Poster Session

Presented in the
Grand Ballroom
Wyndham Grand Pittsburgh Hotel

Thursday, May 7, 2015

10:20-11:20 am
And
3:30-4:30 pm

Listed in alphabetical order by First Author

Standardization of Histopathological Diagnoses from the Dog and Cat Using SNOMED-Based Information Model

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Content:
The World Small Animal Veterinary Association Gastrointestinal Standardization Group proposed standards for reporting the microscopic findings of endoscopic biopsies for the dog and cat. However, these standardization efforts do not include recommendations on terminology and syntax for the morphologic diagnosis based upon the microscopic findings. In this work, an information model was created to provide a standard representation of histopathological diagnoses. These standardized diagnoses can serve as classification categories to facilitate the application of data mining and machine learning methods.

Technology:
Retrospective gastrointestinal biopsy reports were examined from dogs (n=320) and cats (n=125) with clinical gastrointestinal disease. Animals were client owned and presented to the Veterinary Teaching Hospital, Virginia-Maryland Collage of Veterinary Medicine between November 1, 2006 and April 29, 2013. The Systematized Nomenclature of Medicine-Clinical Terms (SNOMED CT) was used as a terminology for the semantic content in the information model for representing the histopathological diagnoses.

Design:
Unstructured textual biopsy diagnoses were cataloged. Unique unstructured diagnoses were mapped to SNOMED. Unique unstructured diagnoses were then expressed as triplets. These triplets were comprised of SNOMED *morphological abnormality* concepts, SNOMED *finding site* relationship, and SNOMED *body structure* concepts.

Results:
The biopsy reports contained 99 unique unstructured diagnoses. These diagnoses were associated with the following anatomic locations: n=41 (27.3 %) stomach, n=50 (33.3 %) small intestine and n=59 (39.3 %) large intestine. SNOMED was only able to directly represent 59 (59.6%) of the unstructured original unique diagnoses. However, using the triplet information model, 100% of the original report diagnoses could be expressed by using 33 SNOMED *morphological abnormality* concepts and 9 SNOMED *body structure* concepts.

Conclusions:
In this study, the information model (*morphological abnormality* Concept *+ finding site* relationship *+ body structure* Concept) was able to represent the gastrointestinal histopathological diagnoses, thus, can be used to extend the World Small Animal Veterinary Association Gastrointestinal Standardization Group's efforts to standardize gastrointestinal biopsy reporting.

Evaluation of Inflammatory Dermatoses using Whole Slide Images: Digital Images versus Glass Slides in the Analysis and Diagnosis of Neutrophilic Dermatoses.

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Content:
The neutrophilic dermatoses are a clinically diverse group of diseases defined by a dense dermal infiltrate of mature neutrophils with leukocytoclasis. However, histologic variants exist and may pose diagnostic difficulty. Whole slide images (WSIs) have been used to assess of pathologic processes in several organ systems but there are few data on their use in Dermatopathology. As part of a study to explore how neutrophil count impacts the development of

histologic features in neutrophilic dermatoses, particularly Sweet's Syndrome, we assessed the utility of high resolution WSIs for assessment and diagnosis. Sweet's Syndrome can occur in the setting of leukemia and lymphoma, and timely diagnosis is desirable in this patient population. The use of WSIs would facilitate on-line collaborative subspecialty Dermatopathology review and aid in the diagnosis of histologic variants of Sweet's Syndrome.

Technology:
Glass slides were digitized using a Philips UFS slide scanner and the WSIs were viewed on https://slide-atlas.org, our high performance web-based viewing platform. Where indicated, local adaptive alignments of sequential WSIs were performed in Slide Atlas, and the aligned WSIs displayed side by side.

Design:
48 cases were selected by searching the laboratory information system for "neutrophilic dermatoses / infiltrates." These were digitized and uploaded to Slide Atlas. The glass slides and then the corresponding WSIs were evaluated with a 2-week "wash out" period. Features evaluated included the density and distribution of the neutrophilic infiltrate, the presence of papillary dermal edema, vasculopathy, leukocytoclasis, or "variant" features (immature neutrophils), and the presence of an associated non-neutrophilic inflammatory infiltrate.

Results:
Neutrophilic infiltrates could be identified on WSIs in all cases. All 16 classic neutrophilic dermatoses were identified on the WSIs. Appropriate differential diagnoses were made for the 3 variant cases (superficial dermal infiltrate) on the WSIs, and equivalent to glass slide exam. WSIs had the advantage over glass slides of improved low zoom architectural assessment, the ability to computer-align sequential sections for limited 3D assessment and collaborative review.

Conclusion:
High resolution WSIs displayed using a high performance viewer can be used in the assessment and diagnosis of neutrophilic dermatoses and inflammatory dermatoses with neutrophilic infiltrates.

Software Tools to Aid Blood Utilization Review

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Content:
Blood management initiatives often involve retrospective analysis of product utilization. Current techniques usually include an automatically generated report which shows unit type, patient location, etc. However, relevant clinical data is often lacking. In this project, custom software was written to correlate issued blood bank products with clinically relevant data including the preceding hemoglobin and platelet levels for red cell units (RBC) and platelet units respectively.

