



Tumor Immune Microenvironment: A Holistic Approach Workshop

April 21-22, 2022 • San Diego and Virtually



Radiomics/Radiology

Integrating tumor heterogeneity for radiomics guided Radio-immunotherapy?

Session Vizualing Tumor Microenvironment

Eric Deutsch MD PhD

Gustave Roussy Villejuif France

DISCLOSURE INFORMATION

Eric Deutsch

- **Personal financial interest :**

Roche, Astrazeneca, , MSD, AMGEN, Accuray, Boehringer

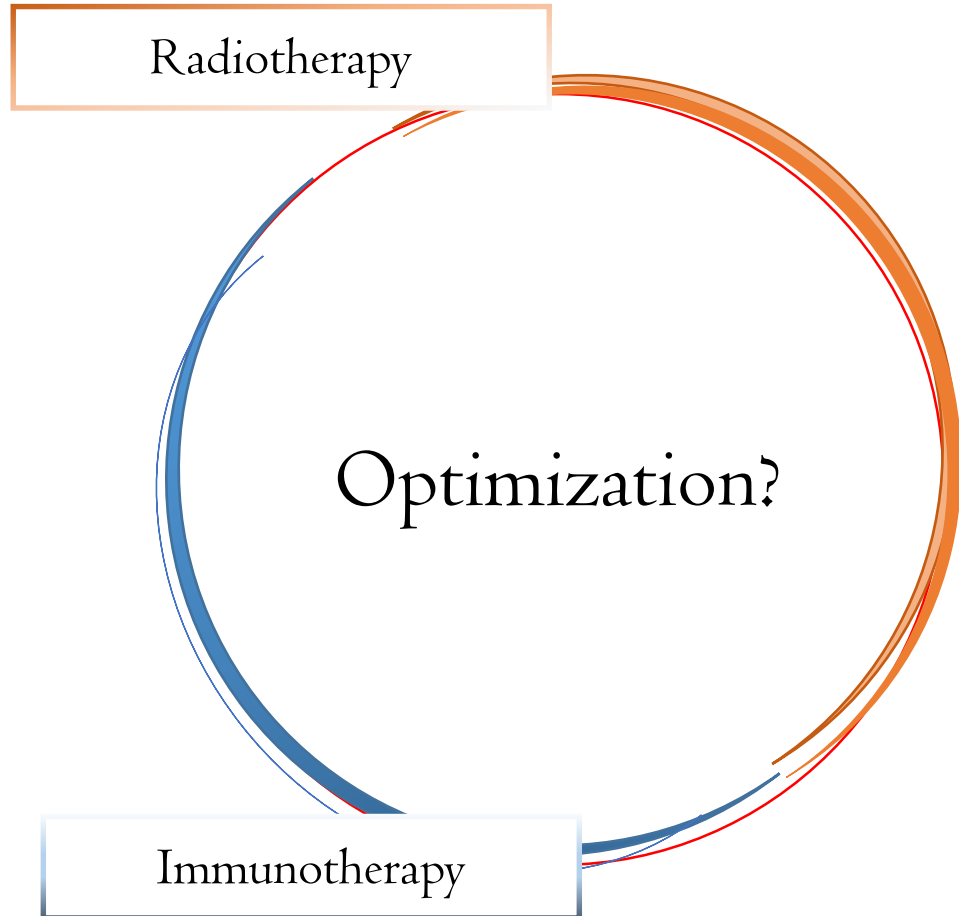
- **Institutional financial interests,**

Boehringer, Astrazeneca, Roche, Amazon AWS, Nanobiotix, Lilly, Servier

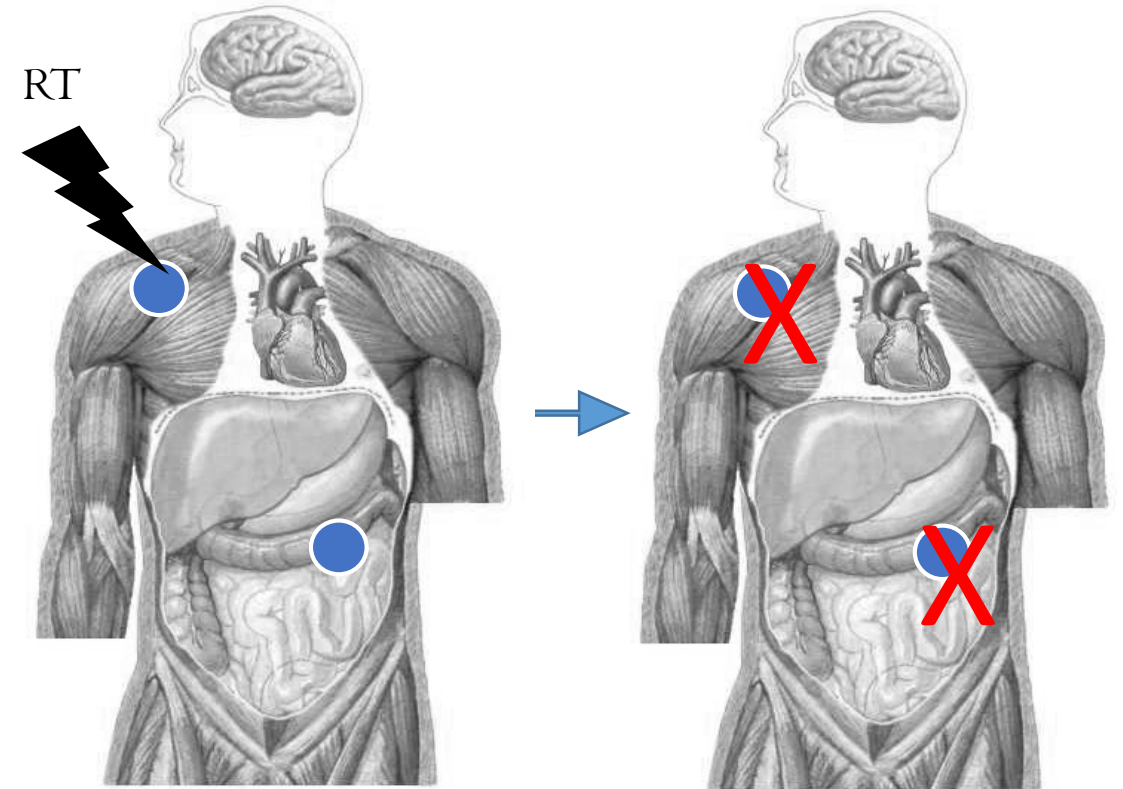
- **- Other :**

Shared patents with NH-Theraguix, Clevexel, Graegis, Joined lab with Therapanacea.

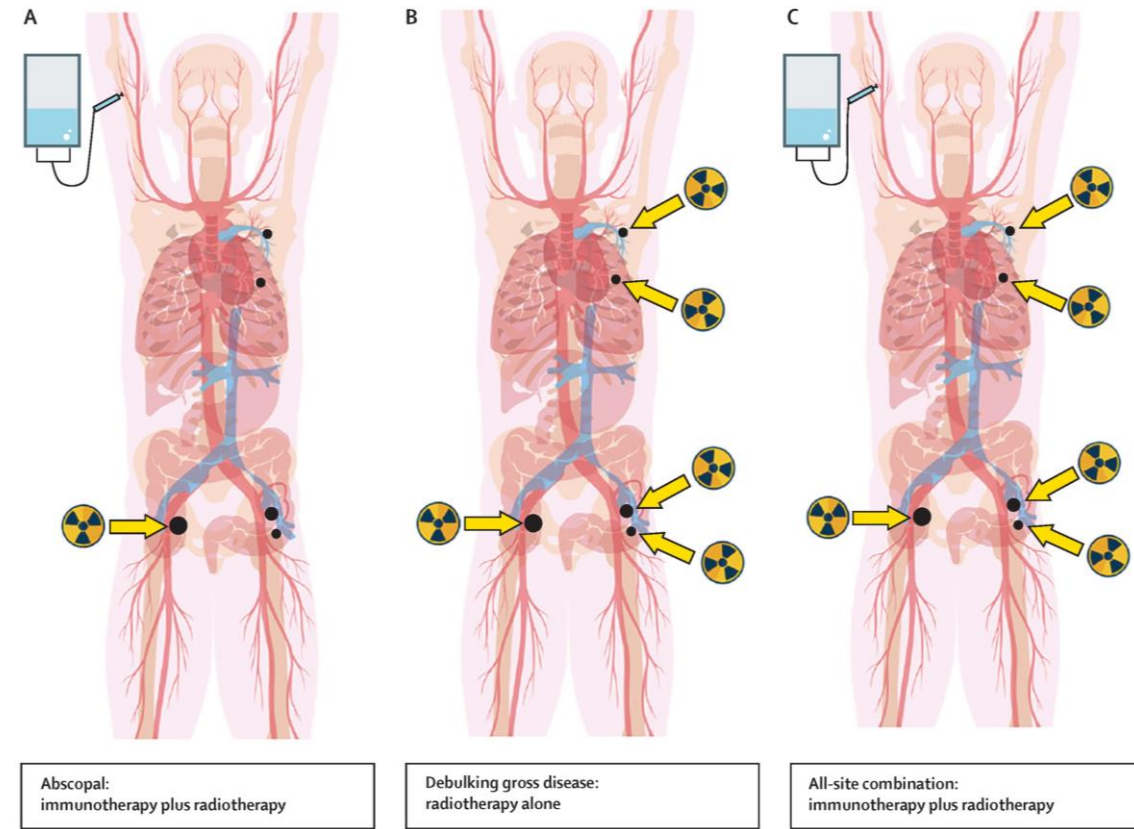
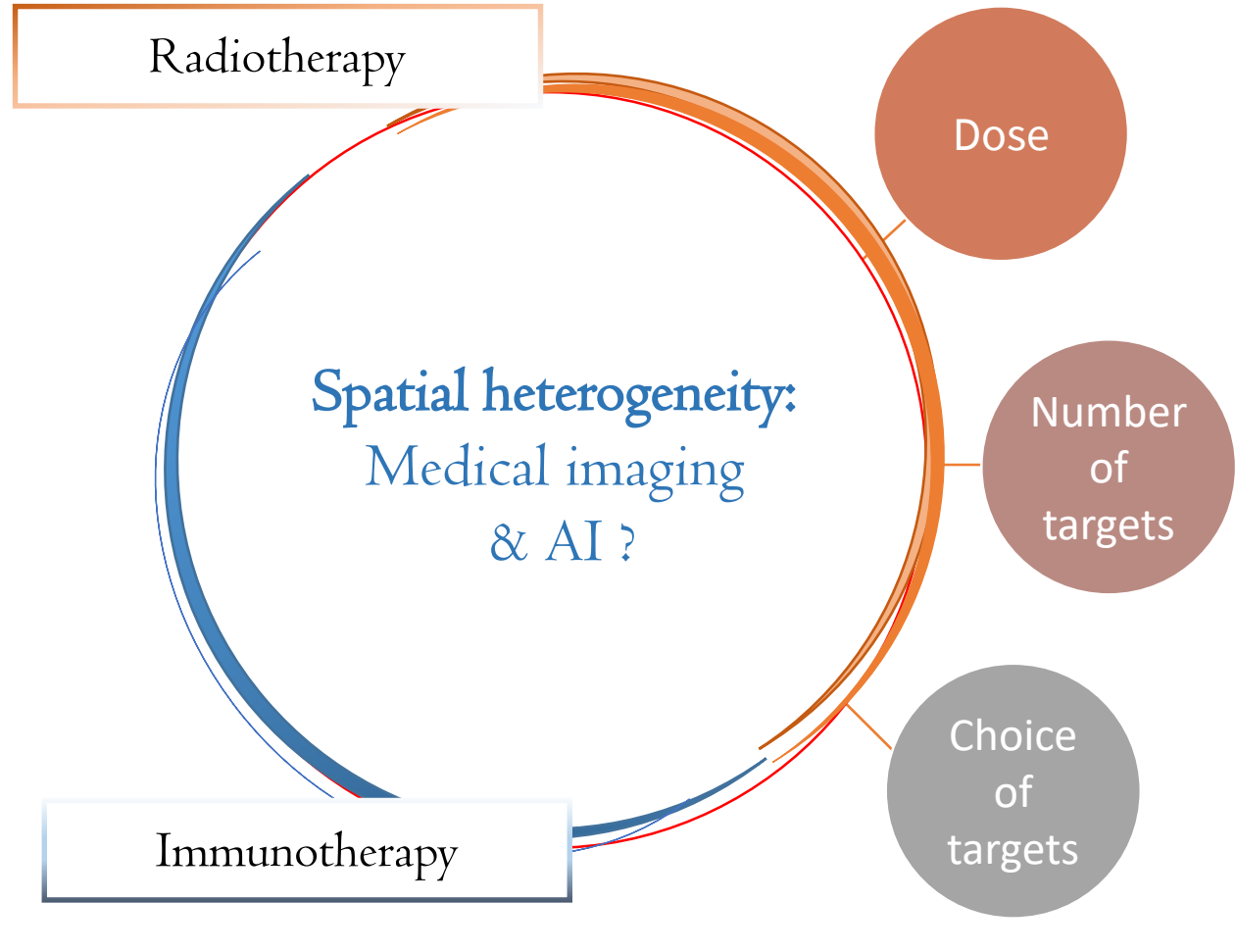
Radioimmunotherapy



