Reimagining Pathology: A Seamless Transformation from Slides to Generative Insight

Osamu Iizuka
Medmain Inc. CEO

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Osamu has a medical background from Kyushu University School of Medicine and extensive experience in AI and software development. After working as a software engineer at a startup and winning first place in a pitch competition in Silicon Valley, he founded Medmain Inc. in 2018 to drive innovation in pathology. In 2020, Osamu was named to the Forbes 30 Under 30 Asia list for his contributions to healthcare and AI.

All-in-One System for Pathological Specimen Storage / Browsing / Sharing / AI analysis

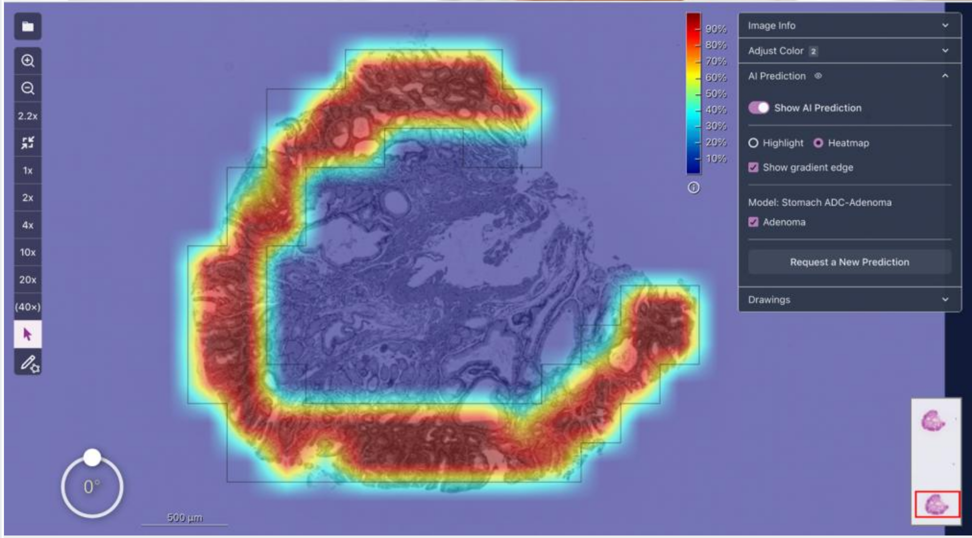
The Next Generation Cloud-Based AI-Mounted Digital Pathology Support System

PidPort

Pathology AI Analysis Solution Introduction of「PidPort」

Medmain develops and provides PidPort, an AI-powered cloud system that supports digital pathology, to solve problems in pathological diagnosis and related fields.

PidPort is a system that has the following three major functions.
①Pathological Image Analysis by AI
②Collaborative functions through inter-facility coordination (Telepathology/consultation, conference, education and research support)
③Digital storage of pathological data



Service Flow

Customer

Pathology Specimen

Pathology Image Data

Digitization

PidPort

Supporting the field of pathological diagnosis with technology

Storage & Managemen t	Pathological image data and case information can be safely stored, managed, and used in the cloud.
Viewing & Sharing	Our own high-speed viewer allows you to view images and share cases easily
AI Analysis	AI, developed through deep learning, can instantly and accurately screen and double check tissues and cells.

Medmain Imaging Center

Support for establishing an environment for digital pathology

Just by sending the pathological specimens, they can be digitized quickly and inexpensively in high quality.

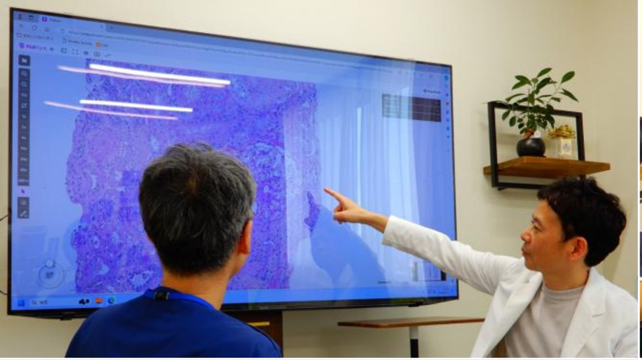
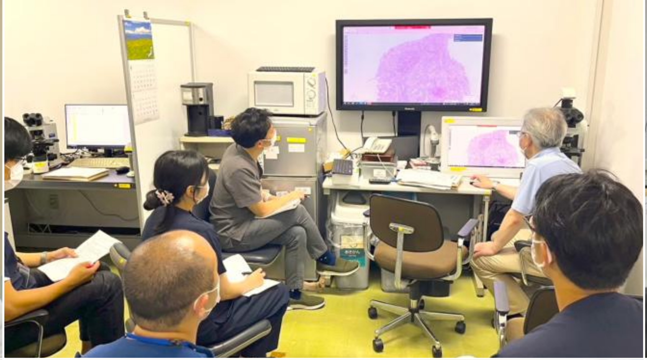
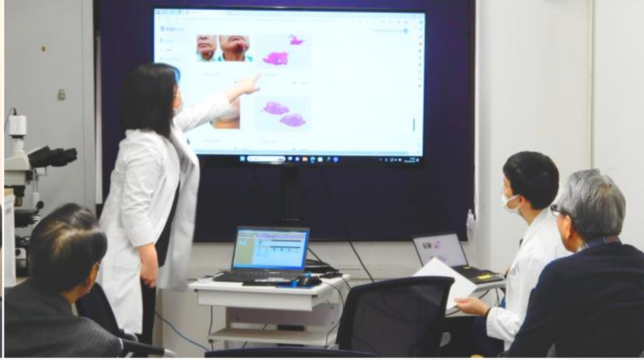
Imaging Center

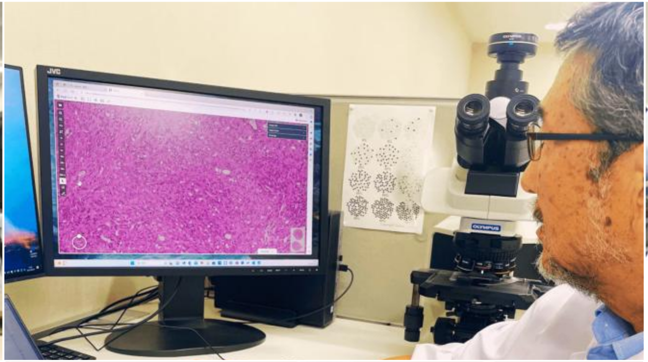
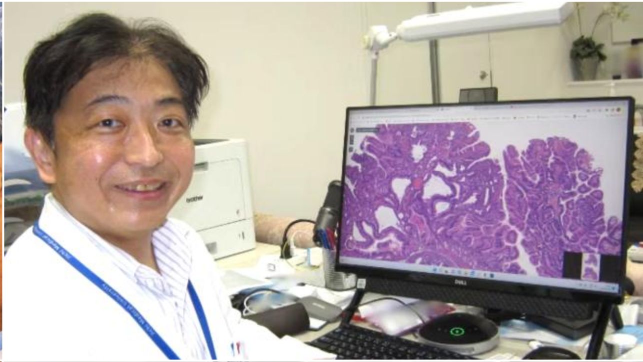
Support Digitization of Glass Slides

Inexpensive and Rapid Digitization Service of Pathological Specimens

In order to promote digitization of glass slides in medical institutions, there are many challenges remain, including purchasing expensive equipment such as special scanners, securing personnel, and controlling quality of images.

We have our own digitization centers for glass slides and support to digitize them rapidly and inexpensively.

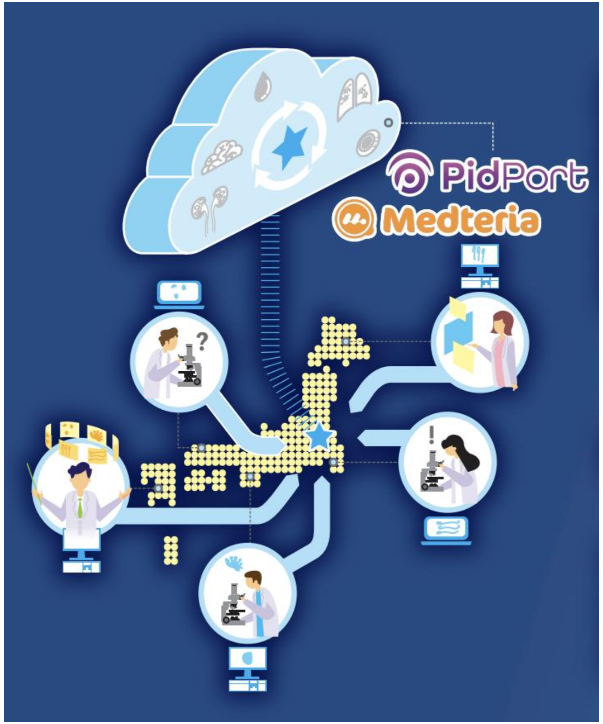





JVC
OLYMPUS



- **Used by over 100 institutions globally**
  Japan, India, Vietnam, Singapore and more
- **60% of medical universities in Japan have adopted PidPort as KOL facilities**

Running the online platform for pathologists.

ANYTIME & ANY PLACE PATHOLOGY；Problem-Solving Platform Among Pathologists



① Online Pathology Consultation

② Online Pathology Conferences

③ Online Seminars & Live Consultation

④ Special Seminar/Symposium, etc.

