MRO.ART, Rome, Italy

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Quantitative imaging for radiation oncologists

Evis Sala, MD, PhD, FRCR, FRCP

ARC Advanced Radiology Center

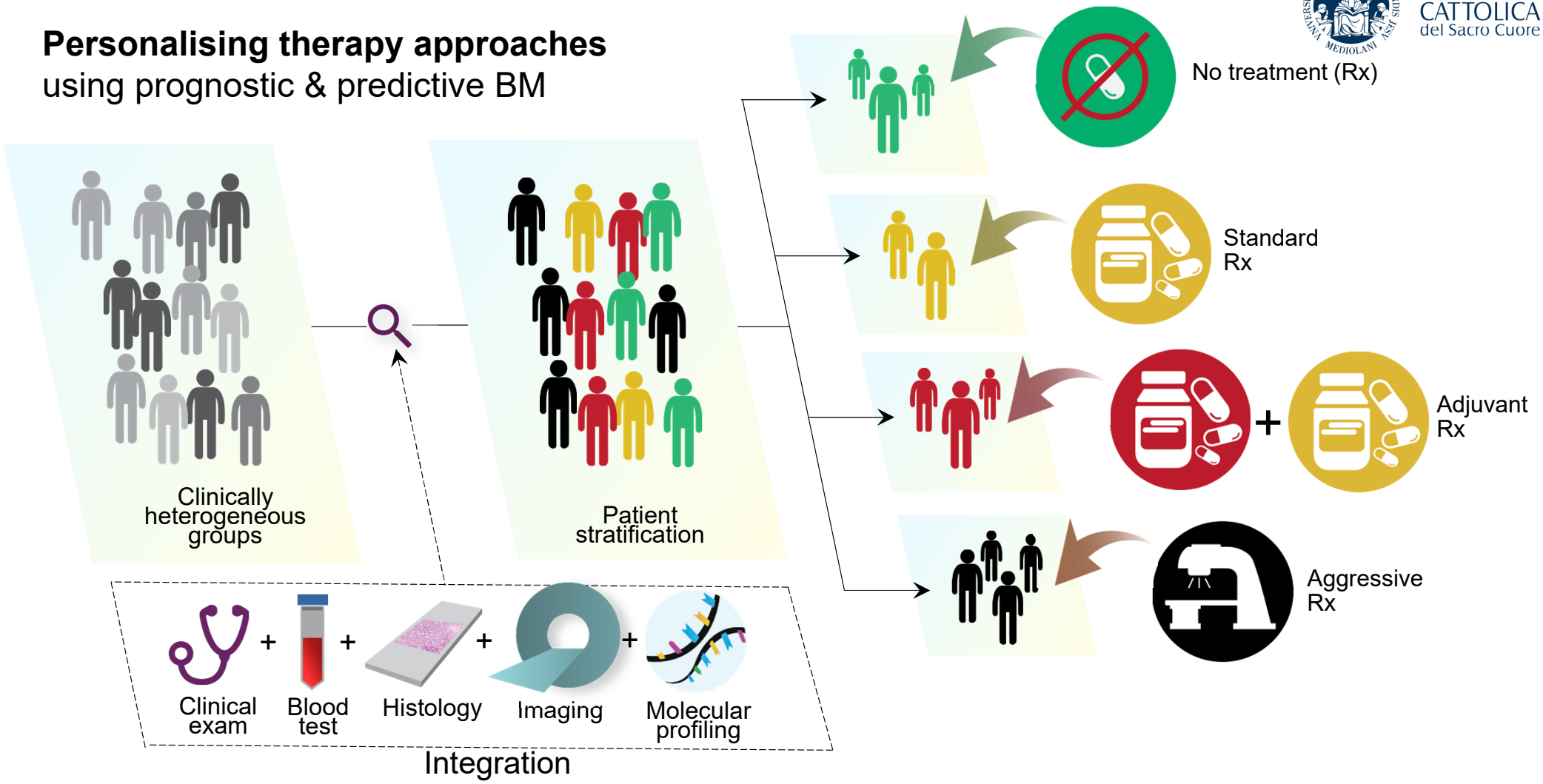
Disclosures

- Co-founder and shareholder, Lucida Medical
- Research support, GEHC, Canon
- Speaker’s bureau, GEHC, Canon

Outline

- Lesion identification and segmentation/contouring
- Clinical decision support fo treatment selection
- Assessment of treatment response
- Prediction of outcome

Personalising therapy approaches
using prognostic & predictive BM



Challenges in tumour response assessment

- RECIST is ill-suited, especially for confluent multi-site disease
  - Automated whole-volume tumour and sub tissue segmentation
- Quantification and monitoring of intra/inter-tumoural heterogeneity
  - Quantitative imaging (e.g. ADC)
  - Robust Radiomics
  - Habitat Imaging (Spatial radiomics)
  - Biological validation
- Detection of treatment resistance
  - Tumour site-level information and integration of ctDNA are needed (esp. in neoadjuvant setting)
- Multimodal and multiomics data integration for assessment of therapy response
  - AI for multi-omics data integration and modelling

Segmentation: Cervical cancer

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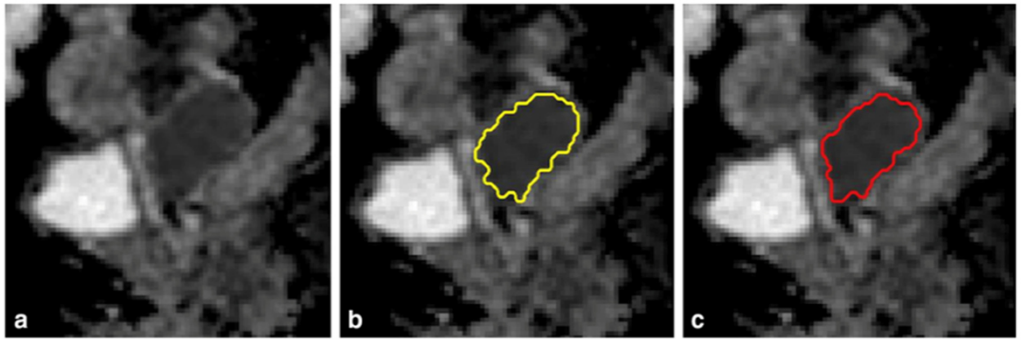
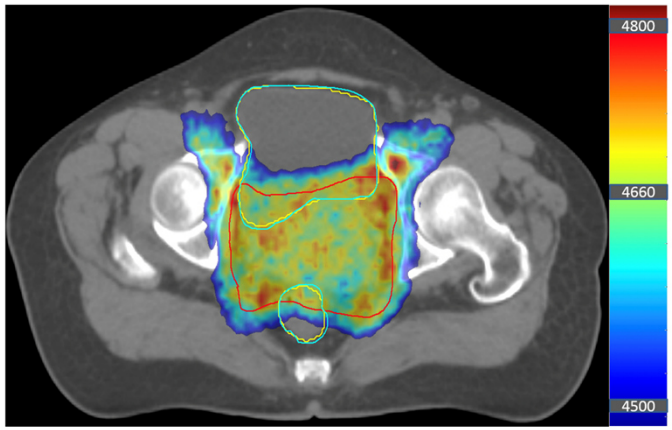
Tumour

- DL-based auto-segmentation
- 160 patients; DWI images as input
- GS: manual segmentations (9 and 11 year-experienced radiologists)
- **DSC test set: 0.82**

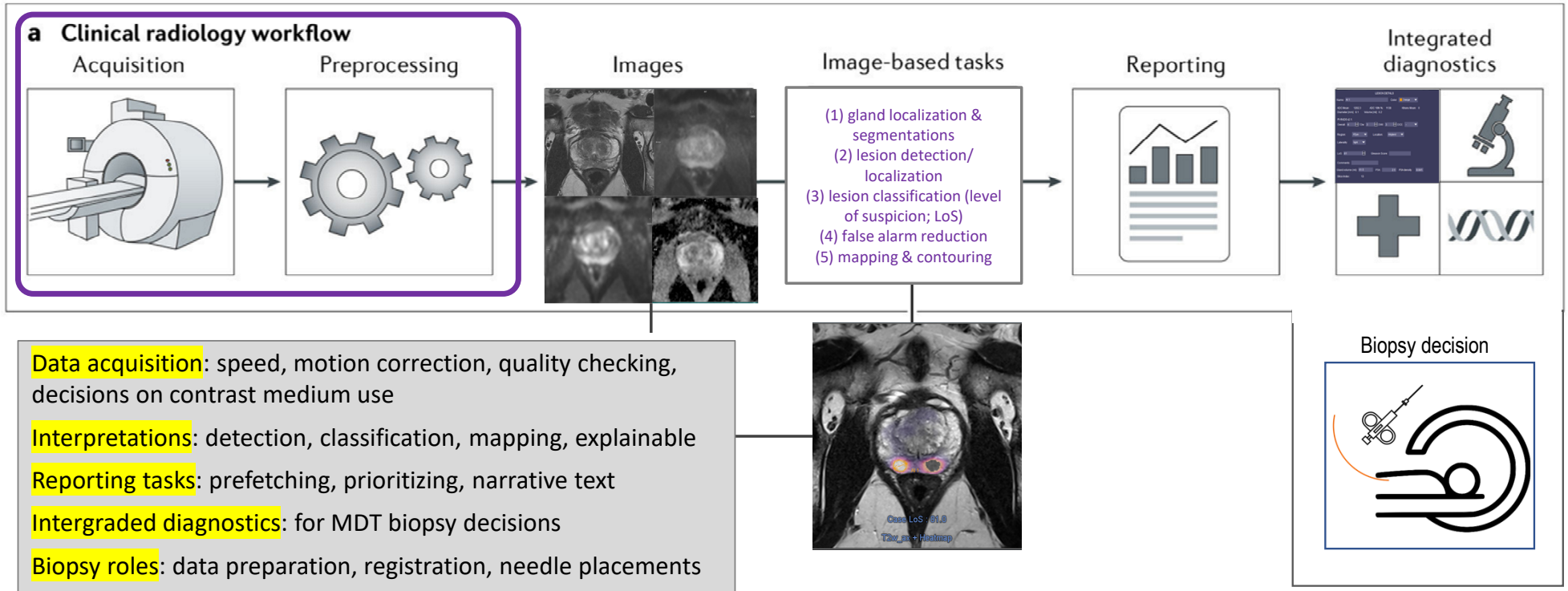


Organs at risk

- DL-based auto-segmentation for radiotherapy
- 127 patients (105 : 22)
- High similarity for bladder, femoral head, kidneys, and pelvic bone, (mean **DSC > 0.94**).



