The Digital Revolution in the Pathology Laboratory

Promises and Challenges of Artificial Intelligence

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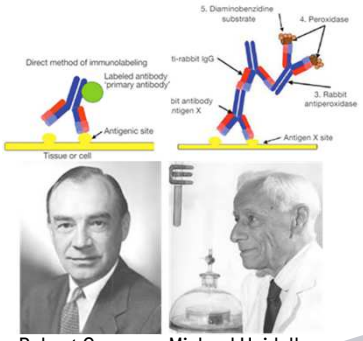
Digitalisation of the Pathology Lab

The fourth revolution in Anatomical Pathology: from the body to omics

Mid XIXth Century

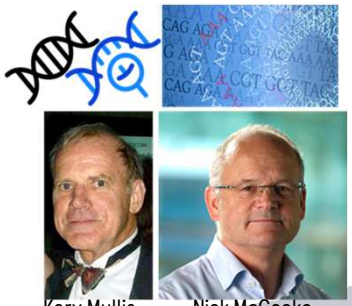
Robert Hooke Anton Van Leeuwenhoek Rudolph Virchow

1970s

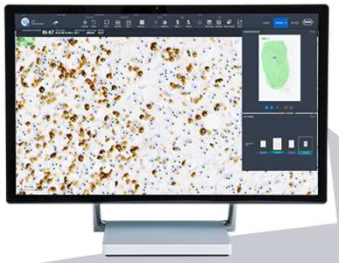


Robert Coons Michael Heidelberger

1990s 2010s
PCR NGS



Kary Mullis Nick McCooke



1990s
2010s

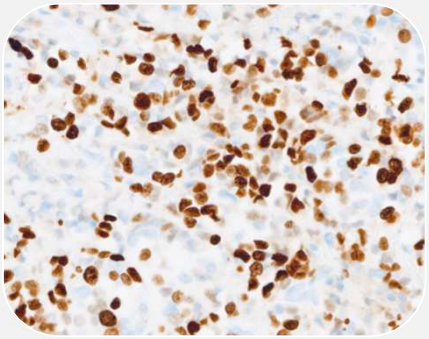
Tissue & Cells | **Proteins & Antigens** | **Genes** | **Digitizing & Image Analysis** | **?**

