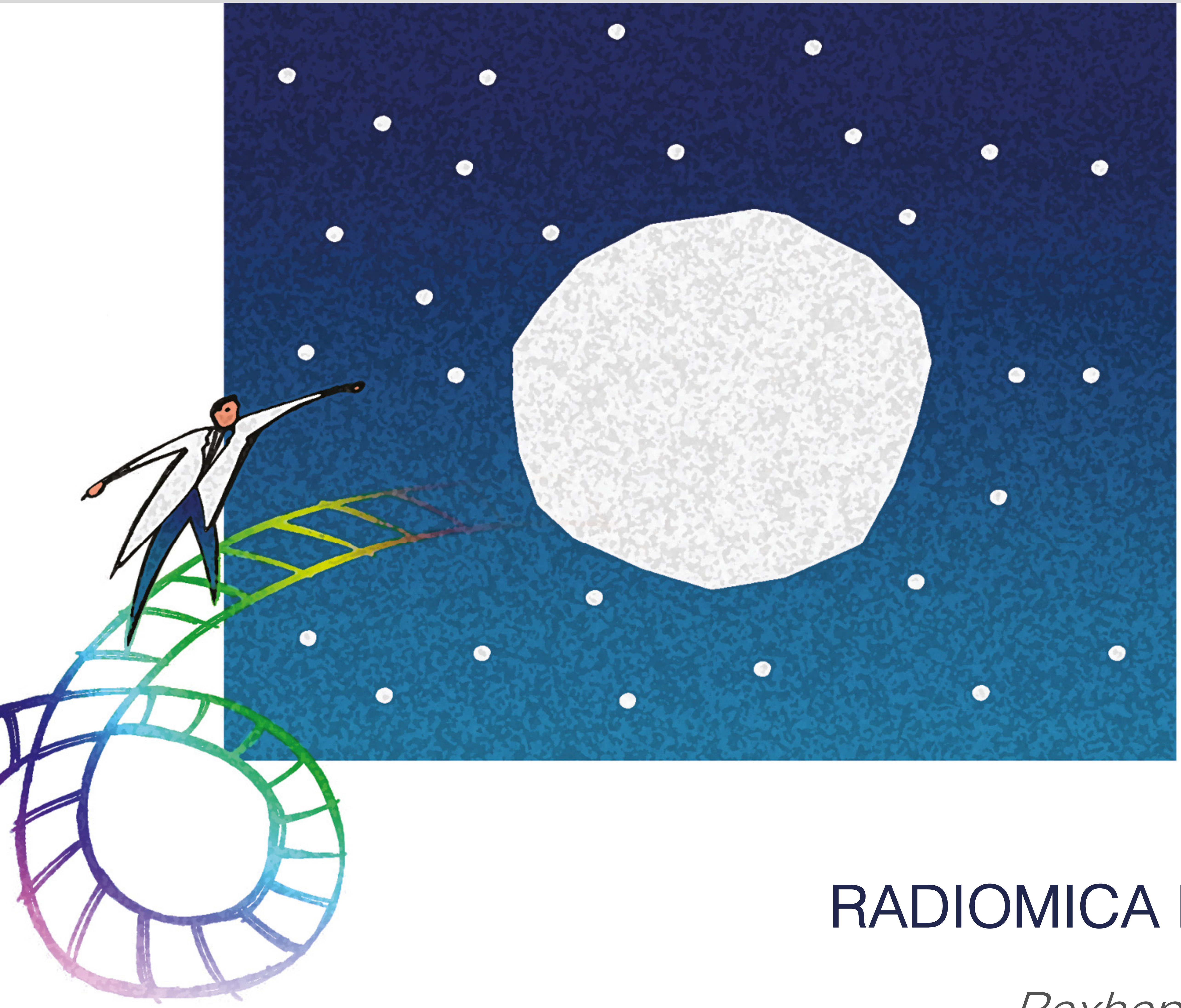


The young side of LYMPHOMA

gli under 40 a confronto

Milano, 14-15 aprile 2023

RADIOMICA NEI LINFOMI

Rexhep Durmo

AUSL-IRCCS REGGIO EMILIA

rexhep.durmo@ausl.re.it

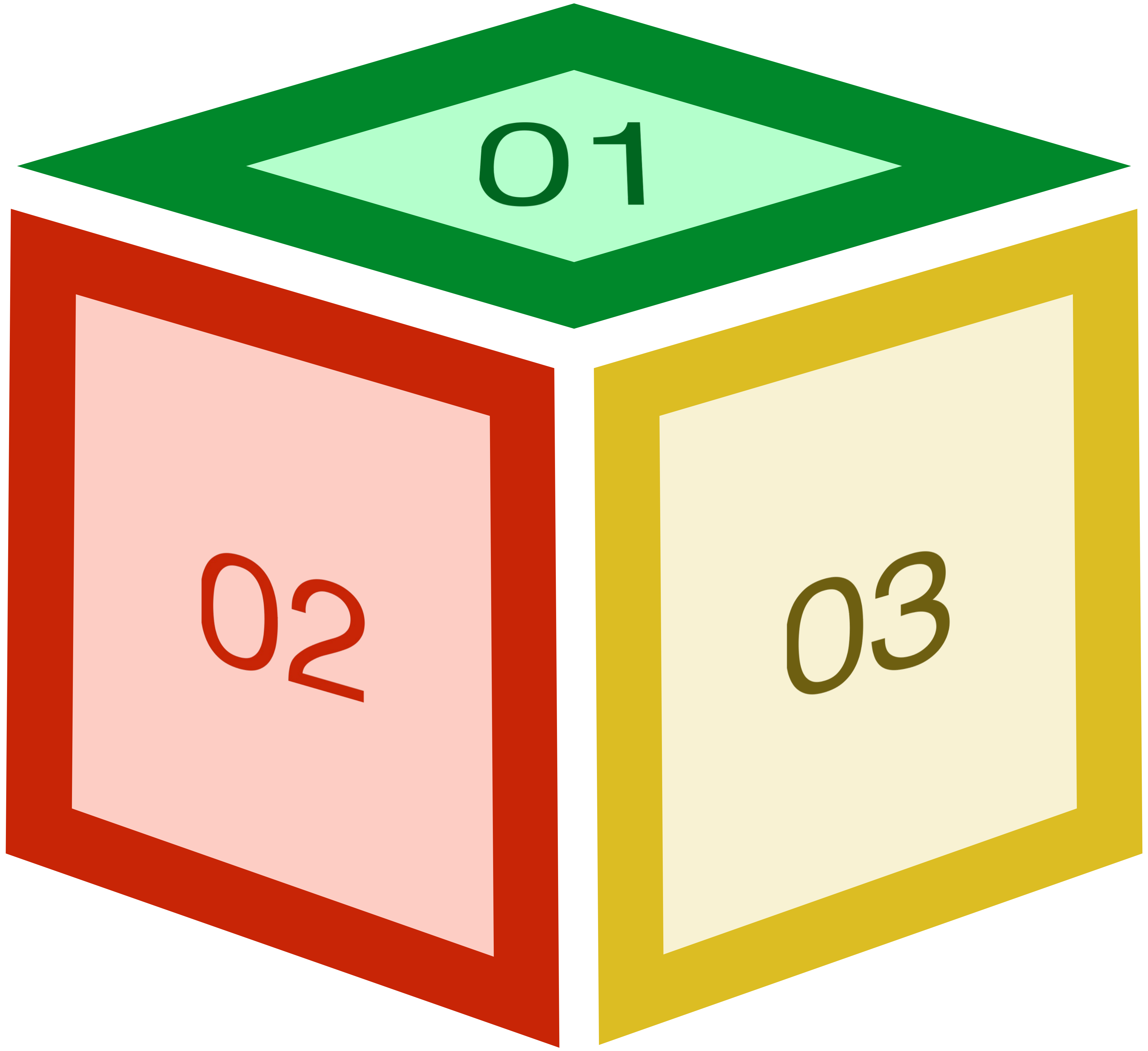
Disclosures of Name Surname

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other

RADIOMICA

Overview of radiomics

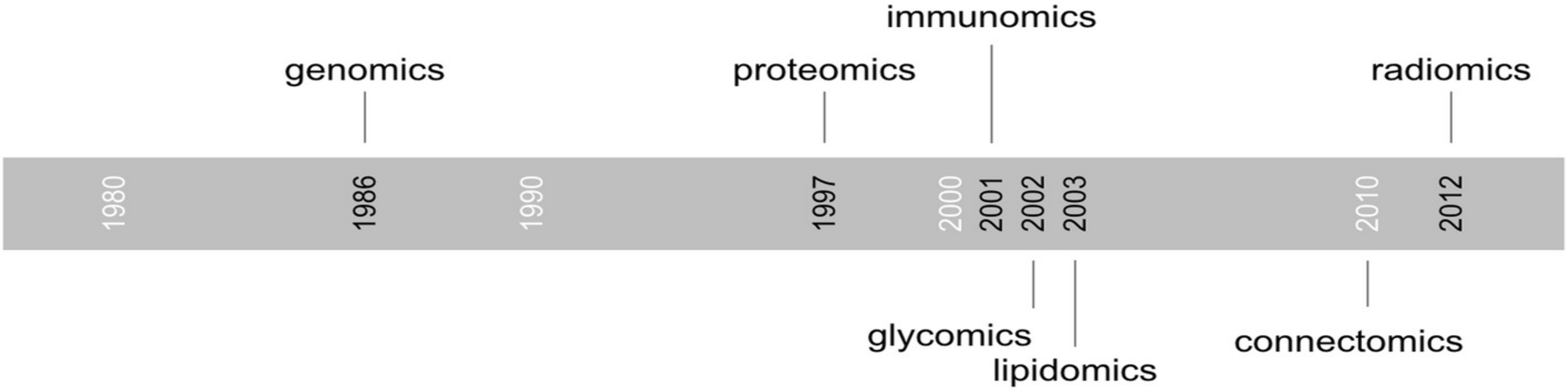
APPLICAZIONI DI RADIOMICA



LIMITI E PROSPETTIVE FUTURE

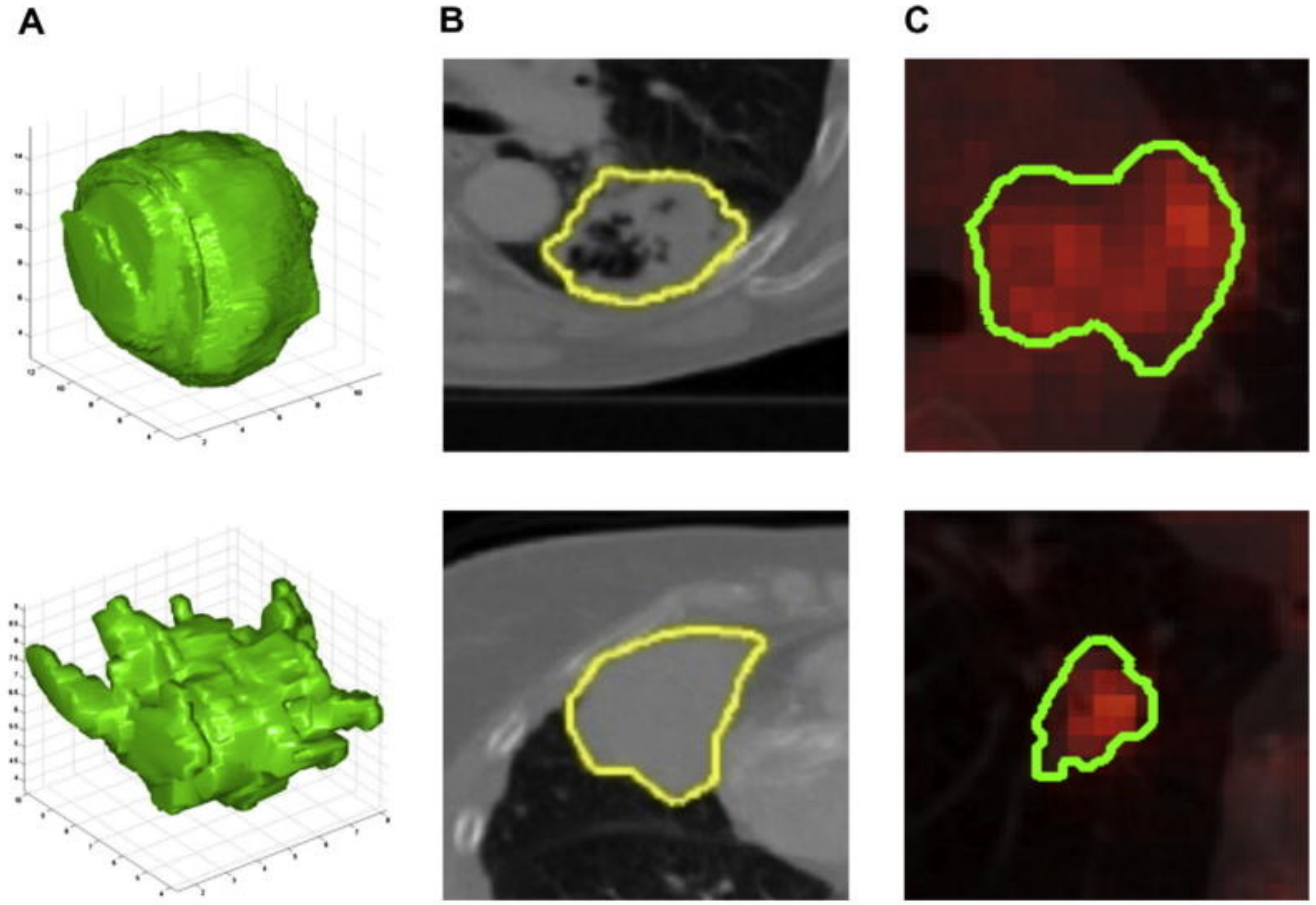
TRECCANI

Si definiscono *scienze omiche* quelle discipline che utilizzano tecnologie di analisi che consentono la produzione di informazioni (dati), in numero molto elevato e nello stesso intervallo di tempo, utili per la descrizione e l'interpretazione del sistema biologico studiato.