« Abscopal » effect

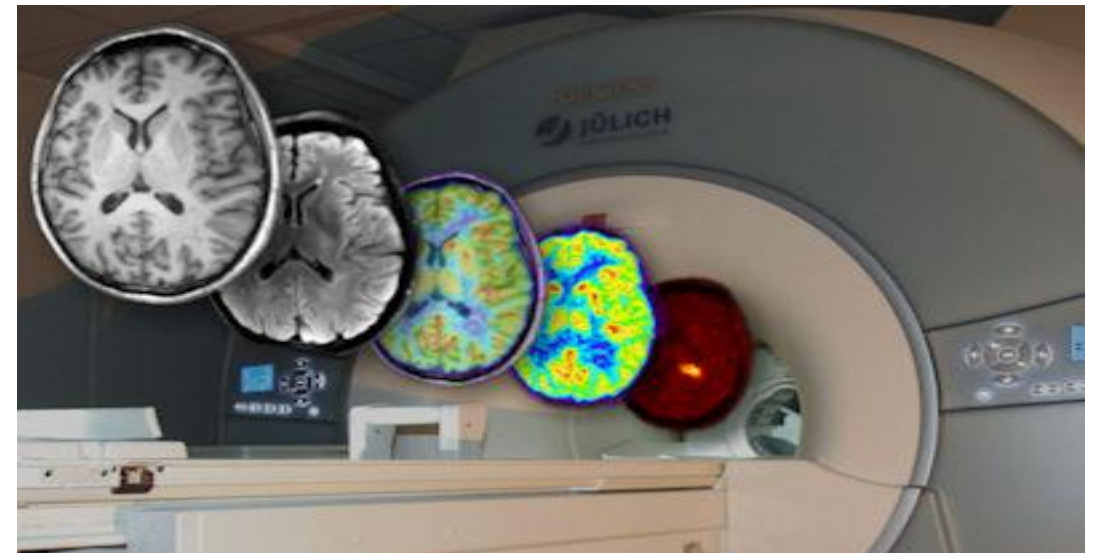
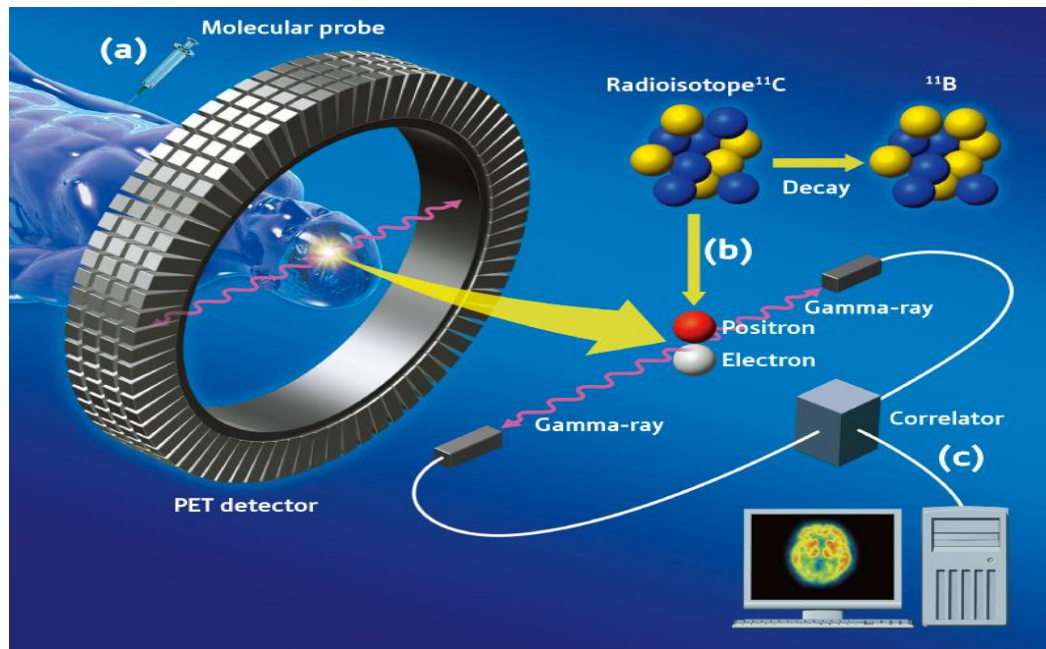
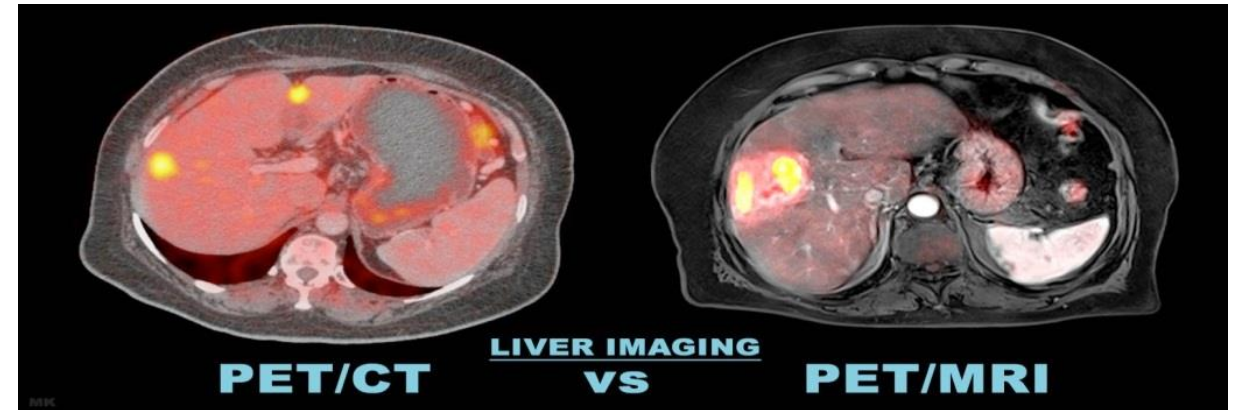
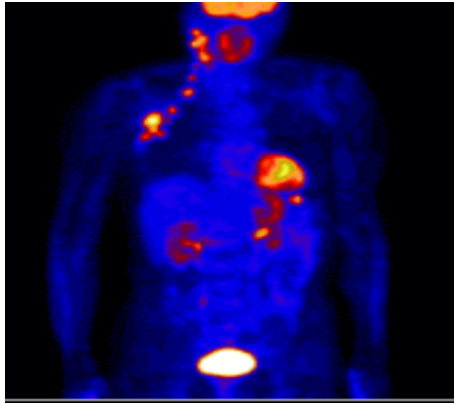


