1573 Whole Genome Sequencing-Based Molecular Epidemiology of Vancomycin-Resistant Enterococcus faecium Pre Versus Post Daptomycin Use in a Suburban New York City Medical Center

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Background: Vancomycin-resistant *Enterococcus faecium* (VREf) belonging to clonal cluster 17 (CC17) has been emerging globally since the 1990's and is now among the predominant group of enterococci causing nosocomial infections of the bloodstream, urinary tract, skin and soft-tissues. The aim of this study was to assess the clonality of temporally spaced VREf clinical isolates using whole-genome sequencing analysis.

Design: Thirty-four and 113 VREf clinical isolates recovered from patients in a tertiary medical center in suburban New York City in 1995 and 2013, respectively, were selected and analyzed. Whole-genome sequencing was performed on the Illumina MiSeq™ or HiSeq™ System by using paired-end methods. Multilocus sequence typing (MLST) and single nucleotide variations (SNVs) data were derived from the genome sequences of each isolate. The genetic relatedness of different enterococcal isolates and sequence types were explored using the goeBURST program.

Results: The predominant strain type for VREf isolates from 1995 was ST17 (79.4%), followed by ST18 (8.8%) and ST323 (8.8%). By contrast, a newly described clone, ST736, accounted for 48.7% of VREf isolates in 2013, followed by ST18 (24.7%) and ST412 (21.2%). Population genetic analysis established that ST736 is a novel clone within CC17 with differences in two alleles from its prototype ST17.

Conclusions: Whole-genome sequencing analysis of VREf clinical isolates demonstrated a dramatic change in dominant strain types and the emergence of a novel clone ST736 in our patient population over the past 18 years.

Informatics

1574 Clinical Genome Analytics (CGA): An Automated Analytical Pipeline for Detection and Annotation of Clinically Relevant Genomic Variants

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Background: The development of next generation sequencing (NGS) and associated target sequence enrichment technologies has enabled time and cost effective detection of clinically relevant molecular alterations in hundreds of genes using a single clinical assay, thus paving the path for personalized medicine. Although data generation is no longer the major hurdle, accurate and time-effective bioinformatic and statistical analysis, and biologically meaningful interpretation of the data remain challenging.

Design: We created CGA (Clinical Genome Analytics), an automated data analysis pipeline that is implemented using Civet, an in-house engineered XML-based framework for building analytical pipelines for efficient multi-step data processing.

Results: CGA includes capabilities for automatic scheduling of jobs, monitoring analysis runs, and automatically saving information about each run (including command line options, versions and standard output/error for each tool). It puts together 17 different tools, from quality control and alignment through local realignment around indels and base quality recalibration to calling SNPs, indels and CNVs, and finally assigning genomic annotations to these variants. CGA takes an average of 6 hr to process samples containing approximately 25M paired-end reads, and ensures high (> 99.4%) sensitivity and specificity for the detection of >= 5% frequency SNPs and indels (<= 50bp) and of copy number changes >= 6.

Conclusions: CGA is an automated analysis pipeline that ensures accurate and sensitive detection and clinical annotation of mutations. It is currently being used as part of an NGS-based molecular diagnostic assay that detects actionable mutations in solid tumors in a CLIA-certified laboratory. It provides not only an accurate analysis of samples in a clinically acceptable short turn-around time, but also the ability to document quality metrics and information on all of the tools, their versions and options, and all reference genomes and databases used, which is key to ensure reproducibility and traceability in a clinical set-up.

1575 Utility of Automated Bioinformatic Pipeline in the Analysis and Interpretation of SNP Microarrays in Neoplasia

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Background: SNP microarrays are being widely used as a tool in a routine oncology diagnostic workflow. The main advantage is its ability to accurately identify the composition of derivative chromosomes & marker chromosomes commonly observed in clonal populations. One of the biggest challenges of interpreting oncology arrays is the lack of bioinformatics tools facilitating the analysis and interpretation of microarray data. Another major challenge is to rule out the common polymorphic genomic variants stored in databases such as DGV, as well as having the ability to tease out potentially relevant copy number variable (CNV) and Loss-Of-Heterozygosity (LOH) regions possibly contributing to the pathogenesis of neoplastic disorder. The aim of this study was to access and configure the utility of an automated bioinformatic pipeline in the analysis and interpretation of SNP Microarrays in neoplasia.

Design: For constitution SNP array's our lab has been using various automated bioinformatics pipelines for data analysis and reporting. For oncology SNP array data analysis and interpretation we collaborated with Cartagenia Inc. Aim is to create a different variant assessment and filtration strategies that can be established and automated for the analysis of SNP microarrays in various leukemias and the utility of the Bench platform in the identification of pathogenic changes. We selected array SNP array data from 42 cases of cytogenetically normal cases of CMML, Myelofibrosis and ALL and subjected to the customized bench.

Results: Our studies have allowed us to establish specific filters for the determination of potentially significant copy number changes (like mosaic deletions and mosaic duplications). SNP microarrays also have the added advantage of identifying regions of LOH which play a very important role in the 2 hit hypothesis in somatic cancers. Our filtration allowed removing germline mutations, stored in databases such as DGV, as well as alignment of genomic variants with control populations or healthy tissue samples. We have also been able to establish an automated filtration and reporting pipeline that allows the identification and reporting of regions of LOH harboring important cancer genes such as CDKN2A and JAK2.

Conclusions: We propose that an automated bioinformatic pipeline for the analysis and interpretation of neoplastic disorders will benefit the labs and oncologists ordering a high-resolution chromosomal microarray in a diagnostic setting.

1576 Diagnostic and Educational Uses of Google Glass in Anatomic Pathology

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Background: Google Glass is a wearable intelligent device permitting the capture and communication of photography and video via its hands-free, voice recognition capabilities. Multiple institutions are investigating the use of Glass technology in health care, most notably within surgical and internal medicine specialties. Glass utilization within pathology has been limited to very few reports. The first study investigated live-streaming of routine specimen dissection; another study described the acquisition and quality of still images in forensic autopsy findings. To date, no studies have applied the use of Glass-acquired data, specifically videos, for subsequent diagnostic and educational purposes in anatomic pathology.

Design: Google Glass (Explorer edition) photography and videography was implemented as an adjunct to routine gross specimen documentation by hand-held digital photography during intraoperative consultations and/or routine permanent processing. Specimens included pulmonary, gynecologic, and gastrointestinal resections. The edited dissection videos were less than 40 seconds in length. Data was obtained, stored, and accessed in the same secure and HIPAA-compliant methodology currently in place for digital gross photography. Specimen photography and videography were evaluated in several clinical and educational capacities, including but not limited to consultations among residents and attendings, gross specimen review at the time of microscopic examination, pathology resident education, and inter- and intra-departmental conferences.

Results: Glass technology obtained images and videos with quality comparable to those by digital photography but without disruption or increase in processing time to pre-existing grossing procedures. The use of Glass was described as more convenient and efficient than conventional photography. Dissection videos of complex resection specimens, beginning from their intact and fresh states to their final sectioning, were reported to be of greater diagnostic and educational utility than both photography and gross specimen review of the fixed and sectioned tissues.

Conclusions: Glass has demonstrated clinical and educational value within anatomic pathology. The analysis of surgical specimens in pathology almost always requires specimens to become disrupted and altered in fixative following dissection. Maintaining quality photographic and video records of the intact and fresh specimens at the time of initial dissection is important for diagnoses and reporting, medical education, and potential error reduction.

1577 FISH Digital Image Capture and Automated Segmentation Improves Laboratory Workflow Efficiency

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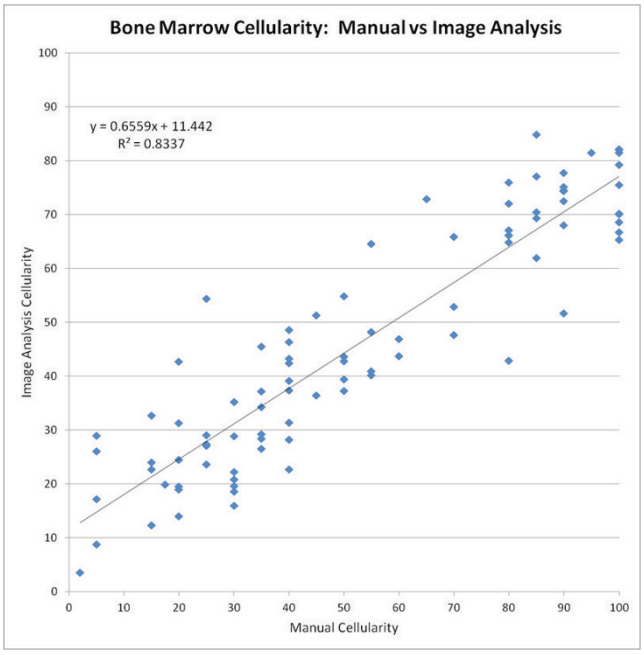
Background: Fluorescence in situ hybridization (FISH) is a laboratory testing modality where fluorescent probes highlight specific chromosomal sequences which are then localized by fluorescence microscopy. Limitations to FISH interpretation include identification of individual cells showing fluorescent signal without cellular overlap. These limitations are exacerbated by manual counting and interpretation, leaving manual FISH analysis subjective and time consuming. As FISH testing is increasingly incorporated in diagnostic pathology, turnaround time with accurate reproducibility of results is of utmost importance to workflow and patient care. We examined if incorporation of automated segmentation protocols on digitally captured images improves cell detection and laboratory workflow efficiency.

Design: FISH cases (hematologic and non-hematologic) were analyzed (5 Her2/neu, 3 FKHR, and 8 MYC) using automated FISH analysis systems (GenASIs, Applied Spectral Imaging, Carlsbad, CA). H&E slides were reviewed and marked by a pathologist. Following image capture by GenASIs, manual and automated segmentation protocols were performed on a minimum of 60 cells (hematopoietic cases) and 120 cells (non-hematopoietic cases) from four to five digital image frames. Manual segmentation involved a technologist circling appropriate cells for analysis with the GenASIs mouse. Automated segmentation by the GenASIs Omni software, was performed on identical frames with manual deselection of inappropriate cells. Both methods were compared for efficiency and accuracy.

Results: Automated segmentation by GenASIs resulted in an overall significant technician time reduction (range 13-19 min, mean 10.7 min) in comparison to manual segmentation, (range 19-85 min, mean 37.2 min) ($p = <0.0001$). Automated segmentation maintained significant time reduction over manual segmentation in each test: Her2/neu ($p=<0.0001$), FKHR ($p=0.0004$), and MYC ($p=0.06$). There was no significant difference in the classification time between methods ($p=0.46$). There was high concordance on both signal scoring pattern ($P=<0.0001$, $r^2=0.98$) as well as 100% concordance on case classification/result interpretation in both methods with gold standard microscopic evaluation.
Conclusions: Digital capture and analysis FISH systems perform automated cell detection much more rapidly than manual segmentation yet maintain high levels of accuracy, thus improving laboratory workflow. Adoption of digital imaging in the clinical laboratory also provides advantages including long term archival and quality assurance measures.

