دانشگاه علوم پزشکی و خدمات بهداشتی، درمانی ایران

Artificial Intelligence in Breast Health and Cancer

دکتر نسیبه رادی راز

Dr. Nasibeh Rady Raz

PhD in Artificial Intelligence and Robotics

Assistant Professor in Artificial Intelligence in Medicine, Faculty of Advanced Technologies in Medicine, Iran University of Medical Sciences, Tehran, Iran

radyraz.n@iums.ac.ir

دانشگاه علوم پزشکی و خدمات بهداشتی، درمانی ایران

بسم الله الرحمن الرحیم

دانشگاه علوم پزشکی و خدمات بهداشتی، درمانی ایران

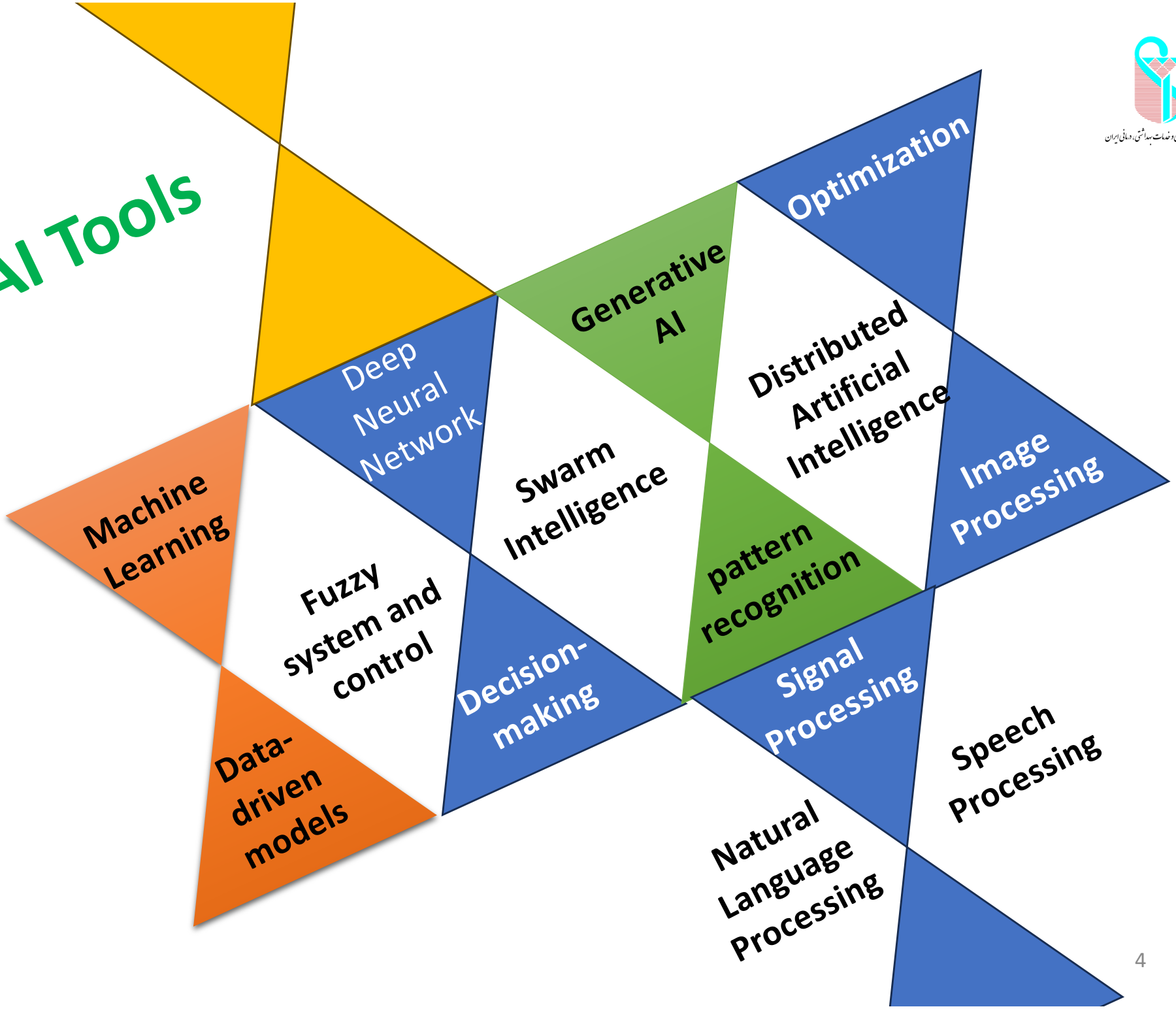
عنوان دوره آنلاین:

هوش مصنوعی در پزشکی با رویکرد بالینی

Online Course: Artificial Intelligence in Medicine with Clinical Approach

Course Topics	عناوین بیست و چهار جلسه	تاریخ جلسات
Artificial Intelligence (AI) in medicine	معرفی هوش مصنوعی در پزشکی	۲۸ بهمن ۱۴۰۲
AI and Fuzzy systems and its applications in medicine	هوش مصنوعی و سیستم های فازی در پزشکی	۵ اسفند ۱۴۰۲
Machine Learning and its applications in medicine	یادگیری ماشین و کاربردهای آن در پزشکی	۱۲اسفند۱۴۰۲
Evolutionary systems and its applications in medicine	الگوریتم های بهینه سازی تکاملی و کاربردهای آن در پزشکی	۱۹اسفند ۱۴۰۲
Neural networks and deep neural networks in medicine	شبکه های عصبی و شبکه های عصبی عمیق در پزشکی	۲۵فروردین ۱۴۰۳
Application of AI in Early Detection of Disease	کاربرد هوش مصنوعی در تشخیص زودهنگام بیماری ها	۱ اردیبهشت ۱۴۰۳
Swarm Intelligence and multi-agent/swarm in medicine	هوش ازدحامی، سیستم های چند عامله/ازدحامی در پزشکی	۸اردیبهشت ۱۴۰۳
Application of AI in Cancer	کاربردهای هوش مصنوعی در سرطان	۲۲اردیبهشت ۱۴۰۳
Application of AI in surgery	کاربردهای هوش مصنوعی در جراحی	۲۹ اردیبهشت ۱۴۰۳
Applications of AI in Neurology	کاربردهای هوش مصنوعی در مغز و اعصاب	۵ خرداد ۱۴۰۳
Application of AI in Internal Medicine	کاربردهای هوش مصنوعی در پزشکی داخلی	۱۲ خرداد ۱۴۰۳
Applications of AI in cardiovascular	کاربردهای هوش مصنوعی در قلب و عروق	۱۹ خرداد ۱۴۰۳
Applications of AI in Breast Disease	کاربردهای هوش مصنوعی در بیماری های پستان	۲۶ خرداد ۱۴۰۳
Application of AI in Ophthalmology	کاربردهای هوش مصنوعی در چشم پزشکی	۲ تیر ۱۴۰۳
Application of AI in Nephrology	کاربردهای هوش مصنوعی در نفرولوژی	۹ تیر ۱۴۰۳
Application of AI in Otorhinolaryngology	کاربردهای هوش مصنوعی در گوش و حلق و بینی	۱۶ تیر ۱۴۰۳
Application of AI in Gynecology and obstetrics	کاربردهای هوش مصنوعی در زنان و مامایی	۲۳ تیر ۱۴۰۳
Application of AI in pediatric medicine	کاربردهای هوش مصنوعی در پزشکی اطفال	۳۰ تیر ۱۴۰۳
Application of AI in anesthesia	کاربردهای هوش مصنوعی در بیهوشی	۶ مرداد ۱۴۰۳
Application of AI in emergency medicine	کاربردهای هوش مصنوعی در پزشکی اورژانس	۱۳ مرداد ۱۴۰۳
Applications of artificial intelligence in orthopedics	کاربردهای هوش مصنوعی در ارتوپدی	۲۰ مرداد ۱۴۰۳
Application of AI in pain management	کاربردهای هوش مصنوعی در مدیریت درد	۲۷ مرداد ۱۴۰۳
Application of AI in pharmacology	کاربردهای هوش مصنوعی در داروسازی	۳ شهریور ۱۴۰۳
Application of AI in dentistry	کاربردهای هوش مصنوعی در دندان پزشکی	۱۰ شهریور ۱۴۰۳

AI Tools


Machine Learning
Deep Neural Network
Generative AI
Optimization
Fuzzy system and control
Swarm Intelligence
Distributed Artificial Intelligence
Image Processing
Data-driven models
Decision-making
pattern recognition
Signal Processing
Speech Processing
Natural Language Processing

Breast Cancer

Lobules
Ducts
Connective tissue

Multifactorial disease
strong interplay between genetic and environmental factors.

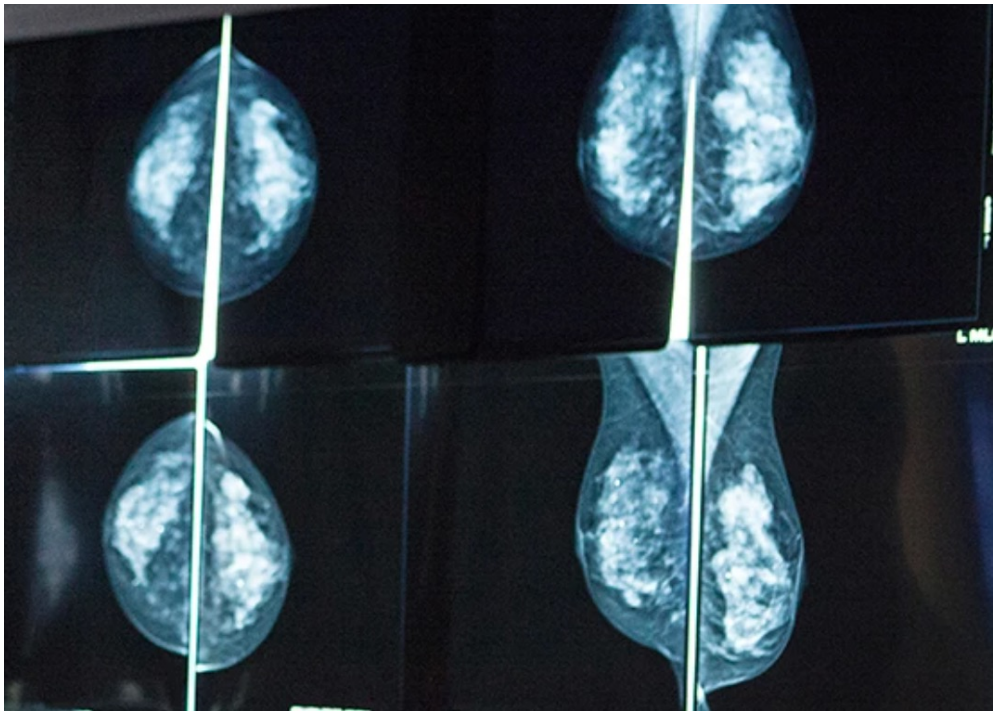
-Ductal carcinoma in situ,
-Invasive ductal carcinoma,
-Inflammatory breast cancer
-Metastatic breast cancer.

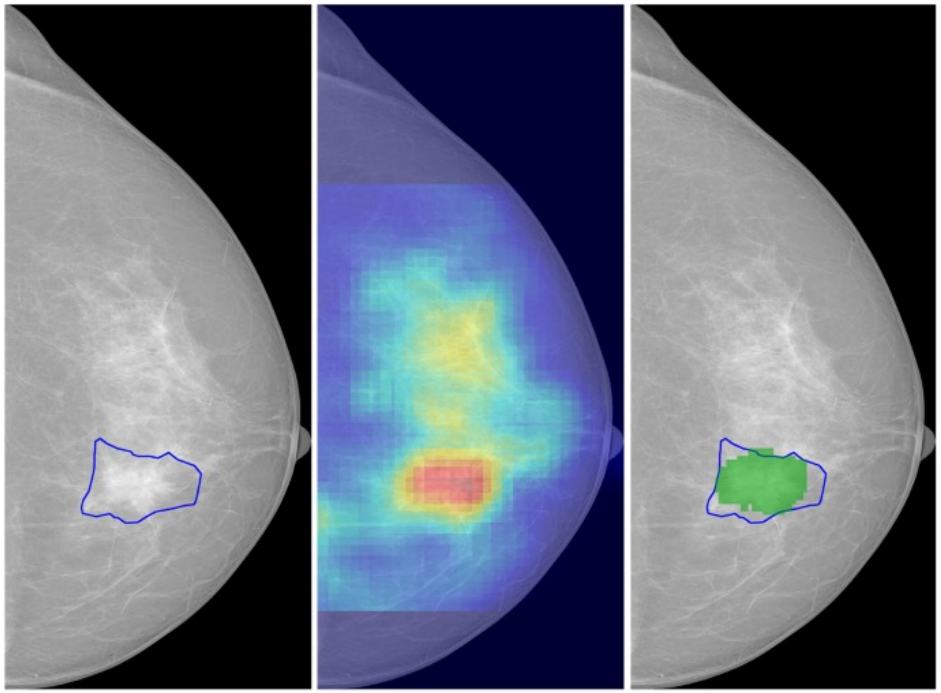
How Common?

QueensCare
HEALTH CENTERS
1 in 8
Women Will Be Diagnosed with Breast Cancer
Know the Warning Signs
New lumps in breast or armpit
Thickening or swelling of the breast
Irritation or dimpling of breast skin

Breast Health

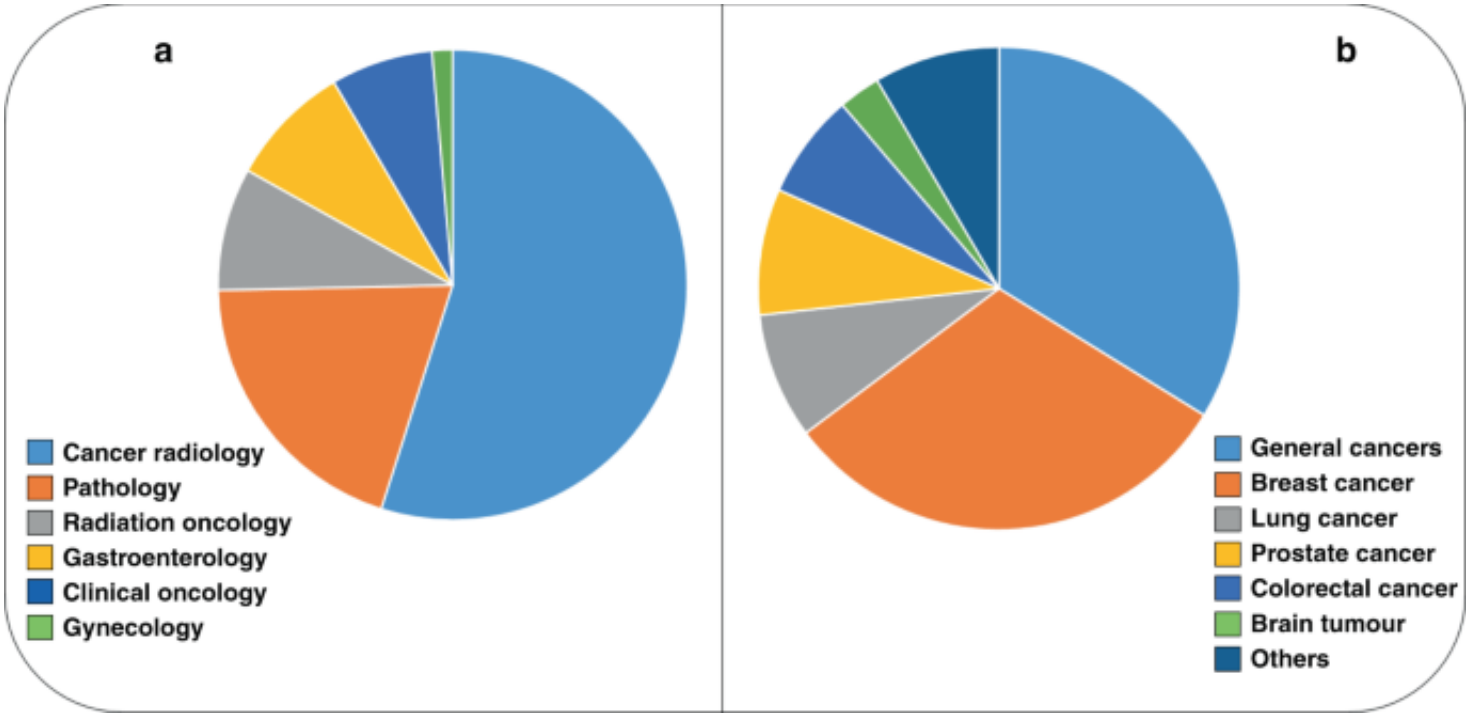
Supplementing human expertise with an automated program means catching more cancers





Nature **620**, 471 (2023)

Current status of Artificial intelligence in Breast Cancer



Claudio Luchini Et al, “Artificial intelligence in oncology: current applications and future perspectives” *British Journal of Cancer*, vol. 126, pages4–9, 2022.

