with positive lymph nodes, lymphovascular invasion and high number of positive lymph nodes in patients with diffuse malignant mesothelioma.

1831 Abstract moved to 327A

1832 Prognostic Significance of Tumor Chronic Inflammatory Infiltrate in Diffuse Malignant Mesothelioma.

W Zhang, M McIntire, R Bueno, J Godleski, L Chirieac. Brigham and Women's Hospital, Boston, MA; Caris Life Science, Newton, MA.

Background: Diffuse malignant mesothelioma is well known to be an aggressive disease. Therefore, identification of histopathologic factors with prognostic value is important for selection of therapeutic modalities. Recent studies in other malignancies have shown that the tumor inflammatory infiltrate has important prognostic value. The aim of the present study was to investigate whether the tumor stromal inflammatory infiltrate represented by CD3 positive cells is a prognostic factor in patients with diffuse malignant mesothelioma.

Design: We studied 204 patients with diffuse malignant mesothelioma (125 epithelioid, 8 sarcomatoid, and 71 biphasic type) who had surgical resection performed at Brigham and Women's Hospital between 2001 and 2008. Paraffin embedded tumor samples were used to construct tissue microarrays. CD3 positivity was evaluated and graded in each tumor as absent (<1%), moderate (<50%), or severe (>50%). Patient age, sex, tumor type, TNM stage, lymphovascular invasion and number of positive lymph nodes were recorded and correlated with CD3 positivity.

Results: In our study, 166 patients (81%) were men and 38 (19%) were women with mean age 63.2 (range 34-84). T category was 1 in 4% of patients, 2 in 24%, 3 in 43% and 4 in 29%. We found that a higher number of CD3 positive lymphocytes were correlated with fewer mediastinal lymph node metastases (p=0.002).

Conclusions: Our results suggest that the degree of chronic inflammatory infiltrate in diffuse malignant mesothelioma has prognostic value. Chronic inflammatory infiltrate may represent an important parameter in the histopathologic assessment of diffuse malignant mesothelioma. An increased number of CD3 positive lymphocytes are associated with fewer lymph node metastases. Stromal chronic inflammatory infiltrate should be considered in the planning of the management of patients with diffuse malignant mesothelioma.

1833 IMP-3 and Ki-67 Expression in Neuroendocrine Tumors of the Lung.

L Zhao, A Fraire, P Cagle, T Allen, K Rock, D Kandil. University of Massachusetts Medical School, Worcester; The Methodist Hospital, Houston, TX; University of Texas, Tyler.

Background: Insulin-like growth factor-II mRNA-binding protein 3 (IMP3) plays a key role in multiple cancers. Ki-67 is a nuclear protein involved in cell proliferation. IMP3 has been shown to have higher expression in high grade tumors and to be a poor prognostic marker for some others. Ki-67 has been reported as a helpful biomarker in differentiating carcinoid tumors from small cell carcinomas (SCC) of the lung. In this study, we explore for the first time the usefulness of IMP-3 in discriminating pulmonary carcinoid tumors from SCC. To our knowledge, this is the first study to evaluate the expression of both IMP3 and Ki-67 in pulmonary neuroendocrine tumors.

Design: Sixty-seven tissue micro-array cases were retrieved from the surgical pathology files of a large academic institution. These included 40 cases of carcinoid tumors (39 typical and 1 atypical) and 27 SCC. All cases were stained with antibodies against IMP3 and Ki-67 proteins, and evaluated independently by 2 observers. IMP3 expression was divided into 2 categories: negative (absent or weak cytoplasmic staining) and positive (moderate or strong cytoplasmic staining with membranous accentuation). Ki-67 expression was scored as negative or low (0-20% positivity) or high (> 20 %).

Results: IMP-3 was expressed in 60% (16/27) of SCC cases. KI-67 expression was high in 48% (13/27) of SCC cases. Combined, IMP-3 and KI67 were expressed in 30% (8/27) of SCC cases. In carcinoid tumors, IMP-3 was expressed in only 5% (2/39) cases, while Ki-67 expression was expressed in 2.5% (1/39) cases. The atypical carcinoid case was positive for both IMP-3 and ki-67. None of the typical carcinoid cases showed positivity for both markers.

Conclusions: In this study, IMP-3 is shown to have higher sensitivity than KI-67 in SCC (60 vs. 48%) and slightly lower specificity (95 vs. 97.5%). However, the combined sensitivity of both markers in SCC was 30%. Our data suggest that IMP-3 is preferentially expressed in SCC than in typical carcinoids. Our findings further suggest that neuroendocrine tumors with equivocal features of SCC but expressing both IMP3 and Ki-67 can be safely classified as SCC.

Quality Assurance

1834 Effect of Fixatives and Duration of Fixation on Expression of MSI Markers.

PA Adegboyega. LSU Health Sciences Center, Shreveport, LA.

Background: Tumors with abnormal DNA mismatch repair (MMR) genes are described as having microsatellite instability (MSI) and have also been shown to have distinctive clinical and pathologic features including tumor response to chemotherapeutic agents and patients' survival. Hence, immunohistochemical expression of MMR gene products is used to screen for MSI status of tumors for therapeutic decisions and determination of prognosis. This study investigates the optimal tissue processing and fixative conditions for immunohistochemical assay of MMR proteins.

Design: Benign samples of 10 routine tonsillectomy specimens and 5 colectomy specimens were fixed separately in 10% neutral buffered formalin (NBF) solution and dissect aid (DA). Matched samples from each fixative were processed for routine paraffin embedding after fixation for 1, 7, 14, 21, 42, 84, 96, and 112 days. Section of each block was immunostained for MLH1, MSH2 and MSH6. Immunoreactivity was scored in a blinded fashion using a semi quantitative score of 0, 1, 2, 3, and 4. The fixatives' code was then broken.

Results: In tonsils, MLH1 expression in germinal centers was comparable in both fixatives for the first 4 weeks; and thereafter begins to fade out in fixative A samples – with even lower scores in the inter-follicular areas and in the overlying squamous mucosa. For fixative B, MLH1 and MSH6 expression were 4+ in all samples and in all compartments of the tonsil throughout the 16 weeks of tissue fixation; MSH2 expression was 3- 4+ but begins to fade out after 4 weeks. Fixative A samples expressed 1-2+ MSH6 only in the germinal centers and MSH2 was undetectable in most cases (8/10) – even with as little as 24 hours of fixation in fixative A.

In the colon, all fixative B samples stained strongly positive for MLH1, MSH2 and MSH6 and the strong staining reaction was maintained throughout the study. In comparison, fixative A samples' MLH1 scores were consistently at least 1+ lower than corresponding scores for fixative B samples. MSH2 and MSH6 had negative staining reaction for all colon samples processed in fixative A – with as early as 24 hours fixation.

Conclusions: The effect of tissue fixatives on levels of MSI markers is tissue dependent and also varies with the gene product examined. In the tonsil, the overlying squamous mucosa and interfollicular lymphoid cells are more negatively affected than the germinal center cells fixed in fixative A (DA). Compared with MLH1, MSH2 and MSH6 are more susceptible to the adverse effects of fixative A in all the tissue types studied. Fixative B (NBF) is the preferred fixative for MSI immunohistochemical assays.

1835 Quality Control in Microsatellite Instability Testing.

AN Bartley, R Luthra, D Saraiya, R Broaddus. The University of Texas MD Anderson Cancer Center, Houston.

Background: Microsatellite instability (MSI) analysis and immunohistochemistry (IHC) for DNA mismatch repair (MMR) gene products are well-accepted methods in the evaluation of cancers for Lynch Syndrome (LS). Additionally, MSI in sporadic colon cancer has important prognostic and therapeutic implications. The concordance between PCR-based MSI analysis and IHC is typically high. However, whether in a large molecular diagnostics lab or a small community practice, problem cases will arise and are not well-described in the literature. We summarize our findings to document the frequency and outcomes of such cases.

Design: The records of 736 patients who underwent MSI analysis and/or IHC from 2002 to 2010 were reviewed. Patients with both MSI and IHC analysis (n=628) were subsequently studied in detail. Discordance was defined as a discrepancy between the result of MSI and IHC. Problem was defined as a case with indeterminate or questionable IHC for one or more of the MMR genes. All discordant/problematic results were re-reviewed by two pathologists.

Results: Discordances (13) and problems (10) were identified in 23/628 (3.7%) of the cases. Most (12/13) discordances were detected in MSI-high cancers with positive IHC for the four MMR proteins, MLH1, MLH2, MSH6 and PMS2. Following genetic counseling, 67% of those who underwent germline MMR testing were identified to have MMR mutations. The ten problematic cases were grouped as selection error (2), pathologist error in IHC interpretation (6), or unusual pattern of IHC expression (2). Selection error cases involved patients with multiple synchronous MSI-high and MS-stable colon cancers. Pathologist error cases involved difficulties with MSH6 IHC interpretation and overlooking a lack of positive internal control staining. One unusual staining pattern identified included a case with heterogeneous MLH1 and PMS2 staining, later explained by methylation of *MLH1*. The second unusual pattern case showed expression of MLH1 and MSH2 with complete loss of MSH6 and PMS2 in a colorectal tumor that was MSI-high.

Conclusions: Through this quality control review, several recurring sources of problems in laboratory testing for DNA MMR genes were identified including selection and interpretation error and unusual IHC patterns. Many of these problems are correctable via pathologist education. Recognition of discordant cases and referral for germline mutation analysis is important, as a relatively high percentage of these patients will have germline MMR mutations.

1836 A 383% Increase in Testing Efficiency in a Diagnostics Molecular Lab: LEAN Work Design and Continuous Process Improvements Are Critical for Maintaining Steady Expansion of Services and Short Turn-Around Times.

M Cankovic, L Whiteley, J Beher, D Lubensky, RJ Zarbo, D Chitale. Henry Ford Hospital, Detroit, MI.

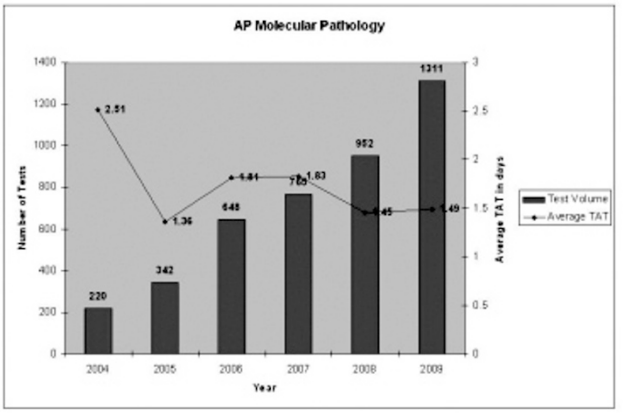
Background: With new cancer biomarkers and targeted therapies growing in number, the demand for molecular oncology lab services has been increasing. In 2006, faced with the necessity to bring on new tests and increase revenue for sustainability, our laboratory made an effort to aggressively eliminate non-value added waste and promote LEAN work practices. Standard activities, direct connections and pathways, and continuous improvement and worker empowerment were focused on. The aim of this study was to evaluate effectiveness and sustainability of LEAN in a laboratory environment with monitoring of total volumes and turn around time (TAT) for clinical tests as the ultimate indicator of lab efficiency and customer satisfaction.

Design: Management and staff received LEAN training in May of 2006 as part of a department-wide effort. All processes, inventories, and customer-supplier connections were evaluated. Specimen delivery, test ordering, reporting of results, inventory, and assay validations were standardized. Teaching modules were developed to educate

suppliers (support personnel, nursing) and customers (physicians). A minimum of 2 process improvements continue to be implemented each month based on PDCA (Plan, Do, Check, Act) principles. Data was collected before and after the implementation of above initiatives which included number of tests, samples, time of receipt and completion of testing for TAT calculation.

Results: Tests offered from rose from 2 in 2004 to 30 in 2009 while the number of clinical samples rose from 220 in 2004 to 1500+ in 2010.

Number of molecular genotyping tests vs average turn around times from years 2004 to 2009.



Conclusions: Over a 4 year period (2006-2009) our laboratory maintained short TAT (1.5-3 business days) with constant staffing levels while significantly increasing the number of tests offered and the samples processed. Additionally, validation studies were done for individual tests before offering them clinically. Creating, structuring and sustaining a culture of continuous improvement allowed us to reduce non-value added waste and allocate resources towards growth and expansion, employee engagement, and greater patient/ clinician satisfaction.

