ECDP2022

18th EUROPEAN CONGRESS ON DIGITAL PATHOLOGY

PROGRAM



15th-18th of June 2022 | Berlin, Germany

#ECDP2022
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ESDIP
EUROPEAN SOCIETY OF DIGITAL AND INTEGRATIVE PATHOLOGY

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NOTES

Dear Colleague,

Welcome to Berlin and to the 18th 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 exciting interdisciplinary environment, where pathologists, computer scientists, biologists, technicians, students, and last but not least, clinicians as well as industry partners discuss the latest topics related to digital and computational pathology.

This year's focus will be on the integration of histology, molecular pathology and clinical data through machine learning/artificial intelligence. While the diagnosis of pathological tissue alterations will continue to be based on histomorphology in the future, novel imaging techniques, such as multiplex immunofluorescence or imaging mass spectrometry, will gain influence and complement conventional approaches.

Moreover, novel molecular methods, such as spatial transcriptomics or single-cell proteomics, offer new opportunities to combine histology with spatially-resolved deep molecular profiling. ESDIP's mission is closely aligned with these developments, where computational pathology is key to analyzing and interpreting the resulting complex data.

ESDIP is gaining new energy and is evolving fast to the benefit of its members, offering novel scientific, diagnostic and educational opportunities, increasing communication and ideas for innovative paths. Please keep following the ESDIP announcements via our channels on social media and our newsletter.

We hope that you will enjoy ECDP2022.
With our best regards, and on behalf of the ECDP2022 Organizing Committee,

Frederick Klauschen
Congress President

CONGRESS PRESIDENT

Frederick Klauschen

Ludwig-Maximilians-Universität München
Thalkirchner Straße 36 | 80337 München
Germany

Charité – Universitätsmedizin Berlin
Charitéplatz 1 | 10117 Berlin
Germany

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LOCATION

Titanic Chaussee Berlin
Chausseestraße 30 | 10115 Berlin
Germany

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Artyom Borbat *Russia*
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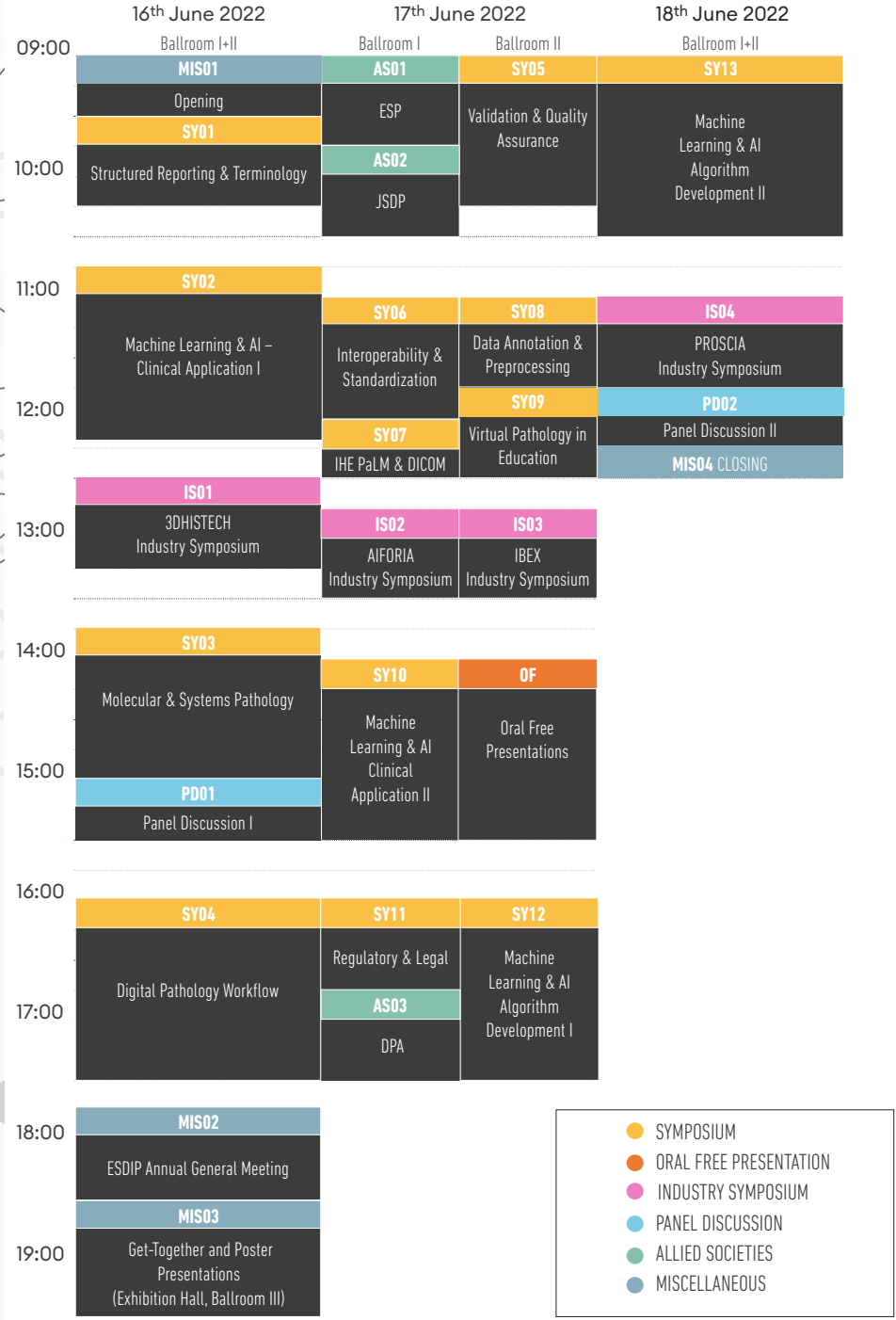
Nora Pohlan *Germany*

PROGRAM OVERVIEW



Ballroom I+II	**MIS01**	**MISCELLANEOUS**
09:00-9:30		**OPENING**
09:00	MIS01.01	**Welcome words from the Congress President** Frederick Klauschen (Germany)
09:05	MIS01.02	**Welcome words from ESDIP** Norman Zerbe (Germany)
09:10	MIS01.03	**Artificial Intelligence in Pathology and Beyond** Klaus-Robert Müller (Germany)
Ballroom I+II	**SY01**	**SYMPOSIUM**
09:30-10:15		**STRUCTURED REPORTING & TERMINOLOGY**
	Chairs	Gunter Haroske (Germany) Sabine Leh (Norway)
	Invited	
09:30	SY01.01	**Datasets and structured reporting: the future of pathology?** Iris Nagtegaal (The Netherlands)
	Abstracts	
09:55	SY01.02	**Specifying a Pathology Structured Report with HL7 FHIR** Andrea Essenwanger (Germany), Gunter Haroske, Thimo Hoelter, Alexander Bartschke, Sylvia Thun
10:05	SY01.03	**Kidney Biopsy Codes: a multi-hierarchical terminology for non-neoplastic kidney biopsies** Sabine Leh (Norway), Hrafn Náttálfur Holger Weishaupt, Amélie Den

Ballroom I+II	SY02	SYMPOSIUM
10:45-12:15		**MACHINE LEARNING & AI - CLINICAL APPLICATION I**
	Chairs	Johan Lundin (Finland) Yuri Tolkach (Germany)
	Invited	
10:45	SY02.01	**Deep learning applications in kidney pathology** Peter Boor (Germany)
	Abstracts	
11:15	SY02.02	**MarrowQuant 2.0: clinical application of a user-friendly digital hematopathology tool for human bone marrow trephine biopsies** Rita Sarkis (Switzerland), Olivier Burri, Claire Royer-Chardon, Sophie Blum, Frederica Schyrr, Mariangela Costanza, Stephane Cherix, Carmen Barcena, Bettina Bisig, Valentina Nardi, Rosella Sarro, Olivier Spertini, Sabine Blum, Martin Weigert, Bart Deplancke, Arne Seitz, Laurence de Leval, Olaia Naveiras
11:25	SY02.03	**AI model trained to detect breast cancer metastasis to lymph node shows robust performance for micrometastases and isolated tumor cells.** Juan A. Retamero (United States), Patricia Raciti, Emre Gulturk, David Klimstra
11:35	SY02.04	**Assessment of glomerular patterns of injury by machine learning methods** Justinas Besusparis (Lithuania), Mindaugas Morkūnas, Arvydas Laurinavičius, Renaldas Augulis
11:45	SY02.05	**Budding-T-cell score is a potential predictor for more aggressive treatment in pT1 colorectal cancers** Linda Studer (Switzerland), John-Melle Bokhorst, Francesco Ciompi, Andreas Fischer, Heather Dawson

11:55	SY02.06	**CYTOFastUrine: An Innovative Integrated Solution For Automated Urine Cytology Diagnostics** Matteo Botteghi (Italy), Francesco Trisolini, Silvia Carattoni, Stefano Martinotti, Antonio Procopio
12:05	SY02.07	**A Multi-Feature AI Solution for Diagnosis Support in Gastric Biopsies: A Prospective Multi-Site Clinical Study** Jessica Calvo (France), Thierry Garcia, Elisabeth Lanteri, Joelle Reyre, Inssaf Laouar, Alona Nudelman, Marina Maklakovski, Anat Albrecht Shach, Ayala Arad, Geraldine Sebag, Maya Grinwald, Judith Sandbank

Ballroom I+II	SY03	SYMPOSIUM
13:45-15:00		**MOLECULAR & SYSTEMS PATHOLOGY**
	Chair	Albrecht Stenzinger (Germany)
	Invited	
13:45	SY03.01	**AI in cancer research and molecular diagnostics** Frederick Klauschen (Germany)
	Abstracts	
14:05	SY03.02	**Machine Learning Models Predict the Primary Sites of Head and Neck Squamous Cell Carcinoma Metastases Based on DNA Methylation** Maximilian Leitheiser (Germany), Frederick Klauschen, Philipp Jurmeister, Michael Bockmayr
14:15	SY03.03	**Using machine learning to infer whole genome duplication from tumour nuclear morphology** John Connelly (United Kingdom), Juliet Luft, Craig J. Anderson, Peter Bankhead, Frances Connor, Liver Cancer Evolution Consortium, Paul Flicek, Núria López-Bigas, Colin A. Semple, Duncan T. Odom, Sarah J. Aitken, Martin S. Taylor
14:25	SY03.04	**Bagging ensemble cNN outperforms conventional laboratory staining methods in predicting molecular subtypes of gastric adenocarcinoma** Nadine Flinner (Germany), Steffen Gretser, Alexander Quaas, Katrin Bankov, Claudia Doering, Reinhard Buettner, Josef Rueschoff, Peter J. Wild
14:35	SY03.05	**Patient-level proteomic network prediction by explainable artificial intelligence** Philipp Keyl (Germany) Michael Bockmayr, Daniel Heim, Gabriel Dernbach, Grégoire Montavon, Klaus-Robert Müller, Frederick Klauschen

14:45	SY03.06	**A deep learning approach in the prediction of gene mutations using hematoxylin-eosin images in breast cancer** Raquel Romero-Garcia (Spain), Antonio Toro Valderas, Irene Bernal Florindo, Lidia Atienza Cuevas, Marcial Garcia Rojo
Ballroom I+II	**PD01**	**PANEL DISCUSSION I**
15:00-15:30		**INTEGRATIVE PATHOLOGY**
	Panelists	Frederick Klauschen (Germany) Peter Hufnagl (Germany) Inti Zlobec (Switzerland) David Horst (Germany)
Ballroom I+II	**SY04**	**SYMPOSIUM**
16:00-17:30		**DIGITAL PATHOLOGY WORKFLOW**
	Chairs	Filippo Fraggetta (Italy) Paul van Diest (The Netherlands)
	Invited	
16:00	SY04.01	**Implementation of a fully digital workflow: a critical review after two years** Philipp Ströbel (Germany)
16:20	SY04.02	**Do the best for your patients - start the digital transformation of your lab!** Catarina Eloy (Portugal)
	Abstracts	
16:40	SY04.03	**A standard-based computational image analysis workflow for scalable and interoperable AI model development and deployment** Chris Gorman (United States), William J. R. Longabaugh, David A. Clunie, Andrey Y. Fedorov, Markus D. Herrmann

16:50	SY04.04	**Technical and Diagnostic Issues with Whole Slide Imaging in Validation Studies** Paola Chiara Rizzo (Italy), Albino Eccher, Liron Pantanowitz, Pietro Antonini, Matteo Brunelli, Nicola Santonicco, Stefano Marletta, Anil V Parwani, Ilaria Girolami
17:00	SY04.05	**An AI-supported solution to improve the digital pathology workflow for optimized breast cancer treatment decision-making** Rutger H.J. Fick (France), Capucine Bertrand, Alireza Moshayedi, Valentina Di Proietto, Agathe de Vulpian, Marvin Akoudad, Stephanie Petit, Saima Ben Hadj
17:10	SY04.06	**A combined molecular/digital approach to the cervical cancer screening program in Sicily (Italy): a preliminary report** Alessandro Caputo (Italy), Simona Vatrano, Chiara Taranto, Lidia Rizzo, Angela Arcoria, Elisabetta Occhipinti, Francesca Santamaria, Filippo Fraggetta
17:20	SY04.07	**Implementation of Digital Pathology Workflow for Routine Primary Diagnosis in a Large Private Hospital Network** Deniz Bayçelebi (Turkey), Emre Karakök, Serdar Balcı, Fatma Aktepe, Gülen Bülbül Doğusoy, İpek Çoban Elbeği, Pembe Gül Güneş, Yıldırım Karslıoğlu, Sezen Koçarslan, Fatma Gülgün Sade Koçak, Murat Oktay, Zeynep Pehlivanoğlu, Türkan Rezanko, Zuhal Silav, Mehtat Ünlü, Şemsi Yıldız, İlknur Türkmen

Ballroom I+II	**MIS02**	**MISCELLANEOUS**
17:45-18:30		**ESDIP ANNUAL GENERAL MEETING**
Ballroom III	**MIS03**	**MISCELLANEOUS**
from 18:30		**POSTER SESSION & GET-TOGETHER**

Ballroom I	AS01	ALLIED SOCIETIES
09:00-09:45		**EUROPEAN SOCIETY OF PATHOLOGY (ESP)**
	Chairs	Norman Zerbe (Germany) Filippo Fraggetta (Italy)
	Invited	
09:00	AS01.01	**Digitalisation and pathology – ESP aspects and strategy** Peter Schirmacher (Germany)
09:20	AS01.02	**Tissue microarrays as tools in the digital era: useful or useless?** Inti Zlobec (Switzerland)

Ballroom II	SY05	SYMPOSIUM
09:00-10:30		**VALIDATION & QUALITY ASSURANCE**
	Chair	Artyom Borbat (Russia)
	Invited	
09:00	SY05.01	**The quest for reproducible quality control in digital pathology** Andrew Janowczyk (United States)
	Abstracts	
09:20	SY05.02	**Physical Color Calibration of Digital Pathology Scanners for Deep Learning Based Diagnosis of Prostate Cancer** Xiaoyi Ji (Sweden), Richard Salmon, Nita Mulliqi, Henrik Olsson, Lars Egevad, Pekka Ruusuvuori, Martin Eklund, Kimmo Kartasalo

09:30	SY05.03	**Quality checkpoint in pathology specimens handling: an AI system to automate fragment detection and count** Tomé Albuquerque (Portugal), Diana Montezuma, Sara P. Oliveira, Pedro C. Neto, João Monteiro, Liliana Ribeiro, Sofia Gonçalves, Ana Monteiro, Isabel M. Pinto, Jaime S. Cardoso
09:40	SY05.04	**Automated Quality Control of Whole Slide Images Using Artificial Intelligence** Vaughn Spurrier (United States), Ramachandra V. Chamarthi, Sean Grullon, Sivaramakrishnan Sankarapandian, Julianna D. Ianni
09:50	SY05.05	**Automated detection of crush artefact in surgical pathology specimens using deep learning** Rasmus Kiehl (Germany), Sebastian Lohmann, Tom Bisson, Oliver Fischer, Benjamin Voigt
10:00	SY05.06	**Building Clinical-Grade Artificial Intelligence-Tools for Breast Cancer from the Ground Up** Rob Sykes (United States), Derek Miller, Hafez Eslami Manoochehri, Ji Wang, Sheheryar Ali Arshad, Payam Khorramshahi, Chad Salinas
10:10	SY05.07	**Profiling images for better Quality Control in Digital Pathology** David Ameisen (France), Julie Auger-Kantor, Emmanuel Ameisen
10:20	SY05.08	**Quality issues while setting up country wide digital pathology consultancy service in a limited resources** Artyom Borbat (Russia), Nikolai Kozlov

Ballroom I	AS02	ALLIED SOCIETIES
09:45-10:30		**JAPANESE SOCIETY OF DIGITAL PATHOLOGY (JSDP)**
	Chairs	Norman Zerbe (Germany) Sabine Leh (Norway)
	Invited	
09:45	AS02.01	**Implementation of digital pathology and AI model to pathology practice in Japan** Junya Fukuoka (Japan)
10:05	AS02.02	**Discover Asia: a brief guide to digital pathology and AI on the continent** Andrey Bychkov (Japan)

Ballroom I	SY06	SYMPOSIUM
11:00-12:00		**INTEROPERABILITY & STANDARDIZATION**
	Chairs	Gunter Haroske (Germany) Mikael Wintell (Sweden)
	Invited	
11:00	SY06.01	**IHE PaLM profiles for Digital Pathology: Enhancing interoperability of digital images across, electronic health record systems (EHR), laboratory information systems (LIS), imaging systems (IMS, PACS), and scanners** Riki Merrick (United States)
11:20	SY06.02	**Enabling quantitative tissue imaging and artificial intelligence in pathology through interoperable tools and services** Markus Herrmann (United States)

	Abstracts	
11:40	SY06.03	**The EMPAIA approach: building bridges between existing AI solutions and digital pathology systems by providing open specifications** Christoph Jansen (Germany), Klaus Strohmenger, Stefan Manthey, Daniel Romberg, Theodore Evans, Peter Hufnagl, Norman Zerbe
11:50	SY06.04	**Anonymization of Whole Slide Images for Research and Education** Michael Franz (Germany), Daniel Romberg, Tom Bisson, Truong An Nguyen, Peter Hufnagl, Norman Zerbe
Ballroom II	**SY08**	**SYMPOSIUM**
11:00-11:45		**DATA ANNOTATION & PREPROCESSING**
	Chairs	Rasmus Kiehl (Germany) Andrew Janowczyk (United States)
	Invited	
11:00	SY08.01	**When AI meets clinical reality - a holistic approach to pathology AI** Anirban Mukhopadhyay (Germany)
	Abstracts	
11:15	SY08.02	**PatchSorter a high throughput open-source digital pathology tool for histologic object labeling** Tasneem Talawalla (United States), Robert Toth, Cedric Walker, Hugo Horlings, Kien Rea, Sven Rottenberg, Anant Madabhushi, Andrew Janowczyk
11:25	SY08.03	**Few-Label Adaptation using Multi-ProtoNets – an Experiment on Urothelial Carcinomas** Rosalie Kletzander (Germany), Daniel Firmbach, Volker Bruns, Carol Geppert, Arndt Hartmann, Markus Eckstein, Michaela Benz

11:35	SY08.04	**Comparison of Consecutive and Re-stained Sections for Virtual Multi-Staining by Image Registration** Johannes Lotz (Germany), Nick Weiss, Jeroen van der Laak, Stefan Heldmann
Ballroom I	**SY07**	**SYMPOSIUM**
12:00-12:30		**IHE PaLM & DICOM WG 26**
	Invited	
12:00	SY07.01	**Current topics from IHE PaLM** Gunter Haroske (Germany)
12:15	SY07.02	**Current topics from DICOM WG-26** Mikael Wintell (Sweden)
Ballroom II	**SY09**	**SYMPOSIUM**
11:45-12:30		**VIRTUAL PATHOLOGY IN EDUCATION**
	Chairs	Vincenzo Della Mea (Italy) Lewis Hassell (United States)
	Invited	
11:45	SY09.01	**Pathology education - anytime, anywhere on any device** Rajendra Singh (United States)
	Abstracts	
12:10	SY09.02	**Alternating a MOOC with face-to-face sessions: a blended design to teach Histology** Laurence Pesesse (Belgium), Céline Tonus, Marie Pirotte, Renaud Vandenbosch, Pascale Quatresooz, Pierre Bonnet, Björn-Olav Dozo, Renaud Hoyoux, Grégoire Vincke, Valérie Defaweux

12:20	SY09.03	**A pilot study for postgraduate teaching pathology with virtual microscopy** Artyom Borbat (Russia), Tatiana Novikova, Petr Bondarenko
Ballroom I	**SY10**	**SYMPOSIUM**
14:00-15:30		**MACHINE LEARNING & AI - CLINICAL APPLICATION II**
	Chair	Peter Boor (Germany)
	Invited	
14:00	SY10.01	**AI implementation in pathology practice: the UMC Utrecht roadmap** Paul van Diest (The Netherlands)
	Abstracts	
14:30	SY10.02	**Prognostic evaluation of endometrial hyperplasia using an AI-based image analysis tool on whole slide images** Emma Rewcastle (Norway), Ivar Skaland, Einar G. Gudlaugsson, Melinda Lillesand, Jan P.A. Baak, Emiel A.M. Janssen
14:40	SY10.03	**Deep Learning for HPV Infection Prediction in Head and Neck Cancers from H&E Whole Slide Images** Ruoyu Wang (United Kingdom), Amina Asif, Syed Ali Khurram, Lawrence Young, Nasir Rajpoot
15:50	SY10.04	**Evaluating the prognostic performance of a deep learning-based model that reproduces NHG histological grading in breast cancer** Abhinav Sharma (Sweden), Yinxi Wang, Philippe Weitz, Johan Hartman, Mattias Rantalainen

15:00	SY10.05	**Can deep learning predict tumor heterogeneity in upper tract urothelial carcinoma?** Miriam Angeloni (Germany), Sebastian Lindner, Sebastian Foersch, Patrick Volland, Carol I. Geppert, Hendrik Heers, Sven Wach, Helge Taubert, Danijel Sikic, Bernd Wullich, Robert Stoehr, Reiner Strick, Pamela L. Strissel, Markus Eckstein, Arndt Hartmann, Fulvia Ferrazzi, Veronika Bahlinger
15:10	SY10.06	**Tumour Region Identification and Tumour Proportion Score Estimation of PD-L1 Expression in Non-Small Cell Lung Carcinoma Using Deep Learning** Nidhi Bhatt (United Kingdom), Aman Shrivastava, Geetank Raipuria, Nitin Singhal
15:20	SY10.07	**Development of cytopathology support system using the homology concept** Kento Iida (Japan), Kazuki Kanayama, Kunimitsu Kawahara, Masako Onishi, Yuhki Yokoyama, Sachiko Nangumo, Hirofumi Yamamoto, Kazuaki Nakane

Ballroom II	OF	ORAL FREE PRESENTATIONS
14:00-15:30		
		ORAL FREE PRESENTATIONS
	Chairs	Vincenzo L'Imperio (Italy) Daniel Racoceanu (France)
	Abstracts	
14:00	OF.01	**Malignant Mesothelioma Subtyping of Tissue Images via Sampling Driven Multiple Instance Prediction** Mark Eastwood (United Kingdom), Silviu Tudor Marc, Xiaohong Gao, Heba Sailem, Judith Offman, Emmanouil Karteris, Angeles Montero Fernandez, Danny Jonigk, William Cookson, Miriam Moffat, Sanjay Popat, Jan Lukas Robertus, Fayyaz Minhas
14:10	OF.02	**DNA methylation-based classification of sino-nasal tumors** Philipp Jurmeister (Germany) Maximilian Leitheiser, Klaus-Robert Müller, Frederick Klauschen, David Capper
14:20	OF.03	**Novel analysis method for in-situ spatial phenotyping of cell populations in multimarker imagery** James Mansfield (Denmark), Fabian Scheider, Alessandro Massaro, Simon Haastrup, Rasmus Lyngby, Johan Dore-Hansen, Jeppe Thagaard
14:30	OF.04	**Validation of automated positive cell detection of immunohistochemically stained laryngeal tumor tissue using QuPath digital image analysis** Hilde J.G. Smits (The Netherlands), Justin E. Swartz, Marielle E.P. Philippens, Remco De Bree, Johannes H.A.M. Kaanders, Sjors A. Koppes, Gerben E. Breimer, Stefan M. Willems

14:40	OF.05	**Application of neural architecture search technique in nuclear and epithelium segmentation in digital pathology images of oral dysplasia** Neda Azarmehr (United Kingdom), Adam Shephard, Hanya Mahmood, Nasir Rajpoot, Syed Ali Khurram
14:50	OF.06	**CohortFinder: an open-source tool for quantitively partitioning datasets to improve deep learning model robustness** Fan Fan (United States), John Shin, Yijiang Chen, Bangchen Wang, Takaya Ozeki, Laura Barisoni, Anant Madabhushi, Andrew Janowczyk
15:00	OF.07	**Ki-67 in breast cancer: do different algorithms and file formats lead to the same results?** Stefan Reinhard (Switzerland), Cédric Pieren, Bastian Dislich, Sandro Wanner, Inti Zlobec, Tilman T. Rau
15:10	OF.08	**Upconversion nanoparticles as labels for histopathological tissue evaluation** Krzysztof Krawczyk (Sweden), Matthias J. Mickert, Stefan Andersson-Engels
15:20	OF.09	**Morphological analysis of nodular and micronodular basal cell carcinoma subtypes through texture analysis and semantic segmentation performance** Mircea-Sebastian Serbanescu (Romania), Raluca Maria Bungardean

Ballroom I	SY11	SYMPOSIUM
16:00-16:45		**REGULATORY & LEGAL**
	Chairs	Kurt Zatloukal (Austria) Christian Dierks (Germany)
	Invited	
16:00	SY11.01	**The road to a CE-marked IVD and the particularities for AI-based medical device software** Janos Hackenbeck (Germany)
16:20	SY11.02	**Legal framework and things to watch in AI for pathology** Christian Dierks (Germany), Markus Gollrad (Germany)
	Abstracts	
16:35	SY11.03	**The role of explainable AI in regulatory practices** Markus Plass (Austria), Theodore Evans, Rasmus Kiehl, Michaela Kargl, Rita Carvalho, Christian Geißler, Heimo Müller, Norman Zerbe, Andreas Holzinger

Ballroom II	SY12	SYMPOSIUM
16:00-17:30		**MACHINE LEARNING & AI-ALGHORITHM DEVELOPMENT I**
	Chairs	Mircea-Sebastian Serbanescu (Romania) David Ameisen (France)
	Invited	
16:00	SY12.01	**Resilience in AI and ML systems** Peter Hufnagl (Germany)
	Abstracts	
16:30	SY12.02	**Deep Learning Optimization for Whole Slide Image Analysis in Low-Resource Environments** Siddhesh Thakur (United States), Sarthak Pati, Junwen Wu, Ravi Panchumarthy, Deepthi Karkada, Prashant Shah, Spyridon Bakas

16:40	SY12.03	**Unsupervised Transfer Learning Boosts AI-based Virtual Staining in Histology** Umair Akhtar Hasan Khan (Finland), Sonja Koivukoski, Leena Latonen, Pekka Ruusuvuori
16:50	SY12.04	**Computer-aided tool for CRC diagnosis: from the AI model to the clinical software prototype** Sara P. Oliveira (Portugal), Diana Montezuma, Sara P. Oliveira, Pedro C. Neto, João Monteiro, Liliana Ribeiro, Sofia Gonçalves, Ana Monteiro, Jaime S. Cardoso, Isabel M. Pinto
17:00	SY12.05	**Tumor detection and regression grading in esophageal adenocarcinomas** Yuri Tolkach (Germany), Lisa-Marie Wolgast, Alexey Pryalukhin, Wolfgang Hulla, Marie-Lisa Eich, Simon Schallenberg, Wolfgang Schroeder, Christiane Bruns, Reinhard Büttner, Alexander Quaas
17:10	SY12.06	**Relieving pixel-wise labeling effort for pathology image segmentation by using self-training to learn from sparsely-annotated data** Romain Mormont (Belgium), Mehdi Testouri, Ba Thien Le, Pierre Geurts, Raphaël Marée
17:20	SY12.07	**A robust artificial intelligence approach for histopathological evaluation of prostate biopsies** Nita Mulliqi (Sweden), Kimmo Kartasalo, Xiaoyi Ji, Kelvin Szolnoky, Henrik Olsson, Anders Blilie, Marcin Braun, Marcello Gambacorta, Kristina Hotakainen, Emilius A. M. Janssen, Svein R. Kjosavik, Roman Łowicki, Bodil Ginnerup Pedersen, Karina Dalsgaard Sørensen, Benedicte Parm Ulhøi, Pekka Ruusuvuori, Lars Egevad, Martin Eklund

Ballroom I	AS03	ALLIED SOCIETIES
16:45-17:30		**DIGITAL PATHOLOGY ASSOCIATION (DPA)**
	Chairs	Norman Zerbe (Germany) Vincenzo Della Mea (Italy)
	Invited	
16:45	AS03.01	**Regulatory considerations for Medical Device Software (MDSW) / Software as a Medical Device (SaMD)** Esther Abels (United States)
17:05	AS03.02	**Current state of digital pathology and ML/AI in the US - the DPA perspective** Matthew Hanna (United States)

Ballroom I+II	SY13	SYMPOSIUM
09:00-10:30		
		MACHINE LEARNING & AI-ALGHORITHM DEVELOPMENT II
	Chairs	Nasir Rajpoot (United Kingdom) Viktor Kölzer (Germany)
	Invited	
09:00	SY13.01	**Linking traditional pathology and novel descriptors by machine learning** Jens Rittscher (United Kingdom)
	Abstracts	
09:30	SY13.02	**Fully Automated Attention based Multiple Instance Learning Predicts the Presence of Oral Epithelial Dysplasia in Whole Slide Images** Adam J Shephard (United Kingdom), R M Saad Bashir, Neda Azarmehr, Hanya Mahmood, Shan E Ahmed Raza, Syed Ali Khurram, Nasir M Rajpoot
09:40	SY13.03	**Deep learning-based renal cell carcinoma detection and classification of common subtypes in histological sections** Marie-Lisa Eich (Germany), Alexey Pryalukhin, Pavel Lazarev, Milana Sitova, Matvey Smirnov, Wolfgang Hulla, Oleg Kheyfets, Marta CarralCrespo, Alexander Quaas, Reinhard Büttner, Yuri Tolkach
09:50	SY13.04	**Tumor-infiltrating lymphocytes recognition in melanoma by open source deep learning convolutional neuronal network** Marco Laurino (Italy), Filippo Ugolini, Sara Simi, Francesca Brutti, Vincenza Maio, Vincenzo De Giorgi, Antonio Cossu, Giuseppe Palmieri, Clelia Miracco, Ketty Peris, Francesco Federico, Mario Mandalà, Romina Nassini, Daniela Massi, Francesco De Logu

SCIENTIFIC PROGRAM

18th JUNE 2022

10:00 SY13.05

Characterization of tumor-microenvironment in H&E stained non-small cell lung cancer samples using immunohistochemistry-informed AI

Thomas Mrowiec (Germany), Sharon Ruane, Simon Schallenberg, Gabriel Dernbach, Rumyana Todorova, Cornelius Böhm, Walter de Back, Blanca Pablos, Roman Schulte-Sasse, Ivana Trajanovska, Adelaida Creosteanu, Emil Barbuta, Marcus Otte, Christian Ihling, Hans Juergen Grote, Juergen Scheuenpflug, Viktor Matyas, Maximilian Alber, Frederick Klauschen

10:10 SY13.06

Automatic quantification of "myxoid" desmoplastic stroma in colorectal cancer: a heterogeneous feature and challenging task

Elias Baumann (Switzerland), Christian Abbet, Heather Dawson, Andrew Janowczyk, Inti Zlobec

10:20 SY13.07

Generation of Synthetic Colorectal Cancer Histology Images from Bespoke Glandular Layouts

Srijay Deshpande (United Kingdom), Fayyaz Minhas, Nasir Rajpoot

Ballroom I+II

11:45-12:15 **PD02** **PANEL DISCUSSION II**

WAYS TOWARDS CLINICAL BENCHMARKING FOR AI

Panelists

Jeroen van der Laak (The Netherlands)
Thomas Wiegand (Germany)
Daniel Racoceanu (France)
Nasir Rajpoot (United Kingdom)
Frederick Klauschen (Germany)
Norman Zerbe (Germany)

Ballroom I+II

12:15-12:30 **MIS04** **MISCELLANEOUS**

CLOSING

NOTES

INVITED TALKS

Thursday

SY01.01: **Datasets and structured reporting: the future of pathology?**

Iris Nagtegaal[1]

[1)] Department of Pathology, Radboud Institute for Health Sciences, Radboud University Medical Center, Nijmegen, the Netherlands.

SY02.01 **Deep learning applications in kidney pathology**

Peter Boor[1]

[1)] Institute of Pathology, RWTH University Hospital Aachen, Aachen, Germany; Division of Nephrology and Immunology, RWTH University Hospital Aachen, Aachen, Germany; Department of Electron Microscopy, RWTH University Hospital Aachen, Aachen, Germany.

SY03.01 **AI in cancer research and molecular diagnostics**

Frederick Klauschen [1,2,3]

[1)] Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt Universität zu Berlin, Institute of Pathology, Berlin, Germany [2)] Institute of Pathology, LMU München, Germany [3)] BIFOLD, Berlin Institute for the Foundations of Learning and Data, Germany

SY04.01 **Implementation of a fully digital workflow: a critical review after two years**

Philipp Ströbel[1]

[1)] Institute of Pathology, University Medical Center Göttingen, Göttingen, Germany.

SY04.02 **Do the best for your patients - start the digital transformation of your lab!**

Catarina Eloy[1, 2, 3]

[1)] Laboratory of Pathology, Ipatimup-Institute of Molecular Pathology and Immunology of University of Porto. [2)] Institute for Research and Innovation in Health, University of Porto. [3)] FMUP-Faculty of Medicine, University of Porto, Porto, Portugal.

Friday

AS01.01 **Digitalisation and Pathology – ESP Aspects and Strategy**

Peter Schirmacher[1]

[1)] Institute of Pathology, University Hospital Heidelberg, Heidelberg, Germany.

