



con il patrocinio di



PROGRESSI E NUOVE FRONTIERE IN
GASTROENTEROLOGIA
ED ENDOSCOPIA DIGESTIVA



BELLUNO
15-16 GIUGNO 2023

Ruolo della Intelligenza Artificiale in epatologia

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Sapienza, University of Rome, Italy



Con il patrocinio di



PROGRESSI E NUOVI
GASTROENTEROLOGIA
ED ENDOSCOPIA

MEDIATECH: Martedì, 30/5/2023

"L'intelligenza artificiale come una guerra nucleare. Umanità a rischio"

L'allarme clamoroso di 350 esperti tra cui l'ad di OpenAI, Sam Altman, e il fisico italiano Roberto Battiston



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ChatGPT, Bard e ErnieBot: perché chiedere all'intelligenza artificiale non è sempre intelligente



Cosa sono e come funzionano i chatbot basati sull'intelligenza artificiale e perché i limiti sono ancora molti

Ethical code related to Artificial Intelligence Tools

This lecture is the result of

Artificial Intelligence

OR

My Natural Deficiency

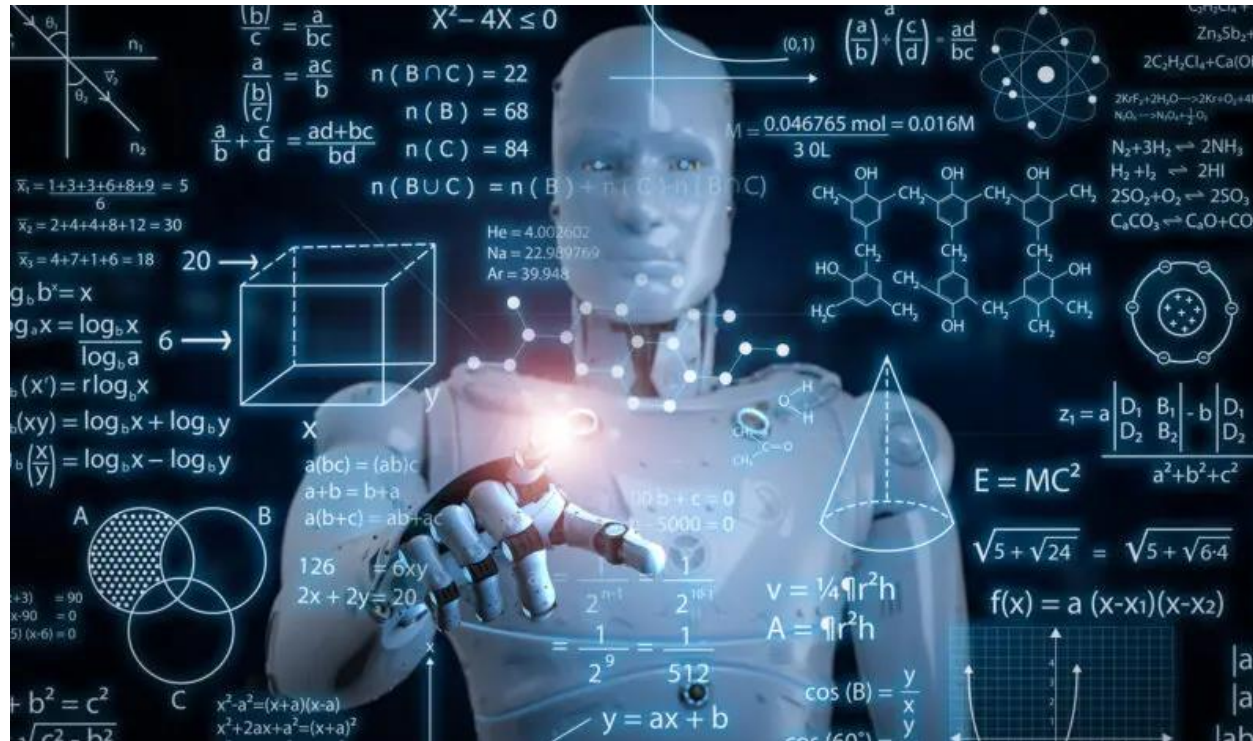
REVIEW ARTICLE

Jeffrey M. Drazen, M.D., *Editor*;
Isaac S. Kohane, M.D., Ph.D., and Tze-Yun Leong, Ph.D., *Guest Editors*

AI IN MEDICINE

Artificial Intelligence and Machine Learning in Clinical Medicine, 2023

Charlotte J. Haug, M.D., Ph.D., and Jeffrey M. Drazen, M.D.



B Advances in Speed

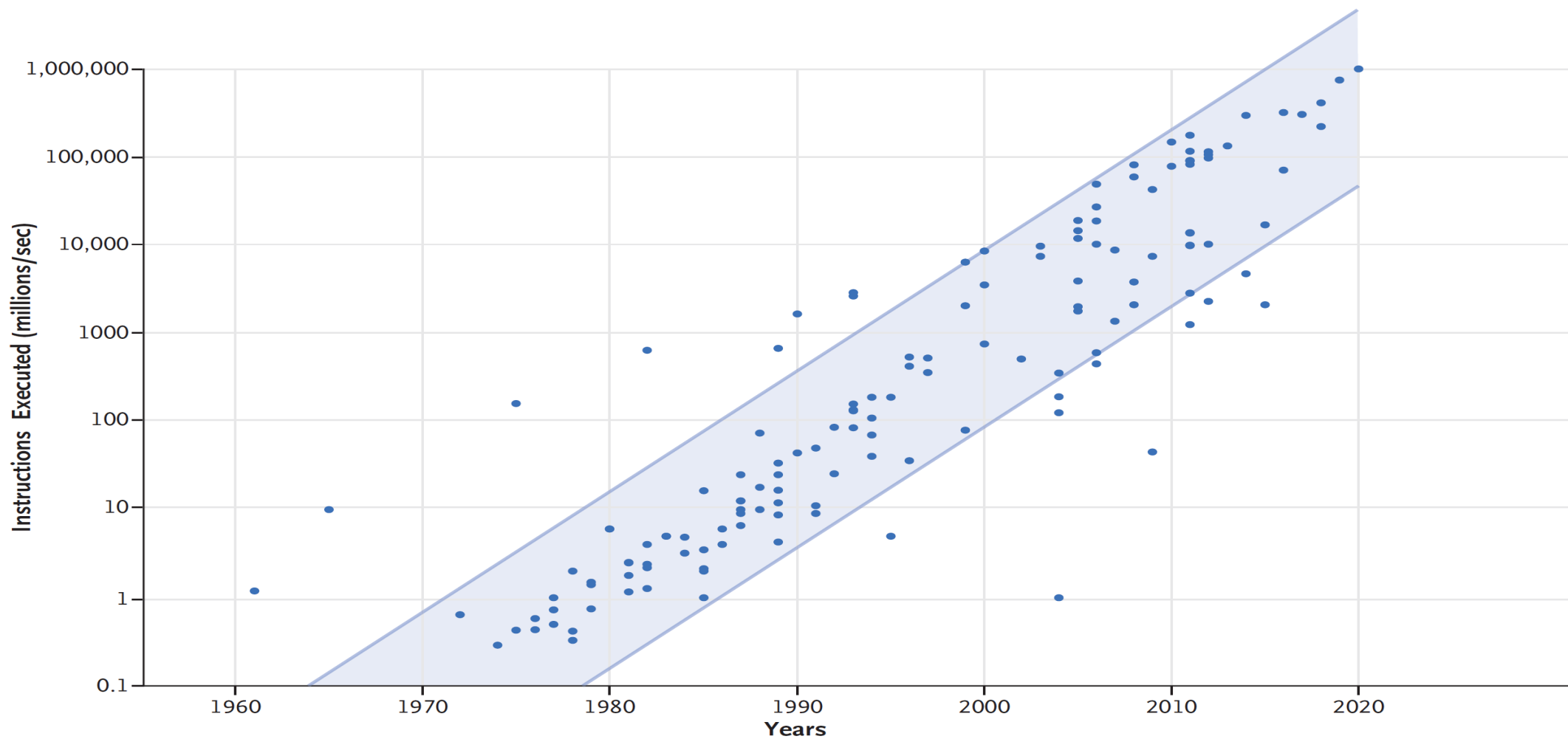
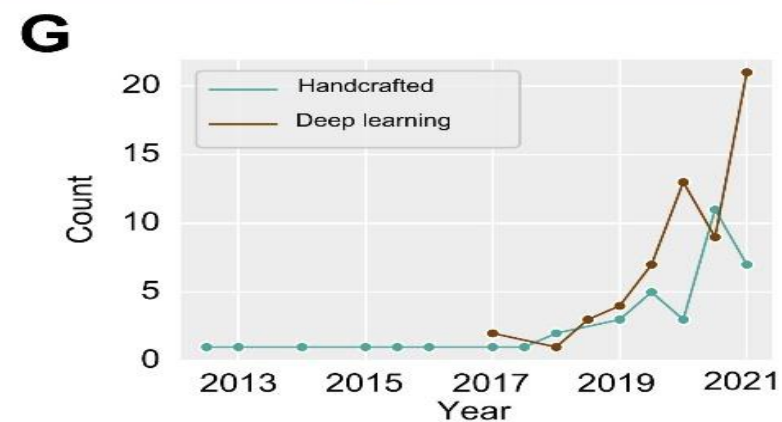
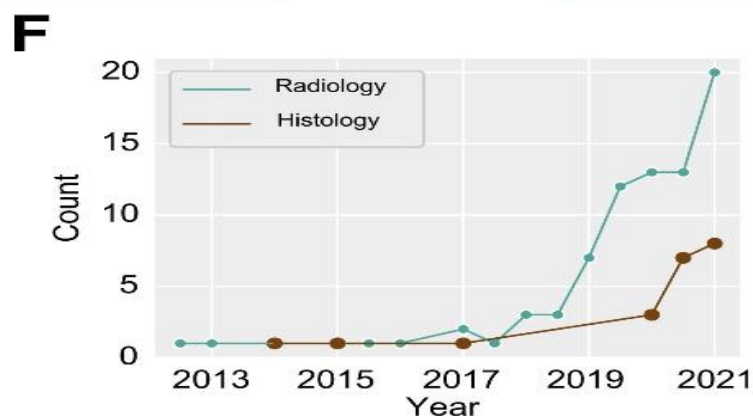
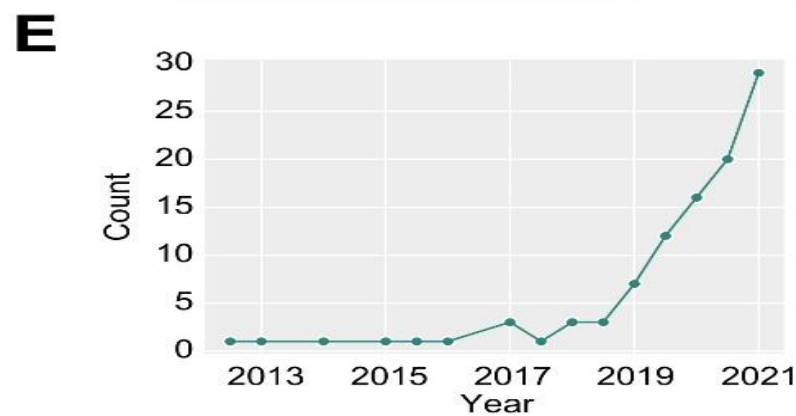
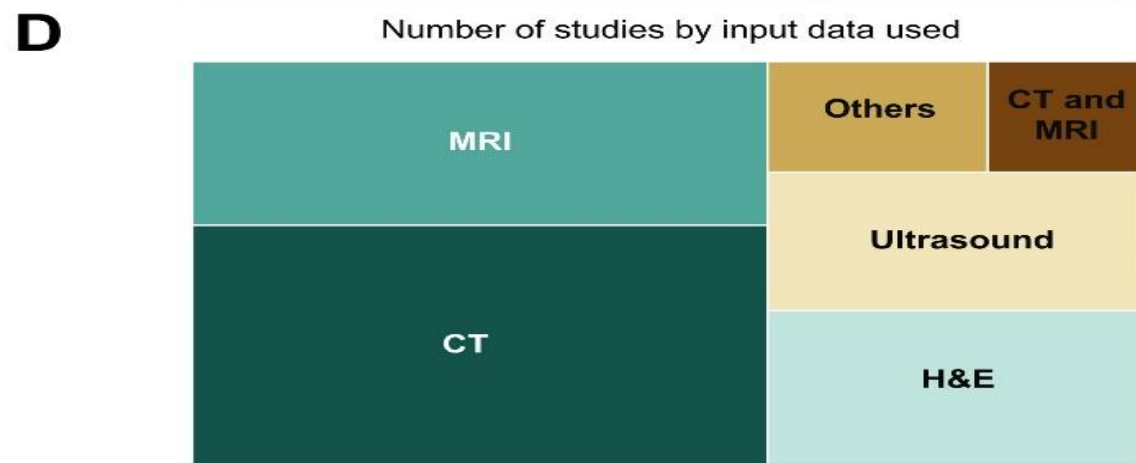
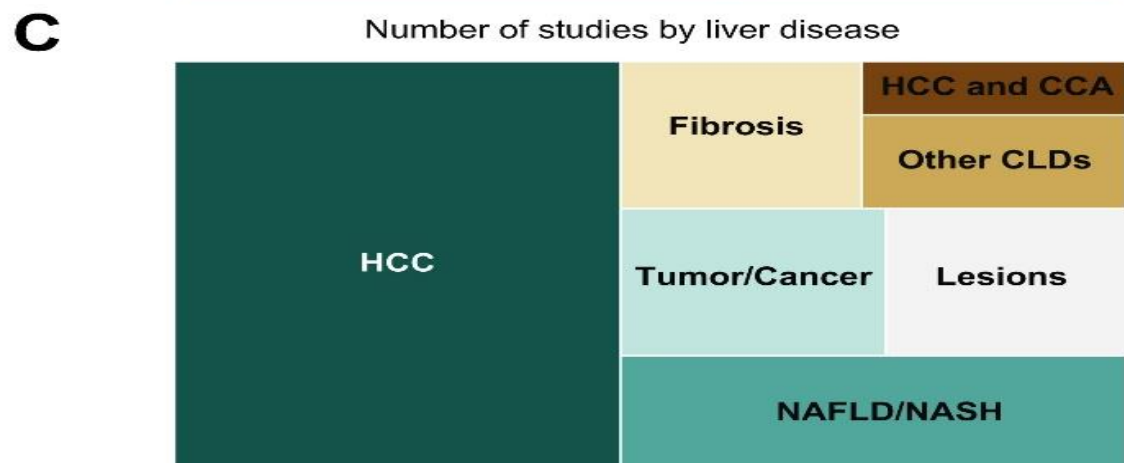
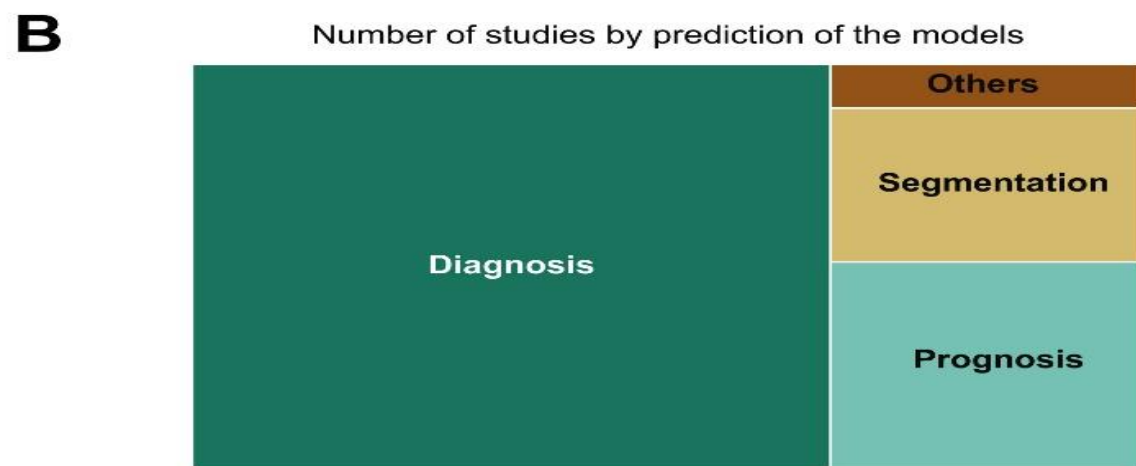
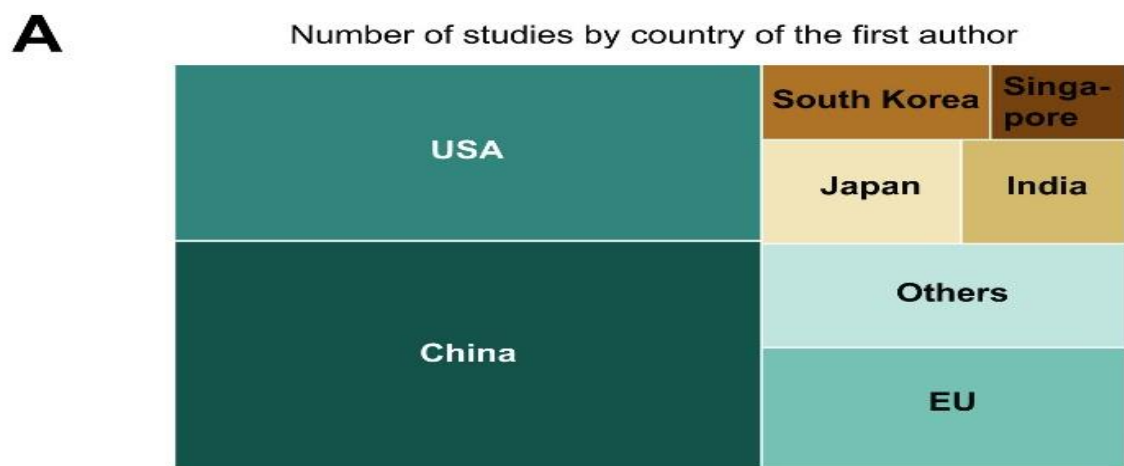