- **Establishment of an online platform for pathologists across Japan**
  A total of 1,000 pathologists - representing 35% of all pathologists in Japan - are participating.

- **Establishment of an online platform connecting pathologists and clinicians (Hematologists, Nephrologists, etc.) in Japan**

Pathology AI Development
High-Speed, High-Accuracy Image Analysis with AI

Through joint research with multiple medical institutions, we have created hundreds of thousands of virtual slides (WSI) and are developing pathology AI using proprietary deep learning and transfer learning technologies, based on training data annotated by a large number of expert pathologists.

Currently, our pathology AI covers a wide range of organs and diseases, including the stomach, colon, lung (malignant epithelial tumors and non-neoplastic lesions), breast (malignant epithelial tumors, benign epithelial tumors, and non-neoplastic lesions), pancreas (detection of adenocarcinoma in endoscopic ultrasound-guided fine-needle aspiration biopsy specimens), prostate (malignant epithelial tumors and non-neoplastic lesions), lymph nodes (detection of metastatic malignant epithelial tumors), and the uterine cervix and urine (cytological determination of tumor presence).

Development of Pathology AI: Core Models for Pathology Diagnosis Support

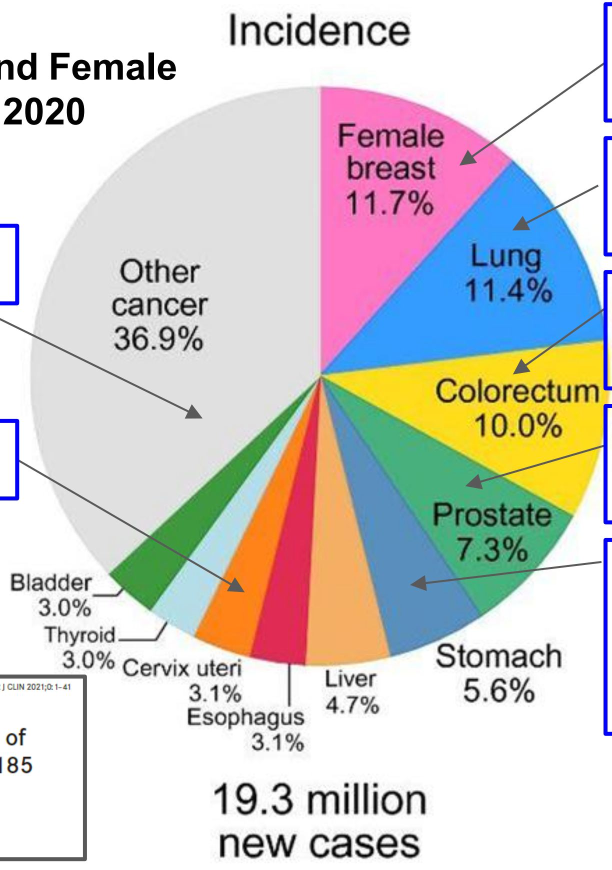
Combined Male and Female Incidence Rate in 2020

Pancreas

Scientific Reports, 11: 8454, 2021.

Cancers, 14: 1159, 2022.

Liquid-based cytology



Virchows Archiv, 480: 1009-1022, 2022
Cancers, 13: 5368, 2021

Scientific Reports, 11: 8110, 2021
Scientific Reports, 10: 9297, 2020

Diagnostics, 11: 2074, 2021
Scientific Reports, 10: 1504, 2020.

Diagnostics, 12: 768, 2022.
Cancers, 14: 4744, 2022.

Scientific Reports, 11: 20486, 2021.
Technology in Cancer Research & Treatment, 20: 15330338211027901, 2021.
Scientific Reports, 10: 1504, 2020.

CA CANCER J CLIN 2021;0:1-41

Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries

Hyuna Sung, PhD [1]; Jacques Ferlay, MSc, ME[2]; Rebecca L. Siegel, MPH [1]; Mathieu Laversanne, MSc[2]; Isabelle Soerjomataram, MD, MSc, PhD[2]; Ahmedin Jemal, DMV, PhD[1]; Freddie Bray, BSc, MSc, PhD[2]

Medmain's Developed AI Models

Medmain AI covers 90% of all the pathological cases and detect cancer

Histology:

① [Stomach] Epithelial tumour screening model of the stomach: adenocarcinoma, adenoma and non-neoplastic lesions
② [Stomach] Adenocarcinoma subtyping model of the stomach: signet ring cell carcinoma
③ [Stomach] Adenocarcinoma differentiation model of the stomach: poorly differentiated adenocarcinoma
④ [Colon] Epithelial tumour screening model of the colon: adenocarcinoma, adenoma and non-neoplastic lesions
⑤ [Colon] Adenocarcinoma differentiation model of the colon: poorly differentiated adenocarcinoma
⑥ [Lung] Screening model for lung cancer: cancer diagnosis
⑦ [Lung] Adenocarcinoma subtyping model of the lung cancer: squamous cell carcinoma, adenocarcinoma, small cell carcinoma
⑧ [Pancreas] Pancreatic cancer screening model within ultrasound endoscopic puncture aspiration micro specimens of the pancreas.
⑨ [Breast] Invasive ductal carcinoma screening model of the breast: cancer diagnosis
⑩ [Breast] Screening model for classification of invasive and non-invasive ductal carcinoma of the breast
⑪ [Prostate] Adenocarcinoma screening model in needle biopsy specimens of the prostate: cancer diagnosis
⑫ [Prostate] Adenocarcinoma screening model in TUR-P specimens of the prostate gland: cancer diagnosis
⑬ [Prostate] Screening model for grading of prostate cancer
⑭ [lymph node] Models for screening adenocarcinoma for multiple organs
⑮ [Stomach] Screening model for poorly differentiated adenocarcinoma in gastric ESD (endoscopic submucosal dissection) specimens
⑯ [Skin] Screening model for cutaneous melanoma

Cytology:

⑰ [Uterine Cervix] Screening model for epithelial neoplastic changes in cervical liquid-based cytology
⑱ [Urine] Screening model for specimens suspected of urothelial carcinoma in urethral liquid-based cytology

Published Pathology AI R&D Paper ①

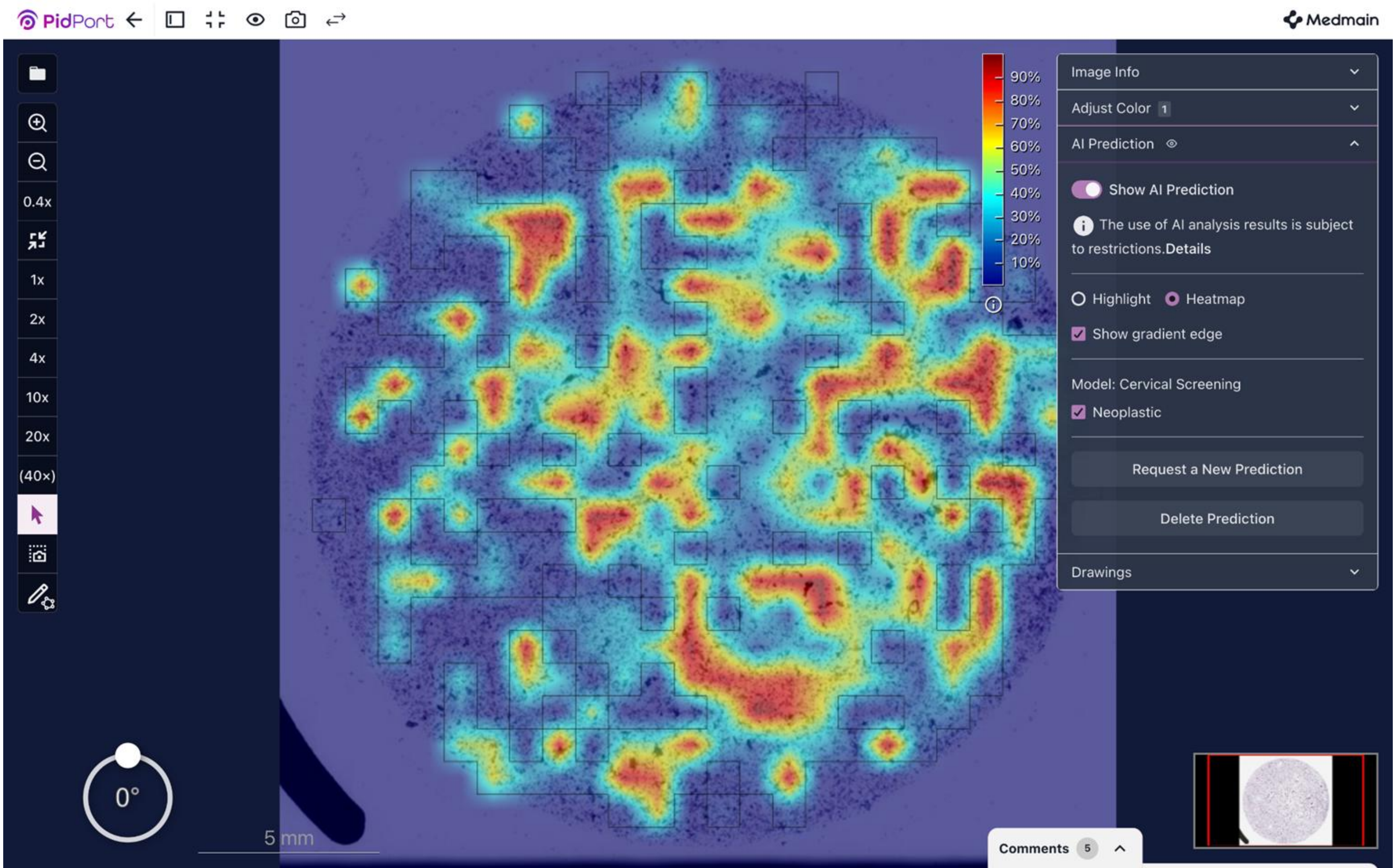
	Organ(s)	Classification	Specimen	Paper	Link
1	stomach & colon	Non-neoplastic lesion, Adenoma, Adenocarcinoma	Biopsy & Surgical specimens	Deep Learning Models for Histopathological Classification of Gastric and Colonic Epithelial Tumours	https://www.nature.com/articles/s41598-020-58467-9
2	lung	Non-neoplastic lesion, Carcinoma	TBLB & Surgical specimens	Weakly-supervised learning for lung carcinoma classification using deep learning	https://www.nature.com/articles/s41598-020-66333-x
3	lung	Non-neoplastic lesion, ADC, SCC, SCLC	TBLB & Surgical specimens	A deep learning model for the classification of indeterminate lung carcinoma in biopsy whole slide images	https://www.nature.com/articles/s41598-021-87644-7
4	pancreas	ADC, non-ADC	EUS-FNA biopsy	A deep learning model to detect pancreatic ductal adenocarcinoma on endoscopic ultrasound-guided fine-needle biopsy	https://www.nature.com/articles/s41598-021-87748-0
5	stomach	Signet ring cell carcinoma, non-signet ring cell carcinoma	Biopsy	Deep Learning Models for Gastric Signet Ring Cell Carcinoma Classification in Whole Slide Images	https://journals.sagepub.com/doi/full/10.1177/15330338211027901
6	stomach	Diffuse-type adenocarcinoma	Biopsy	A deep learning model for gastric diffuse-type adenocarcinoma classification in whole slide images	https://www.nature.com/articles/s41598-021-99940-3
7	uterine cervix	NILM, Neoplastic suspected	LBC	A Deep Learning Model for Cervical Cancer Screening on Liquid-Based Cytology Specimens in Whole Slide Images	https://www.mdpi.com/2072-6694/14/5/1159
8	colon	Poorly differentiated adenocarcinoma	Biopsy	Deep Learning Models for Poorly Differentiated Colorectal Adenocarcinoma Classification in Whole Slide Images Using Transfer Learning	https://www.mdpi.com/2075-4418/11/11/2074
9	breast	Invasive ductal carcinoma (IDC), non-IDC (benign)	Biopsy & Surgical specimens	Breast Invasive Ductal Carcinoma Classification on Whole Slide Images with Weakly-Supervised and Transfer Learning	https://www.mdpi.com/2072-6694/13/21/5368
10	breast	IDC, DCIS, benign	Biopsy & Surgical specimens	A deep learning model for breast ductal carcinoma in situ classification in whole slide images	https://link.springer.com/article/10.1007/s00428-021-03241-z