1578 Comparison of Bone Marrow Cellularity Assessment Using Computational Image Analysis and Conventional Manual (Visual) Cellularity Estimation Scores

Bryan Dangott, Rongqin Ren, Ridas Juskevicius. East Carolina University Brody School of Medicine, Greenville, NC.
Background: Microscopic examination of trephine bone marrow biopsies is a routine part of the hematopathology examination and accurate estimation of the marrow cellularity (ratio of hematopoietic to fat and stromal cells) is an important diagnostic determinant. Manual (visual) assessment of marrow cellularity lacks standardized criteria, which introduces inter and intraobserver variability and makes comparison of cellularity in sequential samples difficult. Reliable cellularity scores are diagnostically essential and clinically important for tracking therapy-related changes and disease progression. The aim of our study is to evaluate feasibility of computational image analysis in an attempt to standardize the cellularity assessment.
Design: 104 consecutive bone marrow biopsies were digitally scanned at 20x magnification using an Aperio CS whole slide scanner. 89 cases had numeric manual cellularity scores and qualified for comparison with digital analysis. Images were annotated manually to isolate the region of interest. An in house developed algorithm was used to process images and determine a cellularity percentage. Manual scores were extracted from the diagnostic pathology reports and compared to the automated image analysis scores.
Results: Our image analysis technique has a good correlation with manually reported cellularity. Linear regression analysis showed an R-squared value of 0.8337.



Automated cellularity scores ranged from 3.5 to 85 while manual scores ranged from 2 to 100. The overall average score for the automated group was 46.3 while the average cellularity by manual (visual) estimation was 53.2. The overall average difference between automated scoring and manual estimation was -6.9.
Conclusions: The correlation between image analysis and manual methods was better than expected. This method provides a consistent and reproducible system for tracking marrow cellularity through time. Few limitations include manual error introduced in selecting the area for scoring, stromal fibrosis, and tissue drop out. Further study may introduce techniques to address these issues.

1579 Histologic: A Comprehensive Web 2.0 Histology Education Wiki

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Background: Medical histology is traditionally taught using paper manuals, kodachromes and glass slides, limiting the majority of learning opportunities to microscope-based laboratory sessions that are labor-intensive on the part of the faculty and generally not well-attended by students. While many efforts to provide online learning resources for histology exist, few are of sufficient quality to significantly contribute to student learning. The purpose of this project was to create an interactive histology learning experience with whole slide images (WSI), infinite extensibility, easy content generation, and high student uptake.
Design: A Dell PowerEdge 2950 running VMWare ESXi 4.1.0 was used to create a LEMP (Ubuntu Linux 12.04.5, nginx 1.7.5, MariaDB 5.5.39, PHP-FPM 5.3.10) stack virtual machine. Customized builds of MediaWiki 1.22, OpenSlide 3.4, VIPS 4.38 and OpenSeadragon 1.1.1 were implemented and deployed atop the stack. Custom extensions allowing for WSI embedding into MediaWiki were programmed and deployed. Finally, a new interactive histology manual codenamed "Histologic" was implemented and deployed atop this highly-customized stack infrastructure.
Results: Histologic was deployed on 7/21/14, and has since then sustained over 5600 views and over 170 collaborative additions and revisions, many of these revisions in response to faculty and student input. It contains 19 chapters of material, presented in an interactive format. Instructional text is seamlessly integrated with still images and over 200 embedded WSIs. In early pilot testing, students and instructors have overwhelmingly preferred Histologic over the more traditional laboratory-based teaching format. Server traffic and bandwidth patterns exhibit large utilization spikes clustered around examination times, suggesting that students are turning to Histologic as a learning resource.
Conclusions: Histologic has enjoyed rapid adoption among our students and faculty. Future goals include continuing additions and revisions, annotating WSI regions of interest, live tutorial sessions, and locally deploying Histologic to African medical schools using Raspberry Pi systems. This effort shows the utility of informaticist-supervised resident/fellow programming projects as learning opportunities and medical education improvement.

1580 Gaze Pattern During Diagnostic Exploration of Whole-Slide Images and Glass Slides

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Background: Digital pathology is a useful tool for applications requiring remote access to diagnostic material. Recent improvements in the production of whole slide images (WSIs) support a viewing experience over standard networks that closely matches the speed and efficiency of examining glass slides on a light microscope. The use of digital pathology will undoubtedly become a viable option to meet the increasing demands of cost reduction, and access to specialist expertise, yet no study to date has quantitatively assessed the visual interaction of the pathologist with WSIs as compared to glass slides during the diagnostic process.
Design: Pathologists were recruited to view and diagnose a set of glass slides and corresponding WSIs. We used a Philips UFS whole slide scanner and hosted the WSIs on https://slide-atlas.org, a high-performance web-based system. Glass H&E slides were controlled by participants and viewed in real-time using an Olympus Bx43 microscope equipped with a digital camera. Through this method, the diagnostic material and characteristics of the viewing screen could be controlled across both viewing modalities. A Tobii X2-60 eyetracker was used to collect continuous gaze data, which was later analyzed with slide movement, and compared across sample categories.
Results: The duration of individual fixations, as well as the localized pattern of gaze, were not significantly different between WSIs and glass slides. Overall, fewer fixations were observed with glass slides, and a greater proportion of fixations were clustered in the upper central portion of the visual field as compared to WSIs ($p<0.05$). A greater number of slide movements and fewer changes in magnification were observed with glass slides than with WSIs.
Conclusions: In this first quantitative comparison of both glass slides and their corresponding WSIs, we observed similarities in localized visual approach, as well as differences in the effect of each modality upon movement of the slide and utilization of visual fields. These findings enhance our understanding of the way pathologists interact with digital platforms, and currently provide the closest comparison of the diagnostic process utilizing WSIs as compared to traditional microscopy.

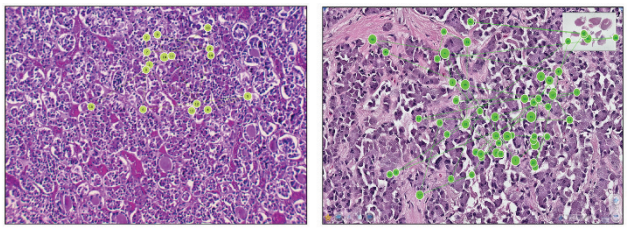


Figure 1: Sample fixations (green dots) on a glass slide (left) and WSI (right).

1581 Alopecia Diagnosis: 3D Analysis of Aligned Serial Whole Slide Images

Edward Fulton, Kristin Burns, Ashley Ward, C Law, Beverly Faulkner-Jones. BIDMC, Boston, MA; Kitware, Inc., Clifton Park, NY.

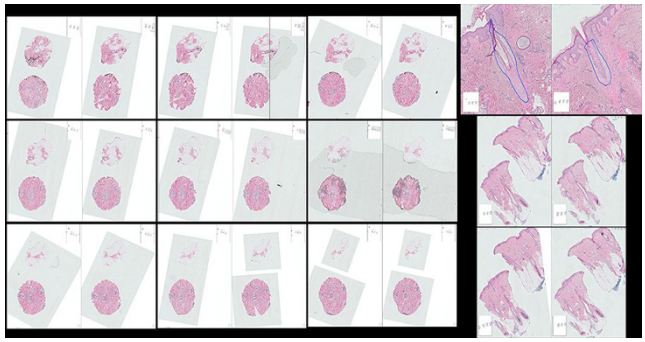
Background: Pathologists render a diagnosis by reading two-dimensional (2D) tissue sections. However, the ability to infer three-dimensional (3D) structure from 2D tissue sections can be crucial for diagnosis, and this is particularly true for alopecia. Multiple sequential sections must be examined to fully evalaute the necessary parameters, a time consuming and subjective process dependent on the skill and experience of the individual pathologist. With advances in digital methods, it is now feasible to present pathologists with aligned whole slide images (WSIs) of serial sections. The expectation is for faster evaluation, greater objectivity, and improved diagnostic accuracy.

Design: Alopecia punch biopsies are sectioned either "vertically" or "horizontally" for analysis. We chose one biopsy processed horizontally and one biopsy sectioned vertically for initial analyses. Slides were scanned using a Philips UFS scanner and whole slide images (WSIs) were displayed via https://slide-atlas.org, a high performance web-based viewer. Tools developed for local adaptive alignment of the serial WSIs were incorporated into the software system. Aligned WSIs were displayed side by side, and could be quickly manipulated. Regions of interest can be compared simultaneously in adjacent sections allowing precise characterization of follicular architecture. Precise alignment is maintained at different zoom levels. Follicular units can be segmented using web-based tools, and then 3D-volume rendered.

Results: All histologic parameters could be rapidly and accurately assessed on the aligned WSIs of the two test cases, chronic traction alopecia and frontal fibrosing alopecia, and a diagnosis rendered. Individual follicular units could be traced, segmented and 3D volume rendered.

Conclusions: Aligned sequential WSIs from alopecia biopsies cut vertically or horizontally allow for more rapid, accurate and comprehensive study than conventional glass slides, and increase our understanding of follicular micro-architecture.

Figure 1. Aligned serial WSIs of alopecia biopsies processed horizontally (left), and vertically (right). Initial segmentation of a follicle with perifollicular fibrosis is shown (top right).



1582 Stain Interpretation Management Program for Liver Lesions (SIMPLL): A Web Application To Aid in the Diagnosis of Well-Differentiated Lesions in the Non-Cirrhotic Liver

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Background: Hepatic adenomas are rare, benign lesions that sometimes occur in women of child bearing age, and who are taking oral contraceptives. It is often challenging for a pathologist to distinguish between Focal Nodular Hyperplasia, Hepatocellular Adenoma, and Well-Differentiated Hepatocellular Carcinoma. The process of distinguishing between these lesions is complex and involves interpreting multiple staining patterns. SIMPLL (Stain Interpretation Management Program for Liver Lesions), is a web application that was developed with the intent to make the process of evaluating rare liver lesions accurate and efficient for pathologists.

Design: The SIMPLL is a web based application. The diagnostic algorithm developed by our resident pathologist is hard coded in the application. The application was tested by comparing the diagnosis of 20 cases with that rendered by the attending pathologist. Slides from 20 cases of well-differentiated non-cirrhotic liver lesions, were pulled from Department of Pathology archives and de-identified. PGY1 to PGY4 residents were asked to render diagnoses with and without the use of SIMPLL. The diagnostic accuracy was determined by comparing the results with the final pathology report, and the process efficiency is determined by comparing the turnaround times for diagnoses rendered with and without the use of SIMPLL.

Results: While using SIMPLL**,** the average turnaround time for PGY-1 residents was 63.4 minutes, while rendering the correct diagnosis in an average of 9/20 cases; 57.1 minutes for PGY-2 residents while rendering the correct diagnosis in an average of 14/20 cases; 45.7 minutes for PGY-3 residents, while rendering the correct diagnosis in an average 16/20 cases; and 39.5 minutes for PGY-4 residents, while rendering the correct diagnosis in an average 18/20 cases. Without SIMPLL, the average turnaround time for PGY-1 residents was 103.8 minutes, while rendering the correct diagnosis in an average of 4/20 cases; 90.2 minutes for PGY-2 residents while rendering the correct diagnosis in an average of 8/20 cases; 81.7 minutes for PGY-3 residents, while rendering the correct diagnosis in an average 13/20 cases; and 63.4 minutes for PGY-4 residents, while rendering the correct diagnosis in an average 16/20 cases.

Conclusions: The SIMPLL web application can be an accurate and efficient decision making aid when evaluating well-differentiated lesions in a non-cirrhotic liver.

