CAREGGI TRA INNOVAZIONE STRATEGICA E INNOVAZIONE DI SERVIZIO

CAREGGI TRA INNOVAZIONE STRATEGICA E INNOVAZIONE DI SERVIZIO

18° FORUM RISK MANAGEMENT

21 NOVEMBRE 2023 dalle ore 14.00 alle ore 18.00

SALA PETRARCA

Impatto clinico delle innovazioni nel Dipartimento delle Diagnostiche

Vittorio Miele, Daniela Massi

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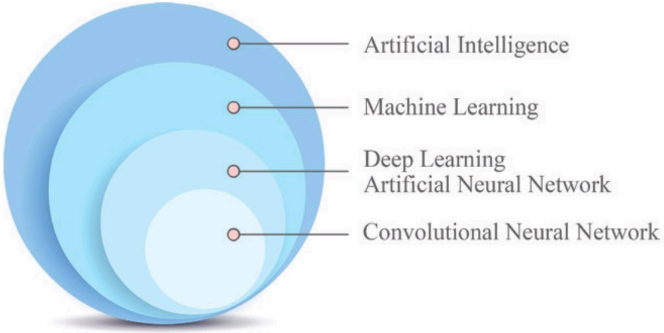
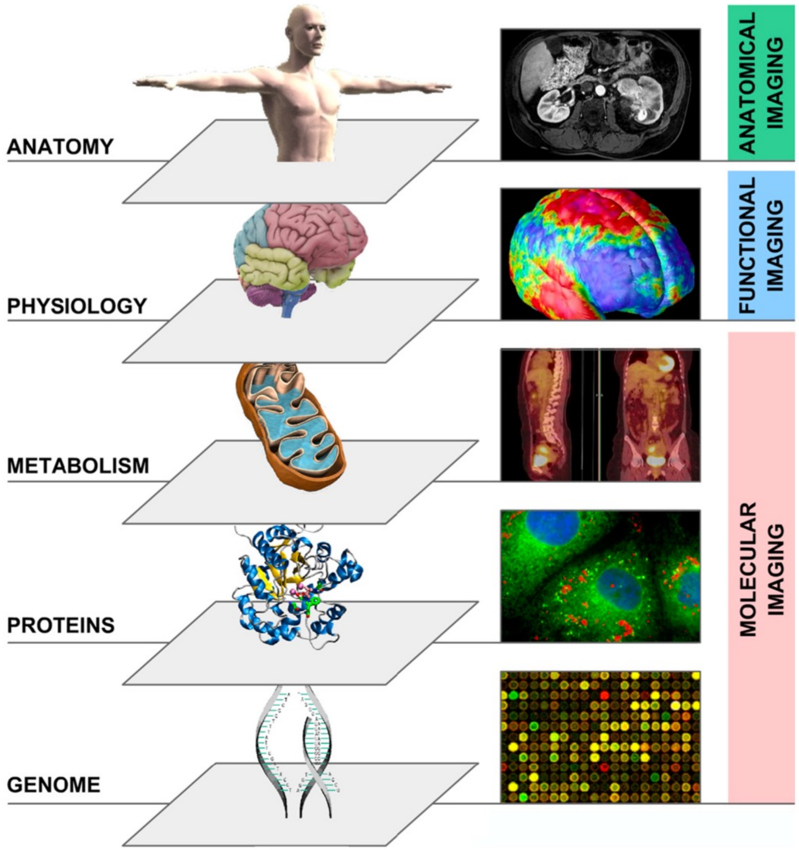


Radiologist work in a complete digitalized environment:

- Image data are collected in PACS from 2001 with **DICOM** standard, an hybrid images' format that combines images information, technical information, time of exams execution, patient's information
- RIS integrated patient anamnestic and personal information and radiological reports

Treatment decision – a multitasking strategy

Diagnostic Imaging – multimodality strategy from Radiology to Molecular Imaging



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Servizio Sanitario della Toscana

Radiomics - data mining from morphological information to functional and genetic information

European Journal of Cancer (2012) 48, 441–446

Available at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.ejconline.com

ELSEVIER EJC

Radiomics: Extracting more information from medical images using advanced feature analysis

Philippe Lambin [a,*,e,f], Emmanuel Rios-Velazquez [a,e], Ralph Leijenaar [a,e], Sara Carvalho [a,e], Ruud G.P.M. van Stiphout [a,e], Patrick Granton [a,e], Catharina M.L. Zegers [a,e], Robert Gillies [b,e], Ronald Boellard [c,e], André Dekker [a,e], Hugo J.W.L. Aerts [a,d,e]

Radiology

ORIGINAL RESEARCH ■ SPECIAL REPORT

Radiomics: Images Are More than Pictures, They Are Data[1]

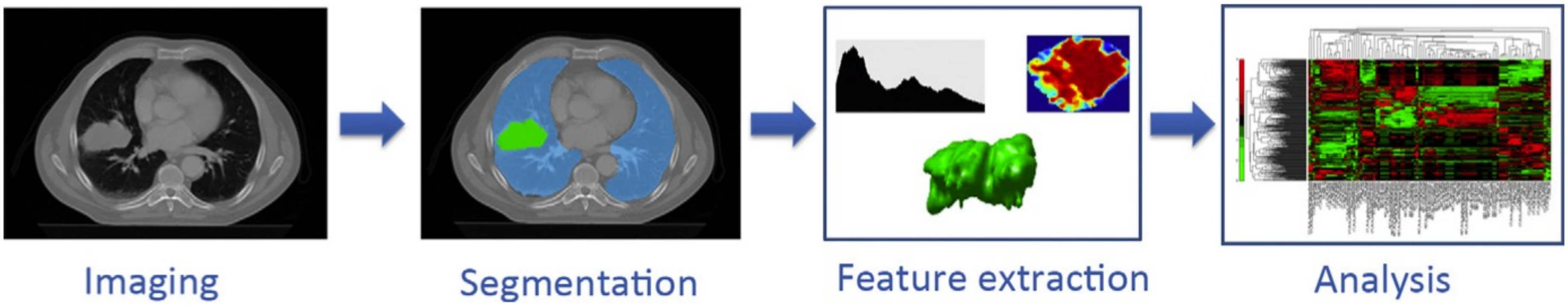
Robert J. Gillies, PhD
Paul E. Kinahan, PhD
Hedvig Hricak, MD, PhD, Dr(hc)

In the past decade, the field of medical image analysis has grown exponentially, with an increased number of pattern recognition tools and an increase in data set sizes. These

Radiomics is defined as the conversion of images to higher-dimensional data and the subsequent mining of these data for improved decision support.

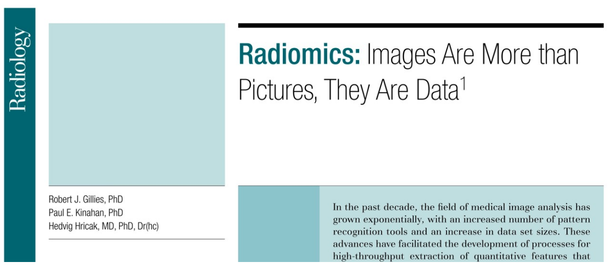
Radiomic analysis promises to increase precision in diagnosis, assessment of prognosis, and prediction of therapy response.

Radiomics - workflow



RADIOMICS

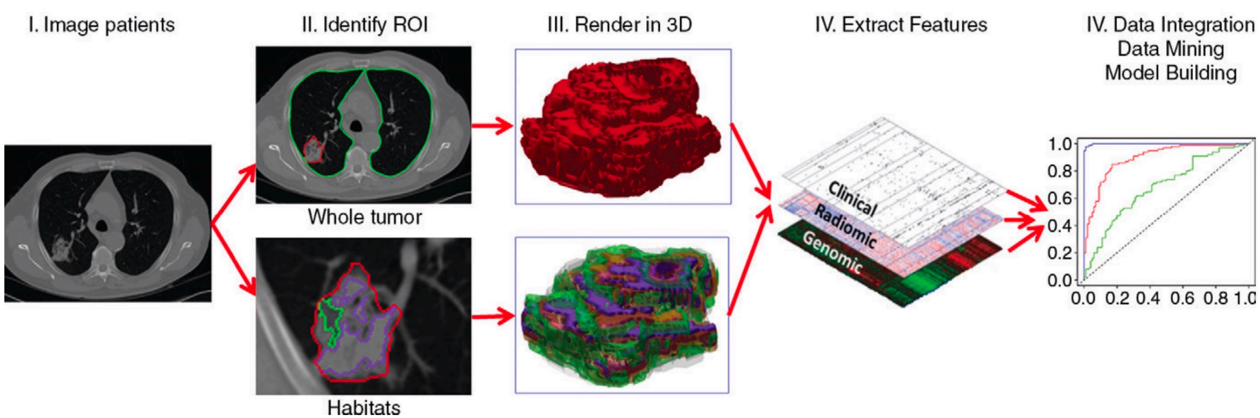
Extraction of quantitative information through radiomics algorithm needs precise measurements of biomarkers that correlate with diseases and their clinical management and prognosis
Extraction of information is obtained by texture analysis with different parameters.
Measurements obtain many data that needs artificial intelligence algorithms that can manage and correlate.


