Short Abstract Presentations

Wednesday, May 25, 2016
8:00 am – 9:00 am

Locations:

Wyndham Grand Pittsburgh Hotel

Grand Ballroom 1

Kings Garden 1

Kings Garden 2/3

Advanced Pathology Informatics Computational Pathology, Imaging Informatics, Applied Pathology Informatics

Grand Ballroom 1

Laboratory Websites Portals as Pathology Educational Resources: The Concept of Combining Apples and Oranges with Other Fruits

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Content
The apparent solution for utilization dispersed on the Internet laboratory pathology websites would be to combine them in specialized portals. Their development depends on three essential conditions: an appropriate institution to handle the design and maintenance, a coordinating organization such as a professional society, and reliable financial support.

Technology
Software platforms, like WordPress, make the site dynamic and manageable by nonprofessionals in computer science. However, aggregating the websites in a portal requires professional approach. The main challenges are the differences between composition and software platforms of the aggregated websites.

Design
The goal of design is that on entering the laboratory website portal's forest, the user would find a particular mushroom under a specific tree. Providing connections between the different websites would thus enable the user to access the technical details of procedures. Resembling portal vein and portacaval anastomoses systems, the "portal hypertension" allows the user to obtain in "anastomoses" specific information without surfing through archives. While following the hierarchical organization of the website's pages, the portal building framework includes reasonable content fragmentation in the presentation of the material ("nested doll principle".)

Results
A laboratory portal predominately aggregates authority websites with a certain "niche of knowledge." Apart from the informative content, which is paramount, the authority site follows a certain set of specific search engine work rules for maximal visibility and sustainability on the Internet. The daily statistic chart provides important information about the topics in which the visitors are interested. Our educational "Grossing Technology in Surgical Pathology" (grossing-technology. com) website, which is more than decade old with an average of 100K views per year, is an example of maintaining an authority website. The website's composition, which contains basic contents, a blog, and an ancillary part, has proven optimal. The ancillary part includes also a mutually beneficial presence of the manufacturers. The website can serve as a framework for an aggregated educational pathology laboratory portal.

Conclusion
Laboratory specialized portals are an untapped resources for pathology informatics. An educational methodological pathology laboratory portal can be one of these resources. A sustainable authority website is the cornerstone of the portal's development.

Straddling the Clinical and Anatomic Pathology Divide, The UCLA Molecular Diagnostic Laboratory's experience transitioning to the AP and CP Epic 2014 Beaker Module

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Content
We will describe the experiences of the UCLA Molecular Diagnostics Laboratories (MDL) in transitioning to Epic's modules of AP and CP Beaker.

Technology
In March 2016, the UCLA Pathology will transition from PowerPath in anatomic pathology and MEDITECH in the lab, to the AP and CP Beaker Modules from Epic, respectively.

Design
This is a descriptive study, systematically assessing our approach towards the Epic AP and CP beaker build that took place between August 2015 and March 2016. We will assess the effect of AP and CP Beaker in build decisions, workflow and reporting within MDL.

Results
In our experience, molecular diagnostic tests with a limited set of reportable analytes (e.g. Factor V and cystic fibrosis genotyping panels) can be readily reported using CP Beaker. We built this subset of high-volume and "simple" tests within CP Beaker to take advantage of batch reporting. AP Beaker is used for the remaining higher complexity tests, including all tissue-based tests. In-depth integration of test orders and reports is performed through electronic linking by specimen.

Tissue-based workflows in MDL will change significantly. Ordering cancer sequencing tests in Beaker is a two-step process, as Beaker 2014 is unable to reliably auto-link physician orders with histology notification for slide recuts. First, the order must be placed electronically by a pathologist/treating physician. MDL receives this order in a shared inbox and must then add notifications for histology to cut slides manually. Once slides are received MDL will create a case for tracking. MDL is thus notified for every tissue-based test upon ordering, allowing us to screen for ordering errors.

For reporting, we have divided complicated reports into discrete fields. This provides a significant upgrade from purely unstructured text and will enable future automated disease-specific snapshots for the treating physician.

Conclusions
The full extent of the consequences of our decisions will become evident after go-live. While the 2014 Beaker modules do not address the full range of needs of a molecular pathology laboratory, we anticipate improvements to specimen tracking, workflow, and aspects of reporting.