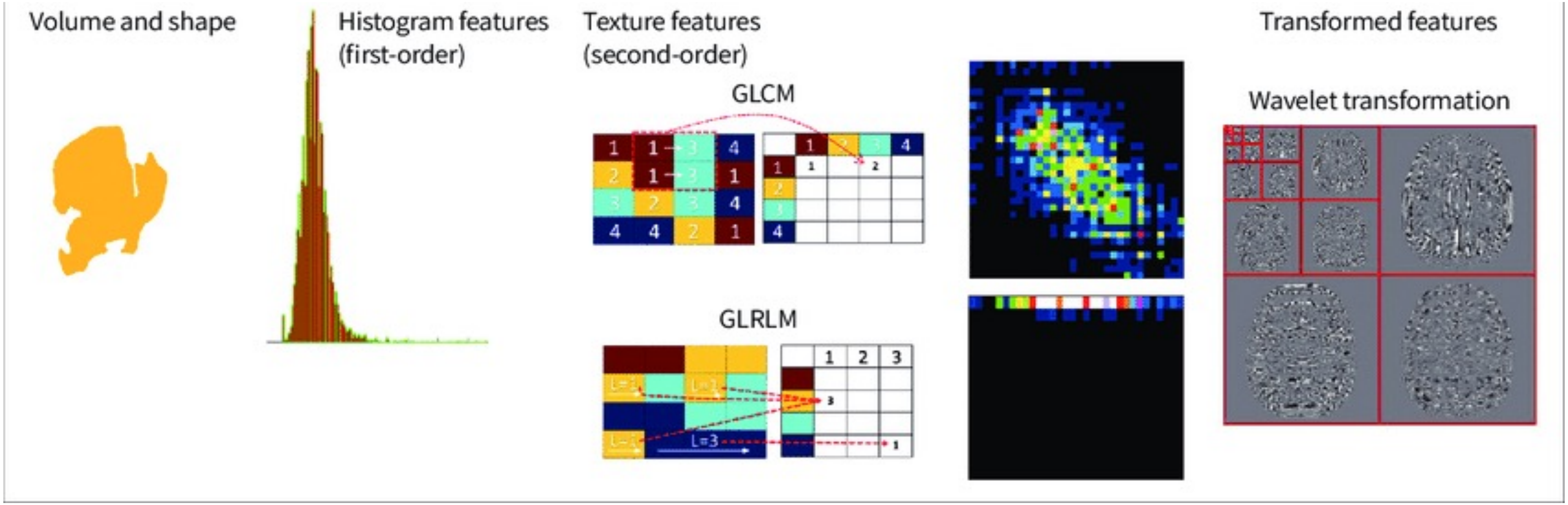


Gatta, R. *et al.* Integrating radiomics into holomics for personalised oncology: from algorithms to bedside. *Eur Radiol Exp* **4**, 11 (2020). https://doi.org/10.1186/s41747-019-0143-0

●Radiomica: l'analisi delle **immagini mediche** volta a ottenere, tramite opportuni **metodi matematici**, informazioni di tipo quantitativo per creare **modelli di supporto alla decisione clinica: Decision Support Systems**



Lambin P, Rios-Velazquez E, Leijenaar R, et al. *Radiomics: extracting more information from medical images using advanced feature analysis*. Eur J Cancer. 2012;48:441–446.



1.First-order features: statistical measurements of the image intensity distribution within the region of interest (ROI) and are related to the histogram of pixel/voxel values.

2. **Second-order features:** texture-based and describe the spatial relationships between pixels/voxels within the ROI. Second-order features are derived from the grey-level co-occurrence matrix (GLCM), grey-level run-length matrix (GLRLM), grey-level size zone matrix (GLSZM), and grey-level dependence matrix (GLDM).

3. **Higher-order features:** These features are derived from mathematical models, such as fractals and wavelets, and describe the more complex structures and patterns within the ROI.

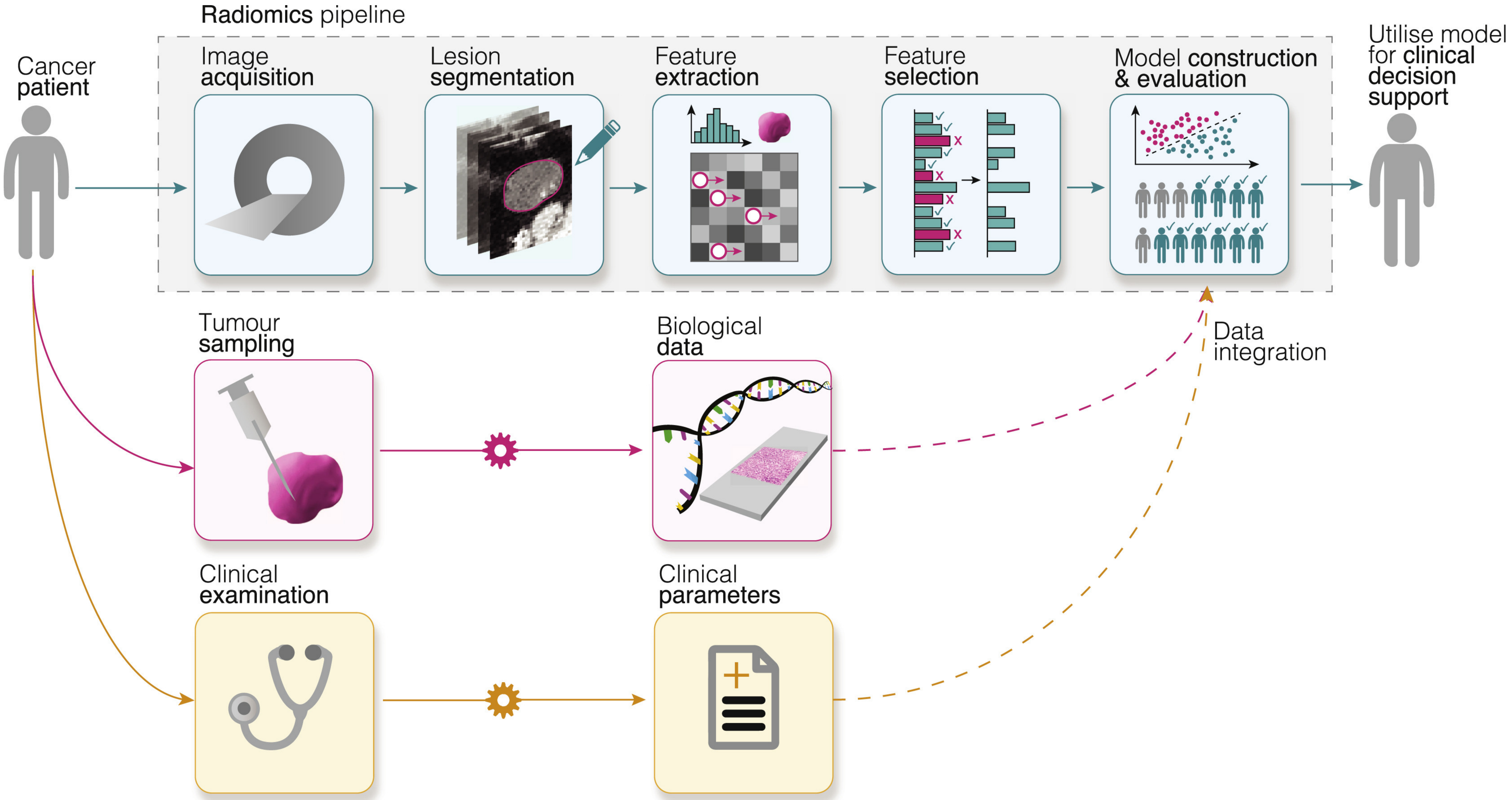
Pengpeng Xu et al. Radiomics https://doi.org/10.1161/CIRCIMAGING.120.011747

First-order texture features

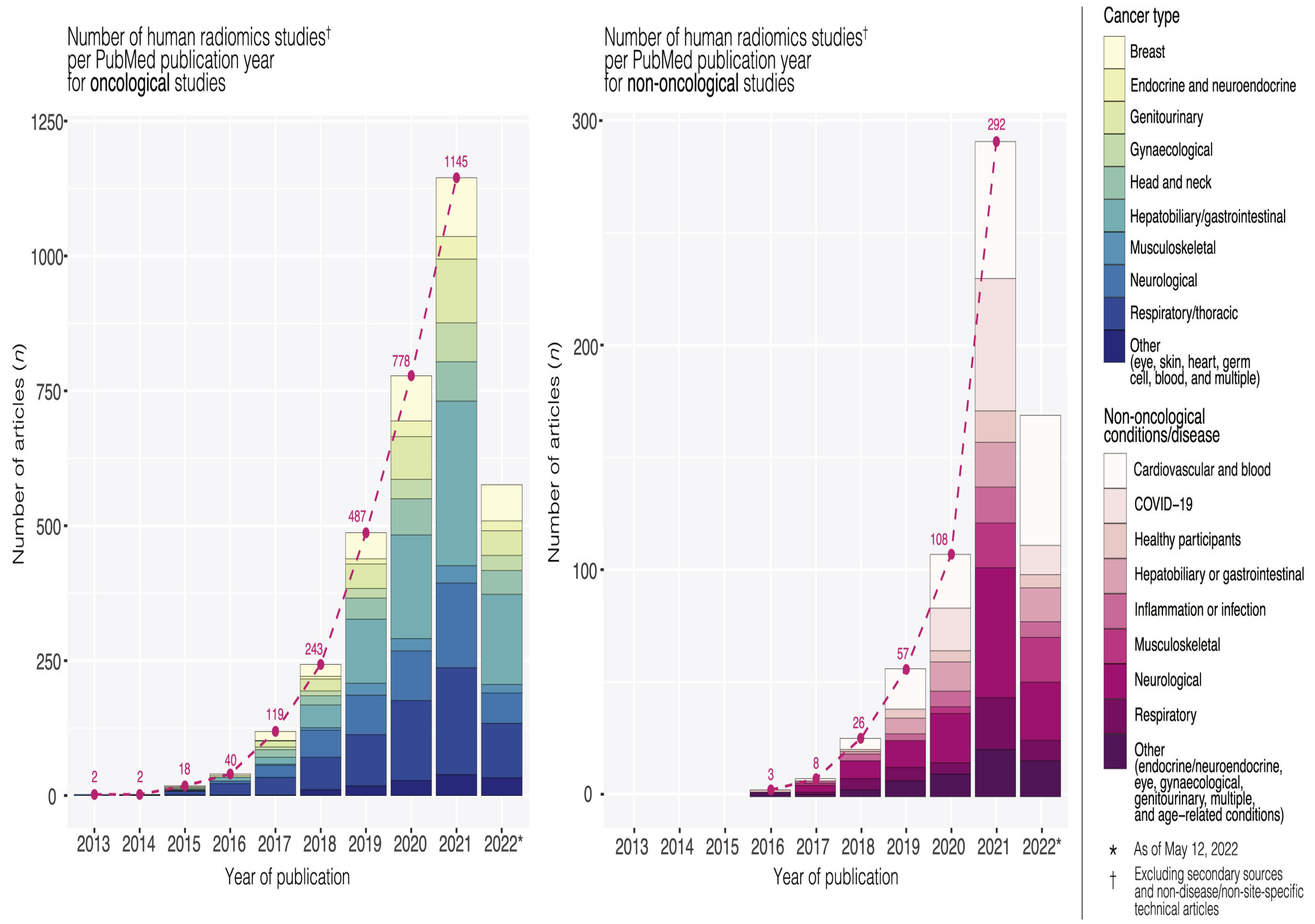
Feature	Definition	Description
SUV_{max}, SUV_{avg}, MTV, TLG	–	Conventional PET parameters
CV	Standard deviation of SUVs/SUV_{avg}	A global heterogeneity marker. Higher values indicate more heterogeneity
AUC-CSH	Percent of total tumor volume above percent threshold of SUV_{max}, which threshold varies from 0 to 100%.	A global heterogeneity marker. Lower values indicate more heterogeneity
Skewness	$\frac{\frac{1}{E}\sum_i \left(HISTO(i)-\overline{HISTO}\right)^3}{\left(\sqrt{\frac{1}{E}\sum_i \left(HISTO(i)-\overline{HISTO}\right)^2}\right)^3}$ (with $E=$ the total number of voxels in the VOI, $\overline{HISTO}=$ the average of gray levels in the histogram)	The asymmetry of the gray-level distribution in the intensity frequency histogram
Kurtosis	$\frac{\frac{1}{E}\sum_i \left(HISTO(i)-\overline{HISTO}\right)^4}{\left(\frac{1}{E}\sum_i \left(HISTO(i)-\overline{HISTO}\right)^2\right)^2}$ (with $E=$ the total number of voxels in the VOI, $\overline{HISTO}=$ the average of gray levels in the histogram)	The sharpness of the peak of the gray-level distribution in the intensity frequency histogram
$Entropy_{histo}$	$\sum_i p(i)\cdot\log(p(i)+\varepsilon)$	The randomness of the gray-level distribution in the intensity frequency histogram

