Ai-based medical solutions

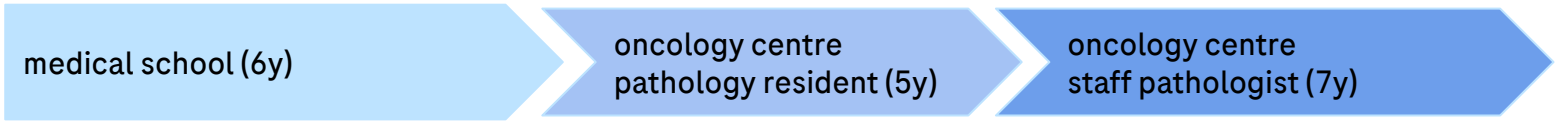
How efficiently bring them to patients

Konstanty Korski, MD, PhD
Digital Pathology Lead, Roche Pharma personalized healthcare group

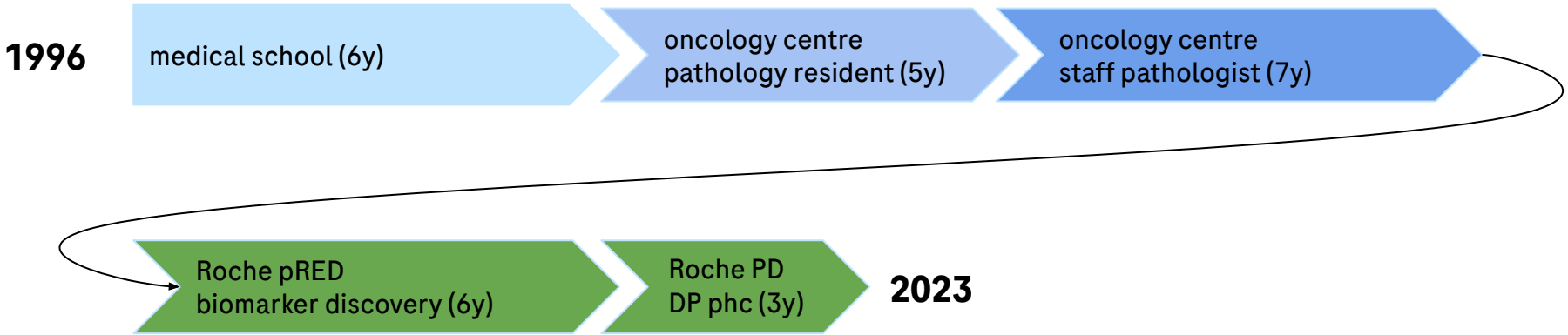
May 23, 2023 | Turing-Roche Knowledge Share Series

my background

1996

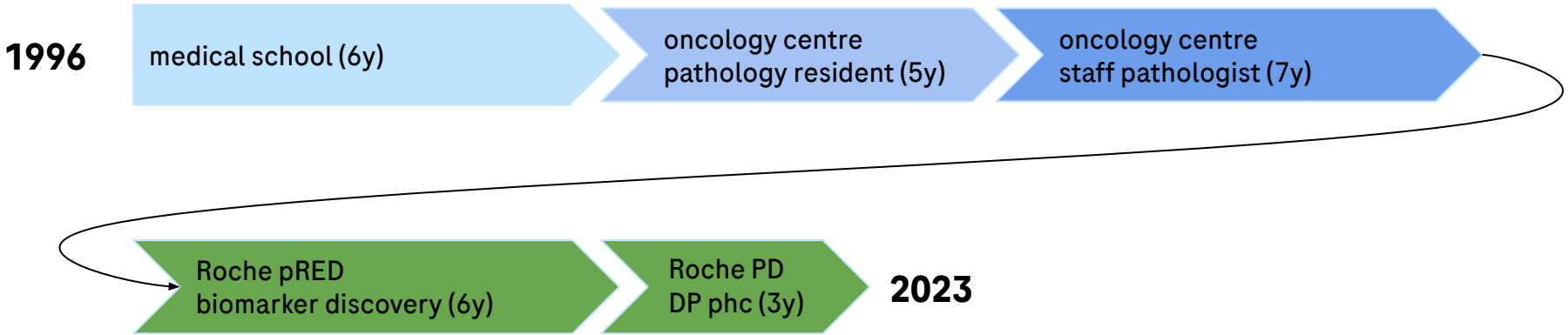


my background



pRED - pharma Research & Early Development
PD - Product Development
DP phc - Digital Pathology - personalised healthcare