Implementation of User-Tailored Data Analytics in a Complex Laboratory Setting

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Content
Laboratories have needs for data analysis for activities like quality management, tracking key performance indicators, monitoring operations, and strategic planning. Laboratory information systems (LISs) may not provide analytical capabilities that meet such needs. Also, being able to combine data from multiple sources can be valuable. This project implemented a system that provides "analytics", or business intelligence, to meet data analysis needs in a complex laboratory environment.

Technology
Kofax Insight business intelligence system (Irvine, CA), CoPath LIS (Cerner, Kansas City, MO), Sunquest Laboratory LIS (Tucson, AZ), MS SQL Server 2008 and Excel 2010 (Microsoft, Redmond, WA).

Design
Functional requirements were determined, with input from departmental end-users. Required data elements were identified in LISs and other sources. Insight tools were used to establish content and timing of data extracts from source systems, with organization into a secondary database. Configurable data displays including dashboards, charts, tables, and calculations were created in Insight based on this database. End-users with domain expertise validated each new data report and dashboard for accuracy prior to its deployment.

Results
Currently 103 dashboards have been deployed. Throughout the laboratories, there are 177 active dashboard users. Eight dashboards combined data from more than one source. Frequency of scheduled data pulls from source systems ranges from minutes to weeks. Applications of dashboards have included data visualization and presentation for daily team huddles, clinical and business metric reviews, critical value report monitoring, dynamic pending logs, and utilization reviews. Data from Insight have replaced the LIS for 58% (34/59) of ad hoc data search requests (July-December 2015). Laboratory end-users are empowered to perform their own analyses. User acceptance was initially slow but escalated as the usefulness of the system has been realized. Because the system is highly configurable, the learning curve was significant, including for system analysts.

Conclusions
A configurable data analytics system can be implemented in a complex laboratory environment and provide substantial value to the laboratory through use of flexible tools for data analysis, presentation, and visualization. Success factors for implementation included commitment through a learning curve, attention to data validation, and tailoring to end-user needs.

Comparison of LOINC Codes for Commonly Ordered Lab Tests Provided by Different Medical Centers

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Content
Standard codes for clinical measurements are essential for optimal exchange of health information. Logical Observation Identifiers Names and Codes (LOINC) is a universal method of normalizing, identifying, and reporting medical laboratory observations. In the USA, the Office of the National Coordinator have chosen LOINC coding as a standard to support healthcare data exchange and interoperability. To the best of our knowledge, a comprehensive analysis of LOINC between disparate health systems has not been undertaken. Therefore, we sought to evaluate the accuracy of LOINC codes assigned to commonly ordered lab tests at three distinct healthcare systems.

Technology
Excel spreadsheets (Microsoft).

Design
Three large tertiary academic medical centers (University of Pittsburgh Medical Center, Cleveland Clinic, MD Anderson Cancer Center) participated. The 300 most commonly ordered clinical lab tests (chemistry, hematology, immunology) at one of the institutions were retrieved from their laboratory information system. Only 249 of these tests were compared, because not all centers offered exactly the same tests (especially for point of care testing). Excel spreadsheets were used to enter and analyze codes to determine universal matching (agreement between all 3 sites), partial matching (agreement between any 2 sites), and if there was no matching (no agreement between sites).

Results
LOINC codes provided showed that there was 44% universal and 30% partial matching of lab tests. For 26% of the lab tests there was zero matching among centers that included hematology (36%), chemistry (35%), urinalysis (12%), immunology (8%) and point of care (7%) tests.

Conclusion
These data show that there was absolute concordance among all three healthcare systems for only 44% of LOINC codes. Reasons for discrepant LOINC coding need to be determined, but may have been limited by providing only the component and property database axes of test descriptors. Given the high discordance of LOINC coding that may occur among different pathology laboratories, additional measures (e.g. external quality control checks) may be necessary before these codes can be reliably used to support interoperability between healthcare systems.

Imaging Informatics

Kings Garden 1

HCV Genie V 2.0: A Web Platform for the Versant Hepatitis C Virus (HCV) Genotype Line Probe Assay

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Content
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 steps of this procedure are a manual, time-consuming, error prone process that involves the identification of bands and comparison of each test strip to a physical reference table. A resident had developed an HCV genotype interpretation platform that identifies the strain of HCV based on the banding. However, identifying bands on the strip was done manually. This study serves as a follow-up with an MD/PhD student porting this system to an open web environment and adding an analytical step utilizing a scanned LiPA image to generate the genotyping results.