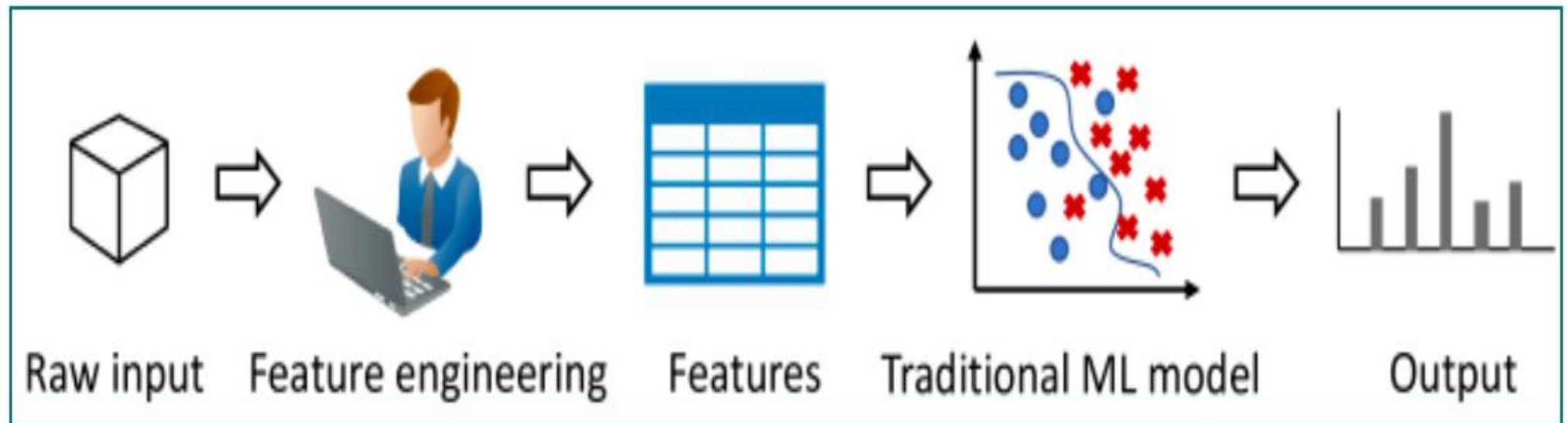
Figure 1. Improvements over 50 Years in the Ability of Computers to Store and Process Data.

Panel A shows advances in data storage, in terms of both physical size and cost per unit of storage. RAMAC denotes random access method of accounting and control. Panel B shows advances in the speed of computing. Each dot represents an individual machine type and the approximate year of its introduction. These improvements in storage and speed have allowed machine learning to progress from a dream to reality. Data in both panels are estimates from many types of system architecture and are derived from multiple public sources.



Il termine **Machine Learning** è stato coniato da Arthur Samuel nel 1959, che lo ha definito come:

«Machine Learning is the field of study that gives computers the ability to learn without being explicitly programmed»



Alcuni compiti non possono essere infatti definiti esaustivamente, tranne che tramite esempi.

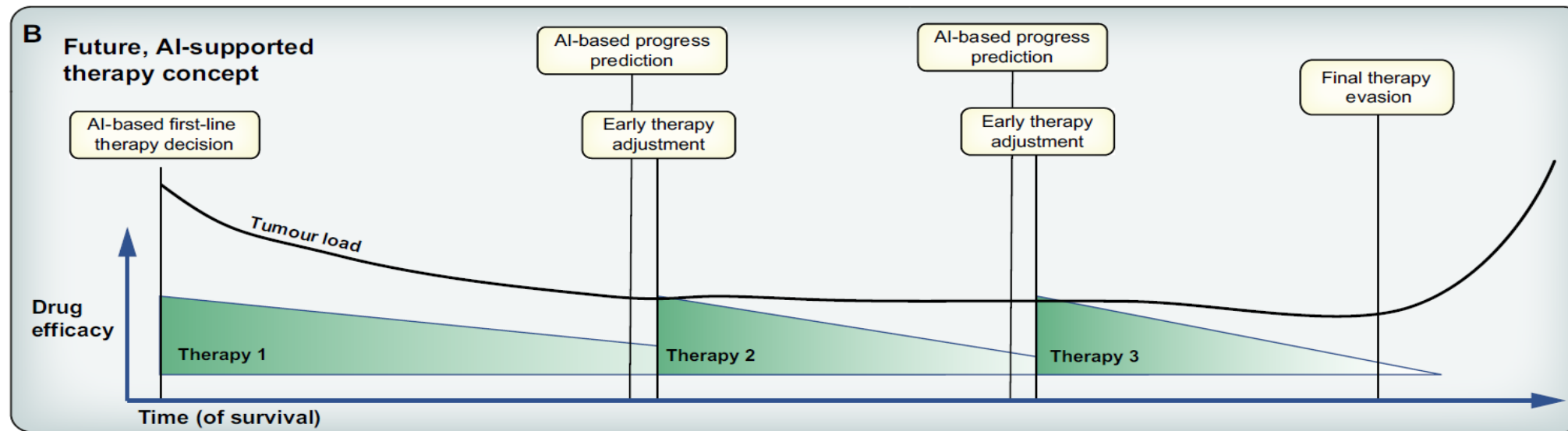
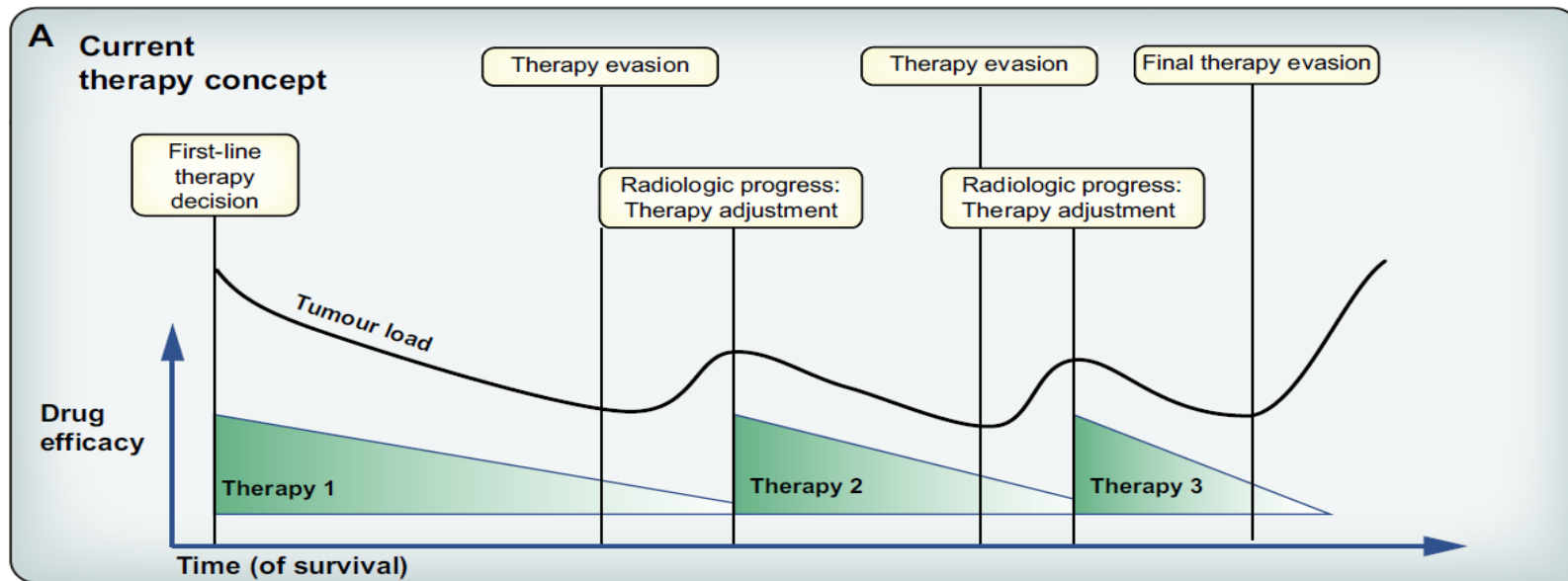
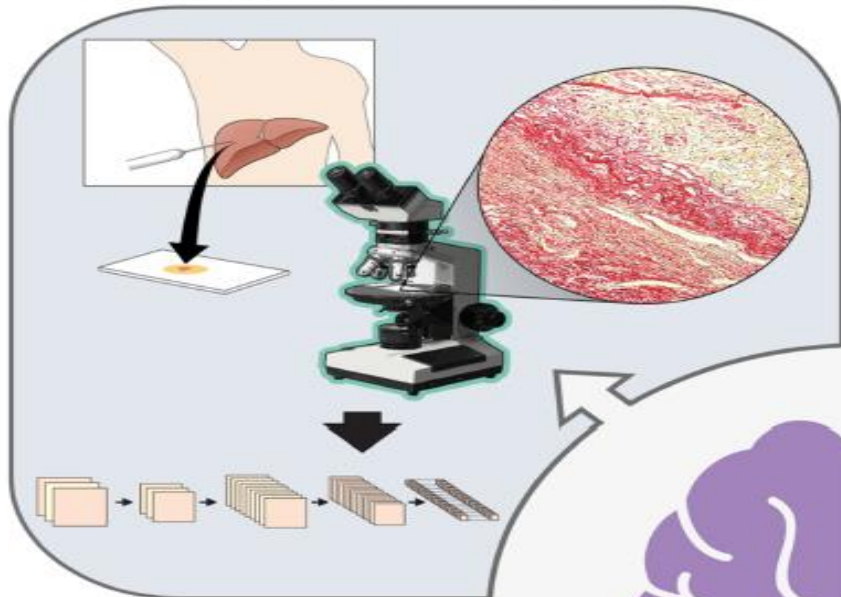
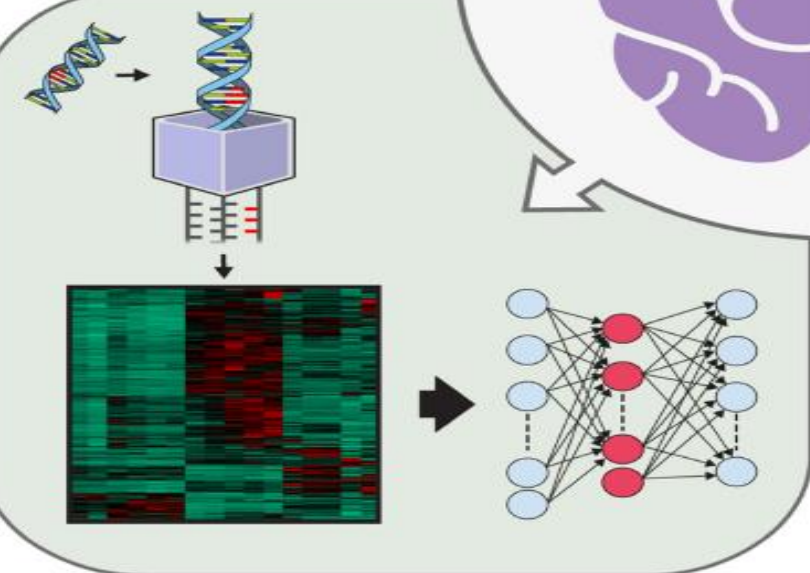
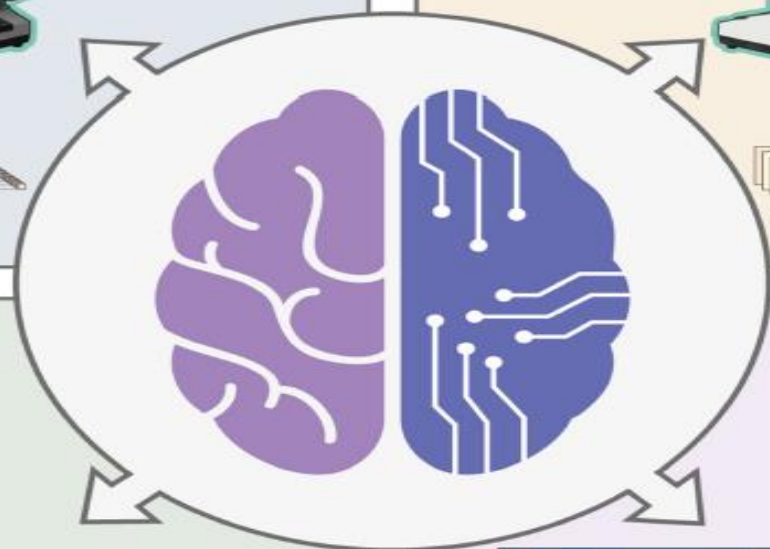
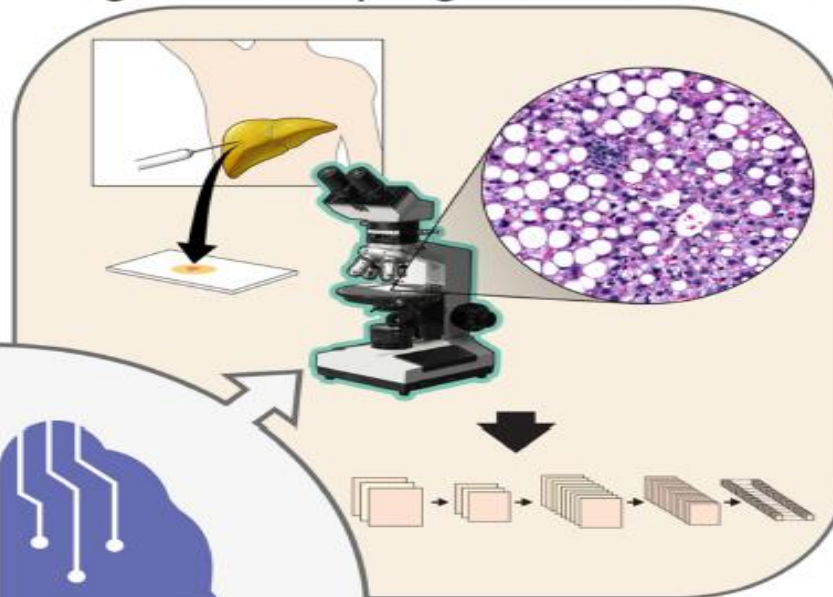


