ECDP 2023

19th EUROPEAN CONGRESS ON DIGITAL PATHOLOGY

14th–17th of June 2023 | Budapest, Hungary

PROGRAM

#ECDP2023

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ESDIP

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WELCOME MESSAGE

Dear friends, dear colleagues,

Welcome to Budapest and the 19th European Congress on Digital Pathology (ECDP), the annual meeting of the European Society of Digital and Integrative Pathology (ESDIP).
We are looking forward to the usual friendly and stimulating environment, where pathologists, biologists, technicians, computer scientists, clinicians, and industry partners will exchange views on the latest topics in digital pathology.

At this year's meeting in the center of Europe, along the Danube River connecting East, West, North and South of Europe, we will gather to share novel aspects of integrative pathology, discuss the strengths of the implementation of a digital workflow and promote the benefits and future applications of an AI-aided working environment.

The integrative dimension of this meeting will be represented by the combination of histology with molecular profiling, once again underlining that ESDIP's mission is closely aligned with these developments, where computational pathology is the key to analyzing and interpreting complex data.

ESDIP members and participants in this meeting will also have the opportunity to interact with colleagues from all over Europe and beyond, including representatives from our allied societies worldwide. ESDIP is gaining new energy and is evolving fast to advance its members, offering novel scientific, diagnostic and educational opportunities, increasing communication and ideas for innovative paths.

We look forward to enjoying ECDP2023 together with you.
With our best regards, and on behalf of the ECDP2023 Organizing Committee,

Andras Kiss, M.D., Sc.D.
Andras Matolcsy, M.D., Sc.D.
Congress Presidents

Congress Presidents

András Matolcsy (Hungary)
András Kiss (Hungary)

Organizing Committee

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Location

Corinthia Budapest
Erzsébet Körút 43-49
Budapest H-1073, Hungary

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Tiago Guedes *(Portugal)*

SCIENTIFIC PROGRAM OVERVIEW

	Thursday - 15.06.2023		Friday - 16.06.2023		Saturday - 17.06.2023
Time	**Grand Ballroom**	**Valletta I**	**Grand Ballroom**	**Valletta I**	**Grand Ballroom**
08:00 - 08:15			Breakfast Symposium	Breakfast Symposium	Breakfast Symposium
08:15 - 08:30					
08:30 - 08:45					
08:45 - 09:00					
09:00 - 09:05					
09:05 - 09:10	Opening		Virtual Pathology in Education	Digital Pathology Workflow	Future Technologies - From Research to Clinical Application
09:10 - 09:30					
09:30 - 09:50					
09:50 - 10:00	Integrative and Molecular Pathology I		Panel Discussion II - Advancing Cooperation of Clinicians and Computer Scientists		
10:00 - 10:20					
10:20 - 10:30					
10:30 - 10:45	Coffee Break		Coffee Break		Panel Discussion III - Global Task Force - Digital Pathology
10:45 - 11:00					
11:00 - 11:30			Interoperability and Standardization	Data Annotation and Preprocessing	
11:30 - 11:50	Machine Learning and AI - Clinical Application I				Coffee Break
11:50 - 12:00				Quality Control in the Real World	
12:00 - 12:15			IHE PaLM and DICOM WG 26		Industry Symposium
12:15 - 12:20					
12:20 - 12:30					
12:30 - 12:45					
12:45 - 13:00					
13:00 - 13:15	Lunch Break/ Lunch Symposium		Lunch Break/ Lunch Symposium	Lunch Break/ Lunch Symposium	Machine Learning and AI - Algorithm Development II
13:15 - 13:30					
13:30 - 13:45					
13:45 - 14:00					
14:00 - 14:20	Synoptic Reporting and Nomenclature				Closing
14:20 - 14:40			Machine Learning and AI - Clinical Application II	Integrative and Molecular Pathology II	
14:40 - 14:50	Panel Discussion I - Impact of Digital Pathology for the Community	Oral Free Presentations			Lunch
14:50 - 15:00					
15:00 - 15:15					
15:15 - 15:30					
15:30 - 15:40					
15:40 - 16:00	Coffee Break		Coffee Break		
16:00 - 16:10					
16:10 - 16:30					
16:30 - 16:50	Machine Learning and AI - Algorithm Development I	Advancements in Digital Cytopathology	ESDIP Challenge	Transforming Pathology with Emerging Technologies	
16:50 - 17:00					
17:00 - 17:10					
17:10 - 17:20					
17:20 - 17:30					
17:30 - 17:45					
17:45 - 18:00	ESDIP Annual General Meeting	Poster Reception			
18:00 - 18:15					
18:15 - 18:30					
18:30 - 19:00					
19:00 - 20:30					
20:30 - 22:00					

June 15

Grand Ballroom

09:00 - 09:30 OPENING

09:00 András Matolcsy (Hungary)
Welcome words from the Congress President

09:05 Norman Zerbe (Germany)
Welcome words from ESDIP President

09:10 András Kiss (Hungary)
AI assisted colorectal cancer screening

09:30 - 10:30 INTEGRATIVE AND MOLECULAR PATHOLOGY I

CHAIRS
Inti Zlobec (Switzerland)
András Kiss (Hungary)

INVITED SPEAKER
09:30 Matteo Fassan (Italy)
Digital pathology and artificial intelligence: new actors in the clinical evolution of pathology

ABSTRACTS
09:50 Bourgade Raphaël (France) et al.
Deep learning for detecting BRCA 1/2 mutations in high-grade ovarian cancer based on an innovative tumor segmentation method from whole-slide images (A61)

10:00 Arwa Al-Rubaian (United Kingdom) et al.
Detection of STK11 mutation in lung adenocarcinoma from WSIs via self-supervised learning (A16)

10:10 Vivien Miczán (Hungary) et al.
The Proteomic Map of Mitosis in Human Tumor Tissue (A02)

10:20 Eric Erak (United States) et al.
Predicting Prostate Cancer Molecular Subtype with Artificial Intelligence (A67)

10:30 - 11:00 Coffee Break

11:00 - 12:30 MACHINE LEARNING AND AI CLINICAL APPLICATION I

CHAIRS
Yuri Tolkach (Germany)
István Csabai (Hungary)

INVITED SPEAKER

11:00 Jeroen Van Der Laak (The Netherlands)
AI for breast cancer diagnostics

ABSTRACTS

11:20 Daniela Rodrigues (United States) et al.
HALO PD-L1 AI: Development and Validation of an Automated PD-L1 Tumour Proportion Scoring Algorithm in Non-Small Cell Lung Cancer (A31)

11:30 Shannon Doyle (The Netherlands) et al.
DCIS risk and outcome prediction using a multi-instance-based deep learning approach (A74)

11:40 Constance Boissin (Sweden) et al.
Deep learning-based risk stratification of pre-operative breast biopsies using histological images (A14)

11:50 Ruoyu Wang (United Kingdom) et al.
Consensus Subtype Classification of HPV+ Cervical Squamous Cell Carcinoma using Routine Histology Slides (A18)

12:00 Rajiv Dhir (United States) et al.
Routine Use of an AI Solution for Primary Diagnosis of Prostate Biopsies in Clinical Practice (A36)

12:10 Guillaume Balezo (Paris) et al.
An HE-only workflow for liver fibrosis assessment using HE-predicted collagen (A37)

12:20 Sarah Schmell (Germany) et al.
Validation of AI-supported assessment of HER2 gene amplification status in fluorescence in-situ hybridization (FISH) whole slide images (A65)

12:30 - 14:00 Lunch Break

14:00 - 14:40 SYNOPTIC REPORTING AND NOMENCLATURE

CHAIRS
Eva Krpelanova (Switzerland)
Sabine Leh (Norway)

INVITED SPEAKER
14:00 Tibor Glasz (Hungary)
Informatic solutions for nationwide use in Hungarian digital pathology

ABSTRACTS
14:20 Harriet Evans (United Kingdom) et al.
Using Systemised Nomenclature of Medicine (SNOMED) codes to select digital pathology whole slide images for long-term archiving. (A49)

14:30 Cleo-Aron Weis (Germany) et al.
Knowledge Graphs in (Nephro-)pathology for decision tree extraction (A07)

14:40 - 15:40 PANEL DISCUSSION I - IMPACT OF DIGITAL PATHOLOGY FOR THE COMMUNITY

PANELISTS
András Kiss (Hungary)
Nina Linder (Finland)
Janina Kulka (Hungary)
Balázs Rozványi (Hungary)

15:40 - 16:10 Coffee Break

16:10 - 17:30 MACHINE LEARNING AND AI ALGORITHM DEVELOPMENT I

CHAIRS
Peter Hufnagl (Germany)
Peter Boor (Germany)

INVITED SPEAKER

16:10 Diana Montezuma (Portugal)
Bridging Art and Pathology: Annotating for ML/algorithm development in Pathology

ABSTRACTS

16:30 Anthony Moreau (France) et al.
A fully automatic TILs assessment tool (A11)

16:40 Tomé Albuquerque (Germany) et al.
Multimodal Identification of Brain Tumor Biomarkers using a Deep Fusion Strategy from MRI and Digital Pathology exams (A05)

16:50 Joona Pohjonen (Finland) et al.
HistoEncoder: Building a foundation model for histopathology (A64)

17:00 Mira Valkonen (Finland) et al.
How many samples is enough? How will self-supervised pre-training affect model accuracy, robustness and generalisation? (A38)

17:10 Abhinav Sharma (Sweden) et al.
Exploring the decision-making of weakly supervised CNN models for histopathology image classification (A78)

17:20 Raja Muhammad Saad Bashir (United Kingdom) et al.
Semi-Supervised Contrastive Learning for Semantic Segmentation of Histology Images (A41)

17:30 ESDIP Annual General Meeting

Valletta I

14:00 - 15:40 ORAL FREE PRESENTATIONS

CHAIRS
Mircea-Sebastian Serbanescu (Romania)
Renate Kain (Austria)

ABSTRACTS

14:00 Iuliu Gabriel Cocuz (Romania) et al.
Digital Pathology awareness on Pathology Residents in Romania – A multicenter study (A23)

14:10 Yuri Tolkach (Germany) et al.
Clinical-grade tumor detection and tissue segmentation in colorectal specimens using artificial intelligence tool (A75)

14:20 David Anglada Rotger (Spain) et al.
A Generic Pipeline for Cell Semantic Segmentation in Histopathological Images (A13)

14:30 Christian Abbet (Switzerland) et al.
Impact of Scanner Variability on Colorectal Cancer Tumor Segmentation (A15)

14:40 Hrafn Weishaupt (Norway) et al.
Deep learning-based segmentation of glomeruli: Detection of erroneous annotations through morphometric analysis (A45)

14:50 Suze Roostee (Sweden) et al.
Decoding the Interplay between Immune Response and Somatic Tumour Mutations in Triple-Negative Breast Cancer (A73)

15:00 Selim Sevim (Turkey) et al.
Artificial intelligence can be handy in detecting lymph node metastases of common tumors (A08)

15:10 Ana Leni Frei (Switzerland) et al.
Swiss national study on the impact of computer-aided diagnosis systems on pathologists' scoring: an application for tumor cell fraction estimation (A62)

15:20 Zehra Talat (Pakistan)
A Novel Deep Learning-Based Mitosis Recognition Approach and Dataset for Uterine Leiomyosarcoma Histopathology (A01)

15:30 Paola Chiara Rizzo (Italy) et al.
Temporal and geographical insight into the global adoption of DP: a review of the published literature (A17)

15:40 - 16:10 Coffee Break

16:10 - 17:30 ADVANCEMENTS IN DIGITAL CYTOPATHOLOGY

CHAIRS
Andrey Bychkov (Japan)
Vincenzo L'Imperio (Italy)

ABSTRACTS

16:30 Kazuki Kanayama (Japan) et al.
Respiratory cytology support system using homology profile for clinical application (A03)

16:40 Martina Verri (Italy) et al.
Instant Immunohistochemistry in Digital Pathology (A55)

16:50 Volodymyr Chapman (United Kingdom) et al.
Automation of cytological grading in Follicular Lymphoma evidences polarising impact of immunochemotherapy in high grade cases (A19)

17:00 Henning Höfener (Germany) et al.
A Workflow for efficient creation of high quality cell classification data sets (A25)

17:10 Farina Kock (Germany) et al.
Transfer learning for cell detection in bone marrow smears (A58)

17:30 - 20:30 POSTER RECEPTION AND GET TOGETHER (EXHIBITION)

17:45 - 18:30 ESDIP ANNUAL GENERAL MEETING

JUNE 16

Grand Ballroom

09:00 - 09:50 VIRTUAL PATHOLOGY IN EDUCATION

CHAIRS
Luca Cima (Italy)
András Matolcsy (Hungary)

INVITED SPEAKER
09:00 Lewis Hassel (United States)
The OPEN Solution: DP opens the way to solving workforce deficit (A06)

ABSTRACTS
09:20 Umair Khan (Finland) et al.
AI-driven multi-organ H&E virtual histopathology staining (A04)

09:30 Markus Plass (Austria) et al.
CARVIS-WSI: An open source tool for Cartographic Visualization of the Diagnostic Path on Whole Slide Images (A57)

09:40 Mohammad Faizal Ahmad Fauzi (Malaysia) et al.
AI for Digital Pathology (AI4DP) Research Excellence Consortium: An Initiative to Kickstart Digital Pathology Research in Malaysia (A54)

09:50 - 10:30 PANEL DISCUSSION II - ADVANCING COOPERATION OF CLINICIANS AND COMPUTER SCIENTISTS

PANELISTS
Sabine Leh (Norway)
Inti Zlobec (Switzerland)
Gloria Bueno (Spain)
Rajiv Kaushal (India)
Marcial Garcia Rojo (Spain)

10:30 - 11:00 Coffee Break

11:00 - 12:00 INTEROPERABILITY AND STANDARDIZATION

INVITED SPEAKER

11:00 Dagmar Krefting (Germany)

ABSTRACTS

11:20 Harriet Evans (United Kingdom) et al.
A proposed approach for standardised semantic annotation of digital histopathology slides at the point of diagnosis (A50)

11:30 Yixiao Zhao (United States) et al.
Standardisation and De-Identification of Whole Slide Images for Digital Pathology Data Management (A44)

11:40 Kai Standvoss (Germany) et al.
Image Standardization in Pathology could improve Learnability for AI Models (A30)

11:50 Richard Salmon (United Kingdom)
A Pathology of Digitisation in Digital Pathology - Scanner Color Standardisation and QA (A43)

12:00 - 12:30 IHE PALM AND DICOM WG 26

12:00 Markus Herrmann (Switerzland)
Report from DICOM Connectathon

12:30 - 14:00 Lunch Break

14:00 - 15:30 MACHINE LEARNING AND AI - CLINICAL APPLICATION II

CHAIRS
Alex Haragan (United Kingdom)
Johan Lundin (Finland)

INVITED SPEAKER

14:00 Yuri Tolkach (Germany)
Diagnostic AI algorithms: from development to application

ABSTRACTS

14:20 Zaibo Li (United States) et al.
Artificial intelligence aided detection of sentinel lymph node metastasis on histologic whole slide images in a digital workflow (A24)

14:40 Bhakti Baheti (United States) et al.
Unsupervised clustering of morphology patterns on whole slide images guide prognostic stratification of glioblastoma patients (A33)

14:50 Yun Joo Cho (South Korea) et al.
Prognostic Impact of Tertiary Lymphoid Structures in Epstein-Barr Virus-associated Gastric Carcinomas measured by Digital Image Analysis (A35)

15:00 Mostafa Jahanifar (United Kingdom) et al.
Robust and Efficient Detection of Mitotic Figures (A20)

15:10 Hilde Smits (The Netherlands) et al.
Using intratumor heterogeneity of IHC biomarkers to classify laryngeal and hypopharyngeal tumors based on histological features (A68)

15:20 Giorgio Cazzaniga (Italia) et al.
Amyloid detection through Congo red fluorescence in the digital nephropathology laboratory (A09)

15:30 - 16:00 Coffee Break

16:00 - 17:30 TRANSFORMING PATHOLOGY WITH EMERGING TECHNOLOGIES

CHAIRS
Nasir Rajpoot (United Kingdom)
Dejan Dobi (Hungary)

INVITED SPEAKER

16:00 Andrey Bychkov (Japan)
Transforming Pathology with Emerging Technologies: A Look into the Future

ABSTRACTS

16:30 Mark Eastwood (United Kingdom) et al.
Interactive Model Visualization on Whole Slide Images (A66)

16:40 Kim Nijsten (Belgium) et al.
Optimization of immunofluorescence slide digitization (A76)

16:50 Daniele Davoli (Italy) et al.
Automated Diagnosis of Pancreatic Cancer through Deep Learning and Ex-vivo Fluorescence Confocal Laser Microscopy: A New Frontier in Digital Pathology (A69)

17:00 Sangjoon Choi (South Korea) et al.
Direct comparison of GeoMX DSP and OPAL multiplex immunohistochemistry for tumor immune microenvironment study (A26)

17:10 Hans M Hertz (Sweden) et al.
Laboratory phase-contrast imaging for 3D tumor resection margin assessment (A79)

Valletta I

09:00 - 10:30 DIGITAL PATHOLOGY WORKFLOW

CHAIRS
Mikael Björnstedt (Sweden)
Arvydas Laurinavicius (Lithuania)

INVITED SPEAKER

09:00 Jordi Temprana (Spain)
Hunting Unicorns: Digital Pathology Workflow at the Catalan Health Institute (ICS). DigiPatICS Project

ABSTRACTS

09:20 Amjad Khan (Switzerland) et al.
Streamlining, executing and validating AI algorithms on remote HPC infrastructure: An integrated approach (A47)

09:30 Rutger Fick (France) et al.
End-to-End Spermatozoid Detection in Cytology WSI: A success story in Forensic Pathology Workflow Optimization (A28)

09:40 Anna Tregubova (Russia) et al.
Automatic Counting of HPV Viral Capsid Proteins expression on Whole Slide Images for Cervical Intraepithelial Lesions Diagnostics (A34)

09:50 Adrien Nivaggioli (France) et al.
Automatic Detection of Lymphovascular Emboli in Whole Slide Breast Histopathology Images (A40)

10:00 Philipp Nolte (Germany) et al.
Post-Sectioning Verification and spatial Correlation of 2D histological Slices with 3D CT-Scans through 3D printed Phantoms (A48)

10:10 Yukako Yagi (United States) et al.
Whole Tissue Imaging and Whole Block Imaging in Pathology Practice and Research (A80)

10:20 Patrick Stünkel (Norway) et al.
Pathology process modelling with Petri-nets on event logs (A72)

10:30 - 11:00 Coffee Break

11:00 - 11:50 DATA ANNOTATION AND PREPROCESSING

CHAIRS
Diana Montezuma (Portugal)
Jeroen Van Der Laak (The Netherlands)

INVITED SPEAKER
11:00 László Székely (Sweden)
Practical aspects of data extraction from digital images

ABSTRACTS
11:20 Tripti Bameta (India) et al.
PathCaptcha: Crowd-sourcing image labeling from experts (A22)

11:30 Mieko Ochi (Japan) et al.
Large-scale histological image dataset with various H&E stain conditions and devices including smartphone for the robust model development (A53)

11:40 Christoph Jansen (Germany) et al.
SlideMaps: An EMPAIA specification for storage and visualization of pixel-wise overlays on Whole Slide Images (A60)

11:50 - 12:30 QUALITY CONTROL IN THE REAL WORLD

CHAIRS
Lilla Madaras (Hungary)
Peter Hufnagl (Germany)

INVITED SPEAKER
11:50 Anirban Mukhopadhyay (Germany)
The Untold Story behind Privacy-Preserving Federated Pathology

ABSTRACTS

12:10 Daniela Rodrigues (United States) et al.
Automated Artificial Intelligence-Powered Artifact Detection for Quality Control of Whole-Slide Digital Pathology Images (A32)

12:20 Mélissande Cossutta (France) et al.
Digital Image Analysis as a Standardized Method for External Quality Assessment of HER2 IHC in Breast Cancer (A39)

12:30 - 14:00 Lunch Break

14:00 - 15:30 INTEGRATIVE AND MOLECULAR PATHOLOGY II

CHAIRS
András Kiss (Hungary)
Rasmus Kiehl (Germany)

INVITED SPEAKER

14:00 Jochen Lennerz (United States)
Unlocking the power of integrated diagnostics for better patient care - A focused approach for clinical implementation

ABSTRACTS

14:20 Neda Zamanitajeddin (United Kingdom) et al.
Integrating Social Network Analysis and Deep Learning for Improved Prediction of Molecular Pathways in Colorectal Cancer (A21)

14:30 Mauro Gwerder (Switzerland) et al.
Characterizing the expression landscape of colorectal tumor buds by machine-learning based analysis of seqIF images (A42)

14:40 Davide Seminati (Italia) et al.
A combined digital and molecular approach to precision oncology: the lung and breast cancer use cases (A10)

14:50 Dea Natalie Munch Jepsen (Denmark) et al.
Infiltration of lymphocytes assessed by deep learning-based algorithms and the association with response to neoadjuvant therapy in rectal cancer (A12)

15:00 Subhash Yadav (India) et al.
Using Deep Learning on H&E stained Histopathology Slides for HPV Detection in Head Neck Cancer (A52)

15:10 Dejan Dobi (Hungary) et al.
Digital pathology and gene expression analysis as potential tools of standardization for renal transplant pathology (A77)

15:20 Sanja Despotović (Serbia) et al.
Altered organization of collagen fibers in the uninvoled human colon mucosa 10 cm and 20 cm away from the colorectal cancer (A70)

15:30 - 16:00 Coffee Break

16:00 - 17:30 ESDIP CHALLENGE

16:00-16:05 Yuri Tolkach (Germany)
Introduction

16:05-16:15 Marie-Lisa Eich (Germany)
SemiCOL Challenge: a focus on the clinical perspective

16:15-16:25 Jonathan Stieber (Germany)
SemiCOL Challenge: Technical Aspects and Evaluation Results

16:25-16:34 Team 1
Presentation of algorithm

16:34-16:43 Team 2
Presentation of algorithm

16:43-16:52 Team 3
Presentation of algorithm

16:52-17:01 Team 4
Presentation of algorithm

17:01-17:10 Team 5
Presentation of algorithm

17:10-17:19 Team 6
Presentation of algorithm

17:19-17:30 Anirban Mukhopadhyay (Germany)
Concluding remarks

June 17

Grand Ballroom

09:00 - 10:30 FUTURE TECHNOLOGIES - FROM RESEARCH TO CLINICAL APPLICATION

CHAIRS

Norman Zerbe (Germany)
Vincenzo L'Imperio (Italy)

INVITED SPEAKERS

09:00 Andrew Smith (Italy)
Rendering the invisible visible: Adding a molecular dimension to pathology with mass spectrometry driven spatial omics

09:20 Miklós Szócska (Hungary)
Data-driven health as systems capability

ABSTRACTS

09:40 Sonja Koivukoski (Finland) et al.
Unstained tissue imaging and virtual HE staining of whole slide images: an assessment of histological feasibility (A71)

09:50 Miklós Vincze (Hungary) et al.
3D visualization in digital pathology using VR technology (A56)

10:00 Aray Karjauv (Germany) et al.
Neural Style Transfer as a Service (A51)

10:10 Bence Biricz (Hungary) et al.
The fundamental points of testing a pathological virtual reality software (A63)

10:20 Teodora Trandafir (The Netherlands) et al.
Artificial Intelligence-Aided Three-Dimensional Quantification of Thrombosis Occurrence in Lungs Affected by COVID-19 (A81)

10:30 - 11:15 PANEL DISCUSSION III - GLOBAL TASK FORCE - DIGITAL PATHOLOGY

PANELISTS
Norman Zerbe (Germany)
Junya Fukuoka (Japan)
Liron Pantanowitz (United States)

11:15 - 11:45 Coffee Break

12:30 - 13:30 MACHINE LEARNING AND AI ALGORITHM DEVELOPMENT II

CHAIRS
Rita Carvalho (Germany)
Vincenzo Della Mea (Italy)

INVITED SPEAKER
12:30 Nasir Rajpoot (United Kingdom)
Interpretable AI for Pathology

ABSTRACTS
12:50 Felipe Miranda Ruiz (Germany) et al.
Using CNN Stability Training increases robustness to scanner and IHC-based image variability for epithelium segmentation in cervical histology (A29)

13:00	Yoni Schirris (The Netherlands) et al. **DeepSTIL: a robust deep-learning based tumor-infiltrating lymphocyte scoring pipeline trained solely on open source data (A46)**
13:10	Matej Gallo (Czech Republic) et al. **Shedding Light on the Black Box of a Neural Network Trained to Detect Prostate Cancer in Whole Slide Images by Occlusion-Based Explainability (A27)**
13:20	Ana Leni Frei (Switzerland) et al. **Merging local cell feature and global tissue structure to learn accurate epithelial cell classification on H&E images (A59)**
13:30 - 13:45	Closing
13:45 - 15:00	Lunch

A01

A Novel Deep Learning-Based Mitosis Recognition Approach and Dataset for Uterine Leiomyosarcoma Histopathology

Zehra Talat[1]
[1)] Pathology department, Jinnah sindh medical university, Pakistan

Introduction

Uterine leiomyosarcoma (ULMS) is a type of rare cancer among malignant gynecologic tumors that arises from the smooth muscle of the uterine wall [1]. Mitosis is an important biomarker widely used for the diagnosis of different cancers including ULMS [2]. In histopathological examinations, it is usually detected via visual inspections of histopathology slide images under high-resolution microscopes. In recent years, technological innovations and new image analysis systems have offered new, reliable, and accurate approaches for a more objective assessment of tumor aggressiveness. Artificial intelligence (AI) is increasingly being used for the automatic counting of mitotic figures [1 &2]. Motivated by these AI-based studies, we aimed to use deep-learning architecture to automate the process of ULMS diagnosis. In this paper, we present an artificial Intelligence (AI) based automatic detection of mitoses in Uterine Leiomyosarcoma.

Material and methods

In this study supervised learning based method was used. We collected our dataset from a local medical facility in collaboration with highly trained pathologists. The dataset was collected at Atia Hospital, Karachi Pakistan under the IRB# AGH/IRB/2021/01 Preprocessing and annotations are performed using standard procedures, and a deep learning-based method is applied to provide baseline accuracies Figures (3&4). The slides were made digital at 40x by microscope connected camera by a pathologist and annotated for mitosis. Computer scientists than trained the annotated data and apply the YOLOv4 model.

Results and discussion

Preliminary results show AI as promising solution for detection of mitotically active regions in Uterine leiomyosarcoma cases and can be used as a second opinion system. The experimental results showed 0.7462 precision, 0.8981 recall, and 0.8151 F1-score. For research and development, the code and dataset have been made publicly available.

Conclusion

In this paper, we presented an AI-based automated method for mitosis detection in uterine leiomyosarcoma (ULMS) histopathology images. Its results were appreciated. We had certain limitations like we made digital slides instead of whole slide images due to unavailabity of scanner. AI based algorithms can work on digital slides as well. So one can start itd digital journey in financial constrains setup as well.

Key words: leiomyosarcoma diagnosis, mitosis identification, deep learning, YOLOv4

A02

The Proteomic Map of Mitosis in Human Tumor Tissue

Vivien Miczán[1], Zsanett Zsófia Iván[1, 2], István Grexa[1, 3], Réka Hollandi[1], Farkas Sükösd [4], Andreas Mund[5], Frederik Post[5], Matthias Mann[5], Péter Horváth[1, 6, 7]
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Introduction

Cancer is consistently among the leading causes of death in Europe. It is therefore crucial to develop new strategies to gain deeper understanding on tumor processes and to develop the most accurate treatment strategies. To achieve this, we aimed to map the morphological and molecular changes during cancer cell division on the single-cell level.

Material and methods

We have built a YOLO (You Only Look Once) model to detect mitotic cells on whole-slide microscopy images of human lung adenocarcinoma HE-FFPE samples and used the Regression Plane concept to determine the current mitotic stages of cells with near-infinite resolution. Our recently presented CAMI (Computer Aided Microscopy Isolation) method allowed isolation of individual mitotic cells by laser microdissection, then ultra-sensitive proteomics was applied to uncover the molecular composition of the cells.

Results and discussion

We have established tissue processing and microscopy protocols for optimal visualization of mitotic morphology, developed deep learning algorithms to detect and segment mitotic cells in human lung cancer tissue and predict their mitotic status. The ultra-sensitive proteomic analysis of the dissected mitotic cells resulted in clear distinction of the mitotic states, and the levels of many well-known mitotic proteins changed according to the literature, moreover, the exact mitotic profile of several proteins were defined and some of them implied previously undetected mitotic function.

Conclusion

We have created a workflow and a database that maps mitosis and serves as a resource for fundamental researchers and clinicians to find new targets in cancer medicine in the future based on single-cell proteome measurements.

Key words: proteomics, mitosis, cancer, FFPE, microdissection, YOLO

A03

Respiratory cytology support system using homology profile for clinical application

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Introduction

In ECDP 2022, we reported that by quantizing the "fineness" of chromatin by the homology-based idea, the histological types in lung cancer could be classified. This analysis was performed with 100x objective lens. As oil immersion is necessary when using 100x, wiping is required. This procedure has been a bottleneck in clinical application. Here, we aimed to examine whether differential of histological types by the homology analysis is possible with an image of 40x objective.

Material and methods

A total of 23 cases of lung cancer (non-small cell carcinoma 16 and small cell carcinoma 7) that diagnosed at Habikino Medical center were selected. Papanicolaou specimens were observed with a 40x objective on a KEYENCE microscopy system, and they were taken by a low-resolution (1920x1440) and high-resolution (4080x3060). The nuclei of cancer cells were randomly extracted and analyzed.

Results and discussion

In low-resolution, the average of the homology features for non-small cell carcinoma and small cell carcinoma was 0.366 and 0.323 ($P > 0.05$). Meanwhile, the average of high-resolution showed 0.059 and 0.040, there was a significant difference between them ($P = 0.0189$). Moreover, the average values for adenocarcinoma and squamous cell carcinoma were 0.077 and 0.039, significantly higher in adenocarcinoma ($P < 0.01$).

Conclusion

Differentiation of cytohistological type is an important key when deciding treatment policy. If this could be supported by an AI system, it would have significant impact on clinical practice. Since we could distinguish them, even with a 40x objective lens if the resolution is sufficient, clinical application of this system could be expected.

Key words: Cytology, Lung cancer, Homology Profile, 40x objective lens, clinical application

A04

AI-driven multi-organ H&E virtual histopathology staining

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Introduction

Virtual staining of unstained tissue images using deep learning-based image-to-image translation models has gained noticeable traction in the recent past. The high-fidelity results produced by virtual staining algorithms have been proven to be concordant with their chemically stained counterparts by other studies and by us, through quantitative evaluation. Some studies have even used virtually stained images in the downstream analysis as an auxiliary evaluation method.

Material and methods

Most previous studies on virtual staining have used specific organ tissue images. We expanded virtual histopathology staining, using a basic brightfield microscopy setup, to multiple organ tissues. We imaged preclinical tissue samples from the liver, kidney, spleen, testis, and seminal vesicle, before and after H&E staining. First, baseline pix2pix models, a commonly used supervised image-to-image translation method, were trained with multi-organ tissue images. Then, DenseU-net-based pix2pix models were trained with the same data.

Results and discussion

For the DenseU-net-based pix2pix models, we observed an increase in both mean PSNR and SSIM scores by approximately 3%. The visual histological analysis further established that the virtually stained images generated by the DenseU-net-based variant were better in quality and had fewer artifacts.

Conclusion

This experiment shows that virtual staining invariably works effectively for different organ tissues and using more dense networks could improve the resulting virtually stained image quality.

Key words: virtual staining, deep learning , computational pathology, image-to-image translation

A05

Multimodal Identification of Brain Tumor Biomarkers using a Deep Fusion Strategy from MRI and Digital Pathology exams

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Introduction

Adult-type diffuse gliomas are the most frequent malignant tumors of the central nervous system. The emergence of targeted therapy alternatives makes molecular biomarkers more appealing and directly influences the prescription of the proper treatment. However, manual screening is time-consuming and error-prone in pathological labs. To overcome this limitation, a multimodal fusion model is proposed to detect the two most critical molecular biomarkers in gliomas (IDH1 and 1p/19q codeletion) using MRI and digital pathology exams.

Material and methods

All experiments were performed on The Cancer Genome Atlas (TCGA) dataset, containing MRI and digital pathology exams for each patient. A dual path convolution neural network fusion model was designed integrating both image modalities to extract semantically consistent representations for biomarkers classification. One path of the network considers 3D tumor segmentations as input, while the other path leverages multiple instance learning techniques based on a 2D residual network as a feature encoder for pathology images.

Results and discussion

The proposed method was trained on 149 digital pathology H&E slides and MRI scans with FLAIR and T1ce modalities. It is then validated on 38 H&E and MRI exams. The proposed model outperformed its unimodal counterparts by obtaining an AUC of 87.69%, 86.32%, and 81.54% for multimodality, MRI, and H&E respectively.

Conclusion

The model achieved high results in several metrics, highlighting the possibilities of detecting semantically meaningful biomarker features and successfully classifying different glioma subtypes using deep learning systems. The model also includes interpretable features by highlighting the most important regions in H&E slides for the decision process.

Key words: Biomarker Detection, Multimodal Learning, Deep Learning, Glioma Subtyping

A06

The OPEN Solution: DP opens the way to solving workforce deficit

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Introduction

Vast segments of the world population are unserved/underserved by pathologists, particularly vexing given projected increased incidence of cancer & other diseases dependent on laboratory diagnosis and management. Virtual education methods based on digital pathology tools presents an opportunity to ameliorate this problem.

Material and methods

Utilizing digital pathology (DP) resources and open source learning management tools, a virtual training program (Open Pathology Education Network) for pathology trainees and others is being deployed at www.open-pathology.org. The method employs extant teaching and DP resources in an organized, sequential fashion to enable virtual training, augmented by live mentoring sessions. Two pilot projects in gynecologic pathology and urine cytology have been in operation for 6-12 months, training mentees in Vietnam entirely remotely as proof of concept.

Results and discussion

Recruitment of interested individuals into training has been highly successful, with potential multiplier effects noted when training occurs in leading provider centers. Time differences for live sessions have been surmounted. Organization and deployment of training materials, self-assessments and pre- and post-test assessments has been facilitated by migration of the materials to a learning management platform. Live mentoring sessions have been well attended. Performance on assessments shows marked improvement, and real-life improvements, based on portion of cases presented in multidisciplinary tumor boards that face diagnostic challenge by external pathology reviewers, are sizable (decreasing from 50% to less than 25% on non-statistical sample). Enthusiastic broad support indicates widespread awareness that this idea has great potential and could fill a large need.

Conclusion

OPEN is a solution to the challenge of insufficient and incompletely trained pathologists worldwide.

Key words: Workforce, low resource settings, pathology education, virtual education, digital pathology

A07

Knowledge Graphs in (Nephro-)pathology for decision tree extraction

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Introduction

Diagnostic expertise in pathology, typically stored in texts, is subject to continuous improvement. To overview this knowledge and to have a diagnostic algorithm for different diagnoses is beyond the capabilities of a single pathologist. Retrieving diagnostic information or algorithms from texts using natural language processing remains challenging. Against this background, in this project, domain-specific knowledge (from nephropathology as a use case) is first stored in a knowledge graph, based on which diagnostic decision trees are generated using different approaches.

Material and methods

Nephropathology knowledge is stored from multiple sources in a Knowledge graph, initially based on the SnomedCT Ontology. It is enriched with information from textbooks and diagnostic texts. For this purpose, the texts must first be decomposed into entities (as nodes) and their relationships (as edges) using Natural Language Processing methods. Each disease is represented by a node, and each case by a subgraph of the knowledge graph. Then different node classification models are trained to predict the diagnoses of different cases to learn relevant relations between certain nephropathological features and diseases. Finally, decision trees are extracted from the node classification model.

Results and discussion

Searching the relation between two entities in pathological texts failed in many cases due to the typical semantic style of such reports. Therefore we are to develop a custom relation extraction model based on the medspaCy-toolkit. Training a MINDWALK-tree leads to comprehensible results since it can utilize the information of the knowledge graph more efficiently.

