.0001, Student's t-test) than on non-BT regardless of AC/NAC nature or city size, with the mean value of poor results on non-BT being approximately twice that of BT.



Conclusions: AC and NAC irrespective of city size were equally successful in CIQC EQA challenges, suggesting that expertise in IHC can be achieved in many types of labs. However, performance on BT was significantly higher than on non-BT in every category, suggesting that emphasis on breast hormone IHC quality assurance in recent years has led to improved results.

2075 Quality Assurance Impact of Diagnostic Discrepancies

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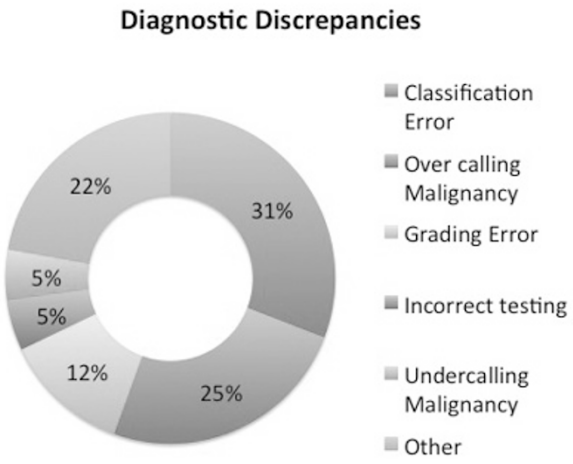
Background: The landmark Institutes of Medicine report, 'Too Err is Human', launched a successful decade of patient safety initiatives and seeded an emerging discipline dedicated to studying diagnostic error, an important, but overlooked aspect of patient safety. We set out to observe how pathology processess, at the inter-institutional transfer of care, can contribute to reductions in patient harm. Understanding discrepancies, in relation to the clinical context, should suggest relevant areas for process optimization.

Design: Patient's transferring care to Stanford are required to have their slides reviewed prior to undergoing treatment. We compared 773 diagnoses spanning a four month period by constructing a relational database, SPIDeR (Stanford Pathology Inside/ Outside Database Review tool), containing scanned PDF of outside reports, and the corresponding diagnosis and comment fields from the pathology database. We examined:the number of diagnostic procedures submitted with the referred material, size and practice type of the originating institution, organ system, diagnosis, prior second opinion, type of outside testing, additional ancillary studies and the clinical significance and reason for disagreement.

Results: We found that 9% of cases had a discrepancy in diagnosis, when comparing the initial working diagnosis to the second opinion (subject to revision pending resolution of diagnostic changes of uncertain signficance). In 3% (n=21) of cases a major discrepancy, expected to alter treatment, was identifed. Significant differences in discrepancy rates were found between organ systems (p<0.01) although discrepancies were identified in nearly all major organ systems. Gynecologic cases had the highest rate of discrepancy at 37%, dermatology cases 26%, and genito-urinary cases were 19% discrepant. The most common reason for a discrepant diagnosis was disagreement about classification.



73% of the referred cases represented a single procedure, 25% represented 2-3 different procedures. Additional testing was performed on 10% of the cases, and 5.4% of the cases had already been seen by a second consultant.
Conclusions: Diagnostic review generates a significant amount of discrepancy and impacts clinical management. Discrepancies are more common in some case types but may not provide reliable predictors to pre-select cases for review.

2076 Implementation of Lean Methods To Improve Histotechnology Productivity

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Background: Lean methods have been increasingly incorporated into healthcare institutional strategies to maximize efficiencies, improve financials, and reduce error. We examined the effectiveness of these methods in improving the productivity of histotechnology services.
Design: We evaluated the turn-around times (TAT) for the processing of surgical tissue blocks over a 5 month period. To affect a reduction in the backlog of uncut blocks and to achieve a 24 hour processing TAT, we employed Lean methods, including creating a visual workplace; 5S of the laboratory; introduction to Toyota work principles; workspace redesign and standardization; employee engagement in work redesign; and assessment of task staffing requirements. Lean Implementation specialists performed root cause analysis to investigate methods of reducing TAT. Pathology residents instituted quality improvement studies to identify areas of over-blocking of surgical specimens.
Results: Initially, we found a backlog of 1989 surgical specimen blocks. Productivity of technologists ranged from 30 slides per day to 150 slides per day with a staff of 14 FTEs. Within the first month, the 5S of the lab created four additional cutting stations that produced a more conducive work area. Employee education encouraged participation from the frontline staff in the evaluation of factors contributing to the backlog of work and in workspace standardization. Reassessment of task staffing requirements removed technologists from 2 assignments that were transferred to laboratory assistants thereby freeing up additional time to cut blocks. Improvement specialists created a visual workplace with daily productivity numbers for the cutters as well as graphs indicating the number of blocks received, in arrears, and cut for the week. Unscheduled absences, as well as the revocation of overtime, were addressed with personnel in an attempt to change the culture of non-attachment to job responsibilities. Pathology residents' quality improvement studies identified areas of over-blocking for placentas, fibroids, and submission of specimens deemed unnecessary for pathologic review. Within the five month period the entire backlog was erased and a 24 hour TAT maintained. Productivity of technologists increased to 80 - 165 slides per day.
Conclusions: We showed that the application of Lean methods resulted in increased productivity. The involvement of front line staff in work redesign created a culture of process ownership. The performance of quality improvement studies and root cause analysis resulted in increased efficiency.

2077 Enhancing Patient Safety through Multi-Departmental Perioperative Surgical Specimen

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Background: Perioperative specimen safety is a focus of proposed standardized processes defined by the World Health Organization Guidelines for Safe Surgery and Association of Operating Room Nurses. Patient identification the #1 national patient safety goal and is addressed by Pathology accrediting bodies. The Michigan Hospital Association Keystone Surgery Initiative is a statewide collaborative of 85 hospitals focused on benchmarking and sharing best practices to increase perioperative patient and specimen safety and quality.
Design: This is the experience of multi-disciplinary teams from Pathology and Surgical Services at Henry Ford Hospital, Detroit in solving specimen safety issues as participants in the statewide collaborative. Using a data-driven PDCA approach to testing interventions through the Henry Ford Production System LEAN quality initiative, we assessed measures of defective labeling and handling of specimens, requisitions, containers over 18 months with a standardized data input tool. We captured failures to provide required information elements on each specimen requisition and container received by Pathology from main hospital operating rooms. Numerous sources of defects of specimen labeling and handling were then targeted by interventions and the effect measured.
Results: Data collection period: January 2010 through September 2011
Interventions tested: 1) regular customer-supplier meetings between OR and Pathology, 2) specimen handling training video for OR surgical services staff, 3) education of surgeons on WHO perioperative read-backs, 4) targeted daily pathology interventions, 5) OR TV to educate surgeons at scrub-in, 5) specimen labeling stations in each OR to standardize handling and labeling pathways for specific specimen streams to include routine, frozen scetion, lymphoma, lung and microbiology tissue samples.
Daily defect data collected:
Surgical requisitions (average 700/month)- January 2010- 7 defects, September 2011- 3 defects
Containers (average 1400/month)- January 2010-15 defects, September 2010- 0 defects
Specimens (average 670/month) January 2010- 19 defects, September 2010-3 defects
Interventions resulted in an overall 84% reduction in specimen defects.
Conclusions: The success in targeting specimen safety is attributed to the team approach to standardizing the numerous specimen hand-offs. The data-driven PDCA approach to monitoring defects and changes is effective in driving and sustaining interventions to ensure that processes are maintained and followed. This also requires ongoing education and support of all in an effort to achieve a zero defect goal.

2078 A Web-Based Tracking System to Facilitate Transfer of Patient Care between Residents in a Multi-Site Academic Anatomic Pathology Department: A Solution to JCAHO and ACGME Mandates for Optimizing Patient "Handoffs"

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Background: Transfer of patient care from one provider to another carries a risk for introducing error, delay, or suboptimal quality of care. These risks are compounded in a training setting where resident-physicians rotate frequently between different patient care services. Recently, both ACGME and JCAHO have mandated hospitals to enact patient care transfer procedures that incorporate both verbal and written communication between the transferring and the receiving physician. We developed a web-based, automated tracking system to facilitate patient handoffs in a multi-site, multi-rotation, academic anatomic pathology department.
Design: The system is a HIPPA compliant web-based Handoff Portal that tracks all incomplete cases on the last working day of each month in our training program's 3 hospitals, including a tertiary care hospital, a county hospital and a Veteran's Administration hospital. Incomplete cases can be organized by resident (transferring or receiving), faculty, specimen number and category of pending issues. The pathology information system at the cancer hospital was programmed to automatically upload these variables from incomplete cases into the Handoff Portal system. At the other hospitals, the variables were manually entered by the transferring resident. On the last working day of each month, the transferring resident confirms their incomplete case data, the receiving resident reviews the list online, and then a verbal discussion occurs. These actions are tracked online with compliance measured by the percentage of total trainees who completed a handoff at the end of the month via both written and verbal documentation.
Results: Since July 1, 2011, the system has been used to track handoffs at the end of each of three 1-month rotation cycles involving 12 rotations at 3 hospitals. A total of 451 cases to be handed off by 28 trainees were tracked. Over the initial 3 months the compliance rate was 93%, 93%, and 86%. Non-compliance trended toward the more senior trainees, in particular, fellows.
Conclusions: A web-based tracking system can facilitate transfer of patient care between residents at the end of rotations. Although automated data entry by linkage to the existing pathology information system reduces labor on residents, the handoff itself represents a system and culture change which may not be as readily adopted by senior trainees. Further study into benefits for turnaround time and quality assurance are needed.

2079 Building a Center of Excellence in Hematopathology: Review of CNB and FNA Samples To Improve the Current Workflow

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Background: Increased clinical demand to diagnose lymphoma from core needle biopsy(CNB) and fine needle aspiration(FNA) samples requires collaboration between radiologists, cyto- and hematopathologists to ensure collection of adequate sample and triage for ancillary studies. No criteria for adequacy are available and the sequence for best tissue retrieval and workflow is not well defined. As part of our performance improvement, we reviewed our work to identify quality gaps and points of intervention to increase the diagnostic accuracy of lymphoma.
Design: Review of 2010-2011 electronic data identified 108 CNB and FNA samples for involvement by lymphoma. Excluded from this study were bone marrow biopsies and metastatic carcinomas; included were samples from superficial and deep seated masses/organ lesions. When available, we reviewed pathology and radiology reports for history, location, quantity of sample collected, flow cytometry, accuracy of correlation between intraoperative cytology interpretation and final diagnosis and/or follow-up resections. Findings were assessed by our radiologists, cyto- and hematopathologists to develop/apply an improvement plan.
Results: 24% of cases had prior history of lymphoma; others were from patients with lymphadenopathy. Most samples were superficial (65%) and the number of cores varied (3-multiple). The needle gauge used was 19-20. In 47 cases, flow samples collected as CNB were diagnostic in 31%. Out of 61 flow samples collected as FNA,

67% were diagnostic. The diagnosis was established in 93/108 cases (86%) and 5/15 nondiagnostic samples had lymphoma on surgical follow-up. Intraoperative consultation by cytopathologists was performed in 104/108 cases and correlated with final diagnosis in 72% cases.

Conclusions: As a result of this review, we built a new requisition for clinical history documentation of lymphoma and CBC. Marked difference in flow-cytometry results where FNA rather than core biopsies were submitted required a new lymphoma biopsy protocol in Radiology. Flow cytometry samples by FNA will be collected first, followed by a CNB using a larger needle gauge(18). In Cytology, verification for adequacy on flow sample in addition to core biopsy touch preps was implemented, and a transfer policy of cases between cyto- and hematopathology staff was created. In Histology, separating core biopsies in 2 blocks was done to secure more tissue for ancillary studies. The effect of the implemented measures will be assessed early January 2012.

2080 Effectiveness and Efficiency in the Evaluation of Pathological Specimens of Limited or No Clinical Value

TR Finch, HS Currens, SS Raab. Memorial University, St. John's, NL, Canada.

Background: In Canada and the United States, many anatomic pathology laboratories do not process or perform gross-only examinations of specimens of limited or no clinical value. The impact on laboratory resources, time, and cost for examining these specific specimen types are theorized to be significant, although this has not been studied.

Design: We evaluated the clinical significance and the efficiency of processing and examining specimens of limited or no clinical value in our tertiary hospital-based Canadian laboratory. We considered 5 specimen types as not requiring submission or gross examination (e.g., aneurysm contents and teeth) and 8 specimen types as requiring gross examination only (e.g., hernia sacs and intervertebral discs). We measured the number of blocks submitted for each specimen type, non-pathologist workload units as a quantifier of laboratory resource utilization (each unit represented one minute of time and $2.65 Canadian), and clinical significance of pathologist final tissue diagnosis.

Results: We processed 274 specimens that generally did not require laboratory submission at a cost of $24,645 and 155 laboratory work hours. We processed 577 specimens that generally required a gross-only examination at a cost of $64,802 and 406.8 laboratory work hours, of which 99.8 hours and $15,872 was spent on block submission. Revision of specimen processing for specimens of limited or no clinical value could potentially save our institution 254.8 laboratory work hours and $40,517 per year. Of the 13 specimen types studied, processing tonsil and adenoid specimens demonstrated the most significant impact on laboratory resources with 307 blocks, 134.6 laboratory work hours, and a cost of $21,399. One incidental dysplastic nevus was found within an abdominal pannus specimen, otherwise there were no other unexpected critical diagnoses. In the tonsil group, we found 6 malignant cases, all with at least a suspicious for malignancy clinical history.

Conclusions: Our findings indicate that tissue block submission and gross examination of specimens generally considered of limited or no clinical value resulted in increased laboratory inefficiencies and costs. If clinicians provide pertinent clinical patient history, lab personnel could perform no or gross-only examination with considerable cost savings and without a sentinel event.

2081 Accuracy of the Measured Depth of Histologic Sections Compared to the Gross Specimen Measurement

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Background: Tissue processing by histology labs is a complicated process, involving replacement of water with a tissue-solidifying medium to allow thin sections to be cut and mounted onto glass slides. This process has the potential to alter tissues. To our knowledge, no previous study has evaluated factors potentially associated with changes in tissue dimensions during processing.

Design: We prospectively analyzed 120 skin specimens with a minimum excisional depth of 0.5 cm. We measured the depth from superficial epidermis to deepest point of: 1) intact gross specimen (gross-I), 2) deepest gross section after sectioning (gross-S), and 3) histologic section of the corresponding tissue block mounted on a glass slide (hist-D). Change in dimension (CID) was calculated as the difference between hist-D and gross-S. These measurements were compared with patient sex, age, anatomical location [head/neck (H/N), trunk or extremity], and technologist. Comparisons were made with Pearson correlation coefficients, t-tests, Kruskal-Wallis rank tests and ANOVA.