Fig. 4. Artificial intelligence could support doctors in decision making in tumour therapy in the future. (A) Current oncologic therapy pattern. After an initial first-line therapy, the tumour is evading therapy through resistance mechanisms. The following tumour growth is recognised during radiologic follow-up leading to therapy adjustment. (B) Hypothetical, future, AI-supported therapy pattern. Initial, individualized first-line therapy decision, accounting for an AI-based recommendation. After an AI algorithm predicts progression of a tumour, doctors decide to adjust therapy before the tumour can develop resistance to therapy and grow again.

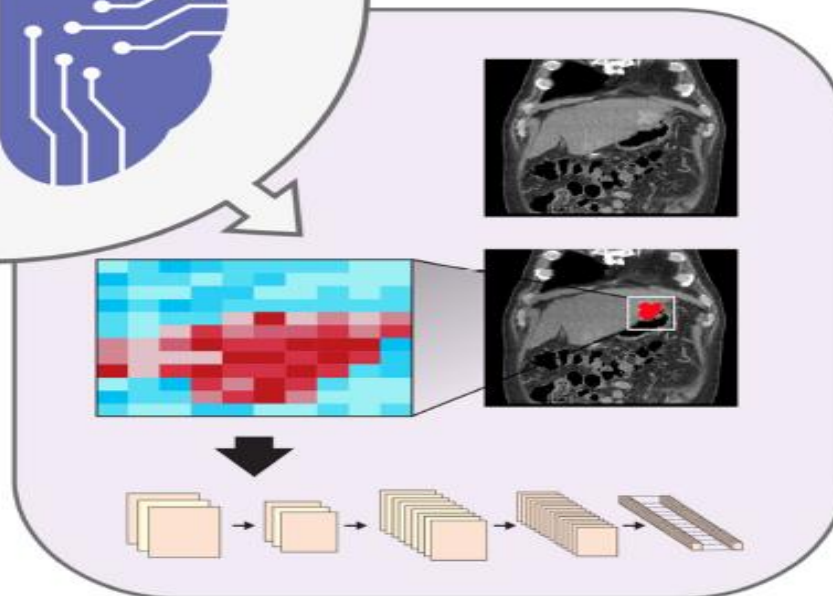
Measurement of liver fibrosis



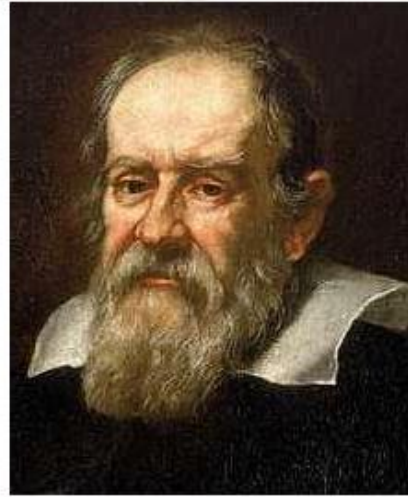
Diagnosis and prognosis of NAFLD



Prediction of disease progression



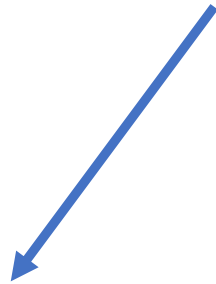
Diagnosis of focal liver lesions



*Misura ciò che è
misurabile, e rendi
misurabile ciò che non lo è*

Artificial Intelligence applications in diagnostic and prognostic imaging in hepatology

IMAGING-DRIVEN DIAGNOSIS and PROGNOSIS



IMAGING ACQUISITION

IMAGING INTERPRETATION



Critical Issues

- **High Subjectivity**
- **Experience and Tiredness**

L'analisi visiva riesce a estrarne solo circa il 10% delle informazioni contenute in una immagine medica digitale

Radiomica = le immagini ottenute dagli esami TAC, RM o PET, vengono convertite in dati numerici.

Se le immagini sono analizzate in dettaglio attraverso dei software di analisi della tessitura dell'immagine è possibile ottenere dati quantitativi oggettivi, in grado di fornire informazioni sui sottostanti fenomeni pato-fisiologici, inaccessibili alla semplice analisi visiva.

Radiogenomica

Mette in relazione i dati quantitativi ottenuti con la radiomica con i dati genomici del tumore.

L'obiettivo è che una semplice analisi radiomica non invasiva possa essere in grado di informarci se un tumore abbia una certa mutazione, evitando analisi di tessuti !!!!



- La Radiomica è spesso applicata in ambito oncologico, allo scopo di porre le basi per la futura

MEDICINA DI PRECISIONE

Un evidente **vantaggio auspicato** degli approcci radiomici in ambito oncologico è quello di **rimpiazzare la biopsia** del tessuto tumorale, e quindi:

- **sostituire una tecnica invasiva con una non invasiva;**
- **ridurre il rischio di errato campionamento dei tessuti**, dato che negli approcci radiomici l'intera lesione viene analizzata.

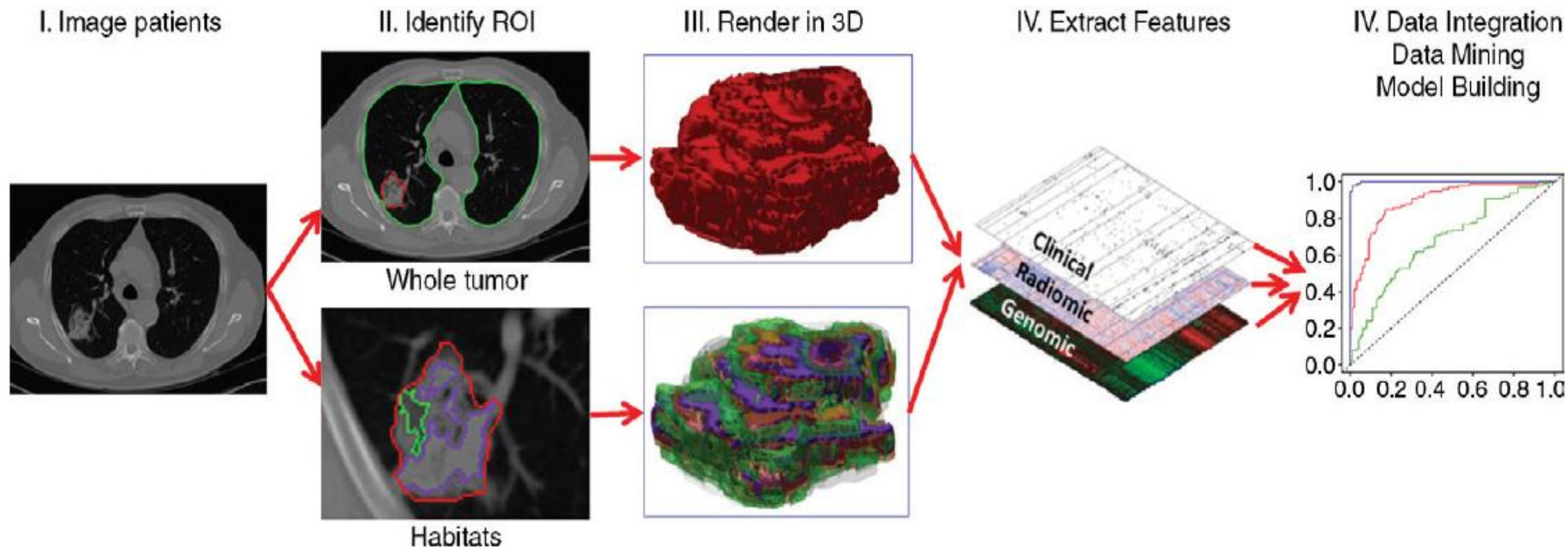
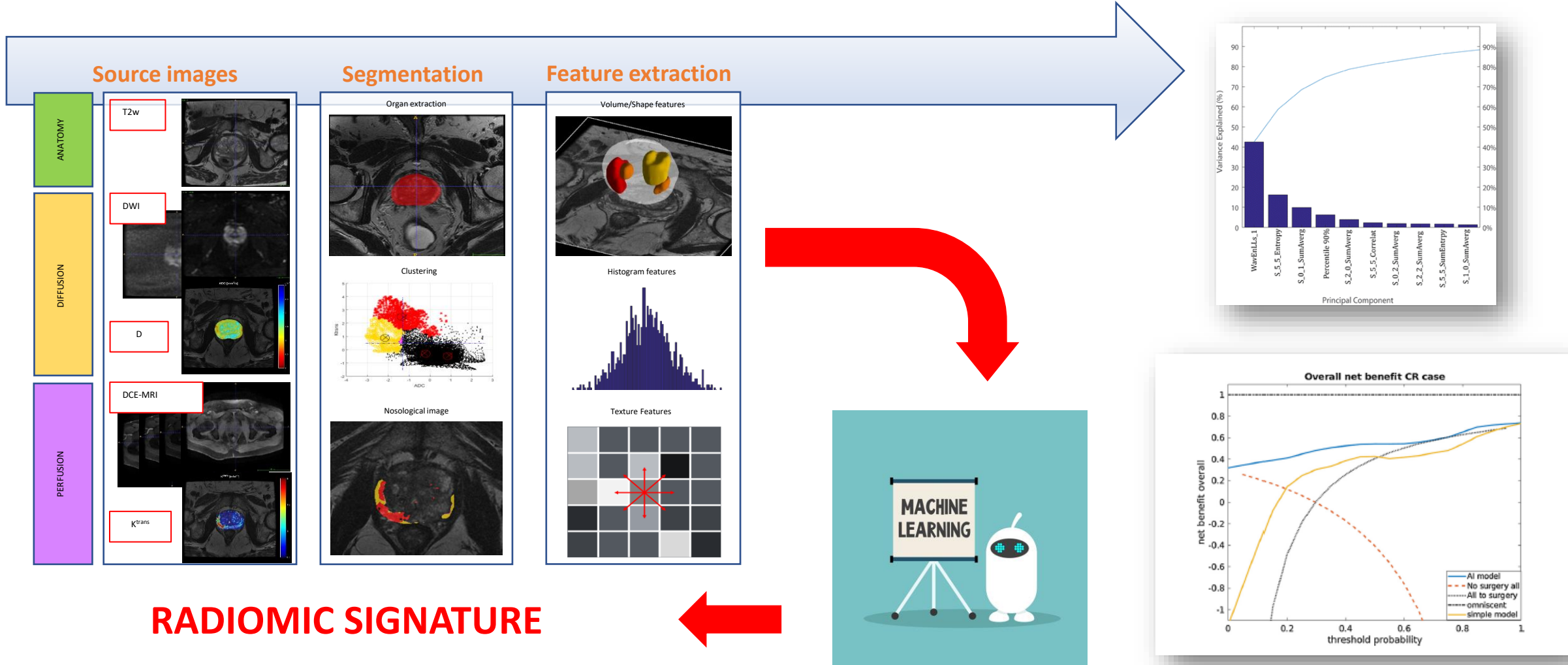
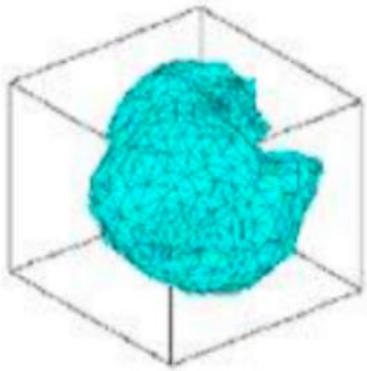


Figure 1: Flowchart shows the process of radiomics and the use of radiomics in decision support. Patient work-up requires information from disparate sources to be combined into a coherent model to describe where the lesion is, what it is, and what it is doing. Radiomics begins with acquisition of high-quality images. From these images, a region of interest (*ROI*) that contains either the whole tumor or subregions (ie, habitats) within the tumor can be identified. These are segmented with operator edits and are eventually rendered in three dimensions (*3D*). Quantitative features are extracted from these rendered volumes to generate a report, which is placed in a database along with other data, such as clinical and genomic data. These data are then mined to develop diagnostic, predictive, or prognostic models for outcomes of interest.