Conclusion

Converting a text classification task to a node classification task benefits from additional information stored within a knowledge graph.

Key words: Diagnostic Decision Trees, Knowledge Graphs, Nephropathology, Text Classification, Node classification , Decision Tree Induction

A08

Artificial intelligence can be handy in detecting lymph node metastases of common tumors

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Introduction

Papillary thyroid carcinoma (PTC) and breast invasive ductal carcinoma (IDC) are common carcinomas which often metastasize to regional lymph nodes (LNs). Although the accurate evaluation of LNs is very important in terms of guiding the treatment, this routine task is time-consuming and tedious. We investigated whether artificial intelligence (AI) can distinguish between metastatic and non-metastatic areas via whole slide images (WSIs) obtained from LNs of PTC and IDC.

Material and methods

HE slides of LNs from 44 PTC, 57 IDC (303 LNs) were scanned (3D HISTECH, Panoramic P250 Flash3). After manual annotation and color normalization, WSIs were used for testing (%20), training (65%), and training validation (15%). UnetPlusPlus, ImageNet, Efficientnet-b3 and Resnet were used for LN segmentation, transfer learning, feature extraction for LN detection and to detect tumors, at different zoom levels (ZL), respectively.

Results and discussion

AUC: 0.9717, accuracy: 0.9554, recall: 0.9702, precision: 0.8492, F-score: 0.8850 were found in LN detection/segmentation. In the IDC and PTC groups, scores for separating tumoral and non-tumoral areas in LNs were found as accuracy: 0.9656/0.9818, recall: 0.9185/0.9507, precision: 0.9248/0.8749, F-score: 0.8727/0.8430 by AI, at 13x ZL, respectively. In distinguishing PTC and IDC; sensitivity, specificity, recall, precision, F-score and accuracy were found to be higher than 0.97, at 13x ZL.

Conclusion

AI recognizes metastases with considerable accuracy. With the perfection of AI algorithms, it can be expected that AI will replace the pathologist in time-consuming tasks in the near future, providing the precious time we need for more sophisticated and enjoyable tasks.

Key words: pathology, artificial intelligence, whole slide imaging, region of interest, lymph node, metastasis

A09

Amyloid detection through Congo red fluorescence in the digital nephropathology laboratory

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Introduction

The digital transition in nephropathology labs needs integration of different imaging sources, including the need to report the Congo red stain birefringence in amyloidosis, but polarized-light scanners are still largely unavailable. Congo red fluorescence (CRF) can be used as an alternative with comparable diagnostic reliability.

Material and methods

Here we evaluated 72 Congo red stained renal biopsies scanned with Nanozoomer S60 (Hamamatsu, Shizuoka, Japan) in bright- and dark-field with a TRITC filter. Two renal pathologists evaluated the slides in blind for CRF and quantified the deposits through Amyloid Score (AS). Cohen's kappa was used to calculate the interobserver agreement, Pearson correlation coefficient has been used to evaluate the variability in the assessment of the different structures (mesangial, capillary, interstitial and vascular).

Results and discussion

Overall, 21% of cases (15/72) were considered CRF+ by at least one observer, with a complete concordance with the traditional birefringence. Optimal inter-observer agreement was recorded for the in blind evaluation of CRF (k=0.86), with no false positive and three false negative cases, characterized by a low amount of amyloid deposits, as determined by the AS (1/12). The evaluation of AS showed excellent correlation overall (r=0.95), with optimal concordance for glomerular capillaries and interstitium (r=0.82 and 0.86), good for vascular (r=0.78) and fair for mesangial areas (r=0.5).

Conclusion

This study demonstrates the reliable role of CRF in the assessment of renal amyloidosis, enabling the extension of digital pathology application also to this field of nephropathology.

Key words: Amyloid, Kidney Biopsy, Fluorescence Scanner, WSI

A10

A combined digital and molecular approach to precision oncology: the lung and breast cancer use cases

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Introduction

Molecular testing has become increasingly important in the diagnosis and treatment of breast cancer (BC) and non-small cell lung cancer (NSCLC). The use of these tests has grown rapidly in recent years as they have been shown to provide more accurate and detailed information about the genetic characteristics of the tumor, leading to more effective treatment options.

Material and methods

In order to assess the impact of molecular testing on a pathology department, data for BC and NSCLC was extracted from the Laboratory Information System (LIS) of the Pathology department of Fondazione IRCCS San Gerardo dei TIntori over the year period from 2020 to 2022. The number and percentage of tests performed were estimated from data extracted and estimation of costs per case was performed based on the currently recognized reimbursement from the National Health System.

Results and discussion

Increased use of Gene Expression Profiling, performed on 4,54% of BC cases in 2022, and Next Generation Sequencing, performed on 42% NSCLC cases in 2022, led to higher average institution costs per patient (54% and 140% rise, respectively). This shift to molecular testing has reduced single gene testing in NSCLC, causing a 58% drop in RT-PCR and 50% decrease in IHC predictive tests.

Conclusion

The paradigm shift in the assessment of BC and NSCLC cases due to the Introduction of molecular tests changed the landscape of pathology departments from an organization and economic point of view. The integration of different data sources thanks to digital pathology and LIS dashboards allowed us to track the dynamic changes of this precision oncology transition.

Key words: laboratory information system, NSCLC, breast cancer, NGS, gene expression profiling

A11

A fully automatic TILs assessment tool

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Introduction

Tumor infiltrating lymphocytes (TILs) quantification has proven a reliable prognosis factor for multiple cancer types in multiple organs and particularly in breast cancer. However, despite efforts to standardize TILs score assessment, this process is subject to substantial inter-reader variability and biases. The interest for computational assessment of TILs score has therefore been growing. In this context, we propose a fully automatic tool for TILs grading on WSI.

Material and methods

To prove reliability and generalizability, the algorithm was tested on publicly available TIGER dataset and on an in-house dataset of both biopsies and surgical samples. The proposed processing pipeline includes three separate steps. The first one consists of a Deep Learning cancer localisation model, trained using CycleGAN augmented data in order to achieve stain invariance. This step is followed by a combined segmentation of stroma and lymphocytes on cancer regions. This is performed using a convolutional backbone with two segmentation heads, that is trained through a custom multi-phase process. The final TILs score is computed from the resulting segmentations.

Results and discussion

The proposed pipeline showed state-of-the-art performance TIGER dataset with a DICE of 84.9 ± 1.0 for stroma segmentation and 84.4 ± 0.4 for TILs nuclei segmentation. Performances were also assessed on an in-house dataset. We investigated the correlation between the final TILs scores and the pathologists scores on both datasets.

Conclusion

The resulting algorithm can be integrated into a WSI analysis pipeline and, with such performance, provide pathologists with an automatic TILs assessment tool.

Key words: TILs, Breast Cancer, WSI, automatic grading

A12

Infiltration of lymphocytes assessed by deep learning-based algorithms and the association with response to neoadjuvant therapy in rectal cancer

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Introduction

The standard treatment strategy in locally advanced rectal cancer (RC) is neoadjuvant chemoradiotherapy (nCRT) followed by surgery. Patients with RC receiving nCRT achieve varying pathological response. The ability to differentiate complete from other responders could potentially save patients from an ineffective treatment. Furthermore, organ sparing in RC is an emerging goal and tools to predict complete responders are warranted. This study aimed to investigate potential differences in histopathological features between complete responders vs. all other groups.

Material and methods

We included 50 patients with RC treated with nCRT. Deep learning-based digital algorithms were developed to assess the epithelium tumor area percentage (ETP) based on hematoxylin and eosin-stained slides, and to quantify the density of CD3+ and CD8+ lymphocytes in immunohistochemically stained slides, from the diagnostic tumor biopsies. The ETP, and density of CD3+, CD8+ lymphocytes as well as the CD8/CD3-ratio were compared according to the Mandard tumor regression grade in the surgical specimens.

Results and discussion

When comparing the complete responders (n=7) to all other groups of response (n=43), there were no significant differences in the ETP ($P>0.05$). Densities of both CD3+ and CD8+ lymphocytes and the CD8/CD3-ratio in the biopsies were significantly higher in the group of complete responders ($P\leq0.05$).

Conclusion

It is well-known that the infiltration of CD3+ and CD8+ lymphocytes in colorectal cancer is a prognostic marker. In the future, assessment of infiltration of CD8+ and CD3+ lymphocytes in diagnostic biopsies of patients with RC may be useful in predicting complete response to nCRT.

Key words: Tumor-infiltrating lymphocytes, Rectal cancer, Neoadjuvant therapy, Digital image analysis, Deep learning

A13

A Generic Pipeline for Cell Semantic Segmentation in Histopathological Images

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Introduction

This work presents an AI-based generic pipeline for cell semantic segmentation in histopathological images. With the increasing digitalization in pathology, efficient image processing algorithms have gained importance. The proposed pipeline inputs a Whole Slide Image (WSI) and outputs the detection and classification of cells of the tissue. This work has been developed within the project DigiPatICS, led by the Institut Català de la Salut (ICS) together with 8 hospitals of Catalunya.

Material and methods

First, tissue is detected using mathematical morphology techniques over a downsampled WSI version, followed by a tiling process over the detected tissue regions in full resolution. Then, a basic Convolutional Neural Network is applied to discard tiles not containing relevant tissue. The next step involves two U-Net architectures, one for cell segmentation and the other for stroma-epithelium region identification. Afterwards, individual tile results are combined to create a representation of the complete WSI.

Results and discussion

This pipeline has been assessed on breast cancer diagnosis using HER2, KI67, RE, and RP stained WSIs. The obtained results have been validated by a group of pathologists from the ICS.

Conclusion

The proposed approach optimizes the segmentation process over regions of interest of WSI and speeds up the cancer diagnosis process, being able to segment and classify all cells in a WSI in 1023 seconds on average. This is an off-line process which delivers precomputed results that pathologists only have to upload and visualize. With the increasing prominence of digital pathology, this pipeline offers a reliable and efficient solution for semantic segmentation in histopathological images.

Key words: Semantic Segmentation, Histopathological Images, Digital Pathology, Cancer Diagnosis, U-Net Architechture, Deep Learning

A14

Deep learning-based risk stratification of pre-operative breast biopsies using histological images

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Introduction

Nottingham histological grade (NHG) is a well established prognostic factor for breast cancer and is important for treatment decisions. However, manual NHG assessment of biopsies are challenging, leading to a large proportion being classified as NHG 2 (intermediate risk), and to large inter-assessor variability. Here, we evaluate whether an existing model for grade-based risk stratification developed using resected tumour specimens could predict risk groups in biopsy specimens.

Material and methods

A total of 9,441,794 tiles from 903 whole slide images of haematoxylin and eosin stained biopsies from 698 patients diagnosed with cancer in Stockholm, Sweden were used to validate the previously published DeepGrade models using biopsy specimens. Classification performance for grade 1 and 3 tumours were evaluated using area under the operating curve (AUC), further subclassification of NHG 2 was performed.

Results and discussion

The DeepGrade model could classify resected tumour grades 1 and 3 using only biopsy specimens with an AUC of 0.88 (95% CI: 0.85;0.91). The model could also predict the biopsy-level NHG assessed on the biopsy of 114 patients with an AUC of 0.97 (95% CI: 0.92; 0.99). Further, out of the 284 NHG 2 tumours, 198 (70%) were classified as DeepGrade2-low, and 86 (30%) were classified as DeepGrade2-high.

Conclusion

We could predict the resected tumour grades 1 and 3 using only the biopsy specimen and sub-classify grade 2 tumours into low and high risks. The results demonstrate that deep learning models can provide decision support for biopsy grading, leading to identifying high-risk tumours earlier on, thus improving treatment decisions.

Key words: breast cancer, biopsy, grading

A15

Impact of Scanner Variability on Colorectal Cancer Tumor Segmentation

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Introduction

The impact of scanner variability on image analysis is widely discussed in digital pathology but has only been quantitatively evaluated for a few tasks, such as lymph node segmentation and prostate cancer detection. Here, we investigate the impact on the task of tissue segmentation in colorectal cancer, which is a crucial step for many downstream analyses.

Material and methods

We scan our cohort of 10 whole slide images (WSIs) with two different scanners from the same vendor (named A and B). For the tissue segmentation, we use our previously published self-supervised tissue segmentation model SRMA (Abbet et al. in Medical Image Analysis 79 (2022)). The performance is evaluated on 15 regions with an average size of 15mm2, where tissue is annotated as either tumor, stroma, or "other".

Results and discussion

When applying the model on scanner A we achieve a Dice score of 69.5% and 75.5% for the tumor and stroma segmentation, respectively. Scanner B outperforms this by nearly 6%, reaching a Dice score of 75.1% for tumor, and 80.6% for stroma segmentation.

Conclusion

We find that even models especially trained for domain shift or using data augmentation fail to completely account for scanner variabilities. Thus, rescanning slides with a different scanner could represent a fast and efficient data augmentation. Additionally, when choosing a scanner, it is also important to evaluate not only the feasibility for the lab, but also the impact on the quality of image analysis. Even between the same scanners, there can be differences depending on factors like color calibration, software version, and scanning profile.

Key words: Colorectal Cancer, Scanner Variability, Tissue Segmentation

A16

Detection of STK11 mutation in lung adenocarcinoma from WSIs via self-supervised learning

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Introduction

Detection of STK11 mutations in non-small cell lung cancer (NSCLC) is of paramount importance as several studies suggest its contribution to precision immunotherapy. Moreover, it has been shown that STK11 mutations are associated with an increased risk of cancer development. Currently these mutations are detected via genetic sequencing, a process that is tissue destructive and incurs extra costs and longer turnaround times. Detecting key mutations from Hematoxylin & Eosin (H&E) whole-slide Images (WSIs) offers the advantages of saving tissue, reduced costs, and turnaround times.

Material and methods

A total of 462 H&E WSIs from TCGA-LUAD cohort were processed at 20× magnification with 14% of the cases having STK11mutations. These slides were selected based on the compatibility of labels from GDC and CBioPortal. A self-supervised approach, in which the student model is trained to match the output of a teacher model over different augmentation of the same image, was used to pretrain the ResNet50 model. The pretrained model was then used as a backbone in the iterative draw and rank sampling (IDaRS) pipeline.

Results and discussion

We used 4-fold cross validation and achieved an average AUROC of 0.71±0.08 for detecting STK11 mutations compared to 0.67±0.06, 0.67±0.09, and 0.68±0.09 using Coudray's et.al pipeline, IDaRS and Resnet50, respectively. Our model can detect other key mutations such as TP53, KRAS, and EGFR with an AUROC of: 0.67±0.07, 0.64±0.09, and 0.64±0.08, respectively.

Conclusion

The preliminary results outperform state-of-the-art methods and show potential for predicting gene mutations from WSIs. Our future plans include enhancing the self-supervised model and the overall pipeline to improve prediction performance.

Key words: Digital pathology, Mutation prediction , Lung cancer, Deep learning

A17

Temporal and geographical insight into the global adoption of DP: a review of the published literature

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Introduction

Digital pathology (DP) is currently in the spotlight and is rapidly gaining ground, even though the history of this field spans decades. Despite great technological progress, the adoption of DP for routine clinical diagnostic use remains limited.

Material and methods

A systematic search was conducted in the electronic databases Pubmed-MEDLINE and Embase. Inclusion criteria were all published studies that encompassed any application of DP, and was designed to be an update of the original search performed by Della Mea in 2011.

Results and discussion

Of 4888 articles retrieved, 4041 papers were included, representing studies dealing with DP published over nearly four decades (between 1984 and 2022). Relevant articles were categorized as "diagnostic" (147/4041, 4%) where DP was utilized for routine diagnostic workflow and "non-diagnostic" (3894/4041, 96%) for all other applications. The "non-diagnostic" articles were further categorized according to DP application including "artificial intelligence", "education", "narrative" for reviews and editorials, and "technical" for pure research publications.

Conclusion

This manuscript provided temporal and geographical insight into the global adoption of DP by analyzing the published scientific literature. Today the literature reveals that DP is a towards mature technology that is currently deployed in many pathology laboratories, it clearly depicts the evolution of DP, from the first application with telepathology to the development of AI.

Key words: artificial intelligence, digital pathology, image analysis, systematic review, whole slide imaging

A18

Consensus Subtype Classification of HPV+ Cervical Squamous Cell Carcinoma using Routine Histology Slides

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Introduction

Identifying prognostically relevant biomarkers for stratifying HPV+ CSCCs remains a challenge. Recently, therapeutic-relevant CSCC subtypes have been identified from transcriptome analyses. We propose a deep learning framework for identifying consensus molecular subtypes from H&E-stained histology slides for HPV+ CSCC stratification.

Material and methods

Two CSCC cohorts (TCGA-CSCC, n=203, and Uganda-CSCC, n=94) collected from 28 medical centres were used as the discovery and validation cohorts, respectively. The two CSCC subtypes (C1 and C2) were identified on the discovery cohort by consensus clustering on gene expression profiles. A ranking based multiple instance learning framework was developed for predicting CSCC subtypes. Salient regions of C1 and C2 were identified using the predicted ranking scores. Cellular composition analysis was performed using an automatic cell detection pipeline.

Results and discussion

The model trained on TCGA-CSCC achieved an AUC of 0.82 for predicting consensus subtypes on the Uganda-CSCC cohort. The group predicted as C1 by our algorithm showed a statistically significant better prognosis than the group predicted as C2 in terms of the overall survival (p=0.041). Cellular composition analyses on salient regions revealed that C1 regions contain more inflammatory cells, while C2 regions contain more connective cells.

Conclusion

We proposed a model for CSCC consensus subtype prediction and showed that it can generate prognostically significant stratification on HPV+ CSCCs without transcriptome analyses. Our cellular composition analyses on salient regions may suggest impact of genetic differences on the tumour microenvironment and lead to a novel way of studying and prognosticating HPV-associated CSCCs.

Key words: Cervical squamous cell carcinoma, human papillomavirus, deep learning, consensus genetic subtypes, cellular composition, H&E

A19

Automation of cytological grading in Follicular Lymphoma evidences polarising impact of immunochemotherapy in high grade cases

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Introduction

Cytological grading in follicular lymphoma (FL) involves quantification of neoplastic cells, centroblasts, within naive B-cell regions of lymph nodes (follicles). Manual grading is laborious, suffers from poor reproducibility, and is susceptible to sampling bias. We present an automated pipeline for cytological grading, facilitating exhaustive and reproducible quantification of cell populations in H&E whole slide images.

Material and methods

H&E-stained whole slide images (WSI), scanned at 40x magnification at time of diagnosis, were available for 122 FL patients, with 6 years of clinical follow-up. For selection of follicles, an ensemble of 3 UNet models were trained on 9 exhaustively-annotated WSIs. 6 additional WSIs were used for evaluation using ROC-AUC. HoVerNet was used to segment nuclei within follicles. 66 features, including area and local binary pattern were extracted for nuclei. Cell type was assigned in a semi-supervised manner using 67,000 pathologist-annotated nuclei. Grade was assigned as per WHO centroblast thresholds, on 50 high power fields – 5x more than required. Grades were compared with outcome using Cox Proportional Hazards models.

Results and discussion

The follicle classifier achieved ROC-AUC of 0.80 on test data. Nuclei clustered into 6 groups, one enriched for centroblasts (75% of all). Consumer hardware was used for grading, processing each WSI in under 6 minutes. Cox proportional hazards models evidenced potential survival differences between high grade (grade 3) cases: hazard ratios of 1.10 (95% CI: 0 – 2.4x10^17) for patients on 'watch-and-wait' and 2.38 (95% CI: 0 – 7.4x10^14) for immunochemotherapy.

Conclusion

Results evidence limited benefit of current immunochemotherapy in treatment of grade 3 FL.

Key words: Automation, Computer vision, Cytological grade, Non-Hodgkin lymphoma

A20

Robust and Efficient Detection of Mitotic Figures

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Introduction

Counting mitotic figures is a crucial step in grading and prognostication of several cancers, but manual counting is tedious and time-consuming. In addition, there is a high degree of discordance among pathologists due to variations in the appearance of mitotic figures. Automatic detection algorithms have been proposed, but they are sensitive to domain shift and are not usually fast enough to be used in clinical practice for mitosis detection in whole slide images.

Material and methods

We propose a two-stage mitosis detection framework that comprises mitosis candidate segmentation and candidate refinement stages. The candidate segmentation model, EUNet, is fast and accurate due to its architectural design. Candidates are then refined using a deeper classifier network in the second stage. Both stages are robust against domain shift by incorporating domain-invariant methods.

Results and discussion

We test our algorithm on the three largest publicly available datasets and show that it outperforms all other state-of-the-art methods on all three datasets. In internal cross-validation experiments, our algorithm achieved F1 scores of 0.785 and 0.781 on the MIDOD21 and TUPAC datasets, respectively. Also, the proposed method is the best-performing algorithm on the external test sets and the winner of the MIDOG21-22 challenges.

Conclusion

The proposed method can detect mitosis with high accuracy, suggesting its potential as a stand-alone tool. It is fast and efficient, making it suitable for clinical practice. Finally, we showcase the utility of the proposed algorithm by processing the TCGA breast cancer cohort to generate and release a repository of mitotic figures.

Key words: mitosis detection, breast cancer, deep learning

A21

Integrating Social Network Analysis and Deep Learning for Improved Prediction of Molecular Pathways in Colorectal Cancer

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Introduction

Conventional techniques for identifying molecular pathways, genetic subtypes and mutations associated with CRC (which are crucial for precision medicine) are costly, time-consuming and tissue destructive. Most recent deep learning methods proposed for this task lack interpretability. We present a new approach that incorporates cell interaction information for the prediction of key mutations and molecular pathways in CRC.

Material and methods

We introduce cell graphs with nuclei as nodes and nuclei connections as edges of the network. We leverage Social Network Analysis (SNA) measures to extract interpretable features that describe cell interactions or distribution in an image. These SNA-based features are incorporated alongside CNN-based image representations in two deep-learning frameworks. We demonstrate the efficacy of our approach on the TCGA-CRC-DX cohort.

Results and discussion

Our method achieves significant improvements in the prediction of CIN, HM, TP53, BRAF and MSI mutations (2.4-4% and 7-8.8% improvement in AUROC and AUPRC on average) compared to the state-of-the-art methods. Furthermore, we achieve outstanding performance in MSI prediction in an external PAIP dataset (99% AUROC and 98% AUPRC). Our results provide insights into the correlation between cell interactions and molecular pathways and key mutations.

Conclusion

Our approach of incorporating SNA-based features provides interpretable information while being computationally efficient and scalable. The results demonstrate the discrimination power of SNA features and how they can enhance deep learning model performance in CRC. This study highlights the potential of incorporating cell interaction information in other biology or pathology image analysis tasks.

Key words: Social Network Analysis, Colorectal Cancer, Deep Learning, Key mutation, molecular pathways

A22

PathCaptcha: Crowd-sourcing image labeling from experts

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Introduction

WSIs are complex and challenging to analyze due to their large size and high resolution. Researchers often break down WSI into smaller patches for AI training-testing. Process requires accurate labels obtained from experts, which is a labour-intensive and time-consuming process. Inter-observer variation and consolidating inputs from multiple pathologists is also challenging.

Material and methods

PathCaptcha is an in-house designed service to source labels from pathologists. A set of known labeled images validate labels received on unknown image patches presented in a 3x3 grid generated randomly, using an API-based patch retrieval. Labels are weighed by pathologists' experience in the field. The process is iterated for multiple pathologists and weights are summed until a cutoff. Patch-level labels are aggregated to generate WSI-level annotation with confidence. Pathologists can choose the frequency of PathCaptcha vs Google ReCaptcha interactions. The process is optimized for speed by limiting to patches from tissue area using a separate algorithm.

Results and discussion

At submission, 110 pathologists (1-30yrs experience) provide labels 1 - 6times/day at the time of login into a reporting platform. A median of 3(1-9) attempts are required to successfully validate a grid with a median of 3(2-24) pathologists providing inputs for each patch. A median of 13(1-24) hours are needed per patch to reach cutoffs. A median of 338(70-480) patches/day reach cut-offs with a median confidence of 0.9(0.5 - 1). The sensitivity/specificity of the method for a task such as "identify patches containing tumor" is 0.86/0.99 respectively.

Conclusion

PathCaptcha is a ReCaptcha-inspired, non-intrusive platform for crowdsourcing image labels from experts with an in-built confidence metric.

Key words: Digital pathology, expert-sourcing label, WSI, AI, multiple noisy labels

A23

Digital Pathology awareness on Pathology Residents in Romania – A multicenter study

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Introduction

Digital Pathology (DP) is evolving daily and has become a routine practice in the Pathology Departments. Due to the interest of the young generation to technology, artificial intelligence (AI) and digitalization, DP demands a high interest in pathology residents. The aim of our study was to assess the DP awareness on Pathology residents in Romania.

Material and methods

Materials and methods We have performed a questionnaire-based study on 36 pathology residents from 7 centers of training in Romania. The study was performed in February 2023 and included 14 multiple choice questions.

Results and discussion

Out of the 36 residents, 27.28%(n=10) were in the first year of residency. 75%(n=27) said that they know the concept of DP and only 13.89%(n=5) apply DP in their department. 25%(n=9) have participated in courses or trainings in DP and almost half (47.22%,n=17) known how AI can be applied in pathology. WSI is used by 27.78%(n=10) and 97.22%(n=35) would consider beneficial a DP fellowship during their training. 100%(n=36) are convinced that AI can be applied in pathology, and 61.11%(n=22) totally agree that the training in digitalization of the health services is necessary for future specialists. 69.44%(n=25) consider that DP will increase the quality of services provided by the Pathology Departments, even though 63.89%(n=23) have observed a reticence in DP.

Conclusion

DP shows an interest to pathology residents and the premises of awareness for the young generation of doctors are increasing. The quality of the services provided by the Pathology Departments can be increased by training the pathology residents for DP during their residency in Romania.

Key words: Digital Pathology, Quality Assurance, Residents, Training

A24

Artificial intelligence aided detection of sentinel lymph node metastasis on histologic whole slide images in a digital workflow

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Introduction

Many institutions are using cytokeratin immunohistochemistry (IHC) to detect sentinel lymph node (SLN) metastasis in invasive breast carcinoma (IBC). We validated an artificial intelligence (AI) algorithm to screen SLN metastasis with aim to replace cytokeratin IHC.

Material and methods

The validation study cohort included 234 SLNs from 108 IBCs and the consensus study cohort included 102 SLNs from 62 IBCs. All SLNs had two levels stained with H&E and one level stained with cytokeratin IHC. All slides were scanned into whole slide images (WSI) during routine digital workflow and WSIs were automatically batch analyzed using Visiopharm (VIS) AI algorithm.

Results and discussion

For validation cohort, VIS AI algorithm detected all 46 metastases including 19 macrometastases, 26 micrometastases, 1 with isolated tumor cells (ITC) with a sensitivity of 100%, specificity of 41.5%, positive predictive value of 29.5% and negative predictive value of 100%. The false positivity was caused mostly by histiocytes (52.7%), followed by crushed lymphocytes (18.2%) and others. For consensus cohort, three pathologists examined all VIS AI annotated H&E slides and cytokeratin IHC slides and showed the same average concordance rate of 99% when using VIS AI annotated slides or cytokeratin IHC slides. However, the average time consumed per VIS AI annotated slide (0.6 minute) was significantly less than the time consumed per IHC slide (1.0 minute).

Conclusion

VIS AI algorithm showed perfect sensitivity and negative predictive value in detecting SLN metastasis and less time, suggesting its utility as a screening modality in routine digital pathology workflow to increase efficiency and decrease cost by eliminating cytokeratin IHCs.

Key words: artificial intelligence, digital pathology workflow, sentinel lymph node metastasis, breast cancer

A25

A Workflow for efficient creation of high quality cell classification data sets

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Introduction

Large, high quality datasets are essential for training and evaluating supervised cell classification algorithms. To reduce efforts for generating such datasets, each sample is usually labeled by only a single observer. However, as inter-observer variability in medical images is often high, this results in suboptimal datasets.

Material and methods

We propose a workflow for rapid labeling of samples by multiple observers. The workflow requires each sample to be labeled by at least two observers and that there is an absolute majority for a label value. The second observer is shown the value of the first label (validation). In case of disagreement, however, further observers cannot see the previous labels. We implemented the workflow as a web-based labeling tool, designed to require minimal interaction to facilitate rapid labeling. Our goal was to label cell images from bone marrow smears. The dataset contains more than 26,000 samples to be assigned to 53 different classes. Using this workflow we can additionally measure agreement between observers.

Results and discussion

In our dataset, labels of different observers did not match in 17.03% of the cells. Cell labeling takes a median of 3.62s in normal mode and 2.08s in validation mode. Considering the number of labels needed, this results in 6.52s (IQR: 4.31s - 11.90s) of labeling time per cell.

Conclusion

The high level of disagreement between observers demonstrates the need for multiple observers combined with a strategy for dealing with conflicting labels in order to produce high quality datasets. Our streamlined workflow facilitates rapid labeling to obtain such datasets in a reasonable amount of time.

Key words: Image Labeling, Cell Classification, Dataset Generation, Inter-Observer Variability, Bone Marrow Smear

A26

Direct comparison of GeoMX DSP and OPAL multiplex immunohistochemistry for tumor immune microenvironment study

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Introduction

Nanostring GeoMx DSP technology allows for digital quantification of multiple proteins enabling simultaneous quantification of target proteins. OPAL multiplex immunohistochemistry (mIHC) has been a widely used method for the comparison of tumor immune microenvironment of various cancer types. In the present study, we aimed to directly compare the results of DSP and OPAL mIHC analyses and evaluated the correlation of the two assays

Material and methods

In 123 tissue microarray (TMA) cores from 46 patients with gastric cancer, GeoMX DSP analysis was performed. In the same tissues, OPAL mIHC with CD11c, VISTA, PD-L1, CD4, CD8, and PanCK were performed. As the 1 mm TMA cores contain tumor- and TIL-rich areas, the average values of each protein expression level (DSP) and percentage of cells positive for each antibody (OPAL) were calculated.

Results and discussion

The correlation of GeoMX DSP and OPAL mIHC analyses was evaluated in the (1) CD45+ segment (DSP) and PanCK- stromal region (OPAL), (2) PanCK+ tumoral segment in DSP and OPAL, and (3) total stromal and tumor areas (OPAL). Of 6 antibodies used for OPAL mIHC, in the stroma, VISTA, CD11c, CD4, and CD8 showed significant correlation ($p<0.05$) with GeoMX DSP results, while PD-L1 showed weak correlation ($p=0.086$, $r=0.26$). In intratumoral areas, only CD8 remained significant ($p=0.020$, $r=0.34$) between the two platforms. In comparison of total areas, PD-L1, VISTA, CD4, and CD8 significantly correlated between GeoMX DSP and OPAL mIHC

Conclusion

We selected six antibodies for comparison and four of them showed significant correlation between GeoMX DSP and OPAL mIHC.

Key words: Comparison, GeoMX DSP, OPAL multiplex immunohistochemistry, tumor immune microenvironment

A27

Shedding Light on the Black Box of a Neural Network Trained to Detect Prostate Cancer in Whole Slide Images by Occlusion-Based Explainability

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Introduction

The neural networks represent a promising tool to assist pathologists in routine diagnostic procedures. However, one major issue with deep learning approaches is their lack of interpretability. They perform admirably, but do not explain how they reach their Conclusions. From the pathologist's point of view, the morphological criteria of malignancy in the prostate are well-established. They can represent a starting point to identify the key morphological features important for the neural network's decision of prostate biopsies.

Material and methods

We developed a deep learning-based system for carcinoma detection in whole slide images of prostate core biopsies, achieving state-of-the-art performance. Furthermore, we investigated various methods to extract the key features used by the neural network for classification.

Results and discussion

The occlusion technique analyzes the sensitivity of the detection system to changes in the input images. Resulting heatmaps indicate which parts of the image have the strongest impact on the system's output that a pathologist can examine to identify the network's reasoning behind a given classification. Reassuringly, these heatmaps identified several prevailing morphological features characterizing carcinoma, e.g. single-layered epithelium, presence of small lumina, and hyperchromatic nuclei with halos. The recognition of their mimickers in non-neoplastic tissue represented a convincing finding.

Conclusion

The neural network uses image patterns, representing a subset of morphological features used by human, to recognize prostatic cancer in biopsy. These patterns can be visualized by explainability heatmaps. This approach provides added value for automated digital pathology to analyze and fine-tune deep learning systems, and improves trust in computer-based decisions.

Key words: deep learning, prostate cancer, explainability, occlusion

A28

End-to-End Spermatozoid Detection in Cytology WSI: A success story in Forensic Pathology Workflow Optimization

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Introduction

Spermatozoid screening based on cytology slides is a routine task at forensic laboratories, aimed at identifying rape suspects through DNA profiling of sperm recovered from victims. Microscope-based slide inspection is both time-consuming and at risk of false negative slide labeling, sometimes containing only a single spermatozoid. To improve the screening sensitivity and throughput, Tribun Health installed a deep learning-based digital workflow to detect spermatozoids on Whole Slide Images (WSI).

Material and methods

Our dataset consists of 200 retrospective single-center cytology WSI – 50 for training and 150 for testing – containing samples recovered from a representative source variety (vagina, anus, hair, clothing). We exhaustively annotated the training set through a 2+1 expert consensus, resulting in 6425 annotated spermatozoids. The test set is equally split between positive, doubtful, and negative slide labels. We trained a state-of-the-art detector/classification ensemble model for object detection, which presents the results on a dedicated desktop with Calopix 5.0.2.2.

Results and discussion

The model achieves a mean 3-fold cross-validation F1 score of 0.87 [0.85-0.89]. Applied on the test set, and verified by an expert cytologist, we found missed spermatozoids in 5/50 of the negative slides and confirmed the presence of spermatozoids in 37/50 of the doubtful slides and 49/50 of the positive slides. The digital workflow reduced the standard workload treatment time of 50 cases from a week to around 2 hours of computation time plus verification of top-scoring objects.

Conclusion

Our installation of a WSI-based spermatozoid detection workflow in a forensic laboratory improved both their caseload throughput and accuracy.

Key words: Sperm Detection, Cytology, Forensics, Workflow Optimization, Deep Learning

A29

Using CNN Stability Training increases robustness to scanner and IHC-based image variability for epithelium segmentation in cervical histology

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Introduction

In digital pathology, image properties such as color, brightness, contrast or blurriness may vary based on the scanner and sample preparation. Convolutional Neural Networks (CNNs) are sensitive to these variations and may underperform on images from a different domain than the one used for training. Here, CNN Stability Training (CST) is proposed as a method to increase CNN robustness to scanner and Immunohistochemistry (IHC)-based image variability.

Material and methods

CST was applied to segment epithelium in immunohistological cervical Whole Slide Images (WSIs). CST randomly distorts input tiles and factors the difference between the CNN prediction for the original and distorted input within the loss function. CNNs with and without CST were trained using a training set of 114 p16-stained WSIs from the same scanner, and evaluated on 6 WSI groups, each group composed of 24 images of the same tissue, but with a specific scanner/IHC combination. Robustness (ΔAUC) was measured as the difference between CNN performance on WSIs from the same domain used for training (i.e. baseline test set) and WSIs with a different scanner/IHC. A lower ΔAUC represents a lower robustness.

Results and discussion

Across all test sets, CST models outperformed "No CST" models ($AUC \in [0.939, 0.986]$ vs $AUC \in [0.840, 0.980]$). At a WSI level CST models show an improved robustness in 117 of the 119 WSIs within the test set ($\Delta AUC \in [-0.046, 0]$ vs $\Delta AUC \in [-0.140, -0.007]$).

Conclusion

CST offers a path to improve CNN performance without the need for more data and allows customizing distortions to specific use cases. A python implementation of CST is publicly available in https://github.com/TIGACenter/CST_v1.

Key words: Digital pathology, deep learning, robustness, stability training, cervical intraepithelial neoplasia, image variability

A30

Image Standardization in Pathology could improve Learnability for AI Models

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Introduction

Image quality and consistency is crucial for the success of AI models in digital pathology. Differences in image properties can substantially affect the performance of AI-based image analysis [Schöming-Markiefka et al, 2021]. Standardization of staining and scanning protocols is one way to address this problem, for instance, through the use of individual slide stainers instead of traditional linear stainers. To measure the impact of standardization on AI models, we performed a quantitative comparison of the effects of stainer and scanner devices on image quality metrics.