Published Pathology AI R&D Paper ②

	Organ(s)	Classification	Specimen	Paper	Link
11	global	ADC, non-ADC	Biopsy & Surgical specimens	Weakly supervised learning for multi-organ adenocarcinoma classification in whole slide images	https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0275378
12	prostate	ADC, benign	Biopsy	A Deep Learning Model for Prostate Adenocarcinoma Classification in Needle Biopsy Whole-Slide Images Using Transfer Learning	https://www.mdpi.com/2075-4418/12/3/768
13	prostate	ADC, benign	TUR-P	Transfer Learning for Adenocarcinoma Classifications in the Transurethral Resection of Prostate Whole-Slide Images	https://www.mdpi.com/2072-6694/14/19/4744
14	prostate	Aggressive, Indolent, Benign	Biopsy	Inference of core needle biopsy whole slide images requiring definitive therapy for prostate cancer	https://bmccancer.biomedcentral.com/articles/10.1186/s12885-022-10488-5
15	stomach	Poorly differentiated adenocarcinoma	ESD & Surgical specimens	Weakly Supervised Learning for Poorly Differentiated Adenocarcinoma Classification in GastricEndoscopic Submucosal Dissection Whole Slide Images	https://journals.sagepub.com/doi/10.1177/15330338221142674
16	skin	Melanoma, non-Melanoma	Biopsy & Surgical specimens	Deep Learning Approach to Classify Cutaneous Melanoma in a Whole Slide Image	https://www.mdpi.com/2072-6694/15/6/1907
17	urine	Negative, Neoplastic	LBC	Deep Learning-Based Screening of Urothelial Carcinoma in Whole Slide Images of Liquid-Based Cytology Urine Specimens	https://www.mdpi.com/2072-6694/15/1/226

	Paper	Link
18	Partial transfusion: on the expressive influence of trainable batch norm parameters for transfer learning	https://openreview.net/forum?id=TjwDWRdfZpg
19	Inference of captions from histopathological patches	https://proceedings.mlr.press/v172/tsuneki22a.html


PidPort
Medmain
Image Info
Adjust Color
AI Prediction
Drawings
0.4x
1x
2x
4x
10x
20x
(40x)
0°
5 mm
Comments 5


PidPort
Medmain
0.4x
1x
2x
4x
10x
20x
(40x)
0°
5 mm
90%
80%
70%
60%
50%
40%
30%
20%
10%
Image Info
Adjust Color 1
AI Prediction
Show AI Prediction
The use of AI analysis results is subject to restrictions.Details
Highlight
Heatmap
Show gradient edge
Model: Cervical Screening
Neoplastic
Request a New Prediction
Delete Prediction
Drawings
Comments 5

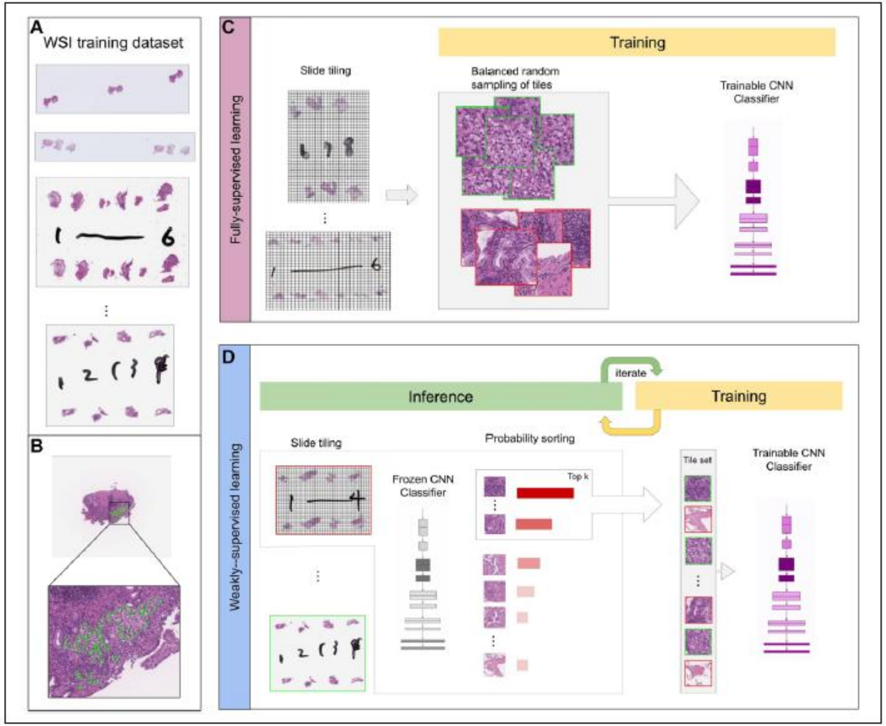
AI Model to Detect Signet Ring Cell Carcinoma in the Stomach

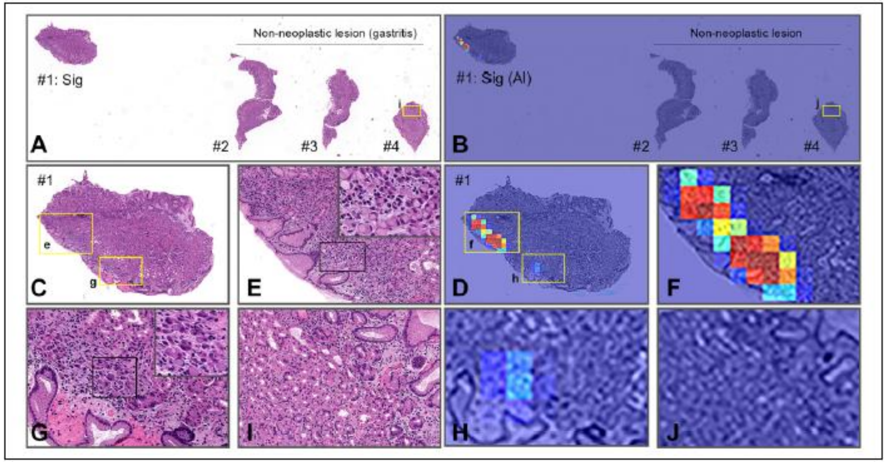
Deep Learning Models for Gastric Signet Ring Cell Carcinoma Classification in Whole Slide Images