Digital Pathology

Slide and stain to Scan to analysis

Slide

H&E or IHC*



Stain

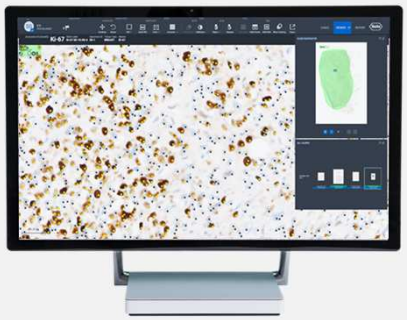
Digitalisation

Slide scanner

High-quality images with accurate, fast, easy-to-use scanners

Digital viewer

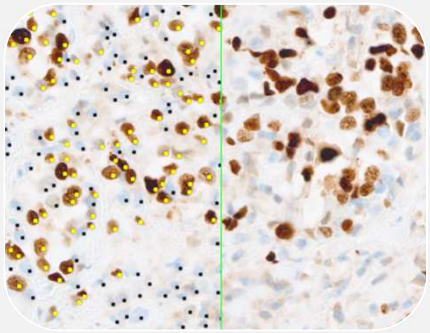
Image Management Software



Pathologist interface offers seamless workflow for analysis

Post analytical/interpretation

Image Analysis



Analyse confidently with **validated and CE-IVD** marked algorithms

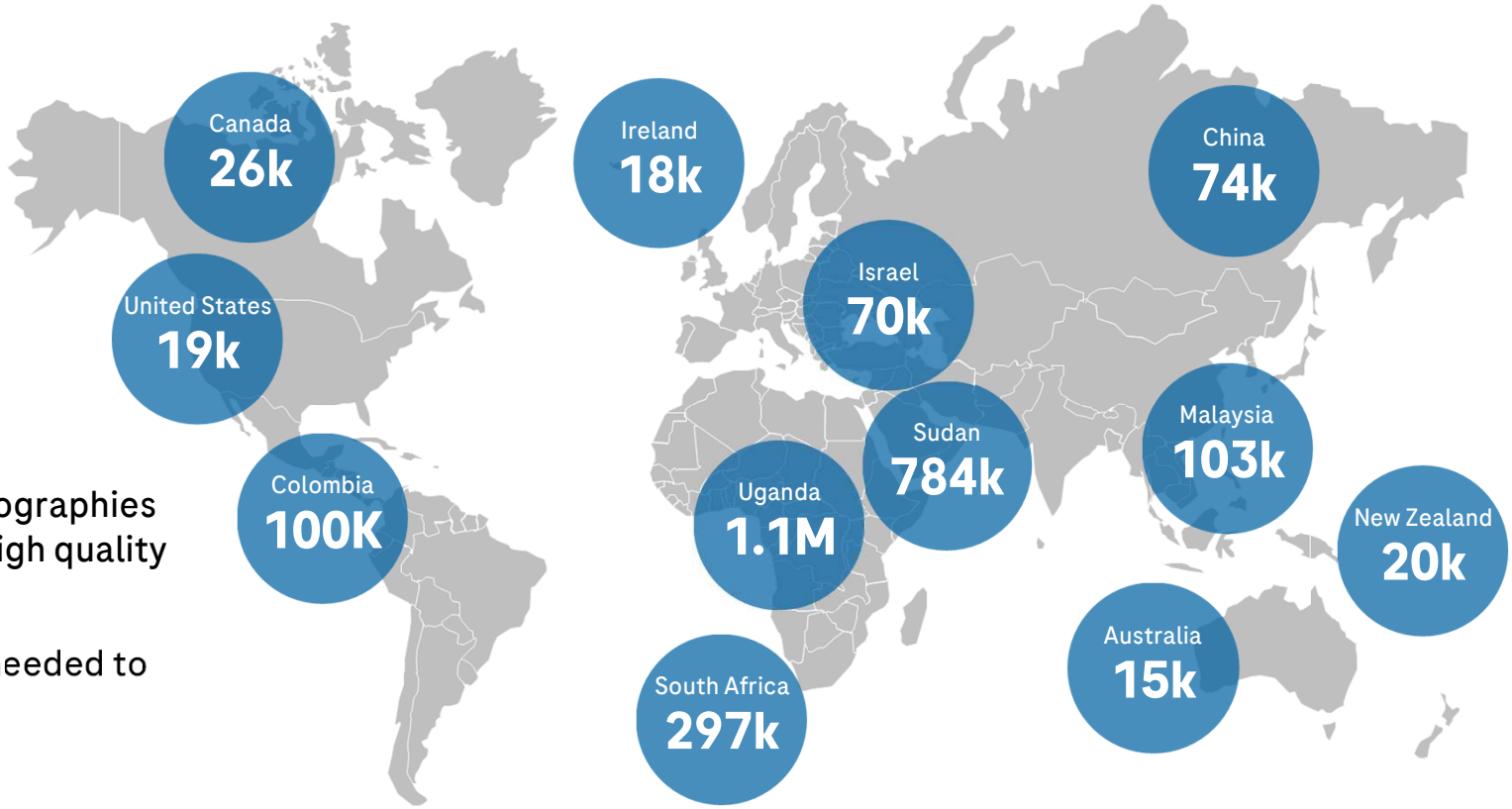
**IHC staining is shown for example.*

The present of AI in Pathology

Digitalisation and AI can support the pathologists' increased workload

And address a critical shortage of pathologists globally

- More than 70% of all diagnoses involve pathology tests
- Shortage of pathologists globally, and the need for second opinion to access experts for equivocal cases
- Remote collaboration between geographies will be crucial for patients to get high quality diagnostics
- Automation in analysis (AI) will be needed to meet demand for cancer testing



Number of Patients per pathologist

1.www.clpmag.com/2017/10/digital-pathology-gives-rise-computational-pathology/
2.The Lancet Oncology. 2013. Adesina et al.
3. www.minsalud.gov.co: Documento Técnico GPES/1682C-13

Values of Digital Pathology and AI

Digital pathology provides value: from workflow benefits up to precision medicine

Taking over time-consuming and repetitive tasks

- Counting mitoses
- Scoring immunohistochemistry
- Scoring immune infiltration
- Grading cancer

Supporting the Pathologist

- Pre-screening slides
- Workflow optimization
- Gain confidence

Optimize / improve classification systems

- Deep learning
- Clinically actionable genetic alterations
- AI driven pathology prediction