Radiomics

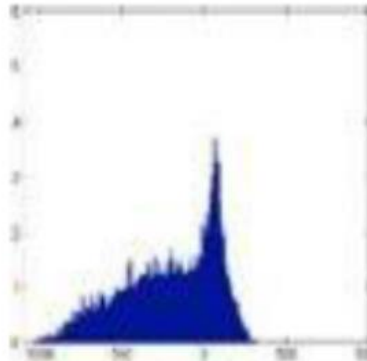
RADIOMICS: the conversion of digital images into mineable data





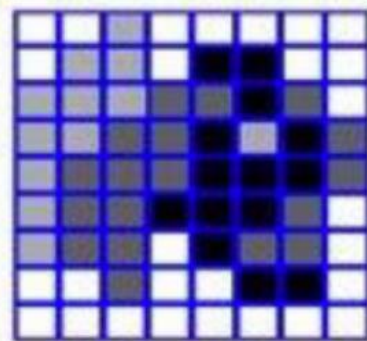
Features relative a
forma e dimensione

Features che descrivono forma
e dimensione della ROI (2D o
3D).



Features statistiche del
primo ordine

Features calcolate a partire
dall'istogramma che
rappresenta la distribuzione dei
valori dei pixel/voxel nella ROI.

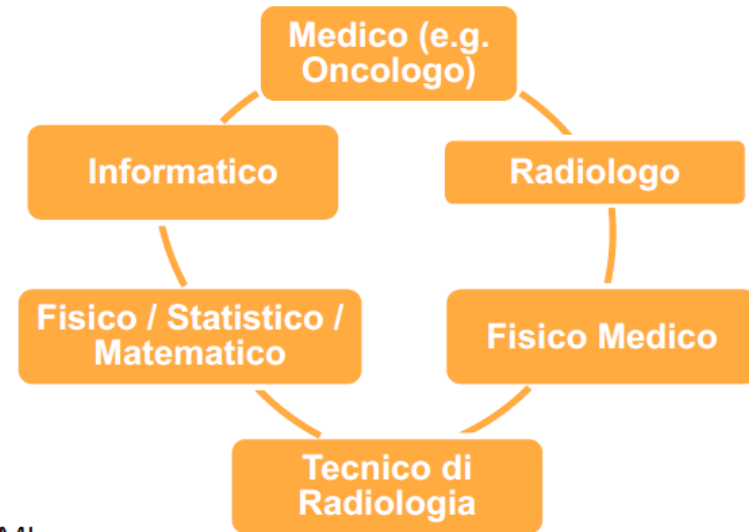


Features statistiche di
ordine superiore

Features che descrivono
relazioni tra i valori di due o più
pixel/voxel nella ROI.

Per effettuare correttamente uno studio di Radiomica + ML è necessario un gruppo di ricerca altamente interdisciplinare, data le molteplici e differenti competenze necessarie:

- Acquisizione dei dati
- Controllo di qualità dei macchinari e dei dati acquisiti
- Segmentazione automatica/manuale delle regioni di interesse
- Annotazione dei campioni
- Preprocessing dei dati
- Estrazione delle features radiomiche
- Addestramento algoritmi di Machine Learning
- Valutazione dei risultati
- Valutazione dell'impatto clinico dei risultati dell'analisi di radiomica + ML



HEAL ITALIA

Health Extended Alliance

for

*Innovative Therapies, Advanced Lab-research, and Integrated Approaches
of Precision Medicine*

Tra gli Obiettivi principali:

Sviluppo di algoritmi per

- diagnosi precoce
- modelli di gestione territoriale patologie alto impatto epid.
- stratificazione personalizzata di rischio di progressione, complicanze e eventi avversi
- benefici ed eventi avversi di terapie farmacologiche
- riposizionamento di farmaci

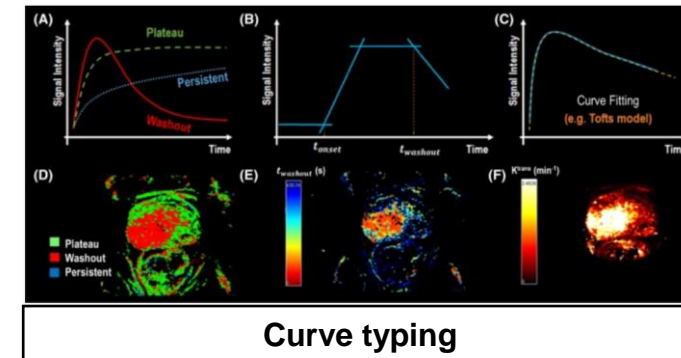
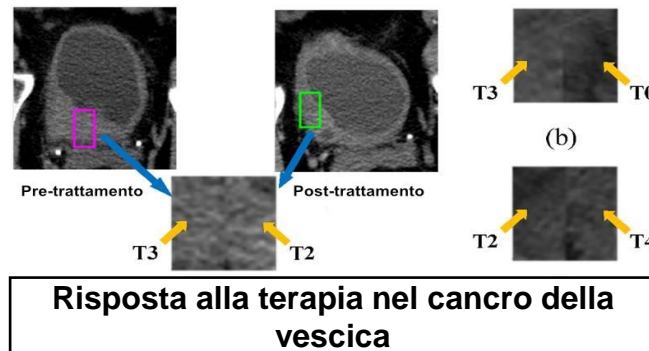
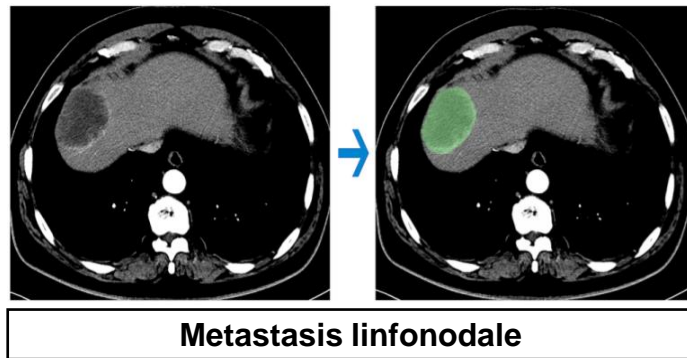
TO
*...a precise cure
for each one!*



Radiomics: Applicazioni cliniche

Ha diverse applicazioni nell'ambito della diagnostica clinica, tra le quali [1],[2],[3],[4]:

1. Previsione della risposta alla terapia del cancro (Treatment response and Outcomes)
2. Stadiazione del tumore (Tumor staging)
3. Aggressività del tumore (Level of malignancy)
4. Identificazione del tessuto e tipizzazione della lesione (Tissue Identification and typing)
5. Valutazione della genetica del cancro (Radiogenomics)



[2] Stephen S F Yip and Hugo J W L Aerts 2016 Phys. Med. Biol. 61 R150

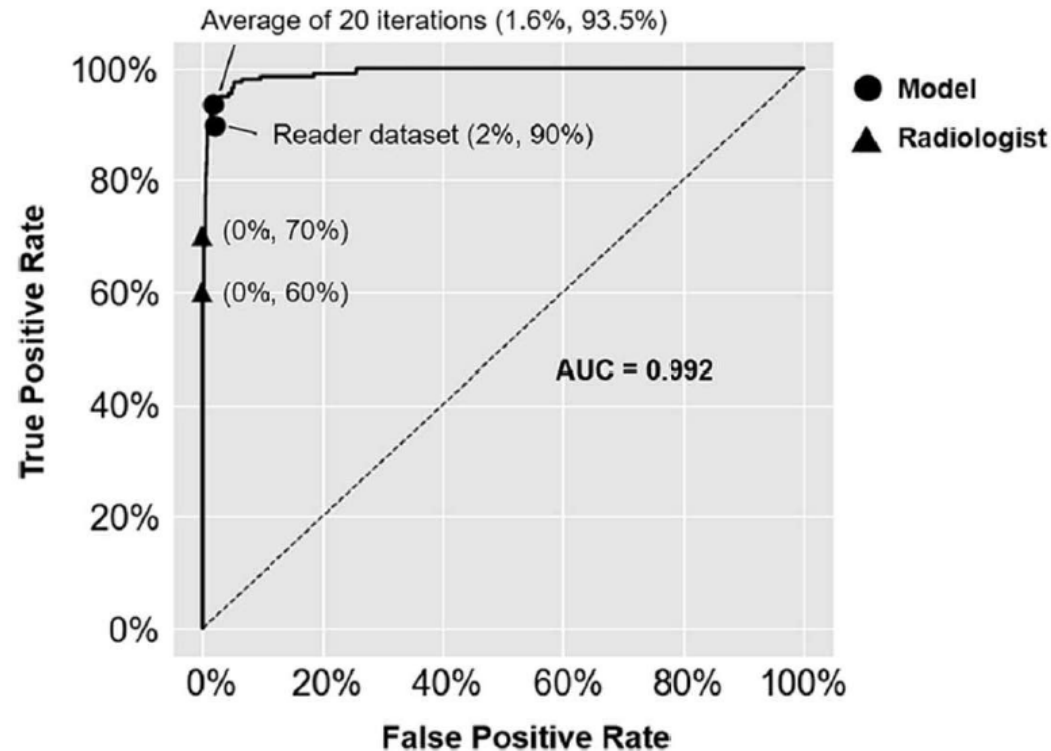
[3] Introduction to Radiomics Marius E. Mayerhoefer, Andrzej Materka, Georg Langs, Ida Häggström, Piotr Szczypiński, Peter Gibbs, Gary Cook Journal of Nuclear Medicine Apr 2020, 61 (4) 488-495

[4] Bogowicz, Marta, et al. "CT radiomics and PET radiomics: ready for clinical implementation?." The Quarterly Journal of Nuclear Medicine and Molecular Imaging: Official Publication of the Italian Association of Nuclear Medicine (AIMN)[and] the International Association of Radiopharmacology (IAR),[and] Section of the Society of.. (2019).



Deep learning for liver tumor diagnosis part I: development of a convolutional neural network classifier for multi-phasic MRI

Charlie A. Hamm^{1,2} · Clinton J. Wang¹ · Lynn J. Savic^{1,2} · Marc Ferrante¹ · Isabel Schobert^{1,2} · Todd Schlachter¹ · MingDe Lin¹ · James S. Duncan^{1,3} · Jeffrey C. Weinreb¹ · Julius Chapiro¹ · Brian Letzen¹



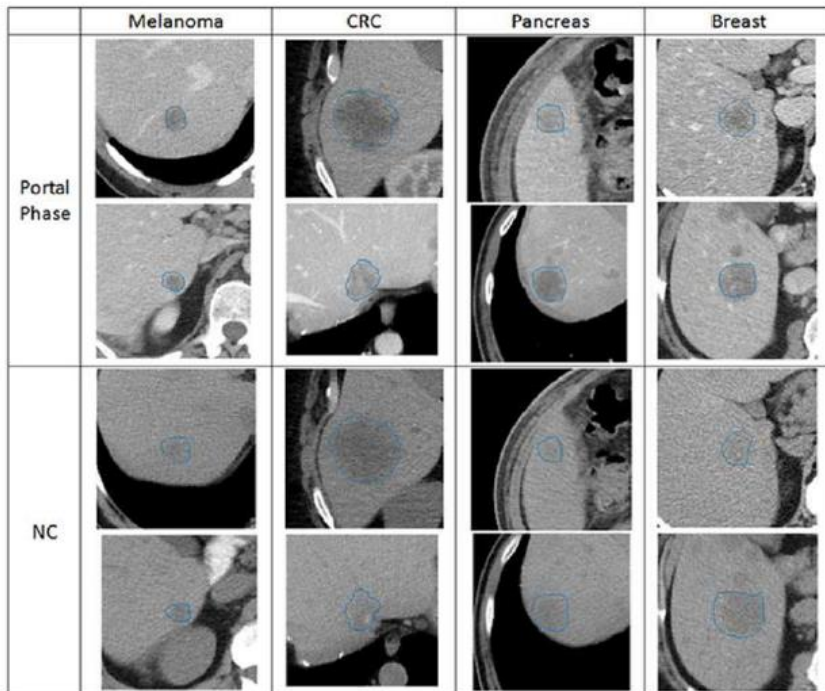
- Four hundred ninety-four hepatic lesions with typical imaging features from six categories (simple cyst, cavernous hemangioma, focal nodular hyperplasia, HCC, intrahepatic cholangiocarcinoma, and colorectal cancer metastasis) were utilized, divided into training ($n = 434$) and test ($n = 60$) sets.
- The ground truth was extracted from official reports
- 20 iterations were performed, randomly splitting lesions into training and test set.
- The model performance was evaluated in distinguishing the six lesion entities as well as three broader categories that simulate the application of a deep learning model to an HCC diagnostic imaging framework such as LI-RADS.
- After model engineering was finalized, classification accuracy for the final CNN was compared with two board-certified radiologists on an identical unseen test set

| | Accuracy of lesion classification (mean \pm SD %) | Accuracy of derived LI-RADS classification (mean \pm SD %) | Runtime (mean \pm SD) |
|---------------------------|---|--|-------------------------|
| Average of 20 iterations | | | |
| Model training set | 98.7 \pm 1.0 | 99.1 \pm 0.7 | 29 min \pm 4 |
| Model test set | 91.9 \pm 2.9 | 94.3 \pm 2.9 | 5.6 ms \pm 4.6 |
| Reader study ($n = 60$) | | | |
| Model | 90.0 | 91.7 | 1.0 ms \pm 0.4 |
| Radiologist 1 | 80.0 | 88.3 | 14 \pm 10 s |
| Radiologist 2 | 85.0 | 88.3 | 17 \pm 24 s |