Technology
Web Server: Github gh-pages; Programming Language(s): JavaScript, HTML5, CSS; User Interface Framework: Bootstrap 3.3.

Design
The student (a) ported the original, clinically validated, HCV genotype interpretation program, "HCV Genie," from an SQL database to JSON object, (b) created image analysis algorithms that convert LiPA images into band and genotype calls, and (c) built a user interface to utilize these tools. Client side JavaScript allows the analysis to be performed without any data leaving the investigator's computer. Additionally, results of the analysis are downloadable as a printable report.

Results
The original HCV Genie was written, deployed, clinically validated, and proven to be identical to human expert interpretation (n = 200). It decreased the time needed to interpret results by 53% for residents, but results among experienced lab technicians were more equivocal. Since the most time-consuming part is to identify each band on the strip, HCV-Genie 2 allows us to further minimize analysis time and eliminate errors, thereby, increasing the quality of patient care. Available at: hcvGenie.com.

Conclusion
This iteration of HCV Genie focused on developing lane and band detection algorithms, and creating a publically available tool that eliminates data privacy concerns. Future iterations of this program will focus on allowing users to store and aggregate results in a database of their choosing, allowing for advanced data analytics of HCV genotypes.

Clinical Lab Manager System V1.0 – A web-based application to manage all workflow in genomic pathology laboratories with interactivity with Beaker and I2B2

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Content

The power of genomic analysis is matched by the challenge of maintaining quality at each step of the process. Complex assays such as next generation sequencing have many procedural steps and are performed at multiple work stations, often by multiple technologists. Management of quality is dependent upon the traceability of the progression of a specimen throughout the process, a capability that is not available through commercial laboratory information systems (LIS). Many laboratories employ the work around of using multiple spreadsheets that lack real-time traceability and status update.

The Clinical Lab Manager System V1.0 (CLMS) is a web-based application that was created to provide continuous access for documenting and reviewing status of diagnostic specimens through all phases. CLMS has been used in our Molecular & Genomic Pathology Laboratory since 2015. It extracts sample accessioning information from the CoPath LIS and tracks all steps of all processes, such as DNA concentration, quality, and QC data for library preparation of next generation sequencing assay and final results review.

Technology

CLMS is a web application created using PHP with a MySQL database backend utilizing R and javascript for various functionalities.

Design

CLMS stores information in MySQL relational database. Front end forms are created in PHP and HTML. Order and result information can be communicated to Beaker via cloverleaf engine.

Results

CLMS manages:

- Specimen information including demographics, diagnoses, specimen type for all current and archived specimens in a single database with interactive front-end
- Assay workflows, by calculating reagent requirements based on specimen number in real-time
- Final result review and storage in the CLMS data base
- Archival of de-identified results in the I2B2 translational research database

Conclusions

CLMS has created a single portal for managing all operational steps with the capability to generate statistics for assay volumes and turn around times, as well as results. It has eliminated many spreadsheets and provided a “modern” working environment, resulting in increased operational efficiency. Bi-directional connectivity to EPIC Beaker has been established, which enables management of all intra-laboratory steps in CLMS and creation of orders and report resulting in Beaker when EPIC goes live in Jefferson Health System.

Fetal Autopsy Report Automation with Microsoft Excel and Word

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Content
Fetal autopsy reports are complex documents which record gross, histologic, and ancillary findings. Body and organ measurements are compared with gestational age and birth status dependent normal reference ranges. Traditional manual writing is notoriously error prone and time consuming, and few attempts have been made to improve it. The aim of this project was to design and validate an automated system for producing fetal autopsy reports using advanced programming functions available in Microsoft Excel and Word.

Technology
An excel spreadsheet fetal autopsy template was created using Microsoft (Redmond, WA) Excel and Word on a PC running Microsoft Windows 7 professional. We extracted all reference values from Potter's Pathology of the Fetus, 2007 and structured the data to allow automatic population of values using lookup and reference functions. Categorical values were set-up as drop down menus or check boxes with Boolean functions. Gross findings were presented as a list of unselected check boxes by default, along with individual text fields where alternative abnormal findings could be reported. Numerical values such as weight, length and body fluids were placed adjacent to normal reference ranges. All input values were inserted into an embedded Microsoft Word document as field codes with pre-populated texts. A macro function removed all field codes after completion of the report to generate "clean" text for copy and paste into Sunquest CoPath 6.1 (Tucson, AZ) for additional review and final sign-out.