1583 LOCHI: A Suite of R Programs To Automate Chimerism Analysis

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Background: Quantitative chimerism is an indicator of the cellular dynamics involving engraftment of donor hematopoietic stem cells (HSCs) or relapse of recipient malignant cells in HSC transplant (HSCT) patients. Currently, the most common method for monitoring chimerism following HSCT is by PCR amplification of short tandem repeat (STR) loci followed by capillary gel electrophoresis. However, this method can be challenging and tedious, including selection of informative loci and the repetition of quantifying chimerism for multiple loci from multiple cell types and multiple patients. Manual computation is not only time consuming but also has the potential of human errors. Currently, there is no free software to fully automate the chimerism analysis.

Design: The algorithm for single donor (SD) chimerism calculation is well established. LOCHI, a suite of R programs, were developed to automatically pick informative loci and calculate chimerism. In short, before transplantation, the donor and recipient alleles at each locus are compared to identify informative loci; after transplantation, chimerism is calculated from the peak areas of the informative loci. Alleles not shared between donor and recipient are used to calculate chimerism. In the case of informative locus with one shared and one unshared alleles, the value of unshared allele is used to estimate the shared allele assuming balanced amplification. The average chimerism value of all informative loci is reported. Similarly, we developed an algorithm to calculate chimerism in double cord blood transplantation and implemented it in LOCHI. R was chosen for programming because it is free and has strong matrix arithmetic capability.

Results: LOCHI starts reading data from files generated by ABI GeneMapper. It filters the input data to get rid of stutter peaks and other noise. In addition to selecting informative loci and calculating chimerism, it also generates the checksum data to help verify the data integrity and pinpoint the outliers. The accuracy of the programs was compared with manual calculation on 20 patient samples. It is 90% concordant with manual calculation. As expected, the non-concordance was due to human errors from the manual calculation.

Conclusions: By automating chimerism analysis, LOCHI significantly saves time and avoids human errors. Even though it was designed for our specific lab procedure, it can be easily adapted to other STR platforms with minor modification. The programs are freely available upon request.

1584 Integrating Online Whole Slide Imaging System and Open-Source Web-Based Questionnaire in a Nationwide Cytopathology Peer-Comparison Educational Program in Taiwan

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Background: Peer-comparison educational program is an important part in quality assurance of cytopathologic practice. However, transferring educational slides among laboratories is a time and cost consuming task. The emerging online whole slide imaging system may eliminate this physical barrier. Nevertheless, it's not a well-accepted method for cytopathologic interpretation. The aim of this study is to evaluate the performance and the acceptance in a nationwide cytopathology peer-comparison educational program using online whole slide imaging system and open-source web-based questionnaire.

Design: Five Papanicolaou smears (HSIL, adenocarcinoma of extra-uterine origin, squamous cell carcinoma, trichomonas infection, and LSIL) and 5 non-gynecologic slides with histologic confirmation (instrumented urine specimen with negative result, ascites with adenocarcinoma, pleural effusion with small cell carcinoma, breast FNA with fibroadenoma, parotid gland FNA with mucoepidermoid carcinoma) were selected by the cytopathology committee of Taiwan Society of Pathology for this educational program. The 10 whole slide images were acquired by Leica SCN-400 system in 40X magnification and hosted in Aperio eSlide Manager Server. Web-based questionnaires generated by Google Forms with online access to the 10 whole slide images were released to the members of Taiwan Society of Pathology and Taiwan Society of Clinical Cytology by emails with a limited answering period.

Results: A total of 302 participants (pathologists/cytotechnicians: 112/190) joined the Papanicolaou smear part and 291 (pathologists/cytotechnicians: 117/174) in the non-gynecologic part. The correct interpretation rates were 82%-94% in the Papanicolaou smears and 22%-93% in the non-gynecologic cases. About 63% of the participants experienced their first time using whole slide imaging system for cytopathology interpretation and most of the participants (88%) thought that the educational program was helpful for their clinical practice. Almost all the participants (98%) would like to participate in a similar program for the next time.

Conclusions: Integrating online whole slide imaging system and open-source web-based questionnaire is an inexpensive and well-accepted method to access nationwide practitioners and to help them identifying diagnostic weak point in clinical practice. The result of the program further guides the continuous medical education in cytopathology in Taiwan.

1585 Data From Words: The Spectrum of Hidden Information in Simple Word Lists from Pathology Reports

Cigdem Himmetoglu Ussakli, Rodney Schmidt. University of Washington, Seattle, WA.

Background: Pathology reports and the laboratory information systems (LIS) that produce them are dense repositories of information that make them high-value targets for queries. However, a variety of privacy and security concerns limit data access to those with special training and permission. When pathology reports are disassembled into lists of words, all linkage to specific patients is lost and such lists can be made available to a broader range of people for business or research analysis. We developed such word lists from all pathology reports issued over a 14 year period with two

intentions: to develop a custom dictionary that could be used with our LIS, and to explore the types of qualitative and quantitative information that could be extracted from word frequency lists.
Design: We used a custom SQL script to parse all pathology reports into annual lists of words and their frequency of use without retention of any links to individual cases or any personal health information. For a custom dictionary, words were sorted in descending frequency, manually reviewed for typographical errors, converted to Unicode format, and imported into Word as a .DIC file. To demonstrate proof of concept for other uses, historical trends in the frequency of use of selected words were compared either with use of other words or with standard, direct metrics.
Results: The custom dictionary developed from word lists integrated smoothly into Word and performed flawlessly. Historical trends were demonstrated for changes in diagnostic terminology (e.g. Hodgkin vs Hodgkin's), test terminology (e.g. FISH, aCGH), and for the dramatic rise in molecular terms in pathology reports (e.g. sequencing and EGFR). Terms like "intraoperative" and "FISH" correlated well with billed CPT codes for frozen and FISH (0.67 and 0.90, respectively). The dates on which specialty labs started using the LIS for reporting were also evident. Slide reviews and consultation requests from other pathology laboratories reflected the diagnostic challenges associated with high volume subspecialty areas such as breast pathology.
Conclusions: Custom dictionaries can be developed from simple word lists extracted from pathology reports. Changes in word frequency can be used to follow qualitative trends but also used to elucidate such things as employment history and work volume. Although word frequency correlates with precise metrics, the correlations may be too low for business decisions except for in special cases.

1586 A 5-Year Evaluation of Barcoding in Surgical Pathology at a Teritary Care Hospital

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Background: Adverse patient events in Anatomical Pathology (AP) from misidentification or mislabeling errors occur largely due to manual tasks and data entry. Barcoding technology offers a solution to reduce such errors. However, unintended errors (e.g. printer problems and failure to read barcodes) have been noted. Our aim was to study the impact of technology-related errors following barcoding in surgical pathology at our institution.
Design: 2D Datamatrix barcode technology integrated with our AP laboratory information system (CoPath Plus, Cerner DHT, Kansas City, MO) was implemented at our institution. We analyzed quality assurance data of reported adverse patient events over a 5-year period (pre-barcode: Jan 2008 to Jan 2009, barcode implementation period: Feb 2009 to Dec 2009, and post-barcode: Jan 2010 to Dec 2012).
Results: Although adverse event reporting practices increased during and post implementation, the mislabeling error rate decreased after barcoding (Table 1). Human related errors contributed to most of the reported adverse events, and increased following implementation. Grossing errors and slide label placement errors by staff were more common after barcoding, and block/slide retrieval errors occurred only in the post-barcode era. Hardware errors were attributed to printer problems. Three manual entry errors were related to a system downtime.

Reported errors	Pre-barcode period (Jan 2008-Jan 2009)	Implementation phase(Feb 2009-Dec 2009)	Post-barcode period(Jan 2010-Dec 2012)
Errorrate (events per 10,000 specimens)	7.7	6.4	6.0
Human related errors	34 (44%)	43 (76%)	135 (75%)
Hardware errors	4 (5%)	3 (5%)	8 (4%)
Downtime errors	0 (0%)	0 (0%)	3 (2%)
Other (unspecified) errors	39 (51%)	11 (19%)	35 (19%)
Total errors	77	57	181

Conclusions: Implementation of barcoding helped reduce, but did not eliminate, misidentification-related errors in our AP laboratory. Such errors may persist or even increase due to better reporting of adverse events (e.g. electronic alerts and heightened user awareness), non-compliance of users (during grossing and block/slide retrieval), and as a result of technology failures (e.g. misplaced barcoded labels, printer errors and system outage).

1587 Computerized Nuclear Shape Analysis of Prostate Biopsy Images Predict Favorable Outcome in Active Surveillance Patients

George Lee, Robert Veltri, Guangjing Zhu, Jonathan Epstein, Anant Madabhushi. Case Western Reserve University, Cleveland, OH; Johns Hopkins University School of Medicine, Baltimore, MD.
Background: Prostate cancer (CaP) is well documented as being one of the most overdiagnosed and overtreated diseases where active treatment of 48 patients over a median of 9 yrs may be necessary in order to prevent 1 CaP specific death. Active surveillance (AS), an accepted monitoring program, may be offered for men with very low risk (VLR) CaP in lieu of immediate intervention to reduce unnecessary treatment and improve quality of life. Our objective is to identify computationally derived features from digitized biopsy core images which can predict favorable and unfavorable outcomes for VLR AS patients.
Design: Based on the NCCN CaP guidelines, CaP patients from the Johns Hopkins Hospital (JHH) were given the option for AS if they were classified as VLR (stage T1c, PSA < 10ng/mL, Gleason sum (GS) <= 6, <= 2 positive cores, <= 50% core involvement, PSA density < 0.15 ng/mL and life expectancy < 20 years). Outcome was deemed favorable if patients under AS did not require re-classification with follow up and deemed unfavorable if disease demonstrated an upgraded GS, increased tumor volume, and/or PSA/PSAD during monitoring. Quantification of nuclear shape based features was performed on 65 H&E stained biopsy core images (30 Favorable, 35 Unfavorable) obtained from 51 AS CaP patients managed at the JHH AS program. Cancerous regions of interest were denoted by our collaborating pathologist, Jonathan I. Epstein at JHH, for the purpose of analysis.
Results: Nuclear shape-based features (Std. Dev. Perimeter Ratio, Std. Dev. Long/Short Distance Ratio, and Mean Long/Short Distance Ratio) were capable of differentiating favorable from unfavorable outcome in 51 AS patients as shown in Figure 1. This ability to identify patients that will fail AS is supported by a Random Forest classifier using these nuclear shape features (AUC = 0.78) compared to GS (AUC = 0.60).

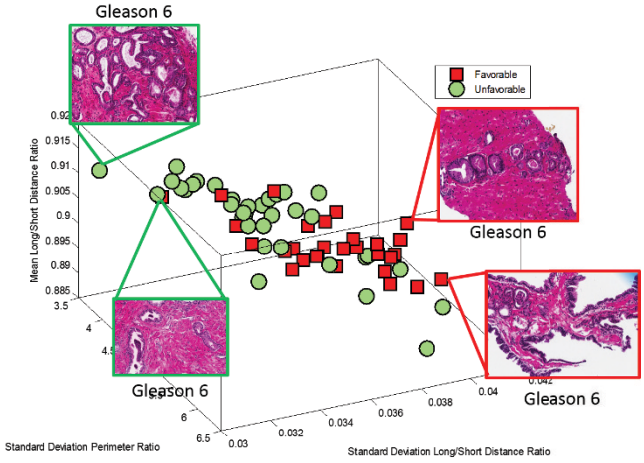

Figure 1: Three shape-based features are shown to differentiate prostate biopsy core images from active surveillance patients associated with favorable and unfavorable outcomes.