Radiology

Radiomics: Images Are More than Pictures, They Are Data[1]

Robert J. Gillies, PhD
Paul E. Kinahan, PhD
Hedvig Hricak, MD, PhD, Dr(hc)

In the past decade, the field of medical image analysis has grown exponentially, with an increased number of pattern recognition tools and an increase in data set sizes. These advances have facilitated the development of processes for high-throughput extraction of quantitative features that



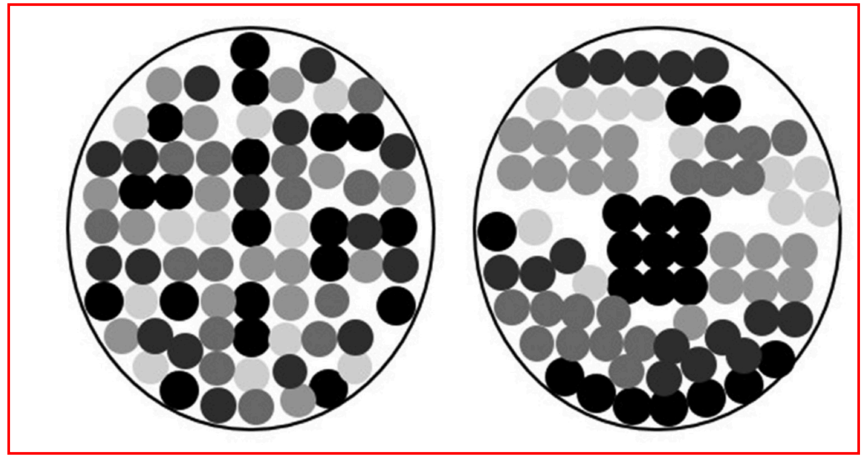
Examples of Semantic and Agnostic Features of Radiomics

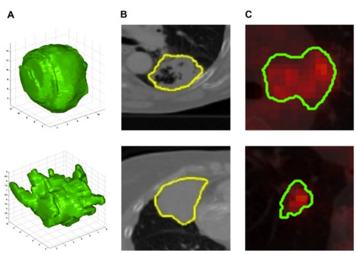
Semantic	Agnostic
Size	Histogram (skewness, kurtosis)
Shape	Haralick textures
Location	Laws textures
Vascularity	Wavelets
Spiculation	Laplacian transforms
Necrosis	Minkowski functionals
Attachments or lepidics	Fractal dimensions

TEXTURE ANALYSIS

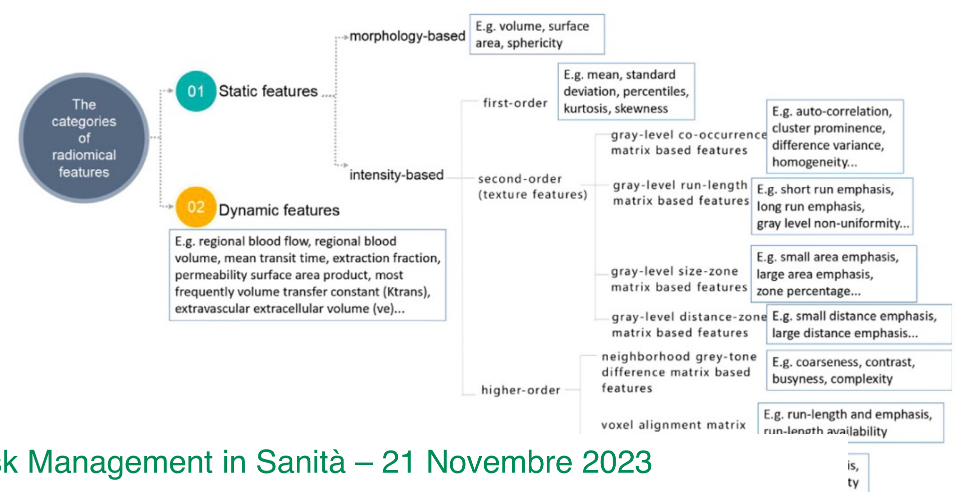
Table 1: Spectrum of Statistical-based First-Order and Higher-Order Texture Features

Texture Feature	Level/Order	Description	Examples	Comments
Intensity of pixel histogram	First order	Histogram where x-axis represents pixel/voxel gray level and y-axis represents frequency of occurrence (Fig 2)	Mean gray-level intensity, threshold, standard deviation or variance of the pixel histogram, skewness, kurtosis, first-order entropy, mean of the positive pixels (MPP)	Takes into account only pixel intensity, not spatial location or relationship of pixels. First-order entropy is the irregularity or complexity of pixel intensities
Run-length matrix	Second order	Adjacent or consecutive pixels/voxels of a single gray level in a given direction	Run-length nonuniformity, gray-level nonuniformity, long-run emphasis, short-run emphasis, fraction	Similar to co-occurrence matrix, takes into account both pixel intensity and spatial relationships
Gray-level co-occurrence matrix	Second order	How often pairs of pixels with specific values in a specified spatial range occur in an image	Contrast, uniformity, second-order entropy, sum of variance, sum of averages, sum of entropy	...
Advanced metrics	Higher order	Comparing differences and relationships between multiple pixels/voxels	Hundreds: autoregressive model, Haar wavelet (wavelet energy), geometry parameters, neighborhood gray-tone difference matrix	...





Same number of grey circle,different distribution different texture parameters



RADIOMICS AND RADIOGENOMICS IMPLEMENTATION
external validation of radiomics data

Radiology

REVIEWS AND COMMENTARY • REVIEW

The Biological Meaning of Radiomic Features

Michal R. Tomaszewski, PhD • Robert J. Gillies, PhD

From the Department of Cancer Physiology, H. Lee Moffitt Cancer Center and Research Institute, 12902 Magnolia Dr, Tampa, FL 33612. Received June 5, 2020; revision requested July 20; revision received July 30; accepted August 17. **Address correspondence to** R.J.G. (e-mail: *Robert.Gillies@moffitt.org*).

Supported by National Institutes of Health grants U01 CA143062 and U54 CA143970.

Conflicts of interest are listed at the end of this article.

Radiology 2021; 298:505–516 • https://doi.org/10.1148/radiol.2021202553 • Content code: IN

1) Radiomic analysis involves the automated extraction of clinically relevant information from radiologic images.
2) The data-driven nature of the radiomic method offers no direct insight into the biological meaning of the findings, thus highlighting the need for external validation.
3) Recent advances in the field are enabling biological validation of the radiomic signatures using a variety of correlates, including genetic and histologic data.
4) We predict that biological correlation will soon become standard in the field of radiomics, thus increasing the reproducibility of the findings and cementing the role of the method in clinical practice.

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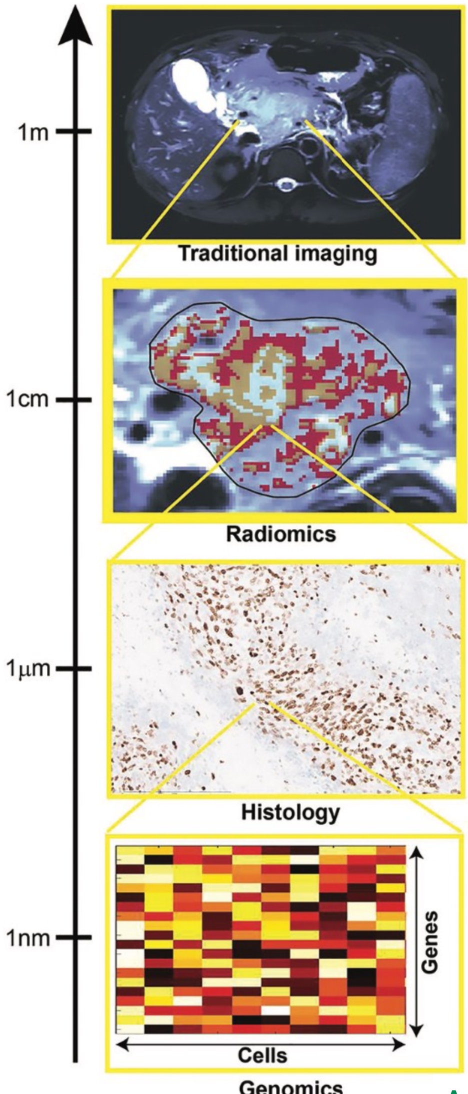

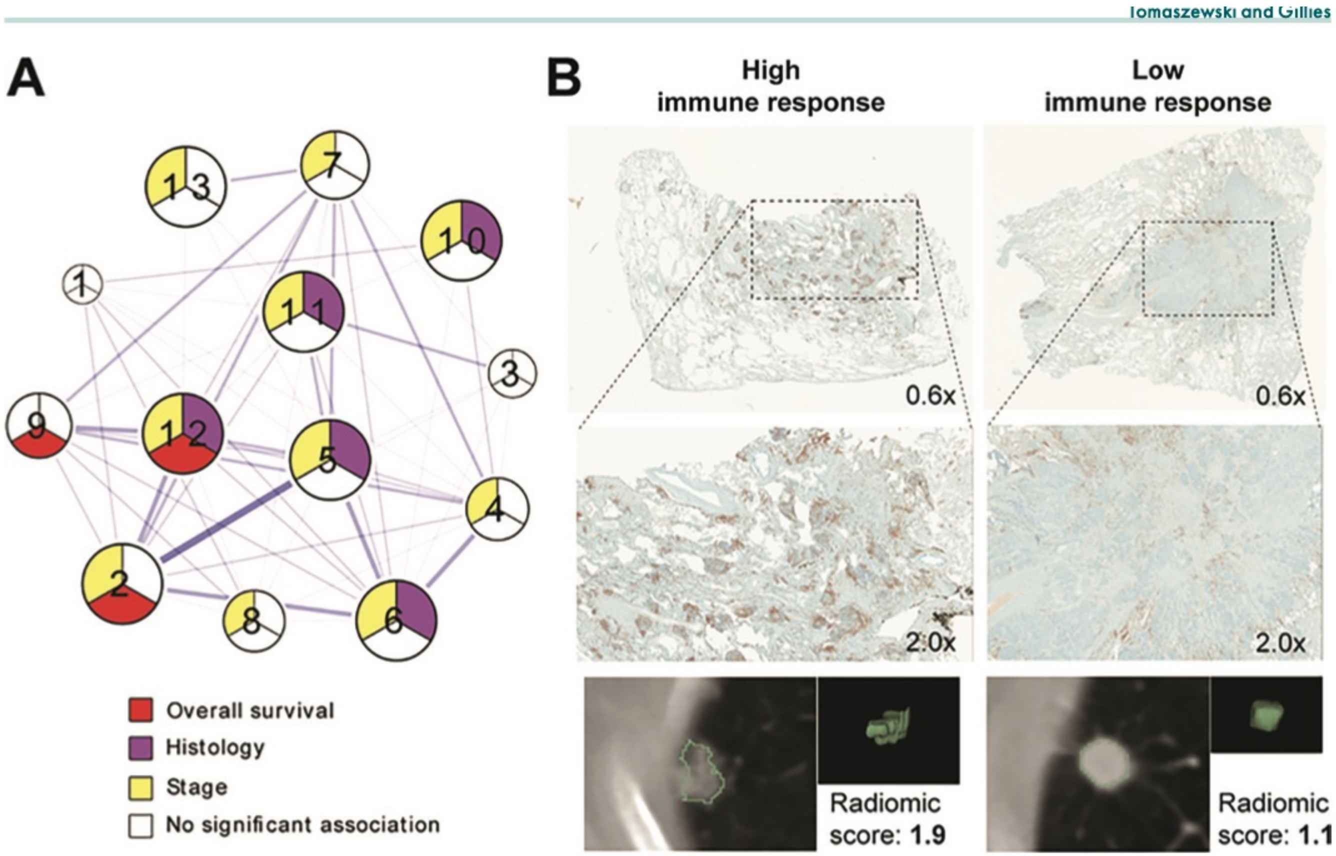

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frontiers in Oncology

REVIEW
published: 26 January 2
doi: 10.3389/fonc.2020.570

The Era of Radiogenomics in Precision Medicine: An Emerging Approach to Support Diagnosis, Treatment Decisions, and Prognostication in Oncology