AS01.02 **Tissue microarrays as tools in the digital era: useful or useless?**

Inti Zlobec[1]

[1)] Institute of Pathology, University of Bern, Bern, Switzerland.

AS02.01 **Implementation of Digital Pathology and AI model to pathology practice in Japan**

Junya Fukuoka[1, 2]

[1)] Department of Pathology, Nagasaki University Graduate School of Biomedical Sciences, 1-7-1 Sakamoto, Nagasaki 852-8501, Japan. [2)] Department of Pathology, Kameda Medical Center, 929 Higashi-cho, Kamogawa, Chiba 296-8602, Japan.

SY04.02 **Discover Asia: a brief guide to digital pathology and AI on the continent**

Andrey Bychkov[1]

[1)] Department of Pathology, Kameda Medical Center, 929 Higashi-cho, Kamogawa, Chiba 296-8602, Japan.

SY05.01 **The quest for reproducible quality control in digital pathology**

Andrew Janowczyk[1,2]

[1)] Department of Biomedical Engineering, Case Western Reserve University, Cleveland, OH, United States.[2)] Precision Oncology Center, Lausanne University Hospital, Lausanne, Switzerland.

SY06.01 **IHE PaLM profiles for Digital Pathology: Enhancing interoperability of digital images across, electronic health record systems (EHR), laboratory information systems (LIS), imaging systems (IMS, PACS), and scanners**

Riki Merrick[1, 2]

[1)] Vernetzt LLC, Wilton, CA, United States. [2)] Association of Public Health Laboratories, Silver Spring, MD, United States.

SY06.02 **Enabling quantitative tissue imaging and artificial intelligence in pathology through interoperable tools and services**

Markus D. Herrmann[1]

[1)] Department of Pathology, Massachusetts General Hospital and Harvard Medical School, Boston, MA, United States

SY07.01 **Current topics from IHE PaLM**

Riki Merrick[1, 2]

[1)] Vernetzt LLC, Wilton, CA, United States. [2)] Association of Public Health Laboratories, Silver Spring, MD, United States.

SY07.02 **Current topics from DICOM WG-26**

Mikael Wintell[1]

[1)] Department of Regional Health, Region Västra Götalandsregionen, Sweden

SY08.01 **When AI meets clinical reality - a holistic approach to Pathology AI**

Anirban Mukhopadhyay[1]

[1)] Department of Informatics, Technische Universität Darmstadt, Darmstadt, Germany.

SY09.01 **Pathology education - anytime, anywhere on any device**

Rajendra Singh[1]

[1)] Northwell Health and Zucker School of Medicine, New York, NY, United States.

SY10.01 **AI implementation in pathology practice: the UMC Utrecht roadmap**

Paul van Diest[1]

[1)] Department of Pathology, University Medical Center Utrecht, Utrecht, The Netherlands.

SY11.01 **The road to a CE-marked IVD and the particularities for AI-based medical device software**

Janos Hackenbeck[1, 2]

[1)] Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt Universität zu Berlin, Institute of Pathology, Berlin, Germany [2)] Berlin Institute of Health, BCRT - Berlin Institute of Health Center for Regenerative Therapies, 13353 Berlin, Germany.

SY11.02 **Legal framework and things to watch in AI for pathology**

Christian Dierks[1]

[1)] Dierks+Company Rechtsanwaltsgesellschaft mbH, Berlin.

AS03.01 **Regulatory considerations for Medical Device Software (MDSW) / Software as a Medical Device (SaMD)**

Esther Abels[1]

[1)] Visiopharm, Westminster, Colorado, United States

AS03.02 **Current state of digital pathology and ML/AI in the US - the DPA perspective**

Matthew Hanna[1]

[1)] Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, NY, United States.

SY12.01 **Resilience in AI and ML systems**

Peter Hufnagl[1, 2, 3]

[1)] Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt Universität zu Berlin, Institute of Pathology, Berlin, Germany

[2)] HTW University of Applied Sciences Berlin, Center for Biomedical Image and Information Processing (CBMI), Berlin, Germany

Saturday

SY13.01 **Linking traditional pathology and novel descriptors by machine learning**

Jens Rittscher[1, 2]

[1)] Department of Engineering Science, Institute of Biomedical Engineering (IBME), University of Oxford, Oxford [2)] NIHR Oxford Biomedical Research Centre, Oxford University Hospitals NHS Foundation Trust, Oxford, Oxfordshire, UK.

PANEL DISCUSSIONS

PD01

Integrative Pathology

Frederick Klauschen[1,2,3], Peter Hufnagl[1,4], Inti Zlobec[5], David Horst[1]

[1)] Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt Universität zu Berlin, Institute of Pathology, Berlin, Germany

[2)] Institute of Pathology, LMU München, Germany

[3)] BIFOLD, Berlin Institute for the Foundations of Learning and Data, Germany

[4)] HTW University of Applied Sciences Berlin, Center for Biomedical Image and Information Processing (CBMI), Berlin, Germany

[5)] Institute of Pathology, University of Bern, Bern, Switzerland.

PD02

Ways towards clinical benchmarking for AI

Jeroen van der Laak[1,2], Thomas Wiegand[3], Daniel Racoceanu[4], Nasir Rajpoot[5, 6], Frederick Klauschen[7,8,9], Norman Zerbe[10]

[1)] Department of Pathology, Radboud Institute for Molecular Life Sciences, and Radboud Institute for Health Sciences, Radboud University Medical Center, 6500HB Nijmegen, The Netherlands.

[2)] Center for Medical Image Science and Visualization, Linköping University, Linköping, Sweden.

[3)] Fraunhofer HHI, Berlin, Germany.

[4)] Sorbonne Universités, UPMC Univ Paris 6, CNRS, INSERM, Laboratoire d'Imagerie Biomédicale (LIB), 75013, Paris, France.

[5)] Tissue Image Analytics Centre, Department of Computer Science, University of Warwick, United Kingdom

[6)] The Alan Turing Institute, The Alan Turing Institute, United Kingdom

[7)] Institute of Pathology, LMU München, Germany

[8)] BIFOLD, Berlin Institute for the Foundations of Learning and Data, Germany

[9)] Institute of Pathology, Charité – Universitätsmedizin Berlin, corporate member of Freie Universitä Berlin and Humboldt- Universität zu Berlin, Berlin, Germany

SY01.02

Specifying a Pathology Structured Report with HL7 FHIR

Andrea Essenwanger[1], Gunter Haroske[2], Thimo Hoelter[1], Alexander Bartschke[1], Sylvia Thun[1]

[1)] Core Facility Digital Health and Interoperability, Berlin Institute of Health at Charité - Universitätsmedizin Berlin, Germany [2)] Digital Pathology, Professional Association of German Pathologists (BDP), Germany

Introduction

Although the need for interoperable electronic health records (EHR) has been increasingly rising during the last couple of years, pathology reports are still missing a standardized structure, which makes accessing and analyzing these reports a tedious task. We propose an HL7 Fast Healthcare Interoperability Resources (FHIR) solution, based on the IHE profile, an HL7 Clinical Document Architecture (CDA) template, for Anatomic Pathology Structured Report (APSR).

Material and methods

An interdisciplinary team of pathology and interoperability experts came together in the context of the German Medical Informatics Initiative (MI-I) with the purpose of developing an interoperable solution for pathology reporting. The initial data model and required terminology standards were reconciliated in Art-Décor. The FHIR profiles are specified with FHIR ShortHand (FSH), a language used for defining FHIR artifacts as part of a FHIR Implementation Guide (IG), using SUSHI (SUSHI Unshortens ShortHand Inputs) as the compiler. These compiled resources are synchronized with Simplifier, where the graphical representation and documentation can be found.

Results and discussion

By combining FHIR's DiagnosticReport and Composition resources, our solution offers a deeply structured core, while still enabling the documentation of the required administrative data. The DiagnosticReport sets the main machine-searchable structure for the pathology report, including references to all clinically relevant information, such as the specimens, their respective observations, and patient data. The Composition incorporates administrative data with the DiagnosticReport, enabling the implementation of a signed FHIR Document.

Conclusion

Our solution is strongly inspired by the IHE APSR profile and unites the best of FHIR and CDA, creating a consistently structured yet human-readable pathology report.

Keywords: Structured pathology reporting, HL7 FHIR, Interoperability

SY01.03

Kidney Biopsy Codes: a multi-hierarchical terminology for non-neoplastic kidney biopsies

Sabine Leh[1, 2], Hrafn Náttálfur Holger Weishaupt[1], Amélie Dendooven[3, 4, 5]

[1)] Department of Pathology, Haukeland University Hospital, Bergen, Norway [2)] University of Bergen, Bergen, Norway [3)] Department of Pathology, University Hospital of Ghent, UZ Gent, Belgium [4)] Department of Pathology, University Hospital of Antwerp, Antwerp, Belgium [5)] University of Antwerp, Antwerp, Belgium

Introduction

Chronic kidney diseases have a major and increasing impact on morbidity and mortality worldwide, placing a heavy burden on health care costs. Often, microscopic analysis of a kidney biopsy is the method of choice to establish a diagnosis, preferably in the early course of a kidney disease. There is an enormous variability in microscopic changes and possible diagnoses combined with scarcity of knowledge and missing evidence-based recommendations for treatment. Accumulation, reuse and exchange of pathology data is therefore crucial. However, no international coding system with sufficient granularity is available. Here we introduce Kidney Biopsy Codes (KBC), a comprehensive terminology for non-neoplastic kidney diseases that allows coding of any diagnosis and/or histomorphological pattern for a non-neoplastic kidney biopsy.

Material and methods

An expert workshop defined the principles of the KBC system. Based on experience, literature review and 60 nephropathology reports, a terminology with synonyms and parent-child relationships was established. Then, a project-internal review process and a second workshop were carried out.

Results and discussion

Currently, KBC consists of 576 active concepts, of which 168 belong to a compact and 408 to a detailed set of terms. The KBC structure is multi-hierarchical with a pattern of injury and a disease concept axis as well as qualifiers for certainty. Concepts are further grouped according to kidney compartments.

Conclusion

A comprehensive coding system for non-neoplastic kidney diseases is established. In order to provide governance and to promote use within existing frameworks, the KBC team aims to collaborate with SNOMED international to make a subset in SNOMED CT.

Keywords: Standard, Interoperability, Terminology, Coding, Diagnosis

SY02.02

MarrowQuant 2.0: clinical application of a user-friendly digital hematopathology tool for human bone marrow trephine biopsies

Rita Sarkis[1, 2, 10], Olivier Burri[3], Claire Royer-Chardon[4], Sophie Blum[2], Frederica Schyrr[2], Mariangela Costanza[5], Stephane Cherix[6], Carmen Barcena[4, 7], Bettina Bisig[4], Valentina Nardi[8], Rosella Sarro[9], Olivier Spertini[5], Sabine Blum[5], Martin Weigert[1], Bart Deplancke[10], Arne Seitz[3], Laurence de Leval [3], Olaia Naveiras[2, 5]

[1)] Institute of Bioengineering , School of Life Science, Ecole Polytechnique Fédérale de Lausanne (EPFL), Switzerland [2)] Department of Biomedical Sciences , University of Lausanne (UNIL), Switzerland [3)] Bioimaging and Optics Core Facility, Ecole Polytechnique Fédérale de Lausanne (EPFL), Switzerland [4)] University Institute of Pathology, Clinical Pathology Service , Lausanne University Hospital (CHUV), Switzerland [5)] Hematology Service, Departments of Oncology and Laboratory Medicine, Lausanne University Hospital (CHUV), Switzerland [6)] Department of Orthopaedics and Traumatology, Lausanne University Hospital (CHUV), Switzerland [7)] Department of Pathology, University Hospital 12 de Octubre, Spain [8)] Department of Pathology, Massachusetts General Hospital, United States [9)] Instituto cantonale di patologia, Locarno, Switzerland [10)] Laboratory of Systems Biology and Genetics, Institute of Bioengineering, School of Life Sciences, Ecole Polytechnique Fédérale de Lausanne (EPFL), Switzerland

Introduction

Bone marrow (BM) assessment is a multiparametric evaluation of which BM cellularity constitutes one of the baseline parameters to evaluate hematological and non-hematological disorders. The original description is based on point-counting, a time and labor-consuming quantitative method. Currently, in clinical routine, the assessment is based on a semi-quantitative estimation. This estimation is rapid but subjective. In this study, we validated MarrowQuant2.0, a user-friendly quantitative digital hemopathology tool integrated within QuPath software, to quantify four compartments within the BM (hematopoietic cells, adipocytes (based on Stradist), interstitium & microvasculature, and bone) and measure the cellularity on BM trephine biopsies.

Material and methods

We calculated the cellularity in a series of retrospective biopsies (training set n=36; experimental set n=157 H&E). Using intraclass coefficient of correlation (ICC), specificity and sensitivity tests, we measured the agreement between MarrowQuant2.0' quantification, visual estimation, and clinical reference. MarrowQuant 2.0 was tested also on a set of prospective BM trephine biopsies from clinical routine diagnosis (test set n=42).

Results and discussion

Our algorithm was capable of accurate, rapid, and robust segmentation (average accuracy 0.86, n=36H&E). There was an excellent agreement between MarrowQuant2.0 and the clinical reference (ICC=0.978, R2= 0.93, n=157H&E). We found a reciprocity among the hematopoietic and adipocytic compartments in the context of extreme cases of BM remodeling except for cases with an expansion of the stroma compartment.

Conclusion

We can conclude that our tool is compatible within research and clinical context. We will use MarrowQuant2.0. to link output with clinical parameters to explore a potential prognostic value in myeloid malignancies. * paper ready for submission

Keywords: Digital Pathology, Hematopathology, Cellularity, Bone Marrow, H&E image

SY02.03

AI model trained to detect breast cancer metastasis to lymph node shows robust performance for micrometastases and isolated tumor cells.

Juan A. Retamero[1], Patricia Raciti[1], Emre Gulturk[1], David Klimstra[1]
[1)] Medical Affairs, Paige AI, United States

Introduction

The assessment of metastatic spread of breast cancer to lymph nodes remains one of the most important aspects in staging breast cancer. However, it is a tedious task for pathologists, and is an area where pathologists show suboptimal diagnostic accuracy, particularly for small metastases. Artificial intelligence systems have been developed to assist pathologists in this aspect, with the expectation to improve diagnostic accuracy, efficiency and reduce immunohistochemistry (IHC) related delays and costs.

Material and methods

An AI system was developed to detect areas suspicious for metastasis in lymphatic tissue, using multiple instance learning. The system was trained using 20,000 unannotated whole slide images (WSIs) . After the model was trained, it was tested in a different dataset comprising 800 slides.

Results and discussion

The system performed with a sensitivity of 0.98 and specificity of 0.90 for macrometastases. For micrometastases, the sensitivity was 0.97, whereas for ITCs the sensitivity was 0.96.

Conclusion

Multiple instance learning is a suitable methodology to train an AI model for the detection of breast cancer metastases to lymphoid tissue. This model shows robust performance across multiple tumor sizes, with the potential to improve pathologist's diagnostic performance and efficiency and to impact turnaround times and IHC requests.

Keywords: Sentinel lymph node biopsy, Screening, AI assisted diagnosis, Generalizability, Diagnostic accuracy, Diagnostic efficiency

SY02.04

Assessment of glomerular patterns of injury by machine learning methods

Justinas Besusparis[1, 2], Mindaugas Morkūnas[1, 2], Arvydas Laurinavičius[1, 2], Renaldas Augulis[1, 2]

[1)]Faculty of Medicine , Vilnius University, Lithuania [2)]National Center of Pathology, Vilnius University Hospital Santaros Clinics, Lithuania

Introduction

Biopsy diagnosis of glomerular diseases requires a visual scoring of active and chronic lesions, represented by various patterns of glomerular injury. Potential value of artificial intelligence tools has been reported to classify glomeruli by patterns of injury. However, inter- and intraglomerular heterogeneity of the lesions and mixed patterns have to be taken into account to assess activity and chronicity of glomerular disease in individual cases. Therefore, we aim to develop tools to assess intraglomerular lesions for a comprehensive pathology report.

Material and methods

Nine patterns of glomerular injury were provided for training Xception neural network. The training and testing datasets consisted of 783 and 351 glomerular images, respectively, selected by 2 nephropathologists reviewing 27,156 glomeruli, extracted by a pretrained glomerular classifier from 655 native kidney biopsy slides stained by picrosirius red.

Results and discussion

The Xception classifier achieved overall 60% glomerular classification accuracy, including: crescentic 61%, endocapillary 42%, focal segmental sclerosis 43%, hypertrophy 45%, membranoproliferative 78%, membranous 76%, mesangioproliferative 36%, normal 71% and global glomerular sclerosis 100%. For each glomerular image, visual attention heatmaps were generated with a probability of class attribution for further intraglomerular quantification.

Conclusion

Our experiment reveals a possibility to achieve medium accuracy for classifying patterns with heterogenous (crescentic, endocapillary) intraglomerular distribution and medium-high accuracy for homogenous patterns (membranoproliferative, membranous). Further improvement of the training sets and strategies is needed to achieve robust intraglomerular segmentation and quantification of the lesions.

Keywords: machine learning, intraglomerular heterogeneity, glomerular patterns, quantification of intraglomerular segmentation

SY02.05

Budding-T-cell score is a potential predictor for more aggressive treatment in pT1 colorectal cancers

Linda Studer[1, 3, 4], John-Melle Bokhorst[2], Francesco Ciompi[2], Andreas Fischer[1, 4], Heather Dawson[3]

[1)] iCoSys, School of Engineering and Architecture of Fribourg, Switzerland [2)] Department of Pathology , Radboudumc, The Netherlands [3)] Institute of Pathology, University of Bern, Switzerland [4)] DIVA Research Group, University of Fribourg, Switzerland

Introduction

As pT1 colorectal cancers (CRC) tend to be overtreated, we investigate the previously proposed budding-T-cell-score (BTS = (#tumor-buds+1)/(#T-cells+1)) as a predictive marker to assess patients' need for resection. BTS was shown to be a better predictor of survival and other clinical factors than individual scoring.

Material and methods

We consider hotspots annotated by a pathologist according to the ITBCC guidelines on double-stained (AE1-AE3 pan-cytokeratin and CD8+) whole slide images from our pT1 CRC cohort (N=573). Within hotspots, tumor-buds and T-cells are automatically detected using convolutional neural networks and counted. The patients are divided into two groups based on their need for resection ("no": N0 / follow-up without recurrence; "yes": N1 / follow-up with recurrence). The dataset is imbalanced ("no": 89.2%, "yes": 10.8%). To predict the patient group, we train a support-vector machine with data-balancing using the tumor-buds or T-cell counts individually, together, and just the BTS. We report the weighted accuracy, and sensitivity and specificity for the "yes" group.

Results and discussion

The highest weighted accuracy (62.8±6.5%) and specificity (17.6±3.7%) are achieved using the tumor-buds count. Using the BTS achieves a sensitivity of 98.3±2.9%, which outperforms the other models by more than 30%.

Conclusion

We show that combined assessment of tumor-buds and T-cells has the potential to serve as a predictive marker for the need for resection in pT1 cancers. However, there is much room for improvement, as the low specificity still leads to overtreatment. We aim to address this in future work by also considering the spatial relationship of tumor-buds and T-cells and other predictive factors of nodal metastasis.

Keywords: Tumour-budding, pT1 colorectal cancer, T-cell scoring, Budding T-cell Score

SY02.06

CYTOFastUrine: An Innovative Integrated Solution For Automated Urine Cytology Diagnostics

Matteo Botteghi[1, 3], Francesco Trisolini[4], Silvia Carattoni[3], Stefano Martinotti[2], Antonio Procopio[1]

[1)] Department of Clinical and Molecular Sciences, Università Politecnica delle Marche, Italy [2)] Unit of Predictive Medicine and Clinical Pathology, CAST Institute, Università degli studi di Chieti-Pescara, Italy [3)] R&D, WorldConnex, San Marino [4)] R&D, Hospitex International, Italy

Introduction

In EU new cases of bladder, kidney and prostate cancer were more than 715,000 in 2020. A proper diagnosis and follow-up could save lives up to 12% of this population. The urine cytology diagnostics performed by pathologists is an expensive and time consuming process. We are developing an innovative computerized diagnostics AI-assisted platform for urine cytology, based on The Paris System standard. The overall saving of early diagnosis through CYTOFastUrine approach in EU can be estimated at around 37 billion €/year, considering that about 18.7% of urinary tract tumours can be cured if early diagnosed.

Material and methods

We developed the complete prototype of CYTOFastUrine made of sample processing with CYTOfast+ system, digitization of samples slides, computerized analysis capable of identifying suspected morphology and aggregates, remote diagnostics reporting through WaidX telemedicine platform. The digitization is managed with automatic slide scanners. Computerized diagnostic algorithms are integrated into the digitization platform. A team of remote pathologists takes care of the validation and quality control of the diagnostic platform. A web-based platform allows the patient to book a cytology test, self-collecting the samples directly at home and receiving the report within 48 hours.

Results and discussion

Algorithm validation is ongoing. An overall of about 300 samples, 100 positive and 200 negative, will be used as initial validation set.

Conclusion

Nowadays, vertical integrated digital pathology solutions for computerized cancer diagnosis with standardized liquid-based cytology aren't available for urine cytology. CYTOFastUrine enables the possibility of installing laboratories everywhere, giving a valid answer to the increasing shortage of pathologists dedicated to urinary cytology.

Keywords: Image Analisys, Urine Cytology, Pathomics, Liquid Based Cytology, CytoFast, WaidX

SY02.07

A Multi-Feature AI Solution for Diagnosis Support in Gastric Biopsies: A Prospective Multi-Site Clinical Study

Jessica Calvo[1], Thierry Garcia[1], Elisabeth Lanteri[1], Joelle Reyre[1], Inssaf Laouar[1], Alona Nudelman[2], Marina Maklakovski[3], Anat Albrecht Shach[4], Ayala Arad[5], Geraldine Sebag[5], Maya Grinwald[5], Judith Sandbank[2, 5]

[1)] MediPath, MediPath, France [2)] Institute of Pathology, Maccabi Healthcare Services, Israel [3)] Department of Pathology, Assuta Ashdod Medical Center, Israel [4)] Department of Pathology, Shamir Medical Center, Israel [5)] Ibex Medical Analytics, Ibex Medical Analytics, Israel

Introduction

Computer-assisted diagnostic solutions to evaluate gastric biopsies hold promise to increase efficiency and accuracy in diagnosis. Despite proof-of-concept studies, there remains a need for an AI solution that detects both cancer and other pathologies (e.g., H. pylori) with high accuracy. Here we validate the performance of such a solution on large dataset of clinical samples from two sites.

Material and methods

The Galen™ Gastric algorithm was examined in a prospective stand-alone performance study using retrospectively collected histopathology slides. We compared ground truth diagnosis of adult gastric biopsies with the algorithmic results on whole slide images). Ground truth was reached by concordance diagnosis between two pathologists (original report and a new blinded diagnosis by a pathologist reviewing slides/WSIs). Discrepancies were adjudicated and reviewed by an expert pathologist

Results and discussion

The algorithm demonstrated very high accuracy for the detection of gastric adenocarcinoma and high-grade dysplasia, with AUC of 0.994 in an internal test. Analyzing 1845 cases (230 positive), demonstrated sensitivity of 96.96%, specificity of 97.28%, PPV of 83.52% and NPV of 99.56%. Additionally, the algorithm achieved an AUC of 0.932 for the detection of H. pylori in analysis of 1743 cases (639 positives), with sensitivity of 87.86%%, specificity of 97.48%%, PPV of 80.66% and NPV of 92.38%. We will further report on additional pathologies, e.g., low-grade dysplasia and Adenoma.

Conclusion

This study reports the successful clinical validation of a multi feature AI-based solution in the detection of gastric adenocarcinoma, H. pylori and other pathologies, offering an important tool for computer-aided diagnosis in routine pathology practice.

Keywords: AI, deep learning, biopsy, Gastric, digital pathology, carcinoma

SY03.02

Machine Learning Models Predict the Primary Sites of Head and Neck Squamous Cell Carcinoma Metastases Based on DNA Methylation

Maximilian Leitheiser[1], Frederick Klauschen[1, 2, 4], Philipp Jurmeister[1, 2], Michael Bockmayr[1, 3]

[1)] Institute of Pathology, Charité - Universitätsmedizin Berlin, Germany [2)] Institute of Pathology, LMU München, Germany [3)] Department of Pediatric Hematology and Oncology, University Medical Center Hamburg-Eppendorf, Germany [4)] BIFOLD, Berlin Institute for the Foundations of Learning and Data, Germany

Introduction

In head and neck squamous cell cancers (HNSCs) that present as metastases with an unknown primary (HNSC-CUPs), the identification of a primary tumor enables a more targeted therapy approach and increases patient survival. However, the currently available diagnostic methods are laborious and do not offer a sufficient detection rate. Recently, machine learning models have been successfully applied to DNA methylation data in various tumor classification problems. In order to improve the diagnostic workup for HNSC-CUPs we extended this technique to HNSCs.

Material and methods

We compiled and annotated a reference cohort of 405 primary HNSC samples as well as an independent validation cohort of 64 pulmonary and lymph node metastasis, including 48 newly measured cases. The reference cohort was used to develop four classifiers based on different machine learning models (random forest (RF), neural network (NN), elastic net penalized logistic regression (LOGREG), support vector machine (SVM)) that predict the primary site of HNSC tumors from their DNA methylation profile. Their performance was evaluated on the validation cohort.

Results and discussion

The models achieved high classification accuracies (RF=83%, NN=88%, LOGREG=SVM=89%) on the validation cohort. The accuracy of all models did not show a significant difference between pulmonary and lymph node metastases and the NN, LOGREG, and SVM models significantly outperformed p16 status as a marker for oropharyngeal origin.

Conclusion

The DNA methylation profiles of HNSC metastases are characteristic for their primary sites, which can be predicted with high accuracy by the classifiers developed in this study. Thus, these classifiers can provide valuable information to guide the diagnostic workup of HNSC-CUP.

Keywords: DNA methylation, cancer of unknown origin, head and neck squamous cell carcinoma, machine learning

SY03.03

Using machine learning to infer whole genome duplication from tumour nuclear morphology

John Connelly[1, 2, 3, 4], Juliet Luft[1], Craig J. Anderson[1], Peter Bankhead[3], Frances Connor[5, 6], Liver Cancer Evolution Consortium[1, 2, 5, 7, 8, 9, 10, 11], Paul Flicek[5, 7], Núria López-Bigas [8, 9, 10], Colin A. Semple[1], Duncan T. Odom[5, 11], Sarah J. Aitken[2, 5, 12, 13], Martin S. Taylor[1]

[1)] MRC Human Genetics Unit, Institute of Genetics and Cancer, University of Edinburgh, United Kingdom [2)] MRC Toxicology Unit, University of Cambridge, United Kingdom [3)] Edinburgh Pathology, Institute of Genetics and Cancer, University of Edinburgh, United Kingdom [4)] Laboratory Medicine, NHS Lothian, United Kingdom [5)] Cancer Research UK Cambridge Institute, University of Cambridge, United Kingdom [6)] Current Address: Wellcome - MRC Cambridge Stem Cell Institute, University of Cambridge, United Kingdom [7)] European Molecular Biology Laboratory, European Bioinformatics Institute, Wellcome Genome Campus Hinxton, United Kingdom [8)] Institute for Research in Biomedicine (IRB Barcelona), The Barcelona Institute of Science and Technology, Spain [9)] Research Program on Biomedical Informatics, Universitat Pompeu Fabra, Spain [10)] Institució Catalana de Recerca i Estudis Avançats, ICREA, Spain [11)] Division of Regulatory Genomics and Cancer Evolution, German Cancer Research Centre (DKFZ) Heidelberg, Germany [12)] Department of Histopathology, Cambridge University Hospitals NHS Foundation Trust, United Kingdom [13)] Department of Pathology, University of Cambridge, United Kingdom

Introduction

Most human cancer genomes exhibit multiple mutational signatures, reflecting the complex milieu of damage and repair occurring during carcinogenesis. We used a robustly controlled, highly powered in vivo experiment to investigate genotype-phenotype correlates.

Material and methods

Inbred mice were exposed to a single dose of diethylnitrosamine shortly after birth. Resultant liver tumours were isolated and submitted for whole genome sequencing, total RNA sequencing, and histopathology. These data have previously been used to demonstrate the phenomenon of lesion segregation, a unifying property of extrinsic mutagenesis.

Results and discussion

The lesion segregation model predicts that around 50% of the autosomal genome will exhibit mutational asymmetry. Instead, in a subset of tumours, we observed a total or near-total absence of this pattern. We hypothesised that this was due to whole genome duplication (WGD) at the first cell division following mutagenesis. We used a deep neural network to segment nuclei in the histopathology images, and quantified nuclear geometry and histochemical staining. We modelled these features using supervised learning to predict WGD and orthogonally validate the genomic inference.

Conclusion

We identified a subset of tumours with unexpected genomic profiles and used machine learning to successfully infer WGD from nuclear morphology. The presence of WGD is highly correlated with a specific genetic background, which suggests that genotype may influence the rate of WGD during tumour evolution. WGD is common in human cancer, associated with poor prognosis, and may be a tractable target for precision therapy. Therefore, scalable methods for WGD detection are of considerable potential importance.

Keywords: Machine Learning, Genomics, Whole Genome Duplication, Mouse, Cancer, Evolution

SY03.04

Bagging ensemble cNN outperforms conventional laboratory staining methods in predicting molecular subtypes of gastric adenocarcinoma

Nadine Flinner[1], Steffen Gretser[1], Alexander Quaas[2], Katrin Bankov[1], Claudia Doering[1], Reinhard Buettner[2], Josef Rueschoff[3], Peter J. Wild[1]

[1)] Dr. Senckenberg Institute of Pathology, University Hospital Frankfurt, Germany [2)]Institute of Pathology, University Hospital Cologne, Germany [3)]Targos Molecular Pathology GmbH, Germany

Introduction

Gastric cancer (GC) is one of the most lethal cancer types. Four distinct molecular subtypes (EBV, MSI, GS and CIN) are defined by the TCGA, each responding differently to immune- or chemotherapy. In practice these subtypes are often determined by IHC.

Material and methods

We trained an ensemble cNN to predict the molecular subtypes in GC using a bagging approach: each individual cNN was trained with 84 randomly selected WSI's (21 per class) from a bigger dataset. This dataset included additional patients for MSI, GS and CIN classes, but not for EBV. In addition, 30 tiles were randomly selected from a pool of ~100 per patients. This procedure ensures that each cNN was trained with slightly different datasets. We compare our prediction results with a classical staining approach and then used OncoScan arrays for clarification.

Results and discussion

Significant differences in GS subtype identification were observed between the staining and the deep learning approach, while the OncoScan array agreed more often with the deep learning results. Using the bagging approach reduced the error rate from 47% to 33% for an external data set, compared to individual cNN's; random guessing would result in error rates of 75% for this problem. In addition, the bagging ensemble also outperformed a vanilla ensemble, which was trained with an invariant dataset. Predictions revealed cases positive for two or more subtypes, challenging the original subtype definition.

Conclusion

A staining-based approach is not suitable for determing the molecular subtype in GC and is outperformed by Deep Learning.

Keywords: Ensemble cNN, gastric adenocarcinoma, molecular subtype prediction

SY03.05

Patient-level proteomic network prediction by explainable artificial intelligence

Philipp Keyl[1], Michael Bockmayr[1,2,3], Daniel Heim[1], Gabriel Dernbach[1,4], Grégoire Montavon[4,5], Klaus-Robert Müller[4,5,6,7], Frederick Klauschen[1,4,8,9,10]

[1)] Institute of Pathology, Charité - Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin and Berlin Institute of Health, Berlin, Germany [2)] Department of Pediatric Hematology and Oncology, University Medical Center Hamburg-Eppendorf, Martinistr. 52, 20246 Hamburg, Germany [3)] Mildred Scheel Cancer Career Center HaTriCS4, University Medical Center Hamburg-Eppendorf Martinistr. 52, 20246 Hamburg, Germany [4)] BIFOLD - Berlin Institute for the Foundations of Learning and Data, Berlin, Germany [5)] Machine Learning Group, Technical University of Berlin, Marchstr. 23, 10587 Berlin, Germany [6)] Department of Artificial Intelligence, Korea University, Seoul 136-713, South Korea [7)] Max-Planck-Institute for Informatics, Stuhlsatzenhausweg 4, 66123 Saarbrücken, Germany [8)] Institute of Pathology, Ludwig-Maximilians-University Munich, Thalkirchner Str. 36, 80337 München, Germany [9)] German Cancer Consortium (DKTK), German Cancer Research Center (DKFZ), Berlin partner site [10)] German Cancer Consortium (DKTK), German Cancer Research Center (DKFZ), Munich partner site

Introduction

Understanding the pathological properties of dysregulated protein networks in individual patients' tumors is the basis for precision therapy. Functional experiments are commonly used, but cover only parts of the oncogenic signaling networks, whereas methods that reconstruct networks from omics data usually only predict average network features across tumors. Here, we show that the explainable AI method Layer-wise relevance propagation (LRP) can infer protein interaction networks for individual patients from proteomic profiling data.

Material and methods

A neural network is trained to predict individual protein abundances based on the abundances of arbitrary sets of other proteins from the same patient. Subsequently, LRP is applied to predict the relevance of each protein for this prediction. This relevance score is then used as an estimate of the interaction strength between every pair of proteins.

Results and discussion

On synthetic data, LRP reconstructs average and individual interaction networks with an AUC of 0.99 and 0.93, respectively, and outperforms state-of-the-art network prediction methods for individual tumors. Using data from The Cancer Proteome Atlas, we identify known and potentially novel oncogenic network features, among which some are cancer-type specific and show only minor variation among patients, while others are present across certain tumor types but differ among individual patients.

Conclusion

Layer-wise relevance propagation allows for the prediction of sample-wise interaction networks based on a proteomic dataset. This approach may in the future support predictive diagnostics in precision oncology by inferring "patient-level" oncogenic mechanisms.