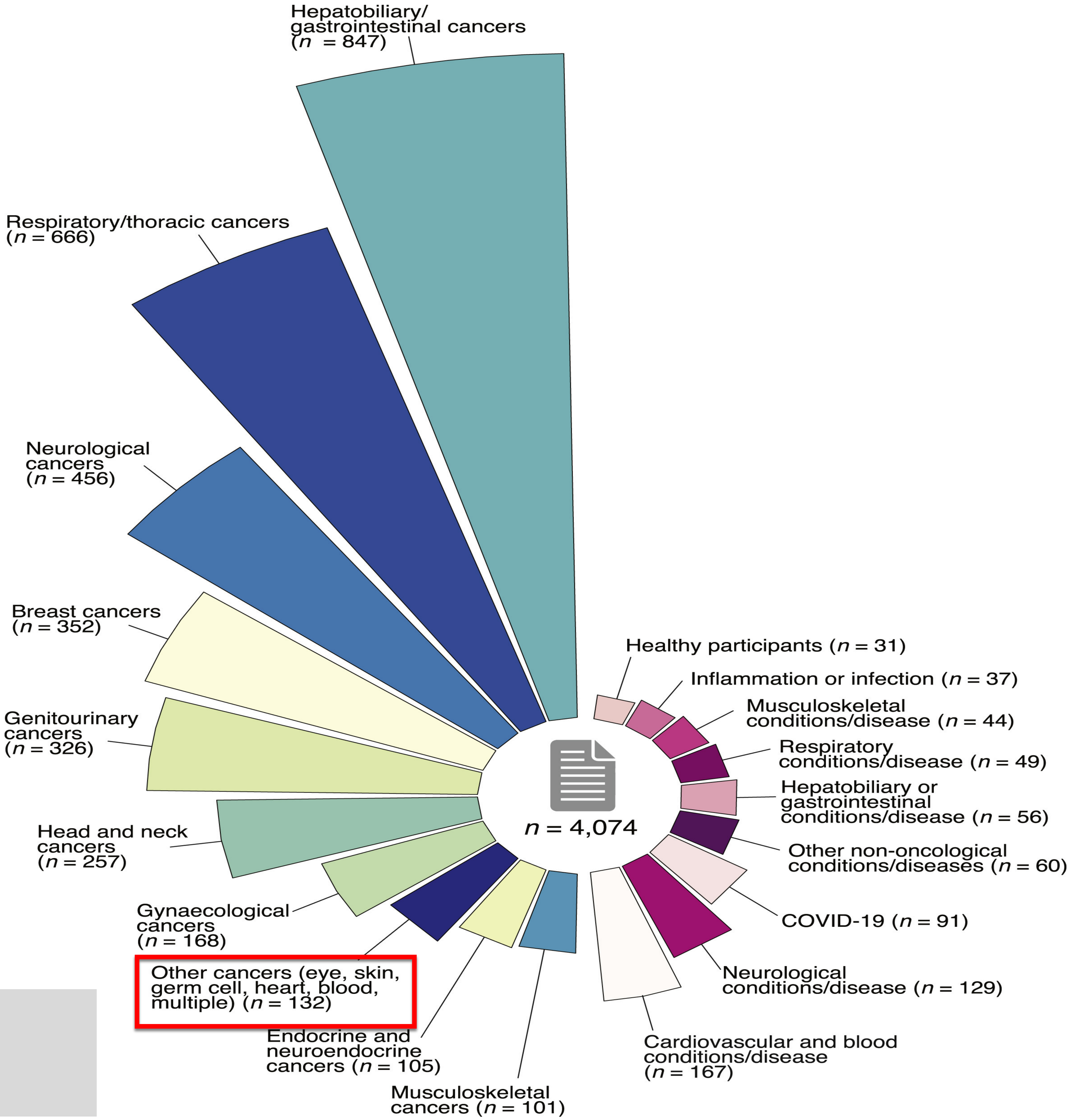
AUC-CSH, area under curve of cumulative SUV-volume histogram; *CV*, coefficient of variation; *MTV*, metabolic tumor volume; *SUV*, standardized uptake values; SUV_{avg}, average of SUVs; SUV_{max}; maximum of SUVs; *TLG*, total legion glycolysis; *VOI*, volume of interest

Ha S. et al. Radiomics in Oncological PET/CT: a Methodological Overview. *Nucl Med Mol Imaging*. 2019;53(1):14-29. doi:10.1007/s13139-019-00571-4



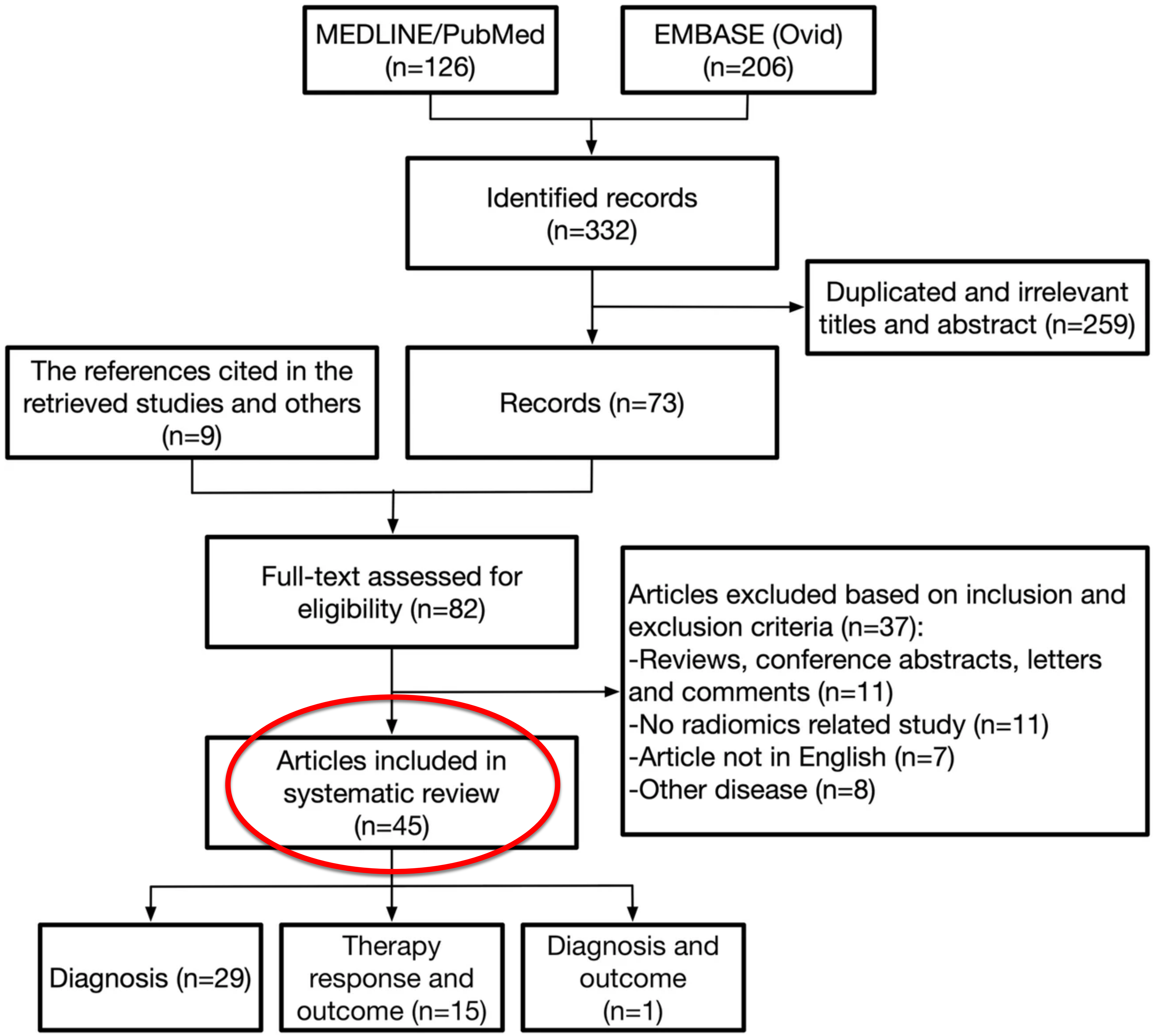
Clinical Radiology 2023 7883-98DOI: (10.1016/j.crad.2022.08.149)





Clinical Radiology 2023 7883-98DOI:
(10.1016/j.crad.2022.08.149)

APPLICAZIONI DI RADIOMICA



Current status and quality of radiomics studies in lymphoma: a systematic review. Wang, H., Zhou, Y., Li, L. *et al.* *Eur Radiol* **30,** 6228–6240 (2020). https://doi.org/10.1007/s00330-020-06927-1

Computer Methods and Programs in Biomedicine 185 (2020) 105153

ELSEVIER

Contents lists available at ScienceDirect

Computer Methods and Programs in Biomedicine

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

Texture analysis and multiple-instance learning for the classification of malignant lymphomas

Marco Lippi[a,j,k,*], Stefania Gianotti[a], Angelo Fama[c], Massimiliano Casali[d], Elisa Barbolini[i], Angela Ferrari[c], Federica Fioroni[b], Mauro Iori[b], Stefano Luminari[c,f], Massimo Menga[g], Francesco Merli[c], Valeria Trojani[h], Annibale Versari[d], Magda Zanelli[e], Marco Bertolini[b]

60 patients

Features extracted from PET/CT, combined with multiple-instance machine learning algorithms

Hodgkin's lymphoma, can be identified from texture information: 97.0% of sensitivity and a 94.1% of predictive positive value (precision)

Subtype	Method	VOIs				Patients			
		A	P	R	F_1	A	P	R	F_1
DLBCL	ES	–	–	–	–	0.778	0.545	0.667	0.600
	ES + R	–	–	–	–	0.806	0.600	0.667	0.632
	ES_ℓ + R	–	–	–	–	0.778	0.571	0.444	0.500
	IS	0.725	0.317	0.394	0.351	0.667	0.364	0.444	0.400
	IS + R	0.765	**0.407**	**0.530**	**0.461**	0.806	0.583	**0.778**	**0.667**
	IS_ℓ + R	**0.800**	0.379	0.512	0.436	**0.833**	**0.714**	0.556	0.625
FL	ES	–	–	–	–	**0.833**	**1.000**	0.333	**0.500**
	ES + R	–	–	–	–	0.778	**1.000**	0.111	0.200
	ES_ℓ + R	–	–	–	–	0.750	0.000	0.000	0.000
	IS	0.504	0.182	0.291	0.224	0.457	0.143	0.222	0.174
	IS + R	0.553	0.292	**0.570**	0.386	0.528	0.250	0.444	0.320
	IS_ℓ + R	**0.565**	**0.316**	0.560	**0.404**	0.639	0.357	**0.556**	0.435
HL	ES	–	–	–	–	0.917	0.875	0.778	0.824
	ES + R	–	–	–	–	0.917	0.875	0.778	0.824
	ES_ℓ + R	–	–	–	–	**0.944**	**0.889**	**0.889**	**0.889**
	IS	0.728	0.294	0.566	0.387	0.722	0.462	0.667	0.545
	IS + R	0.791	0.384	**0.623**	0.475	0.861	0.750	0.667	0.706
	IS_ℓ + R	**0.818**	**0.419**	0.619	**0.500**	0.833	0.714	0.556	0.625
MCL	ES	–	–	–	–	0.556	0.360	**1.000**	0.529
	ES + R	–	–	–	–	0.556	0.360	**1.000**	0.529
	ES_ℓ + R	–	–	–	–	0.611	0.391	**1.000**	0.563
	IS	**0.662**	**0.610**	0.500	**0.550**	**0.806**	**0.600**	0.667	**0.632**
	IS + R	0.625	0.550	**0.500**	0.524	0.722	0.455	0.556	0.500
	IS_ℓ + R	0.593	0.540	0.488	0.513	0.694	0.429	0.667	0.522

Hindawi
Contrast Media & Molecular Imaging
Volume 2019, Article ID 4507694, 9 pages
https://doi.org/10.1155/2019/4507694

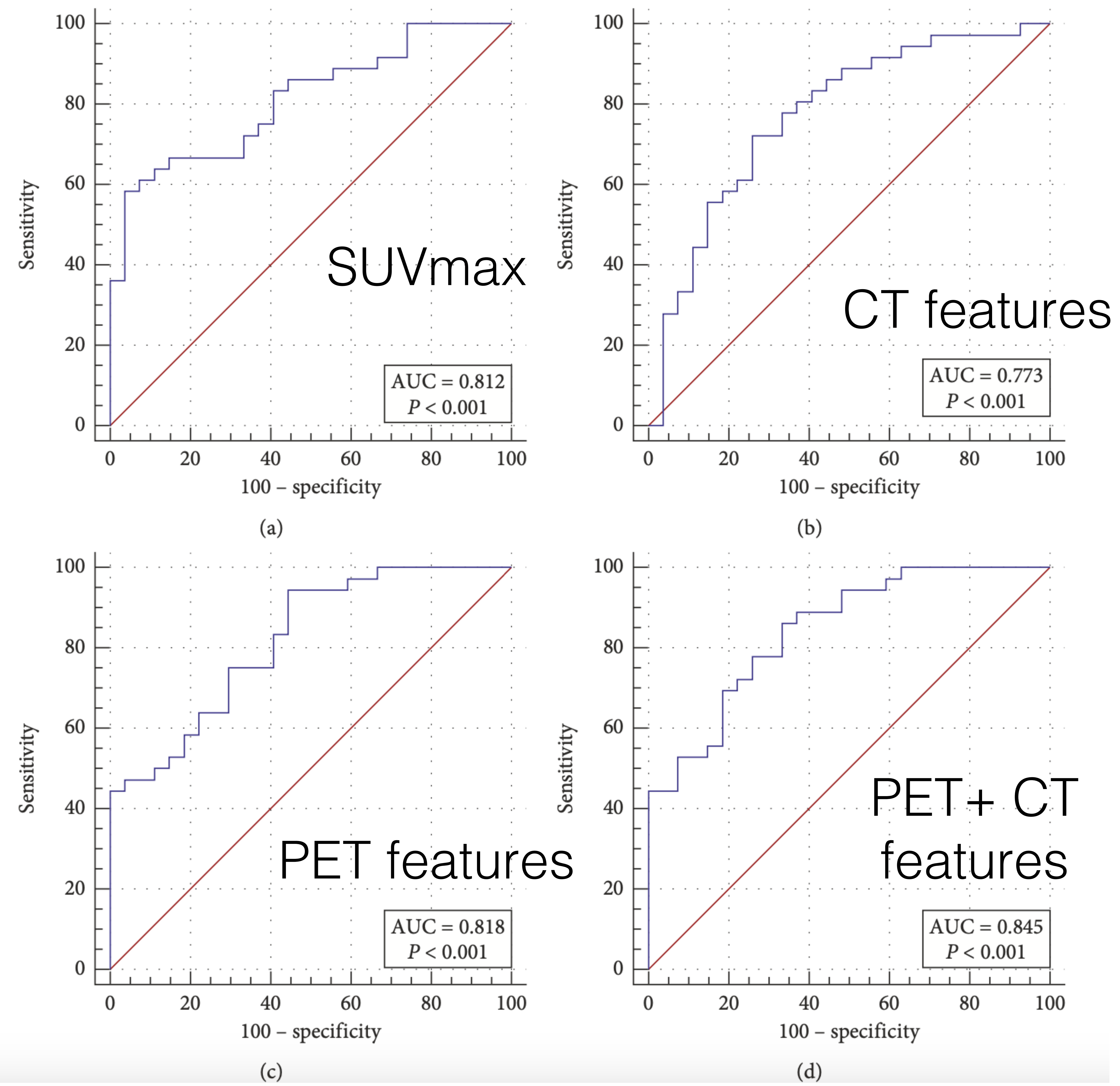
Research Article

Ability of ^{18}F-FDG PET/CT Radiomic Features to Distinguish Breast Carcinoma from Breast Lymphoma