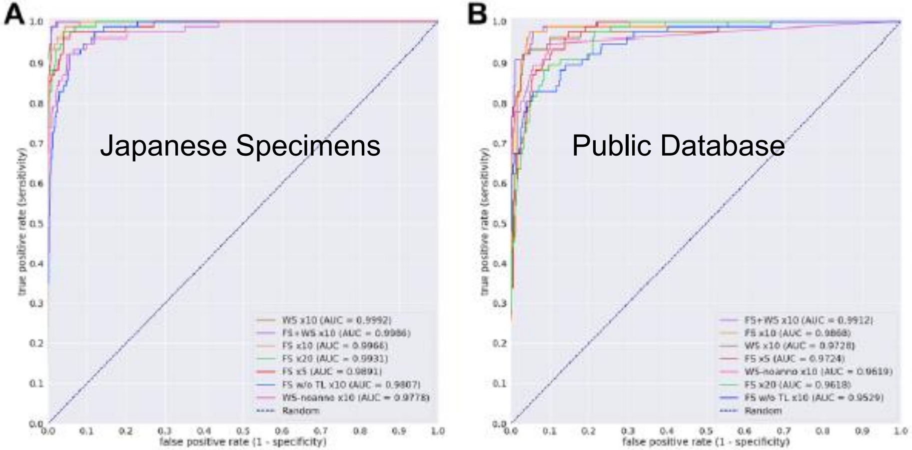
Technology in Cancer Research & Treatment
Volume 20: 1-14

DOI: 10.1177/15330338211027901
journals.sagepub.com/home/tct
SAGE

Fahdi Kanavati[1], Shin Ichihara[2], Michael Rambeau[3], Osamu Iizuka[3], Koji Arihiro[4], and Masayuki Tsuneki[1,3]







AI Model to Classify Lung Cancer Histological Subtypes

www.nature.com/scientificreports

scientific reports

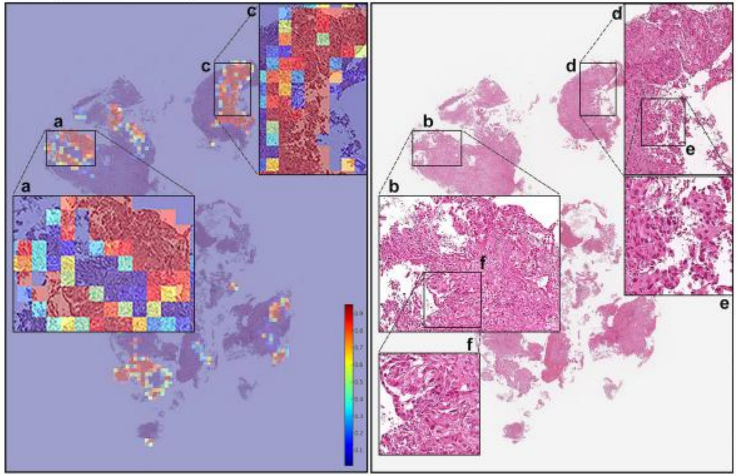
Check for updates

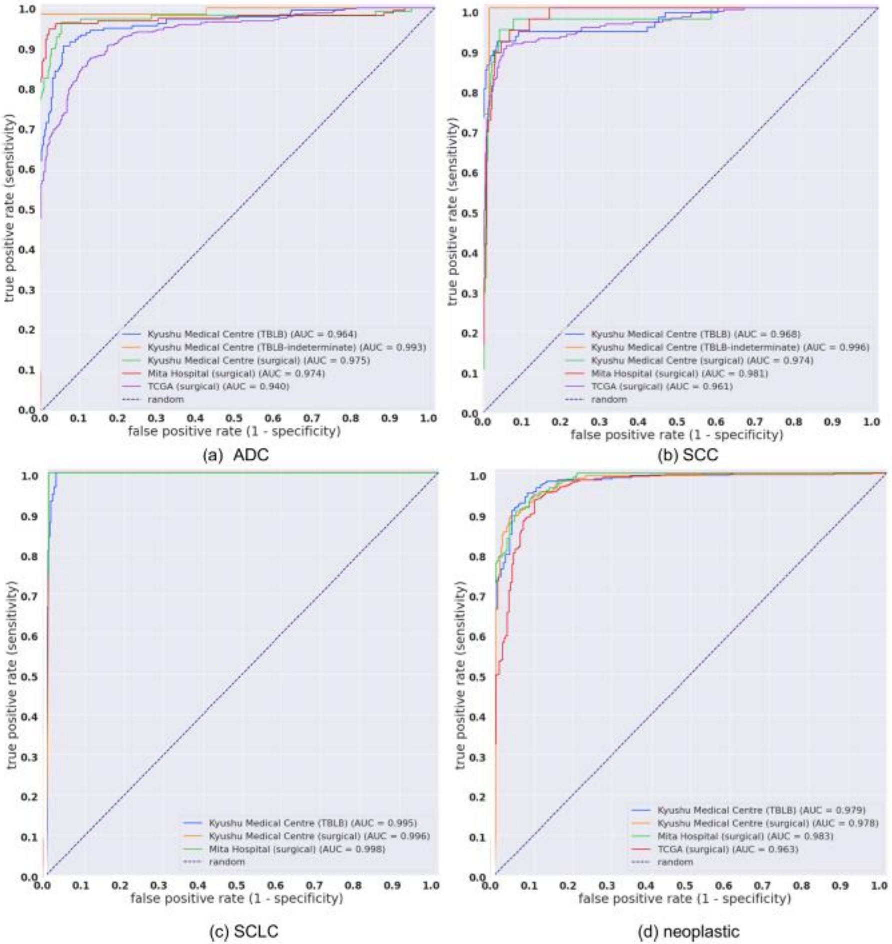
OPEN

A deep learning model for the classification of indeterminate lung carcinoma in biopsy whole slide images

Fahdi Kanavati[1,6], Gouji Toyokawa[2,6], Seiya Momosaki[3], Hiroaki Takeoka[4], Masaki Okamoto[4], Koji Yamazaki[2], Sadanori Takeo[2], Osamu Iizuka[5] & Masayuki Tsuneki[1,5]

A: True positive ADC case (indeterminate TBLB)





Pathology AI Models for Breast Tissue

cancers

Open Access Article

Breast Invasive Ductal Carcinoma Classification on Whole Slide Images with Weakly-Supervised and Transfer Learning

by Fahdi Kanavati and Masayuki Tsuneki *

Medmain Research, Medmain Inc., Fukuoka 810-0042, Japan

* Author to whom correspondence should be addressed.

Academic Editors: Anke Meyer-Baese, Max Zimmermann and Andreas Stadlbauer

Cancers **2021**, *13*(21), 5368; https://doi.org/10.3390/cancers13215368

Received: 30 September 2021 / Revised: 22 October 2021 / Accepted: 23 October 2021 / Published: 26 October 2021

(This article belongs to the Collection Artificial Intelligence in Oncology)

Simple Summary

In this study, we have trained deep learning models using transfer learning and weakly-supervised learning for the classification of breast invasive ductal carcinoma (IDC) in whole slide images (WSIs). We evaluated the models on four test sets: one biopsy (n = 522) and three surgical (n = 1129) achieving AUCs in the range 0.95 to 0.99. We have also compared the trained models to existing pre-trained models on different organs for adenocarcinoma classification and they have achieved lower AUC performances in the range 0.66 to 0.89 despite adenocarcinoma exhibiting some structural similarity to IDC. Therefore, performing fine-tuning on the breast IDC training set was beneficial for improving performance. The results demonstrate the potential use of such models to aid pathologists in clinical practice.

SpringerLink

Original Article | Published: 25 January 2022

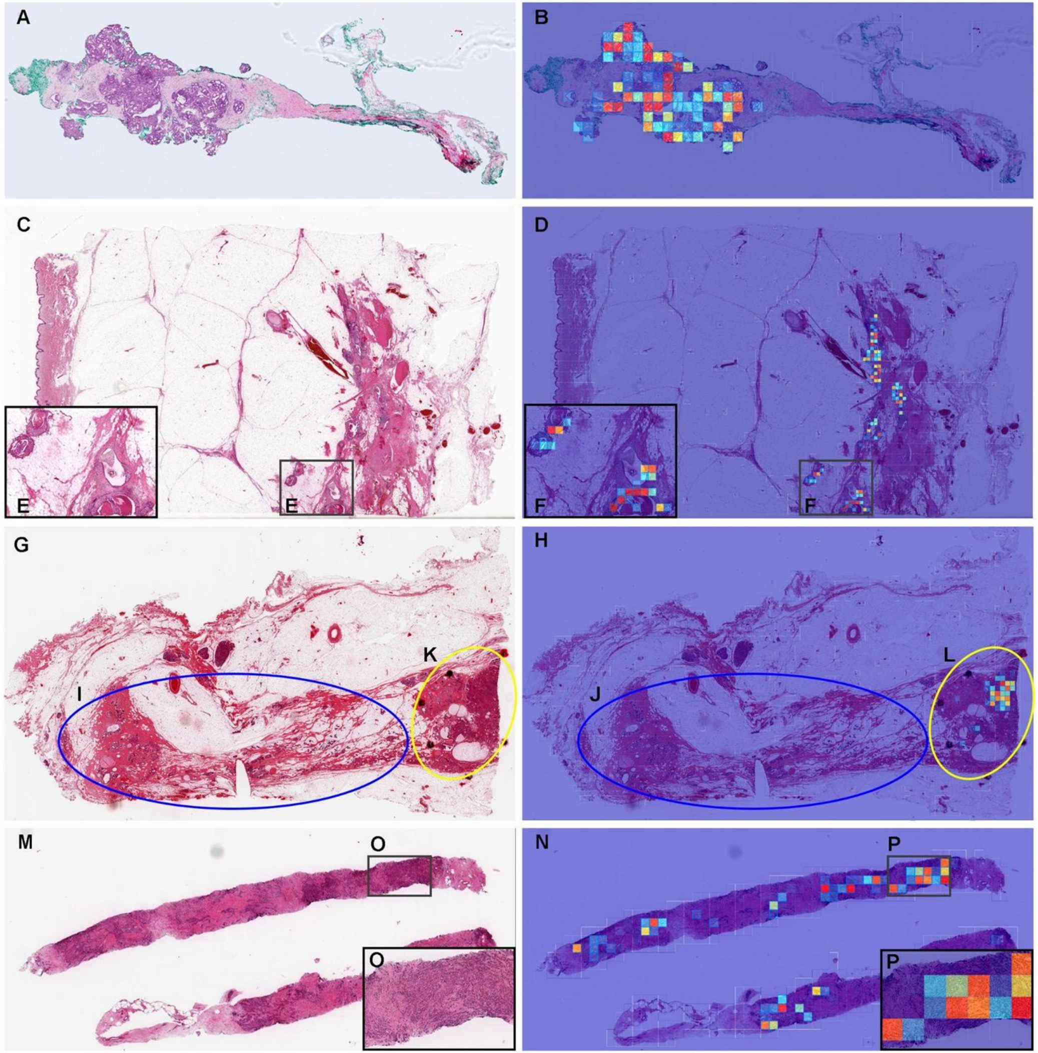
A deep learning model for breast ductal carcinoma in situ classification in whole slide images