Changes in the Patient Journey

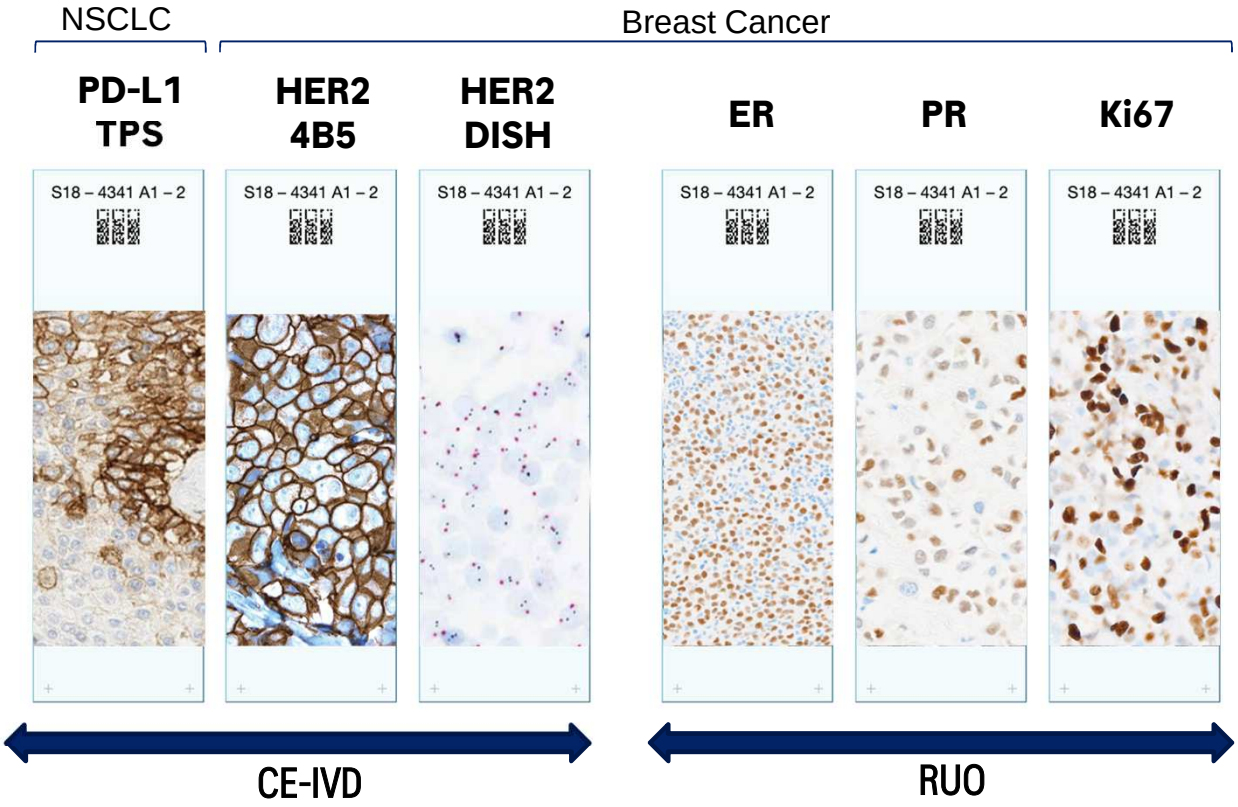
- Patient tailored treatment
- Useable in primary process
- Aging of the population

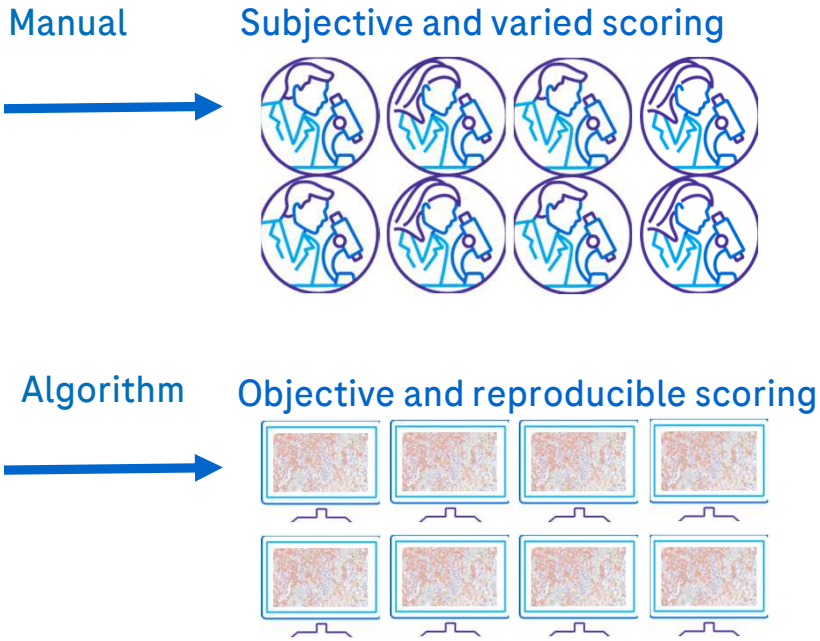
Present of AI

Future of AI

Available algorithms supporting single biomarker evaluation

Algorithms supports pathologist's expertise and increase inter and intra observer reproducibility