Radioimmunotherapy

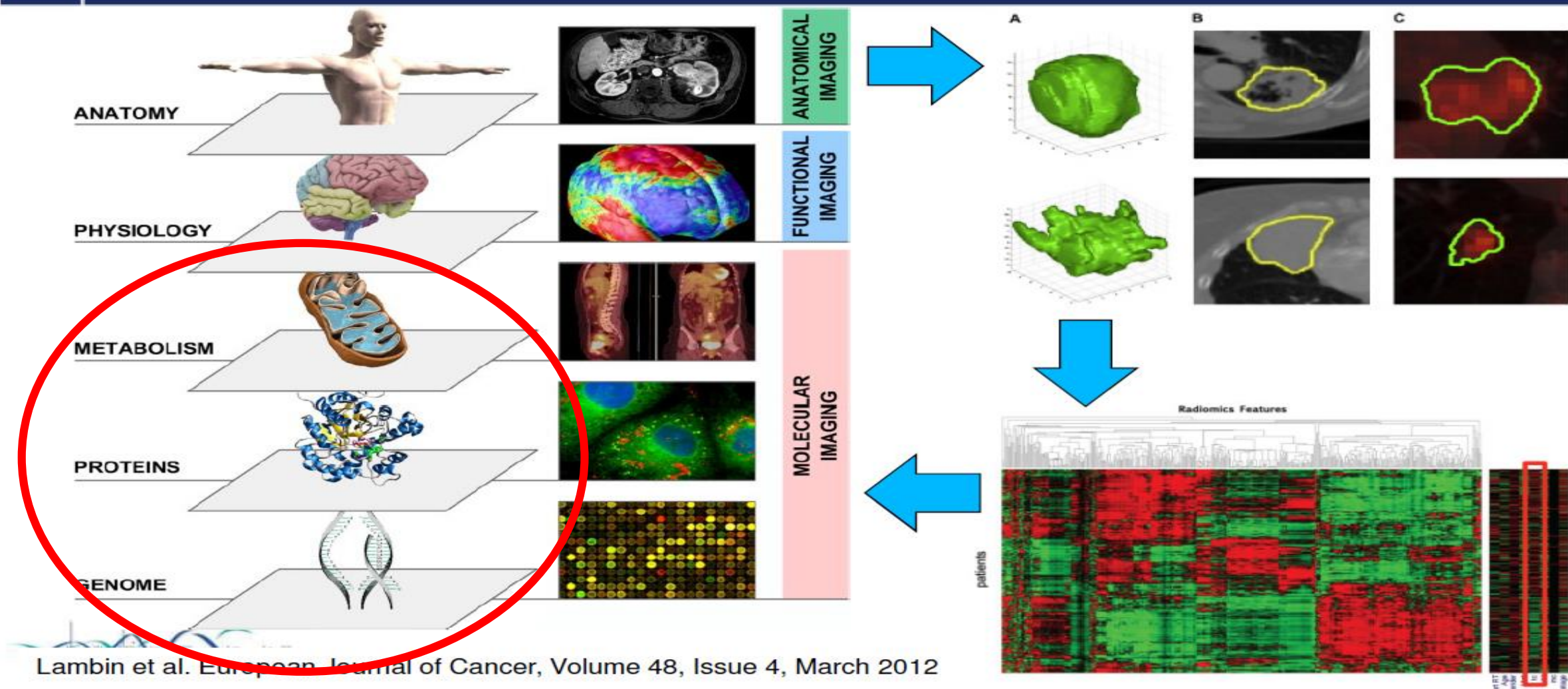


Deutsch *et al.* Lancet Oncol 2019

Imaging

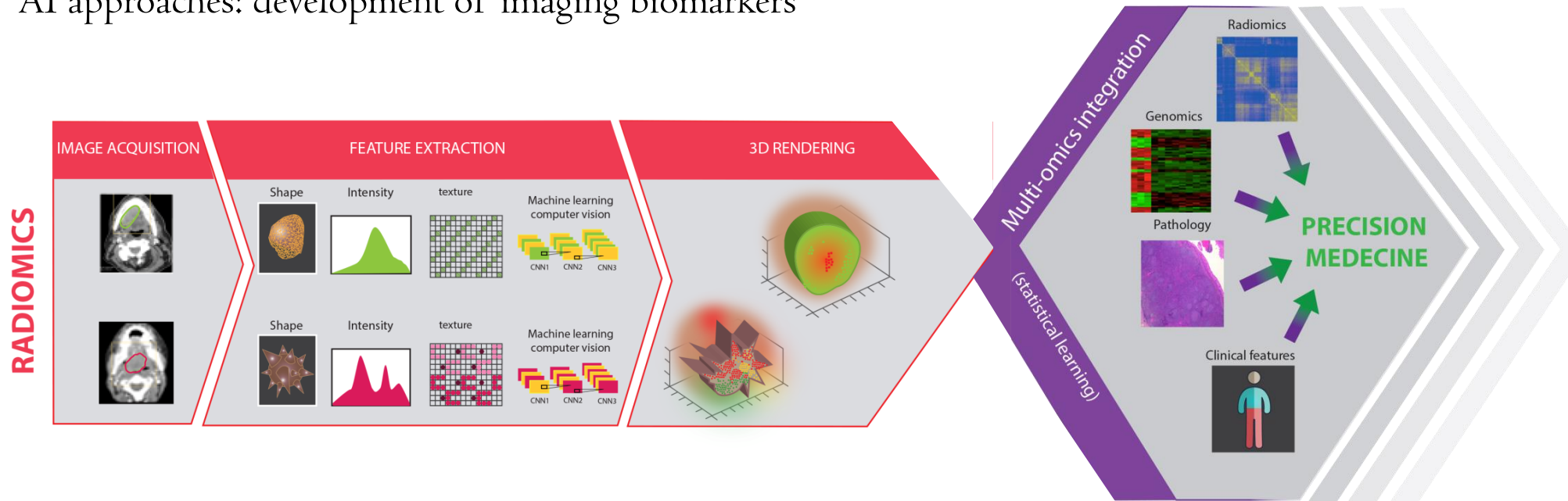


Entering the OMICS era... Radiomics



Radiomics

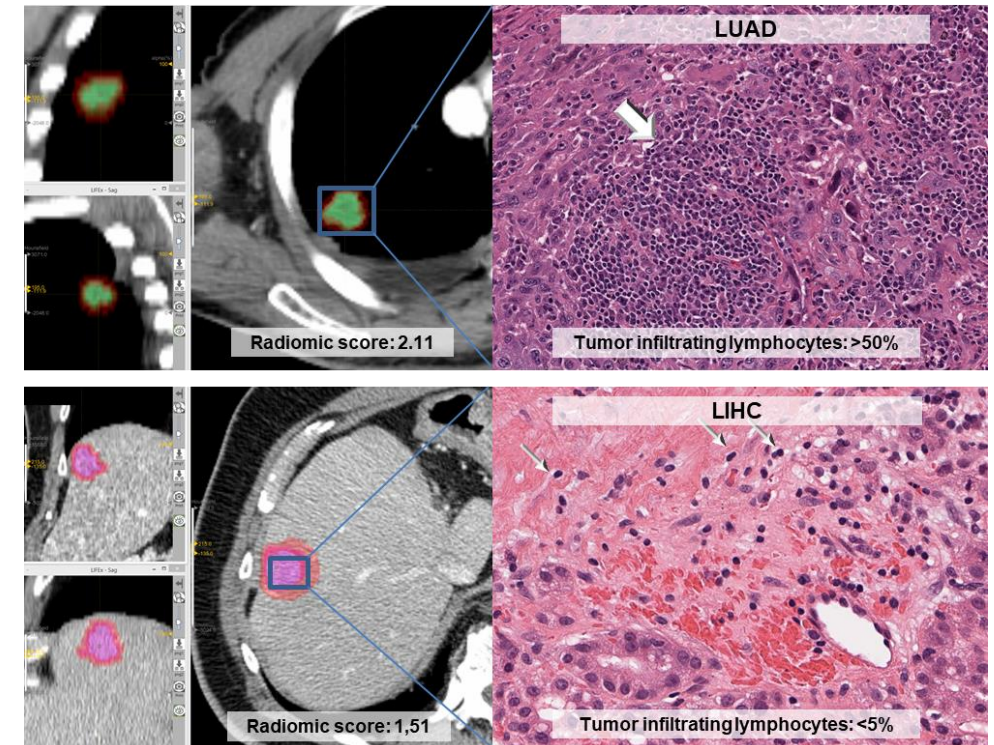
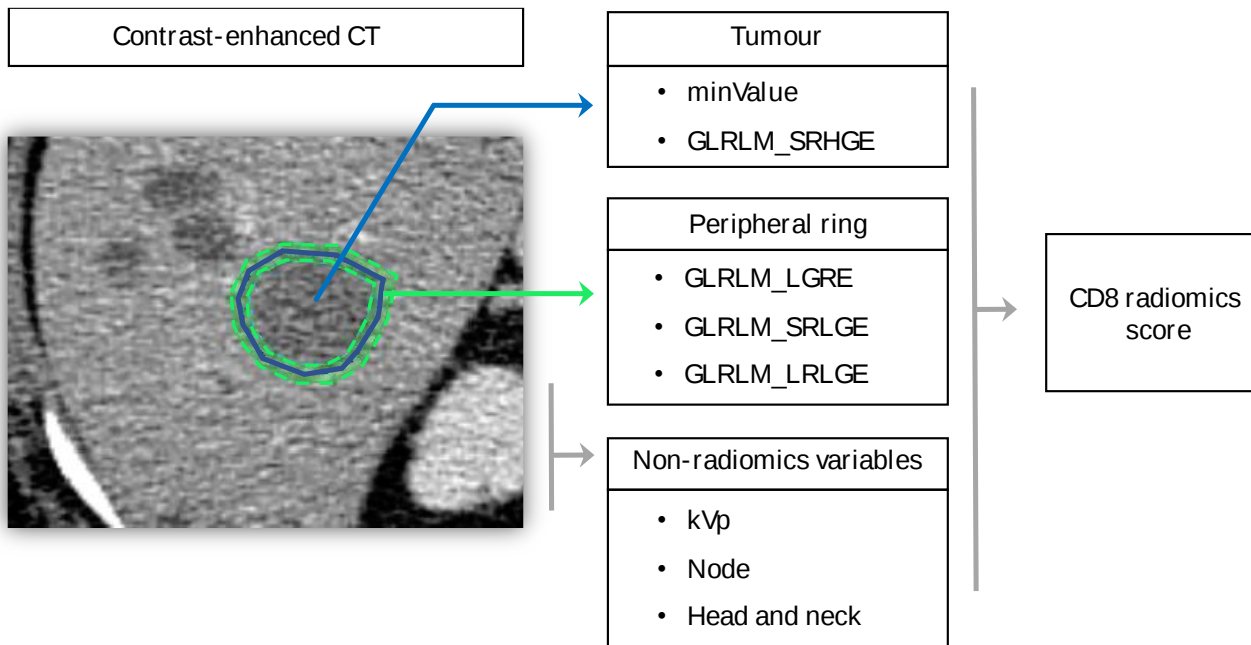
- Translates medical imaging into quantitative data
- Reflects the tumor phenotype (cellular and molecular properties)
- AI approaches: development of imaging biomarkers



Limkin E, Sun R *et al.* Ann Oncol 2017

CD8 Radiomics signature

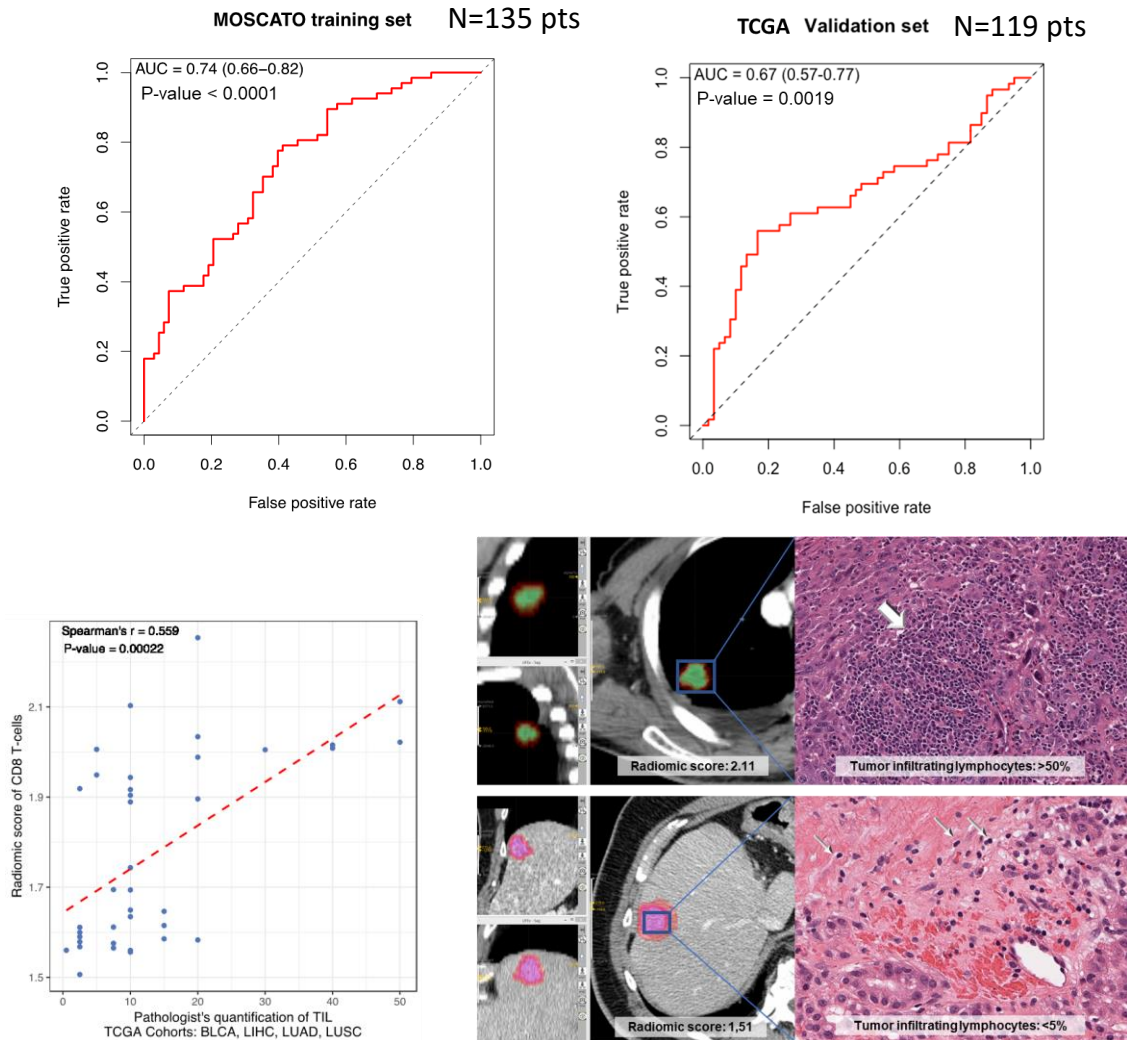
Prediction of CD8 T cells using radiomics on contrast enhanced CTs