Technology:
Custom programming using a mix of MUMPS, korn shell scripts, and perl were written for the Sunquest LIS (Tucson, AZ) to parse the data. By default the scripts run daily to identify transfusion time stamps from the previous calendar day. The time stamps are used to find the most recent hemoglobin and/or platelet values for a transfused patient. If no relevant values are found in a five day look back, the script will abort and move to the next transfusion. The default settings can be overridden by entering a date range to perform retrospective analysis. For this project, anonymized data from calendar year 2014 was exported and subsequently analyzed in Microsoft Excel.

Design:
Extracted variables included: age range, gender, pretransfusion hemoglobin level, pretransfusion platelet count and issued product.

Results:
For all patients the average pre-transfusion hemoglobin level was 7.7 and the average pre-transfusion platelet level was 61. A total of 20,393 red cell products and 2,597 platelet products were issued during the calendar year. Approximately, 75% of both red cell and platelet transfusions took place after age 45. Comparing issued red blood cells with age range shows a bimodal pattern with peaks at 15 to 25 years and 60 to 70 years. The platelet vs age comparison shows a similar bimodal pattern with peaks at 10 to 15 years and 55 to 60 years (Table 1).

Table 1.

AgeRange	Total RBC Units	Average PreTransfusion Hemoglobin	Total Platelet Units	Average PreTransfusion platelet level
<= 5	319	9.0	50	50
> 5 to 10	354	7.9	53	16
> 10 to 15	477	8.2	128	33
> 15 to 20	638	8.1	65	71
> 20 to 25	637	7.5	60	51
> 25 to 30	475	7.1	36	55
> 30 to 35	547	7.2	65	32
> 35 to 40	731	7.8	56	62
> 40 to 45	923	7.3	71	77
> 45 to 50	1143	7.3	205	53
> 50 to 55	1650	7.3	247	57
> 55 to 60	1989	7.5	361	47
> 60 to 65	2285	7.6	311	73
> 65 to 70	2325	7.6	272	64
> 70 to 75	2025	7.7	255	66
> 75 to 80	1584	8.0	175	73
> 80 to 85	997	7.5	69	89
> 85 to 90	400	7.6	29	101
>= 90	894	8.9	89	121

Conclusions:
By using software to incorporate relevant clinical values, blood utilization data can be stratified in ways that are very difficult using manual methods. Custom software allowed a retrospective review to illustrate how blood products are used in our facility. Going forward the implementation of this software will help with blood utilization management.

Integration of third party genetic analysis software into a clinical next generation sequencing data platform

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Content:
Advancements in next-generation sequencing (NGS) technology have allowed researchers and clinicians to generate genome-wide data sets. However, current information systems, which predate the arrival of NGS technology, lack adequate methods for NGS analysis and remain isolated from the systems which generate the data. In order to add

meaningful annotations to clinical NGS data, we developed a system that allows us to request and dynamically format sequencing data for a variety of software applications.

Technology:
The data management system is hosted on Windows Server 2012 (Microsoft, Redmond, WA, USA). Research software packages were run on Linux-based virtual machines running CentOS. Web service responses were consumed and parsed using Python 2.7 then visualized in R (version 3.1.2) using the SciClone R-package.

Design:
In an effort to implement third-party data analysis software, we obtained variant call format (VCF) files from technology agnostic web service endpoints and parsed the data with a python script. Data was formatted with the same Python script for analysis with a locally installed research application, called SciClone, which can be used to assess tumor heterogeneity from NGS results.

Results:
Easily consumable web services support NGS utilization in clinical and research scenarios, without adversely impacting system performance. Results can be sent back to the data management system for use in ongoing clinical trials or for clinical interpretation as appropriate. Researchers or clinicians accessing the results need no additional training, and data can be provided based on available user permissions. Connecting clinicians and researchers to NGS results with a user-friendly environment, provided with visually interpretable graphs, is currently serving to improve turnaround time and closely integrate ongoing research studies with clinical signout in our department.

Conclusion:
The ability to generate genome-wide sequences and analyze the resulting data in a clinically meaningful way are two distinct entities, which have been discordant in their points of evolution. With NGS technology evolving at a rapid pace, the technology used to interpret it struggles to keep up. To increase efficiency and provide increased data access, applications that easily and securely allow access to third-party research applications, such as web services, are important for furthering our understanding of sequencing data.

Whole slide images of prostate core needle biopsies: How do compression levels impact pathologist's interpretation?

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Content:
Compression of whole slide images may improve their transmission rates and need for storage. However, image compression may negatively impact diagnostic performance. The objective of this study is to determine the impact of different image compression levels when interpreting prostate biopsies.

Technology:
Glass slides were scanned using an Aperio ScanScope XT (Leica Microsystems Inc., US). Computer monitors (HP ZR24w 1920x1200) were used to view digital slides with ImageScope software (Aperio ePathology, Leica, US).