AI assistance in the MRI diagnosis workflow



Data acquisition: speed, motion correction, quality checking, decisions on contrast medium use

Interpretations: detection, classification, mapping, explainable

Reporting tasks: prefetching, prioritizing, narrative text

Intergraded diagnostics: for MDT biopsy decisions

Biopsy roles: data preparation, registration, needle placements

Pathology assessments

Monitoring: AS including the need for repeat biopsy

Mata LA, et al. Artificial Intelligence-assisted Prostate Cancer Diagnosis: Radiologic-Pathologic Correlation. Radiographics. 2021 Oct;41(6):1676-1697.

Workflow integration and automation

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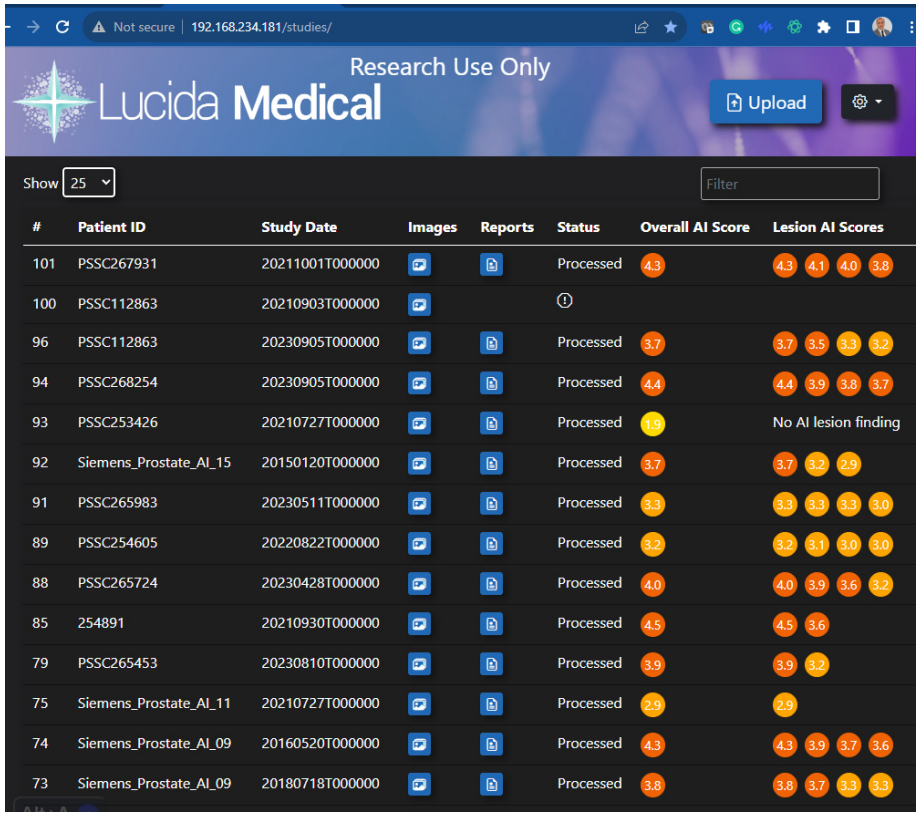
AI examples

Lucida: "semi-automated" concurrent reading for preprocessing, acceptance, and rejection. Patient & lesion prioritization. Report generation.

Siemens AI: requires radiologists to run the AI and results are accepted, rejected, or edited. Report generation. Biopsy export.

Quantib: heatmap that radiologists must segment & classify manually. Manual report.

Semi-automated concurrent reading



#	Patient ID	Study Date	Images	Reports	Status	Overall AI Score	Lesion AI Scores
101	PSSC267931	20211001T000000			Processed	4.3	4.3 4.1 4.0 3.8
100	PSSC112863	20210903T000000					
96	PSSC112863	20230905T000000			Processed	3.7	3.7 3.5 3.3 3.2
94	PSSC268254	20230905T000000			Processed	4.4	4.4 3.9 3.8 3.7
93	PSSC253426	20210727T000000			Processed	1.9	No AI lesion finding
92	Siemens_Prostate_AI_15	20150120T000000			Processed	3.7	3.7 3.2 2.9
91	PSSC265983	20230511T000000			Processed	3.3	3.3 3.3 3.3 3.0
89	PSSC254605	20220822T000000			Processed	3.2	3.2 3.1 3.0 3.0
88	PSSC265724	20230428T000000			Processed	4.0	4.0 3.9 3.6 3.2
85	254891	20210930T000000			Processed	4.5	4.5 3.6
79	PSSC265453	20230810T000000			Processed	3.9	3.9 3.2
75	Siemens_Prostate_AI_11	20210727T000000			Processed	2.9	2.9
74	Siemens_Prostate_AI_09	20160520T000000			Processed	4.3	4.3 3.9 3.7 3.6
73	Siemens_Prostate_AI_09	20180718T000000			Processed	3.8	3.8 3.7 3.3 3.3

Actionable Prostate MRI Report

Gemelli

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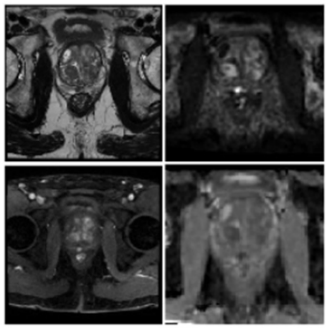
Data Esame :		**Nosografico**	
Paziente :		**Stato**	
Data nascita		**UOC :**	
Cod. Sanitario		**ULD :**	

TECNICA D'ESAME: Esame eseguito ad alto campo 3T, mediante imaging multiparametrico con sequenze T1W e T2W, DWI ed acquisizione dinamica dopo somministrazione ev di radio paramagnetico Gadoterticio 15 ml.
QUALITA' DELLE IMMAGINI: Buona. PI-QUAL score: 6.
INDICAZIONE: Rialzo PSA; PSA: 7.05 ng/mL
CONFRONTO RM: Nessuna
I REPERTI SONO STATI VALUTATI SECONDO I CRITERI PIRADS V2.1.

Reperti:
VOLUME PROSTATICO: 5.0 cm CC x 5.8 cm AP x 5.4 cm LL ; Vol = 74.41 cc; **PSA DENSITY:** 0.09 ng/mlxcc;
IPERPLASIA PROSTATICA BENIGNA: SI
PRESENZA DI ARSE EMORRAGICHE: No
LESIONE:
LESIONE # 1: Area ipointensa nella sequenza T2W che misura: 8mm.
ZONA: Periferica
LOCALIZZAZIONE: enig1endola DX, in sede Posteriore, in regione medio-ghiandolare, in settore PZpm.
CARATTERISTICHE DWI: Ipointensità in DWI con Basai valori di ADC;
CARATTERISTICHE DCE: enhancement Precoce.
CATEGORIA PI-RADS: 4

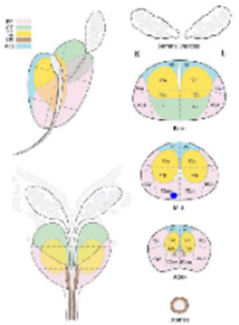
ESTENSIONE EXTRA-PROSTATICA: No
ESTENSIONE VESCICOLE SEMINALI: No
VESCICA: da sforzo.
LINFOADENOMEGALIE: No
VERSAMENTO: Si sono tracce fluide nello scavo pelvico posteriore.
LESIONI OSSEE: No
REPERTI COLLATERALI: Idrocele bilaterale.

CONCLUSIONE: Lesione #1 di 8 mm nel settore PZpm a destra, in regione medio-ghiandolare, PI-RADS 4

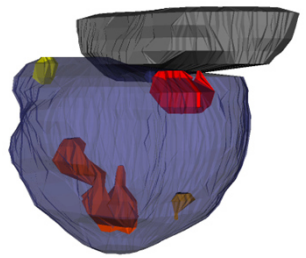


T.S.R.M.

UCRIS, il



Il Medico Radiologo



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Data nascita		UOC :	
Cod. Sanitario		ULD :	

Actionable Imaging in Prostate Cancer

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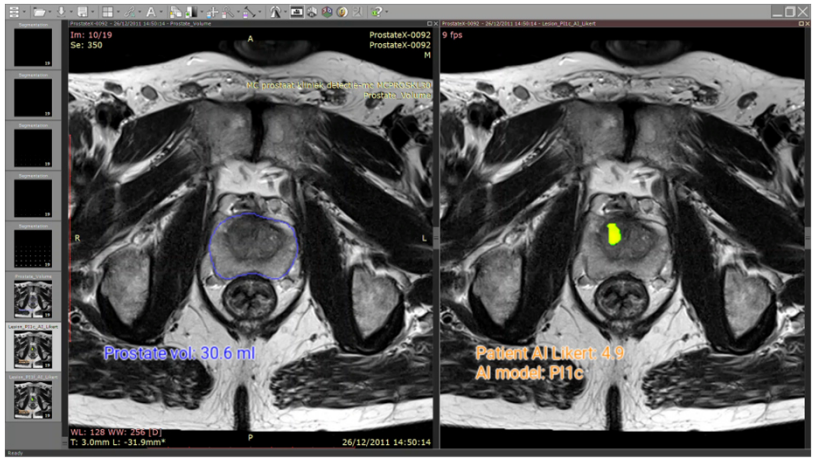
ARTIFICIAL INTELIGENCE GUIDED FOCAL THERAPY IN PROSTATE CANCER



Multi-stage AI analysis system to support prostate cancer delination

Interventional Radiotherapy (brachytherapy) for high dose delivery and organ at risk sparing

better local control of the disease
less side effects
more rapid procedures

- Tagliaferri L, Alemanno G, Fionda B et al. Multiparametric imaging guided HDR interventional radiotherapy (brachytherapy) boost in localized prostate cancer: a multidisciplinary experience. Eur Rev Med Pharmacol Sci. 2023; Article in Press
- Suchanek J et al, Multi-stage AI analysis system to support prostate cancer diagnostic imaging EuSoMII Virtual Annual Meeting, 24 October 2020