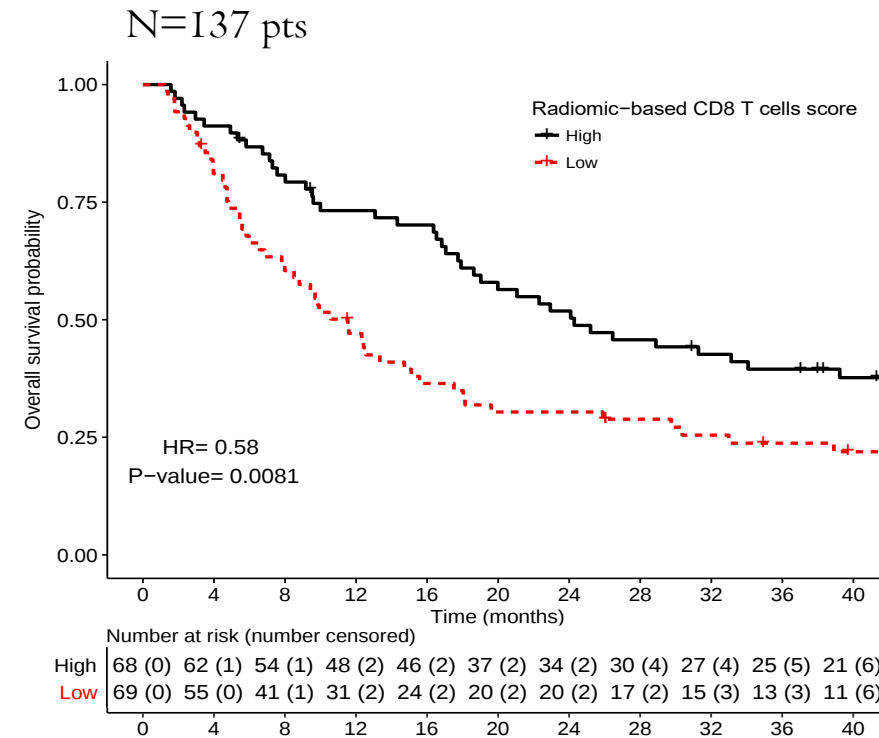
Sun R, et al – Lancet Oncol 2018

CD8 Radiomics signature

The radiomic signature could discriminate high vs low genomic score of CD8 T-cells infiltration



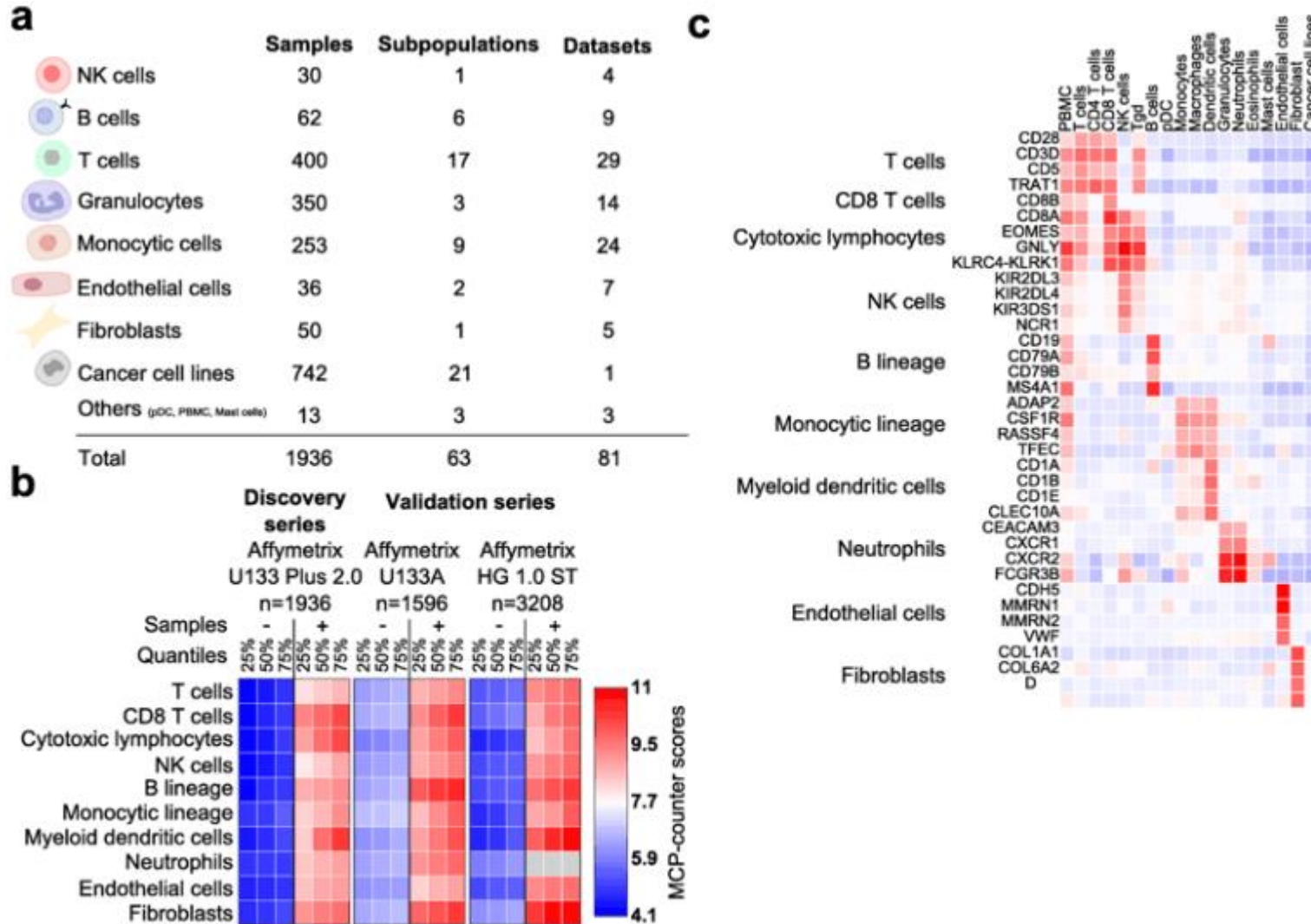
And was associated with OS in patients treated with anti-PD-I/PD-LI



Sun R et al. Lancet Oncol 2018

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MCP counter

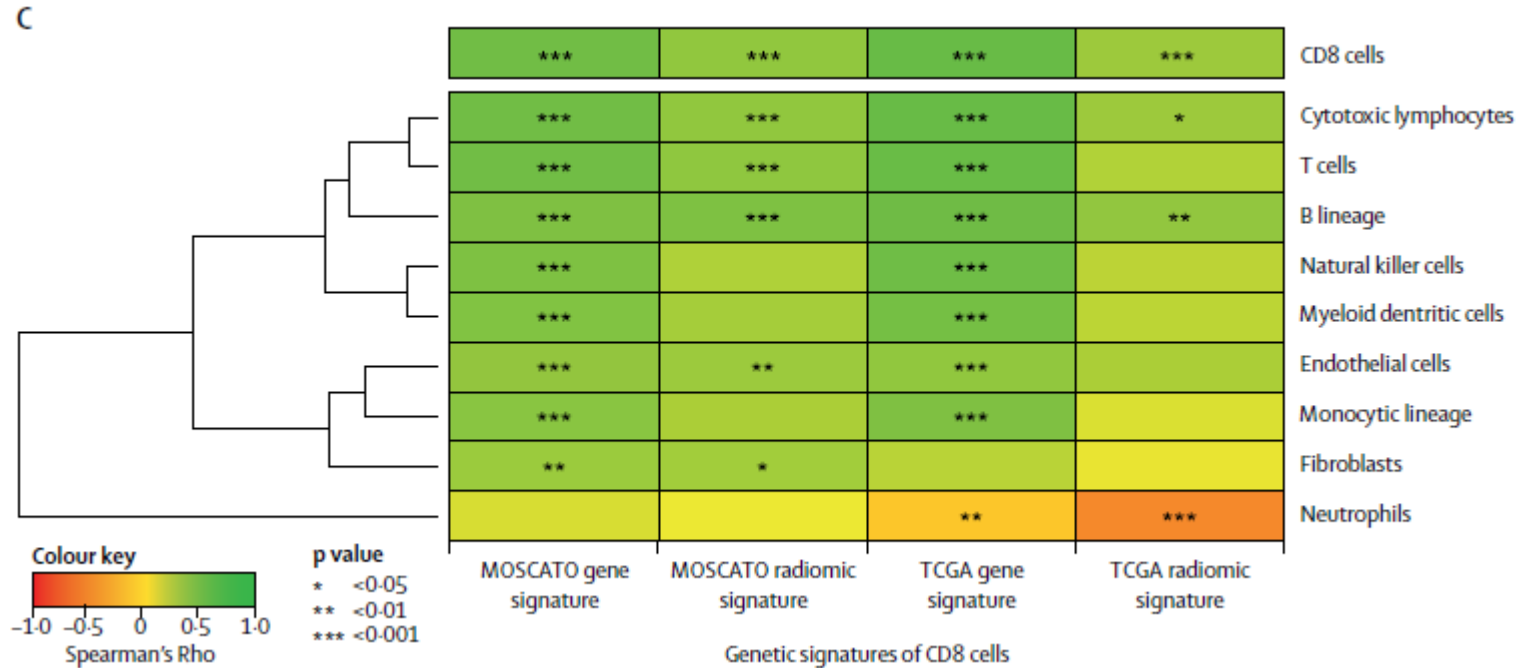


- **MCPcounter** is an R package which predicts the abundance of 10 cell populations from transcriptomic profiles.

Etienne Becht et Genome Biology, 2016 Oct 20;17(1):218.

Correlations between the genomic signatures and radiomic signatures of CD8 T cells and the other cell populations,

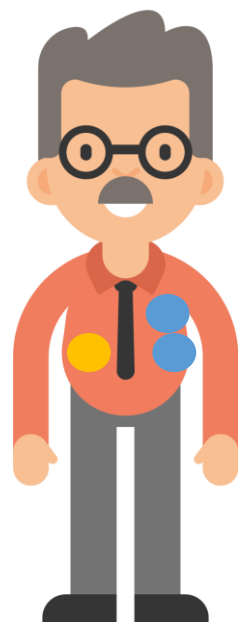
as estimated by the MCP-counter gene signatures



Useful for radioimmunotherapy?