Keywords: Precision Oncology, Protein networks, Proteomics, Layer-wise Relevance Propagation, Explainable Artificial Intelligence

SY03.06

A deep learning approach in the prediction of gene mutations using hematoxylin-eosin images in breast cancer

Raquel Romero-Garcia[1], Antonio Toro Valderas[1], Irene Bernal Florindo[1], Lidia Atienza Cuevas[1, 2], Marcial Garcia Rojo[1, 2]

[1)] Bioinformatics Unit, Institute of Research and Innovation in Biomedical Sciences of the Province of Cadiz (INiBICA), Spain [2)] Department of Pathology, Puerta del Mar University Hospital, Cadiz, Spain

Introduction

Breast cancer is the most prevalent disease worldwide and the leading cause of tumor-related death among women. Single nucleotide variants (SNV) of TP53 and amplification of ERBB2 genes are frequently detected in breast cancer. In this study, it is aimed to predict these mutations in breast cancer using histological hematoxylin-eosin (HE) images.

Material and methods

A total of 684 H&E images (1,60x1,200 pixels) from breast cancer patients were collected from TCGA WSI repository. They were classified according to TP53 SNV and ERBB2 amplification status. Images were divided in 14,432 and 6,638 smaller tiles, respectively. Tiles were used to train an Efficient net B7 neural network to predict these mutations previously described. This network is then evaluated on subsets of test tiles to obtain metrics (4,126 for TP53 and 1,932 for ERBB2). Clinical data were also included in separate experiments.

Results and discussion

Using only histological HE images; sensitivity, specificity and AUC-ROC values obtained in test tiles for SNV in TP53 were 69.99%, 59.67% and 0.7 respectively. For ERBB2 amplification, values were 59.63%, 72.15% and 0.71, respectively. Using only clinical data; sensitivity, specificity and AUC-ROC values obtained in test tiles for SNV in TP53 were 73.3%, 83% and 0.87 respectively. For ERBB2 amplification, values were 68.42%, 78.95% and 0.78, respectively.

Conclusion

Although using only clinical data gives better results, it is important to emphasize that this model generated using only histological images (clinical data are not always available) is also able to predict these TP53 and HER2 mutations in breast cancer.

Keywords: Breast cancer, NGS data prediction, hematoxylin-eosin, deep learning, TP53, HER2

SY04.03

A standard-based computational image analysis workflow for scalable and interoperable AI model development and deployment

Chris Gorman[1], William J. R. Longabaugh[2], David A. Clunie[3], Andrey Y. Fedorov[4], Markus D. Herrmann[1]

[1)] Department of Pathology, Massachusetts General Hospital and Harvard Medical School, Boston, MA, United States [2)] Institute of Systems Biology, Seattle, WA, United States [3)] PixelMed Publishing LLC, Bangor, PA, United States [4)] Department of Radiology, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, United States

Introduction

Exchange and use of imaging data from different devices and sites is critical for AI model development and deployment. However, AI workflows currently developed in research rely on custom data formats and interfaces, which impede interoperability and clinical integration. To bridge this gap, we developed a computational image analysis workflow based on the DICOM standard that facilitates streamlined AI model development and deployment.

Material and methods

As a proof of concept, we implemented a published neural network model architecture for identification and classification of tumors in whole slide images. We then trained models on the National Cancer Institute's Imaging Data Commons (IDC) cloud platform using a data set of 13,593 DICOM images from 38 cancer imaging collections and subsequently deployed the models at our healthcare enterprise to perform inference on a separate set of 1000 DICOM images. All image annotations and analysis results were also encoded in DICOM format and all model input and output was performed using DICOMweb services.

Results and discussion

Using our workflow, we successfully developed models on the IDC platform, accessing over 20 terabytes of DICOM data via more than 15 million DICOMweb requests. We were further able to evaluate models locally by simply pointing our workflow during inference to the DICOMweb endpoint of our local DICOM store. In addition, we could immediately visualize the inference results in DICOM format using the IDC Slim viewer.

Conclusion

Our workflow demonstrates the feasibility of developing and deploying AI models at scale in a standard-conformant, device-independent, and platform-agnostic manner and thereby opens new avenues for realizing AI in pathology.

Keywords: Image Analysis, Artificial intelligence, DICOM, Interoperability, Cloud, Computational Pathology

SY04.04

Technical and Diagnostic Issues with Whole Slide Imaging in Validation Studies

Paola Chiara Rizzo[1], Albino Eccher[1], Liron Pantanowitz[2], Pietro Antonini[1], Matteo Brunelli[1], Nicola Santonicco[1], Stefano Marletta[1], Anil V Parwani[3], Ilaria Girolami[4]

[1)] Department of Pathology and Diagnostics, University and Hospital Trust of Verona, Italy
[2)] Department of Pathology & Clinical Labs, University of Michigan, Ann Arbor, Michigan, United States[3)] Department of Pathology, The Ohio State University, Columbus, OH, United States
[4)] Division of Pathology, Central Hospital Bolzano, Italy

Introduction

Digital pathology with whole-slide imaging (WSI) has shown many potential clinical and non-clinical applications. In the past decade, despite significant advances in WSI technology adoption remains slow for primary diagnosis. The aim of this study was to identify common pitfalls of WSI validation studies and assess potential measures to overcome these challenges.

Material and methods

A systematic search was carried out in electronic databases Pubmed-MEDLINE and Embase. Inclusion criteria were all validation studies designed to evaluate the feasibility of WSI for diagnostic clinical use. Technical and diagnostic problems encountered with the use of WSI during these studies were recorded.

Results and discussion

45 studies were included in which technical issues were reported in 15 studies (33%), diagnostic issues only in 8 studies (18%), and 22 (49%) reported both. Key technical problems were related to scan failures, prolonged time for pathologists to review cases and need for higher magnification. Diagnostic challenges were concerned with grading dysplasia, assessment of mitotic count, identification of microorganisms and defining the invasive front of tumors.

Conclusion

Improvements have occurred with WSI technology, but some critical issues remain. More focus on the quality of pre-scanning phase handling and training of pathologists could help reduce the impact of WSI technical difficulties. Critical issues regarding specific diagnostic tasks also remain a challenge, that likely represent suboptimal reproducibility among pathologists also seen when examining glass slides with conventional light microscopy.

Keywords: Whole Slide Imaging, Digital Pathology, Validation Study

SY04.05

An AI-supported solution to improve the digital pathology workflow for optimized breast cancer treatment decision-making

Rutger H.J. Fick[1], Capucine Bertrand[1], Alireza Moshayedi[1], Valentina Di Proietto[1], Agathe de Vulpian[1], Marvin Akoudad[1], Stephanie Petit[1], Saima Ben Hadj[1]

[1)] Computer vision & AI, Tribun Health, France

Introduction

To optimize breast cancer treatment selection, we introduce a fully integrated AI suite as part of our CaloPix software. It automatically scores the five predictive biomarkers: ER, PR, KI67, and HER2, in addition to the mitotic rate on HE. Our solution is important as it has been shown that the evaluation of these markers is time-consuming and subject to inter-observer variability – especially in intermediate cases. This is due to the evaluation criteria of these markers being based on precise ratios of IHC positive/negative cells – which are in practice eyeballed – or the detection of rare and ambiguous mitotic cells.

Material and methods

Our breast cancer suite is part of the CaloPix software, which runs both locally and in the cloud. The datasets to train each biomarker were sourced through our medical partners. All models were trained using PyTorch, where we focus on enhancing domain generalizability through proven domain-specific augmentation approaches – our mitosis detection algorithm won 3rd place in the 2021 MIDOG challenge.

Results and discussion

The result of our work is an optimized digital pathology workflow that 1. Saves the pathologist time by automatically scoring predictive biomarkers in a few seconds rather than a few minutes with the traditional method 2. Enables the pathologist to make a confident decision by visualizing a mask of the detected cells and their categories

Conclusion

We created a digital pathology workflow that improves the treatment decision in two ways: 1)we supplement the eyeballing approach with the actual cell counts, and 2)we speed up biomarker scoring from minutes to seconds.

Keywords: Breast cancer, workflow, digital pathology, AI, treatment decision, computational pathology

SY04.06

A combined molecular/digital approach to the cervical cancer screening program in Sicily (Italy): a preliminary report

Alessandro Caputo[1], Simona Vatrano[2], Chiara Taranto[2], Lidia Rizzo[2], Angela Arcoria[3], Elisabetta Occhipinti[3], Francesca Santamaria[3], Filippo Fraggetta[2]

[1)] Department of Pathology, University Hospital «San Giovanni di Dio e Ruggi D'Aragona", Italy [2)] Department of Pathology, UOC Anatomia Patologica, Gravina Hospital, Caltagirone, ASP Catania, Italy [3)] Department of Pathology, UOC Patologia Clinica Territoriale, Screening Program, Acireale, ASP Catania, Italy

Introduction

Nowadays cervical cancer screening (CCS) guidelines require sequential assessments consisting in molecular HPV testing and cytological analysis of cervical smears. This implies an interplay of biologists, cytotechnologists, laboratory technicians, and pathologists. In this study we aim to validate the use of WSIs from liquid-based cytology (LBC) in the CCS workflow, thus introducing the benefit of the telecytology.

Material and methods

Cervical samplings are shipped to the main laboratory where automated HPV testing takes place (Roche cobas HPV 4800). Cases positive for HPV are retrieved and used to prepare a LBC slide (HOLOGIC Inc, USA). After staining, the slide is converted into a WSI using a Pannoramic 250 FLASH III (3DHISTECH, Hungary). WSIs are immediately available in a remote lab where expert biologists screen them using telecytology. Their reports are instantly available in the main lab to render the combined final molecular-digital diagnosis.

Results and discussion

In the first month of implementation, we analyzed 2202 cervicovaginal samples with a median turnaround time of 4 days from accessioning to molecular reporting. The 195 cases which tested positive for HPV were used to prepare WSIs which were signed out in a median of 3 days.

Conclusion

The combined molecular biology and digital pathology workflow applied to CCS is feasible, and allows using human expertise where and when resources are present and needed. The presented workflow may represent a solution to the shortage of professionals and open the doors to the application of AI tools in the setting of CCS.

Keywords: Cervicovaginal cytology, pap test, telecytology, hpv testing, screening, digital pathology

SY04.07

Implementation of Digital Pathology Workflow for Routine Primary Diagnosis in a Large Private Hospital Network

Deniz Bayçelebi[1], Emre Karakök[1], Serdar Balcı[1], Fatma Aktepe[1], Gülen Bülbül Doğusoy[1], İpek Çoban Elbeği[1], Pembe Gül Güneş[1], Yıldırım Karslıoğlu[1], Sezen Koçarslan[1], Fatma Gülgün Sade Koçak[1], Murat Oktay[1], Zeynep Pehlivanoğlu[1], Türkan Rezanko[1], Zuhal Silav[1], Mehtat Ünlü[1], Şemsi Yıldız[1], İlknur Türkmen[1]

[1)] Pathology Department, Memorial Hospital, Turkey

Introduction

Our pathology laboratory serves a private hospital network of 11 hospitals in 5 cities. Biopsies were scanned with two Leica Aperio T2 scanners and shared via the Sectra IDS7 system. A total of 6977 biopsies were scanned and archived during a-ten-month period and used in consultation, second opinion, and meetings. To start using the system as a primary diagnostic tool, a validation study is initiated.

Material and methods

Seventeen pathologists (median 17 years (3-33)in practice) have participated. Each has diagnosed routine cases first with digital slides then under microscope. Either 60 cases or as many as the pathologist feels comfortable with the interface and feels safe to give primary diagnosis is aimed. Organ system, both diagnoses, difference if any, causes of difference, and challenges are noted.

Results and discussion

Eight hundred thirty biopsies were reached until this preliminary analysis. Re-scanning was required in 3%, microscopic examination in 5%. There was no difference in the diagnosis in 90% of the cases. The challenges on diagnosis were due to counting mitosis, microorganism (H.pylori) detection, IHC intensity optimisation (HER2), missed tissues in scanning area, dysplasia vs reactive, grading dysplasia, tumor subtyping, missing small tumor foci, focus problems, nuclear details.

Conclusion

Currently two pathologists work completely digitally and others in a hybrid model. Adding digital pathology to our workflow is still in progress and will be suitable for everyday use with a proper implementation, validation, and quality control.

Keywords: Digital pathology validation, routine diagnosis, challenges, scanned slides

SY05.02

Physical Color Calibration of Digital Pathology Scanners for Deep Learning Based Diagnosis of Prostate Cancer

Xiaoyi Ji[1], Richard Salmon[2], Nita Mulliqi[1], Henrik Olsson[1], Lars Egevad[3], Pekka Ruusuvuori[4, 5], Martin Eklund[1], Kimmo Kartasalo[1]

[1)] Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Sweden [2)] Department of Life Sciences, FFEI Ltd, United Kingdom [3)] Department of Oncology and Pathology, Karolinska Institutet, Sweden [4)] Institute of Biomedicine, Cancer Research Unit and FICAN West Cancer Centre, University of Turku and Turku University Hospital, Finland [5)] Faculty of Medicine and Health Technology, Tampere University, Finland

Introduction

Artificial intelligence (AI) has been shown to accurately detect and grade prostate cancer from digitized biopsies. However, a key problem for clinical implementation is decreased diagnostic performance due to technical variation in whole slide images (WSI) acquired using different scanners. We apply a spectrophotometrically characterised color calibration slide for standardizing WSIs of prostate biopsies, and evaluate the impact of calibration on AI performance in detecting prostate cancer.

Material and methods

The AI system in our experiment is adapted from Ström et al., The Lancet Oncology, 2020. For model training, we use 3653 prostate biopsies from 957 patients from the Stockholm-3 trial, scanned on an Aperio AT2 scanner. The tuning (100 WSIs) and testing (230 WSIs) sets were scanned on a Hamamatsu S360. The scanners' ICC profiles were obtained using the Sierra calibration slide (FFEI Ltd., Hemel Hempstead, UK). The generic sRGB profile available at the ICC website is taken as our calibration standard.

Results and discussion

In the independent test set, the AUC of cancer detection on slide-level for the model using original WSIs is 0.949, and 0.983 by using the calibrated WSIs. The Cohen's kappa, measuring the concordance between ISUP grades estimated by the AI and the study pathologist, was 0.728 and 0.383 with or without calibration, respectively. These show an obvious improvement in the performance.

Conclusion

The result so far has provided us solid proof that the spectrophotometric color calibration slide can improve the robustness of AI model performance across different scanner systems. Next, we expect to further confirm the feasibility of this approach in practical applications.

Keywords: Prostate Cancer, Artificial Intelligence, Color Calibration

SY05.03

Quality checkpoint in pathology specimens handling: an AI system to automate fragment detection and count.

Tomé Albuquerque[1, 2], Diana Montezuma[3, 4, 5], Sara P. Oliveira[1, 2], Pedro C. Neto[1, 2], João Monteiro[3], Liliana Ribeiro[3], Sofia Gonçalves[3], Ana Monteiro[3], Isabel M. Pinto[3], Jaime S. Cardoso[1, 2]

[1)] INESC TEC, Porto, Portugal [2)] FEUP, Porto, Portugal [3)] IMP Diagnostics, Porto, Portugal [4)] ICBAS, Porto, Portugal [5)] Cancer Biology and Epigenetics Group, IPO-Porto, Portugal

Introduction

Ensuring that the material available for slide analysis matches the material included after grossing is an essential step to guarantee no valuable loss. However, this is still a time-consuming manual step that delays the availability of the complete case for pathologists. To overcome this limitation, we developed an autonomous deep learning system to detect and count the number of fragments within each WSI.

Material and methods

All experiments were performed on a dataset of digitized histopathological specimens manually labeled with bounding boxes for each fragment and set. We applied a state-of-the-art object detection model, the YOLOv5, followed by several post-processing rules to check if the detected sets in each slide all have the same number of fragments. The deep learning models were fed with the colored images, resized to 512×512px to match the squared input size of the chosen architecture. The model outputs the number and spatial location of the fragments/sets and also gives a warning if the number of fragments per set is not uniform.

Results and discussion

The proposed method was trained on 1275 slides of colorectal samples and evaluated on 420 slides of specimens of other tissue types, obtaining a precision, accuracy, and mean absolute error of 74%, 73%, and 0.41, respectively.

Conclusion

The model achieved good results in several metrics, highlighting the favorable performance gains of using deep learning methods to automatically identify which slides have a different fragment number than the one reported in the macroscopy report. For future work, the model's performance may benefit from the inclusion of more tissue types for training.

Keywords: Quality control, digital pathology, fragment detector, deep learning, whole slide imaging

SY05.04

Automated Quality Control of Whole Slide Images Using Artificial Intelligence

Vaughn Spurrier[1], Ramachandra V. Chamarthi[1], Sean Grullon[1], Sivaramakrishnan Sankarapandian[1], Julianna D. Ianni[1]

[1)] Proscia, Inc., United States

Introduction

Unintentional slide artifacts inhibit pathology workflows by requiring laborious manual slide review of 3-10% of slides and lowering the data quality used in research or clinical practice - including building Artificial Intelligence systems. Artifacts are sometimes introduced during slide preparation, and can include air bubbles underneath the cover slip. Slide pen mark artifacts can obscure tissue during downstream analysis. Finally, digitization can produce artifacts including out of focus regions, missing or unscanned tissue sections, cut off tissue regions, and no scanned tissue.

Material and methods

We built a system, automated quality control (QC), to identify artifacts in Whole Slide Images (WSIs) generated from formalin-fixed paraffin-embedded (FFPE) hematoxylin and eosin (H&E) stained tissue that can be used to flag slides that need to be reprepped/rescanned, or to exclude regions during downstream analysis. Automated QC consists of an ensemble of traditional computer vision and deep learning segmentation models.

Results and discussion

We used 6448 WSIs consisting of eight tissue types from The Cancer Genome Atlas and 1781 additional skin WSIs for training, validation, and testing with a 70%/15%/15% split including data from two scanners (Leica and Hamamatsu). We achieve test set sensitivities/specificities of 90%/84%, 89%/93%, 74%/89%, 85%/77%, 82%/89%, and 98%/99% on the six artifacts outlined above.

Conclusion

Automated QC can run on multiple scanners and tissue types while exhibiting high individual artifact performance, which can improve workflow efficiency by reducing time spent identifying artifacts and improving data quality for research or clinical use.

Keywords: Artificial Intelligence, Quality Assurance, Quality Control

SY05.05

Automated detection of crush artefact in surgical pathology specimens using deep learning

Rasmus Kiehl[1], Sebastian Lohmann[2], Tom Bisson[1], Oliver Fischer[2], Benjamin Voigt[2]

[1)] Institute of Pathology, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany [2)] Centrum für Biomedizinische Bild- und Informationsverarbeitung (CBMI), University of Applied Sciences (HTW) Berlin, Berlin, Germany

Introduction

In surgical pathology specimens, "crush artefact" (CA) is a mechanical change that can affect the microscopic examination. While pathologists can recognize CA, the **introduction** of computational pathology necessitates new quality control mechanisms, as CA can obscure or mimic diagnostic structures.

Material and methods

We built a dataset from 47 H&E-stained stomach biopsies for Helicobacter-associated gastritis. Areas with significant CA were annotated by a pathologist who labelled 3.94% of the tissue as CA. A Resnet50 was trained for patch-based classification utilising a weighted random sampler and a moderate training length of 20 epochs to avoid overfitting on the less-represented class.

Results and discussion

We achieved a mean two-class test accuracy of 84%, whereas CA detection accuracy went up to 98% and non-CA classification to 82%. The difference may reflect the significant imbalance between classes and must be examined in more detail in further experiments.

Conclusion

We found that detection of CA with DL is possible using a Resnet50. This approach could enable automatic quality assurance and pre-screening of histologic images to improve subsequent computational analysis.

Keywords: AI, deep learning, surgical pathology, crush artefact, quality assurance

SY05.06

Building Clinical-Grade Artificial Intelligence Tools for Breast Cancer from the Ground Up

Rob Sykes[1], Derek Miller[1], Hafez Eslami Manoochehri[1], Ji Wang[1], Sheheryar Ali Arshad[1], Payam Khorramshahi[1], Chad Salinas[1]

[1)] Artificial Intelligence and Machine Learning Strategic Business Unit , Leica Biosystems, Vista, CA, United States

Introduction

Artificial Intelligence (AI) holds potential to aid pathologists in routine diagnostics and address increasing imbalances in pathology demand versus capacity. Considering global incidence, mortality, and research investment, there is disproportionate focus on AI for prostate compared to breast cancer, which is the most prevalent cancer worldwide. To develop a ground truth platform for clinical AI development, consideration should be given to ethical patient slide/data access, sample size, number of specialist reviews for each slide, and variation in tissue preparation/staining. Herein, we describe the approach and initial results in a study detecting breast cancer using AI.

Material and methods

800 H&E slides from multiple global locations were annotated at pixel-level detail. A 25+ breast pathologist network was established ensuring each slide is reviewed/annotated by a minimum of 3 specialists, accounting for discordance in breast tissue classification into clinically relevant subcategories. Slides are scanned at 40x on Aperio GT 450/450DX or Aperio AT2 scanners and annotated using stylus and touchscreen technology with a customized viewer.

Results and discussion

Automatically combining annotation inputs and extracting concordant areas is critical to developing a strong data pipeline. Early analysis revealed 12% discordance for 2 pathologists and 22% for 3, supporting a multi-reviewer approach. Early prototype models achieved 70-75% accuracy in detecting diagnostically significant areas against the test set.

Conclusion

Definition of ground truth provides a platform to investigate methodologies for reviewing and analyzing pathology cases, magnification levels, architectural changes and feature extraction. Careful definition of the annotation protocol and pathology tool will ultimately enable development of the best aids to the pathologist.

Keywords: Breast Cancer, Artificial Intelligence, Ground Truth

SY05.07

Profiling images for better Quality Control in Digital Pathology

David Ameisen[1], Julie Auger-Kantor[1], Emmanuel Ameisen[1]
[1)] R&D, imginIT SAS, France

Introduction

Systematic image Quality Control (QC) is essential to Digital Pathology (DP) workflows and Artificial Intelligence algorithms for computer-aided diagnosis. Frameworks for image analysis and QC in Digital Pathology have been developed for artifact-specific, image-specific algorithms. The issue now shifts to providing explainable and interoperable results efficiently whilst adapting to the great diversity of images in DP.

Material and methods

Analyzing over 500 H&E, HES, IHC, special stains and fluorescent Whole Slide Images (WSI) acquired from different scanners for color and artifact diversity, we developed and tested the following new QC algorithms: staining and color range detection, broken glass detection, dynamic tissue sample detection, blur detection, and integrated them in a single, dynamic and orchestrated QC workflow.

Results and discussion

Basic acceptability thresholds were first set to work for all slides. Profiles were then set for each major staining relying on text-based contextual information: file name, Laboratory Information Systems (LIS) and Image Management Systems (IMS) metadata, yielding better results than no profiling or coarse profiling. Relying on the image itself, by detecting the staining of the slide and the color ranges of the digitized image, yields even better results than solely relying on text metadata. This allows WSI auto-profiling, and the detection of inconsistencies between slide staining and IMS or LIS metadata.

Conclusion

We developed coherent, stable, quantifiable and interoperable image QC using fast, no-reference algorithms. While the wide variety of images in DP requires fine calibration of such QC algorithms, efficient profiling of the images benefits image QC, and even improves the general pathology workflow.

Keywords: Quality Control, Calibration, Pathology Workflow, Staining detection, Artifact detection, Sharpness quantification

SY05.08

Quality issues while setting up country wide digital pathology consultancy service in a limited resources

Artyom Borbat[1], Nikolai Kozlov[2]

[1)] Oncology service coordination center, FSBI NMITs of Oncology named after N.N. Blokhin of the Ministry of Health of Russia, Russia [2)] Surgical pathology department, FSBI NMITs of Oncology named after N.N. Blokhin of the Ministry of Health of Russia, Russia

Introduction

In 2021 in Russia telemedicine service for oncology hospitals was launched, which includes digital pathology. As infrastructure is country wide and lot of service being raised from a zero level, pathology service suffers lack of funding while still needs to support oncologists. Many developing countries can face such an issue, so we summarized the main issues we faced the first operation year.

Material and methods

833 cases from 49 regions including 9129 whole slide images for the 2021 dispatched to digital pathology consultations were reviewed for quality issues.

Results and discussion

Overall 22.8% (190) cases demonstrated issues, which influenced consultation time or made it impossible to perform. The majority (70; 37%) was linked to technical issues: server connection and damaged files. Poor histology quality was identified in 54 cases (28%). Laboratory and clinical supplementary information was inappropriate in 30 and 18 cases, respectively. Scanning issues were identified in 18 cases, mostly unfocused images. On a time scale the fourth month demonstrated maximum issue level 40%.

Conclusion

While setting up digital pathology consultancy service in limited resources technical and scanning issues are the main contributors – almost half according to our data – and easily reduced when staff gets experience. Supplementary clinical and laboratory information provide 25% and can be managed with dedicated trainings and staff focus on how important to provide adequate information for distant consultancy services.

Keywords: consultancy service, digital pathology, technical issues

SY06.03

The EMPAIA approach: building bridges between existing AI solutions and digital pathology systems by providing open specifications

Christoph Jansen[1], Klaus Strohmenger[1], Stefan Manthey[1], Daniel Romberg[2], Theodore Evans[3], Peter Hufnagl[1], Norman Zerbe[1]

[1)] Institute of Pathology, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt- Universität zu Berlin, Germany [2)] Institute for Digital Medicine, Fraunhofer MEVIS, Germany [3)] Distributed AI Laboratory, Technische Universität Berlin, Berlin, Germany

Introduction

With the advance of digital pathology, the development of image processing and artificial intelligence (AI) solutions becomes more and more viable. To achieve a satisfying user-experience these solutions must be integrated with a multitude of hardware and software systems. The EMPAIA project presents the Workbench API specification, that for the first time allows the user interface (UI) of an AI app (commercial or research) to be decoupled from the underlying infrastructure.

Material and methods

The project has previously published an App API specification, that decouples the AI's processing logic and allows the developers to focus on their core product. The presented Workbench API specification uses modern browser-based technologies that allow UIs to be delivered to any operating system. Single-page web components communicate via HTTP and are embedded in sandboxed iframes.

Results and discussion

The EMPAIA Workbench Client is a web UI reference implementation that allows pathologists to select a patient's case and use third-party AI apps for examinations. For each app a custom UI component is loaded into an iframe. The component may present an image viewer, let the user draw annotations, specify processing inputs, run the app in the platform backend and fetch results, all via the HTTP API.

Conclusion

The Workbench API allows developers to integrate their UIs in a well-defined way, while maintaining the freedom to deliver a custom user experience. EMPAIA is currently working with six AI companies to integrate existing solutions and gather feedback. The integration of EMPAIA APIs in clinical environments is highly relevant for all stakeholders, as it enables interoperability and vendor-agnostic integration of AI solutions.

Keywords: user interface, user experience, specification, web, artificial intelligence, workbench

SY06.04

Anonymization of Whole Slide Images for Research and Education

Michael Franz[1], Daniel Romberg[2], Tom Bisson[1], Truong An Nguyen[3], Peter Hufnagl[1, 3], Norman Zerbe[1]

[1)] Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt Universität zu Berlin, Institute of Pathology, Berlin, Germany [2)] Fraunhofer, Institute for Digital Medicine MEVIS, Max-von-Laue-Straße 2, 28359 Bremen, Germany [3)] HTW University of Applied Sciences Berlin, Center for Biomedical Image and Information Processing (CBMI), Berlin, Germany

Introduction

Sharing Whole Slide Images (WSIs) is of crucial importance for research and education. For exchange between multiple institutions it is necessary to remove sensitive information that is present in the data. Such a function is not directly available in scanning systems. Standards such as DICOM WSI simplify the anonymization, but are not yet widely adopted. Therefore, an application that provides anonymization for a variety of different WSI formats is required to enable a legally compliant exchange of WSIs.

Material and methods

Our approach is dedicated to anonymization and pseudonymization of WSIs. To achieve this, all sensitive data is removed or replaced by an alias, in case later re-identification is desired. Since common WSI file formats differ in complexity and composition, sensitive information is stored in various locations such as label and macro images or metadata files.

Results and discussion

We have developed an open-source library which provides anonymization for WSI formats from Leica, Hamamatsu, 3DHistech, Philips and Roche. A modular structure facilitates the extension of the software. Integration into external software is enabled through a command line interface and wrappers for multiple programming languages. The library is integrated into the data provisioning workflow of the EMPAIA platform, performing just-in-time client-side anonymization during the upload process.

Conclusion

We would like to initiate the discussion that scanner vendors provide tools for an optional anonymization of their data within their systems. For pseudonymization, more complex steps are necessary, since a re-identification strategy must be implemented. This requires the application of an id management system and establishment of an honest broker.

Keywords: Whole Slide Images, Anonymization, GDPR, Open Source

SY06.05

Slim: interoperable web viewer and annotation tool for computational pathology

Chris Gorman[1], Davide Punzo[2], Igor Octaviano[2], Steven Pieper[3], William J. R. Longabaugh[4], David A. Clunie[5], Ron Kikinis[6], Andrey Y. Fedorov[6], Markus D. Herrmann[1]

[1)] Department of Pathology, Massachusetts General Hospital and Harvard Medical School, Boston, MA, United States[2)] Radical Imaging, Boston, MA, United States [3)] Isomics Inc, Cambridge, MA, United States [4)] Institute for Systems Biology, Seattle, WA, United States [5)] PixelMed Publishing LLC, Bangor, PA, United States [6)] Department of Radiology, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, United States

Introduction

Realization of AI in pathology depends on the ability of machines to exchange and use data for analysis and to display AI outputs to human experts for interpretation and decision making. DICOM is emerging as the standard for communication of digital images and related information in pathology, but interoperable tools are lacking. Slim is a DICOMweb viewer for display and annotation of whole slide microscopy images and derived analysis results together with contextual metadata.

Material and methods

Slim is implemented as a single-page application without any custom server components. Instead, it relies on standard DICOMweb services for data query, retrieval, and storage to achieve interoperability with systems that expose a DICOMweb interface. Decoding, transformation, and rendering operations are based on DICOM data models and efficiently implemented in WebAssembly and WebGL to maximize interoperability and performance.

Results and discussion

Slim enables users to interactively browse and visualize brightfield and fluorescence microscopy images (including highly-multiplexed immunofluorescence imaging data), to annotate images for AI model development, and to review and interpret AI model inference results in the form of geometric objects, segmentation masks, or parametric maps. Slim serves as the pathology viewer of the National Cancer Institute's Imaging Data Commons, where it supports diverse quantitative microscopy imaging use cases on a common, modality-agnostic cloud platform that is shared with the radiology viewer.

Conclusion

By using DICOM, Slim achieves interoperability between image analysis and display systems and facilitates evaluation and integration of AI into digital pathology workflows in a device independent manner. The software is available free and open-source under a permissive license: https://github.com/herrmannlab/slim.

Keywords: Visualization, Interoperability, Artificial intelligence, DICOM, Image analysis, Standards

SY08.02

PatchSorter a high throughput open-source digital pathology tool for histologic object labeling

Tasneem Talawalla[1], Robert Toth[2], Cedric Walker[3], Hugo Horlings[4], Kien Rea[1], Sven Rottenberg[3, 4, 5], Anant Madabhushi[1, 6], Andrew Janowczyk[1, 7]

[1)] Department of Biomedical Engineering, Case Western Reserve University, United States [2)] Toth Technology LLC, United States [3)] Institute of Animal Pathology, University of Bern, Switzerland [4)] The Netherlands Cancer Institute, Division of Molecular Pathology, the Netherlands [5)] Bern Center for Precision Medicine, University of Bern, Switzerland [6)] Louis Stokes Veterans Affair Medical Center, United States [7)] Precision Oncology Center, Lausanne University Hospital, Switzerland

Introduction

A number of computational pathology approaches rely on accurate localization and subtype identification of objects (e.g., cells) present in whole slide images (WSI). While image analysis/segmentation algorithms can identify the location of millions of objects in WSI, a subsequent step is needed to identify their type. Manually assigning labels (e.g., lymphocytes vs non-lymphocytes) to these objects individually is especially laborious and tedious. Here, we present PatchSorter (PS), a browser-based high-throughput object labeling tool which facilitates user review and assignment of labels at a group, as opposed to individual object level, thus greatly improving labeling efficiency. As the user labels groups of objects, PS's deep learning backend iteratively increases separation between target groups within a low-dimensional representational space, thus further improving labeling efficiency.

Material and methods

From the Matador breast cancer trial, ~2.2k random cells from H&E stain WSIs were used to evaluate PS. To compare lymphocyte cell labeling efficiency, a clinical pathologist used for 15 minutes each GIMP (a Photoshop clone) and PS, and labels per second (LPS) were calculated. PS generated labels were manually reviewed to determine label accuracy.

Results and discussion

The GIMP approach resulted in 513 labels (.57 LPS), while PS yielded 2150 labels (2.37 LPS), a notable 317% labeling-efficiency improvement. PS label accuracy remained high at 0.944.

Conclusion

PatchSorter demonstrates an impressive 317% efficiency improvement for assigning labels to cell objects, suggesting PS's potential to be applied at scale to larger cohorts and other histologic objects. PatchSorter will be released into the open-source domain for community review, comment, and usage at patchsorter.com

Keywords: computational pathology, deep learning, open-source labelling

SY08.03

Few-Label Adaptation using Multi-ProtoNets – an Experiment on Urothelial Carcinomas

Rosalie Kletzander[1], Daniel Firmbach[1], Volker Bruns[1], Carol Geppert[2], Arndt Hartmann[2], Markus Eckstein[2], Michaela Benz[1]

[1)] Image Processing and Medical Engineering Department, Fraunhofer Institute for Integrated Circuits IIS, Germany [2)] Institute of Pathology, University Hospital Erlangen, FAU Erlangen-Nuremberg, Germany

Introduction

One of the biggest challenges in computational pathology is creating large labelled datasets to train specific AI models. Few-shot approaches aim to generalize learning so that only a few examples are required to allow adaptation to new tasks.

Material and methods

We investigate the adaptability of a Multi-ProtoNet model originally trained to differentiate seven tissue classes in colon sections. The new task is discriminating between two classes (healthy, tumor) in urothelial carcinomas and assigning all other tissue types to an "unknown" class. As there are various subtypes of urothelial carcinomas differing significantly in appearance, we split our data into two datasets: sections containing the subtype "conventional" (A) and sections containing other subtypes (B). Model A (B) is adapted based on 21 (36) annotations in three (five) sections from group A (A & B), respectively. Both models are evaluated on annotated regions in disjoint test sets: A (11,648 tiles, 2.912 mm^2, six sections) and B (4,591 tiles, 1.148 mm^2, four sections).