Material and methods

Data was collected from 200 biopsies of NSCLC lung cancer patients. To minimize biological variation, two tissue sections were prepared from the same FFPE block. Staining was performed on a Ventana HE600 automatic stainer, as well as two traditional linear stainers. Scanning of both batches was performed on a Ventana DP200 and a Leica Aperio GT450. Image metrics --- comprising color ranges, image contrast, texture, and complexity --- were calculated based on 64x64 px tiles of whole slide images. These metrics were used to perform cluster analyses and compute intrinsic dataset dimensionalities, as a proxy for learnability [Pope et al. 2021].

Results and discussion

Our results show that scanning devices have substantial impact on both contrast and color metrics and different staining devices mainly differ in perceptual color range. Together, the HE600 stainer and DP200 scanner was found to have the lowest intrinsic data dimensionality.

Conclusion

These results suggest that standardization of staining and scanning pipelines could provide benefits for the learnability of AI models.

Key words: Standardization, Learnability, Intrinsic dimensionality, Image metrics

A31

HALO PD-L1 AI: Development and Validation of an Automated PD-L1 Tumour Proportion Scoring Algorithm in Non-Small Cell Lung Cancer

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Introduction

Programmed death-ligand 1 (PD-L1) expression on tumour cells is a response predictor to immune checkpoint inhibitor therapy and the tumour proportion score (TPS) has a crucial role in treatment decision-making for patients with advanced non-small cell lung cancer (NSCLC) (1). However, poor interobserver concordance exists when reporting PD-L1 expression (2). To support pathologist quantification and increase scoring consistency, we developed an AI-based algorithm for scoring tumour PD-L1 expression in NSCLC samples.

Material and methods

HALO PD-L1 AI was developed with routine diagnostic cases stained with either SP263 or 22c3 clones. The algorithm was trained with 146984 expert annotations to identify PD-L1 tumour-positive cells, within automatically segmented tumour regions. The algorithm was validated on 203 SP263-stained whole slide images (WSI) by comparing the algorithm's TPS score with TPS scores from three pathologists. To assess the algorithm generalizability, we compared the algorithm TPS scores to the clinical data from an independent institute across 165 22c3-stained WSI.

Results and discussion

For the SP263 clone, pairwise pathologist agreement ranged from 74.9% to 77.3%. Agreement of the algorithm with the pathologists' mode was 75.4%. Intraclass correlation coefficient (ICC) between the algorithm and pathologists' TPS scores was 0.95 (95%CI 0.93 – 0.97). In 22C3 cases, the overall percent agreement to clinical data was 72.7% and ICC 0.95 (95%CI 0.93 – 0.96).

Conclusion

HALO PD-L1 AI is highly concordant with pathologist TPS scores both for SP263 and 22c3 clones. HALO AI PD-L1 can be implemented to support PD-L1 scoring, saving pathologists' time, and ensuring consistency in the reported results. 1. doi: 10.1177/1758835918763493 2. doi: 10.1158/1078-0432.CCR-17-0151

Key words: PD-L1, NSCLC, artificial intelligence, deep learning

A32

Automated Artificial Intelligence-Powered Artifact Detection for Quality Control of Whole-Slide Digital Pathology Images

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Introduction

Artifacts have a negative impact on the digital pathology workflow and can be introduced at multiple stages during the creation of a whole slide image. Manual quality control is a laborious and qualitative procedure. To allow all samples in a workflow to be assessed and increase the reproducibility of quality control procedures, we developed SlideQC, an AI-based quality control tool to automatically detect and segment tissue artifacts.

Material and methods

SlideQC was developed using 2499 annotations of air bubbles, dust/debris, folds, out-of-focus, and pen marker, across 302 Haematoxylin and Eosin (H&E) and immunohistochemistry (IHC) stained whole-slide images from more than 9 tissue types. The training set was supplemented with a set of 2048 synthetically generated out-of-focus images. SlideQC performance was assessed on 73 external HE (HistoQC Repo) and IHC (LYON19) external test cohort images, across 432 annotations (tissue and artifact).

Results and discussion

SlideQC showed high precision, recall, and F1-score with average values of 0.94, 0.90, and 0.91. For each specific artifact, recall was 0.84 for air bubbles, 0.91 for debris/dust, 0.84 for folds, 0.98 for pen marker, and 0.97 for out-of-focus.

Conclusion

SlideQC achieved high precision, recall, and F1-score in HE and IHC external test cohorts. By identifying and reporting the percentage of artifacts on each slide, SlideQC could provide an automated, measurable quality control procedure. SlideQC could be used both in clinical and research workflows to triage and alert slides containing a high percentage of artifacts or to exclude the artifact regions for downstream analysis

Key words: artifact detection , quality control, artificial intelligence, deep learning

A33

Unsupervised clustering of morphology patterns on whole slide images guide prognostic stratification of glioblastoma patients

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Introduction

Glioblastoma is the most common malignant adult brain tumor with poor prognosis and heterogeneous morphology profiles. Stratifying glioblastoma patients according to overall survival (OS) is a challenging task with direct clinical implications. We hypothesize that computational quantification of morphology patterns present in H&E-stained whole slide images (WSI) can yield biomarkers of prognostic relevance contributing to optimizing clinical decision-making.

Material and methods

H&E-stained WSI from 188 IDH-wildtype GBM (CNS WHO grade 4) patients at 10X magnification were identified, following the TCGA-GBM/TCGA-LGG reclassification according to the 2021 WHO classification criteria and outlier exclusion. These were divided to short- (below 9 months, n=94) and long-survivors (above 13 months, n=94), and then proportionally partitioned to training and hold-out-test subsets (n_training/n_hold-out-test=152 /36). All WSI were split into non-overlapping 256x256 patches, followed by feature extraction (512-dimensional vector) using a pre-trained VGG16. Principal component analysis reduced the feature dimensionality to 32. Unsupervised k-means clustering revealed distinct groups of morphology patterns. The cluster numbers were automatically determined based on Rand index and Silhouette coefficient. Proportions of these patterns describe tumor's spatial heterogeneity, and used to distinguish short- and long-survivors using a decision tree classifier.

Results and discussion

We identified seven clusters of distinct morphology patterns, including 3 categories of tumor cellularity (low/intermediate/high), necrosis/macrophages, and other prognostically-relevant characteristics. Short- and long-survivor classification accuracy, driven by these patterns, is equal to 83.33% on hold-out-test data.

Conclusion

Quantification of morphology patterns from H&E-stained WSI of glioblastoma can accurately stratify patients according to their OS, while providing additional knowledge to the clinical neuropathologist for routine microscopic assessment.

Key words: Glioblastoma, Morphology, Survival, Clustering, Stratification, VGG16

A34

Automatic Counting of HPV Viral Capsid Proteins expression on Whole Slide Images for Cervical Intraepithelial Lesions Diagnostics

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Introduction

Currently there is not any appropriate marker for accurate low grade squamous intraepithelial lesions diagnostics while it is extremely important for patients in IVF programs.

Material and methods

We evaluated 32 patients (cervical biopsies with HSIL and LSIL). Histology was performed with h/e slides, immunohistochemistry was performed with anti-HPV16 L1, L2 antibodies («Biorbyt», UK) assessed with 0-3 scores. For NN construction we used 260 slides with L1 (34%), L2 (34%) and hematoxylin and eosin (32%) staining. From each slide we extracted 20 random tiles 512x512 pixels for binary classification (LSIL yes/no). MobileNetv3_Small and ResNet50 were chosen as architectures of the neural network model. We revealed that ResNet50 application with augmentation was more accurate than MobileNetv3_Small.

Results and discussion

In LSIL samples L1/L2 expression was observed more frequently than in HSIL (p=0.001 and p=0,036 consequently). L1 expression was 1+, 2+ and 3+ scores in 88.9%, 88.9% and 80.0 % for samples with LSIL consequently. L2 expression was 0, 1+, 2+ and 3+ in 25.0%, 50.0%., 16.7% and 8.3% for samples with LSIL consequently. For ResNet50 with augmentation F1 score was 0.56, 0.72, 0.85, 0.90 for h/e slides, L1, L2 and L1+L2; Precision was 0.49, 0.59, 0.75, 0.82 for h/e slides, L1, L2 and L1+L2; recall was 0.65, 0.92, 1.00 and 0.99 for h/e slides, L1, L2 and L1+L2.

Conclusion

L1 and L2 IHC expression can be the useful markers for LSIL and HSIL differentiation. L1- and L2-based neural networks can effectively predict LSIL with random tiles while ensemble of L1- and L2-based NN is more accurate on prediction.

Key words: CNN, WSI, squamous intraepithelial lesion

A35

Prognostic Impact of Tertiary Lymphoid Structures in Epstein-Barr Virus-associated Gastric Carcinomas measured by Digital Image Analysis

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Introduction

Epstein-Barr Virus-associated gastric carcinoma (EBVaGC) is characterized by prominent intratumoral lymphocytic infiltrations and favorable prognosis. Tertiary lymphoid structure (TLS) has been reported to have a positive correlation with more favorable outcomes in various types of cancer. We aimed to evaluate the TLS density, MECA-79 expressing high endothelial venules (HEV) and CD8-positive tumor infiltrating lymphocyte (CD8+ TIL) densities by using digital image analyses in surgically resected EBVaGCs to find their clinical implication.

Material and methods

Among patients who underwent surgery for advanced GC from 2017 to 2019, 72 EBVaGC were identified. TLS, HEV, and CD8+ TIL were identified by immunohistochemistry (IHC) for MECA-79, CD31, and CD8 and the densities of TLS, HEV, and CD8+ TIL were determined by digital image analysis.

Results and discussion

Higher HEV density was significantly associated with negative lymph node metastasis (p= 0.01) and low pT stage (p=0.03). High CD8+ TIL density was significantly associated with low pT stage (p=0.01). Positive MECA-79 expression in cancer cells correlated well with lymph node metastasis (p=0.003) and low TLS density (p=0.04). TLS density showed positive correlation with TA-HEV density (correlation coefficient: 0.53, p<0.001). Unexpectedly, TLS density and CD8+ TIL density showed a weak negative correlation (correlation coefficient: -0.23, p= 0.048). In survival analysis, patients with lower TLS density had a worse prognosis compared to those with higher TLS density (p value = 0.0043).

Conclusion

EBVaGC with high TLS density showed a significantly better prognosis than those with low TLS density. The better prognosis may be caused by the immune response preventing lymph node metastasis.

Key words: Epstein-Barr Virus, Stomach, Tertiary lymphoid structure, Prognosis

A36

Routine Use of an AI Solution for Primary Diagnosis of Prostate Biopsies in Clinical Practice

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Introduction

We present the analysis of a clinically deployed artificial intelligence (AI) decision support solution for prostate biopsies primary diagnosis utilized as first read within a digital pathology workflow.

Material and methods

The AI solution was previously validated in the lab on an independent cohort. Four pathologists underwent training and used the solution for prospective primary diagnosis of consecutive prostate CNBs, reporting on 92 cases (374 parts, 600 H&E slides).

Results and discussion

The AI solution demonstrated high performance when pre-classifying parts with the likelihood to be benign or malignant, with AUC = 0.99 (95% CI: 0.985, 0.997), NPV = 99.1% (108/109), and PPV = 97.6% (200/205), respectively. 16 % of parts have been classified as suspicious by AI. User feedback survey, as reported by pathologists, showed high satisfaction marks for the AI solution, particularly for the Gleason scoring (4.75/5), PNI detection (4.5/5), and tissue and tumor length automated measurement (4.75/5). Pathologists felt there is potential to increase diagnostic efficiency by using the AI tool.

Conclusion

We report here the successful implementation of a multi-feature AI solution that automatically imparts clinically relevant diagnostic parameters regarding prostate cancer, grading, measurements, and other pathologic features. The solution demonstrated its ability to accurately detect cancer and contribute to diagnostic quality. Thus, the AI solution could be used as a significant aiding tool for pathologists in clinical decision-making in routine pathology practice.

Key words: AI, Prostate, Cancer, Machine learning , digital pathology, Image Analysis

A37

An HE-only workflow for liver fibrosis assessment using HE-predicted collagen.

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Introduction

Liver diseases are a significant global health problem, where quantifying fibrosis is essential for monitoring disease progression. To highlight fibrotic collagen, special stains like Masson's Trichrome (MT), Sirius Red (SR), or Saffron (HES) are required. This study aims to highlight collagen directly from Hematoxylin and Eosin (HE) stained liver biopsies using deep learning, eliminating the need for special stains.

Material and methods

We obtained 11 retrospective liver cases with varying degrees of fibrosis. For each case, we collected three consecutive slides, each stained with HE, and separately overstained with either HES, MT, or SR. We registered the HE slides with their respective special stains, used stain deconvolution to extract continuous collagen concentrations, and trained a Unet to predict collagen from HE. We calculated the pixel-wise Pearson correlation and p-value to quantify the similarity between the predicted and special stain collagen maps. To evaluate the practical efficacy of our approach, two pathologists evaluated the METAVIR score on both the special stains and our digital HE-predicted collagen overlaid on the HE (c-HE), with a 15-day washout period.

Results and discussion

We find strong correlations between c-HE and each special stain (HES: 0.87, MT: 0.78, SR: 0.71), p-value<1e-5. The pathologists found agreement in METAVIR score in P1: 10/11, P2: 11/11 cases using either special stains or c-HE.

Conclusion

Our study suggests that collagen content can be accurately inferred from HE-stained liver biopsies, both quantitatively and qualitatively, with a high correlation with any of the standard special stains that highlight collagen, and little influence on METAVIR evaluation quality.

Key words: digital pathology, fibrosis assessment, workflow optimization, collagen prediction

A38

How many samples is enough? How will self-supervised pre-training affect model accuracy, robustness and generalisation?

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Introduction

Clinical pathology will be revolutionized by artificial intelligence (AI) driven decision support systems in the near future. Nevertheless, widespread adaptation of AI systems requires a high degree of accuracy and reliability. Training an accurate model requires a massive amount of labeled training data. With the increasing amount of available data, the future of these methods cannot rely on supervised approaches alone. Self-supervised learning can effectively leverage large amounts of unannotated data to learn useful representations that provide a good basis for supervised downstream task training.

Material and methods

Here, we investigated the number of samples required for building an accurate state-of-the-art deep ensemble model for prostate cancer detection from hematoxylin and eosin stained whole slide images in a supervised setting. Further, we have studied whether the amount of training samples can be significantly reduced with self-supervised pre-training for reaching the same level of accuracy as with the supervised approach. For the self-supervised pre-training, we used 26408 whole slide images of 18 different tissues publicly available in The Cancer Genome Atlas (TCGA) database. In addition to the required sample size, we will investigate the self-supervised model behavior with out-of-distribution or near-distribution outliers samples.

Results and discussion

Our results showed that after a specific amount of training samples, the model performance did not increase significantly in a supervised setting.

Conclusion

Overall, the future work in AI assisted pathology requires building models that can utilise massive amounts of data and generalise well to datasets from different sources. Self-supervised learning provides one potential method for achieving this goal.

Key words: Prostate cancer, Self-supervised learning, Whole slide image analysis

A39

Digital Image Analysis as a Standardized Method for External Quality Assessment of HER2 IHC in Breast Cancer

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Introduction

Treatment of breast carcinoma (BC) rely on accurate HER2 status using immunohistochemistry (IHC) to identify tumors with classical HER2 overexpression and the new HER2-low category (1-2+ unamplified). NordiQC offers external proficiency testing for HER2 IHC. The evaluation of participants' IHC results are conducted by an expert panel assessing analytical accuracy and technical quality. With an increased number of participants, we examined the possibility to use digital image analysis (DIA) as an un-biased assessment method.

Material and methods

105 slides from 6 NordiQC HER2 IHC runs were included comprising 30 different BCs. The slides were selected to include sufficient and insufficient staining qualities characterized by false positive (FP) or false negative (FN) results and technical challenges as excessive cytoplasmic staining. All slides were scored using 2 methods; visually by the NordiQC expert panel and by DIA using a quantitative cell analysis algorithm (IMSTAR PathoScan Tumor-Marker).

Results and discussion

An overall concordance of 94% and 69% was obtained between DIA and the expert panel for HER2-overexpression and HER2-low scores, respectively. DIA-vs-experts agreement was of 100% and 63% for the detection of FP and FN results, respectively. Among FN slides, 6/12 of 2+ amplified BCs were scored as 0-1% by the experts and 12/12 as 2+ by DIA.

Conclusion

DIA accurately categorized HER2 IHC results as sufficient and insufficient despite multiple technical conditions being used. DIA-vs-experts concordance was high for HER2-overexpressing BCs. DIA showed a high accuracy for scoring 2+ amplified BCs, even with a poor staining quality. DIA-vs-experts disagreement needs further studies for more accurate scoring of HER2-low BCs.

Key words: Quality Control, Breast Cancer, HER2 IHC, Artificial Intelligence, Image Analysis, Digital Pathology

A40

Automatic Detection of Lymphovascular Emboli in Whole Slide Breast Histopathology Images

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Introduction

Emboli detection within breast tumors is crucial as it affects both the diagnosis and patient treatment. However, detecting emboli is tedious as they are small and rare objects which can, in addition, be confused with mimickers. Automatic detection of emboli on WSI (Whole Slide Images) could thus be a substantial help to pathologists.

Material and methods

Since emboli are scarce, few annotated data are available. Expert pathologists annotated 1639 slides leading to a dataset of 533 emboli patches vs. 273108 non emboli patches. Traditional deep learning techniques with little data lead to poor performance. To overcome this challenge, we use a pretrained network to project images into a low dimensional feature space. A small classification head is then trained on these embeddings. In a routine setup, the resulting model is applied on patches extracted from the input WSI. The highest scoring patches are then presented to the pathologist for further diagnosis. This dramatically reduces the area of research and therefore the time needed for emboli discovery.

Results and discussion

To capture the help brought to pathologists, we measure the following custom metrics : - Average rank of patches containing emboli among WSI patches : 1 - Proportion of slides where emboli patterns appear in the top : 75%

Conclusion

Emboli patterns are detected in a vast majority of WSI. Results are promising and the detection pipe may be a good assistance to pathologists.

Key words: Deep Learning, Artificial Intelligence, Histopathology, Emboli

A41

Semi-Supervised Contrastive Learning for Semantic Segmentation of Histology Images

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Introduction

Segmentation of histology images is a challenging task due to the scarcity of annotated data. Annotated datasets are costly and time-consuming to obtain. In this work, we present a semi-supervised framework for segmenting histology images by enforcing context-aware cross-consistency training in an unsupervised manner together with entropy minimisation.

Material and methods

Two publicly available datasets, Multi-organ nuclei segmentation (MoNuSeg) dataset and Breast Cancer Semantic Segmentation (BCSS) dataset, were used for this study. MoNuSeg contains 29,000 annotated nuclei of 7 different organ types in 44 images, while BCSS contains over 20,000 annotated images of regions of interest from five categories. We conducted experiments by taking the whole and fractions of training data. The proposed framework utilises contrastive learning, cross-consistency regularisation, and entropy minimisation. While contrastive learning helps the model to distinguish between positive and negative image pairs, cross-consistency helps improve robustness against small perturbations and entropy minimisation improves confidence for accurate predictions.

Results and discussion

The proposed method outperforms several state-of-the-art methods, especially when only 1/8th of the training data is used, yielding a dice score of 61.68, which is 6% better performance than fully supervised DeepLab-v3. Similarly, on MoNuSeg dataset, our model achieved a dice of 85.19 and performed 15% better than the fully supervised DeepLab-v3.

Conclusion

The proposed method shows promising results for segmentation of histology images in a semi-supervised setting, especially when using a small proportion of training data. Future work involves improving contrastive loss for minor classes, targeting histology-specific perturbations, and validating on a large multi-centric histopathological dataset to ensure accurate downstream analysis through segmented histology primitives.

Key words: Computational Pathology, Deep Learning, Semantic Segmentation, Unlabeled , Context-aware

A42

Characterizing the expression landscape of colorectal tumor buds by machine-learning based analysis of seqIF images

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Introduction

Tumor buds are small clusters of cancer cells (less than 5 cells) that are a known independent prognostic factor in colorectal cancer. However, currently no phenotypic marker for tumor buds exists. We propose an analysis pipeline that can automatically detect tumor buds in sequential Immunofluorescence (seqIF) images and is able to characterize their phenotypes in an automated way.

Material and methods

7 CRC sections underwent seqIF protocol on COMET™ (Lunaphore Technologies). Among 1,040,000 epithelial cells, we detected 41,000 tumor buds. Epithelial tissue areas are segmented using random forest classifiers, and individual nuclei are detected using the StarDist algorithm. Within each epithelial area, we classified cells as tumor buds depending upon the local abundance (i.e., when belonging to areas with less than 5 cells in total).

Results and discussion

We were able to uncover downregulated marker expression of E-Cadherin, beta-Catenin and CDX2 in tumor buds with effect sizes d of 0.93, 0.72 and 0.55 respectively (p less than 0.001). We found significant correlations between these markers and the number of cells within a connected tissue region, confirming earlier findings in literature. Furthermore, we identified a subpopulation of tumor buds overexpressing ZEB1 in two of the six slides.

Conclusion

Our findings show that the proposed pipeline is robust to replicate prior findings in an automated way. Crucially, it allows to bypass the labor-intensive manual annotation of tumor buds, which so far has prevented a systematic study of their expression profiles. We also show the sensitivity of the approach by detecting known subpopulations of tumor buds.

Key words: Sequential Immunofluorescence, Tumor buds, Tissue segmentation, Spatial analysis

A43

A Pathology of Digitisation in Digital Pathology - Scanner Color Standardisation and QA

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Introduction

Digital pathology scanners do not reproduce the ground truth color of tissue and vary in accuracy, visible in viewer platforms and relevant to AI reliability and scalability. Clear terminology and accessible metrics must be defined, occurrence and severity in scanners must be measured and then corrected for industry-wide Quality Assurance. Methods must enable all scanner users, AI developers and scanner manufacturers to utilize independently. Scanner color validation and standardisation is essential for QA in digital pathology and AI.

Material and methods

Define: digital scanner color versus stain chemistry variation; absolute standardisation versus arbitrary normalisation; system versus vendor color; variation detection versus impact of correction. Measure: Utilising FFEI's Sierra Slide technology the WSI scanner market was quantified for errors against ground-truth color and aligned against human color resolution standards. Correct: scanner-agnostic validation and independent standardisation of system and vendor color was performed using Sierra ICC profiles and validated across many use-cases. Assess: demonstrate impact on multi-scanner, multi-institute standardisation and integration of ICC profiles into AI workflow.

Results and discussion

Metrology of digital color variation reveals industry-wide standardisation issues. Images from many scanner models and vendors were independently standardised and validated to high color fidelity against international standards. The QA methodology was verified in multiple scanner, viewer and AI deployments.

Conclusion

Scanners and staining differently contribute to color non-standardisation, however digital scanner color can be quantitatively validated and, importantly, corrected to a standard of absolute truth by an independent, scanner-agnostic method. This can deploy in workflow to enable stringent QA to diagnose and eliminate the impact of digital color variation on pathologists and AI.

Key words: standardisation, quality assurance, color, calibration, validation, AI

A44

Standardisation and De-Identification of Whole Slide Images for Digital Pathology Data Management

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Introduction

Standardization of whole slide images (WSI) can enhance the interplay between different digital pathology systems and scanners for data storage and management. A WSI data management system was developed to standardise proprietary file formats of WSI into a long-standing standard format (TIFF) while de-identify patient-associated information from the raw data for sharing and reuse in digital pathology.

Material and methods

50 proprietary WSIs were digitized and collected from multiple scanners including Aperio(svs), Hamamatsu(ndpi), MIRAX(mrxs), and Philips(isyntax). For each proprietary WSI, the tissue-associated region was automatically extracted from a single layer of high-resolution WSI using an learning-based WSI optimization algorithm and restructured to a generic multi-resolution TIFF structure. Along with the standardisation process, the system de-identified patient-associated information of clinical WSI data by detaching image-associated and patient-associated metadata from the raw proprietary WSI. The image-associated metadata was re-bundled to the generated TIFF slide in a performant manner for viewing, reading, and sharing based on non-personal diagnostic results. The patient-associated metadata was stored separately in a patient database allowed for image retrieval based on queries of patient information.

Results and discussion

All proprietary WSI formats were successfully converted to generic TIFF formats. The generated WSI in TIFF can be retrieved by major clinical viewers such as QuPath, Orbit, ASAP and clinical workflow such as Dynamyx from Inspirata.

Conclusion

The proposed WSI data management system can effectively convert and efficiently store and retrieve WSI data in methods that allow for effective transfer of the WSI data through the web for expanded use.

Key words: standardisation, Whole-slide imaging, data management, data storage

A45

Deep learning-based segmentation of glomeruli: Detection of erroneous annotations through morphometric analysis

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Introduction

Deep learning-based segmentation has evolved to a powerful strategy for automatically annotating glomeruli in kidney biopsy images, but any artificial intelligence can make mistakes. Thus, when utilized to gather large collections of glomeruli for downstream analyses, how to quantitatively estimate the amount of faulty annotations and to flag these for subsequent correction, without the laborious task of manually checking each image?

Material and methods

To address this issue, the current project performed an extensive study on the use of shape analysis for automatically evaluating deep learning-derived glomerular segmentations. Specifically, the study evaluated 19 morphometric features for detecting faults among over 220000 glomeruli annotations.

Results and discussion

Three major types of faults were discovered: annotations with horizontal/vertical cuts, annotations with irregular boundaries, and annotations spanning multiple glomeruli. Through shape analysis, these mistakes could be successfully discerned from each other and from accurate segmentations, thus enabling an estimation of the number of errors (~4% in the current dataset), and to flag them for subsequent corrections. Currently, the study is extensively labeling glomerular annotation errors in order to precisely evaluate the accuracy of the various metrics. Nevertheless, a pilot experiment already suggested that presorting annotations via morphometrics might reduce the number of annotations that would have to be manually screened by 95-99%.

Conclusion

In summary, the work demonstrates the methodological aspects and benefits of shape analysis for evaluating glomerular segmentation results. We are convinced that the outlined strategy for detecting segmentation errors will enable a more time-efficient correction of deep learning-derived glomerular annotations.

Key words: Nephropathology, Glomerular segmentation, Annotation validation, Morphometry, Shape analysis

A46

DeepSTIL: a robust deep-learning based tumor-infiltrating lymphocyte scoring pipeline trained solely on open source data

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Introduction

The stromal tumor infiltrating lymphocyte score (sTIL%) is a prognostic and predictive biomarker in certain breast cancer subtypes. Currently, sTIL% scoring requires a trained pathologist and suffers from high intra- and interrater variability. We present results of a pipeline that trains tissue segmentation and lymphocyte detection methods on open-source data, which, combined with heuristic post-processing, provides highly concordant sTIL% scores on an external H&E WSI dataset.

Material and methods

DeepSTIL consists of a learnable stage which 1) segments tissue, 2) segments stroma and tumor tissue, and 3) detects lymphocytes. These outputs are utilized in a non-learnable stage to 4) define the tumor bed, and 5) compute the sTIL% score. The learnable models are U-Net and YOLO networks trained on the TIGER, NuCLS, and BCSS breast cancer datasets (subsets of The Cancer Genome Atlas) from an Aperio scanner. We evaluate DeepSTIL on an external breast cancer dataset (n=252 across molecular subtypes) from ICGC, digitised with a different scanner (Hamamatsu).

Results and discussion

There is an evident linear relationship between DeepSTIL's scores and the pathologist scores (Pearson's r=0.67) and a high goodness-of-fit (R2=0.43). When we define a binary ground-truth label (sTIL-high: >30 sTIL%, sTIL-low: ≤30%), DeepSTIL achieves an AUROC of 0.86.

Conclusion

Leveraging open-source data, DeepSTIL combines deep learning with heuristic post-processing to compute the sTIL% score in H&E WSIs of breast cancer patients. The computationally assessed scores are highly concordant with a pathologist's score on an external dataset from a different scanner. In the future, such methods may be used to access sTIL% scores for translational research.

Key words: Deep learning, tumor infiltrating lymphocytes, breast cancer, heamatoxylin and eosin, whole slide images

A47

Streamlining, executing and validating AI algorithms on remote HPC infrastructure: An integrated approach

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Introduction

Owing to the complexity and large size of image data in pathology, artificial intelligence (AI) algorithms preferably run on a dedicated high-performance cluster (HPC). Validation of newly developed algorithms usually requires integration into an image management system (IMS), which is a time-consuming process. We propose an IMS-independent approach to rapidly validate and deploy AI algorithms in research and diagnostic settings.

Material and methods

A generalizable interface for any image-related AI algorithm has been developed to set up an automatic workflow between the institute and the remote HPC. Once image data is generated, the data flow is managed and monitored by a data and job manager communicating with the HPC. A web-based graphical user interface (GUI) displays the status and allows pathologists to visually evaluate the result in a user-friendly manner and provide instant and structured feedback.

Results and discussion

To test and validate the workflow, an initial implementation is carried out for the extended validation of a recently published algorithm for the detection of lymph node metastases in colorectal cancer. The technical deployment of the workflow has proven to be stable. The GUI and user experience (UX) were also well-received and accepted by pathologists.

Conclusion

In digital pathology, annotation and validation of AI models require specific domain expertise that can only be provided by a trained pathologist. The presented solution allows experts to focus on the validation of results without distraction and time loss due to technical obstacles.

Key words: artificial intelligence algorithms , digital pathology, HPC infrastructure, image management system, Streamlining algorithms, lymph node metastases detection

A48

Post-Sectioning Verification and spatial Correlation of 2D histological Slices with 3D CT-Scans through 3D printed Phantoms

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Introduction

Hard tissue histology is hindered by the fact that the specimen is opaque and therefore the cutting process cannot be targeted to regions of interest. We present a novel workflow using microCT scans prior to cutting. These scans are used for the analysis of the resulting cutting plane. 3D-printed markers embedded together with the specimen are used to register the histological section into the microCT context.

Material and methods

Three cone-shaped phantoms were embedded in combination with different tissue specimens in resin. After polymerization, the blocks were scanned in a microCT at a resolution of 80 µm. A priming cut was performed using a diamond bandsaw . The specimen was then sectioned using a laser microtome. Completed sections were imaged using a microscope. Image analysis was performed using a python script.

Results and discussion

After sectioning the histological image is processed with the aim of retrieving the minor-axis of each cone. Through segmenting and labeling the CT-Scan we obtain the matching diameter for each cone, thus allowing for the estimation of the sectioning plane. This plane is then extracted and defined as a matching candidate. Finally, both modalities are fused by image registration.

Conclusion

We expect that our method could enrich efforts to reconstruct a virtual histology volume, by eliminating the need for corresponding blockface images or costly matching-candidate-algorithms. However, a drawback concerning the printing powder, manifests in the porous phantoms. One solution to address this problem is to investigate sufficient 3D-printable materials that yield sufficient contrast while being resistant to the abrasive processing.

Key words: Computer Tomography, Histology, 3D printing, Image Registration, Tissue Sectioning, Laser-microtomy

A49

Using Systemised Nomenclature of Medicine (SNOMED) codes to select digital pathology whole slide images for long-term archiving.

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Introduction

Digital pathology allows the creation of a digital archive, allowing rapid retrieval of previous cases without the need to acquire them from off-site storage and preventing issues of slide degradation. However, the vast volumes of data created are a significant storage challenge for laboratories, with high associated costs. In the UK, retention of glass slides is recommended for a minimum of 10 years, but it is for individual departments to determine how digital images are archived.

Material and methods

In a retrospective study, we examined the Systemised Nomenclature of Medicine (SNOMED) codes of cases reported between July 2011 and December 2015 and of cases recalled for clinical review more than 12 months after diagnosis at a large digital pathology department. We calculated the recall probability of each SNOMED T and M code combination.

Results and discussion

Our results show that 0.2% (390/162,761) of cases are recalled after 12 months, with SNOMED code being able to predict which cases are likely to be recalled. Using the combination of M and T codes would allow us to store only 38% of cases, with a 100% successful recall rate (AURRC=0.96).

Conclusion

Our study shows that SNOMED T and M codes provide a mechanism for predicting the recall probability of pathology cases from archives. At our centre, this approach could reduce the number of cases archived by 62% and still ensure all cases likely to be recalled remain in the archive. This provides an example of how departments could best manage a digital archive to maximise benefit while minimising cost.

Key words: SNOMED, Archive, Storage, Digital Slides

A50

A proposed approach for standardised semantic annotation of digital histopathology slides at the point of diagnosis.

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Introduction

As digital pathology is replacing conventional glass slides, the annotation of digital pathology whole slide images (WSI) is rapidly becoming part of a pathologist's regular practice. Currently there is no recognisable organisation of these annotations and no preformed motifs to consistently annotate certain regions of interest. As a result, pathologists adopt a haphazard approach to defining annotations which leads to inconsistency and limits the down-stream efficient use of this valuable effort.

Material and methods

We used The Royal College of Pathologists and College of American Pathologists documents, feedback from reporting pathologists in our NHS department and experience in developing annotation dictionaries for PathLAKE research projects to develop a structured approach to the standardised annotation of WSI.

Results and discussion

We formed a list of 167 commonly annotated entities, under 12 speciality subcategories. Each entity is assigned a suitable annotation shape, colour, and SNOMED CT code. Additionally, as an example of how the approach could be expanded, all lung tumours in the WHO classification 2021 are included with a shape, colour, SNOMED CT code and ICD-O code.

Conclusion

We have proposed a structured approach that could be widely adopted to maximise the utility of WSI annotations. By standardising annotations, they become quicker to use, identifiable at low power and are searchable across a case, thus aiding reporting and reviewing cases. Furthermore, it paves the way for the annotations being made during reporting to be used for research, vastly aiding to overcome the hurdle of slide annotation in the development of artificial intelligence-based tools.

Key words: Annotation, Standardisation, SNOMED CT

A51

Neural Style Transfer as a Service

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Introduction

Acquiring large and diverse datasets for effective AI systems while maintaining patient data privacy is challenging. We propose style transfer as a service to learn scanner and staining procedure-specific variabilities from patient data, without releasing the learned model or data. This may allow vendors to augment existing training data without compromising patient privacy. We explore the feasibility of this approach and discuss future research directions.

Material and methods

The study evaluates a style transfer model CycleGAN on the Camelyon16 dataset obtained from two different scanners, denoted style A and B. First, CycleGAN was used to transfer style A to B. Then, the accuracy of a baseline classifier trained on the original images was compared with a classifier trained solely on these synthetic images and evaluated on the real images of style B from the test set.

Results and discussion

The results show that the classifier trained on entirely synthetic images performed approximately 7% worse than that trained on real images. This suggests that while synthetic data may not fully capture the complexity of real-world data, it can still be useful for training AI models.

Conclusion

This study highlights the potential of using style transfer as a service to augment datasets while maintaining data privacy by not disclosing the original data. Further research is needed to determine the extent to which private data can be extracted from augmented images and to evaluate the performance of state-of-the-art models beyond CycleGAN.

Key words: Neural Style Transfer, Generative Adversarial Networks, Privacy, Data Augmentation, Image to Image Translation

A52

Using Deep Learning on H&E stained Histopathology Slides for HPV Detection in Head Neck Cancer

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Introduction

Head Neck cancers are currently classified using Human papillomavirus (HPV) in-situ hybridisation (ISH) into HPV-related and unrelated with prognostic and therapeutic implications. HPV-ISH is a time-consuming, expensive, and elaborate test. P16 immunohistochemistry (IHC) is often used as a surrogate marker. In India, the PPV of p16 IHC for predicting HPV infection is ~50% due to low disease prevalence.

Material and methods

An in-house bioinformatic tool "HPVDetector" was utilized to infer HPV load in cancer genome sequences of the TCGA HN cancer dataset. Further, the dataset was assigned HPV positive and negative labels for three different viral load thresholds (10, 50 and 200). This labelled data was then used to train a deep learning (DL) algorithm on HE-stained whole-slide images (WSI) of the corresponding cases to predict the viral positive and negative labels.

Results and discussion

A total of 438 WSI from 438 patients were used. The model classified HPV Positive vs HPV Negative with an average test area under curve (AUC) of 0.9110 in a 10-fold cross-validation for the TCGA dataset for a threshold of 10 (37 positive and 401 negative).