The shift towards AI driven H&E algorithms as supporting tools

Speeding up, improving accuracy and diagnosis confidence in daily routine

Automated Image analysis for « low level tasks » = object recognition

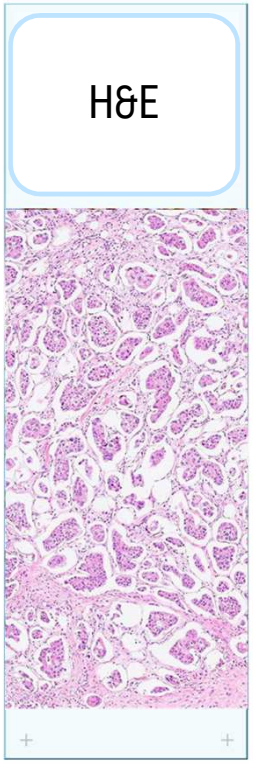
Aims at

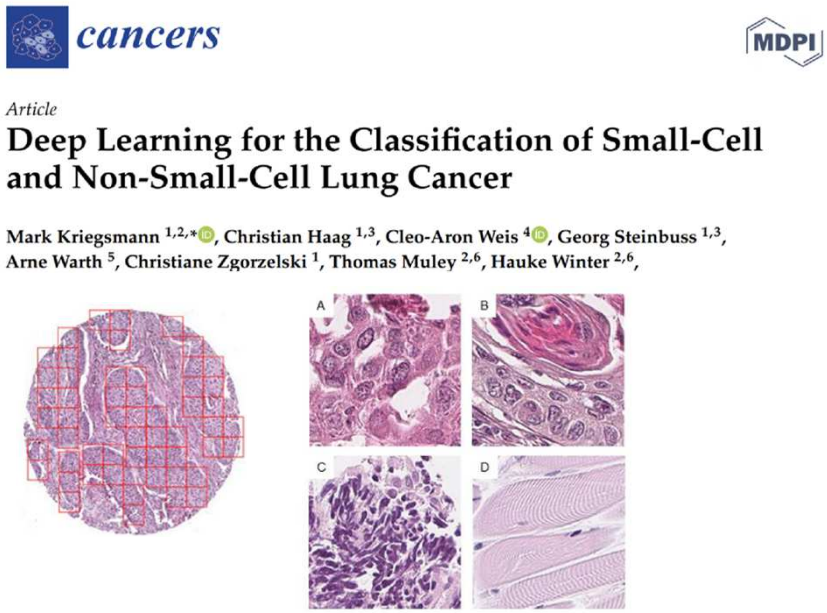
→ Saving pathologists' time

→ Improving consistency and accuracy

Examples

- Tumor detection
- Histotyping (NSCLC)
- Tumor grading
- Detection of metastases in lymph nodes




cancers

MDPI

Article

Deep Learning for the Classification of Small-Cell and Non-Small-Cell Lung Cancer

Mark Kriegsmann [1,2,*], Christian Haag [1,3], Cleo-Aron Weis [4], Georg Steinbuss [1,3], Arne Warth [5], Christiane Zgorzelski [1], Thomas Muley [2,6], Hauke Winter [2,6],

Validation cohorts
High quality data sets

[1] Kriegsmann M et al Cancers 2020, 12, 1604

NSCLC = Non-Small Cell Lung Cancer

The shift towards AI driven H&E algorithms as supporting tools

Extensive digitalisation of slides and resulting massive data lakes (will) open a new era

Advanced automated image analysis, based on **pattern recognition**

- To support and predict disease diagnosis and/or underlying molecular alterations
- To inform prognosis (OS) and/or treatment response on the basis of patterns in the image

nature medicine ARTICLES
https://doi.org/10.1038/s41591-018-0177-5

Classification and mutation prediction from non-small cell lung cancer histopathology images using deep learning

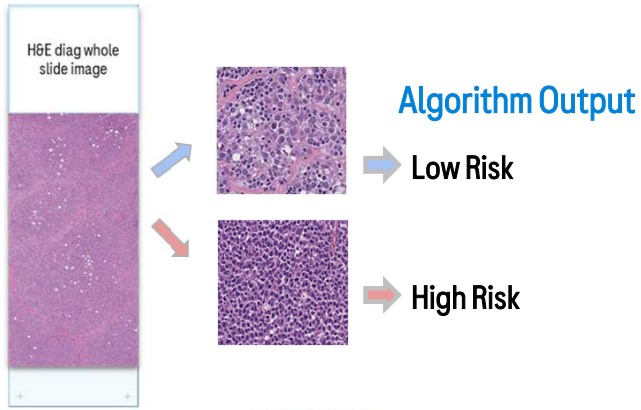
Nicolas Coudray[1,2,9], Paolo Santiago Ocampo[3,9], Theodore Sakellaropoulos[4], Navneet Narula[3], Matija Snuderl[3], David Fenyö[5,6], Andre L. Moreira[3,7], Narges Razavian[8*] and Aristotelis Tsirigos[1,3*]

