Short Abstract Presentations

Wednesday, May 24, 2017
7:45 am – 9:00 am

Locations:

Grand Ballroom 1

Kings Garden 1

Kings Garden 2/3

Brigade Room

Whole Slide Imaging (WSI) and Microsoft HoloLens: A Comparison of WSI Viewers

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Content
Virtual and augmented reality devices used in healthcare offer a novel means for physicians to interact with their surrounding environment. Newer headsets allow users to blend virtual reality with a real life background. The use of a mixed reality device such as the Microsoft HoloLens has great potential in pathology, especially for telepathology. The aim of this study was to investigate the ability of the HoloLens to navigate whole slide images using different WSI viewers.

Technology
Microsoft HoloLens (Development Edition), a wearable holographic computer with sensors and cameras to enable mixed reality human computer interaction. User input included gaze, voice and gestures to interact with holographic content. Microsoft Edge browser was used for viewing WSI with 9 different WSI viewers (AJAX, DBViewer, DigitalScope, Google Maps API, ImageScope, ImageZoomer, Nanozoomer, OpenSlide, Zoomify).

Design
Using the HoloLens 9 different WSI viewers were compared employing gestures to perform navigation tasks including scroll (tapping), panning (drag) and zoom (finger directed up for zooming in and down for zooming out). Compatibility and usability of each WSI viewer was documented.

Results
Three viewers were compatible (DigitalScope, ImageZoomer, Openslide) and permitted digital slides to be viewed and navigated using gestures (Figure 1). Three viewers (AJAX, Google Maps API, Nanozoomer) permitted viewing, but gestures in all navigation modes did not function as intended. Three WSI viewers (DBViewer, ImageScope, Zoomify) were incompatible with the HoloLens, mostly due to JAVA.

Conclusion
Whole slide images can successfully be viewed on the HoloLens device. However, not all WSI viewers are yet configured for use in such a mixed reality environment. Future directions should include developing WSI viewers for easy navigation with virtual and/or augmented reality devices.

Figure 1. WSI navigation in a mixed reality environment with the Microsoft Hololens

Whole Slide Image File Integrity: A 10-year Look Back at Archival Images

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Content

Whole slide images (WSI) can help overcome storage problems with pathology glass slides such as breakage, faded stains, and loss/misplacement. However, we are not aware of literature that has investigated the integrity of long-term archived WSI. The aim of this study was to compare WSI file integrity over a 10-year period.

Technology

Aperio Scanscope T2 (2005-2008), CS (2008-2010), and XT (2010-2016) whole slide scanners were used for scanning. A Microsoft Windows Server (R2 Enterprise, 64 bit, 8GB RAM, Intel Xeon E7-4880 2.4 GHz) was utilized for WSI storage, and included one data migration episode (2012). Adobe Photoshop CC 2017 was employed for image quality measurements.

Design

30 glass slides (24 H&E, 6 immunohistochemistry stains) were retrieved that had been previously scanned on Aperio scanners over a 10-year period (2005-2015). The 30 matching glass slides were re-scanned with an XT scanner for comparison. WSI were categorized as aged (2005-2010 scans), mid-age (2010-2015 scans), and recent (newly re-scanned in 2016). Qualitative and quantitative image quality measurements were performed using Adobe Photoshop to compare image files. All WSI files were also subjected to 100 open/close and compression/decompression cycles.

Results

Subjective human evaluation of WSI showed no difference between archived and newly re-scanned slides. Mean compression ratios for aged, mid-age, and recent archived WSI were 23.2, 27, and 13.6, respectively (41.4% decrease compared to aged, 50% decrease compared to mid-age WSI). Average WSI file sizes for aged, mid-age, and recent WSI were 182, 199, and 214 bytes/pixel, respectively (14% difference from aged, 7% difference from mid-age WSI). Histogram color (RGB) and luminance comparative data are shown in table 1. Aged and mid-age WSI files averaged 7.2% and 3.8% RGB color intensity variation, respectively. Recent images had 10% less noise (via luminance) than aged and mid-age WSI. WSI files showed no degradation after successive open-view-close and compression/decompression cycles.

Conclusions

These data show that the integrity of WSI files archived over a decade satisfactorily represent the glass slides from which they were scanned. Over the years WSI file size has increased, possibly due to improved sensors and/or decreased file compression ratios. Objective analysis showed wider variation in luminance for older WSI, but no notable difference in color. Repetitive opening, viewing, closing and compression-decompression cycles did not appear to impact WSI file integrity. Enhanced whole slide scanner image capture (i.e. sensors) and post-processing (i.e. software) likely play a role in varying WSI file properties.

Table 1. Histogram data comparing WSI of varying ages to newly re-scanned slides

	Adobe Photoshop Histogram Data			
	Color (RGB)		Luminance	
WSI files	Mean	SD	Mean	SD
Aged (2005-2010)	2.2%	7.2%	3.4%	17.6%
Mid-age (2010-2015)	1.5%	3.8%	2.0%	5.1%

Value of Sharing Pathology Educational Digital Slides on Social Media

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Content

The influence of social media is emerging in pathology. Pathology images shared online can be undertaken for educational, consultation and/or marketing interests. Usage statistics and evidence of impact related to sharing digital pathology images via social media are limited in the literature. The aim of this study was to determine the benefit of posting digital images of anatomical and clinical pathology as a “case of the week” on Facebook.