Screening: breast cancer

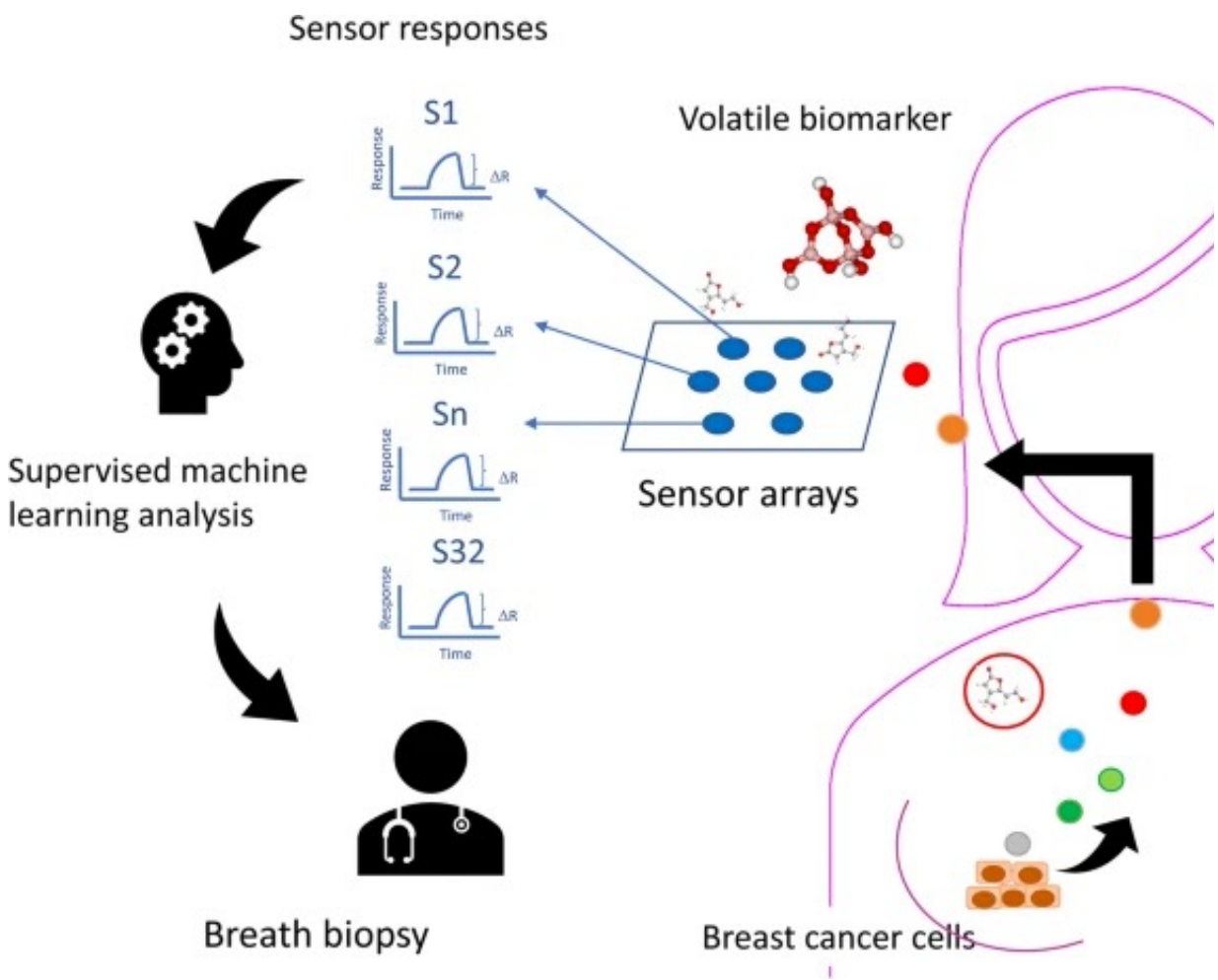
The promise of AI in personalized breast cancer screening

Nature Reviews Clinical Oncology **volume 21**, pages403–404 (2024)

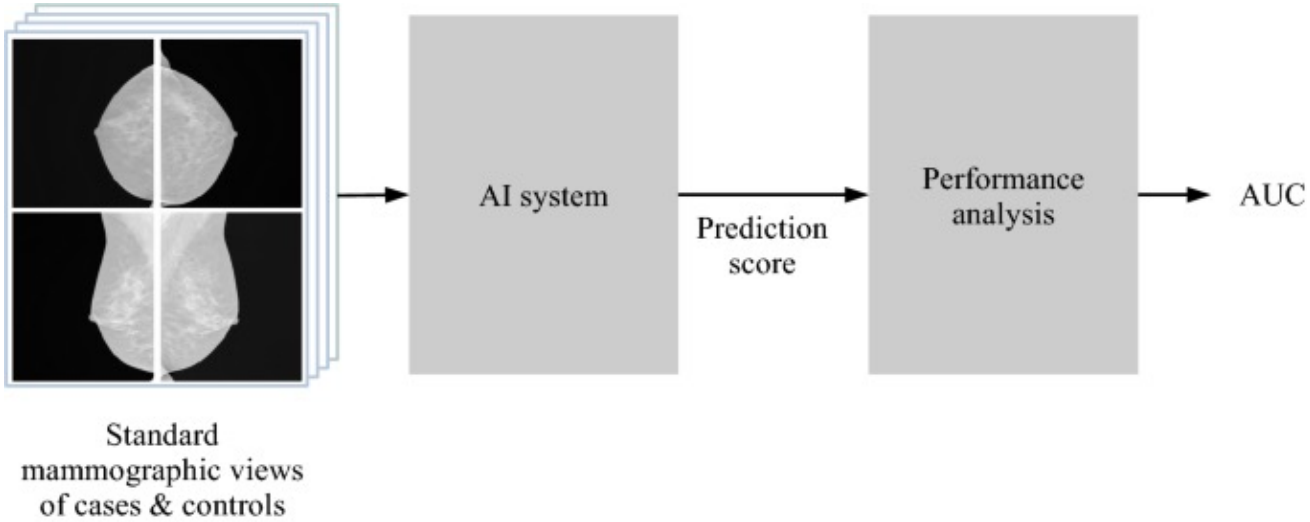
Scott Mayer McKinney et al, “International evaluation of an AI system for breast cancer screening,” Nature volume 577, pages89–94 (2020)

Early Detection of Breast Cance
Using Virtual biopsy

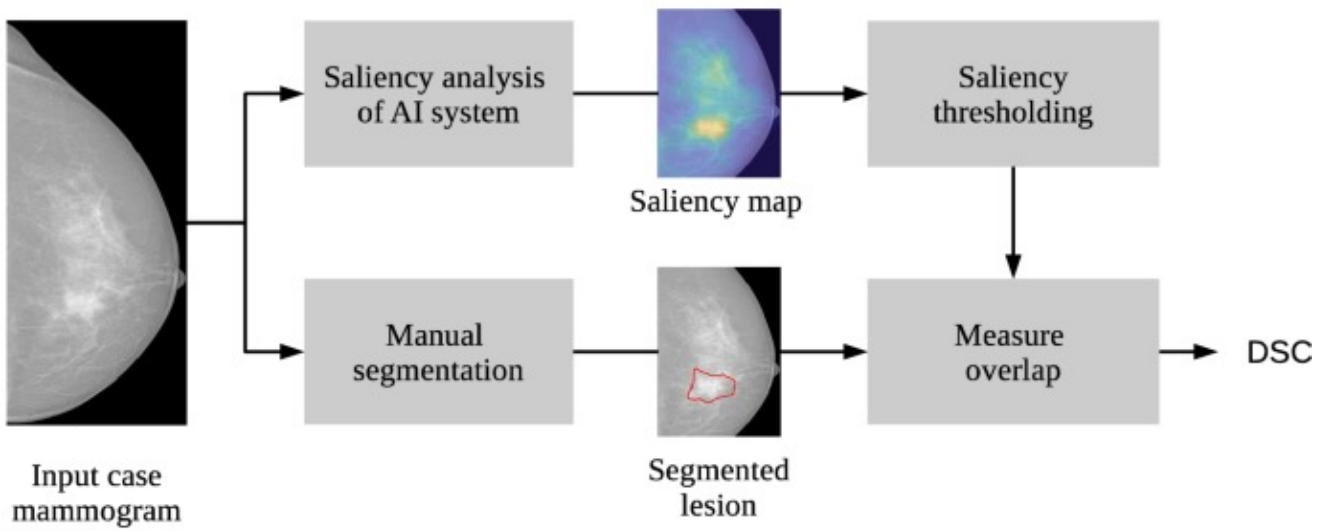
New types of Breast Cancer Biopsy:
Breath biopsy



Breath biopsy of breast cancer using sensor array signals and machine learning analysis, Scientific Reports volume 11, Article number: 103 (2021)



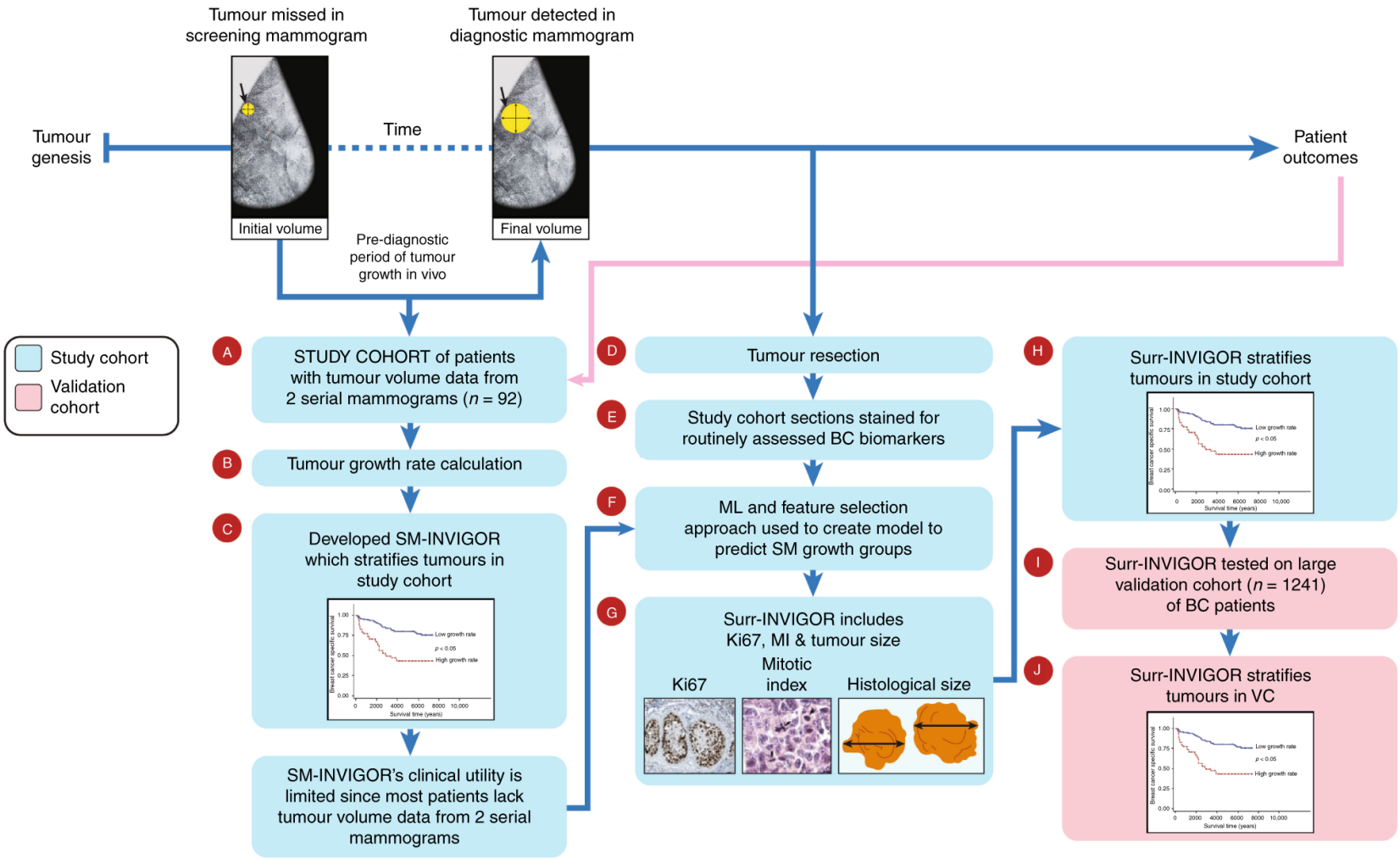
(a)



(b)

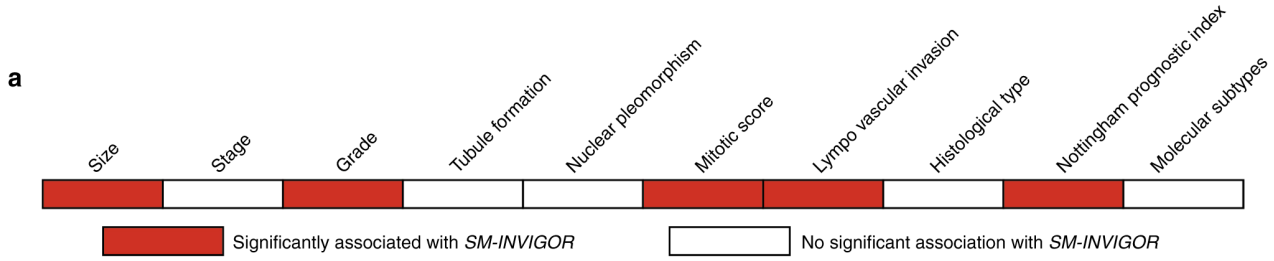
Scientific Reports **volume 13**, Article number: 20545 (2023)

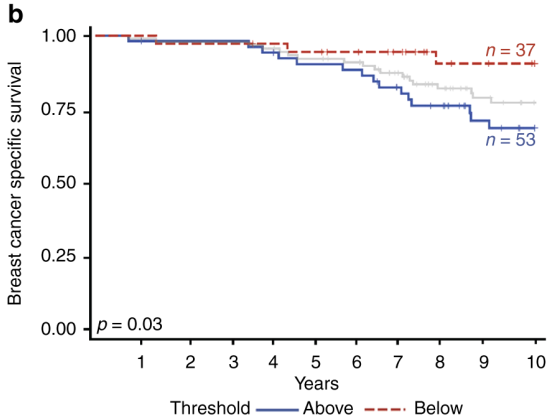
Machine learning-based prediction of breast cancer growth rate in vivo



British Journal of Cancer **volume 121**, pages497–504 (2019)

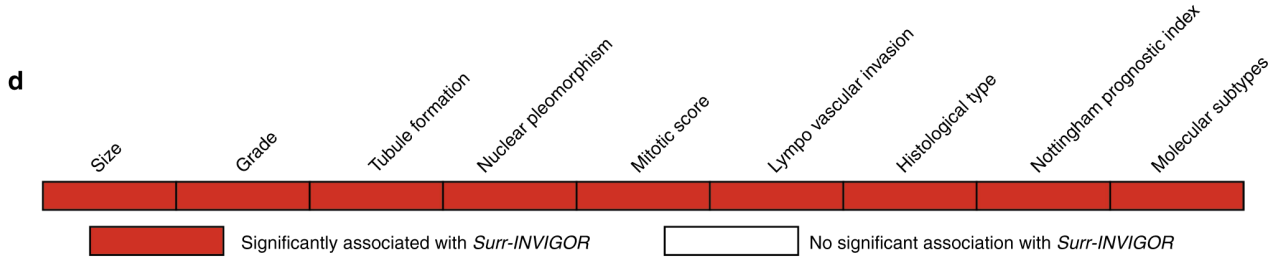
Factors

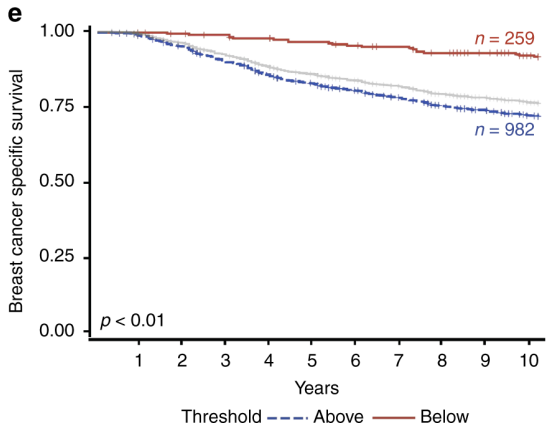




c

Multivariate analysis of the association between clinicopathological variables and patient's outcome in the study cohort			
		Hazard ratio (95% CI)	*p*-value
Overall survival			
Age	≤65 vs >65	0.989 (0.912–1.072)	0.78
ER	Neg	0.836 (0.229–2.98)	0.77
Grade	3	3.684 (0.043–30.623)	0.22
Grade	2	4.877 (0.615–38.702)	0.13
SM-INVIGOR	Above	3.623 (1.014–12.941)	0.04

