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PRECISION ONCOLOGY CONNECT

THE EMERGING ROLE OF ARTIFICIAL INTELLIGENCE IN PRECISION ONCOLOGY

Prof. Albrecht Stenzinger, PhD
Pathologist, Heidelberg University Hospital, Heidelberg, Germany
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DEVELOPED BY PRECISION ONCOLOGY CONNECT

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EDUCATIONAL OBJECTIVES

UPON COMPLETION OF THIS ACTIVITY, THE LEARNER WILL:

- Have a deeper awareness and understanding of the current and future role of artificial intelligence in precision oncology

CLINICAL TAKEAWAYS

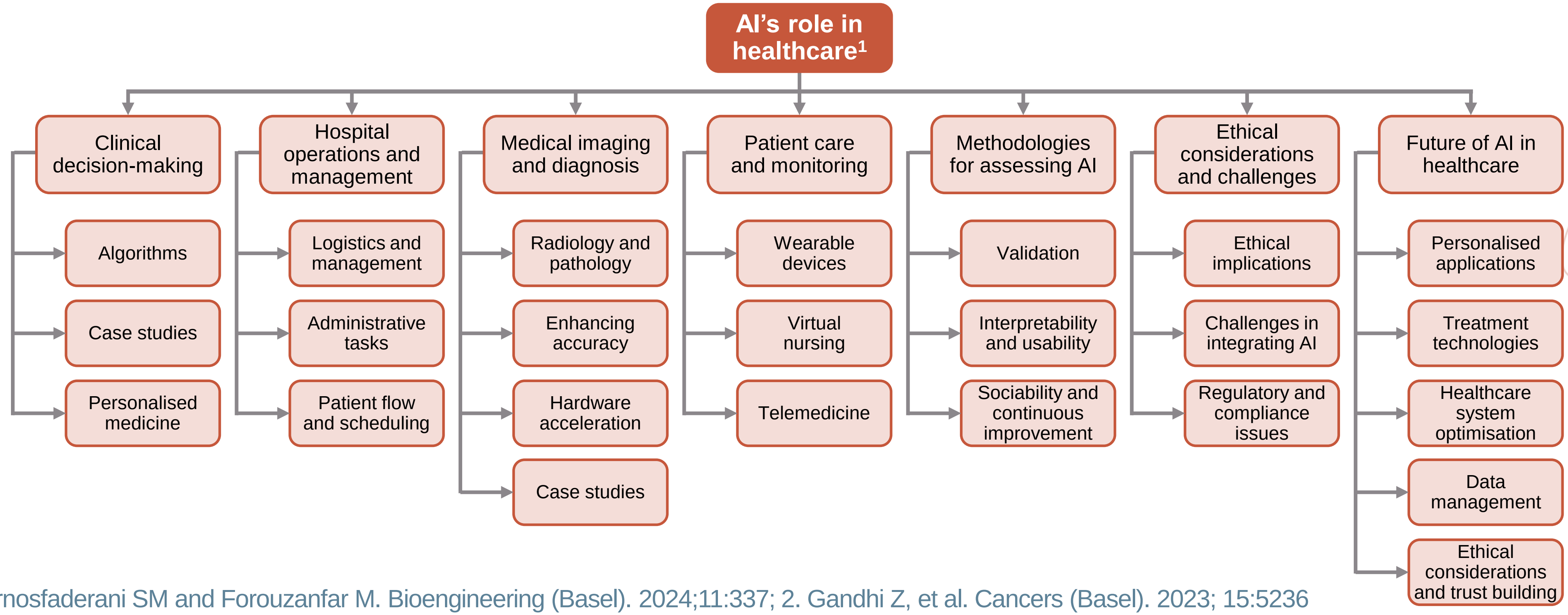
- AI technologies have the potential to support cancer diagnostics and therapy prediction by integrating complex clinical, imaging and genetic data
- Explainable AI is paramount for implementation in diagnostics
- Generalisability of AI is critical for widespread use
- Addressing regulatory and ethical issues, such as ensuring transparency in AI decision-making and maintaining patient data privacy, is essential for the widespread adoption of AI in precision oncology

AI, artificial intelligence

DEVELOPMENT, REQUIREMENTS FOR SUCCESSFUL USE AND CORE CONCEPTS OF AI

INTRODUCTION

- Artificial intelligence (AI) has transformed various fields, including healthcare and has the potential to improve patient care[1,2]
- AI technologies can assist physicians with accurate diagnosis via oncology image-recognition algorithms and can help clinicians estimate the patient's prognosis by predicting drug response, the tumour recurrence rate after surgery, radiotherapy response, and side effects[1,2]



1. Varnosfaderani SM and Forouzanfar M. Bioengineering (Basel). 2024;11:337; 2. Gandhi Z, et al. Cancers (Basel). 2023; 15:5236

PATHOLOGY BECOMES DIGITAL

- **Molecular Pathology**
  - Acquisition of images of molecular features such as specific tagged proteins or RNA or full metabolic, proteomic, or transcriptomic imaging. Digital pathology methods can be applied to molecular pathology imaging
- **Histopathology/surgical pathology**
  - Digital slide scanning and the use of AI
  - Virtual microscopy on the computer, with multiple tools using artificial intelligence and machine learning to support pathologists in their work