Technology

A Panoptiq imaging system (Point Grey digital camera with Sony Pregius IMX249 sensor c-mounted to an Olympus BX45 microscope using Panoptiq 3 software v3.9.3) was used to acquire panoramic images with 4x, 10x, 20x, 40x or 100x oil objectives. All images incorporated embedded z-stack video frames for multiplane focusing of key diagnostic regions.

Design

Glass slides of interesting surgical pathology and hematology cases were used to generate panoramic digital slides with z-stacks (e.g. https://goo.gl/68PXRR). Image files were uploaded to the Panoptiq ViewsIQ portal. ViewsIQ used Amazon’s cloud storage to host files and designed an HTML5 viewer to be cross compatible with different mobile devices. Digital image navigation was tested on an iPhone 6 (iOS 8), iPad air 2 (iOS 9), and Microsoft Surface Pro 3 (Windows 10). Clinical history with quiz questions was compiled for each case using Google Forms. Weekly cases were publicized on Facebook and Twitter (@DigPathologists). Web service analytical tools (Facebook Insights, Twitter Analytics, Google Analytics) were used to capture traffic data.

Results

After 20 weekly posted digital slides, total followers on Facebook increased by 135 and on Twitter by 186. These posts triggered 18,410 social media interactions (average 921/week) from 32 different countries, including likes and/or shares on Facebook (total, 5684; weekly average, 284), and impressions or engagements (e.g. retweets, replies, follows, likes) on Twitter (total, 12726; weekly average, 636). Social media engagement on Twitter was more actively shared by users compared to Facebook, 51% vs 14%, respectively. 64% of users correctly answered quiz questions.

Conclusions

Prior to posting pathology images on social media websites it is important to employ applications that users are not slowed down by having to download and that are guaranteed to run on any mobile device. Amazon's cloud infrastructure provided high uptime, ample speed, and enforced encryption of all communications and storage. Sharing interesting pathology cases on social media that are easy to view is an effective educational tool that can reach a large cohort of users.

Pathpresenter.Com: An Innovative Platform for Teaching, Learning and Sharing Of Pathology Images

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Content

The microscope has been around for more than a 100 years and pathologists love their microscopes. Pathology is image-rich and very visual and pathologists use many types of images and yet the workflow is very manual. Digital pathology has been around for more than a decade and despite the countless advantages it brings, digital pathology has only seen limited adoption.

Technology

Pathpresenter.com is a completely web-based platform, without the necessity for plugins or other downloads. The images are stored on a cloud-based platform with easy accessibility and a robust user interface

Design

PathPresenter.com is an innovative platform that bridges the gap of exposing pathologists to digital pathology for daily use. The platform has three major areas of use: presentations, high yield cases, and an extensive searchable slide library. The platform provides a streamlined workflow for teaching and learning pathology. It converts conventional PowerPoint presentations with static images to live, interactive presentations with whole slide images as digital slides. Annotation and presentation tools are available in presentation mode.

Results

Since launching in January 2017, the platform has had more than 20,000 page visits, 7500 site visits, and with 1642 registered users. The site has been accessed in 120] countries, with the top three being United States, India and Australia. The slide library contains 8400 cases in all medical subspecialties (n=17). Users can upload whole slide images or use from the PathPresenter Slide Library to create presentations saved in the user's profile. Individual whole slide images or presentations can be shared via email. Trainees can learn from and study the high yield cases. The platform is available on smart devices as well as conventional PCs.

Conclusions

Based on the initial feedback, pathologists like the ease and innovative approach to sharing images via PathPresenter.Pathpresenter.com facilitates sharing of slides and presentations with colleagues across the globe. Academicians have access to high quality cases for teaching and have an exhaustive resource of digital slides available for free use anytime, anywhere. The high yield case library is growing in number with more annotations and high quality diagnostic teaching slides.

Implementation of Whole Slide Imaging as a Pathology Teaching Tool and for Institutional Tumor Boards: A resident's experience

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Content

This presentation will describe our experience implementing and utilization whole slide imaging (WSI) as a teaching tool for the pathology residents in Henry Ford Hospital, Detroit as well as our initial efforts to use WSI at institutional tumor boards.

Technology

1. Health system network
2. 2. Roche Ventana iScan HT Whole Slide Scanner (Roche Diagnostics Corporation, Indianapolis, IN) . capable of scanning up to 360 slides at one time.
3. Internet Explorer 11 access to Roche Ventana Virtuoso WSI viewing software
4. Basic Windows workstations as deployed throughout HFHS
5. CoPathPlus (Sunquest Information Systems)

Design

Glass slides were scanned for practice over several weeks to determine basic operation, system performance and workflow processes. Experience quickly showed that the iScan HT could be used to improvement quality and efficiency of weekly unknown slide conference. A proposal was made and accepted to pilot this process. Username's and passwords were given to all the residents allowing them to access the digital slides from any terminal in the hospital campus. Initially there was a lot of reluctance and resistance from the group to use WSI. To increase interest and enthusiasm concordance studies were presented in the monthly journal club which compared WSI and glass slides. To further interest, slides from a recently autopsy were scanned and presented during the journal. In addition, informatics lecture and luncheon meeting topics as well as a grand rounds, presentation on novel ways to use WSI were shared with the residents and other members of the department. This resulted in marked increased interest.

Soon interest grew from attending physicians to use WSI for a subset of tumor boards. The same processes and procedures used for scanning slides for unknown conference were applied.