Design:
Fifteen randomly selected prostate core needle biopsies (97 slides) were diagnosed using conventional light microscopy and digital slides. Slides were scanned at 3 different compression settings: 70 (low quality default setting, low compression), 50 (mid-level compression), and 30 (high compression). Reviewers were blinded to these compression levels and asked to rate image quality and their diagnostic confidence.

Results:
Table 1 shows the differences when evaluating digital slides with different compressions.

Compression	Low	Mid	High
Image quality	Satisfactory	Satisfactory	Satisfactory
Diagnostic confidence	High	High	High
Diagnostic discrepancy with glass slide	10% (10/97 slides)	9% (9/97 slides)	5% (5/97 slides)

Conclusion:
These data show that compression of whole slide images do not impact the diagnostic confidence and perceived image quality by pathologists. Diagnostic discrepancy between glass and digital slides was unrelated to image compression levels.

Are Coverslips Required Before Glass Slides Can be Digitized?

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Content:
Whole slide imaging devices are typically calibrated to scan specific glass slides. A glass "slide" in pathology used for routine work (e.g. surgical pathology, cytopathology) includes a microscope slide (1.0 mm average thickness) and a mounted coverslip (0.15mm average thickness). Some manufacturers recommend scanning with a glass coverslip. However, for some practices (e.g. rapid on-site evaluation of cytology specimens), glass slides may be prepared without coverslips. The effect of scanning glass slides without coverslips has not been well studied. The aim of this study was to determine the impact of uncovered glass slides on the digitization process of various commercially available scanners.

Technology:
Whole slide scanners used: ScanScope XT (Aperio, Leica Microsystems, USA), NanoZoomer HT 2.0 (Hamamatsu, Japan), Mirax midi (3DHISTECH, Hungary), and VL4 (Omnyx, USA).

Design:
Air-dried cytopathology glass slide smears (Diff-Quik stained) were prepared without coverslips. Attempts were made to digitize these uncovered slides using different scanners. The slides were subsequently mounted with glass coverslips and rescanned. The ability to scan slides and the image quality of these digital slides was evaluated.

Results:
The table shows that all tested devices were able to successfully scan uncoverslipped glass slides. While image quality of both uncovered and covered digitized slides were satisfactory for diagnosis, for most scanners the covered digital slides were subjectively sharper in detail.

Whole slide scanner (resolution)	Scanning	Image Quality
Aperio ScanScope XT (0.5 micron/pixel)	Successful	Satisfactory
NanoZoomer HT 2.0 (0.46 micron/pixel)	Successful	Satisfactory
Mirax midi (0.116 micron/pixel)	Successful	Satisfactory
Omnyx VL4 (0.275 micron/pixel)	Successful	Satisfactory

Conclusion:
While some manufacturers claim that uncoverslipped glass slides may fail to scan with their whole slide imaging devices because they require a glass slide-coverslip interface for image capture, this was not observed in the scanners tested. If the presence of a coverslip is required to digitize a glass slide, this may warrant modification of workflow, especially during cytology on-site evaluation.

The Use of Apple's Siri Virtual Assistant & Google's Mobile Application for Rapid Literature Searches

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Content:
Multiple mobile applications are available but pathologists are probably underutilizing them as there is little awareness about their potential to facilitate daily practice. We tested the applicability of a smart phone and two widely available mobile applications from leading information technology corporations to perform rapid literature searches.

Technology:
An iPhone 6 (Apple, Cupertino CA) smart phone equipped with Siri (Apple iOS v. 8.1.3) and Google's (Google, Mountain View CA) mobile application (v. 5.2.0) was used to query for literature information. Both applications use voice activated natural language user interfaces. They function as virtual personal assistants that delegate user requests to various web services and easily enable quick access to large, networked information databases.

Design:
Ten questions pertaining to lung cancer were formulated and dictated to each of the mobile apps. For each query, the total number of retrieved links and the clinical relevance of the first ten links retrieved by each application were recorded. The latter were classified as either relevant or non-relevant, based on our clinical expertise. Results were compared with the F-test.

Results:
Both applications retrieved results surprisingly rapidly, with as many as 24,700,000 links per question in less than 1 second. There was no significant difference in the number of total of links retrieved by either software. On average, 6.5 (± 1.4) and 7.4 (± 1.3) of retrievals by Siri and Google's mobile application, respectively, were relevant. Differences are not statistically significant ($p = 0.72$).

Conclusion:
Smart phones and their intrinsic applications represent vast, untapped resources that can serve multiple purposes because of their portability, ubiquitous Internet access, and ease of use. Both of the tested mobile applications from Apple & Google were easily able to process medical queries using natural language input with reasonable accuracy. Optimization of these natural language-based applications may potentially reduce turn-around-time associated with surgical pathology sign-out by enabling rapid access to pertinent differential diagnostic information

A Comprehensive Web 2.0 Neuropathology Whole Slide Imaging Repository and Teaching Platform

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Content:
Last year, we created an instructional neuropathology wiki for the education of residents and fellows at our institution's Pathology residency and fellowship programs. This wiki is host to a curated collection of digital neuropathology images, presented within their clinical context. With the creation and deployment of a Web 2.0 universal whole slide imaging (WSI) system at our institution, we have chosen to create the largest publicly available neuropathology WSI repository and teaching platform on the web.