AI, artificial intelligence; RNA, ribonucleic acid

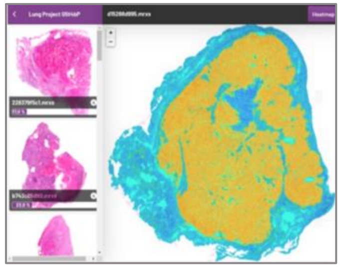
Stenzinger A, et al. Seminars in Cancer 2021: https://doi.org/10.1016/j.semcancer.2021.02.011; Dexter A, et al. J Mol Pathol. 2022;3:168-81

AI-BASED SUPPORT SYSTEMS

- Support tool in the framework of diagnostics – “Copilot“ supporting:
  - Diagnosis[1]
  - Prognosis[1,2]
  - Enrichment of mutational profiles[1]

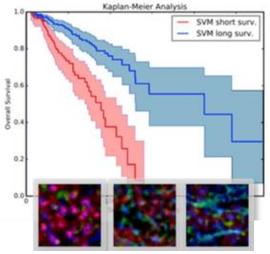
PATHOLOGY AI[1]

Today
Improve analysis



- Disease detection
- Feature quantification

Next
Improve diagnosis



- (Differential) diagnosis
- Outcome prediction
- Treatment suggestion

Future
Multi-modal data integration & clinical decision-making

- AI-based precision medicine: integration of histological, molecular and clinical information
- Independent AI diagnosis of “easy” cases

AI, artificial intelligence

1. Stenzinger A, et al. Semin Cancer Biol. 2022; 84:129-143; 2. Gandhi Z, et al. Cancers (Basel). 2023; 15:5236

A SCALABLE SET-UP

A scalable set-up is required for AI to be successful:

- Hardware (scanner and IT infrastructure)
- Experts familiar with the systems
- Critical Mass
- Significant investments in short innovation cycles

AI, artificial intelligence; IT, information technology

How To Scale AI In Your Organization | IBM (Accessed Oct 2024)

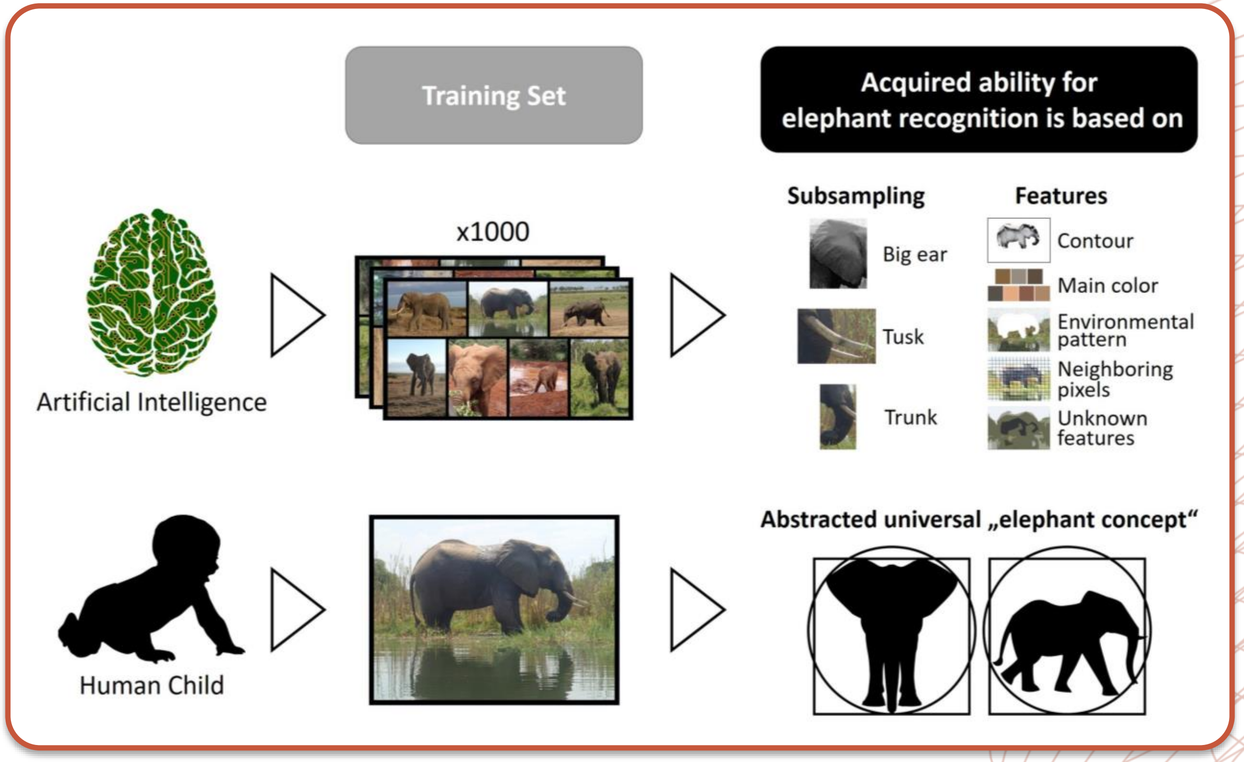
DEVELOPMENT OF AI

Strength in numbers/training sets

- Machine learning tools require large amounts of high-quality data for training purposes and are only able to interpolate the acquired information for a new task
- Human beings can extract highly complex concepts from limited amounts of data to apply it to new tasks beyond the one originally learned