challenge



pRED - pharma Research & Early Development
PD - Product Development
DP phc - Digital Pathology - personalised healthcare

challenge

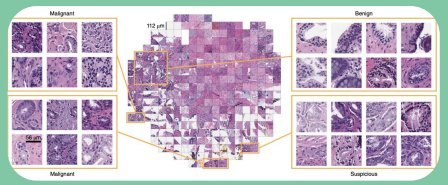
27y (human) ?-> 1y (AI)

Approved DP algorithms for primary Dx

First AI-powered HE-based algorithms to support pathologists

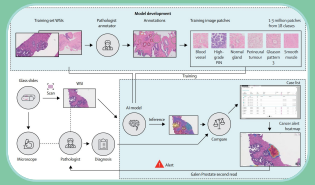
Paige

Prostate Detect



IBEX

Galen™ Prostate

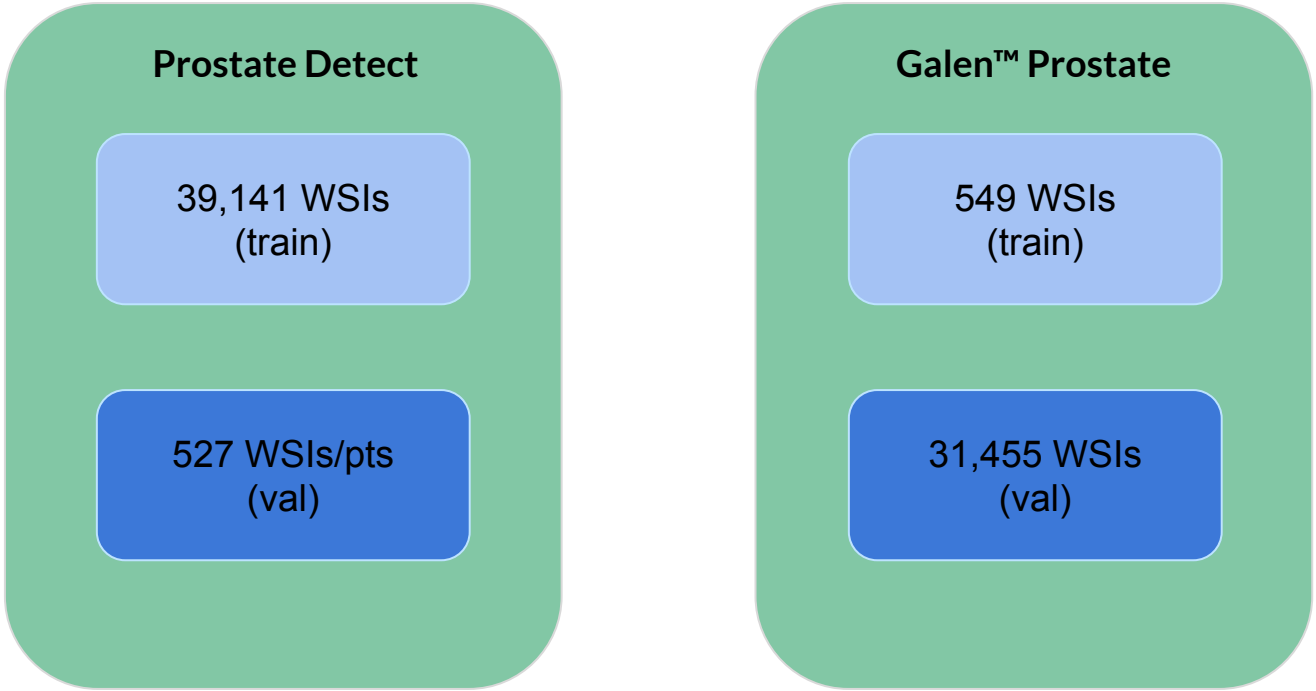


• Campanella, G., Hanna, M.G., Geneslaw, L. *et al.* Clinical-grade computational pathology using weakly supervised deep learning on whole slide images. *Nat Med* 25, 1301–1309 (2019). https://doi.org/10.1038/s41591-019-0508-1