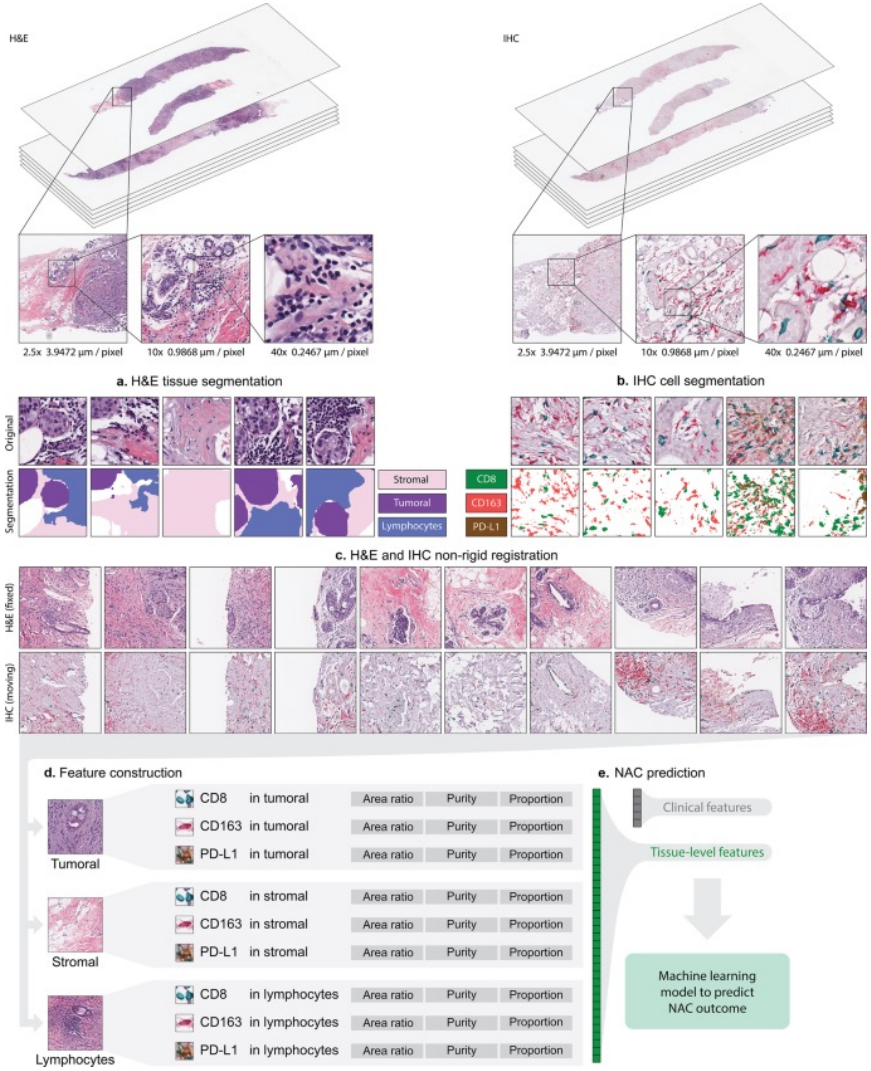




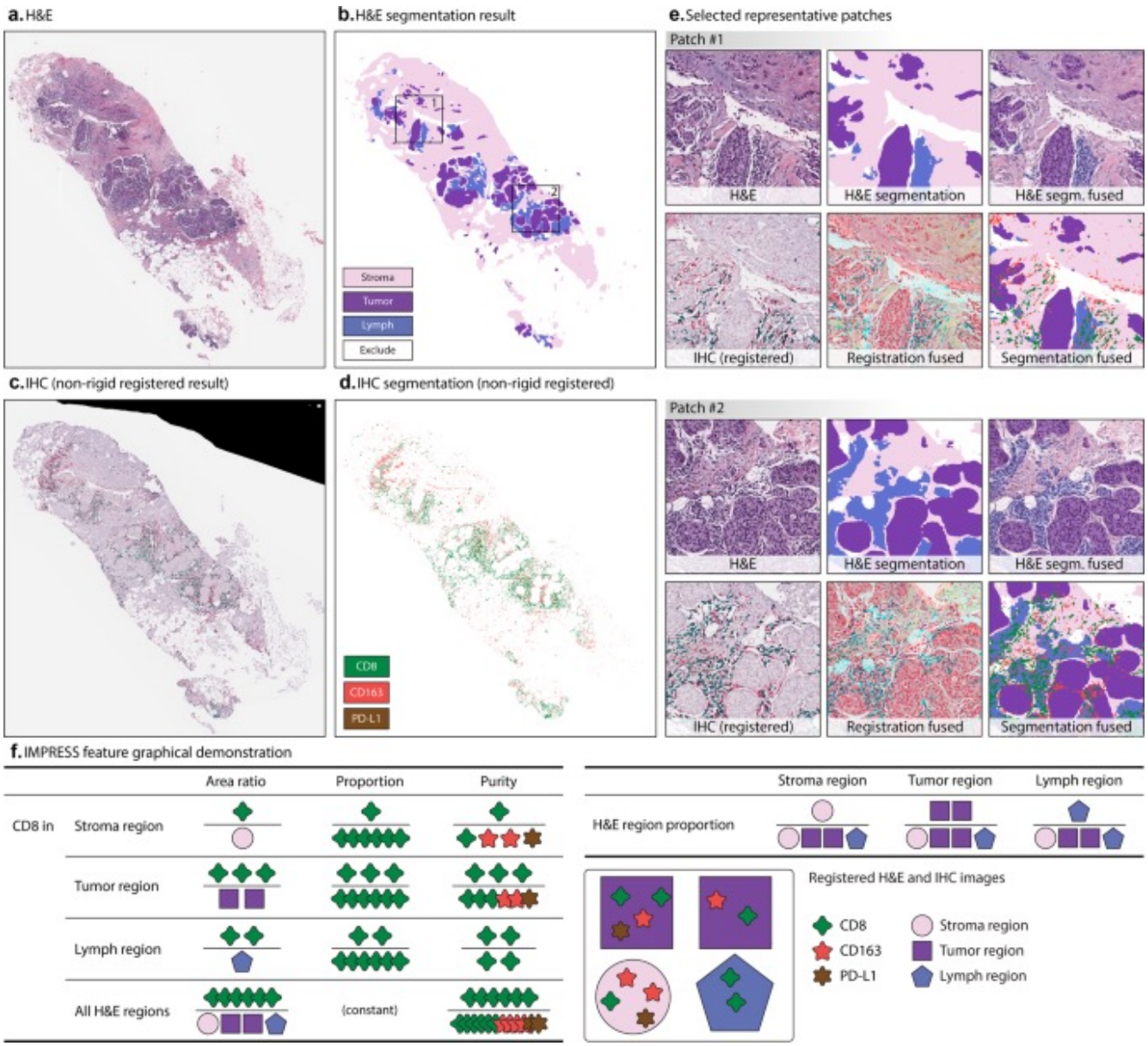
f

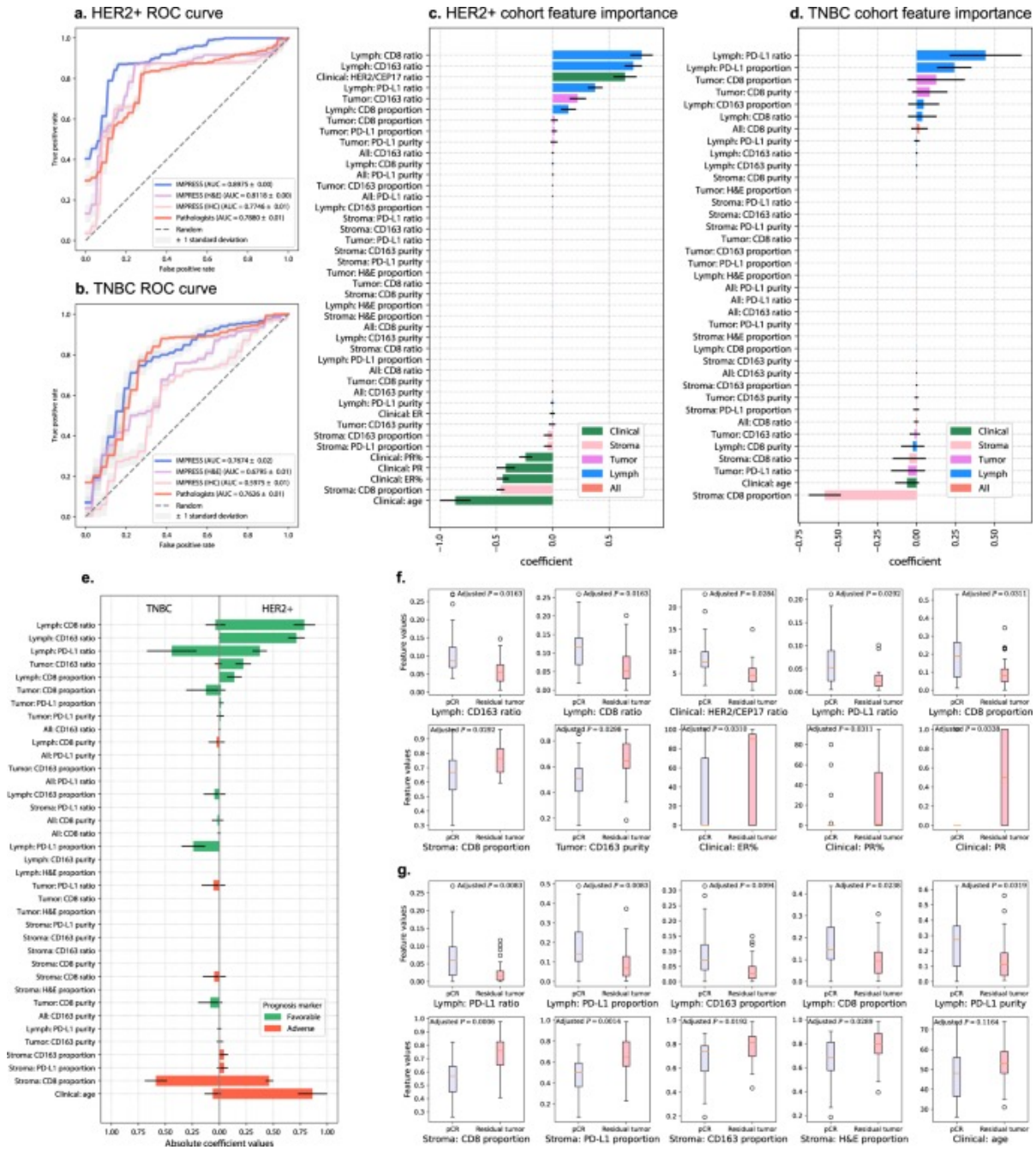
Multivariate analysis of the association between clinicopathological variables and patient's outcome in the validation cohort			
		Hazard ratio (95% CI)	*p*-value
Overall survival			
Age	≤65 vs >65	1.006 (0.994–1.018)	0.3242
ER	Neg	1.312 (1.008–1.707)	0.0435
Grade	3	7.204 (3.609–14.382)	<0.001
Grade	2	3.723 (1.853–7.481)	0.0002
Surr-INVIGOR	Above	2.059 (1.276–3.324)	0.0031

Artificial intelligence reveals features associated with breast cancer neoadjuvant chemotherapy responses from multi-stain histopathologic images

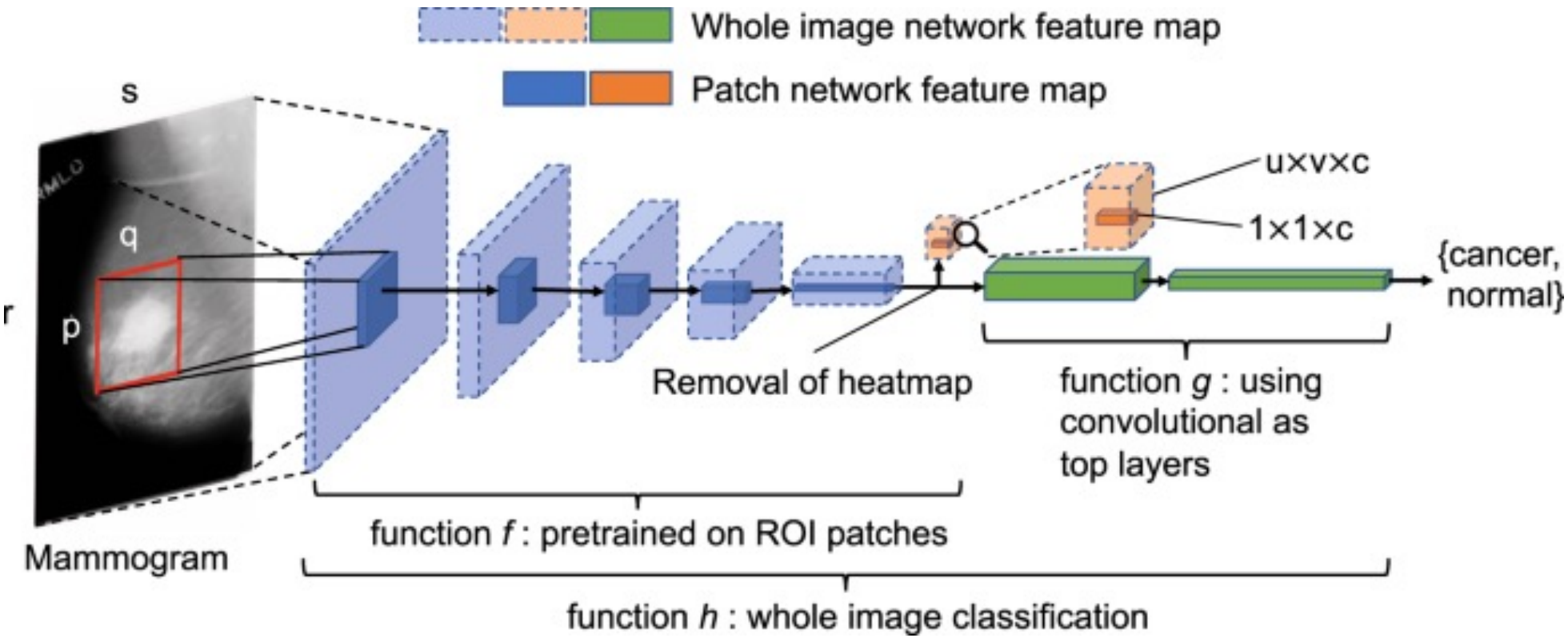


npj Precision Oncology **volume 7**, Article number: 14 (2023)


a. H&E
b. H&E segmentation result
Stroma
Tumor
Lymph
Exclude
e. Selected representative patches
Patch #1
H&E
H&E segmentation
H&E segm. fused
IHC (registered)
Registration fused
Segmentation fused
c. IHC (non-rigid registered result)
d. IHC segmentation (non-rigid registered)
CD8
CD163
PD-L1
Patch #2
H&E
H&E segmentation
H&E segm. fused
IHC (registered)
Registration fused
Segmentation fused
f. IMPRESS feature graphical demonstration
Area ratio
Proportion
Purity
CD8 in
Stroma region
Tumor region
Lymph region
All H&E regions
(constant)
Stroma region
Tumor region
Lymph region
H&E region proportion
Registered H&E and IHC images
CD8
CD163
PD-L1
Stroma region
Tumor region
Lymph region


a. HER2+ ROC curve
b. TNBC ROC curve
c. HER2+ cohort feature importance
d. TNBC cohort feature importance
coefficient
Clinical
Stroma
Tumor
Lymph
All
e.
TNBC
HER2+
Prognosis marker
Favorable
Adverse
Absolute coefficient values
f.
g.
Feature values
pCR
Residual tumor

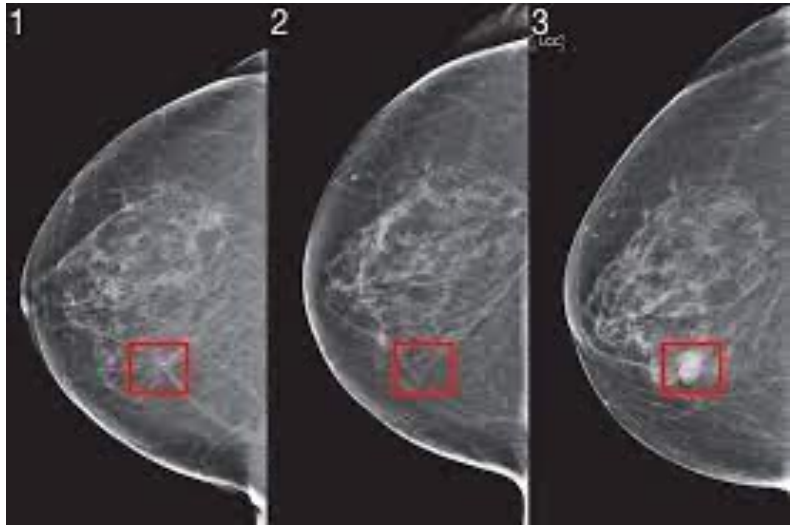
Deep Learning to Improve Breast Cancer Detection on Screening Mammograph



Scientific Reports **volume 9**, Article number: 12495 (2019)

Robust artificial intelligence tools to predict future cancer

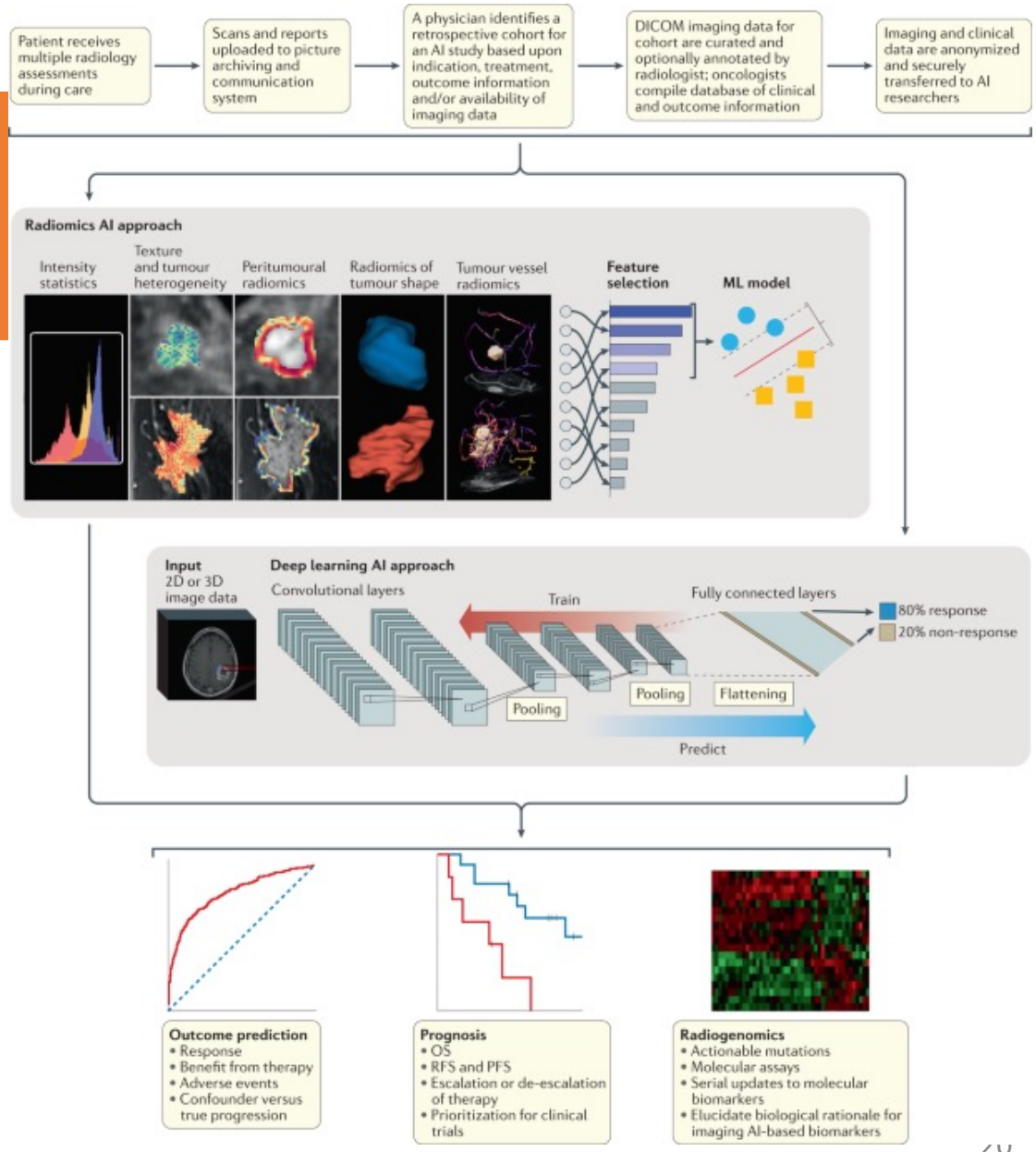
- **created a risk-assessment algorithm**



https://news.mit.edu/2021/robust-artificial-intelligence-tools-predict-future-cancer-0128

Predicting cancer outcomes with radiomics and artificial intelligence in radiology

focusing on hand-crafted radiomic approaches and deep learning-derived representations,



Nature Reviews Clinical Oncology **volume 19**, pages132–146 (2022)