Design
To measure improvements in this new system compared to traditional methods, we used it to review 10 cases of reports that had been previously completed manually and looked for errors in the normal reference ranges and body/organ measurements.

Results
The system detected errors in 4 out of 10 reports with no significant impact on overall diagnosis. The system was well received by both attending pathologists and residents. Since implementation, all users have adopted the system.

Conclusions
We have developed a novel and user friendly fetal autopsy report automation system using commonly available Microsoft Office products. It has improved the autopsy workflow by reducing errors and inefficiencies.

A Brief Technical Note on Microservices Architecture

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Content
The modern software ecosystem is a rapidly evolving landscape. The availability of cloud computing resources has encouraged developers to package applications into small, encapsulated & functional units that easily scale to meet demand. This segmentation is commonly termed as microservices-based architecture, which offers significant advantages over established monolithic architecture including reliability, maintainability, and security.

Technology
The enabling technology, Linux micro-kernels also referred to as "containers", is in some ways an evolution of the virtual machine concept but has actually been around much longer. However, relatively recently this has gone from a relatively obscure concept to dominating much of the literature concerning cloud based services. Many cloud providers, including Amazon and Google, now have native container support. Indeed, even Microsoft has incorporated containers into their Azure service and supports Linux and recently announced Windows Server containers.

Design
Microservice containers are essentially bare-bones operating systems. A lightweight framework on the host handles loading and allocation of system resources. The containers are agnostic, and in fact unaware, as to the host they are on. A variety of management frameworks are available to transparently network microservices together. Thus, containers can be running on a single development system, on a private intranet, or anywhere on the internet and function in exactly the same way.

Results
We have started transitioning portions of our infrastructure to a microservices architecture, with immediately encouraging consequences. Although limited in scope, the transitioned services use fewer system resources, are more fault tolerant, and exhibit improved availability. Tempering this observation is the concurrent reality that many systems also under our stewardship are legacy applications and therefore not amenable to such a change.

Conclusions
Industry is rapidly adopting microservices-based approaches. Laboratory leaders will be well-served to learn best practices in other fields and apply these to their own organizations, or at least keeping it in mind as future roadmaps are being developed. We believe this is more than a passing trend and such solutions will be needed to manage an increasingly complex menagerie of interconnected systems and middleware.

Applied Pathology Informatics

Kings Garden 2 / 3

Evaluation of 3D reconstruction analysis of FISH slides scanned by a confocal WSI scanner

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Content:
Technological advances contribute to a maturation of digital pathology in clinical applications. However, there are few reports on fluorescence scanning especially those include confocal fluorescence imaging technology, which has better resolution in depth compared to wide-field fluorescence imaging. Here, we explored benchmark features of a confocal WSI scanner for application in typical research and diagnostic imaging applications of fluorescence in situ hybridization (FISH) test.

Technology:
Multilayer stacking (Z-stack) which stores all image information from each layer, and extended focus which stores the optimal image information from all scanned layers were used with the Pannoramic Confocal scanner (3DHISTECH Ltd., Budapest, Hungary). 3D reconstruction and automatic quantification of dots inside nuclei were made by Imaris (Bitplane, Zurich, Switzerland).

Design:
10 FISH slides were digitized with the Pannoramic confocal scanner at multiple layers. The objective used was 40× water immersion with a resolution of 0.1625 µm/pixel. Z-stack and extended focus were used for multiple layers scanning with 31 layers and 2 micron interval. Scanning time and file size were recorded, and image quality was assessed by visual comparison. The 3D reconstruction, quantification of dots, and co-localized analysis were made with Imaris.

Results:
Z-stack and extended focus had the same scanning time on the same scanning area, but Z-stack had tremendous file size than extended focus. The quantification of dots inside nuclei analysis showed that extended focus decreased the number of dots (Figure 1A-D). And the co-localization analysis of dots in FITC and TRITC channel indicated that extended focus increased the number of co-located dots (Figure 1E&F). Multiple channels could be used to image various fluorophores, and the number of dots in each channel was quantified automatically (Figure 1G).