Lin Shui[1†], Haoyu Ren[2†], Xi Yang[1†], Jian Li[3], Ziwei Chen[4], Cheng Yi[1], Hong Zhu[1] and Pixian Shui[5*]*

Studies	Study type	No. of specimen	Inclusion criteria	No. and type of Radiomic features	Image Modality	Clinical Characteristics	Statistical analysis
Brain cancer							
Li et al. (61)	Retrospective study	Validation: 84 from TCGA 272(training: validation= 182:92)	Grade II or III glioma	431 (intensity, shape, texture, and wavelet)	T2-weighted MRI	p53 status	Gene ontology (GO) analysis, LASSO Cox regression, SVM classifier, ROC curve analysis
Liu et al. (62)	Retrospective study	41 patients	II or III glioma, GBM	_	MRI	ki-67, TP53 and IDH mutation, EGFR amplification, mTOR activation	hazards regression, Cox proportional hazards model
Mazurowski et al. (63)	Retrospective study	110 patients (TCGA)	Grade	5(shape)	FLAIR sequence MRI	IDH mutation, 1p/19q co-deletion	Univariate Cox proportional
Zinn et al. (64)	Retrospective study	93 patients (TCGA/ TCIA/REMBR/ ANDT)	GBM	310 (intensity, shape, texture, and wavelet)	MRI	Periostin expression	LASSO Cox regression
Hong et al. (70)	Retrospective study	176 patients	GBM	_	MRI	IDH 1/2 mutation, ATRX loss, MGMT promoter methylation	Univariate/multi-variate analysis, Cox regression
Kickingereder et al. (71)	Retrospective study	152 patients	GBM	31 (intensity, shape, texture, and wavelet)	MRI	Global DNA methylation subgroups, MGMT promoter methylation status, and CDKN2A loss, EGFR amplification	Univariate analysis, stochastic gradient, boosting machine, random forest, penalized logistic regression classifiers
Cui et al. (72)	Retrospective study	108 patients (TCIA)	GBM	High-risk volume (HRV)	MRI	MGMT methylation status, NF1 and PIK3CA mutation	Cox regression analysis,
Hu et al. (76)	Exploratory study	48 tissue of 13 patients	GBM	256 (240 MRI-texture features + 16 raw features [mean, SD])	MRI	Image-guided biopsy	Univariate/multi-variate analysis, decision-tree models, chi-square test
Jamshidi et al. (77)	Retrospective study	23 patients	GBM	6(contrast enhancement, necrosis, contrast-to-necrosis ratio, infiltrative versus edematous T2 abnormality, mass effect, subventricular zone involvement)	MRI	messenger RNA expression, DNA copy number variation (CNV)	global gene set enrichment approach, gene set enrichment analysis, Pearson correlation algorithm
Breast cancer							
Li et al. (80)	Retrospective study	453	breast cancer	Coarseness, contrast, percent density, radiographic texture analysis	full-field digital mammograms	BRCA1/2 mutation	Pearson correlation algorithm, ROC analysis
Grimm et al. (81)	Retrospective study	275 patients	breast cancer	56 (size and shape, gradient, texture, dynamic)	DCE MRI	ER, PR, HER2 status	binary multivariate, logistic regression model
Mazurowski et al. (83)	Retrospective study	48 patients	breast cancer	23 (morphologic, textural, dynamic)	MRI	ER, PR, HER2 status	logistic regression, likelihood ratio tests
Zhu et al. (84)	Exploratory study	270 patients	breast cancer	45-56	DCE MRI	ER, PR, HER2 status	off-the-shelf deep features approach, three neural network structures
Yamamoto et al. (97)	Retrospective study	70 patients	breast cancer	47 (geometric, statistical, spatiotemporal)	DCE MRI	ER, PR, p53, HER2 status, lncRNA transcripts	Cox regression analysis, log-rank Mantel-Cox test
Renal cell carcinoma							
Karlo et al. (101)	Retrospective study	233 patients	Clear cell RCC	8 quantitative features	CT	VHL, PBRM1, SETD2, KDM5C, or BAP1 genes	Fleiss k, Fisher exact test, t test
Li et al. (102)	Retrospective study	255 patients	Clear cell RCC	156	CT	VHL mutations	random forest based wrapper algorithm(Boruta),Wilcoxon rank-sum test
Kocak et al. (104)	Retrospective study	45 patients (TCGA)	Clear cell RCC	828 (first-order, texture, and wavelet)	CT	PBRM1 mutation	artificial neural network (ANN) algorithm, random forest

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La radiologia medica (2022) 127:928–938
https://doi.org/10.1007/s11547-022-01529-x

ABDOMINAL RADIOLOGY

Check for updates

Gastroenteropancreatic neuroendocrine neoplasms (GEP-NENs): a radiomic model to predict tumor grade

Giuditta Chiti[1] · Giulia Grazzini[1,2] · Federica Flammia[1] · Benedetta Matteuzzi[1] · Paolo Tortoli[3] · Silvia Bettarini[3] · Elisa Pasqualini[4] · Vincenza Granata[5] · Simone Busoni[3] · Luca Messserini[6] · Silvia Pradella[1,2] · Daniela Massi[4] · Vittorio Miele[1]

La radiologia medica
https://doi.org/10.1007/s11547-023-01609-6

ABDOMINAL RADIOLOGY

Check for updates

Branch duct-intraductal papillary mucinous neoplasms (BD-IPMNs): an MRI-based radiomic model to determine the malignant degeneration potential

Federica Flammia[1] · Tommaso Innocenti[2,3] · Antonio Galluzzo[1] · Ginevra Danti[1] · Giuditta Chiti[1] · Giulia Grazzini[1] · Silvia Bettarini[4] · Paolo Tortoli[4] · Simone Busoni[4] · Gabriele Dragoni[2,3] · Matteo Gottin[2,3] · Andrea Galli[2,3] · Vittorio Miele[1]

La radiologia medica
https://doi.org/10.1007/s11547-023-01592-y

CHEST RADIOLOGY

Check for updates

Reproducibility of CT radiomic features in lung neuroendocrine tumours (NETs) patients: analysis in a heterogeneous population

Eleonora Bicci[1] · Diletta Cozzi[1,2] · Edoardo Cavigli[1] · Ron Ruzga[1] · Elena Bertelli[1] · Ginevra Danti[1] · Silvia Bettarini[3] · Paolo Tortoli[3] · Lorenzo Nicola Mazzoni[4] · Simone Busoni[3] · Vittorio Miele[1]

diagnostics

MDPI

Article

Radiomic Features Are Predictive of Response in Rectal Cancer Undergoing Therapy

Diletta Santini [1], Ginevra Danti [1,*], Eleonora Bicci [1], Antonio Galluzzo [1], Silvia Bettarini [2], Simone Busoni [2], Tommaso Innocenti [3], Andrea Galli [3] and Vittorio Miele [1]

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BIOBANK FOR AI EVALUATION
EUROPEAN PROJECT

NAVIGATOR

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Bournemouth University

University of Cambridge

Società Italiana di Radiologia Medica e Interventistica

Fondazione SIRM

euCanSHare

PRIMAGE Medical imaging Artificial intelligence Childhood cancer research

EUCAN IMAGE

ProCAncer-I

INCISIVE

chAImeleon

Borgheresi *et al.*
European Radiology Experimental (2022) 6:53
https://doi.org/10.1186/s41747-022-00306-9

European Radiology Experimental

GUIDELINE/POSITION PAPER Open Access

NAVIGATOR: an Italian regional imaging biobank to promote precision medicine for oncologic patients

Rita Borgheresi[1], Andrea Barucci[2], Sara Colantonio[3], Gayane Aghakhanyan[1*], Massimiliano Assante[3], Elena Bertelli[4], Emanuele Carlini[3], Roberto Carpi[5], Claudia Caudai[3], Diletta Cavallero[1], Dania Cioni[1], Roberto Cirillo[3], Valentina Colcelli[2], Andrea Dell'Amico[3], Domnico Di Gangi[3], Paola Anna Erba[1], Lorenzo Faggioni[1], Zeno Falaschi[1], Michela Gabelloni[1], Rosa Gini[6], Lucio Lelii[3], Pietro Liò[7], Antonio Lorito[2], Silvia Lucarini[4], Paolo Manghi[3], Francesco Mangiacrapa[3], Chiara Marzi[2], Maria Antonietta Mazzei[8], Laura Mercatelli[4], Antonella Mirabile[2], Francesco Mungai[4], Vittorio Miele[4], Maristella Olmastroni[5], Pasquale Pagano[3], Fabiola Paiar[1], Giancarlo Panichi[3], Maria Antonietta Pascali[3], Filippo Pasquinelli[5], Jorge Eduardo Shortrede[1], Lorenzo Tumminello[1], Luca Volterrani[8], Emanuele Neri[1,9] and on behalf of the NAVIGATOR Consortium Group

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FUTURE: DIGITAL TWIN

DIGITAL HEALTH
Volume 9, January-December 2023

https://doi.org/10.1177/20552076221149651

SAGE journals

Review article

Digital twin in healthcare: Recent updates and challenges

Tianze Sun[1,2,*], Xiwang He[3,*], and Zhonghai Li[1,2]

Abstract

As simulation is playing an increasingly important role in medicine, providing the individual patient with a customised diagnosis and treatment is envisaged as part of future precision medicine. Such customisation will become possible through the emergence of digital twin (DT) technology. The objective of this article is to review the progress of prominent research on DT technology in medicine and discuss the potential applications and future opportunities as well as several challenges remaining in digital healthcare. A review of the literature was conducted using PubMed, Web of Science, Google Scholar, Scopus and related bibliographic resources, in which the following terms and their derivatives were considered during the search: DT, medicine and digital health virtual healthcare. Finally, analyses of the literature yielded 465 pertinent articles, of which we selected 22 for detailed review. We summarised the application examples of DT in medicine and analysed the applications in many fields of medicine. It revealed encouraging results that DT is being increasing applied in medicine. Results from this literature review indicated that DT healthcare, as a key fusion approach of future medicine, will bring the advantages of precision diagnose and personalised treatment into reality.