1837 Standardized Prosection Protocol for Whipple Specimens Does Not Affect Lymph Node Counts.

DH Carpenter, DC Linehan, EM Brunt. Washington University School of Medicine, St. Louis, MO.

Background: Increased attention to circumferential resection margins (CRM) of pancreatoduodenectomy (Whipple) specimens has resulted in a new standardized prosection protocol (SP). The traditional protocol (TP) for 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; lymph nodes (LN) were dissected by palpation or direct visual identification and submitted separately. The new 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 including peripancreatic fat with LN. Thus, each slide contains an inked margin for evaluation. The aim of this study is to evaluate whether the new SP is equivalent to the TP with regard to LN count and status. The hypothesis was there would be an increased number of LN and positive LN in the SP compared to the TP.

Design: All Whipple cases since the change in protocol in Oct 2009, were reviewed (n=81). Consecutive Whipple specimens following the TP from the prior year were the comparator group (n=122). Known non-neoplastic cases were excluded from both groups. The surgeons for both groups were the same, as was the spectrum of final diagnoses. The total and positive number of LN dissected from the Whipple specimens were quantified for each case; LN submitted separately by the surgeon were excluded in order to evaluate only differences in the *prosection* protocols. The mean number of LN for SP and TP was calculated and compared using the t test. For both groups, the number of positive LN per case was calculated, as was the total percent of cases in each group with at least one positive lymph node.

Results: In the TP group, the average number of LN per case was 22.1; in the SP group, the average number of LN per case was 24.5 (p=0.13). The average number of positive LN for the TP and SP groups was 2.2 and 2.3, respectively. Additionally, 51% of cases in the TP group had at least one positive LN, compared to 46% of cases in the SP group.

Conclusions: In spite of serial sectioning of LN by the new SP, the average counts and the number of positive LN per case has not increased in a statistically significant fashion compared to the TP. Thus, the SP provides the benefit of complete margin assessment as well as thorough, but not inflated LN counts.

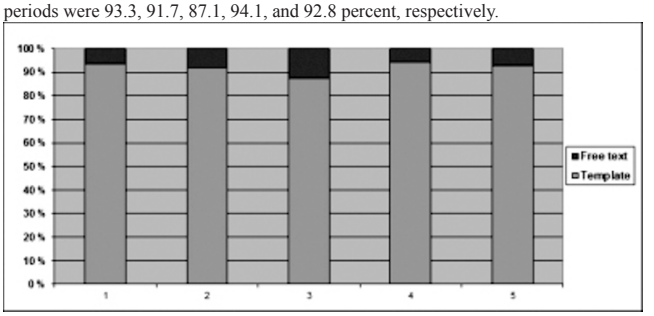
1838 Template Reporting of Colorectal Carcinoma Resections: 5-Year Follow-Up Shows a Stable, High Adherence Rate to the Implemented Guideline.

B Casati, R Bjugn. Akershus University Hospital, Lørenskog, Norway; Oslo University Hospital, Norway.

Background: Several professional pathology organizations have published guidelines to ensure adequate quality of histopathology cancer reports. Template (or synoptic) reporting have been found to be superior in ensuring that key parameters are reported. Studies in clinical medicine have, however, shown that adherence rates to guidelines may return to baseline levels after cessation of the specific implementation strategies. In 2005, a nationwide system for electronic template reporting of colorectal carcinoma resections was introduced in Norway. The present study was undertaken to evaluate the long-term adherence to the use of this template in a routine pathology department.

Design: All histopathology reports on colorectal carcinoma resections for a 5-year period (April 1, 2005 to March 31, 2010) were identified by a systematic search in the full electronic pathology software package being used by the laboratory. The reports were then evaluated with respect to the use of the electronic template. In order to evaluate a possible time-change in adherence to the use of the template, the reports were grouped into five consecutive 1-year periods.

Results: 1186 colorectal resection specimens were identified. The electronic template had been used in 1089 cases (91.8%). The adherence rates in the five consecutive 1-year periods were 93.3, 91.7, 87.1, 94.1, and 92.8 percent, respectively.



Conclusions: Our study shows a high, consistent rate of adherence to the use of the electronic template. The template was implemented in 2005 based on a joint decision among the consultants after just one group discussion. Apart from a quality-survey 18 months after the introduction of the template, no other interventions had been undertaken. Among factors influencing the implementation of such a guideline (characteristics of the guidelines; the implementation strategies; the professionals; the patients; or the environment), we believe the characteristic of the template (experienced simplicity and efficiency in use) and the environment (common decision among consultants and supportive "peers") were the factors ensuring the high adherence rate despite a very simple implementation strategy.

1839 Determination of HER2 Status Variability by Immunohistochemistry in Chile.

L Contreras, M Garmendia, J Levican, A Piottante. Clinica Las Condes, Santiago, Chile.

Background: The cancer treatment based on molecular targets, is in active research and development. The HER2 is one of the most studied drug targets The determination of HER2 gene status in breast cancer is a prognostic and predictive marker. This status must be determined with an exact technique for an adequate therapeutic decision.

Design: During 2008 and 2009 we analyzed 221 biopsies from 221 women with invasive breast cancer sent by 41 chilean pathology laboratories to determine HER2 status by Fluorescent In Situ Hybridization (FISH). 201 biopsies allow analysis (90.1%). In our Lab the HER2 status was determined by IHC and FISH in a standardized way in accordance with the American Society of Clinical Oncology and the College of American Pathologists (ASCO/CAP) recommendations. These results were compared with the original HER-2 IHC reports from different laboratories.

Results: The variability of the assessment of HER2 status in the 41 national laboratories is similar to that described in international literature, reaches 19.7% when compared with standard IHC technique and reach 26.9% when compared with FISH. The rate of false positives in IHC is 15.7% and 25.6% when compared to FISH, the false negative rate reaches 28.7% for both IHC and FISH.

Conclusions: This study confirms the need for Chilean laboratories carrying out the determination of HER2 status to implement validated IHC technique with stringent quality controls both internal and external, employing standardized technical and interpretative procedures according to international recommendations for a proper therapeutic decision.

1840 Enhancing Peri-Operative Tissue Specimen Safety – Standardization of the Surgery-Pathology Hand-Off.

R D'Angelo, R Zarbo, R Varney, F Torres, O Alassi, G Sharma, O Kryvenko, D Lubensky, A Ormsby, N Main, S Richard. Henry Ford Health System, Detroit, MI.

Background: Numerous bodies call for improving effectiveness of communication among caregivers (National Patient Safety Goal #2). A highly recommended process calls for verbal-written specimen identification with perioperative readback verification of verbal communication between caregivers (physician, scrub nurse, circulator) to prevent misinformation (WHO & AORN Guidelines for Safe Surgery). We describe our Lean based process changes to standardize the Surgery to Pathology hand-offs to improve specimen safety as part of the statewide Michigan Hospital Association's Keystone-Surgery initiative.

Design: Customer-Supplier teams trained in Lean process redesign were established between Surgical Services and Pathology at Henry Ford Hospital, Detroit, MI. to define mutual requirements, identify defects, lack of standardization, and brainstorm solutions to improve the quality of specimen hand-offs between caregivers. A daily database maintained by Pathology was created to longitudinally track specimen requisition and container defects related to specimen label, patient identification, numeric identifier, specimen source or type or laterality.

Results: Specimen defects were reduced by 90% in 2010 January (87) to July (8). The following process changes contributed: 1. A perioperative Read-Back was implemented

from surgeon to circulator/scrub nurse to repeat information for each specimen as a standard communication. 2. A 15 minute specimen handoff training video was developed for Surgical Services personnel. Surgeon training consisted of a 30 second video of Read-Back instructions shown within the OR on OR-TV. 3. A chain of custody process was established with the Frozen Section room documenting receipt of specimens. 4. Specific specimen streams were created to standardize the approach to time sensitive (frozen section) or special handling cases. 5. Standardized label stations were created and placed within each OR for accurate specimen identification at the point of collection that provide color coded specimen container label stickers for each specimen stream. 6. Labels were further redesigned for frozen section indication to include a box for diagnosis and margin.

Conclusions: Marked improvement in specimen safety with effective and consistent communication of hand-offs can be achieved through engaged work teams focused on creating standardized work activities, connections, and pathways. The development and use of interim outcome metrics is key to guiding the adoption and understanding the impact of process improvement changes proposed to achieve the goal of zero defects.

1841 Lean Preanalytic Process Improvement of Lymphoma Workup.

R D'Angelo, K Inamdar, R Varney, D Lubensky, G Sharma, J Crane, J Pimentel, ON Kryvenko, RJ Zarbo. Henry Ford Health System, Detroit, MI.

Background: Lymph nodes biopsied for lymphoma work up may require special handling to be processed promptly for work up with portions of tissue directed to numerous laboratories. To address numerous observed defects in this complex pre-analytic process, we describe a Lean process redesign directed at lymph nodes biopsied via CT guided intervention targeting shorter transport to process times.

Design: The preanalytic process was subjected to value stream mapping to identify steps from specimen collection and preparation, transport to the lab, in-house processing and aliquot delivery to an off-site reference laboratory for flow cytometry testing. Each step in the process was analyzed for time waste, process inefficiencies and further opportunities for improvement. The initial condition was evaluated for lymph node biopsies from Aug-Dec 2009. The post process redesign data was derived from January-September 2010. Measures compared were specimen collection to delivery times and total turn around time from collection to pathology report diagnosis.

Results: To address deficiencies we tested and adopted the following interventions:

1. A visual signal to designate STAT delivery status was created to distinguish these specimens from routine specimens derived from the CT suite. Standard work aides were developed to enable staff to consistently place colored stickers on the specimen, information card, container and bag.
2. A direct connection was established between CT and Pathology to assure ASAP specimen transport from 3 floors away directly to the Surgical Pathology Gross Room, bypassing the Clinical Laboratory.
3. A chain of custody hand-offs was created with time/date of each specimen taken and received. This log is the daily metric assuring processing times are met.
4. Enhanced communication was established between all stakeholders to enable real-time feedback to communicate discrepancies and resolutions.

Our baseline of 20 lymph node biopsies was an average preanalytic specimen collection to laboratory delivery time of 4.23 hours. After process redesign, the timeliness of specimen delivery to lab improved by 33% to 1.38 hours. The total turnaround time from biopsy procedure to pathology report improved by 20% from 5 to 4 days.

Conclusions: Using Lean tools of value stream mapping and Lean work rules targeting creation of standardized work, connections and pathways can result in marked reduction of time waste in the preanalytic aspect of lymphoma work up that may impact downstream specimen integrity with potential diagnostic implications.

1842 Immunofluorescent (IF) Slides for Renal Biopsies Can Be Safely Used for Review after One and Half Years of Storage in Room Temperature.

TR Fennell, MT Rooney, PL Zhang. William Beaumont Hospital, Royal Oak, MI.

Background: IF sections for renal biopsies are usually discarded after the diagnosis is reached in many laboratories because of assumed reduced fluorescent intensity over time. IF slides are ideally used for later internal and external reviews in addition to slides for light (LM) and electron microscopy (EM). In this quality control study, we determined whether IF staining intensity was reduced in renal biopsies over one and half years.

Design: We retrospectively queried our database for control cases composed of 21 focal segmental glomerulosclerosis (FSGS) and 35 study cases with immune complex mediated glomerulopathy (ICMG), from 01/2009 to 06/2010. The frozen sections were washed with Difco FA buffer, incubated with specific fluorescein labeled antibodies for 30 min and coverslipped with Permafluor mounting media. IF slides were kept in dark boxes at room temperature after initial evaluation. IF slides for IgG, kappa and lambda were re-examined for fluorescent intensity after a storage time ranging from 1 to 17.5 months (m) and the fluorescent intensity was scored from 0 to 3+. The re-examined scores were compared with initial scores statistically.

Results: Control cases (FSGS) showed no staining in both initial and re-examination. In ICMG group, there was small but non-significant reduction in staining intensity for IgG, kappa and lambda over time; these included 1.3% reduction from 1m to 6 m (n = 13), 10.0 % reduction from 6 m to 12 m (n =10) and 8.3% reduction from 12 m to 17 m (n = 12). Overall (including control and study cases, n = 56), there was significant correlation between initial scores and re-examination scores (IgG, r = 0.924, p = 0.001; kappa, r = 0.878, p = 0.001; lambda, r = 0.879, p = 0.001, by linear regression analysis). One case with remarkable intensity reduction at 14 m was a type 2 lupus nephritis. One anti-glomerular basement membrane (GBM) case did not show intensity reduction at 5 m but another anti-GBM case lost most of staining intensity at 13.5 m.