Results and discussion

The achieved accuracy/F1 scores are: model A on set A: 0.908/0.875, model B on set A: 0.911/0.900, model A on set B: 0.815/0.810, and model B on set B: 0.905/0.941. The qualitative evaluation reveals that model A detects "unknown" tissue types more accurately, especially inflammation.

Conclusion

The results show the adaptability of the Multi-ProtoNet with few annotations. Model B achieves better performance especially on test set B as it was adapted based on all subtypes. However, there is room for optimization regarding the recognition of "unknown" tissue types, which will be addressed in future research.

Keywords: few-shot learning, urothelial carcinomas, prototypical networks

SY08.04

Comparison of Consecutive and Re-stained Sections for Virtual Multi-Staining by Image Registration

Johannes Lotz[1], Nick Weiss[1], Jeroen van der Laak[2], Stefan Heldmann[1]

[1)] Fraunhofer MEVIS, Institute for Digital Medicine, Germany [2)] Diagnostic Image Analysis Group, Radboud University Medical Center, The Netherlands

Introduction

In digital histopathology, virtual multi-staining is important for diagnosis and biomarker research and additionally provides accurate ground-truth for various deep-learning tasks. Virtual multi-staining can be done by using different stains for consecutive sections or by re-staining the same section. Both approaches require image registration to compensate tissue deformations but little attention has been devoted to comparing their accuracy.

Material and methods

Our goal is to compare variational image registration of differently stained consecutive and re-stained sections. We describe a fully-automatic algorithm for deformable (nonlinear) registration and evaluate it on data from the automatic non-rigid histological image registration (ANHIR) challenge (230 consecutive slide pairs) and a new hybrid dataset of re-stained and consecutive sections (HyReCo, 81 slide pairs, ca. 3000 landmarks) that we also make publicly available.

Results and discussion

In the HyReCo dataset we obtain a median landmark error after registration of 13.2 µm (HyReCo) and 38.1 µm (ANHIR) between consecutive sections. The difference between the datasets is likely due to the larger distance between sections and more numerous artefacts. Between re-stained sections, the median registration error is 1.0 µm (HyReCo only). We observe that deformable registration leads to lower landmark errors than affine registration in both cases, though the effect is smaller in re-stained sections.

Conclusion

While the registration of re-stained sections allows nucleus-level alignment, consecutive sections only allow the transfer of region-level annotations. The latter can be achieved at low computational cost using coarser image resolutions. In both cases, registration is a valuable tool for the joint analysis of different stains.

Keywords: image registration, virtual multi-staining, deep learning, ground-truth

SY09.02

Alternating a MOOC with face-to-face sessions: a blended design to teach Histology

Laurence Pesesse[1], Céline Tonus[2], Marie Pirotte[1], Renaud Vandenbosch[1], Pascale Quatresooz[1], Pierre Bonnet[1], Björn-Olav Dozo[2], Renaud Hoyoux[3], Grégoire Vincke[3], Valérie Defaweux[1]

[1)] Department of Preclinic and Biomedical Sciences, Faculty of Medicine, University of Liège, Belgium [2)] CARE Digital Tools, University of Liège, Belgium [3)] Open Source Division, Cytomine cooperative, Belgium

Introduction

Over the past three decades, the surge of educational technologies has thoroughly transformed instructional methods by inducing new ways of teaching using advantage of online resources and digital tools. The teaching of Histology has been revolutionized by the rise of whole-slide scanners and virtual microscopes. For several years, the methods used to teach Histology at the Faculty of Medicine of the University of Liège (Belgium) has been adapted to a flipped classroom model blending online courses and activities (including virtual microscopy) and face-to-face sessions to consolidate the learning outcomes.

Material and methods

The e-learning part of this blended model is a Massive Open Online Course (MOOC) in french entitled "**Introduction** to Histology: exploration of the human tissues" and hosted on the French MOOC platform FUN (France Université Numérique). The virtual microscope is the open-source software CYTOMINE.

Results and discussion

Beyond the advantage offered by online activities during the COVID-19 crisis, a large survey carried out among ULiège students notably showed 85% of students consider this approach more motivating than the traditional method. Other factors related to engagement were also greatly improved.

Conclusion

The french MOOC has been repeated 11 times (ongoing series) and gathered more than 85,000 learners from 85 countries. Building on this success and in view of registrations' explosion during the pandemic, an English edition is now in preparation, to allow worldwide students to learn Histology through a universal and free access to high quality educational resources. Based on this experience, several European universities have also adopted this blended way to teach histology.

Keywords: MASSIVE OPEN ONLINE COURSE, E-LEARNING, VIRTUAL MICROSCOPY, HISTOLOGY TEACHING, DIGITAL TOOLS, INNOVATION

SY09.03

A pilot study for postgraduate teaching pathology with virtual microscopy

Artyom Borbat[1], Tatiana Novikova[1], Petr Bondarenko[2]

[1)] Pathology Department, Burnasyan Federal Medical Biophysical Center of Federal Medical Biological Agency, Russia [2)] Software Development Department, Leycor LLC, Russia

Introduction

The whole slide images (WSI) is a well known technology for pathology consultations and teaching medical students. It gains more attention also for pathology residents. The aim of the study was to perform a pilot study and to learn lessons for next steps in digital approach for postgraduate education.

Material and methods

The study was performed at Burnasyan Medical Biophysical Center. The breast pathology module was built with the SaaS Moodle learning platform. It includes theory, practice and testing. Practice and testing parts use a local server based dataset of 193 slide-based annotated breast pathology WSI, containing 19 morphologic entities. To open the WSI dataset a SaaS software Paithology was used. Eight first and second year residents were asked to use the module as a supplementary tool for the breast pathology course. After the course residents were interviewed on their experience of using the module.

Results and discussion

All the residents used the module when studying breast pathology and resumed to use it later to refresh knowledge. There were no issues for both dealing with software and matching WSI and traditional microscopy. The residents confirmed the module allowed them to review more cases with less time.

Conclusion

The study confirms the WSI virtual module is effective in postgraduate education. The dataset of the module was transferred to a web-based server allowing access to the module with the Internet. It is distributed as a free course for pathology residents. WSI and SaaS technologies allow residents to review lots of cases with few resources.

Keywords: resident pathologist, education, online module, digital pathology

SY10.02

Prognostic evaluation of endometrial hyperplasia using an AI-based image analysis tool on whole slide images

Emma Rewcastle[1, 2], Ivar Skaland[1], Einar G. Gudlaugsson[1], Melinda Lillesand[1, 2], Jan P.A. Baak[1], Emiel A.M. Janssen[1, 2]

[1)] Department of Pathology, Stavanger University Hospital, Norway [2)] Department of Chemistry, Bioscience and Environmental Engineering, University of Stavanger, Norway

Introduction

Prognostic evaluation of endometrial hyperplasia (EH), a condition characterised by excessive proliferation of endometrial glands, is an important step in pathological diagnosis. According to morphological criteria, EH patients are classified as low- or high-risk of progression to endometrial cancer. Over- and under-treatment of EH patients is of concern during this evaluation.

Material and methods

The aim of this study was to develop an automated, reproducible, machine-learning based tool to identify low- and high-risk EH lesions. The study cohort consisted of 386 patients with EH diagnosed between 1980 and 2007 from Stavanger University Hospital, Norway. Of these patients, 42 progressed to cancer and 344 did not, in the follow-up period (median: 146, 0-366months). Whole slide images of pan-cytokeratin stained slides were available for all patients. Using Visiopharm®, an application was developed to measure morphological features including gland density and cytological variation. The application was trained on 29 representative cases and validated on 334 cases (52 were excluded due to poor staining or loss of endometrial tissue).

Results and discussion

The features percentage stroma and the standard deviation of the lesser diameter of epithelial nuclei, were considered the most prognostic predictors in a logistic regression model. A risk score was calculated, with this model, which had an overall specificity of 92%, sensitivity of 50% and accuracy of 88%.

Conclusion

In this study, we establish an application that is able to categorise EH lesions according to progression risk. We demonstrate the potential of using an AI-based tool to assist in and improve prognostic evaluation of EH for better patient treatment.

Keywords: Endometrial hyperplasia, Image analysis, Visiopharm, AI, Prognosis

SY10.03

Deep Learning for HPV Infection Prediction in Head and Neck Cancers from H&E Whole Slide Images

Ruoyu Wang[1], Amina Asif[1], Syed Ali Khurram[2], Lawrence Young[3], Nasir Rajpoot[1, 4]

[1)] Tissue Image Analytics Centre, Department of Computer Science, University of Warwick, United Kingdom [2)] School of Clinical Dentistry, University of Sheffield, United Kingdom [3)] Warwick Medical School, University of Warwick, United Kingdom [4)] The Alan Turing Institute, The Alan Turing Institute, United Kingdom

Introduction

Human papillomavirus (HPV) induced head and neck cancers (HNC) exhibit a different disease course and prognosis compared to HNC driven by non-viral carcinogens such as tobacco or alcohol. While PCR and in-situ hybridisation are used for more precise diagnosis and sub-typing, p16 is a widely accepted surrogate biomarker for HPV infection in HNC (oropharyngeal) patients. We aim to develop a deep learning approach which can predict the HPV infection status from whole slide images (WSI) of H&E slides to reduce the waiting time and extra costs that other assays may incur.

Material and methods

Patches were extracted from WSI regions generated by a pre-trained tumour segmentation model. A multiple instance learning (MIL) strategy was adopted to generate higher scores for HPV+ slides and lower scores for HPV– slides using a custom ranking loss function and attention-based aggregation of prediction scores for all patches in a slide.

Results and discussion

A total of 412 cases from the TCGA-HNSC cohort were used (12% HPV+) using 3-fold strong cross validation. We achieved an average AUROC of 0.87±0.01, compared to the non-MIL baseline method (AUROC=0.80±0.02).

Conclusion

The proposed ranking loss-based MIL deep learning method shows promising improvement for prediction of HPV infection from H&E images of HNC slides. Our future work will investigate histological features associated with HPV related HNC tissues and explore large-scale validation on multi-centric HNC cohorts.

Keywords: Head and Neck, HPV, Multiple Instance Learning, Attention

SY10.04

Evaluating the prognostic performance of a deep learning-based model that reproduces NHG histological grading in breast cancer

Abhinav Sharma[1], Yinxi Wang[1], Philippe Weitz[1], Johan Hartman[2], Mattias Rantalainen[1]

[1)] Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Sweden

[2)] Department of Oncology-Pathology, Karolinska Institutet, Sweden

Introduction

Nottingham Histological Grade (NHG) is a prognostic factor that is routinely assessed in breast tumours. However, NHG suffers from high inter-assessor and inter-lab variability, causing uncertainty in grade assignments. This study aims to develop a deep learning-based model to improve reproducibility and quality in the classification of NHG (Grade1, 2, and 3)from histopathology whole slide images (WSIs).

Material and methods

1436 hematoxylin and eosin-stained WSIs were included for model training and validation. An attention-based deep Convolutional Neural Network (CNN) model was developed for the classification of the three NHG grades from WSIs. The classification performance was evaluated by the prognostic performance and compared against conventional NHG grades. A univariate Cox proportional hazards model was applied for the time-to-event analysis using Recurrence-free survival (RFS) as the outcome.

Results and discussion

We observed similar effect sizes (Hazard Ratio) for grade 2 vs 1, for the conventional NHG method (HR=1.50 (0.73-3.08 95%CI)) and the deep learning model (HR = 1.56 (0.79-3.05 95%CI)). For grade 3 vs 1, we observed effect sizes (HR = 3.50(1.75-7.00 95%CI)) with conventional NHG method and (HR = 3.57 (1.86-6.83 95%CI)) for the deep learning model.

Conclusion

Due to the high degree of inter-assessor variability and uncertainty in routine NHG grade assignments, there is a need for model-based decision support to improve quality in histological grading. We found that a deep learning-based histological grade model that classifies tumours into the conventional three-grade classes provides similar prognostic performance as NHG. The results suggest the feasibility of deep CNN-based models to improve breast cancer histological grading.

Keywords: Breast Cancer, Histological Grading, Deep learning

SY10.05

Can deep learning predict tumor heterogeneity in upper tract urothelial carcinoma?

Miriam Angeloni[1, 2], Sebastian Lindner[1, 2], Sebastian Foersch[3], Patrick Volland[1, 2], Carol I. Geppert[1, 2], Hendrik Heers[4], Sven Wach[2, 5], Helge Taubert[2, 5], Danijel Sikic[2, 5], Bernd Wullich[2, 5], Robert Stoehr[1, 2], Reiner Strick[2, 6], Pamela L. Strissel[1, 2, 6], Markus Eckstein[1, 2], Arndt Hartmann [1, 2], Fulvia Ferrazzi[1, 2, 7, *], Veronika Bahlinger[1, 2, *]

[1)] Institute of Pathology, University Hospital Erlangen-Nürnberg, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany [2)] Comprehensive Cancer Center Erlangen-EMN , CCC ER-EMN, Germany [3)] Institute of Pathology, University Medical Center Mainz, Germany [4)] Department of Urology and Pediatric Urology, University Hospital Gießen and Marburg, Germany [5)] Department of Urology and Pediatric Urology, University Hospital Erlangen, Friedrich-Alexander Universität Erlangen-Nürnberg, Germany [6)] Laboratory for Molecular Medicine, Department of Gynecology and Obstetrics, University Hospital Erlangen-Nürnberg, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany [7)] Department of Nephropathology, Institute of Pathology, University Hospital Erlangen-Nürnberg, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany
[*)] These authors contributed equally as senior authors

Introduction

In recent years the increasing use of high-resolution whole-slide images (WSIs) opened the way to AI-based approaches for the identification of prognostic and/or predictive cancer biomarkers. Upper tract urothelial carcinoma (UTUC) is a rare cancer for which better patient stratification is urgently needed. Here, we propose a deep-learning workflow to predict immunohistochemistry (IHC)-based subtypes from WSIs of UTUC patients.

Material and methods

Molecular subtyping of 100 samples >= pT2 was performed relying on hierarchical clustering of the expression of three luminal (FOXA1, GATA3, CK20) and three basal (CD44, CK5, CK14)IHC markers evaluated on tissue microarrays. H&E slides were digitalized and tumor areas annotated in QuPath. An automated Python-based pipeline was developed to generate, filter, and stain-normalize tiles. A transfer-learning approach was employed for subtype (luminal/basal) prediction by fine-tuning a ResNet50 pre-trained on ImageNet.

Results and discussion

To assess the performance of our workflow, a stratified random split of WSIs into 70% training/30% validation was repeated three times. Our approach achieved a mean accuracy of 0.83 [0.81-0.87], with a mean AUROC of 0.8 [0.72-0.92]. We are currently performing the evaluation with an independent test set. Class activation maps identified dense nuclei with small stroma bridges as morphological luminal features, and dense stroma and keratinization as basal characteristics. Additionally, classification maps allowed the identification of potentially heterogeneous WSIs, as characterized by the co-presence of both subtypes to be verified by expression analysis.

Conclusion

Taken together, our approach could offer a valid support to help pathologists in pre-selecting samples for further investigation to stratify UTUC patients for targeted therapy.

Keywords: deep learning, UTUC, WSI, subtype prediction, tumor heterogeneity, patient stratification

SY10.06

Tumour Region Identification and Tumour Proportion Score Estimation of PD-L1 Expression in Non-Small Cell Lung Carcinoma Using Deep Learning

Nidhi Bhatt[1], Aman Shrivastava[2], Geetank Raipuria[2], Nitin Singhal[2]
[1)] Pathology, North Bristol NHS Trust, United Kingdom [2)] Medical Imaging, AIRAMATRIX PVT. LTD., India

Introduction

The PD-L1 (Programmed Cell Death Ligand 1) protein expression has emerged as a critical biomarker for selecting individuals with advanced lung cancer who are most likely to respond to immune checkpoint inhibitor therapy. The inherent heterogeneous expression of PD-L1 and the availability of multiple PD-L1 assays, detection systems, platforms, and cut-offs have created challenges in ensuring reliable and reproducible reporting which continues to be based on subjective visual assessment by pathologists. Using Deep Learning, we propose a computational technique for recognising tumour cells in whole slide images (WSI) of immunohistochemically (IHC) stained sections from Non-Small Cell Lung Carcinoma (NSCLC) and accurately computing the Tumour Proportion Score (TPS) for PD-L1 expression.

Material and methods

At a magnification of 40x, an Aperio AT2 slide scanner was utilised to digitise IHC stained sections from NSCLC. TPS was calculated using a two-stage computing methodology based on the fraction of positively and negatively stained tumour cells. To begin with, a neural network based on Vision Transformer separated tumour areas from necrosis, benign epithelial cells and stromal regions. Then, using a multi-encoder and decoder architecture, a bespoke cell instance segmentation network recognised diverse cell kinds, including PD-L1 positive and negative tumour cells, lymphocytes, and macrophages. The model was tested on 200 WSIs using 120 WSIs as training data.

Results and discussion

The technique achieved a sensitivity and specificity of 91.2% and 95.8 % respectively, for detection of carcinoma regions. With a Pearson Coefficient of 0.92, we found significant correlation between the predicted TPS score and that assessed by an expert pathologist.

Conclusion

We provide a Deep Learning approach for reproducible and fast identification of tumour cells and accurate TPS grading for PD-L1 expression, in IHC stained WSI from NSCLC. We intend to conduct larger multicentre trials in the future to validate the technique.

Keywords: PD-L1, NSCLC, Deep-Learning, WSI, IHC

SY10.07

Development of cytopathology support system using the homology concept

Kento Iida[1], Kazuki Kanayama[2], Kunimitsu Kawahara [1, 3], Masako Onishi[1], Yuhki Yokoyama[3], Sachiko Nangumo[3], Hirofumi Yamamoto[3], Kazuaki Nakane[3]

[1)]Department of Pathology, Osaka Habikino Medical Center, Japan [2)]Department of Clinical Nutrition, Suzuka University of Medical Science, Japan [3)]Department of Molecular Pathology, Osaka University, Japan

Introduction

Due to the shortage of cytopathologists, the development of computer support systems for cytology is an urgent issue. Morphological information on chromatin is important for diagnose, however, it is very complex. This makes difficult to apply AI systems for analyzing the cytology. Here, we will introduce an image analysis method using the concept of the homology. The homology is a mathematical concept which evaluate "the contact degree". Our method is different from ordinary AI systems and it can be applied for analyzing to complex images, generically.

Material and methods

Specimens collected and diagnosed at Osaka Habikino Medical Center have been used, adenocarcinoma 8, squamous cell carcinoma 11 and small cell carcinoma 13. The specimens were stained with Papanicolaou, and they were taken 100x objective by a high-resolution camera. Non-keratinized cells and keratinized cells have been analyzed separately. An index MHP (Maximum value of the Homology Profile) based on the concept of the homology has been defined. MHP is, so to speak, an index for measuring "fineness".

Results and discussion

The average MHP values for adenocarcinoma, squamous cell carcinoma (non-keratinized cells), squamous cell carcinoma (keratinized cells) and small cell carcinoma are 0.068, 0.038, 0.106, and 0.147, respectively. There was a significant difference between them (t-test p 0.05).

Conclusion

By some ingenuity, the situation of increase of chromatin can be read as a change in contact degree. By defining the index MHP that quantitatively estimates the "fineness" of chromatin, the cancer types have been classified. We have already developed the basic technology, we would like to make sure the POC and develop a GUI system for clinical use in near future.

Keywords: cytology, lung, homology

OF.01

Malignant Mesothelioma Subtyping of Tissue Images via Sampling Driven Multiple Instance Prediction

Mark Eastwood[1], Silviu Tudor Marc[4], Xiaohong Gao[4], Heba Sailem[3], Judith Offman[2], Emmanouil Karteris[5], Angeles Montero Fernandez[6], Danny Jonigk[7], William Cookson[8], Miriam Moffat[8], Sanjay Popat[8], Jan Lukas Robertus[8], Fayyaz Minhas[1]

[1)] TIA Center, Warwick University, United Kingdom [2)] CS, Imperial College, United Kingdom [3)] CS, Oxford University, United Kingdom [4)] CS, Middlesex University, United Kingdom [5)] Medicine, University of Brunel, United Kingdom [6)] Medicine, Manchester University, United Kingdom [7)] Medicine, Medizinische Hochschule Hannover , Germany [8)] Heart & Lung Institute, Kings College London, United Kingdom

Introduction

Malignant Mesothelioma is a difficult to diagnose, highly lethal cancer usually associated with asbestos exposure. It can be classified into three subtypes: Epitheliod, Sarcomatoid, and a hybrid Biphasic subtype. However, the subtyping of malignant mesothelioma is difficult and has a high level of inter-observer variability. Early diagnosis and identification of the subtype informs treatment and can help improve patient outcome. A model capable of subtyping regions of tissue would aid this.

Material and methods

The dataset used is a collection of H&E stained Tissue Micro-arrays (TMAs) of tumor tissue biopsies. It consists of 4 TMA slides scanned at 20x, with a total of 243 cores covering 102 separate cases (patients), where 155 are Epithelioid, 64 Biphasic, and 24 Sarcomatoid cores. We propose a patch-based multiple instance learning (MIL) approach for malignant mesothelioma subtyping. This uses an instance-based sampling scheme for training deep convolutional neural networks on core-level labels that allows learning on a wider range of relevant instances compared to max or top-N based MIL approaches. The proposed MIL approach enables identification of malignant mesothelial subtypes of specific tissue regions.

Results and discussion

We have evaluated the proposed method on the above dataset with an AUROC of 0.87 +/- 0.04. Heatmap overlays of prediction outputs are also produced.

Conclusion

We have developed a model which can identify specific regions of tissue as being associated with Sarcomatoid or Epitheliod subtype. From this a continuous characterization of a sample according to predominance of sarcomatoid vs epithelioid regions is possible. Heatmaps could help a pathologist asses a sample more efficiently and accurately.

Keywords: Malignant Mesothelioma, Multiple Instance Learning, Computational Pathology, Deep Learning

OF.02

DNA methylation-based classification of sinonasal tumors

Philipp Jurmeister[1,2], Maximilian Leitheiser[3], Klaus-Robert Müller[4,5,6,7], Frederick Klauschen[1,2,3,7], David Capper[8]

[1)] Institute of Pathology, Ludwig-Maximilians-Universität München. [2)] German Cancer Consortium (DKTK), Partner Site Munich, and German Cancer Research Center (DKFZ), Heidelberg, Germany. [3)] Institute of Pathology, Charité – Universitätsmedizin Berlin. [4)] Machine-Learning Group, Department of Software Engineering and Theoretical Computer Science, Technical University of Berlin, Berlin, Germany. [5)] Department of Artificial Intelligence, Korea University, Seoul, South Korea. [6)] Max-Planck-Institute for Informatics, Saarbrücken, Germany. [7)] BIFOLD – Berlin Institute for the Foundations of Learning and Data, Berlin, Germany. [8)] Department of Neuropathology, Charité – Universitätsmedizin Berlin.

Introduction

The histopathological diagnosis of sinonasal tumors is challenging due to the number and heterogeneity of diagnoses that have to be considered. Among those, sinonasal undifferentiated carcinomas (SNUCs) are particularly challenging. We evaluated the value of DNA methylation and machine learning to classify these tumors.

Material and methods

We profiled the global DNA methylation signature of a comprehensive reference (n = 395) and test set (n = 52)of sinonasal tumors. A cohort of non-sinonasal samples (n = 8,104)was used to establish a supervised outlier detection. A subset of samples was further analyzed using mass spectrometry-based proteomics and DNA sequencing.

Results and discussion

14 of 18 epigenetic classes were equivalent to their conventional histopathological classification. The remaining four class included a heterogenous set of diagnoses, mainly SNUCs. Two classes had neuroendocrine differentiation in proteomics are were characterized by IDH2 or SMARCA4/ARID1A mutations with an overall favorable clinical course. The third class included tumors driven by SMARCB1-deficiency with poor outcome and the fourth class represented previously misclassified adenoid cystic carcinomas. We trained a support vector machine to classify new cases. It achieved an accuracy of 1.0 on the independent validation set and a sensitivity of 0.904. The outlier detection was highly effective, with a specificity of 0.982. It can be accessed at www.aimethylation.com.

Conclusion

DNA methylation-based classification of sinonasal tumors is highly accurate and could assist pathologists in difficult cases. Furthermore, SNUCs are not as undifferentiated as their current terminology suggests but can rather be reassigned to four distinct molecular classes.

Keywords: DNA methylation cancer of unknown origin head and neck squamous cell carcinoma machine learning

OF.03

Novel analysis method for in-situ spatial phenotyping of cell populations in multimarker imagery

James Mansfield[1], Fabian Scheider[1], Alessandro Massaro[1], Simon Haastrup[1], Rasmus Lyngby[1], Johan Dore-Hansen[1], Jeppe Thagaard[1]
[1)] R&D, Visiopharm, Denmark

Introduction

Spatial biology is increasingly important in immuno-oncology because of the need to understand complex tumor microenvironment architecture, especially regarding the immune contexture in and around solid tumors. Multiplex imaging data is used to segment the tissue into relevant compartments (tumor, stroma, etc.) and perform multiplex phenotyping of the cells. For highplex data (10+ markers), phenotyping has typically used an unsupervised clustering algorithm, but that has many limitations.

Material and methods

We have developed a novel method of phenotyping cells in situ in multiplexed imaging data that involves dividing markers into two user-defined categories: lineage markers and functional markers. Lineage markers are used to identify cellular phenotypes, while functional markers are measured afterwards for their expression levels in across each phenotype and in each individual cell. This new method first uses a supervised classification methodology using lineage markers to find cells with expected phenotypes. In a second step, the levels of functional markers are measured for each cell. Unexpected phenotypes in unclassified cells can then be explored.

Results and discussion

We present data of the novel workflow for 7-plex and 20+-plex data and found that the new method increased the efficiency of setting up complex analysis workflows and improved analysis results. Fewer non-biological phenotypes were found, cell classifications were improved compared to auto-clustering, while still exploring unexpected phenotypes. Interactive exploration of the cell populations enabled quicker validation of results and deeper understanding of the tumor immune contexture.

Conclusion

This new method will improve analyses of the next generation of highplex imaging datasets for many modalities of multiplexed imaging.

Keywords: immuno-oncology, multiplexed pathology, image analysis, phenotyping

OF.04

Validation of automated positive cell detection of immunohistochemically stained laryngeal tumor tissue using QuPath digital image analysis

Hilde J.G. Smits[1], Justin E. Swartz[2], Marielle E.P. Philippens[1], Remco De Bree[2], Johannes H.A.M. Kaanders[3], Sjors A. Koppes[4], Gerben E. Breimer[5], Stefan M. Willems[6]

[1)] Department of Radiotherapy, University Medical Center Utrecht, The Netherlands [2)] Department of Head and Neck Surgical Oncology, University Medical Center Utrecht, The Netherlands [3)] Department of Radiation Oncology, Radboud University Medical Center Nijmegen, The Netherlands [4)] Department of Pathology, Erasmus MC, University Medical Center Rotterdam, The Netherlands [5)] Department of Pathology, University Medical Center Utrecht, The Netherlands [6)] Department of Pathology and Medical Biology, University Medical Center Groningen, The Netherlands

Introduction

This study aimed to validate a workflow for automatic positive cell detection for a nuclear (hypoxia-inducible factor 1a [HIF-1a]) and a cytoplasmatic hypoxia biomarker (pimonidazole [PIMO]).

Material and methods

101 tissue fragments from 58 laryngeal tumor biopsies were immunohistochemically stained for HIF-1a and PIMO. Cell detection was performed in QuPath. HIF-1a staining was very diffuse, so only cells with strongly stained nuclei were considered positive (nuclear optical density ≥0.65). PIMO staining was less intense, so cells with any staining were considered positive (cytoplasmatic optical density ≥0.10). Three pathologists scored the fragments on the area-percentage of positive cells using five categories (0=<1%; 1=1-10%; 2=11-33%; 3=34-66%; 4=>67%). Disagreements were solved by consensus. The observers' score was used as the reference standard.

Results and discussion

For PIMO fragments, the automated positive cell detection was in agreement with observers in 64 fragments (63.4%, quadratic weighted kappa=0.82). In 24 of 37 cases of disagreement (64.9%), the automated detection overestimated the percentage of positive cells. For HIF-1a fragments, the automated detection agreed with observers in 51 fragments (50.5%, quadratic weighted kappa=0.66). In 48 of 50 cases of disagreement (96%), the automated detection underestimated the percentage of positive cells.

Conclusion

The automated positive cell detection was able to assess the percentage of positive cells beyond chance to an excellent degree in PIMO fragments. For the percentage of strong HIF-1a positivity, the automated workflow showed an adequate agreement with observers. To improve agreement, the positivity threshold for HIF-1a should be lowered. With some fine-tuning of thresholds, this method can serve as a valuable tool for pathologists.

Keywords: Validation, Cell-based analysis, QuPath, Positive cell detection, Immunohistochemistry, DAB

OF.05

Application of neural architecture search technique in nuclear and epithelium segmentation in digital pathology images of oral dysplasia

Neda Azarmehr[1], Adam Shephard[2], Hanya Mahmood[1], Nasir Rajpoot[2], Syed Ali Khurram[1]

[1)] School of Clinical Dentistry, The University of Sheffield, United Kingdom [2)] Department of Computer Science, University of Warwick, United Kingdom

Introduction

Oral epithelial dysplasia (OED) is a precursor to oral cancer with significant variations in histological grading. Correct grading is vital for optimal treatment and prognosis prediction. Deep learning has been used to automatically segment OED epithelium into different layers for grading. However, segmentation of regions of interest in whole slide images (WSI) is challenging due to the sheer amount of pixel data in WSIs. We propose a neural network for effective segmentation of the full epithelium with individual nuclear segmentation that can facilitate downstream OED analysis.

Material and methods

43 H&E stained WSI at 20× magnification were obtained. Manual annotation of individual epithelial nuclei by a pathologist served as ground-truth classed as 'epithelial' or 'other' nuclei. The Nu-Click framework was used to generate nuclear boundaries and a Neural Architecture Search (NAS) approach to design a network for more precise and simultaneous segmentation of epithelium and nuclei. The performance of three well-known networks (U-Net, SegNet, DeeplabV3ResNet101) was compared.

Results and discussion

Using an optimal network approach, the full epithelium segmentation task produced an F1-score of 0.935 while the F1-scores from other state-of-the-art models (i.e U-Net, SegNet, DeeplabV3ResNet101) were 0.744, 0.739, and 0.808 respectively. Also, the F1-score for nuclear segmentation achieved by the optimal network was 0.945 (compared to 0.757, 0.660, and 0.895 using U-Net, SegNet, DeeplabV3ResNet101, respectively).

Conclusion

Our initial results achieved using the NAS approach outperformed state-of-the-art deep learning models for epithelium and nuclear segmentation tasks. This work reveals opportunities for further efficient architecture search strategies for segmentation in the area of computational pathology.

Keywords: Artificial Intelligence, Pathology, Oral Dysplasia, Oral Cancer, Deep learning, Image Analysis

OF.06

CohortFinder: an open-source tool for quantitively partitioning datasets to improve deep learning model robustness

Fan Fan[1], John Shin[1], Yijiang Chen[1], Bangchen Wang[2], Takaya Ozeki[3], Laura Barisoni[2], Anant Madabhushi[1, 4], Andrew Janowczyk[1, 5]

[1)] Department of Biomedical Engineering, Case Western Reserve University, United States [2)] Department of Pathology, Duke University, United States [3)] Department of Internal Medicine, Division of Nephrology, University of Michigan, Ann Arbor, United States [4)] Louis Stokes, Cleveland Veterans Administration Medical Center, United States [5)] Precision Oncology Center, Lausanne University Hospital, Switzerland

Introduction

Digital Pathology batch effects (BE) are systematic technical differences in good quality images (e.g., scanner, stain variances), unrelated to biological variation, which can negatively impact generalizability of machine learning models like deep learning (DL). CohortFinder (CF), a new open-source tool, algorithmically divides images containing the same BE (as identified by an open-source quality control tool HistoQC) into training/testing folds. This intentionally increased training set diversity is intended to positively impact DL generalizability.

Material and methods

N=64 PAS-stained kidney images from 20 sites helped evaluate CF in a proximal tubule segmentation task using mean and standard deviation of Dice (segmentation) and F-scores (detection).1 image from 9 sites was randomly held-out for external testing (ET). With the remaining 55 WSIs, 3 scenarios (Average-Case (AC), Worst-Case (WC), and Best-Case (BC)) were explored to assess impact of BE on DL robustness via 3-fold cross-validation (CV). The AC saw random assignment of images to CV folds (current best-practice). WC and BC strategies employed CF to algorithmically create potential (but rare) AC's instances with extreme diversity properties, wherein BE are either grouped or precisely divided between CV folds, respectively.

Results and discussion

In both internal and external testing sets, CF's more diverse training folds (BC) showed consistent performance improvements compared to AC and WC, while also demonstrating the lowest standard deviation. BC=[CV-DICE:0.87±0.13/F-score:0.93±0.04;ET-DICE:0.91±0.03/F-score:0.93±0.01], AC=[CV-DICE:0.85±0.15/F-score:0.92±0.05;ET-DICE:0.90±0.04/F-score:0.93±0.01], WC=[CV-DICE:0.75±0.26/F-score:0.89±0.1;ET-DICE:0.86±0.17/F-score:0.92±0.06].

Conclusion

Quantitatively driven data partitioning provided by CF reduces impact of BEs, helping to improve DL performance and generalizability. CohortFinder will be released into the open-source domain for community review, comment, and usage at cohortfinder.com.

Keywords: batch effects, quality control, deep learning

OF.07

Ki-67 in breast cancer: do different algorithms and file formats lead to the same results?

Stefan Reinhard[1], Cédric Pieren[1], Bastian Dislich[1], Sandro Wanner[1], Inti Zlobec[1], Tilman T. Rau[2]

[1)] Institute of Pathology, University Bern, Switzerland [2)] Institute of Pathology, Heinrich-Heine-Universität Düsseldorf, Germany

Introduction

Ki-67 assessment is well-known to be strongly observer and lab-dependent, but remains a pivotal biomarker for clinical decision-making. Several algorithms based on digital pathology exist to replace the "eyeballing" of Ki-67 in breast cancer. Our aim is to compare Ki67-scores of different algorithms (QuPath and commercial) and two different scanners (3DHistech, Hamamatsu) against ground-truth and routinely collected diagnostic data.