Journal of *Clinical Medicine*

MDPI

Perspective

Digital Twins in Radiology

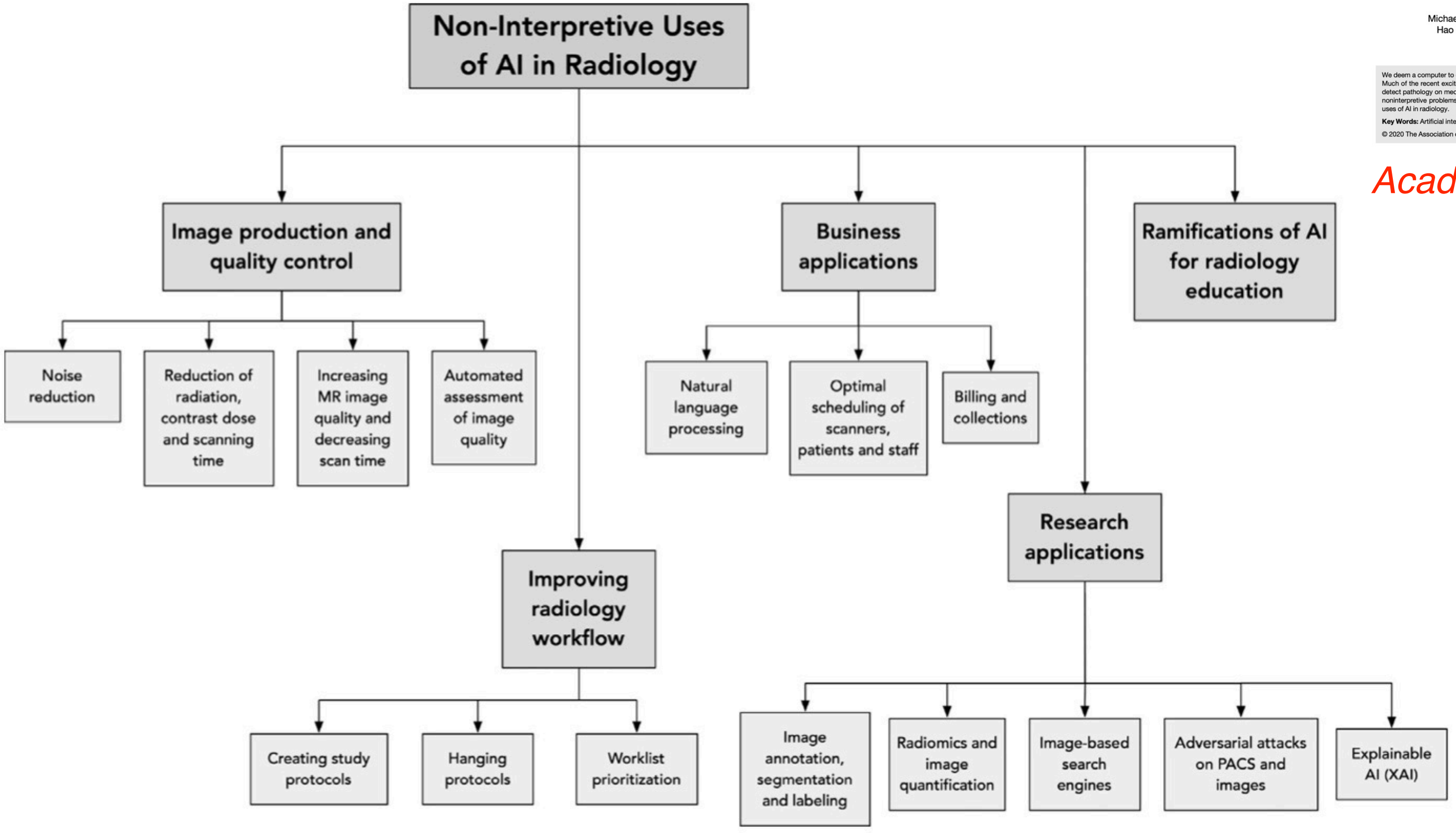
Filippo Pesapane *, Anna Rotili, Silvia Penco, Luca Nicosia and Enrico Cassano

Breast Imaging Division, IEO European Institute of Oncology IRCCS, 20141 Milan, Italy
* Correspondence: filippo.pesapane@ieo.it

Abstract: A digital twin is a virtual model developed to accurately reflect a physical thing or a system. In radiology, a digital twin of a radiological device enables developers to test its characteristics, make alterations to the design or materials, and test the success or failure of the modifications in a virtual environment. Innovative technologies, such as AI and -omics sciences, may build virtual models for patients that are continuously adjustable based on live-tracked health/lifestyle parameters. Accordingly, healthcare could use digital twins to improve personalized medicine. Furthermore, the accumulation of digital twin models from real-world deployments will enable large cohorts of digital patients that may be used for virtual clinical trials and population studies. Through their further refinement, development, and application into clinical practice, digital twins could be crucial in the era of personalized medicine, revolutionizing how diseases are detected and managed. Although significant challenges remain in the development of digital twins, a structural modification to the current operating models is occurring, and radiologists can guide the introduction of such technology into healthcare.

Keywords: digital twins; personalized medicine; digital devices; digital patients; artificial intelligence

NON INTERPRETIVE USE OF ARTIFICIAL INTELLIGENCE



Original Investigation

Noninterpretive Uses of Artificial Intelligence in Radiology

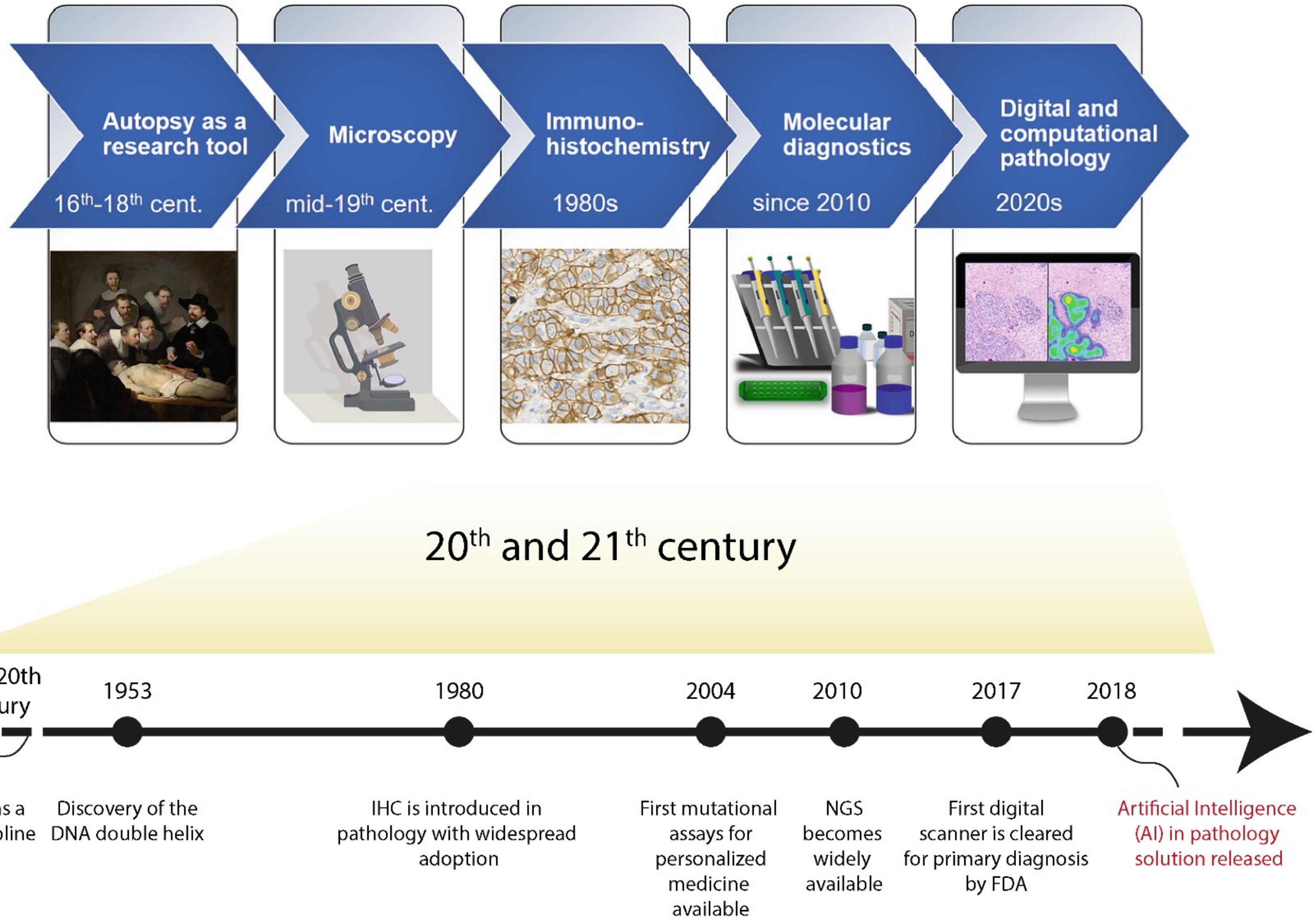
Michael L. Richardson, MD, Elisabeth R. Garwood, MD, Yueh Lee, MD, Matthew D. Li, MD, Hao S. Lo, MD, MBA, Arun Nagaraju, MD, Xuan V. Nguyen, MD, PhD, Linda Probyn, MD, Prabhakar Rajiah, MD, Jessica Sin, MD, Ashish P. Wasnik, MD, Kali Xu, MD

We deem a computer to exhibit artificial intelligence (AI) when it performs a task that would normally require intelligent action by a human. Much of the recent excitement about AI in the medical literature has revolved around the ability of AI models to recognize anatomy and detect pathology on medical images, sometimes at the level of expert physicians. However, AI can also be used to solve a wide range of noninterpretive problems that are relevant to radiologists and their patients. This review summarizes some of the newer noninterpretive uses of AI in radiology.