Conclusions: Our data suggest that IF intensity, corresponding to large immune complex deposits by EM, was relatively well maintained from 1 month to 17.5 m in most cases, particularly when a panel of stains (such as IgG, kappa and lambda) was reviewed and a trend of panel staining was considered together. Small deposits in mesangial areas and anti-GBM staining may be lost after a year. Room temperature is adequate for the storage. This study encourages complete internal or external reviews using all LM, IF and EM slides in each renal biopsy case.

1843 Comparison of Two Staging Systems for Hepatocellular Carcinoma in Post-Transplant Liver Patients.

M Garcia-Buitrago, P Bejarano. University of Miami/Jackson Memorial Hospital, FL.

Background: Several staging systems have been used to predict prognosis and guide therapeutic approach for hepatocellular carcinoma (HCC). Current treatment options include resection and transplantation. The United Network for Organ Sharing organization uses the modified staging American Liver Study Group (ALTSG) to allocate donor livers to patients with HCC who require transplantation. The best staging system remains controversial. The aim of this study is to compare the American Joint Committee on Cancer (AJCC) and ALTSG staging systems.

Design: A search for HCC patients who underwent liver transplant over a 6-year-period was performed. The pathology reports and histology slides of the native livers were reviewed to assess number of tumors, tumor size, lymphovascular and portal invasion. The cases were re-staged using AJCC and ALTSG systems. Survival and recurrence data were collected.

Results: Liver transplantation for HCC was performed in 203 patients (155M, 48F) with a mean age of 58 years (range 29-77). The average follow-up was 29 months (range 0.5-76). Using the AJCC, 43% of patients were stage I, 51% stage II and 6% stage III. Using the MSALTSG, 16% of the patients were stage I, 53% stage II, 18% stage III and 14% stage IV. The overall survival at AJCC and ALTSG stages I-II was 30 and 31 months, respectively. The overall survival at AJCC and ALTSG stages III-IV was 15 and 26 months ($p<0.02$). Recurrence rate at AJCC stages I, II and III are 2%, 10% and 33%, respectively. Recurrence rate at ALTSG stages I, II, III and IV are 3%, 5%, 14% and 18, respectively.

Conclusions: Among the two systems, the AJCC showed better stratification of patients when evaluating the overall survival. However, ALTSG showed better discrimination of recurrence rate. While further studies are performed to establish the ideal staging system in transplanted patients with HCC, we strongly recommend the use of both systems in the synoptic reports.

1844 High Frequency of Instability in Penta D in Microsatellite Instability High Colorectal Cancer: Potential Pitfall in Tumor DNA Identity Interpretation.

MA Grilliot, M Bronner, D Patil, T Plesec, X Liu. Cleveland Clinic.

Background: DNA fingerprinting analysis was originally developed for parental and forensic identity testing using normal tissue. However, it has been increasingly used to confirm identity in possible malignant tissue contaminants on histologic slides or in cases of mislabeled tissue blocks. The Promega PowerPlex 16 System is widely used for tumor DNA fingerprinting and analyzes 15 polymorphic microsatellite loci, including Penta D. This allele is also present in the widely used Promega microsatellite instability (MSI) kit. Penta D instability may lead to false positive non-identity results in MSI-H cancers. This study aims to determine the frequency of Penta D instability in MSI-H colorectal cancers and to raise pathologists' awareness of potential pitfalls in tumor DNA identity interpretation.

Design: Electropherograms for MSI tests performed on colorectal neoplasms from 2009 to 2010 were retrieved. All alleles of Penta D in tumors were recorded and compared to paired normal control tissue to determine the frequency of altered alleles and overall pattern of alleles in MSI-H tumors. MSI-H was determined using the Promega MSI kit in context with paired normal control.

Results: Electropherograms for MSI tests performed on 473 colorectal neoplasms were analyzed. A total of 79 tumors were MSI-H and 394 were microsatellite stable (MSS). Of 79 MSI-H neoplasms, 37 (46.8%) revealed instability in Penta D [vs. 1 of 394 (0.3%) MSS tumors, $p<0.00001$]. In MSI-H tumors with Penta D instability, 22 cases (59.5%) had 3 Penta D peaks, 5 cases (13.5%) had 4 peaks, 7 cases (18.9%) with homozygous Penta D control DNA showed 2 peaks, and other patterns were seen in 3 cases (7.6%).

Conclusions: Penta D instability is common in MSI-H tumors (46.8%); its presence produces a mixed or nonidentity genotype pattern in comparison to known patient DNA. Without attention to this fact, Penta D instability in MSI-H tumor could result in false positive DNA non-identity test results. The rate of instability in MSI-H tumors of the remaining 14 loci comprising the Promega PowerPlex 16 System kit, in addition to Penta D are urgently needed to further address this largely unrecognozided issue.

1845 Use of a Laboratory Information System (LIS) Driven Tool for Cytopathologist Pre-Signout Quality Assurance.

SN Kamat, AV Parwani, W Khalbuss, SE Monaco, SM Kelly, LT Wiehagen, AL Piccoli, KM Lassige, L Pantanowitz. University of Pittsburgh Medical Center, Shadyside Hospital, PA.

Background: A quality assurance (QA) program is designed to detect, control and prevent errors. A novel pre-signout QA tool (PQAT) at our institution allows the LIS to automatically and randomly select an adjustable percentage of non-gynecological cytology cases for prospective review by a second cytopathologist before release of the final report. The aim of this study was to review our experience with using this novel PQAT and to determine its effectiveness in the cytopathology laboratory.

Design: Software modifications were made to the existing LIS application (CoPathPlus, Cerner) to allow for QA peer review of random cases prior to signout. Following implementation of PQAT in February 2009 at two medical centers (UPMC-Shadyside & UPMC-Presbyterian), a cytopathologist had around 8% of their cases randomly selected at the time of electronic signout for peer review by a second cytopathologist. An assigned QA cytopathologist reviewed the selected cases and entered their interpretation (agreement or major/minor disagreement) with comments directly into the LIS. The original pathologist was provided with the opportunity to rectify any detected errors before the case was signed out. The reviewing pathologist was entered into the LIS as a consultant. Data from cases selected for PQAT over an 18 month period (Feb 2009-Aug 2010) were collected and analyzed using descriptive statistics.
Results: The total number of non-gynecological cases subjected to pre-sign out QA review during this time period was 1,339 (7.45%) out of a total of 17,967 cases signed out. For the vast majority of cases (1,304 cases; 97.4%) cytopathologists agreed with the entered diagnosis. There was a disagreement in 2.6% of cases, including 34 (2.5%) with minor disagreements (such as 14 thyroid FNAs involving FLUS cases and 3 bronchoalveolar lavages where fungus was missed) and only one major disagreement identified (overcalled CSF specimen which was confirmed to be negative for leukemia using flow cytometry). Average turn around time of cases selected for the PQAT was 1.56 days, compared to an average of 2 days for all non-gynecological cases signed out.
Conclusions: The PQAT is a novel mechanism in non-gynecological cytopathology that provides an automated prospective QA method for preventing potential diagnostic errors from occurring. This process allows for a second peer review and potential corrective action prior to the reporting of a diagnosis without delaying turn around time, in order to decrease the potential for errors and thereby improve patient safety.

1846 Simulation Based Medical Education (SBME) of Intraoperative Frozen Section Interpretation.

GR Kotnis, TA Wilkerson, CP Yantsides, SS Raab. University of Colorado Denver, Aurora.
Background: A major source of latent error in diagnostic anatomic pathology is secondary to pathologist training. The traditional apprenticeship training model focuses on completion of specifics tasks and not on quality improvement, standardization, and continuous learning. Using standardized SBME modules, we assessed baseline resident performance in intraoperative diagnostic consultation practice as a means to target training for specific weaknesses.
Design: We created a SBME intraoperative consultation program that includes 400 intraoperative cases modules. Slides from each module were reviewed, the original interpretation was confirmed, and a new interpretation in a standard format was generated. A diagnostic difficulty score and a technical quality score, using a five point Likert scale, were assigned. Nine pathology residents representing all five years of post graduate training (PGY) completed the SBME modules to establish baseline competence. The residents were provided the cases using standaridzed answer forms and assigned a technical quality and difficulty score. A total of 30 modules of 5 cases each were completed. The concordance between the technical and diagnostic scores was correlated with the original assessment; the interpretation was examined for error in 2 ways: 1) if the standard and the resident interpretation directly matched, and 2) if the standard and resident interpretation matched in a general, but not a direct sense (e.g. necrotizing granuloma and negative.)
Results: Overall the pathologists in training were 84% correct using the loose criteria and 70% correct using the strict criteria (see Table 1). Segregating the cases by organ system allowed us to track trends, indicating the gynecologic and gastrointestinal specimens had high rates of error, while lymph nodes for metastaic cancer did not. Tracking of technical quality and root cause analysis points to shatter artifact and fat content to be particular reasons for poor technical scoring.

Summary of Results

Total Correct Mean (Loose)	84%	Total Correct Mean (Strict)	70%
Correct Mean (Loose) PGY1	68%	Correct Mean (Strict) PGY1	44%
Correct Mean (Loose) PGY2	87%	Correct Mean (Strict) PGY2	68%
Correct Mean (Loose) PGY3	78%	Correct Mean (Strict) PGY3	66%
Correct Mean (Loose) PGY4	88%	Correct Mean (Strict) PGY4	88%
Correct Mean (Loose) PGY5	94%	Correct Mean (Strict) PGY5	86%

Conclusions: This pilot data show that the the SBME may establish baseline resident competence that correlates with PGY.

1847 Misidentifications as Root Causes for Amended Reports in Surgical Pathology.

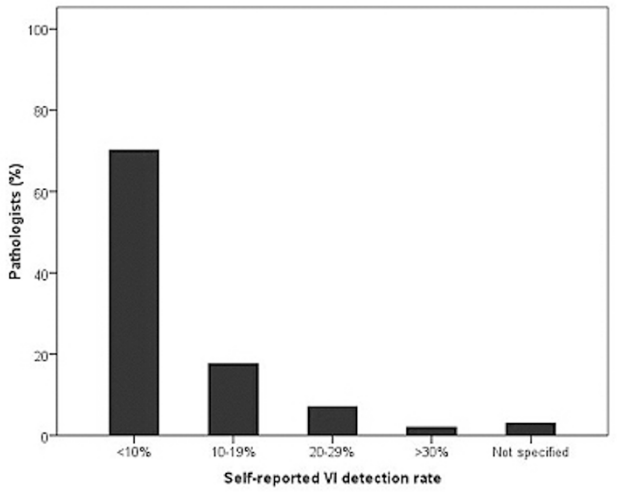
FA Meier, RC Varney, C Neuman, A Ormsby, O Alassi, RJ Zarbo. Henry Ford Hospital, Detroit, MI.
Background: During 2008-2009 we used a previously validated taxonomy of defects (misclassifications, specimen defects, misinterpretations, report defects) to identify causes of amendments in surgical pathology reports. This study assess the contribution of misidentifications (mis-Ids) to amendments and sorts through their root causes.
Design: For the two year period, amendments were classified as they occurred, measured as defects per thousand cases, and placed into the four categories. For the category of mis-Ids, defects were sub-classified as patient, anatomic site, laterality, and tissue type mis-Ids. Among the patient mis-Ids, the loci of misidentification events were further determined to be external (outside the pathology department) vs. internal (inside the pathology department).
Results: 512 amendments were classified as they occurred among 92,509 accessions (5.5 defects/1000 accessions): 12% (62/512) were mis-Ids, 4.7% (24/512) specimen defects, 4.5% (23/512) mis-interpretations, and the remaining 79% (403/512) report defects not qualifying for the previous three categories. Among mis-Ids, 47% (29/62) were of patients, 8% (6/62) of anatomic site, 32% (20/62) of laterality, and 11% (7/62) of tissue type. 38% (11/29) of patient mis-Ids occurred internally – in the pathology department.
Conclusions: During a two year span with a stable defect rate of 5.5 report defects/1000 accessions, mis-Ids accounted for 12% of all amendments; patient mis-Ids accounted for almost half (47%) of all mis-Ids; more than a third (38%) of patient mis-Ids occurred within the pathology department's control. To the extent that mis-Ids lead to amended reports, these three characteristics – the fraction of all amendments caused by mis-Ids, the fraction of all mis-Ids that are patient mis-Ids, and the fraction of patient mis-Ids that occur internally – quantify salient effects of mis-identifcation in the surgical pathology diagnostic process.