• Pantanowitz, L., Quiroga-Garza, G.M., Bien, L., Heled, R., Laifenfeld, D., Linhart, C., Sandbank, J., Shach, A.A., Shalev, V., Vecsler, M., Michelow, P., Hazelhurst, S., Dhir, R., 2020. An artificial intelligence algorithm for prostate cancer diagnosis in whole slide images of core needle biopsies: a blinded clinical validation and deployment study. Lancet Digital Heal 2, e407–e416. https://doi.org/10.1016/s2589-7500(20)30159-x

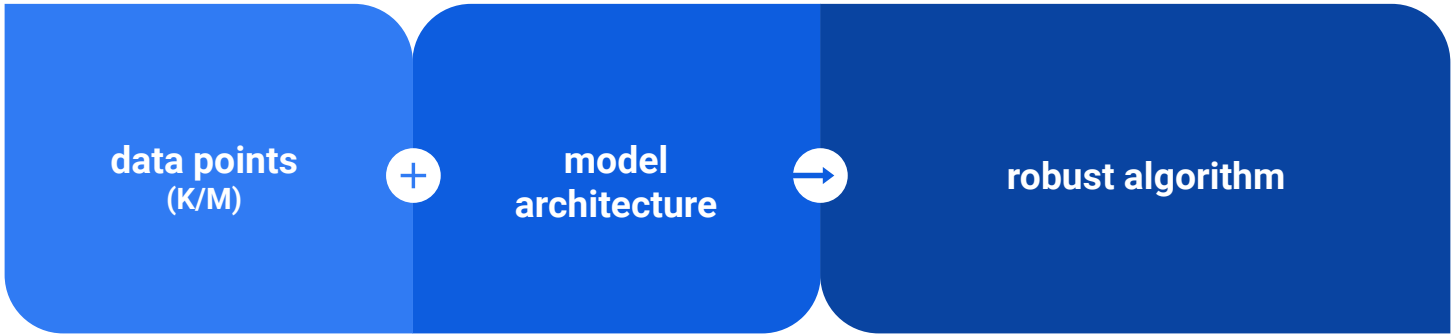
Approved DP algorithms for primary Dx

First AI-powered HE-based algorithms to support pathologists



WSIs - whole slide images; **pts** - patients

Recipe for success ?



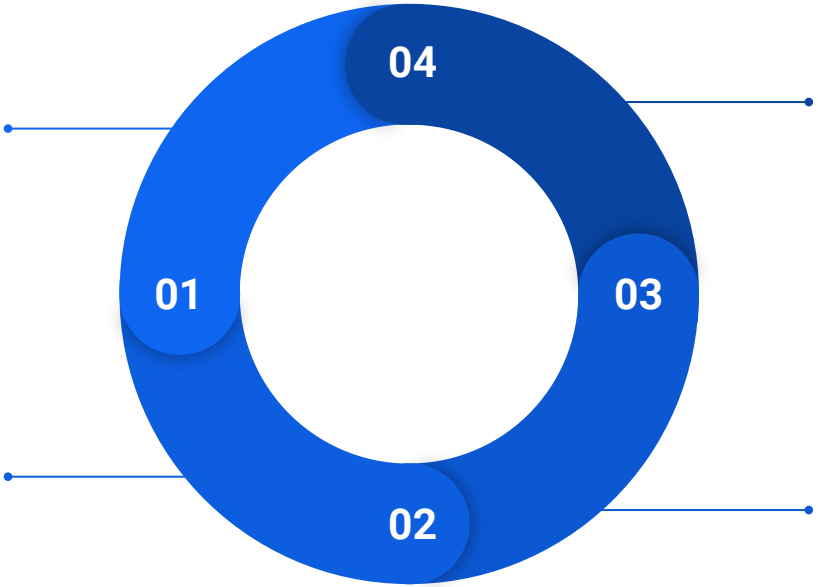
Key challenges for successful deployment of AI-based solutions in medical field

data quality

breadth and depth of data repositories to represent RW diversity

healthcare regulations

meeting legal requirements to ensure safety and accuracy of AI solutions



infrastructure

technical foundation for models (inter)operability

clinical deployment

fit for clinical workflows to ensure high RW uptake

RW - real world

Data quality

strong impact on algorithms' robustness

Percentages of 518 FDA-approved AI products that submitted data covering sources of bias