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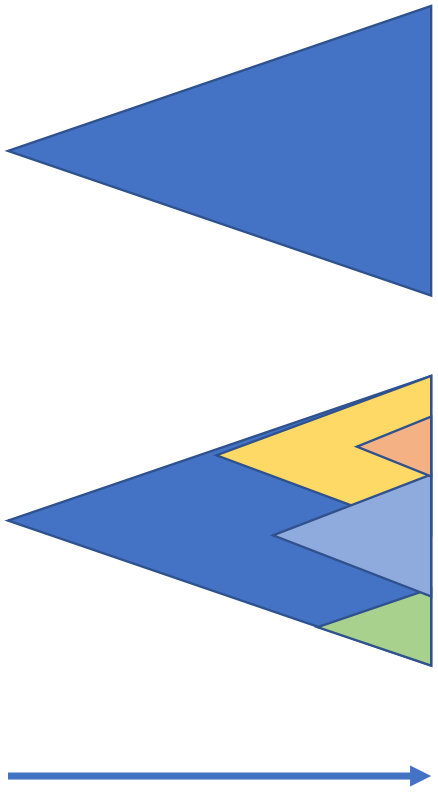
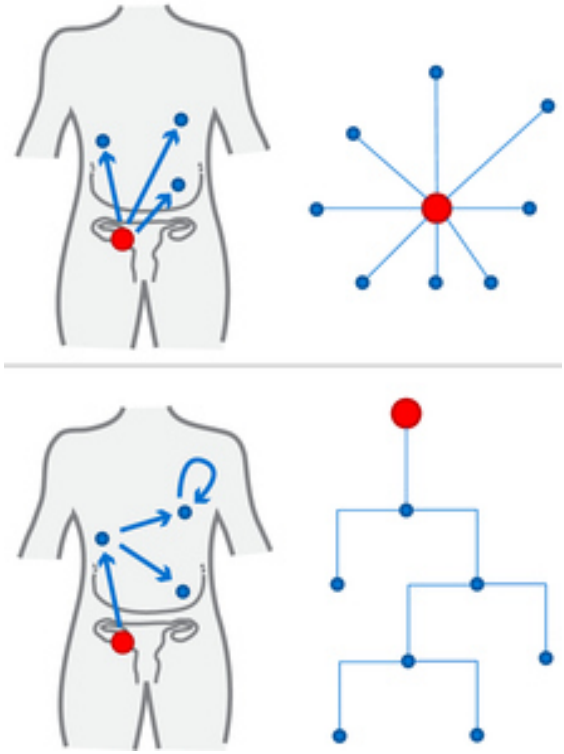
Extraordinary Heterogeneity

Between patients



Within a patient's tumour



Challenge:

- Heterogeneity within a single lesion doesn't capture the entire tumour volume TME heterogeneity which drives the treatment resistance in the metastatic setting

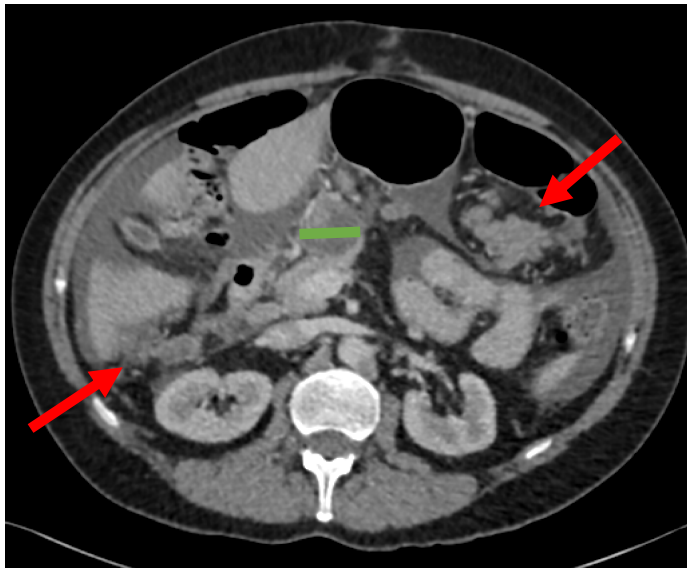
Opportunity:

- Development of new computational methods (AI & radiomics) to capture both spatial and temporal heterogeneity of the entire tumour and unravel distinct phenotypes of the TME

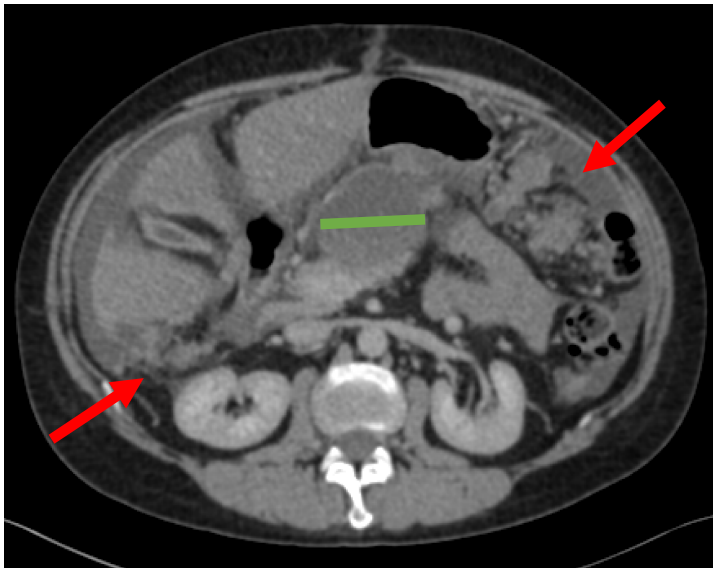
McPherson A, et al. Nat Genet 2016; Zhang K, et al. Cell 2018; Sala E, et al. Clin Radiol 2017

Ovarian Cancer: assessment of response to NACT

Time point 1



Time point 2



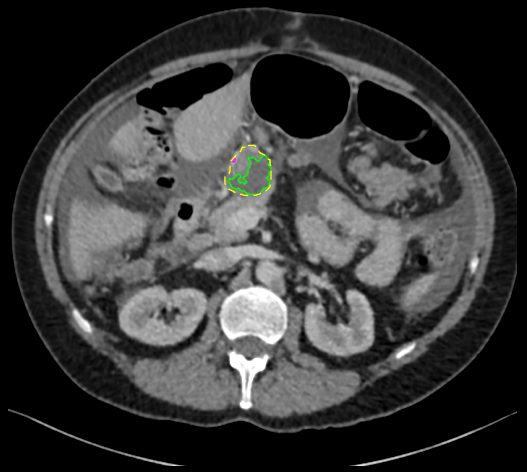
RECIST evaluation:

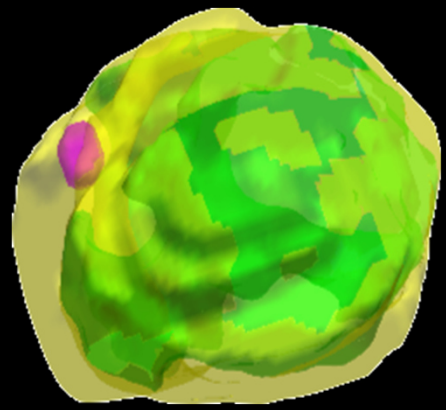
- Lesser sac implant has doubled in size
- Splenocolic and Morrison pouch implants are stable

Progressive disease

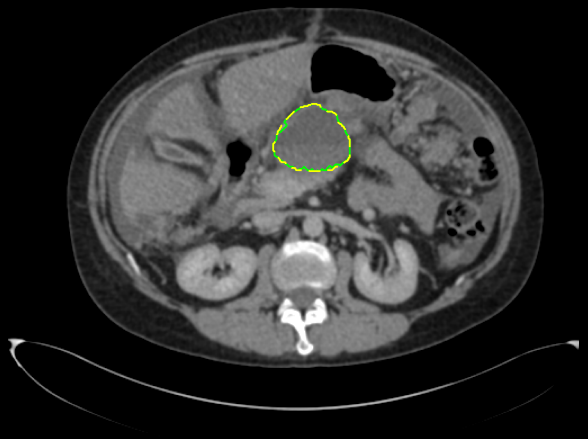
Lesser sac lesion

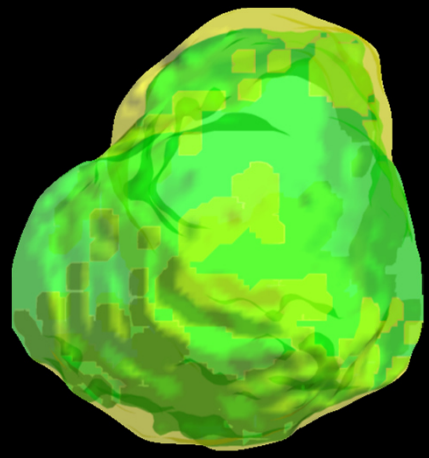
Time point 1





Time point 2





Whole tumour automatic segmentation

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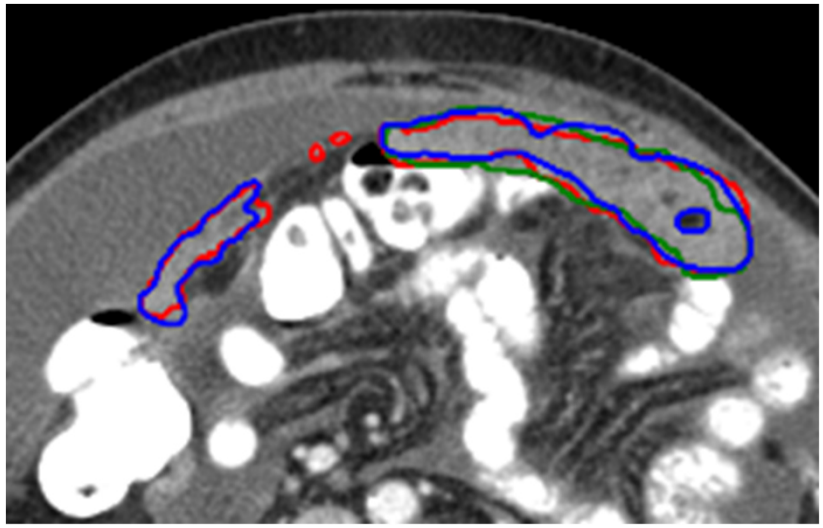
Segmentation