Patients

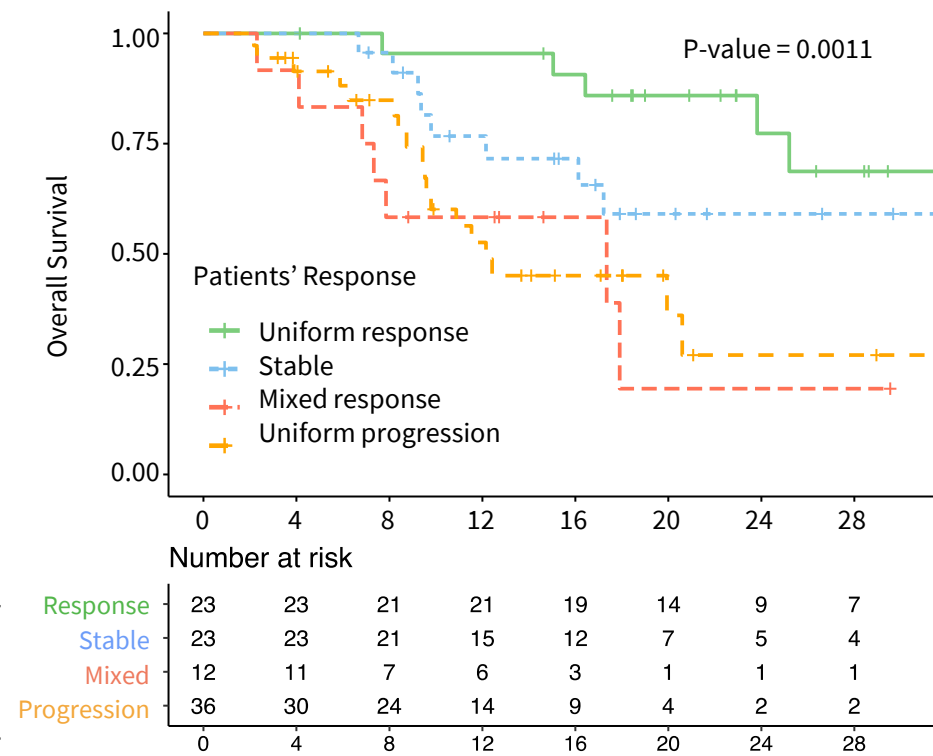
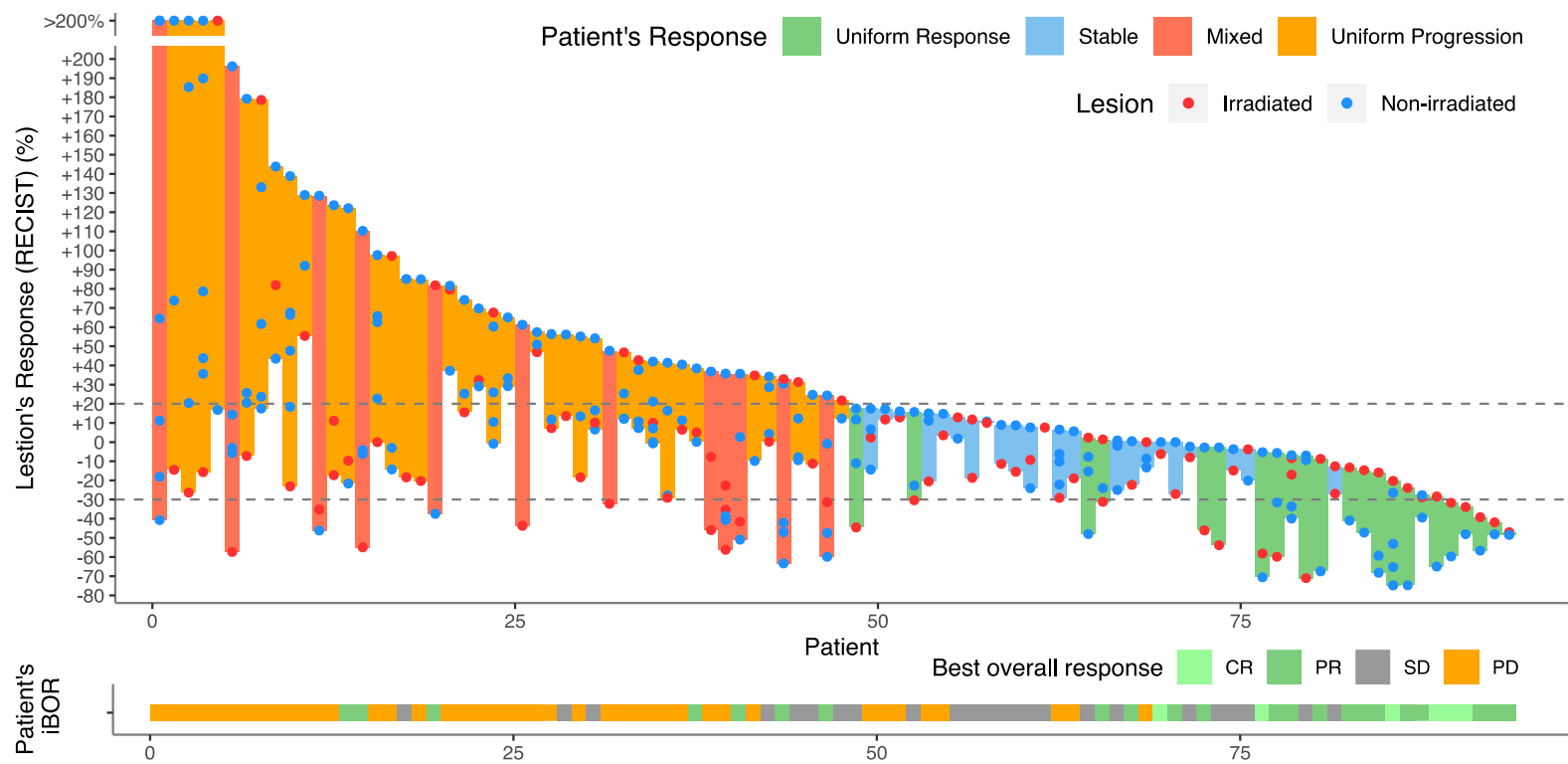
Gustave Roussy	SABR	Phase II CRC, melanoma, lung stage IV	Stereotactic RT (SBRT) : 3 x 15 Gy	Atezolizumab
	Mel-Ipi-Rx	Phase I Melanoma Stage III-IV	Hypofractionated 3 x 3 / 5 / 6 Gy	Ipilimumab
Gent	SBRT Ipilimumab	Phase I Melanoma Stage IV	SBRT : 3 x 8 / 10 / 12 Gy	Ipilimumab
	SBRT Nivolumab	Phase II Melanoma Stage III-IV	SBRT : 3 x 8 Gy	Nivolumab
	SBRT Pembrolizumab	Phase I Urothelial Stage IV	SBRT : 3 x 8 Gy	Pembrolizumab
Erlangen	ST-ICI	Observational H&N, lung Stage III-IV	Palliative and/or curative RT	Nivolumab Pembrolizumab



Sun et al. JITC 2020

RTIO cohort

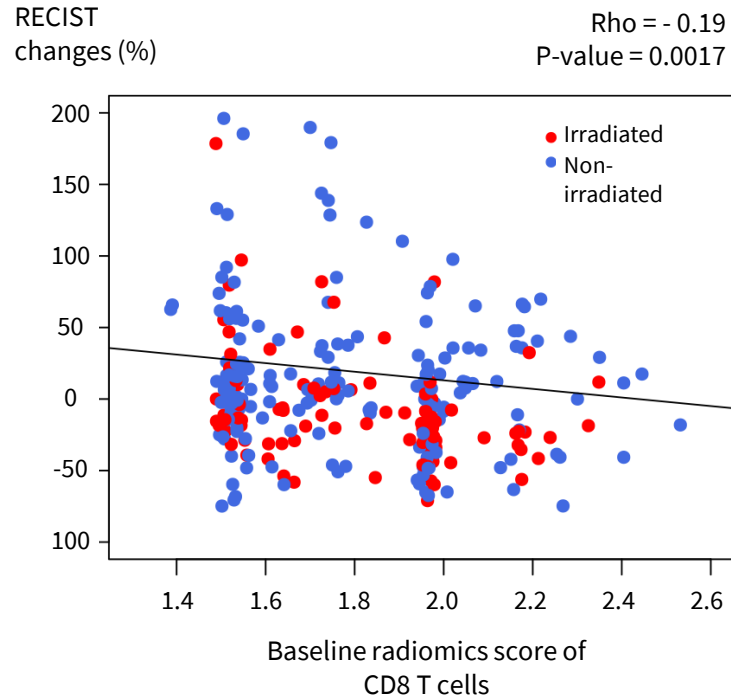
Patient patterns of response



RTIO cohort

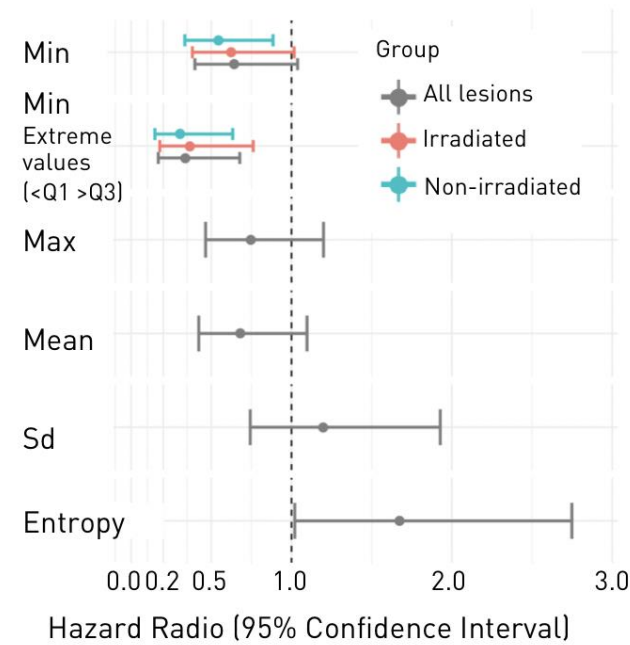
CD8 radiomic score distribution

Lesion response

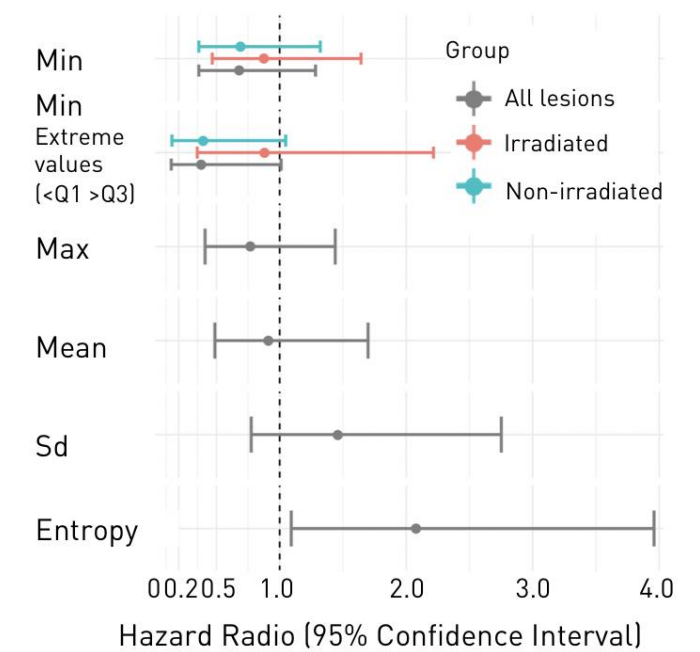


Patient response

RS baseline distribution and PFS



RS baseline distribution and OS



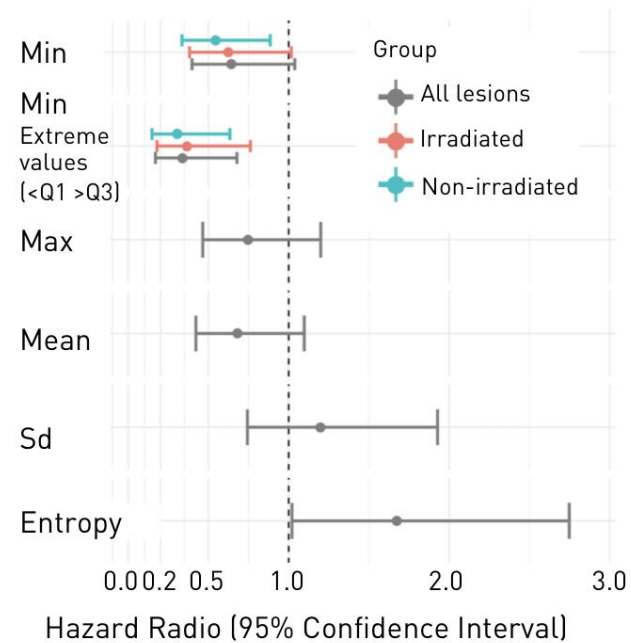
Sun et al. JITC 2020

RTIO cohort

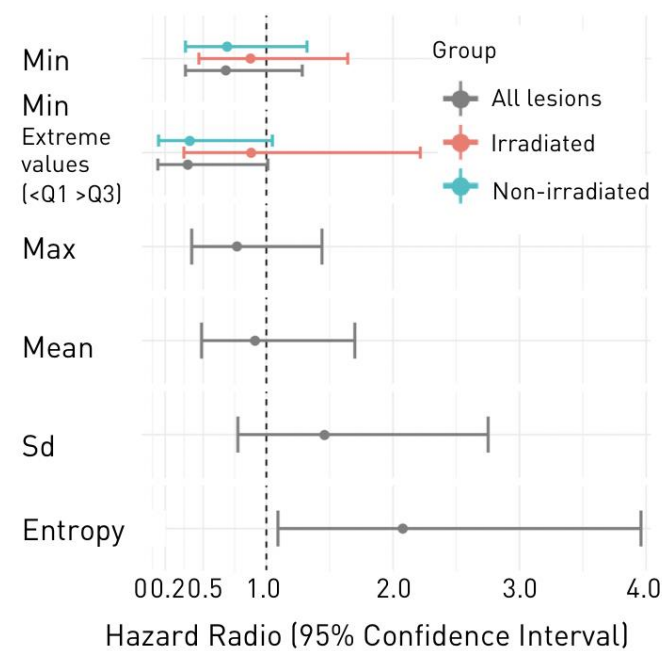
CD8 radiomic score distribution

Patient response

RS baseline distribution and PFS



RS baseline distribution and OS



Min CD8 RScore

Predictive value of the **least immune-infiltrated and non-irradiated** metastasis