Results: Mean patient age was 56 (±17.8). Trunk was the most common site (43%). There were 15 technologists, and each processed between 1 and 17 specimens. Mean gross-I and gross-S were not significantly different from mean hist-D (mean gross-I=8.4mm, mean gross-S=8.7mm, mean hist-D=8.6mm). The correlation coefficients between gross-I and gross-S with hist-D were 0.80 (95% CI: 0.72-0.86) and 0.85 (95% CI: 0.79-0.89), respectively (P<0.0001 for both). No difference in CID was found for sex (P=.21), age (P=0.79), or anatomic site (P=0.32). Specimens from the H/N category yielded smaller CID values (mean ranks: H/N 50.19, Upper Extremity 52.06. Lower Extremity 56.25, Trunk 60.89, Genital 93.50; global P=0.32). Gross-I and gross-S were both negatively correlated with CID, (rho=-0.27 (95% CI: -0.44, -0.91) and -0.29 (95% CI: -0.46, -0.12), respectively). The difference in mean CID between highest and lowest technologists was 3.55.

Conclusions: Processing of tissues for histological analysis is an intricate process with significant potential to change dimensions, and thus altering diagnoses and patient management. We found a negative correlation of both gross-I and gross-S with CID, implying that specimens with greater excisional depth and greater depth of deepest section undergo the least absolute change in size after processing. Age, sex, and anatomic site did not significantly influence the CID.

2082 Assessment of Gross Examination and Tissue Submission Practice in Hysterectomy Specimens with Leiomyomata

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Background: Gross tissue examination and block submission protocols of common specimens, such as hysterectomy specimens for leiomyomata, are often not-standarized in actual practice. We assessed currently used gross descriptors and number of submitted blocks for hysterectomy specimens with leiomyomata to measure current variability in practice and to establish a standardized protocol in order to improve quality.

Design: We conducted a one-year retrospective study to assess the gross description and tissue block submission practices for 175 hysterectomy specimens for leiomyomata. Gross examinations were performed by 4 residents and 3 pathologists assistants. We reviewed pathology reports using a standardized checklist to assess 5 standard internal leiomyoa gross descriptors (eg. number, size, color, texture, and hemorrhage/necrosis), circumscription status, and number of blocks submitted of leiomyomata. We performed descriptive statistics including measures of central tendency and dispersion.

Results: We found that only 5% of the leiomyomata had the 5 standard descriptors, 11.4% had 4 descriptors, 22.8% had 3 descriptors, 42.8% had 2 descriptors, and 17.0% had 1 descriptor. Description of the circumscription status was present in only 10.2% of leiomyomata. In single leiomyoma specimens, 15.7% had 3-4 submitted blocks and 13.5% had more than 5 submitted blocks submitted. We found that the number of submitted blocks per leiomyoma increased as the size of leiomyoma increased; for a large leiomyoma (> 10 cm) the number of blocks ranged from 15-19, without worrisome changes in gross descriptors. One-third of specimens with a single leiomyoma had more than 5 blocks submitted.

Conclusions: We found a lack of standardization and high variability in the use of gross descriptors in the examination of leiomyomata, with the majority of leiomyomata poorly described. Over blocking occurred in large leiomyoma specimens and in one-third of small single leiomyoma specimens. We conclude that a more rigous adoption of standardized grossing protocols for specimens with leiomyomata would improve quality and decrease laboratory inefficiencies.

2083 Whole Slide Imaging Validation Using Cervical Biopsies Yields Significant Interobserver Variability for Low Grade Dysplasias

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Background: Whole slide imaging (WSI) involves scanning glass slides to produce digital images, which may be viewed remotely. Validation requirements have not been adequately addressed, and there are no standard guidelines for validating WSI for diagnostic use in the laboratory. Furthermore, few studies address the utility of WSI in challenging specimens such as cervical biopsies for dysplasia, when high resolution is particularly critical for accurate diagnosis.

Design: Fifty (50) cases with cervical biopsies (103 total specimens) were imaged at 20x magnification using BioImagene iScan Coreo Au scanners. Two examiners then blindly and independently evaluated the WSI using image-viewing software (Virtuoso). The examiners were aware of prior Pap test results for all cases. The histologic diagnoses were then compared to the original glass slide diagnoses. All diagnoses were stratified as: Negative, HPV/CIN 1, CIN 2, and CIN 3.

Results: One hundred and three (103) scanned specimens were collected. Of these, 1 slide had not been scanned and 3 were lacking coverslips or were overstained. Of 200 WSI diagnoses made, no specimen originally diagnosed as high grade dysplasia was called negative. There were 33 minor discrepancies and 14 major (calling a positive finding "negative" or two categorical differences). Seven cases (6.8%) could have had different clinical treatment based on WSI interpretation: 5 cases of HPV/CIN 1 were upgraded to CIN 2/3 and 2 cases of CIN 2/3 were downgraded to HPV/CIN 1 by at least one observer. The overall diagnostic accuracy was 83.5%, using the original glass-slide diagnosis as the gold standard.

Original Diagnosis	Reviewer 1			Reviewer 2			
	Negative	HPV/CIN 1	CIN 2/3	Negative	HPV/CIN 1	CIN 2/3	N/A
Negative	36	9		32	12		1
HPV/CIN 1	3	42	2	10	31	5	1
CIN 2/3		1	7		2	6	

Conclusions: Although whole slide imaging offers a promising new tool for pathologists, validation can be challenging. Here we have shown that for cervical biopsies, where interobserver variability is known to be substantial using glass slides, it is difficult to disentangle the effect of WSI image quality from interobserver variability. We consider our results sufficient to validate WSI as being equivalent to glass slides, but an objective threshold for "acceptable" variability in WSI validation has not been established. Additional studies on intraobserver validation are needed to determine if this is a superior approach.

2084 Immunohistochemistry Validation Procedures and Practices: A College of American Pathologists Survey of 727 Laboratories

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Background: The immunohistochemistry (IHC) lab represents a dynamic area of surgical pathology with limited practice guidelines. Studies have shown significant interlaboratory variability in results. The purpose of this study was to establish baseline parameters for IHC validation procedures and practice, and to assess their feasibility of implementation.

Design: In September 2010, a questionnaire was distributed by the College of American Pathologists (CAP). It was composed of 32 questions relating to non-predictive assays as well as non-FDA approved, predictive IHC assays other than human epidermal growth factor 2 (HER2).

Results: Qualitative aspects of the procedures are shown in table 1. 86% of labs validated the most recently introduced non-predictive antibody. 75% used 21 or fewer total cases for the validation, and 40% used weakly or focally positive cases. 75% of labs validated the most recently introduced predictive antibody other than HER2. Less than half used 25 or more cases for the validation, and 47% used weakly or focally positive cases.

Conclusions: Some laboratories have written validation procedures that appear to build upon HER2 testing guidelines. Some labs also manage to validate new antibodies according to those standards, however many do not. While guidelines for HER2, estrogen receptor, and progesterone receptor help give laboratories some guidance for those IHC procedures, there appears to be a need for further validation guideline development for non-predictive and non-FDA approved predictive antibody assays.

Table 1. Validation Procedures for Immunohistochemistry

Percent of laboratories that include in their written procedure:	Non-predictive	Predictive
Validation of new antibodies	68	46
Specific number of cases required	54	65
Revalidation for introduction of a new lot of antibody	66	64
Revalidation for introduction or change of antigen retrieval	71	80
Revalidation for a change in detection system	74	81
Revalidation for a change in instrumentation	74	78
Revalidation for a change in fixative	65	74
Revalidation for a change in tissue processor instrumentation	49	55
Any specifications for use with cytologic material?	37	42

2085 Effectiveness of Targeted Education in Decreasing Utilization of Prophylactic Plasma Transfusion for Mildly Elevated INR

BT Haws, E Thorpe, LL Tilzer. University of Kansas Medical Center, Kansas City.

Background: Despite the lack of evidence, there continues to be significant prophylactic use of plasma for mildly elevated INR (≤2.0). In an effort to bridge the gap between guidelines and actual clinical practice, a blood management initiative was implemented at our institution aimed at developing more effective educational strategies to increase understanding and compliance with evidence based guidelines. This quality study was designed to evaluate the effect of targeted education towards changes in 1) the overall use of FFP 2) the indications cited for transfusion of plasma, and 3) utilization practices of individual clinical services.

Design: Data was collected retrospectively for one month periods before (June 2010) and after (June 2011) the implementation of educational strategies, which included reporting the June 2010 data in a medical staff newsletter, individual meetings with clinical departments, (focusing on specialties with the most plasma usage for minimally invasive procedures [medicine]) and invitation of guest presenters with expertise in blood management. Plasma transfusion data was abstracted from the laboratory information system, and the following information was collected for each transfusion: pre-transfusion INR, ordering clinical service (cardiothoracic surgery, surgery [including all other surgical specialties], or medicine [GI, ER, internal medicine and critical care]), and indication for order (significant hemorrhage, emergency reversal of warfarin, or prophylaxis prior to procedure [PPP]).

Results:

Table 1. Number of plasma units ordered pre and post educational intervention

	Pre-Intervention	Post-Intervention
Total Plasma	216	266
INR ≤2.0	107 (49.5%)	124 (46.6%)
INR ≤2.0 and indication PPP	68 (31.5%)	72 (27.1%)
Cardiothoracic Surgery	25	22
Surgery	26	44
Medicine	17	6

Conclusions: There was no clinically significant decrease in overall plasma or plasma with an INR≤2 transfused before and after implementation of educational strategies. However, there was a clinically significant decrease (17 vs 6) in plasma utilization by medicine, which was specifically targeted by educational efforts. Surgery showed an increase in the number of units transfused (26 vs 44) which may reflect an unintended result of educational efforts which stressed that INR value ≤2 requires more units of plasma to approach a normal INR. Our data suggests that educational strategies based on clinical trends of plasma utilization improve compliance with evidence based guidelines and help identify additional specialties that need focused educational efforts.

2086 A Resident-Driven Process Improvement Project Decreases Cassette Labeling Errors

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Background: In healthcare, there is increased recognition of the value of process improvement to increase efficiency and improve patient safety. An important challenge for Anatomic Pathology (AP) laboratories is to adopt these techniques and to provide education and experience in this discipline to residents. AP residents identified this need in the context of specimen cassette labeling in the gross room. We used process improvement techniques to identify and resolve both systematic and individual sources of cassette labeling errors, resulting in a measurable and sustained decrease in errors at our institution.

Design: "Errors" were defined as any labeling deficiency that required correction, thus creating non-value-adding labor. These included incorrectly numbered or color-coded cassettes and discrepancies between the histology Laboratory Information System (LIS) worklist and the cassettes received in our off-site histology lab. Institutional data from 360,743 cassettes for 61,581 cases from academic years (AY) 2008-10 were analyzed. The average error rate for AYs 2008-09, 4.1%, was designated as the baseline error rate, with the goal to reduce this error rate by 25%.

A resident committee examined gross room cassette-labeling procedures to identify error-prone steps in specimen processing and transfer to the histology laboratory. Each step was analyzed for process inefficiencies and physical or technological limitations leading to error. "Best practices" were identified by observing the procedures of individuals with low baseline error rates, and used to institute systematic changes in process, procedure, and environment.

Results: The following interventions were made following analysis: replacement/relocation of cassette racks to improve ergonomics, maintenance of cassette labelers to reduce printing malfunctions, LIS programming and procedure changes to improve synchronization of cassette submission with histology worklists, and monthly data analysis with anonymous feedback of individual errors as compared to department averages. These changes reduced the error rate by 30% in AY 2010, and resulted in intangible changes in resident and PA awareness of the causes and impact of labeling error.

Conclusions: Over a 12 month period, this resident-driven project applied process improvement techniques to reduce the block labeling error rate by 30%, improving both laboratory efficiency and patient safety. An additional benefit was the development of a culture of continuous improvement, which resulted in increased housestaff enthusiasm and engagement in error reduction.

2087 Utility of Retrospective Review of Non-Gynecological Cytology Cases

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Background: Retrospective review of routine non-gynecological (non-gyn) cases is infrequently performed in cytology laboratories. We sought to examine the utility of retrospective review of non-gyn cases in our laboratory over a four year period.

Design: We performed a retrospective review of one randomly selected non-gyn case per day (1% of total cases). Urines were excluded. The slides were examined for interpretation accuracy and the requisitions were compared to the electronic report. Diagnostic differences required consensus review (2-3 observers) to be classified as interpretation differences. Corrected reports were issued where management may have been impacted.

Results: Among the 1004 cases reviewed (2007-10), 90 (9%) issues were identified as follows: 49 (55%) accessioning errors (37 typographical errors, 10 incorrect site, 2 incorrect patient/physician identifiers), 16 (18%) interpretation differences/terminology misuse, 14 (16%) report errors (11 typographical errors, 3 negative with comment about atypia), 4 (4%) cases not signed out, 4 (4%) illegible handwriting and 3 (0.5%) incorrect patient identifiers. There were 15 (1.5%) corrected reports issued for 7 accessioning/report errors and 8 interpretation difference/terminology misuse (4 thyroid, 2 breast, 1 soft tissue, 1 fluid).

Conclusions: A review of randomly selected non-gyn cases identified issues in 9% of cases. Rarely, this required a corrected report (1.5%) with over half due to interpretative differences or terminology misuse. Accessioning errors, especially typographical errors, were the most common issues identified at review. Changes to our practice from this analysis include: terminology standardization, recommendations for internal second opinion on certain thyroid diagnoses and double-checking of report against requisition prior to sign-out.

2088 Review of ER, PR, and Her-2/Neu Immunohistochemisty Should Be Performed for Breast Cancer Patients Transferring Care to Another Institution

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Background: Breast cancer patients receive vastly different care depending on ER/PR and Her-2/neu status. Even small differences in interpretation may alter treatment decisions, from which ancillary tests are ordered to which drugs patients ultimately receive.

Design: An electronic database query (1/08-6/11) identified patients seeking second opinion or transfer of care for the diagnosis of invasive breast carcinoma or ductal carcinoma in-situ. Patients were those who had pathology slides, including ER, PR, &/or Her-2/neu immunostains, performed at a contributing institution and reviewed at a referral center. ER/PR were interpretated as negative, weakly positive, and positive if <1%, 1-10%, and >10% of tumor showed nuclear positivity, respectively. Her-2/neu was interpreted as negative, equivocal, and positive if there was 0-1+, 2+, and 3+ membranous staining, respectively. ER, PR, & Her-2/neu status was assigned by retrospective review of reports from contributing and referral institutions. Discordance was defined as any change in interpretation for one or more reviewed stains. Future plans are to review all discordant cases to assess clinical impact.