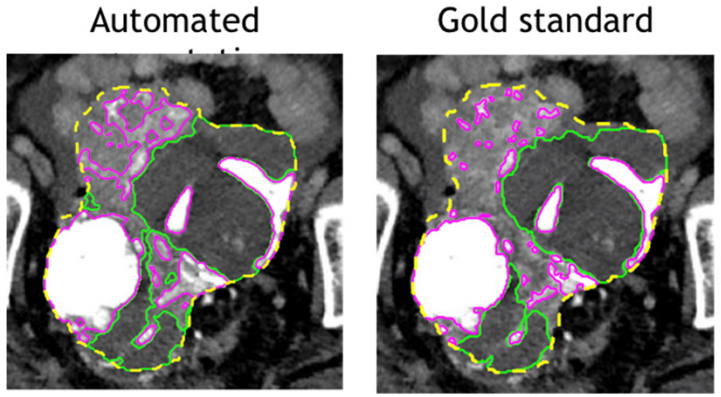
– Automatic – Observer 1 – Observer 2

Obs 1 *vs.* Obs 2 *DSC* = 71.41

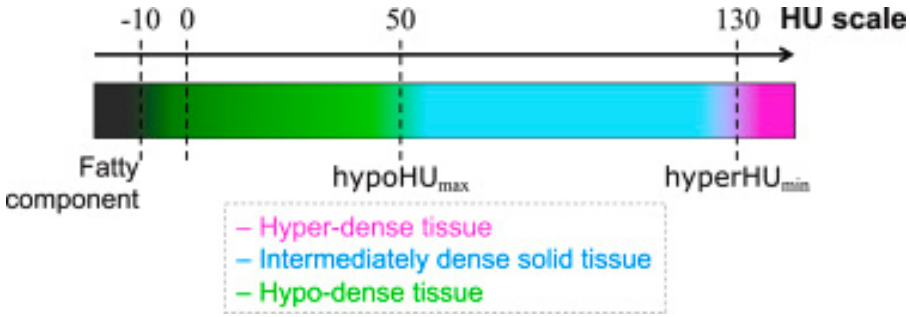
Auto *vs.* Obs 1 *DSC* = 71.85

Auto *vs.* Obs 2 *DSC* = 72.26

Sub-segmentation



Pelvic/Ovarian disease
(26 cases)
DSC = 81.94 ± 4.76
DSC = 87.32 ± 6.01



Rundo L, et al. Computers in Biology and Medicine, 2020
Buddenkotte T, et al. Eur Rad Exp, 2023

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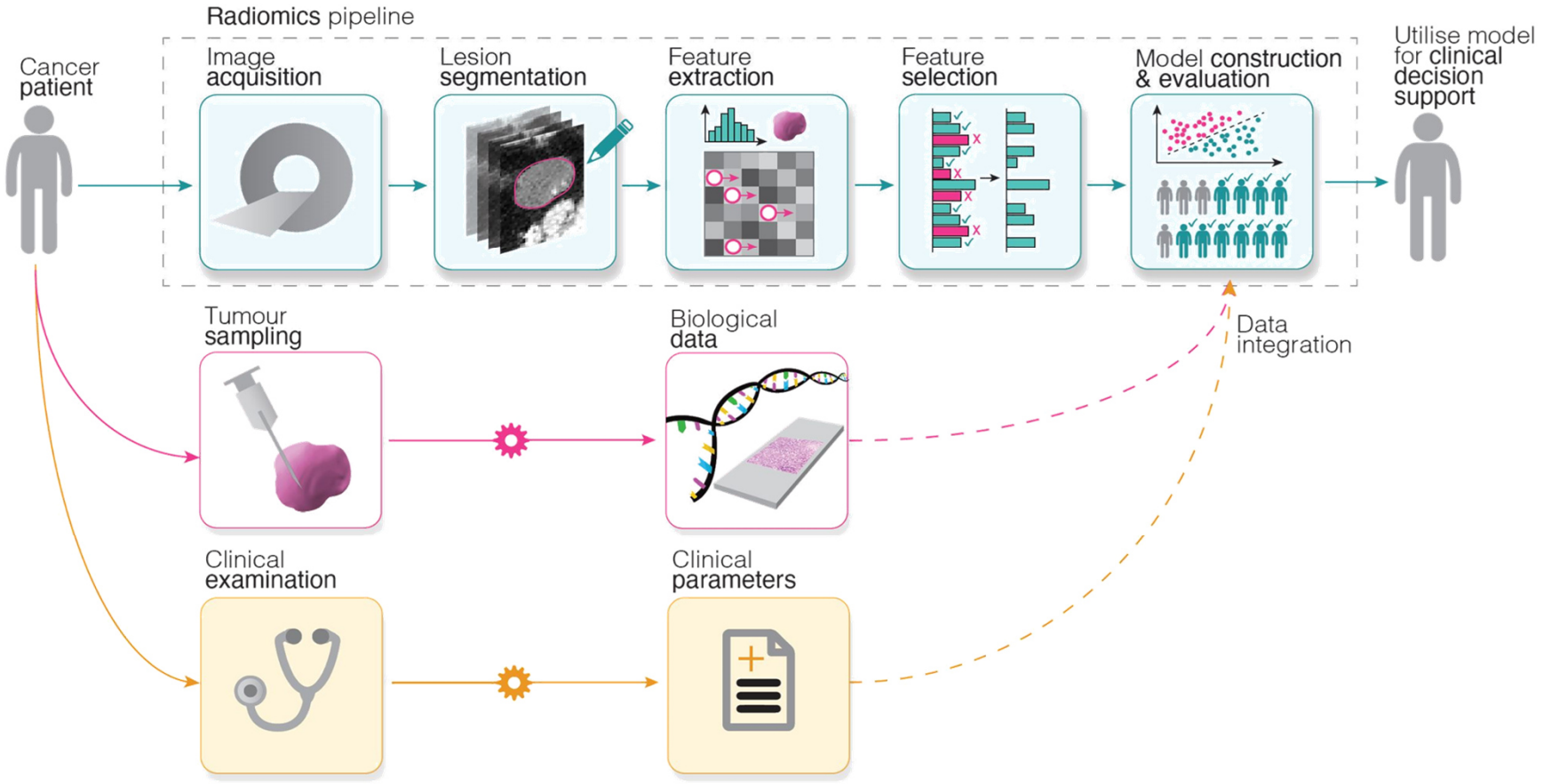
Radiogenomics Framework



A (bit) of art history

Homogeneity

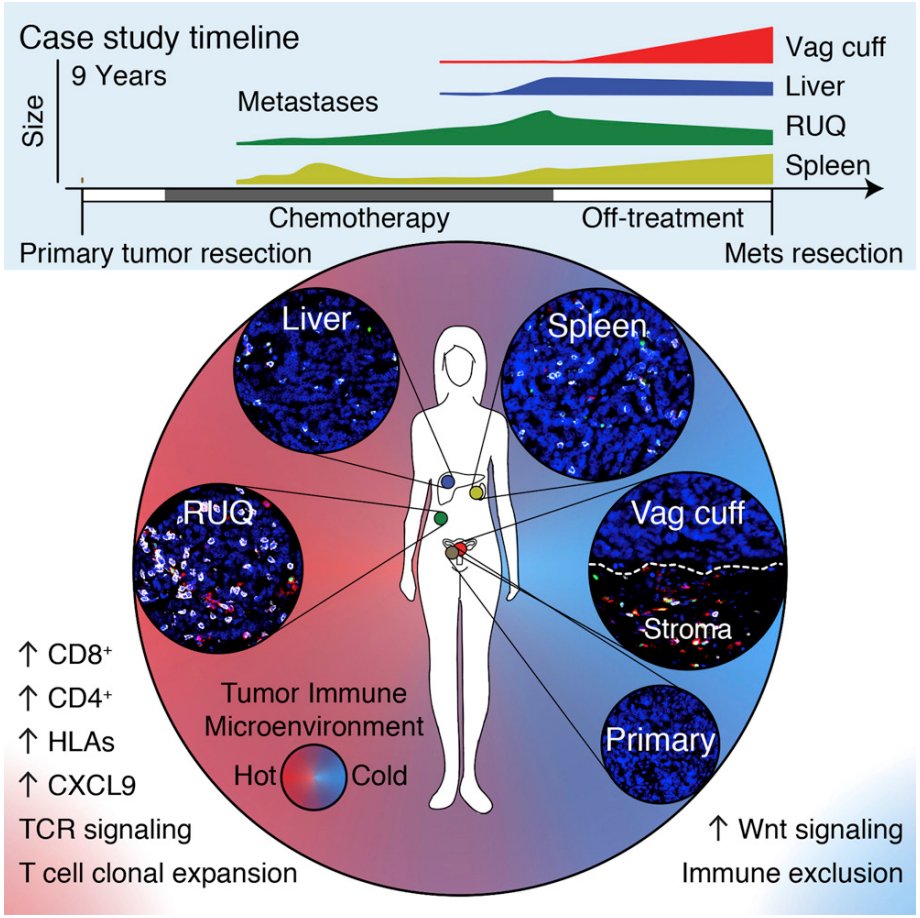
0.54 0.54 0.76 0.79 0.85 0.89

7.84 7.69 7.09 7.37 6.82

Entropy
(Randomness)

a-e) Jackson Pollock f) Mark Rothko

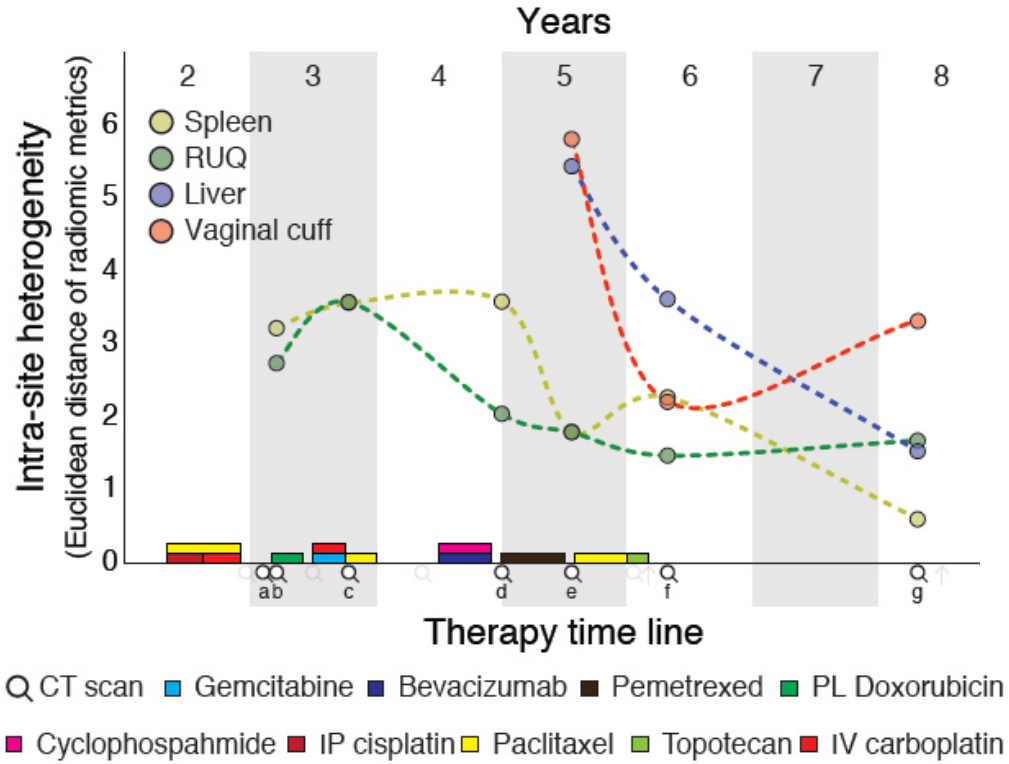
Are Heterogeneous Outcomes of Metastatic Lesions Linked to Immune Escape in Ovarian Cancer?