Conclusion

Our study demonstrates that convolutional neural networks, such as Attention MIL with clustering, can be used to assist in the diagnosis of head and neck cancer from histopathology slides. HPV detection using DL methods on HE-stained WSI is a feasible method for patient management, potentially reducing the costs of tests and time to treatment.

Key words: HPV, WSI, Viral load, Deep learning

A53

Large-scale histological image dataset with various H&E stain conditions and devices including smartphone for the robust model development

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Introduction

Stain conditions and whole slide imaging (WSI) scanners vary across hospitals, causing color and texture variation in the histological images. In various countries, pathologists use smartphones to capture photographs of microscopic images instead of WSI scanners, adding further variation. Such variation limits the utility of machine learning models for pathological diagnosis in clinical settings, highlighting the need for an accurate evaluation of the model's bias and an optimized strategy for color/texture normalizations or augmentations to make robust models. Therefore, we created a large-scale histological image dataset with various stain conditions and devices including smartphones.

Material and methods

Tissue Microarray sections with 46 diverse tissues were stained with eight hematoxylins and one eosin solution to produce 13 H&E-stained tissue slides. They were scanned through seven WSI scanners and seven smartphones. Then, we performed image registration among the image groups with the same field of view. We evaluated whether test-time augmentation (TTA) utilizing our dataset improves the classification performance of datasets with different stains and scanners. We trained ResNet-18 with one dataset and evaluated the performance on the other test dataset with color normalization or augmentation.

Results and discussion

We produced 384,713 image patches. Accurately registered group images enabled us to clarify the image characteristics of each staining and scanner or smartphones. In the classification task, the TTA method using our dataset outperformed conventional color normalization.

Conclusion

We showed that our dataset could be useful for developing robust deep learning models in a downstream task. We will make our dataset available in a public repository.

Key words: test-time augmentation, color normalization, color augmentation, developments of robust models

A54

AI for Digital Pathology (AI4DP) Research Excellence Consortium: An Initiative to Kickstart Digital Pathology Research in Malaysia

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Introduction

Digital pathology has yet to take off in Malaysia, with only a few public hospitals equipped with digital pathology facilities. Correspondingly, while there is extensive work going on in digital pathology research groups worldwide, the research within the local community is still very limited, with only a few research labs actively pursuing research in this niche but very important field.

Material and methods

To elevate the digital pathology research into international standards, three research labs from Multimedia University (MMU), Universiti Kebangsaan Malaysia (UKM) and International Medical University (IMU) banded together to create a research consortium called the AI for Digital Pathology (AI4DP). While the main focus is on the application of artificial intelligence in digital pathology, in the long term the consortium also aims to create awareness among local pathologists on the importance of embracing digital pathology, to become the national referral point in digital pathology research, as well as to work with the relevant bodies in establishing the policy for digital pathology practice in Malaysia.

Results and discussion

The consortium managed to secure an initial funding from the Ministry of Higher Education Malaysia to work on projects exploring both histopathology and cytopathology branches, several machine learning problems (detection, segmentation, diagnosis), and three cancer sites (breast, blood, pancreas).

Conclusion

In this presentation we will share our journey in establishing this consortium as well as present the initial findings for the projects on real-time breast tumor cell detection and segmentation, histological screening for blood cancer, and cytological diagnosis of pancreatic cancer.

Key words: digital pathology consortium, CAD systems, breast cancer, blood cancer, pancreatic cancer

A55

Instant Immunohistochemistry in Digital Pathology

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Introduction

Ex-vivo fluorescence confocal microscopes (FCMs) is a new optical technology for fast microscopic digital imaging of fresh unfixed biological specimens without any slide preparation. However, it still needs additional approaches to support morphological analysis. Infact, modern medicine requires rapid diagnosis and accurate characterization to provide the best therapeutic approach and patients' management. The aim of this study was to integrate instant digital morphology with Immunohistochemistry (IHC) for cell lineage markers or oncoproteins on FCM for immediate and complete samples characterization.

Material and methods

The study was performed on bioptic and cytological specimens from thyroid, pancreatic and lung neoplasms. We used a series of antibody (Pan-CytoKeratin, CytoKeratin 7, Tireoglobulin, Sinaptophysin) labelled with appropriate fluorescent dye for IHC to be observed in real-time at FCM VivaScope®2500 (Vivascope GmbH, Munich, Germany). For each sample, IHC visualized on Vivascope was compared with the paired IHC performed on the final FFPE conventional sections by expert pathologists.

Results and discussion

We set up an IHC workflow that provides the best staining for each protein tested, avoiding cross-reactivity, non-specific bindings and noise background. We also optimized the protocol for antibody incubation and signals visualization at Vivascope to speed up the procedure. The IHC signal visualized at Vivascope was well detectable and similar to that observed on FFPE section after conventional IHC.

Conclusion

IHC integrated with instant digital morphology opens a new way to an innovative real time approach that allows to evaluate biological specimens without fixation or freezing and with immediate effects on fast diagnostic accuracy.

Key words: Instant Digital Pathology, Immunohistochemistry, Ex-vivo fluorescence confocal microscopes

A56

3D visualization in digital pathology using VR technology

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Introduction

The possibilities of 3D virtual reality visualization are still untapped in digital medicine. The application of this visualization technique can provide pathologists with tools that can speed up their daily work, make it more comfortable, and customize their entire work environment. In our paper, we present a solution that innovates 3D visualization in digital pathology using virtual reality.

Material and methods

In our paper, we present a solution capable of 3D visualization in virtual reality, for which the input data is digitized pathological serial section. We developed our solution with the help of a so-called graphics engine.

Results and discussion

The visualization solution presented by us gives the user an optimized implementation that can be widely used in digital medicine. With our solution the user is able to examine pathological serial sections reconstructed in 3D in a virtual examination space. Our solution provides an opportunity for the pathologist to carry out the diagnosis in a customizable, comfortable environment, and if necessary, he can even share the virtual space with other colleagues, so even establishing a joint diagnosis is a possible option among use cases.

Conclusion

As a result, we created a solution that can reconstruct complete pathological serial sections in 3D and then visualize them in virtual reality. Based on virtual reality, we have created an examination space in which the user can perform routine pathological examinations comfortably, away from the distractions of the outside world. We determined three areas in which the virtual reality 3D visualization can be useful in digital medicine: diagnostics, consultation, education.

Key words: 3D visualization, digital pathology, virtual reality, digital medicine

A57

CARVIS-WSI: An open source tool for Cartographic Visualization of the Diagnostic Path on Whole Slide Images

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Introduction

Focus of the presented software solution is the visualization of the pathologist's complex "diagnostic path" at a glance, using methods for information visualization as an overlay to Whole Slide Images (WSIs). CARVIS-WSI facilitates a detailed exploration of the multidimensional time- and space-related attributes describing the diagnostic process in histopathology by solving the problem of simultaneously depicting time-flows of viewed area, observation-duration, and slide-magnification.

Material and methods

To describe the relevant aspects of the diagnostic process in histopathology, CARVIS-WSI renders and displays the pathologist's visual tour through the histopathological slide. This tour is captured by screen recording the evaluation in QuPath and tracking eye-movement data with the iMotions Biometric Research Platform software and a Tobii Pro Fusion eye-tracker.

Results and discussion

The CARVIS-WSI Tool enriches the histopathological slide image with the above mentioned multidimensional attributes describing the diagnostic process. These attributes are mapped to the histopathological slide image in an overlay, similar to visualizations known from cartography. This results in an image that comprehensively represents the pathologist's decision path including all attributes of the diagnostic process. CARVIS-WSI is available on Github (https://github.com/human-centered-ai-lab/CARVIS-WSI).

Conclusion

CARVIS-WSI utilizes a combination of multiple approaches to develop a multiscale visualization of a pathologist's diagnostic path, extending previously known and used methods, such as heat maps on gigapixel images. The proposed visualization would not only be useful for training of pathologists and self-evaluation of pathologists working in diagnostics, but would also help to gain deeper insights into comparative histopathology studies, or user behavior studies for improving digital pathology software solutions.

Key words: Visualization, Diagnostic Path, Observation Path, Histopathology, Cartography

A58

Transfer learning for cell detection in bone marrow smears

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Introduction

With increasing availability of medical datasets from multiple sources, the use of transfer learning can enhance the performance of deep neural networks. In this study, we compare different strategies to include external data sources into the training to boost the performance of a network with respect to our internal dataset while maintaining generalizability.

Material and methods

We use an external dataset of 512 regions of interest (ROIs) and a smaller internal dataset of 172 ROIs, both for cell detection in bone marrow smears. We train CenterNet and Faster R-CNN (FRCNN) on these datasets in different ways, namely a) each of the two datasets individually, b) both datasets combined (with and without balancing), and c) pre-training on the external dataset and fine-tuning on the internal dataset (with and without frozen backbone).

Results and discussion

When evaluated on the internal test set, both architectures show low F1-scores for a) when trained on external data only (CenterNet: 0.73, FRCNN: 0.79) and high scores on internal data only (CenterNet: 0.94, FRCNN: 0.9). However, external test quality is low in the latter case. We can further observe that training strategy b) is outperformed by strategy c) without frozen backbone (CenterNet: 0.92, FRCNN: 0.9). Furthermore, average distance between predicted and reference cells is lower for FRCNN (2.27 vs. 13.34).

Conclusion

While CenterNet provides better F1-scores, FRCNN predicts cell positions much more accurately. To increase cell detection quality in bone marrow smears while maintaining generalizability, pre-training on the larger external dataset and fine-tuning with the internal dataset appears to be the best strategy.

Key words: Transfer Learning, Cell Detection, Bone Marrow Smear, Deep Learning

A59

Merging local cell feature and global tissue structure to learn accurate epithelial cell classification on H&E images

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Introduction

In cell-level tissue analysis from H&E digital images, available datasets and models propose an epithelial class without further differentiating between normal and malignant. This distinction can be challenging due to the high morphologic heterogeneity of malignant cells. We propose here a new method based on the aggregation of local and global tissue features to accurately differentiate between normal and malignant cells.

Material and methods

Epithelial graphs were built on a subset of patches from Lizard and Bern datasets for training and TCGA and PanNuke for testing that were specifically annotated for normal/malignant epithelial cells. Nodes were individual epithelial cells and attached features were locally extracted from the H&E image to reflect cell morphology. Delaunay triangulation was used to build the edges. Graph convolution networks were trained and optimized for node classification using different message passing (MP) functions, followed by postprocessing (graph clustering and median filtering) to smooth the predictions inside individual glands.

Results and discussion

The best performance was obtained with graph attention (GAT) MP. The graph-based cell classification significantly ($p < 0.05$) improved the F1 score on both testsets compared to ResNet, achieving 97.8% F1 score on TCGA and 100% on PanNuke (91.7% and 99.0%, respectively, using ResNet).

Conclusion

Structural context, captured by graphs, showed to be an important feature for epithelial cell classification. The model we propose can be applied on top of any other method that identifies epithelial cells to further differentiate between normal and malignant cells and get an accurate estimation of the epithelial cells' composition for downstream analyses.

Key words: colorectal cancer, cell classification, cell-based graphs, graph convolutional networks, graph attention, malignant epithelial cells

A60

SlideMaps: An EMPAIA specification for storage and visualization of pixel-wise overlays on Whole Slide Images

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Introduction

Image processing applications (Apps) for digital pathology produce output of various data types, such as numerical scores, contours of cells and pixel-wise results. The EMPAIA App Interface is an open and vendor-agnostic specification for integrating Apps into pathology workstations. We hereby propose the SlideMap datatype as a specification extension for pixel-wise overlays on WSIs to enable more detailed analysis and accurate diagnoses.

Material and methods

WSI overlays support many different use-cases: Quality control algorithms highlight digital artifacts like blurry areas as sharpness maps. Explainable Artificial Intelligence (xAI) methods may visualize the prediction confidences or highlight the importance of pixel areas as saliency or attention maps. Apps can automatically produce heat maps of tumor hotspots or tissue segmentation maps on large tissue areas.

Results and discussion

The SlideMap specification describes HTTP API endpoints to write and read pixel-wise binary data and describes the byte-level data layout. The basic idea is to store medical or technical meaningful values instead of a color encoding, allowing the client to mix and render data channels to the user's preference. SlideMaps are being transferred on a per-tile basis, where each tile may have multiple data channels and corresponds to a location on a specific WSI image layer.

Conclusion

The highly requested SlideMap feature is being discussed with AI researchers and industry partners of the EMPAIA Consortium to meet the requirements of existing and future use cases. The datatype is being developed to functionally match the related DICOM supplements. All stakeholders are invited to contribute to the further development and review of this specification.

Key words: specification, web, artificial intelligence, image processing, visualization, datatype

A61

Deep learning for detecting BRCA 1/2 mutations in high-grade ovarian cancer based on an innovative tumor segmentation method from whole-slide images

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Introduction

BRCA mutations constitute a significant proportion of Homologous Recombination Deficiency (HRD) and represent a reliable effective predictor of sensitivity of high-grade ovarian cancer (HGOC) to poly(ADP-ribose) polymerase inhibitors. However, their testing by NGS is costly, time-consuming, and can be affected by various preanalytical factors. In this work, we present a novel approach for predicting BRCA mutations in ovarian cancer using deep learning (DL).

Material and methods

The dataset includes 775 patients with HGOC and BRCA somatic mutational status. To optimize the training of the classifier, a first step of tumor segmentation based on an innovative DL technique was performed. A total of 1,69M tumor tiles were predicted over the whole dataset. We used 599K tiles to train a ResNet-50 with a momentum contrast approach while 1,087M tiles were used to train a BRCA classifier with an attention-based multiple-instance learning mechanism.

Results and discussion

The segmentation model trained on 8 WSI achieved a Dice Score of 0.915 and an IoU of 0.847 on a test set of 50 WSI. The BRCA classifier obtained an AUC of 0.741 in 5-fold cross-validation, 0.673 on the test set, and 0.631 on an independent test set from TCGA. We performed additional multi-scale approaches suggesting that the relevant information for predicting BRCA mutations is more located in the tumor context than in the cell morphology.

Conclusion

Our results suggest that BRCA mutations have a discernible phenotypic effect which could be detected by DL and could be used as a pre-screening tool. This pipeline needs to be conducted on ovarian cancer with other homologous recombination anomalies.

Key words: High-grade ovarian cancer, BRCA mutation, Deep learning, Computational pathology, Segmentation, Momentum Contrast self-supervised learning

A62

Swiss national study on the impact of computer-aided diagnosis systems on pathologists' scoring: an application for tumor cell fraction estimation

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Introduction

Tumor cell fraction (TCF) estimation is a common clinical task with well-established large inter-observer variability. It thus provides an ideal testbed to evaluate potential impacts of employing a computer-aided diagnostic (CAD) tool to support pathologists' evaluation.

Material and methods

During a National Slide Seminar event, pathologists (n=69) were asked to visually estimate TCF in 10 cropped H&E colorectal cancer images intentionally curated for diverse tissue compositions, cellularity, and stain intensities. Next, they re-evaluated the same images while being provided a computationally created overlay highlighting predicted tumor versus non-tumor cells, together with the corresponding TCF percentage. Participants also reported confidence levels in their assessments using a 5-tiered scale, indicating no confidence to high confidence, respectively. The TCF ground truth (GT) was defined by manual cell-counting by experts.

Results and discussion

When assisted, inter-observer variability significantly decreased, showing estimates converging to the GT. This improvement remained even when CAD predictions deviated slightly from the GT. The standard-deviation of estimated TCF to the GT across images was 9.9% vs 5.8% with CAD, $p < 0.05$. The intraclass correlation coefficient increased from 0.8 to 0.93 (CI95% [0.65, 0.93] vs [0.86, 0.98]) and pathologists stated feeling more confident when assisted (3.67 +/- 0.81 vs. 4.17 +/- 0.82 with CAD).

Conclusion

CAD TCF estimation support demonstrated improved scoring accuracy, inter-pathologist agreement and scoring confidence. Interestingly, pathologists also expressed more willingness to use such a CAD tool at the end of the survey, highlighting the importance of training/education to increase adoption of CAD systems.

Key words: inter-observer variability, computer-aided diagnosis, tumor cell fraction, scoring agreement

A63

The fundamental points of testing a pathological virtual reality software

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Introduction

The utilization of virtual reality (VR) is gaining traction in scientific research and industrial fields. Even though there has been significant progress in the development of VR software, identifying the specific features that contribute to its quality, user-friendliness, and effectiveness still a challenge. The use of VR for scientific purposes has the potential to revolutionize the human-computer interface. In our paper, we present aspects that can be used to test the usability of the software.

Material and methods

Using the defined metrics, our solution allows usability testing of a pathological VR software. The Godot engine was used to create a VR environment for development. The SteamVR Plugin was used to integrate the HTC Vive headset with the Godot engine. The software application was tested in Godot environment, and usability metrics such as hand and head movement were measured and evaluated. A usability study was conducted with participants to evaluate the user experience of the software application.

Results and discussion

Our proposed testing approach can evaluate the user's head, hand, and eye movements, as well as detect any inconsistencies between the real-world and virtual environments presented through VR headsets and controllers. Usability testing aims to determine how comfortable, fast, and learnable a particular software is to use.

Conclusion

The scientific use of virtual reality is based on quality factors of virtual reality software, which are not yet fully developed. Discovering and developing these aspects can advance the development of quality VR software. As a result, we created a solution that can test usability aspects of a virtual reality software.

Key words: usability testing, digital pathology, virtual reality, Godot

A64

HistoEncoder: Building a foundation model for histopathology

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Introduction

Deep learning models perform superior to human observers in many digital pathology tasks, although training reliable models require large annotated datasets and access to high computing environments. Foundation models are pre-trained with massive datasets and fine-tuned for specific downstream tasks, which require less computing power and annotated data. Foundation models have already transformed language processing and fine-tuning models pre-trained on natural images is already common practice in digital pathology, although natural images differ radically from histological images. Currently, there are no foundation models pre-trained with histological data.

Material and methods

Here, we train a self-supervised encoder model with 50 million images from thousands of prostate tissue samples on Europe's largest supercomputer LUMI and demonstrate the shortcomings of models pre-trained on natural images.

Results and discussion

During pre-training, the encoder learns to distinguish different histological patterns. Visualising the encoded features after dimensionality reduction reveals clear clusters for Gleason grades and even patterns associated with prostate cancer-specific death, which are not visible with a model pre-trained with natural images. Fitting a nearest neighbour prostate cancer classifier with the encoded features requires no training, while still outperforming an end-to-end fine-tuned natural image model. Fine-tuning the models with limited training data, reveals the encoder requires up to 17 times less data to achieve similar results.

Conclusion

Encoding useful features without fine-tuning enables researchers for example to easily combine histopathology data with other data modalities, and automatically label histological samples based on feature clusters. Our results demonstrate that foundation models pre-trained with histopathology images are superior to models pre-trained with natural images.

Key words: foundation models, prostate cancer, image analysis, transfer learning, deep learning

A65

Validation of AI-supported assessment of HER2 gene amplification status in fluorescence in-situ hybridization (FISH) whole slide images

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Introduction

Evaluating the HER2 gene amplification status in breast cancer tissue is the gold standard for treatment decisions with trastuzumab. However, manual assessment is a time-consuming task that is subject to substantial interrater variability. We developed a decision support system called PAIKON that assists pathologists with the detection and classification of nuclei and gene signals. Here, we present preliminary results of a validation study of PAIKON.

Material and methods

We retrospectively collected and scanned tissues from 71 breast cancer cases (incl. 24 HER2 positive) from routine diagnostics at the Institute of Pathology at the Carl Gustav Carus University Hospital in Dresden. Three trained assistants assessed the mean HER2/CEN17 ratio per case under three conditions: (1) under an analogue microscope, and in the PAIKON-based digital slide viewer (2) without AI-support, and (3) with AI-support.

Results and discussion

Concordance between HER2/CEN17 ratios was quantified using Lin's correlation coefficient (ccc), while Cohen's kappa (kappa) was used to measure concordance between positive/negative cases. Very high concordance (ccc=0.86, kappa=0.95) was observed between analogue and digital assessment. When directly comparing human and AI-assisted assessment, a high concordance (ccc=0.75, kappa=0.93) was found, but a slight proportional bias was observed that could be attributed to clusters of HER2 signals. We also validated the assessment of a much larger number of nuclei than stated in the guidelines (e.g., 500 vs. 20 nuclei per slide) where we found excellent concordance with routine diagnostics (kappa=0.96).

Conclusion

Our preliminary validation study of PAIKON shows very promising quantitative results with respect to the AI-assisted assessment of the HER2 gene amplification status.

Key words: FISH, HER2, Artificial Intelligence, breast cancer, whole slide imaging, PAIKON

A66

Interactive Model Visualization on Whole Slide Images

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Introduction

We have developed a visualization tool tailored for the overlay of outputs of machine learning models onto whole slide images, in a fully zoomable, interactive, and customizable viewer. The tool can be used locally, but can also be packaged into a docker to make a visualization available for online viewing/sharing.

Material and methods

We leverage open-source projects bokeh (bokeh.org) for development of the browser-based UI, and tiatoolbox (https://github.com/TissueImageAnalytics/tiatoolbox) for slide reading, serving image tiles, and annotation storage/rendering. The tool is written in python and is available publicly at https://github.com/measty/tiatoolbox.

Results and discussion

We are able to overlay any combination of the following onto a WSI: 1. Annotations stored as geometries paired with property dictionaries. This is the most flexible mode for display of model outputs. The way that annotations are coloured and displayed can be chosen interactively in a variety of ways, such as a colour mapping of some continuous property, or colouring annotations of specific types according to a colour dictionary. 2. Lower resolution images such as pre-generated heatmaps, provided as .png or .jpeg files 3. A graph provided as a dictionary of nodes and edges. Both nodes and edges can be toggled on/off, and it is possible to provide features or model outputs associated with nodes that are displayed as a hovertool when a node is moused over.

Conclusion

We provide a powerful and general way to explore model predictions on WSIs, which is flexible enough to accommodate visualizations for a variety of model types including patch-based models, semantic segmentations of histological entities such as cells or glands, and graph-based models.

Key words: Model Visualization, Machine learning, Digital Pathology, Whole Slide Images, Slide Viewer

A67

Predicting Prostate Cancer Molecular Subtype with Artificial Intelligence

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Introduction

Visual microscopic examination of prostate cancer has not shown a consistent connection between tumour molecular subtype and morphologic characteristics, unlike other genitourinary malignancies. Deep learning-based algorithms trained on Hematoxylin and Eosin (H&E) stained whole slide images (WSI) from large cohorts with proven molecular classification may outperform the human eye and provide a cost-effective and rapid technique to find clinically relevant genomic abnormalities. We present an approach to identify prostate tumours with ERG fusions and/or PTEN loss.

Material and methods

We created a deep learning system that extracts non-linear characteristics from histopathology imaging data for improved prediction of molecular markers. Using genetically confirmed immunohistochemical testing for ERG/PTEN status, the algorithm was trained using H&E-stained WSI from 242 tumours from a previously reported Johns Hopkins radical prostatectomy (RP) cohort.

Results and discussion

ERG algorithm performance was assessed on three RP cohorts, including 64 additional WSI held out from the pre-training cohort (AUC: 0.91) and 248 WSI (AUC: 0.86) & 375 WSI (AUC: 0.89) from independent RP cohorts. In addition, we tested the algorithm in 202 WSI from a needle biopsy cohort of patients undergoing radiation therapy (AUC: 0.80). PTEN algorithm performance was assessed using 64 additional WSI held out from the pre-training cohort (AUC: 0.81) and a cohort of 214 WSI of Grade Group 2 needle biopsies (AUC:0.74).

Conclusion

A deep learning method to predict ERG status from H&E-stained WSI performed well across three independent testing cohorts, including RP and needle biopsies. The PTEN status prediction system is promising but may need additional training to account for frequent heterogeneous and subclonal loss.

Key words: Molecular Markers, Prostate Cancer, Deep Learning, Histopathology

A68

Using intratumor heterogeneity of IHC biomarkers to classify laryngeal and hypopharyngeal tumors based on histological features

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Introduction

Haralick texture features are used to quantify the spatial distribution of signal intensities within an image. In this study, the heterogeneity of proliferation (Ki-67 expression) and immune cells (CD45 expression) within tumors was quantified and used to classify histological characteristics of larynx and hypopharynx carcinomas.

Material and methods

Of 21 laryngectomy specimens, 74 whole-mount tumor slides were scored on histological characteristcs. Ki-67 and CD45 immunohistochemistry was performed and all sections were digitized. The tumor area was annotated in QuPath. Haralick features independent of the DAB-intensity were extracted from the isolated DAB-signal to quantify intratumor heterogeneity. Haralick features from both biomarkers were used as input for a principal component analysis (PCA). A linear support vector machine was fitted to the first four principal components for classification and validated with a leave-one-patient-out cross-validation method.

Results and discussion

Laryngeal vs. hypopharyngeal tumors and cohesive vs. non-cohesive growth showed significant differences in individual Haralick features. Therefore, these were used for classification. The linear classifier resulted in a classification accuracy of 85% for site origin and 81% for cohesive vs. non-cohesive growth. A leave-one-patient-out cross-validation resulted in an error rate of 0.27 and 0.35 for both classifiers, respectively.

Conclusion

In this study, we show a method to quantify intratumor heterogeneity of IHC biomarkers using Haralick features. This study also shows the feasibility of using these features to classify tumors by histological characteristics. The classifiers created in this study are a proof of concept, since more data is needed to create robust classifiers, but the method shows potential for automated tumor classification.

Key words: Haralick features, Intratumor heterogeneity, Tumor classification, Whole Slide Imaging, Immunohistochemistry

A69

Automated Diagnosis of Pancreatic Cancer through Deep Learning and Ex-vivo Fluorescence Confocal Laser Microscopy: A New Frontier in Digital Pathology

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Introduction

The recent technological advances in Artificial Intelligence (AI) and particularly in Deep Learning (DL) models have the potential to improve performance of automated computer-assisted diagnosis tools in digital pathology and reduce subjectivity. Simultaneously, ex-vivo Fluorescence Confocal Laser Microscopy (FCM) has emerged as a new optical technology intended for fast microscopic digital imaging of fresh unfixed biological specimens without any slide preparation that gives less noisy digital images.

Material and methods

In this study 25 digital FCM images of endoscopic ultrasound guided fine needle biopsy samples (EUS-FNB) from solid lesions of the pancreas were annotated and segmented by pathologist and were subjected to DL techniques for tumor cell detection, classification and segmentation. To train and infer the AI tasks, Convolutional Neural Networks (particularly U-Net architecture) were extensively used along with the Sørensen-Dice coefficient, which served as both the training loss function and performance score.

Results and discussion

Preliminary results show that the best trained model achieved performances greater than 0.7 for Sørensen-Dice Score and 0.8 for sensitivity. A quality assessment was also conducted by a pathologist; the outcome shows that almost all regions of tumor tissue were segmented but the segmentations also included the adjacent class of atypical tissue and minimal regions of other types of tissue consistently with the obtained sensitivity.

Conclusion

The promising results obtained will be able to provide immediate unassisted evidence of the adequacy of the specimen at the time of sample collection. Further improvements can be reached by incrementing the dataset size and labeling the atypical tissues, mitigating the misclassification of tumoral and atypical tissues.

Key words: deep learning, computer-assisted diagnosis, instant digital pathology, pancreas lesions, ex-vivo technology

A70

Altered organization of collagen fibers in the uninvolved human colon mucosa 10 cm and 20 cm away from the colorectal cancer

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Introduction

Remodelling of collagen fibers has been described during every phase of cancer genesis and progression. Changes in morphology and organization of collagen fibers contribute to the formation of microenvironment that favors cancer progression and development of metastasis. However, there are only few data about remodelling of collagen fibers in healthy looking mucosa distant from the cancer.

Material and methods

Using SHG imaging, scanning electron microscopy (SEM), specialized softwares (CT-FIRE, CurveAlign and FiberFit) and novel morphological method, we objectively visualized and quantified changes in morphology and organization of collagen fibers. SHG polarization anysotropy was used to quantify alignment of collagen molecules inside fibers. Using immunohistochemistry (staining with anti-alphaSMA, anti-LOX, anti-MMP2 and anti-MMP9) we investigated possible causes of collagen remodelling (change in syntheses, degradation and collagen cross-linking) in the colon mucosa 10 cm and 20 cm away from the cancer in comparison with healthy mucosa.

Results and discussion

We showed that in the lamina propria this far from the colon cancer, there were changes in collagen architecture (width, straightness, alignment of collagen fibers and collagen molecules inside fibers), increased representation of myofibroblasts and increase expression of collagen-remodelling enzymes (LOX and MMP2).

Conclusion

Thus, the changes in organization of collagen fibers, which were already described in the cancer microenvironment, also exist in the mucosa far from the cancer, but smaller in magnitude.

Key words: collagen, human colon mucosa, colorectal cancer

A71

Unstained tissue imaging and virtual HE staining of whole slide images: an assessment of histological feasibility

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Introduction

Hematoxylin and eosin (HE) is the standard stain for histology. The main purpose of histological staining is to make tissues visible to the human eye by highlighting certain cellular and tissue structures. This chemical technique, however, is irreversible, making the tissue unusable for other methodologies. Here, we develop and evaluate techniques to perform HE staining computationally from preclinical whole slide images (WSIs) acquired with brightfield microscopy.

Material and methods

We first optimized laboratory preparation protocol for virtual staining using five tissue section thicknesses and three unstained conditions (unprocessed, deparaffinized, and coverslipped). We used CycleGAN, an unsupervised deep learning approach, to virtually stain the samples, and compared the results to chemically stained HE reference. With the optimized conditions, we then utilized supervised deep learning with pix2pix network for virtual staining of prostate tissue and tested the effect of different network capacities on staining performance. Finally, we tested performance of the most successful architecture with six other tissues. All virtual stainings were thoroughly assessed quantitatively and histologically.

Results and discussion

We found that 5 micron deparaffinized tissue sections have the best reproducibility for virtual staining whereas increasing tissue content with thicker sections is disadvantageous. Utilizing a supervised deep learning model significantly improves the results compared to an unsupervised approach, and increasing network capacity further improves the accuracy of virtual staining.

Conclusion

Our findings highlight the potential of virtual HE staining of brightfield WSIs for both research and clinical histopathology while simultaneously opening possibilities for histological staining to become more sustainable and streamlined.

Key words: computational histology, digital pathology, HE staining, histopathology, virtual staining, whole slide imaging (WSI)

A72

Pathology process modelling with Petri-nets on event logs

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Introduction

Traditionally, the focus of digital pathology has been on artificial intelligence methods in digital image analysis to assist the pathologist in examining slides. In this study, we extend the scope of digital pathology to all stages of the diagnostic process, explicitly including tissue preparation. Specifically, we report on a project conducted at Haukeland University Hospital (Norway) with the aim of supporting and improving the performance of the entire "pathology process" by using the available data in novel ways.

Material and methods

While the whole slide imaging system contains unexploited value in the form of images, the laboratory information system contains unexploited value in the form of event logs. We use process mining to obtain a process model from the raw event logs. Simulation based on Petri-nets and queuing theory then utilises the resulting process model to make predictions about process turnaround times.

Results and discussion

As first preliminary results of our project, we present a dashboard that visualises the current "production" of cassettes, blocks and slides in real time, as well as a graphical Petri-net simulation engine that can predict key performance indicators of the laboratory for selected time ranges.

Conclusion

By combining heterogeneous methods from data science, operations research and artificial intelligence, it is possible to visualise, explore and predict laboratory processes. We conclude with a vision of an integrated pathology process intelligence system capable of predicting future workloads, suggesting optimal resource allocations, and facilitating integrated tracing allowing patients and clinicians to directly track the status of the specimen.

Key words: Workflow Analysis, Process Mining, Simulation, Petri-nets, Dashboards

A73

Decoding the Interplay between Immune Response and Somatic Tumour Mutations in Triple-Negative Breast Cancer

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Introduction

Breast cancer is the most common cancer among women worldwide and the immune response is a known prognostic factor in triple-negative breast cancer (TNBC). To improve our understanding of the role of somatic mutations in shaping the tumour microenvironment, we combine automated in-situ histological cell counts with genomic data to shed light on the complex relationship between mutational processes in TNBC and the immunological tumor microenvironment.

Material and methods

We developed a cell counting pipeline to quantify immunologically stained cells in Tissue Microarrays (TMAs) in a large population-based TNCB cohort (n=218). The pipeline was built using colour deconvolution for staining separation and implemented starDist for cell segmentation.

Results and discussion

Our results revealed a strong correlation between automated cell counts from IHC staining and p53 mutation status. Integrating homologous recombination deficiency (HRD) status and CD3 cell counts, we saw that patients with HRD-positive tumours and higher CD3 counts have better clinical outcomes. Moreover, we found that a positive HRD status is not equivalent to an 'immune hot' phenotype and that p53 protein staining is associated with TP53 mutations but not necessarily with a pathogenic mutation.

Conclusion

Our findings demonstrate the importance of integrating somatic tumor features with in situ TME estimates in breast cancer. Through this integrative approach we hope to improve patient stratification and prognostication through a more comprehensive understanding of the interplay between the immune response and tumour-intrinsic features in TNBC.

Key words: breast cancer, image analysis, tumour microenvironment

A74

DCIS risk and outcome prediction using a multi-instance-based deep learning approach

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Introduction

Ductal Carcinoma in Situ (DCIS) is a potential precursor for ipsilateral invasive breast cancer (iIBC). Patients are treated with radiotherapy to prevent progression to iIBC. However, it is known that a majority of these women would not experience a recurrence within their life-time. To reduce overtreatment with radiotherapy, we have developed a deep-learning pipeline that predicts iIBC recurrence from whole-slide images (WSIs) of H&E histopathology slices of DCIS lesions that outperforms existing biomarkers.

Material and methods

Our dataset consists of WSIs of the primary DCIS lesion from 249 patients with follow-up recurrence status for 10 years (125 recurrences). The included patients did not receive any subsequent treatment such as radio- or endocrine therapy. Our proposed deep-learning pipeline follows a two step approach: 1) Detection of mammary ducts using an object detection model with a shared ResNet- Feature Pyramid backbone. 2) Prediction of DCIS recurrence status with a ResNet backbone using a multi-instance learning approach with average pooling. For both steps, ResNet backbones were pretrained using self-supervised learning on the publicly available TCGA-BRCA data.

Results and discussion

The proposed deep-learning pipeline achieves an AUC of 0.8 for predicting 10-year iIBC-recurrence on the test set (n=75).

Conclusion

In Conclusion, a multiple instance learning model trained on features extracted from automatically detected ducts on H&E WSIs of DCIS lesions can predict iIBC recurrence better than existing biomarkers, promising to reduce overtreatment of breast cancer patients in clinical practice. Our current work is focused on training several WSI-based prediction models, as well as validating our models on an external dataset.

Key words: Digital Pathology, AI , Breast Cancer, Deep Learning

A75

Clinical-grade tumor detection and tissue segmentation in colorectal specimens using artificial intelligence tool

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Introduction

Digital pathology adoption allows for applying computational algorithms to routine pathology tasks. Our study aimed to develop a clinical-grade AI tool for precise multi-class tissue segmentation in colorectal specimens (resections and biopsies) and clinically validate the tool for tumor detection in biopsy specimens.

Material and methods

The training dataset included 241 precisely manually annotated whole slide images from multiple institutes. The algorithm was trained for semantic segmentation of 11 tissue classes with an additional module for biopsy whole slide image classification. Six case cohorts from 5 pathology departments (four countries) were used for formal and clinical validation, digitized by four different scanning systems.

Results and discussion

The developed algorithm shows high precision of segmentation of different tissue classes in colorectal specimens with composite multi-class Dice score of up to 0.895 and pixel-wise tumor detection specificity and sensitivity of up to 0.958 and 0.987, correspondingly. In the clinical validation study on multiple external cohorts, the AI tool reached sensitivity 1.0 and specificity of up to 0.969 for tumor detection in biopsy whole-slide images. The AI tool analyzes most biopsy cases in < 1 min allowing effective integration into clinical routine.