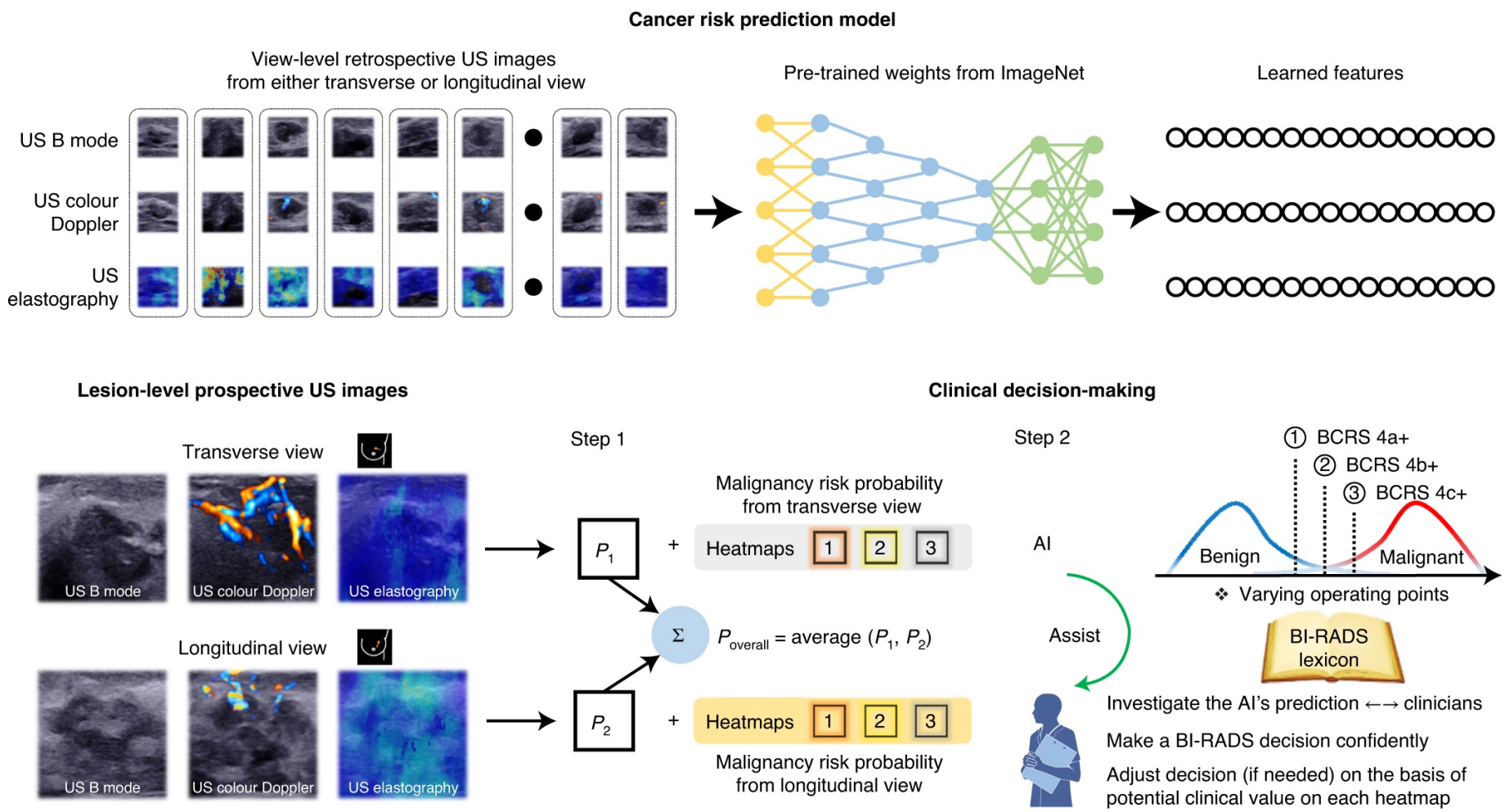
Classification and diagnostic prediction of breast cancer metastasis on clinical data using machine learning algorithms

develop a non-invasive breast cancer classification system for the diagnosis of cancer metastases.

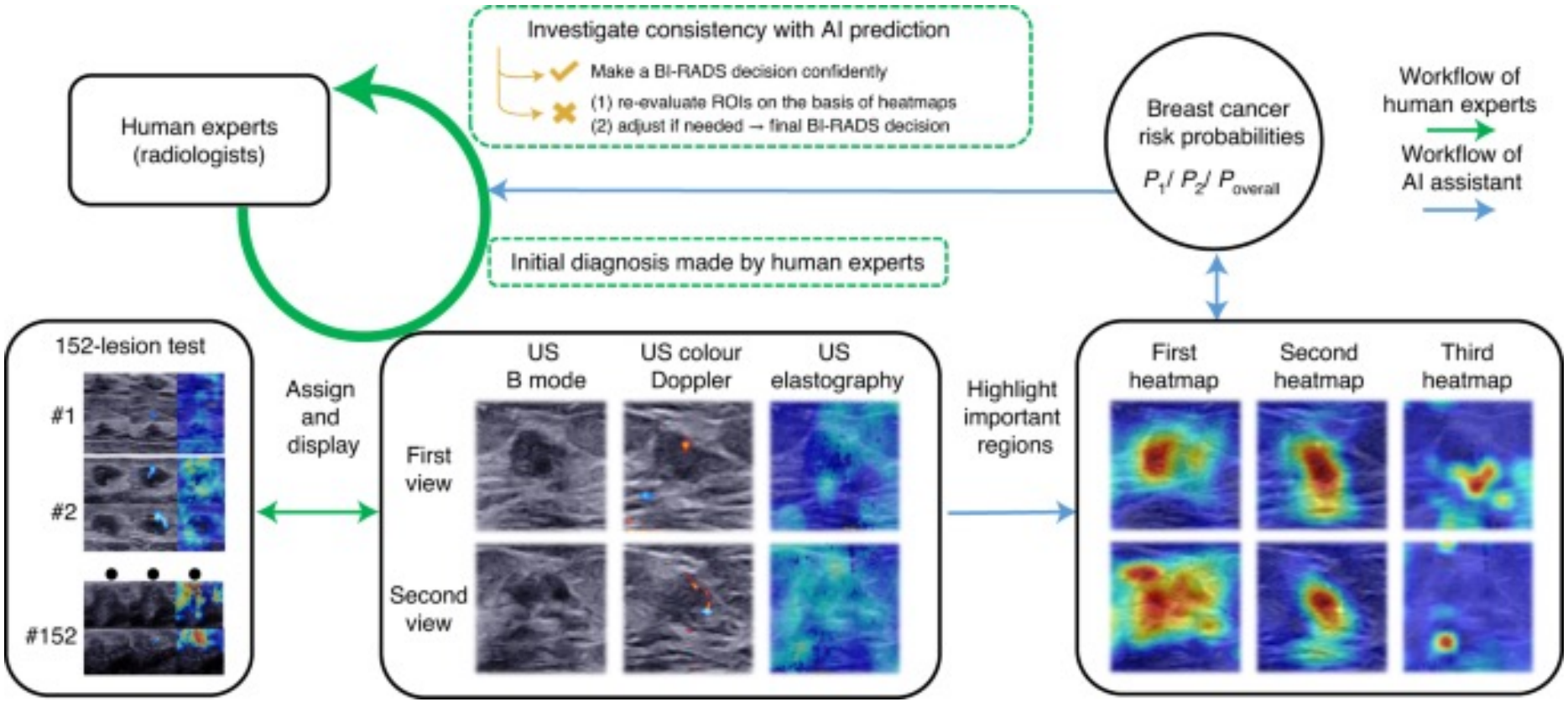
Hematological parameters such as ‘hemoglobin content’, ‘red cell’, ‘white blood cell’, ‘neutrophils’, ‘lymphocytes’, and ‘monocyte counts’ were extracted from the medical records for the selected cancer patients.

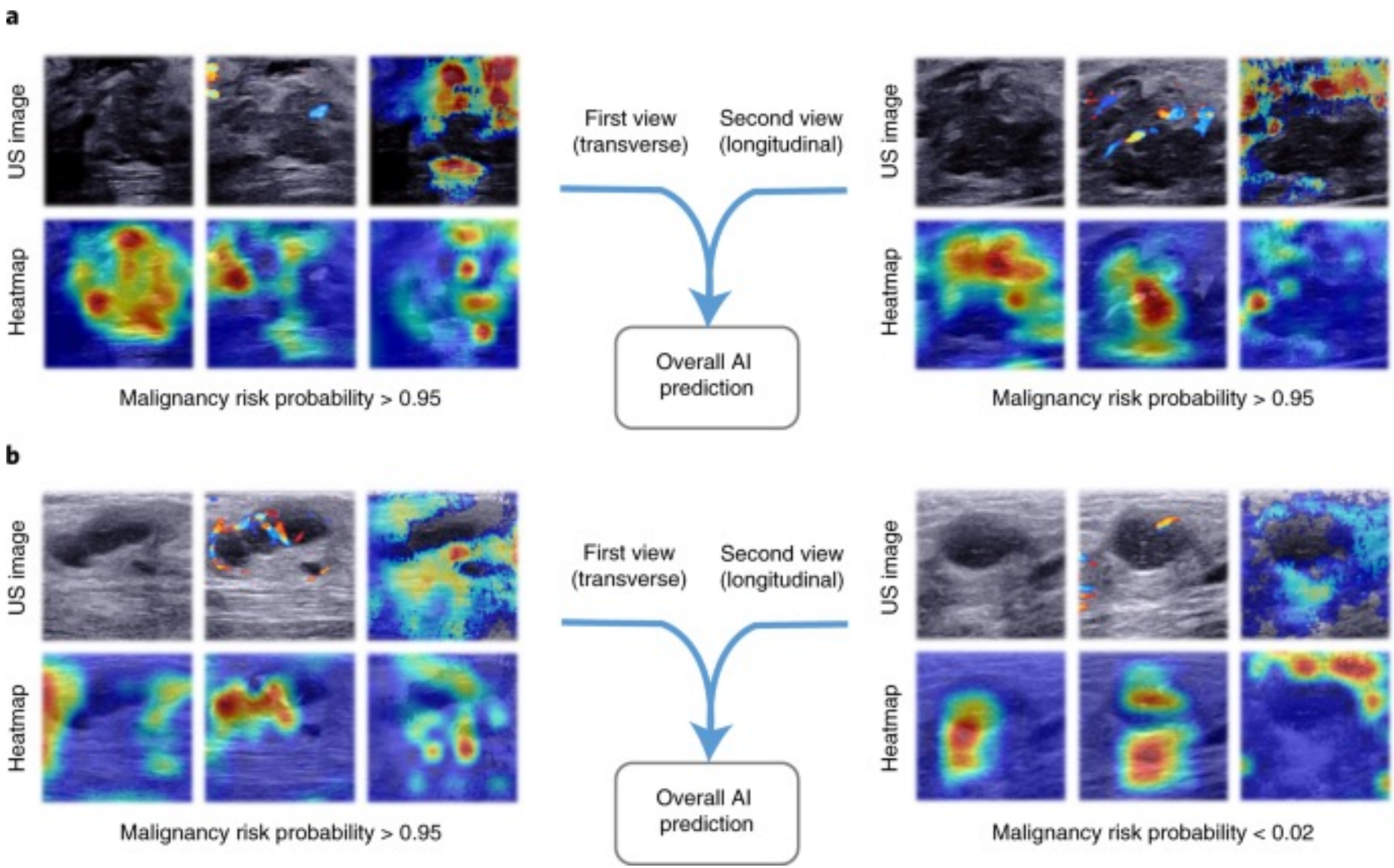
Scientific Reports **volume 13**, Article number: 485 (2023)

Prospective assessment of breast cancer risk from multimodal Multiview ultrasound images via clinically applicable deep learning

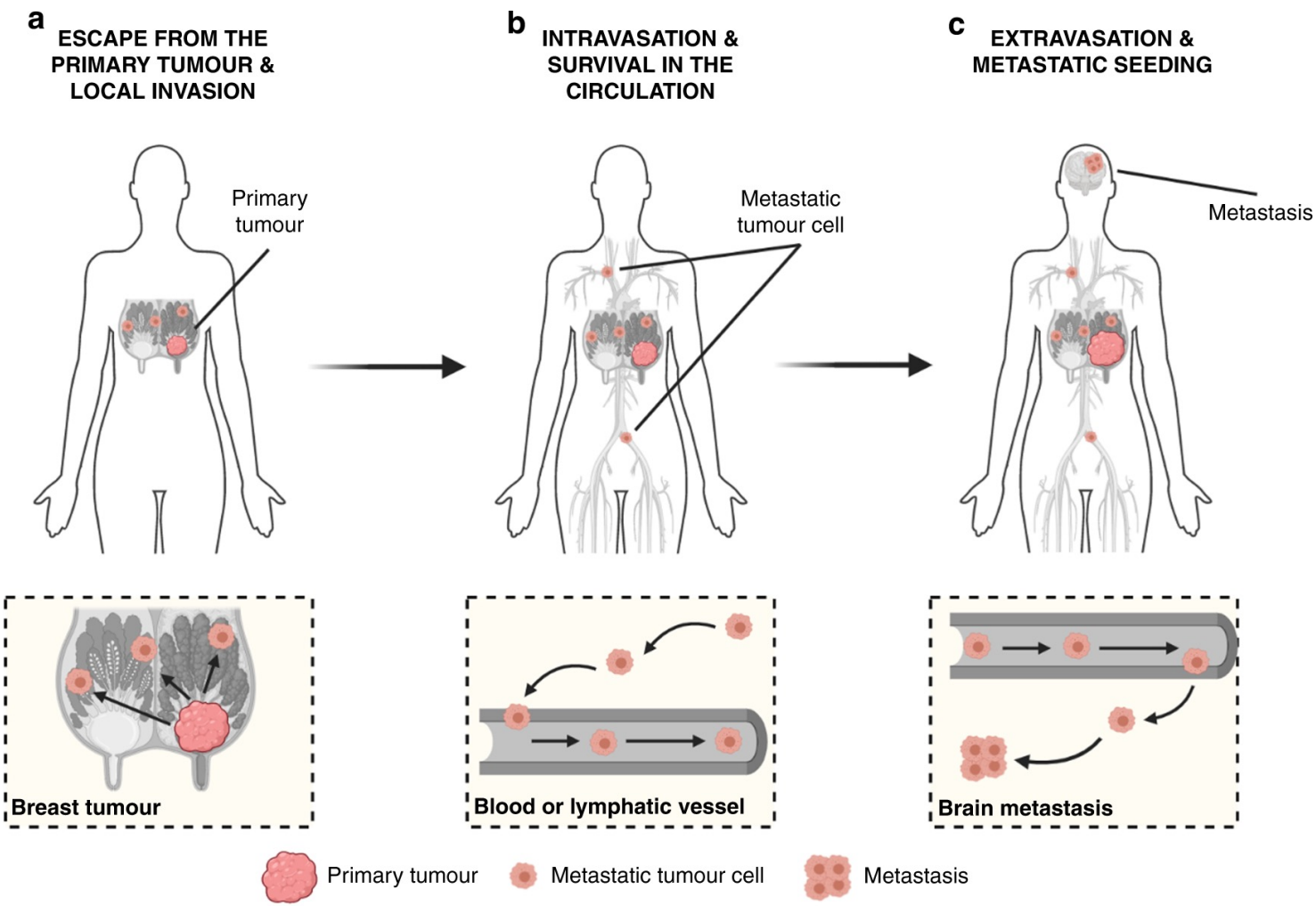


Nature Biomedical Engineering **volume 5**, pages522–532 (2021)


Investigate consistency with AI prediction
Make a BI-RADS decision confidently
(1) re-evaluate ROIs on the basis of heatmaps
(2) adjust if needed → final BI-RADS decision
Human experts (radiologists)
Breast cancer risk probabilities
P_1/ P_2/ $P_{overall}$
Workflow of human experts
Workflow of AI assistant
Initial diagnosis made by human experts
152-lesion test
#1
#2
#152
Assign and display
US B mode
US colour Doppler
US elastography
First view
Second view
Highlight important regions
First heatmap
Second heatmap
Third heatmap


a
US image
Heatmap
Malignancy risk probability > 0.95
First view
(transverse)
Second view
(longitudinal)
Overall AI
prediction
US image
Heatmap
Malignancy risk probability > 0.95
b
US image
Heatmap
Malignancy risk probability > 0.95
First view
(transverse)
Second view
(longitudinal)
Overall AI
prediction
US image
Heatmap
Malignancy risk probability < 0.02

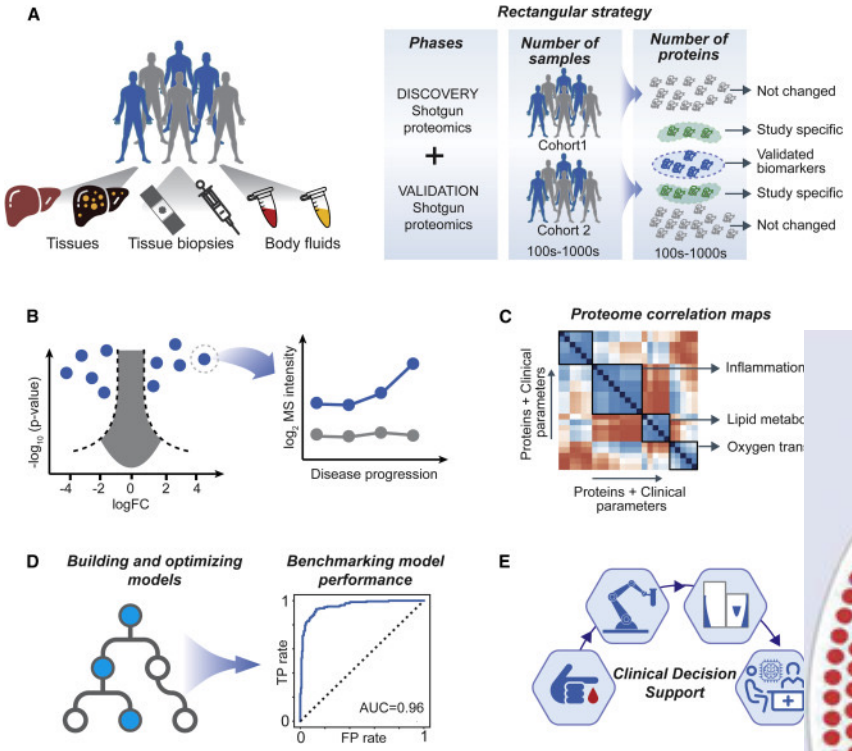
AI traces mysterious metastatic cancers to their source