Further development of AI tools

- Human features like cognition and extrapolation are core examples of AI-based approaches that still require enormous scientific advancements

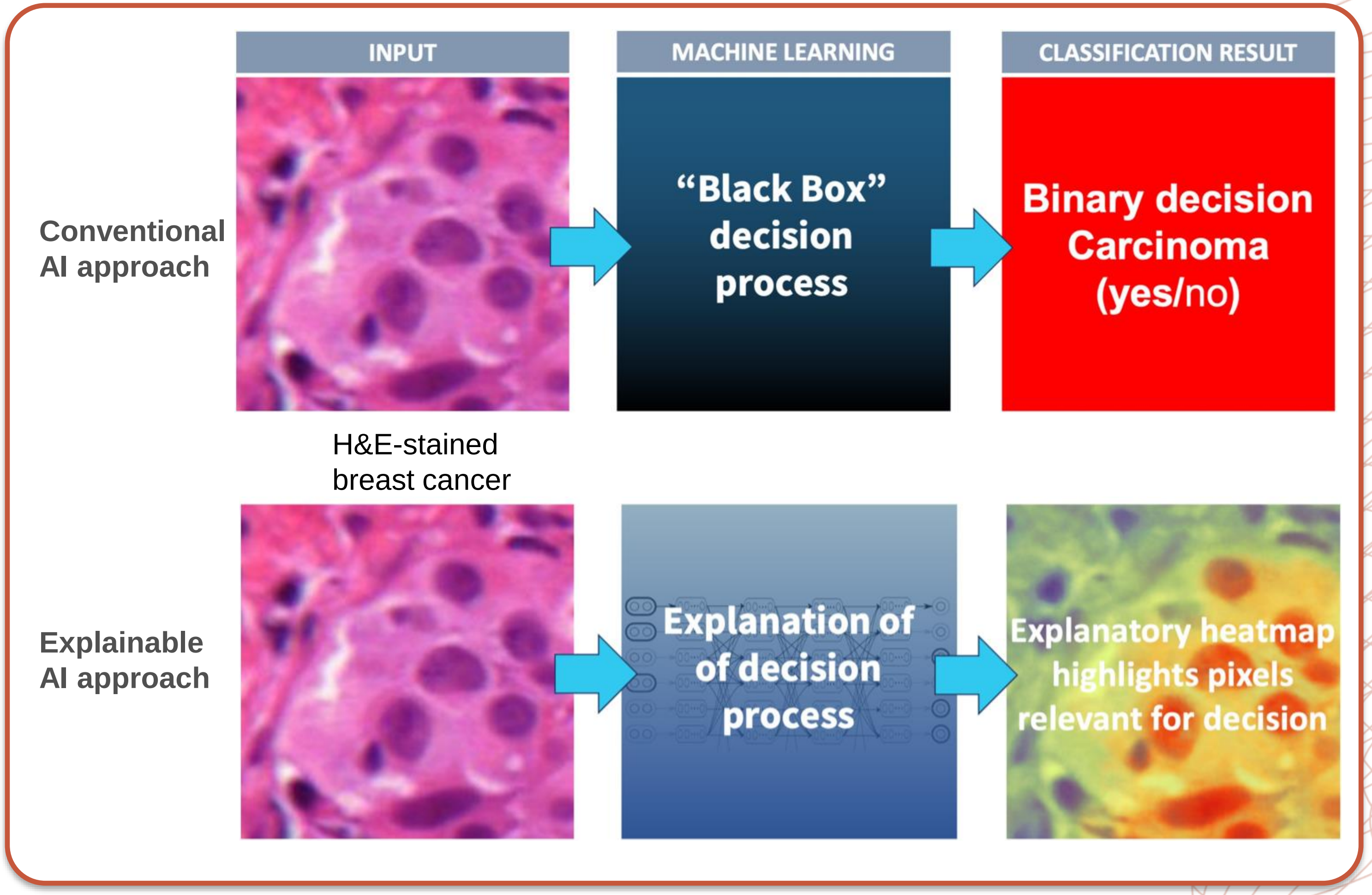


AI, artificial intelligence

Stenzinger A, et al. Semin Cancer Biol. 2022; 84:129-143

IMPLEMENTATION OF AI

- **Generalisability**
  - The data generated in one dataset need to be transferable to another dataset/institution
- **Explainability**
  - Conventional AI leaves the decision process intransparent (“black box”) and provides a binary decision without “explaining” why
  - Explainable AI uses layer-wise-relevance propagation to open the black box and provide pixel-wise scores that contribute to the decision “carcinoma”



AI, artificial intelligence; H&E, haematoxylin and eosin stain

Stenzinger A, et al. Semin Cancer Biol. 2022; 84:129-143

CONSIDERATIONS FOR CLINICAL IMPLEMENTATION

Barriers:

- Lack of quality medical data can result in inaccurate outcomes[1]
- Lack of large clinical datasets to train the model[2]
- Data privacy, availability and security issues[1]
- Determining relevant clinical metrics and methodology[1]
- Lack of human expertise[1]

Solutions:

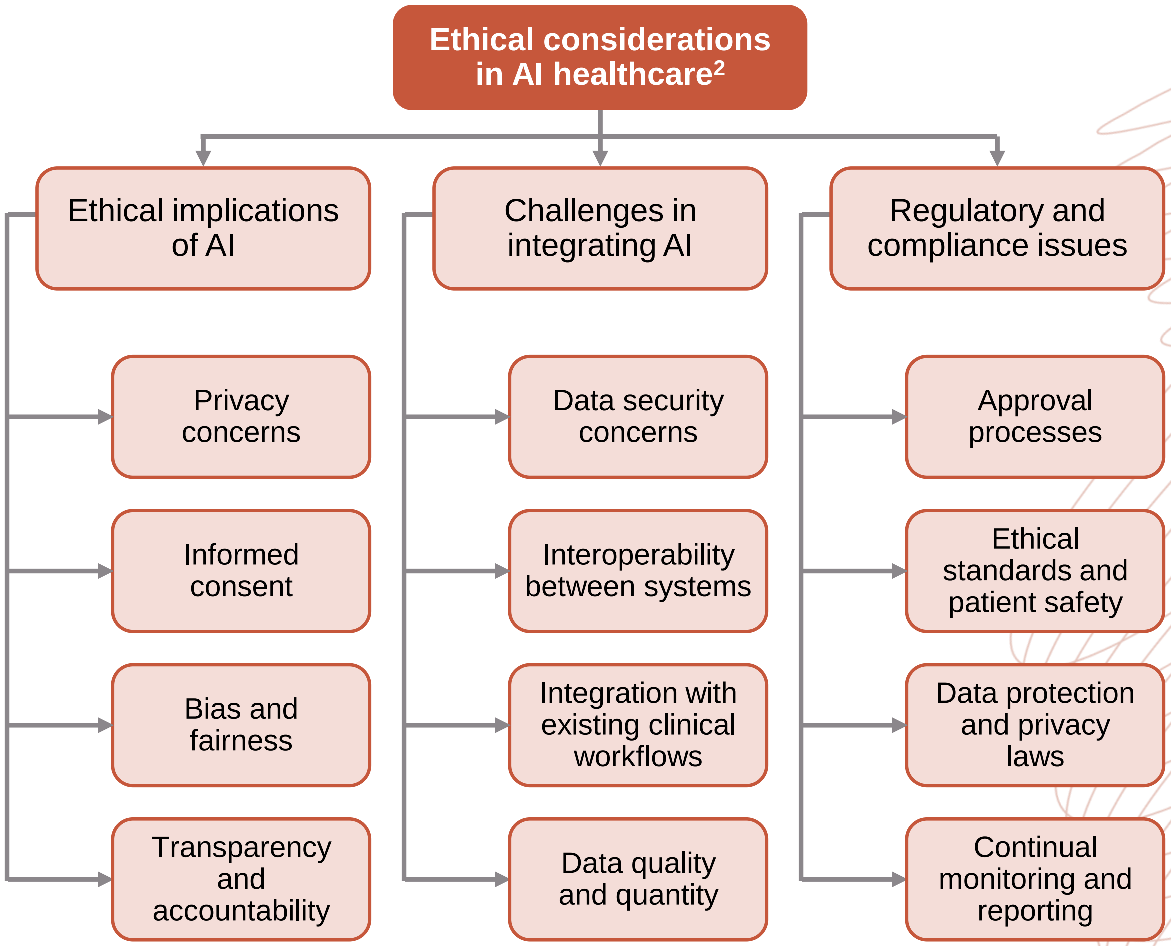
- Multidisciplinary approach[1]
- Innovative data annotation methods[1]
- Development of more rigorous AI techniques and models[1]
- Data sharing between multiple health care settings[1,2]
- Training and education of students and healthcare professionals[1]

AI, artificial intelligence

1. Alowais SA, et al. BMC Med Educ. 2023;23:689; 2. Gandhi Z, et al. Cancers (Basel). 2023;15:5236

ETHICAL, LEGAL AND REGULATORY ASPECTS OF AI

- **IVDR and other regulations[1]**
  - applies to in vitro diagnostics containing AI/ML-based software
  - Validation of any AI approach requires careful standardisation of datasets in a highly controlled environment
- **Acceptable error margin[1]**
  - Defining an error margin that we would be willing to accept when applying AI
  - What is the human error rate in comparison
- **Liability of the AI report provider[1]**



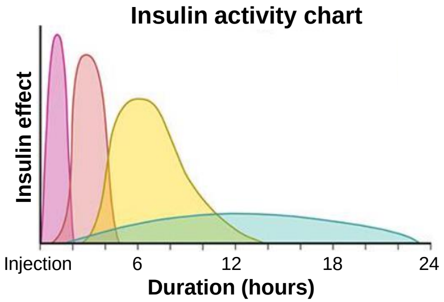
AI, artificial intelligence; IVDR, in-vitro diagnostic regulation; ML, machine learning

1. Stenzinger A, et al. Semin Cancer Biol. 2022; 84:129-143; 2. Varnosfaderani SM and Forouzanfar M. Bioengineering (Basel). 2024;11:337;