Material and methods

96 slides were collected and annotated by pathologists. The ground-truth of all ROI was counted on 2000 cells and validated manually. A comparison to routine data from two pathologists was performed. Transfer of ROI annotations was used to compare the performance among the systems as well as the second scanner option. This way different resolution and color variability were integrated into the study setup. Pearson correlation and intraclass correlation coefficients (ICC) were used to determine the association between and across different methods and vendors.

Results and discussion

The mean ground-truth score over the whole dataset was 19.6% (range: 18.4% to 25%), whereas the correlations of all algorithms were highly significant $p < 0.0001$ or larger and an ICC greater than 0.94. Beside the high correlation several slides were identified which deviate markedly from the ground-truth counts regardless of file format or algorithm.

Conclusion

Overall, all algorithms perform similarly and lead to high correlations with ground-truth. Of note, while differences among vendors remain in terms of certification, open-source, inter-operability with the pathologist and flexibility of the systems, the herein tested systems and conditions were all suitable for automated analysis.

Keywords: Ki-67, breast cancer, image analysis, scanners, open-source, algorithms

OF.08

Upconversion nanoparticles as labels for histopathological tissue evaluation

Krzysztof Krawczyk[1], Matthias J. Mickert[1], Stefan Andersson-Engels[2]
[1)] Lumito AB, Lumito AB, Sweden [2)] Biophotonics@Tyndall, Tyndall National Institute, Ireland

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.

Keywords: digital pathology, upconversion nanoparticles, breast cancer, visualisation, WSI, scanner

OF.09

Morphological analysis of nodular and micronodular basal cell carcinoma subtypes through texture analysis and semantic segmentation performance

Mircea-Sebastian Serbanescu[1], Raluca Maria Bungardean[2]

[1)] Department of Medical Informatics and Biostatistics, University of Medicine and Pharmacy of Craiova, Romania [2)] Department of Pathology, Iuliu Hatieganu University of Medicine and Pharmacy, Romania

Introduction

Current guidelines recommend the division of basal cell carcinoma (BCC) subtypes into low-risk (LR) and high-risk (HR) groups based on recurrence risk, or into "easy-to-treat" and "difficult-to-treat". Based on clinical observation, we emphasize that the nodular (LR) and micronodular (HR) subtypes are different tumors with different behavior due in part to different surrounding stroma and in part to different tumor morphology.

Material and methods

Nodular (n=100) and micronodular (n=100) BCC microscopic images were manually segmented by two pathologists. Four classes of objects were segmented: tumor, touching tumor (peripheral palisading), touching stroma (cleft formation), and stroma. Classical pattern analysis using Haralick texture features was used to describe the four classes of the segmented data. A Deeplab v3+ semantic segmentation network with weights initialized from a pre-trained Resnet-18 network was trained, aiming to differentiate between nodular and micronodular subtypes.

Results and discussion

10 out of 14 computed Haralick texture features show no statistical differentiation between the tumor class of the two BCC subtypes, with more differentiation in the other three classes. The semantic segmentation network archives good accuracy (ACC=0.80795) and weighted intersection-over-union (wIoU=0.71877) on segmenting the images into the four classes. When assessing between nodular and micronodular subtypes ACC and wIoU increased to 0.87954 and 0.81789 showing that there is enough morphological information to distinguish the two subtypes.

Conclusion

Having low texture differentiation and high segmentation output, we conclude that nodular and micronodular subtypes are different tumors not only through their tumor-stoma ratio, but also through the tumor architecture itself. Research funded by the University of Medicine and Pharmacy of Craiova, grant 26/24c/13.07.2021.

Keywords: basal cell carcinoma, semantic segmentation, Haralick texture features, low and high risk, nodular subtype, micronodular subtype

SY11.03

The role of explainable AI in regulatory practices

Markus Plass[1], Theodore Evans[2], Rasmus Kiehl[3], Michaela Kargl[1], Rita Carvalho[3], Christian Geißler[2], Heimo Müller[1], Norman Zerbe[3], Andreas Holzinger[4]

[1)] Diagnostic and Research Center for Molecular BioMedicine, Diagnostic & Research Institute of Pathology, Medical University of Graz, Austria [2)] DAI-Labor, Technical University Berlin, Germany [3)] Institute of Pathology, Charite – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Germany [4)] Institute for Medical Informatics, Statistics and Documentation, Medical University of Graz, Austria

Introduction

In the context of digital pathology and in-vitro diagnostics, Artificial Intelligence (AI) must empower (bio)medical professionals to take responsibility for their decision-making, raising the demand for explainable AI. The US Food and Drug Administration (FDA) and the European In-Vitro Diagnostics Regulation (IVDR) address explainability in their recommendations and documents. However, to achieve efficient and effective explanations in AI systems, it is essential to know who uses which type of AI-solution for what purpose and how the human-AI interface is designed.

Material and methods

We propose definitions for AI solutions in the field of digital pathology, including the classes of algorithms involved and how these may be applied. We identify the stakeholders using such applications,their aims and potential requirements. We define a taxonomy describing the interface between the AI solutions and their stakeholders, as well as varieties of explanations and metrics for their quality.

Results and discussion

Usability encompasses measurements for the quality of use, and causability encompasses measurements for the quality of explanations produced by explainable AI methods. We describe both concepts and give examples of how both are essential for demonstrating scientific validity, as well as analytical and clinical performance in digital pathology.

Conclusion

Explainable AI methods provide answers to important questions in scientific validation and the evaluation of analytical and clinical performance of AI solutions in digital pathology: "Why does an AI solution generate reliable results for an intended purpose?", "Why did it produce a specific result?", "Was the explanation satisfactory for the user?".

Keywords: In-vitro diagnostics, Validation, Causability, Explainable AI, Usability

SY12.02

Deep Learning Optimization for Whole Slide Image Analysis in Low-Resource Environments

Siddhesh Thakur[1, 2, 3], Sarthak Pati[1, 2, 3, 4], Junwen Wu[5], Ravi Panchumarthy[5], Deepthi Karkada[5], Prashant Shah[5], Spyridon Bakas[1, 2, 3]

[1)] Center for Biomedical Image Computing and Analytics, University of Pennsylvania, United States [2)] Department of Pathology and Laboratory Medicine, Perelman School of Medicine at the University of Pennsylvania, United States [3)] Department of Radiology, Perelman School of Medicine at the University of Pennsylvania, United States [4)] Department of Informatics, Technical University of Munich, Germany [5)] Intel Health and Life Sciences, Intel Corporation, United States

Introduction

Histopathology tissue assessment is the gold standard for cancer diagnosis and prognosis. Digitization of glass tissue slides in whole slide images (WSI) enabled the proliferation of deep-learning (DL) towards automating quantitative assessments. However, DL solutions have large computational footprint and require specialized hardware (e.g., DL acceleration cards) limiting their use in low-resource environments, such as clinical settings. Here we seek the optimization of DL-based tumor segmentation in colorectal adenocarcinoma WSI, towards assessing potential clinical deployment.

Material and methods

We identified 250 H&E-stained WSI with apparent tumor, from the DigestPath2019 challenge, and downsampled them to 10x magnification level. Each WSI underwent background/non-tissue removal, followed by partitioning to 500 (512x512)patches, resulting in 125,000 patches collectively. These were divided to independent training (80%) and testing (20%) cohorts, to develop a tumor segmentation model, based on UNet with residual connections. Majority voting was used for overlapping patch regions, to generate the complete WSI mask. Post-Training-Optimization (PTO) and Quantization-Aware-Training (QAT) were evaluated on typical clinical hardware of consumer-grade CPU (Intel Core i7-1185G7).

Results and discussion

Current preliminary analysis yielded hardware-specific 5-fold speedup improvements on average during inference for both PTO and QAT (compared to the original PyTorch v.1.10.0 FP32 model), as well as memory footprint improvements (from 118MB to 22.25MB with PTO and to 15.57MB with QAT), with only negligible Dice differences.

Conclusion

Both Post-Training-Optimization and Quantization-Aware-Training in DL inference workflows for tumor segmentation in WSI, obviate the need for specialized hardware and reveal speedup and memory footprint improvements without noticeable performance differences, thereby showing promise for their potential clinical translation.

Keywords: Deep Learning, Medical Imaging, Digital Pathology, Optimization, Segmentation, Low Resource Environments

SY12.03

Unsupervised Transfer Learning Boosts AI-based Virtual Staining in Histology

Umair Akhtar Hasan Khan[1], Sonja Koivukoski[2], Leena Latonen[2], Pekka Ruusuvuori[1]

[1)] Faculty of Medicine, University of Turku, Finland [2)] Institute of Biomedicine, University of Eastern Finland, Finland

Introduction

Conventional histopathology staining has been indispensable for tissue analysis and diagnosis of different diseases, especially cancer. Recently, however, several studies have successfully used AI-based image-to-image translation methods to virtually stain tissue images with high accuracy. These methods have two main categories: supervised and unsupervised. While supervised methods are coveted because of their high translational accuracy, their performance is strictly tied to paired image data. They require special tissue preparation protocols and a non-trivial image-to-image registration step to align the tissue image pairs. Unsupervised methods don't require paired data, but they typically suffer from lower quality virtual staining results. We present a hybrid approach to virtual staining utilizing the benefits of both method types.

Material and methods

We utilize histological images of murine prostate tissue to train three image-to-image translation models on the virtual staining task 1) A supervised training model called Pix2Pix with randomly initialized weights, 2)An unsupervised training model called CycleGAN, and 3)A boosted Pix2Pix with pretrained unstained-to-stained generator weights from the CycleGAN training.

Results and discussion

Using pre-trained generator weights (even from an unsupervised training method) in the Pix2Pix training improves the mean SIMM score by 2.81% and 0.59% (in trainings with rigidly and elastically registered image data, respectively) compared to the Pix2Pix training with randomly initialized weights.

Conclusion

This experiment shows that transfer learning, even unsupervised, has the potential to improve the robustness of supervised virtual staining, especially when paired data is scarce. Future experiments can include unsupervised transfer learning from different tissue types or stain normalization to virtual staining.

Keywords: virtual staining, unsupervised transfer learning, supervised learning, histology

SY12.04

Computer-aided tool for CRC diagnosis: from the AI model to the clinical software prototype

Sara P. Oliveira[1, 2], Diana Montezuma[3, 4, 5], Sara P. Oliveira[1, 2], Pedro C. Neto[1, 2], João Monteiro[3], Liliana Ribeiro[3], Sofia Gonçalves[3], Ana Monteiro[3], Jaime S. Cardoso[1, 2], Isabel M. Pinto[3]

[1)] INESC TEC, Porto, Portugal [2)] FEUP, Porto, Portugal [3)] IMP Diagnostics, Porto, Portugal [4)] ICBAS, University of Porto, Portugal [5)] Cancer Biology and Epigenetics Group, IPO-Porto, Portugal

Introduction

With the advent of digital pathology, the development and integration of automatic, robust, high-performance and interpretable diagnostic support tools can be valuable in helping pathologists with their daily workload. Thus, we present an AI-based clinical software prototype for colorectal samples classification and tissue mapping.

Material and methods

The prototype was developed as a server-side web application that can be accessed from any workstation in the lab. It is designed to evaluate a single slide, or a batch of slides simultaneously, in real-time. Moreover, the latest results are cached, allowing re-evaluation without the need to re-upload slides. In addition to displaying the slide diagnosis, and its confidence level, a visual prediction map is also retrieved, explaining the diagnosis itself and drawing the pathologist's attention to key tissue areas within each slide. Furthermore, the prototype also allows user feedback, an important feature for active learning, software update and research development.

Results and discussion

The model was developed to classify colorectal samples into non-neoplastic, low-grade or high-grade. On a set of 4433 slides, it achieved an accuracy of 90.2%, a sensitivity of 98.8%, a specificity of 85.7%, and a quadratic weighted kappa of 0.888.

Conclusion

This prototype can aid in the analysis of CRC slides by detecting high-grade lesions in colorectal biopsies with high sensitivity and focusing the pathologist's attention on key areas, by visually displaying tissue classification. Thus, it can be used as a second opinion and even as a flag for details that may have been missed at a first glance.

Keywords: Software Prototype, AI, Computational Pathology, Colorectal Cancer

SY12.05

Tumor detection and regression grading in esophageal adenocarcinomas

Yuri Tolkach[1], Lisa-Marie Wolgast[1], Alexey Pryalukhin[2], Wolfgang Hulla[2], Marie-Lisa Eich[1], Simon Schallenberg[3], Wolfgang Schroeder[4], Christiane Bruns[4], Reinhard Büttner[1], Alexander Quaas[1]

[1)] Institute of Pathology, University Hospital Cologne, Germany [2)] Institute of Pathology, Landeskrankenhaus Wiener Neustadt, Austria [3)] Institute of Pathology, University Hospital Berlin-Charité, Germany [4)] Department of General, Visceral and Cancer Surgery, University Hospital Cologne, Germany

Introduction

Resections due to esophageal adenocarcinoma (EAC) are among the largest and time-consuming pathological specimens. As most of the patients receive neoadjuvant therapy (NT), two of the common pathological diagnostic tasks are detection of tumor and fibrotic regression tissue as well as quantification of their volume (regression scoring). In this study, we create a digital pathology (DP) tool aimed at detection of 11 tissue classes in esophageal resection specimens.

Material and methods

Manually annotated digitized histological slides from specimens of patients with EAC after NT were used: 1) Training dataset (slides/patients n = 193 / 98) from Institute 1; 2)Four test datasets: from Institute 1 (hold-out cases, n = 22 / 20), Institute 2 (n = 62 / 15), Institute 3 (140 / 44), and The Cancer Genome Atlas (TCGA) cohort (n = 22 / 22; NT-naive patients). Deep learning algorithms were based on InceptionResNetV2 architecture. Final version of training dataset consisted of approximately 1.200.000 patches from 11 tissue classes.

Results and discussion

High algorithm accuracies for detection of tumor and regression tissue were received on all four test datasets. Tumor detection sensitivity from a native algorithm output without thresholding was up to 0.978, with a specificity of up to 0.996, also for TCGA dataset with therapy-naive tumors. Regression tissue detection sensitivity was slightly lower, up to 0.923, with high specificity of up to 0.990.

Conclusion

The developed DP algorithm for detection of tumor and regression tissue in patients with EAC shows high accuracy and allows for optimization of the routine pathology work.

Keywords: deep learning, tumor, regression, detection, pathology, tool

SY12.06

Relieving pixel-wise labeling effort for pathology image segmentation by using self-training to learn from sparsely-annotated data

Romain Mormont[1], Mehdi Testouri[1], Ba Thien Le[1], Pierre Geurts[1], Raphaël Marée[1]

[1)] Montefiore Institute, University of Liège, Belgium

Introduction

Data scarcity is a common issue when training deep learning models for digital pathology. Large exhaustively-annotated segmentation datasets are difficult to obtain. In this context, two questions arise: is exhaustive labeling required to train reliable models and can these models be improved by exploiting only sparsely-annotated images? Here, we investigate a self-training approach using a training set composed of two subsets, denoted subsets A and B, respectively containing exhaustively- and sparsely-annotated images, sparse annotations being cheaper to produce.

Material and methods

Our workflow first consists in training a U-Net architecture on subset A for a few epochs. Then, we repeat the following process at every subsequent epoch until convergence: pseudo-labels are generated for the unannotated pixels of images from subset B using the currently trained model and the pseudo-labeled images are included in the training set for the next epoch. We furthermore apply weights on pseudo-labeled pixels to account for model uncertainty and also propose an auto-calibration approach for pseudo-labels generation.

Results and discussion

We use MoNuSeg and SegPC cell segmentation datasets and simulate sparsity by randomly removing annotated cells from the masks. We also validate our findings on an in-house dataset. We observe that, even in extreme scarcity (>95% missing annotations), self-training brings a significant improvement over using only subset A and yields only a marginal drop of performance compared to using exhaustively-annotated images from both subsets.

Conclusion

In this work, we show that using a self-training approach can help to significantly relieve the labeling effort. Moreover, we plan to integrate our method into the Cytomine open-source platform.

Keywords: image segmentation, self-training, semi-supervised learning, deep learning, data scarcity, digital pathology

SY12.07

A robust artificial intelligence approach for histopathological evaluation of prostate biopsies

Nita Mulliqi[1], Kimmo Kartasalo[1], Xiaoyi Ji[1], Kelvin Szolnoky[1], Henrik Olsson[1], Anders Blilie[2], Marcin Braun[3], Marcello Gambacorta[4], Kristina Hotakainen[5], Emilius A. M. Janssen[6], Svein R. Kjosavik[7], Roman Łowicki[8], Bodil Ginnerup Pedersen[9], Karina Dalsgaard Sørensen[10], Benedicte Parm Ulhøi[11], Pekka Ruusuvuori[12], Lars Egevad[13], Martin Eklund[1]

[1)] Medical Epidemiology and Biostatistics, Karolinska Institutet, Sweden [2)] Faculty of Health Science, University of Stavanger, Norway [3)] Department of Pathology, Medical University of Lodz, Poland [4)] Department of Pathology, Synlab, Italy [5)] Department of Clinical Chemistry, University of Helsinki, Finland [6)] Department of Chemistry, Bioscience and Environmental Engineering, Faculty of Science and Technology, Norway [7)] The General Practice and Care Coordination Research Group, Stavanger University Hospital, Norway [8)] 1st Department of Urology, Medical University of Lodz, Poland [9)] Department of Clinical Medicine, Aarhus University, Denmark [10)] Department of Molecular Medicine, Aarhus University Hospital, Denmark [11)] Department of Pathology, Aarhus University Hospital, Denmark [12)] University of Turku, Institute of Biomedicine, Finland [13)] Department of Oncology and Pathology, Karolinska Institutet, Sweden

Introduction

Examination of biopsies determines the diagnosis and treatment of prostate cancer but is complicated by a global deficiency in pathology expertise and inter- and intra-rater variability. Artificial Intelligence (AI) can aid with these challenges, but its widespread implementation requires tackling diverse patient populations and clinical settings. Biopsies from different clinics vary in sample preparation, scanning and morphological heterogeneity. We propose an AI approach for robust clinically applicable biopsy evaluation.

Material and methods

We aim to incorporate four concepts: scanner calibration, improved algorithms, dataset upscaling and morphological heterogeneity modelling. To train robust AI models, we obtained clinical samples with pathology information from 9 European laboratories, resulting in a diverse dataset of ~95,000 whole slide images on various scanners. We apply scanner calibration as data augmentation and novel weakly supervised AI algorithms for improved robustness. Additionally, we model perineural invasion and cribriform morphologies.

Results and discussion

An initial prototype trained on a single-clinic dataset (N=6682)can detect prostate cancer: correctly classifying >85% of benign biopsies while detecting >99% of cancerous cores in a test set (N=1631). In Gleason grading, concordance of the AI with experts (mean pairwise linear Cohen's kappa 0.62)is comparable to a standardisation panel of 23 experienced uropathologists.

Conclusion

AI can differentiate between malignant/benign and grade prostate biopsies comparably to experts. However, robust performance across laboratories and scanning equipment in real clinical settings remain to be improved. We empirically identify 4 components to achieve better prognostication and Gleason grading and allow for evaluating the system in a diagnostic clinical trial.

Keywords: Digital Pathology, Artificial Intelligence, Prostate cancer, Gleason grading, Generalization, Scanner variation

SY13.02

Fully Automated Attention based Multiple Instance Learning Predicts the Presence of Oral Epithelial Dysplasia in Whole Slide Images

Adam J Shephard[1], R M Saad Bashir[1], Neda Azarmehr[2], Hanya Mahmood[2], Shan E Ahmed Raza[1], Syed Ali Khurram[2], Nasir M Rajpoot[1]

[1)] Tissue Image Analytics Centre, Department of Computer Science, University of Warwick, United Kingdom [2)] School of Clinical Dentistry, University of Sheffield, United Kingdom

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 provides an exciting opportunity to improve the efficiency of OED diagnosis.

Material and methods

134 H&E stained whole slide images (WSIs) were collected at 40× magnification (n=108 OED, n=26 controls). A pathologist segmented the intra-epithelial layers (basal, epithelium, keratin) in 21 OED cases, and added point annotations (each nucleus) in 10 large regions (labelled as epithelial or other nuclei). NuClick, with manual refinement, was used to generate nuclear instance segmentations. HoVer-Net+ was then finetuned to perform simultaneous nuclear instance segmentation and intra-epithelial layer segmentation, before inferring on all WSIs. Patch-level morphological features were generated in the detected epithelium and used in attention-based Multiple Instance Learning (MIL) to predict which WSIs contained OED.

Results and discussion

For the segmentation of the basal, epithelial and keratin layers, HoVer-Net+ obtained an F1-score of 0.73, 0.88 and 0.82, respectively. We achieved an F1-score of 0.84 for epithelial nuclei segmentation and 0.78 for other nuclei. For case-control prediction, an F1-score of 0.86 and an AUROC score of 0.82 was achieved.

Conclusion

We show the potential of HoVer-Net+ to be applied to oral dysplasia analysis with finetuning. We also demonstrate the use of MIL approaches for histopathological diagnosis using an end-to-end fully-automated pipeline. In the future we plan to target OED detection and grade prediction on a large multicenter cohort.

Keywords: Oral Epithelial Dysplasia, Instance Segmentation, Segmentation, Multiple Instance Learning, HoVer-Net+

SY13.03

Deep learning-based renal cell carcinoma detection and classification of common subtypes in histological sections

Marie-Lisa Eich[1], Alexey Pryalukhin[2], Pavel Lazarev[3], Milana Sitova[3], Matvey Smirnov[3], Wolfgang Hulla[2], Oleg Kheyfets[4], Marta CarralCrespo[4], Alexander Quaas[1], Reinhard Büttner[1], Yuri Tolkach[1]

[1)] Institute of Pathology, University Hospital Cologne, Germany [2)] Institute of Pathology, Landesklinikum Wiener Neustadt, Austria [3)] Saint-Petersburg State Pediatric Medical University, Saint-Petersburg, Russia [4)] Clinic of Urology, Landesklinikum Wiener Neustadt, Austria

Introduction

Digital pathology allows for the automatization and objectivization of many pathology tasks. In this study, we create a deep learning-based tool for the detection of renal cell carcinomas (RCC) in histological sections (hematoxylin&eosin) and their subtyping (common histological RCC subtypes).

Material and methods

A large training dataset of 442 digitized histological slides from patients with RCC (1 slide / patient; The Cancer Genome Atlas, TCGA, cohort) with detailed manual annotations for 12 classes (9 benign and 3 tumor classes) was used for algorithm training: clear cell RCC (ccRCC) n = 131, papillary RCC (pRCC) n = 256, and chromophobe RCC (chrRCC) n = 55; overall number of image patches 1.016.551 (size 250 px at mpp 1.0). Deep learning algorithms were based on Inception-ResNetV2 architecture. Four test cohorts consisting of manually annotated digitized histological sections: 1) Hold-out cases from TCGA cohort (ccRCC/pRCC/chrRCC n = 376/24/63). 2)Institute 1 (n = 84/28/40), 3)Institute 2 (n = 178/52/26), 4)Institute 3 (n = 35/11/8).

Results and discussion

Extensive data augmentation without stain normalization was sufficient to achieve high accuracies in most cases, given a large, well-annotated training dataset. High sensitivity and specificity were achieved in test datasets for benign and tumor tissue detection of up to 0.995 and 0.994, and 0.994 and 0.995, correspondingly. Sensitivity and specificity for ccRCC, pRCC, and chrRCC subtypes were 0.988 and 0.975, 0.954 and 0.97, and 0.992 and 0.991, respectively, at patch level.

Conclusion

High levels of accuracy were achieved for a supervised deep-learning algorithm for RCC detection and subtyping in histological sections.

Keywords: Renal cell carcinoma, Deep learning, Pathology, Tool, Subtyping, AI

SY13.04

Tumor-infiltrating lymphocytes recognition in melanoma by open source deep learning convolutional neuronal network

Marco Laurino[1], Filippo Ugolini[2], Sara Simi[2], Francesca Brutti[1], Vincenza Maio[2], Vincenzo De Giorgi[3], Antonio Cossu[4], Giuseppe Palmieri[5], Clelia Miracco[6], Ketty Peris[7], Francesco Federico[8], Mario Mandalà[9, 10], Romina Nassini[11], Daniela Massi[2], Francesco De Logu[11]

[1)] Institute of Clinical Physiology , National Research Council, Pisa, Italy [2)] Department of Health Sciences, University of Florence, Florence, Italy [3)] Department of Dermatology , University of Florence, Florence, Italy [4)] Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy [5)] Institute of Genetic and Biomedical Research, National Research Council, Sassari, Italy [6)] Department of Medicine, Surgery, and Neurosciences, University of Siena, Siena, Italy [7)] Department of Surgery and Translational Medicine, Catholic University, Rome, Italy [8)] Department of Life Sciences and Public Health, Catholic University, Rome, Italy [9)] Division of Pathological Anatomy, Papa Giovanni XXIII Hospital, Bergamo, Italy [10)] Department of Medical Oncology, University of Perugia, Perugia, Italy [11)] Department of Health Sciences, University of Florence, Florence, Italy

Introduction

Tumor-infiltrating lymphocytes (TILs) are associate with a favorable prognosis in primary cutaneous melanoma (PCM). To date, this prognostic variable has not seen broad adoption due to lack of standardization. Automation could represent a solution. Here, using open-source software, we develop a new convolution neural network (CNN) for image-based automated assessment of TILs infiltration on hematoxylin-eosin stained sections in whole slide image (WSI) of PCM.

Material and methods

A CNN based on a pre-trained Inception-ResNet-v2 was trained using a retrospective cohort of 306 PCMs including two independent cohorts, one training set of (N = 238 WSI for 46204 patches) and one validation set (N = 68 WSI for 29533 patches). After the classification of PCM areas, we define an AI-based TILs density index (AI-TIL) as the ratio between the areas define TILs present and TILs absent. AI based TILs index was correlated with conventional TILs evaluation and clinical outcome.

Results and discussion

The results of the automatic score on the WSI patches of PCM show a recognition accuracy equal to 99.98% (testing set). AI-TIL index significantly discriminate WSI in three class absent, non-brisk, or brisk ($p<0.001$) and in three score class 1+, 2+ and 3+ ($p<0.001$). We show that the automated TIL scoring algorithm separates patients into favorable and poor prognosis cohorts, where higher AI-TILs scores are associate with favorable prognosis.

Conclusion

With further studies, we plan to implement the algorithm creating an easy-to-use tool that could assist pathologists to standardize the recognition of TILs in PCM.

Keywords: Melanoma, TILs, CCN, Algorithm, WSI

SY13.05

Characterization of tumor-microenvironment in H&E stained non-small cell lung cancer samples using immunohisto-chemistry-informed AI

Thomas Mrowiec[1], Sharon Ruane[2], Simon Schallenberg[4], Gabriel Dernbach[2, 3, 4], Rumyana Todorova[5], Cornelius Böhm[2], Walter de Back[2], Blanca Pablos[2], Roman Schulte-Sasse[2], Ivana Trajanovska[2], Adelaida Creosteanu[2], Emil Barbuta[2], Marcus Otte[1], Christian Ihling[1], Hans Juergen Grote[1], Juergen Scheuenpflug[1], Viktor Matyas[2], Maximilian Alber[2, 4], Frederick Klauschen[3, 4, 5, 6, 7]

[1)] Merck Healthcare KGaA, Darmstadt, Germany[2)] Aignostics, Berlin, Germany [3)] BIFOLD, Berlin, Germany [4)] Institute of Pathology, Charité Berlin, Germany [5)] Institute of Pathology, LMU Munich, Germany [6)] German Cancer Consortium (DKTK), Partner Site Berlin, German Cancer Research Center (DKFZ), Heidelberg, Germany [7)] BIH, Berlin, Germany

Introduction

Automated cell-level characterization of the tumor microenvironment (TME) is essential for data-driven immuno-oncology. The need for manual pathologist annotations limits H&E-based models, both in number and accuracy. Accurately co-registered immuno-histochemistry stains provide cell-specific labels, which improve this accuracy and can facilitate automated label extraction.

Material and methods

239 NSCLC tumors were first stained for H&E and then with CK-KL1, CD3+, CD20, Mum1, CD68 and MPO antibodies to label carcinoma (CA), lymphocyte (LY), plasma (PL), macrophage (MA) and granulocyte (GR) cells, respectively. For evaluation, representative regions were annotated by 3 trained pathologists. Same-section H&E and IHC stained images were co-registered to single-cell precision. Cells were detected in H&E and labeled using rule-based algorithms incorporating IHC information. This H&E data was used to train deep neural networks (DNNs).

Results and discussion

Correlation between pathologists (measured in cell count correlation) annotating on H&E alone is increased by 0.08 on average when registered IHC images are provided. DNNs trained with IHC-informed extracted labels outperform pathologists annotating on H&E alone (for lymphocytes, plasma cells, macrophages and granulocytes) or perform similarly (carcinoma).

Conclusion

Here, we demonstrate and quantify the improvement in inter-rater agreement when a co-registered IHC stain is provided as compared to human cell-level annotations on H&E alone. We then utilized registered same-section H&E and IHC stains to simultaneously automate the extraction of H&E training data and captured the increase in annotation quality achieved when humans had access to IHC.

Keywords: Image analysis, Artificial intelligence, Whole slide images, Immunohistochemistry, H&E, NSCLC

SY13.06

Automatic quantification of "myxoid" desmoplastic stroma in colorectal cancer: a heterogeneous feature and challenging task

Elias Baumann[1], Christian Abbet[2], Heather Dawson[1], Andrew Janowczyk[3, 4], Inti Zlobec[1]

[1)] Institute of Pathology, University of Bern, Switzerland [2)] Signal Processing Laboratory 5, EPFL, Switzerland [3)] Department of Biomedical Engineering, Case Western Reserve University, United States [4)] Precision Oncology Center, Lausanne University Hospital, Switzerland

Introduction

Myxoid stroma (MS), which contains high amounts of ground substance (GS) and is commonly observed at the invasive tumor front of colorectal cancers (CRC), has been associated with unfavorable patient outcome. To date, most studies evaluating MS are performed by visual assessment on single slides. This study aims to determine feasibility of a quantitative evaluation of GS within tumor stroma.

Material and methods

GS was estimated on H&E whole slides images (WSI@.24mpp) from two pT3 CRC cohorts (C1 n=33 patients/33 WSI for histopathological associations, C2: n=30 patients/422 WSI for heterogeneity assessment). H&E channel thresholding was applied on C1, while a U-Net segmentation model was used on C2. Tumor center, invasion front, and stroma regions were identified by a tile-based tissue-type classifier. GS-scores are defined as the sum of the five largest areas with GS>20% within a 40x microscope field equivalent (d=450µm) from WSIs with maximal GS.

Results and discussion

GS is detected in both tumor center and invasion front, yet only the latter correlates with features of tumor dissemination (lymphatic vessel invasion, p=0.02, venous invasion p=0.007). In C2, top five GS WSIs by GS-score are considered. Largest two/five GS-regions originate from 1.5/2.5 slides (respectively) indicating that large GS areas are distributed over several WSI.

Conclusion

Automated quantification of GS is feasible, however numerous challenges need to be overcome, including similarity with mucin, and dependency on stain and scan quality. Despite intra-patient heterogeneity, employing solely the slide with the largest amount of GS seems to be indicative of a more aggressive CRC.

Keywords: Colorectal Cancer, Stroma, Desmoplastic, Myxoid, Segmentation, Heterogeneity

SY13.07

Generation of Synthetic Colorectal Cancer Histology Images from Bespoke Glandular Layouts

Srijay Deshpande[1], Fayyaz Minhas[1], Nasir Rajpoot[1]
[1)] Tissue Image Analytics Centre, University of Warwick, United Kingdom

Introduction

Collection of annotated data for data-hungry algorithms in computational pathology requires highly trained pathologists. For tasks like gland segmentation, manual generation of annotations/component masks highlighting glandular regions can be a laborious task. Generating synthetic images reduces the cost of annotations and can help with pre-training of deep-learning models whose results can be further utilized for downstream analysis tasks for computer-assisted diagnostic and prognostics.

Material and methods

We propose a Generative Adversarial Network based framework that can generate colon images along with component masks simultaneously from bespoke glandular layout, a layout where users can specify locations and sizes of the glands. The glandular layout is consumed by the mask generator to generate respective binary glandular masks. These masks are then wrapped into an intermediate tensor, which is then passed through the neural models generating the component mask and the final tissue image subsequently. For evaluation, we use the DigestPath dataset that contains colon cancer images with annotated glandular regions.

Results and discussion

While comparing with real images, we obtain Frechet Inception Distance, a proximity metric, of 134 for synthetic images and 485 for the random noise. To assess the utility of generated annotated pairs for evaluation of gland segmentation algorithms, we train U-net on training images, compute segmentation masks of both real and synthetic images from the test set, and obtain an average Dice index of 0.9022 and 0.9001, respectively.

Conclusion

The proposed framework can generate annotated pairs of realistic colon tissue images and their component masks. We demonstrate the applicability of synthetic annotated pairs for evaluation of gland segmentation algorithms.

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

ABSTRACTS: POSTER PRESENTATIONS

P01

Virtual multidisciplinary tumor board impact after the COVID-19 pandemic

Peter Ouillette[1], Liron Pantanowitz[1]
[1)] Pathology, University of Michigan, United States

Introduction

The COVID-19 pandemic stressed the practice of pathology. Digital pathology offers a solution for many pathology laboratories to sustain clinical patient care during the pandemic. The aim of this study was to determine how the COVID-19 pandemic impacted virtual multidisciplinary meetings at our institution.

Material and methods

At our institution representative glass slides for tumor boards are selected for scanning. Links to WSIs and LIS reports are displayed in an online interface developed specifically for tumor boards. Images are available for immediate retrieval for three years, and thereafter archived to tape. The utility of our institution's virtual tumor board service was evaluated before and since (March 1, 2020) the COVID-19 pandemic.

Results and discussion

Prior to the pandemic, 9 tumor boards were already digital, whereas this increased to 12 post-pandemic. Scanning activity for tumor boards increased from around 500 slides/month pre-COVID to up to 700 slides/month post-COVID. However, since overall slide scanning activity in our department experienced robust year-on-year growth, this proportion of work was negligible.

Conclusion

Having an existing infrastructure to support virtual multidisciplinary tumor boards made it easy for our department to sustain this clinical service with the arrival of the COVID-19 pandemic. The utilization of virtual tumor boards increased moderately in our pathology department after the COVID-19 pandemic. However, the workload impact for our digital pathology service of increased tumor board scanning during the COVID-19 pandemic has been negligible.