Results: Partial analysis yielded 700 cases, 640 (91.4%) of which had concordant and 60 (8.6%) had discordant interpretations. Patients in both groups had no significant difference in clinicopathologic characteristics.

Clinicopathologic Features

	Concordant (N=640)	Discordant (N=60)
Age (yrs)	54.0	52.9
Sex (N, %)		
F	638 (99.7)	60 (100)
M	2 (0.3)	0 (0)
Procedure (N, %)		
Core	489 (76.4)	47 (78.3)
Excision/Lump	128 (20)	11 (18.3%)
Mastectomy	14 (2.2)	1 (1.7)
Other	9 (1.4)	1 (1.7)
Histology (N, %)		
DCIS/microinvasive	71 (11.1)	6 (10)
IDC	500 (78.1)	46 (76.7)
ILC	51 (8)	7 (11.6)
Other	18 (2.8)	1 (1.7)
Grade (N, %)		
1	152 (23.7)	10 (16.7)
2	247 (38.6)	19 (31.7)
3	241 (37.7)	31 (51.6)

Of the 60 discordant cases 55 (91.7%) had discordance in hormonal receptor (ER &/or PR) interpretation, 3 (5%) had Her-2/neu discordance, and 2 (3.3%) had ER/PR and Her-2/neu discordance. Discordance was most often due to ER/PR (PR>ER) disagreement of single interval change.

Discordant Cases

	Neg ⇔ Weak/Equiv (N, %)	Weak/Equiv ⇔ Pos (N, %)	Neg ⇔ Pos (N, %)
ER (N=60)	8 (13.3)	9 (15)	0 (0)
PR (N=60)	21 (35)	17 (28.3)	3 (5)
Her-2/neu (N=50)	3 (6)	2 (4)	0 (0)

Conclusions: ER, PR, and Her-2/neu interpretation is subject to interobserver variability, this study resulting in small but significant discordance rate of 8.6%. As their interpretation may change clinical management review should be performed for patients seeking second opinion or care at another institution.

2089 Effectiveness of Reporting Significant Diagnosis in Anatomic Pathology: Pathologists' Roles and Challenges

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Background: Communication of an anatomic pathology significant diagnosis has been controversial since the College of American Pathologists (CAP) and the Association of Directors of Anatomic and Surgical Pathology (ADASP) first implemented it in 2006. Since then, there has been an increasing demand for hospital administration to impose this responsibility onto the pathologist, as reporting a significant diagnosis is an essential component in patient care. Yet, the pathologist may spend time trying to communicate a significant diagnosis to a clinician, at times with no success. Thus, the current challenge is defining the pathologist's role in reporting a significant diagnosis and understanding the most effective means of communicating these results to the clinician.

Design: An eleven-item survey was distributed to all medical specialties in our institution. The survey consisted of closed-ended questions relating to the role of the pathologist and effectiveness of significant diagnosis notification. In addition, our department developed a centralized system for communicating a significant diagnosis and this survey was used to analyze the effectiveness of this system.

Results: A total of one hundred and twenty seven clinicians and eleven pathologists responded to the survey. Most pathologists (73%) consider our mechanism of reporting a significant diagnosis to be effective. 41% of clinicians reported that our mechanism of reporting a significant diagnosis is not well defined. The most effective method of reporting a significant diagnosis was reported as email (63% of clinicians and 73% of pathologists,) however both clinicians and pathologists agree that a flag is needed to attract the clinician's attention if the report is sent via email.

Conclusions: In the continuously growing field of pathology, the pathologist has had increasing responsibilities in patient care. The perception of this clinical survey reveals that it is the pathologist's responsibility to monitor the clinician's response to a significant diagnosis notification. Subsequently, it is crucial for our clinicians to be well introduced to a centralized system of reporting a significant diagnosis in order to receive this information in a timely manner. Accordingly, although multiple modalities exist to report a significant diagnosis, standardization of reporting is crucial to most effectively improve the pathologist's communication with the clinician. As a result, this will optimize patient care. Ultimately, increasing responsibilities and demands from hospitals may continue to change future practice.

2090 An Audit of Dermatopathology Requisitions: Hand Written vs Electronic Medical Record Data Entry Accuracy

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Background: At NorthShore University HealthSystem, dermatopathology (DP) case requisitions are received in hand written form or via electronic medical record (EMR). There are multiple categories for requisition data entry including patient demographics, physician name, and procedure site/date. Data entry error propagates inaccurate patient information and potentially delays billing/revenue collection. The DP service maintains a high case volume and thus systematic data entry problems potentially cause considerable documentation error. We reviewed DP data entry errors on hand written requisition forms compared to data entry errors via EMR.

Design: 11,475 DP requisitions (8,545 hand written, 2,930 EMR) were included in the study (4/1/2011-9/30/2011). Data entry errors were documented and categorized as cases were accessioned and reviewed.

Results: Results are illustrated in table 1.

Category of error	# of hand written requisition errors	# of EMR requisition errors	Total # of errors
Mismatch between existing computer demographics/hand requisition	37	NA	37
Illegible requisition/container label	3	0	3
Requisition with incomplete/absent demographics	3	0	3
Requisition with no physician indicated	1	0	1
Requisition with wrong collection date	1	2	3
Specimen container not labeled	2	1	3
Specimen container with no patient name	10	0	10
Mismatch between patient name on requisition form/ container	8	0	8
Specimen container with no procedure site	152	95	247
Mismatch between procedure site on requisition form/ container	35	13	48
Wrong patient accessioned	4	0	4
Other	2	2	4
Total Errors	258	113	371
Total requisitions	8545	2930	11475
Overall error rate	3.0%	3.9%	3.2%

The majority of errors occurred with container labelling. More specifically, procedure site was either not on the container or there was a discrepancy between the site indicated on the container and on the requisition. Container labelling is currently a hand written process. The EMR does not generate labels and 109/113 EMR errors (96%) were related to container labelling.

Conclusions: 1.With both hand written and EMR requisitions, the most common source of error is specimen container labelling.

2.Currently, even with EMR, containers are hand labeled and 96% of EMR errors occurred during this process. Other EMR data entry errors are extremely uncommon (4/2930 cases). This suggests introduction of a labelling process linked to EMR data entry could nearly eliminate data entry errors.

3. Although this study focused on DP cases, the findings can be applied to all types of specimens.

2091 A Retrospective Review of Parathyroidectomy Specimen Pathology: A Diagnostic Accuracy Study

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Background: Parathyroidectomy is most often performed to treat hyperparathyroidism. Hyperparathyroidism can either be primary, secondary or tertiary depending on etiology. Certain histologic patterns are suggestive of etiology and even inherited endocrine syndromes. The pathology of the parathyroid gland can be largely divided into three categories: normal, hyperplastic and neoplastic. These categories can be further subdivided. The hyperplasias can be categorized as diffuse, nodular, primary and secondary. The neoplastic category includes parathyroid adenoma, atypical adenoma and parathyroid carcinoma. We reviewed parathyroidectomy cases to determine if there was a difference between the diagnoses made by general surgical pathologists versus a sub-specialized endocrine pathologist.

Design: We reviewed 169 parathyroidectomy specimens received between 1999 and 2009 from patients with secondary or tertiary hyperparathyroidism. These cases were originally diagnosed by general surgical pathologists and were subsequently reviewed by an endocrine pathologist. We evaluated the differences between the diagnoses made by both types of pathologist.

Results: The differences between the type and number of each diagnoses made by a general pathologist versus an endocrine pathologist are summarized in [table 1]. Of note, four cases (2%) were considered to be atypical adenomas when reviewed by an endocrine pathologist, which had been previously diagnosed as either parathyroid tissue or hypercellular parathyroid tissue. There was no diagnosis of atypical adenoma made by the general surgical pathology group. Sixty-five cases (38%) were re-classified as neoplastic upon review by an endocrine pathologist.

Parathyroidectomy:Type and Number of Diagnoses by Pathologist Type

Diagnosis	No. of Diagnoses made by General Surgical Pathologist	No. of Diagnoses Made by Endocrine Pathologist
Parathyroid Tissue	36 (21%)	0 (0%)
Normocellular	9 (5%)	7 (4%)
Hypercellular	28 (17%)	9 (5%)
Hyperplasia	75 (44%)	56 (33%)
Nodular Hyperplasia	14 (8%)	25 (15%)
Adenoma	5 (3%)	14 (8%)
Adenoma Arising in Hyperplasia	2 (1%)	54 (32%)
Atypical Adenoma	0 (0%)	4 (2%)

n=169

Conclusions: In this study, thirty-eight percent of reviewed parathyroidectomy specimens were reclassified as neoplastic when reviewed by an endocrine pathologist as compared to general surgical pathologists. This is suggestive of the improved diagnostic accuracy of sub-specialized pathologists. These findings support the present tendency towards sub-specialized pathology sign-out currently found in many academic centers.

2092 Reprocessing Unsatisfactory ThinPrep Papanicolaou Smears: A Tool for Reducing Unsatisfactory Rate and Enhancing Disease Detection

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Background: Longitudinal studies have shown that cervical cytology specimens classified as unsatisfactory have an increased risk of being associated with disease, including carcinoma. We conducted this study to assess the effect of reprocessing ThinPrep slides on the unsatisfactory rate and subsequent detection of epithelial cell abnormality over a 3-year period at our institution.

Design: All unsatisfactory ThinPrep samples submitted between January 2008 and March 2011 were reprocessed using a glacial acetic acid wash.
Results: A total volume of 24345 ThinPrep samples were evaluated over a three year period. The unsatisfactory rate prior to reprocessing was 2.3 % (627 of 24345). After reprocessing all the unsatisfactory smears, the reprocessing rate was reduced to 0.07% (17 of 24345). Of the 627 samples that were reprocessed, 97.3% (610 of 627 TP samples) were changed from unsatisfactory to satisfactory. Of these 610 satisfactory reprocessed paps 81% (495) were negative for intraepithelial lesion or malignancy, 8.6% (53) were atypical squamous cells of undetermined significance, 0.81% (5) were atypical glandular cells of undetermined significance, 4.4% (27) were low-grade squamous intraepithelial lesions, 1.5% (9) were high-grade squamous intraepithelial lesions, 0.67% (4) were carcinoma and 2.8% (17) were 'other' category.
Conclusions: Reprocessing unsatisfactory ThinPrep Papanicolaou smears with glacial acetic acid serves as a useful tool for reducing unsatisfactory rate and enhancing cervical disease detection.

2093 Improving Patient Safety: Instituting Mandatory "Pathology Specimen Time-Out" in the Operating Room as a Means for Reducing Patient/Specimen Identification Errors

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Background: The national drive towards establishing a comprehensive Electronic Medical Record (EMR) underscores the importance of accuracy of such records. ACGME specifically requires training programs to educate residents in identification and prevention of human/system errors and implementation of solutions, as components of practice-based learning and improvement, and systems-based practice. Our previous study of root cause analysis of surgical pathology reports released on the wrong patients revealed that incorrect entry of patient or specimen information occurred most frequently in the operating room (OR), due to high volume of specimens received from the OR. The objective of our current study is to prevent errors through implementation of mandatory "pathology specimen time-out" (PSTO) in our institution's OR policy. Here we report results of our performance improvement measure for reducing patient/specimen misidentification by the OR.
Design: We implemented mandatory PSTO in our OR policy in June 2010. PSTO was defined as "patient re-identification and re-confirmation of specimen site and laterality" at the time of acquisition of the specimen in the OR. Subsequently, all amended surgical pathology reports released on wrong patients from July 2010 through August 2011 were reviewed. In addition, we reviewed all "near-misses" from OR, defined as "improper or incorrect patient and/or specimen identification recognized by pathology staff before completion and release of report," thus preventing patient or specimen misidentification and avoiding an amended report.
Results: Before institution of the mandatory PSTO, 16 reports were released on wrong patients out of a total of 50,000 surgical pathology reports from January 2006 to June 2010 at our institution. In the subsequent 13 months following institution of mandatory PSTO, 4 reports were released on wrong patients out of a total of 14,000 surgical pathology reports, and none of these amended reports occurred due to OR entry error. All 4 amended reports were a result of entry error at clinics where mandatory PSTO had not been implemented. In addition, there was a progressive decline in "near misses" from the OR during this 13 month period.
Conclusions: Mandatory PSTO implementation in the operating room is an effective preventive mechanism for reducing patient/specimen entry errors into EMR, thus contributing to patient safety and should be adopted as a national/global standard of care.

2094 Clinician Compliance with Laboratory Regulations Requiring Submission of Appropriate Clinical Data: A One Year Retrospective Analysis

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Background: The evaluation of tissue samples submitted to Surgical Pathology is a consultation composed of evaluation of pertinent patient history, clinical findings and morphologic analysis. The College of American Pathologists (CAP) recognizes the need for clinical data in the interpretation of specimens submitted for histopathologic evaluation. The CAP regulation (CAP GEN.40100 Specimen Collection Manual Elements) includes instructions for a number of elements which include the need for appropriate clinical data, when indicated. In a note they state, "Because of the importance of clinical information in the practice of Surgical Pathology and Cytopathology, requisitions for such specimens should include pertinent clinical data, as well as preoperative and postoperative diagnosis." Anecdotal evidence indicates that clinician compliance with such requests is variable and at times poor.
Design: ARUP Laboratories and the Department of Pathology at the University of Utah have recognized inclusion of clinical history on Surgical Pathology request forms as a clinical indicator for quality assurance. The quality assurance data from August 1, 2010 to September 31, 2011 were searched for all cases flagged as containing no clinical history. Additionally, four consecutive weeks of Surgical Pathology request forms were reviewed to determine the presence or absence of clinical history, correlation was made with specimen type and clinical service requesting the pathology consultation. QA data was also reviewed to determine if the clinical history was accurate.
Results: Between August 1, 2010 and July 31, 2011, 21,700 surgical pathology cases were accessioned. Within this group, 1,293 (5.9%) requisitions contained no clinical history. The four week review found that 140 of 1,698 (8.2%) of requisitions contained no clinical history or only a specimen site of origin. This analysis also revealed that 4 cases contained substantially incorrect or incomplete clinical history (0.2%).
Conclusions: Our review indicates a significant number (5.9%) of requisitions contain no clinical history on the request form. A more in depth review reveals that approximately 8% contain either no clinical history or simply a body site in the clinical history request area and in 0.2% of cases, the clinical history was factually incorrect. Compliance with requirements for clinical history is poor and reveals the need to educate clinicians to provide this information.