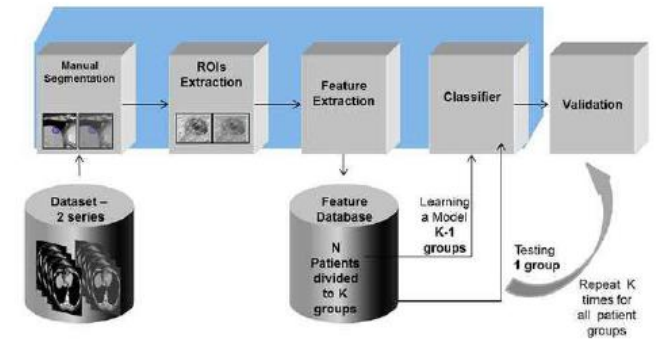
Original Investigation

CT Image-based Decision Support System for Categorization of Liver Metastases Into Primary Cancer Sites: Initial Results

Avi Ben-Cohen MSc^a, Eyal Klang MD^b, Idit Diamant MSc^a, Noa Rozendorn BSc^b, Stephen P. Raskin MD^b, Eli Konen MD^b, Michal Marianne Amitai MD^b, Hayit Greenspan PhD^a



- 50 lesion cases taken from 29 patients were selected for the development set; 142 lesion from 71 patients were chosen for the evaluation set.
- The data include various liver metastatic lesions derived from different primary sites showing melanoma, breast cancer, colorectal cancer, and pancreatic cancer
- For each lesion, two 2D images (portal phase and non contrast CT) were available



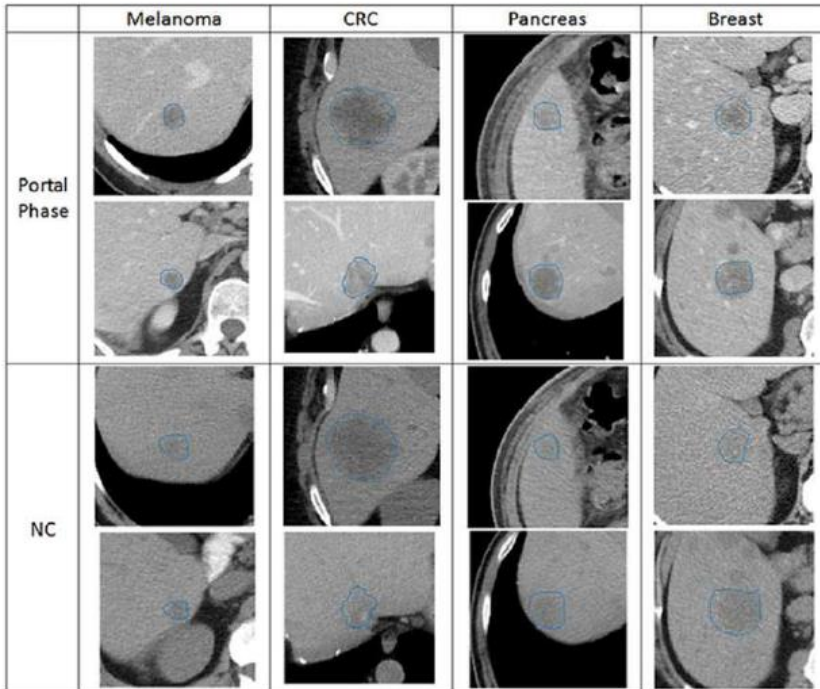
In a multicategory classification task, into the four different primary sites, the first expert achieved a classification accuracy of **42%** and the second expert **33%**

| Features | Top-1 ACC | Top-2 ACC | Top-3 ACC |
|-------------------------|-----------|-----------|-----------|
| Texture | 0.56 | 0.66 | 0.90 |
| CNN low-layer selection | 0.50 | 0.66 | 0.90 |

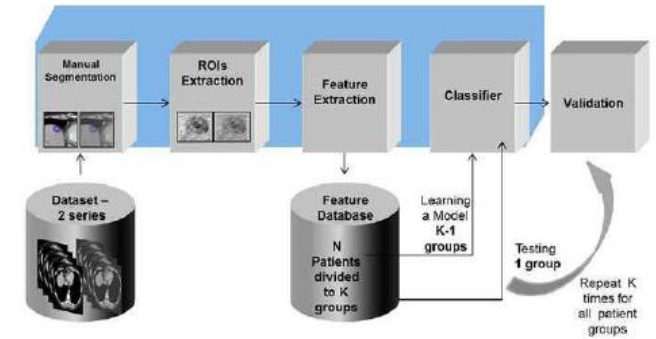
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In a multcategory classification task, into the four different primary sites, the first expert achieved a classification accuracy of **42%** and the second expert **33%**

TABLE 4. Top-1, Top-2, and Top-3 Accuracy Results Comparison on the Evaluation Set Using Texture Features, Features Extracted From the CNN, and Age and Gender Information

| Features | Top-1 ACC | Top-2 ACC | Top-3 ACC |
|--------------------------------------|-----------|-----------|-----------|
| Age and gender | 0.54 | 0.76 | 0.94 |
| Texture, age, and gender | 0.61 | 0.81 | 0.94 |
| CNN low selection and age and gender | 0.56 | 0.83 | 0.99 |

Radiomics-Response Prediction



Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad



Radiomics diagnosed histopathological growth pattern in prediction of response and 1-year progression free survival for colorectal liver metastases patients treated with bevacizumab containing chemotherapy

- 119 affected by liver metastases in CRC treated with bevacizumab
- Manually 3D segmentation on non-contrast CT phase
- Radiomics model designed to identify histopathologic growth pattern
- To predict early response
- To predict 1-year PFS

Radiomics in early response:

- AUC 0.707 per-lesion, AUC 0.720 per-patient

Radiomics 1-year PFS:

- Was the only independent predictor of 1-year PFS

Univariable and Multivariable Cox Proportional Hazards Models for 1-Year Progression-Free Survival.

| Covariate | Univariable analysis | | Multivariable analysis | |
|----------------------|------------------------|---------|------------------------|---------|
| | HR (95% CI) | P value | HR (95% CI) | P value |
| RAD_HGP | 0.339 (0.176–0.655) | 0.001 | 0.396 (0.195–0.804) | 0.010 |
| ER_PVP | 0.561 (0.314–1.001) | 0.050 | | |
| Liver resection | 0.247 (0.060–0.918) | 0.053 | | |
| Morphologic response | 0.268 (0.268–0.846) | 0.011 | 0.676 (0.365–1.253) | 0.214 |

Wei S I et al., EJR 2021

histopathologic growth pattern (HGP)



Radiomics-Response Prediction

LIVER METS

JNCI J Natl Cancer Inst (2020) 112(9): djaa017

doi: 10.1093/jnci/djaa017
 First published online February 4, 2020
 Article

| Analysis | Anti-EGFR treatment | | No anti-EGFR treatment | |
|--------------------|----------------------|----------------------|------------------------|---------------------|
| | FOLFIRI + cetuximab | | FOLFIRI only | |
| | mCRC | | mCRC | |
| | CRC-FC ^{HQ} | CRC-FC ^{SD} | CRC-F ^{HQ} | CRC-F ^{SD} |
| Reference standard | OS | OS | OS | OS |
| No. patients | | | | |
| Total | 116 | 186 | 129 | 236 |
| Training | 78 | 124 | 78 | 159 |
| Sensitive | 48 | 71 | 42 | 85 |
| Resistant | 30 | 53 | 36 | 74 |
| Validation | 38 | 62 | 51 | 78 |
| | | | | 42 |
| | | | | 36 |

Random Forest
 Shape SI4
 LoG Z Entropy
 GTDM Contrast
 LoG X Entropy

Radiomics Response Signature for Identification of Metastatic Colorectal Cancer Sensitive to Therapies Targeting EGFR Pathway

Radiomics-derived support tools could give clinicians an early prediction of the success of treatment with FC using conventional standard-of-care CT scans

- 667 metastases
- Segmentation
- 3499 features
- To predict tumor sensitivities to CHT

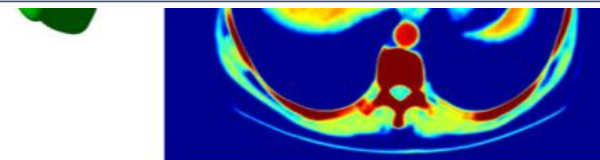
Performance

| | OS >17.7 mo | OS >17.7 mo | OS >17.7 mo | OS >17.7 mo |
|-------------------|------------------------------|------------------------------|------------------------------|------------------------------|
| Tumor sensitivity | | | | |
| AUC, training | 0.83 (95% CI = 0.75 to 0.95) | 0.84 (95% CI = 0.76 to 0.89) | 0.75 (95% CI = 0.63 to 0.85) | 0.75 (95% CI = 0.67 to 0.82) |
| AUC, validation | 0.80 (95% CI = 0.69 to 0.94) | 0.72 (95% CI = 0.59 to 0.83) | 0.59 (95% CI = 0.44 to 0.72) | 0.55 (95% CI = 0.43 to 0.66) |

Association with OS

| Cox regression | | | | |
|----------------|------------------------------|----------------------------|---------------------------|----------------------------|
| Hazard ratio | 44.3 (95% CI = 6.4 to 307.7) | 6.5 (95% CI = 1.8 to 23.6) | 1.9 (95% CI = 0.4 to 8.4) | 0.96 (95% CI = 0.2 to 4.3) |
| Death | 31/38 | 53/62 | 42/51 | 69/78 |
| P | .0001 | .005 | .43 | .96 |

Dercle L et al., JNCI 2020



Radiomics-Response Prediction

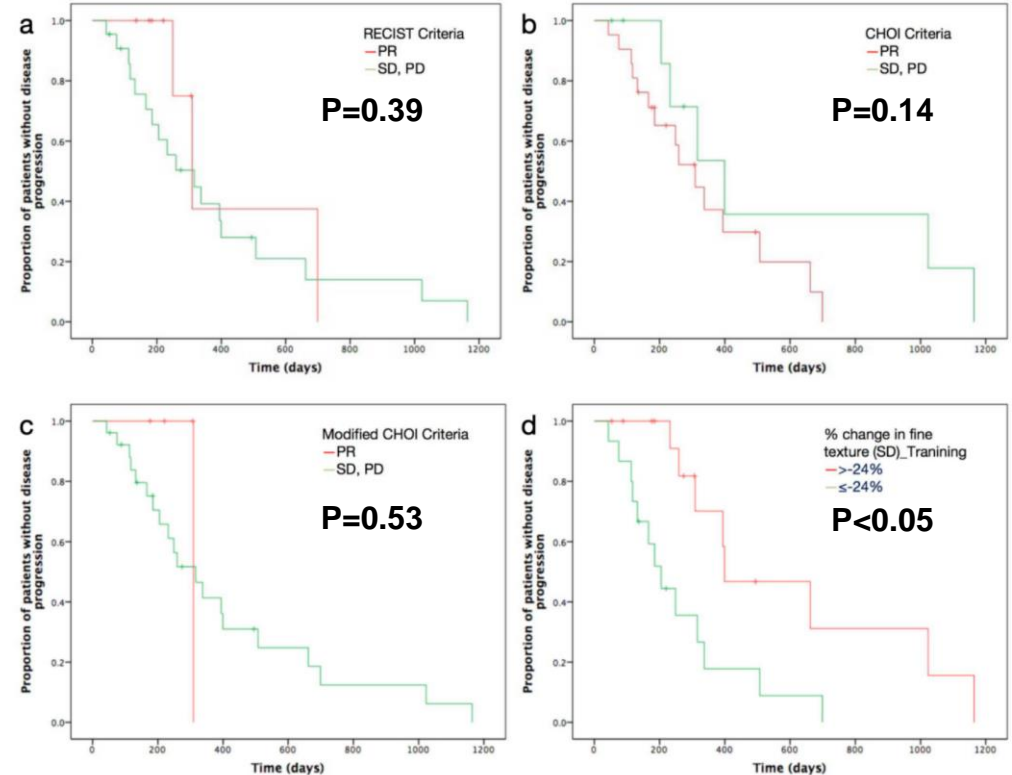
Article

Assessment of Response to Chemotherapy in Pancreatic Cancer with Liver Metastasis: CT Texture as a Predictive Biomarker

AIM: To test CT texture of metastatic in comparison with RECIST 1.1, Choi and modified Choi criteria in evaluating treatment and determining time to progression (TTP) in metastatic PDAC

5. Conclusions

Our findings indicated that the existing assessment criteria, including RECIST 1.1, Choi and modified Choi, were not sufficient for the evaluation of tumor response to treatment. We found that the percentage change in texture SD of liver metastatic lesions derived from contrast-enhanced CT texture analysis, might better predict tumor response and TTP in pancreatic patients with liver metastasis undergoing chemotherapy. Therefore, CT texture was proved to be an effective assessment tool and biomarker that predicted tumor response and TTP in a manner that was superior to traditional response criteria based on enhancement change, size change, or both.