Technology:
Server Hardware: Dell Precision T3600; Host Virtualization Hypervisor: VMWare ESXi 4.1.0; Guest Operating System: Ubuntu Linux Server 14.04 LTS 64-bit; Web Server: nginx 1.7; Database Management System: MariaDB 10.0; Programming Language: PHP-FPM 5.5; User Interface Framework: Twitter Bootstrap 3.3; Rapid Publication Environment: MediaWiki 1.22; WSI Conversion Software: libVIPS 4.32 and OpenSlide 3.4; WSI Server System: PEIR-VM 0.2

Design:
We gathered all of our glass-slide neuropathology teaching sets, cataloged them, made fresh recuts where necessary, and most critically compiled detailed metadata on each slide into a CSV file. This CSV file was then fed into our existing PEIR-VM system, and all slides were scanned. The scanned slides were converted into DZI pyramids via libVIPS and OpenSlide; these DZI pyramids were then transferred to PEIR-VM for final display. The WSIs (complete with relevant metadata) can be directly viewed from PEIR-VM, or they can be embedded in their clinical context at our neuropathology teaching wiki.

Results:
Over the course of several months, over 150 slides were vetted, scanned, compiled with metadata, and inserted into PEIR-VM. We now have a full library of neuropathology WSIs against which both teaching and image analytics

research can be done. Our WSI library is fully integrated into our existing neuropathology teaching wiki, allowing residents and fellows to read full slides instead of having to be guided by static images alone.

Conclusions:
The addition of our Neuropathology WSI library, while time-consuming and system resource-intensive has been worthwhile. We will continue to maintain this library as time goes on, adding new cases culled from our clinical service as appropriate. We are considering a parallel version of this system for clinical case archiving.

Impact of Monitor Color Calibration on Digital Pathology Interpretation

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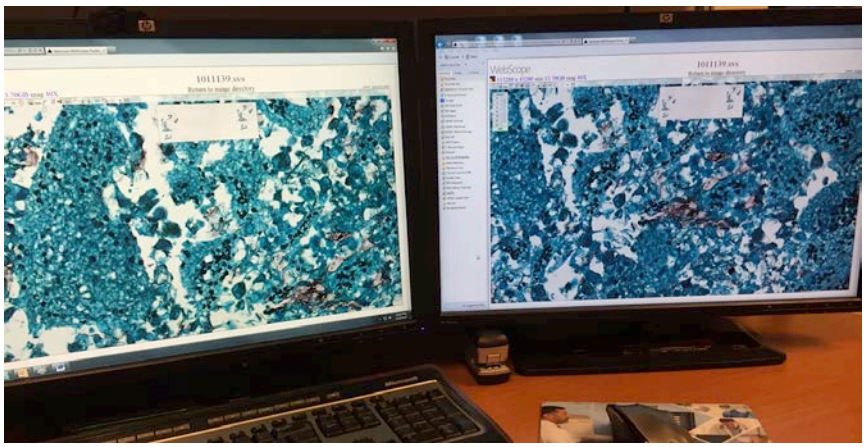
Content:
Color is emerging as an important parameter that may impact digital imaging in pathology. Color in digital images is impacted by tissue stains, image acquisition devices, and computer displays used to view images. Color calibration of stained slides, whole slide scanners and/or monitors is alleged to be important in standardizing digital pathology. This study aimed to determine if color calibration of monitors produced a noticeable difference when interpreting digital slides.

Technology:
Digital slides scanned at 40x magnification using an Aperio ScanScope XT (Leica Biosystems, USA) were viewed on 24 inch widescreen Hewlett-Packard displays (ZR24w monitor, HP, USA) with 1920 x 1200 resolution. Display color calibration was performed using Spyder4 Pro (Datacolor, Lawrenceville, NJ, USA) software and a color sensor attached via USB to each monitor workstation.

Design:
Two pathologists each interpreted 12 whole slide images using side-by-side HP monitors with equivalent display brightness, contrast ratio, pixel pitch and color gamut. Digital slides of various stains were selected (H&E, Diff-Quik, Papanicolaou, trichrome, Gram, acid fast, Grocott's methenamine silver, India ink, immunohistochemistry). One monitor had baseline factor settings, while the other was color calibrated using Spyder4 Pro adjusting for ambient light. Pathologists were blinded as to which monitor was calibrated. Their preference for monitor, color predilection and diagnostic accuracy was recorded.

Results:
Pathologists overall preferred (92% and 75% of cases) viewing digital slides on the uncalibrated monitor. They favored image color and brightness on the uncalibrated display. The calibrated monitor appeared to have a blue undertone compared to the affable yellow uncalibrated monitor (Figure 1). Calibration nor lack thereof did not affect diagnosis.

Figure 1. Comparison of “yellow” uncalibrated (left) and “blue/true white” calibrated (right) HP desktop monitors. The digital image shown is Pneumocystis (Grocott's methenamine silver stain).