Conclusion:
Extended focus decrease file size and storage, but could cause incorrect analysis due to overlapping information in depth. We foresee confocal Z-stack scanning as a digital pathology tool for FISH imaging and automated diagnosis in future.

Acknowledgement: The authors thank 3DHISTECH and Bitplane for technical support.

*See Figure 1A-G on next page

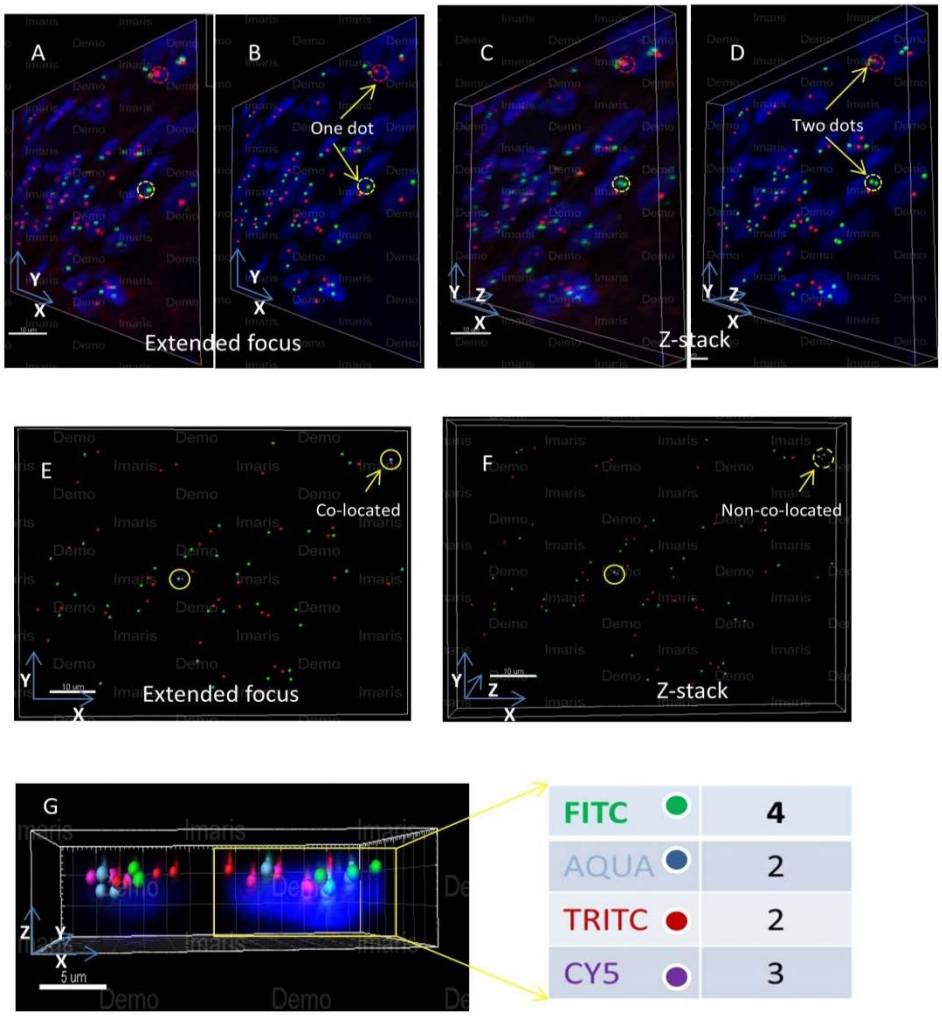

Figure 1 Comparison of extended focus and Z-stack for analysis of dots inside nuclei.

Three-Dimension (3D) Whole-slide Histological Image Analytics

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Content:
Whole-slide histological images encode a wealth of information on tissue morphological and pathological signatures at the cellular level, allowing researchers to better understand the underlying mechanisms of disease onsets and evolutions. Therefore imaging analytical approaches for quantitative analysis of histological structures (such as nuclei and vessels) with microscopy images are in great demand. This is especially true for those enabling studies on 3D structural changes and 3D spatial relationships. We report such a method for 3D primary vessel reconstruction with a set of histological whole-slide images of liver sequential tissue sections, and a mechanism for characterizing 3D spatial relationships between nuclei and vessels by distance measurement.