	Aggregate reporting	Stratified reporting
Patient cohort	less than 2% conducted multi-race/gender validation	less than 1% approvals with performance figures across gender and race
Medical device	8% conducted multi-manufacturer validation	less than 2% reported performance figures across manufacturers
Clinical site	less than 2% conducted multisite validation	less than 1% approvals with performance figures across sites
Annotators	less than 2% reported annotator/reader profiles	less than 1% reported performance figures across annotators/readers

Enes Hosgor and Oguz Akin *Four types of bias in medical AI are running under the FDA's radar.* STAT+, Jan 9, 2023

Healthcare regulations

evolving guidelines for AI-based algorithms clearance to ensure their accuracy and safety

Table 2: US Food and Drug Administration and European classification for *in vitro* diagnostic medical devices

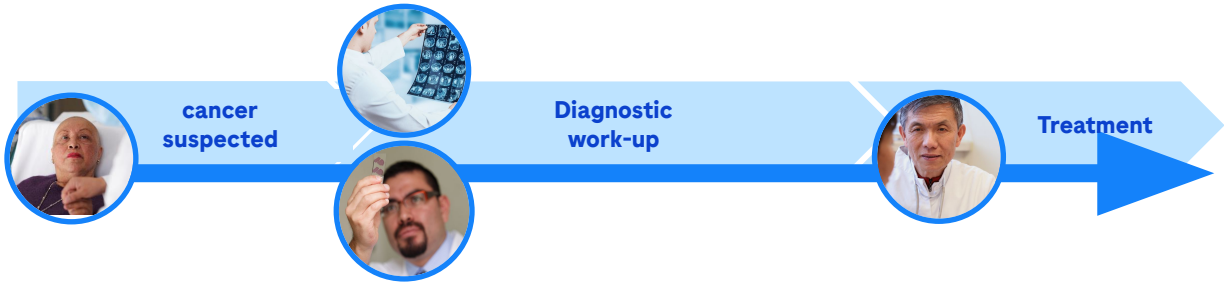
US FDA	Regulation (EU) 2017/746
Class III	Class D
Highest risk	High risk of infection or specific blood groupings
General controls	Manufacturer performs tests on each manufactured batch of devices
PMA	Expert panel/EU reference laboratory evaluates the manufacturer performance evaluation report
Clinical studies needed^	Class C
Class II	Detection of nonhigh risk infectious agents, managing life-threatening disease or condition, companion diagnostics
Moderate risk	Class D and C require
General controls and special controls	Notified body conformity assessment*
Premarket notification 510(k)	EU type-examination certificate
Substantial equivalence to a predicate	Quality management system assessment
	Safety and performance evaluation document should be publicly available, updated at least annually
	Clinical studies needed^
	Synergies with EU database for clinical trials on medicinal product
	Postmarket surveillance: PSUR at least annually
-	Class B
	Many self-testing devices (glucose, erythrocytes, leucocytes, and bacteria in urine)
	Notified body conformity assessment*
Class I	Class A
Low risk	General laboratory products
General controls (GMP)	Manufacturer conformity assessment
510(k) exempt	
Registration and listing	

^Clinical studies are needed. The study must demonstrate that clinical interpretations (diagnoses) made based on the digital pathology images are comparable to those made using glass slides. In case technological characteristics are modified, clinical studies are not needed if substantial equivalence to the previous version can be demonstrated with attributes such as the intended use/indications for use, technology and design features, and safety and effectiveness, *When the device clinical performance which cannot be fully determined by analytical performance studies, literature, and/or previous experience gained by routine diagnostic testing, clinical performance studies are necessary to demonstrate compliance with the relevant general safety and performance requirements. GMP: Good manufacturing practices, PMA: Premarket approval, PSUR: Periodic safety update report, EU: European Union, FDA: Food and Drug Administration