Fahdi Kanavati, Shin Ichihara & Masayuki Tsuneki

Virchows Archiv **480**, 1009–1022 (2022) | Cite this article

Abstract

The pathological differential diagnosis between breast ductal carcinoma in situ (DCIS) and invasive ductal carcinoma (IDC) is of pivotal importance for determining optimum cancer treatment(s) and clinical outcomes. Since conventional diagnosis by pathologists using microscopes is limited in terms of human resources, it is necessary to develop new techniques that can rapidly and accurately diagnose large numbers of histopathological specimens. Computational pathology tools which can assist pathologists in detecting and classifying DCIS and IDC from whole slide images (WSIs) would be of great benefit for routine pathological diagnosis. In this paper, we trained deep learning models capable of classifying biopsy and surgical histopathological WSIs into DCIS, IDC, and benign. We evaluated the models on two independent test sets (n= 1382, n= 548), achieving ROC areas under the curves (AUCs) up to 0.960 and 0.977 for DCIS and IDC, respectively.



<DCIS (Core Needle Biopsy)>

The AI accurately detected the area of DCIS presence.

<DCIS (Surgical Specimen)>

The AI accurately detected the area of DCIS presence.

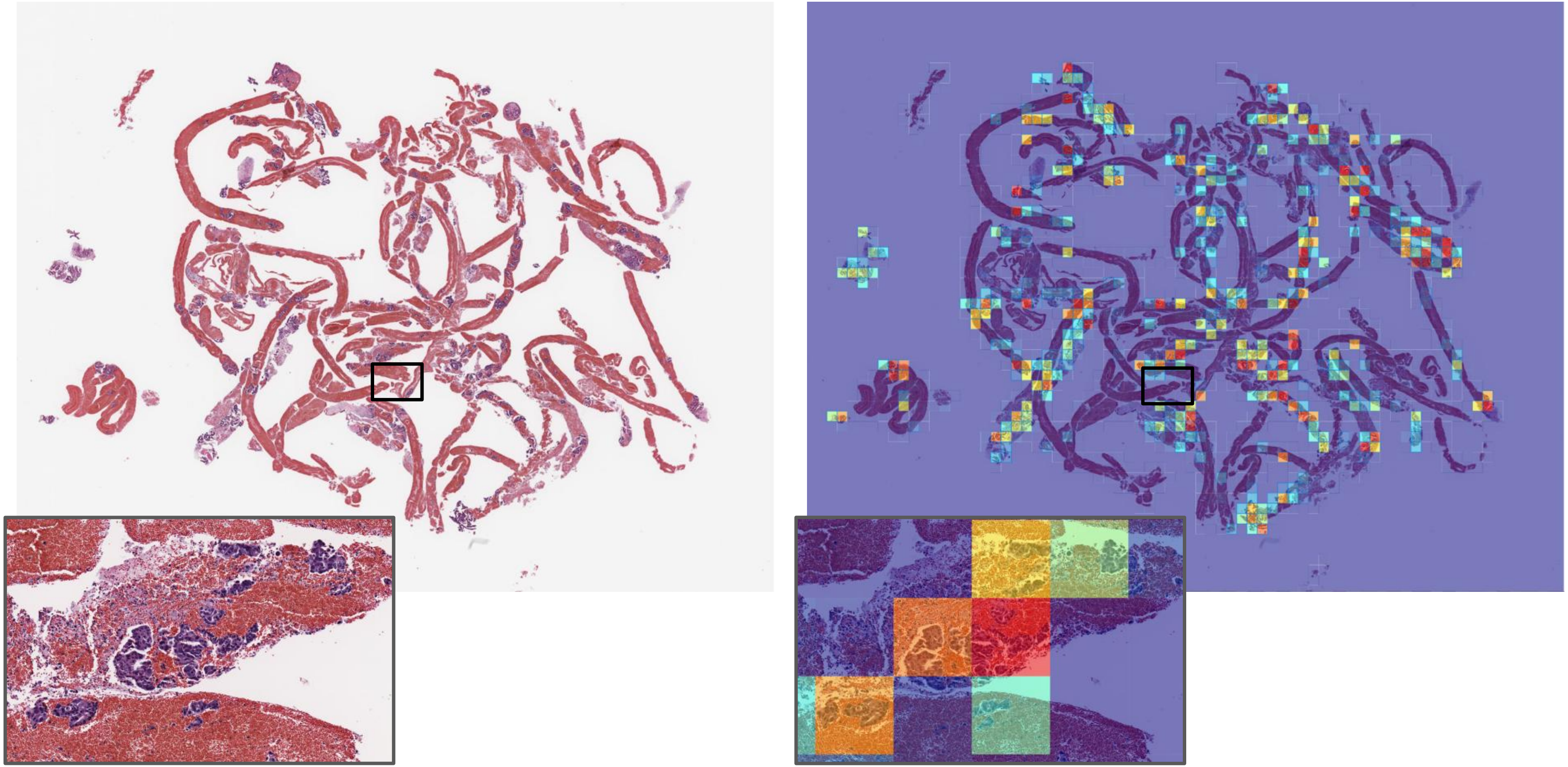
<DCIS (Surgical Specimen)>

Even in the presence of mastopathy or adenosis in the background, the AI accurately detected the area of DCIS.

<IDC (Core Needle Biopsy)>

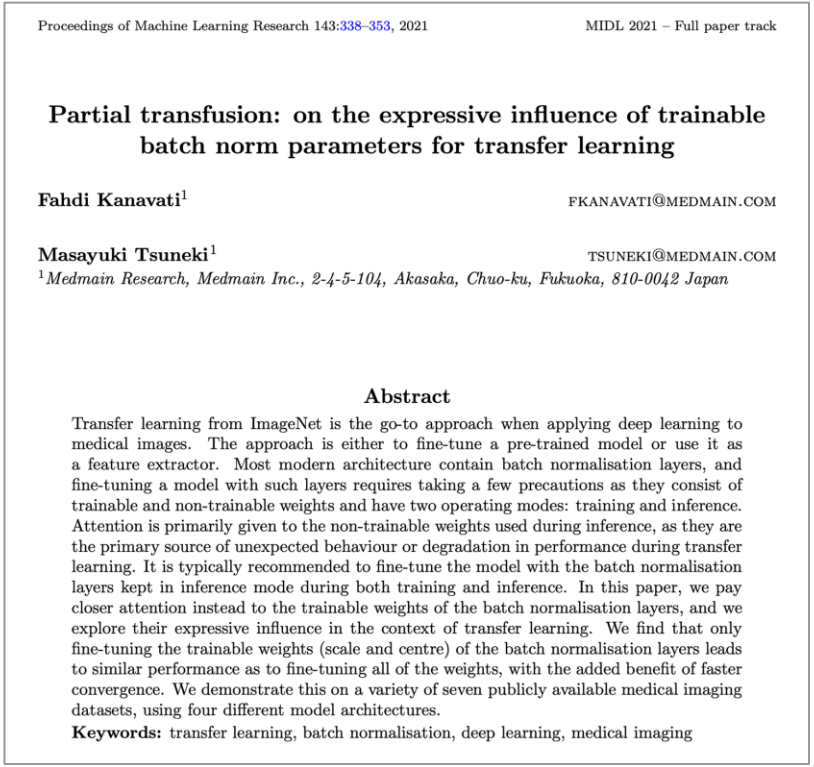
The AI accurately detected the area of IDC.

AI for Detecting Adenocarcinoma in Pancreatic EUS-FNA Specimens



Unique Technology to Accelerate Transfer Learning

Medmain has unique technology to accelerate transfer learning of deep learning.
With this technology, we can develop AI models quickly with less teaching data.