Technology:
With a stack of registered microscopy images, we segment primary vessels by an improved level set method with prior information on vessel wall probability for the energy minimization paradigm. We achieve the optimal vessel associations by local bi-slide vessel mapping and global vessel structure association within a Bayesian Maximum A Posteriori (MAP) framework. We visualize the reconstructed 3D primary vessels by a 3D mesh model, and perform 3D spatial analytics on the reconstructed vessels and simulated 3D nuclei by a distance-based query over Hadoop platform.

Design:
Our 3D primary vessel reconstruction framework consists of image registration, primary vessel segmentation, vessel cross-sections association, vessel interpolation and 3D reconstruction. After registering all the slides to a reference image, we segment primary vessels with an improved level set method. We associate the segmented vessel cross-sections in all slides by generating bi-slide vessel components and recovering the global vessel structures. We perform B-Spline interpolation between adjacent associated vessel objects and volumetrically render 3D vessel structure with a mesh representation. Additionally, we compute distances between 3D nuclei and vessels for spatial analytics.

Results:
We have tested our framework with a set of 54 whole-slide images of sequential liver tissue sections stained by Immunohistochemistry (IHC). Experiments present satisfactory results and quantitative evaluations demonstrate the efficacy of our method. The proposed framework for 3D vessel reconstruction and spatial analysis is generic and can be readily applied to the analytics of other 3D biological entities of common interest to a large number of studies using whole-slide microscopy imaging data.

Conclusions:
3D modeling and spatial analysis of micro-anatomic objects in histological whole-slide images are essential for researchers and pathologists to understand both normal and disease processes. Our framework can automatically reconstruct the primary vessel structures in 3D with microscopy images and explore spatial patterns across 3D histological objects. In future work, we will develop a system that can dynamically analyze whole-slide images at higher resolutions to accommodate micro-vessel analysis and propose scalable and high-performance platforms for spatial analysis of 3D pathologic structures.

Lessons Learned from Integration of Digital Pathology into Gastrointestinal Pathology

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Content
Numerous studies have shown the equivalency of digital images to glass slides. We have integrated digital pathology into our workflow for gastrointestinal pathology at the University of Pittsburgh Medical Center. Herein, we describe our experience with adoption of digital pathology into our gastrointestinal pathology signout.

Technology
A VL120 scanner (Omnyx) and Integrated Digital Pathology solution (version 1.3, Omnyx) directly interfaced with the Anatomic Pathology Laboratory Information System (APLIS, CoPath Plus V2014.01.1.106, Cerner). The cases with images were viewed at Omnyx workstations.

Design
Over a 3-month period, 529 were randomly selected from the daily gastrointestinal biopsy bench for digital evaluation with each case required to have less than 3 parts. For each case, a pathologist would first render a diagnosis based on digital images, followed by review of glass slides. The two reviews were compared for discrepancies. The histology laboratory created two workflows – one to divert slides for digitalization and one for the standard histology workflow. All slides were scanned at 40x and then sent to the signout pathologists with the remaining gastrointestinal slides for that day. No delays in the usual receipt time of slides was experienced.

Results
Over the course of the study period, the APLIS integration experienced minor technical difficulties (predominantly related to the query service component of the integration) reducing the ability to access clinical information for many of the cases. Fifteen cases contained only partial diagnoses for the entire case based on the digital images and were excluded. Four hundred and seventy cases (91%) were interpreted the same as the final glass slide review. No major discrepancies occurred during the study period. Fifty four cases showed discrepancy between the Omnyx diagnosis and the final diagnosis. These discrepancies were minor in nature and would have limited impact on the patient management. The majority (70%) of these discrepancies involved the evaluation of inflammation within the tissue or the lack of confidence about identifying Helicobacter organisms.

Conclusion
In the evaluation of inflammation and Helicobacter organisms, digital images are difficult to interpret compared to glass slides. We were able to implement a gradual integration of digital pathology into our workflow for gastrointestinal pathology with agreement between the digital images and the glass slides. This work represents a partial adoption of digital imaging and future directions, which will include improving the workflow within the histology lab (convert to a complete digital workflow), scanning gastric biopsies with potential Helicobacter pylori at 60x and pathologists adjusting to this new workflow.