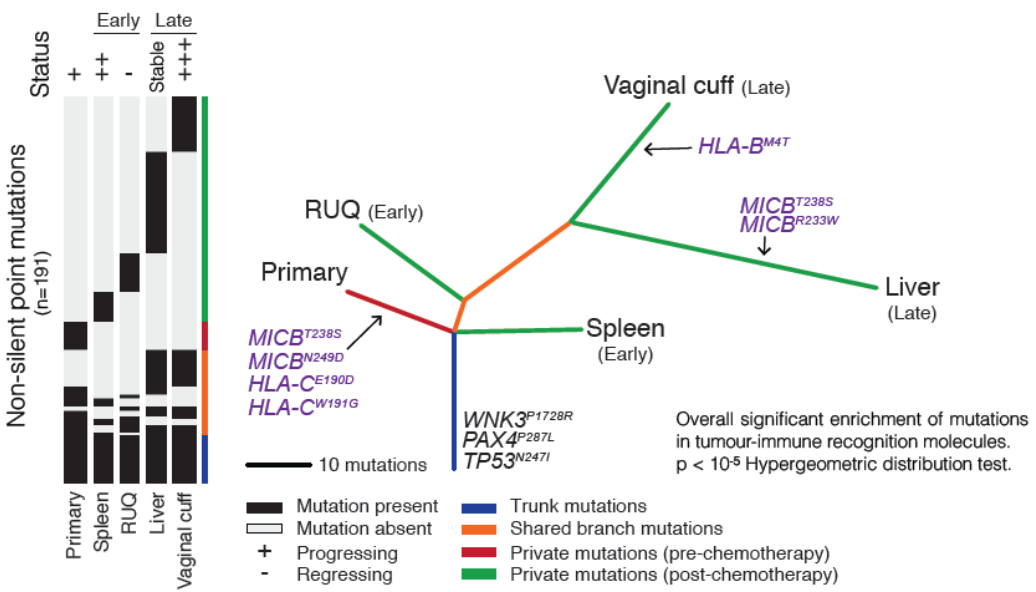


- The interaction between cancer, host immune response and chemotherapy is largely unknown
- Analysis (in both space and time) of patient matched primary and metastatic disease is crucial
- Metastatic tumors exhibit intra-patient heterogeneous tumour growth and somatic mutation patterns after multi-line chemotherapy

Reuben A. et al. NPJ Genom Med 2017; Jimenez... Sala... Snyder, Miller. Cell 2017

Understanding tumour immune microenvironment in HGSOC





- Late metastases (liver & vaginal cuff) are phenotypically more heterogeneous
- Is there a matching genomic heterogeneity?

Late metastases (liver & vaginal cuff) have a higher mutation rate

“Spatial” Radiogenomics

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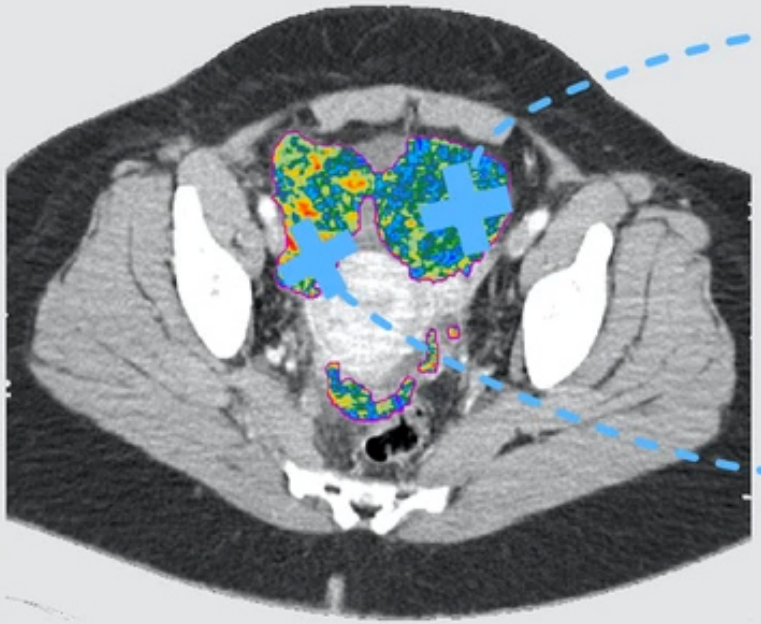
Targeted approach: radiomic maps + multiple targeted biopsies



Molecular profile 1
associated with
local radiomic
feature values

Molecular profile 2
associated with
local radiomic
feature values

P. Martin-Gonzalez, MCO, et al., Insights into Imaging 2020

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Habitat imaging predicts genetic heterogeneity

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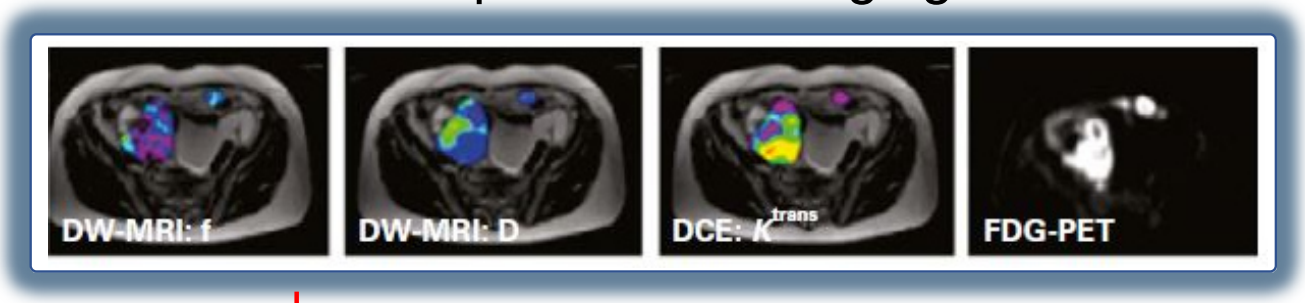
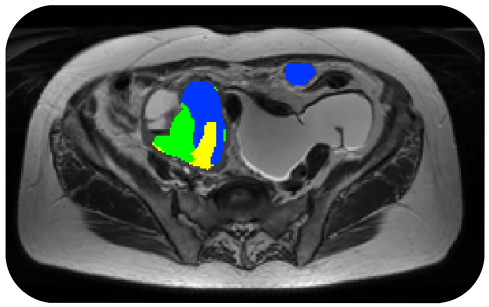
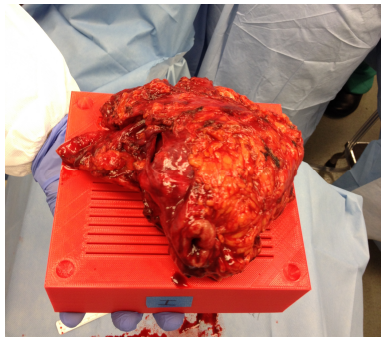
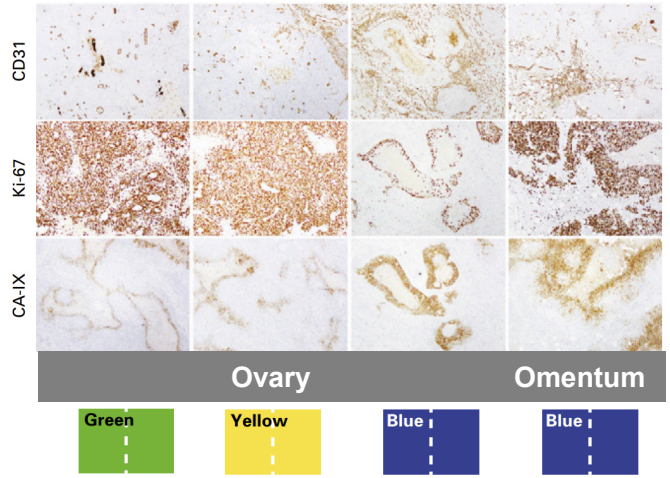
Multiparametric Imaging