Xuejin Ou,[1,2] Jian Wang,[3] Ruofan Zhou,[1] Sha Zhu,[1] Fuwen Pang,[4] Yi Zhou,[4] Rong Tian,[4] and Xuelei Ma[5]

44 patients: 25 with breast cancer and 19 with lymphoma

Histogram and texture features were extracted independently from PET and CT images



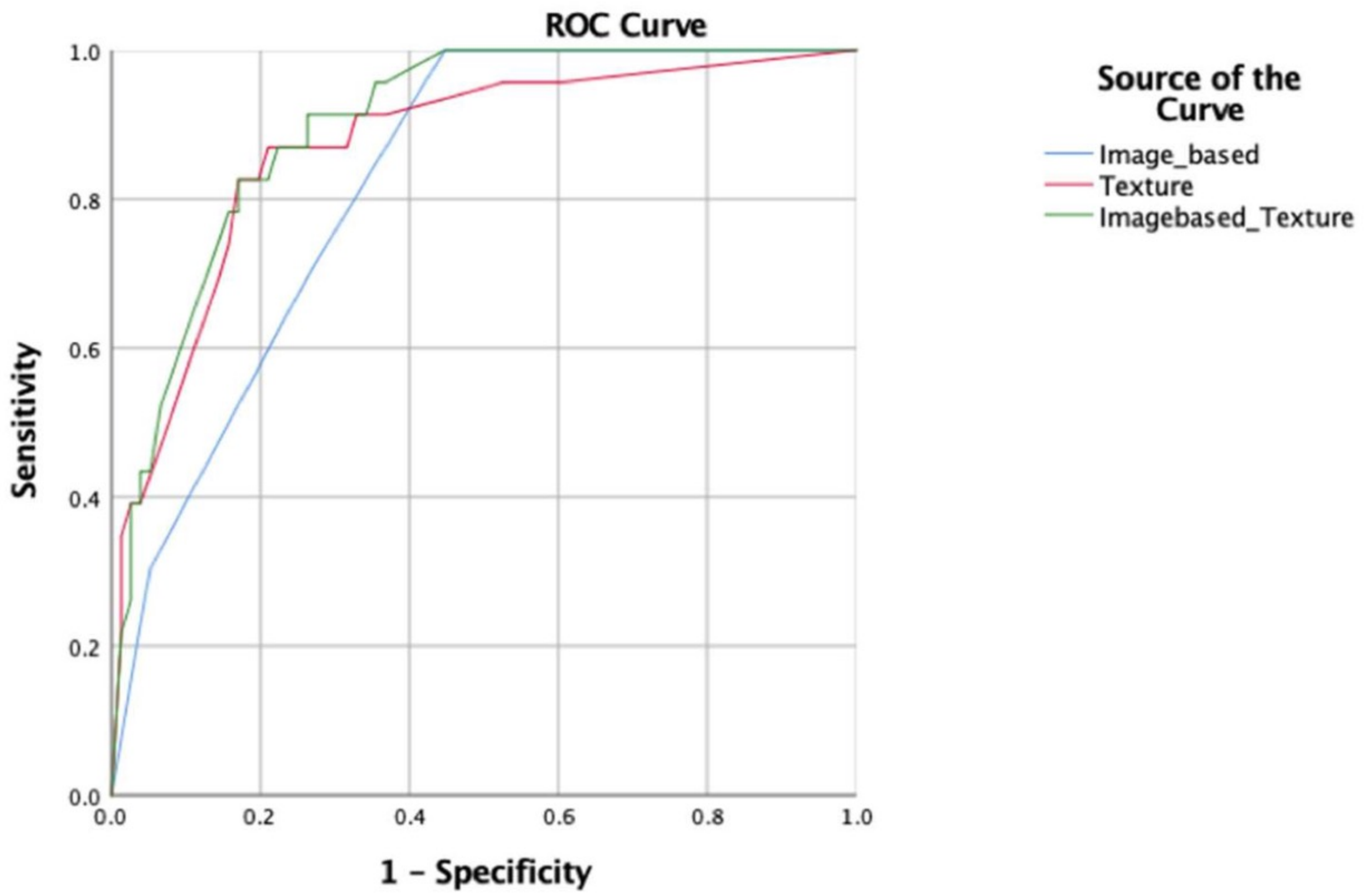
frontiers in Oncology

ORIGINAL RESEARCH
published: 03 September 2019
doi: 10.3389/fonc.2019.00844

Three-Dimensional Texture Analysis Based on PET/CT Images to Distinguish Hepatocellular Carcinoma and Hepatic Lymphoma

Hanyue Xu[1,2], Wen Guo[2], Xiwei Cui[2], Hongyu Zhuo[3], Yinan Xiao[2], Xuejin Ou[2], Yunuo Zhao[2], Tao Zhang[2] and Xuelei Ma[1,3*]

99 patients: HCC (*n* = 76) and HL (*n* = 23)
Histological confirmation as gold standart



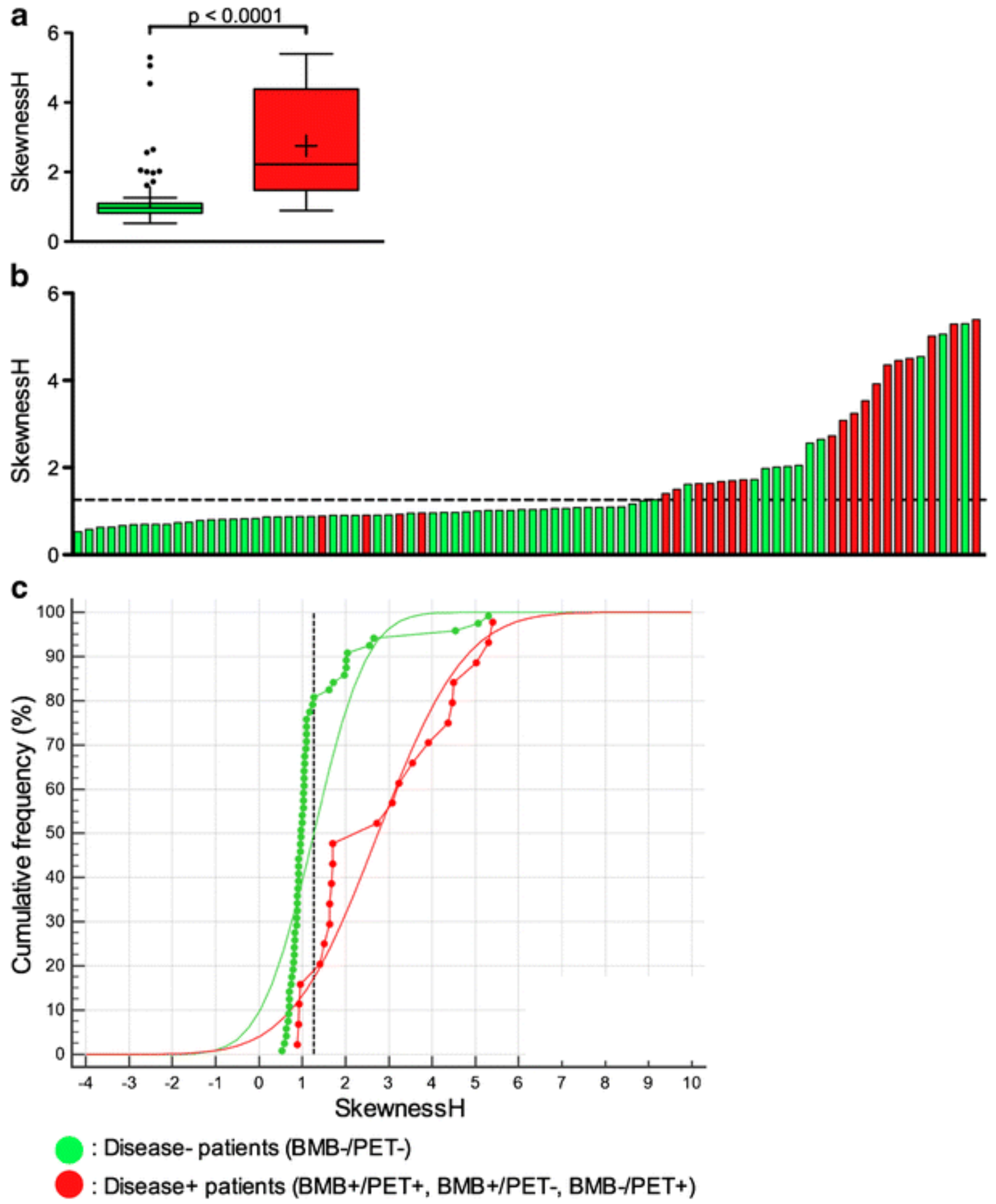
	AUC	SENSITIVITY	SENSIBILITY
SUVmax	0.822	0.696	0.737
Texture	0.870	0.913	0.776
SUVmax + Texture	0.898	0.913	0.776

Original Article | Open Access | Published: 07 December 2017

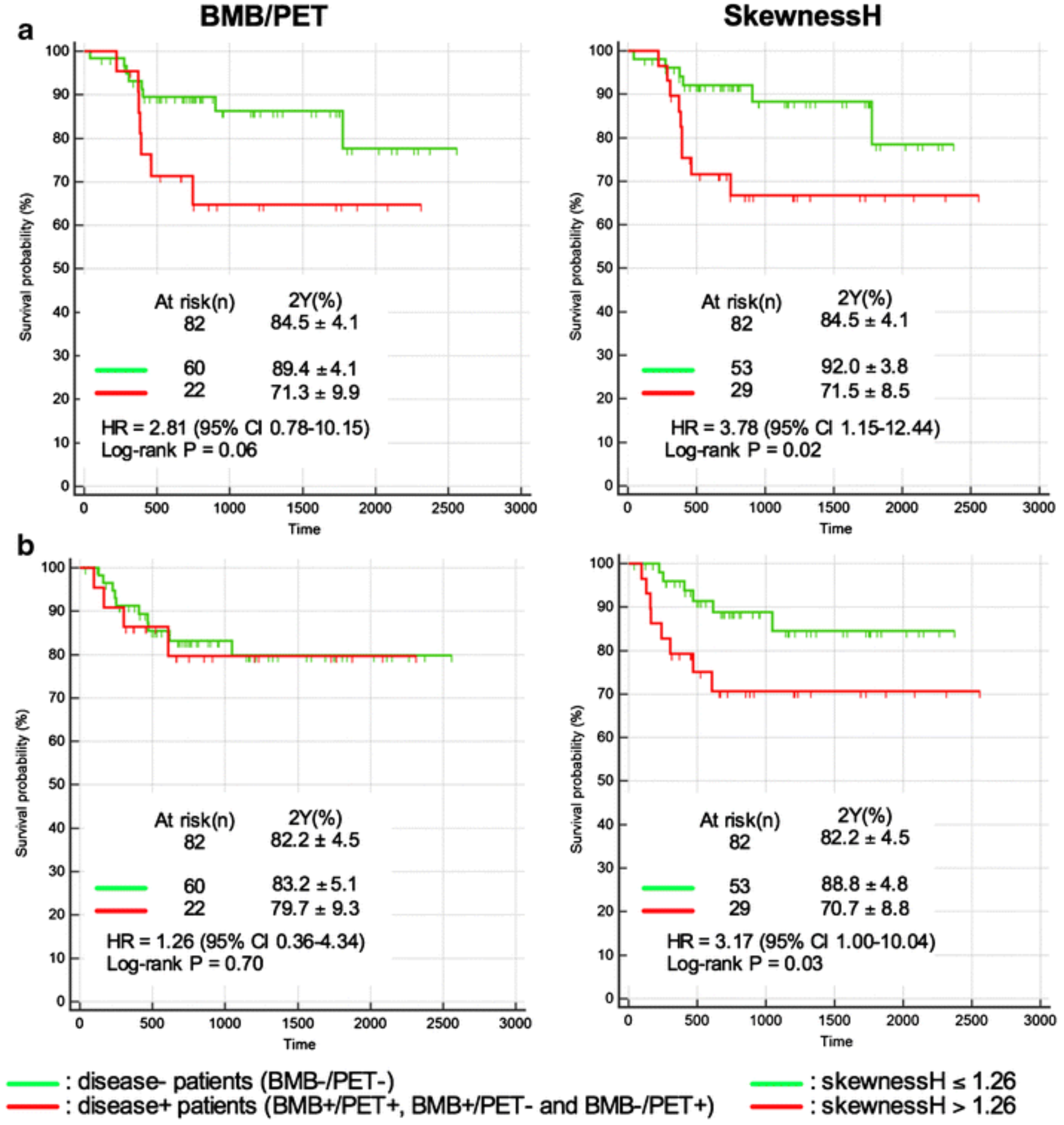
Diagnostic and prognostic value of baseline FDG PET/CT skeletal textural features in diffuse large B cell lymphoma

Nicolas Aide, Marjolaine Talbot, Christophe Fruchart, Gandhi Damaj & Charline Lasnon

European Journal of Nuclear Medicine and Molecular Imaging 45, 699–711 (2018) | Cite this article