Deep convolutional neural network enabled (CNN) on whole slide images (WSI) to accurately

- Classify tumours according to histotype (AUC* 0.97/pathologists
- Assist pathologists in the detection of cancer subtype/gene mutations (6/10 most common mutated genes in Lung Adenocarcinoma (including EGFR, KRAS, TP53, STK11)

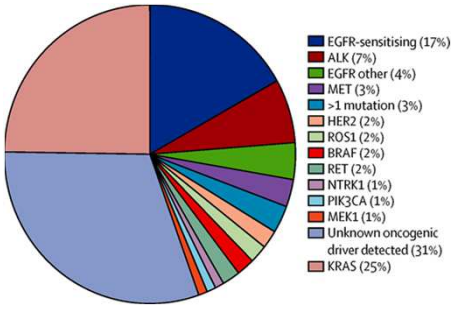
- **Aggressive lymphoma algorithm**

Identification of **high risk DLBCL**** patients for **next generation Heme trials**



- **Lung Adenocarcinoma algorithm**

Mapping morphology to the molecular landscape of targetable **actionable fusion positive NSCLC**



Frequency of molecular aberrations in driver oncogenes in lung adenocarcinoma.

1 Coudray, Ocampo et al 2018, Nature Medicine
2 Hirsch et al, Lancet 2017.

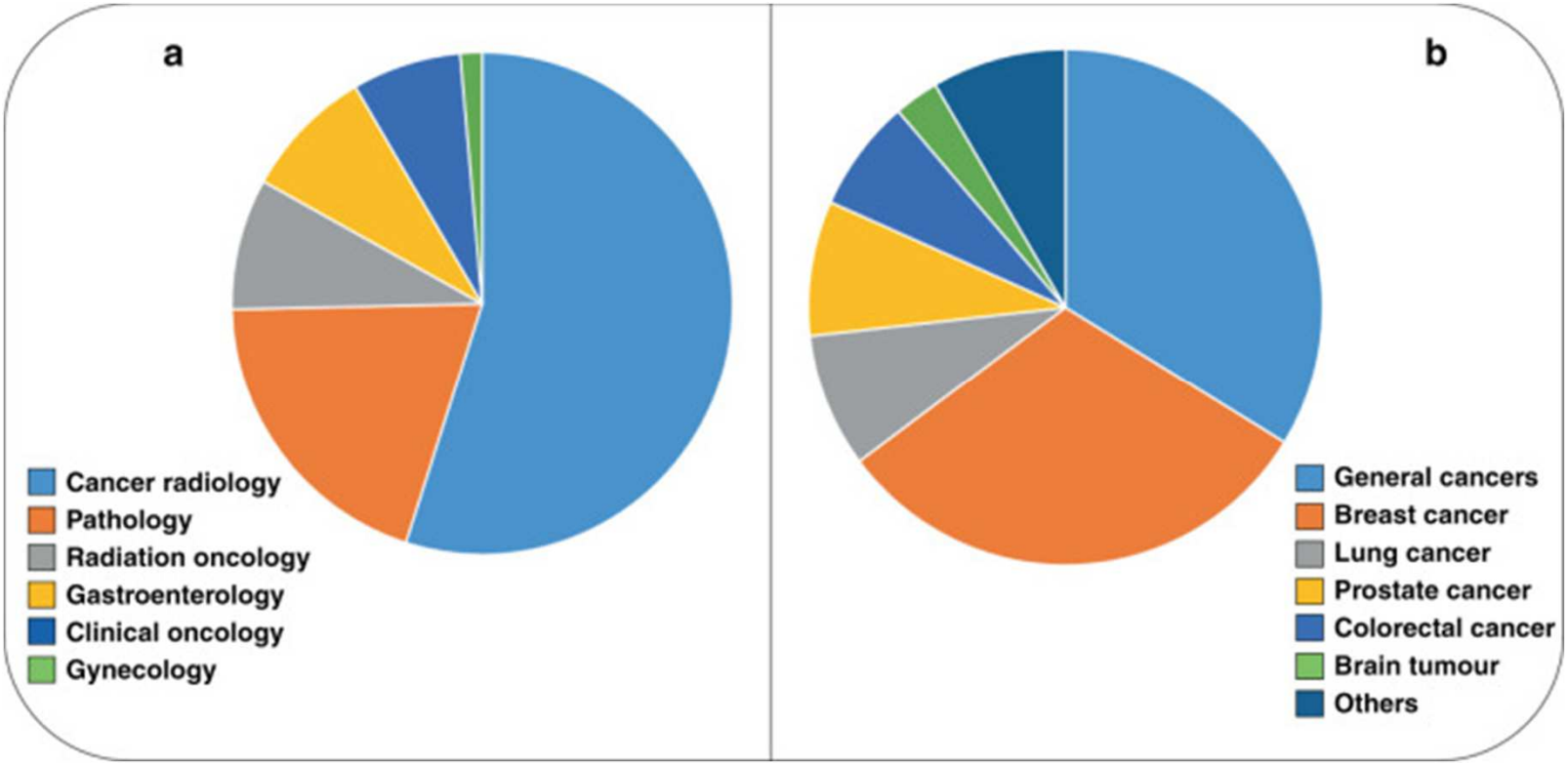
*AUC = Area Under the Curve is the measure of the ability of a classifier to distinguish between classe.
The higher the AUC, the better the performance of the model at distinguishing between the positive and negative classes (max = 1).