Result

In Oct 2016unknown slide conference was presented using WSI. The reaction to the quality of the histopathology system usage was excellent: nuclear contours and nucleoli were clear; navigation easy; response time was excellent with no screen lag. The conference was well received. The residents and attending loved the new format. Since then unknown conference has been presented monthly using WSI.

In November 2016, we started presenting cases on WSI in GYN tumor board. GYN tumor board is unique as we typically need to present entire slides,not just the static picture of a relevant area. To do so we would project the slides via a microscope connected to the TV in the tumor board conference room a stressful and inefficient task. WSI, eliminated many problems went away in an instant rapid navigation toarea(s) of interest, ease of switching between slides and ease of switching cases. were ecstatic after the tumor board. The resident was super confident and was able to explain everything in detail using WSI without fumbling. The Attending, clinicians and residents were enthused at the new format; Some had no idea that this was even technically possible. All GYN weekly tumor boards are presented using WSI.

Conclusion

Whole slide imaging is a useful tool for teaching and presentation purposes. It can be easily implemented and integrated into our day to day pathology practice and resident training. The reluctance to use WSI is initially high among pathologists, but enthusiasm increases once implemented into regular practice. WSI provides for efficiencies and ease of collaboration in both educational and clinical case review settings such as institutional tumor boards.

Machine Learning Strategies to Optimize in Silico Genetic Variant Effect Predictions Informed by TP53 Functional and Clinical Data

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Content:
Predicting the impact of genetic variants of uncertain significance (VUS) is a major challenge for clinical genomics. Numerous *in silico* variant effect prediction (VEP) algorithms purport to address this, but better validation is needed, especially to improve specificity and prevent potentially harmful false-positive results. Using a public database of TP53 variants curated with clinical and functional data, we compared several common VEP algorithms alone and in combination using support vector machine (SVM) and deep neural network (DNN) techniques.

Technology:
Python language (3.5.2) with TensorFlow (0.11.0, Google, Mountain View, CA) library; R language (3.3.2); ANNOVAR (2/1/2016)

Design:
Tumor and germline databases of TP53 mutations were downloaded in CSV format from the UMD TP53 website (http://p53.fr, accessed 10/5/2016). Missense variants with preserved function in yeast studies selected from the tumor database were compared against inactivating germline variants associated with heritable tumor syndromes. Variant function was annotated with precompiled *in silico* predictions from the dbNSFP database, version 3.0, via ANNOVAR. Receiver-operator characteristics (ROC) of 21 VEP algorithms were analyzed in R. Based on the five best performing classifiers, a SVM was trained on a random 70% sampling of the variants in R, then tested on the remaining 30%. Using the same testing and training sets, a DNN with 3 layers of 30 nodes each was composed using TensorFlow.

Results:
The training set contained 230 inactivating variants and 352 with preserved function; the test set contained 101 and 148, respectively (831 total). Based on AUC, the five best performing individual algorithms were VEST3, FATHMM, MutationAssessor, PROVEAN and Polyphen-2 HVAR. Optimization based on ROC analyses generally improved specificity at a modest cost to sensitivity, relative to default interpretations available for 10 VEP. The accuracy of the SVM classifier was 0.933 in a 5-fold cross-validation of the training data and 0.936 with test data (AUC of 0.921). The DNN yielded an accuracy of 0.940 and an AUC of 0.976, the latter essentially similar to the AUC of VEST3. **See table** for sensitivity/specificity calculations.

Conclusion:
Optimization of VEP algorithms for individual genes is possible given sufficient functional training data. Ensemble VEP classifiers do not necessarily outperform the best individual component.

Table on next page

Table: sensitivity/specificity calculations

Existing classifiers via dbNSFP	Individual vs ensemble classifier	AUC	Sensitivity (initial → optimized)	Specificity (initial → optimized)
VEST3	individual	0.977	N/A → 0.946	N/A → 0.93
FATHMM	individual	0.934	1 → 0.882	0 → 0.912
MutationAssessor	individual	0.928	0.97 → 0.921	0.66 → 0.786
PROVEAN	individual	0.926	0.95 → 0.9	0.76 → 0.846
Polyphen2 HVAR	individual	0.912	0.98 → 0.912	0.62 → 0.838
Polyphen2 HDIV	individual	0.902	1 → 0.894	0.53 → 0.858
SIFT	individual	0.889	0.99 → 0.955	0.63 → 0.772
FATHMM-MKL	individual	0.83	0.97 → 0.934	0.43 → 0.688
SiPhy 29-way log odds	individual	0.809	N/A → 0.779	N/A → 0.714
LRT	individual	0.789	0.93 → 0.949	0.71 → 0.624
GERP	individual	0.765	N/A → 0.834	N/A → 0.61
phastCons 7-way vertebrate	individual	0.745	N/A → 0.752	N/A → 0.716
phastCons 20-way mammalian	individual	0.647	N/A → 0.855	N/A → 0.538
phyloP 7-way vertebrate	individual	0.637	N/A → 0.707	N/A → 0.612
MutationTaster	individual	0.602	0.96 → 0.97	0.47 → 0.234
phyloP 20-way mammalian	individual	0.591	N/A → 0.909	N/A → 0.45
fitCons	individual	0.491	N/A → 0.97	N/A → 0.054
MetaLR	ensemble	0.939	1 → 0.894	0.03 → 0.92
CADD (raw)	ensemble	0.889	N/A → 0.84	N/A → 0.798
DANN	ensemble	0.868	N/A → 0.722	N/A → 0.858
MetaSVM	ensemble	0.65	1 → 0.792	0.03 → 0.606
Novel classifiers		**AUC**	**Sensitivity**	**Specificity**
Novel 5-way SVM classifier	ensemble	0.921	0.921	0.946
Novel 5-way DNN classifier	ensemble	0.977	0.95	0.932