Conclusions: We demonstrated the ability of computerized nuclear shape features to predict favorable from unfavorable outcomes in AS using biopsy images statistically significantly ($p<0.05$) better than GS.

1588 Prostate Cancer Recurrence Can Be Predicted By Measuring Cell Graph and Nuclear Shape Parameters in the Benign Cancer-Adjacent Field of Surgical Specimens

George Lee, Robert Veltri, Sahirzeeshan Ali, Jonathan Epstein, Christhunesa Christudass, Anant Madabhushi. Case Western Reserve University, Cleveland, OH; Johns Hopkins University School of Medicine, Baltimore, MD.
Background: The 'field effect' describes the micro-environment around the site of the tumor which may lead to a progression of disease. The field effect phenomenon is interesting for the investigation of disease progression in prostate cancer (CaP) primarily because CaP is known as a heterogeneous and multi-focal disease, where 50-76% of all radical prostatectomy (RP) cases have been reported to contain multiple tumor regions. Since the surrounding benign regions may contain molecular/or morphologic clues for cancer progression, we show that disease progression can be predicted via computational analysis of benign stromal tissue adjacent to cancerous regions of interest.
Design: We investigated cell graphs of the benign regions surrounding the tumor area in addition to nuclear shape in cancerous regions (Figure 1 (a-l)) for the purpose of identifying progression via biochemical recurrence (BCR) in 70 CaP patients following RP, 22 of whom displayed signs of BCR, and 48 who did not.

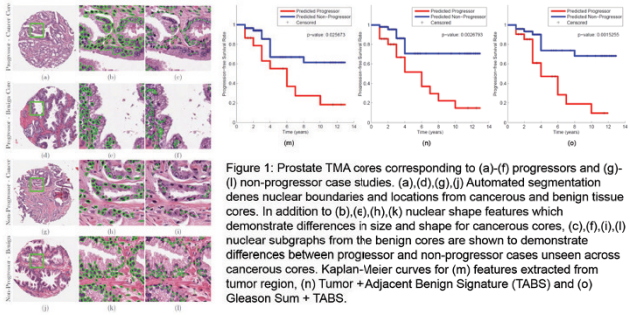

Figure 1: Prostate TMA cores corresponding to (a)-(f) progressors and (g)-(l) non-progressor case studies. (a),(d),(g),(j) Automated segmentation denes nuclear boundaries and locations from cancerous and benign tissue cores. In addition to (b),(e),(h),(k) nuclear shape features which demonstrate differences in size and shape for cancerous cores, (c),(f),(i),(l) nuclear subgraphs from the benign cores are shown to demonstrate differences between progiessor and non-progressor cases unseen across cancerous cores. Kaplan-Meier curves for (m) features extracted from tumor region, (n) Tumor +Adjacent Benign Signature (TABS) and (o) Gleason Sum + TABS.

Results: Nuclear shape descriptors were found to be the most useful for the analysis of CaP regions, while nuclear subgraph and nuclear density features were more useful for extracting discriminatory information from the benign cancer-adjacent regions. These top features were combined to produce a 10 feature Tumor + Adjacent Benign Signature (TABS) for predicting BCR which produced a classification AUC of 0.74. We found that the addition of cell graph features from benign cancer-adjacent regions of the excised prostate could improve prediction of BCR over Gleason sum (GS) (AUC = 0.72) and

nuclear shape features extracted from cancer regions alone (AUC = 0.72). Combining TABS with GS further improved the identification of BCR (AUC = 0.82) and similarly improved prediction of progression free-survival (Figure 1 (m-o)).
Conclusions: We found the combined TABS feature set to outperform the gold standard for clinical CaP tissue analysis, Gleason sum. Furthermore, combining TABS with Gleason sum significantly improves upon the predictive performance of Gleason sum alone.

1589 Documenting Communication of Significant Pathology Results Using the LIS and the EMR

Cesar Llanos, Joseph Zeitouni. University of Miami Miller School of Medicine, Miami, FL.
Background: In the United States close to 30 million pathology reports that contain urgent or significant results, are sent to treating physicians. In 11 to 30% of these, the responsible providers were not aware of the results, despite requirements by the Joint Commission on Accreditation of Health Organizations (JCAHO) to have approved criteria for the immediate notification and follow up of these results. While the federal SAFER Guides recommends flagging of results, the ADASP has published criteria for the significant pathology result (SPR), and our pathologists have been documenting these as free-text, our department decided to implement an additional, more proactive approach to help our clinical colleagues manage these results using the LIS and the EMR.
Design: Since automated flagging as with clinical lab results, is not possible for most pathology results, we concluded that our pathologists would have to manually flag their reports in the LIS at the time of sign out. We asked the LIS vendor to create a pop-up window to answer: "Is this an SPR?", and they will classify the SPR from a list compiled from ADASP criteria for surgical pathology significant/critical results with input from clinicians at our local institution. After the case is signed out, the HL7 message will carry an SPR flag in OBX-8 concatenated with the codes for the SPR reason to the interface engine. If the SPR fields and retrieval flags are present in a specific SPR translation table, the interface engine will send this message to the EMR.
Results: Currently, the SPR prompt is functional in our LIS testing environment. We are testing EMR functionality that includes a physician in-basket notification with a specific SPR icon, requiring forced documentation of the provider's action. Additionally, the SPR flags sent from the LIS will be stored and monitored in the EMR with several ad-hoc reports used by scheduling and the department of patient safety to monitor the rate and timeframe within which these results are appropriately communicated and follow-up visits.
Conclusions: Amid growing adoption of EMR technology, and interfaced laboratory results, pathologists have opportunities to modify and leverage their LIS to play central roles as members of the clinical management team. They must assume responsibilities of ensuring that patients are managed appropriately based on the findings from diagnostic tests or procedures. By doing so, they extend their influence beyond the four walls of the laboratory and can reestablish themselves as being physicians at the center of patient care.

1590 Fractal Descriptors Accurately Distinguish Between Growth Patterns of Prostate Cancers

Zhaoxuan Ma, Yuan Xiaopu, Mahul Amin, Beatrice Knudsen, Arkadiusz Gertych. Cedars-Sinai Medical Center, Los Angeles, CA.
Background: There are no image analysis tools that can accurately distinguish benign (BN), low-grade (Gleason pattern 3 (G3)), high-grade cribriform (G4-C), and high-grade non-cribriform (G4-NC) prostate cancer (PCA). Fractal dimension (FD) and lacunarity (LA) are complementary pattern recognition tools that we applied to classify binary nuclear masks from H&E images of radical prostatectomies (RP).
Design: Digital images (20X) from 20 RPs were generated with the Leica scanner (SCN 400) and divided into squared tiles. Binary nuclear masks were derived from randomly selected tiles containing benign glands (BN, n=161), G3 (n=51), G4-C (n=54) or G4-NC (n=90) and analyzed to obtain 3 FD and 3 LA numerical features using small and large scanning boxes. These descriptors were fed into a linear classifier system to distinguish: BN from PCA, G3 from G4 or BN, and all four tissues. A 7-fold cross validation scheme (15% of samples for testing and 85% for training) was used to validate the accuracy of predicting cancer and cancer grades in each tile.
Results: FD and LA features from PCA images formed clusters for each of the grades

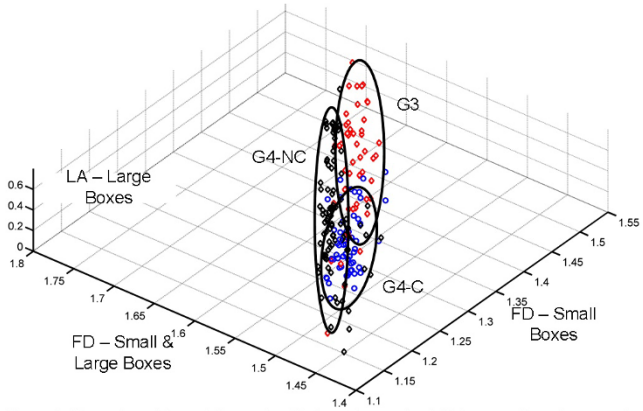

Figure.1. Clustering of fractal dimension (FD) and lacunarity (LA) features from images of low-grade (G3) and high grade (G4) cancer.

The separation of clusters was improved through the combination of scanning boxes of different sizes. The prediction of PCA and BN areas using FD and LA was correct in 97% of cases.

Tissue/Feature	PCA or BN	G3 or G4 or BN	G3 or G4-NC or G4-NC or BN
LA	95.5%	88.7%	75.5%
FD	97.1%	86.2%	78.9%
LA + FD	97.4%	92.4%	85.3%

When the PCA category was divided into G3, G4-C and G4-NC, the prediction was less accurate due to overlaps between G3, G4-NC and G4-C clusters. When combined, FD and LA yielded the highest correct classification rates, higher than FD and LA alone.
Conclusions: Along with ongoing efforts on morphological refinements in the Gleason system, image analysis offers a promise as an independent approach to quantify PCA. FD and LA derived from binary nuclear masks can distinguish four tissue components. Combining multiple FD and LA values is a new approach that can aid in the assessment of PCA grades by imaging.

1591 Poster Presentations 2.0 – Using Mobile Device-Based Augmented Reality To Enhance Pathology Poster Presentations

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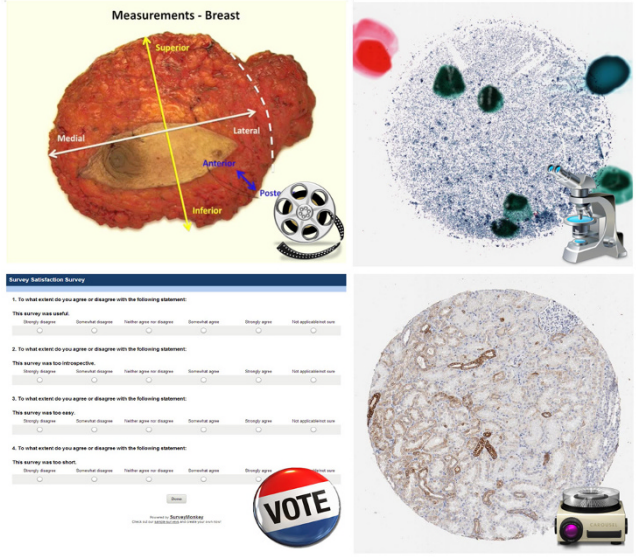
Background: Poster presentations are a staple of pathology conferences and form the nidus of thousands of academic conversations each year, many of which spark new ideas, collaborations, and further research. While the process of making posters has evolved with computing and printing technology, they remain limited by their primary distribution medium–paper. These posters can't present information dynamically or interactively and each poster is limited in the amount of information it can display. With the ubiquity of smartphones and tablets today, we explore how augmented reality technology can transform the traditional paper poster into a modern, interactive digital experience.
Design: A poster is constructed as usual and a digital copy uploaded to an augmented reality platform (www.layar.com). Specific areas are then chosen to link to supplementary dynamic web components, including movies, photo/image carousels, audio, or interactive features such as online polls, maps, or social media features. An augmented reality app (specific to the augmented reality platform, Layar here) is then downloaded and installed on the user's mobile device from the appropriate app store (Apple iOS, Android, or Blackberry). After launching the app, the user points the mobile device's camera at the poster, the live video feed is analyzed, and the augmented reality areas are recognized and overlaid onto the video feed. The user then selects an augmented area by touch to display or interact with the associated digital media. Pathology-specific features, such as whole slide images, can be incorporated by launching apps or websites.
Results: We created a poster with several augmented reality regions, with each region demonstrating a different supplementary medium.