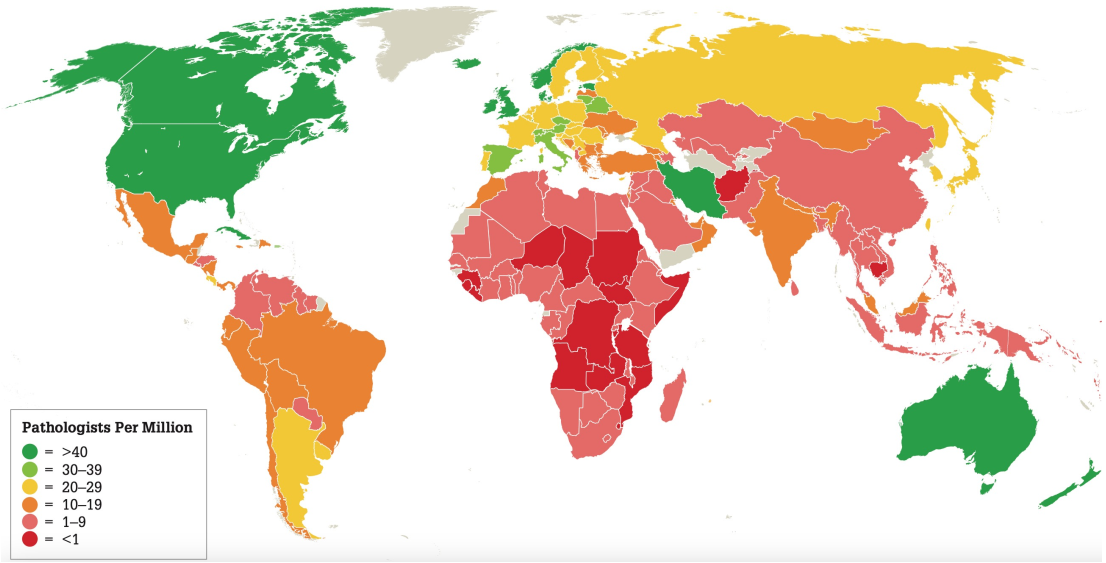
Key Words: Artificial intelligence; Deep learning; Radiology applications; Radiology education.

Academic Radiology, 2020

The Future of Diagnostics is Digital



The Shortage of Pathologists



By 2030 the number of active pathologists may have dropped by 30 percent compared to 2010 levels

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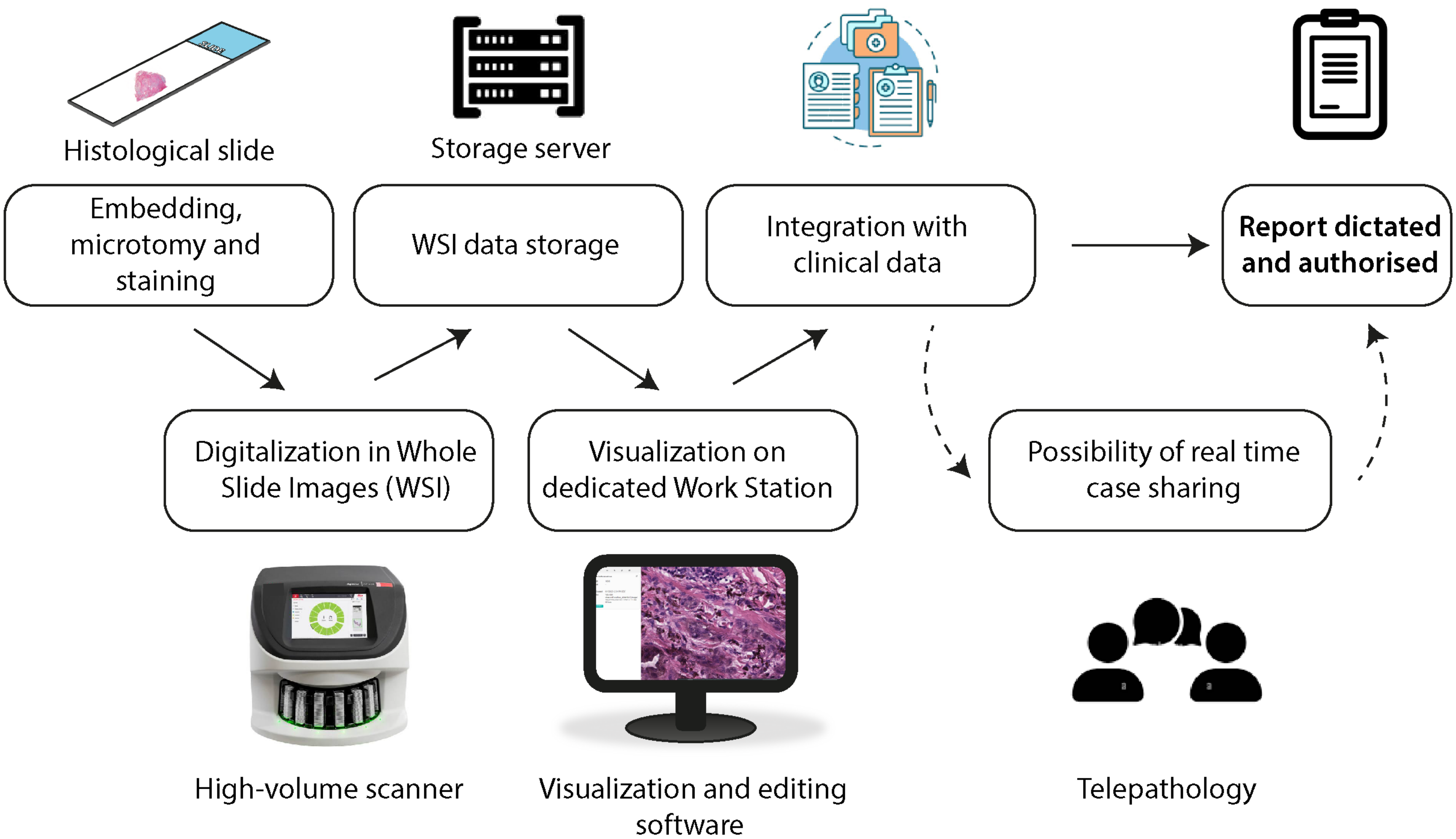
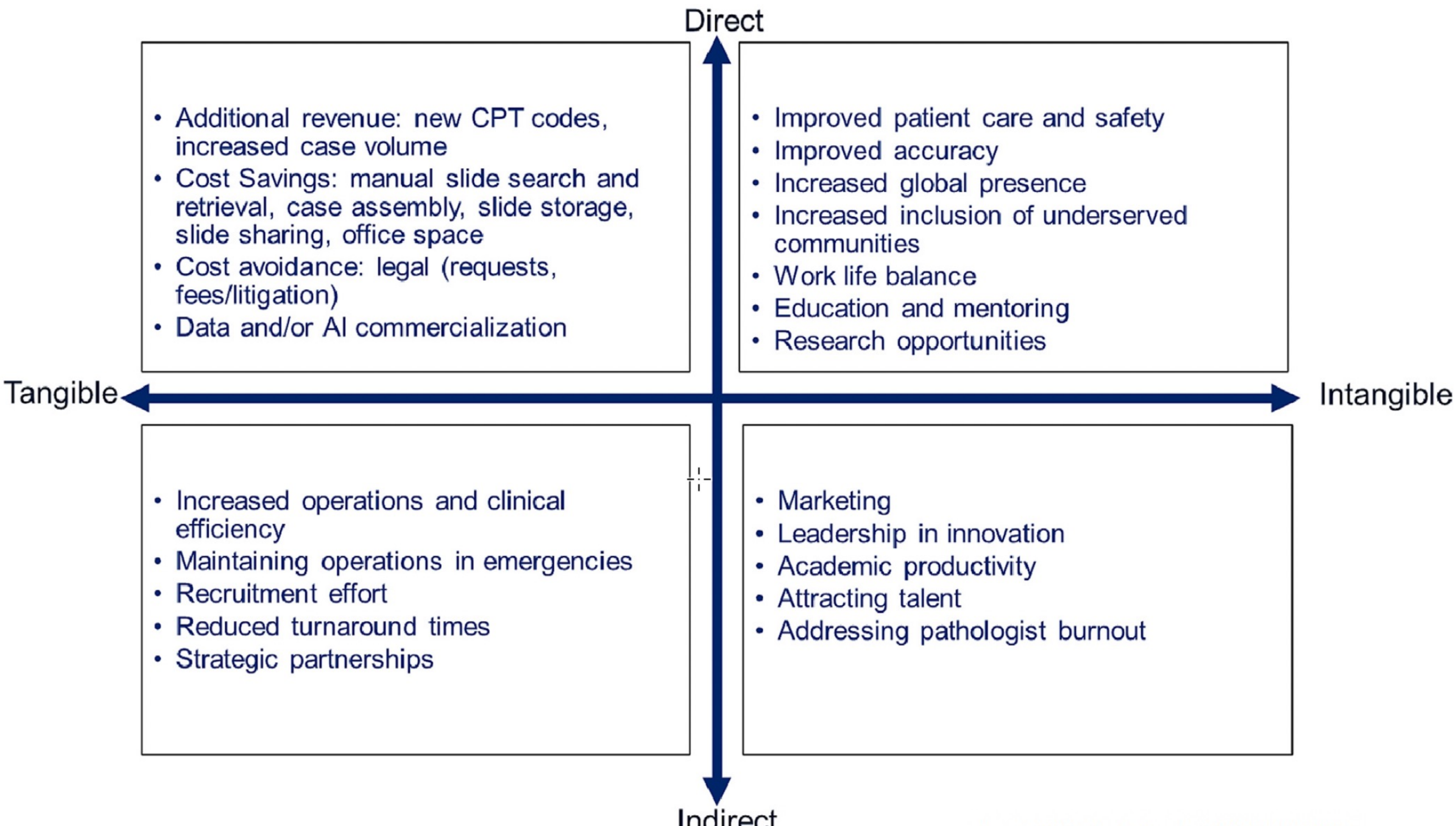
DIGITAL PATHOLOGY WORKFLOW