2095 Use of GEWF Solution in the Gross Examination of Colorectal Adenocarcinoma Resection Specimens Is Associated with Increased Lymph Node Yield but Not Improved Survival

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Background: The number of lymph nodes identified in colorectal adenocarcinoma (CRC) resection specimens correlates positively with clinical outcomes. The identification of a greater number of lymph nodes increases the likelihood of appropriate staging, and the identification of 12 lymph nodes is a key quality measure for colon cancer care. Rectal resections and some colon resections may be associated with suboptimal lymph node yields (LNY). GEWF solution (glacial acetic acid, ethanol, water, formalin) is a safe, simple, and inexpensive lymph node highlighting (not fat-clearing) solution that has been demonstrated to result in significantly improved lymph node retrieval. Whether its use is associated with improved clinical outcomes has not been studied.
Design: Patients with stage I-III CRC who underwent primary surgical resection at two partner institutions were selected sequentially from 2002-2004; an *a priori* power analysis was performed to determine an adequate sample size for detecting survival benefit. GEWF solution was routinely used for lymph node retrieval in the study group and not in the control group. Clinical and pathologic features including LNY, disease-free survival (DFS), and overall survival (OS) were compared.
Results: One hundred fifty-three resections were examined using GEWF solution, and 169 resections were examined without GEWF. Use of GEWF solution was associated with significantly greater LNY (21.0 ± 10.1 vs. 13.2 ± 7.2, $P < 0.0001$) and a greater number of positive lymph nodes (1.7 ± 3.5 vs. 1.1 ± 2.2, $P < 0.05$). Twelve or more lymph nodes were more frequently identified in specimens examined with GEWF (82.4% vs. 50.0%, $P < 0.0001$). Use of GEWF was more often associated with adequate LNY in rectal specimens (80.0% vs. 37.9%, $P < 0.05$) and specimens measuring ≤ 15 cm in length (68.9% vs. 48.4%, $P < 0.05$). No differences in DFS or OS were noted between the two groups (mean follow-up = 63.2 ± 27.7 months). The two groups were otherwise similar with respect to patient and tumor characteristics.
Conclusions: Use of GEWF solution in the gross examination of CRC specimens is associated with improved LNY and a larger number of positive nodes. Although routine use of GEWF does not lead to improved patient outcomes, laboratory quality measures may be more readily achieved with its use, particularly when assessing problematic specimens.

2096 Communicating Diagnostic Uncertainty in Surgical Pathology Reports: Disparities between Sender and Receiver

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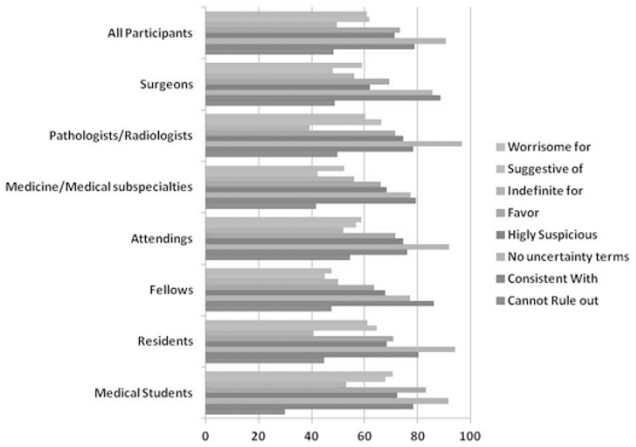
Background: Conveying diagnostic uncertainty in surgical pathology is a daily practice however there is no standardized wording for communication of uncertainty to clinicians.
Design: Attendees at multi-disciplinary tumor boards completed an anonymous survey that asked them to estimate the degree of certainty associated with eight diagnoses. One diagnosis contained no expression of uncertainty while the other seven contained the following phrases: cannot rule out; consistent with; highly suspicious; favor; indefinite for; suggestive of; and worrisome for. A total of 57 responses were received.
Results: For analysis the respondents were divided into the following groups: medical students, residents, fellows, attendings, medicine/medical subspecialties, pathologists/radiologists, and surgeons. The variations in the level of perceived certainty is quantified by the standard deviations from the means (table 1) and shown graphically (Figure 1).

Table 1: Standard deviations for the degree of certainty associated with phrases.

	Medical Students	Residents	Fellows	Attendings	Medicine	Pathologists/ Radiologists	Surgeons
Cannot rule out	18	25	25	27	31	21	30
Consistent with	16	21	8.9	24	16	25	13
No uncertainty terms	8.3	8.1	30	15	30	6	13
Highly suspicious	27	23	27	18	26	19	27
Favor	10	23	23	24	24	25	23
Indefinite for	29	19	25	28	21	24	31
Suggestive of	22	26	23	25	26	23	29
Worrisome for	22	24	19	23	22	23	22

Figure 1: Interpretation of degree of certainty associated with phrases



Conclusions: We found that all groups show marked variability between respondents in the degree of certainty they associated with the phrases. The high standard deviations for all phrases indicate that there is substantial ambiguity in these terms, even amongst pathologists who routinely use these phrases in their own reports. These preliminary findings highlight the need for more explicit communication of uncertainty between pathologists and clinicians. Clearly, we are not adequately communicating our intended level of diagnostic uncertainty with the phrases studied here. This communication gap opens the door for medical errors. While a more extensive study is necessary, we see the need to foster dialogue and actions to insure more accurate communication.

2097 Interobserver Variability of Lymph Node Count in Pelvic Lymph Node Dissection for Prostate Cancer

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Background: The prognostic significance of lymph node (LN) status is well established in prostate cancer. Data suggest that examination of greater than 10 LNs is associated with a 15% lower risk of prostate cancer death, even amongst patients with negative nodes. This study examines the variability of pathologist's role in LN counts for pelvic lymph node dissection (PLND).

Design: LN slides from 12 radical prostatectomy cases were distributed to four pathologists. Each pathologist was instructed to report the number of LNs per case. From this data interobserver agreement was calculated. Concomitantly, 696 prostatectomy cases from our database were analyzed. From these data, multiple regression was used to determine what factors were most significant to the number of LNs reported. The average number of LNs per pathologist was also calculated. From this data pathologists were grouped into quartiles. Average LN count was compared by quartile.

Results: Interobserver agreement of LN count was very poor (Fleiss kappa -0.12). Multiple regression analysis of LN counts using independent variables of pathologist, surgeon, organ weight, patient age, Gleason score, presence of metastases, extracapsular extension, extensive perineural invasion, lymphovascular space invasion, surgical stage and the number of LN packets submitted found that only the number of node packets was a statistically significant factor in the number of LNs counted (p=<0.0001). Quartile analysis of all pathologists showed that the lowest quartile (Q1) reported 5.5 fewer LNs on average than the top quartile (Q4, p=<0.0001, 95% CI 3.4 to 7.6 nodes). In the cases where only two LN packets were submitted, Q1 reported 3.5 fewer LNs when compared to Q4 (p=0.0009, 95% CI 1.5 to 5.5). Q2 and Q3 also reported significantly fewer nodes than Q4 for all cases (p=0.001 and 0.007, respectively) and for those cases where only two LN packets were submitted (p=0.0012 and 0.026, respectively).

Conclusions: Interobserver agreement in LN counts in PLND is very poor. Analysis of LN counts by all pathologists at our institution indicate that counting may be biased, since the top quartile of pathologists reports significantly more nodes than the other three, even when controlling for the most significant factor affecting LN counts (number of packets submitted). These data suggest that pathologists do not use the same criteria for LN counts and calls into question studies use LN counts as a metric of clinical outcome or quality of surgery or pathology. We recommend developing a national consensus for how pelvic LNs are counted.

2098 Image Cytometric Proliferation (MIB-1): Interinstitutional and Interobserver Validation

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Background: Proliferation (MIB-1 labeling index [LI]) is used to assess prognosis, and hence, management in breast carcinoma, gastrointestinal tract, neuroendocrine, and brain tumors. Thus, LI needs to be accurately quantitated. Two institutions with a total of three observers performed a validation study in order to assess concordance of results between institutions and among observers.

Design: Two sets of 30 formalin fixed paraffin-embedded breast carcinomas, chosen at institution 1 were immunostained (IHC)(Dako MIB-1 antibody) at two institutions designated 1 and 2 respectively. Quantification was by image cytometry (IA)(ACIS, Dako) by three observers (A,B,C). Results from IHC_1/IA_1 were compared to those from IHC_2/IA_2 by observers A and C respectively, who routinely perform daily quantitation. The results of IHC_1/IA_1, IHC_2/IA_2, IHC_1/IA_2, IHC_2/IA_1 each quantitated by A, B, and C were compared using cutoffs low (≤ 10%), intermediate (11-20%), and high (>20%).

Results: Substantial agreement was demonstrated between both institutions and observers despite differences in both analytical and preanalytical variables.

Comparative Statistics

	Concordance	R2
IHC1/IA1 vs. IHC2/IA1	26/30 (87%)	0.89
IHC1 A/B	25/30 (83%)	0.79
IHC1 A/C	27/30 (90%)	0.74
IHC1 B/C	24/30 (80%)	0.86
IHC2 A/B	22/30 (73%)	0.63
IHC2 A/C	22/30 (73%)	0.65
IHC2 B/C	24/30 (80%)	0.68

Differences in Preanalytic and Analytic Methods

	Preanalytic	Analytic
Institution 1	Ventana platform, Hematoxylin	8-10 average representative fields, 40X
Institution 2	Dako autostainer,Light Hematoxylin	3 "Hotspots", 20X

Conclusions: Comparing IHC between institutions using IA from the same institution showed strong agreement with one observer. When IHC from one institution was quantitated at a different institution by 3 different observers, results showed very good or substantial agreement. Standardization of preanalytic and analytic methods as suggested by an international panel of investigators in March, 2010, should improve concordance.

2099 Low Accuracy of Manual White Blood Cell Count in Amniotic Fluid

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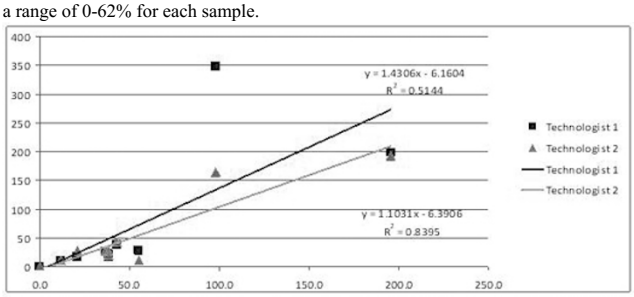
Background: Intraamniotic infection (IAI) is a common cause of preterm labor. Of the laboratory tests for IAI, amniotic fluid (AF) WBC count can be performed rapidly. An elevation of AF WBC over 50 cells/mm^3 has been reported to be 36-64% sensitive and 72-95% specific for IAI. However, cell count on amniotic fluid is not routinely performed in the laboratory, nor is it offered at any of the major reference labs. At the request of clinicians, accuracy of manual AF WBC count was determined.

Design: Ten AF samples sent to the laboratory for routine AFP measurement were randomly selected for analysis. Two technologists performed cell counts on each sample using a hemocytometer. A total of 100 fields were counted. To assess accuracy of WBC counts at various concentrations, AF samples that had no WBCs were spiked with blood from CBC specimens with known WBC counts, producing samples with calculated WBC counts ranging from 11-195 WBC/μL. Cell counts were performed on the ten spiked samples, including a negative control. The WBC counts for all 20 specimens were then compared to the calculated expected value for WBC.

Results: No debris was reported. The initial WBC count on the non-spiked samples ranged from 0-4/mm^3. Comparison between the technologists' manual WBC count on the spiked samples to the expected WBC count yielded R^2 coefficients of 0.51 and 0.83. When technologist results were averaged together, the R^2 coefficient between the manual count and the expected WBC count was 0.66. Percent agreement between the technologists was 80%, with an R^2 coefficient of 0.83. The average CV was 21% with a range of 0-62% for each sample.



Conclusions: There was moderate correlation between the manual and the expected WBC in the spiked AF samples. The coefficient of determination from the averaged results was lower than usual acceptable criteria. Using a threshold of 50 cells/mm^3 as the cutoff for infection, one sample would have erroneously been reported as less than 50, while the expected count was 54 cells/mm^3. The accuracy of the WBC count may be increased by averaging the WBC counts reported by two technologists. The decision to perform amniotic fluid cell counts should involve a discussion with clinicians about the accuracy of the test and the potentially high CV associated with this test.

2100 Studying Patient Misidentifications in the Surgical Pathology: Identifying the Root Cause of a Rare but Major Defect

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Background: A systematic approach to rare defects is a major challenge in surgical pathology continuous quality improvement. Patient misidentifications (patient misIDs) are infrequent but major defects in the surgical pathology process.

Design: We investigated the distribution throughout the entire surgical pathology testing process of defects that led to amended reports. Among 315 amendments in 2010, as we we processed 63,308 cases [5 amendments /1000 cases], 31 amendments were due to misidentifications [9.5 %], 8 to specimen defects [2.5 %], 16 to misinterpretations [5%], and 260 to report defects [83%] (Report defects were errors that did not involve misidentifications, specimen problems, or misinterpretations.) Of the 31 misidentifications, 6 were errors in determining laterality, 2 errors that designated the wrong tissue, and 1 error in designating location within a tissue. The remaining 22 misidentifications were of pateints. We specified the root cause for all of these 22 cases.

Results: Among more than 63,000 surgical specimens, 22 patient misIDs [3.5 misIDs/10,000 specimens] were indeed rare events. 13 (59%) occurred before arrival in the pathology department: 3 at patient registration (2 involving patient impersonation and 1 confusing mother and daughter), 10 at specimen collection: 5 skin biopsies in dermatologists' practices; 2 endometrial biopsies, one in a clinic, one in an emergency department; 2 placentas from two different labor and delivery units, and 1 transplant kidney biopsy from nephrology. Of the 9 patient misIDs in the pathology department, 3 skin biopsies, 3 liver biopsies, and 1 prostate case were confused at pathologist sign-out; 2 colon biopsies were confused at microtome sectioning.

Conclusions: Biopsies accounted for 16/22 (73%) and skin biopsies alone for 8/22 (36%) of all patient misIDs. The physical similarity of biopsies from different patients –at collection (8/10 cases) and at sign-out session (5/7 cases)- emerged as the main root cause. The same root cause also appeared for placentas confused at the point of colection and for GI biosies confused at microtome sectioning. Physical similarity lastly appears as the cause of confusion at specialty sign-out for standardized prostate resections. For the 19/22 patient misIDs that were not primary registration errors, failing to distinguish between grossly identical specimens was the root cause in all cases detected, both external and internal to the pathology department.