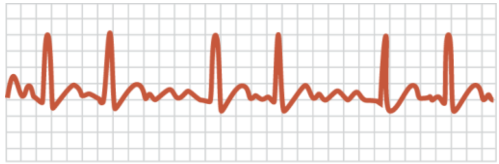
CLINICAL APPLICATION OF AI

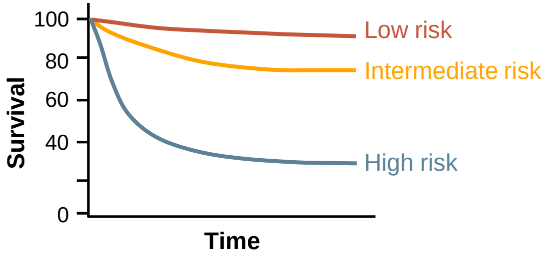
AI, artificial intelligence

AI-POWERED PREDICTIVE ANALYSIS IN CLINICAL PRACTICE



Analyses both historical and current data





It requires:
1. Quality data
2. Technological infrastructure
3. Human supervision

Beneficial outcomes	
Improve patient outcomes	Identifying patients at risk and target interventions to prevent or treat them
Predicting hospital readmissions	Reduce healthcare costs

AI, artificial intelligence

Alowais SA, et al. BMC Med Educ. 2023;23:689;

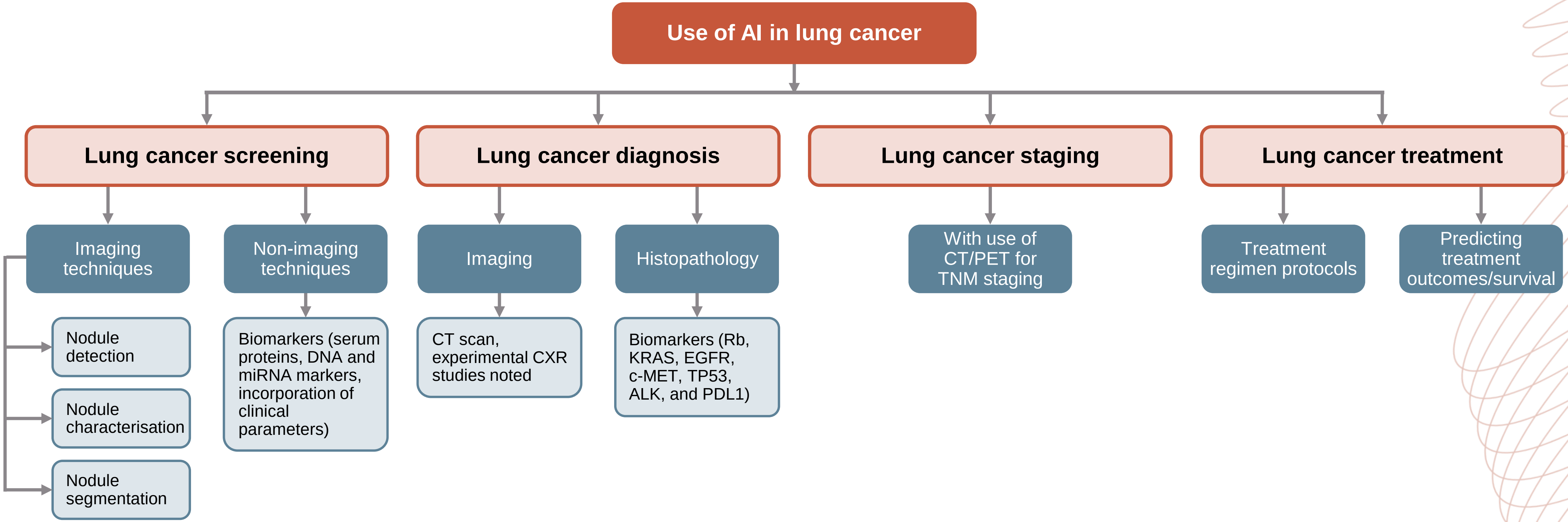
CLINICAL APPLICATION OF AI IN ONCOLOGY

- **AI Applications in Cancer Genomics**
  - Analysing large-volume multiomics data (exome, transcriptome, and epigenome) combined with clinically annotated datasets has led to the identification of drug-susceptibility genes, variant detection, new cancer biology insights, and prediction of RNA splice sites
- **AI Applications in Cancer-related Image Analysis**
  - AI-based models are now routinely part of breast imaging
  - Software program allows comprehensive detection and tracking of pulmonary nodules, prediction of lung malignancy among detected lesions on low-dose CT images
  - Deep neural networks have been developed to detect enlarged lymph nodes or colonic polyps in CT images and to enhance colon polyp detection during colonoscopy with a real-time DL computer-aided detection system
  - Augmented interpretation of endoscopic images using AI consistently improves accuracy in the detection of oesophageal cancer
  - Analysis of pathologic images for diagnosis, grading, and prognostic biomarker interpretation

AI, artificial intelligence; CT, computed tomography; DL, deep learning; RNA, ribonucleic acid