Conclusions: Poster presentations are a valuable component of many scientific conferences, including national pathology meetings such as the USCAP Annual Meeting. We have demonstrated how the traditional paper poster can be augmented with a wealth of supplementary dynamic media, using current technology to extend the reach of static printed materials and to enrich conference attendees' experiences.

1592 Computer Analysis of Benign and Malignant Breast Specimen Images By Graph Extraction and Adjacency Matrices

Amir Momeni Boroujeni, Raavi Gupta, Elham Yousefi. SUNY Downstate Medical Center, Brooklyn, NY.

Background: The pathologists' eyes and judgement have been the gold standard for diagnosis of breast tissue pathologies. Just as the pathologists use visual patterns they see in the slides in order to call a diagnosis; we propose that a computer can also pick up the patterns in the slides. In this study we analyzed and compared the patterns in benign and malignant breast lesions.

Design: For our study we chose to compare sclerosing adenosis as an example of a benign breast lesion and grade III infiltrating ductal carcinoma as an example of a malignant breast lesion. Four cases of sclerosing adenosis and four cases of infiltrating ductal carcinoma were randomly chosen. The slides were reviewed by a pathologist and two points of interest were chosen at 40x by the pathologist for each slide. The points of interest were chosen based on the pathologist's interpretation that they showed the intended pathology (either sclerosing adenosis or infiltrating ductal carcinoma). High resolution TIF images were then taken from the points of interest. The images were then binarized and the resulting binary images were segmented and skeletonized using ImageJ software in order to extract the cell-graph. We then used MATLAB software to identify the network of the cells; in order to do this we extracted the adjacency matrices of the binarized and segmented image. The data extracted was then used to define a network for each point of interest in Cytoscape software and the network was analyzed in order to understand its properties. We then used SPSS software to compare the network properties in our 8 benign and 8 malignant points of interest.

Results: When we compared the network data of the two different lesions, It was shown that the two lesions have significant differences in network properties which enables our model to differentiate between the benign and malignant lesions. The multivariate analysis we used had an accuracy of 100% in differentiating sclerosing adenosis from infiltrating ductal carcinoma.

Conclusions: The morphologic differences between sclerosing adenosis and high grade infiltrating ductal carcinoma are considerable and this allows the application of computerized image analysis to differentiate between them; our learning technique is based on graph theory and similar studies have supported its applicability for devising mathematical models for differentiating breast lesions. The challenge is to devise models for differentiating morphologically similar lesions and integration of histologic features such as nuclear grading and number of mitosis in such models.

1593 Reducing Unnecessary Send Out Testing at an Academic Teaching Hospital

Pawel Mroz, Gregory Retzinger. Northwestern University, Chicago, IL.

Background: Laboratory testing is a necessary and central part of modern medicine and is a single highest-volume medical activity with the estimated 5 billion tests performed across United States per year. Overutilization and inappropriate testing however, can cause harm and lead to medical errors increasing the likelihood of false-positive results, longer hospital stays and liability. Most importantly, it can significantly drive up the costs of patients care. Studies have showed that educational efforts directed at changing physician practice as well as changes in requisition design may have significant effect but are labor-intensive and require substantial subspecialty expertise.

Here we report an attempt to significantly reduce the number of send out tests and associated costs based on the implementation of an electronic medical records integrated send out alert supplemented by pathologist triage protocol.

Design: We conducted the analysis of send out tests ordered at our institution in a period between January 30th 2014 and August 11th 2014 that triggered an electronic medical records integrated send out alert or pathologist triage protocol. We reviewed the costs of individual tests as well as the total costs of send out tests ordered in this period and analyzed the effects of the proposed system on the overall number of ordered tests as well as savings associated with test reconsideration/cancellation.

Results: We analyzed total of 4579 send out tests ordered between January 30th 2014 and August 11th 2014. Of those 4222 we used for final analysis. All of those tests triggered the electronic medical records integrated send out alert and resulted in successful immediate reconsideration/cancelation of 317 tests or 12%. Remaining 3704 tests were ordered despite triggering the electronic medical records integrated send out alert and 891 or 21% were subsequently cancelled or subjected to pathologist triage. Overall this approached led to 33% reduction in send out tests ordered within studied period and allowed for significant cost reduction.

Conclusions: The implementation of the electronic medical records integrated send out alert did not completely eliminate overutilization of send out testing but led to significant number of tests being immediately reconsidered and cancelled. Additional review of send out orders by pathologist led to further decrease in overall numbers and costs of send out tests. The results may provide a basis for development of clinician education program as well as reduction of overall cost of send out tests.

1594 Use of Histology Pattern Recognition Software for PD-L1 Immunoprofiling of Lung Cancer

Edwin Parra, Barbara Mino, Junya Fujimoto, Ximing Tang, Neda Kalhor, Annikka Weissferdt, Carmen Behrens, Julie Izzo, Cesar Moran, Ignacio Wistuba, Jaime Rodriguez-Canales. University of Texas MD Anderson Cancer Center, Houston, TX.

Background: Immunohistochemical (IHC) analysis of tumor-inflammation markers have become relevant for tumor immunoprofiling and cancer immunotherapy. These analysis require computer aided scoring (CAS) of multiple markers through algorithms for the analysis of nuclear, membrane or cytoplasmic IHC markers. However, CAS algorithms alone cannot identify morphological patterns such as tumor cells versus stroma. This limitation is critical for PD-L1 (CD274) which can be expressed by tumor cells, macrophages and lymphocytes. GENetic Imagery Exploration (GENIE) is an image pattern recognition software recently incorporated into Aperio digital pathology for histology pattern identification. Our goal is to explore the application of image pattern recognition software for CAS of PD-L1 in tumor cells excluding stroma, compared with CAS analysis without histology pattern recognition.

Design: 214 lung cancer specimens were stained with PD-L1. IHC slides were scanned using an Aperio ScanScope and analyzed using ImageScope software (Aperio). All slides were first analyzed using a membrane algorithm on 5 random 1mm square tumor areas selected by a pathologist providing a H-score of PDL1 expression as the average of the 5 areas. The same cases where analyzed using GENIE for pattern recognition of the tumor in the whole slide, excluding stroma and normal cells, and then applied the membrane algorithm for H-score of PD-L1 on all the cells selected by GENIE. Both results, with and without GENIE, were compared and correlated.

Results: Using the membrane algorithm alone for the scoring of PD-L1 provided an H-score of 44.16 ± 45.26 (mean and standard deviation (SD). Using GENIE for pattern recognition of tumor on the same cases provided a PD-L1 H-score of 13.75 ± 28.20 (mean and SD). The CAS without GENIE was statistically significantly higher compared with CAS obtained with GENIE ($P<0.001$). Spearman correlation between the PD-L1 expression using GENIE and PD-L1 expression without GENIE was $R=0.656$ ($P<0.001$). A review of the IHC images by the pathologists showed that without GENIE the CAS algorithm counted all IHC staining including tumor and inflammatory cells in the lung stroma, instead GENIE successfully enriched for tumor cells for the IHC scoring.

Conclusions: When compared both CAS methods for PD-L1 IHC scoring, the use of a histology pattern recognition software (GENIE) improved significantly the IHC scoring of PD-L1 excluding the staining present in macrophages and inflammatory cells. However, both CAS methods, with and without GENIE, require the supervision by a pathologist.

1595 AutoStitcherTM: An Automated Program for Accurate Reconstruction of Digitized Whole Histological Sections From Tissue Fragments

Gregory Penzias, Andrew Janowczyk, Asha Singanamalli, Mirabela Rusu, Natalie Shih, Michael Feldman, Satish Viswanath, Anant Madabhushi. Case Western Reserve University, Cleveland, OH; University of Pennsylvania, Philadelphia, PA.

Background: While whole-mount tissue specimens are most optimal for whole-slide disease annotation and correlating pathology with radiology, preparation of whole tissue specimens is not always feasible. In such cases, accurate reconstruction of digitized pseudo whole-mount histological sections (PWMHSs) from smaller image fragments can ensure minimal disruption of pathology workflows. We recently presented a memory efficient, flexible tool called HistoSticher™ for manual reassembly of image fragments. However, this technique still requires laboriously manually identifying matching locations ("fiducials") prior to reconstruction. We present preliminary results of an automated method of reconstructing PWMHSs from tissue fragment images, thus removing a major impediment to pathology-radiology correlation research.

Design: Data utilized in this study comprises quartered and digitized histological sections. For each pair of image fragments, the algorithm: (1) pre-processes to separate tissue from background, and rotates fragments into a common reference frame; (2) "stitches" adjacent fragments by ensuring contiguity of edges; and (3) identifies pairs of fiducials along the stitched edge. Optimal PWMHS reconstruction was calculated by transforming all 4 fragments such that the fiducials for the 4 edge-pairs are as spatially close as possible.

Results: AutoStitcher results were compared to manual PWMHS reconstructions obtained via HistoStitcher (Figure 1). Quantitative evaluation required computing the mean distance between fiducials identified at the midpoints of each fragment's edge (and thus independent of fiducials used for PWMHS reconstruction by either AutoStitcher or HistoStitcher). AutoStitcher demonstrated a mean error of 7.10 pixels compared to an error of 8.13 pixels for HistoStitcher in a cohort of 4 *ex vivo* prostate sections.

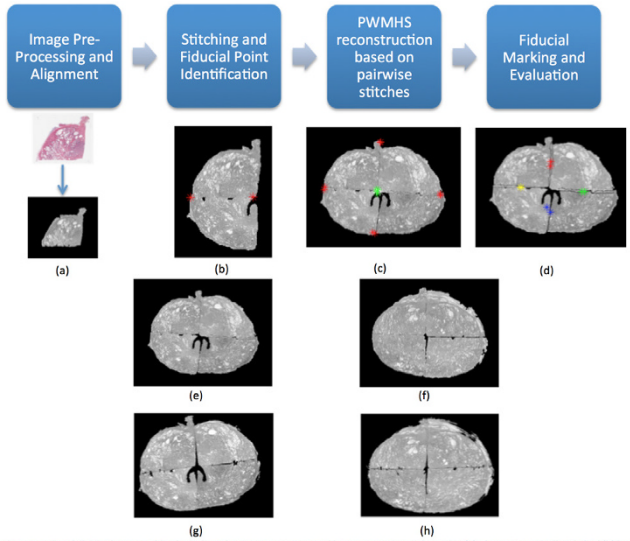


Figure 1: Pairs of digitized prostate histological quadrants are pre-processed by segmentation and rotation (a), then automatically stitched (b) by ensuring contiguity of edges. Two fiducial points are automatically marked on each of these stitches (b), then the full PWMHS is reconstructed using all eight pairs of fiducial points (c). PWMHS stitches are evaluated by automatically marking a fiducial at the midpoint of each edge (d), then computing the mean separation distance of the four pairs. AutoStitcher (e, f) appears to yield similar reconstructions compared to HistoStitcher (g, h) images for real *ex vivo* prostate PWMHSs. Note that (e, f, g, h) resized to 5% of 2x resolution.