Proceedings of Machine Learning Research 143:338–353, 2021 MIDL 2021 – Full paper track

Partial transfusion: on the expressive influence of trainable batch norm parameters for transfer learning

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Masayuki Tsuneki[1] TSUNEKI@MEDMAIN.COM

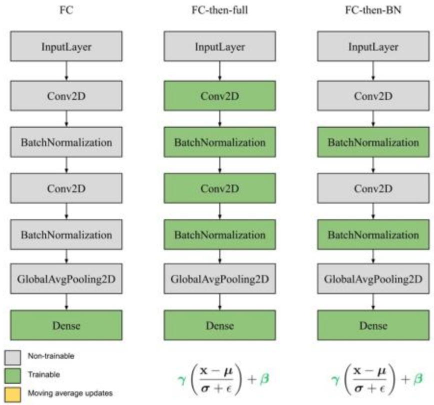
[1] *Medmain Research, Medmain Inc., 2-4-5-104, Akasaka, Chuo-ku, Fukuoka, 810-0042 Japan*

Abstract

Transfer learning from ImageNet is the go-to approach when applying deep learning to medical images. The approach is either to fine-tune a pre-trained model or use it as a feature extractor. Most modern architecture contain batch normalisation layers, and fine-tuning a model with such layers requires taking a few precautions as they consist of trainable and non-trainable weights and have two operating modes: training and inference. Attention is primarily given to the non-trainable weights used during inference, as they are the primary source of unexpected behaviour or degradation in performance during transfer learning. It is typically recommended to fine-tune the model with the batch normalisation layers kept in inference mode during both training and inference. In this paper, we pay closer attention instead to the trainable weights of the batch normalisation layers, and we explore their expressive influence in the context of transfer learning. We find that only fine-tuning the trainable weights (scale and centre) of the batch normalisation layers leads to similar performance as to fine-tuning all of the weights, with the added benefit of faster convergence. We demonstrate this on a variety of seven publicly available medical imaging datasets, using four different model architectures.

Keywords: transfer learning, batch normalisation, deep learning, medical imaging

https://proceedings.mlr.press/v143/kanavati21a.html

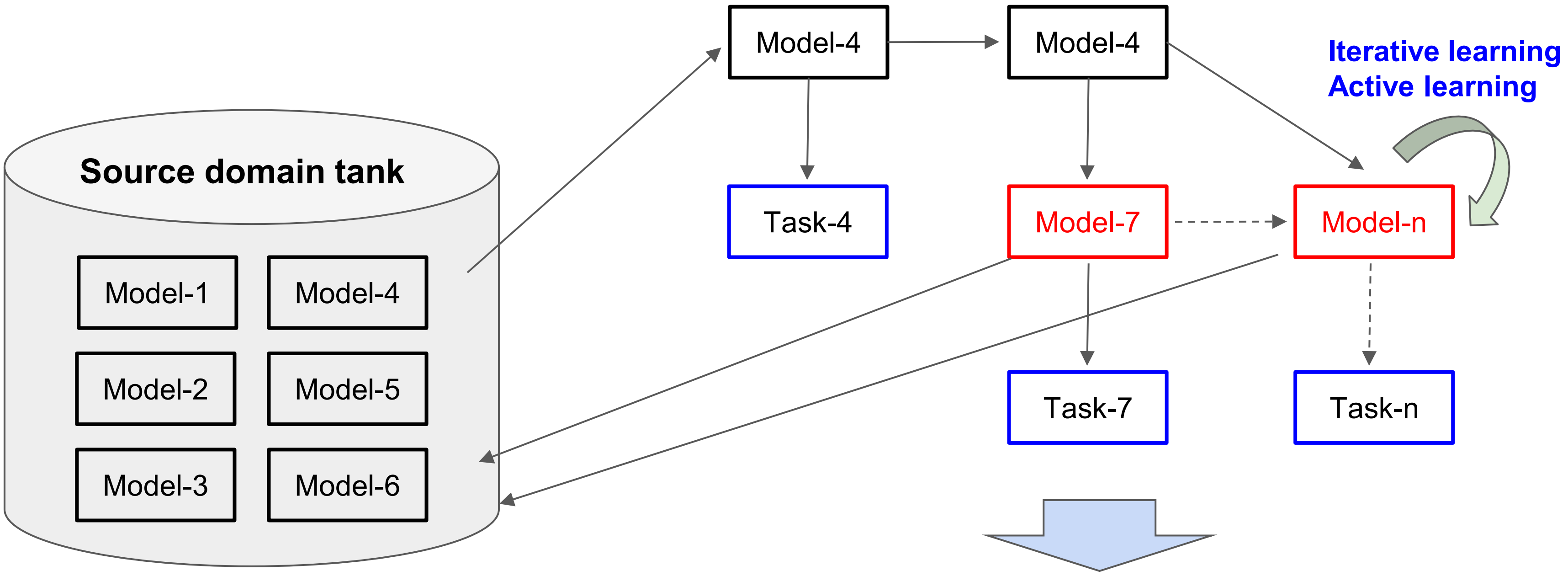


Non-trainable moving averages

$$\gamma\left(\frac{\mathbf{x}-\boldsymbol{\mu}}{\boldsymbol{\sigma}+\epsilon}\right)+\boldsymbol{\beta}$$

Trainable/differentiable affine parameters

Seamless AI Development through Transfer Learning



Model-1, Model-2,........., Model-n-1, Model-n

Task-1, Task-2,........., Task-n-1, Task-n

Ensemble: Model-1+2+5, Model-3+7+n-1,......

Joint Research and Usage Result of Medical Facilities in Japan and Overseas

Number of Joint Research and Facilities Using the System

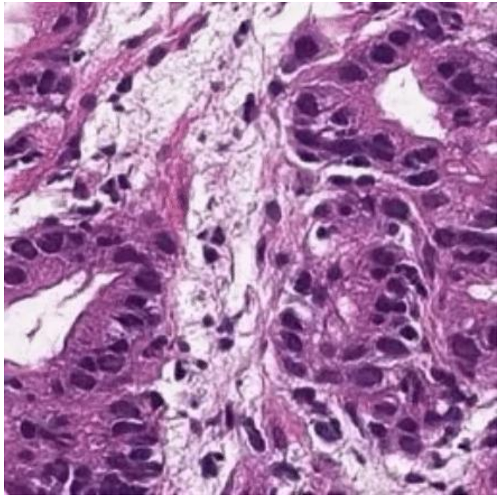
100 +Facilities

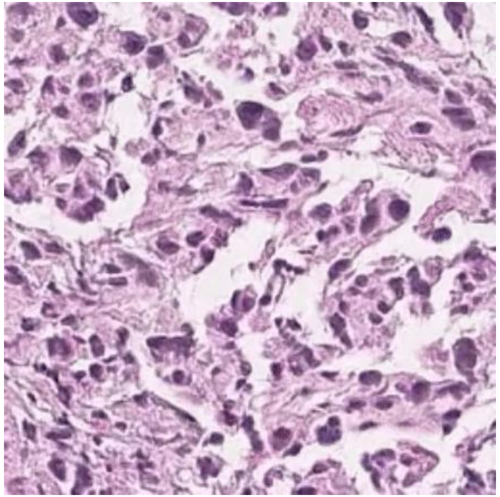
Japan / India / Thailand / USA / Singapore and more

- In Japan, 23 of the 82 medical universities (around 25%) are supporting Medmain’s pathology AI development through data contribution and annotation efforts.
- Using 5 million cases globally as a database for pathology AI development

Generative AI for Pathology Image Creation

Achieved wide-range generation of synthetic pathology images, covering well-differentiated to poorly differentiated adenocarcinomas. AI models are also capable of generating surrounding stromal components—such as fibrous tissue, blood vessels, and blood cells—faithfully reproducing typical tumor architecture in high resolution.

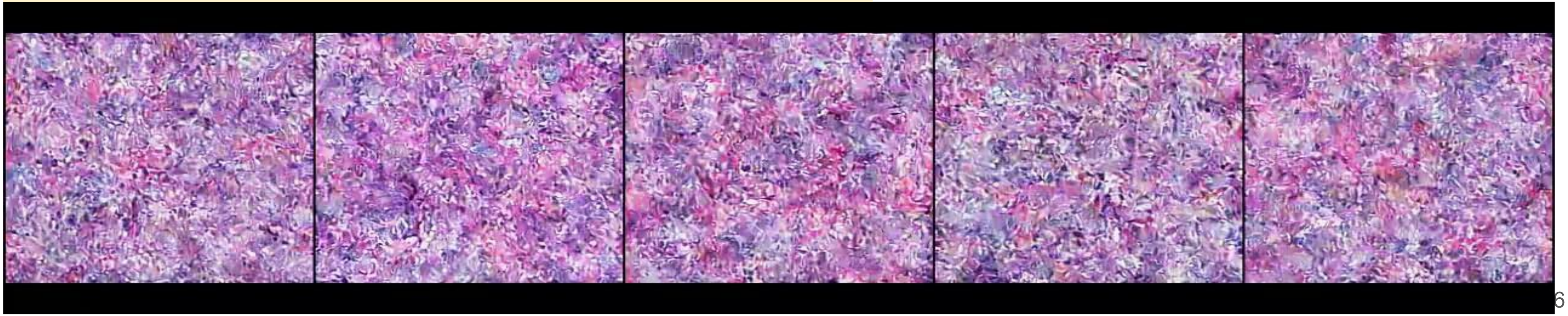




Diffusion models for generating pathological images from keywords

1. Keyword: stomach, adenoma

2. Keyword: stomach, poorly differentiated adenocarcinoma



Diffusion models for generating pathological images from keywords

3. Keyword: colon, adenocarcinoma

4. Keyword: breast, carcinoma

Deep learning models to write diagnostic reports from pathology images

Proceedings of Machine Learning Research 172:1–16, 2022 Full Paper – MIDL 2022

Inference of captions from histopathological patches

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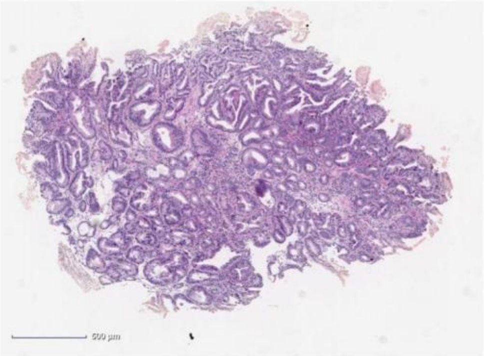
Abstract