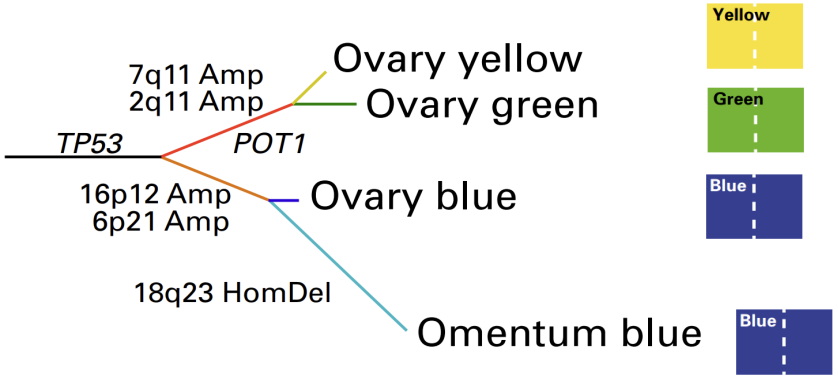


K-means clustering









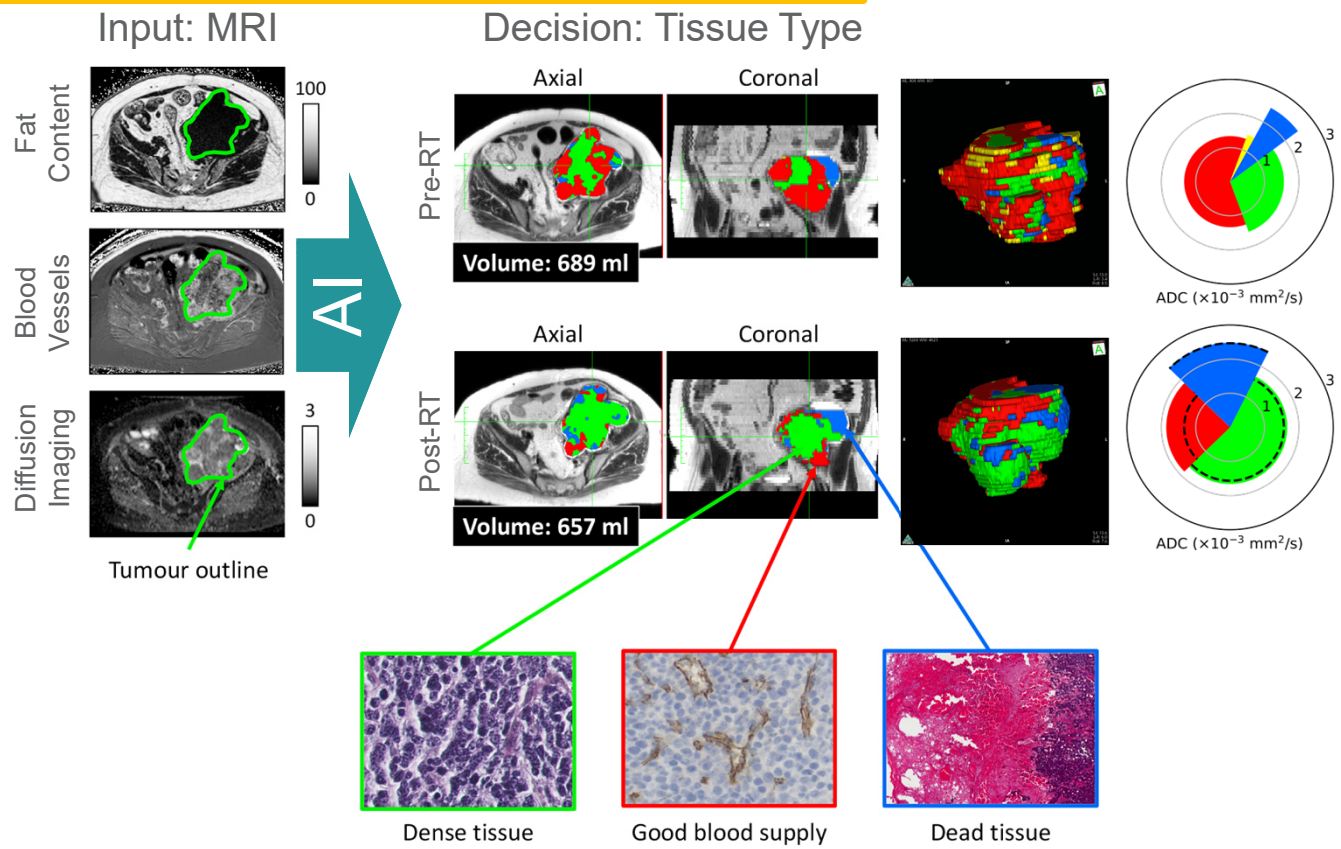
Weigelt B, Vargas AH, et al. JCO Precision Oncology 2019; Jimenez-Sanchez A, et al. Nat Genet 2020

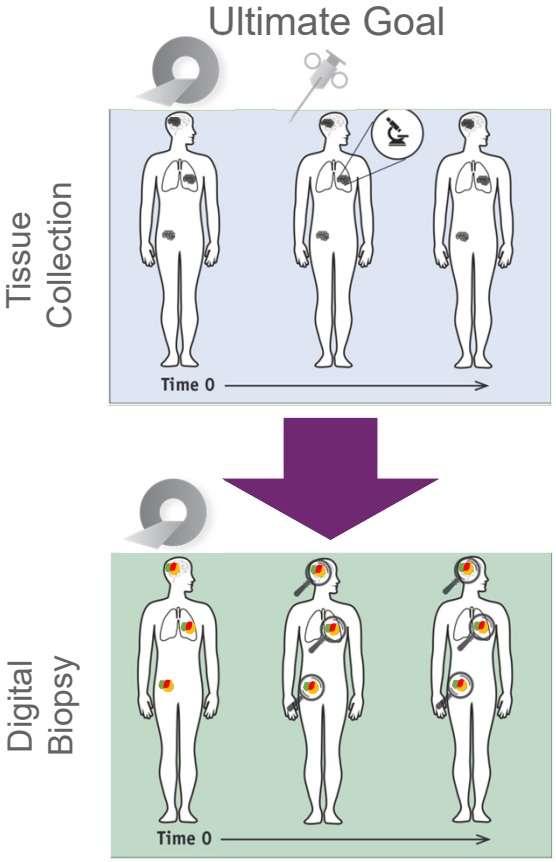
Habitat Imaging for Virtual Biopsy

frontiers in Oncology

Supervised Machine-Learning Enables Segmentation and Evaluation of Heterogeneous Post-treatment Changes in Multi-Parametric MRI of Soft-Tissue Sarcoma

Matthew D. Blackledge[1*†], Jessica M. Winfield[1,2*†], Aisha Miah[3,4], Dirk Strauss[5], Khin Thway[3,6], Veronica A. Morgan[1,2], David J. Collins[1,2], Dow-Mu Koh[1,2], Martin O. Leach[1,2] and Christina Messiou[1,2*]





Radiogenomic response predictor for HGSOC

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Patient cohort (n=138)

n=92 eligible patients

n=46 External validation

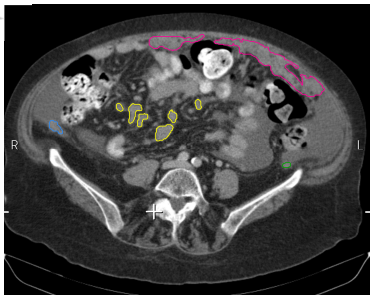
n=72 Training

n=20 Hold-out validation

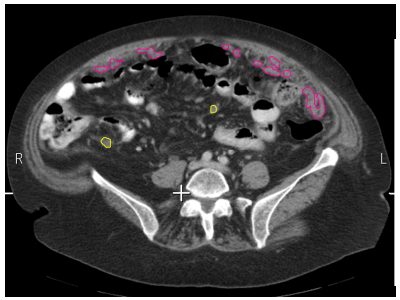
Predict response to neoadjuvant chemotherapy (NACT) [change in tumour volume] from baseline scans

Manual segmentations of whole tumour burden

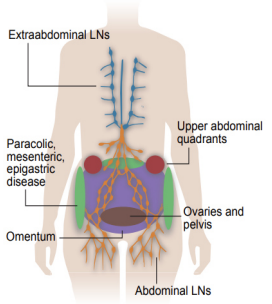
CT scans



Pre-NACT



Post-NACT



Crispin-Ortuzar M & Woitek R et al. *Nat Comm (in press)*

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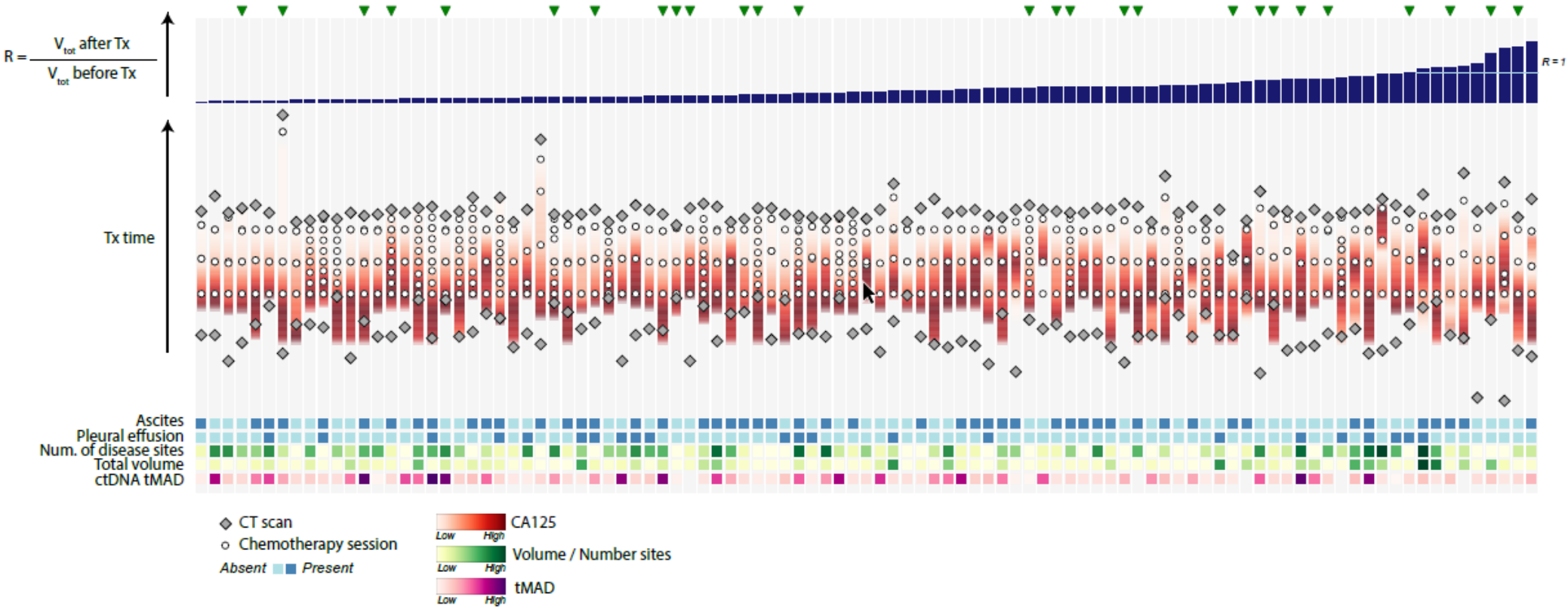
Data integration for response prediction

Can we predict response to NACT at baseline and help patient stratification?