2101 Frozen Section – Permanent Correlation: An Audit of 3950 Cases

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Background: The correlation of intra-operative frozen section diagnosis with the final diagnosis on permanent sections is an integral part of quality assurance in anatomical pathology laboratories.

Design: We reviewed the slides and reports of 3950 cases of frozen sections and corresponding permanent sections including those from Surgical Pathology, Neuropathology and Paediatric Pathology practices. The types of discrepancies were classified based on the criteria set by the Association of Directors of Anatomic and Surgical Pathology. Reasons for discrepancies were analyzed.

Results: Summary of Correlation data.

Results

	Neuropath	Pediatrics	Surgpath	Total
Total reviewed	225	190	3535	3950
Agreement	212 (94.2%)	141 (74.2%)	3196 (90%)	3549 (89.9%)
Deferred -appropriate	3 (1.3%)	36 (18.9%)	106 (3.0%)	145 (3.7%)
Deferred -inappropriate, minor	1 (0.4%)	0	4 (0.1)	5 (0.1%)
Deferred -inappropriate, major	2 (0.9%)	0	0	2 (0.0%)
Discordance -minor	4 (1.8%)	0	127 (3.6%)	131 (3.3%)
Discordance major	1 (0.4%)	2 (1.0%)	75 (2.1%)	78 (2.0%)
Reasons				
Block sampling	0	0	51 (1.4%)	51 (1.3%)
Specimen sampling	4 (1.8%)	0	21 (0.6%)	25 (0.6%)
Technical inadequacy	0	0	2 (0.0%)	2 (0.0%)
Lack of Clinical data	0	0	0	0
Interpretation	1 (0.4%)	9 (4.7%)	104 (2.9%)	114 (2.9%)
Other	1 (0.4%)	0	0	1 (0.0%)

Conclusions: Specimen sampling errors were more common in Neuropath cases likely due to surgical difficulties in accessing the tumor tissue. Deferrals and interpretation errors were more common in paediatric cases, caused by high frequency of small round cell tumors and congenital disorders that was difficult to diagnose in the intraoperative setting. Lessons learned from detailed analysis of the data could help to reduce errors, reduce the number of deferrals and improve the accuracy of frozen section diagnosis.

2102 Potential Diagnostic Pitfalls Related to Bone Marrow Biopsy Quality in Staging Diffuse Large B-Cell Lymphoma

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Background: Diffuse large B-cell Lymphoma (DLBCL) is a common and an aggressive subtype of non-Hodgkin lymphoma (NHL). International Prognostic Indices (IPI) guide clinical management and prognostication at primary diagnosis. Morphologic evaluation of the bone marrow in combination with sensitive ancillary studies such as immunohistochemistry (IHC), flow cytometry (FCM) and molecular studies for B- cell clonality (IGH) are critical for staging DLBCL. Variability of marrow space involvement by DLBCL and sampling discrepancies can affect diagnostic outcome across these methods. In this study we looked at the frequency of discordant results across different diagnostic techniques, the effect of trephine core length on morphologic diagnostic outcome, and the potential influence of these discrepancies on staging of DLBCL.

Design: There were 174 DLBCL staging bone marrow biopsies from year 2003-2010, with concurrent FCM and IGH data available for review at RPCI. Length of the trephine core biopsies and the extent of marrow space involvement by DLBCL were recorded. FCM and IGH data was correlated with morphologic diagnosis. FCM and IGH assays were performed using standard laboratory protocols.

Results: Average length of trephine core biopsies was 8.4mm, range of 2mm to 50mm. 152/174 (87.4%) were of inadequate length (<15mm). Morphology, FCM and IGH were positive in 8/174 (4.6%), negative in 121/174 (69.5%), and discordant across the three methods in 45/174 specimens (25.8%). Within the discordant group, the trephine core biopsy was of inadequate length in 41/45 (91.1%), with a negative morphologic diagnosis in 35/45 specimens (77.7%). Clinical staging data was available in 36/45 among the discordant cases. 18/36 cases were assigned a Stage I-II status, of which 16/18 (89%) were of sub-optimal length and morphology for diagnosis, with a negative morphologic diagnosis in 17/18 (94%) cases.

Conclusions: Inadequate marrow trephine core biopsy length contributes significantly to discordant diagnostic data, creates interpretive pitfalls, and can lead to a false negative morphologic diagnosis in staging bone marrow biopsies. This diagnostic disparity can potentially lead to inaccurate clinical staging. The outcome of upstaging disease status based on positive ancillary data, independent of marrow morphology is unclear at this time.

2103 The Effect of General Versus Sub-Specialty Sign-Out on the Reporting of Lung Transplant Biopsy Rejection

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Background: Lung transplantation is an established treatment modality for patients with end-stage lung disease. Surveillance for rejection is based on spirometry parameters and pathologic evaluation of protocol biopsies in stable grafts; additional biopsies are performed for clinical indications in failing grafts. However, the detection of rejection is dependent on the observer's experience in allograft pathology interpretation. We sought to compare the % of reporting of rejection by general surgical pathology versus sub-specialty sign-out.

Design: We reviewed all lung transplant biopsies performed at our institution between 2005 and 2010 for the reported degree of rejection, underlying lung pathology leading to transplantation, age at the time of biopsy and correlated the results with the type of sign-out (general versus subspecialty). 1034 lung biopsies from 224 patients were reviewed; 41 patients who were < 40 years old all suffered from cystic fibrosis while 183 patients who were > 40 years old suffered primarily from idiopathic pulmonary fibrosis and COPD. Prior to 2008, lung transplant biopsies were handled by general pathologists but since 2008 this is done by a sub-specialty sign-out.

Results: Among 1034 biopsies reviewed, 362 were performed during 2005-2007 and 672 were performed from 2008-2010. The reported % of rejection (see table) doubled with subspecialty sign-out: 10.5 versus 22.5%. While this was mainly due to increased reporting of A1, there was also a 70% increase in the reporting of clinically significant (A2) grades of rejection. Moreover, reporting of minimal rejection (A1) was clinically helpful in patient management and planning for a possible re-biopsy. There was no statistically significant difference in reporting rejections in different patient age-groups and underlying lung pathology.

2005-2007		2005-2007, <40		2005-2007, >40	
A0%	89.5%	A0%	89.2%	A0%	89.6%
A1%	6.1%	A1%	4.8%	A1%	6.5%
A2%	3.6%	A2%	4.8%	A2%	3.2%
A3%	0.8%	A3%	1.2%	A3%	0.7%
2008-2010		2008-2010, <40		2008-2010, >40	
A0%	77.7%	A0%	76.5%	A0%	77.9%
A1%	14.7%	A1%	13.9%	A1%	14.9%
A2%	6.1%	A2%	6.1%	A2%	6.1%
A3%	1.5%	A3%	3.5%	A3%	1.1%

Conclusions: Introduction of sub-specialty sign-out doubled the overall % of reported rejections and, most importantly, increased by 70% the reporting of clinically significant, A2, rejections. While the latter leads to an immediate change in clinical management, the reporting of minimal rejection (A1) has also been helpful in overall patient management. Our study further supports the advantages of sub-specialty sign-out as an important quality assurance measure in surgical pathology.

2104 A Method for Decreasing Interobserver Variability in Quantitative HER2 Immunohistochemistry

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Background: Over-expression of the HER2 receptor is associated with aggressive breast cancer development. The highly specific immunotheraputic targeting of HER2 by mABs and TKIs, as well as, the high cost of these treatments make accurate assessment of HER2 status essential. Currently, the main techniques used to assess HER2 status are FISH and IHC. FISH is limited to laboratories with fluorescent microscopy capabilities while IHC is the most prevalent technique for quantifying HER2 status. However, quantitative immunohistochemistry (qIHC) shows poor reproducibility between observers. Here we report a method to decrease inter-observer variability in HER2 qIHC through the inclusion of reproducible standard controls.

Design: Four immortalized cancer cell lines with consistently differing levels of HER2 expression (MCF-7, BT-20, MDA-MB-453 and SKOV-3) were grown, pelleted, formalin fixed and paraffin embedded. Control strips were made from 2 mm cores of these cell lines. Eight cases of breast carcinoma known to express HER2 as previously assessed by FISH were cut on a slide with the control strips. The optimum incubation and concentration of a mAB (CB11) for HER2 was found such that an intensity breakpoint was seen between 2+ and 3+ staining patterns corresponding to a HER2/CEP17 ratio of 1.8. Next, an additional 19 cases of breast carcinoma with HER2/CEP17 ratios ranging between 1.0 and 7.2 were evaluated by 5 pathologists using the control strip in addition to ASCO guidelines. Five additional pathologists assessed HER2 status without the control strip. The data was analyzed using Fleiss' correlation and chi-square analysis.

Results: The analysis of HER2 expression by use of control strips and ASCO guidelines significantly decreased inter-observer variability compared to analysis using only ASCO guidelines, (k=0.5686 vs k=0.4337) with a mean difference of 0.1349 (95% CI 0.0591 to 0.2107). Receiver Operating Characteristic curves for the experimental group showed an area-under-curve (AUC) of 0.888 while the control group showed an AUC of 0.856 (not significant).

Conclusions: We describe a new method for decreasing inter-observer variability using qIHC to score HER2 expression. These control strips are easily made from cultured cells and provide sufficient control material to run a large number of quantitative tests. qIHC may serve as a useful and important tool in determining HER2 status in small laboratories lacking the ability to assess HER2 status by FISH or in specimens with small tumor foci where FISH may fail.

2105 Thyroid FNAs and Clinical Outcomes: An Institutional Quality Assurance Project

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Background: Since The National Cancer Institute's summation for thyroid fine needle aspirations (FNAs) in 2008, multiple studies have confirmed the Bethesda System's utility in standardizing terminology and predicting malignancy rates for thyroid FNAs. The goals of our review were to determine: 1. our adherence to the Bethesda terminology; 2. our malignancy rates in comparison to the literature; 3. how we can improve patient care through multidisciplinary education; and 4. how ancillary molecular testing may improve patient care.

Design: Our study reviewed every thyroid fine needle aspirate performed in 2010, totaling 243 FNAs from 178 patients. For each patient, any previous and subsequent (until May 2011) FNAs were also reviewed. Each FNA was classified and data gathered as to clinical follow-up, including ancillary molecular studies.

Results: Of 243 FNA's, 17% were unsatisfactory (Unsat), 39% benign (Ben), 25% atypical/follicular lesion of undetermined significance (AFLUS), 12% suspicious for follicular neoplasm (SFN), 3% suspicious for malignancy (SM), and 5% malignant (Mal). 13% of FNA diagnoses did not adhere to the Bethesda terminology and were placed into the most appropriate category for the purposes of this study. Sixty-three cases had follow-up histology, and malignancy rates for the Bethesda categories are as follows: Ben 17%, AFLUS 20%, SFN 29%, SM 83%, and Mal 100%. 28% of patients with AFLUS diagnosis received a repeat FNA. Ten patients received a molecular panel (BRAF, RAS, RET/PTC, Pax8/PPARγ) to aid in management decisions; based on negative molecular panels, 6 of 10 patients received clinical management only.

Conclusions: Our institution's percent of each FNA category per the Bethesda terminology was consistent with the literature, except for our 25% rate of AFLUS diagnoses, for which we may need to institute a quality control measure. In addition, our cytopathologists do not consistently use the Bethesda terminology, which likely results in confusion among clinicians and may affect patient care. We therefore recommend strict adherence to the Bethesda terminology, with description as needed. Furthermore, our rates of malignancy in patients with histologic follow-up are similar to those reported in the literature. Because only 28% of AFLUS-diagnosed patients are receiving a repeat FNA, we recommend a multi-disciplinary workshop to discuss patient management for each Bethesda category. Last, ancillary molecular testing indicates that, for our patient population, a molecular panel may be an excellent ancillary test in patients who do not desire surgery and have an AFLUS or SFN diagnosis.

2106 On-Site Adequacy Assessments of Fine Needle Aspiration Biopsies

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Background: On-site assessment of fine needle aspiration biopsies provides valuable feedback on specimen adequacy and allows for further sampling and ancillary studies. This study sought to 1) determine the accuracy of on-site adequacy assessments (OSAA) provided by our laboratory's cytotechnologists; and 2) identify reasons for differences between OSAA and final sign-out adequacy assessment (FAA).

Design: OSAA from Oct 09- June 11 were compared to FAA. Re-review of cases with differences between OSAA and FAA was performed by comparing OSAA and FAA slides.

Results: Among 1060 cases, OSAA and FAA comparison yielded 1017 (96%) concordances and 43 (4%) differences. Six (0.5%) cases adequate at OSAA were unsatisfactory at FAA, and 37 (3.5%) cases unsatisfactory at OSAA were adequate at FAA. Reasons for differences in adequacy included: diagnostic material present only on fixed smears, ThinPrep and/or cell block (54%); amount of diagnostic material on rapid assessment smears borderline for adequacy, *i.e.* at "threshold" (22%); contributory clinical information (10%); and diagnostic pitfalls (10%). Slides were not available for review in 4% of cases. Diagnostic pitfalls were interpretation of lung parenchyma as neoplastic and salivary gland acinar cells as lymphocytes; and missed granulomas.

Conclusions: The accuracy of OSAA provided by our cytotechnologists is high (96%). Differences between OSAA and FAA occurred in a minority of cases with only rare cases resulting in an unsatisfactory overall outcome. Reasons for differences were most commonly due to diagnostic material on additional slides not reviewed at OSAA. An interpretative issue was identified in a small percentage of cases.

2107 Digital Cytopathology and Whole Slide Imaging – Exploring Its Application in Cytology Education and Proficiency Testing Programs in Ontario, Canada

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Background: The Quality Management Program-Laboratory Services (QMPLS) plays a key role in the health-care system through its focus on quality assurance and analysis of proficiency testing (PT) performance by licensed laboratories in Ontario, Canada. Digital Morphology (DM) utilizes computers to review and interpret digitized images of microscopic preparations along with data management, web accessibility, annotations, and automated image analysis. This technology allows pathologists and cytotechnologists to review images from any computer and enables consultation within and among different facilities. The purpose of our survey was to test digital images for use in PT.

Design: A pilot survey was conducted by QMPLS in 2010. The participants were asked to download the viewing software Image Scope provided by Aperio. QMP-LS distributed the software to 51 participants within Ontario. The participants were asked to view and analyze eight digital images obtained from various preparation techniques and body sites.