Conclusion

We developed and extensively validated a highly accurate, clinical-grade tool for assistive diagnostic processing of colorectal specimens. This study is a foundation for a SemiCOL computational challenge. We open-source multiple manually annotated and weakly-labeled test datasets, representing an enormous contribution to the colorectal cancer computational pathology field.

Key words: colorectal cancer, tumor detection, segmentation, biopsy, diagnostic tool, pathology

A76

Optimization of immunofluorescence slide digitization

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Introduction

Digitization of tissue slides is an emerging concept in the field of research and pathology. Currently, the focus is more on brightfield imaging, yet fluorescence images can reveal more information regarding multiplexing for different cell types. The digitization of fluorescence samples is more complex than brightfield imaging because it requires a superior signal-to-noise ratio. Therefore, it is important to acquire an optimal staining as well as scanning protocol to obtain high-quality reproducible images, especially in the context of downstream data analysis. The aim of our study was to optimize a tissue staining protocol for mouse lung tissue as well as the digital image acquisition protocol.

Material and methods

To optimize the staining protocol, we used paraffin-embedded mouse lung tissue. For tissue clearing, different agents were compared including Xylene and Neo-Clear. In addition, the antigen retrieval method was optimized for the mouse lung tissues, in which three methods were compared: intermittent antigen retrieval using a microwave, long antigen retrieval using a microwave and a steaming technique. Furthermore, we optimized an image acquisition protocol for fluorescence imaging using the Zeiss Axioscan.Z1 digital slide scanner.

Results and discussion

By adjusting laser intensities and exposure times, the signal-to-noise ratio was optimized. The use of the xylene substitutes as a clearing agent enhances the fluorescence signal for slide digitization.

Conclusion

Together with a stable antigen retrieval methods and an optimized scanning protocol, we successfully digitized mouse lung tissue slides. These digital whole-slide images will be used for data analysis purposes and the development of artificial intelligence algorithms in the future.

Key words: slide digitization, optimization, immunofluorescence

A77

Digital pathology and gene expression analysis as potential tools of standardization for renal transplant pathology

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Introduction

The diagnosis of T-cell mediated rejection in the transplanted kidney is based on the microscopic analysis of the biopsy sample. The Banff classification which provides the framework for the diagnostic process uses semi-quantitative lesion scores that are inherently prone to inter- and intraobserver variability. In this study, we used the tools of digital and molecular pathology to explore potential ways to improve the current diagnostic system.

Material and methods

The enrolled kidney biopsies covered the entire spectrum of the T-cell alloimmune response, from normal morphology to borderline changes to T-cell-mediated rejection (n = 96). Histological sections from formalin-fixed, paraffin-embedded (FFPE) tissue blocks were stained with multiplexed immunohistochemistry, then were digitized and analyzed using machine learning algorithms. Gene expression studies were also performed on sections from FFPE tissue on the Nanostring platform.

Results and discussion

The F-score, recall and precision for the glomeruli were 0.91, 0.89 and 0.94 respectively. Similarly excellent parameters could be achieved for the tubules (0.93, 0.95 and 0.91). Object recognition capacity for inflammatory cells (0.79, 0.84 and 0.74) and peritubular capillaries (0.66, 0.82 and 0.60) were fair. The variables generated with the help of the algorithm showed a moderate to strong correlation with the gene sets characteristic of T cell-mediated rejection.

Conclusion

Digital pathology methods and gene expression testing are useful additional tools for semiquantitative kidney biopsy evaluation.

Key words: multiplexed immunohistochemistry, renal pathology, transplant pathology

A78

Exploring the decision-making of weakly supervised CNN models for histopathology image classification

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Introduction

In computational pathology, there is a rise of weakly supervised learning models where slide-level labels are either available on patient or tumour level, e.g. histological grading or patient outcome. However, spatial interpretability is often desirable to understand which tissue areas are important in the classification but is not intrinsically available in weakly-supervised tile-based models. In this study, we have proposed a direct methodology based on backward selection to determine WSI regions that are necessary for the classification of a WSI in the context of weakly-supervised CNN model.

Material and methods

We optimised and validated ResNet-18 models for histological grade 1 vs 3 classification on SöS-BC-4 cohort (n = 1695) using 5-fold CV. Two different tile-to-slide level aggregator functions were evaluated: the 75th percentile of the tile-level prediction probabilities, and a trainable attention layer. In both modelling strategies, we iteratively remove the highest-ranking tile until the slide-level classification flips.

Results and discussion

Removed tiles represent regions-of-interest for spatial visualisation and we observed an average of 32.34% (95% CI: 29.69% - 34.99%) and 44.97% (95% CI: 41.69% - 48.26%) of the WSI regions that contributed to the classification of Grade 3 in the CNN with 75th percentile and attention layer based tile-to-slide level aggregator respectively.

Conclusion

There is a need for interpretability and understanding of the decision-making of weakly supervised deep CNN models in both research and clinical applications. Here we proposed and evaluated a methodology for interpretability that is directly linked to predictions provided by weakly-supervised tile-based deep learning models, which can improve understanding of the classification decisions.

Key words: Weakly-supervised learning, Interpretability, Histological grading

A79

Laboratory phase-contrast imaging for 3D tumor resection margin assessment

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Introduction

Accurate assessment of the resection margin is essential for determining patient outcome in surgical oncology. Presently this typically is done by classical histology, which is time-consuming (several days) and gives only two-dimensional information. Here we propose laboratory phase-contrast computed tomography (CT) as an alternative and a complement. Phase-contrast CT has the unique advantages of giving cellular-resolution three-dimensional (3D) data rapidly. Such a laboratory system has the potential to provide intra-operative feedback to the surgeon.

Material and methods

Our high-resolution (< 10 um) propagation-based phase-contrast CT system relies on a liquid-metal-jet x-ray source in combination with a CMOS detector. It features tailored acquisition and reconstruction algorithms for optimizing 3D soft-tissue contrast and resolution. We started by demonstrating the method on, e.g., mice blood vessels , zebra fish muscles and human coronary arteries . We then continued with paraffin-embedded non-stained human tumor samples from the liver and pancreas including comparisons with classical histology of the same samples. In spite of the difference in contrast mechanisms and slight deformation during slicing for histology, the CT and microscopy images show great resemblance.

Results and discussion

More recently we have investigated fresh non-stained samples of colorectal liver metastasis, cholangiocarcinoma, hepatocellular carcinoma (all liver) as well as bone and soft-tissue sarcomas.

Conclusion

The results are promising, opening up for 3D virtual histology with potential for intra-operative assessment of tumor resection margins in the future.

Key words: Phase-contrast CT, virtual histology, resection margin

A80

Whole Tissue Imaging and Whole Block Imaging in Pathology Practice and Research

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Introduction

Micro-computed tomography (micro-CT) is a novel in vitro tomographic method allowing examination of fresh or fixed tissues and formalin fixed paraffin embedded (FFPE) tissue blocks non-destructively with a spatial resolution up to the level of 1 µm. Previous studies for breast cancer suggested that micro-CT images of fresh specimen, which is so-called whole tissue image (WTI), to showed structures indicating vessel network, metastatic tumor, and lymph node tissue. There is a need for analytical methods such as those implemented in the software used with clinical CT, because it is a difficult task to make sense of the vast amount of 3-dimensional information. In this study, we have evaluated micro-CT technology and feasible clinical utilities in pathology first. Then using the results, we have been developing 3-dimensional analysis methods for micro-CT image and effective visualization method.

Material and methods

Over 2600 samples were scanned (430 fresh tissue samples; 569 fixed tissue samples; 1620 FFPE block samples including 573 3x2 inch block) since February 2017. The micro-CT imaging system was a custom built micro-CT scanner (3DHistech, Hungary). The highest voxel resolution was 1.0 mm/voxel. Re-constructed imaging data was then visualized and analyzed by using commercially software and in-house application. Prior to clinical studies, we have established all necessary standard operating procedure such as material handling, scanning protocol and imaging assessment per organ and per application. After scanning, 1-350 H&E slides from one block were prepared for image assessment and AI development.

Results and discussion

Adding WBI and WTI with micro-CT of entire resected tissue's information, pathologists can evaluate tissue in 3D, seeing critical pathological changes anywhere in the tissue, in a clinical setting. We have confirmed that WBI can improve current WSI based 3D imaging; WBI and/or WTI can reveal additional information beyond what can be ascertained from the H&E in pathology diagnosis in all investigated organ systems.

Conclusion

WBI and WTI using micro-CT have huge potential in future medicine. Combining AI, deep learning, and WBI/WTI–micro-CT imaging technology, new lifesaving and life-extending clinical guidelines for many diseases can be established.

Key words: whole tissue imaging, whole block imaging, pathology practice, research

A81

Artificial Intelligence-Aided Three-Dimensional Quantification of Thrombosis Occurrence in Lungs Affected by COVID-19

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Introduction

Pulmonary thrombosis is common in COVID-19 pneumonia. To expand the understanding of the pathogenesis of (micro-)thrombotic and haemorrhagic events caused by COVID-19 in the lungs, we aim to reconstruct and quantify their extent in post-mortem formalin-fixed paraffin-embedded (FFPE) tissue blocks from victims of this disease.

Material and methods

Six representative FFPE tissue blocks of examined lungs containing thrombi and/or haemorrhages caused by COVID-19 were selected. 3D images of the entire specimen were obtained non-destructively using soft tissue-optimised X-ray micro-computed tomography (µCT). Afterwards, serial sections of 4 µm thickness were cut across the whole FFPE block and every 10th section was stained with haematoxylin-eosin (H&E). For these sections, whole-slide images (WSI) were digitised. On these WSI, thrombi and haemorrhage regions were automatically segmented from surrounding lung tissue using a deep learning pipeline (based on U-net), which was trained and validated on a separate cohort of H&E-labelled WSI from similar cases of influenza and COVID-19. The resulting 2D segmentation labels were registered onto the corresponding 3D µCT level to enable the segmentation of the volumes.

Results and discussion

Comparing to the ground truth annotated by specialists, our segmentation model achieved a dice similarity coefficient of 0.84 and 0.74 for thrombosis and haemorrhage histology structures, respectively. Using the predicted annotations for the non-sequential histology slides of the six COVID-19 FFPE blocks, we could inform the continuous 3D µCT reconstruction. Once registered, each object of interest can be traced throughout the whole tissue block, and its volume quantified.

Conclusion

Our study is a first attempt to accurately segments thrombi and haemorrhages in conventional histology slides using deep learning. This 2D information, once registered onto the corresponding depth levels of the 3D µCT data, provides a basis for the reconstruction of the 3D volumes of the thrombi and the degree of lung tissue affected by haemorrhage in COVID-19 patients. Thus, our work is a first step into the automation of microstructural labelling of µCT tissue scans, by informing regions of interest from 2D histology scans, which add comprehensive morphological information.

Key words: Artificial Intelligence, Thrombosis, Lungs, COVID-1

P01

Introducing ChatGPT to Image Classification for Histopathology

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Introduction

ChatGPT is an AI model that uses generative pre-training transformer (GPT), and it has been optimized using supervised and reinforcement learning. OpenAI offers the ability to fine-tune GPT models, such as: Ada, Babbage, Curie, and Davinci, to perform specific tasks. The objective of this research is to utilize these models to classify images. The challenge of this task is to represent images as strings - an image-to-text task.

Material and methods

A dataset of 50 histological images of fallopian tubes was used. Of these images, half were labeled positive as they exhibited signs of tubal ectopic pregnancy, while the other half were classified as negative as they did not show any evidence of pregnancy. Taking in consideration the fallopian tubes' anatomy, the dataset was augmented using rotation. To represent an image using characters, we utilized the classification scores associated with the class labels of the pre-trained AlexNet network. The network generates a probability value ranging from 0 to 1 for each of the 1000 output classes, indicating the likelihood of the corresponding class being present in the image. We resampled this probability interval into 26 classes (the number of letters in the English alphabet). This enabled us to obtain a 1000-character string representation of the image, similar to a hash. This resulting string, along with its corresponding image class, was then used to fine-tune the GPT models.

Results and discussion

In a 10-fold cross-validation scenario, we obtained classification accuracies over 80% for all models taken in consideration.

Conclusion

GPT models will find their way into histopathological diagnosis and, later, into result generation. Research funded by the University of Medicine and Pharmacy of Craiova, grant 26/24c/13.07.2021.

Key words: generative pre-training transformer (GPT), image classification, histopathology, image representation, image-to-text

P02

Dawn of AI enabled digital pathology in developing world- From benefits to challenges and possible solutions

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Introduction

The practice of pathology is undergoing a rapid transformation and multiple tools such as digital imaging, advanced artificial intelligence algorithms, computer-aided diagnostic techniques etc are being linked with molecular pathology resulting in increased diagnostic speed and accuracy based on the ability of modern-day pathologists to use these new tools and to interpret the data generated by them. Digital and computational pathology are new and emerging field of pathology. The promises of digital and computational tools are beyond the scope of traditional microscopy. In developing countries like Pakistan, the adoption of digital and computational techniques is not very fast like developed part of the world because of many reasons like financial constraints and absence of infrastructure required for the implementation. Not all hopes are lost, still we can start our journey.

Material and methods

We did several piolet studies on digital slides and put them on either commercial based AI software or through the help AI scientists on different projects like Malaria, Leukemia, Chorionic villi identification, ER/PR quantification, Ki-67 quantification and mitosis detection in leiomyosarcoma cases of uterus.

Results and discussion

Though these were all the pilot projects but the results were impressive particularly in terms of quantification.

Conclusion

Digital and computational pathology are significantly newer modalities but they have a definite role in modern pathology in terms of telepathology and computational pathology. These tools will open new horizons of precision medicine in the era of personalize medicine. Challenges are there but can be solved with the passage of time.

Key words: digital pathology, artificial inteligence, developing world

P03

Augment like there's no tomorrow: Consistently performing neural networks for medical imaging

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Introduction

Deep neural networks have achieved impressive performance in a wide variety of medical imaging tasks. However, these models often fail on data not used during training, such as data originating from a different medical centre. How to recognize models suffering from this fragility, and how to design robust models are the main obstacles to clinical adoption. Here, we present general methods to identify causes for model generalisation failures and how to circumvent them.

Material and methods

First, we use distribution-shifted datasets to show that models trained with current state-of-the-art methods are highly fragile to variability encountered in clinical practice, and then develop a strong augmentation strategy to address this fragility.

Results and discussion

Distribution-shifted datasets allow us to discover this fragility, which can otherwise remain undetected after validation against multiple external datasets. Strong augmentation allows us to train robust models achieving consistent performance under shifts from the training data distribution. Importantly, we demonstrate that strong augmentation yields biomedical imaging models which retain high performance when applied to real-world clinical data.

Conclusion

Our results pave the way for the development and evaluation of reliable and robust neural networks in clinical practice.

Key words: generalisation, augmentation, validation, deep learning, neural networks, medical imaging

P04

Harry Potter: a AI tool for diagnostic purposes

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Introduction

Artificial intelligence is quickly becoming an important resource in the medical field. In particular, deep learning-based pattern recognition methods can advance the field of pathology by incorporating data which enables the pathologist to be quicker and more precise in ascertaining a particular diagnose. In countries such as Portugal, where the prevalence of the infection by Helicobacter pylori is high and the incidence of gastric ulcers and cancer is bigger, the empirical strategy (test and treat) or endoscopy is more adequate.

Material and methods

We introduced digital in 2017 and our laboratory receive around 400 gastric biopsies/day, most of them for the sole purposes of identifying the bacteria. We became aware that artificial intelligence could be of great help in shortening the time it takes for the pathologist to search for the microorganisms thus reducing the added costs of non-reimbursed histochemical techniques performed to achieve a better diagnosis.

Results and discussion

We began perfecting an algorithm with a workgroup of six pathologists who would review the same biopsies and thereafter score the samples with 0, 1+, 2+ and 3+, and later on 0/1+ and 2+/3+ according to the established criteria. We met several times in the course of six months in order to reach a consensus regarding the cut-offs of each level.

Conclusion

The final AI algorithm was baptized "Harry Potter". Since most of the times the diagnosis can be achieved with the help of immunohistochemistry or PCR alone, the AI algorithm has been a valuable tool in selecting samples to which apply additional staining methods or eventually PCR and antibiotic resistency tests.

Key words: Artificial intelligence, Helicobacter pylori, digital pathology, gastric biopsy

P05

Three dimensional surface scanning of surgical specimens for potential incorporation into routine macroscopic examination workflow- a pilot study

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Introduction

Three dimensional (3D) scanning has recently been integrated into various medical disciplines. 3D scanning of surgical pathology specimens and its potential utility has been reported in anatomical pathology for clinical care, documentation and education.

Material and methods

We introduced a commercially-available 3D scanner (EinScan pro, Shining 3D) workstation in our department to capture and digitally reconstruct the 3D surface topography of formalin fixed surgical specimens to study the feasibility of incorporating this technology into our laboratory's routine workflow.

Results and discussion

The pilot study comprised 14 cases of large resection specimens from different organs and systems such as breast, uterus, kidney, prostate, liver, pancreas, femoral bone, maxilla as well as a complex retroperitoneal sarcoma resection. All scanning and subsequent surface topography processing could be managed by one operator. The time for scanning and processing ranged from 5 to 22 minutes (average 9.6 minutes) with the size of image files ranging from 20.1 to 184 Megabytes (average 141.1 Megabytes).

Conclusion

This pilot study shows promising initial results for a single-operator 3D scan workstation, with scanning/processing time and file size/storage measurements within practical limits for incorporation into the routine macroscopic examination workflow. The findings provide the basis for a holistic digital technology solution which can be applied to lesion and margin annotation, multimedia pathology reporting, and augmented reality multidisciplinary medical team discussions for both clinical care and education.

Key words: 3D scanning, macroscopic examination, routine workflow

P06

The ACROBAT 2022 Challenge: Automatic Registration Of Breast Cancer Tissue

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Introduction

WSI registration is an enabling technology both for research and diagnostics. The ACROBAT 2022 challenge aimed to evaluate image registration algorithms that align WSIs of differently stained histopathological slides that originate from routine diagnostics.

Material and methods

The data set that was published for the challenge consists of 4,212 WSIs of resection specimens from 1,153 breast cancer patients. For each patient, one H&E WSI is available. The training set consists of 750 cases (3,406 WSIs), with one to four IHC WSIs each from the routine diagnostic stains ER, PGR, HER2 and KI67. The H&E WSIs in the validation set (100 cases, 200 WSIs) and test set (303 cases, 606 WSIs) are paired with one randomly selected IHC WSI each. 13 annotators generated ca. 37,000 pairs of corresponding landmarks in the validation and test set image pairs. Within each image pair, the 90th percentile of distances between registered and annotated landmarks was computed. Participants were then ranked on the median of these 90th percentiles.

Results and discussion

Median 90th percentiles for eight teams that were eligible for ranking in the test set ranged from 60.1 µm to 15938.0 µm. The best performing method therefore has a score slightly below the median 90th percentile of distances between first and second annotator of 67.0 µm.

Conclusion

The ACROBAT 2022 challenge contributed to establishing the state-of-the-art in WSI registration under realistic conditions. Top-performing methods exceeded our expectations regarding robustness and precision and will enable future avenues of research.

Key words: registration, tissue alignment, challenge, breast cancer, WSI

P07

Use Of Novel Opensource Deep Learning Platform For Quantification Of Ki-67 In Breast Cancer Patients Of South Asian Descent – Analytical Validation

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Introduction

Ki-67 scoring is essential for the diagnosis, classification, treatment, and prognosis of invasive ductal carcinoma of breast. Traditional manual scoring of Ki-67 is not just time consuming and tedious for the pathologist but also prone to intra- and inter-observer variability. Every pathology lab is equipped with a computer system nowadays. Using more advanced automated methods for Ki-67 proliferative index estimation could help pathologists with more accurate reporting in many different tumors including breast carcinomas while making the entire process more efficient and reproducible. This can be useful in tumor grading as well.

Material and methods

The slides of tumor were selected retrospectively and randomly from 140 patients, spanning different subtypes. They were stained with the Ki-67 antibody. An expert pathologist evaluated the Ki-67 index in the hotspot fields using the eyeball method. Digital images were captured from the hotspot regions using microscope attached camera at 10x. The images were uploaded to the opensource DeepLIIF cloud platform (https://deepliif.org) to compute the exact percentage of Ki-67 positive cells. The results obtained through automated quantification were compared against those from manual interpretation and relevant concordance/consensus metrics were computed

Results and discussion

The manual and automated scoring methods showed strong positive correlation with Pearson's correlation coefficient of 0.98. The p-value was also statistically significant, $p < 0.05$.

Conclusion

Our study demonstrates that automated scoring of Ki-67 staining has tremendous potential in the future increasing its clinical value as the issues of consistency, reproducibility and accuracy can be eliminated. In the era of personalized medicine, pathologists can efficiently give a precise clinical diagnosis with the support of AI.

Key words: Ki-67 , Breast cancer, automated detection, Digital pathology

P08

Use Of Novel Opensource Deep Learning Platform For Quantification Of Ki-67 In Neuroendocrine Tumors – Analytical Validation

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Introduction

Ki67 is a widely used biomarker for quantifying cellular proliferation in tumors, including neuroendocrine tumors. The Ki67 index is calculated by dividing the number of Ki67 positive cells by the total number of cells evaluated in a tissue sample. A higher Ki67 index indicates a higher rate of cellular proliferation and is associated with a more aggressive tumor phenotype. In neuroendocrine tumors, Ki67 quantification is used to help determine the tumor grade and prognosis as well as to monitor response to treatment. However, it is important to note that Ki67 is not specific for neuroendocrine tumors and its expression can be influenced by other factors such as the stage of the cell cycle. Therefore, Ki67 should be interpreted in the context of other clinical and pathological features. In this study we compare the automated detection of Ki-67 with the manual eyeball/hotspot method.

Material and methods

The slides of tumor were selected retrospectively and randomly from previously diagnosed cases of neuroendocrine tumors. The slides were stained with the Ki-67 antibody. Two expert pathologists evaluated the Ki-67 index in the hotspot fields using the eyeball method. Digital images were captured from the hotspot regions using microscope attached camera at 10x. The images were uploaded to the opensource DeepLiiF cloud platform (https://deepliif.org) to compute the exact percentage of Ki-67 positive cells. The results obtained through automated quantification were compared against those from manual interpretation and relevant concordance/consensus metrics were computed

Results and discussion

The manual and automated scoring methods showed strong positive correlation with Pearson's correlation coefficient of 0.97. The p-value was also statistically significant, $p < 0.05$.

Conclusion

Artificial intelligence (AI) can be used to support the detection and quantification of Ki67 in neuroendocrine tumors. This can be done using a variety of techniques such as deep learning algorithms, computer vision and image analysis. However, it is important to note that deep learning algorithms in neuroendocrine tumor analysis are still in the stage of development and require validation. Also, comparison of AI based Ki 67 quantification to traditional manual methods is needed to ensure its accuracy and reliability

Key words: Ki-67 , Neuroendocrine tumors, automated detection

P09

End-to-end pipeline for automatic grading of IHC biomarkers

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Introduction

Immuno-histochemistry (IHC) is a staining process that highlights prognostic and predictive biomarkers. Grading IHC-stained whole-slide-images (WSIs) involves * identifying invasive carcinoma (IC) regions in hematoxylin-eosin stained WSIs and locating them in associated IHC-stained WSIs and * evaluating the presence and the intensity of target antigens for each cell. This process is tedious and time consuming. Because the score is evaluated using an eyeballing method, it has also proven to hold high inter-observer variability. Artificial intelligence (AI)-based systems could efficiently assist pathologists in a more accurate clinical diagnosis.

Material and methods

Existing tools are only semi-automatic and require pathologists to select IC regions on IHC slides manually or by registration. In this study, we leverage a CycleGAN-based data augmentation strategy to train a model that directly identifies cancerous regions on IHC WSIs. In those identified regions, we apply our automated scoring method for IHC biomarkers including Ki-67 and ER/PR based on AI methods.

Results and discussion

We show that our method consistently and precisely locates IC regions in IHC WSIs directly by comparison with pathologists ground truth annotations on a set of WSIs. We also demonstrate the robustness of our automatic IHC grading tool with accuracy and efficiency metrics at slide-level on a multi-centric dataset.

Conclusion

In this work, we introduce an end-to-end automatic pipeline capable of * identifying IC regions directly on IHC WSIs with no need of human intervention or registration step and * performing the grading process quickly and accurately. Therefore, our method has the potential to streamline pathology laboratories workflow significantly.

Key words: immuno-histochemistry, cancer detection, grading, cycleGAN

P10

Integrating AI into pathologists' work life

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Introduction

AI is expected to increase quality and effectivity of the pathologist's work. On our way to present lesions to the pathologists, a lot of fundamental questions have been raised. 1. Situations, where pathologists require AI-based support. 2. The best way to integrate AI in the pathologists' workflow.

Material and methods

We integrated the slide overlays with annotations into two environments, where pathologists can read WSI's. The pathologists could try both integrations for four weeks. After that we gathered their feedback concerning the workflow integration. Scientific questions were excluded.

Results and discussion

We grouped the pathologists' feedback into three categories - problems addressed with the help of AI the pathologists would like to use information of model-based predictions in case they are insecure about a potential finding. - integration into the pathologists' workflow The pathologists want to be able to see the prediction for a specific slide on demand, while they are reading it. Pathologists do not want to see predicted lesions before they see the WSI the first time. - Additional findings Pathologists told us, that they need to understand the reasoning of a model to predict a lesion to understand its robustness. We expect the request for models and predictions to grow once the pathologists start using it. A way how to add models to the system need to be defined during setup of the workflow.

Conclusion

The experiment motivates the pathologists to reflect the potential of AI and leads to a clear way towards an AI-landscape in pathology.

Key words: AI-integration, model based predictions, Value-adding AI, Workflow definition, workflow experiment, towards AI in pathology

P11

Halo Breast AI: a Deep Learning Workflow for Clinical Scoring of HER2, ER, PR & Ki67 Immunohistochemistry (IHC) in Breast Cancer Tissue

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Introduction

Immunohistochemical assessment of HER2 status, hormone receptors ER, PR, and proliferation marker Ki67 forms part of the routine clinical diagnostic pathway for invasive breast carcinomas, informing both prognosis and patient management. Pathologist scoring of IHC at the microscope is time-consuming and prone to observer variability. Here we present HALO Breast AI, a deep learning algorithm designed to improve efficiency and diagnostic accuracy through automating whole slide image (WSI) scoring.

Material and methods

A tumour detection, DenseNet-v2 classifier (4,937 annotations), and a cancer cell classifier, Resnet 18-based network (123,901 annotations) were developed to segment tumour regions across a WSI and classify cells as 'cancer' or 'other' within these regions. Data was sourced from two independent institutions. HALO Breast AI was validated on 80 images unseen during algorithm development, using 1,216 and 58,796 pathologist-reviewed annotations for the tumour region and cellular classifiers respectively. The HALO Breast AI HER2 score, and ER, PR & Ki67 positivity were compared against scores assigned by 3 pathologists.

Results and discussion

The median image F1-score for tumour classification was 0.91, while the median image F1-score for cell level validation was 0.96. The clinical scores included from HALO Breast AI and 3 expert pathologists gave agreement scores of 95% for ER, 85% for PR, 85% for Ki67 and 80% for HER2.

Conclusion

HALO Breast AI accurately detects tumour regions and tumour cells within breast cancer tissue and demonstrates high clinical agreement when scoring routine diagnostic IHC. This classifier can support pathologists by improving workflow efficiency and standardising results.

Key words: Artificial Intelligence, HER2, Estrogen Receptor, Progesterone Receptor, Ki67, Clinical Translation

P12

Uncertainty calibrated deep tissue classification in histopathology

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Introduction

Deep learning based methods have been successfully employed for a variety of tasks in computational pathology, including delineation of tissue types. However, if models are to be deployed into the field, it is essential they recognize out-of-distribution data they have not been trained on.

Material and methods

Our training and validation datasets are created from 122 hematoxylin and eosin (H&E) stained colon tissue sections comprising 2,173,515 labeled image patches (224 x 224 pixels) for training and 719,000 patches for validation assigned into seven tissue classes (tumor, mucosa, connective/adipose tissue, muscle, inflammation, mucus, necrosis). The test dataset comprises 15 (H&E) stained colon and lymph node sections specifically selected to contain artifacts such as tissue folds or out-of-focus areas. In addition to small areas containing the seven training classes (8,132 patches), three new classes representing "out-of-distribution" data were manually annotated: artefacts (8,132 patches), debris (1,304 patches) and blood (2,046 patches). We chose for our experiments a ResNet-50 architecture a) unmodified (as baseline) and b) modified using a Spectral-Normalized Neural Gaussian Process (SNGP). Both were trained on the training set applying additional color augmentations. The predicted class'es calibrated softmax value was used as confidence metric.

Results and discussion

The average confidence for correctly classified in-distribution patches is slightly higher for the standard (0.976) compared to the SNGP (0.932) model. The difference in confidence for out-of-distribution data is more pronounced, where the uncalibrated model is overly confident (standard: 0.778; SNGP: 0.583).

Conclusion

An uncertainty calibrated neural network reliably indicates out-of-distribution data by low confidence values.

Key words: Uncertainty, Spectral-Normalized Neural Gaussian Process, Tissue Classification, Out-of-distribution detection

P13

Evaluation of Bone Marrow Stromal Edema by quantitative digital pathology

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Introduction

Bone Marrow Edema(BME) results from an abnormal accumulation of interstitial fluid in the bone marrow(BM). Our analysis of a longitudinal acute myeloid leukemia(AML) cohort revealed that BME is frequent after intensive chemotherapy and associated with higher levels of neoplastic cell infiltration at diagnosis. We thus hypothesized that stromal edema could be a marker of stromal remodeling with potential prognostic value, likely correlating with inflammatory parameters, and thus a possible target for therapy.

Material and methods

In this study, the stromal compartments were quantified using the MarrowQuant2.0 algorithm at different timepoints post-intensive chemotherapy, and an AI-based algorithm(DeepMarrow) was developed to quantify BME. The quantification was performed on a set of 72 time-sequential H&E BM images from 18 patients with AML. One BM biopsy was annotated by a hematopathologist to generate the ground-truth labels. DeepMarrow algorithm was trained on a dataset of 600 tiled images and tested on a dataset of 40 tiled images from the same BM biopsy.

Results and discussion

We explored the effect of different contexts and tile sizes, and of different training parameters including data augmentation, initial layers, pooling steps, and input channels. The algorithm was able to detect BME regions within BM biopsies with a good Intersection over Union(IoU) score (0.69). We are currently implementing DeepMarrow quantifications within an open-source platform, QuPath to enable a full slide BME quantification.

Conclusion

DeepMarrow algorithm could be used with MarrowQuant 2.0 to assess BM morphological stromal changes including BME and could potentially offer valuable insights on disease diagnosis and progression in the context of hematological malignancies.

Key words: Deep learning, MarrowQuant 2.0, stromal edema, bone marrow

P14

A longitudinal Australasian review of consultant driven synchronous large group pathology education using digital slides

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Introduction

Internationally, the disruption of the COVID-19 crisis precipitated an immediate need for creativity in pathology education. An emergency altruistic "fix" developed into an extensive digital pathology learning experiment.

Material and methods

In response to SARS-Cov 2, Australia and NZ implemented restrictive stay-at-home orders. Over 24 weeks from April to September 2020 a committed online instructor (Pathology Consultant) curated and guided interactive digital pathology slide tutorials for Anatomical Pathology trainees each Saturday morning. The initiative was initially limited to examination candidates, but subsequently, all trainees were included, with slides available before each session. Professional adult learners with widely differing knowledge bases were accommodated.

Results and discussion

180 pathology trainees in Australia, New Zealand, Singapore, and Hong Kong voluntarily attended out-of-hours digital slide tutorials. Restriction of the Zoom Chat function to the host enabled all participants to submit diagnostic suggestions. Incorporation of a Poll function encouraged wide participation and active learning; in addition to guiding the consultant to address misconceptions and misunderstandings. A sense of community developed with participants supporting each other and sharing resources.

Conclusion

While the benefits of online asynchronous learning have been reported, our cohort stated that the synchronous nature of the digital learning benefitted them most and facilitated knowledge retention. Live discussions provided context and promoted measurable improvement in diagnostic skills. The combination of digital pathology slides from a curated repository with a committed and passionate online expert guiding learners is a more powerful tool for teaching junior pathologists than access to digital or glass slide resources alone.

Key words: digital pathology slides, WSI live learning, collaborative synchronous learning

P15

Ki 67 Quantification by Digital Image-Based AI Software & Its Correlation with Eye Ball Method in Breast Cancer

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Introduction

Breast cancer is the most common cancer in women worldwide. Ki 67 scoring is essential for the diagnosis, classification, treatment and prognosis of invasive ductal carcinoma of breast. The conventional manual counting method of Ki67 detection is prone to intra and inter observer variability. Using automated method for detection of Ki 67 proliferative index would help the pathologists to give accurate results in many different tumors including breast carcinomas. It will make the process faster and more reproducible. The objective of this study was to compare the automated detection of Ki67 with the manual eye ball / hotspot method and validate it in our population.

Material and methods

The slides of tumor were selected retrospectively and randomly from 60 patients. They were stained with the Ki 67 antibody. An expert pathologist evaluated the Ki67 index in the hotspot fields using eye ball method. Digital images were taken from the hotspots using microscope attached camera. The images were uploaded in the Mindpeak software to detect the exact percentage of Ki 67 positive cells. The results obtained through automated detection were compared with the results drawn by expert pathologist to see the concordance.

Results and discussion

The manual and automated scoring methods showed strong positive correlation as the Pearson's correlation coefficient was 0.93 and significant. The p value was 0.00 indicating a significance level of $p<0.05$.

Conclusion

Our study demonstrates that automated scoring of Ki-67 staining has tremendous potential in the future increasing its clinical value as the issues of consistency, reproducibility and accuracy can be eliminated.

Key words: Ki-67, breast cancer, automated detection, AI, Digital pathology

P16

Uncertainty-guided iterative training of supervised deep learning algorithms for digital pathology

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Introduction

Most deep learning (DL) algorithms developed and deployed in digital pathology practice are segmentation algorithms trained in a supervised setting, i.e. on ground truth labels generated by pathologists. While this guarantees a high accuracy of the algorithm prediction on data similar to the data used for the training, it often requires additional labels when the algorithm´s scope is expanded (e.g., a different assay for the same target or a different indication).

Material and methods

We here aim to reduce the effort to generate additional labels by estimating the algorithm's uncertainty and subsequently use this estimate to guide the annotation process on novel training data. This is executed on a DL model segmenting Monoplex-IHC into epithelium and non-epithelium. We are using Monte Carlo Dropout to measure the model uncertainty and show that a modification of this method using spatial dropout results in the most accurate uncertainty prediction.

Results and discussion

Unseen whole slide images (WSI) are ranked by the model uncertainty and the most uncertain slides and slide areas are selected to be labeled by a pathologist. Since the slide's uncertainty correlates with the segmentation error rate, our approach preferentially selects slides and regions on which the algorithm performed poorly. We show that models refined on data using this uncertainty-guided selection process outperform models refined in a random selection process, demonstrating the potential of our method.

Conclusion

In summary, we significantly reduced the required amount of ground truth data for (re-)training of supervised deep learning algorithms, which is a critical factor of the iterative training workflow's effectiveness.

Key words: Deep learning, Uncertainty prediction, Iterative training workflow, Supervised training

P17

Automated Nuclei Segmentation of H&E and IHC stained Whole Slide Images of Diffuse Large B-Cell Lymphoma

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Introduction

The field of digital pathology has seen remarkable advancements in recent years, with a particular focus on nuclei segmentation and classification of H&E-stained histological whole slide images (WSI). This step is crucial in the diagnostic process, but it presents a major challenge due to the diverse types of nuclei, some of which have significant intra-class variability, such as tumor cell nuclei. Although diverse datasets have been published combining H&E WSIs of various cancer types, there is a lack of annotated data and research for lymphoma types, particularly diffuse large B-cell lymphoma (DLBCL).

Material and methods

To address this gap, we present a solution by extending the current research to DLBCL. Additionally, there is a scarcity of nuclei segmentation and classification methods for IHC-stained WSIs, which are also an important part of cancer diagnosis and treatment decisions. To address this, we utilize HoVer-Net to automatically segment and classify nuclei in H&E and IHC-stained WSIs, using our own exhaustively annotated datasets containing H&E and IHC images of DLBCL.