Conclusions:
This study unexpectedly revealed that when viewing whole slide images from a desktop workstation, in the majority of cases pathologists prefer an uncalibrated computer monitor to one that is color calibrated. Additional studies comparing different color calibration techniques and display settings are needed to better appreciate how adjustment of color affects digital pathology.

Pathology Informatics Essentials for Residents (PIER): A Novel Curriculum for Educating Pathology Residents

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Content:
Multiple factors are driving an increased need for pathologists to be proficient in informatics. However, adequate informatics training is currently lacking in most pathology residency programs. We report a cross-organizational initiative to develop a pathology informatics curriculum for residents aimed at providing training in core informatics knowledge and skills that are important for current and future pathology practice.

Technology:
Interactive Portable Document Files (Acrobat, Adobe, San Jose, CA). Microsoft applications (Word and PowerPoint, Microsoft, Redmond, WA).

Design:
The College of American Pathologists, Association of Pathology Chairs, and Association for Pathology Informatics convened a joint workgroup consisting of about nineteen pathologists expert in informatics. A core team of three pathologists and education specialists provided oversight and project management. The workgroup met by conference calls over a period of about 7 months. A subset of the workgroup met in person to finalize the first release. PIER is aimed at training all pathologists, not informatics specialists.

Results:
The group developed Pathology Informatics Essentials for Residents (PIER). Release 1 of PIER launched in September 2014. PIER contains 4 Essentials, each with a set of peer-reviewed informatics knowledge and skill statements, designed with increasing complexity. PIER content is mapped to recent American Council on Graduate Medical Education informatics milestones for residents. PIER materials consist of an instructional resource guide and interactive toolkit (http://www.apcprods.org/pier/). The toolkit enables residents and program directors to track and to document individuals' progress through PIER. Alpha testing has begun at 14 training programs of diverse size and settings.

Conclusions:
PIER is a novel curriculum developed by experts that pathology residency program directors may use to address their informatics training needs. This flexible curriculum is designed to easily align with American Council on Graduate Medical Education milestones. We anticipate widespread adoption and implementation, to ensure that all pathology residents acquire the informatics training needed for modern pathology practice.

Identifying Prognostic Immunophenotypic Profiles of Germinal Center Type Diffuse Large B-Cell Lymphoma through Hospital Information Systems

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Content:
Diffuse large B-cell lymphoma (DLBCL) is the most common type of aggressive non-Hodgkin's Lymphoma (NHL). There are currently two broad categories of DLBCL based on the immunophenotypical profile, germinal center origin or non-germinal center origin. Within the germinal center DLBCL, it is unclear as to which immunophenotypical profile has a worse outcome. Using Clinical Looking Glass (CLG), a Montefiore Medical Center created program, we retrospectively looked at DLBCLs and their immunophenotype with regards to CD10, BCL-2, BCL-6, MUM1 and their Ki67 index.

Technology:
A combination of CLG and Microsoft Excel were used to identify and sort patients with DLBCL and their immunohistochemical profile at diagnosis. CLG centralizes and anonymizes all of our institutional information systems into one searchable database. This provides current retrospective information on patient data. The output of CLG is an Excel table, which allows for further analysis.

Design:
CLG was used to search for surgical pathology reports during a 10 year span of patients with a diagnosis of DLBCL. Reports containing the initial diagnosis of DLBCL and CD10, Ki67, Bcl2, Bcl6, or MUM1 were extracted to Excel with clinical information including age, gender, and survival data. Several Excel functions were used to categorize each patient's immunoprofile from their pathology report. This information, combined with survival data, was used to analyze prognostic value of the immunohistochemical markers.

Results:
166 patients were identified with germinal center DLBCL. Cox Proportional-Hazards Regression showed significantly better prognosis in patients with a Ki67 of 40% or less vs greater than 40% (P=0.01). Kaplan Meier curves suggest that Bcl6- may have a poorer prognosis than Bcl6+. It is not clear if CD10, Bcl2, or MUM1 status individually have prognostic value at this time.

Conclusion:
This study demonstrated how powerful tools like CLG and Excel can analyze large amounts of retrospective data. By doing so, prognostic indicators can be identified and better indicate which patient populations require more aggressive treatments. Further study is necessary to identify which immunophenotypical profiles of DLBCL have predictive value.

An Accurate Nuclei Detection and Segmentation Method based on Multi-scale Edge Selection in Polar Space

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Content:
Cell nuclei in 2D pathology images can yield quantitative information about the presence or the absence of disease processes. Segmenting nuclei correctly with minimum human effort is important for problems involving large numbers of cells, and patients. We describe an alternative nuclei segmentation method, which we call multi-scale edge selection in polar space (MESPS). It takes as input 2D pathology images and outputs segmentation results with little effort for parameter tuning or human intervention.

Technology:
1. Nuclei detection
We construct a filter bank composed with rings of different sizes. Then the input image is convolved with the filters to generate the response map via normalized cross correlation. The peaks in the response map are thresholded and the seeds are finally obtained by calculating the mass center of each connected component.