82 DLBCL patients
BM and PET as gold standart



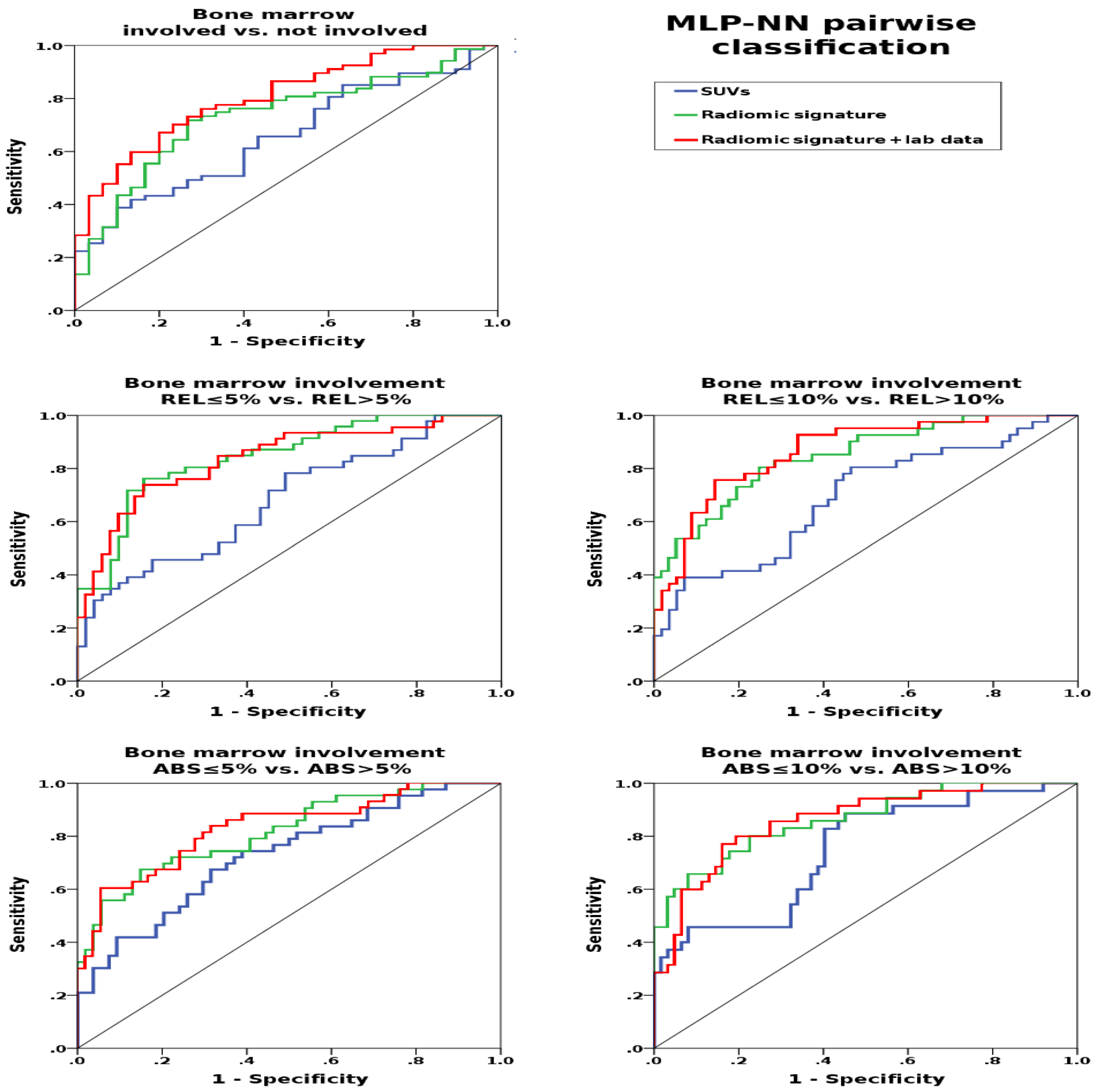
Cancers (Basel). 2020 May 2;12(5):1138. doi: 10.3390/cancers12051138.

[18F]FDG-PET/CT Radiomics for Prediction of Bone Marrow Involvement in Mantle Cell Lymphoma: A Retrospective Study in 97 Patients

Marius E Mayerhoefer [1, 2], Christopher C Riedl [1], Anita Kumar [3], Ahmet Dogan [4], Peter Gibbs [1], Michael Weber [2], Philipp B Staber [5], Sandra Huicochea Castellanos [1], Heiko Schöder [1]

97 patients with MCL (70% training and 30% validation)
BM as gold standart

SUVs alone: AUC of up to 0.66
16 GLCM features : AUC of up to 0.73
radiomic + lab (WBC and LDH): AUC of up to 0.81



European Journal of Nuclear Medicine and Molecular Imaging
https://doi.org/10.1007/s00259-019-04420-6

ORIGINAL ARTICLE

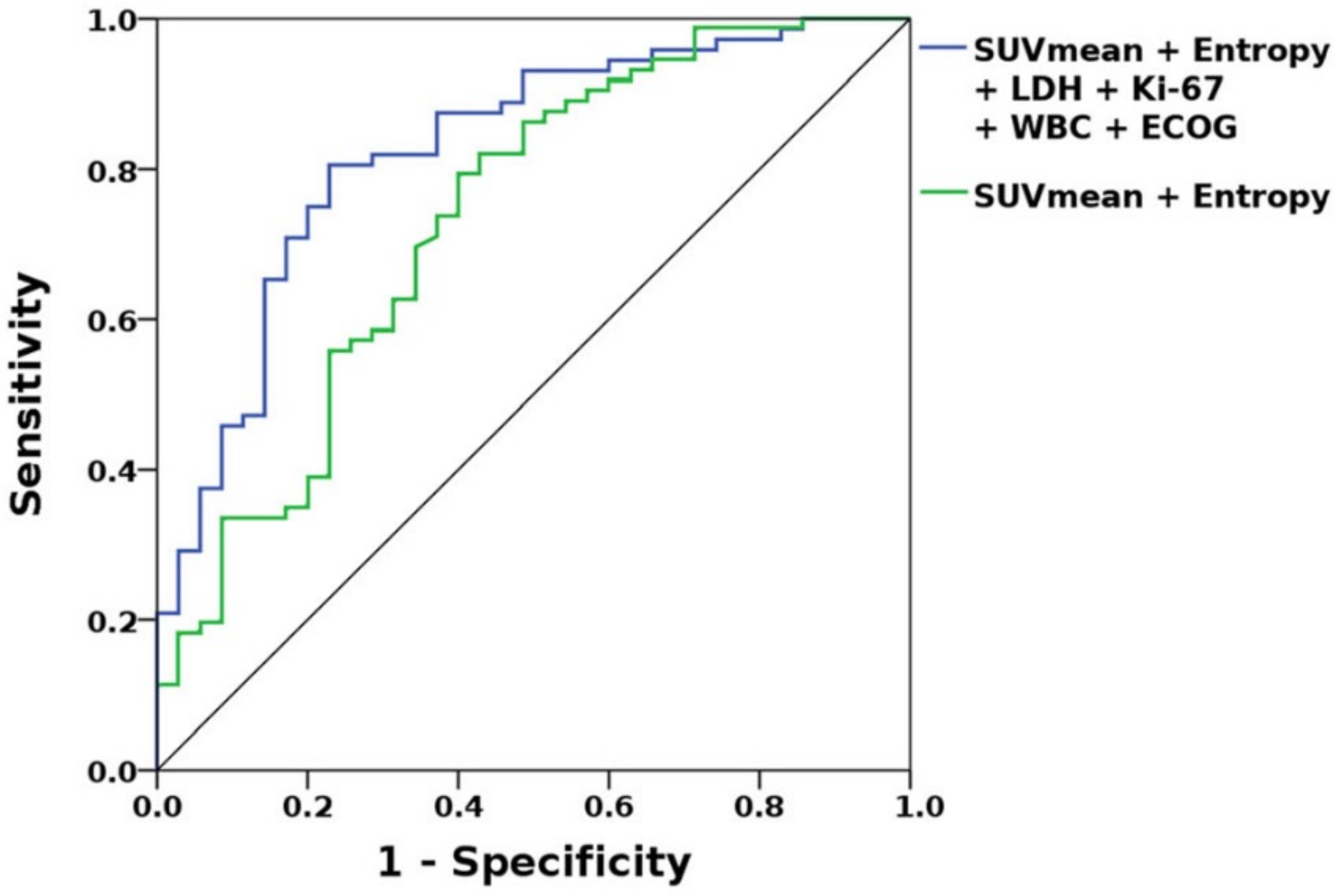
Check for updates

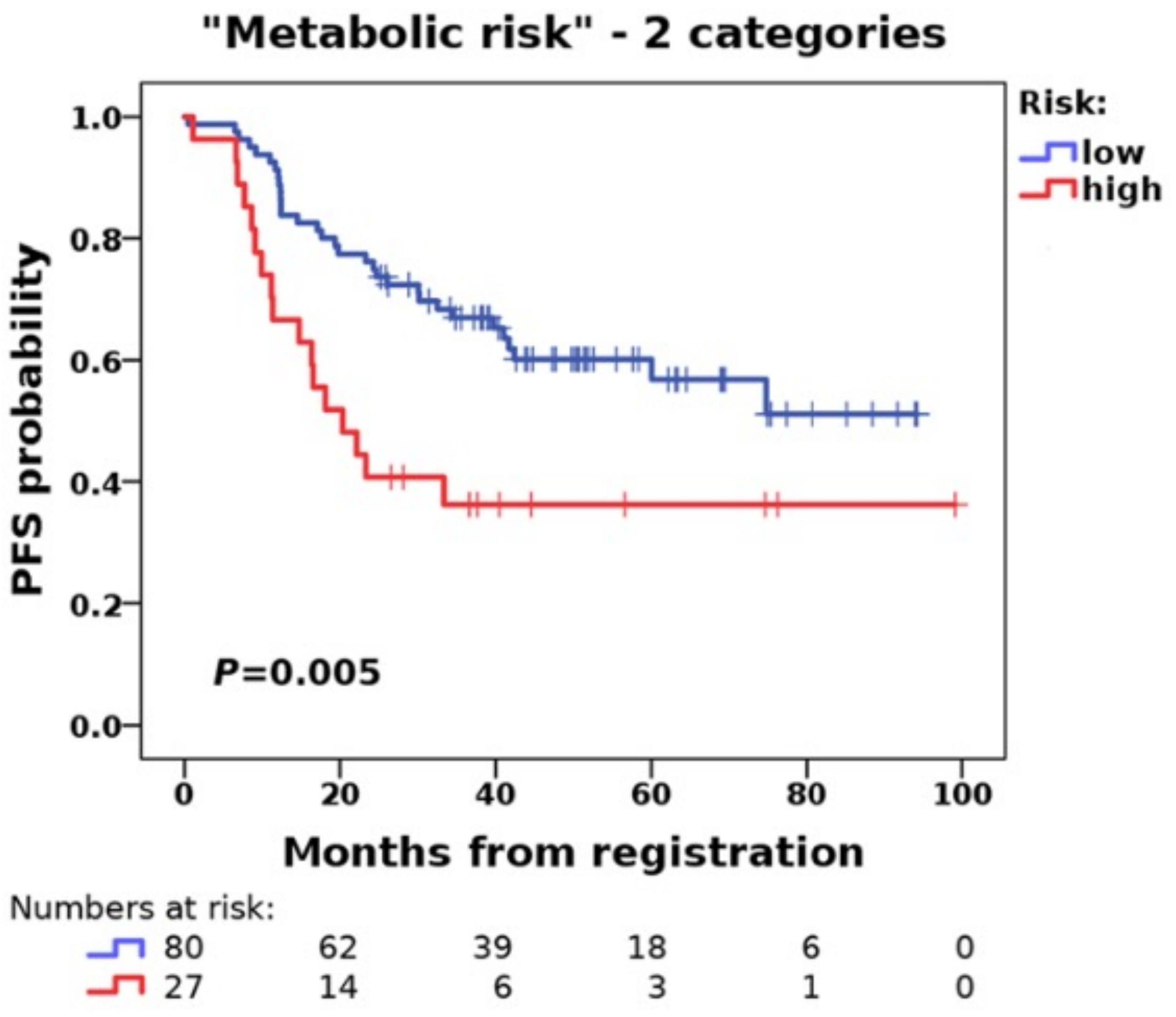
Radiomic features of glucose metabolism enable prediction of outcome in mantle cell lymphoma