Computational histopathology has made significant strides in the past few years, slowly getting closer to clinical adoption. One area of benefit would be the automatic generation of diagnostic reports from H&E-stained whole slide images which would further increase the efficiency of the pathologists' routine diagnostic workflows. In this study, we compiled a dataset (PatchGastricADC22) of histopathological captions of stomach adenocarcinoma endoscopic biopsy specimens, which we extracted from diagnostic reports and paired with patches extracted from the associated whole slide images. The dataset contains a variety of gastric adenocarcinoma subtypes. We trained a baseline attention-based model to predict the captions from features extracted from the patches and obtained promising results. We make the captioned dataset of 262K patches publicly available.

Keywords: Histopathology, caption prediction, adenocarcinoma, stomach

https://proceedings.mlr.press/v172/tsuneki22a/tsuneki22a.pdf



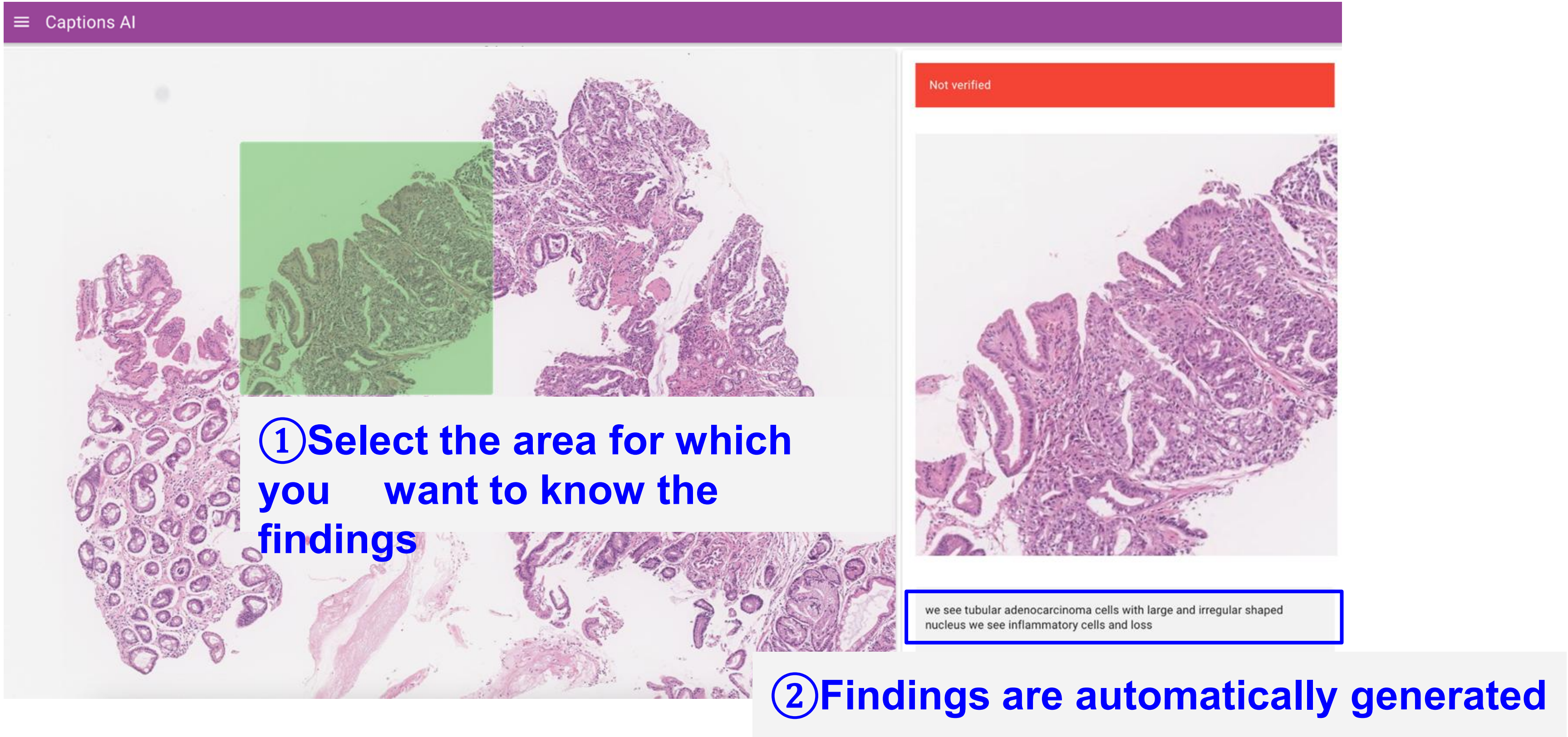
AI Output

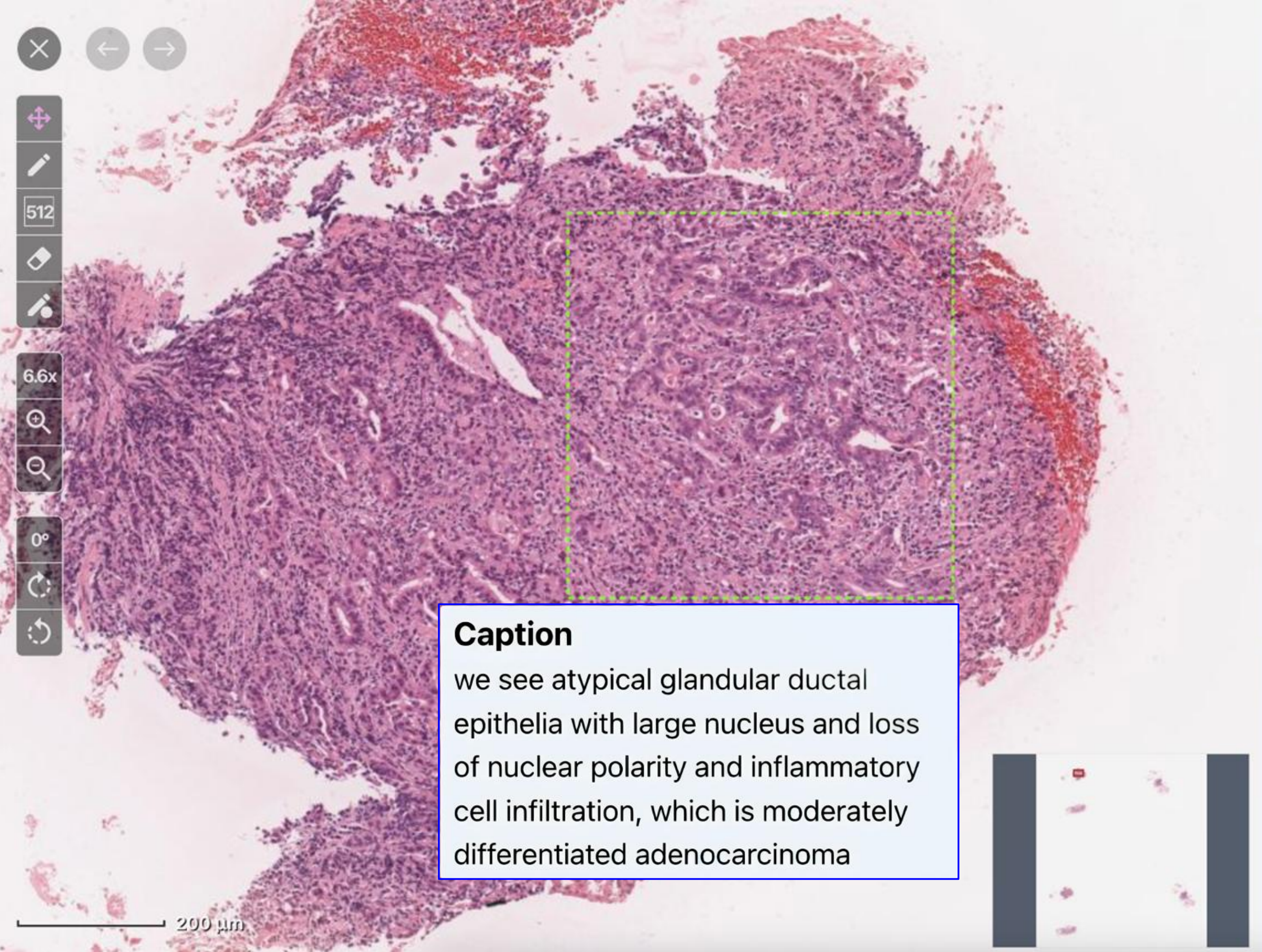
in the superficial epithelium tumor tissue that invades by forming medium sized to small irregular ducts is observed moderately differentiated tubular adenocarcinoma

tumor tissue consisting of cord like or small irregular glandular ducts fused and infiltrated is observed in the superficial epithelium poorly differentiated adenocarcinoma non solid type

Generative AI for Pathological Findings

- Developed AI to generate pathology findings from pathology images
- Designed for applications beyond pathological diagnosis, including use in the drug discovery process.