2. Nuclei segmentation
Edge maps are generated at different levels of image blurring followed by edge selection performed at each level in polar space. With an edge continuity constraint, the algorithm takes selected edges at coarser scales as guidance to select edges at finer scales. The algorithm outputs final contour with the highest likelihood of being correct, as measured through a well-defined energy term.

Design:
We demonstrated the performance of our method on liver histopathology and mesothelioma cytopathology datasets. With hand segmented "ground truth data", the segmentation results are quantified using area error rate (AER) and normalized sum of distances (NSD). Moreover, we compared our method with several state of the art methods level set, template matching, the ovuscule.

Results:
The quantified segmentation results are shown in Table 1.

Table 1. Segmentation results on two datasets (AER/NSD (10x)).

Algorithms	Level set	Template matching	The ovuscule	Our method
Liver dataset	63.32% /5.12	35.29% /1.32	22.31% /0.75	19.39% /0.38
Mesothelioma dataset	7.93% /0.29	13.38% /0.56	10.86% /0.47	7.99% /0.25

Conclusion:
The proposed method showed satisfying performance by quantitative evaluation on real datasets. Most importantly, the algorithm is automatic and robust. Edge iteration in our method can make the contour tightly attached to the borders of nuclei, which can reduce the noisy information induced in segmentation step and thus potentially improve the classification accuracy.

A Clinical-Grade Variant Template Designed to Support Genomic Data Integration into Clinical Applications

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Content:
The absence of adopted standards for representing human genomic sequence variants detected by clinical next-generation sequencing is a challenge to developing interoperable systems for clinical and public health applications. We present a clinical-grade variant template that provides a model for genomic data representation that addresses these challenges.

Technology:
Health information systems and messaging formats are evolving to manage genomic data. The Clinical-Grade Variant Template was developed to support clinical genomic sequencing applications by providing a format and constrained data fields amenable to the messaging of a patient's genomic data generated from next-generation sequencing technologies.

Design:
A national workgroup was convened and facilitated by the Centers for Disease Control and Prevention to develop a clinical-grade variant file template. To assure synergy with existing initiatives, the workgroup collaborated with a number of federal partners (US Food and Drug Administration, National Institute of Standards, National Center for Biotechnology Information), and others in public and private settings.

Results:
The workgroup developed a clinical-grade variant template. The template contains three sections: 1) general data about the patient and test methods, 2) the clinically relevant findings, and 3) the sequence dataset generated by

genomic sequencing prior to clinical assessment (The VCF specification is recommended for this latter element). Certain laboratory methods require standardization to permit the generation of constrained data. For example, the designation of consistent position assignments requires alignment against the human genome reference assembly. The workgroup also recommended that variant callers be set to output reference variant, no call, and local phasing data, at least in clinically important regions of the genome to reduce ambiguity in variant descriptions. Other constrained data were recommended as relevant to data exchange among clinical entities and consistent with other initiatives (e.g., the HL7 Clinical Genomics Workgroup). However, the description of quality metrics remains challenging because calibration protocols vary by method and laboratory setting.

Conclusion:
The clinical-grade variant template is designed to inform processes for genomic data representation amenable to clinical applications and to support of systems interoperability. Currently, the workgroup is designing a use case to evaluate the utility of the template.

Creating a Wiki for the Adaptation, Management and Execution of PIER

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Content:
A lack of structured educational resources regarding informatics is a common occurrence in pathology residency programs. This often leads to deficiencies in the core knowledge and skill sets required by graduating pathologists. At our institution, laboratory management and informatics is a required one-month rotation, and a review of its syllabus revealed unstructured objectives without clear expectations, necessitating improvements based on a newly released research-based instructional resource guide: Pathology Informatics Essentials for Residents (PIER).

Technology:
In order to actively implement PIER, the need for a system that would allow for the creation and modification of content was identified, and the dynamic framework of a wiki (content management system) was most suitable for this function. MediaWiki, a free, server-based, scalable, and feature-rich wiki application was installed and configured in an Apache Linux web server, which uses PHP to process and present information stored in a MySQL database.

Design:
A wiki (http://slrbimcpathology.com/wiki) with a minimalistic user interface was created as a platform to manage the educational objectives formulated by PIER. In order to create and edit content, residents acquire a user account, whose access and ability permissions need to be approved by the wiki administrator, restricting content modification to authorized users.

Results:
By utilizing MediaWiki's revision history tracker and a mobile timekeeping application, it was determined that the manual installation of the wiki, database configuration, and user interface design, comprised a total of 6.5 hours. As an initial assessment of the project, three residents with an interest in pathology informatics were assigned a PIER Essentials 1 topic and asked to populate a wiki page based on the 'Rationale', 'PIER Outcomes', and 'Content' described in the toolkit. Following a short instructional tutorial on a MediaWiki's wikitext format, the average time to completion of a topic page by a contributing resident was 67 minutes.