May help to guide radiotherapy

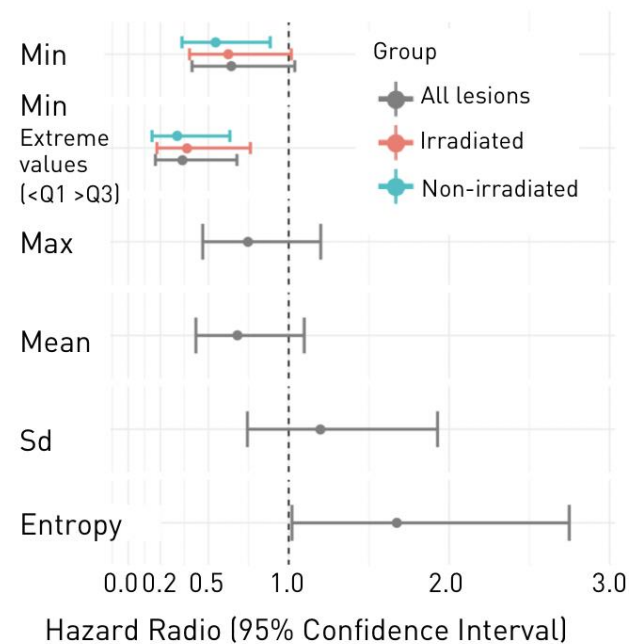
Sun et al. JITC 2020

RTIO cohort

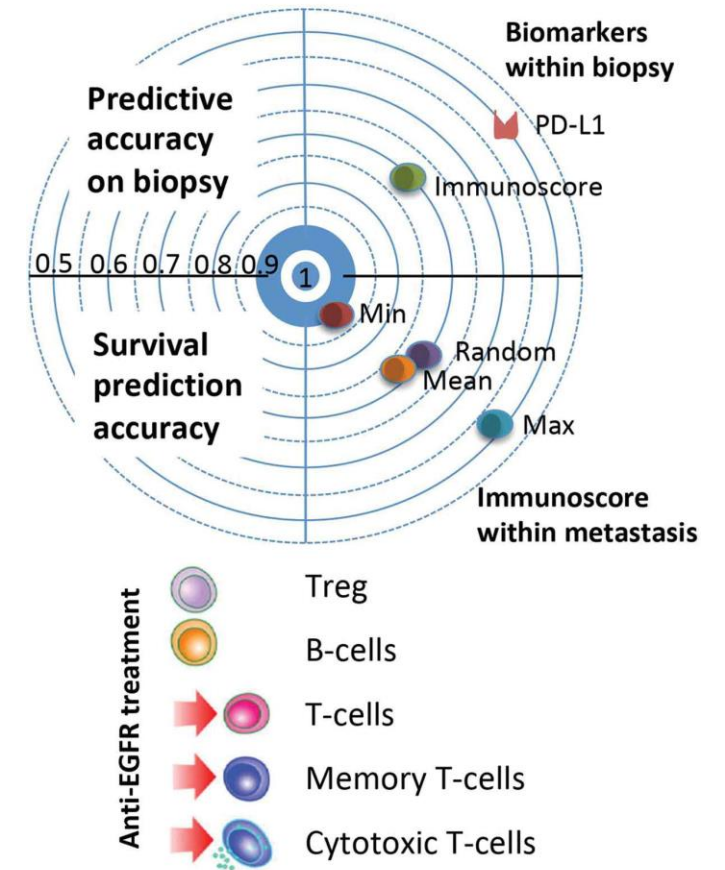
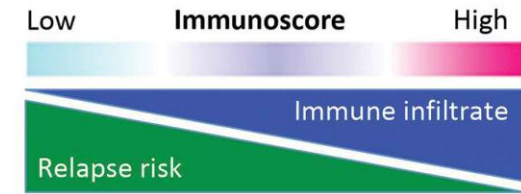
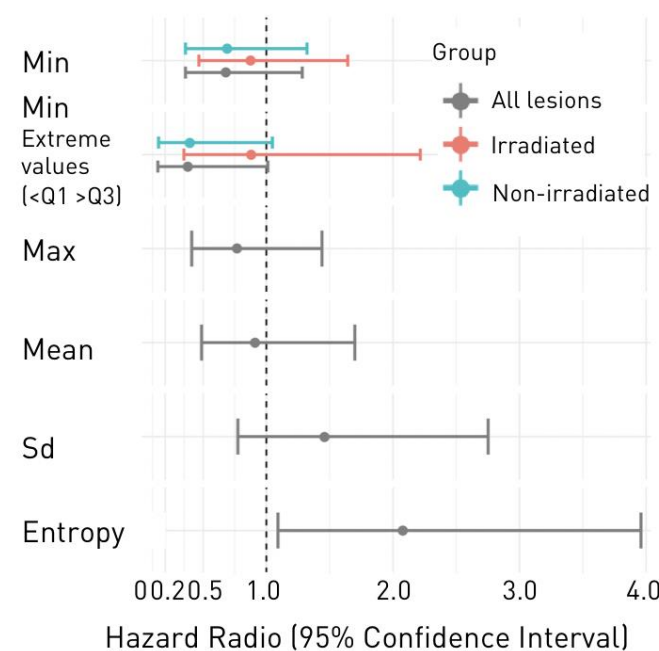
CD8 radiomic score distribution

Patient response

RS baseline distribution and PFS



RS baseline distribution and OS



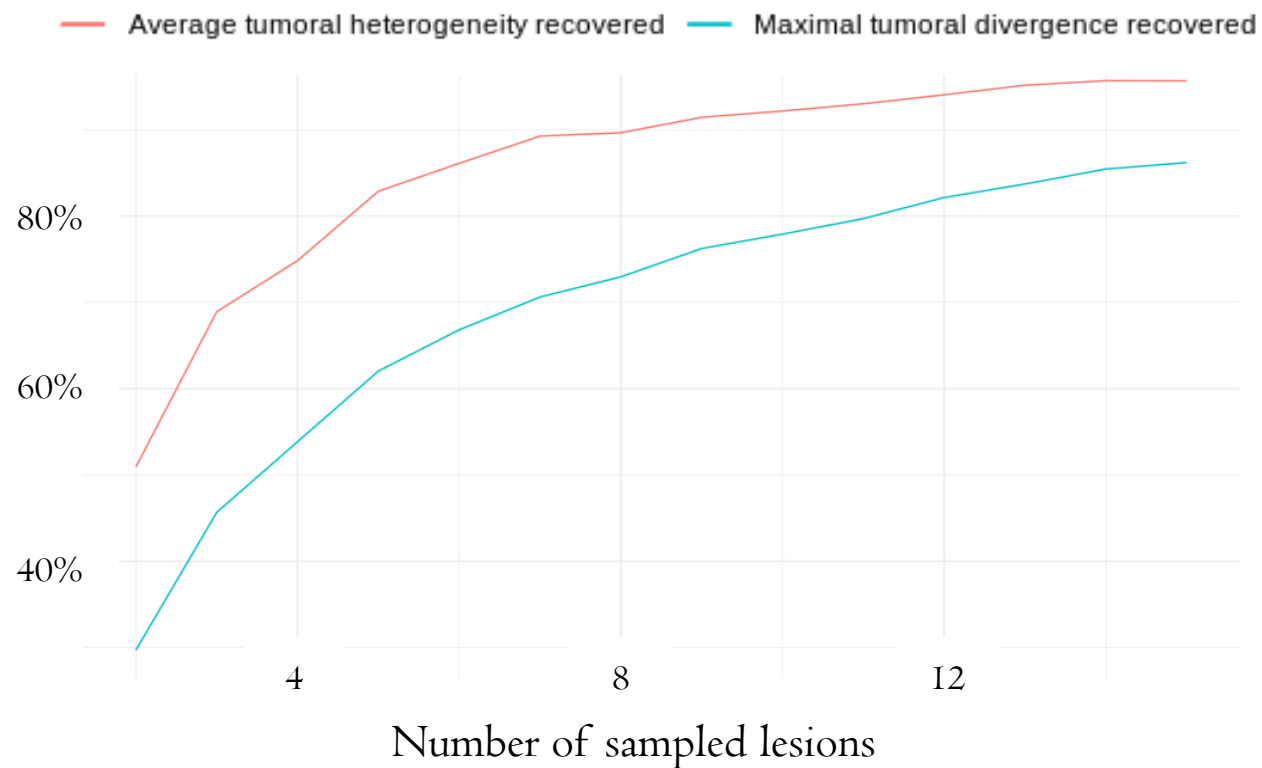
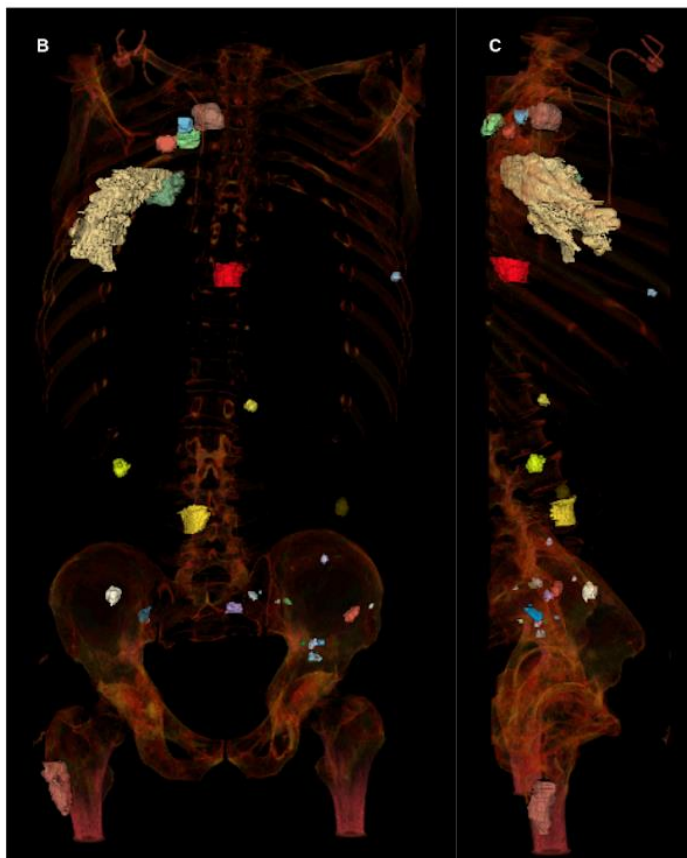
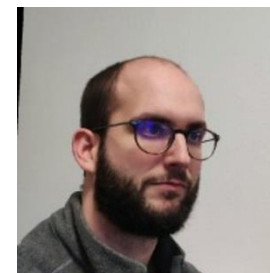
the most immune-infiltrated metastasis was not significantly predicting outcome, whereas the least immune-infiltrated metastasis was best in predicting clinical outcome