Results: Over 85% of participant responses matched the assigned value, except for one case of a respiratory bronchial washing conventional smear, where the thickness of the sample interfered with visualization of the malignant cells. The results showed that LB preparation slides are better suited for DM since they have smaller areas to scan. The image quality and the ability to focus on the image and cells were the two most important factors for successful application of DM in PT. One of the main hurdles was downloading the Image Scope software because of hospitals' and community laboratories' firewalls, though after reconfiguring firewall and proxy settings all participants were able to proceed with the survey.

Conclusions: By using digital images, External Quality Assessment (EQA) programs can provide the means for participants to view and interpret microscopic preparations of small volume, unique or difficult to obtain patient material for assessment and/or education. The benefits of this technology are conducive to revolutionizing traditional cytology surveys.

The pilot survey identified optimal sample types for future DM surveys and the the feedback will help guide QMP-LS in using DM in future surveys.

2108 Evaluation of Communicating Frozen Section Diagnoses with Surgeons

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Background: Communicating the frozen section (FS) diagnosis to the surgeon is a critical component of the FS process. Unfortunately, this often involves reporting a diagnosis via telephone to operating room (OR) staffs other than the surgeon. This may lead to miscommunication and thereby affect patient care. The aim of this study was to evaluate the accuracy of communicating FS diagnoses during intra-operative consultations at our institution.

Design: A total of 300 consecutive cases, where a FS was performed (9 month in 2009), were retrieved from the anatomic pathology laboratory information system (CoPath, Cerner). Cases were included if there was a corresponding OR note in the electronic medical record which described the surgeon's interpretation of the FS diagnosis. Pre-operative diagnosis, intra-operative question, specimen type, FS diagnosis (called to the OR), surgeon's interpretation, final pathologic diagnosis and patient outcome (per clinical notes) were recorded for all cases. Discrepancies between the FS diagnosis and surgeon's interpretation were recorded as a miscommunication and further classified as major (clinical impact) or minor (no clinical impact).

Results: A variety of specimen types were received for FS requesting a diagnosis (59.3%), margin status (30.6%), both a diagnosis and margins (6.6%), or lymph node status for cancer (3.5%). There were 8 (2.6%) miscommunications, all of minor clinical impact, most (88%) of which had a FS diagnosis that was deferred to permanents. Miscommunications in these cases involved reporting "loaded" neutrophils in bone tissue, deferred grading for a sarcoma, interpretation of margins as "excellent" for urothelial dysplasia at ureteral margins, interpretation of a low grade spindle cell proliferation as an inflammatory lesion by the surgeon, and partial documentation in the OR note of two specimens that were submitted for FS diagnosis. In 6 other cases (2%) FS and final pathologic diagnoses were discrepant; however there was no miscommunication of these FS diagnoses to the OR.

Conclusions: The rate of miscommunicated FS diagnoses to surgeons was low at our institution with no adverse patient outcome. Reporting of FS diagnoses using non-standard terminology and indeterminate diagnoses (ie. deferrals) were the most frequent cause for miscommunication. Miscommunications may be circumvented by maintaining a good working relationship with surgeons, requesting immediate acknowledgement following a verbal FS diagnosis and displaying the FS diagnosis in real-time on a monitor in the OR.

2109 Receiver Operating Characteristics (ROC) Application to Immnuhistochemistry for Determining Optimal Antibody Concentration: A Mathematical and Novel Application for Quality Control

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Background: No standards exist by which working antibody concentrations are determined in clinical immunohistochemistry (IHC) laboratories. Such decisions are made by microscopic examination of the staining intensity of differing antibody concentrations using selected tissue sections, and choosing an "optimal" concentration (that which yields the stongest true staining and weakest false staining) "by eye." We utilized a mathematical approach derived from signal detection theory, receiver operator characteristics, coupled with computer image analysis to create a quantitative algorithm for IHC optimization.

Design: Immunohistochemical staining of formalin-fixed paraffin embedded normal kidney tissue using antibodies against Multi-cytokeratin AE1/AE3 (Novocastra; Wetzlar, Germany; #NCL-AE1/AE3) was performed at concentrations 1:1, 1:2, 1:4, 1:40, 1:400, 1:4,000, 1:40,000, and 1:400,000 using standard methods on a Leica Bond instrument using the Novocastra Bond Polymer Refine Detection System. For each antibody concentration, the signal intensity of the tubules (biologic positive) and interstitium (biologic negative) per cell was measured by InForm® data collection software. The area under the curve (AUC), as metric of test performance and standard deviation were calculated. Considering each dilution as an individual "test", we compared the AUC among each "test" and chose the "test" with the highest AUC as the optimal antibody concentration.

Results: The performance of the AE1/AE3 antibody was high across most antibody dilutions (1:1, 1:2, 1:4, 1:40, 1:400, 1:4,000, 1:40,000, and 1:400,000) despite dropping signal intensity. For each respective antibody dilution the AUC was 0.97, 0.91, 0.94, 0.99, 0.97, 0.98, 0.5, and 0.5 (S.D. <.0001)and the average tubule signal was 0.28, 0.22, 0.22, 0.34, 0.19, 0.13, 0, and 0.

Conclusions: Our application of ROC analysis to IHC-based staining is a quantitative, rigorous, mathematical method to determine an optimal antibody concentration for reliable performance. When the performance characteristics (AUC) of a particular antibody are high across multiple dilutions, other factors, such as signal intensity and reagent costs, may be used to determine an optimal antibody concentration. Our methodology will enhance quality control and optimization of IHC staining and also enable comparison of antibody performance over time and among different laboratories and platforms.

2110 Labeling Errors in a Surgical Pathology Gross Room: A Root Cause Analysis

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Background: Medical errors can occur in the pre-analytic, analytic and post-analytic phases of specimen evaluation. Mislabeling of specimens is an infrequent but significant cause for diagnostic error. Specimen labeling errors may occur before receipt in the Surgical Pathology laboratory, during the grossing process, slide preparation and report dictation. Specimen accessioning and "grossing-in" appear to be sites where a significant number of mislabeling errors occur. Root cause analysis of gross room errors could lead to an understanding of causes for mislabeling and a reduction in mislabeling and associated errors.

Design: The Quality Assurance records of ARUP Laboratories were reviewed for all labeling errors between July 2009 and April 2011. Root cause analysis was undertaken to identify circumstances (what, who, when, where) of the error. Analysis of error descriptions included the point in the process where the error occurred, error impact (within case vs between case), and error type (e.g., transposition of numbers, "one-off" shift in digits). Logistic regression was used to explore associations between errors and causal factors such as daily case load, time of day, day of week, case complexity and employee category. Quality analysis tools such as a process flow diagram, a control chart, cause and effect diagrams and "five-why" analysis were used to explore causal relationships.

Results: 85 labeling errors were identified in 42,684 specimens processed during the study period. The error rate was stable over this period and was almost 10 times higher for residents than for regular staff ($p<0.001$). The error rate varied by specimen type being lowest for dermatology specimens ($p< 0.001$). Among non-dermatology specimens, the error rate was significantly higher for complex specimens ($p<0.001$). Errors were unassociated with daily case load, day of week or time of day; there was a significant increase in errors at the end of the day on Friday and Saturday. Errors were evenly divided between within-case and between case errors. Root cause analysis identified work space crowding, cassette printer design and cassette handling mechanisms as possible contributors to error.

Conclusions: Labeling errors are associated with specific factors (employee type, specimen type and particular time periods). Improved supervision of house staff and error prone processes may reduce labeling errors. Increased oversight of labeling of complex specimens and specimens processed during particular times of days may improve specimen labeling.

2111 Rapid On-Site Evaluation of Endobronchial Ultrasound Guided Transbronchial Needle Aspiration: A Practice To Preserve or Retire?

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Background: Endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA) has become an integral tool in the diagnosis and staging of malignant tumors of the lung. Rapid on-site evaluation (ROSE) is a central part of the practice of cytology, to assess for adequacy and provide a preliminary diagnosis. Although ROSE has proven to increase diagnostic accuracy for other sites, few studies have specifically investigated its utility in the assessment of EBUS-TBNA specimens. This study critically evaluates the possible diagnostic benefit and true utility of ROSE for EBUS-TBNA specimens.

Design: The pathology files at our institution were searched for all EBUS-TBNAs performed from 1/10 to 6/11. Data points included number of patients undergoing EBUS-TBNA, number of sites sampled per patient, location of site(s) sampled, use of ROSE, preliminary on-site diagnosis, final cytologic diagnosis, cell blocks produced and ancillary studies performed.

Results: A total of 953 EBUS-TBNA specimens, 854 (90%) lymph nodes and 99 (10%) lung lesions, were collected between 1/10 and 6/11 from 461 patients. ROSE was performed for 394/953 (41%) cases, from 202 patients. The on-site and final diagnoses were concordant in 205 (52%) and discordant in 189 (48%) cases. The main source of disagreement [100 (25%) cases], was the lack of site specific/diagnostic tissue present in on-site smears, but diagnostic tissue present in liquid based preparations and/or cell blocks. Diagnostic specimens were obtained in 366/394 (93%) cases with ROSE and 495/559 (89%) without ROSE. The final diagnosis was malignant in 171/394 (43%) cases with ROSE and 129/559 (23%) without ROSE and benign (excluding granulomatous inflammation) in 146/394 (37%) with ROSE and 328/559 (59%) without ROSE. A cell block was obtained in 364/394 (92%) cases with ROSE and 511/559 (91%) of cases without ROSE.

Conclusions: No significant difference was seen in diagnostic yield for EBUS-TBNA cases with and without ROSE. The main cause for discordant preliminary and final diagnoses in cases with ROSE was the lack of site specific/diagnostic tissue on preliminary smears, suggesting that liquid based preparations and cell blocks may offer advantages for processing these specimens. Despite the benefits of ROSE, in this era of personalized medicine and increasing health-care costs, forgoing ROSE may lead to cost savings as well as increased diagnostic material available for immunohistochemical and molecular testing in EBUS-TBNA specimens.

2112 Analysis of Immunohistochemical Usage in Different Pathology Practice Settings

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Background: Immunohistochemistry (IHC) is a standard diagnostic tool in pathology practice, but the frequency of its use may differ among practice settings. This study analyzes the application of IHC for the diagnosis and classification of carcinoma in several practice types.

Design: Two hundred recent carcinomas (chiefly in biopsies) from patients referred to our institution for treatment were "blindly" and individually reviewed by three of the authors. They included a resident, a mid-level faculty pathologist, and a senior faculty member. The diagnoses, number of cases with IHC stains, and the number of stains performed by the referral pathologists were recorded. To help overcome the inherent bias in the study, a control group of 200 recent consecutive site-matched biopsies performed for cases at our institution were tabulated for the use of IHC stains; these cases were signed-out by pathologists other than those in this study. The referral cases included: prostate (41), endometrium (33), other genitourinary (29), gastrointestinal and hepatobiliary tracts (27), lung (21), head and neck (19), breast (16), other gynecological (11), and bone/soft tissue (3).

Results: Overall diagnostic agreement between study and referral pathologists was 98%. Referral and study pathologists used IHC stains in 26% and 11% of cases, respectively ($p < 0.0001$). The senior pathologist used stains in 6%, the mid-level pathologist in 14% and the resident in 10% of cases. Pathologists from commercial laboratories (12% of cases from referral practices) used IHC in 38% of cases, while those from private or hospital-based laboratories (86% of referral practice cases) used them in 24%. The mean number of stains used per case by pathologists from private or hospital based laboratories was four, while it was three for those in commercial laboratories, as well as for the study reviewers.

The greatest differences between referral and study pathologists in IHC usage were seen for the following sites: lung (71% vs. 38%) ($p=0.06$), prostate (27% vs. 5%) ($p=0.01$), breast (31% vs. 13%), and other gynecological (27% vs. 9%).

For the site-matched control group, the overall IHC rate was 13%. IHC was used for 24% of lung, 17% of prostate, 0% of breast, and 9% of other gynecological cases.

Conclusions: Although diagnostic agreement among pathologists was high, referral pathologists used IHC for more cases than study pathologists. The frequency of use of IHC likely varies for a number of reasons; our study shows that its use reflects, at least in part, the degree of experience of the pathologist as well as the type of pathology practice setting.

2113 Post-Analytical Phase Detection of Identification Errors in Anatomic Pathology

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Background: Identification errors in anatomic pathology may be related to misidentification of the patient, site, or procedure and can occur during any phase (pre-analytical [requisition], analytical [interpretation] and post-analytical [transmission of results]). When these errors are identified and corrected during the analytical phase, they constitute a "near-miss." If they are identified afterwards, they are misses. Many groups now encourage a variety of processes to detect identification errors during the analytical phase. Nonetheless, some identification errors escape detection during the analytical phase and result in post-analytical errors which may have consequences. In this study, we investigate the details of post-analytical phase identification errors.

Design: Surgical pathology and cytopathology reports from 2008 to 2011 with subsequent amendments were identified. The reports and original requisitions were reviewed to classify the error by the subspecialty service involved, type of error, source of error, and the personnel involved in identifying the error.

Results: We identified 75 cases with subsequent amendments. The errors involved all anatomic pathology subspecialties (Table 1). The most frequent type of error was the "wrong anatomic site" provided on the requisition form (Table 2). The source of error was attributed to the submitting clinical staff in 59%, pathology department in 36%, and other sources in 5% of cases. Identification of the errors was made by clinicians in 60% of the cases, pathology department personnel in 34%, others in 6%.

Table 1. Number of errors in subspecialty services

Service	Number of Errors
Gastrointestinal	17
Head and Neck Pathology	10
Transplantation	1
Thoracic	9
Neuropathology	3
Genitourinary	4
Bone and Soft Tissue	19
Consultation Service	4
Cytology	6
Hematopathology	2

Table 2. Type and number of errors

Type of Error	Number of Errors
Wrong site by Pathology	5
Wrong site on requisition	32
Change in final diagnosis	4
Specimen switch (same patient)	4
Wrong pathology procedure	4
Other	15
Wrong procedure on requisition	9
Identity issue	1
Accessioned to wrong patient	1

Conclusions: Post-analytical errors most frequently occurred due to inaccurate documentation (e.g. site). In daily practice, pathology department personnel may be limited in the means to verify the precise documentation of each specimen. Nonetheless, quality improvement may be accomplished by communicating and providing feedback to the clinical and pathology groups involved and focusing on the common types of errors.