Shreve J, et al. Am Soc Clin Oncol Educ Book. 2022;42:1-10

APPLICATION OF AI IN LUNG CANCER

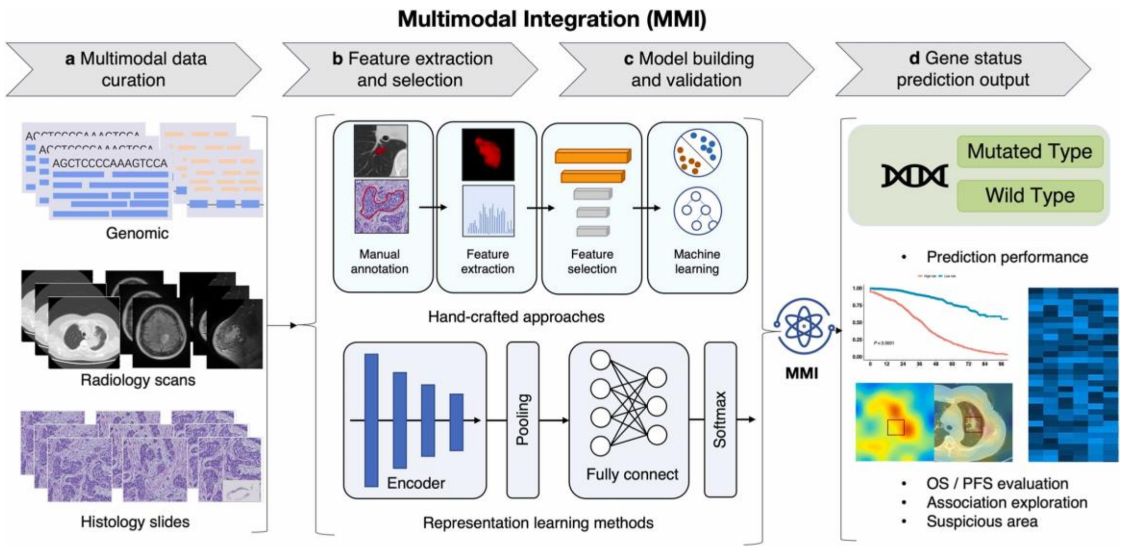


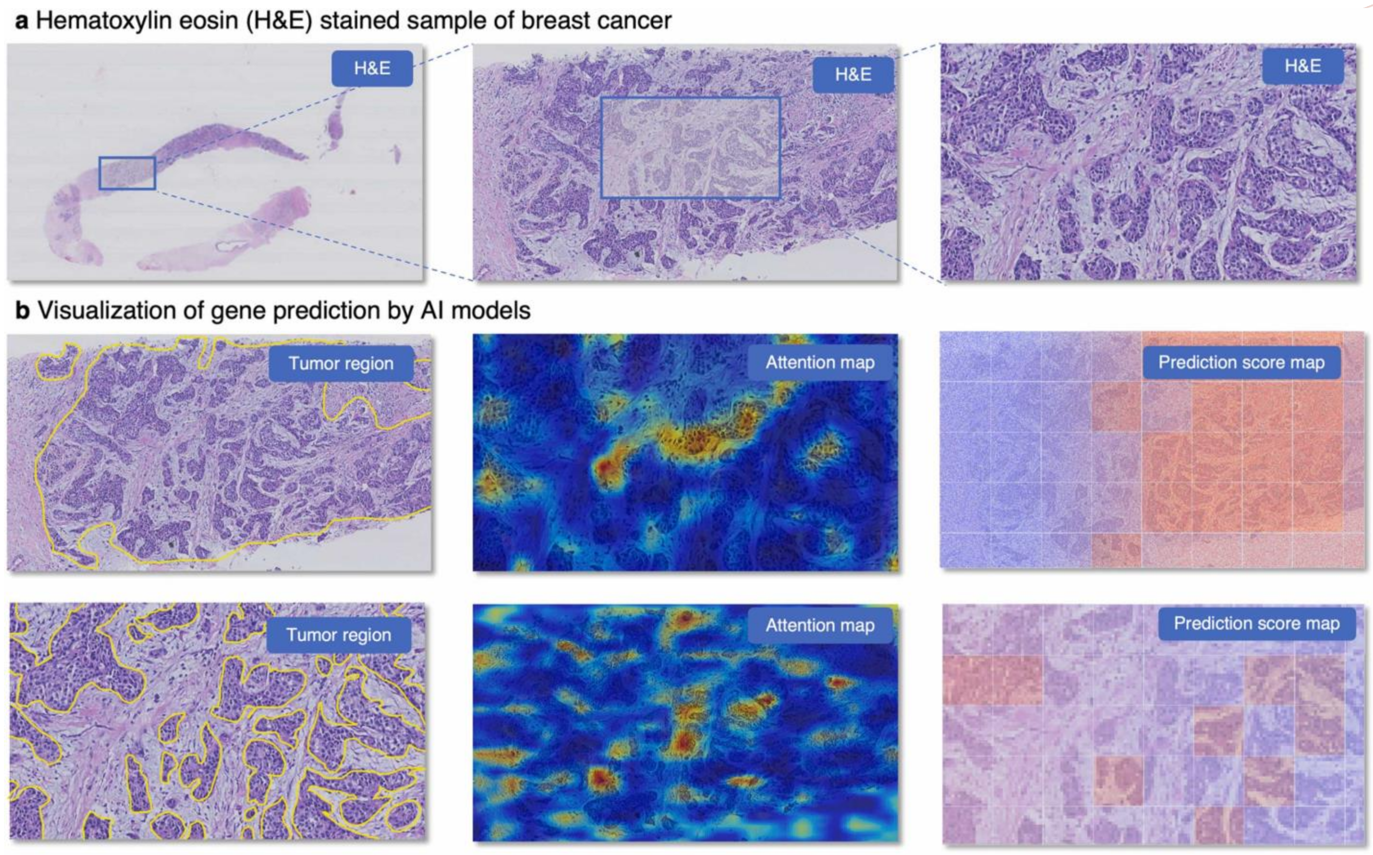
AI, artificial intelligence; ALK, anaplastic lymphoma kinase; c-MET, mesenchymal-epithelial transition factor; CT, computed tomography; CXR, chest x-ray; DNA, deoxyribonucleic acid; EGFR, epidermal growth factor receptor; KRAS, Kirsten rat sarcoma viral oncogene homolog; miRNA, microRNA; PD-L1, programmed death-ligand 1; PET, positron emission tomography; Rb, retinoblastoma protein; RNA, ribonucleic acid; TNM, tumour, node, metastasis; TP53, p53 protein