García-Rojo M, De Mena D, Muriel-Cueto P, Atienza-Cuevas L, Domínguez-Gómez M, Bueno G. New European union regulations related to whole slide image scanners and image analysis software. J Pathol Inform 2019;10:2. DOI:10.4103/jpi.jpi_33_18

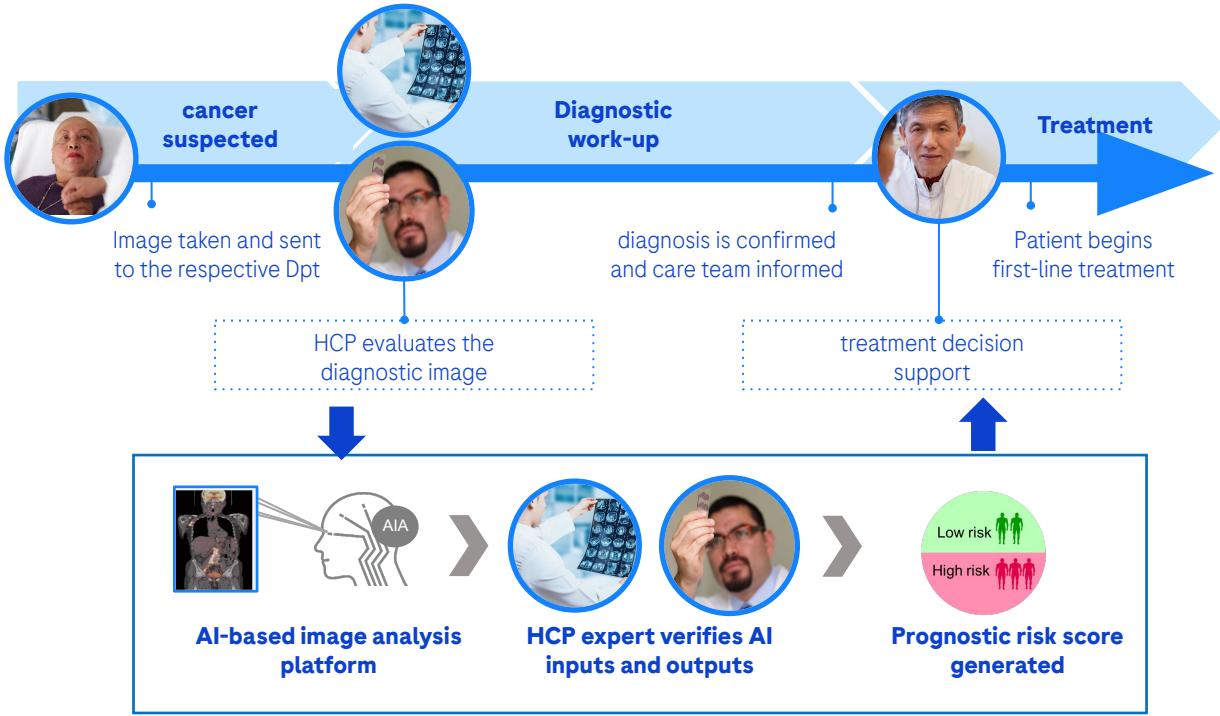
Clinical deployment

in search for “seamless disruption”



Clinical deployment

in search for “seamless disruption”