**DLBCL = Diffuse Large B Cell Lymphoma

Combining and integrating pathology, genomics and radiology with the help of AI, to better inform patient care

FDA approved-AI in Oncology and Related Field

Cancer, Pathology and Radiology as booming fields



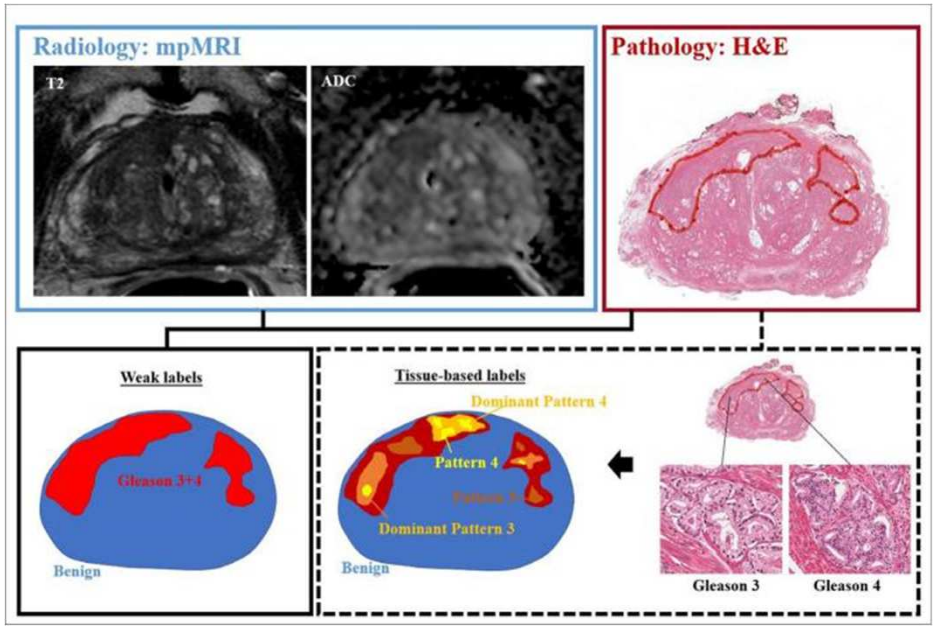
Luchini C et al 2022, Br J Cancer

The AI power of combining Imaging and Pathology

Radiomics informed by Pathology

Better grade Prostate Cancer and develop AI [1]

- AI methods show promise in aiding the **detection** and **assessment** of imaging-based tasks
- AI applied to mpMRI* and digital pathology in prostate cancer enables advanced characterization of disease through combined radiology-pathology assessment.
- Opportunities for improved spatial learning include density mapping of dominant pathologic grading and exclusion of non-cancerous structures within tumor field.



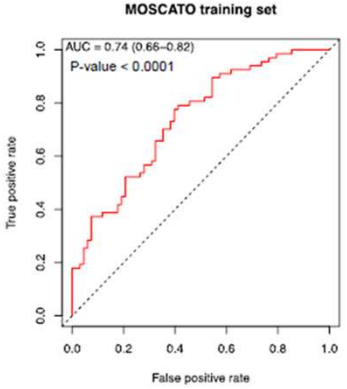
1 Harmon et al, 2019, Diagn Interv Radiol