Conclusions: We have presented preliminary results of a completely automated algorithm that successfully reconstructs PWMHS images from digitized tissue fragments, with relatively low error compared to manual reconstruction. Additional validation is currently underway on a larger dataset and higher resolution.

1596 'Lean' Laboratory Requests: Mobile Apps for Immunohistochemistry and Molecular Test Requests

Keith Pilson, Michael Bennett, Julie McCarthy. Cork University Hospital, Cork, Ireland.

Background: 'Lean' is a management framework for maximizing value and minimizing waste. It has origins in the automotive manufacturing industry and has been utilized successfully in many other non-manufacturing processes. There has been a strong emphasis on 'leaning' processes within the histopathology department at our institution in recent years, with several 'lean' projects bringing significant time and cost savings to the department. One such project was the introduction of an email ordering system for immunohistochemical tests to replace an antiquated paper-based ordering system. Molecular test requesting by clinicians via an email based system was also developed at the hospital. The present work involves refining the simplistic email based systems to increase their utility and time savings using a smartphone as a platform.

Design: Mobile applications to facilitate laboratory test requesting were developed using Xcode and the Objective C programming language. The apps were designed to protect patient anonymity. A bar code scanner was incorporated into the apps to help reduce erroneous requests by scanning case number bar codes. Users specify and store immunohistochemistry panels and other requests for single tap retrieval. The time spent ordering various laboratory tests using the apps was compared with desktop email ordering. The apps were made available as a free download in the Apple App Store.

Results: The apps expedited the laboratory test ordering process and added significant utility by storing frequently used orders and allowing requests to be made away from the office, during a sign-out or at an MDT with convenient access to the request history at all times.

Conclusions: We present a 'lean' method for requesting immunohistochemistry and molecular tests using a smartphone. Our testing shows a time saving compared with desktop email ordering. Development of the applications is on-going with implementation of a data-collection and audit system in progress.

1597 Multi-Head Miscroscope Simulation To Tackle Diagnostic Discordance on Mesothelioma Difficult Cases

Julien Pontoizeau, Celine Lize-Dufranc, CNR MESOPATH Panel, Arnaud Renouf, Gaetane Blaizot, Annabelle Gilg Soit Ilg, Francoise Galateau -Salle. CHU, Caen, Normandy, France; DATEXIM, Caen, Normandy, France; French National Health Institute, Saint Maurice, Ile de France, France.

Background: MESOPATH/IM@EC is a national and international Excellence Reference Center specialized in mesothelioma (MM) diagnosis. Due to a compulsory declaration of disease in France, each case samples with a first diagnosis of MM are certified according to a pathological standardized procedure. Telepathology is used to reduce the reviewing process time, to store expertise for educational purpose and to share knowledge between pathologists. In case of diagnostic discordances, a virtual multi-head functionality is used to finalize a collegial review.

Design: A full web application named CytoSuite allows the pathologists panel to review easily and securely the cases from anywhere: its HTML5 full compliance allows using it on any devices, without any restrictions regarding operating systems nor any plug-in installation. The virtual multi-head functionality of this application proposes online meetings where one of the pathologists can control the other pathologists slide viewers in order to explain the process he used to review the slides and to make them understand his point of view. At any moment, the possibility to drive the application can be given to one of the other pathologists for him to describe what he saw.

Results: The time to reach a collegial diagnosis is reduced because meetings can be taken online and pathologists do not have to be located physically in the same room to exchange on the slides. It is easy for them to explain the process they used to reach their diagnosis and they can demonstrate it to the other pathologists. During the last session, three online pathologists settled on three discordant cases in 45 minutes and in a completely secured way. They reviewed together 42 virtual slides made available through this virtual multi-head tool.

Conclusions: Full-web technology brings secured, immediate and direct access to slides and virtual multi-head functionality allows pathologists to exchange rapidly on difficult cases in order to tackle diagnostic discordance. The accessibility provided by this technology is an advantage really appreciated by pathologists because they can use it anywhere on any device (even on tablets) avoiding them to be on a dedicated workstation. Virtual meetings can be easily and more often organized reducing the time to diagnosis on discordant cases.

1598 Histology – CT Fusion Facilitates the Characterization of Suspicious Lung Lesions With No, Minimal, and Significant Invasion on CT

Mirabela Rusu, Michael Yang, Prabhakar Rajiah, Frank Jacono, Robert Gilkeson, Philip Linden, Anant Madabhushi. Case Western Reserve University, Cleveland, OH; University Hospitals, Cleveland, OH; Louis Stokes Cleveland VA Medical Center, Cleveland, OH.

Background: For pulmonary adenocarcinomas, invasive and *in situ* components may co-exist within the same nodule resulting in a heterogeneous ground glass nodule on CT. Currently radiologists are unable to distinguish no, minimal and frank invasion on CT. The definitive identification of the extent of invasion within a nodule is only possible on histopathology. We aim to use histologic reconstruction and deformable co-registration to precisely map the invasion from corresponding histopathology onto the CT. Ultimately, this facilitates the computer-based learning of the CT appearance of invasive adenocarcinoma and permits assessment for the presence of significant invasion (>5 mm).

Design: Histology and CT of resected ground glass nodules with significant (n=9) and minimal or no (n=5) invasion were included. Following high-resolution scanning of the H&E-stained slides, the expert pathologist outlined the invasive and in situ components. The outlines were mapped onto CT through careful co-registration of histology and CT images. First, an interactive CT nodule sectioning (red plane, Fig. 1a) allows to identify the CT tumor plane (Fig 1b) that best matches the histology slice (Fig 1d) by visually matching anatomic landmarks existing on both modalities. Second, elastic registration aligns the 2D histology and the corresponding 2D CT slices (Fig. 1e). Finally, CT-derived features such as intensity statistics, Haralick and Gabor (Fig. 1f) characterize the textural appearance of the nodule and are utilized to identify those features that distinguish invasive from in situ disease.

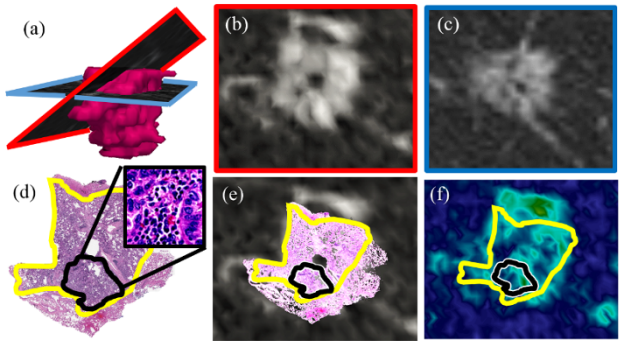


Figure 1. Ground glass nodule histology-CT fusion; (a) 3D view of nodule with axial (blue) and oblique (red) cutting plane; (b) CT intensities (oblique cut); (c) CT intensities (axial cut); (d) H&E section corresponding to the oblique cut (b); invasion (black) and adenocarcinoma in situ + invasion (yellow); (e) the interactive alignment of histology and CT allows to map extent of invasion from histology onto CT; (f) CT-based textures will be included in a predictor

Results: Preliminary results indicate that an accurate registration of histology and CT is possible, thus mapping the invasive and *in situ* components from histology onto CT. The accuracy of the registration may be assessed by measuring the deviation of anatomic landmark, e.g. blood vessels, between the histology and CT.

Conclusions: Histology-CT fusion and image analytics may facilitate the early detection of invasive adenocarcinoma on pre-operative CT, enabling the early intervention for invasive tumors, and avoiding biopsy or surgery for benign nodules.

1599 Whole-Slide Imaging in the Routine in a Pathology Laboratory: Can File Storage Requirements Be Reduced By Deleting Unnecessary Images?

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Background: Whole slide imaging (WSI) allows performing the histological diagnosis of pathological specimens in digitized entire glass slides. A major concern about the use of WSI in the routine practice is the huge server requirements and the high costs of file storage. However, as the process of digitization implies computerization, automatic mechanisms of deletion of unnecessary images could be easily applied after the end of the diagnostic process plus a security period (i.e. 1 year). This study aims to evaluate whether file storage requirements could be reduced by applying a policy of eliminating WSI images and glass slides.

Design: We conducted the study at the department of pathology of a University Hospital. The study involved consecutive slides generated in gynecological (GYN) and pulmonary (PUL) pathology, from May to July 2014 (n=2,293; GYN=1,630; PUL=663). The slides were digitized in a Ventana iScan HT. We reviewed all the WSI images, the glass slides, and the paraffin blocks in order to classify them as candidates to be eliminated or maintained in the files. The main criteria for keeping WSI images were the presence of malignant or premalignant lesions and the relevance for the diagnosis or the staging. Only one representative WSI image was kept. The main criteria for maintaining glass slides was the scant or absence of adequate residual material in the paraffin block.

Results: Overall, 88.4% of the WSI images and 95.8% of the glass slides were classified as candidates for deletion and elimination. In GYN pathology WSI images were less frequently considered as candidates for deletion than in PUL pathology (85.6% vs. 95.6%). This was related to the significantly higher number of biopsies with premalignant HPV related lesions in GYN pathology that were considered as necessary for the adequate follow-up evaluation. Conversely, the reverse occurred for the glass slides: 99.0% of the GYN slides and only 88.0% of the PUL pathology slides were candidates for elimination. This difference was attributed to the higher number of cases with scant material that could be necessary for molecular or immunohistochemical studies in PUL pathology.

Conclusions: The introduction of policies of deleting unnecessary WSI images and glass slides can significantly reduce file storage requirements and consequently reduce the high costs associated with filing in the departments of pathology. Criteria for deletion of WSI images and glass slides should be refined and standardized and the legal issues addressed before implementing these strategies.

1600 HCV Genie: A Web-Based HCV Interpretation Platform for the Versant HCV Genotype 2.0 Line Probe Assay

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Background: Hepatitis C virus (HCV) genotyping at our institution is performed using the Versant Hepatitis C virus genotype 2.0 Line Probe Assay (LiPA). The last step of this procedure is a manual, time-consuming, and error prone process that involves the comparison of bands on a test strip to a physical reference table. The aim of this project was to develop a web-based HCV genotype interpretation platform that would (a) minimize interpretation time, (b) reduce error, and therefore (c) increase the quality of patient care delivered through this test methodology.

Design: Under the supervision of a clinical informaticist, a resident with no prior programming experience utilized a Dell Precision T3600 (Intel Xeon E5-1603 @ 2.8 GHz; 16GB DDR3 SDRAM; 256GB SSD; 1TB HDD; Microsoft Windows 7 x64) to create and host a standard LEMP (Ubuntu Linux Server 14.04 LTS x64, nginx 1.7.5, MariaDB 10.0.14, PHP 5.5.9) stack virtual machine on Oracle VM Virtualbox 4.3.12 virtualization software. Using this stack, she (a) designed, built, and deployed and automated HCV genotype interpretation program called "HCV Genie," (b) populated the reference database of that program utilizing a comma-separated value (CSV) derived from Versant's physical reference table, (c) built a user interface for band pattern query, and (d) clinically validated the final program against the current manual interpretation methodology.