Dynamic Models for Precision and Personalized Pathology

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Content
Dynamic models of pathological phenomena in diseases such as cancer are very useful tools to understand the pathogenesis of disease progression and development. These models study physiological and pathological phenomenon at cell and tissue level focusing not only on components within cells and tissues but also on the evolution of diseases in time and space. In this work, the implications of these models for precision and personalized pathology are discuss using dynamic models of cell death pathways in cancer.

Technology
Dynamical and mathematical models were used to establish a general pipeline for precision and personalized pathology. Computational methods to detect and determine parameter spaces and finding sensitive parameters were applied.

Design
Signaling pathways controlling cell death modalities (mainly apoptosis, necrosis and autophagy) in cancer were translated into a set of ordinary differential equations and the parameter spaces that give robustness to these models were found. These parameters were assigned to biomarkers available for quantitative measurements in patients. The predictive ability of these models was verified within current pathology literature.

Results
Analysis of parameter spaces of cell death pathways in cancer showed some sensitive parameters which can clinically be translated to some biomarkers. These biomarkers are the main determinants of disease progression and variations in their levels can be used to make personalized diagnosis and find the prognosis for each individual patient more accurately.

Conclusions
In the era of big data in medicine, dynamic models can be used for personalized and precision diagnosis of cancers and other diseases. Introducing them to the field of pathology requires development of basic mathematical and computational pipelines. Current example of cell death pathways and their dynamical models is a general pipeline for establishing the field of precision and personalized pathology.

Discovery of prognostic factors for gastric cancer based on KI67(+) immune and epithelial cells using deep learning

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Content

Gastric cancer is among the leading causes of cancer-related deaths worldwide. To improve treatment success, particularly for upcoming immunotherapies, it is important to characterize spatial properties of tumor-infiltrating immune cells and co-localized cancer cells. We present an automatic approach to identify prognostic factors related to KI67(+) cells based on clinical trial data comprising 248 gastric cancer patients treated at Kanagawa Cancer Centre Hospital, Japan.

Technology

We used a convolutional neural network (CNN) to predict heatmaps of KI67(+) immune and epithelial cell densities on tissue microarray (TMA) data. Based on these heatmaps we computed features characterizing each patient, and automatically identified prognostic factors by correlating such features with clinical outcome in a Tissue Phenomics workflow.

Design

Based on manual annotations of positive cells we generated training patches (128x128 pixels²) with six patch classes: all negative (0), KI67(+) epithelial cells medium (1) and high (2) density, KI67(+) immune cells medium (3) and high (4) density, and both KI67(+) epithelial and immune cells mixed (5) (Fig. 1B). A reduced GoogLe net was trained with 100k iterations using 30k augmented patches from a patient subset reserved for training by transfer learning. By applying the network for patch-based prediction we generated KI67(+) cell density heatmaps for all TMA cores (Fig. 1A). Ratios and percentages of all classes in tumor and normal tissue cores were computed (n=43) and systematically mined as to their prognostic value.

Results

Quantitative evaluation of the predicted heatmaps yielded 75.5% accuracy on the patient test set. Data mining identified features with high prognostic value using 100x10-fold Monte Carlo cross-validation. The percentages of class 1-patches (KI67(+) epithelial cells) in tumor (see Kaplan Meier plot Fig. 1C) and class 4-patches (KI67(+) immune cells) in tissue turned out to be stable and strongly positive prognostic factors for cancer-specific death (p-value<0.05).

Conclusions

KI67(+) epithelial and immune cell densities provide prognostic value for gastric cancer patients, which we found using a CNN with the Tissue Phenomics methodology without explicit cell segmentation. We will validate the discovered factors using data from another clinical site.

Acknowledgment:
We thank Prof. H. Grabsch, Maastricht University, NL, for providing the data, and S. Kisliak, W. Susanto, and R. Menendez for their contribution to cell annotations.

Generalizing Deep Learning Models for Histology Data

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Content

Cancer cellularity is an important component of residual cancer burden in breast specimens from patients treated with neoadjuvant systemic therapy. This task is traditionally performed manually (eyeball estimation), which is not only time-consuming but also introduces inter-and intra-rater variability. Considerable progress has been made in the field of image analysis in digital pathology, increasing throughput and improving standardization. Here we propose a method for automatically determining cancer cellularity by analyzing digital slides using deep learning techniques. We develop a method for capturing complex textural appearances of cell nuclei and surrounding tissue to automatically classify image patches into one of four groups: normal tissue and, low, medium and high cellularity. Specifically, we aim to generalize our model to give high performance on a held-out test set.

Technology

Deep learning has had significant impact in digital pathology resulting in state-of-the-art performance on a wide range of tasks. Specifically, convolutional neural networks, or CNNs, encompass a series of convolution and downscaling operations which enable complex textures to be captured at multiple scales without explicit modelling of tissue or cellular structures. To prevent overfitting, dropout layers can be added to reduce the size of the network thus making it more generalizable. This property is ideally suited for histology data which contains highly variable structures particularly in datasets containing cancerous tissue.