Cox regression analysis showed:

- percentage change in SD was an independent predictor of TTP ($p = 0.016$)
- confirmed in the validation cohort ($p = 0.019$)

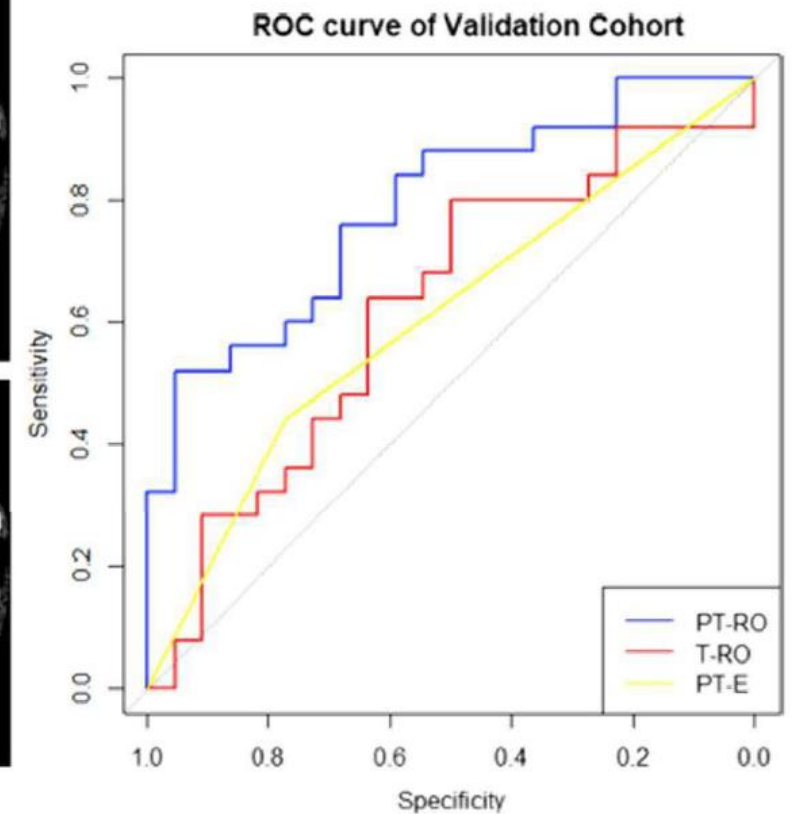
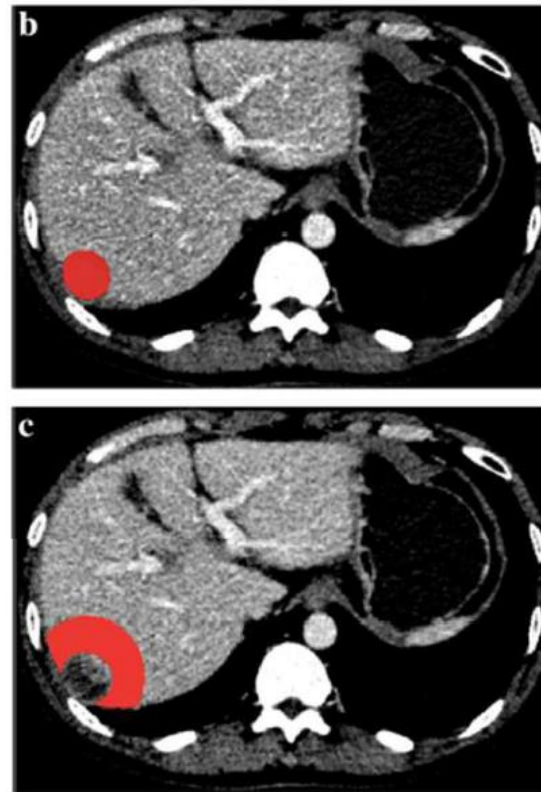
CT-based peritumoral radiomics signatures to predict early recurrence in hepatocellular carcinoma after curative tumor resection or ablation



Quan-yuan Shan¹, Hang-tong Hu¹, Shi-ting Feng², Zhen-peng Peng², Shu-ling Chen¹, Qian Zhou³, Xin Li⁴, Xiao-yan Xie¹, Ming-de Lu^{1,5}, Wei Wang^{1*} and Ming Kuang^{1,5*}

- A prediction model based on peritumoral radiomics signatures from pretreatment CT images was constructed to predict early recurrence of HCC after curative treatment.
- 156 patients randomly divided into training cohort (109 patients) and validation cohort (47 patients).
- Early recurrence was defined as the presence of new intrahepatic lesions or metastasis with typical imaging features of HCC, or atypical findings with histopathological confirmation within 2 years after curative resection or ablation of HCC.
- A region of interest (ROI) was manually delineated around the lesion for tumoral radiomics (T-RO) feature extraction, and another ROI was outlined with an additional 2 cm peritumoral area for peritumoral radiomics (PT-RO) feature extraction.
- The T-RO and PT-RO models were constructed using LASSO logistic regression and compared to the peritumoral Enhancement (PT-E) detected by a radiologist.

| Models | AUC | | cfNRI | | | IDI | | PPV | | NPV | |
|--------|-------------------|--------|--------|--------|--------|------|--------|------|--------|------|------|
| | AUC [95%CI] | P | cfNRI+ | cfNRI- | P | IDI | P | PPV | P | NPV | P |
| PT-RO | 0.79 [0.66, 0.92] | - | - | - | - | - | - | 0.93 | - | 0.64 | - |
| T-RO | 0.62 [0.46, 0.79] | < 0.01 | -0.47 | -0.32 | < 0.01 | 0.22 | < 0.01 | 0.63 | < 0.01 | 0.65 | 0.92 |
| PT-E | 0.61 [0.47, 0.74] | < 0.01 | -0.24 | -0.41 | 0.02 | 0.20 | 0.01 | 0.69 | < 0.01 | 0.55 | 0.38 |



umor. A region of interest (ROI) was manually delineated around the lesion for tumoral radiomics (T-RO) feature extraction, and another ROI was outlined with an additional 2 cm peritumoral area for peritumoral radiomics (PT-

Radiomics and CCA

| First author [Ref.] | Year | Images | Methods | Subjects, Purpose <i>n</i> | AUC |
|---------------------------|------|--------|-------------------------------------|---|--------|
| Matake et al. [104] | 2006 | CECT | ANN | 120 To evaluate the performance of ANN for differential diagnosis of hepatic masses, including CCA | 0.961 |
| Logeswaran [25] | 2009 | MRCP | MLP | 648 To differentiate images with CCA from those without | - |
| Pattanapairoj et al. [26] | 2015 | No | C4.5, ANN | 85 To improve the diagnostic power of serum markers using C4.5 and ANN | - |
| Sadot et al. [27] | 2015 | CECT | Multiple linear regression analysis | 56 To investigate associations between imaging features of CCA and texture analysis | - |
| Liang et al. [28] | 2018 | CECT | LASSO | 209 To develop a novel radiomics nomogram for predicting ER of ICC | 0.90 |
| Shao et al. [105] | 2018 | No | BP-ANN | 288 To predict early occlusion of bilateral plastic stent placement for inoperable HCC | 0.9648 |
| Ji et al. [106] | 2019 | CECT | LASSO | 103 To develop a radiomics model for predicting LNM of ICC and to determine its prognostic value | 0.9244 |
| Ji et al. [107] | 2019 | CECT | LASSO | 247 To evaluate a radiomics model for predicting LNM in BTCs and to determine its prognostic value | 0.81 |
| Xu et al. [108] | 2019 | MRI | SVM | 148 To develop a prediction model for preoperative LNM in ICC patients | 0.870 |
| Peng et al. [109] | 2019 | US | LASSO, SVM | 128 To develop radiomics signatures based on US to assess the biological behaviors of ICC | 0.930 |
| Yang et al. [110] | 2020 | MRI | Random forest | 100 To evaluate diagnostic performance of radiomics models of MRI in the detection of DD and LNM of ECC | 0.90 |

Prediction for early recurrence of intrahepatic mass-forming cholangiocarcinoma: quantitative magnetic resonance imaging combined with prognostic immunohistochemical markers

Li Zhao¹, Xiaohong Ma¹, Meng Liang¹, Dengfeng Li¹, Peiqing Ma¹, Sicong Wang¹, Zhiyuan Wu¹ and Xinming Zhao^{1*}



Research Paper

2019; 9(18): 5374-5385. doi:10.21515/therno.34149

A radiomics approach based on support vector machine using MR images for preoperative lymph node status evaluation in intrahepatic cholangiocarcinoma

Lei Xu^{1,2*}, Pengfei Yang^{1,2,3*}, Wenjie Liang⁴, Weihai Liu⁴, Weigen Wang⁵, Chen Luo^{4,5}, Jing Wang^{4,5}, Zhiyi Peng⁶, Lei Xing⁷, Mi Huang⁸, Shusen Zheng⁹, Tianye Niu^{1,2,3*}



ORIGINAL RESEARCH
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Novel Nomogram for Preoperative Prediction of Early Recurrence in Intrahepatic Cholangiocarcinoma

Wenjie Liang^{1,2*}, Lei Xu^{1,2,3*}, Pengfei Yang^{1,2,3*}, Lile Zhang^{1,2,3}, Dalong Wan¹, Qiang Huang¹, Tianye Niu^{1,2,3*} and Feng Chen^{1*}



RESEARCH ARTICLE

Cholangiocarcinoma: Correlation between Molecular Profiling and Imaging Phenotypes

Eran Sadot¹, Amber L. Simpson^{1,2}, Richard K. G. Do², Mithat Gonen², Jinru Shia³, Peter J. Allen¹, Michael I. D'Angelica¹, Ronald P. DeMatteo¹, T. Peter Kingham¹, William R. Jarnagin^{1*}

European Radiology (2019) 29:3725–3735
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HEPATOBIILIARY-PANCREAS

A radiomics approach to predict lymph node metastasis and clinical outcome of intrahepatic cholangiocarcinoma

Gu-Wei Ji^{1,2}, Fei-Peng Zhu³, Yu-Dong Zhang³, Xi-Sheng Liu³, Fei-Yun Wu³, Ke Wang^{1,2}, Yong-Xiang Xia^{1,2}, Yao-Dong Zhang^{1,2}, Wang-Jie Jiang^{1,2}, Xiang-Cheng Li^{1,2}, Xue-Hao Wang^{1,2}

Yang et al. Oncology 2021

Radiomics and CCA

European Radiology
<https://doi.org/10.1007/s00330-020-07250-5>

COMPUTED TOMOGRAPHY



Radiomics using CT images for preoperative prediction of futile resection in intrahepatic cholangiocarcinoma

Hongpeng Chu¹ · Zelong Liu² · Wen Liang³ · Qian Zhou⁴ · Ying Zhang¹ · Kai Lei¹ · Mimi Tang⁵ · Yiheng Cao⁴ · Shuling Chen² · Sui Peng^{4,6} · Ming Kuang^{1,2}

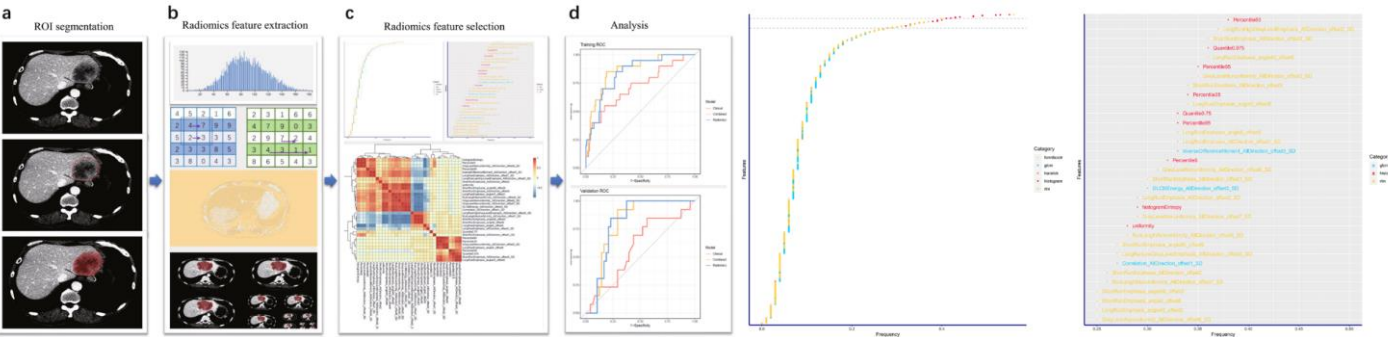


Table 2 Performance of three prediction models: the clinical model, the radiomics model, and the combined model

| | Group | Radiomics | Clinical | Combined model |
|----------------------|------------|----------------------|----------------------|----------------------|
| AUC (95% CI) | training | 0.838 (0.751, 0.924) | 0.716 (0.582, 0.849) | 0.864 (0.781, 0.947) |
| | Validation | 0.804 (0.697, 0.912) | 0.59 (0.415, 0.765) | 0.8 (0.69, 0.909) |
| Accuracy (95% CI) | training | 0.739 (0.659, 0.809) | 0.683 (0.6, 0.759) | 0.817 (0.743, 0.877) |
| | Validation | 0.787 (0.663, 0.881) | 0.59 (0.457, 0.714) | 0.754 (0.627, 0.855) |
| Sensitivity (95% CI) | training | 0.85 (0.621, 0.968) | 0.65 (0.408, 0.846) | 0.85 (0.621, 0.968) |
| | Validation | 0.846 (0.546, 0.981) | 0.692 (0.386, 0.909) | 0.923 (0.64, 0.998) |
| Specificity (95% CI) | training | 0.721 (0.633, 0.799) | 0.689 (0.598, 0.769) | 0.811 (0.731, 0.877) |
| | Validation | 0.771 (0.627, 0.88) | 0.562 (0.412, 0.705) | 0.708 (0.559, 0.83) |
| NPV (95% CI) | training | 0.967 (0.907, 0.993) | 0.923 (0.848, 0.969) | 0.971 (0.916, 0.994) |
| | Validation | 0.949 (0.827, 0.994) | 0.871 (0.702, 0.964) | 0.971 (0.851, 0.999) |
| PPV (95% CI) | training | 0.333 (0.208, 0.479) | 0.255 (0.143, 0.396) | 0.425 (0.27, 0.591) |
| | Validation | 0.5 (0.282, 0.718) | 0.3 (0.147, 0.494) | 0.462 (0.266, 0.666) |