1848 A New Resident QA System, an Interesting Self Study Activity in Pathology Residency Training.

MP Menon, M Hure, BA Woda, P Miron, L Savas, Z Jiang. University of Massachusetts Medical School, Worcester.
Background: Our residency program instituted a quarterly resident quality assurance (QA) system to evaluate residents' performance in their daily pathology practice. Each quarter, senior residents evaluate several aspects of resident performance. The purpose of our resident QA program is to identify systemic problems and individual resident mistakes at any point in the course of processing surgical pathology specimens.
Design: Data was collected by senior residents, laboratory directors, managers, LIS specialists and traditional log books in a quarterly fashion from May 2009 to April 2010. The specific items addressed include each resident's total number of errors when processing specimens, the accuracy of labeling specimens with the correct accession numbers and patient initials, any delays in the processing or reprocessing of specimens and any inadequacies in processing, such as thick tissue sections. Each quarter, a senior resident summarizes the data and presents the findings during a resident meeting, which is also attended by the Program Director and the Associate Director. The Director of Anatomic Pathology also reviews the QA data as one of the important parts of our departmental QA program. The residents, Program Director, and Associate Director analyze the data and compare the current data to the previous quarters' QA data to track performance.
Results: Analysis of the data showed several interesting observations. There was no significant difference in the total error rate across different post-graduate levels. However, as expected, specific errors like processing errors were represented more in the junior residents. Also, the average error rate per resident/quarter (number of errors per resident/quarter) was observed to be lower as compared to the error rate of Pathology Assistants (3.9 vs. 7.6). In addition, since the inception of this program, specific pre-analytical errors that could seriously impact patient care such as wrong surgical numbers, wrong cassette codes and wrong patient initials were dramatically reduced. Specifically, the number of cases with wrong surgical numbers dropped from 22/quarter (May2008-May2009) to 7/quarter (January to April 2010).
Conclusions: The UMass resident QA process has created a good opportunity for residents to identify their errors when grossing and processing specimens. As a result, the number of both minor and egregious mistakes, e.g. not detecting mislabeled specimens, has been significantly reduced. Resident QA is an excellent learning and self improving activity for our residency training program.

1849 Current Practice Patterns among Pathologists in the Assessment of Venous Invasion in Colorectal Cancer.

DE Messenger, DK Driman, RS McLeod, RH Riddell, R Kirsch. Mount Sinai Hospital, Toronto, ON, Canada; London Health Sciences Centre, ON, Canada.
Background: Venous invasion (VI) is an independent prognostic indicator of recurrence and decreased survival in colorectal cancer. The Royal College of Pathologists (RCPath) recommends that extramural VI should be detected in at least 25% of specimens, although the College of American Pathologists' protocol does not provide a reference standard. There is widespread variability in the reported incidence of VI, which may impact on patient access to adjuvant therapy. This study aims to clarify the current practice patterns of pathologists regarding the assessment of VI and to identify factors associated with an increased self-reported VI detection rate.
Design: A population-based survey was mailed to all pathologists in the province of Ontario, Canada.
Results: Surveys were mailed to 361 pathologists. The overall response rate was 64.9%. Most pathologists were practicing in community-based centers (66.2%) and aprroximately half had been in practice for over 15 years (53.5%). A sub-specialist interest in gastrointestinal (GI) pathology was declared by 27.3% of pathologists. The majority of pathologists (70.2%) reported the detection of VI in less than 10% of resections, with only 9.1% reporting detection rates above 20%.



Standardized reporting criteria were applied by 62.1%. Special stains to enhance the detection of VI were used routinely by 11.1%, whilst 57.6% used special stains if VI was suspected with hematoxylin and eosin. Practice in a university-affiliated center, a sub-specialist interest in GI pathology and the acceptance of the 'orphan arteriole' criterion were all independently associated with a self-reported VI detection rate above 10% on multivariate analysis.

Conclusions: Self-reported VI detection rates are low among most pathologists. Even among specialist GI pathologists practicing in university-affiliated centers, few achieved the RCPath reference standard. Strategies to increase the detection of VI may be warranted, although the findings of this study first require verification with actual data from pathology reports submitted to the provincial cancer agency.

1850 Image Analysis of the HER2 Immunohistochemical (IHC) Stain – A Study Comparing a Lab Validated Scoring Method and the Manual Assessment Method.

DM Minot, JS Voss, SB Rademacher, TY Lwin, JL Orsulak, A Nassar, B Chen, AC Clayton. Mayo Clinic, Rochester, MN.

Background: The HER2 IHC stain can be assessed quantitatively using digital image analysis (IA) to identify HER2 positive tumors. The goals of this study are to examine the concordance of IHC and FISH and the reproducibility of HER2 IHC interpretation by manual and automated methodologies.

Design: This retrospective study included 154 tumors with both HER2 IHC and FISH analyzed. Manual assessments of HER2 IHC were performed by 3 pathologists (PA) and 3 cytotechnologists (CT). The 3 CTs also performed IA using a laboratory validated scoring method with the ACIS III (Dako, Carpinteria, CA), which consists of a mean score from 2 areas each of tumor with high, moderate, and low intensity staining (6 areas total). Concordances with FISH results were determined. Intraobserver variability was tested by reanalyzing 20 cases by all observers and methods.

Results: Concordances with FISH were very good for IHC negative (0, 1+) and IHC positive (3+) tumors by all methods (Table 1). CT manual and CT ACIS undercalled two cases (IHC-/FISH+), while PA manual and CT ACIS had one overcall (IHC+/FISH-). The ACIS method had fewer 2+ results overall (n=16) compared to both CT manual (n=23) and PA manual method (n=25) and had a higher concordance with FISH (31% vs. 26% for CT manual and 20% for PA). CTs had higher interobserver reproducibility by both manual (0.747) and ACIS (0.779) methods than PAs (0.697) (Table 2). CTs had better intraobserver reproducibility (0.882) using ACIS method than manual assessment by either CT (0.828) or PA (0.766).

Table 1. Specimens per HER2 IHC Score by Assessment Type with FISH Results

	Score				
	(0)	(1+)	(2+)	(3+)	Total
PA Manual	29 (0)	88 (1)	25 (20)	12 (92)	154
CT Manual	21 (0)	101 (2)	23 (26)	9 (100)	154
CT ACIS	45 (0)	82 (2)	16 (31)	11(91)	154

* Percentages of cases that are FISH positive (ratio >2.2) are shown in parentheses

Table 2. Intra- and Inter-Observer Reproducibility of HER2 IHC Scores by Assessment Type

Comparison (Average)	Interobserver (Avg. Kappa)	Intraobserver (Avg. Kappa)
PA Manual	0.697	0.766
CT Manual	0.747	0.828
CT ACIS	0.779	0.882

* Negative categories (0 and 1+) are combined

Conclusions: ACIS-assisted analysis can improve inter- and intraobserver reproducibility in HER2 IHC assessment. In addition, ACIS-assisted analysis may lower the number of IHC 2+ cases reflexed to FISH while increasing the number of FISH positives in this cohort and maintain high negative (IHC0, 1+/FISH-) and positive (IHC 3+/FISH+) concordances with FISH.

1851 Cholangiocarcinoma: Causes of Failure in Detection in Biliary Brushing Specimens.

FN Moore, SB Sams, SS Raab. University of Colorado at Denver Health Science Center, Aurora.

Background: Our study aims to determine the causes of error in detecting cholangiocarcinoma in bile duct brushings by performing root cause analysis of false-negative bile duct brushing cases to assess (1) specimen and (2) sampling quality. Determining root cause allows for the design of quality improvement initiatives to detect high-grade dysplasia and cholangiocarcinoma.

Design: We performed a 5 year retrospective review of all false-negative bile duct brushings in patients who were diagnosed with either high-grade dysplasia (n=17) or cholangiocarcinoma (n=15) in bile duct biopsies obtained at the time of bile duct brushing. The mean age of patients was 66 years old (range = 43-82 years old). Original bile duct brushing specimens were re-screened by 2 board certified pathologists and one senior resident and reclassified accordingly. Root cause analysis was performed on each case to determine specimen quality and sampling quality. Quality specimens were defined as specimens without processing artifact or obscuring components. Quality sampling was defined as specimens with identifiable tumor.

Results: The frequency of a positive bile duct brushing for suspicious and malignant bile duct biopsies was 19% (n=64). Re-screened sensitivity and specificity of bile duct brushing for either high-grade dysplasia or cholangiocarcinoma were 43% and 86.5% respectively. In 59.3% of cases, failure in detection was seen with a poor quality specimen and poor sampling quality; a system-related error. In 25% of cases, failure in detection was seen with a poor quality specimen and adequate sampling; a combination of system-related and pathologist-related error. In 9.3% of cases, failure in detection was seen with an excellent quality of specimen and poor sampling; a system-related error. In 6.3% of cases a cause of failure was seen with an excellent specimen quality and adequate sampling; a pathologist-related error. System-related error was due to poor sampling, processing, and lack of quality control methods. Pathologist-related error was due to cognitive error.

Conclusions: The causes of false negative bile duct brushing were multifactorial and included system and pathologist-related error. Poor specimen quality and poor sampling quality appeared to have the most significant role in false-negative bile-duct brushing. Pathologist-related error may benefit from consensus by a second pathologist as a meaningful quality improvement measure and warrants further investigation.

1852 How Adequate Are Head and Neck Fine-Needle Aspiration Specimens for HPV Molecular Analysis? An Institutional Experience.

MO Nakashima, D Nielsen, VM van Deerlin, GS Weinstein, KT Montone, VA LiVolsi, ZW Baloch. Hospital of the University of Pennsylvania, Philadelphia.

Background: Human papilloma virus (HPV) testing on head and neck squamous cell carcinomas is being increasingly performed in this era of "personalized medicine". At our institution HPV testing is often requested on fine needle aspiration (FNA) specimens, usually of metastatic lesions, either prior to treatment or after recurrent/metastatic disease. In this study we report our experience with HPV testing on FNA specimens with regards to adequacy of specimen for molecular analysis and if it is affected by method of acquisition (manual v. radiologic guidance, # of passes) and quality of specimen (presence or absence of tumor necrosis).

Design: We searched our institutional pathology files for FNA specimens on which HPV testing (Hologic) was performed. The following data points were recorded: patient demographics, site of lesion, method of FNA procedure, quality and adequacy of specimen for molecular analysis.

Results: A cohort of 42 specimens diagnosed as squamous cell carcinoma (SCC) on FNA were selected in 40 patients (29 men & 11 women, average age 61 yrs); 16 had a prior diagnosis of oropharyngeal (OP) SCC at time of FNA. Thirty-six (86%) specimens were obtained from lymph nodes (cervical-32, supraclavicular-1, submandibular-1, level 7-1, level 11-1) and 6 from other sites (parotid, soft palate lesion, jaw mass, tonsil, lung, chest wall). Of the 42 specimens, 27 were from patients with primary OP lesions, 9 had lesions in oral cavity or larynx and 6 in other sites (parotid, esophagus, lung, cervix, neck, scalp). Thirty-three (79%) FNA specimens were obtained manually and 9 (21%) with radiologic guidance (average # passes 2.2). On-site assessment was performed in 41 (98%) cases; 31 (76%) were diagnosed as SCC and 5 (12%) as atypical/suspicious. A final FNA diagnosis of SCC was rendered in all cases; 9 FNA specimens showed extensive (>80%) tumor necrosis. DNA was adequate for molecular analysis in 28 (67%) specimens (19 positive, 9 negative for high risk HPV) including 7 with extensive tumor necrosis. Results in 14 cases were inconclusive due to inadequate DNA. In addition, 24 of 33 (73%) specimens obtained manually had adequate DNA compared to 4 of 9 (44%) collected with radiologic guidance. Primary OP tumors were more likely to have adequate DNA than non-OP (78% v. 47%).