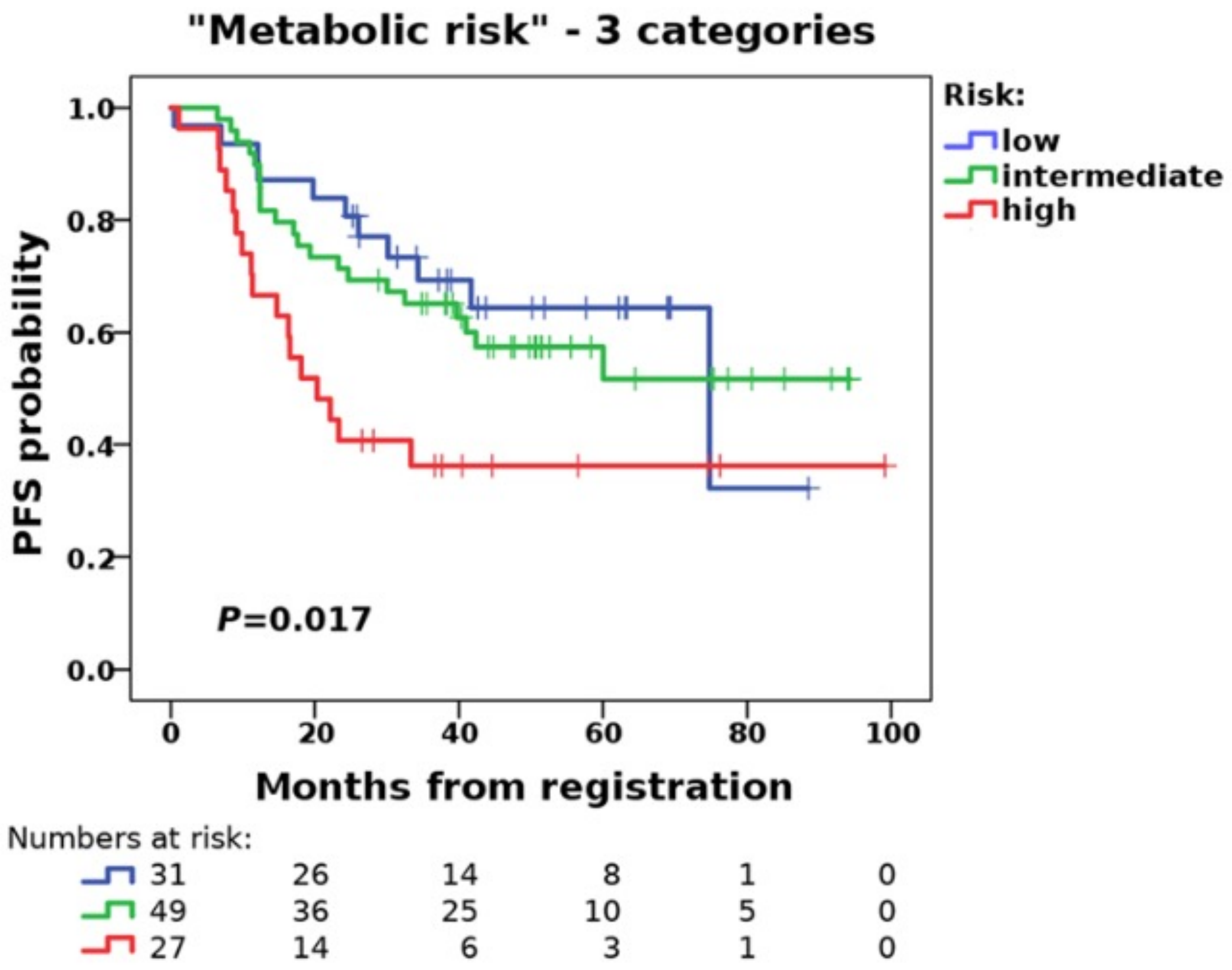
Marius E. Mayerhoefer[1,2] · Christopher C. Riedl[1] · Anita Kumar[3] · Peter Gibbs[1] · Michael Weber[2] · Ilan Tal[4] · Juliana Schilksy[1] · Heiko Schöder[1]

107 patients with MCL
(70% training and 30% validation)

SUVmean (P = 0.013) and Entropy (heterogeneity of glucose metabolism; p=0.027) were significantly predictive of 2-year PFS

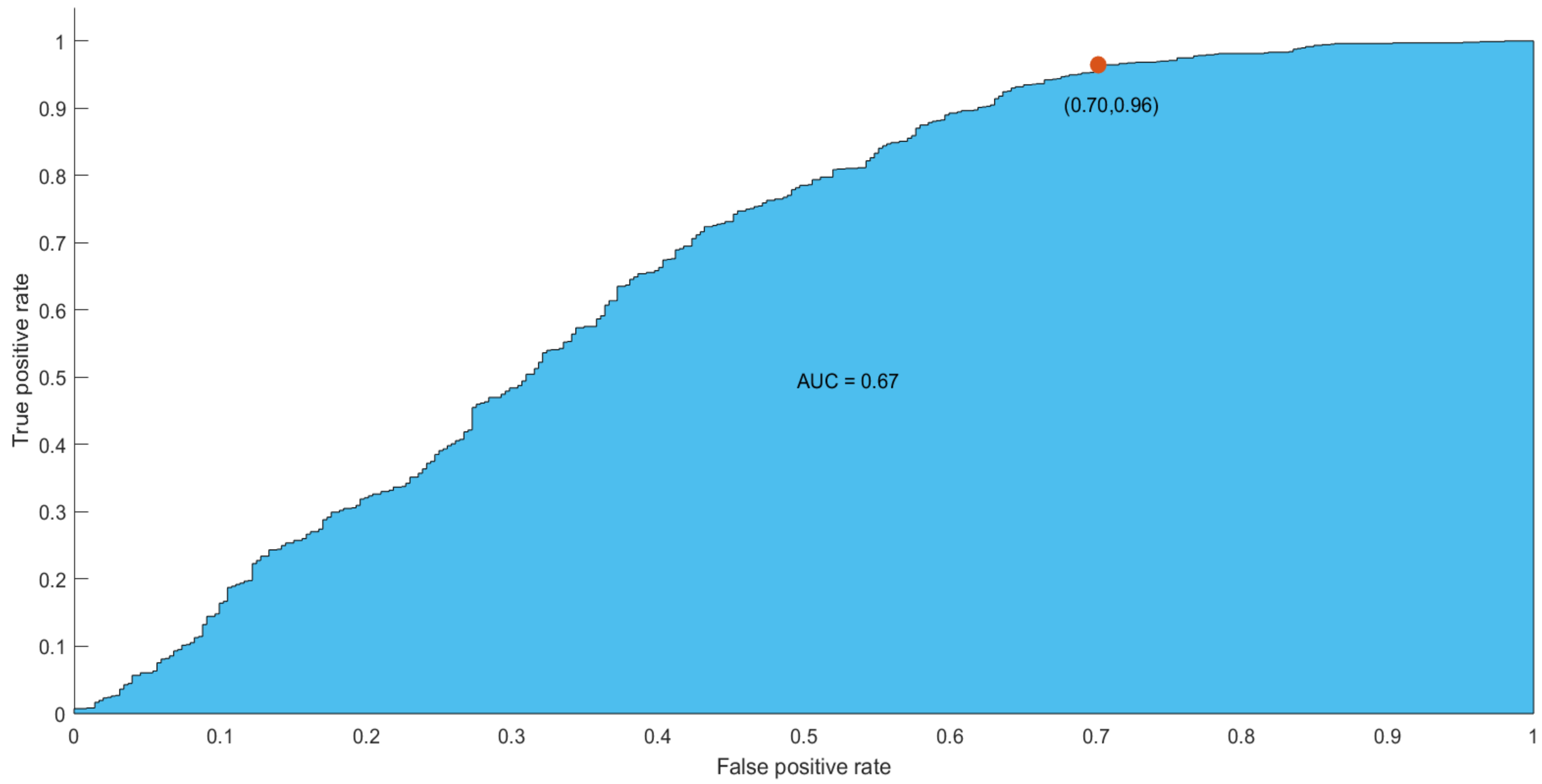






A radiomic signature based on features extracted from baseline 18F-FDG PET/CT predicts 2-year PFS in Hodgkin Lymphoma patients

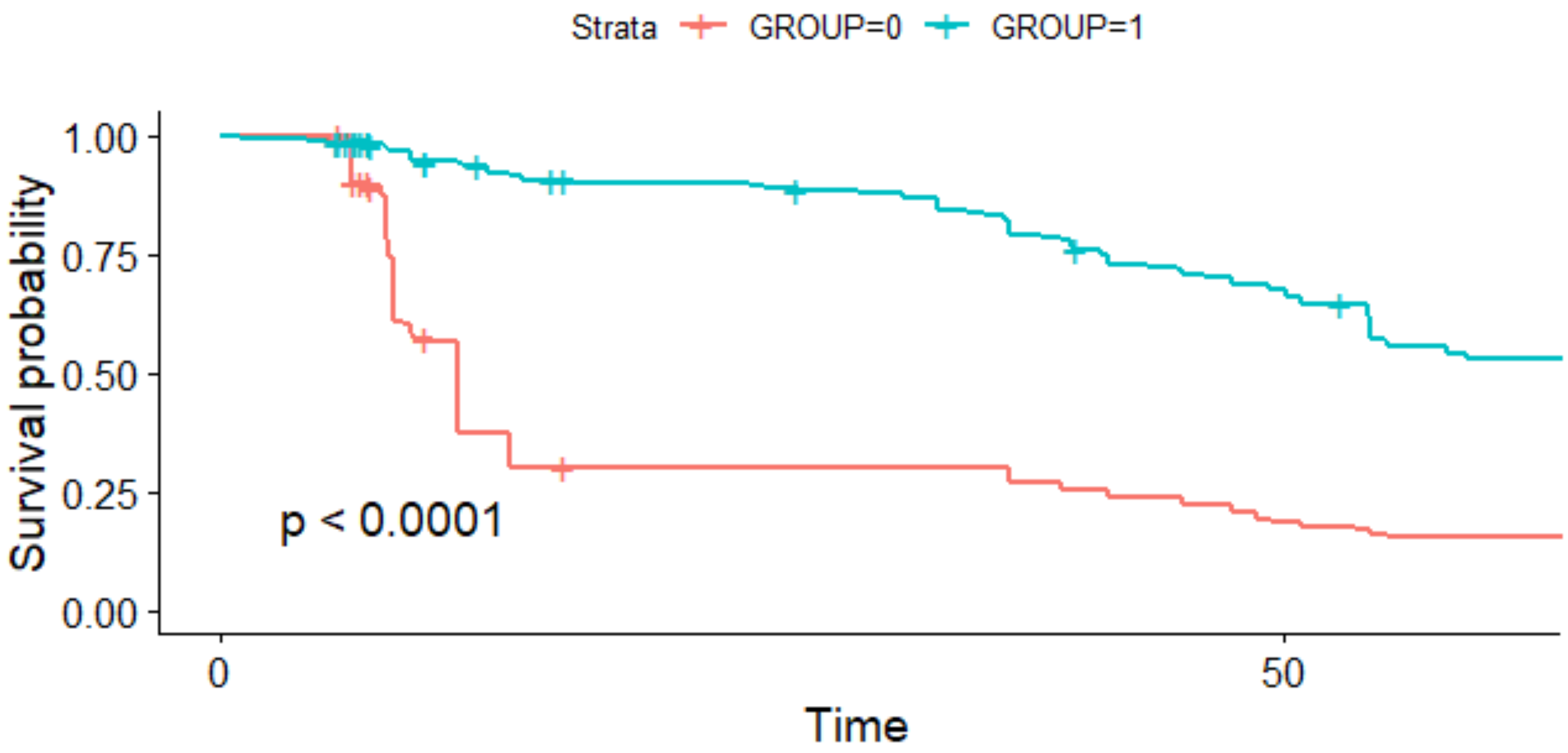
- A total of 1503 radiomic features were extracted, including shape-based features, first-order histogram features, high-order textural features, and waveled-filtred features.
- Based on the LASSO regression analysis, 6 wavelet image-filtered features resulted significant and selected to establish the radiomic signature
- The radiomics model showed an AUC of 0.67 (CI 0.64-0.71) with true positive rate of 96% and false positive rate of 70%



Durmo et al. Eur J Nucl Med Mol Imaging (2021) 48 (Suppl 1): S1–S648DOI: 10.1007/s00259-021-05547-1

A radiomic signature based on features extracted from baseline 18F-FDG PET/CT predicts 2-year PFS in Hodgkin Lymphoma patients

- 2-year PFS 74.9% (95% CI 72.7% - 77.2%)



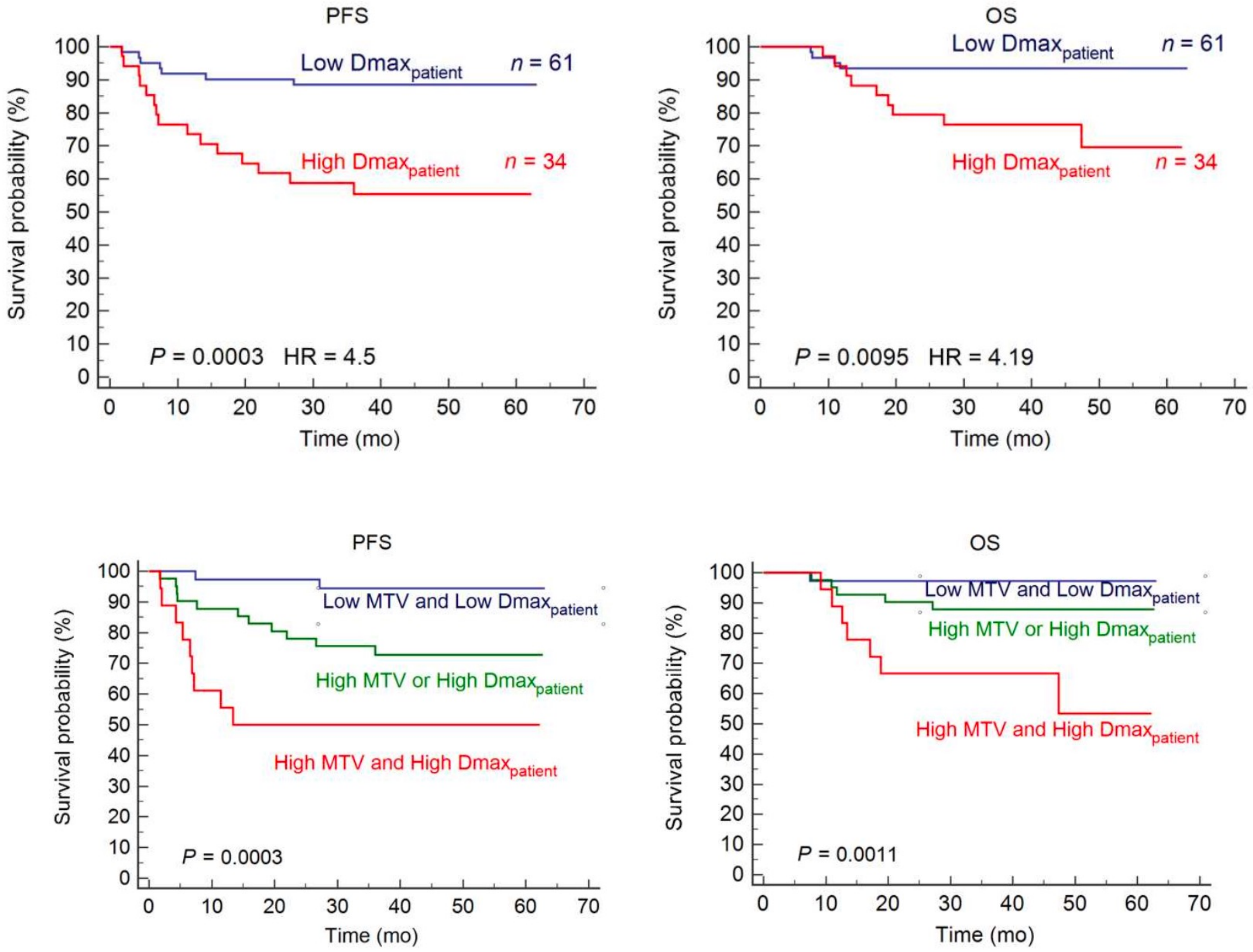
Durmo et al. Eur J Nucl Med Mol Imaging (2021) 48 (Suppl 1): S1–S648DOI: 10.1007/s00259-021-05547-1