Conclusion:
By using a wiki as an educational tool for pathology informatics training, we have been able to restructure our laboratory management and informatics rotation. Through the creation and editing of content, it is our impression that residents will be actively engaged in the learning process allowing them to better retain the knowledge and skills obtained. Future aims include the continuous maintenance of up-to-date wiki topics, evaluation of residents' pre and post pathology informatics competency, as well as an assessment of PIER outcome achievements.

Impact of Social Media on Scholarly Informatics Articles

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Content:
Citations in peer-reviewed journals and impact factors are currently considered the gold-standard of gauging the scientific influence of published articles. However, formal citations in the literature take time to accumulate. Traditional journal metrics such as citation index have also been influenced by the launch of Open Access journals. The role of alternative metrics (aka altmetrics) such as mentions in blogs and social media platforms for measuring the impact of scholarly publications is uncertain. Our aim was explore the impact of social media websites on articles published in the Journal of Pathology Informatics (JPI).

Technology:
JPI (published by Medknow, part of Wolters Kluwer) is an Open Access peer-reviewed journal. Facebook and Twitter accounts were established to publicize JPI articles.

Design:
Two articles both about digital imaging in pathology that were published close together in JPI were chosen for this study. Article #1 was posted as a hyperlink on Facebook and Twitter two days following publication. Article #2 was not mentioned on any of the JPI social media websites. We evaluated the statistics (number of views, prints, emails, and downloads) for these two articles from the JPI website at 3 and 6 months following publication.

Results:
The JPI Facebook homepage has 5,541 likes and Twitter account 496 followers. The table compares the statistics for these two articles.

Article	Published	Posted on Twitter and Facebook	# of views	# of prints	# emailed	# of PDF downloads
#1	7/28/2014	7/30/2014	448	35	0	102
#2	11/28/2014	Never	338	14	1	179

Conclusion:
These data do not support the notion that publicizing scholarly articles with social media greatly influences their popularity. Perhaps following more and different types articles over longer time frames and using other measures (e.g. rate of re-posting articles by followers) may be more informative. Additional investigation into cyberpsychology and the role of social media on scientific research and articles is warranted.

EGFR-Sure Gold Nanorods Precisely Quantify EGFR Expression

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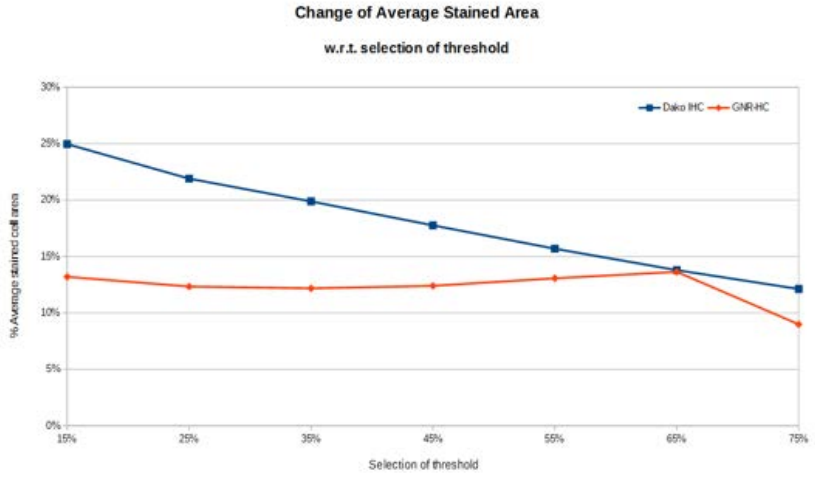
Content:
Epidermal growth factor receptor (EGFR) is a cell surface receptor that is overexpressed in a variety of epithelial tumors such as colon carcinoma and non-small cell lung carcinoma. Precise determination of the EGFR expression levels is important in the selection of therapeutic approaches such as Cetuximab therapy. The only FDA approved

test for EGFR is the immunohistochemical (IHC) method called EGFR PharmDx Kit developed by Dako. Several studies have confirmed that IHC methods are not sufficiently accurate in determining EGFR expression. Here, we report an automated image analysis method to show that our previously developed nanotechnology based EGFR detection kit (EGFR-Sure) is able to consistently quantify EGFR expression.

Technology:
Gold nanorods (GNR) were synthesized at University of Missouri and linked with peptides engineered to bond with EGFR. Images of lung and colon carcinomas stained with an immunohistochemical method (EGFR PharmDx Kit) by Dako and EGFR-Sure nanorods were taken with a Leica DM5500 microscope. In-house developed image analysis software written in Matlab by Mathworks was used to analyze images.

Design:
Several fields of lung and colon adenocarcinomas stained with EGFR-Sure and PharmDx Kit were imaged to compare the robustness of quantification. Specimens were also stained with DAPI nuclear stain. In-house developed software first finds the nuclei in the images by running an active contour algorithm. Then, cytoplasm regions were computed by a watershed algorithm for each nucleus. The amount of stain was computed as a percentage per cell area by thresholding the stain channel and counting pixels within the cytoplasm. Several different thresholds were used to analyze robustness of the quantification.