Keywords: Tumor board, COVID-19, Whole slide imaging

P02

Automated Scoring System of HER2 in Pathological Images under the Microscope

Zichen Zhang[1, 2], Lang Wang[2], Shuhao Wang[2]

[1)] MSCS, Macalester College, United States [2)] R & D, Thorough Images, China

Introduction

Breast cancer is the most common cancer among women worldwide. The human epidermal growth factor receptor 2 (HER2)with immunohistochemical (IHC) is widely used for pathological evaluation to provide the appropriate therapy for patients with breast cancer. However, the deficiency of pathologists is extremely significant in the current society, and visual diagnosis of the HER2 overexpression is subjective and susceptible to inter-observer variation. Recently, with the rapid development of artificial intelligence (AI) in disease diagnosis, several automated HER2 scoring methods using traditional computer vision or machine learning methods indicate the improvement of the HER2 diagnostic accuracy, but the unreasonable interpretation in pathology, as well as the expensive and ethical issues for annotation, make these methods still have a long way to deploy in hospitals to ease pathologists' burden in real.

Material and methods

We propose a HER2 automated scoring system that strictly follows the HER2 scoring guidelines simulating the real workflow of HER2 scores diagnosis by pathologists. Unlike the previous work, our method takes the positive control of HER2 into account to make sure the assay performance for each slide, eliminating work for repeated comparison and checking for the current field of view (FOV) and positive control FOV, especially for the borderline cases. Besides, for each selected FOV under the microscope, our system provides real-time HER2 scores analysis and visualizations of the membrane staining intensity and completeness corresponding with the cell classification.

Results and discussion

Our rigorous workflow along with the flexible interactive adjustion in demand substantially assists pathologists to finish the HER2 diagnosis faster and improves the robustness and accuracy.

Conclusion

The proposed system will be embedded in our Thorough Eye® platform for deployment in hospitals.

Keywords: HER2, rigorous workflow, automated scoring system

P03

Automatic lymphocyte quantification in virtual CD20-CD3 staining generated from H&E images using GAN colorization

Huu-Giao Nguyen[1], Jose A. Galvan[1], Heather Dawson[1], Alessandro Lugli[1], Inti Zlobec[1]

[1)] Institute of Pathology, University of Bern, Switzerland

Introduction

CD20 and CD3 are commonly used specific markers of B- and T-lymphocytes, respectively, and help identify and quantify tumor infiltrating lymphocytes (TIL). The quantification of lymphocytes on H&E stains, however, can be challenging for both human observers and machine learning algorithms. The study aims to automatically detect and count B- and T- lymphocytes in virtual CD20-CD3 staining generated from corresponding H&E stains using a generative adversarial network (GAN) method and color deconvolution.

Material and methods

An in-house training dataset with 34790 H&E images (at 40x) and its re-staining CD20-CD3 images extracted from 1160 TMA spots of 315 patients was considered. We applied the tissue structure extractor on input H&E image (color wash-out) and generator and discriminator networks to learn the CD20-CD3 color (re-stain). A color deconvolution was applied to create fluorescence-like images from virtual CD20-CD3 generated. Finally, we extracted the bounding-box of two cell populations B-cell (brown) and T-cell (red).

Results and discussion

Based on a validation set of other 2100 H&E images, a high correlation was obtained with the Intersection over Union score (92.1%) of the bounding boxes between real and generated images. We also obtained an excellent score (0.865) of Intraclass Correlation Coefficient, the agreement between algorithm and human lymphocyte counts, whereby the overlap of cells in a small area remains challenging.

Conclusion

This study introduces an effective solution for lymphocyte quatification in H&E images, a baseline for TIL analysis or immunoscore measure. It also helps to quickly create and extend a lymphocyte training dataset (deep learning enhancement).

Keywords: tumor infiltrating lymphocytes, CD20-CD3 staining, lymphocyte quatification, immunoscore measure, generative adversarial network, image colorization

P04

A Pix2Pix model for Ki-67 tissue expression prediction on H&E-stained OSCC histopathological images

Francesco Martino[2], Gennaro Ilardi[1], Silvia Varricchio[1], Rosa Maria Di Crescenzo[1], Stefania Staibano[1], Francesco Merolla[3]

[1)] Department of Advanced Biomedical Sciences, Pathology Unit, University of Naples , Italy
[2)] Dedalus HealthCare, Division of Diagnostic Imaging IT, Austria [3)] Department of Medicine and Health Sciences , University of Molise, Italy

Introduction

Anatomical Pathology is living its third revolution through AI. Other than classification, detection, and segmentation models, the spotlight is on predictive models capable of generating virtual slides representative of what would be produced by laboratory activity, reducing the usage of consumables and the turn-around time.

Material and methods

We trained a deep learning model to generate virtual Ki-67 immunohistochemistry slides from H&E images. To train our model, we retrieved 175 Oral Squamous Cell Carcinoma from the archives of the Pathology Unit of the University Federico II and built four TMAs. We obtained one slide from each TMA; each slide was firstly stained with H&E protocol and subsequently destained and converted to anti-Ki-67 immunohistochemistry. After digitizing the slides, we used a dearray procedure to disassemble the cores, tiling them to create a dataset to train a Pix2Pix model.

Results and discussion

Our model resulted in realistic synthetic images, as a panel of interviewed pathologists could not recognize the synthetic image. In contrast, the IHC positivity, quantified using QuPath, resulted in high levels of concordance between real and synthetic images, achieving an accuracy of 74.51%, with high sensitivity (76.67%) and specificity (71.43%) at a 5% cut-off.

Conclusion

Overall, our model allows us to foresee a promising method to collect Ki-67 positivity information directly on H&E slides, limiting the laboratory workload, speeding up the TAT of histological samples, and improving the management of patients.

Keywords: OSCC, Ki-67, Proliferation, Pix2Pix, GAN

P05

Prediction of Ki67 scores from H&E stained breast cancer sections using convolutional neural networks

Philippe Weitz[1], Balazs Acs[2, 3], Johan Hartman[2, 3], Mattias Rantalainen[1]

[1)] Department of Medical Epidemiology and Biostatistics, Karolinska Institute, Sweden
[2)] Department of Oncology-Pathology, Karolinska Institute, Sweden [3)] Department of Clinical Pathology and Cytology, Karolinska University Laboratory, Sweden

Introduction

Ki67 is an established clinical marker of proliferation in breast cancer that is quantified by an immunohistochemistry (IHC)-based assay and associated scoring of positively stained cells. However, clinical IHC-based assays are resource-intensive to maintain and thus not available in all environments. Here we assess to what extent it is possible to predict Ki67 scores directly from whole-slide-images (WSIs) of routine hematoxylin and eosin (H&E) stained tissue sections, which could increase access in settings where IHC is unavailable.

Material and methods

We compared four different deep learning-based approaches to predict Ki67 scores in a dataset that consists of matched H&E and Ki67 WSIs from 126 female primary breast cancer patients. The first method uses WSI-level labels to optimize models. The second approach generates local labels through WSI H&E and IHC registration. The third and fourth method rely on digital restaining with generative-adversarial-networks (GANs).

Results and discussion

Spearman correlations for the different methods range from 0.428 for digital restaining to 0.527 for the registration-based approach in 5-fold cross-validation (CV). This corresponds to AUROCs ranging from 0.783 to 0.827 for classifying WSIs against a dichotomized Ki67 score at 20% positively stained cells.

Conclusion

These findings suggest that it is possible to predict Ki67 scores from H&E stained WSIs to some extent. We are therefore currently expanding the study to a cohort with approximately 2,000 matched Ki67 and H&E WSIs.

Keywords: deep learning, Ki67, registration, digital restaining, WSI, image analysis

P06

Cell segmentation and quantification on H&E images using vision transformer model

Thien Do[1, 2], Tuan-Anh Tran[2], Inti Zlobec[1], Huu-Giao Nguyen[1]

[1)] Institute of Pathology, University of Bern, Switzerland [2)] Faculty of Computer Science & Engineering, Ho Chi Minh City University of Technology, Vietnam

Introduction

Nucleus segmentation, classification, and quantification within H&E stained histology images can be challenging for both human observers and machine learning algorithms. It plays an important role to enable the extraction of interpretable cell-based features and explainable machine learning models in digital pathology. Here, we apply the vision transformer model for semantic segmentation and counting of different nucleus categories in H&E colorectal cancer images.

Material and methods

We used Lizard, a publicly available dataset, of 4'981 non-overlapping H&E images at 20x objective magnification (~0.5 microns/pixel) from six different data sources. For each image, each instance was segmented and classified into one of six following categories: epithelial, lymphocyte, plasma, eosinophil, neutrophil, or connective tissue. We apply the Segmenter, a state-of-the-art vision transformer architecture that relies on the output of a sequence of patch embeddings, and a point-wise linear decoder for a segmentation map.

Results and discussion

The multi-class panoptic quality (mPQ) is used to evaluate the performance of the model. It includes segmentation quality (based on the Intersection Over Union of our segments and ground truth) and recognition quality (based on the precision and recall of object prediction). We obtained the mPQ of 0.354 ± 0.017 (a better result compared with 0.265 ±0.013 of U-Net model). Especially, the detection of lymphocytes is higher with the PQ score of 0.525 ± 0.027.

Conclusion

This study introduces an end-to-end effective solution for nucleus semantic segmentation in H&E images based on a recent vision encoder-decoder transformer. It is a first step towards the solution for tumor environment representation and understanding.

Keywords: Nucleus segmentation, lymphocyte, vision transformer, digital pathology

P07

Quantification of the Immune Content in Neuroblastoma: Deep Learning and Topological Data Analysis in Digital Pathology

Nicole Bussola[1, 2], Bruno Papa[1], Ombretta Melaiu[3], Aurora Castellano[3], Doriana Fruci[3], Giuseppe Jurman[1]

[1)] Data Science for Health, Bruno Kessler Foundation, via Sommarive 18, 38123 Trento, Italy
[2)] CIBIO Department, University of Trento, via Sommarive 14, 38123 Trento, Italy [3)] Department of Paediatric Haematology/Oncology and of Cell and Gene Therapy, Ospedale Pediatrico Bambino Gesù IRCCS, Piazza di Sant'Onofrio 4, 00165 Roma, Italy

Introduction

WSI original data are leveraged here to design a human-in-the-loop ML framework that could aid clinicians in NB risk assessment. DL predictive models with SOTA architectures are trained to count lymphocytes, followed by a post processing pipeline able to detect nuclei from the predicted density maps.

Material and methods

EUNet (U-Net + EfficientNet) is trained to detect lymphocytes in WSIs stained by CD3 marker. Training set consists of 3782 images from an original 54 WSIs OPBG collection with 73,751 manually annotated lymphocytes. Resampling strategies, data augmentation and Transfer Learning are adopted for reproducibility and overfitting/selection bias reduction. Topological Data Analysis, Persistence Diagram and Betti curves are used to define activation maps from different layers of the neural network at different stages of the training process, integrated with UMAP and HDBSCAN for clustering relevant subgroups and structures. TwoNN is leveraged to study the variation of the intrinsic dimensionality of the model. All the experiments were run on the Microsoft Azure cloud platform.

Results and discussion

The model achieves MAE 3.1 on test set, showing agreement between densities estimated by EU-Net and by pathologists. UMAP algorithm unveils interesting patterns consistent with pathological characteristics, highlighting novel insights into the dynamics of the intrinsic dataset dimensionality at different stages of the training process.

Conclusion

The promising results pave the way towards the development of an effective learning tool aimed at timely and precisely quantifying the immune content within cancer cells, representing a precious support for the pathologist, with an effective impact on the daily routine in a clinical setting.

Keywords: Machine learning, Topological Data Analysis, Density Maps

P08

Improving cell classification with hard negative mining: an example of lymphocyte classification in colorectal cancer

Ana Frei[1], Andreas Fischer[2], Inti Zlobec[1]

[1)] Institute of Pathology, University of Bern, Switzerland [2)] Institute of Complex Systems, University of Applied Sciences and Arts Western Switzerland (HES-SO), Switzerland

Introduction

Precise estimation of the cellular composition within colorectal cancers could be used as a biomarker in different clinical scenarios, including predicting therapy response and patient outcome. However, the automated classification of cells (primarily lymphocytes) on H&E images is difficult due to high intra-class nuclei heterogeneity. To alleviate this issue, we used hard negative mining to learn complex sample representation and improve model performance.

Material and methods

The cell classification model was trained on Lizard dataset (20x), containing cell labels for five different colorectal datasets. 16x16px patches were cropped around the cells of interest in the original images. ResNet50 was trained from scratch to perform binary classification: lymphocytes vs all other cell types, using balanced classes. To tackle the overclassification of lymphocytes, the trained model was applied on the whole training data, containing unseen examples, to highlight misclassified samples and those with low probability predictions. The model was then finetuned on these complex samples. The whole finetuning process was repeated a second time to get the final model.

Results and discussion

The classification F1 score improved by 3% after two consecutive hard negative mining steps. The final model achieved an 89.2% average weighted F1 score on the unseen test set.

Conclusion

Hard negative mining significantly improved binary cell classification ($p < 0.001$). The final model reasonably estimates the cellular composition of the images. In future work, this cell classification will be used to study the spatial organization of these cells in the tumour microenvironment and their predictive power regarding therapy response and patient outcome.

Keywords: automated cell classification, hard negative mining, lymphocyte classification

P09

A deep learning framework for stratification of Alzheimer's disease patients using whole slide histopathological brain tissue images

Anuradha Kar[2], Gabriel Jimenez[2], Mehdi Ounissi[2], Lea Ingrassia[2], Susana Boluda[1, 2, 3, 4, 5], Benoit Delatour[1], Lev Stimmer[4], Daniel Racoceanu[1]

[1)] Sorbonne Université, Sorbonne Université, France [2)] ICM, Institut du Cerveau -Paris Brain Institute, France [3)] CNRS, CNRS, France [4)] Inserm, Inserm, France [5)] Laboratoire de neuropathologie Raymond Escourolle, Hôpital de la Pitié Salpêtrière, France

Introduction

Aß peptides and tau protein aggregates present in brain gray matter are considered as the biomarkers of Alzheimer's disease (AD). This study aims to understand how the topography and morphology of these aggregates can be used for stratification of AD patients into very rare, rapidly progressive AD and other common forms of AD. For this, a deep learning based image analysis framework is developed for automatic localization and characterization of peptide aggregates. It includes multiple deep learning architectures aiming to extract a wide range of quantitative information on the aggregates, i.e. diffuse plaques and neurofibrillary tangles within histopathological whole slide images (WSIs) of human brain tissue.

Material and methods

A dataset of 6 whole slide images of postmortem human brain tissue is used in this study. These are fully annotated by neuropathologists yielding a set of more than 30,000 annotated plaques and tangle objects A deep learning pipeline combining a classifier and a UNet model is trained initially for detection and segmentation of tau aggregates in WSIs. Other deep learning architectures used in this framework include attention-UNet models and graph based networks.

Results and discussion

With the framework it is currently possible to detect a majority of the tau aggregates and determine aggregate boundaries with high accuracy. Other derivable parameters include surface area, perimeter, circularity, convexity, proximity and density of the aggregates.

Conclusion

The proposed WSI analysis framework would provide novel insights into the evolution of AD as well as facilitate the patients' stratification through studying the correlation between patient's characteristics and the morphological statistics of AD biomarkers.

Keywords: deep learning, whole slide images, histopathology, Alzheimer's disease, segmentation, stratification

P10

Evaluating generic AutoML tools for computational pathology

Lars Ole Schwen[1], Daniela Schacherer[1], Christian Geißler[2], André Homeyer[1]

[1)] Fraunhofer MEVIS, Institute for Digital Medicine, Germany [2)] DAI-Labor, Technische Universität Berlin, Germany

Introduction

Image analysis tasks in computational pathology are commonly solved using convolutional neural networks (CNNs). The selection of a suitable CNN architecture and hyperparameters is usually done by exploratory iterative optimization, which is computationally intensive and requires a lot of manual work. There are tools for automated architecture search and hyperparameter optimization, but these are generic and not designed specifically for computational pathology.

Material and methods

We performed a comprehensive evaluation [Schwen et al., Informatics in Medicine Unlocked 2022, http://doi.org/10/gn8zkh] of two generic AutoML tools by repeating experiments from literature for three common classification tasks for histological images: tissue classification [Coudray et al., Nature Medicine 2018, http://doi.org/10/ctzr], mutation prediction [Kather et al., Nature Medicine 2019, http://doi.org/10/ggsd8z], and grading [Arvaniti et al., Scientific Reports 2018, http://doi.org/10/gd4gcs]. One tool ran on-premises (AutoGluon) and the other in the cloud (Google AutoML Vision).

Results and discussion

We found that the default CNN architectures and parameterizations of the evaluated AutoML tools already yielded classification performance on par with the original publications. Despite additional computational effort, hyperparameter optimization for these tasks did not substantially improve performance. However, performance varied substantially between classifiers obtained from individual AutoML runs due to non-deterministic effects.

Conclusion

Generic CNN architectures and AutoML tools can provide a viable alternative to manual optimization of CNN architectures and parametrizations. This allows developers of software solutions for computational pathology to focus on more difficult-to-automate tasks, such as data curation.

Keywords: Convolutional neural networks, AutoML, Tissue classification, Hyperparameter optimization, Reproducibility

P11

Adoption of digital techniques and use of artificial intelligence in Histopathology - A validation study on Chorionic Villi

Talat Zehra[1]

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

Introduction

The ever increasing use of digitization and artificial intelligence has left its impact on every field of life. Since the last one year, due to Covid-19 pandemic, the world has witnessed an exponential digital adoption in every field of life. With the aid of Artificial intelligence, the work of pathologist can become much easier, as these techniques can accurately quantify, measure and picked up small pathologies which can be missed by pathologist if he is overworked

Material and methods

We took 60 slides of previously diagnosed cases of products of conception which is a very common pathology a pathologist come across in his routine practice. Glass slides were scanned into digital slides using microscope camera at 4x objective. Digital slides were imported into Aiforia Oy software for all subsequent steps, including annotation, training, and analysis of digital slides

Results and discussion

Out of 60 cases of previously diagnosed cases, the software was able to diagnose 50 cases correctly. The concordance between manual diagnosis versus automated detection was 83.33%

Conclusion

Though, digital pathology and artificial intelligence are relatively new and novel techniques but now there is growing adoption of these techniques worldwide. So it is the right time for the people of developing world to adopt this novel technique as it can overcome the scarcity of pathologists all over the world in general and in developing world particularly. The results of this study were encouraging. We had certain limitations because of the unavailability of digital microscope or a pathology slide scanner

Keywords: Digital pathology, Artificial intelligence, Chorionic villi

P12

Oral Squamous Cell Carcinoma Image Segmentation Using a Multi-encoder U-Net

Andrea Pennisi[1], Domenico D. Bloisi[2], Daniele Nardi[3], Stefania Staibano[4], Francesco Merolla[5]

[1)] Department of Computer Science, University of Antwerp, Belgiumm [2)] Department of Mathematics, Computer Science, and Economics, University of Basilicata, Italy [3)] Department of Computer Science, Control, and Management Engineering, Sapienza University of Rome, Italy [4)] Department of Advanced Biomedical Sciences, Pathology Unit, University of Naples "Federico II", Italy [5)] Department of Medicine and Health Sciences "V. Tiberio", University of Molise, Italy

Introduction

Oral malignancies are responsible for approximately 170,000 deaths worldwide each year. We focused on oral squamous cell carcinoma (OSCC), which accounts for 80-90 percent of all malignant oral neoplasms.

Material and methods

We describe a new deep learning-based method for pixel-level segmentation of whole slide image (WSI) data. The suggested method adds a multi-encoder structure to the well-known U-Net design. Our multi-encoder U-Net network, in particular, is a multi-encoder single decoder network that takes an image as input and separates it into tiles.

Results and discussion

Each tile in the latent space is encoded by an encoder, which is followed by a convolutional layer that merges the tiles into a single layer. The previous up-sampled layer is taken by each layer of the decoder.

Conclusion

Experiments were conducted on the ORal Cancer Annotated (ORCA) dataset, which contains annotated data from the TCGA repository and is freely available. The success of the suggested approach is demonstrated by quantitative experimental findings acquired using three separate quality metrics (Pixel-wise Accuracy, Dice Similarity Coefficient, and Mean Intersection Over Union).

Keywords: OSCC, Segmentation, ORCAset, U-NET

P13

Fine-grained two-step segmentation approach to process digital pathology images in breast cancer

Daniel García León[1], Yinxi Wang[1], Philippe Weitz[1], Mattias Rantalainen[1]

[1)] Medical Epidemiology and Biostatistics Department, Karolinska Institutet, Sweden

Introduction

Tissue segmentation, including background and adipose tissue segmentation, is a key pre-processing step in AI-based computational pathology that still suffers from poor performance. Here, we present a two-step segmentation pipeline to improve quality in whole slide image pre-processing.

Material and methods

We included 200 hematoxylin and eosin test images from two breast cancer studies (s1 and s2). Five baseline algorithms were considered: Otsu-based (OB), Foreground Extraction from Structure Information (FESI), Improved FESI (iFESI), TissueLoc (TL), and Histomics (Hist). First, a background removal step was benchmarked after defining our reference. Secondly, we targeted fat in the benchmark reference. To do so, 100 additional train images were fed to a Gaussian mixture model per study, implementing a non-stained regions (NSR) filter. Both sensitivity, specificity and intersection-over-union (IoU) test metrics were calculated per step.

Results and discussion

Among considered approaches, FESI defined our reference. Baseline algorithms exhibited variable performance (median IoU) to target background: OB (s1:71%; s2:26.4 %), iFESI (s1:83.2%; s2:46.5 %), TL (s1:56%; s2:14.1%) and Hist (s1:72.1%; s2:30.7%). Given the diverse presence of adipose tissue in all segmentations, we decided to exploit this to refine our reference. By adding a second step NSR filter, it was possible to improve pixel-level segmentation performance (median IoU) in our reference: OB (s1:87.5%; s2:71.2%), iFESI (s1:81%; s2:50.1%), TL (s1:78.8%; s2:35.4%) and Hist (s1:81.8%; s2:59.5%).

Conclusion

Adding a NSR filter as a second step after FESI improved segmentation concordance with all evaluated algorithms, suggesting that a two-step approach may increase segmentation granularity in digital pathology applications.

Keywords: Segmentation, Breast cancer, Computational pathology

P14

Retaining Whole Slide Image Information for Cancer Prediction

Robin Sebastian Mayer[1], Steffen Gretser[1], Brahima Malle[1], Peter Wild[1], Nadine Flinner[1]

[1)] Computational Pathology, Dr. Senckenbergisches Institut für Pathologie Frankfurt, Germany

Introduction

Whole Slide Images (WSI) are high resolution images of tissue slides used in pathology. However, at full resolution WSI's result in several gigabyte large files. This poses a challenge for hardware e.g. for training convolutional neuronal networks (cNN). Therefore, WSI's are generally tiled into smaller patches. However, by separating WSI's into smaller tiles, global information is lost. For a multi resolution approach it is essential that training works for different scaling levels.

Material and methods

WSIs were annotated by a pathologist by encircling cancerous areas. Then the described tiling technique was applied and an ensemble cNN was trained on the TCGA-OV dataset and tested on an external KGU dataset. Based on the predictions from the first round of training, we selected tiles for the pathologist's revision of the labels. Then, corrected tile level annotations were used. Finally, tiles were rescaled and training was repeated.

Results and discussion

After training we achieved an AUC of 0.95 in validation and 0.91 for our external KGU dataset. Additionally, the validation AUC could be further improved to 0.98 using the corrected labels. For the test, where no label correction was applied, the AUC increased to 0.92. When training with scaled input data, a performance loss of ~30% is observed for the TCGA dataset, while the KGU test set maintains its performance.

Conclusion

The established technique of tiling WSIs is effective to achieve high performance for cross institute WSI analysis. When scaling images for machine learning tasks, it is important to monitor the performance impact as datasets respond differently.

Keywords: whole slide image, label quality, scaling

P15

Will an AI algorithm ever replace the dermatopathologist? A single institutional study

Gerardo Cazzato[1], Anna Colagrande[1], Giuseppe Ingravallo[1], Eugenio Maiorano[1], Angelo Vacca[2], Alessandro Massaro[2]

[1)] Section of Pathology, Department of Emergency and Organ Transplantation (DETO), University of Bari "Aldo Moro", Bari, 70124, Italy., University of Bari , Italia [2)] Department of Biomedical Sciences and Human Oncology Chief Clinica Medica , University of Bari, Italia

Introduction

Although this is the prerogative of the informatics and technological branches, the use of software and new technologies has spread to many different fields of medicine, indeed to practically all branches, including pathological anatomy and, therefore, also the subbranch of dermatopathology

Material and methods

The artificial intelligence image processing algorithm used to classify and to enhance anomalies contained in the microscope image is the Fast Random Forest (FRF). The learning process of the algorithm is based on a preliminary classification of cluster of pixels of the same image [*] including possible Melanoma's areas: the preliminary identification of Melanoma morphological features, represents the labelling approach typical of machine learning supervised algorithms. The FRF testing provides as output the processed image with colored enhanced Melanoma pixel clusters (each class selected in the learning step is represented by a color), probabilistic maps (high probability highlighted by white to identify an anomaly in a specified image region), and algorithm performance indicators (precision, recall, and Receiver Operating Characteristic -ROC-curves.

Results and discussion

The adopted image vision diagnostic protocol, is structured in the following steps: 1) image acquisition by selecting the best zooming of the microscope; 2)preliminary identification of macro-areas of defect in each pre-selected image; 3)identification of a class of a defect in the selected macro-area; 4)training of the supervised machine learning FRF algorithm, by selecting the micro-defect in the macro-area; 5) executing of the FRF algorithm until image vision performance indicator is good; 6)analysis of the output images enhancing lesion defects.

Conclusion

The probability image is useful to better discriminate information about ambiguous lesions. A single probability image is referred to a particular class of "defect", and enhances, by the white color, the defect distribution in the whole analyzed image.

Keywords: Dermatopathology, AI, Digital Pathology, Algorithm, WSI, Malignant melanoma

P16

AI-assisted detection of Perineural Invasion by Multiple Instance Learning shows robust diagnostic output

Patricia Raciti[1], Juan A. Retamero[1], Emre Gulturk[1], David Klimstra[1]
[1)] Medical Affairs, Paige AI, United States

Introduction

The detection of perineural invasion (PNI) in prostatic core needle biopsies (PCNB) is an independent prognostic factor in clinically localized disease and might make active surveillance for prostatic cancer a less viable option. Detection of PNI can be challenging and time consuming. AI-based digital diagnostics for the detection of PNI can alleviate these challenges when applied to whole side images (WSIs) of PCNB.

Material and methods

An AI-based PNI detection system was developed using multiple instance learning, which is an unsupervised training method that requires no pathologist annotations. The system was trained using several thousand WSIs. The PNI model is applied only to WSIs that are suspicious for cancer by Paige Prostate Detect, which utilizes a multiple instance learning approach based on Campanella et al. (2019) to train a whole-slide image classifier using an SE-ResNet50 convolutional neural network.

Results and discussion

The AI-based PNI detection system shows an AUC of 0.965. Importantly, on WSIs with ISUP 1-5, sensitivity is maintained. Pathologists are presented with a tissue map that demonstrates the foci that are suspicious for PNI as a model output, thus allowing the user to detect the presence or absence of this feature while also provide a total burden of PNI.

Conclusion

A highly accurate, efficient and robust AI-based PNI detection system applied to WSIs can enhance the detection of PNI particularly in cases in which active surveillance/watchful waiting might be a consideration. This facilitates the pathologist's detection of PNI, also in cases with high tumoral burden and also in specimens with high grade cancer.

Keywords: Prostatic biopsy, Perineural invasion (PNI), AI assisted diagnosis, Pathologist , Diagnostic accuracy , Diagnostic efficiency

P17

Improvement of detection accuracy of deep learning in thyroid cancer cells using several histological resources

Satomi Hatta[1, 2], Kunihiro Inai[1], Shohei Higuchi[1, 2], Yoshiaki Imamura[2], Yoshihito Ichiuji[3], Shingo Mabu[3], Hidekata Hontani[4], Soji Kido[5], Hironobu Naiki[1]

[1)] Division of Molecular Pathology, University of Fukui, Japan [2)] Division of Diagnostic/Surgical Pathology, University of Fukui Hospital, Japan [3)] Graduate School of Sciences and Technology for Innovation, Yamaguchi University, Japan [4)] Department of Computer Science, Nagoya Institute of Technology, Japan [5)] Department of Artificial Intelligence Diagnostic Radiology, Osaka University Graduate School of Medicine, Japan

Introduction

Deep learning has been studying as an automatic identification technique of malignant tumors in HE images, however, the discrimination performance depends on the quality and quantity of training images such as the imbalance of each histological type and the staining procedures among facilities. Using thyroid cancer cases, we investigated to improve the accuracy by focusing on the equilibrating the frequency of histological imbalance and the compensation of color variation among samples.

Material and methods

The HE-stained thyroid cancer images in our facility were digitally captured and they were annotated as 6 histological patterns. Commercially available tissue microarrays (TA) were purchased to supplement the tissue images with low frequency. CycleGAN was used to transform the color tone of the TA images to that of our facilities followed by evaluating the efficiency of color correction. Additionally, we explored the best discriminative condition for intra-operative frozen specimens (FS) from following four slide sets: in-house HE, in-house FS, or combinations of them with or without color-adjustment.

Results and discussion

Mean recall of all histological types was improved in conjugation with color-corrected TA (from 69.9% to 75.0%). Especially in 3 minor populations, the value, which represented rather lower than initial value (38.9%) by addition of color-untransformed TA (34.1%), turned into an increase (55.1%) by the color-adjustment. Concerning FS-discrimination, the best discriminator was constructed only from own FS.

Conclusion

These findings suggest that the use of color-corrected TA was useful for resolving sample imbalance, whereas FS may be rather desirable to build an independent detector.

Keywords: deep learning, pathology, thyroid

P18

Implementation of an AI Solution for Primary Breast Cancer Diagnosis and Reporting in Clinical Routine

Judith Sandbank[1, 2], Alona Alona [2], Ira Krasnitsky[2], Yuval Raz[2], Raz Ziv[2], Assaf Peled[2], Tal Patalon[3], Maya Grinwald[2], Manuela Vecsler[2], Chaim Linhart[2]

[1)] Institute of Pathology, Maccabi Healthcare Services, Israel [2)] Ibex Medical Analytics, Ibex Medical Analytics, Israel [3)] Kahn Sagol Maccabi Research & Innovation Center, Maccabi Healthcare Services, Israel

Introduction

There is high demand to develop clinically useful computer-assisted diagnostic solutions to bring significant efficiency improvements for pathologists, reduce turnaround times, decrease error rates, and provide objective and reproducible diagnoses. This study aims to introduce an AI tool to support the pathologists in their review and reporting of breast biopsies in a centralized pathology laboratory.

Material and methods

A two-arm study comparing the standard of care (using a microscope) with pathologists conducting the reporting using an AI solution workflow. Nine pathologists reported on 100 breast biopsies. Each case was reported twice, both with microscope and with the AI solution. Discrepant reports were adjudicated and reviewed by a breast specialist pathologist

Results and discussion

The AI algorithm demonstrated high performance with an AUC = 0.99 for cancer detection and with NPV of 100% and PPV of 93%, respectively. The overall agreement between the two arms on benign and invasive cases was 100%, while on DCIS/ADH was 83.3%. Four cases originally diagnosed as ADH were diagnosed with the AI as benign, 3 were adjudicated benign and 1 case as ADH. In addition, in the AI arm there was a 30% reduction in ordering of IHC slides

Conclusion

This study reports the first successful implementation of a multi feature AI solution that automatically reports clinically relevant diagnostic parameters regarding invasive and in situ breast carcinoma, offering an important tool for computer-aided diagnosis in routine pathology practice.

Keywords: AI, deep learning, biopsy, Breast, digital pathology, carcinoma

P19

Cytomorphologic evaluation of bone marrow single-cell images using deep learning methods

Christian Matek[1, 2]

[1)] Universitätsklinikum Erlangen [2)] Institute of AI for Health, Helmholtz Zentrum München

Introduction

Cytomorphologic evaluation of bone marrow samples is a key step in the diagnostic workup of hematologic diseases, and is routinely performed by cytomorphologists differentiating and counting various malignant and non-malignant cell types using a light microscope.

Material and methods

From the perspective of image classification, recent progress in algorithms is promising to support human examiners in the tedious and time-consuming task of bone marrow cell differentiation. Here, we present an expert-annotated database of more than 170,000 single bone marrow cells, compiled in a large laboratory specializing in leukemia diagnostics. It represents the largest publicly available data source of its kind to date, allowing development of accurate data-driven algorithms for single-cell classification.

Results and discussion

A residual convolutional neural network (RexNeXt-50) is trained using the image database compiled. Performance of the algorithm is evaluated both internally, and using independent external validation data as well as explainability methods. We find that the algorithm exhibits high performance levels for most diagnostically important cell classes. Furthermore, the algorithm shows a deviation pattern from ground truth similar to human examiners. Both GradCAM and saliency maps suggest the algorithm has learned to focus on the relevant image content, i.e. the main leukocytes shown, and maps out known key features of specific cell classes. Analysis of the hidden network layers shows clustering of extracted features according to ground truth annotation. We also discuss generalization to related diagnostic settings, e.g. differentiation of peripheral blood, or other patient cohorts.

Conclusion

Residual networks allow developing a powerful algorithm for leukocyte differentiation using a large, expert-annotated morphology database of a wide spectrum of hematologic diseases. Using explainability methods, individual classification decisions can be investigated, showing similarities to known features of specific cell classes.

Keywords: Hematology, blood smears, Leukemia diagnostics, residual networks, Explainable AI

P20

Artificial Intelligence for Detecting Perineural Invasion in Prostate Biopsies

Kimmo Kartasalo[1], Peter Ström[1], Pekka Ruusuvuori[2, 3], Hemamali Samaratunga[4], Brett Delahunt[5], Toyonori Tsuzuki[6], Martin Eklund[1], Lars Egevad[7]

[1)] Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Sweden [2)] Institute of Biomedicine, University of Turku, Finland [3)] Faculty of Medicine and Health Technology, Tampere University, Finland [4)] School of Medicine, Aquesta Uropathology and University of Queensland, Australia [5)] Department of Pathology and Molecular Medicine, Wellington School of Medicine and Health Sciences, University of Otago, New Zealand [6)] Department of Surgical Pathology, School of Medicine, Aichi Medical University, Japan [7)] Department of Oncology and Pathology, Karolinska Institutet, Sweden

Introduction

Perineural invasion (PNI) is associated with poor prognosis in prostate cancer. However, assessing PNI in prostate biopsies is labor intensive for pathologists. We developed an artificial intelligence (AI) algorithm to automatically detect and segment PNI from whole slide images.