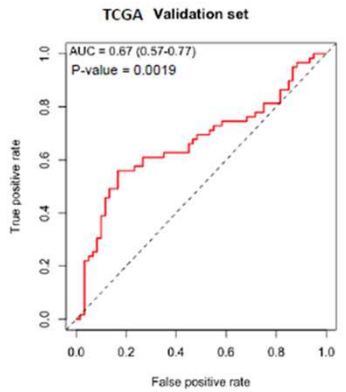
*mpMRI = multiparametric MRI

AI powered Integrated Diagnostics

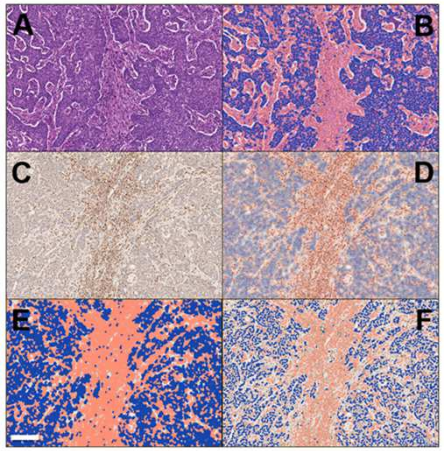
Radiomics informed by Pathology, Genomics supporting AI driven Pathology

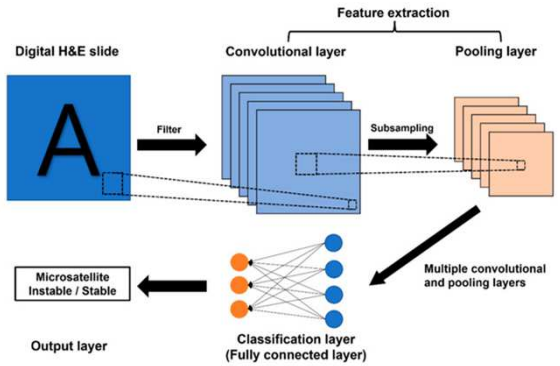
- **Radiomic signature (CT-scan) for CD8+ infiltration, predicting immune phenotype and treatment response to ICPI*[1]**
- Validated on 3 independent cohorts of patients with adv solid tumors
- Radiomic signature for CD8 cells validated with the gene expression signature of CD8 (RNA Seq)
- Signature can discriminate inflamed vs immune desert tumours
- High baseline radiomic score associated with a higher proportion of patients with objective response with anti PD1 and anti PDL1 therapies





- **Predicting Microsatellite instability based on histomorphology[2]**
- CRC: AI-based systems show excellent performance (highest standard of 0.972)
- Gastric and endometrial carcinoma: lower but satisfactory performance (0.81 and 0.82 respectively)
- Confirmation test required for positive AI test