Design

We designed a CNN architecture to automatically classify 2,579 image patches extracted from breast tissue whole slide images stained with H&E. The goal of the CNN is to assign a single label to image patches which represent varying degrees of cellularity. Our CNN contains three convolutional and max-pooling layers as well as two fully connected layers, the last of which outputs class predictions. We also investigated the use of dropout to improve generalizability. Our experimental setup consisted of separate train, validation and test sets; results are reported over five repeated experiments.

Results

The addition of dropout in our CNN increased test accuracy performance from 51.89 ± 0.95% to 62.83 ± 1.84% (dropout rate=0.7), showing considerable performance gain by reducing network size. Confusion matrices showing prediction accuracies on the test set are shown in Figure 1. With the introduction of dropout, correct predictions increased significantly for the normal (0), low cellularity (1) and high cellularity (3) classes.

Conclusion

Our results demonstrate the importance of introducing generalizability when training CNNs with histology data, due to high variability between samples, cases and cohorts. We demonstrate impressive accuracy rates on a cell classification problem which includes normal healthy tissue, which has in the past shown to be challenging to model using hand-crafted features. Our results show CNNs can be used effectively in digital pathology with some minor adjustments.

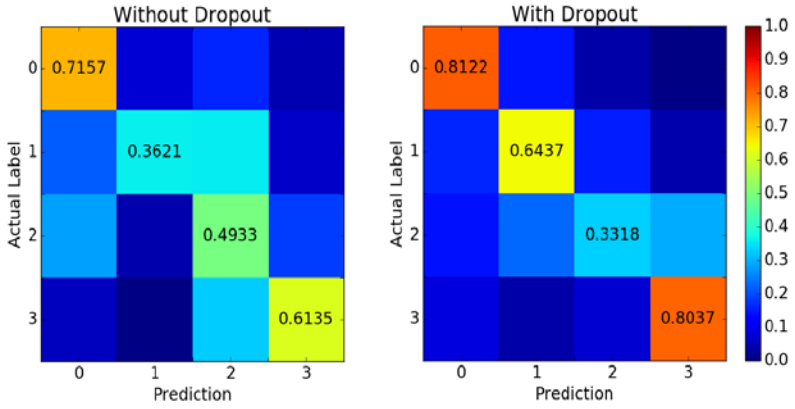

Figure 1: Confusion matrices showing test accuracies per class: 0=normal, 1=low cellularity, 2=medium cellularity, 3=high cellularity. Correct predictions are shown across the diagonal from top-left to bottom right.

An Open Source Web Application for Real-Time Display of Pending Orders

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Content
Many laboratory information systems (LIS) do not provide real-time notification of new orders, relying instead on batched, asynchronous display of information such as printed pending lists. To improve situational awareness of pending laboratory orders, we developed a web application (the "Pending Log Monitor") that displays data continually updated from our LIS on large wall-mounted monitors or PC workstations. Users may enter comments associated with individual items. A survey was administered to evaluate usage patterns.

Technology
The application is implemented in Python 2.7 using the Flask web microframework, and is hosted on a virtual machine running Ubuntu 14.04. Data is extracted from the LIS database (Sunquest Information Systems, Tucson, AZ) using custom code written in Cache (InterSystems Corporation, Cambridge, MA), and is transferred to the application server by a batched process using secure shell. User-provided comments associated with pending tests are stored in an SQLite database.

Design
The application was designed for maintainability, ease of customization, stability, and rapid recovery in the result of a component failure. Logic for display and formatting of pending tests is implemented as Python functions. A simple JSON-format specification can accommodate any tabular data. Lists of pending tests defined for a given area typically correspond to one or more worksheets defined in the LIS.

Results
Customized displays of pending tests have been implemented for over 35 combinations of worksheets in multiple lab areas. Pending orders for each lab area are filtered, ordered, and color coded based on elapsed time since order or receipt, priority, specimen stability, or other criteria. Data is transferred from the LIS by a batched process every four minutes. This application has replaced the use of printed pending lists in many areas. The majority of survey respondents described the application as "very important" to lab operations, with many lab areas referring to the monitor "constantly." Use of comments varies widely between lab areas, but most respondents strongly agreed with the statement that comments improve communication.

Conclusion
A simple web application implemented at low cost using open source technology has provided significant workflow and communication improvements throughout the laboratory.

Potential Benefits and Barriers for Implementing a Digital Communication System for Intraoperative Pathology Consultation

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Content
Timely and properly performed intraoperative pathology consultation often provides critical information to ensure the success of a surgery. This is a highly stressful process for both surgical and pathological teams. Many team members with different understandings of the work flow are involved in the process. Multiple steps need to be accomplished. A complicated process like this is prone to encounter errors and delays.

Common errors and delays can often be traced back to particular communication errors. These include (1) mis-labeled specimens, (2) illegible or incomprehensible requisition sheets, (3) confusing specimen orientation, and (4) suboptimal telecommunication hardware connecting the consultation lab and the operating room. In this simulation study, we attempt to systemically analyze the current work flow of intraoperative pathology consultation in a tertiary medical center, list the problems and barriers for achieving optimum efficiency and minimizing error rate, and propose a computer workstation-based or mobile device app based digital communication solution to replace the current analog environment, and compare the two systems.