Material and methods

Approximately 80,000 biopsy cores from the STHLM3 trial were assessed for PNI, resulting in 485 positive cores. We additionally scanned a selection of negative cores (N=8,318). A random split of 80%-20% was used to assign patients to training and test sets. We used ensembles of 10 Xception models for classification and 10 UNet models for additional pixel-wise segmentation.

Results and discussion

The area under the receiver operating characteristic curve for detecting cores with PNI was 0.98 (CI: 0.97-0.99) (106 positive, 1,652 negative cores), corresponding to sensitivity of 0.87 and specificity of 0.97 at a pre-specified operating point. For pixel-wise segmentation, the average intersection over union was 0.50 (CI: 0.46-0.55). On a subset (106 positive, 106 negative cores) assessed by multiple pathologists, the concordance between the AI and pathologists (mean pairwise Cohen's kappa 0.74)was comparable to concordance between pathologists (0.68-0.75).

Conclusion

We showed that detection of PNI in prostate biopsies using AI is feasible. This could aid pathologists by reducing the number of biopsies that need to be assessed for the presence of PNI or by flagging potentially missed positive biopsies. Moreover, highlighting the potential PNI regions could speed up the pathologist's workflow.

Keywords: Prostate cancer, Perineural invasion, Artificial intelligence

P21

But will AI work on my patients? Generalizability is critical for the clinical use of AI in prostatic biopsy diagnosis and opens its use in screening.

Juan A. Retamero[1], Patricia Raciti[1], Emre Gulturk[1], David Klimstra[1]
[1)] Medical Affairs, Paige AI, United States

Introduction

Artificial intelligence (AI) applied to pathology is the basis of computational pathology, the so called 'fourth revolution' in Pathology. To date, there is limited evidence of AI use in a clinical setting. "Generalizability" refers to the ability of algorithms to perform across broad populations, coping with whole slide images (WSI) from different laboratories, without requiring refitting or calibration. We tested algorithm performance for tumor detection on prostatic core biopsies on an international dataset to test generalizability.

Material and methods

An AI-based prostate cancer detection system was developed using multiple instance learning, which is an unsupervised training method that requires no pathologist annotations. The system was trained using>33,000 slides from circa 7,000 patients, originating from over 800 labs worldwide. The algorithm was then used to review two separate cohorts from different countries that comprised 218 patients and circa 2500 previously diagnosed prostatic biopsy WSIs.

Results and discussion

Without calibration or retraining, the AI system performed with very high sensitivity and specificity (both > 97%) across this external dataset. Interestingly, the Negative Predictive Value approached 100% on a patient level, which opens the possibility of using AI models as screening tools in prostatic biopsy specimens.

Conclusion

Pathology AI algorithms trained with multiple instance learning provide robust outputs that are generalizable across different populations without requiring further training or recalibration. These algorithms offer high diagnostic accuracy as both a standalone tool and to help pathologists screen prostatic biopsies, with the associated increase in efficiency and accuracy.

Keywords: Prostatic biopsy, Screening, AI assisted diagnosis, Generalizability , Diagnostic accuracy , Diagnostic efficiency

P22

Accurate colorectal cancer lymph node metastasis detection using ensemble models trained on breast sentinel nodes

Amjad Khan[1], Philipp Zens[1], Felix Müller[1], Heather Dawson[1], Jean-Philippe Thiran[2], Alessandro Lugli[1], Annika Blank[3], Inti Zlobec[1]

[1)] Institute of Pathology, University of Bern, Switzerland [2)] Swiss Federal Institute of Technology Lausanne (EPFL), Signal Processing Laboratory (LTS5), Switzerland [3)] Institute of Pathology, City Hospital Zurich Triemli, Switzerland

Introduction

Pathologists' microscopic evaluation of lymph node (LN) metastasis for colorectal cancer (CRC) patients can be time-consuming and laborious. We propose an assisting deep learning tool for CRC LN metastasis detection by leveraging ensemble models trained on a public dataset of breast cancer LN.

Material and methods

A cohort of 100 slides from 14 CRC patients is used to train a UNet model for LN segmentation by including the capsular regions. In order to detect LN metastasis, Xception and Resnet50 deep learning models are trained on the public breast cancer dataset, PatchCamelyon. An ensemble model is created to obtain single patch scores and validated on 353 slides of 55 CRC patients using AUC, sensitivity and specificity on a whole slide level.

Results and discussion

In the validation cohort, the proposed pipeline achieves an AUC of 0.85 with a very high sensitivity of 0.99 and specificity of 0.71, aggregating patch-based class probabilities applying a threshold of 0.5 to calculate the slide label. One positive LN slide was misclassified due to small isolated tumour cell clusters (≤43µm largest diameter). Similarly, special morphologies such as mucinous adenocarcinoma were also challenging due to the absence of such examples in the training data.

Conclusion

With 0.99 sensitivity, the proposed pipeline could be included in the routine diagnostic workflow as an assisting tool for faster LN screening. Nevertheless, future work is needed for improving model performance in challenging cases such as cases with isolated tumour cell clusters.

Keywords: colorectal cancer , lymph node metastasis, metastasis detection, lymph node segmentation, breast sentinel nodes, ensemble models

P23

Image analysis of diaphragm muscle cells in Covid-19 patients

Maria Orsaria[1], Vincenzo Della Mea[2], Letizia Casarotto[1], Carla Di Loreto[1, 3], Daniele Orso[6], Tiziana Bove[3, 6], Luigi Vetrugno[4, 5]

[1)] Anatomic Pathology Institute, ASUFC University Hospital of Udine, Italy [2)] Department of Mathematics, Computer Science and Physics, University of Udine, Italy [3)] Department of Medicine, University of Udine, Italy [4)] Department of Medical, Oral and Biotechnolocial Sciences, University of Chieti-Pescara, Italy [5)] Department of Anesthesiology, Critical Care Medicine and Emergency, SS. Annunziata Hospital, Chieti, Italy [6)] Department of Anesthesia and Intensive Care, ASUFC University Hospital of Udine, Italy

Introduction

Diaphragm disorders are present in 60% of critical patients at hospital admission, increasing to 80% after prolonged mechanical ventilation. Different medications are known to be associated to diaphragm atrophy. This is true also for COVID-19 patients. Up to now, no anatomopathological quantitative evaluation has been carried out on diaphragm muscle cells to evaluate the consequences of COVID-19 disease and prolonged mechanical ventilation.

Material and methods

H-E sections of the diaphragm of 24 patients admitted to ICU were acquired as whole slides at 40x using a Leica Aperio AT2 slide scanner. Regions of interest per each slide were annotated using an Omero server. Quantitative evaluation has been carried out with a macro for the ImageJ image analysis software. For each ROI, the software calculated a variety of morphological features of the fibers.

Results and discussion

Level of sedation, fibers density, average perimeter and thickness of fibers were found to be significantly different between two groups of patients with different mechanical ventilation parameters. A group was characterized by a greater number of fibers (422 vs 140, $p = 0.05$) but of a lower caliber than the other group (64.8 vs 136, $p < 0.001$). We also found a direct linear correlation between diaphragmatic fiber diameter and median tidal volume used, and between the fraction of diaphragmatic thickening and the overall time spent in pronation.

Conclusion

This is the first study that morphologically evaluates the diaphragm fibers in prolonged mechanical ventilation and that apply digital image analysis to the quantification of fiber features, allowing to correlate them to patient's clinical outcome.

Keywords: image analysis, Covid-19, WSI, diaphragm, ventilation, morphometry

P24

Image analysis for cervical cancer screening using deep learning

Tomasz Religa[2], Artur Olszewski[2], Piotr Religa[1, 2]

[1)] Medicine, Karolinska Institutet, Sweden [2)] Alcid , Sp.zoo, Poland

Introduction

Cervical cancer is ranked fourth among frequent cancers in women. Consequently, cervical cancer screening is an important part of the woman's routine health checkup, with over 50 million done in US annually. Computer-assisted diagnosis is key for scaling up cervical cancer screening and to significantly reduce error rate and increase productivity. Deep Learning methods that have been applied so far to this problem use highly customized networks trained from scratch.

Material and methods

Here, we develop an approach of fine-tuning the existing deep neural network (DNN) architecture of YoloR that has been previously pretrained on massive image datasets of >300,000 images. This transfer learning approach takes advantage of the hidden representations learned by the DNN from the massive database.

Results and discussion

We evaluated our approach using a benchmark dataset from Liang et al.(2019), where we obtained mean Average Precision (mAP) of 65%, which is >16% higher than the baseline. Our Average Recall (AR) was 80%, which was 16% than previously reported. Modern DNN network architectures pre-trained on large datasets and fine-tunes to the task of interest have potential to significantly outperform current methods used in digital pathology

Conclusion

The proposed method holds promise for the development of automation-assisted cervical cancer screening systems.

Keywords: Cervical cancer, Screening, Artificial Inteligence, Image analysis

P25

Deep learning for sub-classification of Gleason pattern 4 in prostate cancer

Pedro Oliveira[1], Dinisha Kadam[2], Owaish Salim[2], Saikiran Bonthu[2], Nitin Singhal[2]

[1)] Pathology, Christie Hospital NHS Foundation Trust, United Kingdom [2)] Digital Pathology , AIRAMatrix Private Limited, India

Introduction

GP4 shows a heterogeneous presentation comprising morphological variants like poorly formed glands, glomeruloid structures, cribriform glands, and fused glands. The cribriform pattern, is associated with an aggressive clinical course and is a reliable predictor of distant metastases and disease-specific death. However, although glomeruloid pattern is considered by some to be an early stage of cribriform pattern, the impact in prognosis is controversial. Using Deep Learning, we developed a computational technique for identification and quantification of Cribriform and Glomeruloid patterns in whole mount images (WMI) in radical prostatectomy (RP) specimens.

Material and methods

Whole-mount H&E stained histopathological sections of formalin fixed RP specimens showing a mixture of different GP4 subtypes were digitised at a magnification of 40x using Olympus VS200 scanner. A neural network based on U-Net++ with EfficientNet backbone was trained to identify and separate Cribriform and Glomeruloid glands from benign, other tumour pattern, and stromal regions. 13 RP images annotated by two pathologists showing perfect consensus were employed for training the model. 42 RP images were used to test the model.

Results and discussion

On the test dataset, the model performed well, with AUCs (Area Under Curve) of 0.87 for Cribriform and 0.81 for Glomeruloid gland identification. For the two patterns, the segmentation model achieved an F1-score of 0.83 and 0.80, respectively.

Conclusion

Using Deep Learning, we propose a method for automatically localising Cribriform and Glomeruloid growth patterns in radical prostatectomy images. In the future, we intend to conduct multicentre trials on larger data sets for validation of this technique.

Keywords: Gleason 4 pattern, cribriform, glomeruloid, deep learning, prostate, carcinoma

P26

AI in routine prostatic biopsy diagnosis leads to improved diagnostic accuracy and efficiency gains

Juan A. Retamero[1], Patricia Raciti[1], Emre Gulturk[1], David Klimstra[1]
[1)] Medical Affairs, Paige AI, United States

Introduction

Artificial intelligence (AI) applied to pathology diagnosis promises improved diagnostic accuracy and efficiency for overstretched pathology labs. There is mounting evidence to show diagnostic accuracy gains associated to AI use, but relatively little evidence exists to support any efficiency claims.

Material and methods

An AI system was developed to assist pathologists in finding suspicious areas for cancer in prostatic needle biopsies. This model was trained using multiple instance learning, using more than 33,000 slides originating from over 7,000 patients worldwide. The system was tested in two separate experimental settings to assess whether it helped pathologists improve their diagnostic accuracy, their reading times, and the deferral rates for immunohistochemistry (IHC) or other ancillary tests.

Results and discussion

When assisted by AI, pathologists significantly improved their sensitivity and specificity in diagnosing prostatic biopsies. In addition, the reading times were shortened. Also, AI helped pathologists reduce the number of unnecessary deferrals.

Conclusion

When used as a diagnostic adjunct, AI can help pathologists improve their diagnostic accuracy and enhance their efficiency, by diminishing reading times and deferring cases for ancillary testing more judiciously.

Keywords: Prostatic biopsy, Deferrals, AI assisted diagnosis, Generalizability, Diagnostic accuracy, Diagnostic efficiency

P27

Pathologist-driven experience dictates design of AI-based digital diagnostics

Jillian Sue[1], Juan A. Retamero[1], Patricia Raciti[1], David Klimstra[1]
[1)] Medical Affairs, Paige AI, United States

Introduction

Digital pathology and artificial intelligence (AI) for routine clinical diagnosis is a novel, growing area. User experience (UX) research is critical to ensure pathologists can effectively and efficiently use digital viewing software and integrated AI solutions in daily clinical practice.

Material and methods

To understand how to deliver the most value from using a highly accurate AI-based digital diagnostic for breast cancer, various user research methods were employed including contextual inquiry and concept testing with 8 Breast pathology specialists. Additional investigative methods included qualitative interviews and quantitative surveys with both US-based and European-based general and sub-specialized pathologists.

Results and discussion

75% of pathologists surveyed (36/48) were interested/very interested in using AI in digital workflows. The desired level of explainability of AI results depended on the pathologist's level of confidence in identifying diagnostic features and their use setting (clinical v. non-clinical). Additionally, observing pathologists review AI results as a heatmap (visualization technique to display magnitude of findings) revealed an opportunity for improved usability; Pathologists consistently hid the heatmap to evaluate the underlying tissue identified by the AI. Consequently, a new visualization technique that avoids obscuring tissue identified by the AI was developed, resulting in greater satisfaction. Beyond slide-level visualization, AI-enabled case prioritization was perceived as high value for efficiency gains.

Conclusion

Majority of surveyed pathologists believe the incorporation of AI into digital pathology workflows has the potential to save time and reduce workload. These gains in efficiency and quality can only be achieved with thoughtful design powered by user-driven research and insights that focus on enhancing the Pathologist-AI interaction.

Keywords: AI design, User experience, AI assisted diagnosis, Pathologist , Diagnostic accuracy , Diagnostic efficiency

P28

Use of Artificial Intelligence in diagnosing malaria - An endemic disease of developing countries

Talat Zehra[1]

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

Introduction

Malaria is an acute febrile illness caused by Plasmodium parasites. According to WHO in 2019, there were an estimated 229 million cases of malaria worldwide. Most of the malaria cases are reported in developing part of the world where there is also the shortage of pathologists and at the same time pathologists working in these areas are overworked. Delayed and wrong diagnosis is also associated with increase morbidity and mortality of precious lives

Material and methods

It was a pilot study done on previously diagnosed cases of Malaria. The slides were taken from archives. We use microscope connected camera for making slides digital at 40x. The slides were annotated and then trained by Aiforia Oy, a Finland based software. The study was conducted at Jinnah Sindh Medical University from September 2020 to October 2020.

Results and discussion

Though it was a pilot study but the results were appreciating. After training the software was able to pick up almost all the infected RBCs present on the digital slide. The concordance between manual verses automated identification was around 98%. Our study was limited due to the absence of digital microscope or a slide scanner.

Conclusion

Adoption of digitization has revolutionize the field of pathology. Integration of artificial intelligence can further ease the work pf pathologist as it can easily quantify, measure and pick up a small pathology which can be missed by a pathologist if he is overworked. This was just a small study but its results were appreciating. Adoption of these techniques can provide fast and rapid diagnosis of patients

Keywords: Digital pathology, Artificial intelligence, Malaria

P29

Computer-Aided System for Hormone Receptor Expression in Breast Carcinoma

Mohammad Faizal Ahmad Fauzi[1], Wan Siti Halimatul Munirah Wan Ahmad[1]

[1)] Faculty of Engineering, Multimedia University, Malaysia

Introduction

Hormone receptor status is determined primarily to identify breast cancer patients who may benefit from hormonal therapy. The current clinical practice for hormone receptor testing, using either Allred score or H-score, is still based on manual counting and estimation of the amount and intensity of positively-stained cancer cells in immunohistochemistry (IHC)-stained slides. This approach is not only tedious and time consuming for the pathologists, but is also prone to errors and inaccuracies.

Material and methods

Estrogen receptor (ER) is one of the best recognized markers in hormone receptor testing in helping pathologists to decide whether the cancer is likely to respond to hormonal therapy or other treatments. In this work, we proposed a cell detection and classification system based on convolutional neural network model for use with the Allred scoring system for breast carcinoma ER status testing. The system classifies each cell in the ER-IHC stained whole slide images into negative, weak, moderate and strongly stained cells, before Allred scoring is carried out to recommend hormonal treatment options.

Results and discussion

Experimental result shows very promising observations for both the detection and classification process, as well as the Allred scoring computation, with 82.5% agreement with the pathologists in terms of hormonal treatment recommendation. This is very promising as it demonstrates that this time-consuming exercise can be automated to provide fast and reliable assistance to pathologists and medical personnel.

Conclusion

To the best of our knowledge, this is the first work of its kind in developing such a system, which would be a valuable tool for histopathologists in improving the reliability of predictive tumor marker reporting as well as reducing manual intervention workload. The system could also contribute in improving the overall standards of prognostic reporting for cancer patients, benefiting not only the pathologists and patients, but also the public at large.

Keywords: breast carcinoma, tumor biomarker, hormone receptor, estrogen receptor, Allred scoring

P30

Performance study of CLEO Mitosis, an automatic mitosis detection tool for invasive breast cancer

Clara Simmat[1], Loris Guichard[2], Stéphane Sockeel[5], Nicolas Pozin[1], Magali Lacroix-Triki[3], Catherine Miquel[4], Marie Sockeel[6], Sophie Prevot[7]

[1)]Primaa, Paris, France [2)]Hôpital Bicêtre (APHP - Université Paris Saclay), Bicêtre, France [3)]Institut Gustave Roussy (Université Paris Saclay), Villejuif, France [4)]Hôpital Saint-Louis (APHP - Université Paris Diderot), Paris, France [5)] Primaa, Paris, France [6)]Primaa, Paris, France [7)]Hôpital Bicêtre (APHP - Université Paris Saclay), Bicêtre, France

Introduction

Mitotic count is part of the Scarff-Bloom-Richardson histopronostic score modified by Elston and Ellis for invasive breast cancer. In digital pathology, mitoses identification is reported as difficult even after digitalization. It enables pathologists to better detect mitoses, while fitting perfectly into the digitalized laboratory workflow and minimize the volume of storage.

Material and methods

After the first identification step of areas of invasive carcinoma on the whole slide image (WSI), CLEO Mitosis automatically detects mitoses and propose the most mitotic areas. Trained on a set of infiltrating breast carcinoma slides with 2838 mitoses identified, from two different sources, CLEO Mitosis is a 2 stages process consisting of a RetinaNet detector with an EfficientNetB0 backbone, followed by a classification algorithm based on an EfficientNetB0 to refine detected mitotic candidates.

Results and discussion

These preliminary results were measured on 18 WSI. The detector, at a threshold of 0.40, gives a recall of 67% and a precision of 2.49%. The classifier has an AUC of 98.76 and for a threshold of 0.182, a balanced accuracy of 80.3%, a recall of 80.2% and a precision of 10%. The CLEO interface allows the pathologist, to easily interact with the hot spot(s) and the mitoses proposed by the algorithm and thus improve the precision up to around 100%, while keeping a high recall.

Conclusion

This study is the first performance study of CLEO Mitoses. It verifies a complete, interactive, simpler, and faster mitosis counting tool for pathologists, easily integrated in the digitalized laboratory workflow. It is suitable with any type of magnification scanning.

Keywords: Mitosis, breast cancer, automatic detection, whole slide image, artificial intelligence

P31

Classification of DCIS and Invasive cancer in Breast Cancer slides

Leslie Solorzano[1], Philippe Weitz[1], Yinxi Wang[1], Stephanie Robertson[2], Johan Hartman[2], Mattias Rantalainen[1]

[1)]Medical Epidimiology and Biostatistics, Karolinska Institutet, Sweden [2)]Department of Oncology-Pathology, Karolinska Institutet, Sweden

Introduction

In breast cancer (BC), distinguishing from Ductal Carcinoma In-situ (DCIS) and Invasive Cancer (IC) is crucial. However, much of the effort in AI -based image analysis of breast cancer focuses on manual annotation of IC in images. At a glance, DCIS and IC can be indistinguishable, the main difference being the presence of surrounding epithelium on the lesion, only for the trained pathologist the differences become apparent. An automated method for distinguishing DCIS from IC would allow for improved downstream analysis, such as DCIS grading, and prognostic and predictive models, where mainly IC is of interest.

Material and methods

Currently, a set of 500 slides (400 for training, 100 for validation) representative of a BC population sample from Stockholm, have been exhaustively annotated for IC pathologies and partially annotated for DCIS, Invasive lobular cancer, lobular cancer in situ, lymphovascular invasion, non-malignant changes and artefacts. 200 additional slides are currently being annotated (independent test set). Annotated slides will be used to optimise a convolutional neural network (CNN) ensemble for segmentation. The CNN architecture is Tiramisu, an extension of DenseNets to deal with the problem of semantic segmentation.

Results and discussion

Evaluation will be performed on tile level and pixel level.

Conclusion

An automated method will allow to distinguish DCIS from IC which is difficult and currently done only manually due to their visual similarity. A Tiramisu network is suited for this task and will allow for segmentation of the tissue.

Keywords: Breast cancer, Invasive Cancer, Ductal carcinoma in-situ

P32

Development of an AI-based tool for classification of OSCC histopathological images.

Vincenzo D'Angelo[1], Francesco Martino[2], Daniela Russo[1], Massimo Mascolo[1], Stefania Staibano[1], Francesco Merolla[3]

[1)]Department of Advanced Biomedical Sciences, Pathology Unit, University of Naples, Italy [2)]Dedalus HealthCare, Division of Diagnostic Imaging IT, Austria [3)]Department of Medicine and Health Sciences «V.Tiberio", University of Molise, Italy

Introduction

Oral squamous cell carcinoma (OSCC) is the most common malignant tumor of the head and neck district. To the best of our knowledge, analyses of whole slide images related to OSCC cases are scarce in the literature. An AI tool was developed to prioritize cases of OSCC.

Material and methods

We selected 390 OSCC images from the TCGA image database and the archives of Federico II Pathology Unit in Naples. The selected images were cropped and scaled to 228px x 228px with an RGB color profile using OpenCV. Then a model was developed to classify neoplastic from non-neoplastic lesions. The metric used was Area Under Curve. We built the model on normal images and images normalized using a histogram matching approach.

Results and discussion

The results show that, although the normal RGB images trained model had a better AUC, training the network on normalized images produced a more robust model because it was less affected by overfitting.

Conclusion

The CNN obtained represents an AI tool that efficiently prioritizes OSCC cases starting from normalized images. As a computer-aided diagnostic tool, we envisage its employment in a pathologist's daily routine to prioritize the work allowing the pathologist to focus first on more urgent cases.

Keywords: OSCC, CLASSIFICATION, CNN

P33

Self-Rule to Multi Adapt automates the tumor-stroma assessment in colorectal cancer

Christian Abbet[1, 3], Linda Studer[2, 3], Jean-Philippe Thiran[1], Inti Zlobec[3]

[1)] Electrical Engineering, EPFL, Switzerland [2)] Computer Science, School of Engineering and Architecture of Fribourg, Switzerland [3)] Institute of Pathology, University of Bern, Switzerland

Introduction

To validate our recently proposed Self-Rule to Multi-Adapt method, which performs tissue segmentation, in a clinically relevant task, we aim to automatically compute the tumor-stroma ratio (TSR) on whole slide images (WSIs). TSR has been shown to be an independent prognostic factor in colorectal cancer, a lower ratio is associated with poorer patient outcomes.

Material and methods

To ensure the quality of the automatically computed TSR, we compare it to the TSR scored by pathologists (high/low, cutoff=50%) on a validation cohort (N=10). We further analyze its clinical impact using 274 H&E stained WSI from 227 patients diagnosed with adenocarcinoma and no prior treatment from the TCGA cohort. We compute TSR over the WSIs using a sliding window (2500 µm). The predictions are aggregated patient-wise by averaging.

Results and discussion

TSR achieves a 100% correspondence of high/low cases on the validation cohort. On TCGA, TSR does not correlate (chi-squared-test $p>0.05$) with either pT, TNM, or pN. Using a univariate Cox model to predict overall survival, we find a hazard ratio (HR) of 0.67 (0.53-0.85) with $p=0.001$ for TSR. When adjusting for pT, TNM, and pN using a multivariate Cox model, TSR still acts as an independent prognostic factor while improving prognostic capability.

Conclusion

We show that our method has the potential for automated TSR assessment to be included in standard reporting. This would not only save time for pathologists but also provide additional information for diagnosis. For future work, we will validate our findings on additional cohorts, as well as investigate the link between TSR and other clinical parameters.

Keywords: TSR, Self-supervised, Survival, Colorectal cancer

P34

Design and Development of Intelligent Cancer Screening System for Highly Occurred Cancers among People of Europe

Rohit Thanki[1]

[1)] Research and Development, Prognica Labs, UAE

Introduction

In 2019, the healthcare system of every country got limelight due to the COVID-19 pandemic. But before COVID-19, a few deadly diseases such as cardiovascular, stroke, cancers, etc., already occurred in the human body, which causes many deaths every year. Recently, literature identified challenges such as the availability of less specialized physicians and nurses, less facility available for early detection of deadly diseases such as cancer and Alzheimer's, etc., in the existing healthcare system of many European countries. Among these diseases, cancer can be controllable and reduce death's risk factors using early detection, diagnosis, and prevention methods. On the other hand, various cancers such as lung, colorectum (colorectal), breast, and prostate highly occur in people of Europe. Different imaging techniques and data from the laboratory aim to identify cancer in organs at earlier stages of the tumor when treatment can be more successful. Unfortunately, despite screening programs, the interpretation of medical images for early cancer detection is affected by high rates of false positives and false negatives.

Material and methods

The purpose of this research will be to investigate the challenges in the existing conventional cancer screening system in European countries and provide solutions for these challenges. This research's main aim is to provide retrospective as well as prospective study and analysis of the reading performance of medical images by radiologists and artificial intelligence (AI) based screening systems. Also, this research helps to make some policies regarding the usage of AI-based screening systems for the early detection and diagnosis of cancer in hospitals or healthcare centers.

Results and discussion

Development of the System is under process.

Conclusion

Provide an intelligent cancer screening System that can be used for early detection of cancer tumors.

Keywords: Artificial Intelligence, Cancer, Early Detection, Medical Imaging, Retrospective, Screening

P35

Application of Deep Learning in the histopathological diagnosis of breast cancer as a first Moroccan experience on a private dataset

Hajar El Agouri[1], Mohamed Azizi[2], Hicham El Attar[3], Mohamed El Khannoussi[2], Soumaya Echcharif[1], Chaimaa Mounjid[4], Basma El Khammoussi[1]

[1)] Pathology department, Oncology National Institute, Faculty of Medicine and Pharmacy, Mohammed V University, 10100 Rabat, Morocco [2)] Datapathology, 20000 Casablanca, Morocco [3)] Anatomic pathology laboratory Ennassr, Anatomic pathology laboratory Ennassr, 24000 El Jadida, Morocco [4)] Pathology department, Oncology National Institute, Faculty of Sciences, Mohammed V University, 10100 Rabat, Morocco

Introduction

Breast cancer is a critical public health issue and a leading cause of cancer-related deaths among women worldwide. Its early diagnosis using artificial intelligence (AI) tools is emerging, which can help in increasing the chances of survival rate. However, laboratories with integrated digital pathology workflows are still sparse todays. In Morocco, as a developing country, we were the first pathologists to introduce AI in routine pathology workflow, through our project initiated in January 2020.

Material and methods

We collected overall 1229 digital slides, from 440 of surgical breast specimens diagnosed with invasive breast carcinoma of non-specific type, and referred to the histopathology department of the National Institute of Oncology in Rabat. We opted for a hybrid pipeline: Data preprocessing, an unsupervised feature extraction phase using the Xception architecture, and a prediction stage using a supervised machine learning algorithm. The model will accurately classify the images into: normal tissue-benign lesions (groupe0), in situ carcinoma (groupe1) or invasive carcinoma (groupe2).

Results and discussion

We reported high degrees of overall correct classification accuracy (92%), and sensitivity (94%) for detection of carcinoma cases, which is important for diagnostic pathology workflow in order to assist pathologists for diagnosing breast cancer with precision.

Conclusion

In this paper, we proposed a simple and effective method for the classification of histological breast cancer images with good generalization performance. Our results are very encouraging and comparable to the state of the art application of deep learning in the histological diagnosis of breast cancer.

Keywords: Artificial intelligence, Deep leraning, Breast cancer, digital pathology, whole slide images

P36

Standardized phenotypic description of datasets of histological sections

Markus Plass[1], Rita Carvalho[2], Theodore Evans[3], Michaela Kargl[1], Tom Bisson[2], Peter Regitnig[1], Patrick Nitsche[1], Andreas Holzinger[4], Christian Geißler[3], Peter Hufnagl[2], Heimo Müller[1], Norman Zerbe[2]

[1)] Diagnostic and Research Center for Molecular BioMedicine, Diagnostic & Research Institute of Pathology, Medical University of Graz, Austria [2)] Institute of Pathology, Charite – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt- Universität zu Berlin, Germany [3)] DAI-Labor, Technical University Berlin, Germany [4)] Institute for Medical Informatics, Statistics and Documentation, Medical University of Graz, Austria

Introduction

Whole Slide Images (WSI) are playing an important role in medical research and AI algorithm development. Especially in the field of machine learning, large amounts of data are required and many projects and institutions are in the process of creating WSI collections. Such a collection also consists of corresponding metadata to enable a FAIR (Findable, Accessible, Interoperable, and Re-usable) data management. These metadata require a standardized, catalog-based description of samples.

Material and methods

An important part of a metadata catalog is the description of the sample and histological structures in analogy to a feature map. Such pre-classification of samples, regions, and structures is often used by Machine Learning (ML) algorithms, but with different codings and semantic depth depending on the specific usecase. However, to achieve interoperability between different catalogs to enable the combination of collections is needed. We used existing standardized nomenclatures (SNOMED, ICD-10, UMLS) based on domain specific ontologies (Uberon, BRENDA Tissue Ontology) to create a common data format (syntax) and agreement in the meaning of the codes (semantics)

Results and discussion

We propose a description divided into four hierarchical layers: organ, tissue type, structure, and pathological alteration. For each layer, we have selected appropriate nomenclature and developed a method to define use case specific profiles.

Conclusion

For surgical pathology, we have defined first versions of such profiles and demonstrated how descriptions of entire samples or certain regions of interest (ROI) can be stored and exchanged. All our results are available in a GitHub repository, which also provides a discussion platform and version management system.

Keywords: Metadata Catalog, Ontologies, Nomenclature, Hierarchical feature maps

P37

Unsupervised quantification of IHC stains in triple-negative breast cancer

Suze Julia Roostee[1], Johan Staaf[1], Mattias Aine[1]

[1)] Division of Oncology, Department of Clinical Sciences, Lund University, Sweden

Introduction

Breast cancer is the most common cancer among women worldwide. Tissue microarray (TMA) collection may create an increased understanding of the heterogeneous molecular profiles in breast cancer. Despite standardization efforts, inter-and intravariability in pathologist scorings persists. Standardization and reproducibility of quantitative results and spatial patterns in TMA analysis could serve as an important step towards new insights into and a better understanding of breast cancer.

Material and methods

We developed an unsupervised cell quantification pipeline. Images of TMAs stained for six immune cell markers on a triple-negative breast cancer cohort (n=216) were deconvoluted using Red Green Blue to Hematoxylin Eosin DAB color deconvolution. The DAB layer was selected for further processing and a thresholding algorithm separated stained areas from the background. Stained areas were segmented and quantified using watershed segmentation.

Results and discussion

Quantification of the immune cell markers showed good correlations with available pathologist scorings (PDL1-sp142, CD20). CD3 counts in TMAs showed an association to TILs in whole-slide tissue. Low CD3 counts also showed an association with decreased invasive disease-free survival.

Conclusion

Our results show that this pipeline can be applied for more standardization and reproducibility of IHC assay scoring in research through quantification of marker stains and capture of spatial patterns.

Keywords: unsupervised image analysis, triple-negative breast cancer, digital pathology, immunohistochemistry

P38

Image Acquisition Algorithms to Enable Archival of Old Slides with Artefacts

Dr Jaya Jain[1], Raghubansh Gupta[1], Pavani Pallavi Pelluru[1], Shilpa G Krishna[1], Durgaprasad Dodle[1], Priyanka Golchha[1], Prasanth Perugupalli[2]

[1)] Nference, Bangalore, India [2)] Pramana, Cambridge, United States

Introduction

Digitization of the old archival slides poses a huge challenge as most of the scanners require refinement in the slide making process and accept only clean and freshly prepared slides. With the use of intelligent image acquisition algorithms, we obtained WSIs with good image quality in old archive slides with artefacts such as bubbles, dirt and DPX overflow.

Material and methods

50 old H&E slides with artefacts such as bubbles, dirt and DPX overflow were scanned using Pramana scanner with concomitant use of intelligent image acquisition algorithm with and without any specific pretreatment like cleaning and recoverslipping of the slides. Both the WSI groups (with and without pretreatment) were compared for various quality parameters like tissue coverage, focus error and stitching error.

Results and discussion

In all the 50 H&E slides, tissue coverage was 100% in both groups. The difference in focus and stitching error percentage between the slides in two groups were less than < 1 %. Upon visual inspection of WSI, acceptable image quality similar to microscope was achieved despite the presence of bubbles and dirt on slides without pretreatment. DPX overflow over the slide surface (in pretreatment slides) resulted in optical artefacts in the WSI as observed in microscopes which were resolved post cleaning of slides with xylene.

Conclusion

Use of image acquisition algorithms while scanning the old slides with artefacts such as bubbles, dirt and DPX overflow has helped in improving the WSI image quality, thus obviating the need for pre-treatment like cleaning and recoverslipping of old slides.