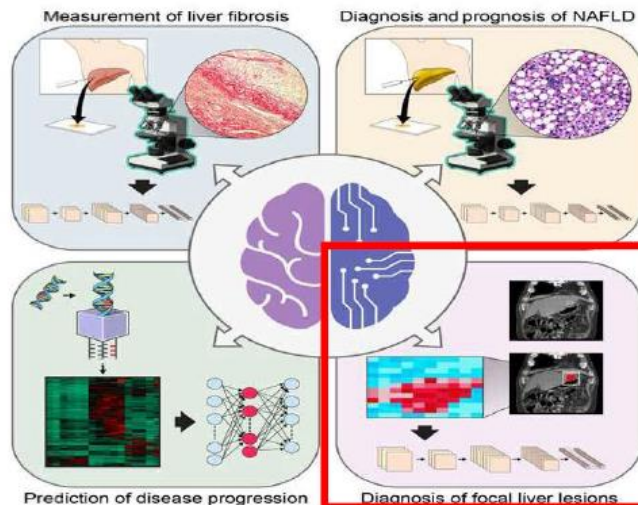
Table 1 Baseline clinical characteristics of the training and validation cohort

| Variables | Levels | Total | Training | Validation | p value |
|------------------------------------|-----------|------------------------|------------------------|------------------------|---------|
| n | | 203 | 142 | 61 | |
| Age, years | | 58.00 [51.00, 67.00] | 57.00 [50.00, 66.00] | 59.00 [54.00, 68.00] | 0.169 |
| Gender | Male | 105 (51.7) | 71 (50.0) | 34 (55.7) | 0.551 |
| | Female | 98 (48.3) | 71 (50.0) | 27 (44.3) | |
| History of previous cholelithiasis | No | 174 (85.7) | 120 (84.5) | 54 (88.5) | 0.595 |
| | Yes | 29 (14.3) | 22 (15.5) | 7 (11.5) | |
| Liver cirrhosis | No | 201 (99.0) | 140 (98.6) | 61 (100.0) | 1.000 |
| | Yes | 2 (1.0) | 2 (1.4) | 0 (0.0) | |
| History of previous liver surgery | No | 192 (94.6) | 134 (94.4) | 58 (95.1) | 1.000 |
| | Yes | 11 (5.4) | 8 (5.6) | 3 (4.9) | |
| CT reports | | | | | |
| Tumor size, mm, mean ± SD | | 63.4 ± 27.2 | 64.60 ± 27.56 | 60.61 ± 26.19 | 0.338 |
| Number of tumor | 0* | 2 (1.0) | 1 (0.7) | 1 (1.6) | 0.811 |
| | 1 | 160 (78.8) | 114 (80.3) | 46 (75.4) | |
| | 2 | 13 (6.4) | 8 (5.6) | 5 (8.2) | |
| | 3 | 3 (1.5) | 2 (1.4) | 1 (1.6) | |
| | > 3 | 25 (12.3) | 17 (12.0) | 8 (13.1) | |
| | Not sure | 32 (15.8) | 18 (12.7) | 14 (23.0) | |
| | clear | 22 (10.8) | 15 (10.6) | 7 (11.5) | |
| Tumor boundary | obscure | 149 (73.4) | 109 (76.8) | 40 (65.6) | 0.164 |
| | clear | 54 (26.6) | 33 (23.2) | 21 (34.4) | |
| Bile duct stone | No | 148 (72.9) | 103 (72.5) | 45 (73.8) | 0.993 |
| | Yes | 55 (27.1) | 39 (27.5) | 16 (26.2) | |
| Bile duct dilatation | No | 104 (51.2) | 70 (49.3) | 34 (55.7) | 0.491 |
| | Yes | 99 (48.8) | 72 (50.7) | 27 (44.3) | |
| Bile duct invasion | No | 178 (87.7) | 124 (87.3) | 54 (88.5) | 0.995 |
| | Yes | 25 (12.3) | 18 (12.7) | 7 (11.5) | |
| Lymph node metastasis | No | 119 (58.6) | 82 (57.7) | 37 (60.7) | 0.818 |
| | Yes | 84 (41.4) | 60 (42.3) | 24 (39.3) | |
| Adjacent tissue invasion | No | 193 (95.1) | 135 (95.1) | 58 (95.1) | 1.000 |
| | Yes | 10 (4.9) | 7 (4.9) | 3 (4.9) | |
| Ascites | No | 197 (97.0) | 137 (96.5) | 60 (98.4) | 0.671 |
| | Yes | 6 (3.0) | 5 (3.5) | 1 (1.6) | |
| Cirrhosis | No | 192 (94.6) | 134 (94.4) | 58 (95.1) | 1.000 |
| | Yes | 11 (5.4) | 8 (5.6) | 3 (4.9) | |
| Splenomegaly | No | 180 (88.7) | 124 (87.3) | 56 (91.8) | 0.495 |
| | Yes | 23 (11.3) | 18 (12.7) | 5 (8.2) | |
| Time between CT and surgery | | 6 (4.00, 10.00) | 7 [4.00, 10.75] | 6 [3.00, 8.00] | 0.194 |
| Laboratory data | | | | | |
| HbsAg | Positive | 160 (78.8) | 117 (82.4) | 43 (70.5) | 0.086 |
| | Negative | 43 (21.2) | 25 (17.6) | 18 (29.5) | |
| WBC, 10 ⁹ /L | | 7.33 [5.86, 9.14] | 7.41 [6.00, 9.12] | 7.18 [5.40, 9.16] | 0.458 |
| NLR | | 2.62 [1.87, 3.84] | 2.72 [2.03, 4.07] | 2.49 [1.67, 3.40] | 0.045 |
| Hb, g/L | | 40.10 [36.65, 42.90] | 39.95 [36.50, 42.57] | 40.50 [37.40, 43.30] | 0.462 |
| Total bilirubin, μmol/L | | 12.10 [9.30, 17.00] | 12.15 [9.40, 16.68] | 12.10 [9.20, 18.80] | 0.953 |
| Direct bilirubin, μmol/L | | 3.00 [2.10, 4.70] | 2.90 [2.00, 4.59] | 3.50 [2.20, 5.00] | 0.193 |
| ALT, U/L | | 25.00 [16.50, 47.50] | 24.00 [15.25, 43.50] | 28.00 [19.40, 60.00] | 0.081 |
| AST, U/L | | 28.00 [23.90, 42.35] | 28.00 [22.25, 42.75] | 29.00 [25.00, 41.30] | 0.541 |
| PT, s | | 11.90 [11.40, 12.60] | 11.90 [11.40, 12.80] | 11.80 [11.40, 12.40] | 0.275 |
| AFP, μg/L | | 3.49 [2.42, 5.63] | 3.20 [2.34, 5.39] | 3.98 [2.71, 7.21] | 0.038 |
| CEA, ng/mL | | 3.23 [1.95, 9.83] | 3.16 [1.81, 10.03] | 3.25 [2.03, 8.45] | 0.812 |
| CA19-9, U/mL | | 64.57 [14.03, 1020.23] | 78.39 [14.46, 1009.90] | 40.86 [13.81, 1779.80] | 0.631 |
| Surgical outcome | Futile | | | | |
| | No | 170 (83.7) | 122 (85.9) | 48 (78.7) | 0.201 |
| Yes | 33 (16.3) | 20 (14.1) | 13 (21.3) | | |

AI and Liver Cancer

Detection/Diagnosis of focal liver lesions

| Task | Type | Accuracy | Ref |
|---|---|----------|--------------------------------|
| Predicting the primary origin of liver metastasis | Radiomics and Deep learning based on CT | 56% | <i>Ben Cohen A, 2017</i> |
| Detecting liver new tumors | Deep learning based on CT | 86% | <i>Vivanti R, 2017;</i> |
| Detecting focal liver lesions | Deep learning based on ultrasound | 89% | <i>Tiyarattanachai T, 2021</i> |
| Detecting liver tumors | Deep learning based on MRI | 90% | <i>Kim J, 2020</i> |
| Detecting and distinguishing different focal liver lesions. | Deep learning based on ultrasound | 97.2% | <i>Hassan TM, 2017</i> |
| Detecting metastatic liver malignancy | Deep learning based on PET/CT | 90.5% | <i>Preis O, 2011</i> |
| Evaluating focal liver lesion | Deep learning based on MRI | 92% | <i>Hamm C, 2019</i> |
| Evaluating focal liver lesion | Deep learning based on CT | 84% | <i>Yasaka K, 2018</i> |



Focal liver lesion **detection**

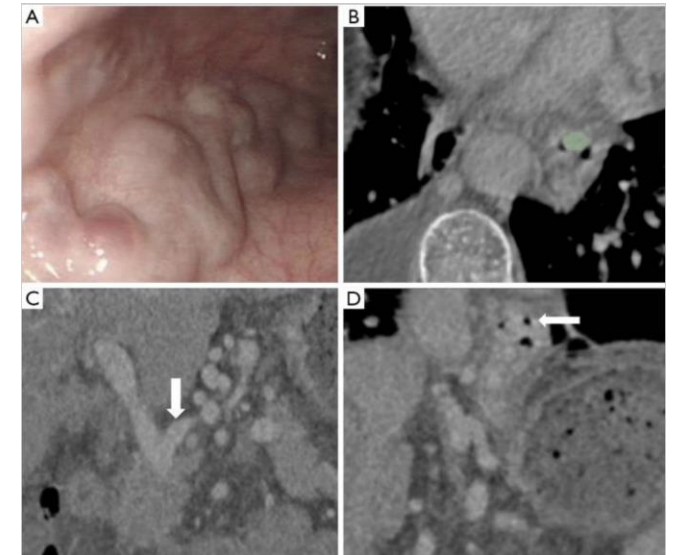
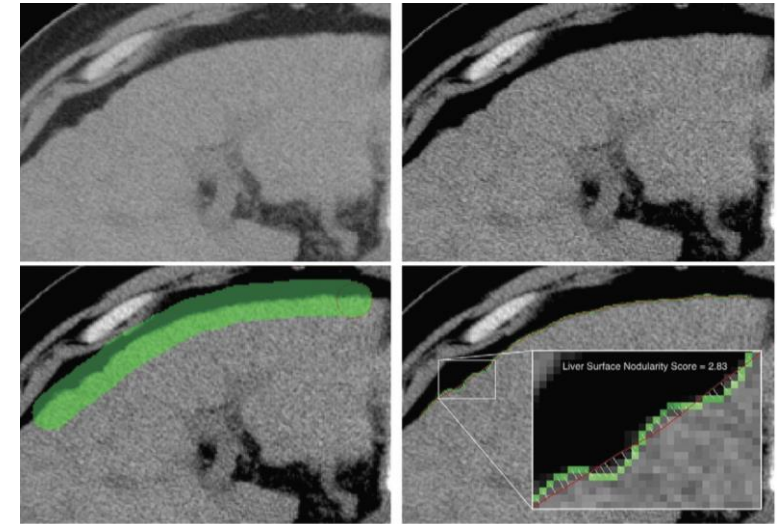
Focal liver lesion **evaluation**



CLINICAL IMPACT ON LIVER IMAGING

DIFFUSE LIVER DISEASES

- Non-contrast-enhanced CT texture analysis predicted **non-alcoholic steatohepatitis**
- Deep learning system allows for accurate staging of liver **fibrosis** by using enhanced CT images
- Diagnose clinically significant **portal hypertension** and predict **esophageal varices severity**



Liu F. et al. E. bio. Medicine 2018

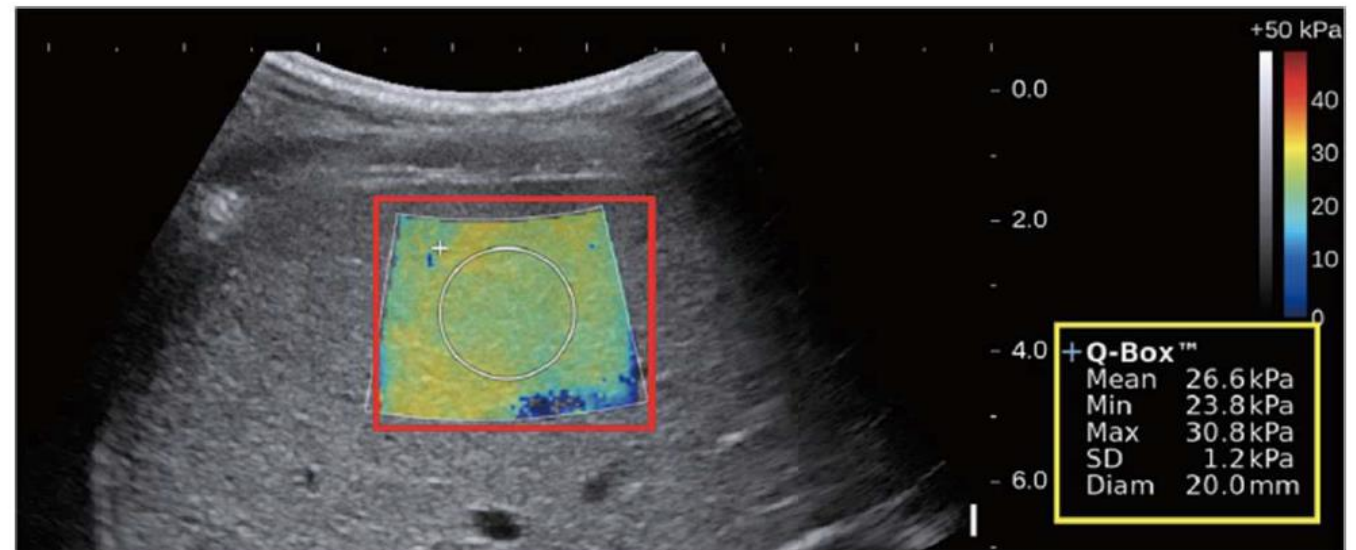
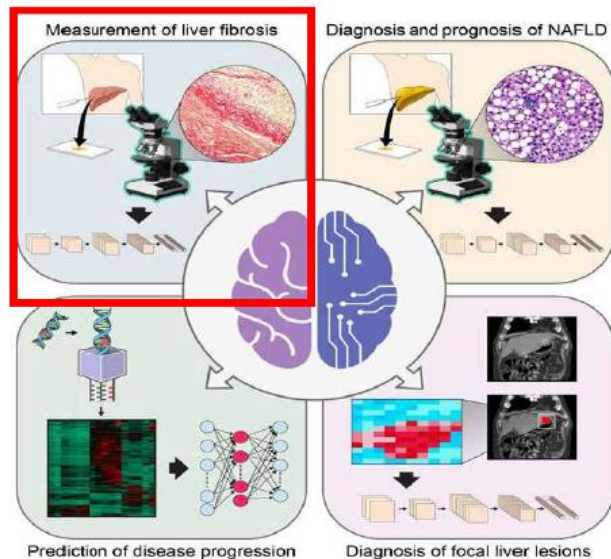
Wan s. et al. Ann. Transl. Med. 2020