Results: Our program was written, deployed, clinically validated, and proven to be identical to human expert interpretation (n = 200) over the course of 2 weeks. It decreases the time needed to interpret results by 53% in residents, but results among experienced lab technicians are more equivocal.

Conclusions: Our program provides results that are identical to the manual workflow, but (a) with reduced manual steps and (b) in a timeframe similar to that of the most well-trained manual interpreter, regardless of the program user's experience level. Future iterations of this program will focus on minimizing user input even further, and as user experience with our program grows, we expect further decreases in interpretation time.

Significance: This program is already a useful and portable tool to cross train technicians, residents, and physicians in the molecular/infectious disease laboratories. Future plans are to completely automate the interpretation step by scanning and automatically interpreting the band pattern on test strips. This effort shows the utility of informaticist-supervised resident/fellow programming projects as learning opportunities and workflow improvements both.

1601 A Novel Pathology-Radiology Fusion Workflow for Predicting Treatment Response and Patient Outcome in Rectal Cancers

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Background: Most rectal cancer patients undergo chemoradiation followed by a total mesorectal excision, but there is no definitive predictor for early treatment outcome in this disease. Information unused in this regard includes *in vivo* pre-surgical MRI which is used only to restage tumor extent, as well as *ex vivo* excised rectal specimen on which different tissue types and pathologies are evaluated. We present a novel workflow for pathology-radiology fusion in rectal cancers, which will enable spatial correlation and integration of these modalities. By combining *in vivo* tumor stage and appearance (from imaging) with detailed *ex vivo* tissue characteristics (from pathology), we could quantify treatment response in rectal cancers and build a quantitative predictor for early patient outcome.

Design: Figure 1 depicts our workflow:

Step 1: Excised rectal specimen is sectioned and stained with H&E, undergoes digitization. An expert pathologist annotates regions of: (a) residual tumor, (b) benign treatment effects of ulceration and fibrosis, (c) normal tissue such as mucosal layers, muscle, and fat.

Step 2: A pathologist and a radiologist confer and visually correlate corresponding sections between *ex vivo* rectal pathology and *in vivo* rectal MRI. Visually discernible landmarks are identified, together with gross anatomical correspondences.

Step 3: Quantitative fusion of pathology and radiology is done via a thin-plate spline based elastic registration scheme so that matched landmarks and gross anatomy are warped into spatial alignment.

Step 4: Spatially correlated MRI and pathology can now be quantitatively fused and integrated.

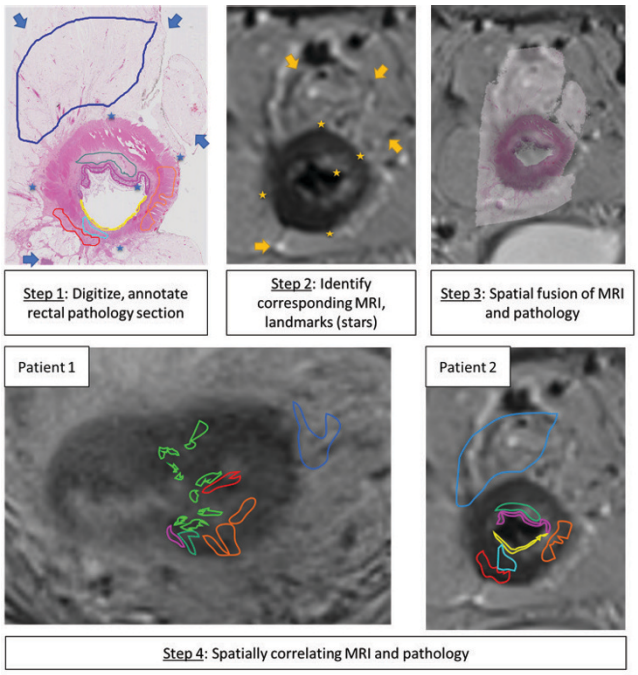

Figure 1: Depicting different steps of pathology-radiology fusion workflow. Key to annotations in Step 1 is below. In Steps 1 and 2, identified landmarks and gross anatomy are highlighted via blue/yellow stars and blue/yellow arrows. Step 4 shows results of spatially correlating pathological information on MRI for 2 different patients, including highly detailed spatial mapping of different tissue types onto imaging.

Annotations key: green – rectal cancer, yellow – ulcer surface, red – fibrosis, light blue – fibrosis+muscle, purple – mucosa, turquoise – submucosa, orange – muscularis propisa, deep blue – perirectal fat

Results: Excellent correspondence was observed between expert-identified landmarks and known tissue types (fat, muscle, rectal wall) for 2 different spatially fused digitized rectal pathology sections and rectal MRI sections. This enabled unique mapping of exact pathological extent on MRI for different treatment effects (ulceration, fibrosis) as well as residual rectal cancer.

Conclusions: Our novel fusion workflow may enable discovery of integrated radiology/pathology information to predict treatment response and early patient outcome in rectal cancer.

1602 Diagnostic Time in Digital Pathology: A Comparative Study on 400 Cases

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Background: Numerous validation studies in digital pathology confirmed its value as a diagnostic tool. However, a longer time to diagnosis than traditional microscopy has been currently seen as a significant barrier to the routine use of digital pathology. As a part of our validation study, we compared digital and microscopic diagnostic time in the routine diagnostic setting.

Design: One senior staff pathologist reported 400 consecutive cases (1396 slides) in histology, non-gynaecological and fine needle aspiration cytology, by means of digital pathology and traditional microscopy (20 sessions, 20 cases/session), over four weeks time. Complex, difficult and rare cases were excluded from the study in order to reduce the bias. Primary diagnosis was digital, followed by traditional microscopy, six months later. Only request forms were available for both primary and secondary diagnosis. Microscopic slides were scanned at X20 using ScanScope AT Turbo (Aperio, Leica Biosystems). Digital slides were accessed through the fully integrated laboratory information management system (LIMS) SymPathy (Tieto) and viewed in ImageScope (Aperio, Leica Biosystems) on double 23" displays (resolution 1920x1200). Microscopic diagnosis was made on an Ecclipse 80i light microscope (Nikon). A median broadband speed was 299/55 Mbps (download/upload). Diagnostic time was measured from the point slides were made available to the point diagnosis was made or additional investigations were deemed necessary, recorded independently in minutes/session and compared.

Results: Digital and microscopic diagnostic time was 1841 (92.05/session) and 1956 (97.8/session) minutes, respectively. Digital diagnostic time was shorter than microscopic in 13 sessions. Four sessions with shorter microscopic diagnostic time included more cases requiring an extensive use of magnifications over X20. The diagnostic time was similar in three session.

Conclusions: Diagnostic time in digital pathology can be shorter comparing with traditional microscopy, in the routine diagnostic setting, when adequate and stable network speeds and fully integrated LIMS are achieved. This also relates to better ergonomics, larger viewing field and absence of physical slide handling, with effects on both diagnostic and non-diagnostic time. Possible reasons for differences with previous studies may be their setting, image size, network speed and participant's level

of confidence and experience in digital reporting. Further advancements in working stations and gained experience in digital reporting are expected to improve diagnostic time and widen applications of digital pathology.

1603 Does "July Effect" Affect Frozen Section Turnaround Time? Appraisal of 1,333 Consecutive Trainee-Participated Single-Sample Frozen Sections From an Academic Pathology Residency Program

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Background: Earlier report by College of American Pathologists Q-Probes study suggested that non-teaching hospitals are associated with superior frozen section turnaround time (TAT) than their counterparts with pathology residency programs. The association between worsened patient outcomes during the beginning of academic calendar year, attributed in part a lack of experience, has been demonstrated in various medical settings. This phenomenon is called the "July Effect." However, such effect on pathology laboratory efficiency, specifically frozen section TAT, in academic teaching hospitals has not been studied.

Design: Our institutional record of 1,333 consecutive trainee-prepared single-sample frozen sections, spanning 4 academic years, was retrospectively reviewed for turnaround time. The trainees' frozen-section preparation experience was categorized as inexperienced (zero baseline), experienced (1 to 2 months), and Fellows (3-6 months). A multivariate logistic regression model was fitted to evaluate predictors of TAT ≥ 20 minutes.

Results: Inexperienced residents, experienced residents, and Fellows participated in 480, 323, and 530 cases, respectively. There was no group difference in the distribution of case types ($p = 0.13$). The overall average TATs for the three groups were 14.7 ± 5.3, 14.9 ± 5.6, and 16.4 ± 8.1 minutes, respectively ($p < 0.000$). Resident trainee-participated frozen sections average TAT is ≤ 20 minutes across all case types (**Figure 1**). Controlling for case types, Fellows were 70% more likely to have TAT ≥ 20 minutes than inexperienced and experienced residents (OR 1.70, 95%CI 1.3 - 2.2, $p < 0.000$).

Conclusions: Frozen section turnaround time is not susceptible to the "July Effect." Other influential factors related to Fellow status may be responsible for the paradoxical association of prolonged TAT and increased experience level. Importantly, in contrast to the earlier report that teaching hospitals performs worse than non-teaching hospitals in TAT, resident trainee-participated frozen sections have average TATs that meet national standard.

1604 Integrative Bioinformatical Analysis of Clear Cell Renal Cell Carcinoma

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Background: Clear cell renal cell carcinoma (ccRCC) is the most common adult kidney neoplasm. Clear understanding of the molecular pathogenesis will lead to better unfolding new biomarkers and therapeutic targets. Our aim was to assemble transcriptomic, proteomic and miRNA data using an integrative approach for investigating ccRCC pathogenesis.

Design: Publically available mRNA, miRNA and protein data were collected from 593 ccRCC and 389 normal kidneys. We performed pathway analysis and built a network of ccRCC pathogenesis. TCGA database and immunohistochenmitry were used for validation. Functional analyses were done in multiple cell line models.

Results: Metabolic processes were the most significant signalling pathways, and we validated Aryl-Hydrocarbon Receptor (AHR) signalling to be involved in tumorigenesis, and as a prognostic marker. Using network analysis, we identified GRHL2 as diagnostic marker and potential drug target. KIAA0101 was found to enhance tumor cell migration and invasion. We also demonstrated that KIAA0101 overexpression correlated with poor prognosis and also a diagnostic marker. We identified miR-139-5p as an important miRNA influencing the ccRCC disease network through targeting ZEB1, TCF4, ETS1 and CCND2.

Conclusions: Using integrative bioinformatic analysis, we identified a number of significant pathways and molecules among which some of them are applicable for biomarkers or new, potential drug targets.

1605 An Optimized Color Space for the Analysis of Digital Images of H&E Slides

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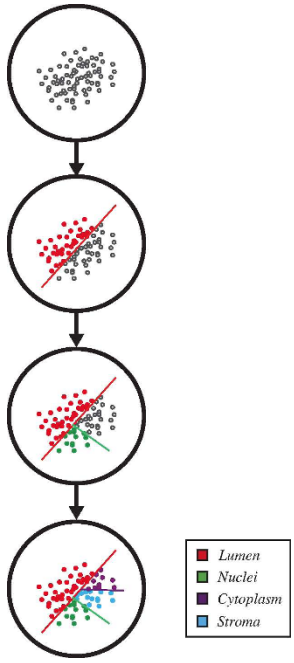
Background: H&E staining is ubiquitous in pathology practice and research. As digital pathology has evolved, the reliance of quantitative methods that make use of H&E images has similarly expanded. One of the major obstacles to quantitative analysis of H&E images is the high degree of variability often observed between different laboratories and samples. Variability makes images difficult to model and causes the generalizability of most algorithms to suffer. To characterize this variability, as well as to provide a substrate that can mitigate this factor in quantitative image analysis, we developed a technique to project H&E images into an optimized space more appropriate for many image analysis procedures.