Conclusions: In our experience HPV testing can be successfully performed on FNA specimens. Neither lack of radiologic guidance for obtaining FNA specimens nor presence of extensive tumor necrosis appears to decrease the likelihood of obtaining adequate DNA for HPV analysis.

1853 Mislabeling Rates of Cases, Specimens, Blocks and Slides; a College of American Pathologists Study of 136 Institutions.

RE Nakhleh, MO Idowu, R Souers, LG Bekeris. Mayo Clinic Florida, Jacksonville; VCU Health System, Richmond, VA; Phoenixville Hospital, PA; College of American Pathologists, Northfield, IL.

Background: Proper specimen labeling is a major safety initiative by the Joint Commission and the College of American Pathologists. Mishaps in specimen labeling have led to patient injury due to wrong side or wrong patient treatment or due to delay

in diagnosis. Our aim is to quantify the rates of mislabeled cases, specimens, blocks and slides and identify the sources of error as well as how they are detected.
Design: This was conducted as a voluntary subscription Q-Probes study. Participants prospectively reviewed surgical pathology cases for an eight week period or until 30 errors related to mislabeled cases, specimens, blocks and slides were identified. Information collected on each labeling error included the work location, what was mislabeled, the number affected, the point of detection, and the outcome. Institutional demographics and practice variables were also collected. The rates of mislabeled cases, specimens, blocks and slides were tested for association with institutional demographics and practice variables.
Results: 136 institutions provided information on a total of 1811 mislabeling occurrences. The overall rate (per 1000) of mislabeling were 1.1 cases, 1.0 specimen, 1.7 blocks and 1.1 slides. In terms of frequency 27.1% were cases, 19.8% specimens, 25.5% blocks and 27.7% slides. 20.9% of errors occurred before accessioning, 12.4 at accessioning, 21.7% at block labeling, 10.2% during grossing and 30.4% at tissue cutting. Errors were typically detected in the 1-2 steps following the error. Lower mislabeled slide rates were associated with continuous individual case accessioning and having formal checks at accessioning. Lower mislabeled specimen rates were associated with routinely including a statement in the gross description that the specimen is labeled with the patient's name and is properly identified. In 96.7% of errors the only outcome was correction of the error, in 3.2% a corrected report was issued, but in 1.3% patient care was affected.
Conclusions: This study demonstrated the mislabeling rate of cases (0.11%), specimens (0.1%), blocks (0.17%) and slides (0.11%). Errors in labeling appear nearly equally throughout the system of accessioning, grossing and tissue cutting. Errors are typically detected in the immediate steps following where the errors occurred reinforcing the need for quality checks throughout the system.

1854 Solid Tumor Molecular Diagnostics: Workflow Challenges for Anatomic Pathology and Molecular Testing.

R Ochs, C Deshpande, C Watt, K Montone, V VanDeerlin, A Sepulveda. Hospital of the University of Pennsylvania, Philadelphia.
Background: With recent clinical evidence guiding treatment decisions, demand for molecular characterization of solid tumors is increasing, presenting distinct challenges to molecular and surgical pathology laboratories. Testing is frequently requested on outside submitted specimens (OSS) that require review by an anatomic pathologist. Submitted material is often a small surgical biopsy or cytopathology cell block and this material may be exhausted during initial diagnosis. Communicating with clinicians regarding receipt of outside slides and/or paraffin blocks and specimen adequacy can be complex. Here we report our experience with solid tumor molecular diagnostics following transition to a laboratory information system (LIS) based specimen tracking system handled by a dedicated Molecular Anatomic Pathology service.
Design: Solid tumor testing requested on paraffin-embedded tissue was tracked using an internally generated report in the LIS during a three month period (July to September 2010) following transition from a manual tracking system. Comparison of overall turn-around time (TAT), specimen type received and specimen adequacy was performed on OSS and our institutional specimens (OIS). TAT comparison with our prior manual system was also performed.
Results: Analysis performed for melanoma, lung and colon cancer specimens (n=115) revealed 68 OIS and 47 (41%) OSS requests. Significantly shorter average TAT for OIS-11.8 workdays compared to 15.4 workdays for OSS ($p<0.05$) was noted. Specimens submitted for molecular testing included 73 *KRAS*, 67 *EGFR*, 33 *BRAF*, and 21 *CKIT* requests. Thirteen tests were cancelled for inadequacy due to low tumor volume (12.8% for OSS, 10.2% for OIS) including 6 fine needle aspiration (FNA) specimens (43% of FNA's) and 7 surgical pathology biopsy specimens (15% of biopsies). Three tests were cancelled because adequate outside materials were not received within two weeks of the initial request (6.4% of OSS). Average TAT in a prior manual system for a representative molecular assay was 18.4 workdays.
Conclusions: Solid tumor testing at an academic referral center results in requests for testing on same institution specimens as well as a high proportion of outside specimens. This leads to challenges for laboratory personnel, including issues with efficient communication and difficulties that arise from processing test requests unaccompanied by adequate or appropriate specimens. Our experience supports the role of a dedicated Molecular Anatomic Pathology service with an integrated LIS solution for efficient workflow.

1855 Making a Case for Rapid Prescreening of Pap Tests in Quality Assurance/Quality Control and Systems Based Approach to Reducing Errors.

V Padmanabhan, SQ Armstrong, DM Green, FM Quinlisk, SL Augustinowicz, VE Johncox. Dartmouth Hitchcock Medical Center, Lebanon, NH.
Background: To increase the sensitivity of Pap tests, 10% of randomly selected negative Papanicolaou (Pap) smears are rescreened as a quality control (QC) measure. This has been mandated to reduce the false negative rate. Recently, there has been an interest in alternatives to the 10% QC, either rapid prescreening (**RPS**) or rapid rescreening (RRS). In the United Kingdon, **RPS** is the most widely used QC method though this is not the practice in the U.S. In this study, we use **RPS** as a tool for QC and as a system absed approach to reduce errors.
Design: Four hundred and forty seven ThinPrep Pap test smears were reviewed. These cases were initially processed on the ThinPrep Image system. **RPS** was performed by the cytopatholgy supervisor at a rate of 1 slide a minute. Additional time was taken to enter the interpretation in a standardized work sheet. No marks were made on these slides. These cases were then given to the cytotechnologists for review on the ThinPrep Image system review microscopes. **RPS** diagnosis and final diagnosis by the cytotechnologists and/ or the cytopathologists were noted (Table 1). Cases where the **RPS** diagnosis and the final diagnosis were negative were not reviewed; but cases with a difference of diagnosis between the 2 were reviewed. After a full manual rescreen, those cases that needed review by the pathologist were submitted to the pathologist. Cases with 10% QC diagnosis were also noted (Table 2).
Results:

Table 1

n= 447	RPS	FD
Unsatisfactory	4	5
NILM	383	398
Ractive/ Repair	3	9
ASCUS	37	23
ASC-H	0	3
LSIL	16	7
LSIL, cannot exclude HSIL	1	2
HSIL	3	0

Rapid prescreening (RPS) assessment versus final diagnosis (FD)

Table 2

	RPS	10% QC review
ASCUS	6	4
ASC-H	2	0
LSIL	1	0
Total	9	4

RPS versus 10% QC review diagnosis

Conclusions: RPS identified more disease (9 cases) than the 10% QC (4 cases); 2.01% versus 0.89% respectively. Automated rescreening methods have been shown to be better than manual rescreening in some studies. In spite of using automated methods like the ThinPrep image system, the final interpretation is given by the cytotechnologist who has to decide whether the cells present in the fields of view are abnormal. The experience of the cytotechnologists varies in most laboratories, including ours. This is a good system-based approach to monitor new cytotechnologists and improve sensitivity and reduce false negative rates in the laboratory. In summary **RPS** is an inexpensive and efficient method to improve the sensitivity of the Pap test.

1856 Adherence to ASCO/CAP HER2 Testing Guidelines: Equivocal Rates and Impact on Management within a Single Institution.

BP Portier, E Downs-Kelly, C Lanigan, C Cotta, D Patil, G Procop, JR Cook, H Moore, GT Budd, RR Tubbs. Cleveland Clinic, OH; Taussig Cancer Institute, Cleveland, OH.
Background: The American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) HER2 guidelines utilize immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH) algorithms to improve HER2 testing. Our aim was to evaluate adherence to ASCO/CAP guidelines within a single institution performing a high volume of HER2 testing, to assess the ability of the guidelines to resolve equivocal results, and to assess the impact of unresolved equivocal HER2 results on patient management.
Design: All patients (1,770) with breast carcinoma tested for HER2 within the Cleveland Clinic system from January 2008 to June 2010 were included. HER2 status and clinicopathologic data (age, tumor grade and stage, hormone receptor status, *HER2*/CEP17 ratio, and treatment) was retrieved from the electronic medical record. The primary method of HER2 testing at our institution is a dual probe FISH assay (PathVysion, Abbott-Vysis, Chicago, IL) with reflex testing of equivocal cases by HER2 IHC (PATHWAY anti-HER2/neu, Ventana, Tucson, AZ).
Results: A total 1,770 cases were analyzed by FISH over the study period; 79 (4.4%) were identified as equivocal. All 79 were rescored by a second technologist and then reflex tested via IHC (100% ASCO/CAP compliance). IHC resolved the equivocal status in 55 (70%) patients, with 12 (15%) identified as positive (3+) and 43 (55%) as negative (0 or 1+). A double equivocal result by both FISH and IHC was seen in 24 (30%) cases. Within this double equivocal group, 6 patients (25%) received Trastuzumab (Herceptin; Genentech, South San Francisco, CA). The only statistically significant clinicopathologic factor in patients that were treated with Herceptin was age <50 ($p = 0.003$).
Conclusions: Previous literature has shown that employing FISH rather than IHC as the primary HER2 testing methodology results in fewer equivocal cases (5% versus 32%, respectively Grimm et al 2010); our current study shows a similar equivocal rate (4.4%) by primary FISH. Reflex HER2 IHC testing resolved 70% of the equivocal FISH cases, however 30% were equivocal by both methodologies. These double equivocal cases are problematic in that there is no accepted guideline for the management of these patients. Outcome studies with long-term follow-up are needed to establish an optimal management plan for the double equviocal subset of breast cancer patients.

1857 Validation of Pathologist Use of Whole Slide Images for Remote Frozen Section Evaluation.

JP Ramey, K Fung, LA Hassell. Oklahoma University Health Sciences Center, Oklahoma City; Oklahoma City Veterans Affairs Medical Center, OK.
Background: Telepathology has been used for remote evaluation of frozen sections (FS) with acceptable results for many years. Advances in whole slide imaging (WSI) and other technologies introduce new possibilities to apply to this challenge. Validation, regulatory and credentialing issues associated with WSI appear important. Previous studies have limited case types evaluated rather than looking at a broad spectrum of cases referred for FS evaluation.
Design: A series of 72 consecutive cases with FS requests were selected for study. FS slides were scanned using an Aperio Scanscope scanner at 20x magnification. All materials utilized in the FS consultation including gross images (if available) and descriptions, clinical information, cryostat sections and cytologic preparations (if available) were catalogued with the images. Scan times were recorded. WSI FS cases

were presented to 8 pathologists for diagnosis on desktop or laptop computers using Webscope or Imagescope viewing software. Time to diagnosis and other parameters of evaluation were noted. The WSI FS results were compared to original reported and final diagnosis to derive kappa values. Cases with discrepancies were subjected to further consensus review of the original glass slides. Cases are available to pathologists at http://moon.ouhsc.edu/kfung/HR2010/Default.htm for additional data accrual and educational purposes.

Results: Average scan time was 2 minutes 14 seconds per slide. Computer hardware in use showed the following minimal specifications: monitor resolution 1024x768 pixels; processor speed 2.59gHz, memory (RAM) 2 gb. Evaluation times for WSI FS averaged 4 min 13 seconds/slide, of which an average of 55 seconds was spent at magnifications above 10x. Complete concordance between initial FS diagnosis (FSdx) and WSI FSdx was observed in 91% of cases. Minor discrepancies resulting in no change in management were observed in 7% of cases. Overall method kappa value was calculated to be 0.84. Type of FS request (margin, etc.) did not influence performance in this series.

Conclusions: WSI offer an acceptable solution for remote FS consultation on a wide variety of cases. Scanning and examination times should not pose a barrier to meeting service time demands intraoperatively. Existing standard hardware in use generally offers acceptable performance. Validation within institutions should include system processes or procedures, hardware and personnel considerations and be be thoroughly tested prior to adoption in routine use.