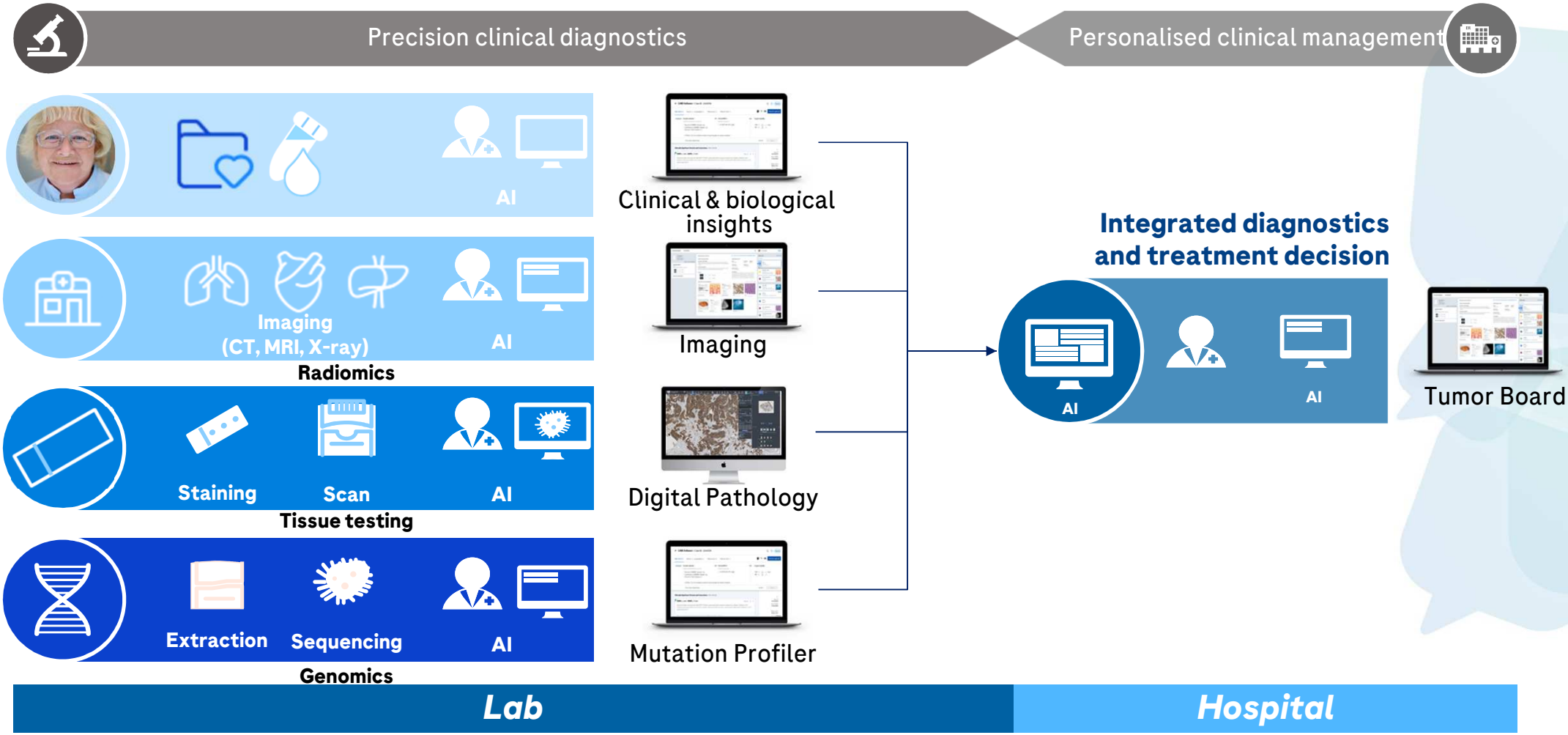




1 Sun et al, 2018, Lancet Oncology
2 Park et al 2022, Int J Mol Sci
*ICPI = Immune CheckPoint Inhibitor

Digital transformation of oncology

Integrating clinical insight, imaging, pathology and molecular genomics

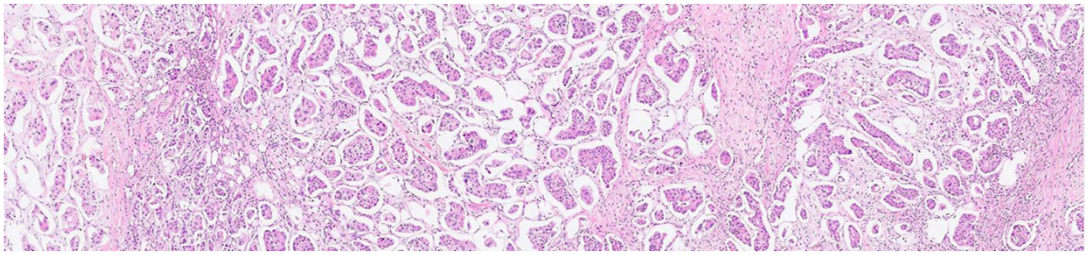


No company will be able to develop everything alone

Partnerships, consortia and open environment are key for success

Roche Digital Pathology Environment

- Accelerate image analysis algorithm development
- Allow for partnerships between researchers and developers, which can result in greater access to innovative imaging tools for laboratories and healthcare providers.



« Providing pathologists with access to innovative digital tools from Roche and our collaboratours through an open environment is critical for laboratory customers and the patients they serve. » Thomas Schinecker, CEO Roche Diagnostics

Public affairs initiatives: the example of the EU beating cancer plan

"...a political commitment to leave no stone unturned to take action against cancer"

- Tackle the **entire disease pathway**, structured around four key action areas : (1) prevention; (2) early detection; (3) diagnosis and treatment; and (4) quality of life of cancer patients and survivors
- Focus on **research** and **innovation**, tap into the potential that **digitalisation** and **new technologies** offer, and mobilise **financial instruments**

Flagship Research, Innovation and Digitalization

European Commission

Europe's Beating Cancer Plan

Launch a **European Cancer Imaging Initiative** to support the **development of new computer-aided tools** to improve personalized medicine and innovative solutions – 2022.

Take aways

A bright future for digitalisation and AI in the pathology lab to improve patient care

- Digitalisation and AI is a booming field in medicine, including the Pathology Lab (the « fourth revolution »)
- AI has the potential to increase speed and accuracy of diagnosis and now on improve prognostication to serve precision medicine.
- Integration with other insights (clinical, biological, radiomics and genomics) will play a major role.

- Some challenges to overcome:
  - → Integrate AI methods into pathology educational programs
  - → Regulatory, key to ensure reliability of the AI tools, secure trust in use and in the public
  - → Technical and biological challenges (big data and data integration, tumor heterogeneity)
  - → Large multicentric studies required to unravel the full potential of AI in the complex and fast evolving field of Oncology
  - → Financial burden and barriers especially for low income countries

Take aways

A bright future for digitalisation and AI in the pathology lab to improve patient care
..... and supporting Pathologist's unique expertise !

Could pathologists soon be replaced by robots ?

" AI won't replace pathologists, but pathologists who use AI will replace pathologists who don't. "

Harry Adams
(Royal College of Pathology, 2020)

Doing now what patients need next