Results and discussion

Our approach delivers results comparable to existing methods for other cancer types and surpasses current state-of-the-art results for lymphoma data and IHC-stained images.

Conclusion

Combining both, segmented H&E and IHC WSIs yield a much more descriptive overview of the tumor microenvironment. For future approaches, the generalizability of our model could be improved by including other H&E lymphoma data sets or even datasets of different cancer types. As for IHC, the dataset could be extended by additional relevant markers to guarantee inter-marker generalizability.

Key words: diffuse large B-cell lymphoma, nuclei segmentation, immunohistochemistry, hematoxylin & eosin

P18

Improving the Reliability of Deep Learning in Computational Pathology

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Introduction

In computational pathology, deep learning methods rapidly reduce the time and effort needed for image processing. However, for accurate classification or segmentation, a robust model is crucial. Despite deep learnings impressive results in laboratory settings, minor differences in image acquisition or staining protocols can cause specific artefacts that challenge automated image processing, even with prior image quality control.

Material and methods

To address these issues, we have developed FrOoDo, a framework for out-of-distribution detection. FrOoDo implements several methods to detect artefacts in a post-hoc fashion. This enables model quality control for unseen data in the downstream applications. We added advanced simulations for the artefacts to ensure realism and better testing.

Results and discussion

The results show that as the severity of artefacts increases, their adverse effect on prediction performance also increases. FrOoDo successfully excludes patches from a whole slide image that are not suited for further analysis, because they likely decrease the prediction accuracy. We could show that the usage of FrOoDo with appropriate out-of-distribution detection methods leads to more accurate disease prediction.

Conclusion

Our work highlights the importance of robust models in automated image processing and the challenges posed by artefacts in image acquisition or staining protocols. FrOoDo provides a solution to this problem by enabling model quality control for unseen data, leading to more accurate disease prediction. The code is open-source and available at: https://github.com/User/Project.

Key words: AI, Out-of-Distribution Detection, Model Quality Control, Artefacts, Open-source

P19

Virtual cytokeratin and LCA staining of gastric carcinomas to classify tumor microenvironment

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Introduction

The tumor microenvironment helps the growth and expansion of cancer cells. Fibroblasts, various immune cells, nerves, and vessels constituent the tumor microenvironment.

Material and methods

We classified the tumor microenvironment of gastric carcinoma into tumor/stroma ratio (TSR)-high and -low using digital deep learning-based virtual cytokeratin staining and tumor immune microenvironment into tumor infiltrating lymphocytes (TIL)-high and -low using deep learning-based virtual leukocyte common antigen (LCA) staining algorithms in 326 gastric carcinoma samples with known genomic profiles and prognosis of patients.

Results and discussion

Finally, gastric carcinomas were classified into 56 TSR-low/TIL-high, 68 TSR-high/TIL-low, 128 TSR-low/TIL-low, and 74 TSR-high/TIL-high subtypes. Matching with genomic alterations and prognosis of patients showed that TSR/TIL subtypes were closely associated with numbers of frameshift mutations, microsatellite-instability status, tumor mutational burden status, and survival of patients.

Conclusion

Unlike previous studies that used small sample sizes or focused on particular immune-cell subtypes, our digital-based virtual tumor stroma and immune microenvironment classification system using H&E-stained sections for gastric carcinoma has prognostic significance and was associated with molecular characteristics.

Key words: Digital, Deep-learning, Virtual staining

P20

Segmentation of epithelial cells in hematoxylin and eosin-stained histopathological breast cancer slides

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Introduction

Most pathology laboratories experience a significant increase in workload. Automatic methods for assessment of histopathological slides could therefore be important. In cancer diagnostics, correct identification of invasive epithelial cells in hematoxylin and eosin (HE) stained tissue slides would be the first step for automatic interpretation. In this study, we aim to use deep learning to segment invasive epithelial cells, benign epithelial cells, and in situ lesions directly from HE stained slides.

Material and methods

We use a dataset comprising tissue microarrays (TMAs) from 992 patients. The TMAs, and four whole slide images (WSI), were derived from five cohorts of breast cancer patients. Each slide was stained with HE and scanned at 40x. To obtain ground truths, the sections were then restained with the antibody cytokeratin (CK) AE1/AE3 and scanned again. This resulted in corresponding HE/CK image pairs. The CK DAB-channel was thresholded to create epithelial masks. Two pathologists annotated benign epithelium and in situ lesions to separate them from the invasive epithelial cells. The TMA-cores from the HE and CK slides were registered, and ground truth masks comprising the three classes were created. A U-Net was trained to perform the segmentation.

Results and discussion

The model achieved a Dice similarity coefficient of 0.501, 0.701 and 0.703 for for the benign, in situ, and invasive classes, respectively. Qualitative assessment of the model's performance on a WSI identified regions where the model struggled, possibly reflecting features in the WSI that were poorly represented in the TMAs.

Conclusion

Further method development is required to reach performance of clinical value.

Key words: Segmentation, Epithelium, Hematoxylin and Eosin, Cytokeratin, Deep Learning

P21

Teaching Digital Pathology to future laboratory technicians: the Udine experience

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Introduction

The role of Laboratory Technicians in the concrete implementation of Digital Pathology is well known and recognised also in the ESDIP recommendations for the Digital Pathology Workflow (Diagnostics 2021; 11, 2167). The present Abstract describes the actions taken at the academic teaching level to innovate the course contents related to digital pathology.

Material and methods

Within the measures foreseen in the University Strategic Plan 2015-2019, one was aimed at improving digital pathology teaching in the Biomedical Laboratory Techniques (BLT) degree. For this funding was set to buy a scanner, and actions were taken to implement innovations.

Results and discussion

In the BLT degree, traditionally there were two informatics modules, at the first and at the third year. The third year module was modified in two modules, with one entitled "Digital Pathology". Furthermore, an introductory practical activity on digital pathology has been set at the second year, during which students take a short seminar on digital slides and scanning, followed by practical activities with the scanner. At the third year, a deeper introduction to medical imaging and digital pathology applications is then provided to consolidate and enrich knowledge.

Conclusion

Students of the last 3 years of the BLT course, for a total of about 45, had the opportunity to know theoretically and practically the emerging field of digital pathology.

Key words: digital slides, education, digital pathology

P22

A Fully Automated Pipeline for the Prediction of Malignant Transformation in Oral Epithelial Dysplasia

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Introduction

Oral epithelial dysplasia (OED) is a premalignant condition arising in the lining of the oral mucosa. Cytological/architectural histological features of OED can be modelled through the segmentation of nuclei and intra-epithelial layers, potentially providing important diagnostic features. Computational pathology, supported by AI, provides an excellent opportunity to explore data-driven prediction of malignant transformation.

Material and methods

A total of 270 H&E whole-slide images (WSIs) for a cohort of 193 OED patients were collected at 40× magnification. In the cohort, 42 patients (with 57 slides) transformed to malignancy. After sourcing point annotations by a pathologist, NuClick with manual refinement was employed to generate nuclear instance segmentations, followed by a fine-tuned version of our in-house HoVer-Net+ to perform simultaneous nuclear instance segmentation and intra-epithelial layer segmentation. Finally, patch-level morphological features were extracted from the epithelium and used in a relatively simple and fast-to-train neural network to predict which OED cases are likely to transform.

Results and discussion

For the prediction of malignant transformation, our algorithm achieved an AUROC value of 0.78. A log-rank test showed a significant difference in survival between cases that were predicted to transform or not, and a potentially superior prognostic utility (C-index = 0.77) when compared to the binary grading system (C-index = 0.68).

Conclusion

We propose a novel AI algorithm for the prediction of malignant transformation in oral dysplastic lesions. We demonstrate the use of the proposed algorithm for the prediction of malignancy transformation, and its potential when compared to current grading systems. Our future work will be aimed at validating the algorithm on multi-centric cohorts.

Key words: Oral Epithelial Dysplasia, HoVer-Net+, Segmentation, Weakly-Supervised Learning, Malignancy Transformation

P23

Few-shot learning of domain-invariant networks for domain-agnostic nuclei instance segmentation

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Introduction

Neural networks do not generalize well between domains, making it necessary to train multiple models using domain-specific annotations. To overcome this limitation, we propose a few-shot and domain-invariant network for nuclei instance segmentation that generalizes across immunohistochemistry (IHC) and multiplexed immunofluorescence (mIF).

Material and methods

The DARCNN network [Hsu et al.,2021] combines a maskRCNN with a domain separation network to perform instance segmentation and unsupervised domain adaptation of the embedding space respectively. We extend this approach to a few-shot learning setting between IHC and mIF which allows us to leverage the few annotations (10 FOVs) available on the target mIF domain together with the annotations (200 FOVs) available on the source IHC domain. We compare the so-obtained model to a first baseline network trained only on the IHC domain and to a second baseline, trained on the few mIF annotations and CycleGAN-translated data from IHC.

Results and discussion

In comparison to the first baseline, the proposed model yields an increase from 0.60 to 0.69 of the detection f1-score on the mIF domain while retaining its good performance on the IHC domain (f1=0.80). In comparison, the second baseline model yields f1=0.66 and only f1=0.08 on the mIF and IHC domain respectively versus f1=0.63 and f1=0.76 for the DARCNN network.

Conclusion

The proposed model for few-shot joint domain adaptation and instance segmentation enables accurate analysis of nuclei in both IHC and mIF and shows improvement to the original unsupervised method. As such the amount of annotation needed for training can be significantly reduced.

Key words: nuclei segmentation, domain adaptation, image analysis

P24

Ensembles for improved detection of invasive breast cancer in histological images

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Introduction

Accurate detection of invasive breast cancer (IC) can provide decision support to pathologists as well as improve downstream computational analyses, where detection of IC is a first step. Tissue containing IC is characterized by the presence of specific morphological features, which can be learned by convolutional neural networks (CNN). Here, we compare the use of a single CNN model versus an ensemble of several base models with the same CNN architecture, and we evaluate prediction performance as well as variability across ensemble based model predictions.

Material and methods

Three datasets are used in this work. Clinseq(n=232);SöS(n=355) were used to train and test, and an external dataset to test (TCGA-BC(n=157)). Clinseq is annotated exhaustively for IC and SöS is exhaustively annotated for IC pathologies and partially annotated for DCIS, Invasive lobular cancer, lobular cancer in situ, lymphovascular invasion, non-malignant changes and artefacts. TCGA IC annotations were available from previously published studies. All annotations were converted to binary tile-level labels (IC vs non-IC) and an ensemble of inception V3 CNN networks were trained with cross validation.

Results and discussion

Composed of ten networks, the ensemble increased accuracy over all datasets and provided a measure of agreement that, when visualized, points to areas more difficult to characterize and provides insight into the confusion with other of the labels in SöS, particularly DCIS.

Conclusion

The ensemble improved accuracy substantially over the single CNN model and generalized to the previously unseen TCGA data. Variability in predictions across base models provides information about areas where there is greater amount of uncertainty in the classification.

Key words: Breast cancer, Invasive cancer, DCIS, Ensemble, CNN, Visualization

P25

Exploring CNN activation patterns associated with the size of cancerous area in histopathology image and its relationship with model feature maps

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Introduction

Convolutional neural networks (CNN) are widely utilized in digital pathology with extraordinary capability in solving clinically relevant computer vision tasks, while remaining as a black-box. In many applications the focus has been on interpreting results from a visual perspective, seldom paying attention to the process of converting image to numerically predicted probabilities of the CNN. In this study, we hypothesised that CNN activation patterns have a relationship with the area of region-of-interest in the patches from whole slide image, and its influence on the feature map is described.

Material and methods

We investigated a VGGNet for binary classification in the PAIP dataset, and statistical features of 100,000 image patches were derived from the model. The Pearson correlation coefficient was applied to measure the linear relation between the percentage of cancerous area in image patches and the predicted class probabilities and the features from different layers.

Results and discussion

The results demonstrate the existence of a moderate linear relationship between the size of input target and the output score of network, with an increasing association when considering the mean of all values in activation map. Furthermore, this expression of quantity relies on minority high values in the feature map, which explains the incompleteness of semantic features in class activated map (CAM).

Conclusion

This study reveals the possibility to directly obtain a numerical estimation of the cancerous area, and the direction of refining the CAM, which can contribute to improving weakly supervised semantic segmentation.

Key words: Activation patterns, Cancerous area estimation, Model interpretability, Class activated map

P26

Interactive Synthesis of Histology Images from Bespoke Cellular Layouts

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Introduction

Generating customized synthetic tissue images with annotations is beneficial since it reduces the expenses associated with collecting and annotating real data, which typically requires highly-trained pathologists. The ability to control the generated image's nuclei through bespoke layouts is useful for applications such as overcoming data imbalance in cellular composition prediction tasks where certain types of nuclei are underrepresented.

Material and methods

We propose an interactive generative adversarial network based framework that generates tissue images using a series of neural networks from user-defined cellular layouts, giving users control over cell type and location. It also generates images based on cell counts by converting them into a cellular layout using a parametric model. We evaluated the performance of the proposed method using the Lizard dataset of colon cancer images with annotated nuclei.

Results and discussion

The framework outperforms other generative models in terms of the Frechet Inception Distance metric. The quality of the generated images has been deemed comparable to real images by 4 trained pathologists. The addition of cell-type specific synthetic images also improves the performance of a cellular composition predictor resulting in an increase of 11% for neutrophils and 8% for eosinophils in terms of Spearman's correlation.

Conclusion

The proposed model generates synthetic histology images based on user-defined cellular layouts. It may be used to extend already existing segmentation datasets for histology image analysis, enabling researchers to improve the performance of automated segmentation approaches for computational pathology. This framework can be generalized for producing a large number of customized images for different types of carcinomas and tissue types.

Key words: Computational Pathology, Generative Adversarial Networks, Image Synthesis, Deep Learning, Annotated Data Generation

P27

Decision-Making Support System For Diagnosis Of Oncopathologies

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Introduction

The study considers the machine learning method, which in contrast to existing Data Mining methods, allows giving diagnostic DSS adaptability properties of decisive rules to arbitrary conditions of histological imaging and flexibility in retraining the system by expanding the recognition classes alphabet that characterizes different tissue structures.

Material and methods

The aim of the study is to increase the functional efficiency of the machine learning decision support system (DSS) for the diagnosis of oncopathology on the basis of tissue morphology. The method of hierarchical information-extreme machine learning of diagnostic DSS is offered.

Results and discussion

The method is developed within the framework of the functional approach to modeling natural intelligence cognitive processes at the formation and acceptance of classification decisions. This approach, in contrast to neuronal structures, allows diagnostic DSS to adapt to arbitrary conditions of histological imaging and flexibility in retraining the system by expanding the recognition classes alphabet that characterizes different structures of tissue morphology. In addition, the decisive rules built within the geometric approach are practically invariant to the multidimensionality of the diagnostic features space. The developed method allows the creation of information, algorithmic, and software of the automated workplace of the histologist for diagnosing oncopathologies of different genesis. The machine learning method is implemented in the example of diagnosing prostate cancer.

Conclusion

The proposed method allows you to automatically generate an input learning matrix, take into account the individual characteristics of the patient and retrain the system when expanding the recognition classes alphabet.

Key words: decision, support system, hierarchical information-extreme machine learning, information optimization criterion, histological image, prostate cancer

P28

Deep Learning Model for Grading Head and Neck Squamous Lesions with a Grade-Sensitive Confidence Measure

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Introduction

Diagnosis of head and neck (H&N) squamous dysplasia and carcinomas is critical for patient care, cure and follow-up. The grading of dysplasia is challenging: the inter and intra-observer variability remains substantial especially for non-specialized pathologists, while early diagnosis of precancerous lesions can prevent cancer development in 88% of cases. In this study we investigated the potential of deep learning to assist the pathologist with automatic and reliable classification of H&N squamous lesions following the 2022 WHO classification system.

Material and methods

We created a large histological database (2000 samples) and developed a weakly supervised model performing classification from Whole Slides Images. We evaluated our model on a dual-blind review test set and defined a confidence score for predictions to identify ambiguous and difficult case.

Results and discussion

On the gold standard test set, our model was able to classify lesions with high accuracy on every class (average AUC: 0.878 (95% CI:[0.834-0.918])). When separating low and high confidence predictions with our grade-sensitive confidence measure (threshold of 0.5), the overall AUC improved by 4.5% (0.931 [0.892-0.965]) and no carcinoma slides were missed. Conversely, the overall AUC on the uncertain slides was equal to 0.764 [0.672-0.848].

Conclusion

We present the first deep learning model for the difficult task of grading H&N squamous lesions. The grade-sensitive confidence measure is an original and efficient way to assess the reliability of the model's predictions, allowing AI algorithm to be used as diagnostic assistance to manage pathology labs' workflow, especially for subjective tasks such as grading H&N squamous lesions.

Key words: Head and Neck precancerous lesions, Dysplasia;, grading, deep learning, Confidence score, augmented pathology

P29

Cancer Imaging Biobank(CAIB)-AI ready health data from India

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Introduction

AI models have a crucial role in augmenting oncologists' capabilities but are often a reflection of the datasets they are trained on and incorporate biases specific to these cohorts. These AI models trained on western datasets often do not perform equally well on Indian patients, due to non-representation along with epidemiological, clinical-pathological differences of cancer in India.

Material and methods

A nationwide, retrospectively curated database is being created for various cancers comprising all WSI and radiology images originating in routine patient care, along with linked clinical, treatment, reports, genomic information, & outcomes data from four tertiary cancer centers. Inclusion criteria are complete baseline information, at least 1 WSI, and an event-free follow-up of 18 months or the presence of an adverse event (progression/death). Expert-manual, semi-automated, and automated annotations, segmentation, and labels along with QC and confidence metrics will also be included in the database for every image.

Results and discussion

At submission, patients with head-neck cancer (3000) and lung cancer (1500) with 12000 DICOM studies (CT, MR, PET, XRAY) and 15951 WSI (tumor, nodes, normal, immunohistochemistry) from different time points in the patient's journey have been included with their linked clinical information from four centers. The data is expected to be made public after adequate quality/accuracy checks and announced through marker papers. CAIB is funded by DBT, India and can be followed at https://caib.actrec.gov.in.

Conclusion

CAIB is expected to become a valuable resource for researchers for training, testing, and validating AI/ML/DL solutions tailored to Indian Patients.

Key words: AI in Oncology, Cancer Imaging Biobank, Whole Slide Image, AI ready Health Data, Data Preprocessing, Radiology

P30

¿Is DICOM really important? What we have learned during our digital transformation process

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Introduction

In our current journey conducting a DP implementation in a network of 14 hospitals in Spain, we have learned that one of the most significant challenges we can encountered of digital technologies is the ability of slide scanners and IT systems to communicate with each other, regardless of vendor. Scanners may generate image files of different formats, and it is not uncommon that the proprietary format files can be viewed and processed only by systems provided by the same manufacturer.

Material and methods

This lack of standardized file formats for slide scanner files, significantly hampers the ability to share digital pathology images, prospects of collaboration, teaching and consulting cases. The Digital Imaging and Communications in Medicine (DICOM) standard has been evolving to support other medical specialties, first radiology and now pathology, to become the single standard throughout medical imaging, but is being slow.

Results and discussion

We have learn that standardized digital pathology is important for workflow efficiency, storage data and associated metadata and security, and we believe it will prove to provide large benefits for health care providers and will enhance patient care by making pathology data accessible.

Conclusion

Therefore, identifying and implementing solutions that allow flexible access to digital pathology images across multiple platforms from different manufactures is fundamental for an efficient pathology workflow.

Key words: Dicom, pathology, digital, interoperability

P31

Virtual stain-multiplexing CD68 for PD-L1 IHC 22C3 pharmDx scanned NSCLC tissue slides

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Introduction

PD-L1 expression in NSCLC is determined by using Tumor Proportion Score (TPS), which is the percentage of viable tumor cells showing partial or complete membrane staining at any intensity. The TPS scoring protocol calls for the exclusion of the staining of immune cells including of macrophages which is known to be difficult. Combined staining of PD-L1 with CD68 can highlight the macrophages and assist clinical pathologists in scoring more accurately, but it is costly and requires additional tissues. Virtual stain multiplexing of CD68 and PD-L1 has the potential for improving pathologists scoring accuracy without these drawbacks.

Material and methods

A pathologist selected 30 NSCLC tissues, based on the closeness to clinically relevant TPS thresholds of 1% and 50%, focusing on difficult cases where macrophages were identified as infiltrating PD-L1 positive tumor areas. The selected tissues were sequentially stained with CD68 on top of the PD-L1 stain. The sequentially stained slides were scanned and the WSI aligned to their matching PD-L1 WSI. A Neural Network model was trained to predict the CD68 stain using matched pairs PD-L1 (input) & PD-L1+CD68 (ground-truth) patches extracted from pathologist-annotated tumor regions of the aligned WSIs.

Results and discussion

We trained the model to yield virtual CD68 staining, which when used as an assistive layer significantly improved performance of the pathologist to identify macrophages.

Conclusion

We demonstrated a promising CD68 virtual stain-multiplexing model, able to identify and virtually stain macrophages. Such virtual stain multiplexing could serve in the future as an assistive layer, allowing pathologists to score PD-L1 slides more accurately and reliably.

Key words: virtual staining, PD-L1, AI

P32

Interpretable whole slide image prognostic stratification of glioblastoma patients furthering current clinical knowledge

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Introduction

Glioblastoma is the most common malignant adult brain tumor, with grim prognosis and heterogeneous morphology profile. Robust prognostic patient stratification from whole slide images (WSI) using interpretable computational methods could contribute to improved disease understanding and patient management.

Material and methods

Reclassification of TCGA-GBM/TCGA-LGG based on 2021 WHO criteria revealed 188 IDH-wildtype GBM (CNS Grade 4) cases, with available overall survival (OS) data and H&E-stained FFPE WSI of 20X/40X magnification. These were divided into short-OS (below 9 months, n=94) and long-OS (above 13 months, n=94). WSI underwent comprehensive preprocessing for background/artifact elimination and patch extraction (256x256). A weakly-supervised multiple instance learning algorithm gave attention scores/heatmaps used in stratification. Evaluation was based on 10-fold cross-validation, using training(80%), validation(10%), and unseen-test(10%) sets.

Results and discussion

Quantitative results yielded Area-Under-Curve of Validation_AUC/Test_AUC=0.75/0.68. Qualitative heatmap assessment contributed in interpreting algorithmic decisions with insights of prognostically-relevant histologic regions. For correctly-predicted long-OS, the heatmaps unexpectedly weighted histologically malignant areas (traditionally considered indicative of short-OS), warranting further interrogation for improved clinical assessment. Correctly-predicted short-OS weighted infiltrative features that should be further investigated. For incorrectly-predicted long-OS necrotic areas were not weighted and gemistocytic cells were densely-packed rather than on infiltrating arrangement.

Conclusion

Our findings support data-driven histology interpretation of algorithmic decisions, contributing to furthering understanding of GBM and identifying morphology patterns with prognostic relevance. Tumor aggressiveness may be partially ameliorated by reactive responses (e.g.,fibrosis), and patient's brain ability to mount this response can be accounted and targeted.

Key words: Glioblastoma, Survival, Morphology, Interpretability, Attention, Multiple Instance Learning

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Tumor infiltrating lymphocytes recognition in primary melanoma by deep learning convolutional neuronal network

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Introduction

The presence of tumor-infiltrating lymphocytes (TIL) has been associated with a favorable prognosis of primary cutaneous melanoma (CM). The recent development of the artificial intelligence (AI) based approach in digital pathology has been proposed for the standardized assessment of TIL on hematoxylin and eosin (H&E)-stained images (whole slide images, WSI).

Material and methods

Here, we have applied a new convolution neural network (CNN) analysis of PM WSI to automatically assess the infiltration of TILs and extract a TILs score. A CNN was trained and validated in a retrospective cohort of 307 primary CMs including a training set (237 WSI, 57,758 patches) and an independent testing set (70 WSI, 29,533 patches). After the classification of tumor patches by the presence or absence of TILs, we identified an AI-based TILs density index (AI-TIL).

Results and discussion

The proposed CNN demonstrated high performance in recognizing TILs in Primary CM WSI, showing specificity and sensitivity of 100% on the testing set. We demonstrated that the AI-based TILs index correlated with conventional TILs evaluation and clinical outcome. The AI-TIL index was an independent prognostic marker directly associated with a favorable prognosis.

Conclusion

A fully automated and standardized AI-TIL appears to be superior to conventional methods at differentiating primary CM clinical outcome. Further studies are required to develop an easy-to-use tool to assist pathologists to assess TILs in the clinical evaluation of solid tumors.

Key words: AI algorithm, Primary Cutaneous Melanoma, TILs, Convolution neural network, Whole Slide Images, Clinical outcome

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The reading paradigm: How the sequence and presentation of AI results to pathologists influences endpoints and outcomes

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Introduction

With the increasing availability and market clearances of artificial intelligence (AI) – based algorithms for pathology, there is strong focus on clinical performance and safe use. Consequently, clinical performance studies are evolving from standalone performance studies (human vs. AI) to studies that look at combined human+AI performance. Such studies can be further classified according to workflow: second read, screening tool, or concurrent read.

Material and methods

Four studies were undertaken with Paige Prostate Detect, an FDA-cleared AI-based algorithm that classifies digital whole slide images of prostate core needle biopsies as either 'suspicious' or 'not suspicious' for harboring cancer. Two studies used the system as a standalone second read modality and considered the implications of a screening use case; one study used a before-after second read workflow; and one study employed a concurrent read design.

Results and discussion

Using an AI-based algorithm as a second read modality can significantly increase human+AI diagnostic accuracy, and potentially help pathologists identify otherwise missed foci of cancer. However, the greatest efficiency gains may be realized with a screening use case (65.5% reduction of time; 68.6% reduction of volume of slides reviewed) or concurrent read (>20% timesaving).

Conclusion

In the EU and UK, health economics are a key consideration for adoption of AI algorithms and the screening and concurrent workflows, as opposed to second read, would offer efficiency gains. Given the higher risk profiles of these use cases, a highly accurate and robust AI system is required, and further clinical validation guidelines should be developed for safe implementation in clinical practice.

Key words: artificial intelligence, prostate cancer, screening, workflow, health economics, efficiency

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To err or to say "I don't know"? A study on the usage of efficient mixed supervision with a rejection option to diagnose colorectal lesions on WSI

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Introduction

Biopsy samples are the main approach in diagnosing colorectal cancer and preneoplastic lesions. In previous works, we developed a mix-supervision approach, with a sampling technique for efficient training, to detect high-grade lesions in colorectal biopsies with high-sensitivity. Herein, we investigate a rejection option method to improve the model.

Material and methods

The dataset contains 10,496 colorectal WSI divided into three diagnostic classes: non-neoplastic, low-grade and high-grade lesions (encompassing high-grade adenomas and invasive adenocarcinomas). The model was first trained on annotated samples (10% of the dataset) in a supervised manner. After, based on a ranking scheme with the expected value, 200 tiles were sampled from each slide, reducing the training tiles by a factor of 6x. With this scheme, the model was further iterated in a weakly-supervised fashion, using the remaining set of data efficiently. Then, we developed the rejection option based on the predicted probabilities of the classification model, i.e, rethinking cases with low-probability for the predicted class as "unknown".

Results and discussion

The model was tested on 900 cases, trained and validated on the remaining, achieving an accuracy of 93.44%. With the proposed rejection option, we excluded for manual revision 5%, 8%, and 20% of the cases with the lowest predicted top probabilities, and the accuracy increased to 95.32%, 96.01%, and 98.19%, respectively.

Conclusion

Computer-aided diagnosis systems should assist pathologists' work. In this study, we introduce a rejection option scheme that can remarkably reduce the pathologists´ workload by 80% or more, with highly accurate results. This procedure makes these systems more reliable for clinical deployment.

Key words: Colorectal Samples, Whole-Slide Images, Artificial Intelligence, Mixed-supervision, Reject Option

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ACROBAT 2023: Analysis of multi-stain WSI registration algorithms under domain shift

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Introduction

Multi-stain WSI registration is a challenging and active research area, with applications such as biomarker guided learning and 3D histology. In 2022 we organized the ACROBAT challenge that found new state-of-the-art with robust and accurate algorithms. Now we will organize a second round of the challenge with focus on evaluation of methods under domain shift to study methods' generalizability. The ACROBAT 2023 challenge will be hosted at the Grand Challenge platform and the results will be announced in MICCAI2023.

Material and methods

The challenge includes a new hidden test set of 200 uncurated cases of breast cancer resection from clinical practices with undisclosed stains. To evaluate the submitted methods, the challenge will be hosted as type 2 challenge where the training and validation sets are publicly accessible, but the test set is private and participants are required to submit their methods in containers. There will be monetary prizes for the top performing teams and teams who publish open source implementations. The challenge is open for submissions from June 15th to August 19th.

Results and discussion

Compared with the previous challenge, the evaluation metric was changed to mean 90th percentile to further emphasize robustness. This time, also the deformation fields are accepted from participants to have a more comprehensive evaluation. Hosting a type 2 challenge will also allow assessment of computation time in a fair manner.

Conclusion

We expect the ACROBAT 2023 challenge to highlight algorithms in terms of generalization ability in domain shift conditions. The results will be a step towards more generalized and clinically applicable registration methods.

Key words: computational pathology, WSI registration, multi-stain, immunohistochemistry, domain shift, challenge

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Upconversion nanoparticles as labels for histopathological tissue evaluation

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Introduction

For decades, haematoxylin and eosin (H&E) stains together with a horseradish peroxidase (HRP) label and diamino benzidine (DAB) as a chromogenic substrate, have been the gold standard to visualise tissue morphology and to detect markers of interest. However, these methods suffer from a narrow dynamic range, difficulties in quantification and limited possibilities regarding multiplexing. Fluorescent IHC techniques open the possibility for a quantitative readout but suffer from photobleaching and spectral overlapping emission bands in multiplexed applications. Here we present an upconversion nanoparticle (UCNP)-based technique to visualize the breast cancer marker HER2 in tissue sections, that allows to overcome problems associated with commonly used labelling techniques.

Material and methods

Formalin-fixed paraffin-embedded breast cancer cell line and human breast cancer tissue were sectioned and labelled. Upconversion imaging of the human tissue sections was conducted in our prototype device and compared with a standard DAB-based IHC. The combination of UCNP and H&E counterstaining on the same slide was investigated.

Results and discussion

Images obtained with our novel device demonstrate that our UCNP bioconjugates are excellent labels for the detection of cancer markers in tissue sections. Brightfield images prove that UCNPs do not interfere with the standard tissue evaluation by a pathologist. Additionally, brightfield and luminescent images can be merged to provide a better understanding of tissue morphology.

Conclusion

Staining solutions and a novel device developed by us give hope for more accurate diagnosis by keeping the advantage of H&E staining and combining it, in one image, with the luminescent data, ideal for generating ground truth for machine learning algorithms.

Key words: upconversion nanoparticles, UCNP, breast cancer, tissue imaging, HER2

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Towards pan-cancer histology image classification with knowledge distillation

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Introduction

Deep networks have shown considerable promise for histology image analysis across diverse cancer-related problems in computational pathology. However, most existing solutions focus on only one specific cancer type. Pan-cancer solutions would help to analyse differences/similarities between various cancer types. Moreover, pan-cancer solutions are a step towards AI generalizability. In this study, we evaluate the ability of deep networks trained on one cancer type to classify images from another cancer type.

Material and methods

We used two public datasets: PatchCamelyon (PCam) and Kather100K, consisting of tissue images from breast and colorectal cancer, respectively, to classify them into tumour/normal. PCam contains 262K training, 32K validation and 32K test image patches, whereas Kather100K contains 100K training and 7K validation. We trained three different frameworks using Kather100K-train dataset: 1. randomly initialised (RI) 2. transfer learning (TL), i.e., pretrained on PCam-train, and 3.knowledge distillation (KD) (teacher: PCam-train and student: Kather100K-train). We evaluated these frameworks using three datasets: 1.Kather100K-valid 2.PCam-valid and 3.PCam-test.

Results and discussion

The proposed KD framework outperforms RI and TL to classify patches across different cancer types. We conduct multiple experiments using various proportions of data (e.g., 25%, 50% and 75%). We achieved median F1 score of 0.67±0.07 with the proposed KD framework across the three evaluation datasets. In contrast, the best median F1 score of RI and TL was 0.55±0.19.

Conclusion

The proposed KD framework shows better performance in pan-cancer image classification, as we can distil the information from one cancer type while training the model using another cancer type. These results open new options towards developing algorithms for pan-cancer histology image analyses.

Key words: knowledge distillation, pan-cancer, tumour/normal classification

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Classification of Nasopharyngeal Cases using DenseNet Deep Learning Architecture

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Introduction

Nasopharyngeal carcinoma (NPC) is one of the understudied but deadliest cancers in South East Asia. In Malaysia, the prevalence is identified mainly in Sarawak, among the ethnic of Bidayuh. NPC is often late-diagnosed because it is asymptomatic at the early stage. This paper is our first initiative to identify the difference between NPC, nasopharyngeal inflammation (NPI) and normal cases with the help of local pathologists from the prevalence state.

Material and methods

Seven whole slide images (WSIs) from seven different patients and two hospitals were experimented using two test set-ups, for proof-of-concept and real-test. Image-set-1 has 4 WSIs, and the diagnosed regions are in concordance with at least two pathologists. While image-set-2 has 3 WSIs, with mixed regions of both concordance (NPC), and non-concordance (normal and NPI). The tissue regions from both image sets are patched into 256x256 pixels blocks and randomly chosen for training and testing of deep learning model. 5,000 patches from each class (with a total of 15,000 patches) are taken from image-set-1 for training. For testing, two setups are proposed: Test-1 with 500 patches per class from image-set-1 but not within the 15,000 training patches, and Test-2 with 500 patches per class taken from image-set-2. The patches are classified using DenseNet-21 architecture, trained with 5 epochs.

Results and discussion

The accuracy achieved for NPC class is 94.8% for Test-1 and 67.0% for Test-2.

Conclusion

Following this preliminary experiment, many other potential experimental works can be done provided more time, resources, and collaborative assistance by the pathologists.

Key words: deep learning, densenet, whole slide image, digital pathology, nasopharyngeal carcinoma

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Whole Slide Image scoring using DenseNet for ER-IHC: in search of optimal configuration

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Introduction

Nuclei classification is a mandatory process to obtain scoring information for a whole-slide image. In immunohistochemistry (IHC) staining specifically for estrogen-receptor (ER) biomarker, an Allred score based on the proportion and intensity of cancer nuclear staining is widely used in histopathology practice to predict response to hormonal treatment. This manually exhaustive process can be accelerated with the help of machine learning.

Material and methods

In this article, we present a thorough analysis of 37 whole slide images of breast cancer cells, where ER-stained nuclei were classified into negative, weak, moderate and strong intensities by using DenseNet deep learning architecture, contributing to Allred scoring. Several methods and configurations were exhaustively tested to obtain the scoring reaching best concordance with the pathologist's manual score.

Results and discussion

Out of 37 WSIs, 21 of them obtained concordance on the Allred score, and 30 of them are concordance to the suggested hormonal treatment. We also have identified several causes that leads to the non-concordances, particularly on the confusion of dark blue stains, brownish small cells which are actually non-cancerous stromal cells but detected as nuclei, and also confusion of the nuclei with both bluish hue and brownish hue. Another issue is on the inaccurate segmentation, where many of the non-nuclei cells or artefacts were segmented and wrongly classified as one of the four classes.

Conclusion

This study provides a basis for the development of more complex deep learning models particularly for nuclei classification of ER-IHC stained whole slide images.

Key words: ER-IHC, whole-slide image, nuclei classification, DenseNet, TensorFlow, PyTorch

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Characterization of chronic kidney diseases with Self-Supervised Learning techniques

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Introduction

One of the biggest hindrances to the broader adoption of AI in digital pathology is the need for annotated datasets. The available data increases in volume at a much higher speed than the ability of the community of AI researchers to produce correct labels. For this reason, supervised learning techniques cannot be properly applied to facilitate the research. As an alternative, methods of self-supervised learning (SSL) are used more often than in the past due to their ability to handle raw datasets well without proper annotations.