Infrastructure

digital solutions require interoperable digital ecosystem

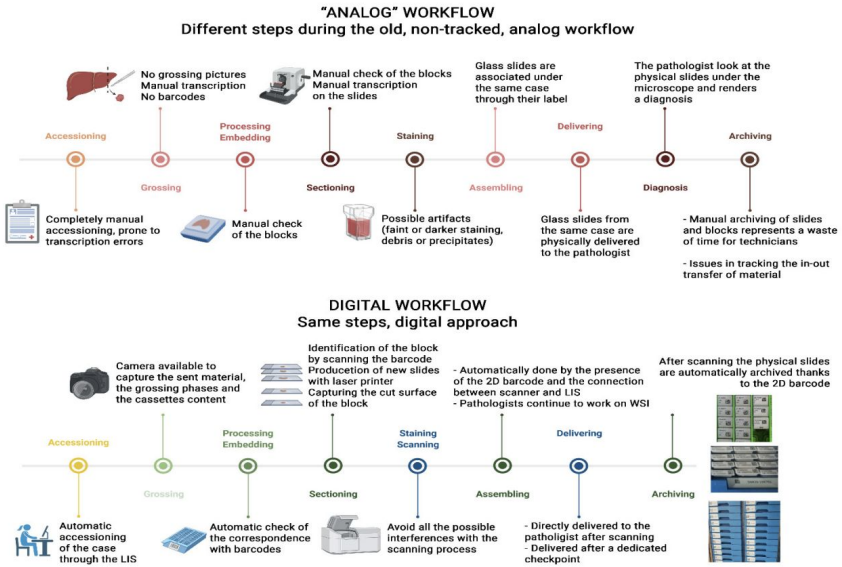


Figure 1. Differences among analog and the digital workflows. Credit: created with BioRender.

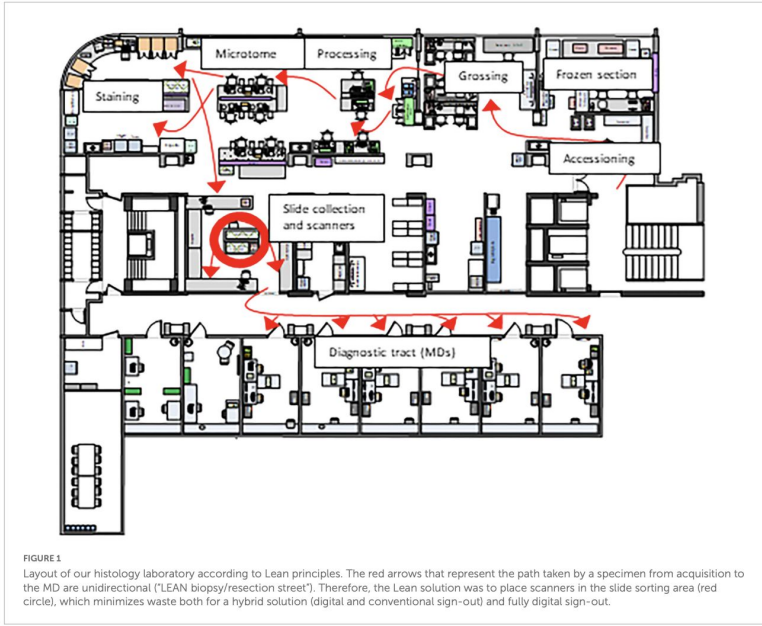


FIGURE 1

Layout of our histology laboratory according to Lean principles. The red arrows that represent the path taken by a specimen from acquisition to the MD are unidirectional ("LEAN biopsy/resection street"). Therefore, the Lean solution was to place scanners in the slide sorting area (red circle), which minimizes waste both for a hybrid solution (digital and conventional sign-out) and fully digital sign-out.

Fraggetta, F. et al. Best Practice Recommendations for the Implementation of a Digital Pathology Workflow in the Anatomic Pathology Laboratory by the European Society of Digital and Integrative Pathology (ESDIP). Diagnostics 2021, 11, 2167. https:// doi.org/10.3390/diagnostics11112167

Dawson H (2022) Digital pathology – Rising to the challenge. Front. Med. 9:888896. doi: 10.3389/fmed.2022.888896

the ultimate challenge - Human

algorithms are used by humans for humans

Sunday November 13 2022, 12.01am GMT, The Sunday Times

"I often tell my students not to be misled by the name 'artificial intelligence' - there is nothing artificial about it. AI is made by humans, intended to behave by humans, and, ultimately, to impact humans' lives and human society."