2114 In Pursuit of Comprehensive Pathology Reports: Implementing Electronic Cancer Checklists

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Background: Cancer pathology reports must include all required elements listed in the College of American Pathologists (CAP) Cancer Protocols according to Standard 4.6 of the American College of Surgeons Commission on Cancer, the CAP laboratory accreditation program, and many state cancer registries. Our institution recently implemented a new Anatomic Pathology information system, which enabled data entry into electronic Cancer Checklists (eCCs) including associated algorithms for completeness and accuracy. The previous system relied on free text templates ("Manual" method).

Design: Consecutive pathology reports for breast, kidney, prostate, lung, and colon cancer that included a synoptic report based on the 2009 CAP Protocols were reviewed. Signed reports using "Manual" and eCC methods were compared for 1) percentage of cases containing all required elements, and 2) number and type of missing required elements. If data elements were not applicable to the specimen they were not counted in the total.

Results: 758 "Manual" and 341 eCC reports were analyzed (see Table for results). The most common missing elements in "Manual" reports were margins/distance to margin (92 breast, 20 lung, 6 colon), presence/absence of lobular carcinoma in situ (57 breast), ancillary studies (39 breast), and evaluation of non-neoplastic kidney (19 kidney). Only four eCC reports had a missing element: distance to margin (3 lung) and ancillary studies (1 breast).

	No. of Cases Reviewed		Cases Containing All Required Elements, No. (% of Total)		No. of Cases Missing 1, 2, 3, ≥4 Required Elements	
	"Manual"	eCC	"Manual"	eCC	"Manual"	eCC
Breast	341	126	176 (51.6)	125 (99.2)	104, 52, 7, 2	1, 0, 0, 0
Kidney	131	64	105 (80.2)	64 (100.0)	24, 1, 1, 0	0, 0, 0, 0
Prostate	121	39	107 (88.4)	39 (100.0)	14, 0, 0, 0	0, 0, 0, 0
Lung	98	68	78 (79.6)	65 (95.6)	18, 2, 0, 0	3, 0, 0, 0
Colon	67	44	54 (80.6)	44 (100.0)	6, 3, 2, 2	0, 0, 0, 0
Total	758	341	520 (68.6)	337 (98.8)		

Conclusions: Switching to eCCs dramatically improved the percentage of cancer reports containing all required elements (from 68.6% to 98.8%). For certain required elements in "Manual" reports, it was often not clear if the element was missing due to an oversight or because it was not applicable to the specimen. The consistent use of "absent" or "N/A" in eCC reports for such elements eliminated this ambiguity. Overall, laboratories using manual methods should consider changing to eCCs in order to increase compliance with cancer reporting requirements.

2115 Objective Histologic Stain Quality and Variability Analysis through Digital Imaging: The Effect of Staining Automation

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Background: Histologic staining variability often poses difficulty in pathologic diagnosis and can be a source of frustration for practicing pathologists. However, assessment is often based upon subjective eyeball evaluation of glass slides. Digital image analysis provides the ability to objectively quantify such evaluations, and allow for regimented quality control over this portion of the hospital laboratory.

Design: Twenty-four daily Masson's Trichrome control slides (12 hand-stained, 12 automated) from available nearest consecutive days prior to and after the implementation of automated staining were digitally scanned with an Aperio Scanscope XT. Two 10X screenshots of representative vasculature were captured from each whole slide file in Aperio Imagescope. Using the open source GNU Image Manipulation Program (GIMP), the optical color components of hue, saturation, and intensity value (HSV) were systematically recorded for 10 points of perivascular fibrous tissue of each vessel. Combined HSV measurements were averaged for each day and analyzed for mean deviation and day-to-day variability.

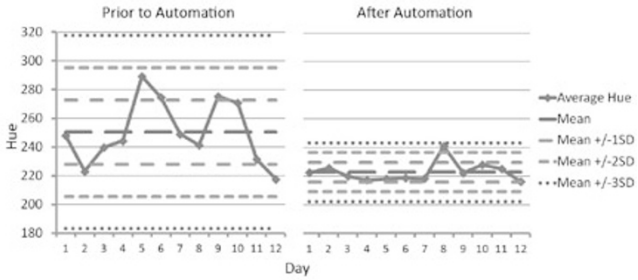
Results: Automation resulted in statistically significant differences in both stain appearance and day-to-day variability. Mean perivascular stain hue and saturation differed significantly ($p = 0.002$ and 0.0006, respectively), while value showed no significant change.

Mean HSV measurements

	Pre-automation	Post-automation
Hue (95% CI)	250.4 (237.7-263.1)	222.7 (218.9-226.6)
Saturation (95% CI)	43.5 (36.9-50.1)	65.1 (57.9-72.5)
Value (95% CI)	64.3 (60.0-68.6)	63.7 (60.2-67.2)

*Hue, saturation, and value are unitless measurements

Additionally, day-to-day hue variability was significantly decreased using an automated stainer (Pre- and post-automation hue standard deviations 22.4 and 6.8, respectively).



Conclusions: Initiation of automated staining yielded significant changes in hue and saturation and decreased day-to-day staining variability. Digital HSV analysis can be a viable method of objectively assessing stain quality and variability within the histology laboratory. Using acceptable hue and saturation error levels, histologic stain quality can be quantitatively assessed in similar fashion to analytical tests within the clinical laboratory.

2116 Pitfalls in Flow Cytometry: Diagnostic Challenges for a Pathologist

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Background: Flow cytometry (FC) is important in the diagnosis of lymphoma or leukemia, but results can be misinterpreted. The aim of this study was to identify uncommon diagnostic pitfalls.

Design: FC analyses performed for clinical suspicion of lymphoma or leukemia at our center between July, 2010 and June, 2011 were reviewed as a part of quality assurance. Cases with significant discordance between FC and morphologic results not explained by sampling were analyzed.

Results: 1362 specimens [bone marrow, blood, fine needle aspirate, body fluids, or lymph node and other tissue biopsies] were reviewed. Three unusual cases were identified as shown in table.

	Case 1	Case 2	Case 3
History	74/M with history of myelodysplasia	60/F with 3 cm PET+ bone mass. No prior history of cancer.	59/M with 8 cm retroperitoneal mass. No prior history of cancer.
Specimen	BM	FNA of mass	FNA of mass
Clinical impression	MDS progression to leukemia	Plasmacytoma	Lymphoma
FC results	38% blasts, (CD45dim+, CD34+, CD13dim+, CD117-, CD33-, HLADR-), consistent with acute leukemia.	30% plasma cells (CD45-, CD38+, CD138+, CD3-, CD19-,CD20-, κ-, λ-).	Nondiagnostic. 90% large CD45- cells, unusually high side scatter. Dimly+ for CD20, CD38, CD138, dual (nonspecific) staining for κ, λ.
Pathology results	BM biopsy showed only 10% CD34+ blasts. MDS with numerous CD34+ CD61+ dysplastic megakaryocytes.	Metastatic adenocarcinoma. Cells had plasmacytoid morphology, but MUM1-, κ-, λ- and CD138dim+. Cytokeratin stains (AE1/AE3, CK7) and TTF1 were positive.	Large B-cell lymphoma with Burkitt-like features. Large, atypical lymphoid cells, high N/C ratio, nuclei with irregular outlines, discernible nucleoli, and vacuoles in cytoplasm.
Resolution of discrepancy	Erroneously high CD34+ blast count on FC was due to fragments of dysplastic CD34+ megakaryocytes with light scatter properties of lymphocytes/blasts.	Carcinoma cells expressed CD138 and were misinterpreted as plasma cells on FC.	PET scan showed a 5 cm testicular mass prompting re-biopsy of the retroperitoneal mass. On IHC, large cells were CD117+, Oct3/4+, PLAP+, consistent with metastatic seminoma.

BM = Bone marrow, FC = Flow cytometry, FNA = Fine needle aspirate

Conclusions: These cases revealed dysplastic CD34+ megakaryocyte fragments that mimic blasts, metastatic CD138+ adenocarcinoma cells that look like plasma cells, and a metastatic germ cell tumor imitating large B lymphoma. They underscore the value of resolving any discrepancies among FC, clinical, and morphologic findings when rendering a diagnosis.

2117 Adrenal Mass Fine Needle Aspriations and Their Radiologic and Clinical Correlation

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Background: The increasing use of imaging techniques has contributed a great deal to the detection of adrenal gland lesions that may be as small as 1 cm. The most common indication for adrenal gland fine needle aspiration (FNA) biopsy is to detect a metastatic lesion for staging a malignancy. Primary adrenal gland neoplasms are very infrequent and many of them are incidental findings. The radiologic/clinical correlation with the FNA interpretation is especially important since only a small percentage of adrenal masses are resected.

Design: Thirty-one cases of adrenal gland FNAs were retrieved from NorthShore University HealthSystem pathology database from 2001 to 2011. The radiologic reports and clinical follow-up were obtained from the patients' electronic medical records. The correlation between all three parameters was analyzed.

Results: Of the 31 cases evaluated, 16 were women and 15 were men, with ages ranging from 48 to 87 years (mean 54 years). The sizes of the adrenal masses ranged from 1.2 cm to 8.0 cm. 71% (22 cases) were detected as part of the work-up of metastatic disease, while the remaining 9 lesions (29%) were found incidentally. The incidental lesions ranged in size from 2.0 to 8.0 cm, with a mean of 3.7cm.

Of all 31 cases, 18 (58%) showed satisfactory concordance between the cytology findings and the radiologic impression, while 10 (32%) were discordant, and 3 had imaging done at an outside hospital. Of the 10 discordant cases, all were suspected to be metastatic disease radiologically, based on masses detected elsewhere and/or positron emission tomography (PET) status. Each of the cases was found to be a benign lesion upon FNA. 9 (90%) of the discordant cases were adrenal masses less than 3.0 cm in size.

In this study cohort, only four cases had subsequent resection specimens. All of the surgical resctions correlated with the original FNA interpretation, with 2 cases as primary adrenal neoplasm (3.0 cm and 4.5 cm) and 2 cases as metastatic carcinoma.
Conclusions: Adrenal gland FNA is mainly reserved for masses suspected to represent metastasis. Radiologic and FNA discordance is fairly frequent (32%) and most common with lesions less than 3.0 cm. Therefore, FNAs of adrenal masses should be used in a more selective fashion, especially when measuring less than 3.0 cm.

2118 The Specimen Handling of GI Mucosal Biopsy: A Simple and Effective Quality Improvement Initiative

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Background: GI mucosal biopsy plays important roles in several clinical situations. Many specific diagnoses could be reached from the biopsy of patients present with GI symptoms with or without endoscopic abnormality. Diagnostic foci may be patchy or exclusively locate in certain areas of mucosa e.g. on surface of the mucus layer, tip of the villi or deep within the crypt epithelium. A perpendicular plane of tissue from surface to muscularis mucosae could increase diagnostic yield since they demonstrate the entire layer of mucosa as well as preserve its anatomic architecture. Starting in February 2010, Department of Pathology Faculty of Medicine Siriraj Hospital launched the 2 steps quality development program to improve the quality of GI mucosal biopsy slides.
Design: First step at pathology laboratory, embedding technicians were trained to recognized GI mucosal biopsy and embed tissues in a perpendicular plane not to exceed 4 tissue pieces per block. After a month, second step at endoscopy unit was introduced. Endoscopic nurses were trained to spread the tissue on a mesh before fixing it in formalin. Then 3 sets of fifty slides were collected for evaluation from before, after step 1 and after step 2 period of quality development program. All slides were independently assessed by one pathology resident (TT) and one general pathologist (JT). Any conflict in reporting was resolved by consensus. Total number of tissues and number of tissues with perpendicular plane on each slide were recorded. Slides contain tissues with perpendicular plane over a half of the tissue pieces were considered as satisfactory. Diagnosis of each slide was also recorded. The study was approved by Siriraj Institution Review Board and supported by Siriraj Research Development Fund (Managed by Routine to Research: R2R)
Results: Numbers of statisfactory slides are significantly increased from 46% to 60% and 74% (p value 0.017) and shown in Table 1.

Number of satisfactory slides among three sets.

	Before (Feb 2010) n=50 (%)	After step 1 (Nov 2010) n=50 (%)	After step 2 (Dec 2010) n=50 (%)
Satisfactory slides	23 (46)	30 (60)	37 (74)
Unsatisfactory slides	27 (54)	20 (40)	13 (26)

Conclusions: The quality of GI mucosal biopsy slides were significantly improved after a simple and feasible program. Educating and training medical personals involved in tissue procurement and tissue processing are crucial. Benefits from these high quality slides will be further investigated.

2119 Public Domain Image Analysis Program Can Quantitate Nuclear Immunostains as Accurately as Proprietary Software

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Background: Various nuclear immunostains including estrogen (ER) and progesterone (PR) receptor and Ki67 are routinely quantitated in the pathology laboratories as predictive or prognostic markers. A number of commercial slide scanners with proprietary image analysis software are available for automated quantitation, but are expensive and in most cases restricted to images produced by specific scanners.
Design: We created a public domain image analysis program entitled Subcellular Stain Analyzer (SCSA), a Java written plugin for ImageJ, which can be run on any Java-enabled operating system. We compared the accuracy and efficiency of automated quantitation of PR immunostain between SCSA and the Aperio IHC Nuclear Image Analysis algorithm (Aperio, Vista, CA) on triplicate core tissue microarrays (TMAs) built from 310 resection specimens of breast carcinomas clinically tested for ER, PR and HER2 at the British Columbia Cancer Agency recently. The TMAs slides were digitized using Aperio Scanscope; areas of invasive carcinoma were manually selected for each tissue core and at least 50 cells per core were analyzed. PR quantitation with the Aperio IHC Nuclear Image Analysis algorithm and SCSA provided continuous output of percent of positive cells, which was further ranked according to the principles of visual scoring. Statistical analysis was performed using PASW 17.0 (IBM Corporation, Armonk, NY).
Results: Automated unsupervised image analysis provided similar results between the two image analysis applications, with a Pearson correlation coefficient of 0.946 ($p < 0.000001$). When continuous scores were dichotomized into negative (0-1% positive cells) and positive (>1% positive cells), kappa statistics between two programs was 0.721.
Conclusions: SCSA, based on public domain image analysis software, may be as accurate and efficient in the quantification of PR immunostaining, when compared with the commercially available Aperio IHC Nuclear Image Analysis algorithm, and may offer a very cost effective alternative in both clinical and research settings. Future studies will involve comparison of quantitative image analysis of ER staining using these two applications with visual scores reported by pathologists.