Results:
Quantification of the developed GNR is consistent among a variety of thresholds in comparison to conventional IHC stain as shown in the figure. Variance of IHC stain quantity is about three fold greater than that of EGFR-Sure, and is dependent on the selection of the threshold.



Threshold	Dako IHC	GNR-HC
15%	0.250	0.132
25%	0.219	0.123
35%	0.199	0.122
45%	0.178	0.124
55%	0.157	0.131
65%	0.138	0.136
75%	0.121	0.090
stdev	**0.0456**	**0.0154**

Conclusions:
Developed GNR is robust to the choice of parameters and produces consistent quantitative values. It provides precise quantification of EGFR expression and has also great potential to be suitable for precision medicine applications.

CubiePEIR: A Next-Generation Linux/armhf Single Board Computer with an Integrated Pathology Learning Environment and a Telepathology Platform

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Content:
One year ago, we sent a Raspberry Pi Linux /armv6 single board computer loaded with educational content to medical schools in Zambia. This computer (codenamed 'RaspberryPEIR'), while successful in its mission, had

significant I/O and processing bottlenecks. As a result, as demand for RaspberryPEIR and its resources grew, perceived and actual systems performance was dramatically reduced. Furthermore, there arose a need for telepathology that RaspberryPEIR could not meet. We therefore designed and implemented a next-generation single board pathology informatics support environment codenamed "CubiePEIR".

Design:
CubiePEIR utilizes a CubieTruck, which integrates an AllWinner A20 SoC. This SoC integrates two ARM Cortex-A7 CPU cores (instruction set architecture: ARMv7 with hardware floating-point unit), 2GB DDR3 SDRAM, an integrated 802.11n chip, and Serial ATA connectivity. The vastly increased performance of this unit allowed us to (a) directly connect a Serial ATA hard drive as a boot and storage device, (b) compile software natively on the system to maximize performance, and (c) introduce a stripped-down, commodity telepathology system based on our previous work in commodity telepathology.

Technology:
Hardware: CubieBoard CubieTruck (AllWinner A20 SoC, 2GB DDR3 SDRAM, Broadcom BCM4392 802.11n) and Western Digital 500GB SATA HDD; Operating System: Cubian Linux; Web Server: nginx 1.6; Database: MySQL 5.5; Programming Language: PHP-FPM 5.5; Web-Based WSI: OpenSlide 3.4.0, OpenSeadragon 1.0.0; Wireless Routing: ISC-DHCP-Server 4.1 and Bind9 9.8; Telepathology: OpenTelePath 0.2

Results:
CubiePEIR exhibits I/O performance that is an order of magnitude higher than that of RaspberryPEIR. It also integrates a much more advanced learning environment, including twice the number of whole slide images that were shipped with RaspberryPEIR, a full online course in Histology, and the ability to stream histology teaching sessions from a microscope via OpenTelePath.

Conclusions:
The use of cheap commodity computing as a means to provide medical education in underserved countries is both cost-effective and sustainable. CubiePEIR will allow greater numbers of trainees to have access to PEIR content, furthering medical education in regions of the world where the limitation of resources serves as a formidable barrier to education.

Lab Med Wiki: A Resource for Institution-Specific Knowledge Developed by and for Residents

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Content:
Well-established mechanisms to store, organize, and disseminate medical and scientific knowledge are readily available to residents training in laboratory medicine. However, residents also require a great deal of institution-specific knowledge to excel in their training programs. Often working in a new and unfamiliar health care system, residents begin each rotation unable to find contact information, schedules, patient data, instrument manuals, and other resources essential to their decision making process. Unfortunately, this institution-specific knowledge is often fragmented and difficult to access and can even go undocumented entirely. To address this problem, we created Lab Med Wiki, a wiki application to store, organize, and disseminate institution-specific knowledge for laboratory medicine residents.

Technology:
Server Hardware: Dell PowerEdge R720, 32x2.3Ghz CPU cores, 192GB memory;
Server Host Virtualization Hypervisor: VMWare ESXi 5.5; VM operating system: Ubuntu 14.04.2 LTS. Programming Language: PHP-FPM 5.3; Rapid Publication Environment: MediaWiki 1.24.1.

Design:
A standard LAMP (Linux, Apache, MySQL, and PHP) stack was installed, and MediaWiki was installed and configured by residents with the assistance of the pathology department's information technology staff. Initial wiki pages were constructed based on extant department-reviewed service manuals ("survival guides") for each lab medicine service. Access to the wiki was provided to all laboratory medicine residents and fellows, and a brief introduction to the Wikimedia platform was provided at a department-wide meeting and through an instructional email.

Results:
Lab Med Wiki was used to consolidate and organize institution-specific knowledge in the laboratory medicine environment. Several examples of residents updating and utilizing the wiki will be shown. Up to date usage statistics including unique users and total uploaded content will also be presented.

Conclusion:
Lab Med Wiki has provided our residents with an organized platform to search and create institution-specific knowledge that has traditionally been difficult to access. By using Mediawiki, an open source platform, we will allow other departments and institutions to adopt the wiki format as a model to organize institution-specific knowledge.