Keywords: digitization, WSI, acquisition, algorithm, artefacts, quality

P39

Correlation and colocalization of HIF-1a and pimonidazole staining for hypoxia in laryngeal carcinomas: a digital, single-cell-based analysis

Justin E. Swartz[1], Hilde J.G. Smits[2], Marielle E.P. Philippens[2], Remco De Bree[1], Johannes H.A.M. Kaanders[3], Stefan M. Willems[4]

[1)] Department of Head and Neck Surgical Oncology, University Medical Center Utrecht, The Netherlands [2)] Department of Radiotherapy, University Medical Center Utrecht, The Netherlands [3)] Department of Radiation Oncology, Radboud University Medical Center Nijmegen, The Netherlands [4)] Department of Pathology and Medical Biology, University Medical Center Groningen, The Netherlands

Introduction

Tumor hypoxia results in worse local control and patient survival. We performed a digital, single-cell-based analysis to compare two biomarkers for hypoxia (hypoxia-inducible factor 1-alpha [HIF-1a] and pimonidazole [PIMO]) and their effect on outcome in laryngeal cancer patients treated with accelerated radiotherapy with or without carbogen breathing and nicotinamide (AR versus ARCON).

Material and methods

Immunohistochemical staining was performed for HIF-1a and PIMO in consecutive sections of 44 tumor biopsies from laryngeal cancer patients randomized between AR and ARCON. HIF-1a expression and PIMO-binding were correlated using digital image analysis in QuPath. High-density areas for each biomarker were automatically annotated and staining overlap was analyzed. Kaplan-Meier survival analyses for local control, regional control and disease-free survival were performed to predict a response benefit of ARCON over AR alone for each biomarker.

Results and discussion

106 Tissue fragments of 44 patients were analyzed. A weak, significant positive correlation was observed between HIF-1a and PIMO positivity on fragment level, but not on patient level. A moderate strength correlation ($r=0.705$, $p<0.001$) was observed between the number of high-density staining areas for both biomarkers. Staining overlap was poor. HIF-1a expression, PIMO-binding or a combination could not predict a response benefit of ARCON over AR.

Conclusion

Digital image analysis to compare positive cell fractions and staining overlap between two hypoxia biomarkers using open-source software is feasible. Our results highlight that there are distinct differences between HIF-1a and PIMO as hypoxia biomarkers and therefore suggest co-existence of different forms of hypoxia within a single tumor.

Keywords: Cell-based analysis, QuPath, Hypoxia Inducible Factor 1-alpha, Pimonidazole, Correlation, DAB

P40

Digital quantification of proliferation rate of the invasive breast carcinoma - inter-observer agreement and clinical validation

Gabriela Izabela Baltatescu[1, 2], Nicolae Dobrin[2, 3], Constanta Stefanov[2, 3], Mariana Aschie[1, 4], Anca Florentina Mitroi[1, 2], Georgeta Camelia Cozaru[1, 2], Anca Antonela Nicolau[1, 2], Mariana Deacu[1, 4], Manuela Enciu[1, 4]

[1)] Clinical Service of Pathology, "Sf. Apostol Andrei" Emergency County Hospital, Constanța, , Romania [2)] Center for Research and Development of the Morphological and Genetic Studies of Malignant Pathology- CEDMOG, "Ovidius" University of Constanța, Romania. [3)] TEM Laboratory, Faculty of Medicine, "Ovidius" University of Constanța, Romania [4)] Department of Pathology, Faculty of Medicine, "Ovidius" University of Constanța, Romania

Introduction

Despite the remarkable progress made in the last two decades in terms of means of diagnosis and treatment options, invasive breast carcinoma (IBC) still continues to rank first in incidence and mortality in females. Ki67 biomarker is indicated to distinguish molecular subtypes of luminal carcinoma types: luminal A versus luminal B-HER2neu. Reproducible of tumor proliferation assessment by quantification of KI67 index is affected by inter-observer variability. The aim of this study is to analyze the degree of reproducibility in the quantification of the Ki67 index between two pathologists using both usual methods, according to clinical guidelines, and automatic quantification using the QuPath computer platform for luminal A and luminal B-HER2neu IBC cases.

Material and methods

This retrospective study includes 115 patients diagnosed in the Clinical County Emergency Hospital Constanța, Romania between 2010-2014. The slides had been digitized using the HURON-TissueEscope 4000x scanner. Kappa coefficient (k) was calculated to evaluate the degree of variability or concordance between the values obtained by two pathologists, evaluating the inter-observer degree.

Results and discussion

Using the visual quantification method, k coefficient was 0.812 when only the areas with intense immunolabeling were evaluated and k=0.868 when the entire digitized image has been analyzed. By computerized analysis of the digitized images, a degree of correlation was obtained between the two doctors of k=0.856 when only the areas with intense immunolabeling were analyzed and of k=0.902 when the entire tumor was considered.

Conclusion

Digital quantification of the Ki67 index by the digital method diminishes the inter-observer variability in establishing the proper molecular profile of IBC.

Keywords: whole slide imaging, proliferation rate, digital quantification, immunohistochemistry, invasive breast carcinoma, Ki67 index

P41

Quantitative Colour: Metric-Based QA for WSI Colour and Impact of Standardisation on Digital Pathology and AI

Richard Salmon[1], Craig Revie[1, 2], John Stevenson-Hoare[1], Jacqui Deane[1], Mark Wootton[1]

[1)] FFEI Life Science, FFEI, United Kingdom [2)] Medical Imaging Working Group, International Color Consortium, Worldwide

Introduction

Colour differences are apparent in visual assessment of Whole Slide Imaging (WSI) scanner output, both when compared to glass slides and across scanner models. Tools that enable the quantitative analysis and universal calibration of WSI scanner colour allow cross-industry end-users of digital pathology the opportunity to standardise and report on the fidelity of images. Integration of independent, metric-based approaches into digital pathology workflow and AI will assist and improve the development of new methodologies in a regulated way. Quantitative colour calibration, validation and standardisation should form an essential part of digital pathology QA.

Material and methods

Utilising FFEI's Sierra Slide, ICC profiles and colour management software, extensive end-user environments have been evaluated to generate universally obtainable colour metrics that provide stringency, reliability and interoperability in a variety of QA workflows. Output colours were cross-analysed to establish the scanner-agnostic validation and standardisation it is possible to sustainably achieve by correction to ground-truth absolute colour.

Results and discussion

Real-world quantitative data from a blend of industry, research, AI and clinical applications reveals the impact, advantages and future-proofing of applying independent, metric-based colour QA. Viability, adoptability and sustainability is demonstrated for quantitative validation and standardisation of WSI to high colour fidelity irrespective of scanner model or use environment.

Conclusion

WSI colour can be validated and standardised by independent, scanner-agnostic methods that are complementary to digital pathology workflow and AI analysis. Quantitative analysis and calibration to defined numerical accuracies can be deployed to develop stringent QA methodologies that minimise or remove the impact of colour variation on ground-truth analysis by human or AI.

Keywords: Colour, Quality, Standardisation, Workflow, Metrics, Validation

P42

Rating Whole Slide Imaging Validation Studies in Cytology according to College of American Pathologists Guidelines

Pietro Antonini[1], Nicola Santonicco[1], Ilaria Girolami[2], Giovanni Negri[2], Matteo Brunelli[1], Stefano Marletta[1], Paola Chiara Rizzo[1], Anil Parwani[3], Liron Pantanowitz[4], Claudio Luchini[1], Albino Eccher[1]

[1)] Department of Pathology and Diagnostics, University and Hospital Trust of Verona, Italy [2)] Department of Pathology, Central Hospital of Bolzano, Italy [3)] Department of Pathology, The Ohio State University, OH, United States [4)] Department of Pathology, University of Michigan, MI, United States

Introduction

In 2021 the College of American Pathologists (CAP) published their updated guidelines for validating whole slide imaging (WSI) for diagnostic purposes in pathology. At that time, evidence supporting the application of these guidelines to cytopathology was considered immature, pending additional research. The aim of the study was to investigate the literature for evidence of WSI in cytology according to 3 strong recommendations (SR) and 9 good practice statements (GPS).

Material and methods

A literature search for relevant papers was completed using PubMed and Elsevier Embase including full-text articles about human cytopathology comparing conventional microscopy to WSI up until 2022. A total of 26 of 3963 papers were included and appraised according to their compliance with SR (strong evidence to base as a recommendation) and GPS (important and intuitive but lack evidence on which to base a recommendation).

Results and discussion

Our review showed that 4/26 papers (15%) fulfilled all 3 SRs. Only 1 publication (4%) satisfied all 3 SRs and 9 GPSs. Moreover, 10/26 papers (38%) did not specify their compliance to at least one SR and 25/26 (96%) did not specify their compliance to at least one GPS.

Conclusion

Increasing experience and published data support the diagnostic use of WSI for cytopathology. However, validation for clinical diagnostic use in pathology practice is still required. While guidelines for validation of WSI technology promote safety, standardization and digital pathology adoption, more evidence is needed to support utilizing current CAP guidelines for WSI in cytopathology.

Keywords: Whole slide imaging, Validation, Cytology

P43

Validation of Artificial Intelligence – Based System for Prostate Cancer Detection and Grading

Taryme Lopez Diaz[1], Dibson Dibe Gondim[1]

[1)] Department of Pathology and Laboratory Medicine, University of Louisville, United States

Introduction

Paige Prostate Detect (Paige.AI Inc., New York, USA) is the first FDA-approved artificial intelligence (AI)-based system created to assist pathologists to detect and grade prostate cancer. Our goal is to present the results of a validation study of this system in an academic center.

Material and methods

40 prostate biopsy cases were randomly selected from a list of 60 consecutive cases. All HE-stained slides (619) were scanned in a Leica Aperio GT450 (400x magnification). Paige Prostate Detect was applied to each slide and results were compared with the original diagnoses. Diagnostic discrepancies were evaluated by pathologists.

Results and discussion

AI output was recorded for each whole slide image. On the other hand, pathologists provided results based on the evaluation of two or more glass slides per biopsy location. 36 disagreements were identified (5.8%) in all slides. Agreement on the case level required that all slides of a case had concordant diagnosis between AI-system and pathologist. 16/40 cases had disagreements The AI-system helped to detect focal cancer in a case with no prior definitive cancer diagnosis. Multiple discrepancies related to atypical small acinar proliferation (ASAP) were identified. Since the system was not trained to make a diagnosis of ASAP, these cases were either diagnosed as carcinoma or benign.

Conclusion

Validation of pathology AI-systems is essential before clinical adoption. This system shows potential to locate low-volume cancer in cases with no definitive diagnosis of malignancy. In the case of ASAP, pathologists should use well-defined criteria to render this diagnosis and should not rely on AI impression.

Keywords: Artificial intelligence, Validation study, Prostate cancer, Histopathology

P44

EMPAIA Academy – a free advanced training program of the EMPAIA project

Rasmus Kiehl[1], Rita Carvalho[1], Norman Zerbe[1]

[1)] Institute of Pathology, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt- Universität zu Berlin, Berlin, Germany

Introduction

The EMPAIA (EcosysteM for Pathology Diagnostics with AI Assistance) Project is building an ecosystem for the development and use of validated and certified AI solutions in the routine practice of diagnostic pathology. A diverse audience of professionals in medical and life sciences but also in the IT/AI sectors is involved. Consequently, the objectives of EMPAIA must include competency building.

Material and methods

A mechanism was therefore required to facilitate the transfer of knowledge, specifically to bring domain expertise of pathology to IT/AI professionals and conversely IT/AI knowledge to pathologists and trainees. This was the rationale for developing the EMPAIA Academy, a series of courses at basic and advanced levels. We conducted a survey of existing resources in this field and assembled an Academy curriculum.

Results and discussion

Distinguished speakers from the fields of IT, artificial intelligence and pathology speak about their experiences, use cases and the latest developments in the field. The recordings of the latest half-day virtual Academy seminars are available to the international audience via the EMPAIA website.

Conclusion

We evaluate the experiences from the Academy courses that took place so far and present our perspectives for future events.

Keywords: education teaching digital computational pathology artificial intelligence

ACKNOWLEDGEMENTS

3DHISTECH
Leica BIOSYSTEMS
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INDUSTRY SYMPOSIA

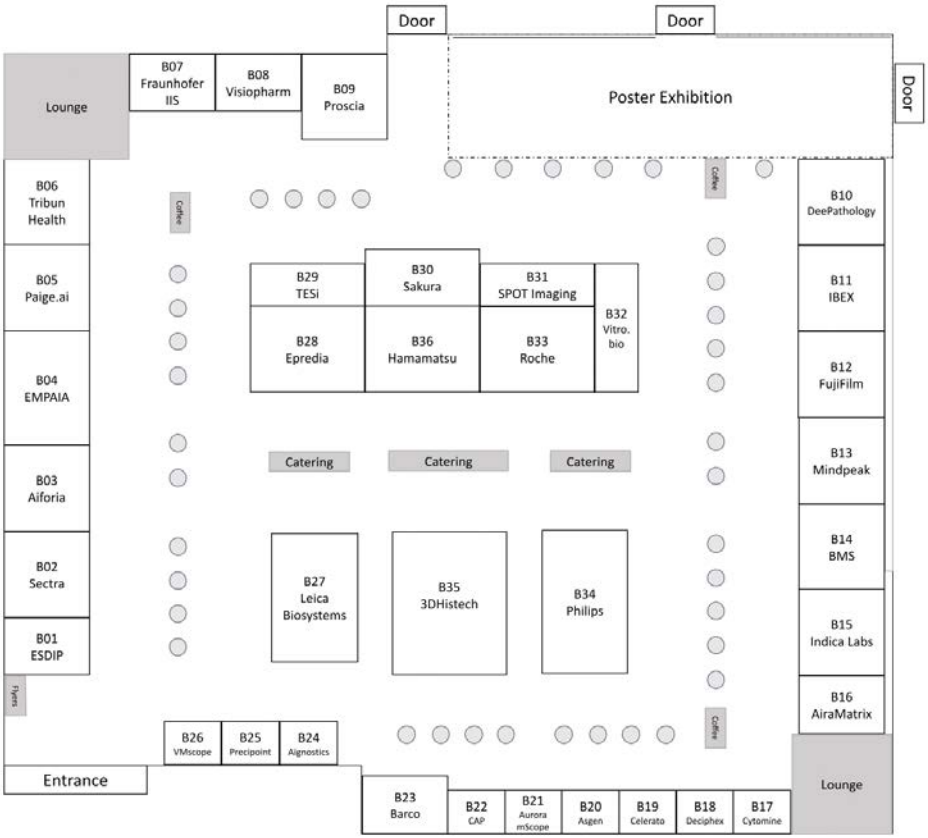
Ballroom I+II 16.06.2022 12:30-13:15	**IS01**	**INDUSTRY SYMPOSIUM** **3DHISTECH** **True insights & best practices - transforming the pathology workflow** More information at www.ecdp2022.org
Ballroom I 17.06.2022 12:45-13:30	**IS02**	**INDUSTRY SYMPOSIUM** **AIFORIA** **Introduction to the role of AI in diagnostic pathology and recently CE-IVD marked clinical AI tools for breast and lung cancer** More information at www.ecdp2022.org
Ballroom II 17.06.2022 12:45-13:30	**IS03**	**INDUSTRY SYMPOSIUM** **IBEX** **AI-powered diagnosis: from vision to clinical impact and patient benefit** More information at www.ecdp2022.org
Ballroom I+II 18.06.2022 11:00-11:45	**IS04**	**INDUSTRY SYMPOSIUM** **PROSCIA** **Improvement in operational efficiency for dermpath case review using AI solutions: insights from a high-throughput lab** More information at www.ecdp2022.org

15th JUNE 2022

	Münnchen	Dresden	Stuttgart
10:00			**WS01** **ESDIP, IHE PaLM WG and DICOM WG-26** Interoperability Roundtable
11:00	**WS02** **EMPAIA** EMPAIA Academy...	**WS03** **ROCHE** Real World Applications of Artifi cial Intelligence in Assessing PD-L1 Status in NSCLC	
12:00			
13:00			
14:00	**WS04** **PAIGE.AI** Will AI Work on my Patients? Generalizability is Critical for AI in Clinical Use	**WS05** **PRECIPOINT** Is it Possible to Digitize Intra-Operative Procedures? What do we Gain? What Does it Take?	
15:00			**WS06** **DICOM** WG-26 Meeting
16:00	**WS08** **VISIOPHARM** Digital Pathology: Motivation, Setup, Challenges and Outlook		
17:00			**WS09** **IHE PALM WG + DICOM WG-26** Joint Meeting
18:00	**WS10** **HAMAMATSU** Deep Dive into Digital Pathology: Experiences from the Scanner to the Diagnostics Platform		
19:00			

	WS	PRE-CONFERENCE WORKSHOPS
10:00-11:00 Room Stuttgart	WS01	**ESDIP, IHE, PaLM WG and DICOM WG-26** Interoperability Roundtable
11:00-12:30 Room München	WS02	**EMPAIA** EMPAIA Academy Hands-On Workshop
11:00-12:30 Room Dresden	WS03	**ROCHE** Real World Applications of Artificial Intelligence in Assessing PD-L1 Status in NSCLC
13:30-15:00 Room München	WS04	**PAIGE.AI** Will AI Work on my Patients? Generalizability is Critical for AI in Clinical Use
13:30-15:00 Room Dresden	WS05	**PRECIPOINT** Is it Possible to Digitize Intra-Operative Procedures? What does it Take? What do we Gain?
15:00-16:30 Room Stuttgart	WS06	**DICOM** WG-26 Meeting
15:30-17:00 Room München	WS08	**VISIOPHARM** Digital Pathology: Motivation, Setup, Challenges and Outlook
17:00-18:30 Room Stuttgart	WS09	**IHE PaLM WG + DICOM WG-26** Joint Meeting
17:15-18:45 Room München	WS10	**HAMAMATSU** Deep Dive into Digital Pathology: Experiences from the Scanner to the Diagnostics Platform

INDUSTRY EXHIBITION



OPENING HOURS EXHIBITION

16th June, 09:00–20:30
17th June, 08:30–17:30
18th June, 08:30–13:30

CONTACT

David Ameisen - Industry Liaison
partner@ecdp2022.org

Tiago Guedes - General Manager
office@ecdp2022.org

INDUSTRY EXHIBITION

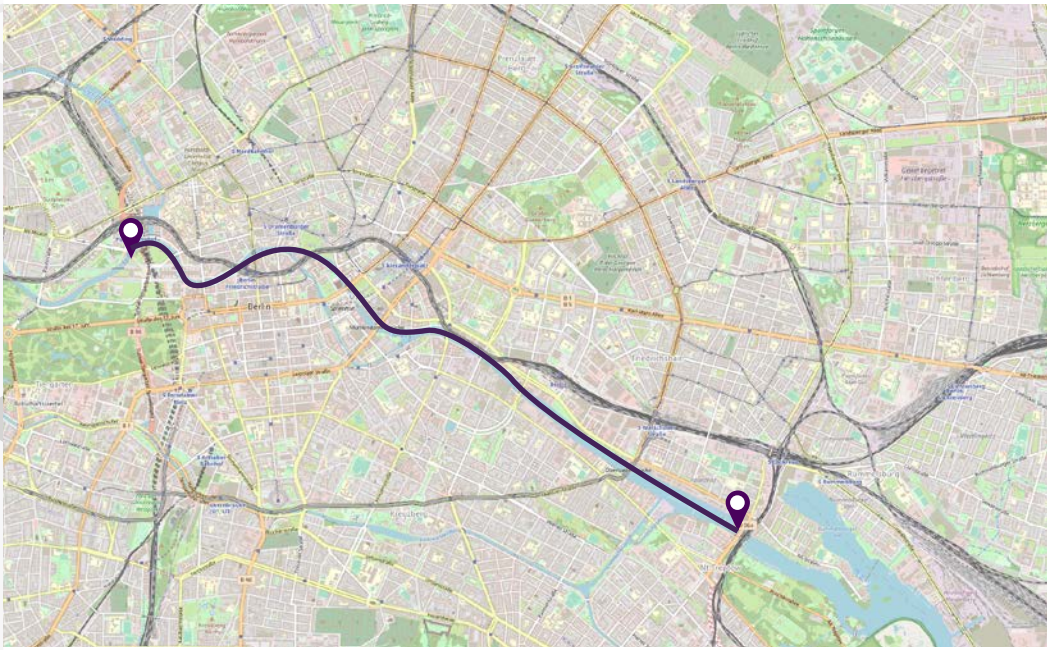
Booth No	Company
B01	European Society of Digital and Integrative Pathology
B02	Sectra Imaging IT Solutions AB
B03	Aiforia Technologies Plc
B04	EMPAIA Consortium
B05	Paige
B06	Tribun Health
B07	Fraunhofer IIS
B08	Visiopharm A/S
B09	Proscia
B10	DeePathology Ltd.
B11	Ibex Medical Analytics
B12	FUJIFILM Europe B. V.
B13	Mindpeak GmbH
B14	Bristol Myers Squibb GmbH & Co. KGaA
B15	Indica Labs
B16	AIRA Matrix Private Limited
B17	CYTOMINE CORPORATION SA
B18	Deciphex Ltd.
B19	Celerato AG
B20	asgen GmbH & Co. KG
B21	Aurora mScope Inc.
B22	College of American Pathologists
B23	Barco NV
B24	Aignostics GmbH
B25	PreciPoint GmbH
B26	VMscope GmbH
B27	Leica Biosystems Lda.
B28	Microm International GmbH (Epredia)
B29	Tesi Elettronica e Sistemi informativi S.P.A.
B30	Sakura Finetek Europe B.V.
B31	Spot Imaging - Diagnostic Instruments, Inc.
B32	VITRO S.A.
B33	Roche Diagnostics Deutschland GmbH
B34	Philips Medical systems NL BV
B35	3DHistech Ltd.
B36	Hamamatsu Photonics Deutschland GmbH

SOCIAL EVENT

All congress delegates, speakers and exhibitors are invited to the ECDP2022 social event which will take place on the evening of Friday, 17th June from 19:00 until 22:00.

Join us for a 3-4h boat trip on the river Spree that runs through the heart of Berlin. This guided tour will pass the government district, the historic center, including the Museum Island, along the East Side Gallery, up the Treptower Park and back to the pickup point (please see map below). The tour will also include the congress dinner on the boat.

The starting point will be close to Berlin Hauptbahnhof. A complimentary 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). Ticket price is 50€/person. Participation is on a first come, first served basis (max. 180 guests).



SOCIAL EVENT

The address of the pier is as follows:

Willy-Brandt-Straße | Moltkebrücke
GPS: 52.52226, 13.36975

We thank our sponsors Dell and SVA for supporting this event.

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CONGRESS INFORMATION

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.

CLOAKROOM

The cloakroom is near the registration desk in the foyer.

CONTINUING MEDICAL EDUCATION (CME) CREDITS

An application for CME accreditation of ECDP2022 was submitted to the Berlin Medical Association (Ärztekammer Berlin) for participants from Germany.
A parallel CME application was submitted to the European Association Council for Continuing Medical Education (EACCME), which provides credits for the attendance at the scientific sessions of the core programme. Through an agreement with the American Medical Association, physicians may convert EACCME® credits to an equivalent number of AMA PRA Category 1 Credits.

CONGRESS HOMEPAGE

www.ecdp2022.org

CONGRESS LANGUAGE

The official language of the congress will be English. Simultaneous translation will not be provided.

CONGRESS VENUE

Titanic Chaussee Berlin
Chausseestraße 30 | 10115 Berlin
Germany

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.

INDUSTRY EXHIBITION

The industry exhibition is located in Ballroom III.

Opening Hours:
16th June, 09:00–18:30
Poster Session & Get-Together, 18:30–20:30
17th June, 08:30–17:30
18th June, 08:30–13:30

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

The media check is located on the ground floor in the Speakers' Ready Room. 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 – should it be the first lecture of the day, please submit the day before (exception 17th June 2022). Please refer to the presentation guidelines guidelines sent via email.

Opening Hours
16th June 8:00-19:00
17th June 8:00-18:30
18th June 8:00-12:00

NAME BADGE

Your 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 a lost or forgotten badge, an administrative fee of 10€ will be charged.

POSTER SESSION & GET-TOGETHER

The Get-Together will take place on Thursday, 16th June 2022 from 18:30-20:30.

PRE-CONFERENCE WORKSHOPS

Pre-conference workshops will take place on Wednesday, 15th June, 2022. Please see page 9 for further information.

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 situated in the foyer on the ground floor. 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.

For on-site registrations, we will only accept cashless payments (all major credit cards, Chip & PIN, contactless NFC payments, as well as Apple Pay and Google Pay). Unfortunately, we cannot accept ESDIP membership fee payments on-site. If you wish to take advantage of the membership benefits when registering on site, please submit the online form and pay your membership fee ahead of time (by PayPal or WireTransfer). We are sorry for this inconvenience.

Opening Hours Registration	**Opening Hours Exhibition**
15th June, 9:00-18:00	–
16th June, 8:00-18:00	16th June, 8:30-21:00
17th June, 8:00-18:00	17th June, 8:30-18:30
18th June, 8:00-12:00	18th June, 8:30-14:00

SOCIAL EVENT

Boat Trip & Congress Dinner

All Congress delegates, speakers and exhibitors are invited to the ECDP2022 social event, which will take place on the evening of Friday, 17th June. Please see pp. 158-159 for details.

SMOKING

Smoking is strictly prohibited in the congress venue by law.

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NOTES

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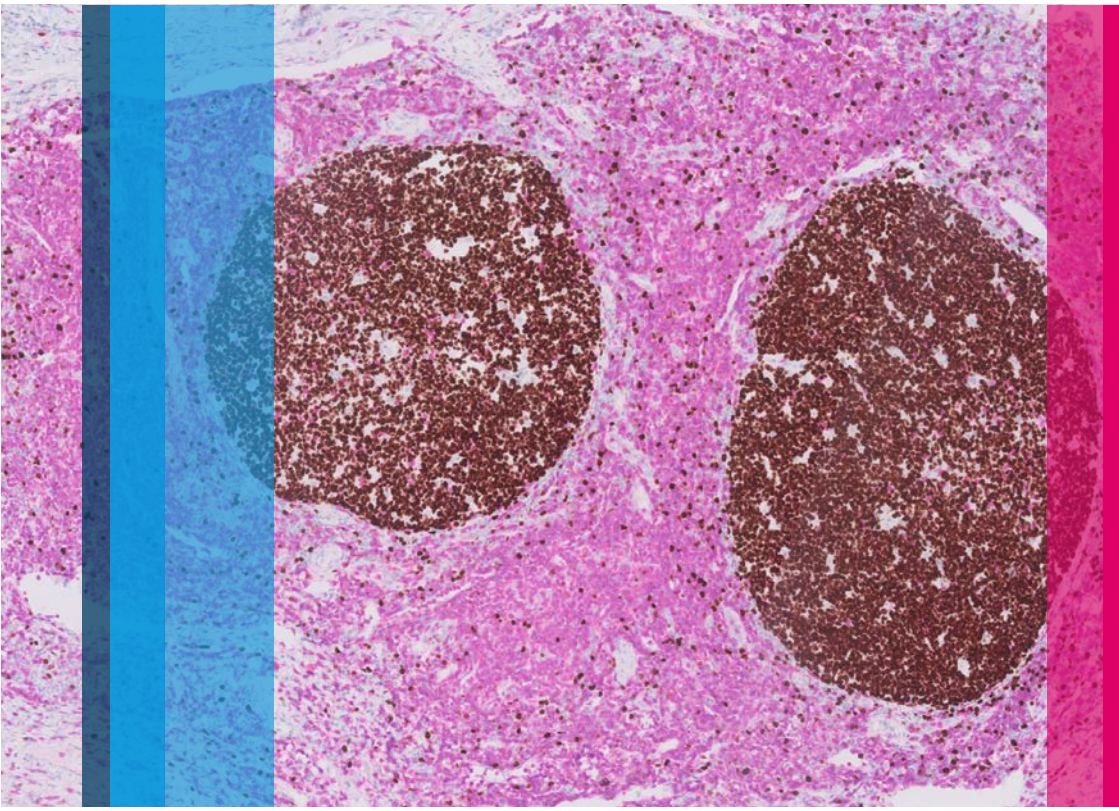

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Image Caption: Tonsil, sequential staining of Ki-67 (DAB, nuclei) in germinal centers and CD3 (HRP Magenta, cytoplasm and membranes of T cells) in the mantle zone.

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Travelling by train from Berlin Brandenburg Airport (BER) via Berlin central train station

The Airport Express (FEX) and other regional trains will take you to the central train station Hauptbahnhof Berlin in 30 minutes. From there you are just 10 minutes away with public transit (see local map on right). Exit the train station on the north side onto Europaplatz and you will see the tram station. You can take tram lines M8 (direction Ahrensfelde) or M10 (direction S+U Warschauer Str.). Exit at the second stop (" Naturkundemuseum"). Turn left onto Chausseestraße. After a 3-minute walk, you will see the congress venue the right side.

Other local and regional public transit

The local transportation company BVG has an app ("BVG Fahrinfo-App", on Apple App Store, Google Playstore) for access to information on all stops and timetables for local transit.

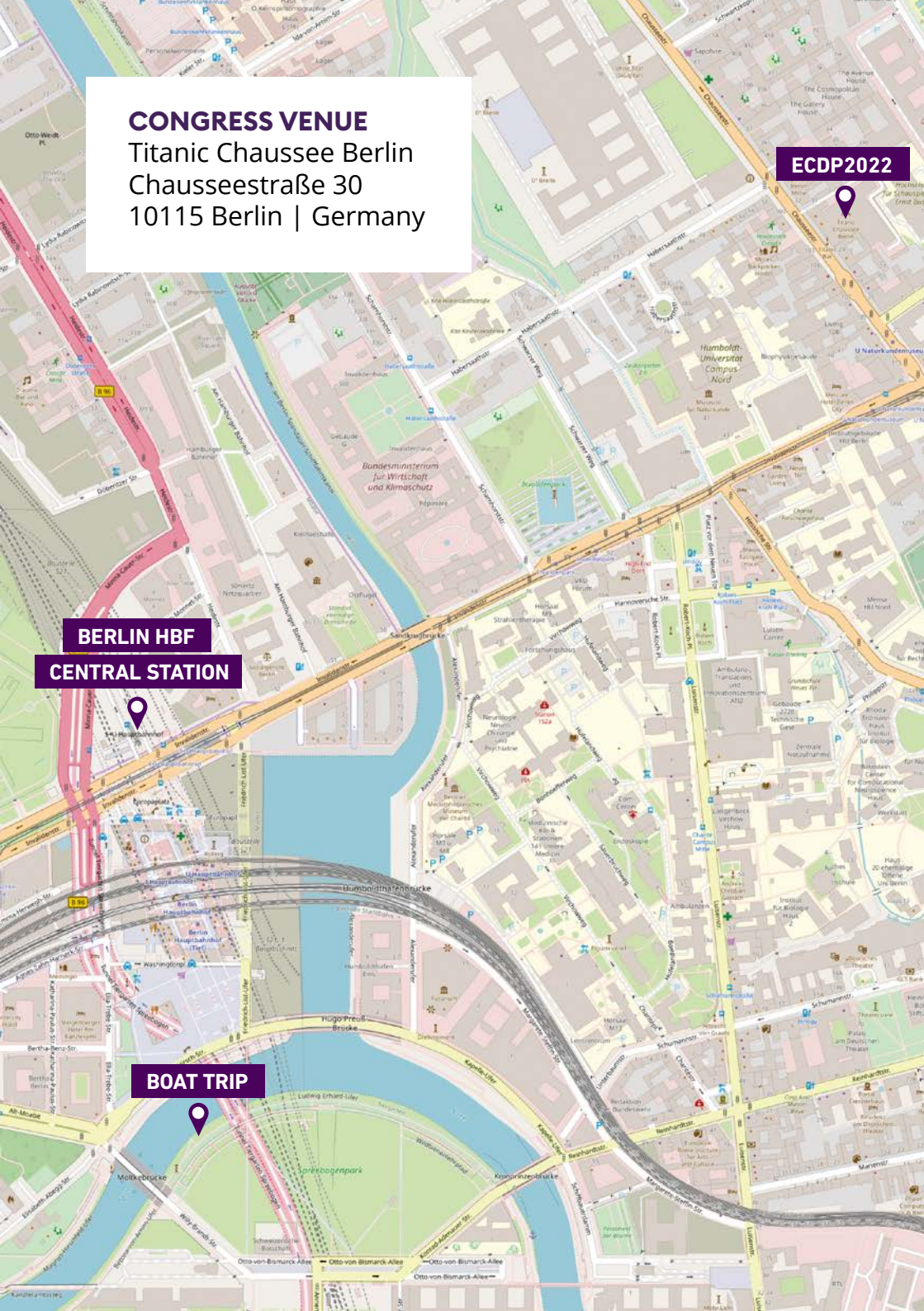
Starting in June 2022, a so-called "9€ Ticket" is available. For just €9, this ticket is valid for regional transportation across the whole of Germany for the entire month.

Berlin also has an official tourist ticket: Berlin WelcomeCard 2022. It includes public transport, a city guide and map, and allows you to save up 50% at top attractions.

Travelling by car

The exit from the A100, Wexstraße, will take you to Martin-Luther-Straße. Follow the road and go across Schöneberger Ufer. Then you will reach the B96 across Potsdamer Platz and the tunnel Tiergarten until the main train station Hauptbahnhof Berlin. Turn right onto Invalidenstraße. After approx. 200m, turn left into Scharnhorststraße. After passing Invalidenpark, turn right into Habersaathstraße. At the end of this street, you will find the Chausseestraße. Make a right turn and you will see our venue Titanic Chaussee Berlin. Please note that a pollution badge is required in case you want to access Berlin City Center by car (more information at berlin.de)

Taxi: If you plan to take a taxicab, you can find all the information you need at visitBerlin.de.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ECDP2022
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BOAT TRIP

IMPRINT

ORGANIZER

ESDIP – European Society of Digital and Integrative Pathology
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CONGRESS PRESIDENT

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Ludwig-Maximilians-Universität München
Thalkirchner Straße 36 | 80337 München
Germany

Charité – Universitätsmedizin Berlin
Charitéplatz 1 | 10117 Berlin
Germany

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CONGRESS HOMEPAGE

www.ecdp2022.org

TIME OF PRINTING

7th June 2022
All information regarding speaker and times is subject to change.

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