JNM The Journal of NUCLEAR MEDICINE

18F-FDG-PET dissemination features in diffuse large B cell lymphoma are prognostic o outcome

Anne-Segolene Cottereau, Christophe Nioche, Anne-Sophie Dirand, Jerome Clerc, Franck Morschhauser, Olivier Casasnovas, Michel A. Meignan and Irene Buvat

J Nucl Med.
Published online: June 14, 2019.
Doi: 10.2967/jnumed.119.229450

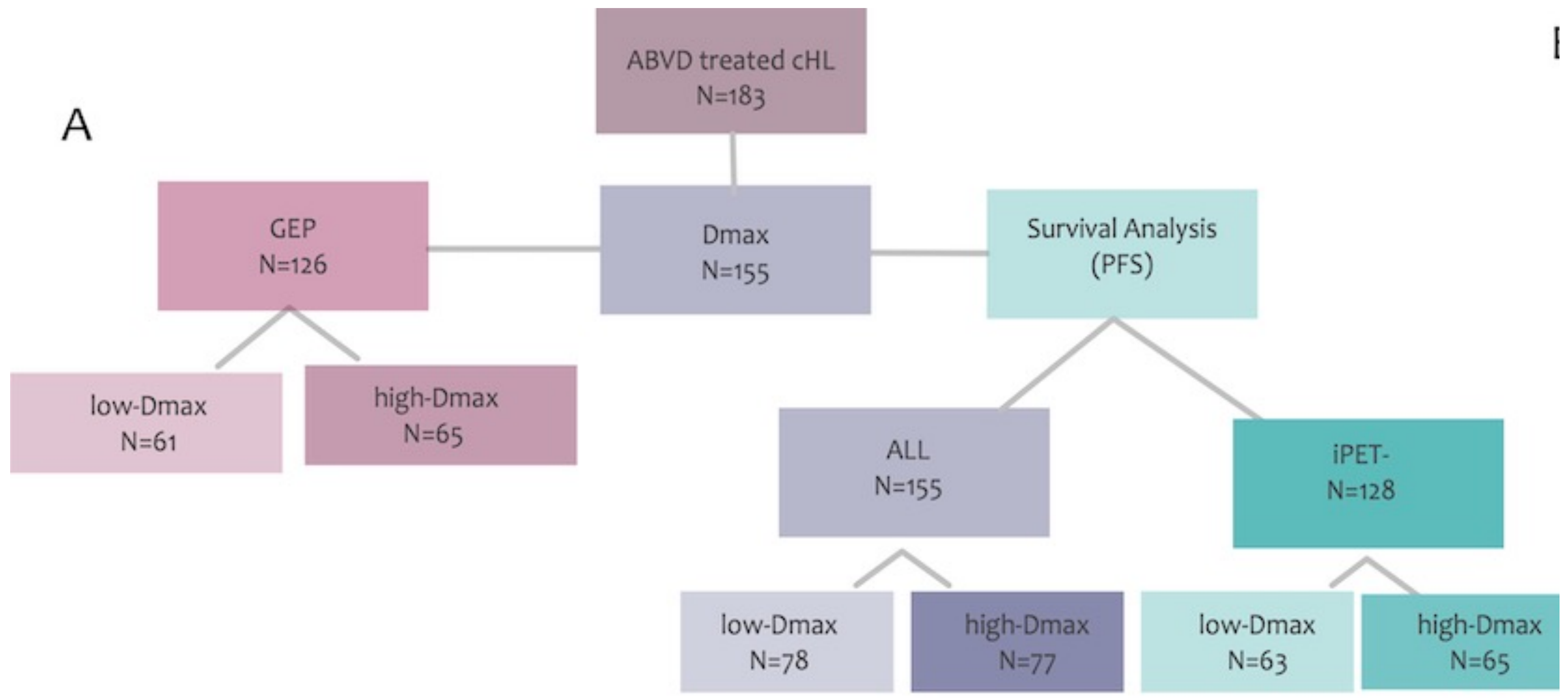


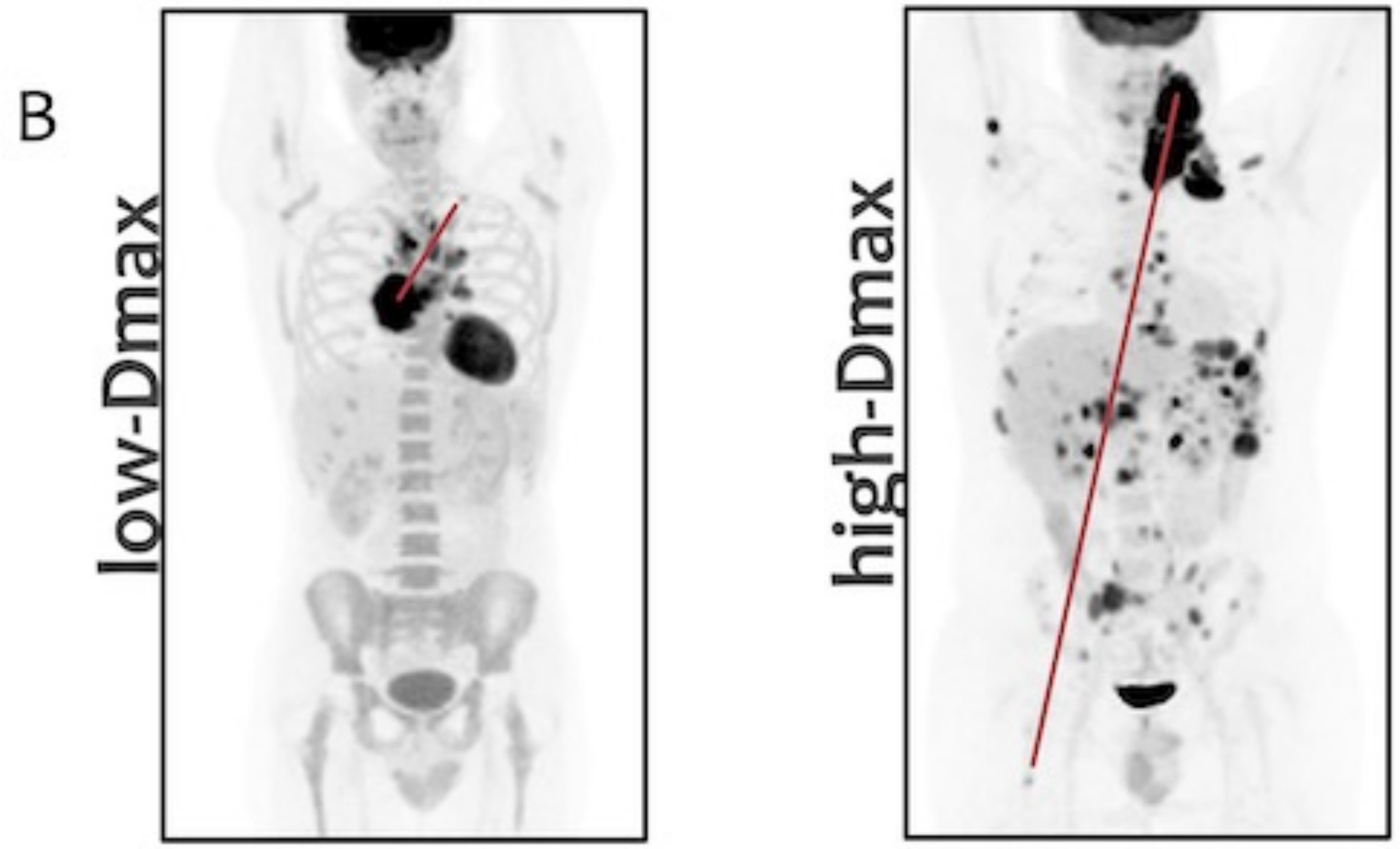
n=95 DLBCL patients
Median MTV= 375 cm3
Median Dmax = 45 cm

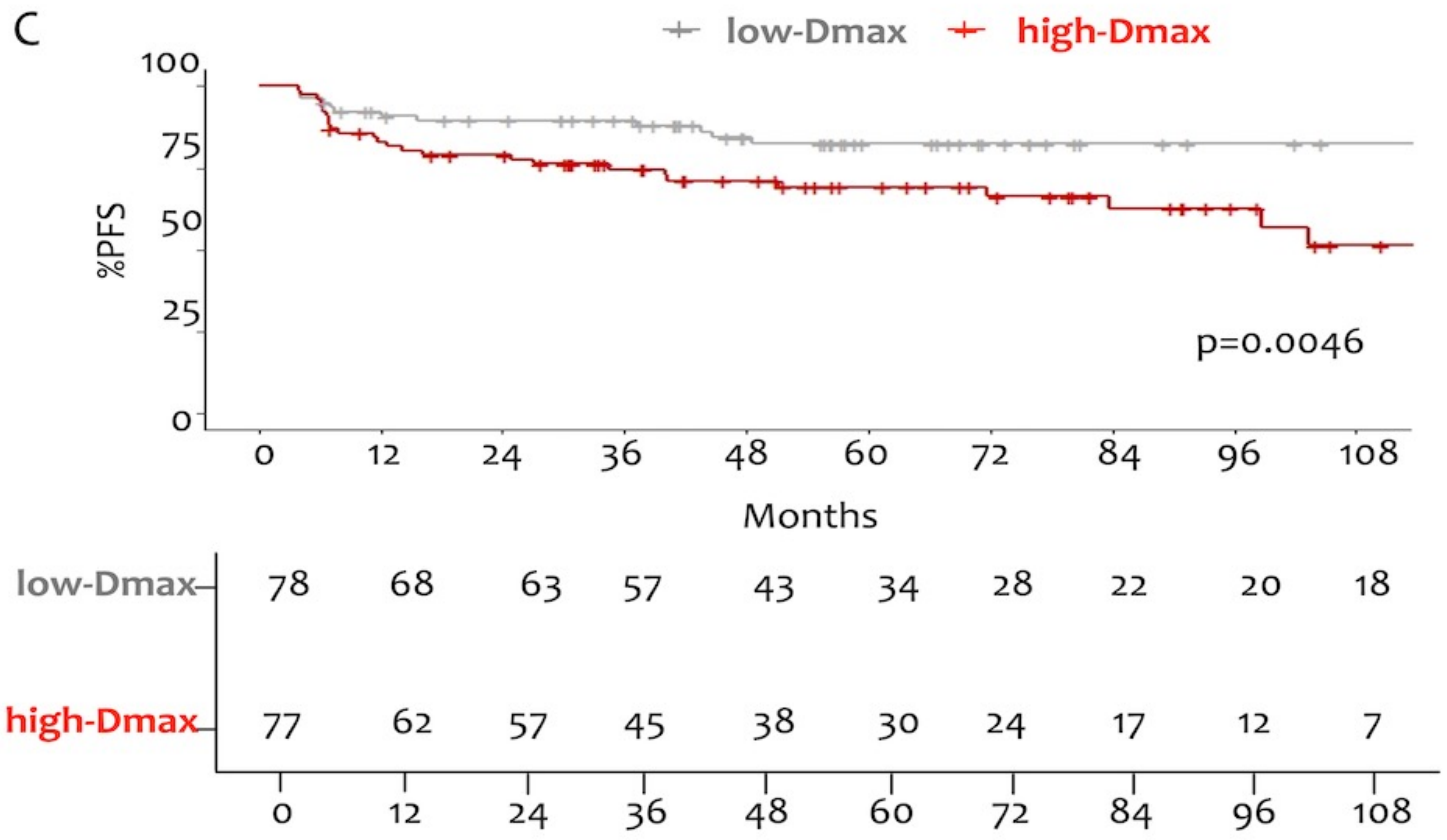
Hematol Oncol. 2022 Oct; 40(4): 645–657.
Published online 2022 May 30. doi: 10.1002/hon.3025
PMCID: PMC9796042
PMID: 35606338

Prognostic value of lesion dissemination in doxorubicin, bleomycin, vinblastine, and dacarbazine-treated, interimPET-negative classical Hodgkin Lymphoma patients: A radio-genomic study

Rexhep Durmo,[1,2] Benedetta Donati,[3] Louis Rebaud,[4,5] Anne Segolene Cottereau,[6] Alessia Ruffini,[7] Maria Elena Nizzoli,[7] Sabino Ciavarella,[8] Maria Carmela Vegliante,[8] Christophe Nioche,[4] Michel Meignan,[9] Francesco Merli,[7] Annibale Versari,[1] Alessia Ciarrocchi,[3] Irene Buvat,[4] and Stefano Luminari[7,10]







Hematol Oncol. 2022 Oct; 40(4): 645–657. PMCID: PMC9796042
Published online 2022 May 30. doi: 10.1002/hon.3025 PMID: 35606338

Prognostic value of lesion dissemination in doxorubicin, bleomycin, vinblastine, and dacarbazine-treated, interimPET-negative classical Hodgkin Lymphoma patients: A radio-genomic study