Technology
We studied the intraoperative consultation process at Buffalo General Medical Center (BGMC), Buffalo NY. for the analog work flow analysis. A simulated digital communication system will be proposed and applied to the work environment to replace the current work flow.

Design
The digital system attempts to completely or partially automate the steps of specimen labeling, requisition sheet fill-out, specimen tracking, specimen accessioning. Advanced communication between operating room and pathology lab with real-time video on gross and microscopic findings is also included. A detailed comparison for potential benefits and drawbacks will be performed.

Results
Multiple steps of current intraoperative consult process at BGMC are prone to errors. In the simulated work flow with an integrated digital communication system, errors in multiple analog work flow steps can be successfully eliminated or minimized. Compared to analog process, the major potential drawbacks of the digital system include system malfunctioning/break down, and workforce compliance with the new workflow.

Conclusion
A digital communication system for intraoperative pathology consultation reduces error and increases efficiency. A properly designed system (computer workstation or mobile app) will improve intraoperative pathology consultation significantly.

Baikal: Streaming Data Science Platform for Laboratory Business Intelligence

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Content

In the era of healthcare system expansion and centralization of laboratory resources, monitoring quality improvement (QI) metrics becomes increasingly critical and challenging. Emerging data management technologies offer novel approaches to enhance QI practices. To this end, we present a component of a data science platform developed at our institution – Baikal – that allows for stream processing and analysis of laboratory orders and results.

Technology

Primary components include the Hortonworks Data Platform (version 2.4.2; Hortonworks, Santa Clara, CA, USA) and Hortonworks Data Flow (HDF) version 1.2 (Hortonworks, Santa Clara, CA, USA). Custom Python (version 2.7) scripts are executed within NiFi to calculate laboratory QI metrics on streaming laboratory data. QI metrics currently include turn-around time (TAT) for lab results, outstanding orders, and order volumes. Data from Health Level 7 (HL7) ORU messages and QI metrics are stored in Elasticsearch (version 2.4.2; Elastic, Mountain View, CA, USA) and can be readily visualized with Kibana (version 4.3.1; Elastic, Mountain View, CA, USA). For laboratory and EHR-related data, Cloverleaf (Infor, NY, USA) was used as the interface and integration engine.

Design

A custom emissary service was deployed to receive a stream of HL7 ORU messages from Cloverleaf. HL7 messages were validated and transformed into JSON documents for structured storage and stream processing. Custom Python (version 2.7) scripts were implemented in NiFi to denormalize messages and calculate QI metrics. Raw messages were stored in Hadoop Distributed File System and processed messages with QI metrics are routed to Elasticsearch for visualization with custom dashboards in Kibana.

Results

Baikal was deployed in July of 2016. In a representative two-month period between August 1st, 2016 and November 1st, 2016; 1.3 million tests were ordered with a total of 10.3 million subcomponents resulted. Messages indexed to Elasticsearch and visualized with Kibana allows interactive exploration of QI metrics filtered by indexed fields.

Conclusion

This work demonstrates that adoption of emerging data management technologies can offer extended capabilities for laboratory QI and business intelligence. Future research will seek to evaluate implementation studies to determine the benefit of QA policies based off streaming laboratory QI metrics.

A Mobile App to Calculate Minimum Blood Volume Needed for Testing

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Content
Iatrogenic anemia, often caused by excessive blood drawn for laboratory testing, is a major risk factor for patient morbidity especially in the pediatric population. While reducing the volume of blood drawn for testing to a minimum has been shown to decrease incidence of iatrogenic anemia, determining the minimum volume needed for various combinations of laboratory tests is often difficult and requires laboratory assistance.

Technology
We have developed a mobile app (iOS, Android) to facilitate such calculations at the patient bedside.

Design
Users input tests, selected from the institutional testing menu, while the application outputs which types of, and how many, blood collection tubes are needed as well as the minimum blood volume required within each tube. Instrument dead volume, hematocrit correction, and other relevant parameters are accounted for. The app incorporates 168 tests and panels, encompassing 13 central laboratory instrument systems, 10 collection tube types and 5 specimen types.

Results
Our house staff and nurses will integrate the app into their clinical workflow to reduce the number of tubes and volume of blood drawn. Usage, user feedback, specimen collection patterns, and patient outcomes will be followed for a longitudinal period and reported.

Conclusion
In response to a clinical need, we have developed a mobile app for calculating the minimum volume of blood required for any given set of tests. The app will integrate into our hospital workflow with the primary goal to reduce iatrogenic anemia especially in the pediatric setting.

Imaging Informatics
Applied Pathology Informatics

Brigade Room
7:45 am

HCV Genie: A Web Platform and Workflow Optimization for the Versant Hepatitis C Virus (HCV) Genotype Line Probe Assay Version 2.0

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Content
Hepatitis C virus genotyping at our institution is performed using the Versant Hepatitis C virus genotype 2.0 Line Probe Assay. This procedure relies on multiple labor-intensive steps; last of which is a manual, time-consuming, and error prone process that involves the comparison of bands on a test strip to a physical reference table. We have streamlined this entire procedure by updating the manual preparation steps for storage a scanned line probe assay image. This is then fed through our image analysis algorithm to determine the banding pattern and the genotype of any number of samples.