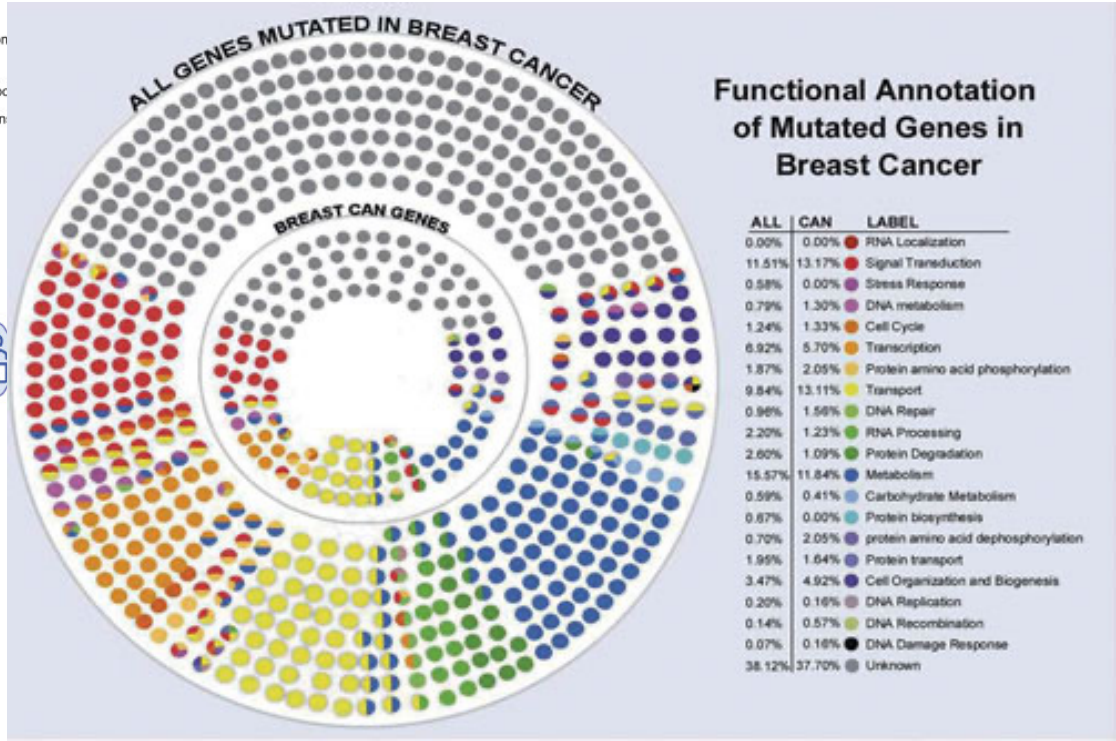


- **The algorithm examines images of metastatic cells to identify the location of the primary tumor.**

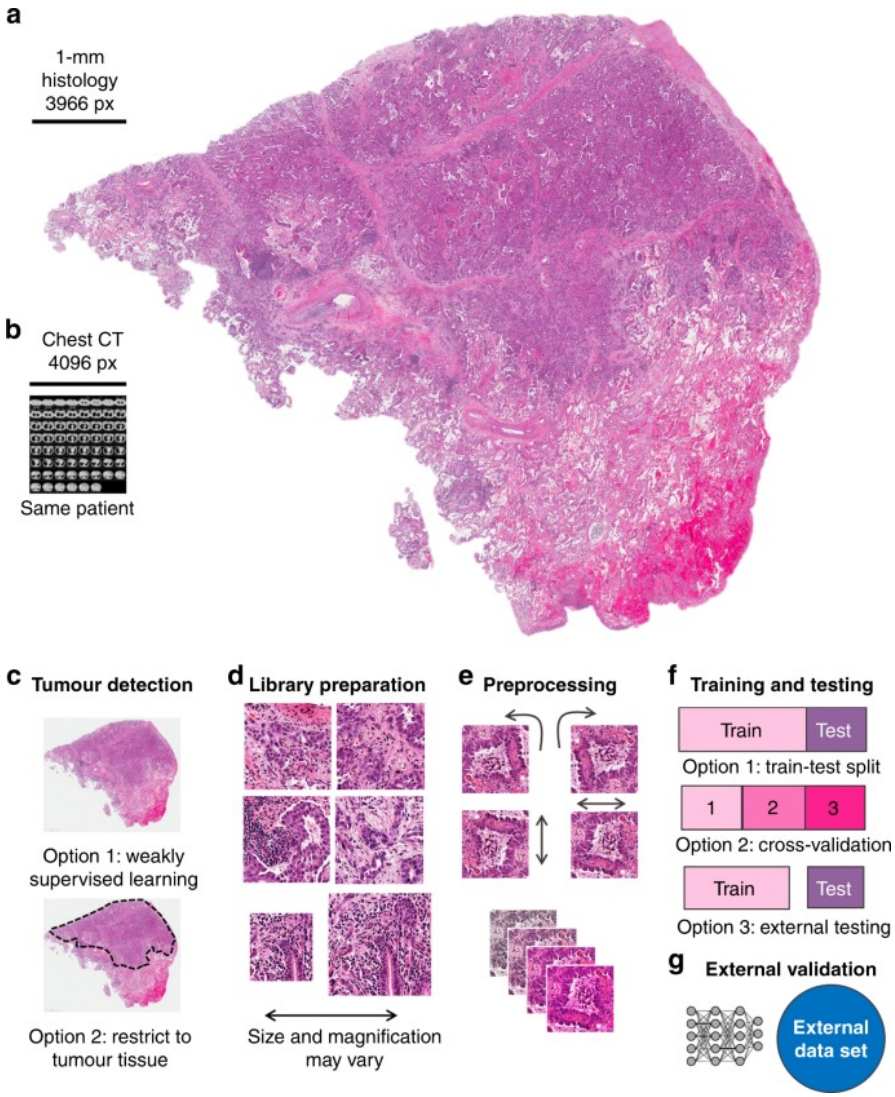
https://www.nature.com/articles/d41586-024-01110-8

Biomarker Discovery in Breast Cancer





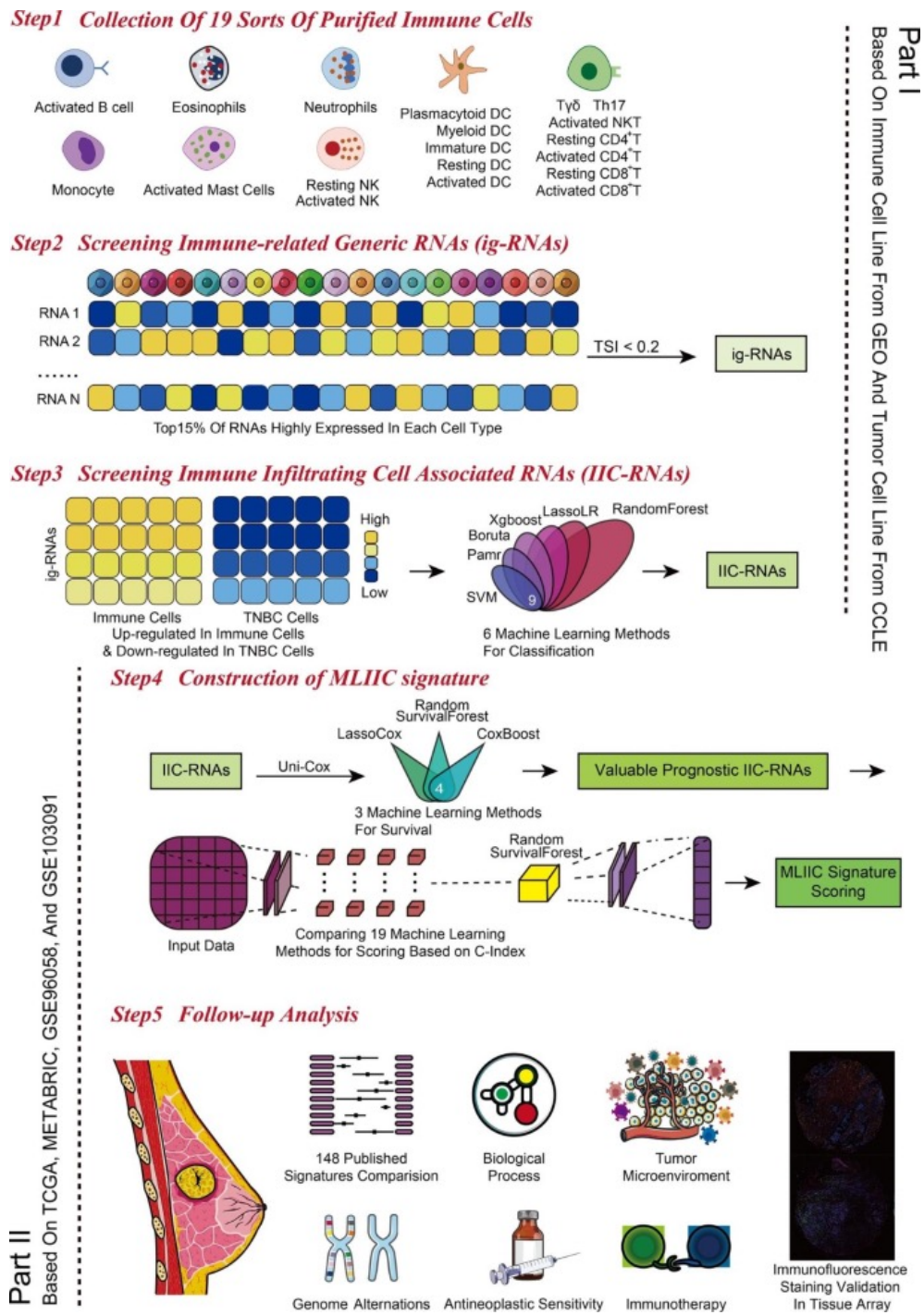
Deep learning in cancer pathology: a new generation of clinical biomarkers



Amelie Echle, “Deep learning in cancer pathology: a new generation of clinical biomarkers,” British Journal of Cancer volume 124, pages686–696 (2021)

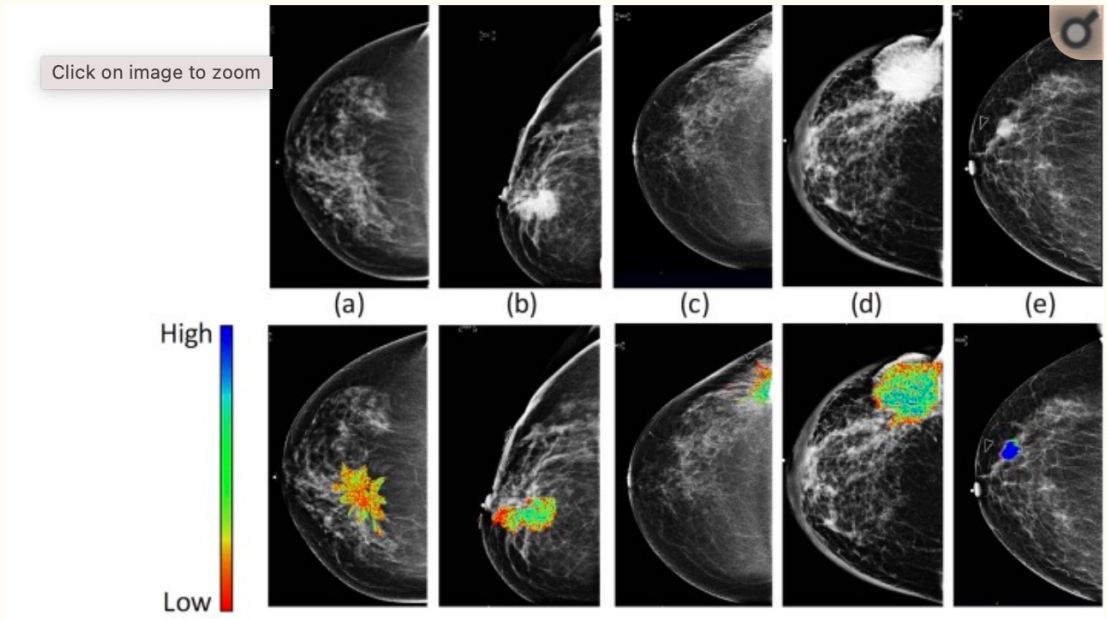
Breast cancer recurrence

There's a 25% chance of cancer recurrence.



Journal of Big Data **volume 10**, Article number: 132 (2023)

Breast Cancer Recurrence Prediction

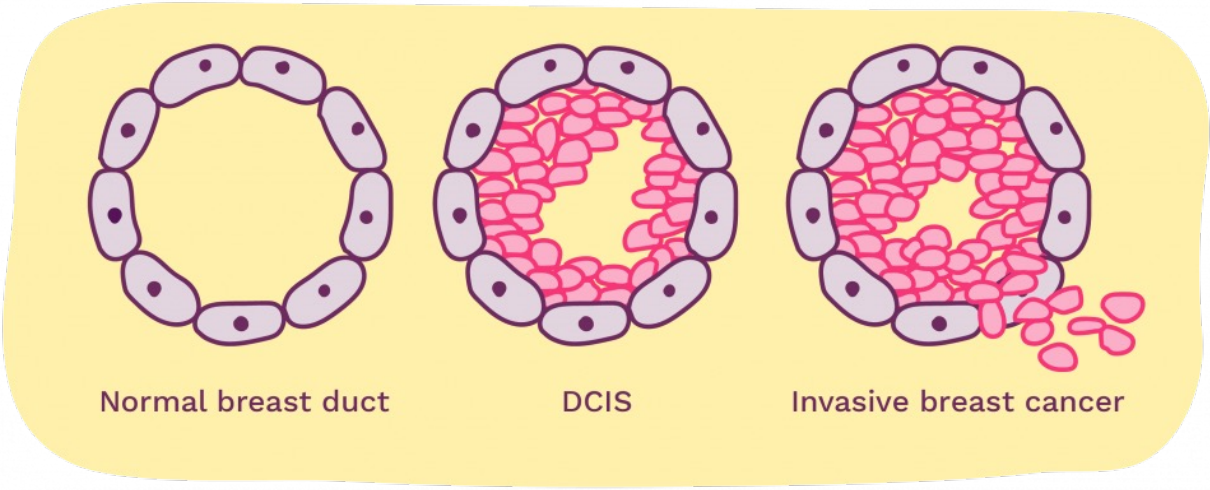


	(a)	(b)	(c)	(d)	(e)
ID Patient	12	156	5	142	2
Side, View	Right, CC	Left, CC	Right, CC	Left, CC	Right, CC
TNM	T1N0M0	T2N1M0	T2N1M0	T2N2M0	T3N1M0
OncotypeDX RS	6.6	-6.7	92.4	141.8	172.1
OncotypeDX Risk	Low	Low	High	High	High
PAM50	Normal-like	LumA	LumB	Basal-like	Her2
Relative Fractal Dim.	-1.53%	2.56%	5.57%	5.84%	5.00%

The lingering mysteries of metastatic recurrence in breast cancer, British Journal of Cancer volume 124, pages13–26 (2021)

دانشگاه علوم پزشکی و خدمات بهداشتی، درمانی ایران

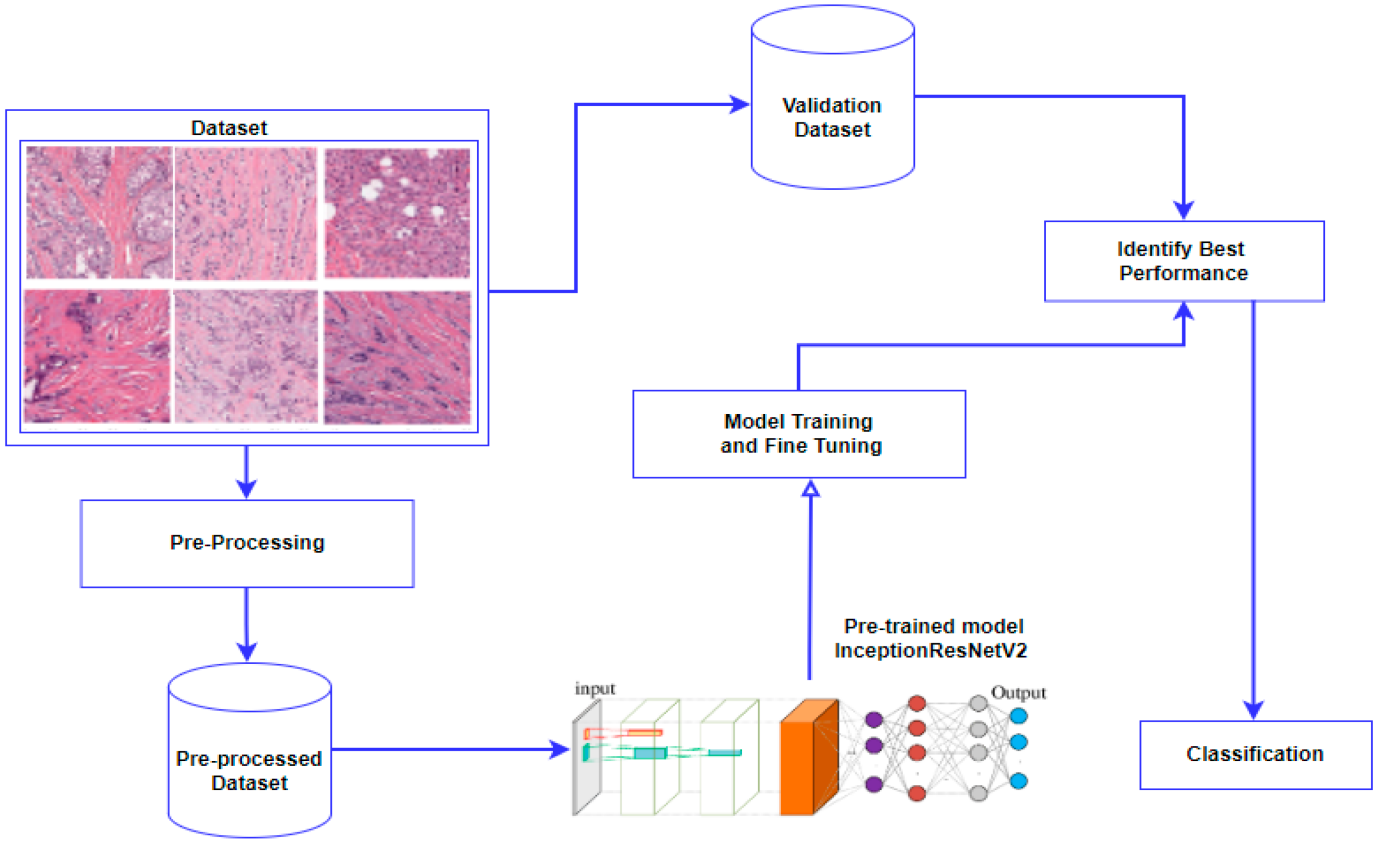
Invasive ductal carcinoma Detectio



- Early detection of breast cancer and its correct stage determination is important for prognosis and rendering appropriate personalized clinical treatment to breast cancer patients.
- To differentiate the early and late stages of IDC. The prediction models are trained with RNA-seq gene expression profiles.