Van den Eynde et al. Oncoimmunology 2020

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Challenges

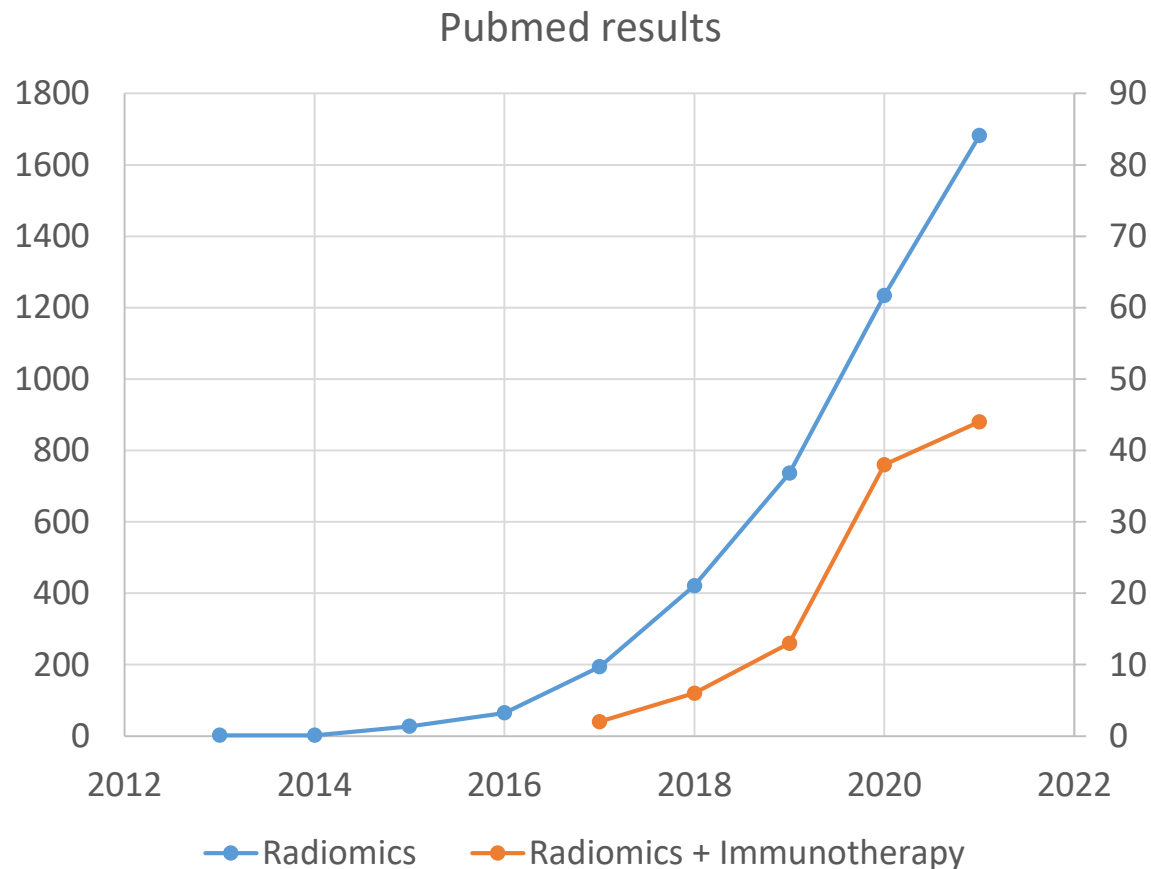
Spatial heterogeneity assessment



Henry T et al. submitted

DO NOT POST

Other promising radiomics signature?



Molecular pathways of immune response, inflammation, TILS, PD-L1

Grossman et al. eLife 2017

Tang et al. Sci Rep 2018

Chen et al. Eur Radiol 2019

MSI: Golia Pernicka et al. Abdom Radiol 2019

Microenvironment > IO response

CD8: Sun et al. Lancet oncol 2018

TMB: He et al. J Immunother Cancer. 2020

PDL1: Mu et al. J Immunother Cancer. 2021

Hypoxia: Tunali et al. JNCI Cancer Spectr. 2021

Response to IO directly

Tunali et al. Lung Cancer 2019

Trebeschi et al. Ann oncol 2019

Khorrami et al. Cancer Immunol Res 2019

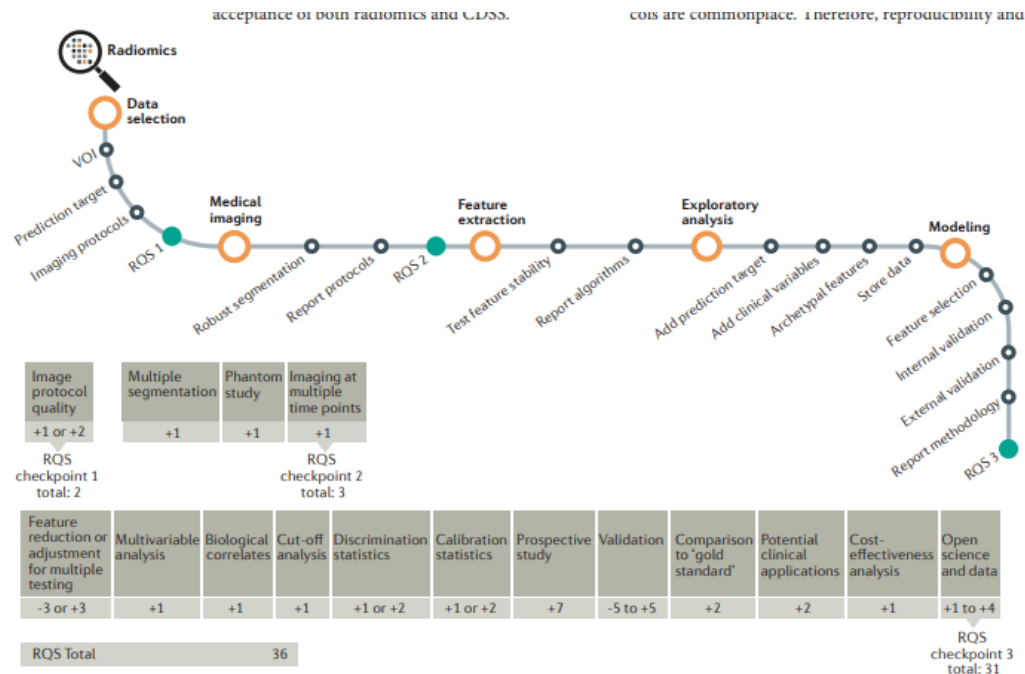
Mu et al. EJNMMI 2020

Liu et al. Front Oncol 2021

MDSC-targeting immunotherapy : Devkota Sci Adv. 2020 (mice)

Validity of radiomics studies

Radiomics Quality Score



Lambin et al, NRCO 2017

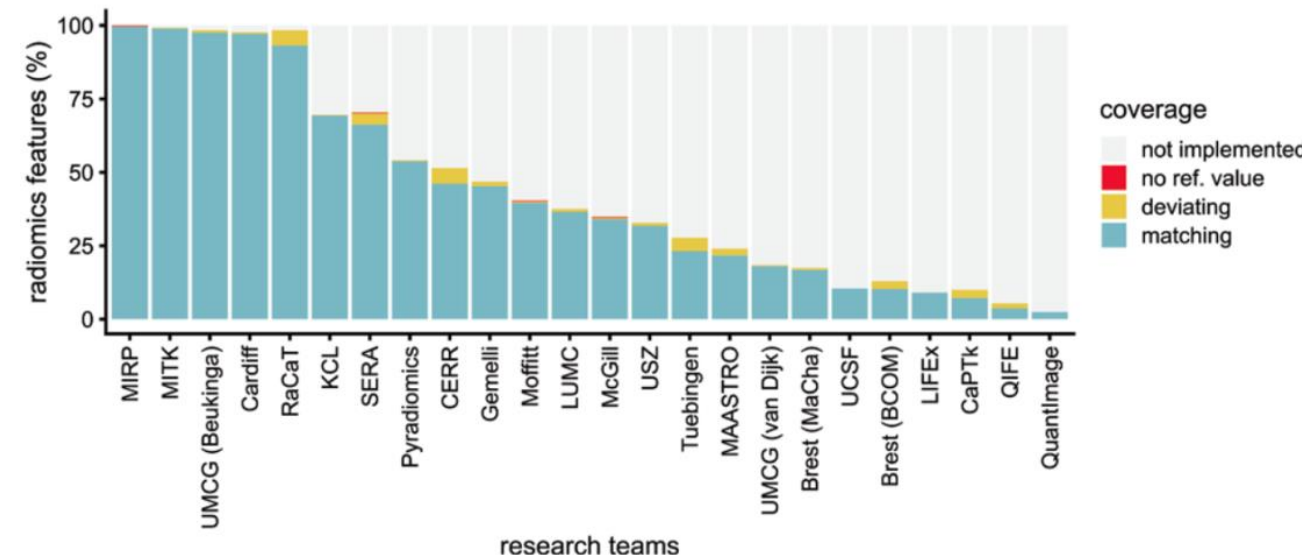
Radiology

ORIGINAL RESEARCH • COMPUTER APPLICATIONS

The Image Biomarker Standardization Initiative:

Standardized Quantitative Radiomics for High-Throughput Image-based Phenotyping

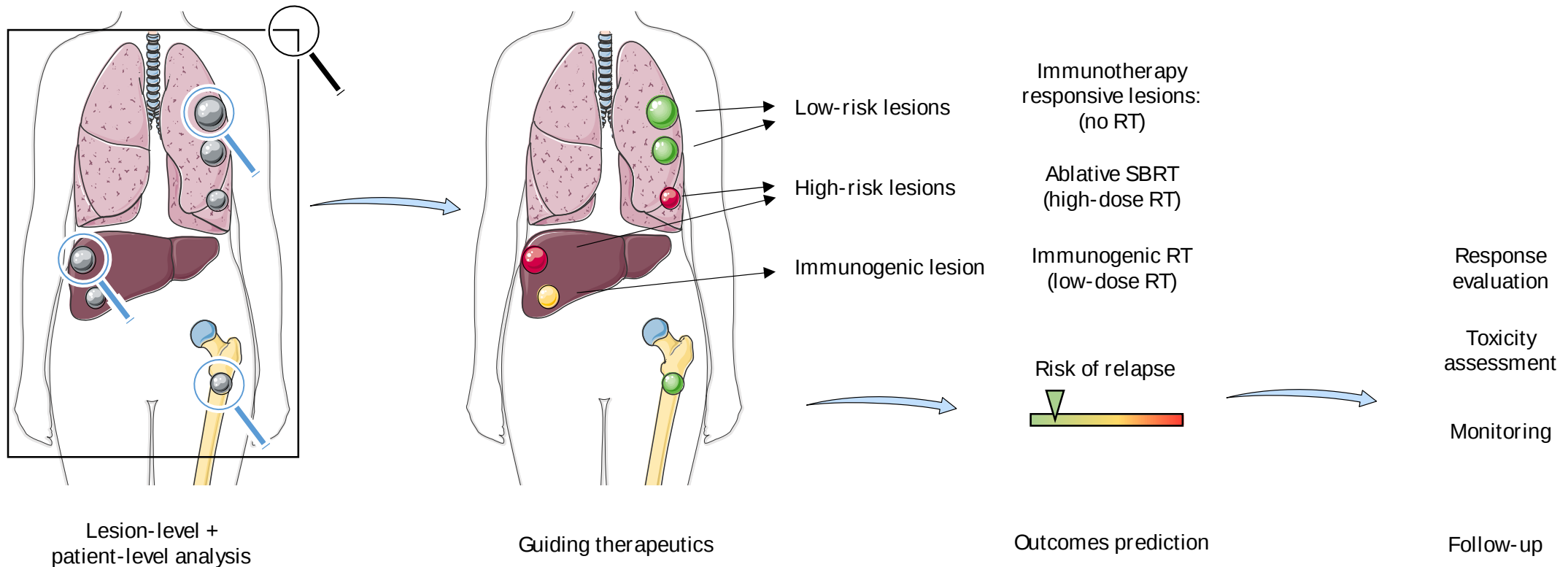
Alex Zwanenburg, PhD* • Martin Vallières, PhD* • Mahmoud A. Abdalah, PhD • Hugo J. W. L. Aerts, PhD • Vincent Andrearczyk, PhD • Aditya Apte, PhD • Saeed Ashrafinia, PhD • Spyridon Bakas, PhD • Roelof J. Beukinga, PhD • Ronald Boellaard, PhD • Marta Bogowicz, PhD • Luca Boldrini, PhD • Irène Buvat, PhD • Gary J. R. Cook, PhD • Christos Davatzikos, PhD • Adrien Depeursinge, PhD • Marie-Charlotte Desseroit, PhD • Nicola Dinapoli, PhD • Cuong Viet Dinh, PhD • Sebastian Echegaray, PhD • For the Group¹ •



Zwanenburg A et al. Radiology 2020

Toward ultra-precision radioimmunotherapy ?

Imaging-biomarkers guided radiotherapy



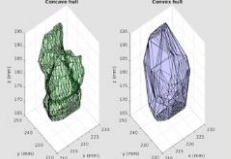
Sun R et al (submitted)

Data Collection

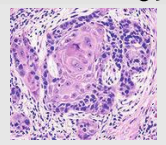
Medical Imaging



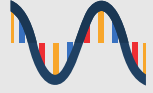
Tumor Geometry



Pathology



Genomic data

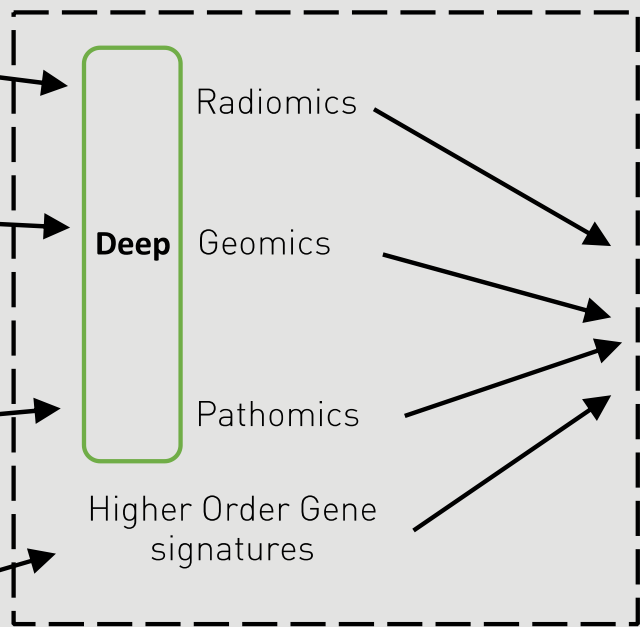


WP1

Seeing the invisible

Deep learning
UberNet

polycephalic/polypodic network



WP2

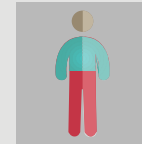
Predicting the outcomes

Advanced machine learning
& artificial intelligence

Training set



Clinical response to
Immunotherapy or
Immuno+radiotherapy
combination



Validation set

Retrospective

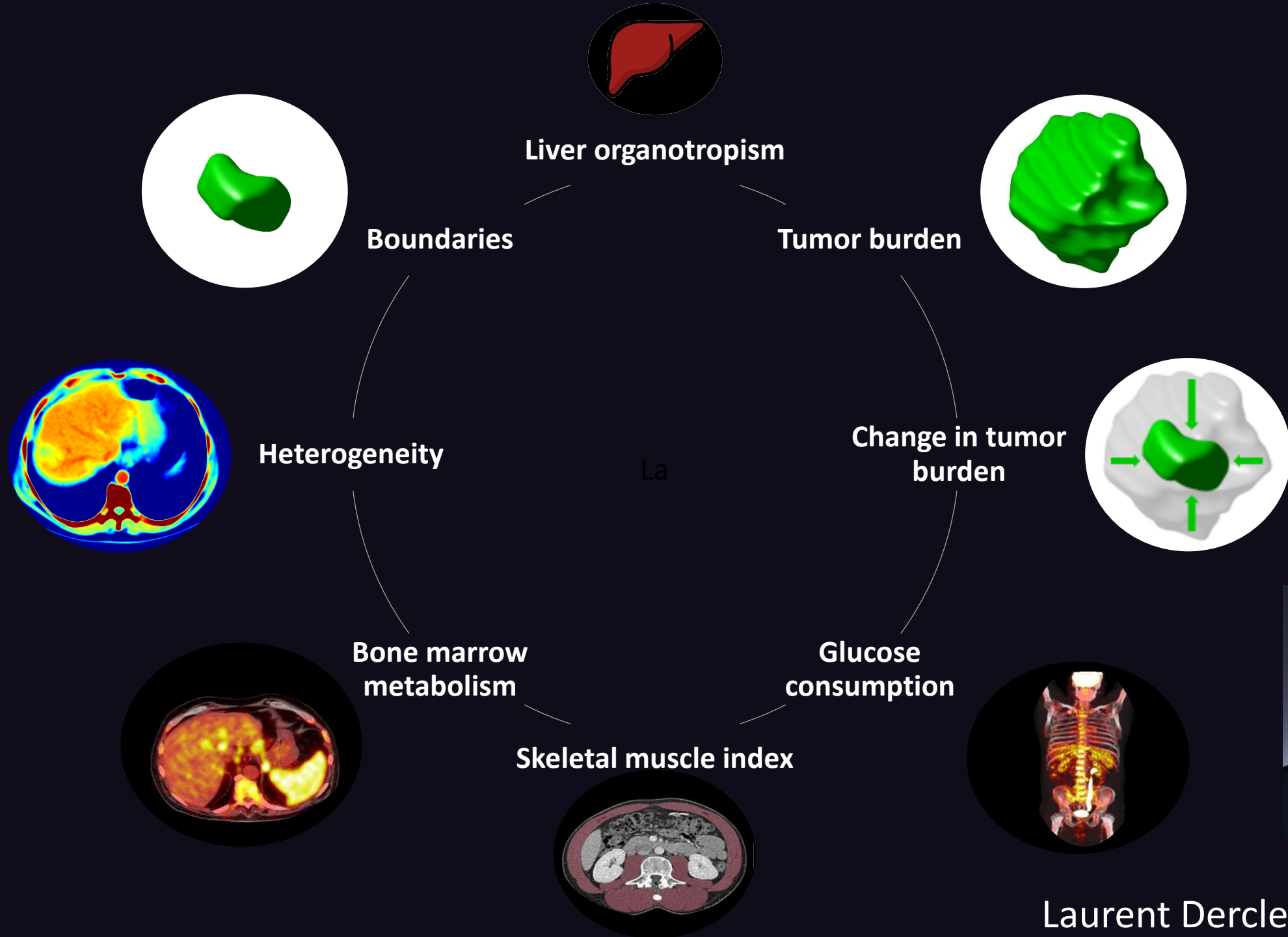
Prospective

WP3

WP4

Training the architecture with all cohorts simultaneously

Training each cohort separately



Laurent Dercle, Columbia

What we still do not really know?

Overlapp between biomarkers for IO and IO + RT ?



Conclusions

- Heterogeneity is a major challenge for radiomics studies
- Improve knowledge: tumor biology & radioimmunotherapy
- Non-invasive way for selection of radiotherapy targets
- Importance of appropriate radiomics study design
- A methodology that can encompass TME component beyond CD8

U1030 and collaborations

Pr. Éric DEUTSCH (PU-PH)

- **Researchers**

Dr. Charlotte ROBERT (MCU)

Dr. Maria VAKALOPOULOU (MCU)

Ibrahima DIALLO (IR)

Cristina VERES (IR)

- **Post-doc**

Dr. Rahimeh ROUHI (Gustave Roussy)

- **PhD students**

Nathan BENZAZON

Théophraste HENRY (MD)

Marvin LEROUSSÉAU

Amaury LEROY (Therapanacea, Gustave Roussy)

Sonia MARTINOT (Therapanacea, Gustave Roussy, Centrale Supélec)

Stéphane NIYOTEKA (Doctorant)

François DE KERMENGUY (Paris Saclay)

- **Chef de projet**

Vjona CIFLIKU

- **CentraleSupélec / Therapanacea**

Pr. Nikos Paragios

- **Ghent university**

Pr. Piet Ost

Dr. Nora Sundahl

Dr. Mathieu Spaas

- **Erlangen Strahlenklinik**

Pr. Rainer Fietkau

Dr. Udo Gaipl

Dr. Markus Hecht

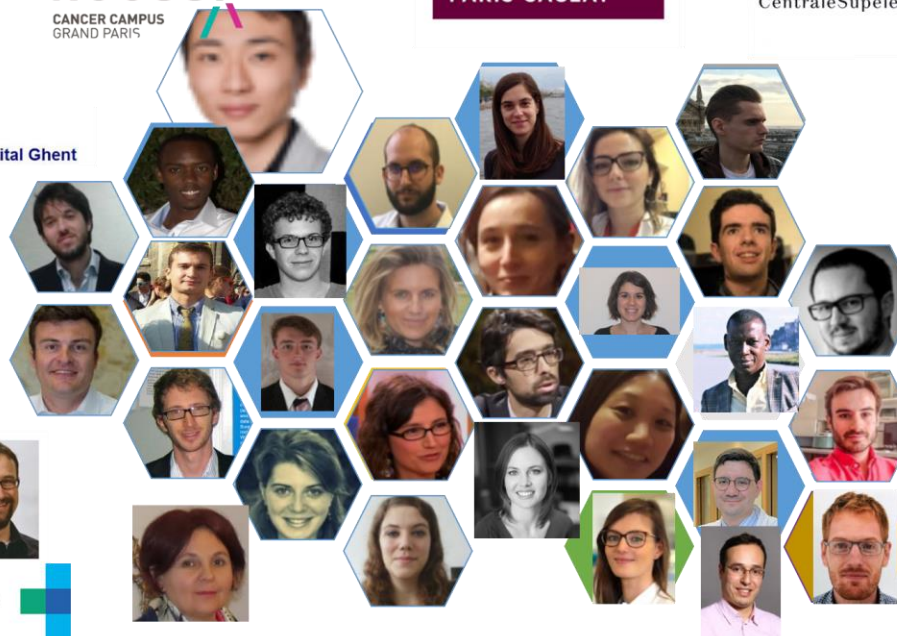
- **Parma university**

Dr Giulia Mazzaschi

- **Fondazione IRCCS Policlinico San Matteo di Pavia**

Pr. Andrea Filippi

Dr Andrea Lan



Columbia NY