Design: We used hierarchical clustering, machine learning, and color space transformations to classify 44 H&E stained whole slide images of resected breast tumors according to the biological structures that are present. This procedure takes a single H&E image as an input and produces a classification map of the image that predicts the likelihood of a pixel belonging to any one of a set of user-defined structures (e.g. cytoplasm, stroma). By reducing these maps into their constituent pixels in color space, an optimal reference vector is obtained for each structure, which identifies the color attributes that maximally distinguish one structure from other elements in the image.



Results: We show that tissue structures can be accurately classified using this semi-automated technique. By comparing reference vectors across different images, we obtained a quantitative depiction of H&E variability for each structure.

Conclusions: The variability of H&E stained images can be definitively measured using the proposed technique. This measurement can potentially be utilized in the laboratory to help calibrate daily staining or identify troublesome slides. Furthermore, by aligning reference vectors derived from this technique, images can be transformed in a way that standardizes their color properties and makes them more amenable for image processing.

1606 University of Pittsburgh Medical Center (UPMC) and Kingmed (China) International Telepathology Consultation: Analysis of 1251 Cases

Chengquan Zhao, Tao Wu, Xiangdong Ding, Anil V Parvani, William Cable, Hualin Chen, Jeff McHugh, Qinling Xie, Gonzalo Romero Lauro, Xiaodong Feng, Shangwei Wu, Samuel Yousem, Liron Pantanowitz. University of Pittsburgh Medical Center, Pittsburgh, PA; Kingmed Diagnostics, Guangzhou, China.

Background: The data on digital use in the clinical practice is limited. KingMed Diagnostics is the largest independent pathology laboratory in China. Since 2012, UPMC and KingMed have established an international telepathology consultation service for Chinese patients.

Design: This is a retrospective study that summarizes telepathology consultation results between UPMC and KingMed from January 2012-August 2014. Whole slide imaging technology is used for the telepathology consultation service.

Results: A total of 1251 cases were submitted for telepathology consultations, including 144 cases in 2012, 614 in 2013, and 493 in the first 8 months of 2014. Most cases (59%) were referred by pathologists, 39% by clinicians, and 2% by patients. Hematopathology received the most cases, followed by bone/soft tissue and gynecologic/breast subspecialties. Average TAT per case was 6.8 days in 2012 and 5.4 days in 2013 ($p<0.05$), and 5.5 days in 2014. Immunostains were required for most of the cases, which extended the TAT. 591 cases (47.2 %) were submitted without a primary diagnosis. Among 660 cases with a primary diagnosis, the final diagnoses rendered by UPMC pathologists were identical in 23.9% of cases, mildly modified in 21.2%, and significantly modified (treatment plan altered) in 54.9% of cases. The natures of the lesions diagnosed by UPMC pathologists included malignancies (62.7%), benign (22.8%) and neoplasm/borderline (14.5%). 81.2% cases had a definite diagnosis and 8.1% with an uncertain diagnosis UPMC pathologists.

Sub-specificities	Case Number	Percentage (%)	TAT (days)
Hematopath	310	24.9	7.0
Bone/soft tissue	267	21.3	5.2
GYN / Breast	259	20.7	4.3
Head/Endo/Thyroid	93	7.4	6.6
GI	89	7.1	5.2
Derm/melanoma	66	5.3	4.2
Thoracic	52	4.2	5.0
GU	48	3.8	8.5
Neuro	33	2.6	3.6
Liver	23	1.8	7.9
Pediatric	6	0.5	6.0
Others	5	0.4	6.6
Total	1251	100	5.5

Conclusions: Our results indicate that international telepathology consultation can significantly improve patient care by facilitating access to pathology expertise. The success of this international digital consultation service was dependent on strong commitment and support from leadership, information technology expertise, and dedicated pathologists. Challenges included internet speed and firewalls, difference in languages, cultures, and health care systems.

Kidney/Renal Pathology (including Transplantation)

1607 Molecular Diagnostics for Antibody-Mediated Rejection in Formalin-Fixed, Paraffin-Embedded Human Renal Allograft Biopsies

Benjamin Adam, Bahman Afzali, Nikhil Shah, Reeda Gill, Luis Hidalgo, Patricia Campbell, Michael Mengel, Banu Sis. University of Alberta, Edmonton, AB, Canada.

Background: In 2013, the Banff classification adopted molecular diagnostics (gene expression) as an adjunct for the diagnosis of antibody-mediated rejection (ABMR) in renal allografts. The new NanoString nCounter gene expression platform is unique in its ability to use samples derived from formalin-fixed paraffin-embedded (FFPE) tissue. We aimed to utilize this method to assess the validity of gene expression quantification for the diagnosis of ABMR in routine clinical FFPE renal allograft biopsies.

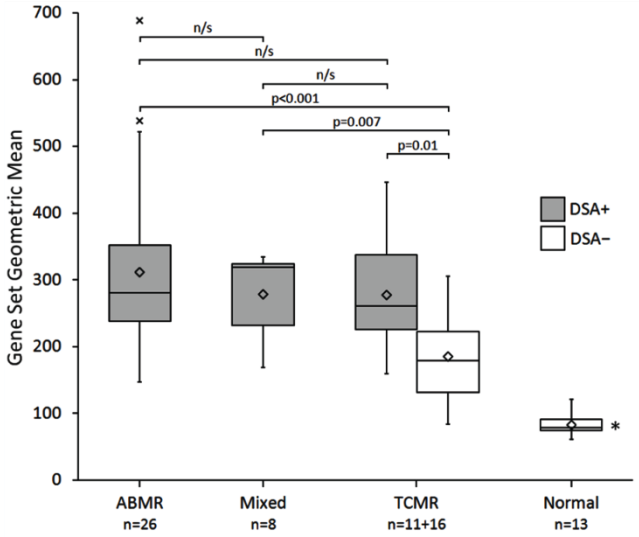
Design: 34 genes previously shown to be associated with ABMR were compiled into a gene set. RNA was isolated from 109 archival FFPE renal allograft biopsies. Gene set expression was quantified with the NanoString assay and correlated with clinical, serologic, and histologic data.

Results: The geometric mean of the gene set correlated with the presence of donor-specific antibodies (DSA) as well as histologic lesions of microcirculation injury and inflammation, but not tubulitis or arteritis.

Table 1: Correlation between gene set expression and serohistologic data.

Serologic/histologic feature	Correlation coefficient (r)	p-value
Donor specific antibodies (DSA)	0.51	<0.001
Glomerulitis (g)	0.41	<0.001
Transplant glomerulopathy (cg)	0.45	<0.001
Interstitial inflammation (i)	0.24	0.010
Interstitial fibrosis (ci)	0.40	<0.001
Tubulitis (t)	0.08	0.403
Tubular atrophy (ct)	0.32	<0.001
Intimal arteritis (v)	0.00	0.987
Fibrous intimal thickening (cv)	0.18	0.061
Arteriolar hyaline thickening (ah)	0.28	0.004
Mesangial matrix increase (mm)	0.44	<0.001
Peritubular capillary margination (ptc)	0.42	<0.001
Total interstitial inflammation (ti)	0.43	0.004
C4d staining (IF/IHC)	-0.09	0.387

Biopsies with a diagnosis of ABMR or mixed ABMR/T-cell mediated rejection (TCMR) had increased gene set expression compared to normal controls and DSA-negative TCMR. Interestingly, DSA-positive cases that met histologic criteria for TCMR, but not acute or chronic active ABMR, still had higher expression than DSA-negative TCMR, suggesting that some TCMR cases would be reclassified as mixed rejection when molecular diagnostics are added, as per the recent Banff 2013 recommendation.



ABMR, antibody-mediated rejection; TCMR, T-cell mediated rejection; DSA, donor-specific antibody; n/s, not significant (p>0.05).
*p<0.001 for heteroscedastic two-tailed t-test between normal controls and all other diagnostic categories.

Figure 1: Gene set expression versus histologic diagnosis.

Conclusions: Our results demonstrate the feasibility of robust multiplexed gene expression quantification from FFPE renal allograft biopsies. We validated the diagnostic potential of a literature-derived ABMR gene set in routine FFPE biopsies with the NanoString platform. These data suggest a method for molecular diagnostics to be introduced into clinical transplantation pathology.

1608 Spectrum of Glomerular Disease Between the Years 2003 and 2014: Review of 11451 Cases in a Colombian Population

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Background: Glomerular diseases (GD) are an important cause of chronic renal failure. Prevalence of GD varies according to different socio-demographic characteristics, in Europe and North-America the most common are focal and segmental glomeruloesclerosis (FSGS) and IgA nephropathy (IGAN). Information related to GD is not very well known in Colombian patients. The aim of this study was to describe the prevalence of GD in a population from multiple areas in Colombia.

Design: Between January2003-September2014, we studied 16820 renal biopsies from multiple areas of Colombia, we excluded cases diagnosed as interstitial or tubular disease and conditions where the main damage was related with vascular injury, final sample of 11451 cases (M=5108, F=6343) age range 1 month-91 years corresponded to GD. Each case was studied with light, immunofluorescence and electron microscopy. For each biopsy information regarding age, gender, histopathological diagnosis and additional findings was available, unfortunately complete clinical information and follow up was not obtainable for most the cases. The classification of GD was based on ¨Armed Forces Institute of Pathology-2005¨ and 3 further groups of diagnostics commonly included in the hospital not included in AFIP list.

Results: From the total 11451 biopsies reported as GD, 82.3% of the cases corresponded to 5 types; first FSGS group corresponded to more frequent 22.20%(2542), the IGAN 20.13%(2305), lupus nephritis (LN) 17.30%(1981), membranous glomerulonephritis (MG) 13.06%(1496) and thin basement membrane disease (TBMD) 9,61%(1101). In relation with groups of patients under and over 18-years old (children and adults respectively), IGAN 22%(1982) was the most common in adults and FSGS 17,68%(701) in children, equally important cases included minimal change disease (MCD)17% (319), LN 15%(388), TBMD 13%(335), IGAN 13%(323) in children, and FSGS 21%(1841), NL 18%(1593), MG 15%(1350) and TBMD 9%(766) in adults.

Conclusions: This unique large cohort can serve for comparison with data from different geographic locations through the world. The information presented in this study reveals the tendency of GD in Colombian population. We confirm that FSGS is the most representative GD in children and IGAN in adults. This information will be the base to make much more specific subsequent prospective studies involving large-scale clinic-pathological correlation analysis.

1609 Dendritic Cells (DCs) in Kidney Transplant Biopsies Cluster With T Lymphocytes and Are Associated with Graft and Systemic Inflammatory Milieu and Poor Allograft Survival

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Background: Long-term renal allograft survival continues to lag behind the progress seen in short-term transplant outcomes. The negative prognostic implication of inflammation in areas of tubular atrophy (iatr) seen in kidney transplant biopsies has been increasingly recognized, however, the immunological mechanisms behind the development of such "active" atrophy have not been deciphered. DCs are the most efficient antigen-presenting cells, but surprisingly little attention has been paid to them in transplanted organs.