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

Design
Using a standard web environment (JavaScript, HTML5, CSS), we (a) ported the original, clinically validated, automated HCV genotype interpretation program called "HCV Genie," from PHP to JavaScript, (b) created image analysis component that converted LiPA images into band and genotype calls, (c) built a user interface for editing banding calls and (d) created a new time saving workflow in the molecular lab. The final tool utilizes code migration, a native component of JavaScript, to allow the code to go to the data without the data ever leaving the investigators computer, eliminating any potential data privacy concerns. Finally the, results of the analysis are downloadable as a printable, human readable report.

Results
Both “HCV Genie” (n=200) and “HCV Genie 2” (n=176) deployed, clinically validated, and proven to be identical to human expert interpretation. HCV Genie decreased the time needed to interpret results by 53% in residents, but results among experienced lab technicians are more equivocal. HCV Genie 2 decreased the total technician interpretation time by 71%.

Conclusions
Our original program provided 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. This iteration’s new features allowed analysis time to further decrease to a timeframe much faster than even the most well-trained interpreter while creating a digital record for laboratory and physician use.

Image Standardization and Its Impact On Whole Slide Image Analysis

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Drexel University College of Medicine

Content
Computational analysis of H&E images relies on the staining and digitization process to produce an image that conforms to an expected range of color. Attempts to improve image analysis often begin with a color normalization step to force the data set to conform to this expectation. However, the impact of standardization on image analysis and whole slide viewing is largely unknown.

Technology
We used image processing to develop and apply a novel color normalization algorithm to whole-slide images. We used eye tracking and psychovisual analysis to measure pathologist gaze patterns to evaluate the impact of color normalization on histology analysis.

Design
We analyzed the color properties of publicly available H&E image sets as well as those acquired from the Drexel University cancer databank to better understand the color attributes commonly encountered in digital pathology. We used these quantities to guide the development of an algorithm that normalizes images by anchoring histologic structures to a set of target colors with the aid of a previously reported structure classification algorithm. We measured pathologist gaze patterns and diagnostic performance while they viewed unnormalized, normalized, and artificially manipulated images to characterize the impact of normalization on diagnosis.

Results
We found an approximate 10-fold decrease in inter-image variability after applying color normalization. Importantly, loss associated with this transformation, as measured by the normalized mutual information, was very small, indicating its potential utility as a preprocessing step for advanced image analysis and whole-slide viewing. However, despite improvements in computational image analysis performance, we observed only modest differences in whole-slide viewing due to normalization.

Conclusion
As regulatory policy continues to take shape in the arena of whole-slide imaging, a quantitative treatment of color becomes an important factor to help refine these policies. We present a novel algorithm for color normalization that substantially reduces inter-image variability while retaining the inherent information in the image, leading to greater standardization in pathology and its measurably positive impact on image analysis. More generally, we describe a color representation paradigm that enables a pathology-specific quantitative framework for color, promoting a platform by which we can compare diagnostic performance and image attributes.

An Update on the DICOM Digital Pathology Connect-a-thon

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Content

The digital imaging and communication in medicine (DICOM) standard is the most widely used medical imaging standard around the world and has been used to archive more than 10 billion medical images. DICOM provides data standards and communication protocols for imaging that currently support more than 60 modalities including whole slide imaging and pathology metadata.

Many digital pathology vendors and pathology associations, such as the College of American Pathologists, have contributed to the standard since 2005 through the DICOM Pathology Working Group (WG-26). WG-26 is currently working on a number of initiatives to expand the capabilities of DICOM for anatomic pathology including support for multispectral imaging, standards for communicating structured reports, standardized workflows for digital pathology and a multi-vendor connect-a-thon to demonstrate the benefits of a DICOM-based workflow for digital pathology. This talk focuses on the motivations for the connect-a-thon.

Technology

The DICOM digital pathology connect-a-thon will demonstrate benefits of interoperability using DICOM to the pathology community. DICOM is natural choice for achieving interoperability in digital pathology since it provides familiar standards for handling, storing, printing, and transmitting medical images.

Design

The connect-a-thon will demonstrate a vendor neutral pipeline that allows imaging, archival and review (Figure 1). All digital pathology vendors will be invited to participate with the overarching goal to show a wide range of scanners and viewing software.

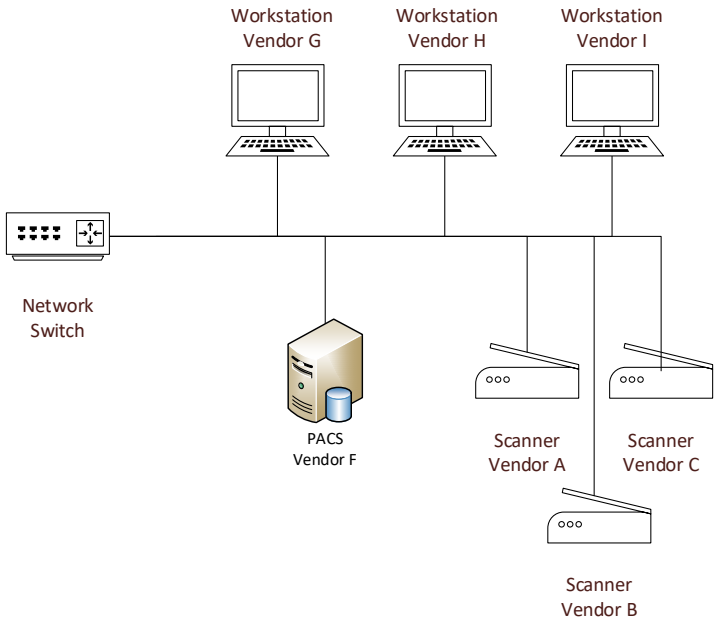

Figure 1: DICOM digital pathology connect-a-thon configuration

Results

The DICOM digital pathology connect-a-thon is currently in the early planning stages. The goal of the WG-26 committee is to organize the connect-a-thon for the fall of 2017.