1858 Do Neoplastic Surgical Pathology Reports Contain Redundant Information?

N Rassaei, CE Parra-Herran, V Nose. University of Miami – Jackson Memorial Hospital, FL.

Background: The College of American Pathologists (CAP) requires the CAP cancer protocol to be completed for each cancer case. Some institutions such as ours include two parts in their cancer surgical pathology reports (CSPR), one contains the main diagnosis and histologic findings as sequenced by the pathologist and the second part includes the CAP cancer protocol. With an increasing array of additional studies and information reported, the CSPR may contain redundant information, raising the question as to whether the clinician can glean the essential information required for diagnosis and patient management by one or another and/or both sections.

Design: Our clinicians and pathologists were asked to complete a survey and rank which part of the reports is most important to them with the purpose to have a feedback from clinicians on the content of our CSPR. Our survey asked clinicians and pathologists to rank the parts of the CSPR as follows; A: the initial section including the main diagnosis and histologic findings as sequenced by the pathologist, B: the CAP cancer protocol, C: both sections.

Results: Twenty-five clinicians of different subspecialties (Oncology-surgery, oncology, gynecology-oncology, hemato-oncology, pulmonology, radiation-oncology, and radiology) and twelve pathologists returned our survey. From our clinicians, 68% consider both sections as essential in the CSPR, among which, surgeons and oncologists in particular, consider both parts as essential. 24% consider the section A as sufficient in CSPR. 8% consider the CAP protocol to be complete and sufficient for diagnosis and patient management. From the 12 pathologists that participated in this survey, 41% consider both sections should be included in the CSPR, 25% consider the CAP protocol as sufficient to convey the essential information to the clinicians and 34% of pathologists consider the initial section containing all the diagnostic information as sequenced by themselves to be sufficient.

Conclusions: Adequate and continuous communication between pathologists and clinicians is essential to deliver important diagnostic findings for the appropriate patient management. Feedback from our clinicians, as our customers, is crucial as a quality management tool. This study shows that our clinicians prefer a complete report with cancer CAP protocol, and with the inclusion of a heading highlighting the main diagnosis and important findings.

1859 An Audit of Surgical Pathology and Cytopathology Amended Reports over a 5 Year Period in a Tertiary Care Hospital.

C Rowsell, M Sidiropoulos, Z Ghorab, MA Khalifa. Sunnybrook Health Sciences Centre, University of Toronto, ON, Canada.

Background: Amended pathology reports (AmR) document changes in information that are made after a report is released. These may include changes in the diagnosis, comment, macroscopic and microscopic description, clinical information, and patient identification. We performed an audit of AmR over a 5 year period focussing on total AmR rates and types of changes in order to identify areas for quality improvement.

Design: Analysis of AmR in surgical pathology and cytopathology for the calendar years 2005-2010 at Sunnybrook Health Sciences Centre was performed. AmR were collated for each quarter (Q) of the year and the following parameters were recorded as a percentage per total cases signed out: total AmR and AmR by type of change (changes in diagnosis comment, macroscopic description, microscopic description, clinical information, patient identification).

Results: A total of 937 surgical pathology and 141 cytopathology AmR were reviewed over the 5 year period. Total AmR cases reviewed and AmR rates per total accessions are listed in Table 1. Surgical pathology AmR due to corrections in clinical information (0.22% in Q1 2005, 0.07% in Q2 2010) and cytopathology AmR due to changes in diagnosis/comment (0.07% Q1 2005, 0.01% Q2 2010) both showed a downward trend from 2005 to 2010, but otherwise no significant changes or trends were seen over the study period.

Table 1.

	Total AmR	Total AmR %	Change diagnosis/ comment %	Change micro %	Change macro %	Correct clinical info %	Correct patient ID %
Surgical pathology	937	0.57 (range 0.27-0.93)	0.26 (range 0.13-0.43)	0.04 (range 0-0.07)	0.09 (range 0-0.23)	0.16 (range 0.07-0.48)	0.015 (range 0-0.05)
Cytopathology	141	0.09 (range 0.01-0.18)	0.046 (range 0-0.08)	0.001 (range 0-0.01)	0.014 (range 0-0.08)	0.018 (range 0-0.05)	0.006 (range 0-0.03)

Conclusions: Changes in diagnosis/comment are the most common type of amendment for both surgical pathology and cytopathology reports in our department. Future quality assurance initiatives should focus on the reasons for these changes and the clinical impact of the change in diagnosis. Patient ID corrections were relatively rare, but due to the potentially dire consequences of such errors, new workflow solutions have been introduced to attempt to reduce or eliminate such errors.

1860 An Analysis of Amendments of Diagnoses in Surgical Pathology Reports.

C Rowsell, M Sidiropoulos, MA Khalifa. Sunnybrook Health Sciences Centre, Toronto, ON, Canada.

Background: Amended reports (AmR) are defined as supplemental or secondary reports issued to change original information on a report that has already been issued. Reviewing AmR may be a useful quality assurance tool as they document defects or errors in diagnosis that may have implications for patient safety. We performed a review of our AmR in surgical pathology, focussing on changes in diagnosis/comment with the goal of identifying specific areas for quality improvement.

Design: All AmR over a 27- month period (April 2008 – June 2010) with a change in the final diagnosis and/or comment field of surgical pathology reports were reviewed. Number of amended reports by organ site and day of the week of initial case sign-out were recorded. Other variables investigated included reason for change, as recorded by the pathologist, and type of information changed within the diagnosis/comment field (primary diagnosis, grade, stage, comment, biomarkers, other prognostic factors).

Results: Over the study period, a total of 73, 437 cases were accessioned and 209 AmR for diagnosis/comment were issued (0.28%). AmR occurred most commonly in breast (68; 33% of AmR) and gynecologic (61; 29%) cases, followed by skin (24; 11%), gastrointestinal (20; 10%), genitourinary (19; 9%), and others (17; 8%). For comparison, the percentage of cases accessioned to these groups was as follows: breast 9%; gynecologic 34%; skin 14%; gastrointestinal 21%; genitourinary 6%. No trend was identified with respect to day of the week of initial sign-out. The most common reason given for AmR was typographical error (125; 60%), followed by new macroscopic/microscopic information (37; 18%), immunohistochemical studies (28; 13%), new clinical information (13; 6%), FISH (5; 2%) and EM (1; <1%). The most common components changed were primary diagnosis (109; 52%), comments (40; 19%), staging information (23; 11%), biomarkers (16; 8%), other prognostic factors (13; 6%) and grade (8; 4%).

Conclusions: Our review enabled us to identify areas with a disproportionate amount of amended reports compared to case volume. In a subspecialized practice like ours, this may be helpful in targeting quality assurance initiatives. Although "typographical error" was the most common reason for amendment given by pathologists, local quality improvement guidelines need to emphasize that pathologists are ultimately responsible for the content of the final report regardless of how the diagnosis is entered or by whom.

1861 Validating a Checklist for the Gross Examination of Benign Uteri.

MS Ryan, ML Smith, GR Kotnis, TA Wilkerson, SS Raab. University of Colorado, Aurora.

Background: Checklists are a means to standardize and improve work quality. Although published manuals describe a standard process of gross tissue examination, the development, validation, and implementation of grossing checklists has not been reported. We describe the method of checklist development and validation for benign uteri, based on an assessment of current practice.

Design: We developed a novel benign uterus checklist that included the important components of the gross dictation, including specimen condition, weight and measurements, description of the serosa, exocervix, os, endocervix, endometrium and myometrium, and the listing of sections submitted. The content of the checklist was based on expert opinion, clinical experience and previously published gross examination protocols. Five participants independently reviewed 25 actual surgical pathology reports of benign uteri and assessed 62 components of the gross dictation report using the checklist. For each item, the participants selected whether the gross activity had been performed well, performed poorly, or not performed. We validated the checklist by assessing the level of observer agreement. Items that had >75% agreement were considered validated in the assessment process.

Results: Out of the 62 checklist items, 50 of the items were validated by the 5 participants. There was not concordance among the graders regarding the description of anatomic structures present and the specimen condition. For these two components of the checklist, there was only 60% and 64% concordance, respectively. Specific items, such as the color and texture of the endometrium, were not validated on 8 and 7 specimens, respectively (32% and 28%); for these items, observers ranged in classification from performed well to performed poorly to not performed. The description of most pathologic lesions (e.g., leiomyoma) were not validated (only 36% of myometrial lesions were validated). The sufficiency of sections submitted was very poorly agreed upon, with only 12%, 48%, and 44% agreement for the adequacy of submitted sections from the serosa, endometrium and myometrium, respectively.

Conclusions: Using standardized checklists, observers were not able to validate approximately 20% of benign uterine grossing metrics. These findings indicate that a challenge in gross tissue examination is the high level of variability in the assessment of whether grossing practices were performed well or poorly.

1862 Improving Patient Safety: Root Cause Analysis of Surgical Pathology Reports Released on Wrong Patients.

S Shuja, B Villas, K Lee. University of Florida, College of Medicine-Jacksonville, Jacksonville.

Background: The national drive towards establishing a comprehensive Electronic Medical Record System underscores the importance of accuracy of such records. The ACGME specifically requires training programs to educate residents concerning identification and prevention of human and system errors and implementation of solutions. We present Root Cause Analysis (RCA) for surgical pathology reports released in error on wrong patients at our institution during last 4 years. The objective of our analyses is to educate and provide feedback to all personnel participating in the health care system, and especially residents in-training.

Design: All amended surgical pathology reports that were released on wrong patients since 2006 were pulled and reviewed, as a component of Quality Assurance and Quality Improvement measure. For RCA, two patient identifiers were compared between correct patient and wrong patient. These included name (last and first) and date of birth (DOB) (month, day and year). Also, individual departments where incorrect electronic entries were generated were identified in each case.

Results: Of approximately 50,000 surgical pathology reports, 16 reports were released on wrong patients, error rate being approximately 1 in 3,000 reports. In 69% of cases (11 of 16 cases) correct and wrong patients had the same last names. Six of 11 patients had the same last and first names, however, the DOB were different in the correct and wrong patients. The remaining 5 of the above 11 cases with identical last names, had different first names. In 5 cases out of the total of 16 cases patients had different names and DOB (month or day in DOB was similar in two cases). Incorrect electronic entry originated in various departments, however, most of them occurred in the operating room (OR).

Conclusions: Our analysis indicates that the most frequent cause of incorrect entry into the electronic system was identical last names of correct and wrong patients (69% cases). Among this group, confirmation of first name reduced the error by 30%. In the remaining 39% of cases, the error could be avoided by confirming the DOB of the patient. Of last 31% (5 of 16 cases), erroneous entry was made in spite of different names and dates of births of the patients. The finding that incorrect entry most frequently occurred in the OR was due to the fact that most specimens were received from the OR. All errors could potentially be avoided by educating and emphasizing to the staff the importance of confirming two identifiers in each patient, during every electronic entry.

1863 Documentation of Quality Assurance Activities in Surgical Pathology: 5-Year Experience Post Introduction of a Comprehensive Quality Assurance Program.

M Sidiropoulos, MA Khalifa, C Rowsell. Sunnybrook Health Sciences Centre, Toronto, ON, Canada.

Background: A comprehensive quality assurance (QA) program can greatly enhance the quality and efficiency of the surgical pathology laboratory by documenting processes, identifying discrepancies, and ultimately illuminating areas for potential improvement. The success of such programs, however, is largely dependent upon participation by departmental staff. A comprehensive QA program with quarterly reporting of QA activities was introduced in our department in 2006. We performed an audit of our overall QA program from 2006-2010 to document changes in QA participation.

Design: QA data in surgical pathology was collected every quarter (Q) since the second quarter of 2006. The following parameters were tracked: recording of intraoperative consultation (IOC) vs final diagnosis correlation, prospective reviews, retrospective reviews, and total QA activities documented in surgical pathology. In addition, total amended reports and turnaround time (TAT) measures were documented.

Results: Total QA activities recorded increased from 8% in Q2 2006 to 15% in Q2 2010. This was largely due to the increase in recording of prospective reviews from 3% to 8% over the same period. There was no significant change in retrospective reviews (range 1- 3%). Total recording of IOC vs final correlation by pathologists was 96% in Q2 2006, rose to a high of 99% in Q4 2006, had a low of 83% in Q3 2008, and rose to 100% in Q2 2010.