Material and methods

In the following work, which is related to nephrology, several self-supervised learning methods were tested with the assumption that they can be used to build a spectrum of disease states from healthy tissue to the apparent illness. In order to achieve this goal, it is crucial to compare images with each other using their numeric representations which are also called embeddings. It was assumed that by using methods of SSL, it is possible to generate embeddings that encode the most universal and important features. To achieve this result, the methods Bootstrap Your Own Latents, SimCLR, and MoCo were used, and their performance metrics were compared.

Results and discussion

The spectrum of disease states shown as a scatter plot was built through the visualization of high-dimensional embeddings by t-SNE. In addition to this, the quality and predictive power of embeddings were evaluated using Random Forest and Gradient Boosting.

Conclusion

The findings proved the usefulness of SSL methods for the characterization of chronic kidney disease progression.

Key words: Self-Supervised Learning, Dataset, Annotations, Nephrology, Chronic Kidney Disease, AI

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Triple-negative breast cancer: structure and morphological features of immunohistochemical subtypes

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Introduction

Triple-negative breast cancer (TNBC) is the most aggressive types of breast cancer. According to recent studies, Basal-Like (BL), Mesenchymal-Like and Luminal Androgen-positive (LAR) immunohistochemical subtypes TNBC demonstrate different responses to cytotoxic therapies. Objective was to study the structure and morphological features in patients with different immunohistochemical subtypes of TNBC.

Material and methods

Biopsy material from patients with TNBC (n=91) was immunostained (IHC) with Cytokeratin5/6 (CK5/6), Cytokeratin14 (CK14), Claudin3 (CLN3), Claudin7 (CLN7), Androgen Receptor (AR), EGFR. Digital analysis of cytoplasmic, nuclear and membrane expression was performed using QuPath-0.3.2 software with calculation of the positivity for CK5/6, CK14 expression, share of positive tumor cells for AR, H-score and Allred score for CLN3, CLN7, EGFR expression.

Results and discussion

Three IHC subtypes of TNBC have been identified: BL (78%), LAR (9%), mesenchymal with stem-like cells and low expression of CLN3/7 (MSL, claudin-low – 2%) and mixed subtypes (11%). The levels, their variability, and cut-off points of CK5/6, CK14, LAR, CLN3, CLN7, and EGFR expression for each IHC subtype were determined. Pilot results (median follow-up of 2.1 years) and the significance of IHC subtypes in prognosis and response to chemotherapy are shown.

Conclusion

The structure of TNBC was dominated by BL and LAR subtypes with single cases was regarded as MSL claudin-low subtype. The TNBC IHC subtypes criteria we have defined and available in the literature, as well as the role of IHC subtypes in determining prognosis and response to chemotherapy, suggest that identification of IHC subtypes in clinical practice is possible and necessary to introduce in order to personalize therapy and improve treatment strategies.

Key words: triple-negative breast cancer, immunohistochemistry, image analysis, claudin, androgen-receptor, cytokeratin

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Automatic detection of Lymph node metastasis: twenty years of evolution

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Introduction

One of the most relevant prognostic factors in cancer staging is the presence of lymph node (LN) metastasis. Evaluating the presence of cancerous cells can be a lengthy and error-prone process. Thanks to digital pathology, Artificial intelligence (AI) can be exploited for automatic detection of metastatic tissue. The aim of this study was to review the literature regarding the implementation of AI as a tool for the detection of metastasis in LNs on whole slide images (WSI).

Material and methods

A systematic literature search was conducted in several electronic databases. Studies involving the application of AI techniques to automatically analyze the LN status were included.

Results and discussion

Of 4584 retrieved articles, 23 were included. Relevant articles were categorized into 3 different categories sorted by the accuracy of the AI in evaluating LN. Nineteen (19/23, 87%) of the included studies employed fully supervised algorithms, while the remaining four (4/23, 13%) used weakly supervised one. Three articles (3/23, 13%), were challenges studies, encompassed a combination of deep learning algorithms, ranging from 4 to 37.

Conclusion

Published data overall indicate that the application of AI in detecting LN metastasis, with due care, is promising for the near future of digital pathology and can be proficiently employed in daily practice.

Key words: digital pathology, artificial intelligence, lymph node, metastasis

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Is Stain Augmentation All You Need for Domain Generalization?

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Introduction

Domain Shift is a prevalent issue in computational pathology, where variability in staining protocols and scanners can lead to significant differences in tissue appearance and consequently to potentially significant degradation of deep learning models' performance. The proposed method focuses on learning stain-invariant representations to address this challenge.

Material and methods

We used two publicly available datasets of colorectal cancer histopathology images, Kather-19 (source domain) with 100,000 images and Kather-16 (target domain) with 5,000 images to evaluate the proposed method for 7 classes. Our model can learn stain-invariant feature representations from source domain and can generalize well on target domain for tissue classification. It generates stain augmented random crops of the same image and uses a deep feature encoder to extract their feature representations, together with a domain regularization loss on the encoder feature layer to enforce similar representation learning for original and augmented images.

Results and discussion

Our model achieved accuracy of 90.1% as compared to ResNet-50 that achieved 79.8% accuracy when trained on Kather-19 (source) and tested on Kather-16 (target). We found that normalizing the dataset using the same stain vectors degrades performance by around 5-6% compared to when using the non-normalized images.

Conclusion

We propose a method to address domain shift by enforcing the model to learn domain-invariant representations and reducing the dependency on stain-specific features. We demonstrate the effectiveness of our approach in handling the domain shift problem. In future, we aim to explore its application to other problems in the area of computational pathology.

Key words: Domain Shift, Computational Pathology, Deep Learning

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Intraoperative Cytological Diagnosis of Brain Tumors: A Preliminary Study Using Deep Learning Model

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Introduction

Intraoperative pathological diagnosis of central nervous system (CNS) tumors is essential in neuro-oncology to plan the patient management. Frozen section slides and cytological preparations provide architectural and cellular details analyzed by the pathologists to reach an intraoperative diagnosis. With the progress in artificial intelligence and machine learning fields, AI systems have significant potential in providing highly accurate real-time diagnosis in cytopathology. We aimed to investigate the efficiency of machine learning models in intraoperative cytological diagnosis of CNS tumors.

Material and methods

We trained a deep neural network to classify 4 major brain biopsied lesions for intraoperative tissue diagnosis. Overall, 205 medical images were obtained from squash smear slides of histologically correlated cases, with 18 high-grade and 11 low-grade gliomas, 17 metastatic carcinomas, and 9 non-neoplastic pathological brain tissues. The neural network model was trained and evaluated using 5-fold cross-validation.

Results and discussion

The model achieved 95% and 97% diagnostic accuracy on the patch-level classification and patient-level classification tasks, respectively.

Conclusion

We conclude that deep learning-based classification of cytological preparations may be a promising complementary method for rapid and accurate intraoperative diagnosis of CNS tumors.

Key words: artificial intelligence, brain tumor, cytopathology, deep learning, intraoperative diagnosis, neural networks

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Mapping the tumor microenvironment: Deep learning-based quantification of eosinophils and lymphocytes for patient outcome prediction in colon cancer

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Introduction

Eosinophils are granulocytes typically associated with allergies and infections. However, multiple studies also suggest an involvement in tumor immune response. In this study, we analyzed the relevance of eosinophil presence and their interactions with tumor infiltrating lymphocytes (TILs) for patient outcome on colorectal cancer H&E WSI.

Material and methods

A nuclei segmentation model trained on the publicly available lizard dataset was applied to TCGA colorectal cancers (CRC) (n=341, all Stages). Scores were computed by counting immune cells within a radius (r=[50,100,200,500] µm) of tumor epithelial cells and normalizing by the total number of tumor epithelial cells. Immune cells close to normal colon mucosa and intraepithelial lymphocytes were considered separately. Corresponding RNA-Seq data for expression analysis was retrieved. A tissue microarray (TMA) CRC cohort (n=267, all Stages) with density scores was used to further validate the work.

Results and discussion

On TCGA, eosinophils (r=50) in a multivariate cox regression (TNM stage, age, sex, therapy, TILs) are statistically significant: Overall survival (OS): p=0.02, HR=0.45, Disease specific: p=.006, HR=0.36. Based on AIC, r=50 shows the best fit. Eosinophils positively correlate with TILs (CC= 0.5) and are more abundant in lower stage (p=0.006). On TMAs, more eosinophils are associated with more TILs (CC=0.49), higher Klintrup–Mäkinen grade (p<0.001), and lower stage (p=0.03). Differential expression analysis on bulk RNA-Seq data (eosinophils High vs. Low) reveals upregulation of genes related to T-regs, T-helper and cytotoxic T-cells.

Conclusion

Eosinophils in the TME are a highly prognostic biomarker quantifiable directly on CRC H&E WSI. Yet, interactions with TILs, especially specific subsets require further investigation beyond the H&E.

Key words: Computational Pathology, Nuclei Segmentation, Microenvironment, Deep Learning

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Effect of stain normalization on estimation of kidney fibrosis with image analysis

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Introduction

The extent of kidney fibrosis – scarring of the kidney – is a prognostic marker and predicts the development of chronic kidney disease. Its standard (visual) evaluation has a poor reproducibility. Automatic image analysis could overcome this; but it is hampered by variations in laboratory procedures, such as staining. To address this issue, we explored the usefulness of stain normalization.

Material and methods

Digital slides from 10 Sirius red-stained kidney biopsy sections with various amounts of fibrosis and visually confirmed stain variation were used. The ground truth (percentage of fibrosis) was established with point counting by an experienced pathologist. Stain normalization was carried out via the Macenko, Reinhard, and Structure Preserving methods. The percentage of fibrosis was then estimated by image analysis (with color thresholding), before and after stain normalization, and finally was compared with the ground truth.

Results and discussion

Color thresholding before stain normalization had a good agreement with the ground truth (ICC=0.88). The same was true for color thresholding after stain normalization with Macenko (ICC=0.81) and Structure Preserving method (ICC=0.89), but visual inspection revealed that both stain normalization methods had introduced undesirable color distortions in some images. On the contrary, stain normalization with Reinhard gave a poor agreement with the ground truth (ICC=0.47), while visual inspection showed a better adaptation to the chosen reference image.

Conclusion

Stain variation was assumed to affect the robustness of image analysis (with color thresholding). However, none of the stain normalization methods investigated in the current project facilitated an improved agreement between the resulting fibrosis quantification and the ground truth.

Key words: image analysis, kidney fibrosis, stain normalization

P48

Digital Markers of Tumour Infiltrating Lymphocytes Predict Locoregional Recurrence-Free Survival in Nasopharyngeal Carcinoma

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Introduction

Nasopharyngeal carcinoma (NPC) is a malignancy of epithelial tissue in the nasopharynx which closely associated with Epstein-Barr virus (EBV) infection. Several studies have shown that a higher number of tumour-infiltrating lymphocytes (TILs) is associated with better prognosis in NPC. However, this measurement is prone to the subjectivity of the pathologist. This study examined the prognostic significance of digital markers of TILs from haematoxylin & eosin-stained whole slide images (WSIs) for locoregional recurrence-free survival (LRFS) in NPC.

Material and methods

Our cohort comprises 367 cases with 385 WSIs and right censored at 5 years. Our method consists of three main stages. First, we detected and classified all nuclei in the WSIs with HoverNet, which trained on the PanNuke dataset. Next stage, we clustered tumour nuclei based on their density. Digital TILs scores were then computed from each cluster and averaged for the final TILs scores. Finally, we utilised digital TILs score for training the Random Survival Forest model on three-fold cross-validation to generate a risk score.

Results and discussion

The average concordance index of the validation set on cross-validation was 0.763. In univariate analysis with a Cox-PH model, our risk score was the only marker with a significant association with LRFS (P=0.01) compared to clinical features such as T, N, stage and EBV-DNA copies data.

Conclusion

The digital TILs showed significant prognostic value for LRFS in NPC in our cohort. To the best of our knowledge, this is the first attempt to automate the quantification of TILs in NPC for survival prediction.

Key words: NPC, TILs, survival, prognosis, LRFS, EBV

P49

PathLAKE Portal: A Hybrid Platform for Showcasing and Sharing PathLAKE Whole-Slide Images

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Introduction

The rapid growth of computational pathology has been led by 'data hungry' deep learning (DL) algorithms, increasing the demand for digitised histology image datasets and corresponding annotations that are required for robust development, validation and testing of new algorithms before being deployed in the clinic. The size of Whole-Slide Images (WSIs) makes them inherently difficult to collect, store and share at scale. We propose a solution to share histology datasets with academic and industrial partners.

Material and methods

The PathLAKE consortium collected WSIs from laboratories across the United Kingdom, including four exemplar projects. Work was undertaken to standardise the metadata, thus allowing us to provide an easy-to-use search functionality to aid with the discovery and selection of slides.

Results and discussion

PathLAKE Portal provides a gateway to over eighty thousand WSIs, covering more than a dozen tissue types along with their clinical metadata through a web-based search and exploration platform. This platform has also been designed to be compatible with other data lakes and compute providers. Users can filter the slide collection based on a range of attributes such as tissue type, stain, patients' age range and gender. Each slide has a corresponding thumbnail, while we also provide a smaller number of high-resolution sample slides to view. Users can then create their own baskets of datasets from the available cohorts, which can be used to develop new models and/or validate existing models.

Conclusion

We believe that the portal will aid in the development of the next generation of machine learning models.

Key words: portal, cloud, gateway, datasets

P50

Morphologic criteria and CD138-positive cells counting for chronic endometritis: manual versus AI-based algorithms

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Introduction

Chronic endometritis (CE) is one of the most impactful causes of female infertility. Accurate CE diagnosis is extremely important for proper management of such patients. The most significant feature of CE is plasma cell in the endometrium. Thus, the purpose of our survey was to develop a reproducible neural network (NN)-based algorithm for accurate plasma cells counting.

Material and methods

Three pathologists independently evaluated 50 endometrial biopsies morphologically and immunohistochemically (IHC)(CD138) (the cutoff for EC diagnosis was≥5 plasma cells (10 HPF). Then we digitilized the slides (whole slide image,WSI) and developed a two-stage algorithm for CE diagnostics. The first stage is a fine-tuned neural network dividing the stromal and epithelial cells. The second stage is an algorithm based on computer vision methods that identifies and counts plasma cells.

Results and discussion

Interobeserver reproducibility was minimal (0.253-0.389) for hematoxylin and eosin-stained slides and was moderate to perfect for IHC slides (0.670-1.000) (manual assesment). The NN model of the first stage was trained on the EndoNuke dataset and fine-tuned on additional data. The additional data was annotated using the CVAT. The agreement between annotators was assessed using Cohen's kappa and reached 0.85 value. The neural network on validation dataset reached 0.74 mAP. The second stage algorithm is currently being finalized in order to find optimal threshold values.

Conclusion

Plasma cell marker CD138 application improved the interobserver reproducibility significantly. Also, it can be successfully used for automatic counting with NN-based algorithm. Nevertheless, CD138 has two main disadvantages for automatic counting: membranous staining and positive internal control (glandular epithelium staining). Funding: State Assignment 223013000171-4

Key words: chronic endometritis, plasma cell, whole slide image, reproducibility, EndoNuke, neural network

P51

A retrospective evaluation of artificial intelligence solution for prostate biopsies

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Introduction

AI builds the future in pathology. We have implemented routine digital pathology diagnosis in two years, later started evaluating image analysis solutions. Here we discuss retrospective evaluation of the Paige Prostate on our cohort.

Material and methods

60 consecutive cases included (scanned Aperio AT2, with 20x-40x, diagnosed on Sectra). Images were anonymised before uploading. Report diagnoses were compared with AI.

Results and discussion

836 biopsy cores evaluated. 601(72%) were labeled as benign both by AI and pathologists; 199(24%) as tumor both by AI and pathologists. 8 cores were diagnosed as benign by AI, but malignant by pathologists (3 blurred, 4 processing artifacts thus excluded from further analysis). One labeled as benign by AI, but malignant by pathologists with IHC confirmation. 27 cores were labeled as tumor by AI, but diagnosed as benign by pathologists (3 diagnosed as benign, 2 as ASAP). Remaining 22 were reevaluated by expert pathologist with IHC. 14 were finalised as benign, 1 ASAP, 7 tumor. These foci were minute and 3+3 grade. On case basis 4(7%) were discrepent where benign foci labeled as tumor by AI. Overall AI had 92.1% and 90% positive predictive value, 99.8% and 100% negative predictive value on core and case based analysis respectively.

Conclusion

The Paige Prostate was found to be helpful for prostate biopsy interpretation. Processing and scanning artifacts cause errors, thus images should be checked for quality. AI found minute tumors missed by pathologists, which had no impact on patient management since other cores also contained tumor. AI sensitivity with pathologists specificity will improve patient care.

Key words: prostate, AI, diagnosis

P52

The BosomShield project: an integrative approach to diagnosis and prognosis of breast cancer relapse based on radiologic / pathologic image biomarkers

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Introduction

Breast cancer (BC) produces 600,000 deaths yearly. Oncologists, radiologists, pathologists may exploit radiological and histopathological imaging to analyze tumors, study their immune microenvironment, and predict the probability of relapse for distant metastasis, also by means of biomarkers. The BosomShield MSCA doctoral network aims to improve the diagnosis and prognosis of breast cancer relapse by means of integrated radiologic- and pathologic-imaging biomarkers

Material and methods

To accomplish the research goal, our contribution includes 1) determining BC molecular subtypes and main characteristics of the relapse by merging morphology, texture, and volumetric features, 2) developing fully automated volumetric methods of breast density that can be used for local recurrence prediction, 3) digital image standardization or color normalization methods so that the results obtained by the application of the digital image analysis methodologies are similar and convergent regardless of the WSI scanner, 4) developing robust biomarkers for detecting primary tumor and axillary tumor microenvironment to predict the risk of metastases and 6) analyzing the relationship between localization, morphology and functions of immune biomarkers extracted from WSI and radiological images to quantify the BC relapse leveraging explainable AI models.

Results and discussion

The project is at the very first stages; however, the enrollment of PhD students has been completed, analysis and development of relevant ML models have begun, and the 1st Summer School on the project topics has been designed.

Conclusion

Based on a dataset of 10 hospitals around Europe, our ongoing results are promising for a reliable prognostic supporting tool for clinicians to define personalized treatment plans for BC patients.

Key words: AI, breast cancer, digital pathology, radiology

P53

A deep-learning framework to dissect histological age patterns of the breast tissue

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Introduction

During the ageing process, structural and functional changes in the female human breast are due to complex mechanisms determined by intrinsic and extrinsic factors, which act synergistically. This study aims to determine and quantify the epithelial histological patterns of the breast emerging over a woman's lifespan.

Material and methods

A collection of 632 H&E-stained normal breast tissue images from women across different age groups was collated from distinct sources, including healthy donors and healthy patients undergoing reduction mammoplasty/risk-reducing mastectomies from 5 research institutes. Tissue-type histological visual features were extracted using a convolutional neural network framework established after extensive modelling. The epithelial features were grouped accordingly to Lloyd's algorithm - statistical analysis and cellular segmentation, characterised clusters morphology and factor/functional associations. Neighbourhood enrichment analysis disclosed the cluster's spatial interactions.

Results and discussion

Deep learning (DL) visual features outlined inter and intra-variance of the normal breast epithelial histological patterns underlying the ageing process in normal tissues. Higher inter variability was associated with higher body mass index in pre-menopausal women and later menarche in post-menopausal. Results correlated to the degree of lobular development annotated by a senior pathologist who performs routine histopathological diagnoses. The histological pattern predominantly linked to young women exhibited acinar structures that were

more densely packed, with a higher glandular to stromal ratio. Spatial analysis disclosed higher neighbourhood enrichment of such regions.

Conclusion

The proposed DL-based framework identifies specific histological patterns in the breast tissue occurring during the women's life course associated with biological factors and processes, manifesting the potential of capturing biological ageing patterns.

Key words: Normal breast tissue, Histological age patterns, Biological age, Spatial statistics, Deep Learning features

P54

Expression of metalloproteinases in assessing the effectiveness of therapy in patients with aggressive periodontitis

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Introduction

The dynamics of metalloproteinases (MMPs) levels is exceptional importance for the manifestation and progression of periodontal disease, the expression levels can be used in evaluating the effectiveness of therapy. Objective was to study the levels of metalloproteinases expression before the start of therapy and at intervals of 1, 6, 12 months.

Material and methods

Gingival biopsy from patients with aggressive periodontitis (AP, n=19) was immunostained (IHC) with MMPs -1,-2,-9,-14. Image analysis of cytoplasmic expression was performed using AperioImageScope v12.4.0.5043. Therapy included gingival curettage with insertion of an antiseptic pledget containing hemostatic sponge with tricalcium phosphate, eugenol and iodoform in periodontal pockets; NSAIDs were used in case of suppuration.

Results and discussion

According to our results, opposite dynamics of the levels of different types of MMPs in the course of AP therapy was revealed. We found a tendency to a systematic increase in the expression of MMP1 during the whole period of monitoring, a consistent decrease in the expression of MMP2 by 6 and 12 months of observation, and a decrease in the expression of MMP9 and MMP14 by 6 months with a subsequent increase by 12 months. These wave-like changes in MMP9 and MMP14 expression correlated with clinical signs of inflammation progression and periodontal tissue destruction.

Conclusion

Decrease of MMP2, MMP9 and MMP14 expression during 6-12 months suggests them as markers of the efficacy of the treatment applied. At the same time, a systematic increase of stromal expression of MMP1 during 12 months and wave-like changes in MMP9 and MMP14 expression may indicate their role in the progression of periodontitis.

Key words: aggressive periodontitis, immunohistochemistry, image analysis, metalloproteinase, therapy

P55

Multitask pretraining outperforms ImageNet in learning general representations in computational pathology

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Introduction

Effective deep learning requires vast amounts of accurately annotated training data, whereas usually, only small amounts of patch-level annotations are available in computational pathology. We investigated if histology-specific representations allow sample-efficient learning on unseen tasks by pretraining a joint model on publicly available datasets using multi-task learning.

Material and methods

We created a large-scale multi-task database comprising 10 public histology datasets covering cancer classification and segmentation, mitosis detection, and nuclei identification on a variety of different H&E stained tissue types. On this database, we trained a generalist model using multi-task learning. Our model was evaluated by predicting inclusion of invasive breast cancer on two datasets and estimating cancer cellularity on one dataset. Results were compared to those obtained using ImageNet pretraining. For the evaluation process, the pretrained model was frozen and the latent representations of the evaluation tasks were used as inputs to task-specific random forest predictors that learned task outputs. These predictors were trained multiple times on differently sized subsets of the unseen evaluation data. We evaluated the transfer performance using the F1-score and the mean squared error.

Results and discussion

Compared with the baseline, the mean F1-scores for the breast cancer classification improved from 63.50% to 75.22% for task one and from 40.41% to 52.53% for task two. The mean squared error in cellularity estimation improved by 11.8% from 0.0566 to 0.0506.

Conclusion

Pretraining on a diverse multi-label database generates general representations suitable for effectively detecting malignant tissue components in breast cancer. Partly funded by the German ministry of education and research (BMBF), project: SynDICAD (01IS21067C)

Key words: Multi-task learning, representation learning, sample-efficiency

P56

Stratipath Breast: Deep Learning-Based Risk Stratification of Intermediate Risk Breast Cancers

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Introduction

Nottingham Histological Grading (NHG) is an established prognostic marker for breast cancer patients that is essential for treatment decisions. However, more than 50% of all breast cancer patients are currently assigned an intermediate risk (NHG 2), which is not sufficiently informative to guide treatment decisions without further diagnostics. Stratipath Breast is the first CE-IVD marked solution for AI-based WSI analysis that can further stratify intermediate risk patients into low- and high-risk groups.

Material and methods

We evaluated the prognostic performance of the predicted risk classes for 901 NHG 2 primary breast cancer patients, 204 originating from the TCGA BRCA study and 697 from a Swedish study. Prognostic performance was quantified by computing hazards ratios for recurrence with Cox proportional hazards models.

Results and discussion

The point estimate for the marginal hazards ratio between predicted risk groups in this particular test data was found to be 2.2. Adjusting for clinical covariates yielded a hazards ratio of 2.1 across all patients.

Conclusion

Stratipath Breast enables risk-stratification of intermediate risk tumors into low- and high-risk groups, while significantly reducing costs and turn-around times compared to molecular assays. Its integration into routine clinical workflows therefore has the potential to benefit both patients and healthcare providers and to expand access to precision diagnostics.

Key words: Breast cancer, Risk stratification, Computational pathology, CE-IVD, Nottingham Grading, Prognostic

P57

Quantifying micro- and macrovesicular steatosis in preclinical mouse models of NAFLD by a deep learning based image analysis of whole slide images

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Introduction

Non-alcoholic fatty liver disease (NAFLD) is an increasing health concerns worldwide, increasing along with obesity. Thus, innovative methods to study the manifestation of NAFLD on pre-clinical models of the disease are needed.

Material and methods

We developed a convolutional neural network (CNN) -based deep learning model in order to quantify micro- and macrovesicular steatosis in the liver. The method applies hematoxylin-eosin stained whole slide images (WSIs), combined with the cloud-based AI-platform (Aiforia Create, Aiforia Technologies, Helsinki, Finland). The CNN model was trained with more than 100 WSIs from various dietary interventions and genetically modified (GM) mouse models with various degree of liver steatosis. The CNN was first trained to detect liver parenchyma, excluding the blood vessels and any artefacts generated during tissue processing and image acquisition, and then to recognize and differentiate the areas of micro- and macrovesicular steatosis. Finally, the percentages of the areas containing micro- and macrovesicular steatosis were quantified by the model in the separate validation set and the image analysis result was compared to other fat measurements and to pathologists´ evaluation.

Results and discussion

The results provided by the model well replicated the assessment by pathologists, and correlated with the liver fat content measured by EcoMRI ex vivo and with the concentration of the triglycerides measured in the liver homogenates.

Conclusion

In conclusion, we have developed a deep learning based model that facilitates fast and reliable quantification of the amount and type of liver steatosis on paraffin sections of preclinical studies with mice.

Key words: Image analysis, Deep-learning, NAFLD, Liver steatosis, Mouse models, Whole slide images

P58

Multicentre and Prospective: Multiplying the complexity to evaluate the health economics of AI for prostate cancer

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Introduction

Market-cleared artificial intelligence (AI)-based algorithms for pathology are available to be used in clinical care. Yet the majority of published clinical efficacy studies are on retrospective, non-consecutive cohorts from a single institution. To study the health economics and the suitability of these systems for routine clinical use, studies need to reflect the complexity of the real-world clinical setting.

Material and methods

In the Articulate Pro study, Paige Prostate, an AI-based software system to help pathologists diagnose prostate cancer in core needle biopsies, is being evaluated prospectively across three NHS trusts in the UK serving distinct patient populations. To create a robust multicentre study protocol and health economic models, the standard of care, reporting practices, and diagnoses from a 12-month period were determined across the three institutions.

Results and discussion

Prostate biopsy cases across the three trusts are distinct in terms of the prevalence of benign cases (38% ; 23% ; 21%). The individual trust detailed case reporting conventions, and the approaches used to prepare cases for multidisciplinary team (MDT) review, also differ across the three trusts and this impacts study design.

Conclusion

Moving from a single-institution study, and to using whole cases instead of single slides, reflects real-life practice yet adds complexity from a conventional retrospective reader study. The integration of AI assistance into clinical practice needs to account for aspects of the full diagnostic pathway beyond the primary review of a single pathologist. A complex data capture system can record resource use and map all of the workflow steps and how AI is integrated into the workflow.

Key words: artificial intelligence, prostate cancer, health economics, prospective, reporting

P59

Age related remodeling of aortic diameter

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Introduction

Aorta is the main representative of the group of arteries that carry large amounts of blood, called elastic arteries. The authors aimed to quantitatively assess the age variation of aortic diameters (D_AO).

Material and methods

Four aortic rings from four main regions (Base – Ao-B; Cross – Ao-C; Thoracic – Ao-T; Abdominal – Ao-Ab) were taken during autopsies from 90 cases (55 men and 35 women), fixed in neutral buffered formalin and photographed together with a ruler. Age was stratified in four main periods: AP1-Childhood+Adolescence, AP2-Young Adulthood, AP3-Mature Adulthood and AP4-Senescence. Average (AV) D_AO was determined using an in-house built software, after prior image calibration and compared with "t" test for two independent samples (Two tailed), Anova: Single factor test and Pearson's test.

Results and discussion

AV D_AO had an obvious increasing trend with age (Pearson's test "p" < 0.0001), more pronounced in men (higher coefficient of determination-R2). The increasing trend is present in each AO region throughout life (AP1-AP4) (Anova's test "p" < 0.0001), in both sexes, being higher in men than in women in each life period. In turn, AV D_AO had an obvious decreasing trend from proximal to distal aortic regions (Ao_B-Ao_Ab) in each period of life (Anova's test "p" < 0.0001) being also higher in men than in women in each aortic region.

Conclusion

AV D_AO underwent a divergent remodeling process in both sexes related to topography and age, its values decreasing constantly from proximal to distal regions but increasing constantly from youth to senescence. AV D_AO values were always higher in men than in women both throughout life and aorta length.

Key words: aorta, ageing, morphometry

P60

Aortic diameter remodeling depending on patient's cause of death

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Introduction

Alterations of cardiovascular system are the leading cause of death, followed by cancer, although there are significant variations between countries. The authors aimed to quantitatively assess the variation of aortic diameters (D_AO) in relation with the disease that caused the patient's death.

Material and methods

Four aortic rings from four main regions (Base – Ao-B; Cross – Ao-C; Thoracic – Ao-T; Abdominal – Ao-Ab) were taken during autopsies from 90 cases, fixed in neutral buffered formalin and photographed together with a ruler. Causes of death were stratified in: V_P-Vascular pathology (25 cases); NV_P-Nonvascular pathology (37 cases); NV_NP-death caused by non-pathologic conditions (28 cases). Average (AV) D_AO was determined using an in-house built software after prior image calibration. AV values were compared using "t" test for two independent samples (Two tailed), Anova: Single factor test and Pearson's test.

Results and discussion

AV D_AO had an obvious and homogenous (Pearson's test "p" < 0.0001) decreasing trend throughout AO length (Ao_B-Ao_Ab) in all three groups (Anova's test "p" < 0.0001) in both sexes, being higher in men than in women in each group. However, D_AO was significantly larger in Ao-B than in the other three regions. AV D_AO values were almost similar throughout the aortic length in V_P and NV_P groups, slightly pronounced in the latter in the proximal regions and significantly higher than in NV_NP group.

Conclusion

The AV D_AO underwent a similar remodeling process depending on the cause of death throughout the aortic length, with higher values in men than in women and in V_P and NV_P groups as compared to the NV_NP group.

Key words: aorta, cause of death, morphometry

P61

Prediction of NMIPUC Relapse from Hematoxylin-Eosin Images using Deep Multiple Instance Learning in patients treated with BCG immunotherapy

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Introduction

Tumor grade is one of the most important features in risk assessment of non-muscle-invasive papillary urothelial carcinoma (NMIPUC) yet it is poorly reproducible. Here we present our preliminary results of tumor risk assessment from NMIPUC resection tissue samples based on image features retrieved by computer vision methods.

Material and methods

We used a set of H&E whole slide images (WSIs) from 981 NMIPUC patients (one WSI per patient) to train the patch-based deep feature extraction network. This network was applied patch-wise to the epithelial compartment of H&E-stained tumor tissue WSIs from an independent cohort of 164 NMIPUC patients treated with transurethral resection followed by intravesical BCG immunotherapy. Extracted features were used to identify patients with tumor relapse within 2-year period after BCG induction. To predict tumor relapse from extracted image features using only weak slide-level labels for training, we employed a neural multiple instance learning (MIL) network.

Results and discussion

We explored alternative feature extraction frameworks and the impact of patch size, training set size, length of feature vector, network architecture, and training strategy on the accuracy of feature extractor network (0.289 – 0.587 classification accuracy). Our MIL network trained to predict 2-year relapse achieved 0.562 mean prediction accuracy and 0.588 F1-score in a 5-fold cross-validation setting.

Conclusion

We achieved an image-based computational method to predict a relapse of NMIPUC in 2-years after BCG immunotherapy induction. These patients represent a relatively homogeneous and aggressive subset of NMIPUC, while previous studies reported comparable stratification accuracy in full spectrum of NMIPUC with highly variable clinical behavior and histologic features.

Key words: Papillary urothelial carcinoma, Multiple instance learning, BCG immunotherapy, Feature extraction

P62

Improving the efficiency and robustness of phenotyping in multiplex immunofluorescence whole slide imaging

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Introduction

Phenotyping of cells in multiplex immunofluorescence (mIF) images is crucial to investigate the spatial interactions between immune and tumor cells in search for new biomarkers or spatial signatures. However, there is a lack of efficient and reliable methods that enable phenotyping across a set of whole slide images (WSIs) with minimal human annotations.

Material and methods

We develop a semi-supervised pipeline to perform simultaneous nucleus segmentation and classification based on a sparse set of point annotations. We combine sparse point annotations with nucleus segmentations obtained from a pre-trained deep learning model, and perform label propagation based on image and shape features. The expanded training set is used to train a deep learning model for end-to-end nucleus segmentation and phenotyping directly from image data.

Results and discussion

We demonstrate our pipeline on a set of 45 mIF WSIs of colon cancer with 6-plex staining of immune cells [Kießler et al., J Immunother Cancer, 2021]. Sparse point annotations were acquired in Akoya's inForm software. Results are compared with vendor-provided phenotyping methods in terms of quality and reliability of segmentation and classification. Although in-depth quantitative evaluation is pending, preliminary results show substantial improvements in nucleus detection and promising results in consistency of phenotyping across different WSIs.

Conclusion

Large-scale analysis of mIF WSIs of the tumor microenvironment requires robust and efficient algorithms for cell phenotyping. By combining efficient sparse point-wise annotations with robust deep learning models that learn phenotyping directly from image data, our pipeline can provide considerable improvements for biomarker research in spatial biology.

Key words: spatial biology, multiplex immunofluorescence, phenotyping, artificial intelligence, deep learning, spatial biology

P63

Auto-NuClick: A dual-stage neural network for nuclear instance segmentation

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Introduction

In computational pathology, cell-based features are often extracted from the digital Haematoxylin and Eosin (H&E) stained histology images and used in the downstream explainable models. We introduce Auto-NuClick, a lightweight and fast dual-stage neural network for automatic nuclear instance segmentation, to address the challenge of sourcing time-consuming and expensive manual dotting of nuclei in histology images. It shows promising results on the largest publicly available dataset.

Material and methods

First, we employ the Efficient-UNet model to detect the nuclei in a given H&E image, which is an encoder and decoder architecture, both with efficient-net backbone. Then, detection output is transformed into inclusion and exclusion maps concatenated with RGB patches, serving as the input of NuClick, a nuclei instance segmentation model requires dots as its input, for the initial prediction. We perform additional post-processing to remove spurious objects and aggregate patch-level maps into the tile-level nuclear instance prediction maps.

Results and discussion

The proposed method was trained using various masks, with the distance map being the most effective. Auto-NuClick achieved a 0.612±0.007 binary panoptic quality score, outperforming HoVer-Net by 4.9% in PQ, half of the standard deviation, with 40% faster inference speed on the 3-fold cross-validation experiment on the Lizard dataset. The method can accurately segment even the smallest cells in crowded areas where HoVer-Net fails.

Conclusion

We proposed the Efficient-UNet model for nuclei detection, combined with NuClick as a dual-stage method for nuclei instance segmentation task, which is 61.9% lighter in parameter size than YOLOv5 combine with NuClick. Future work will focus on designing a nuclei classification branch.

Key words: Nuclear instance segmentation, Computational pathology, Machine learning

P64

Diffusion models for WSI generation: a synthetic step towards supporting sharing and mitigating imbalance

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Introduction

Whole slide images (WSIs) are marking the advent of the new paradigm of Digital Pathology, an ideal testbed for exploiting AI techniques. Nonetheless, the greed for data of Deep Learning methods still represents a major hindrance for the optimal training of the algorithms: here we propose a solution employing synthetic data produced by advanced generative models.