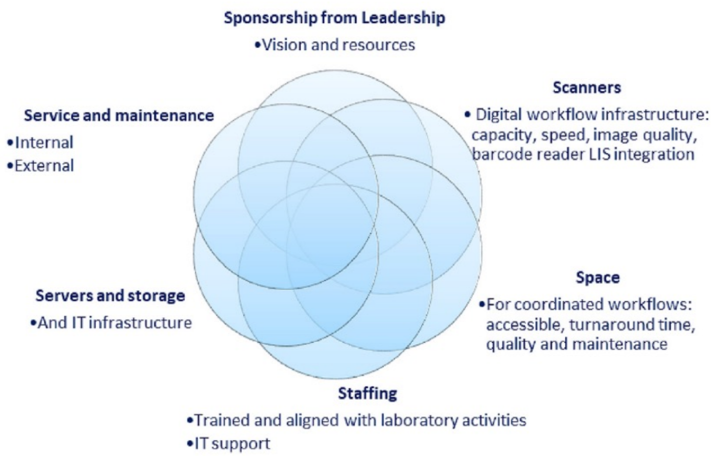
Digital Pathology Benefits



Journal of Pathology Informatics 14 (2023) 100318

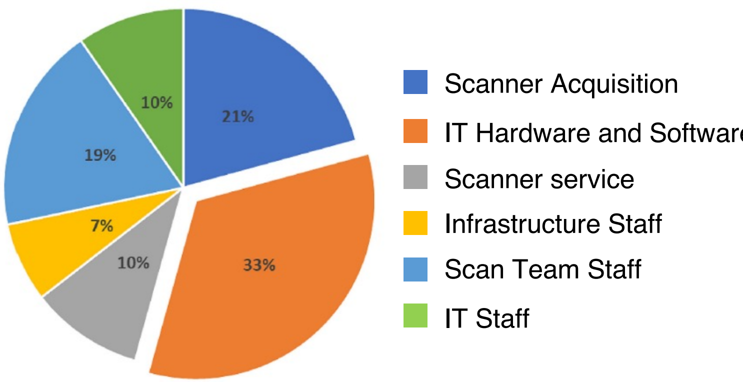
Digital Pathology Challenges

- Organization level



J Pathol Inform. 2023 May 16;14:100318

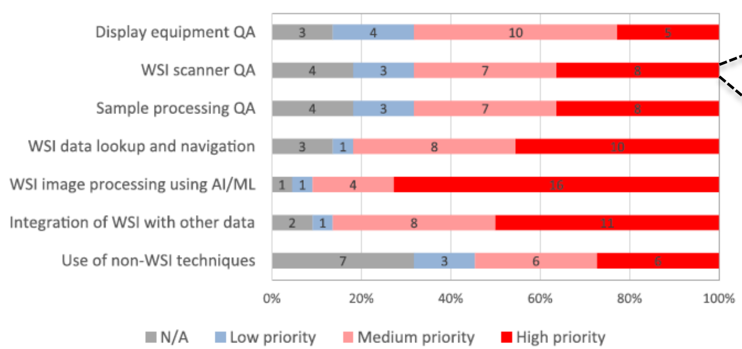
Digital pathology cost categories



J Pathol Inform. 2023 May 16;14:100318

- Pathologists' level

Prioritised challenges in digital pathology



J Pathol Inform. 2022;13:100157

Mod Pathol. 2022 Feb;35(2):152-164.

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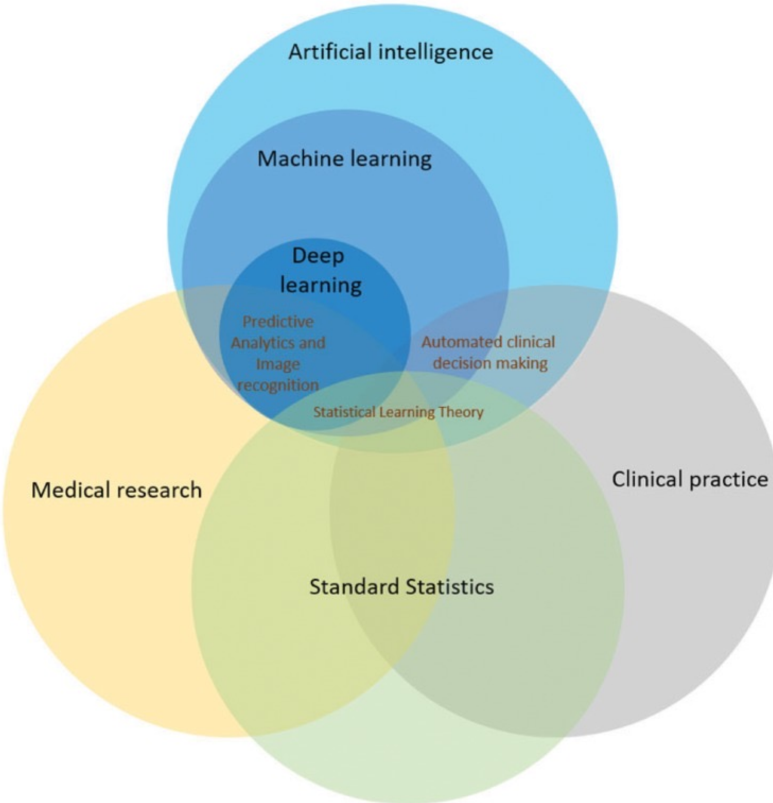
Digital Pathology

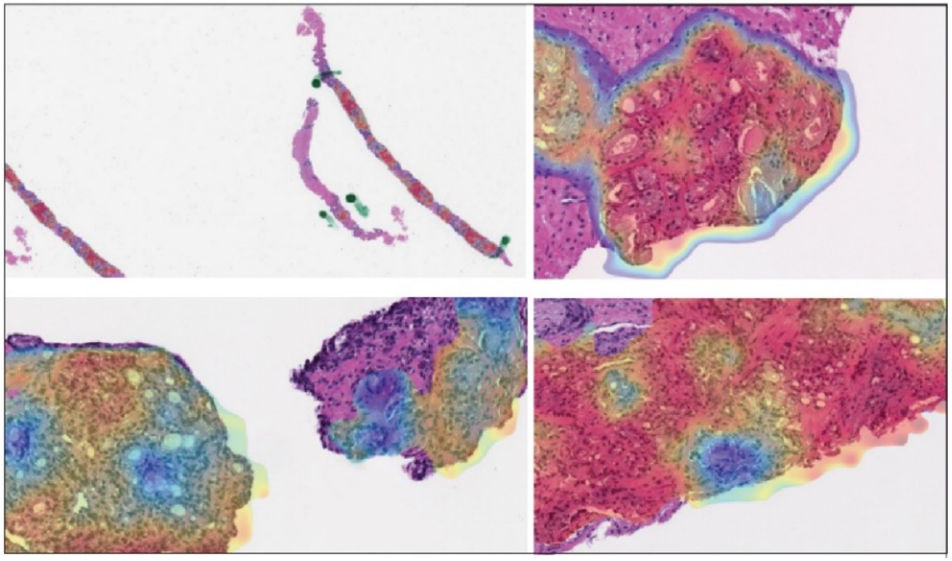
AI Algorithms



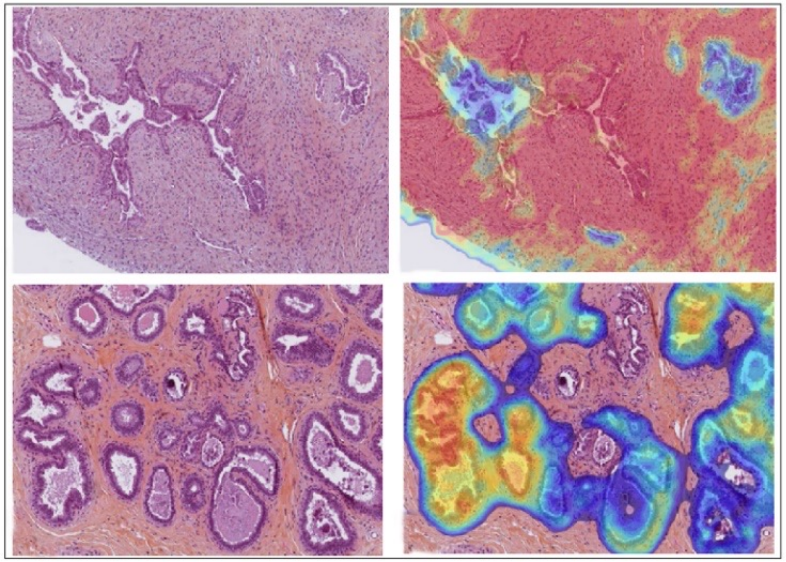
Translate whole slide images into discoveries, decisions and diagnoses

Real World Clinical Applications

Prostate Cancer



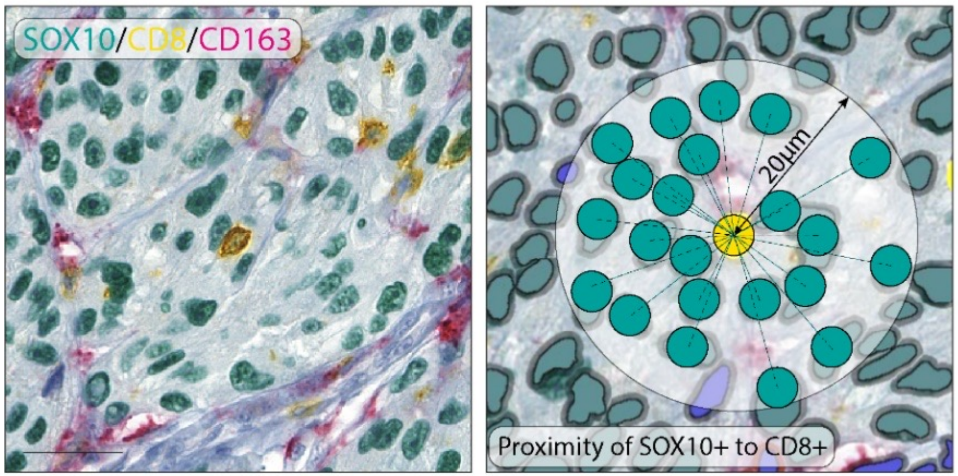
Breast Cancer



- Pre- Post- human analysis screening
- Quick detection of tumor areas
- Qualitative Measurements (tumor heatmap)
- Quantitative Measurements (areas, mitosis, grading)