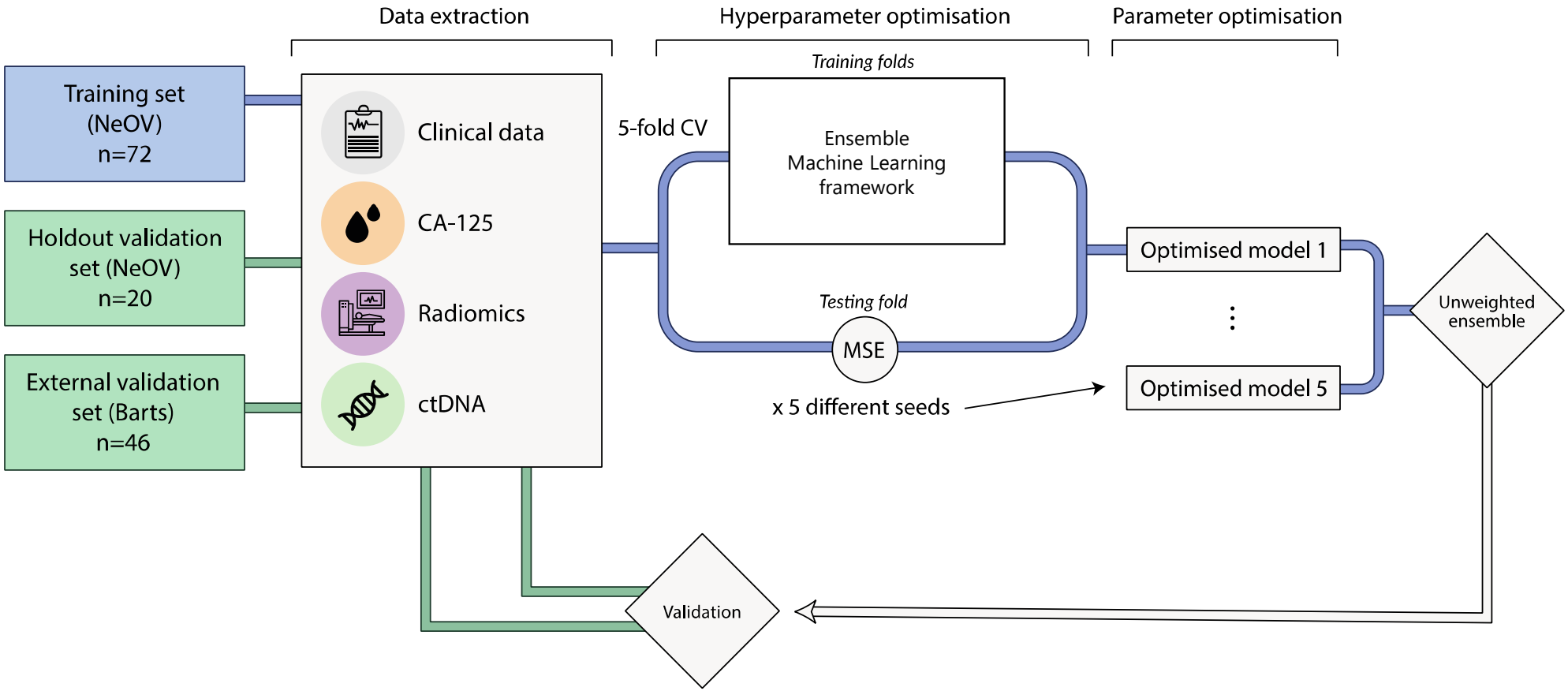


We have curated a rich integrated dataset including clinical data, CA 125, radiomics, and ctDNA

Crispin M, Woitek R, et al. Nature Comm (in press)

Data integration improves response prediction

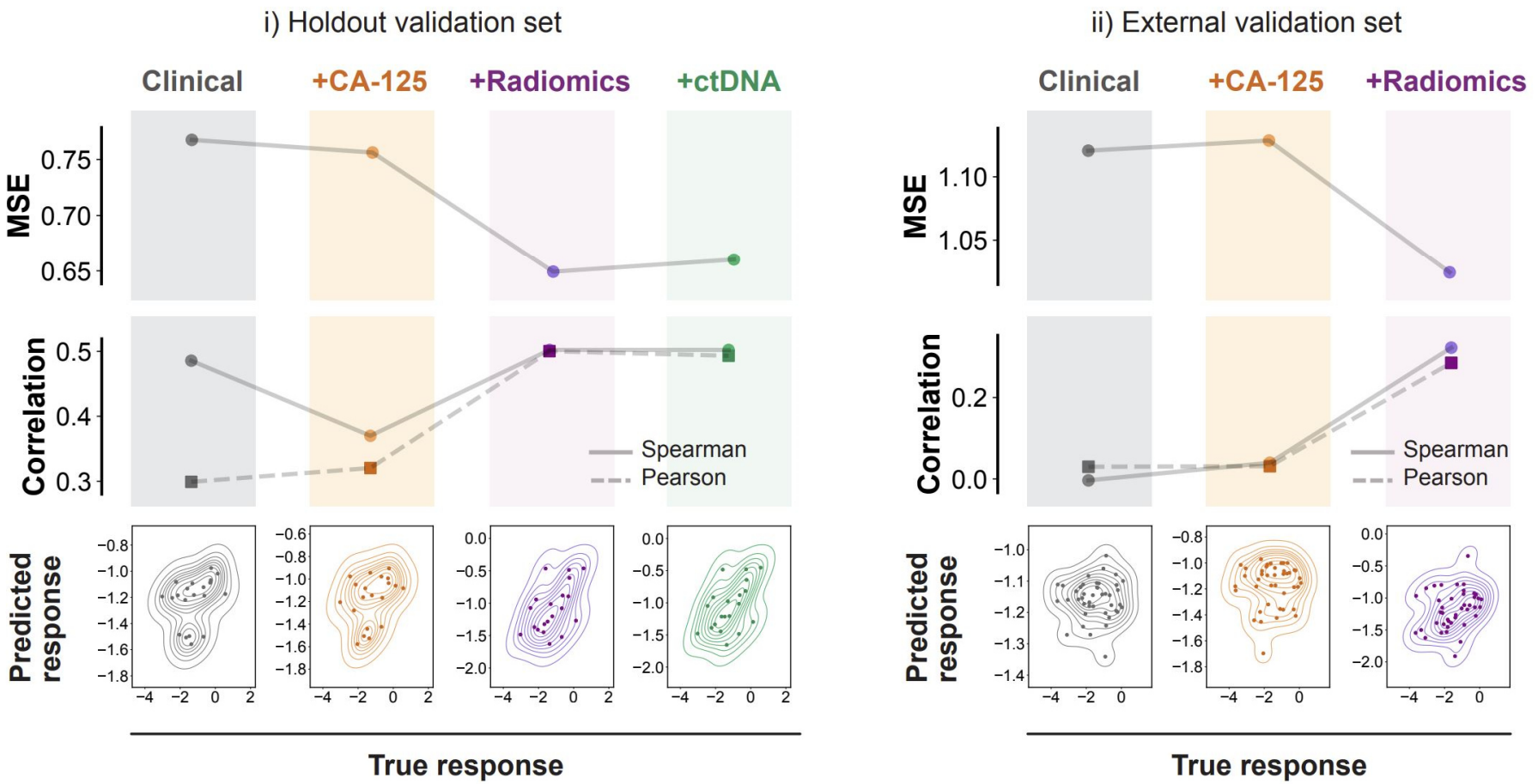
Our ML framework integrates clinical data, CA 125, radiomics, and ctDNA



Crispin M, Woitek R, et al. Nature Comm (in press)

Data integration improves response prediction

Clinical data, CA 125, radiomics, and ctDNA with external validation



Crispin M, Woitek R, et al. Nature Comm (in press)

Radiogenomics for patient stratification

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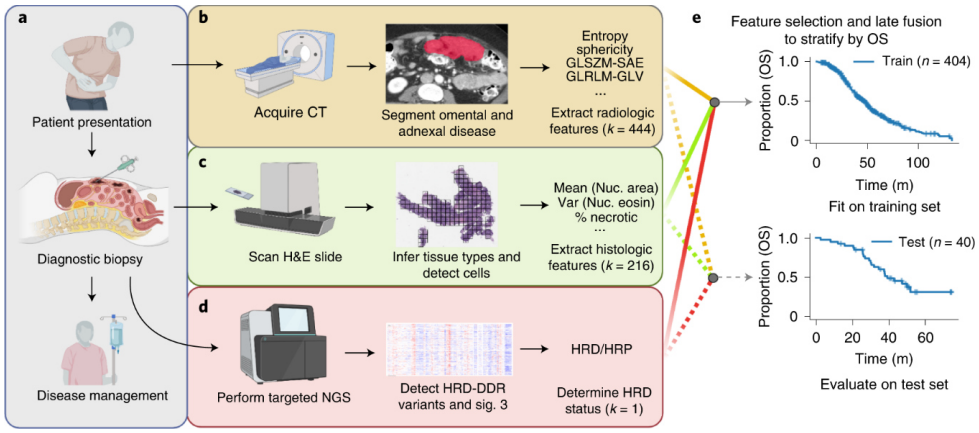
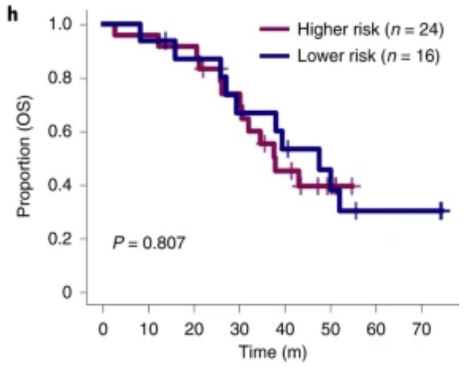
Patient stratification based on multiomics

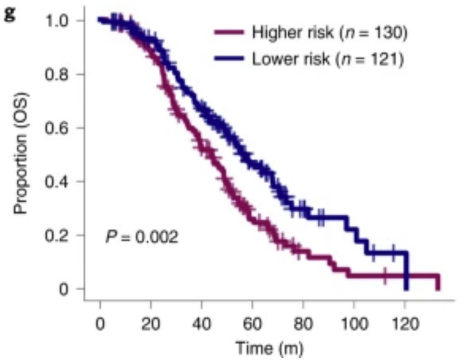
- CT
- H&E tissue sections (dig. Pathology)
- HRD/HRP (NGS)



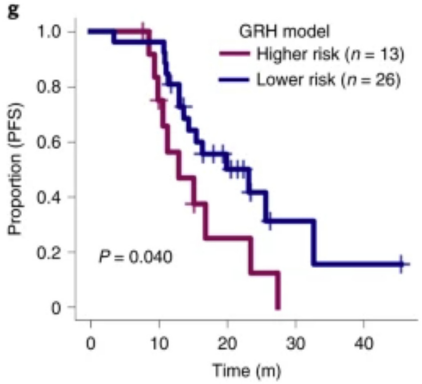
Adnexal radiomics



Omental radiomics



Multimodal data (incl. omental radiomics)



Boehm et al. Nat Cancer 2022

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Cervical cancer: Prediction of response to CTRT/DFS

- LACC standard treatment: CT-RT + brachytherapy
- 60-90% complete response rate
- Early identification of poor responders → adjust treatment consequently