2120 Review of Tumor Board Cases as Part of a QA Program: Impact on Clinical Care in a Non-Subspecialized Tertiary Hospital: A Review of 2,604 Cases

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Background: Part of our current QA process includes the review of slides of all cases presented at all Hospital tumor boards. The review is done by attendings with interest/expertise in each subspecialty area. Results are tabulated by 2 senior pathologists on a quarterly basis, presented at the QA meetings and kept in computerized format.
Design: We reviewed the results of all QA tumor boards from January 2009 until March 2011. This review covers 10% of the total yearly workload of the department and is designed to address errors in all phases of surgical pathology including change in diagnosis or stage, typographical errors, errors in patient's information, inadequate clinical history or incomplete data in the cancer CAP sign out templates.
Results: 2604 cases from 395 tumor board meetings were reviewed including: Breast 722, gynecology 348, gastrointestinal 309, melanoma 275, leukemia/lymphoma 271, urology-188, thoracic 176, head and neck 154, soft tissue 88, and pediatrics 73. In total, 46 issues (1.76%) were identified including 7 (0.27%) in the pre-analytic phase, 1 (0.034 %) in the analytic phase and 38 (1.46%) in the post-analytic phase. In the pre-analytic phase, there was inadequate clinical history in 4 cases, wrong patient's DOB in 1 case, wrong clinician's name in 1 case, and a grossing error in 1 case (failure to identify two separate tumor nodules in a lung specimen). In the analytic phase there was one false positive margin status due to the presence of therapy artefact. In the post-analytic phase: 16 cases had a change in pathologic staging; 15 cases had typographical errors, and 7 cases had incomplete CAP reporting.
Conclusions: Review of tumor board cases can be used as an internal benchmark to monitor error rate in surgical pathology in the pre, post and analytic phases. In our series, patient care benefited from this review in at least 25 cases (0.9%) in which therapy, and prognosis were affected when pathologic staging was changed, CAP reports added important missing information, and one margin was found to be negative rather than positive.

2121 Use of 2D Bar Code Technology and Single Piece Throughput in the Reduction of Specimen Labeling Errors

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Background: Specimen labeling errors are an inherent risk in Anatomic Pathology. A 2009 CAP Q-Probe Study which focused on labeling errors in Surgical Pathology found a median rate for mislabeled blocks of 1.0 per 1000 and mislabeled slides of 1.2 per 1000. In 2011, Dartmouth-Hitchcock's Anatomic Pathology and Histology laboratories began a 2D barcoding initiative with a goal of reducing slide and block labeling errors by 50%.
Design: This initiative is designed to implement 2D barcoding throughout Anatomic Pathology and Histology. 2D barcodes on specimen labels, tissue cassettes and slides contain patient, specimen, and tissue section specific information. Specimen labels, cassettes and slides are printed on demand to support single piece flow throughout the system. Custom programming in the Cerner Millennium Laboratory Information System (LIS) performed by the Laboratory's IT Specialist enables the print devices to access specific case and block information.
Tissue cassettes are printed on Thermo-Scientific Microwriters at the time of specimen setup. Technicians are instructed to work on one case at a time, and each cassette has a corresponding 2D barcode linking it to the LIS with case and block identification data. Each histotech is provided with a slide writer, the Thermo-Scientific Slidemate. The histotech scans the block which interfaces with the LIS. The slide writer prints all slides based on requests pending for that block. The slides are verified in the LIS when completed, and subsequent requests can be entered and printed for recuts and special stains.
Results: During the baseline period (March - May, 2011), the laboratory averaged 2.5 mislabeled blocks per 1000 and 0.086 mislabeled slides per 1000. The data for the implementation month (June) were not counted as several process adjustments were required during that time. During the three months post implementation (July - August), the laboratory averaged 0.7 mislabeled blocks per 1000 and 0.017 mislabeled slides per 1000 resulting in a 73% and 80% improvement, respectively.
Conclusions: The utilization of barcode technology coupled with single piece throughput offers a safer system in terms of maintaining the integrity of specimen labeling throughout the system. Mislabeling events still occur. Data collection in Surgical Pathology is now enhanced to identify where in the process errors occur, i.e. during setup of specimens, reprinting of cassettes, or gross dissection of specimens. Additional process redesign is planned to address these errors when the areas of greatest risk are identified.

2122 Placenta Submissions: Are the Appropriate Indications Being Met?

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Background: Obstetric services informally and formally use clinical indicators to determine a practice of placental submission for pathologic examination. In cost-contained systems, clinical indicator triage algorithms balance patient safety (appropriate diagnosis) with efficiency and may be used to assess the appropriateness of submission practices.
Design: We performed a one-year retrospective medical record review of all submitted placentas (n = 600) to determine if the obstetrical clinical history contained appropriate indicators for placental submission for pathologic examination. We selected a random sample of 119 placentas and recorded if a clinical indicator was provided. If an indicator was present, we classified the indicator into one of three categories: maternal,

fetal, and placental. Each of these indicators consisted of 3 or 4 conditions (e.g., fetal indicators: fetal compromise, fetal phenotype abnormality, or multiple gestations). We determined the level of concordance between clinical indicator condition and placental pathologic diagnosis.
Results: Of submitted placentas with clinical indicators (81%), 49% were maternal indicators, 31% fetal, and 19% placental. In 64% of placentas, the pathologic diagnosis correlated with the clinical indicator. The highest concordance (100%) was with the suspected condition of chorioamnionitis/infection and the lowest level of concordance (33%) was with suspected placental conditions (e.g., previa, retained products, etc.). In 19% of specimens, an appropriate clinical indicator was not provided and the majority was from women who had a Cesarean section with bilateral tubal ligation and no maternal, fetal or placental indications of disease. None of these placental specimens had significant pathologic findings. Extrapolated to the entire year, our laboratory performed a placental examination without appropriate clinical indication in 114 cases.
Conclusions: We hypothesize that a standard clinical indicator checklist may be used to triage placentas for pathologic examination. Providing clinicians with correlation of clinical indicator-pathologic findings also may be used to evaluate the utility of the clinical indicator assessment. Improved lab efficiency may be achieved by limiting unnecessary placental examinations without compromising safety.

2123 Specimen Consideration for EGFR Mutatiopnal Analysis in Non-Small Cell Lung Cancer

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Background: Between 05/2010 and 02/2011, we tested 93 cliinical specimens for mutations in exons 18 to 22 encoding TK domain of EGFR, among which 9 cases failed in the PCR amplication. In this study, we attempted to examine the properties of speicmens that may contribute to failure. The findings will help clinicians and pathologists choose the optimal specimens for EGFR mutational study.
Design: For EGFR mutation testing in our institution, speimens were first tested for the common mutations, including exon 19 deletion by fragment analysis and L858R by melting curve analysis following PCR amplficaiton. Negative cases were subsequently submitted for sequencing of exon 18 to 22. All 93 cases were included in the study. The following information was documented, including pathological diagnosis, type of speicmen (FNA, biopsy, or resection), anatomical site, referring hospital, decalcification status, size of the specimen subject to test, tumor cell per centile, DNA yield, and EGFR mutation status. For the 9 failed cases, we also documented what stage the failure occured as well as the clinical outcomes.
Results: Among 93 cases, EGFR mutation was deteted in 24% of cases and no mutation was deteded in 67% of cases. 9 cases (9%) failed for the study due to insufficient DNA for PCR amplification. Among the failed cases, 1 case turned out to be breast cancer and was subsequently exlucded from the study. In terms of specimen type, cytology specimens had the highest failure rate. The anatomical sites significantly associated with test failure inlcuded brain and bone. The size of specimen in failed cases was significantly smaller than the one in the successful cases. All the failed cases had DNA yield <2ug while majority of successful cases had DNA yield >2 ug. The failure rate in specimens <5mm^3 was 15% while the failure rate was 0 in specimen >5mm^3. Interestingly, only 1 out of 5 decalcified specimens (20%). In terms of outcomes, 2 cases had additional tissue from the same procedure that were successfully tested. The remaining cases had not 2nd biopsy for EGFR testing.
Conclusions: The size of the specimen is the most important factor assoicated with failure in EGFR mutational analysis of NSCLC in our study. There is 15% failure rate if the specimen is <5mm^3. If sufficient sample is obtained (>5mm^3), the EGFR mutational analysis has 100% successful rate. The significance of delcalcification remains unclear in this relatvely small study.

2124 Validation Study of Telepathology on Frozen Section Diagnosis in a Multi-Hospital Subspecialized Pathology Department

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Background: Telepathology is increasingly used for intraoperative frozen section (FS) with great accuracy. In our department, 2 rotating on-duty specialty pathologists cover FS in 3 hospitals, located about a 15-minute-walking distance from each other. Offices for the pathologists are located in 2 of the 3 hospitals. Telepathology has the great potential to improve the turnaround time (TAT) and facilitate consultation. We explored the feasibility of implementing dynamic telepathology for FS in our department.
Design: Our telepathology system includes an Olympus BX40 microscope, an Olympus DP71 camera and MicroSuite Pathology Edition software in the FS suite. Access to the internet and internet browser are the only requirements for the pathologist's computer terminal. For this study, 10 FS cases were randomly chosen by an assistant. The slides were transmitted in real time to 10 specialty pathologists by a junior resident. Short patient history and specimen site were provided. The pathologists independently evaluated each FS slide and rendered a telepathology diagnosis (TPD). Afterward, the glass slides were reviewed and each gave a light microscope diagnosis (LMD). Neither the resident nor the pathologists knew the original FS diagnoses (FSD) or the permanent section diagnoses (PSD). There were no discrepancies between the FSD and PSD.
Results: There were 100 TPD and LMD diagnoses among the 10 pathologists. The overall TPD accuracy was 97%; the LMD accuracy was 98%. For 12 of the 100 TPD responses, the diagnoses were made by pathologists who are specialists in the specimens being evaluated. For the remaining 88 TPD responses, the pathologists were evaluating specimens outside their specialty areas. Nine out of 88 diagnoses (10%) made by specialists outside their own specialty area included diagnoses that were less specific, requested additional tissue or deferred the diagnosis to permanent sections. This did not occur for any of the 12 diagnoses (0%) made by the pathologists in their specialty area.
Conclusions: The diagnostic accuracy of telepathology for FS is good (97%), similar to the conventional method (98%). Therefore, it appears to be a valid alternative, especially when there is an emergent situation to improve the TAT. Additionally, the specialists' diagnoses within their specialty area are more specific and well-defined. Therefore, by facilitating consultation, telepathology holds the promise to improve the overall FS diagnostic accuracy with minimal delay of the TAT.

2125 Large Specimen Surgical Pathology Reporting Facilitated by Lean Workflow and Rapid-Cycle Microwave Processor

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Background: Timeliness of pathology reporting is one of the most common challenges in Surgical Pathology, particularly for large and complex specimens resections requiring more intensive workup for diagnosis. This even more challenging for teaching institutions that integrate residents and education into a large specimen dissection service and can be compounded by Core Histology Laboratory operations that serve as central processing units for numerous remote hospitals.
Design: Pathology workflow in the Henry Ford Hospital Surgical Pathology and Histology Core Laboratory was optimized for continuous flow from work processes of accessioning through gross dissection, histology tissue processing, slide cutting and delivery to pathologists. In this work system, we tested integration of a rapid-cycle microwave processor (Logos, Milestone Medical, Kalamazoo, MI) into continuous flow work for large specimens. The isntrument was initially validated for processing times according to submitted specimen thicknesses from 1-3mm. All specimens were dissected fresh with occurrence of both fixation and processing on the instrument for total processor times ranging from 1.25-3 hours. We then compared surgical pathology report TAT from our previous July 2011 condition of overnight processing of large specimens to the new August 2011 condition of continuous flow processing of larger/complex specimens corresponding to CPT codes 88307 and 88309. Specimen dissection was performed by pathologists' assistants and residents.
Results: 37 large specimen cases (33 coded as 88307 and 4 coded 88309) were dissected fresh at 3mm thickness with formalin fixation and processing in continuous flow on the rapid-cycle processor. TAT from time of accession to case signout was 3.2 days. This is a reduction of 36% from the previously attained TAT of 5 days for both large specimen classes of 88307 and 88309. No histology processing or slide stain quality defects were observed.
Conclusions: Efficient work system designs in surgical pathology and histology can be enhanced with integration of rapid-cycle processors that promote the proven Lean efficiency concept of continuous flow. In teaching institutions, quality and consistency of the work product requires a gross dissection discipline by pathology residents and a different approach that shrinks the non-value added time waste associated with historical overnight or late afternoon batch mode gross dissection.

Techniques

2126 Effects of Long Term Tissue Fixation on the Immunohistochemical Expression of MSI Makers in Colon Adenocarcinoma

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Background: Colorectal adenocarcinomas with microsatellite instability (MSI) do not respond well to Fluorouracil-based chemotherapy and do have treatment outcome that differs from that seen in microsatellite stable tumors. In clinical settings, immunohistochemical staining for makers of MSI [Mismatch repair (MMR) gene products] is used to screen for the presence of MSI; and has been shown to have comparable sensitivity and specificity with MSI detection by PCR. It was recently shown that routinely used tissue fixative such as dissect aid negatively impacts MMR proteins immunohistochemistry. 10% Neutral Buffered Formalin (NBF) was shown to be the optimal tissue fixative for MMR protein immunostaining in routine surgical pathology practice. This study explores the effects of long term NBF tissue fixation on the immunohistochemical expression of three MMR gene products (MLH1, MSH2 and MSH6).
Design: Study materials consisted of cases of colonic adenocarcinoma: 7 primary colectomy and 1 secondary hepatectomy specimens received for tumor diagnosis and staging. Samples of normal colon and tumor from each specimen were fixed in NBF and submitted for routine processing with paraffin embedding after fixation for 1 day, 1 month, 3 months, 6 months and 1 year. Immunohistochemistry for MLH1, MSH2 and MSH6 was performed on representative sections of each block. Immunoreactivity scoring was done using a semi-quantitative score of 0, 1, 2, 3 and 4.
Results: MLH1 immunoreactivity scores for all the samples were strong for the samples within the first 3 months of fixation (previous findings) but thereafter became drastically reduced and is completely negative in 5 of 8 cases for MLH1, 3 of 8 cases for MSH2 and 2 of 8 cases for MSH6 after one year of fixation.
Conclusions: Although 10% Neutral Buffered Formalin solution is the preferred fixative for MMR immunohistochemical assay, long term tissue fixation (greater 3 months) results in loss of immunoreactivity of MMR proteins in tissue sections and so may produce spurious results (false MSI status).

2127 Detection of KRAS Mutations by Locked Nucleic Acid PCR Sequencing in Pancreatic Cyst Fluid Cells

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Background: Mutation of *KRAS* is one of the earliest alterations in pancreatic adenocarcinoma (PA). As such, in combination with clinical and cytologic findings, detection of *KRAS* mutations may have a role in the pre-operative management of