Material and methods

We leveraged a diffusion probabilistic model to generate new images which follow the original distribution. Starting from 150 WSI of 5 different body districts from TCIA, we first produced 49284 tiles and then we trained the model to generate new images that contained the characteristics of the original classes. Fabricated images were evaluated by a panel of 3 pathologists, asked to identify the original class, given a set of 4 homogeneous synthetic and actual images, and whether the tile was real or synthetic. 60 questions for the first part and 22 for the second.

Results and discussion

The pathologists achieved a mean accuracy of 90% in detecting the origin of the tissue, with the wrong answers arising from 7 synthetic and 11 actual images. Considering the second task the mean accuracy was 59% with a recall of 72.7%, true negative rate of 45.5%.

Conclusion

Synthetic tiles are qualitatively comparable with the actual ones, and they contain tissue-specific morphologies. This procedure can anonymize WSI without losing morphological information, shortening time needed to reach research centers and re-balance biases in the dataset. Future developments include a classifier to evaluate the quality of the dataset and generating higher resolution images.

Key words: synthetic data, diffusion models , data privacy, unbalanced datasetes, generative models, anonymization

P65

Fully Automated Artificial Intelligence Solution for Accurate HER2 IHC Scoring in Breast Cancer: Multi-Reader Study

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Introduction

Human visual interpretation of HER2 IHC staining can be subjective, despite established guidelines, leading to intra- and inter-pathologist variability. Recent findings on the efficacy of HER2-targeted therapy on HER2-low patients raise the need for accurate and reproducible scoring. This study aimed to validate the use of an artificial intelligence (AI) solution for interpreting HER2 scores in breast samples, based on ASCO/CAP 2018 guidelines.

Material and methods

Two-arm multi-reader study on 120 cases from four sites compared the performance of pathologists without AI versus with an AI HER2 solution. Both arms were compared to rigorous ground truth (GT) established by five breast subspecialists, i.e. agreement of at least 4 out of 5 pathologists.

Results and discussion

The AI solution showed a very high average agreement of 92.4% with GT for cases with robust GT (N=92). For the same cases, the pathologists aided by AI reached an average agreement with the GT of 88%, while the pathologists without AI assistance showed 85.3% agreement, respectively. For HER2 0 and 1+ cases, pathologists with AI were more consistent with an inter-observer agreement of 87.4% vs. 69.8% for pathologists without AI assistance ($p<0.05$) and showed higher average agreement with GT than pathologists without AI, 88.8% vs 81.9%, respectively.

Conclusion

This study reports improvements in HER2 IHC scoring accuracy by pathologists assisted by an AI solution, specifically for HER2 0 and 1+. AI solutions could be used as decision-support tools for pathologists, enhancing the reproducibility and consistency of HER2 scoring, thus enabling optimal treatment pathways and better patient outcomes.

Key words: AI, deep learning, Cancer, Breast, HER2, Image Analysis

P66

Semantic Segmentation of DCIS in Breast Cancer Histopathology Whole Slide Images with Deep Learning

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Introduction

The accurate detection of invasive cancer (IC) regions in whole slide images (WSI) is a pre- requisite for many computational pathology methods. Some morphologies, such as ductal carcinoma in situ (DCIS) in breast cancer, can be difficult to distinguish from IC regions. Therefore, the inspection of morphology at multiple magnification level in addition to potentially immunohistochemistry staining is often required to correctly classify tissue regions. In this study, we investigate the potential of using deep learning methods to detect areas of DCIS in haematoxylin and eosin (H&E) stained WSIs of primary breast cancer resection specimens.

Material and methods

This study includes 346 H&E stained WSIs from 346 female primary breast cancer patients diagnosed in Sweden. Regions of DCIS and IC were annotated by a clinical pathologist. DeepLabV3+ models were trained and evaluated using 5-fold cross validation (CV) at magnifications 0.625X, 1.25X, 2.5X, 5X, 10X.

Results and discussion

At the best performing magnification of 5X, the AUC of the validation folds were 0.9723, with a median slide-level sensitivity of 0.71 at a median specificity of 0.99 and a median slide-level accuracy of 0.91.

Conclusion

The study shows the possibility to detect and segment DCIS in H&E stained WSIs with reasonably high accuracy using models that operate at a single magnification level. However, due to the high interclass similarity of DCIS and IC cells, multi-resolution models considering the spatial distribution of the data has the potential to improve DCIS segmentation.

Key words: DCIS, Semantic segmentation, Computational pathology, Breast cancer, Whole slide image

P67

Assessing Risk of Prostate Cancer Metastasis by Deep Learning in Surgically-Treated Patients

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Introduction

Pathologic grade remains one of the most important predictors of prostate cancer metastasis after radical prostatectomy (RP). Here, we tested whether deep learning algorithms applied to hematoxylin and eosin (H&E)-stained whole slide images (WSI) of prostate tumors and paired clinical-pathologic data can improve on standard metastasis prediction scores such as CAPRA-S.

Material and methods

We developed a system that integrates multi-modality data from histopathology images and clinical parameters (age, race, pre-operative PSA, pathologic T- and N-stage and margin status). The system includes tumor identification in H&E-stained WSI or tissue microarray (TMA) samples followed by a classification model. The algorithm was trained on 446 patients from previously published Johns Hopkins RP cohorts and validated on 110 additional patients, as well as tested in an independent RP cohort comprised of 346 patients. Model performance was assessed using AUC and compared to the logistic regression model with CAPRA-S alone.

Results and discussion

The baseline AUC for CAPRA-S was 0.851 compared to an AUC of 0.911 using an algorithm incorporating WSI and clinical-pathologic parameters. In the test cohort, the AUC for CAPRA-S was 0.850 versus an AUC of 0.899 using WSI and clinical-pathologic parameters. Similar algorithms using images of 4 tumor punches on TMA from the dominant nodule and clinical-pathologic parameters achieved an AUC of 0.845 on the test cohort.

Conclusion

Deep learning algorithms incorporating WSI or TMA images from the dominant tumor nodule and clinical-pathologic parameters outperform current clinically-utilized prognostic nomograms such as CAPRA-S for prediction of metastasis. Validation in additional multi-institutional as well as racially diverse cohorts is underway.

Key words: Histopathology, Metastasis, Prediction, Deep Learning

P68

Deep Learning-Based Identification of Lymph Node Metastasis in Prostate Cancer

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Introduction

Pelvic lymph node metastasis in prostate cancer is associated with poor prognosis among surgical candidates and these patients may benefit from adjuvant or salvage radiation and hormonal therapy. Thus detecting the presence of metastatic foci in pelvic lymph node dissections is critical for clinical decision-making, post-treatment planning, and outcome prediction for patients. However, this lymph node screening task is tedious for most pathologists and highly amenable to deep-learning-based tools to assist pathologists in identifying micro-metastatic foci on digitized images.

Material and methods

The approach was built on whole slide images (WSI) of H&E-stained sections from pelvic lymph node dissections performed at the time of radical prostatectomy. WSI from 42 patients and 81 patients were used for training and validating the algorithm, respectively. The algorithm was trained by a Transformer-based segmentation model to identify and segment metastatic areas in these images. Based on the detection of malignant regions, the algorithm further categorised the WSI as "metastasis detected" or "no metastasis detected".

Results and discussion

On the internal test cohort, the algorithm demonstrated good diagnostic discrimination between the two diagnosis groups with sensitivity of 95% and specificity of 81%. For segmenting metastatic areas, an F1-score of 89% was obtained.

Conclusion

The proposed approach assists the pathologist in detecting lymph node metastasis in prostate cancer patients. Future development will incorporate external validation of the solution.

Key words: Pelvic lymph node metastasis, prostate cancer, deep learning, histopathology

P69

Z stacking for WSI generation improves the TIL detections algorithm performance in Breast cancer cases

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Introduction

Tumor infiltrating lymphocytes (TILs) are an important predictive biomarker for immunotherapy in breast cancer and other solid tumors, so it's imperative that TILs detection need to be accurate. Here we present a study of 50 breast cancer cases where TILs counting was done in WSIs with and without Z stack fusion WSI

Material and methods

50 cases of Breast cancer were scanned using Spectral HT scanner from Pramana with and without Z stacks. Numbers of Z stacks required for a given biopsy were determined by tissue thickness evaluation and focus content distribution across stacks and subsequently Z stacks were fused. A deep learning based single-stage-detector trained for TILs and nuclei detection was evaluated on both the WSIs (with and without stack fusion) for 50 independent breast cancer cases.

Results and discussion

For all the cases there was significant improvement in the TILs detection and scoring algorithm in the WSIs with fused image post Z stacking in comparison to WSI without Z stacking. Even the overall nuclei counts of different cell types were higher in the fused stack images than best focus WSI across all cases as the focused content in all the layers are available together in fused stack image, whereas in best focus image few cells are not in focus and the cellular details are thus lost

Conclusion

Z stacking and fused stack images capture better nuclear and cytoplasmic details than best focus image, thus TILs detection and scoring algorithm shows improvement in results when run on fused stack WSI in comparison to best focus WSI

Key words: lymphocytes, tumor, cancer, Z stacks, nuclei, infiltrating

P70

Multi-site validation of digital pathology for the routine reporting of histopathology samples

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Introduction

Digital pathology (DP), i.e. the use of high throughput digital slide scanners to digitise histopathology slides is now well established. Many laboratories are using this as their preferred method of diagnosis. In order to spread this practice beyond the early adopters additional data is needed to validate equivalence of DP to light microcopy (LM) including its use for cancer screening samples and samples requiring specialist techniques such as immunofluorescence and immunohistochemistry.

Material and methods

We conducted a multi-site study across 6 centres in the UK comparing LM with DP. Two thousand cases including 600 breast, gastrointestinal and skin and 200 renal biopsies were used. Cases were complete including all parts special stains immunocytochemistry and for renal biopsies immunofluorescence. Sixteen pathologists participated each reporting all the cases in one specialty area on both platforms, separated by a 6 week washout period and with the order randomised. Differences in reports were identified by independent reviewers and passed to an arbitrator for classification as clinically significant or insignificant. Clinically significant difference were reviewed by the reporting pathologists to agree consensus ground truth.

Results and discussion

Intra-observer agreement and agreement with ground truth were measured for each reading. The results will be presented.

Conclusion

The study provide definitive evidence of comparison between DP and LM measured across 2000 cases using for 16 pathologists from 6 different sites, and include cancer screening cases as well as special stains immunocytochemistry and immunofluorescence.

Key words: Digital pathology, validation, cancer screening, immunofluorescence, breast cancer, renal biopsy

P71

On robustness and domain generalization of classification systems for leukocytes in peripheral Blood and Bone Marrow

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Introduction

In recent years, several AI-based image analysis systems have been developed in order to facilitate classification of diagnostically relevant leukocyte patterns relevant in the diagnosis of leukemia. Here, we present neural network-based algorithms for classification of leukocytes in both peripheral blood and bone marrow, and assess their generalizability between different source domains.

Material and methods

We present two neural network-based single cell classification systems for classification of malignant and non-malignant leukocyte classes developed using two publically available datasets of single-cell leukozyte microscopy. We assess performance of the classifiers on external data from different source domains and disease distributions, and test the effectiveness of several domain-generalization methods on the cell classification problem.

Results and discussion

State-of-the-art single-cell classification systems attain a human-level classification performance in several key classification tasks such as myeloblast recognition in peripheral blood. Using domain generalization methods, we find that thier performance can be extended to datasets from other laboratories obtained using different scanning equipment. Furthermore, models can be rendered robust against significant class imbalance, which is a hallmark of many datasets in hematology

Conclusion

Modern neural network-based methods allow development of powerful classifiers for leukocyte classification with the help of large, expert-annotated image datasets. Using domain generalization methods, these classification algotihms can be rendered robust againgst domain shift and class imbalance.

Key words: Digital Cytology, Leukemia, Robustness, Domain Generalisation, Neural Nets, Classification

P72

Digital pathology - from clinic to research. The UZBrussel - VUB experience

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Introduction

The emergence of digital pathology has changed the pathology ecosystem in clinical practice. At present enormous volumes of WSI (whole slide image) and WSI related data remains unexploited for research purposes. We present the establishment of an infrastructure to transfer whole slide image data, annotations and metadata from our diagnostic environment to the separate research environment.

Material and methods

Starting from the 'wet lab', all tissue glass slides are affixed with a barcode label generated by the pathology laboratory information system (LIS). The barcodes are read by the image management system in order to automatically assign the WSIs to the correct cases and patient in the LIS system and to parse the WSIs into a tree-based folder system to guarantee the best tile streaming performance and user experience.

Results and discussion

A tool allowing researchers to compile datasets for (computational) pathology research including anonymized or pseudonymized WSIs, pathology report coded data, scanning device lifecycle data, staining protocol data, slide quality and on slide control tissue data was developed in house. To guarantee patient safety and privacy, a full audit trail was implemented to comply with regulatory security requirements. Researchers are granted, within the constraints of a specified study protocol and period, viewing and/or download rights of the WSI data and associated metadata.

Conclusion

The generation of digital pathology creates novel challenges for the histopathology community in managing, processing, and governing the use of these data for research purposes. Further efforts will be needed to design a performant data governance policy to cope with the new data generated.

Key words: WSI, anonymized, pseudonymized, quality, infrastructure, LIS

P73

Multivariate modelling of mid-infrared spectra of colorectal cancer

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Introduction

The applicability of techniques based on spectroscopy outside the visible light range is increasingly being investigated. The mid-infrared technique is non-invasive and non-destructive, which is one of its main advantages over the use of ionizing radiation. In addition, it can provide sufficient chemical information to effectively predict whether a patient has cancer using appropriate machine learning methods.

Material and methods

Sections of tissue microarrays of formalin-fixed tissue samples embedded in paraffin-embedded tissue were selected and analysed. Spectra were acquired using a Fourier transformation mid-infrared Perkin Elmer Spotlight microscope. Conventional H&E stained sections were digitized using a 3DHistech P1000 scanner. The 32 cores are containing intact colon mucosas (NC) and primary colorectal carcinomas (CRC). A digital database was created to organize and assemble data from different modalities. Both unsupervised (PCA) and supervised methods (Random Forest, Linear Discriminant Analysis, Support Vector Machine, XGBoost, U-Net) were used to process the data.

Results and discussion

7744 spectra were collected from each core. Point clouds visualized for the first two principal components of PCA show some mixing of tumor versus normal spectra. The Random Forest algorithm resulted in a model accuracy of 0.575, Linear Discriminant Analysis 0.644, Support Vector Machine 0.593, XGBoost 0.592 and the U-Net 0.532. Linear Discriminant Analysis produced the highest sensitivity of 0.885.

Conclusion

The accuracies were poor in the discrimination of normal colon mucosa from colorectal cancer on the non-filtered spectra. Therefore, data preprocessing is suggested to be performed on larger cohort after spectral background filtration.

Key words: infrared, FTIR, colorectal, spectroscopy

P74

Reconstructing 3D histological structures using machine learning (AI) algorithms

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Introduction

Histomorphometry is currently the gold standard for bone micro-architectural examinations, however, it relies on two-dimensional sections to deduce the spatial properties of structures. Micromorphometric parameters are calculated from these sections based on the assumption of a plate-like three-dimensional microarchitecture, resulting in the loss of three-dimensional structure due to destructive nature of the classic histological processing.

Material and methods

To overcome limitation of histomorphometry and reconstruct 3D architecture of bone core biopsy samples from 2D histological sections, bone core biopsy samples were decalcified and embedded in paraffin. Subsequently, 5 µm thick serial sections were stained with hematoxylin and eosin and scanned using a 3DHistech Pannoramic® 1000 Digital Slide Scanner. Region of interest was preprocessed and oriented, and semantic segmentation of the bone, bone graft material, and soft tissue was performed. Faulty sections were filtered out using unsupervised filtering based on mutual information. 3D reconstruction was created using ASIFT feature matching and homography.

Results and discussion

Our method achieved an overall accuracy of 96% with an F-score of 0.967 for the segmentation of bone tissue. Filtering process accuracy was 89.7%, with a precision of 0.96 and a recall of 0.88.

Conclusion

This method enables the examination of tissue microarchitecture in 3D with an even higher resolution than microcomputed-tomography (micro-CT), without losing information on cellularity. However, the limitation of this procedure is its destructive nature, which precludes subsequent mechanical testing of the sample or any further secondary measurements. Furthermore, the number of histological sections that can be performed from a single sample is limited.

Key words: machine learning, histology, image matching, digital whole slide

P75

Colorectal cancer screening aided by AI

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Introduction

Hungarian national screening program was started in 2018 to reduce the mortality. To expedite the process and reduce the number of unnecessary biopsies, a machine learning-based algorithm is being developed to pre-filter cases that are likely to be true negatives. This algorithm will use artificial intelligence (AI) approaches on large datasets.

Material and methods

A total of 2,300 colorectal biopsies were scanned using a P1000 digital slide scanner (3DHistech.). A 40x magnification objective was used for scanning. A Convolutional Neural Network (CNN) was trained on 2000 slides, and 300 slides were set aside for testing. The annotations were done in three stages: global, textual annotation for general diagnosis, local, textual annotation for specific tissue parts, and graphical, pixel-level annotation for local tissue parts.

Results and discussion

Out of the 217 adenomas were 187 rightly classified by AI, however, 20 cases were regarded as non-neoplastic lesions and 10 cases as CRCs. All CRCs except one (listed as non-neoplastic lesion) were classified correctly by AI. The separation of negative and non-neoplastic lesion samples are less sufficient, 32 negative cases were classified as non-neoplastic lesion by the neural network.

Conclusion

Incorporating a decision support module into the digital pathology software infrastructure could help reduce the workload on pathologists and would allow doctors to focus on the more complex cases and provide necessary supervision to the AI when needed. The fact, that the model predicts probabilities, enables the possibility of selecting a probability threshold, which can trade sensitivity for specificity based on the need.

Key words: colorectal, WSI, CNN, screening

P76

Screening of Normal Endoscopic Large Bowel Biopsies with Interpretable Graph Learning

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Introduction

Increasing screening rates for early detection of colon cancer are placing significant pressure on already understaffed and overloaded histopathology resources worldwide.

Material and methods

We developed an interpretable AI algorithm, incorporating pathologist domain knowledge, to rule out normal large bowel endoscopic biopsies. 6,591 whole-slides images of endoscopic large bowel biopsies were used from 3,291 patients (54% Female, 46% Male). One UK NHS site was used for model training and internal validation, while two other NHS sites and one site in Portugal were used for external testing.

Results and discussion

Model training and internal validation were performed on 5,054 whole slide images of 2,080 patients from a single NHS site resulting in an AUC-ROC of 0.98 (SD=0.004) and AUC-PR of 0.98 (SD=0.003). We validated the performance using 1,537 whole slide images of 1,211 patients from three independent external datasets with mean AUC-ROC = 0.97 (SD=0.007) and AUC-PR = 0.97 (SD=0.005). At a sensitivity threshold of 99%, the model can reduce the number of normal slides to be reviewed by a pathologist by 55%. Also, IGUANA can provide an explainable output highlighting potential abnormalities in a whole slide image. Example results can be viewed at https://iguana.dcs.warwick.ac.uk/.

Conclusion

An interpretable AI model was developed to accurately screen abnormal cases for review by pathologists. Explainable predictions of IGUANA can guide pathologists in their diagnostic decision making and help boost their confidence in the algorithm.

Key words: Colon Biopsy Screening, Transparent AI, Interpretable, Graph Neural Network

WELCOME TO BUDAPEST

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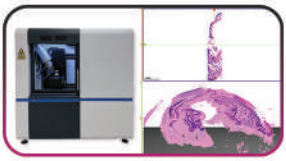
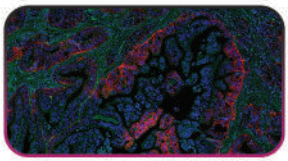
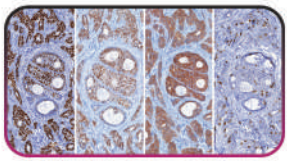

DIAGNOSTICS & RESEARCH

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June 15

Grand Ballroom

13:00 - 13:45 **3DHISTECH**
Digital Pathology – Back into the Future

June 16

Grand Ballroom

08:00 - 08:45 **Roche Diagnostics International**
Developing personalized healthcare solutions to address unmet medical needs of cancer patients

13:00 - 13:45 **Ibex Medical Analytics Symposium**

Valletta I

08:00 - 08:45 **NanoString Technologies Europe Limited**
The Spatial Biology Revolution: multi-omic tissue analysis powered by a cloud-based, fully-integrated informatics platform

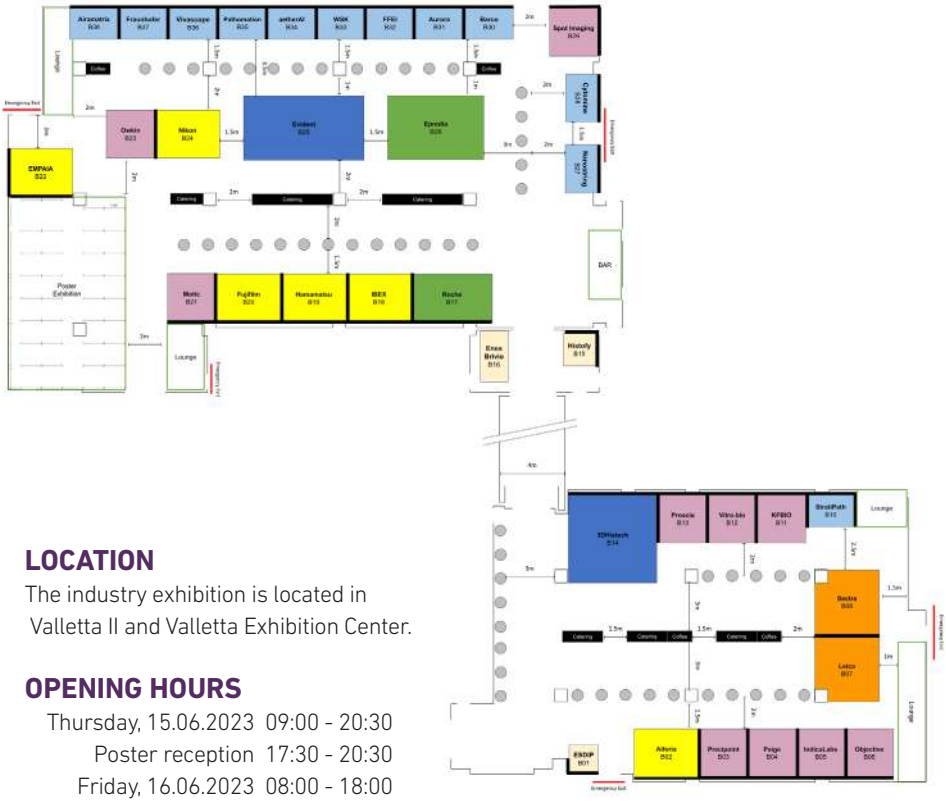
13:00 - 13:45 **AIRA Matrix Private Limited Symposium**

June 17

Grand Ballroom

08:00 - 08:45 **Epredia Symposium**

11:45 - 12:30 **EMPAIA Symposium**



LOCATION

The industry exhibition is located in Valletta II and Valletta Exhibition Center.

OPENING HOURS

Thursday, 15.06.2023 09:00 - 20:30
Poster reception 17:30 - 20:30
Friday, 16.06.2023 08:00 - 18:00
Saturday, 17.06.2023 08:00 - 15:00

Booth Nr.	Company
B01	European Society of Digital and Integrative Pathology
B02	Aiforia Technologies Plc
B03	Precipoint GmbH
B04	Paige
B05	Indica Labs
B06	Objective Imaging Ltd
B07	Leica Microsistemas Lda.
B08	Sectra Imaging IT Solutions AB
B10	Stratipath AB
B11	Ningbo Konfoong Bioinformation Tech Co., Ltd.
B12	VITRO S.A.
B13	Proscia
B14	3DHISTECH LTD
B15	Histofy Ltd
B16	ENEA BRIVIO di SIMONE BRIVIO
B17	Roche Diagnostics International
B18	Ibex Medical Analytics
B19	Hamamatsu Photonics Deutschland GmbH
B20	FUJIFILM Europe GmbH
B21	MOTIC EUROPE SLU
B22	EMPAIA Consortium
B23	Owkin
B24	Nikon Europe B.V.
B25	Evident Europe GmbH
B26	Epredia
B27	NanoString Technologies Europe Limited
B28	CYTOMINE CORPORATION SA
B29	SPOT Imaging
B30	BARCO NV
B31	Aurora mScope
B32	FFEI
B33	WSK Medical
B34	aetherAI Co., Ldt.
B35	Pathomation
B36	VivaScope GmbH
B37	Fraunhofer IIS
B38	AIRA Matrix Private Limited

	Tuesday - 13.06.2023	Wednesday - 14.06.2023				
Time	WS ROOM ROYAL LOUNGE BOARDROOM I	WS ROOM ARANY AND KRUDY	WS ROOM PETOFI AND MIKSZATH	WS ROOM JOKAI	WS ROOM DERY	WS ROOM ROYAL LOUNGE BOARDROOM I
08:00 - 08:15						
08:15 - 08:30						
08:30 - 08:45						
08:45 - 09:00						
09:00 - 09:15	IHE PaLM meeting			Several Research Project Meetings	DICOM WG -26 Meeting	IHE PaLM Meeting
09:15 - 09:30						
09:30 - 09:45						
09:45 - 10:00						
10:00 - 10:15						
10:15 - 10:30						
10:30 - 10:45						
10:45 - 11:00						
11:00 - 11:15		WS1.2 EMPAIA	WS2.2			
11:15 - 11:30						
11:30 - 11:45						
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13:00 - 13:15						
13:15 - 13:30						
13:30 - 13:45		WS1.3 AIFORIA	WS2.3 3DHISTECH			
13:45 - 14:00						
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15:00 - 15:15						
15:15 - 15:30						
15:30 - 15:45		WS1.4 Hamamatsu	WS2.4			
15:45 - 16:00						
16:00 - 16:15						
16:15 - 16:30						
16:30 - 16:45						
16:45 - 17:00						
17:00 - 17:15					IHE PaLM and Dicom - Wg-26 Joint Meeting	
17:15 - 17:30						
17:30 - 17:45		WS 1.5 Roche	WS2.5			
17:45 - 18:00						
18:00 - 18:15						
18:15 - 18:30						
18:30 - 18:45						
18:45 - 19:00						

June 13

Room Royal Lounge Boardroom I

09:00 - 16:30 **IHE PaLM**
IHE PaLM Meeting

June 14

Room Royal Lounge Boardroom I

09:00 - 16:30 **IHE PaLM**
IHE PaLM Meeting

Room Dery

09:00 - 16:30 **DICOM**
DICOM WG-26 Meeting

Room Jokai

09:00 - 19:00 **Individual Research Projects Meetings**

Room Arany and Krudy

11:00 - 12:30 **EMPAIA Consortium**
EMPAIA Academy Hands-On Workshop

Room Arany and Krudy

13:30 - 15:00 **Aiforia Technologies Plc**
Aiforia Research and Clinical Journey
+ PD-L1 AI pratice session

Room Petofi and Mikszath

15:30 - 17:00 **3DHISTECH LTD**
Digital Microscopy - The Past of the Future

Room Arany and Krudy

15:30 - 17:00 **Hamamatsu Photonics Deutschland GmbH**
Implementing Digital Pathology in your lab: The process of integrating Digital Pathology into a working pathology department

Room Dery

17:00 - 18:30 **IHE PaLM and DICOM**
WG-26 joint meeting

Room Petofi and Mikszath

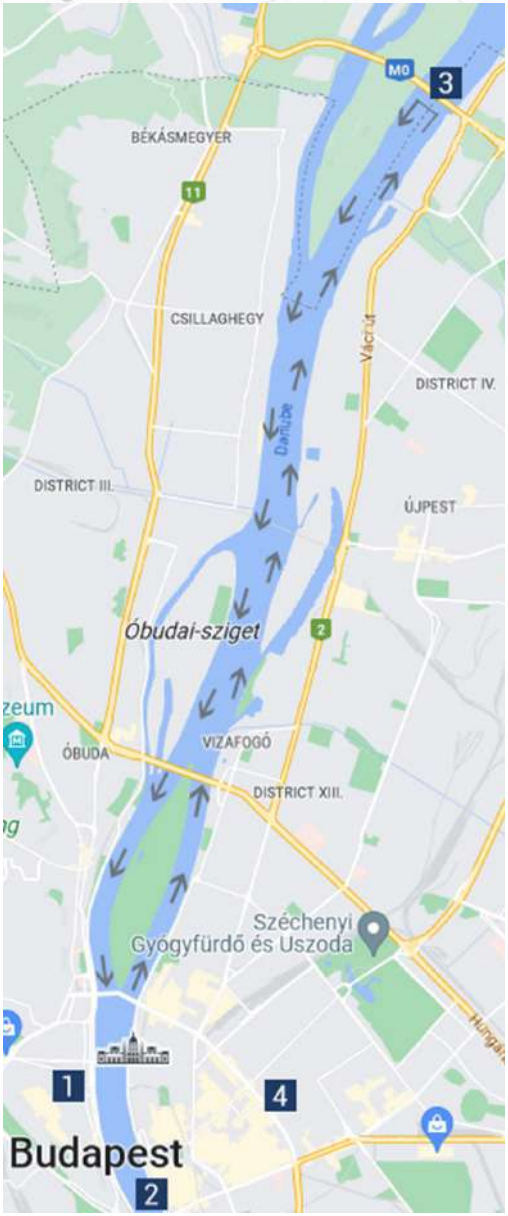
17:30 - 19:00 **Roche Diagnostics International**
Network Meeting on Digital Pathology with a Focus on Precision Medicine

SOCIAL EVENT

All Congress delegates, speakers, and exhibitors are invited to the ECDP2023 social event, which will take place on the evening of Friday, June 16th.
Join us for a 3-4h boat trip on the river Danube that runs through the heart of Budapest (please see map below). The tour will also include the Congress dinner on the boat.
The starting point will be Batthyány Square. A shuttle service from the venue will be provided. Please note that a dedicated registration for the event is required in advance (available via the registration page). The ticket price is 50€/person. Participation is on a first-come, first-served basis (max. 300 guests).

We thank our sponsor 3DHISTECH for supporting this event.

3DHISTECH
THE DIGITAL PATHOLOGY COMPANY



1 **Port of departure and arrival**
Batthyány Square

2 **Southmost point of the cruise**
Rákóczi Bridge

3 **Northmost point of the cruise**
Megyeri Bridge

4 **Congress Venue**
Corinthia Hotel
Erzsébet krt. 43-49.
Budapest H-1073

Route is subject to change depending on weather and water level.

ACT OF GOD

It is mutually agreed that in the event of total or partial cancellation of the Congress due to fire, strike, natural disaster (either threatened or actual), government regulations, or incidents not caused by the organizer, which would prevent its scheduled opening or continuance, the Congress may be partially postponed or terminated as a whole. In this case, participants are not entitled to reclaim refunds on no account. Participants are obliged to have civil liability insurance.

CERTIFICATE OF ATTENDANCE

All participants will receive a certificate of attendance by email after the Congress.

CONTINUING MEDICAL EDUCATION (CME) CREDITS

A CME application was submitted to the European Association Council for Continuing Medical Education (EACCME), which provides credits for attendance at educational events to individual medical specialists.

CONGRESS HOMEPAGE

www.ecdp2023.org

CONGRESS LANGUAGE

The official language of the Congress will be English. Simultaneous translation will not be provided.

CONGRESS VENUE

Corinthia Budapest
Erzsébet Korút 43-49
BUDAPEST H-1073, HUNGARY

DATA PROTECTION

The protection of your data is important to us. All presentation files provided will be deleted immediately after the end of the Congress.

GASTRONOMY

During the official coffee and lunch breaks participants will be offered snacks and beverages in the industry exhibition.

INTERNET ACCESS

Free WiFi will be available at the Congress venue. Login details will be provided on-site.

LIABILITY DISCLAIMER

The organizers cannot be held liable for any hindrance or disruption of Congress proceedings arising from political, social, or economic events or any other unforeseen incidents beyond their control. The organizers will accept no liability for any personal injuries sustained or for loss or damage to property belonging to Congress participants, either during or as a result of the Congress or during all tours and events. Registration of a participant entails acceptance of these conditions.

LOST & FOUND

A Lost & Found box will be placed at the registration desk.

MEDIA CHECK

Access to the media check is from Valetta I. Foyer. Speakers are kindly asked to hand over their presentation at the media check at your earliest convenience but not later than 1 hour before the session.

NAME BADGE

The name badge will be the official conference document and should be worn at all times in order to gain entry to the conference rooms and the exhibition hall. Admission to the conference will not be allowed without badge identification. In case of lost or forgotten badges, an administration fee of 10€ will be charged.

PRE-CONGRESS WORKSHOPS

Pre-Congress workshops will take place on Wednesday, June 14th, 2023.

POSTER RECEPTION

The Poster Reception will take place on Thursday, June 15th, 2023 from 17:30 until 20:30.

PROGRAM CHANGES

The organizer reserves the right to make changes if necessary. No full or partial refunds are made to the attendees in the event of cancellations or other changes in the program.

REGISTRATION DESK

The registration desk is right at the entrance to the convention area that can be reached via the stairs at the end of the Corinthia lobby. Registration is only valid if the complete payment of the congress fee as well as of other services booked has been made. Registration on-site is possible during the entire congress within the opening hours of the registration desk.

SOCIAL EVENT

Boat Trip & Congress Dinner

All congress delegates, speakers, and exhibitors are invited to the ECDP2023 social event which will take place on the evening of Friday, June 16th. Please see page 192 for details

SMOKING

Smoking is strictly prohibited in the conference venue by law.

ADDRESS AND CONTACT

Corinthia Budapest
Erzsébet Körút 43-49
BUDAPEST H-1073, HUNGARY
Phone: +36 1 479 4000
Email: budapest@corinthia.com

HOW TO GET THERE

From Liszt Ferenc International Airport Budapest (BUD)

Distance: 18 km
Estimated time:
30 minutes by car
Taxi approx. 25 min., 25€
Public transit: approx. 50 min.
several possible routes

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Western Railway Station; distance 2 km
Southern Railway Station; distance 4.5 km
Népliget Bus Station; distance 4.4 km

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ORGANIZER

ESDIP - European Society of Digital and Integrative Pathology
Rua da Constituição nº668, 1º esq/traseiras, 4200-194 Porto, Portugal

CONGRESS PRESIDENTS

Andras Kiss (Hungary)
Andras Matolcsy (Hungary)

ORGANIZING COMMITTEE

András Kiss (Hungary)
András Matolcsy (Hungary)
Endre Kontsek (Hungary)
Norman Zerbe (Germany)

CONGRESS HOMEPAGE

www.ecdp2023.org

TIME OF PRINTING

May 30, 2023
All information regarding speakers and times is subject to change.

EVIDENT

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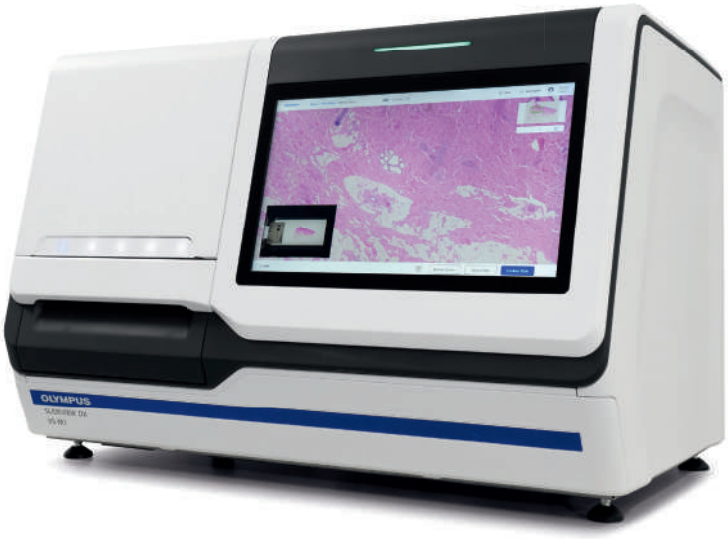
Digital Pathology Slide Scanner

SLIDEVIEW DX PREMIERING AT ECDP 2023



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