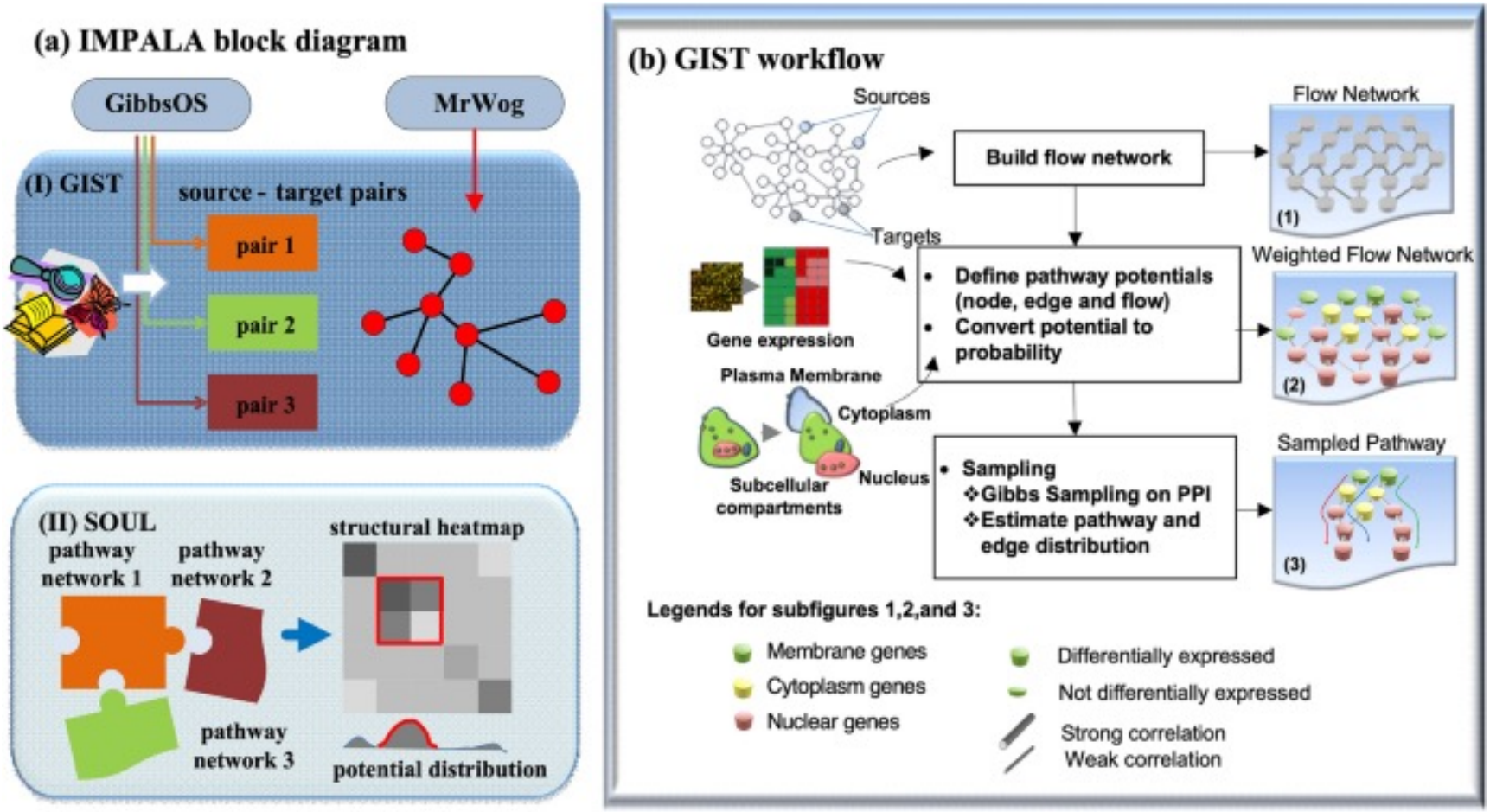
Shikha Roy Et al., Classification models for Invasive Ductal Carcinoma Progression, based on gene expression data-trained supervised machine learning, Scientific Reports volume 10, Article number: 4113 (2020)

Predicting the Risk of Breast Cancer



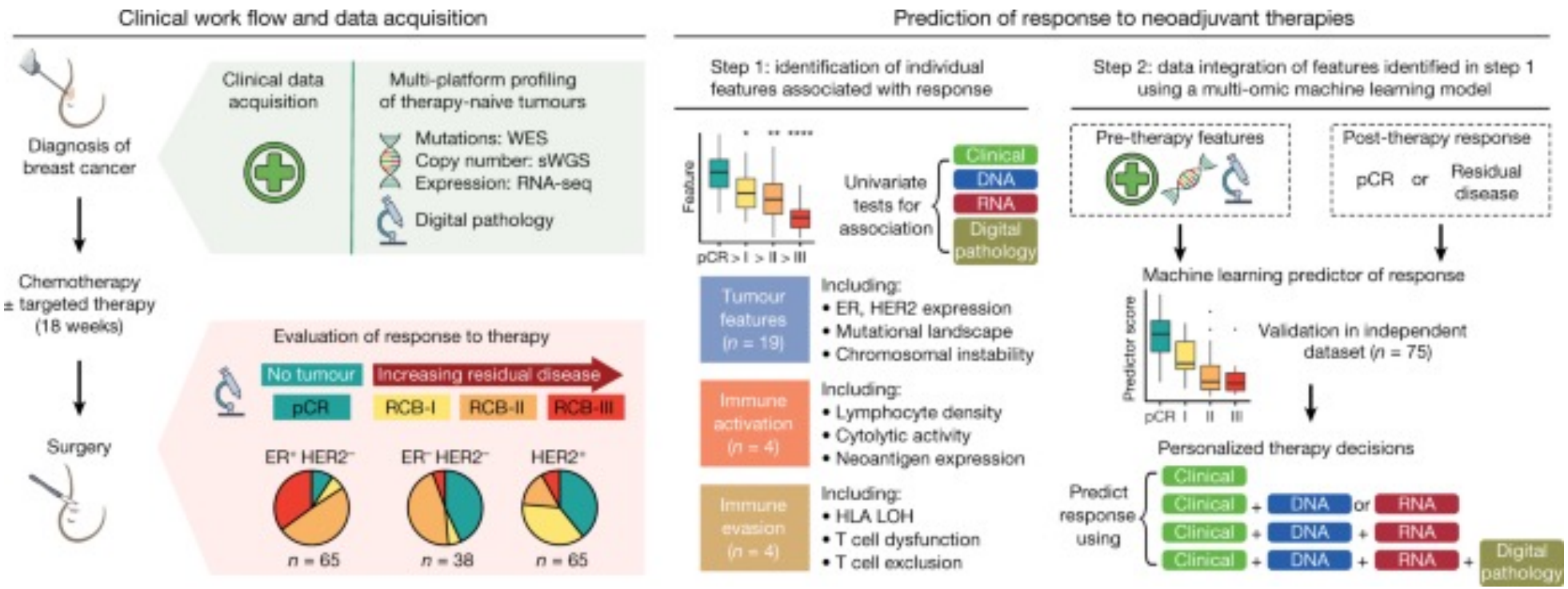
Electronics **2023**, *12*(2), 403;

Analyzing Signaling Pathway for therapeutic targets



Scientific Reports **volume 11**, Article number: 385 (2021)

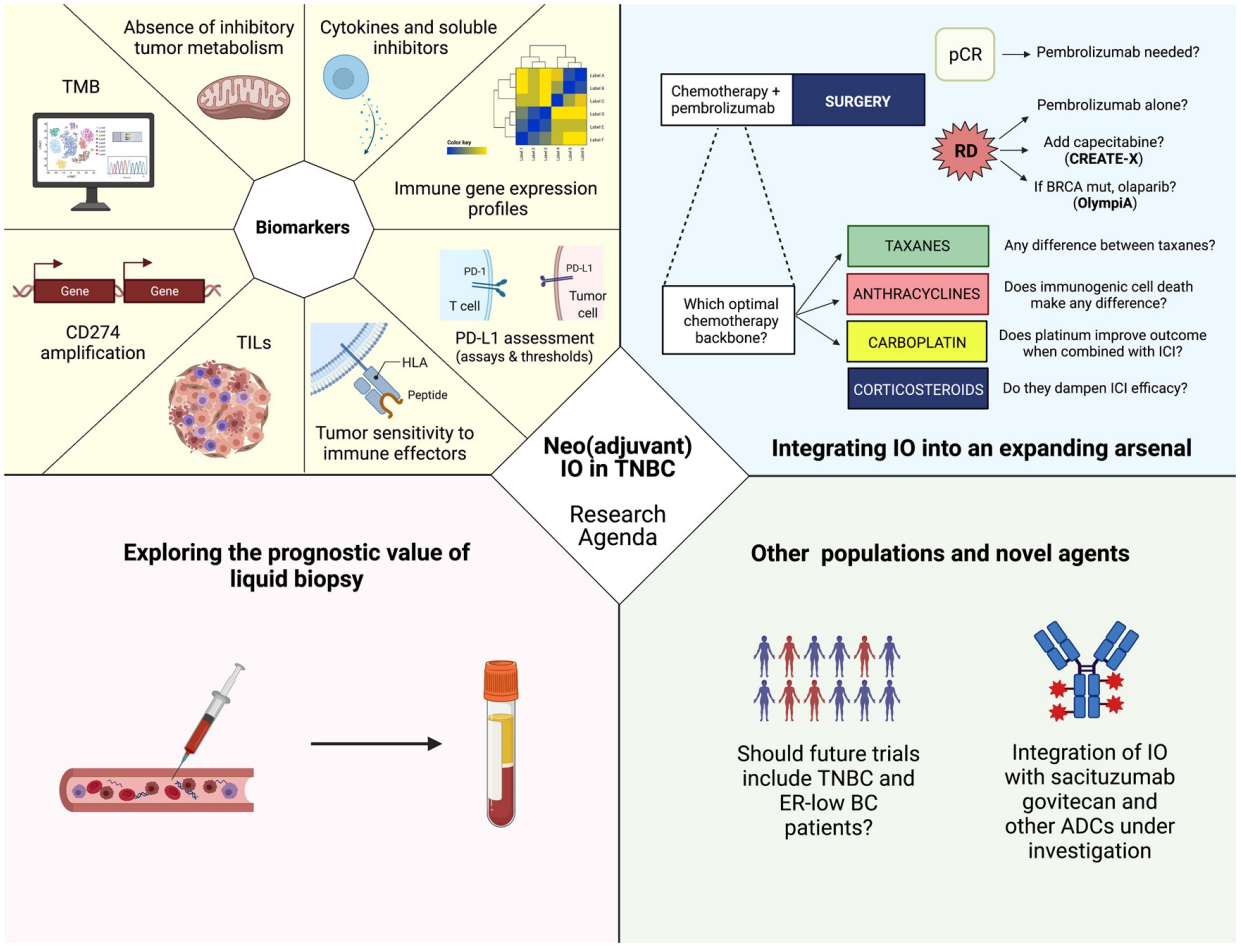
Predicting Mortality and Morbidity



Nature **volume 601**, pages623–629 (2022)

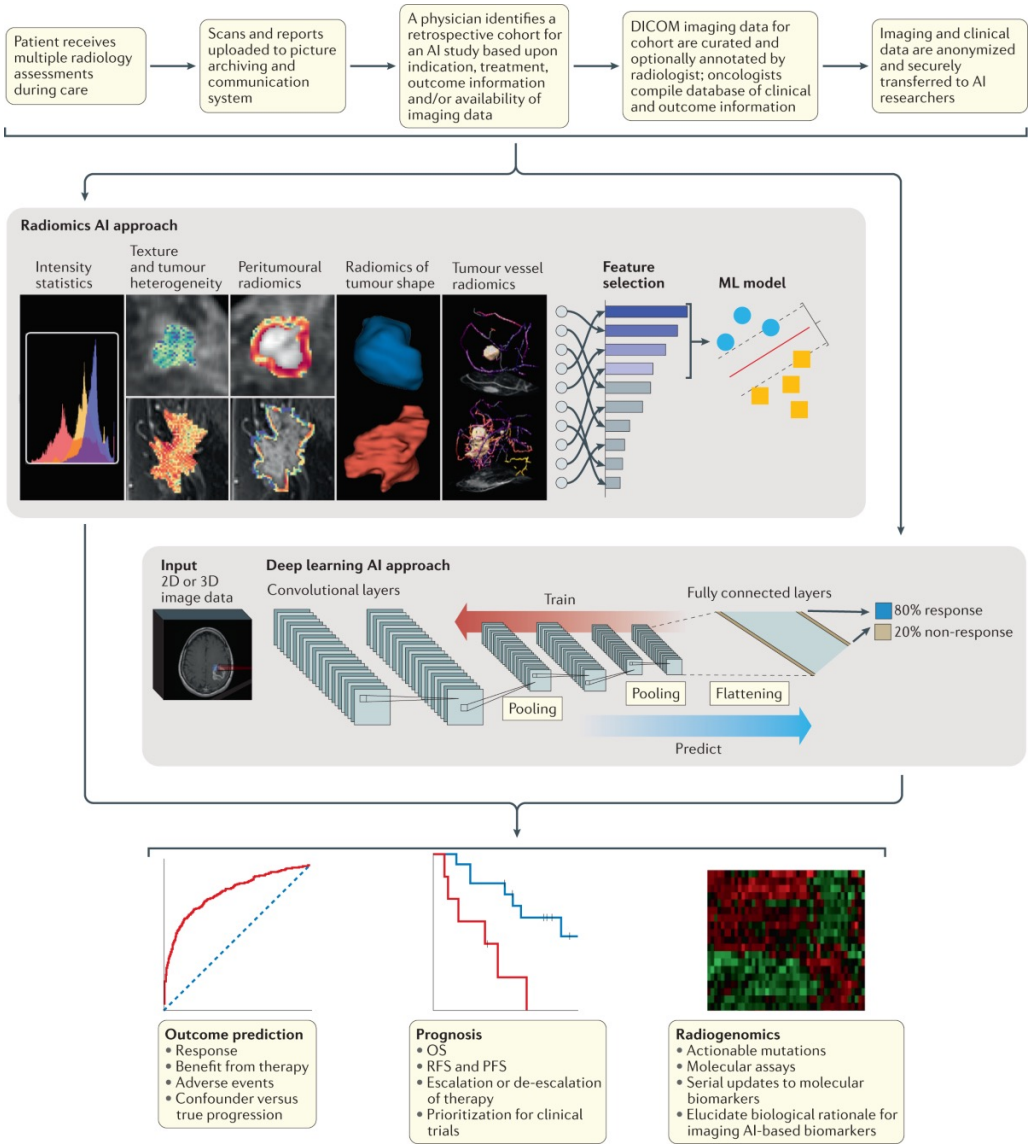
Prediction Breast Cancer Treatment complications

- predict treatment-related toxicity related to radiation and chemotherapy.
- Improvements have been made in the early diagnosis of risk groups in oncological diseases, in radiology, pathology, and imaging technologies, in cancer staging and management.
- Predict the outcome in chemotherapy treatment of oncological diseases.
- Decrees side effect of combinational therapy



Prediction of chemotherapy-related complications in pediatric oncology patients: artificial intelligence and machine learning implementations, Pediatric Research (2022)

predicting treatment response



Nature Reviews Clinical Oncology **volume 19**, pages132–146 (2022)

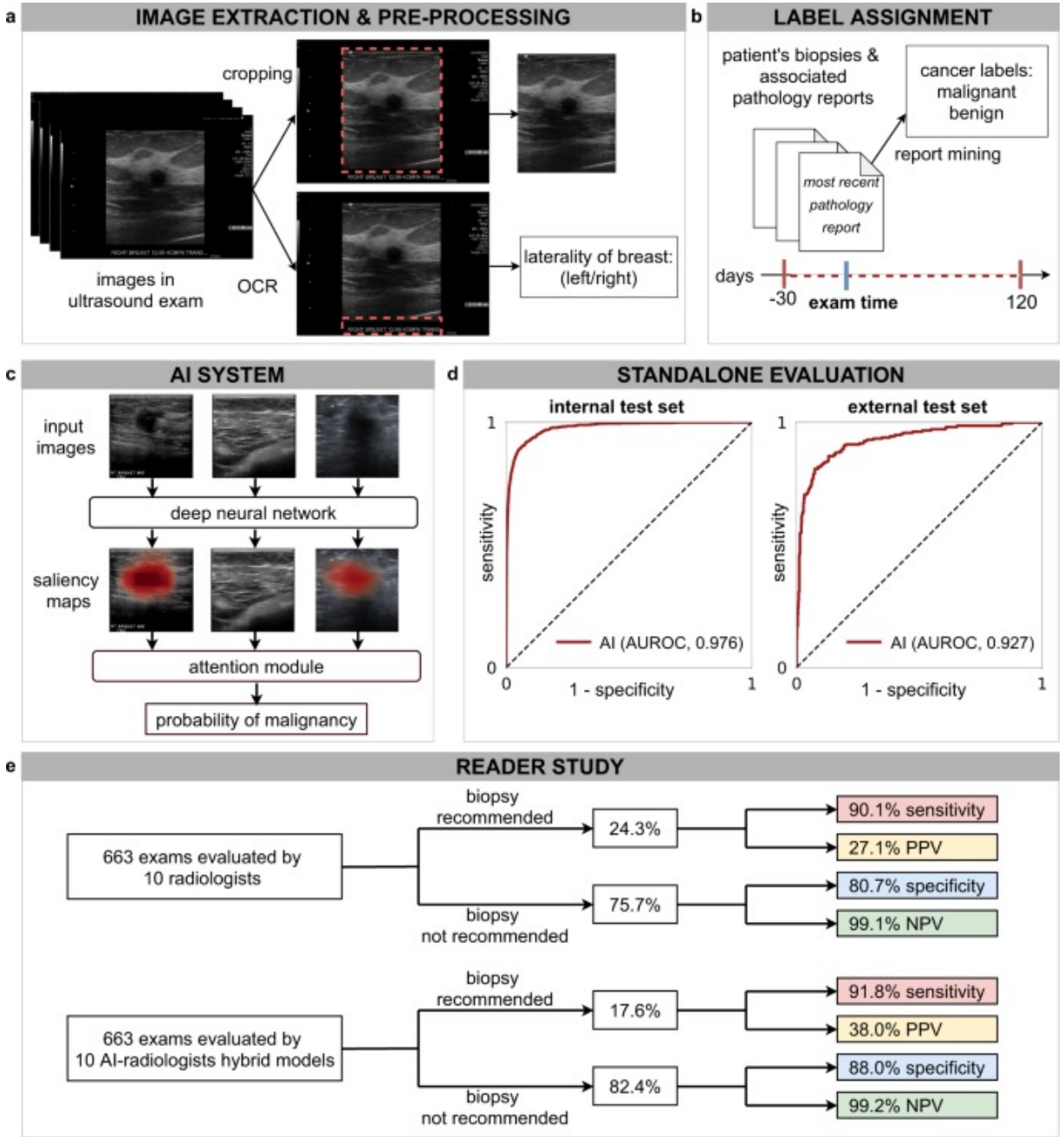
Cancer Radiology

- January 2021: Visage Breast Density (Visage Imaging)

- The software application is intended for use with compatible full-field digital mammography to aid radiologists in the assessment of breast tissue composition

Claudio Luchini Et al, “Artificial intelligence in oncology: current applications and future perspectives” *British Journal of Cancer*, vol. 126, pages4–9, 2022.