Total amended reports decreased from 0.93% in Q2 2006 to 0.53% in Q2 2010. Overall TAT remained consistent over the study period ranging from 4-6 days; however improvements were seen in number of cases signed out within 48 hours (21% in Q2 2006; 33% in Q2 2010).

Conclusions: After the introduction of a comprehensive QA program in surgical pathology, we have seen a significant increase in documentation of QA activities over a five-year period. Factors which may have played a role in the increase include introduction of prospective review policies for targeted specimens and monthly reminders to pathologists to record QA activities. Our experience illustrates that creating a learning, non-punitive environment focussing on patient safety rather than "errors" encouraged pathologists to report their review results and comply with QA guidelines.

1864 Standardized Synoptic Cancer Pathology Reports: So What and Who Cares? A Population Based Survey of 970 Pathologists , Surgeons, and Oncologists.

J Srigley, S Lankshear, M Yurcan, T McGowan, D Divaris, R Rossi, J Ross, J Brierley, C Sawka. Cancer Care Ontario, Toronto, Canada; McMaster Univ., Hamilton, ON, Canada; Univ.of Toronto, ON, Canada.

Background: The benefits of standardized synoptic cancer pathology reporting include enhanced completeness and improved consistency in comparison to narrative reports. The purpose of this study was to determine the impact of standardized synoptic pathology reporting on physician satisfaction regarding process (e.g. timeliness, and completeness) and practice (e.g. clinical decision making).

Design: A descriptive, cross sectional design was utilized including 970 clinicians (e.g. pathologists, surgeons, medical and radiation oncologists) across 27 hospitals. The 11 item survey used an established quality indicator framework as a guide to obtain information regarding timeliness, completeness, clarity and usability. Open-ended questions were also employed to obtain qualitative comments. Data collections following the Tailored Design Method as described by Dillman (2007) and incorporated both a secure web-based survey or hard copy/faxed surveys.

Results: 498 surveys were completed representing a 51% overall response rate, and by specialty ranging from 68% (Pathologists), to 39% (Surgeons) with 45% and 55% response rate from Medical Oncologists and Radiation Oncologists respectively. Descriptive statistics reveal that based on a 5 point Likert scale with 1 = synoptic reports as significantly worse than narrative and 5 = synoptic reports as significantly better than narrative reports, the mean satisfaction score was 4.63 indicating that physicians perceive synoptic reports as significantly better than narrative reports. Correlation analysis revealed a positive relationship between respondents' perceptions of overall satisfaction with the level of information provided in synoptic reports and perceptions of the completeness for clinical decision making [r =.750, p = .000], ease of finding information for clinical decision making [r = .663, p = .000] and the report's ability to facilitate a consistent approach to diagnostic and prognostic factors [r = 717, p = .000]. Dependent t-tests showed a statistically significant difference in the satisfaction scores of pathologists and oncologists *[t* (169) = 3.044, p = .003]. Content analyses of qualitative comments reveal technology related issues as the most frequently cited factor impacting timeless of report completion.

Conclusions: This study provides evidence of strong physician satisfaction with standardized synoptic cancer pathology reporting as a clinical decision support tool in the diagnosis, prognosis and treatment of cancer patients.

1865 Standarized Synoptic Cancer Pathology Reporting: Implementation Strategies for a Population-Based Change Management Initiaitve Involving 400 Pathologists across 86 Hospitals.

J Srigley, D Divaris, T McGowan, M Yurcan, C Sawka, J Ross, MJ King, T Yardley, K Milnes, J Mazuryk, J Irish, R McLeod. Cancer Care Ontario, Toronto, Canada; McMaster Univ, Hamilton, ON, Canada; Univ. of Toronto, ON, Canada.

Background: Standardized (synoptic) cancer pathology reports (SCPRs) facilitate clinical management and data collection by cancer registries (CR), accrediting bodies and planning agencies. This project led by the provincial cancer agency in partnership with 400 pathologists within 86 hospitals, aimed to implement electronic, discrete data field (DDF) synoptic reporting of cancer resection specimens based on the College of American Pathologists (CAP) checklists (2005) to the provincial CR. Change management and knowledge transfer (KT) strategies were employed to optimize physician, vendor and organizational engagement.

Design: Strategies utilized to enable population based implementation of SCPRs in DDF format by all cancer treating hospitals to the CR included: establishing clinical leadership at provincial and local hospital levels to lead the adoption of the CAP standard; enabling interoperability between CR and hospitals with common data and messaging standards; providing hospital funding for synoptic reporting eTools in lab systems; leading KT education and outreach to pathologists; facilitating community of practice groups with synoptic tool vendors and hospitals; and monthly reporting of clinical indicator results to hospital leads on SCPR completeness and surgical quality i (e.g. % of colorectal resections with more than 12 lymph nodes examined and % positive margins in pT2 prostate carcinomas).

Results: The success of the change management strategies utilized is evident in the extent of hospital implementation and population level reporting of pathology and surgical indicators. All 86 hospitals have implemented synoptic reporting e-Tools, and are reporting against CAP standards. Of the five most common anatomic sites, which account for over 50% of all resections, 94 % were submitted in DDF synoptic format and 94% were found to be complete against the CAP standard. With respect to surgical pathology quality indicators, 87% (1812/2093) colon and 79% (637/807) rectal and rectosigmoid resections had 12 or more lymph nodes examined. The overall rates of margin positivity for pT2 prostate cancer based on radical prostatectomy reports was 22% (254/1140).

Conclusions: Adoption of a common reporting standard by pathologists is unprecedented for a jurisdiction of this size and complexity, therefore the utilization of a multi-faceted approach to the implementation of a population level practice change was a key enabler.

1866 Secondary Review of Surgical Pathology Materials for Patient Referred to the Mayo Clinic: An Evaluation of Major Disagreements.

RE Swapp, W Shon, N Campbell, ME Fidler, MC Aubry, DR Salomao, D Schembri-Wismeyer, L Padley, GL Keeney, JC Cheville. Mayo Clinic, Rochester, MN.

Background: Original outside surgical pathology materials are reviewed by Mayo Clinic pathologists for patient referrals. The objective of this study was to identify the

rate of major disagreements with diagnoses from outside institutions, categorize them according to organ system, and determine how these major disagreements affected clinical management.
Design: All surgical pathology cases reviewed between 2005 and 2010 were identified to determine the overall frequency of major disagreements. Major disagreements were defined as any change that significantly affected treatment. Furthermore, a subset of cases with major disagrees (reviewed between July, 2009 and September, 2010) were reviewed to determine the specific type of major disagreement and the effect on patient management and prognosis.
Results: After a retrospective review of 66,215 cases, from 2005 to 2010, 429 major disagreements (0.65%) were identified. Most frequent major disagreements occurred in areas of gastrointestinal (78 cases), lymph node (71) and bone/soft tissue pathology (47), followed by genitourinary (41), breast (34), head and neck (27), pulmonary (25), gynecologic (20), endocrine (18), dermatologic (14), neuropathology (10), and cardiovascular pathology (9). In the subset of 94 major disagrees (of a total of 16,462 cases), treatment was affected in 75 cases (79.8%), and prognosis was affected in 79 cases (84.0%). In 20 cases, the diagnosis was changed from benign to malignant, 19 cases were changed from malignant to benign, in 16 cases tumor classification was changed, 5 cases were changed from invasive carcinoma to in-situ, 4 cases were considered non-neoplastic which were previously classified as neoplastic, and 3 were determined to be neoplastic processes which were previously diagnosed as non-neoplastic. Change of tumor grading and staging was changed in two and one cases, respectively. Twenty-four cases were changed for various other reasons that were considered a major disagreement and that affected treatment.
Conclusions: While major disagreements are rare, they often significantly impact patient treatment. This study highlights the value of secondary review of pathologic materials for patient referrals. It further suggests that secondary review is an important quality control activity which detects diagnostic errors and thereby improves patient care.

1867 EGFR Mutation Analysis: What's Being Tested? The Experience of a Single Academic Medical Center.

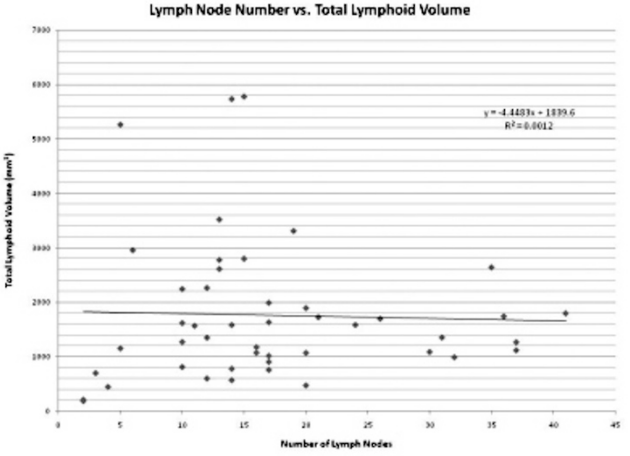
LJ Tafe, MC Schwab, JA Lefferts, C Hart, CC Black, VA Memoli, V Padmanabhan, GJ Tsongalis. Dartmouth-Hitchcock Medical Center, Lebanon, NH.
Background: Testing for *EGFR* mutations is an important tool to guide molecularly targeted therapy in patients with pulmonary non-small cell carcinoma (NSCLC). Diagnostic molecular pathology laboratories receive specimens for *EGFR* mutation analysis from a variety of sources. In this study, we review our experience with the types and appropriateness of specimens submitted to us for *EGFR* mutation testing.
Design: A database was created to record information on the specimens submitted to our molecular pathology laboratory during the 15 month interval that we have offered *EGFR* mutation analysis as a clinical test. Information recorded included specimen preparation (i.e. fresh/formalin fixed), type of specimen (i.e. FNA, core biopsy, excision), clinical status of tested tumor (i.e. primary, metastasis, recurrence) and the diagnosis of the primary tumor with site of origin. All in house specimens were reviewed by a pathologist for adequacy of material for testing.
Results: From May 2009 to August 2010, our laboratory evaluated 242 specimens for *EGFR* mutation status. Twenty-two (9%) were submitted by outside institutions, 75 (31%) by cytology and 145 (60%) by surgical pathology. Overall, only 4 cases did not have sufficient DNA to complete the analysis. Of the 238 evaluable cases, 216 were formalin-fixed paraffin-embedded (FFPE) and 22 were fresh frozen. Most specimens were surgical resection/excisions (98, 41%) and core biopsies (94, 39%) followed by FNA cell blocks (30, 13%); others included pleural fluids, sputum and washes. The primary tumor was most frequently tested (149, 63%) followed by metastases (75, 32%) and rarely recurrent and second primaries. As expected, the overwhelming majority of tumors were diagnosed as adenocarcinoma or poorly differentiated/NOS NSCLC (208 and 12 respectively). However, 3 squamous cell carcinomas and 1 large cell neuroendocrine carcinoma of lung were also tested. Interestingly, 9 cases of metastatic carcinoma of other known primary and 5 cases of metastatic carcinoma of unknown primary were submitted. In total, 4 were insufficient for genotyping, 24 were positive for an *EGFR* mutation and 214 were non-mutated.
Conclusions: Overall, our clinicians and pathologists are submitting samples appropriate for *EGFR* mutation analysis that can be successfully evaluated. Rarely, the test is probably ordered inappropriately in instances where a known carcinoma other than NSCLC is the diagnosis. Our study also shows that at times physicians are using *EGFR* mutation analysis to aid in the diagnosis and possibly treatment of a carcinoma of unknown primary.