Gandhi Z, et al. Cancers (Basel). 2023; 15:5236

EXAMPLES OF AI USE (I)

WORKFLOW FOR PREDICTING GENE STATES



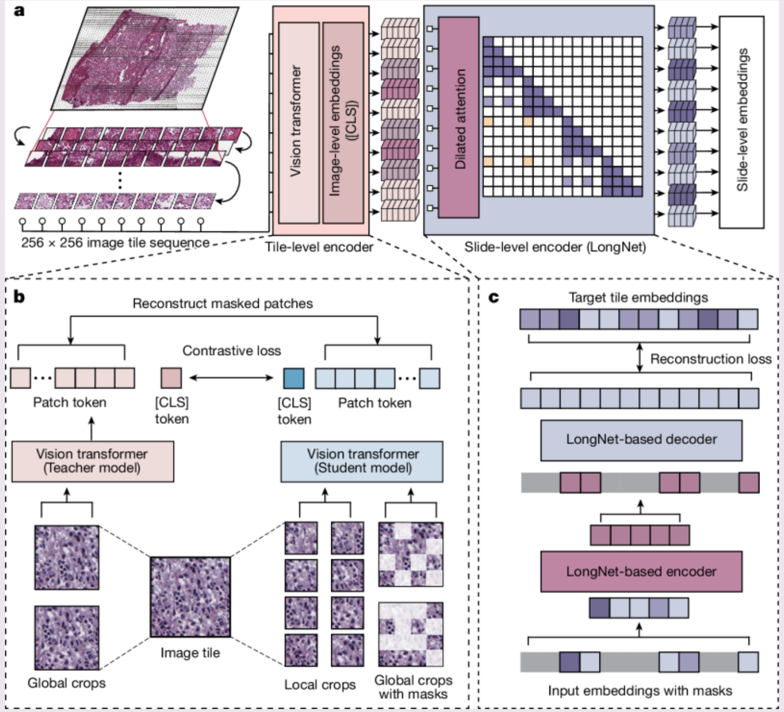


AI, artificial intelligence; OS, overall survival; PFS, progression-free survival

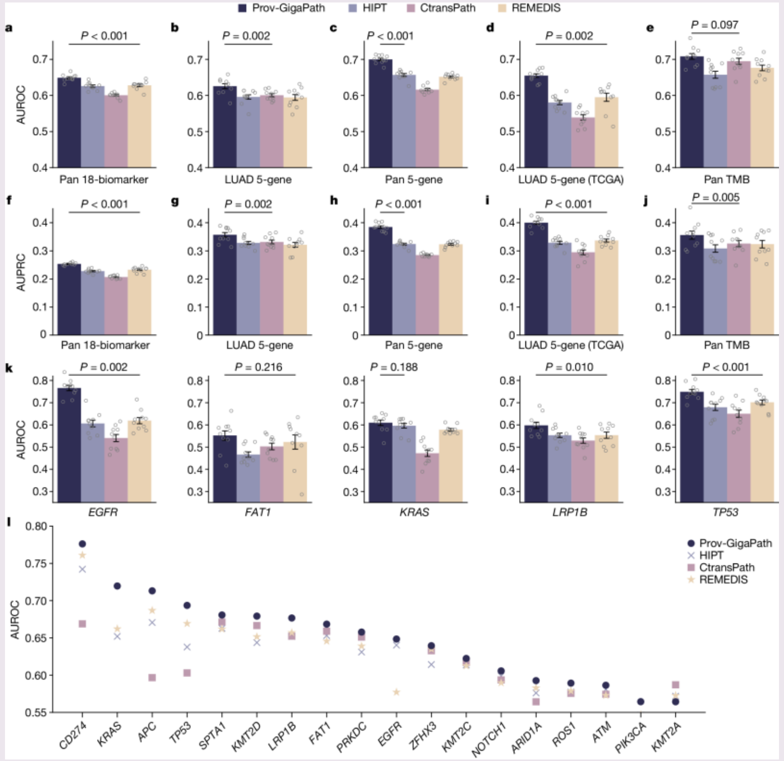
Shao J, et al. Semin Cancer Biol. 2023; 91:1-15

EXAMPLES OF AI USE (II)