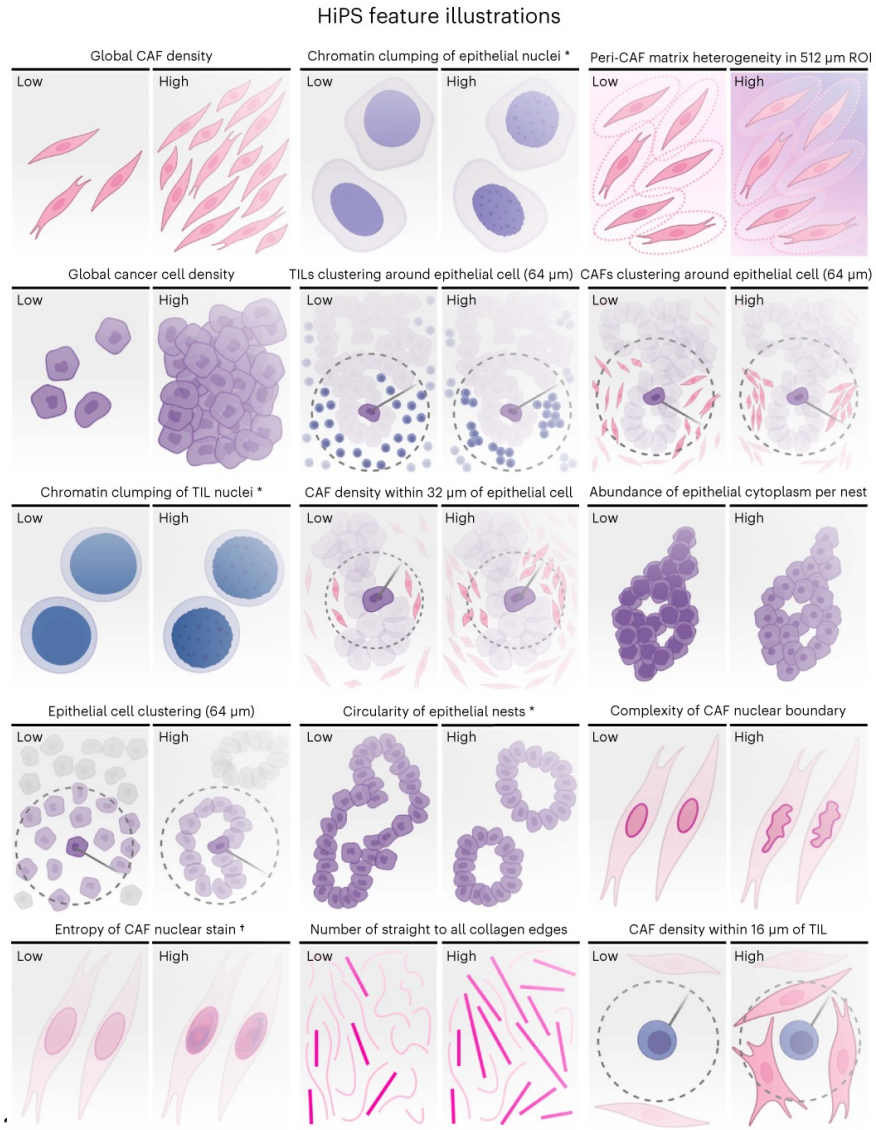
Artificial intelligence system reduces false-positive findings in the interpretation of breast ultrasound exams



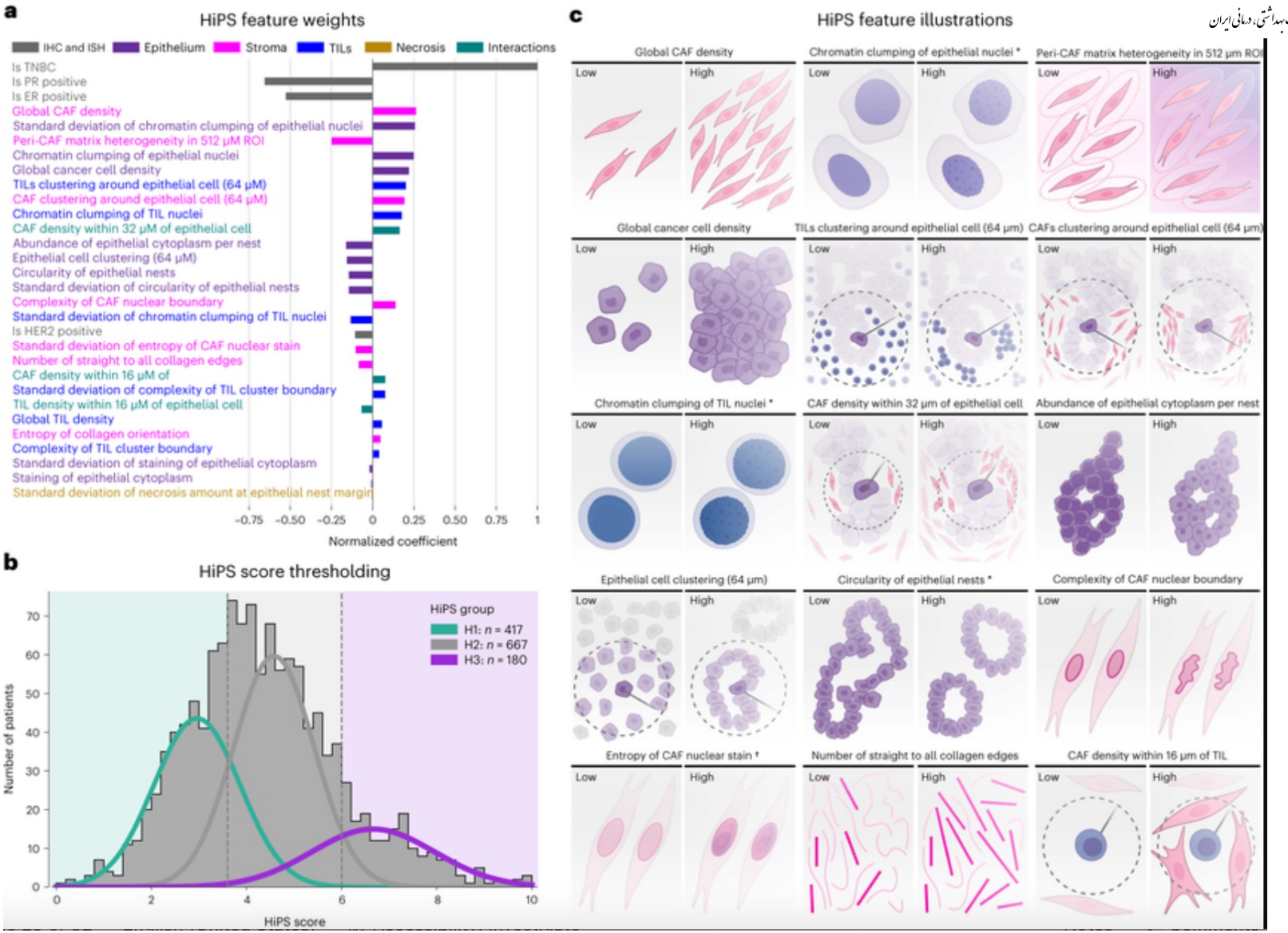
Nature Communications **volume 12**, Article number: 5645 (2021)

Machine learning improves prediction of clinical outcomes for invasive breast cancers

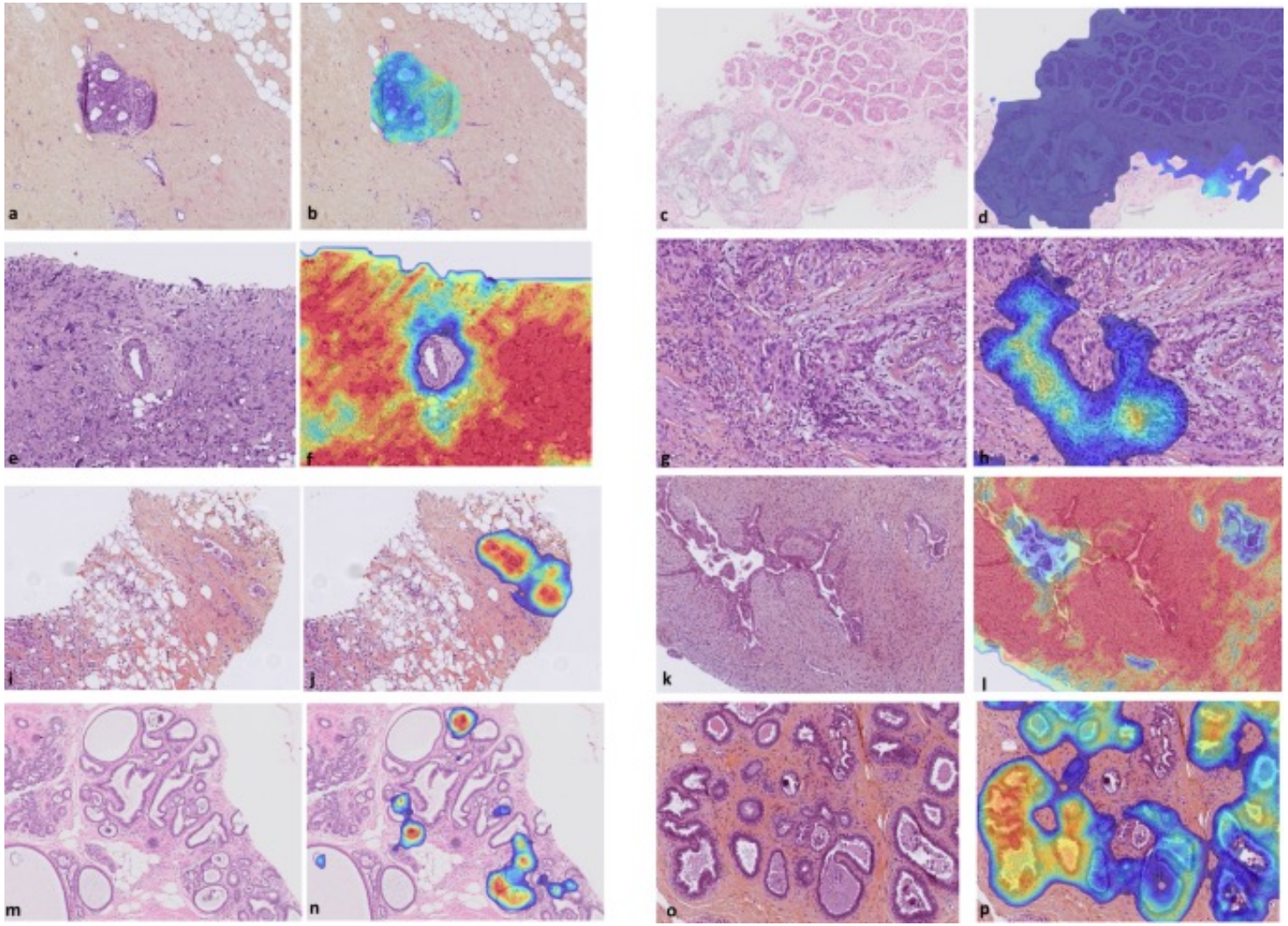
A prognostic model for invasive breast cancer that is based on interpretable measurements of epithelial, stromal, and immune components outperforms histologic grading by expert pathologists.



Nature Medicine **volume 30**, pages41–42 (2024)


a
HiPS feature weights
IHC and ISH
Epithelium
Stroma
TILs
Necrosis
Interactions
Is TNBC
Is PR positive
Is ER positive
Global CAF density
Standard deviation of chromatin clumping of epithelial nuclei
Peri-CAF matrix heterogeneity in 512 μM ROI
Chromatin clumping of epithelial nuclei
Global cancer cell density
TILs clustering around epithelial cell (64 μM)
CAF clustering around epithelial cell (64 μM)
Chromatin clumping of TIL nuclei
CAF density within 32 μM of epithelial cell
Abundance of epithelial cytoplasm per nest
Epithelial cell clustering (64 μM)
Circularity of epithelial nests
Standard deviation of circularity of epithelial nests
Complexity of CAF nuclear boundary
Standard deviation of chromatin clumping of TIL nuclei
Is HER2 positive
Standard deviation of entropy of CAF nuclear stain
Number of straight to all collagen edges
CAF density within 16 μM of
Standard deviation of complexity of TIL cluster boundary
TIL density within 16 μM of epithelial cell
Global TIL density
Entropy of collagen orientation
Complexity of TIL cluster boundary
Standard deviation of staining of epithelial cytoplasm
Staining of epithelial cytoplasm
Standard deviation of necrosis amount at epithelial nest margin
-0.75 -0.50 -0.25 0 0.25 0.50 0.75 1
Normalized coefficient
b
HiPS score thresholding
HiPS group
H1: n = 417
H2: n = 667
H3: n = 180
Number of patients
0 10 20 30 40 50 60 70
0 2 4 6 8 10
HiPS score
c
HiPS feature illustrations
Global CAF density
Chromatin clumping of epithelial nuclei *
Peri-CAF matrix heterogeneity in 512 μm ROI
Global cancer cell density
TILs clustering around epithelial cell (64 μm)
CAFs clustering around epithelial cell (64 μm)
Chromatin clumping of TIL nuclei *
CAF density within 32 μm of epithelial cell
Abundance of epithelial cytoplasm per nest
Epithelial cell clustering (64 μm)
Circularity of epithelial nests *
Complexity of CAF nuclear boundary
Entropy of CAF nuclear stain †
Number of straight to all collagen edges
CAF density within 16 μm of TIL
Low
High

Validation and real-world clinical application of an artificial intelligence algorithm for breast cancer detection in biopsies

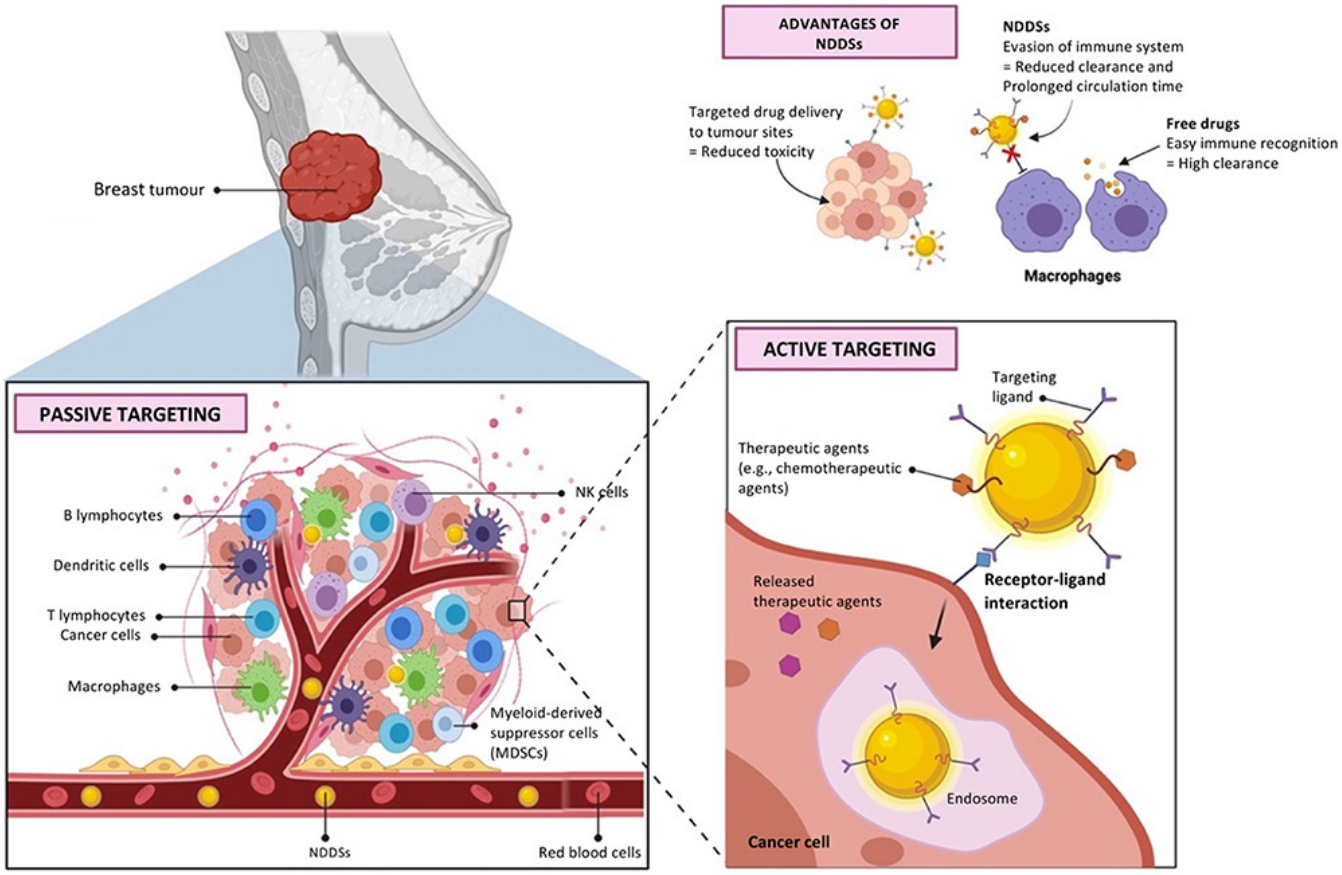


npj Breast Cancer **volume 8**, Article number: 129 (2022

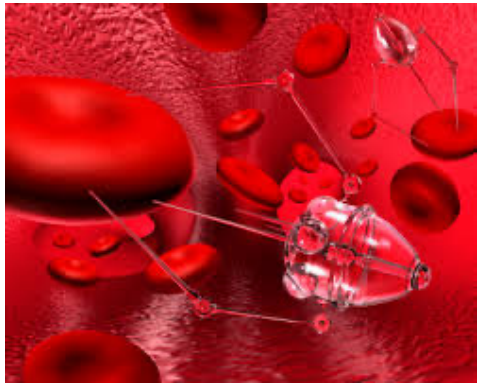
Drug Discovery and Targeted Drug Delivery