1868 Reduction of Labeling Errors in Surgical Pathology by Barcoding.

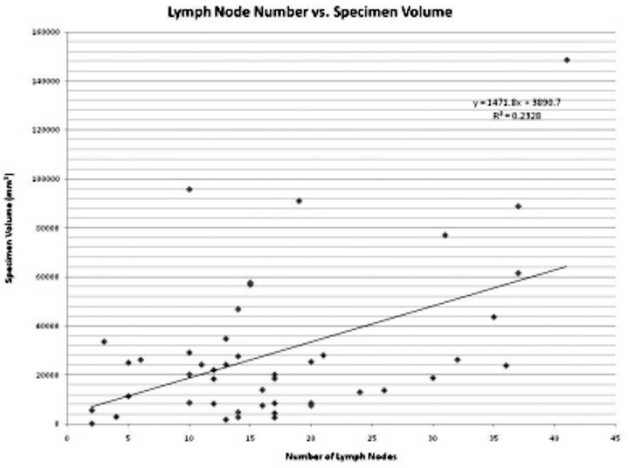
GA Talmon, T Rinehart, M Gerken, J Gerriets, D Muirhead, S Smith, AJ Lazenby. University of Nebraska Medical Center, Omaha.
Background: Most quality control (QC) literature in surgical pathology focuses on diagnostic error and interobserver reproducibility. Few have examined operational issues such as specimen mislabeling and of these, most focus on errors prior to receipt in pathology. Intradepartmental labeling errors (paraffin blocks, glass slides) are potential sources of specimen misidentification. Barcoding (BC) can reduce errors by switching from a human- to an electronic-driven system for labeling, reading and verification of specimen numbers. We examined the process changes in BC and compared labeling errors in the gross room and histology pre- and post-BC.
Design: Sequential cases for a 3 month period pre and post BC implementaion were used. Blocks and slides were examined for alteration of identification numbers (erasures, strikeouts, overwrites). Data collected included number of blocks, slides and cases with error. This reflected gross room or histology errors caught and corrected prior to delivery to pathologists. QC logs, incident reports and results of molecular identity testing were used to identify labeling errors that reach the pathologist. Work processes, including QC pre- and post-BC were also compared.
Results: Following BC, workflow changed from possible batch to obligate single part process. Also, manual/visual identification and QC were replaced by electronic labeling and verification. Material from 6,104 cases (21,067 blocks;38,264 slides) from the pre-BC period and 5,964 cases (23,531 blocks;38,946 slides) from the post-BC period were examined. Pre-BC period: 200 blocks (0.9%) and 809 slides (2.1%) were initially mislabeled, involving 81 (1.1%) and 331 cases (4.5%) respectively. Through multiple QC steps, each error was corrected before slide delivery. From QC and incident logs, 5 mislabeled cases were delivered to pathologists (<.001%). No cases were found to be discrepant by DNA testing. Post-BC period: no block labeling errors occurred (0%). QC and incident reports showed 3 cases with mislabeled slides reached pathologists (<.001%, due to histotech ignoring computer error message). No cases were discrepant by DNA testing due to block or slide mislabeling.
Conclusions: Labeling errors reaching pathologists were rare. Pre-BC, errors made in block and slide labeling were substantial (0.9%, 2.1%) but multiple QC steps corrected them prior to delivery to a pathologist. Post-BC, there was a dramatic reduction in block and slide labeling (0%, <.001%). BC technology switches from a manual/visual system with human QC designed to catch and correct errors to an electronic system that prevents errors.

1869 Accuracy and Significance of Lymph Node Count in Endometrial Cancer.

TA Thurow, I Check, W Watkin. NorthShore University HealthSystem, Evanston Hospital, IL; University of Chicago Pritzker School of Medicine, IL.
Background: The importance of lymphadenectomy (LA) in women with endometrial carcinoma (EC) has been established. Recent studies have tried to define adequacy criteria for lymph node (LN) sampling. The GOG protocol 210 requires 12 LN for eligibility. In our experience, pelvic LN dissections often consist of matted, fatty-replaced LN in which it is difficult to determine an accurate LN count. As a result, studies using LN number as an important parameter may be suspect. In this study, we examine the relationship between LN number and actual LN volume and whether either correlates with the detection of metastases in EC.
Design: 46 cases from 2009 of EC treated with hysterectomy and LA, in which the LA specimens were entirely submitted, were reviewed. Age, tumor type, grade, stage, LA specimen size, and LN number were obtained from pathology reports. The size of actual lymphoid tissue on each slide was measured in two dimensions and assigned a width of 0.3 cm, approximating cassette thickness. Lymphoid volume was calculated using the ellipsoid approximation formula. Regression analysis was performed for correlation.
Results: Patient ages were 41 to 87 years (mean 64). Total LN number per patient ranged from 2 to 41 (median 15, mean 17). 6 patients had positive LN. There was no correlation between the LN number and lymphoid volume (figure 1) or between lymphoid volume and specimen volume (R^2=.06).



There was a weak correlation between LN number and specimen volume (figure 2).



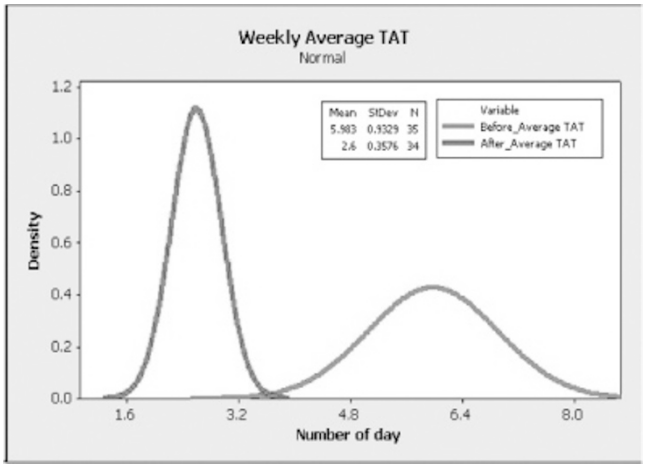
LN positivity did not correlate with either LN number (p=.28) or volume (p=.57).
Conclusions: The number of LN identified in LA is variable and does not correlate with lymphoid tissue volume. Variability in LN numbers may result from counting sectioned single LN as multiple LN. A standard method of dissecting pelvic LN should be developed before LN numbers are used in treatment protocols or as study eligibility criteria.

1870 Pre-Dissection Review of Ultrasound Report Increases Accuracy of Gross Thyroid Tumor Measurements.

LYA Watts, LA Emery, A de las Morenas. Boston Medical Center, MA.
Background: Cancer staging is invariably dependent on primary tumor size. However, discrepancies may exist between preoperative and postoperative measurements, which may affect staging. There are systematic ways in which organs are evaluated according to predetermined dissection techniques. In the thyroid, serial slices are made perpendicular to the long axis of each lobe. Measurements of lesions found are impacted by these initial incisions and may engender the discrepancy from radiographic measurements. We propose a pre-dissection evaluation of the ultrasound (US) report so that the initial cut is made into the lesion in the plane of maximum dimension.
Design: Retrospective patients were screened from our pathology database by searching total thyroidectomy specimens. Patients included in the analysis had discrete nodules measured on gross pathology as well as on US. Prospective patients were those receiving total thyroidectomies with US reports showing dominant nodules. Thyroids flagged as having dominant nodules were grossed with particular attention to the plane of maximum dimension, in that the initial cut into the lesion was made in this plane. Thus, the correlation between gross and US measurements for retrospective patients was made after gross dissection whereas for prospective patients the US measurements were used as a guide for dissection. For both retrospective and prospective patients, gross pathology measurements were compared to US measurements of the dominant nodule(s) and differences in maximum dimension were recorded.
Results: Six retrospective and six prospective patients were analyzed. The retrospective group was found to have a mean maximum difference between US and gross measurements of 0.67 cm (SD:0.4) and the prospective group 0.1 cm (SD: 0.06). Results were statistically significant with a 2-tailed p-value of 0.011 (CI: 0.161-0.972).
Conclusions: Predissection review of the US report in a patient with a dominant thyroid nodule guides pathologic evaluation to more accurately measure tumor size, which ultimately may impact patient management.

1871 Application of Lean Principles To Improve Turn Around Time in Gynecologic Cytology Laboratory.

RJ Wong, M Harigopal, K Schofield, D Chhieng, A Levi. Yale University School of Medicine, New Haven, CT.
Background: Our cytology laboratory, like many others, is under pressure to improve quality and provide test results faster while decreasing costs. We sought to address these issues by applying Lean principles and methodologies. The objective is to determine the impact of Lean principles on the turn around time (TAT) and productivity of the gynecologic cytology operation.
Design: We established a baseline measure of the TAT of Pap tests. We then compared this to performance 6 month after implementing the location guided imaging system and Lean methodologies. The latter included workstation and equipment relocation, redesign of workflow, and visual control.
Results: The average TAT for Pap tests before and after the implementation of new imaging system and Lean principles were 5.98 ± 0.93 days and 2.60 ± 0.38 days, respectively. The improvement in the average TAT was statistically significant (t-test $p < 0.001$). In addition, there was also significant reduction in the variability as evidenced by the reduction in the standard deviation (F-test, $p < 0.001$).



In addition, the productivity of staff was improved by 17%, i.e. the same volume of Pap tests were handled by 2 fewer full-time cytotechnologists who voluntarily resigned.
Conclusions: Implementation of Lean principles in cytology laboratory resulted in shortened and more consistent TAT for Pap tests while improving productivity at the same time.

Pan-genomic/Pan-proteomic Approaches to Diseases

1872 High Levels of Necrosis in TCGA Glioblastoma Samples Are Associated with the Mesenchymal Gene Expression Class and Characterized by Enhanced Expression of Master Transcriptional Regulators of Mesenchymal Transition.

DJ Brat, DA Gutman, LAD Cooper, J Kong, C Chisolm, EG Van Meir, JH Saltz, CS Moreno. Emory University School of Medicine, Atlanta, GA.
Background: The Cancer Genome Atlas (TCGA) project defined four clinically relevant subsets of glioblastoma (GBM) based on gene expression: mesenchymal, classical, proneural and neural. Genomic alterations were identified for each class, yet complete correlation with expression was not evident, suggesting tumor micro-environment may contribute. We investigated if the degree of necrosis within GBM samples used for TCGA studies was associated with a specific expression class and examined which genes were most tightly correlated with extent of necrosis.
Design: We utilitzed publicly available digitized frozen section slides from 79 GBMs used for quality assurance before molecular testing by TCGA. Necrotic foci in each slide were outlined using a machine-human interface. Extent of necrosis (% tissue area) was correlated with expression class. Using the Significance Analysis of Microarray (SAM) survival module, a Cox regression analysis was performed using TCGA Affymetrix U133 expression data to identify genes correlated with %-necrosis. The SAM survival module used a permutation algorithm to correct for multiple hypothesis testing and identify correlated probes with a false discovery rate cutoff of < 4%. 1026 probes were positively associated with %-necrosis and 18 were negatively associated. These 1044 probes were used as input for Ingenuity Pathway Analysis (IPA) to identify enriched networks.
Results: The mesenchymal expression class was enriched with high %-necrosis GBMs (33% with > 25% necrosis) compared to the other 3 classes (2% with > 25% necrosis). Average %-necrosis was higher in mesenchymal GBMs (21.2%) than the other 3 classes (7.4%; one-way ANOVA $p = 0.0022$). Regression analysis of genes correlated with %-necrosis revealed strong upregulation of transcription factors identified as master regulators of mesenchymal transition (Carro, et al. Nature 263: 318-25, 2010), including C/EBP-B, C/EBP-D, FOSL2, STAT3 ($p < 0.005$) and RUNX1 ($p < 0.01$). Increased expression of hypoxia-inducible genes, including VEGF, validated the analysis. FOSL2 and C/EBP-B were strongly correlated with extent of necrosis within the mesenchymal class ($p < 0.00001$).
Conclusions: Our results suggest that the degree of necrosis in GBM is closely related to the mesenchymal gene expression class.

1873 Application of Reverse Phase Protein Lysate Array (RPPA) to Formalin-Fixed, Paraffin-Embedded Tissues.

R Broaddus, S-S Xie, C Wei, E Euscher. M.D. Anderson Cancer Center, Houston, TX.
Background: RPPA is a high-throughput analysis in which dilutions of protein lysate are spotted on nitrocellulose slides (maximum 1,152 spots per slide). Each slide is probed with a different antibody. A DAKO-catalyzed signal amplification system is used for signal detection. RPPA requires less protein than Western blots. An advantage over immunohistochemistry is that RPPA is quantitative rather than qualitative. A current limitation of RPPA is that protein is typically derived from cell lines or frozen tissues, restricting its use to research settings. The RPPA platform incorporates many antibodies directed to phosphorylated proteins; these same antibodies typically do not work well for immunohistochemistry using formalin-fixed, paraffin-embedded (FFPE) tissues. It would therefore be advantageous if RPPA could be adapted to FFPE tissues.