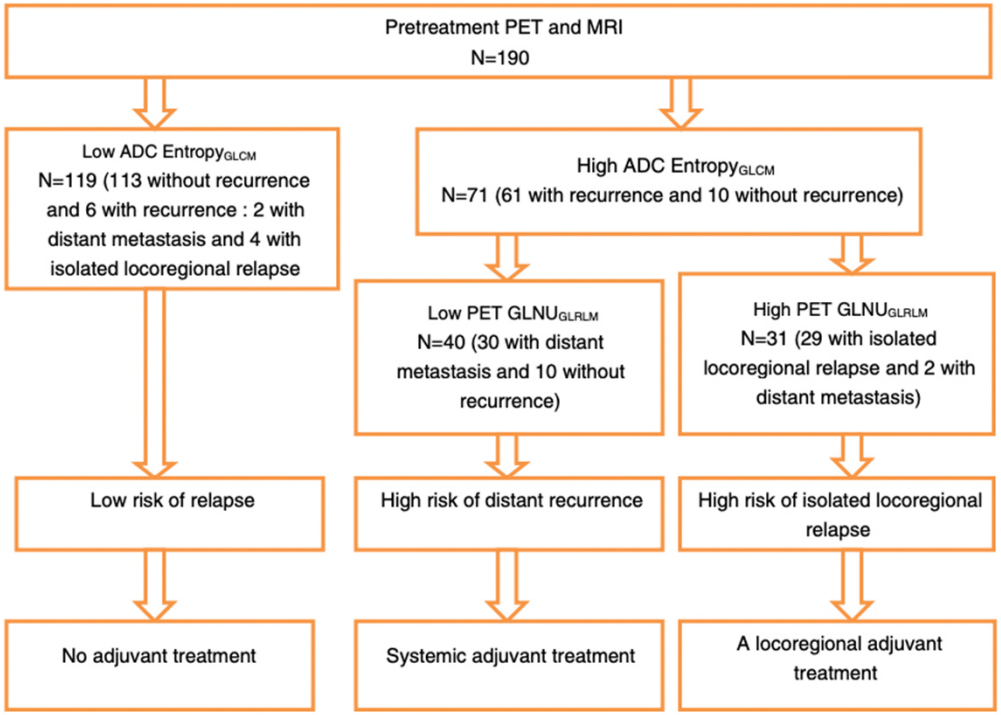
External validation of a previously developed radiomic model:

- $GLNU_{GLRLM}$ derived from PET/CT predicts LRC
- $Entropy_{GLCM}$ derived from ADC map predicts DFS

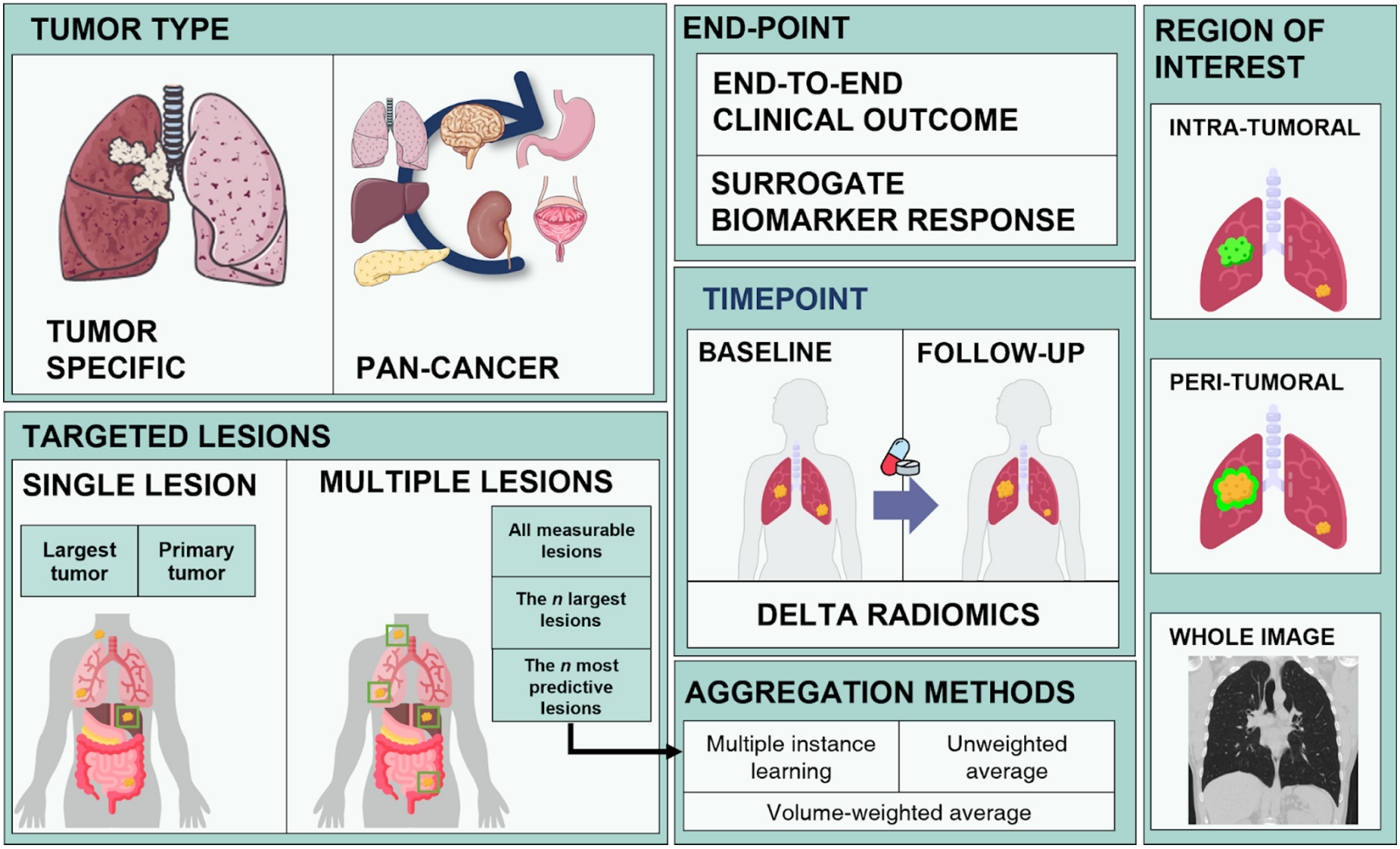
Powerful predictors of the efficacy of CT-RT before treatment with higher accuracy than standard post-treatment metabolic response assessment

Higher value of $GLNU_{GLRLM}$ and $Entropy_{GLCM}$ → worse outcome

→ more heterogeneous tumours have poorer prognosis

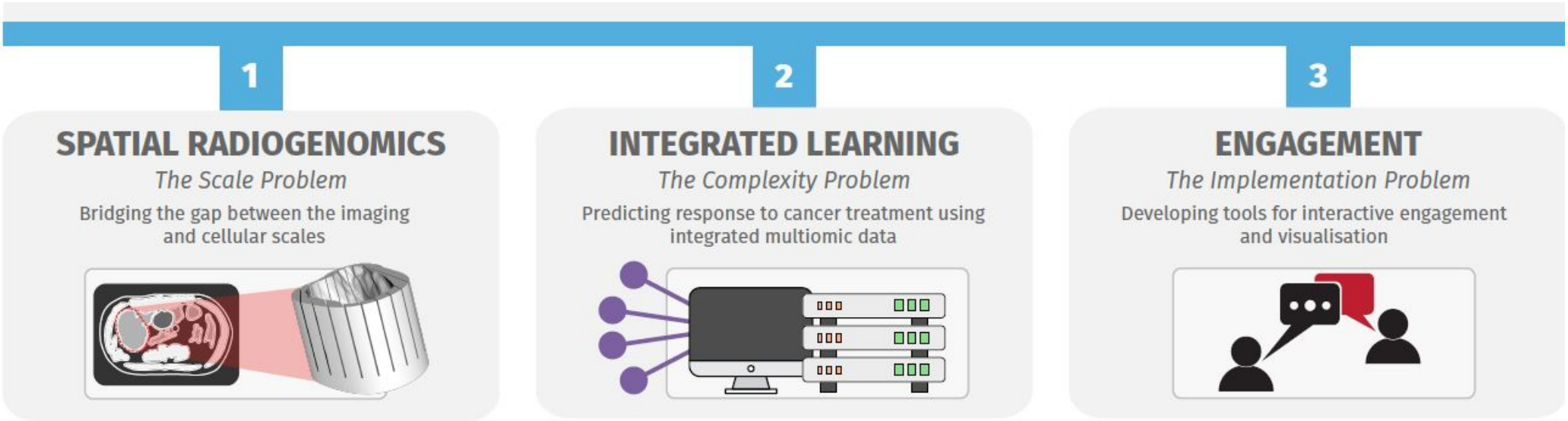


Radiomics Framework



Vision (next 5 years)

Develop integrated frameworks that bridge the gap between imaging and cellular scales (research line 1), predict response to treatment (research line 2), and engage interactively with patients and clinicians (research line 3)



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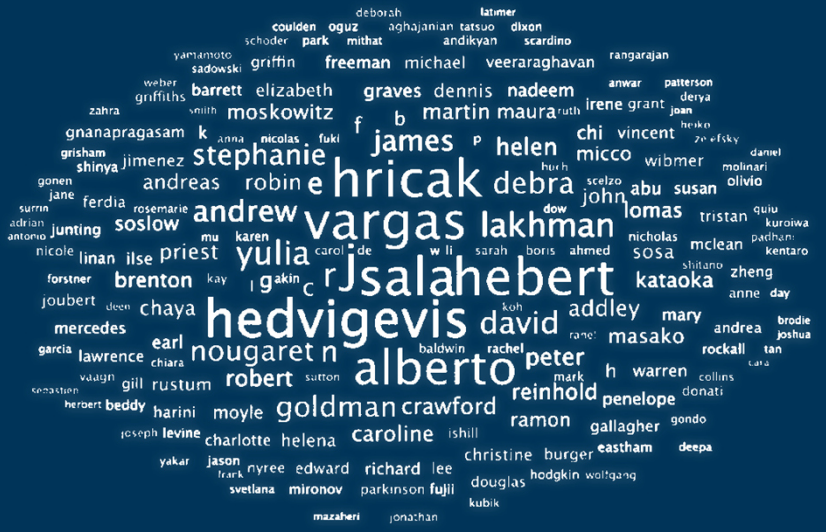
Delivering a New Paradigm of Personalised Cancer Medicine



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The Mark Foundation for Cancer Research

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