Conclusions

While the use of DICOM as a data and communication standard in digital pathology is still nascent, there is growing demand for DICOM in the pathology community. This demand is driven by the need to reduce disparate data formats and to future proof investments in digital pathology infrastructure.

DICOM includes a file format definition and communication protocol that allow devices and software to interoperate within a networked environment. Thus it becomes possible to create a vendor neutral workflow that comprises image scanners, image archives and workstations.

Barcode Beware: Using ISBT 128 in Positive Patient Identification for Blood Administration

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Content
Positive patient identification (PPID) blood administration systems improve safety by ensuring correct pairing of patient to blood product. The selection of a blood administration PPID system was performed at Children's Healthcare of Atlanta (CHOA). Regulatory, accreditation and safety issues were found during system selection which merit dissemination.

Technology
A transfusion safety project considered two systems for PPID for blood administration in 2016. The Electronic Health Record (EHR) vendor differs from the blood bank (BB) information system (BBIS). The application names are hidden because the discovered issue is system-agnostic.

Design
Two systems were compared for cost, integration and safety. Compliance with the following regulatory and accrediting agencies: FDA, AABB and The Joint Commission. ISBT 128 is the only barcoding and labeling system approved by the FDA.

Results

	System A	System B
Cost	+	+++
Integration with EHR	+++	++
Integration with BBIS	No integration	+++
FDA 510(k) Cleared	Yes	Yes
Rapid infusion module	No	No
Degree of Difficulty: - Nursing workflow - BB Workflow - EHR implementation - BBIS implementation	 + +++ + ++	 ++ + +++ +
Blood Product Unit Number and Product Code Matching: - dependent on interfaced data from BBIS - acquired from ISBT 128 compliant barcode reads	 Yes Depends on setup	 No Yes

System A met all criteria for selection except that it was dependent on interfaced blood product ISBT 128 codes which the BBIS could not provide discretely, introducing the potential for human error. Scanning ISBT 128 barcode data into free text fields is not an option because section 2.2 of the ISBT 128 technical specification requires software to ensure data integrity prior to acceptance. This ISBT 128 compliance issue was not known to any stakeholders prior to system comparison. A search of the medical literature did not reveal this as a potential compliance issue with these systems.

Conclusions
System B was chosen because of its enhanced patient safety due to compliance with ISBT 128. FDA clearance and barcoding may provide a false sense of security with PPID blood administration systems. Healthcare institutions should have full knowledge of ISBT 128 requirements prior to implementing them.

Feasibility of Converting and Viewing Whole Slide Images in DICOM Format

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Content

The current lack of standards with whole slide imaging (WSI) file formats has limited interoperability. In particular, the use of proprietary WSI formats has hindered incorporating WSI images into enterprise-wide imaging systems (e.g. picture archiving and communication systems) that deal with Digital Imaging and Communications in Medicine (DICOM) images. DICOM is a known standard for medical imaging, but has yet to be fully adopted in pathology. The aim of this study was to determine the feasibility of converting proprietary WSI files and viewing them in DICOM format.

Technology

Glass slides were scanned on an Aperio scanner at 20x magnification (0.5 micron/pixel). Software used for DICOM conversion included a command line tool plug-in DICOMizer (Orthanc) and FFEI Sierra OpenSlide to DICOM Converter. DICOM conversion was performed on a Hewlett-Packard Z420 PC (3.2 GHz, 64-bit, 16GB RAM). DICOM files were imported to www.orthanc-server.com and viewed using their WSI webviewer powered by OpenLayers toolkit.

Design

WSI of glass slides scanned on an Aperio scanner and publically available WSI files (NDPI, SCN, MRXS, TIFF, BIF) from OpenSlide were converted to DICOM using Orthanc and FFEI Sierra converter software. The process of DICOM conversion and viewing was compared to using radiology DICOM images.

Results

All WSI file types successfully converted to DICOM. Conversion times averaged 0.0003 seconds/MB with Orthanc DICOMizer and 0.002 seconds/MB with FFEI Sierra converter. DICOM file sizes for converted images were 52% smaller than original native WSI files. DICOM converted WSI files were supported by the WSI webviewer, which allowed pan and zoom functionality. However, the default color profile (e.g. YBR) of only Orthanc converted files differed from the original WSI (Figure 1).

Conclusions

The conversion of WSI with different file formats into DICOM format is possible and can be performed using freely available open-source software (e.g. Orthanc). Viewing DICOM converted WSI is achievable, but depending on the photometric interpretation employed (i.e. YBR_422) may result in altered color representation. RGB color space profile converted files retained source WSI color fidelity. Converted DICOM file sizes were at least half the size of original proprietary WSI files, which thus necessitate less storage space.

Figure 1. (a) Original WSI (SVS format) of an H&E stained renal biopsy compared to the (b) DICOM converted file with default YBR color space profile.