AI and Liver Fibrosis

Measurement of liver fibrosis

| Type | AUC Cirrhosis | AUC Advanced fibrosis | AUC significant fibrosis | Ref |
|--|---------------|-----------------------|--------------------------|-----------------------|
| Deep learning based on contrast enhanced MRI | 0.84 | 0.84 | 0.85 | <i>Yasaka K, 2017</i> |
| Deep learning based on contrast enhanced CT | 0.95 | 0.97 | 0.96 | <i>Choi K J, 2018</i> |
| Deep learning based on shear wave elastography | 0.97 | 0.98 | 0.85 | <i>Wang K, 2019</i> |
| Deep learning based on ultrasound | 0.90 | - | 0.90 | <i>Lee J H, 2019</i> |
| Radiomics based on contrast enhanced MRI | 0.87 | 0.88 | 0.91 | <i>Park H J, 2019</i> |



Noninvasive Diagnosis of Nonalcoholic Fatty Liver Disease and Quantification of Liver Fat with Radiofrequency Ultrasound Data Using One-dimensional Convolutional Neural Networks

Aiguo Han, PhD • Michal Byra, PhD • Elbatmy Heba, MD¹ • Michael P. Andre, PhD • John W. Erdman, Jr, PhD • Rohit Loomba, MD, MHSc • Claude B. Sirlin, MD • William D. O'Brien, Jr, PhD

- Raw radiofrequency ultrasound contain more information than do gray-scale B-mode images because information is lost or altered when B-mode images are generated from the raw data
- A one-dimensional CNNs for NAFLD diagnosis and liver fat quantification was developed, using MRI PDFF as the reference standard.
- 204 participants were prospectively enrolled, equally divided into training (n = 102) and test (n = 102) groups by using stratified randomization NAFLD was defined as MRI PDFF of 5% or greater.
- Two one-dimensional CNN algorithms were developed: a binary classifier and a fat fraction estimator. For each RF signal input, the classifier output an NAFLD classification score between 0 and 1, and the fat fraction estimator output the predicted fat fraction as a percentage.

| Performance Metrics | Input: RF without TGC |
|---------------------|-----------------------|
| Sensitivity | 97 (90, 100) [68/70] |
| Specificity | 94 (79, 99) [30/32] |
| PPV | 97 (90, 99) [68/70] |
| NPV | 94 (79, 98) [30/32] |
| Accuracy | 96 (90, 99) [98/102] |

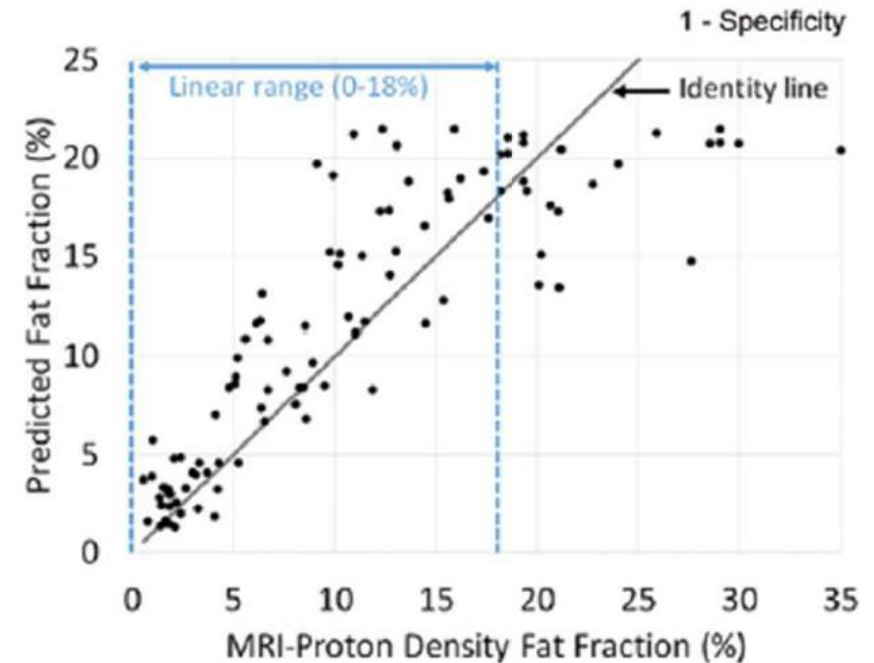
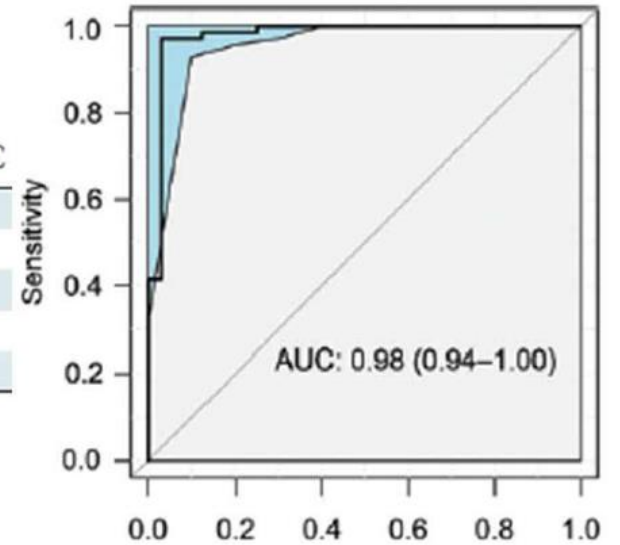


Figure 3. ROC curves of the models for predicting the stage of liver fibrosis and the grade of inflammatory activity

(a), (b) ROC curves for models built based on radiomics features of T_1W , T_2WFS , and $T_1W&T_2WFS$ images for discriminating fibrosis stage $F \geq 1$ and $F \geq 2$; (c), (d) ROC curves for models built based on radiomics features of T_1W , T_2WFS , and $T_1W&T_2WFS$ images for discriminating inflammatory activity grade $A \geq 1$ and $A \geq 2$. ROC, receiver operating characteristic.

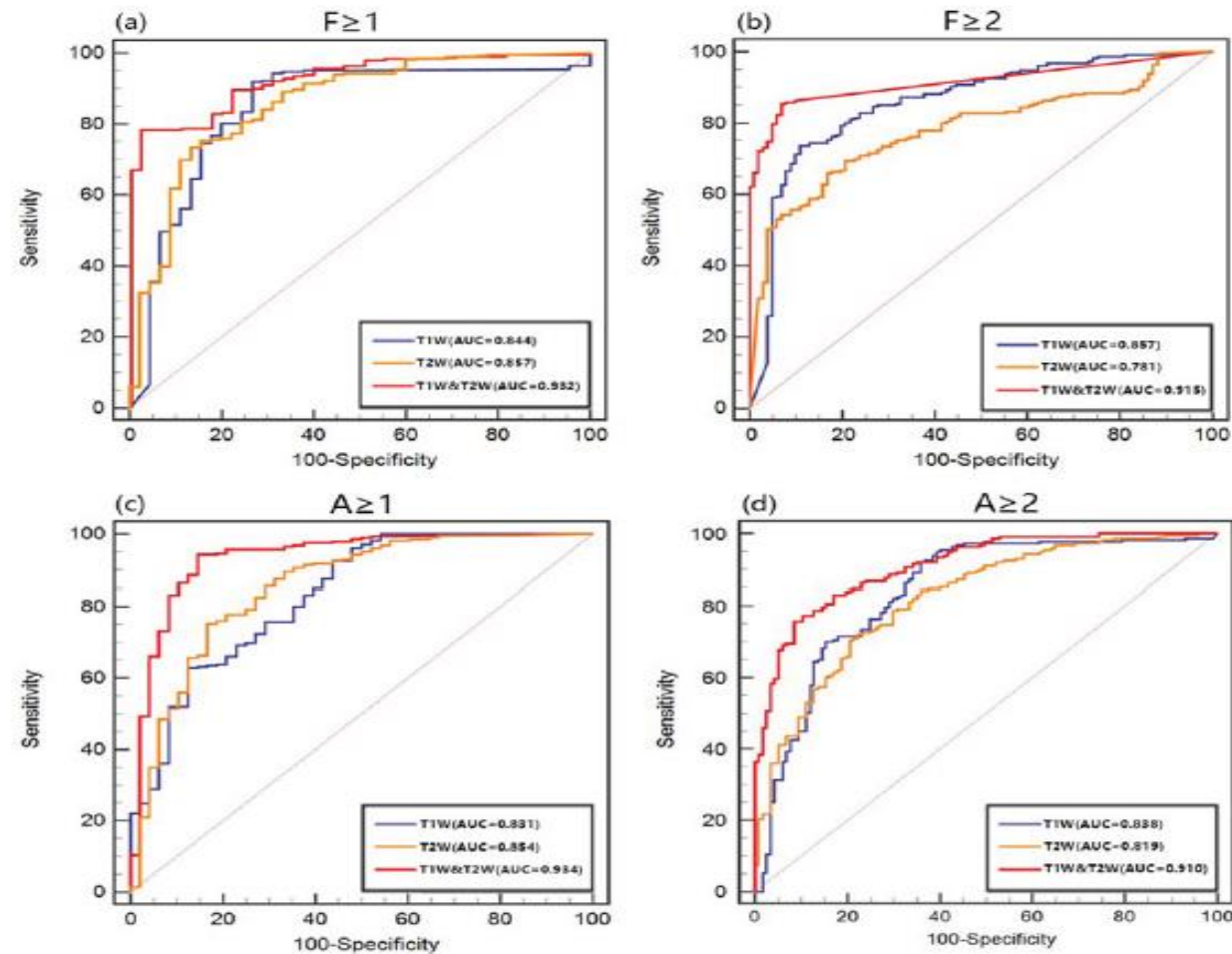


Table 2. Magnetic resonance

| Magnetic resonance sequence |
|-----------------------------|
| T_1W |
| T_2WFS |

FOV, field of view; NEX, number

| | Resolution ratio | |
|----|--------------------|--|
| nm | 0.74×0.74 | |
| nm | 0.74×0.74 | |

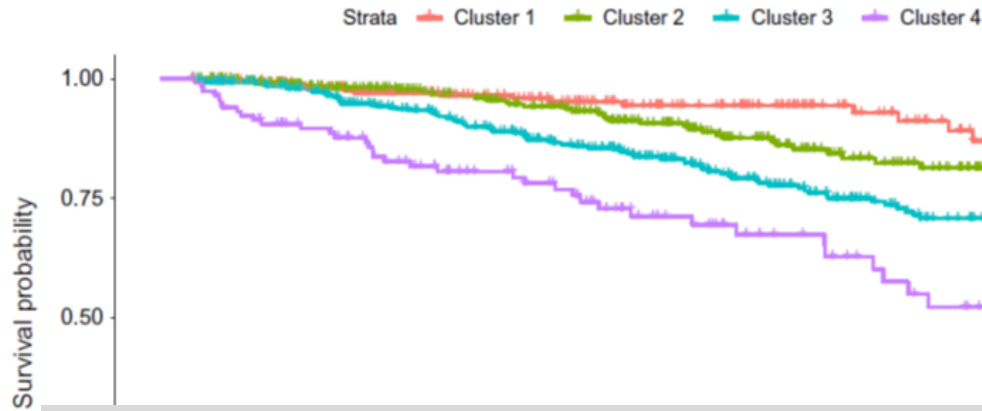


FIGURE 3 Transplant-free survival of patients by cluster membership in the validation set. The survival function within each cluster of patients with primary biliary cholangitis in the validation set was estimated using the Kaplan–Meier method and compared using the log-rank test

Conclusions: Unsupervised ML identified four novel groups of PBC patients with different phenotypes and prognosis and highlighted subtle variations of albumin within the normal range.

| Strata | Number at risk | | | |
|-----------|----------------|-----|-----|----|
| | 0 | 5 | 10 | 15 |
| Cluster 1 | 225 | 159 | 84 | 32 |
| Cluster 2 | 333 | 223 | 119 | 38 |
| Cluster 3 | 393 | 287 | 159 | 64 |
| Cluster 4 | 118 | 70 | 31 | 12 |

| Patient ID | Serum bilirubin at diagnosis (x ULN) | Serum albumin at diagnosis (x LLN) | Serum ALP at diagnosis (x ULN) |
|------------|--------------------------------------|------------------------------------|--------------------------------|
| DD | 1.00 | 1.11 | 7.45 |
| LF | 0.73 | 1.23 | 1.09 |
| PV | 1.32 | 1.11 | 2.19 |

TABLE 3 Features at diagnosis of three newly diagnosed patients with primary biliary cholangitis

Abbreviations: LLN, lower limit of normal; ULN, upper limit of normal.

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