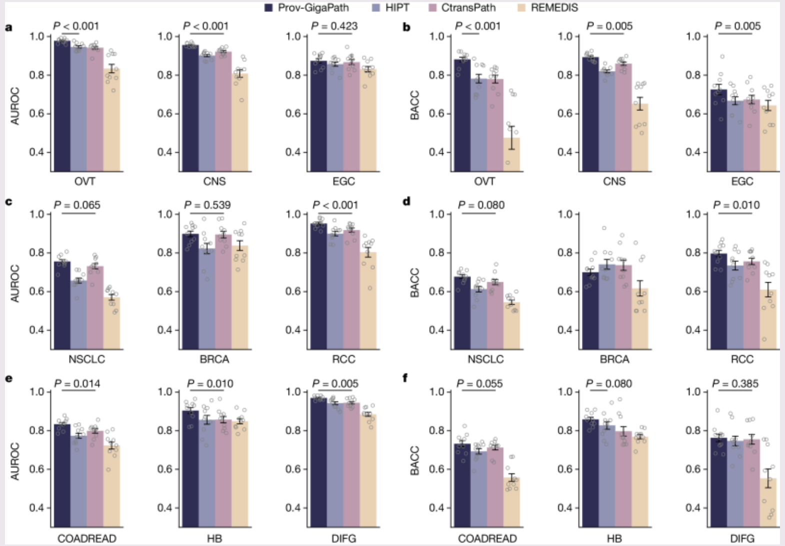
OVERVIEW OF PROV-GIGAPATH



PREDICTION OF MUTATIONS



COMPARISON OF CANCER SUBTYPING



[CLS], “classification” token; APC, adenomatous polyposis coli; ARID1A, AT-rich interactive domain-containing protein 1A; ATM, ataxia-telangiectasia mutated; AUROC, area under the receiver operating characteristic curve; BRCA, breast invasive carcinoma; CD274, programmed death-ligand 1 (PD-L1); CNS, central nervous system; COADREAD, colorectal adenocarcinoma; DIFG, diffuse intrinsic pontine glioma; EGC, early gastric cancer; EGFR, epidermal growth factor receptor; FAT1, FAT atypical cadherin 1; HB, hepatobiliary; HIPT, hierarchical image pyramid transformer; KMT2A/C/D, lysine methyltransferase 2A/C/D; KRAS, Kirsten rat sarcoma viral oncogene homolog; LRP1B, low-density lipoprotein receptor-related protein 1B; LUAD, lung squamous cell carcinoma; NOTCH1, neurogenic locus notch homolog protein 1; NSCLC, non-small cell lung cancer; OVT, ovarian cancer; PIK3CA, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; RCC, renal cell cancer; ROS1, ROS proto-oncogene 1; SPTA1, spectrin alpha, erythrocytic 1; TCGA, The Cancer Genome Atlas; TMB, tumour mutational burden; TP53, p53 protein; ZFHX3, zinc finger homeobox 3

Xu H, et al. Nature 2024;630:181-188

FUTURE USE OF AI

WIDESCALE ADOPTION AND APPLICATION OF AI IN HEALTHCARE

Timeline	Connected/ augmented care	Precision diagnostics	Precision therapeutics	Precision medicine	Summary
Short-term: 0-5 years	• Internet of things in healthcare • Virtual assistants • Augmented telehealth • Personalised mental health support	• Precision imaging (e.g. diabetic retinopathy and radiotherapy planning)	CRISPR (increasing use)	Digital and AI enabled research hospitals	• AI automates time consuming, high-volume repetitive tasks, especially within precision imaging
Medium-term: 5-10 years	• Ambient intelligence in healthcare	• Large-scale adoption and scale-up of precision imaging	• Synthetic biology • Immunomics	• Customisation of healthcare • Robotic assisted therapies	• AI uses multi-modal datasets to drive precision therapeutics
Long-term: >10 years	• Autonomous virtual health assistants, delivering predictive and anticipatory care • Networked and connected care organisations (single digital infrastructure)	• Holographic and hybrid imaging • Holomics (integrated genomic/radiomic/ proteomic/clinical/ immunohistochemical data)	• Genomics medicine • AI driven drug discovery	• New curative treatments • AI empowered healthcare professionals	• AI enables healthcare systems to achieve a state of precision medicine through AI-augmented healthcare and connected care

Timings are illustrative to widescale adoption of the proposed innovation taking into account challenges/regulatory environment/use at scale

AI, artificial intelligence; CRISPR, clustered regularly interspaced short palindromic repeats

Bajwa J, et al. Future Healthc J. 2021;8:e188-e194

SUMMARY

SUMMARY

- AI can be used to diagnose diseases,[1] develop personalised treatment plans,[2] and assist clinicians with decision-making[2]
- Rather than simply automating tasks, AI is about developing technologies that can enhance patient care across healthcare settings[2,3]
- However, challenges related to data privacy, bias, and the need for human expertise must be addressed for the responsible and effective implementation of AI in healthcare[2,4]
- Collaboration amongst stakeholders is vital for robust AI systems,[4] ethical guidelines,[2] and patient and provider trust[2]
- The future of precision oncology, in which databases of multimodal datatypes are recursively used to improve clinical models,[5-7] may have beneficial outcomes across wide-ranging aspects of healthcare in oncology[4]

AI, artificial intelligence

1. Gandhi Z, et al. Cancers (Basel). 2023; 15:5236; 2. Varnosfaderani SM and Forouzanfar M. Bioengineering (Basel). 2024;11:337; 3. Shreve J, et al. Am Soc Clin Oncol Educ Book. 2022;42:1-10; 4. Alowais SA, et al. BMC Med Educ. 2023;23:689; 5. Bajwa J, et al. Future Healthc J. 2021;8:e188-e194; 6. Stenzinger A, et al. Semin Cancer Biol. 2022; 84:129-143; 7. Shao J, et al. Semin Cancer Biol. 2023; 91:1-15

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