Whole-image annotations

No whole-image annotations.

Add

Polygon annotations 2

Caption 2 Trash

Add Mark all as verified

Multi-point annotations

Attachments

No attachments.

Add

Datasets

No datasets.

Metadata

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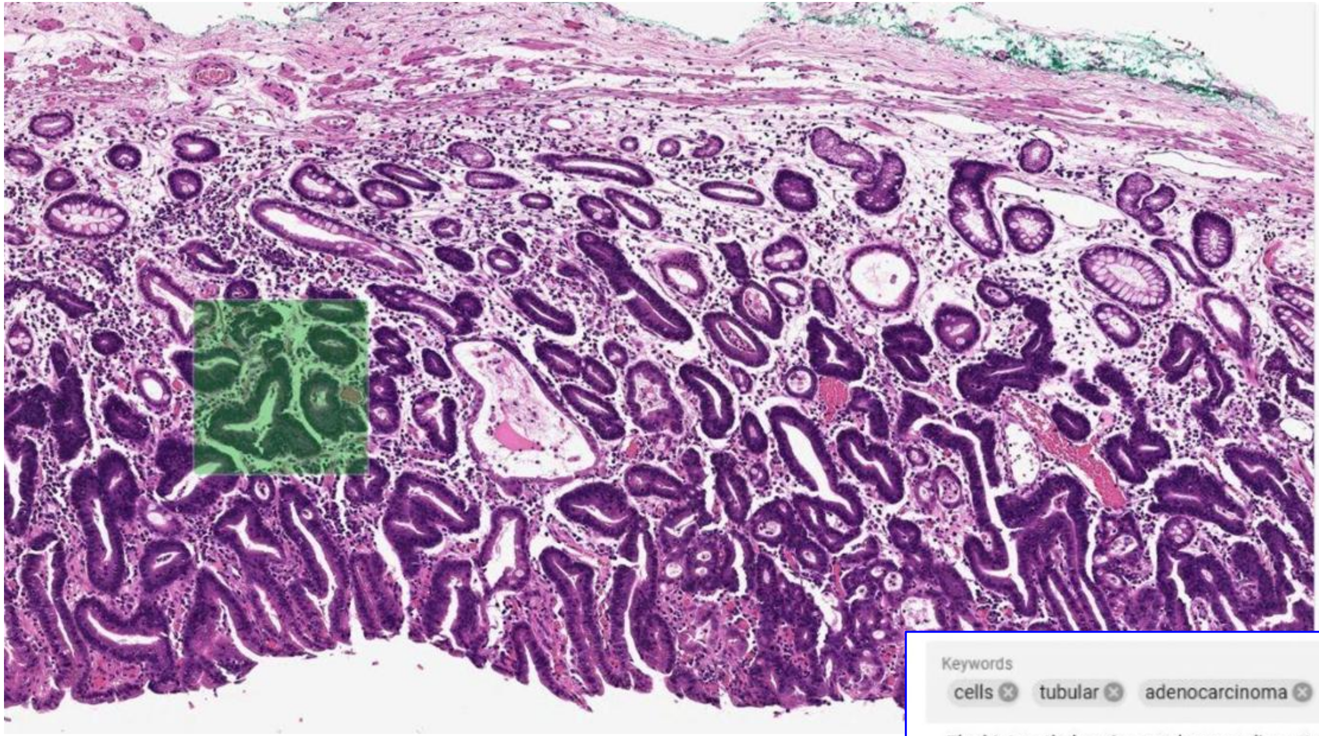
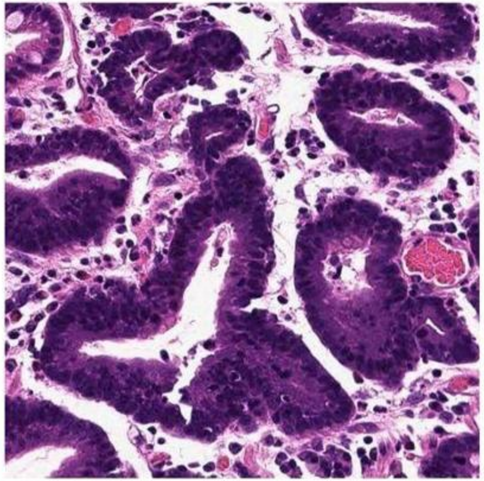
Keyword-Guided Generation of Accurate Pathological Findings from Pathology Images





Keywords

cells · tubular · adenocarcinoma · glandular · malignancy

The histopathology image shows malignant cells forming glandular structures consistent with tubular adenocarcinoma.

Unlocking Possibilities with Structured Pathology Data, Collaborative Networks, and AI

Improving diagnostic turnaround time and accuracy, and reducing the burden on doctors.

- **With pathology AI models, we can:**
  - **Detect, classify, and visualize lesions**
  - **Generate pathological findings as structured textual data**
  - **Automatically generate draft diagnostic reports**
- **Telepathology by collaborative networks enhances diagnostic accuracy and reliability, and helps address geographic barriers and workforce imbalance among pathologists.**

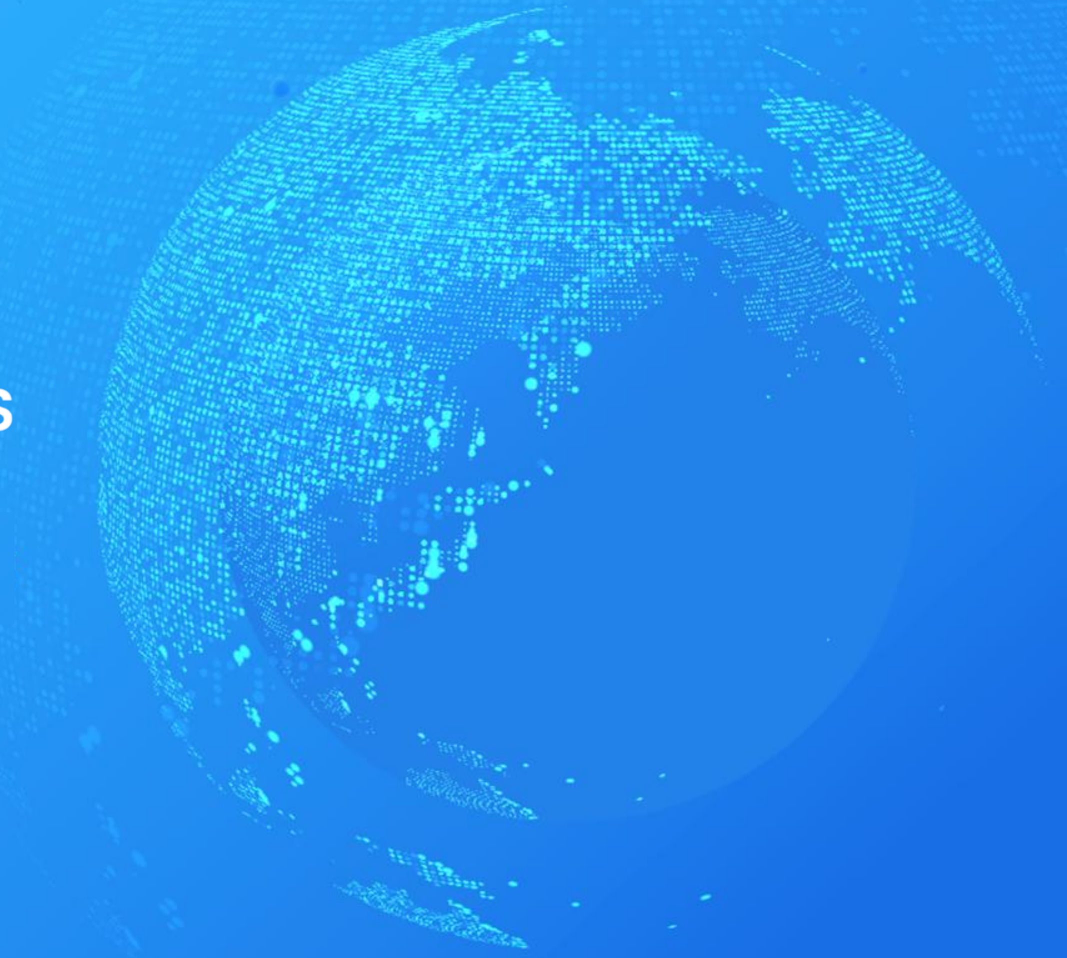
Deliver more advanced outputs:

- **Prognosis prediction and gene mutation estimation**

Quantification and standardization of pathological evaluations:

- **Applications in drug discovery: target identification, preclinical evaluation, biomarker discovery, clinical trials, companion diagnostics development.**

TO CREATE A WORLD
WHERE MEDICAL SERVICES
CAN BE ACCESSED WITH
TECHNOLOGY
ANYWHERE, ANYTIME



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