*M*ulti-*d*imensional *nano*scale nuclear *a*rchitecture *m*apping (md-nanoNAM) for prospective prediction of cancer progression in inflammatory bowel disease (IBD) colitis patients

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Content

We present md-nanoNAM, a derivative of Fourier-domain optical coherence tomography (FD-OCT), to perform nanoscale nuclear architecture mapping of unstained FFPE tissue sections to a multi-dimensional feature space characterizing the three-dimensional optical density alterations in nuclear architecture at nanometer precision (~1 nm). We perform ***md-nanoNAM*** on normal-appearing rectal biopsy to detect the presence of dysplasia throughout the entire colon and predict risk in developing colorectal cancer in patients with IBD colitis.

Technology

A three-module optical system that combines bright-field, common-path FD-OCT and quantitative phase imaging was developed. It builds in pathological identification of epithelial nuclei, along with an algorithm we developed for extracting Fourier phase in FD-OCT, for mapping nanoscale nuclear architecture to a higher-dimensional feature space. The higher-dimensional space is used to identify IBD colitis patients at-risk of developing dysplasia/cancer by learning the feature sub-spaces in which these at-risk patients lay.

Design

We prospectively recruited 107 colitis patients undergoing surveillance colonoscopy with colon biopsies taken per the recommended surveillance guidelines. Two extra biopsies from normal-appearing rectum were analyzed via md-nanoNAM. The patients were grouped into low- and high-risk groups based on histologic diagnoses of all random biopsies from the initial and any available follow-up colonoscopies. We analyzed the initial biopsy to assess if we can both identify the presence of dysplasia anywhere throughout the entire colon, and predict cancer progression for those with follow-up colonoscopies.

Results

Our preliminary results, shown in Fig. 1, indicate that md-nanoNAM is able to identify
1. The presence of dysplasia/cancer found either concurrently or in the follow-up, and
2. Those initially classified as low-risk, but dysplasia was found later in the follow-up colonoscopy.

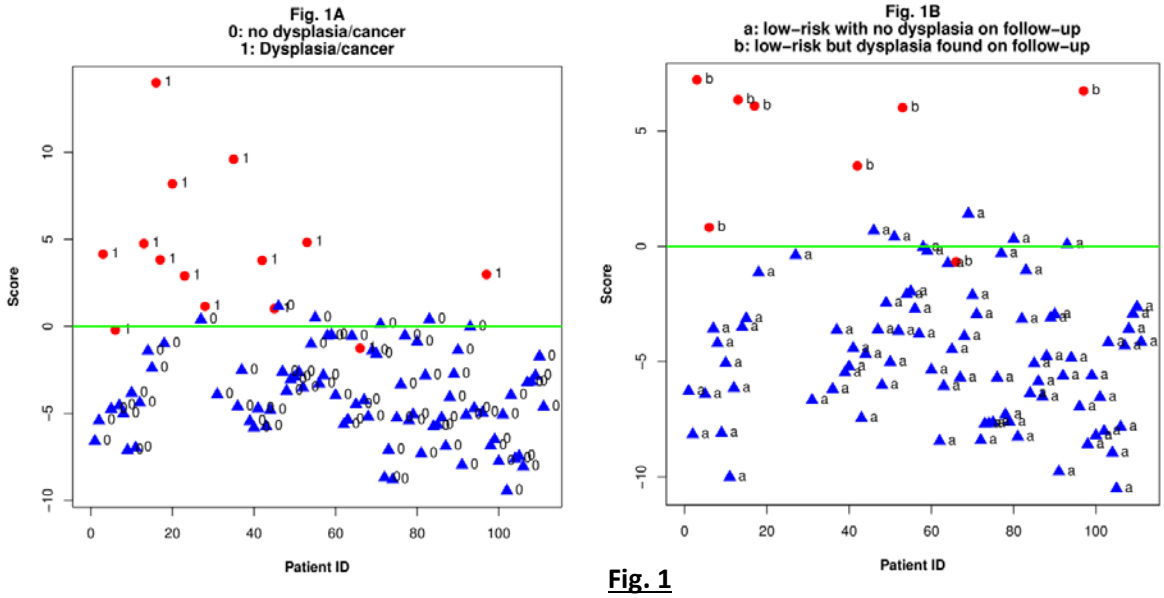

Fig. 1

Conclusions

This initial success of md-nanoNAM in detecting dysplasia from normal-appearing rectum is currently being extended to risk stratification.

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