Research Applications

Computational Pathology

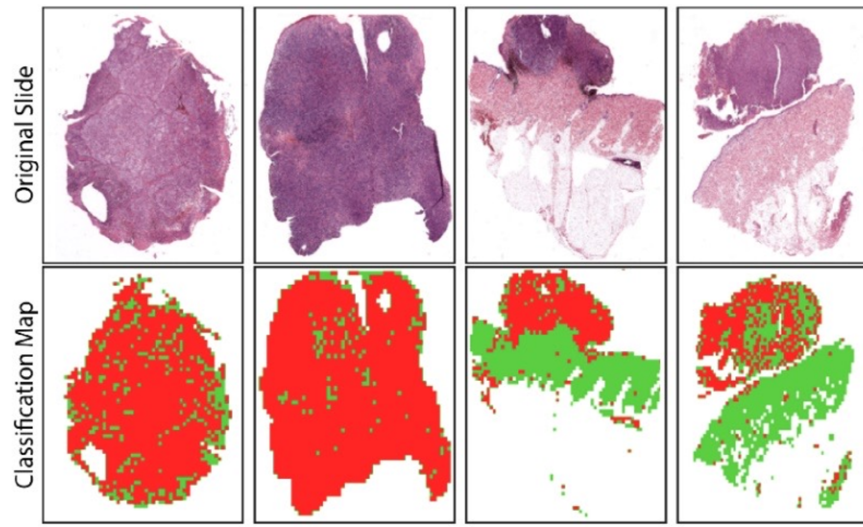


SOX10+ proximity within 20μm to CD8+

Cells. 2021; doi: 10.3390/cells10020422

Lab Invest. 2023; doi:0.1016/j.labinv.2023.100259

Classifier based on Deep Learning



Healthy Tissue
Melanoma

Front Oncol. 2020 ;. doi:10.3389/fonc.2020.01559

Am J Pathol. 2023; doi: 10.1016/j.ajpath.2023.08.013

Focus on Two Integrated Digital Image Systems:

- **Ophtalmic Pathology**
- **Neuropathology**

Improving our value as gatekeepers for subspecialty expertise and for patient information, and integration of diagnostic data from *any* source

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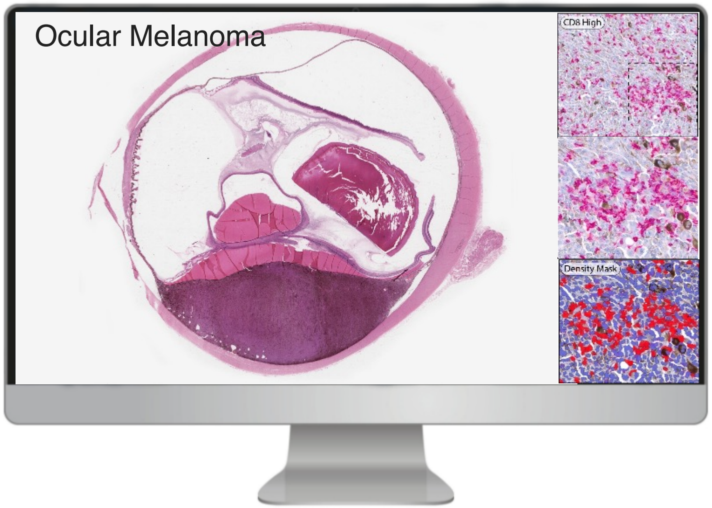
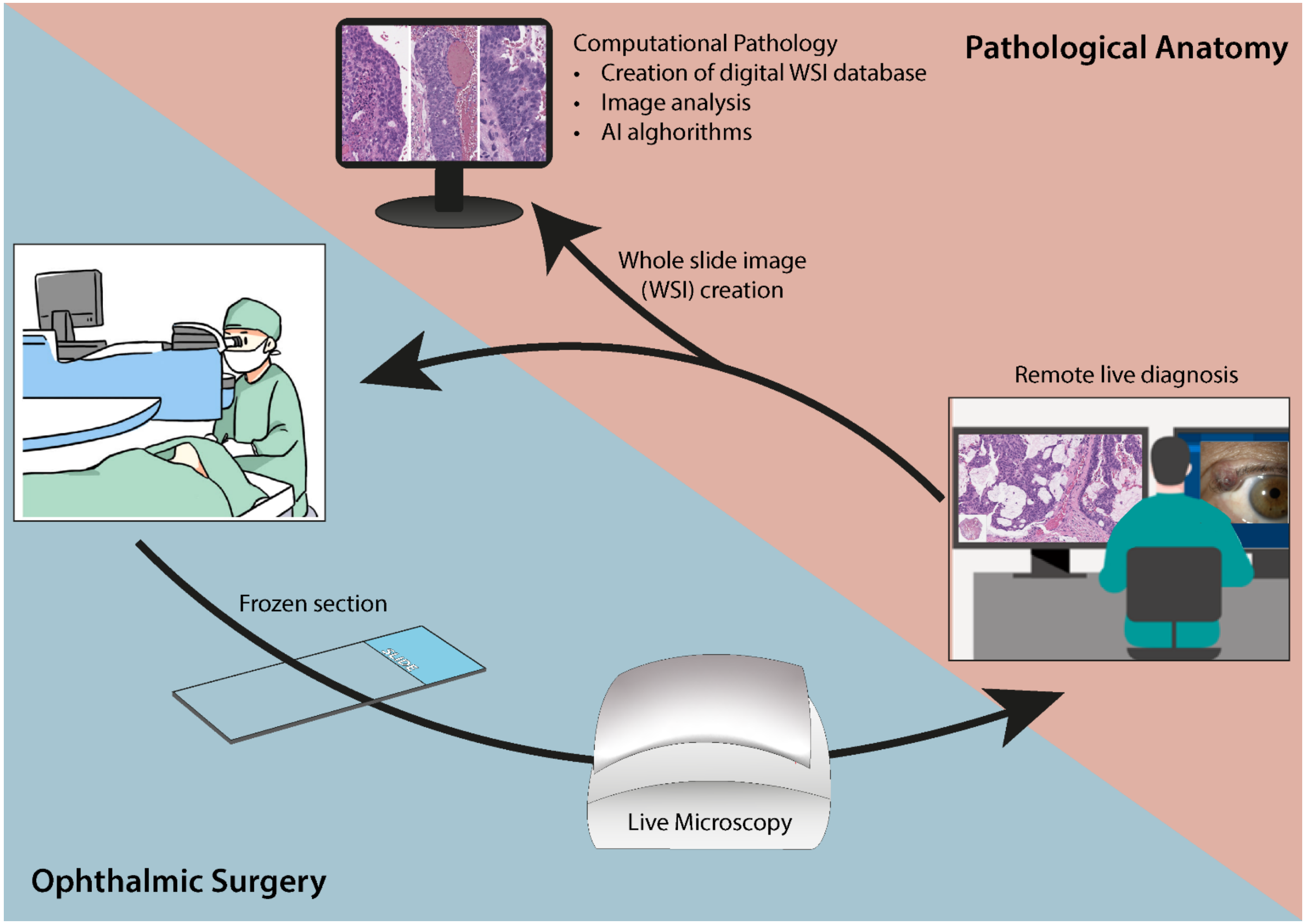
Ophthalmic Pathology Imaging Integration



- Wide-Field Imaging (WF)
- Ultra-Wide Field Imaging (UWF)
- Swept Source Optical Coherence Tomography (SS-OCT)
- Fluorescein Angiography (FA)
- OCT Angiography (OCTA)
- Ultrasound Imaging (US)
- Ultrasound Biomicroscopy (UBM)

- Whole Slide Imaging
- Ready access to digital slides database
- Telepathology (live microscopy)
- Computational Pathology
- AI based tools

Ophthalmic Pathology



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Ophthalmic Pathology

- Ophthalmic data management environment, connected to all devices, enabling a fully electronic innovative workflow and increased functionality and multidisciplinary collaboration
- Multimodal clinical data resource to improve quality measurements and patient safety
- Image repository of digital slides, second opinions, intra and live operative teleconsultation
- Real-world research including tumor classification prognostic evaluation with AI systems

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Neuropathology

Confocal laser live endomicroscopy (Optical Biopsy)

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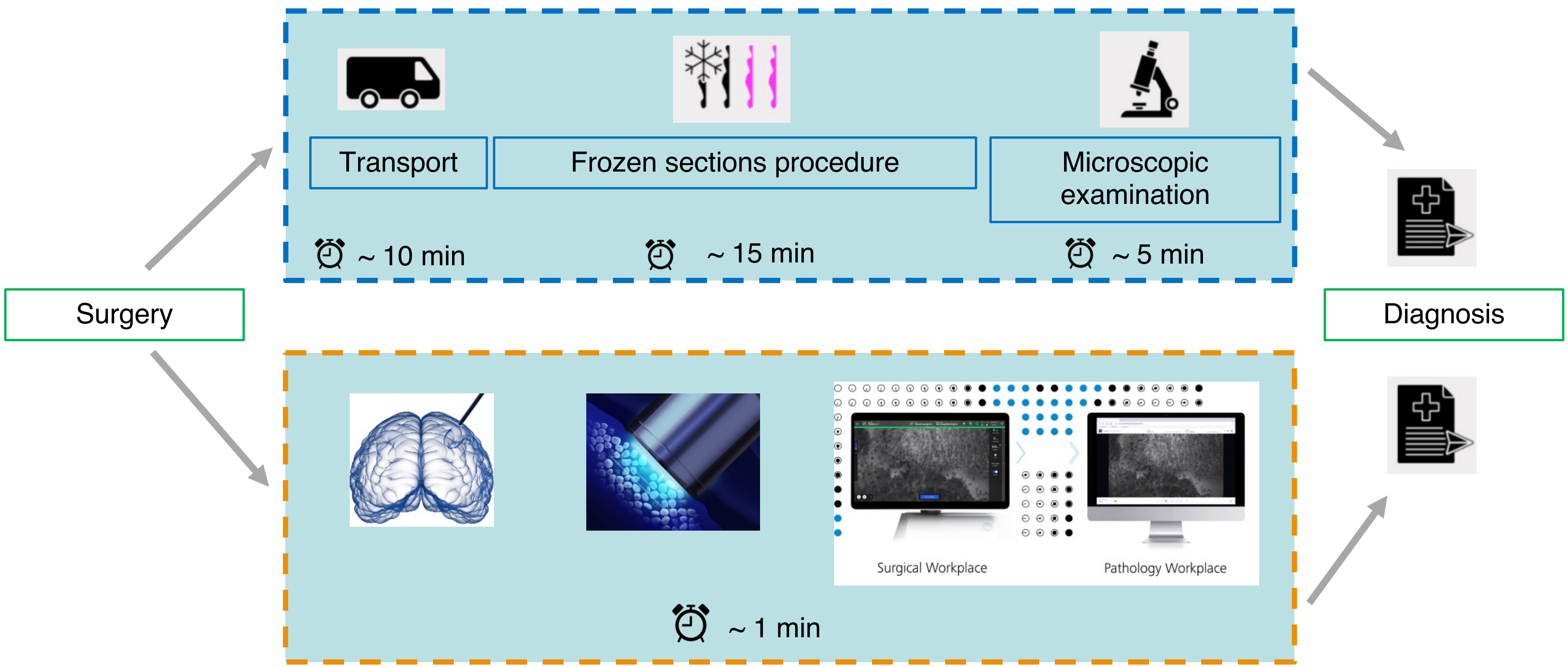
Traditional intraoperative examination and in-vivo digital biopsy: workflow comparison