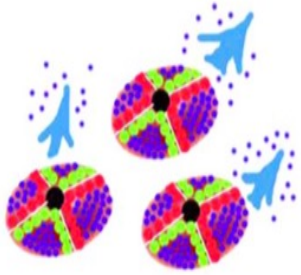
Properties

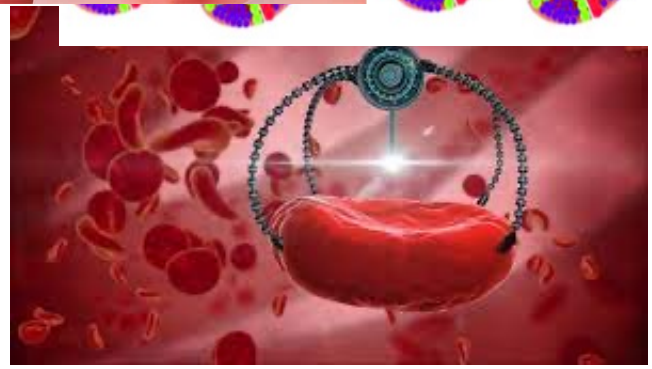
- **Sustained release behavior**
- **Targeting properties**
- **Biocompatibility**
- **Biodegradability**
- **Biodistribution**
- **Low toxicity**

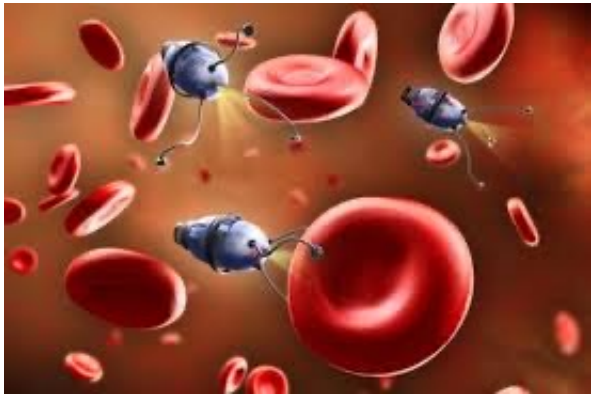


Nanomedicine







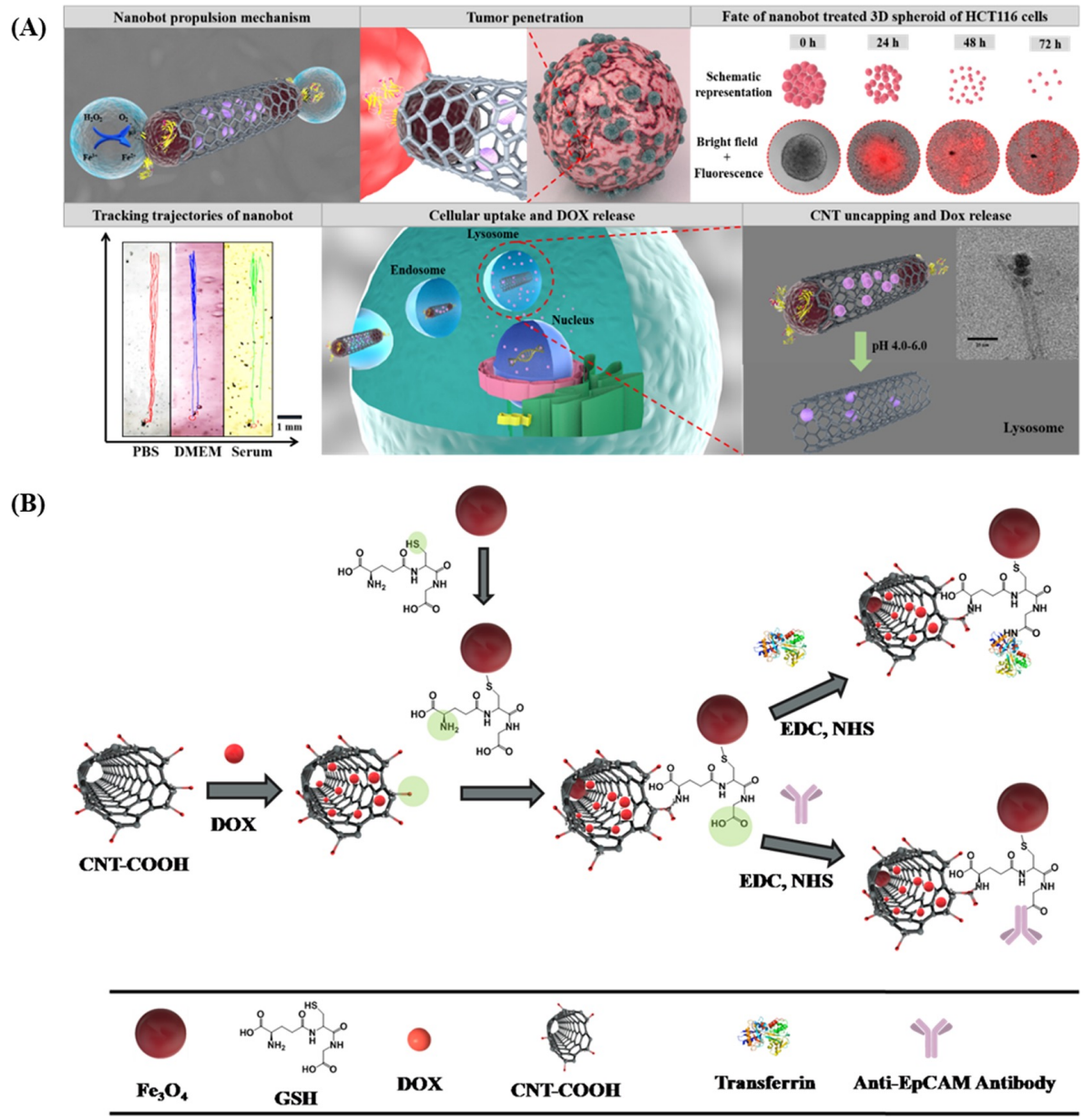


[1] N. Rady Raz, M. R. Akbarzadeh T., "Target Convergence Analysis of Cancer Inspired Swarms for Early Disease Diagnosis and Targeted Collective Therapy,"*IEEE Transactions on Neural Networks and Learning Systems*, 2022.

[2] N. Rady Raz, M. R. Akbarzadeh T., "Swarm-Fuzzy Rule-Based Targeted Nano Delivery Using Bioinspired Nanomachines,"*IEEE Transactions on NanoBioscience*,Vol.18, No.3, pp. 404 - 414, July 2019.

[3] N. Rady Raz, M. R. Akbarzadeh T., M. Tafaghodi, "Bio-Inspired Nanonetworks for Targeted Cancer Drug Delivery,"*IEEE Transactions on NanoBioscience*,Vol.14, No.8, pp. 894-906, Dec. 2015.

Self-Propelling Targeted Magneto-Nanobots for Deep Tumor Penetration and pH-Responsive Intracellular Drug Delivery



Scientific Reports **volume 10**, Article number: 4703 (2020)

clinical trust and adoption of AI technology

Fairness	Universality	Traceability
Usability	Robustness	Explainability

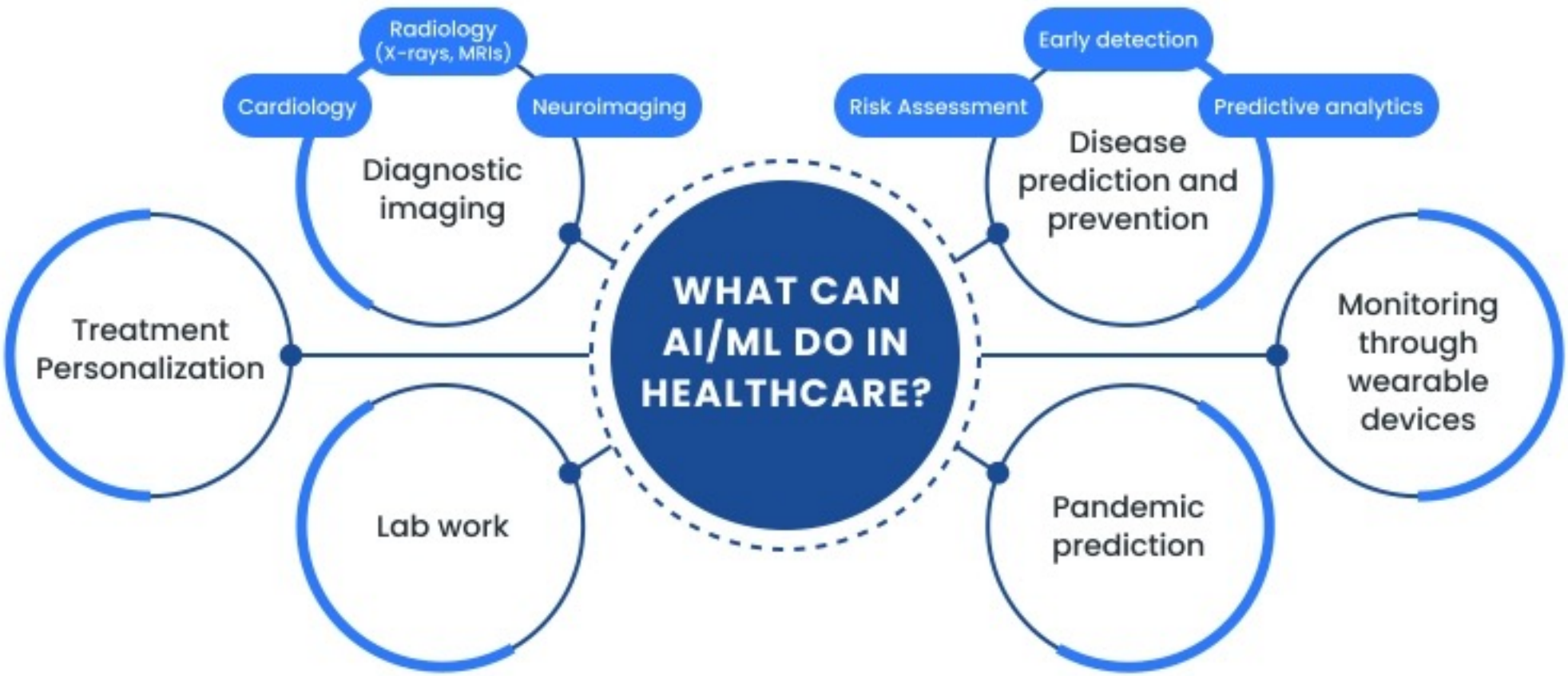
European Journal of Radiology Volume 175, June 2024, 111457

Challenges and Ethical Considerations

data privacy,

potential biases in datasets

interpretability of algorithms,

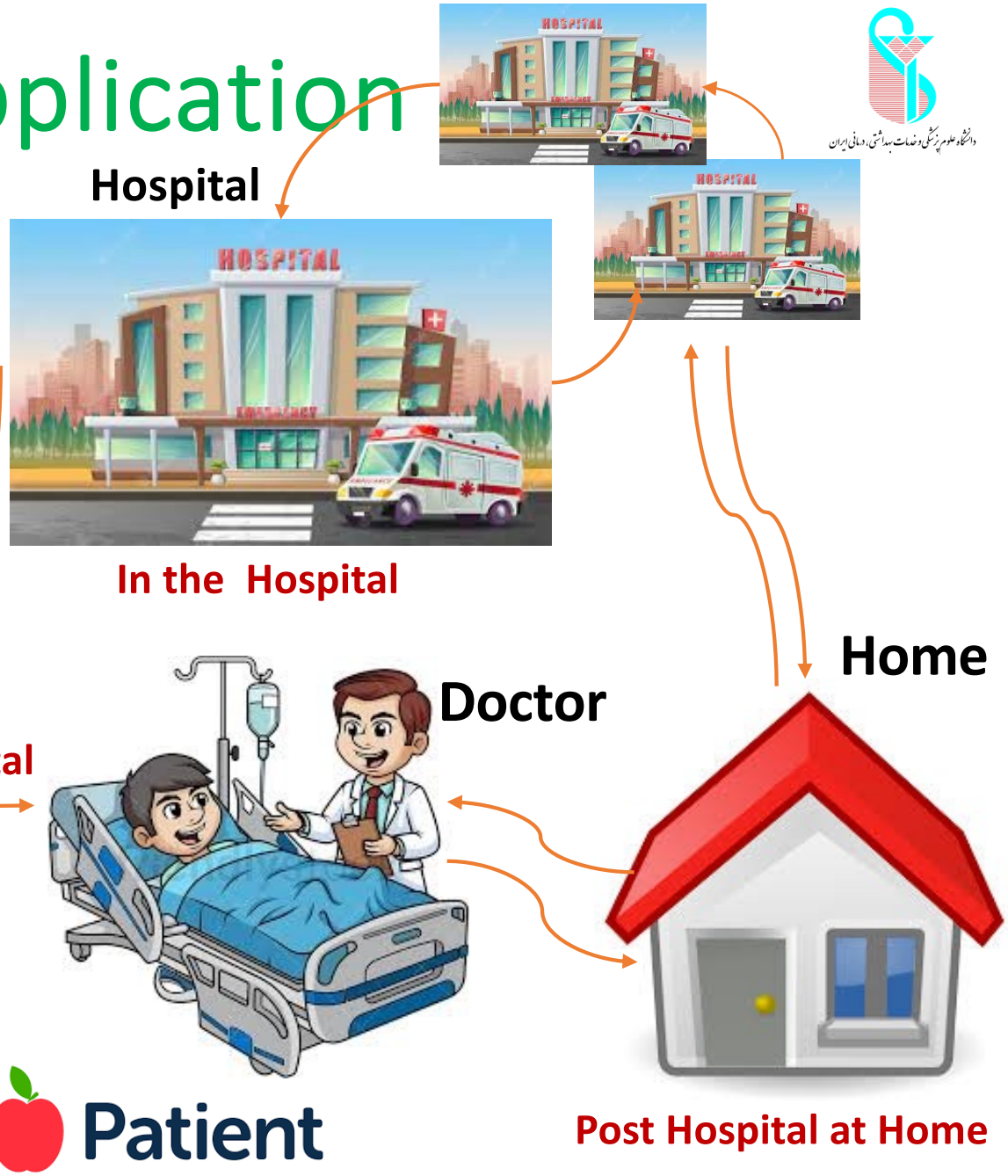


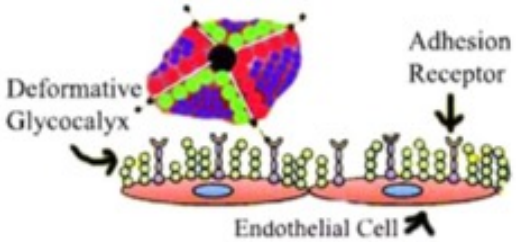
Note that!!

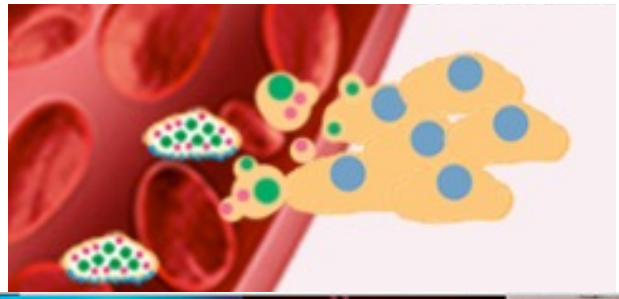
- AI may not replace human doctors.
- Since doctors are trained to not only diagnose and treat diseases but also to provide emotional support to patients.
- AI cannot replace the empathy and compassion that doctors bring to their work.

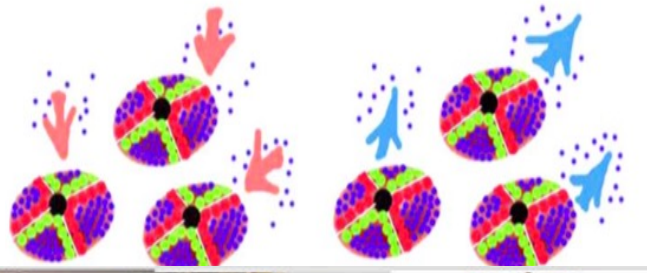
8-AI Medical Application

Prevention	Screening
Early Detection	Diagnosis
Recurrence Prediction	Critical Decision Making
Treatment Selection and Analysis	Mortality and Morbidity Prediction
Triage	…









Nasibeh Rady Raz, Ph.D.

Department of Artificial Intelligence in Medicine, Faculty of Advanced Technologies in Medicine, Iran University of Medical Sciences, Tehran, Iran

MA, Ph.D., and Postdoc in Artificial Intelligence and Robotics

Website: http://radyraz.student.um.ac.ir/

Email: radyraz.n@iums.ac.ir , radyraz@mail.um.ac.ir, radyraz@yahoo.com

Research Interest:

Artificial Intelligence, Artificial Intelligence in Medicine, Complex Systems, Biomimicry, Cognitive Science, Swarm Intelligence, Nanomedicine, Targeted Drug Delivery, Early Detection of Disease, Swarm Nano Robotics, Cancer Research, Fuzzy Logic and Control, Soft Computing, Neural Networks, Machine Learning, Multi-agent Systems, Distributed Decision Making, Biomarkers, Biophysics, Nature Inspired Algorithms, Computational Cellular/Molecular Biology, Protein Folding

Artificial Intelligence for Good (AI for Good)

- Fairness. AI algorithms should maintain the same performance when applied to similar individuals (individual fairness) and across subgroups of individuals, including under-represented groups (group fairness).

- Universality. This principle recommends the definition and application of (technical, clinical, ethical, and regulatory) standards during AI development, evaluation, and deployment. This will increase the interoperability and applicability of AI tools across clinical centers.

- Traceability. Medical AI algorithms should be developed with mechanisms for documenting and monitoring the development process, as well as be paired with methods to continuously or periodically monitor their functioning in the clinical environment.

- Usability. Medical AI tools should be usable, acceptable, and deployable for the real-world end users (i.e., physicians, radiologists, and other end users).

- Robustness. This principle refers to maintaining AI's performance and accuracy when it is applied under the highly variable conditions that could be encountered in the real world, outside the controlled environment of the laboratory where the algorithm was built and initially tested.

- Explainability. Medical AI algorithms should be able to provide meaningful and actionable explanations of their predictions to the end users. Explainability provides insight into the algorithmic mechanisms behind the AI decision-making processes.