- Fei-Fei Li

Healthcare professionals need time to build trust in AI

transparency and reliability of the algorithms are the key to success

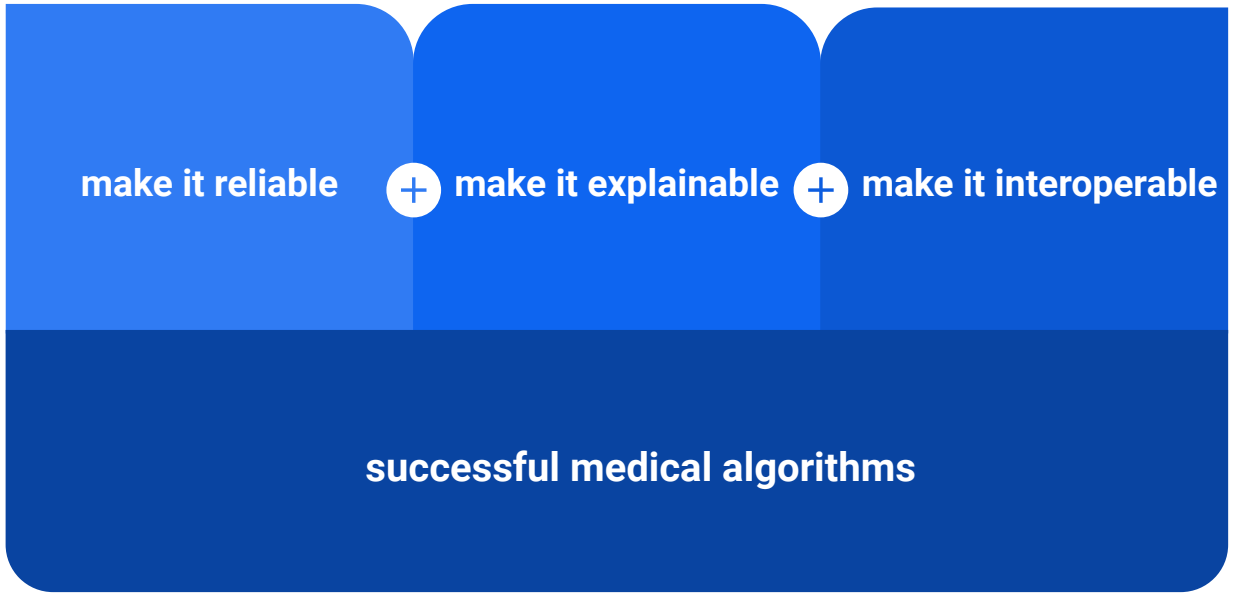
By 2030, regarding the integration of AI in pathology ...

Aspect	Item #	Mode (%)	Mean (SD)	Median (IQR)	Likelihood
A set of new guidelines will be developed, specifically addressing the integration of AI in pathology	150	7 (79.2)	6.63 (0.82)	7.0 (7.0–7.0)	Very strongly agree
Specific validation procedures for different types of AI tools will be defined by regulatory bodies	151	7 (58.3)	6.46 (0.72)	7.0 (6.0–7.0)	Very strongly agree
The introduction of AI-based diagnostic modalities will require regulatory supervision, both related to the quality of the rendered diagnosis and the ultimate destination of the diagnostic information	161	7 (87.5)	6.83 (0.48)	7.0 (7.0–7.0)	Very strongly agree
As long as AI is used as a supportive method, ethical issues will be minor. However, when AI takes over tasks from the pathologist, i.e., making a diagnosis without human oversight, it will face major ethical challenges.	166	7 (75.0)	6.58 (0.93)	7.0 (6.5–7.0)	Very strongly agree
Pathologists will still be legally responsible for diagnoses made with the help of AI	173	7 (62.5)	6.25 (1.39)	7.0 (6.0–7.0)	Very strongly agree

Berbís MA, McClintock DS, Bychkov A, Laak JV der, Pantanowitz L, Lennerz JK, et al. Computational pathology in 2030: a Delphi study forecasting the role of AI in pathology within the next decade. Ebiomedicine. 2023;88:104427.

Key take home message

What to think about while developing algorithms for medical field




AI will probably most likely lead to the end of the world, but in the meantime, there'll be great companies.
Sam Altman
BrainyQuote

Doing now what patients need next