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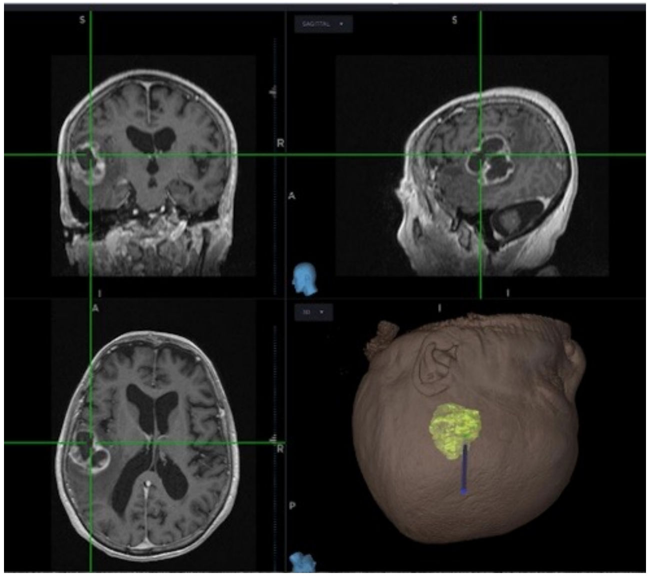

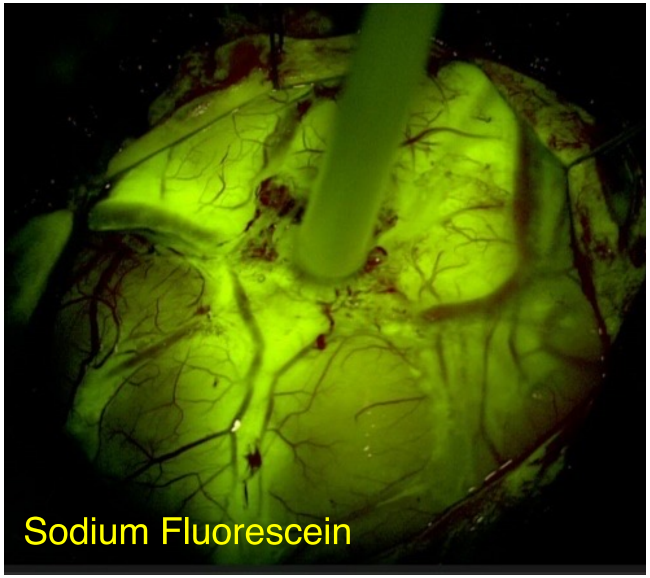

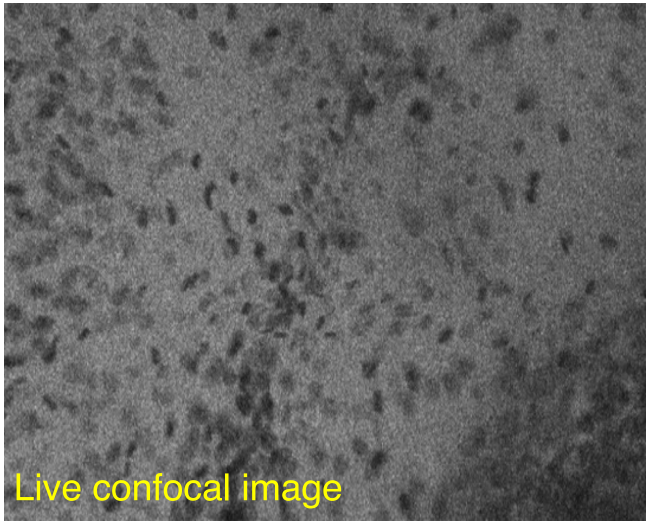

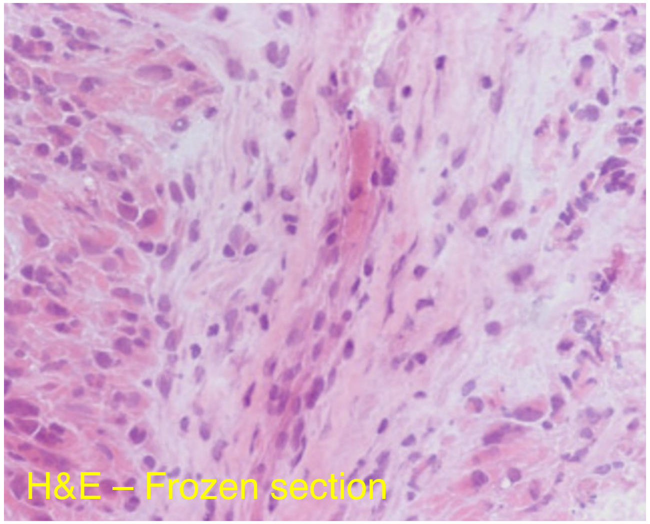

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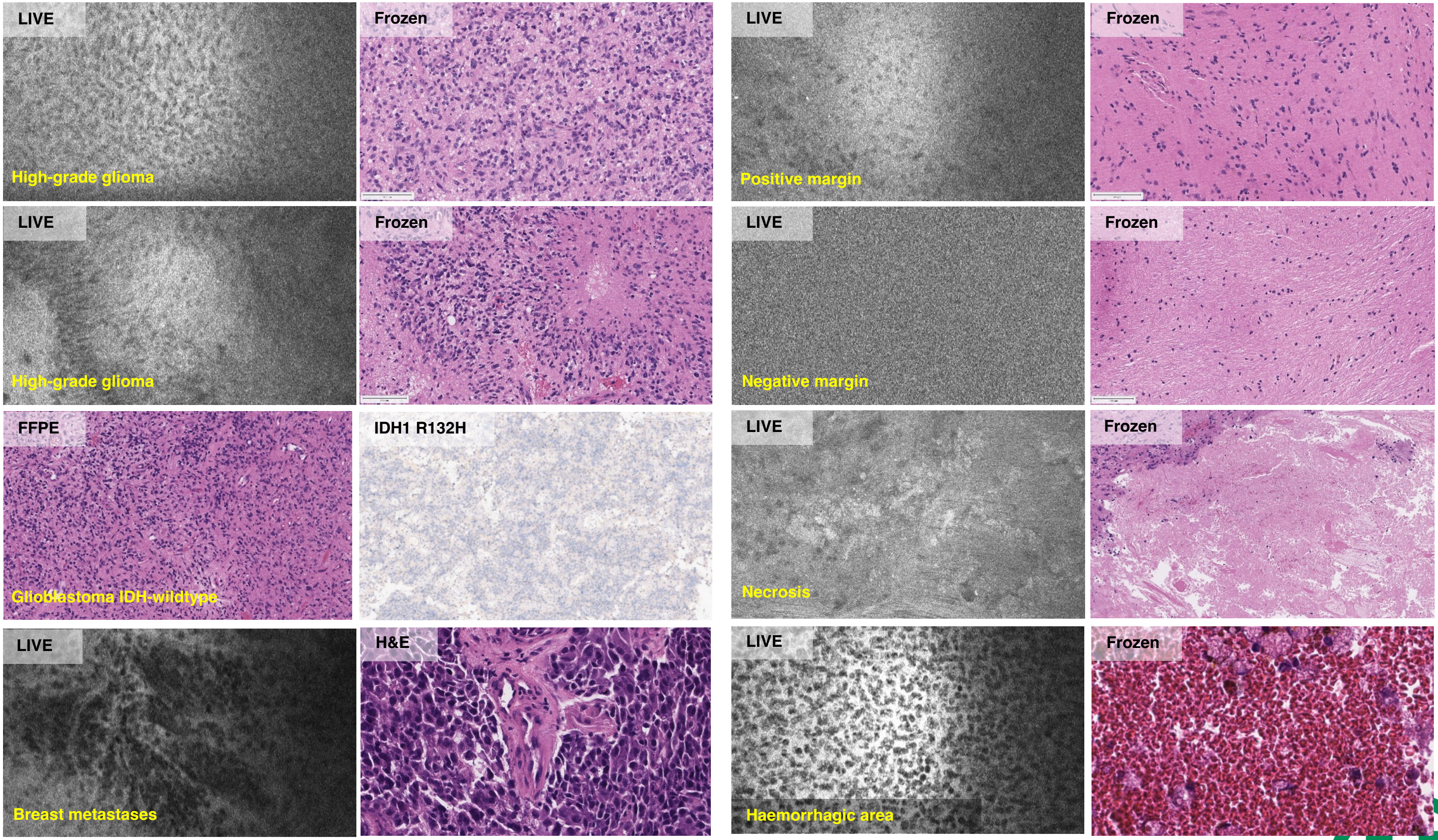

Neuropathology

The Pathology Suite enables real-time feedback on tissue microstructure through consultation and sharing of digital images (confocal laser endomicroscopy, CLE) with a multidisciplinary approach

Main fields of use: high-grade gliomas and brain metastases, where surgical radicality is the main prognostic factor

Main challenges:

- Specific training and a learning curve to interpret the acquired information
- It requires established workflows to optimize costs and benefits
- Technical issues: image resolution, small field of view, image acquisition timing rate, laser stability during image acquisition

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Take Home Messages

- Radiology and pathology are transforming faster than any other medical discipline
- Integrated digital imaging health systems for each specified intended use case
- Regional, national, or international initiatives to drive digital pathology/AI into mass adoption
- Planning and coordination with multiprofessional staff and stakeholders

Process Engineers
Suppliers Scanners
Professional Pathology Associations
Marketing Companies
Biomedical Scientists
Developers algorithms
Ethicists
Developers PACS
Information technology personnel
Patients Organizations
Hospital Executives Process Engineers
Bioinformaticians
Clinicians
Developers Biomarkers
Lawyers
Managers
Molecular Biologists
Radiologists
Pathology Laboratories