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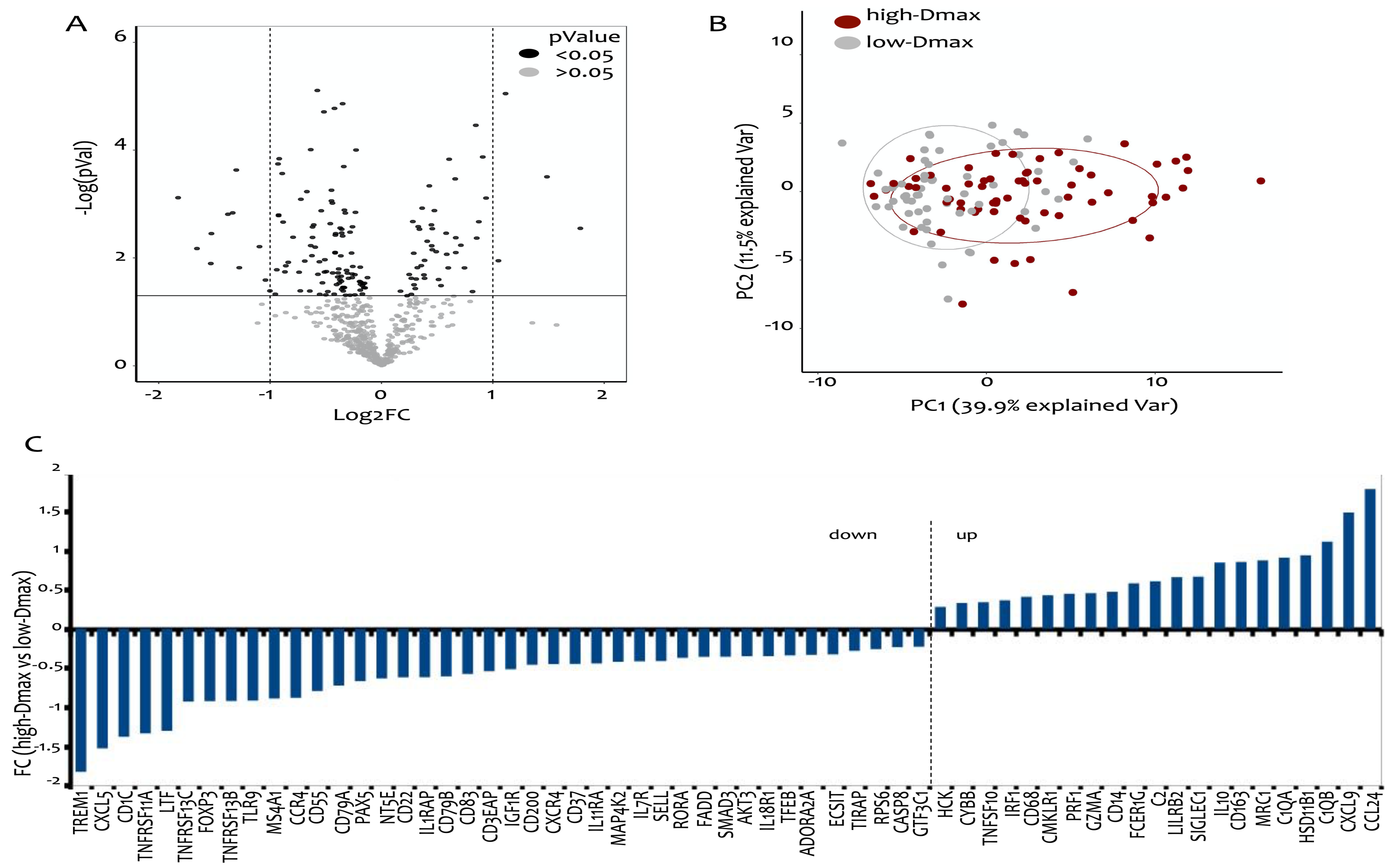
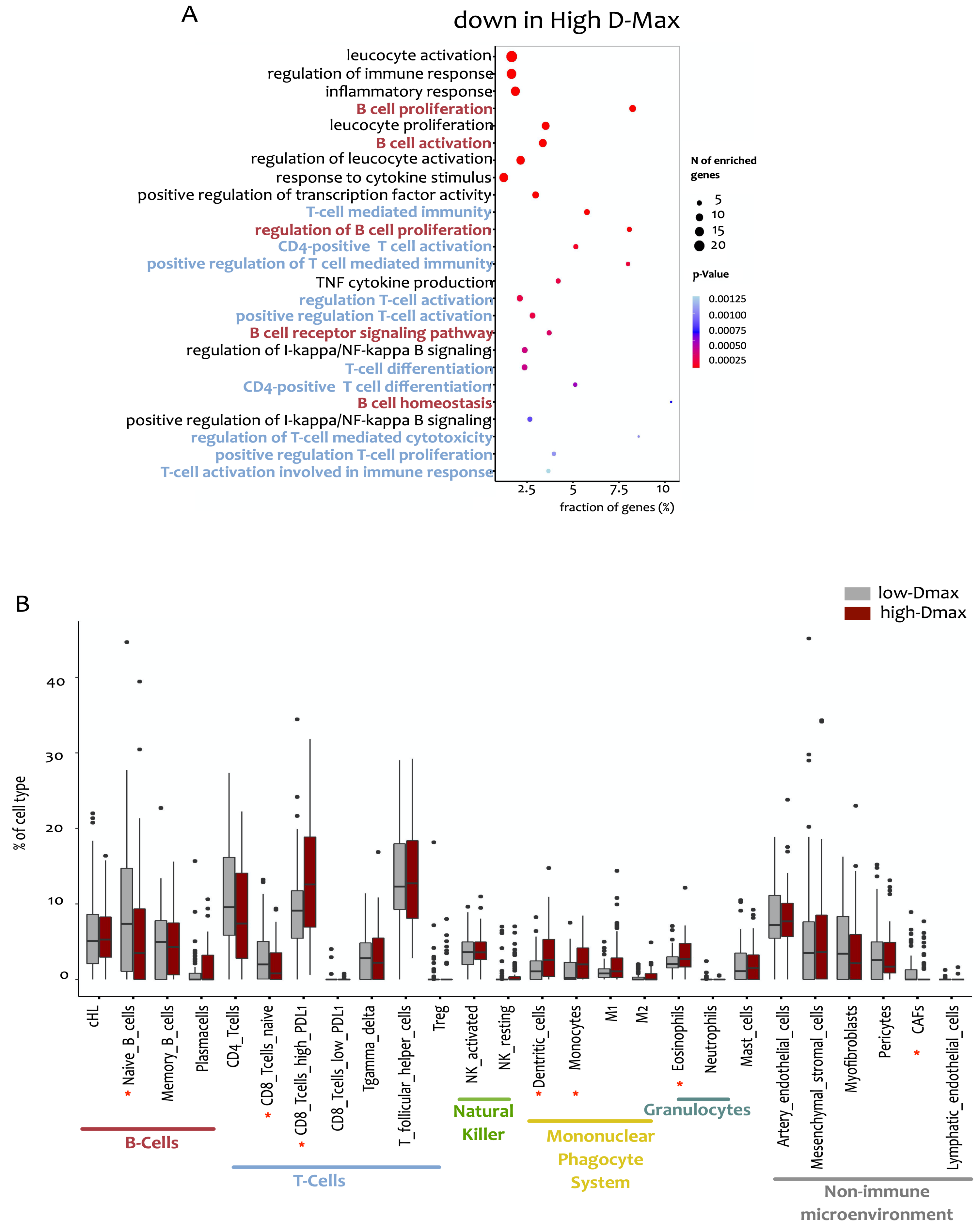
FIGURE 3



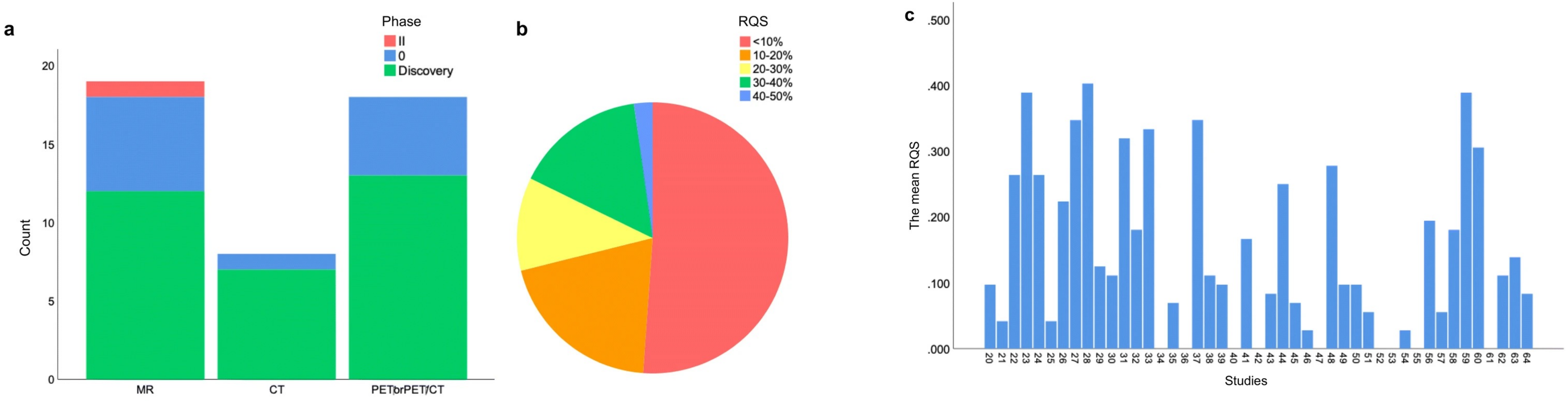
- 21 genes were up-regulated and 40 down-regulated in high-Dmax versus low-Dmax

FIGURE 4



- naïve B and T cells were strongly enriched in the low-Dmax subgroup. By contrast CD8+ T cells expressing high level of PDL1, dendritic cells, monocytes and eosinophil were enriched in the high-Dmax samples.

LIMITI E PROSPETTIVE FUTURE



Current status and quality of radiomics studies in lymphoma: a systematic review. Wang, H., Zhou, Y., Li, L. *et al.* *Eur Radiol* **30,** 6228–6240 (2020). https://doi.org/10.1007/s00330-020-06927-1

LIMITI

Lack of Standardization

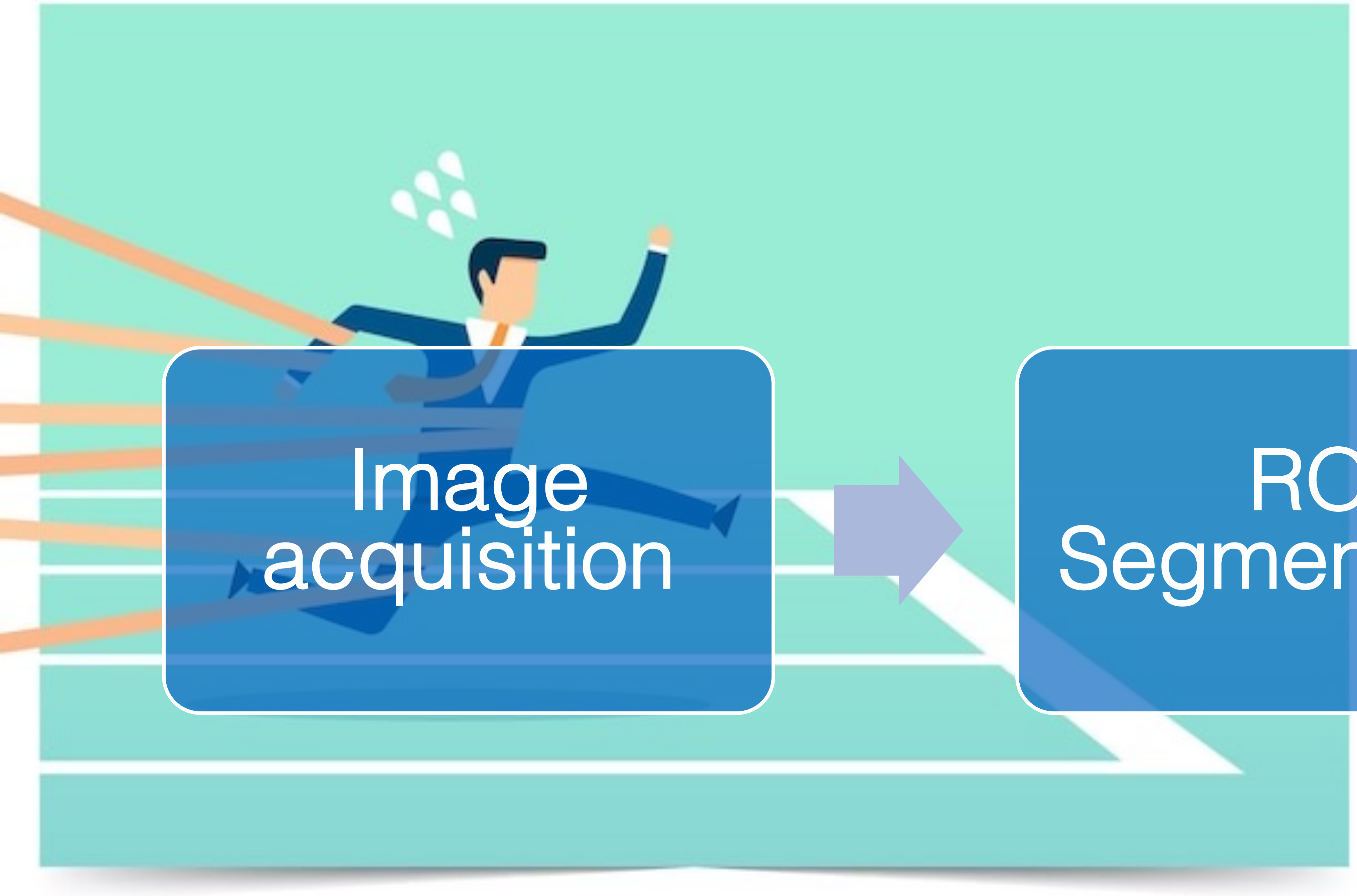
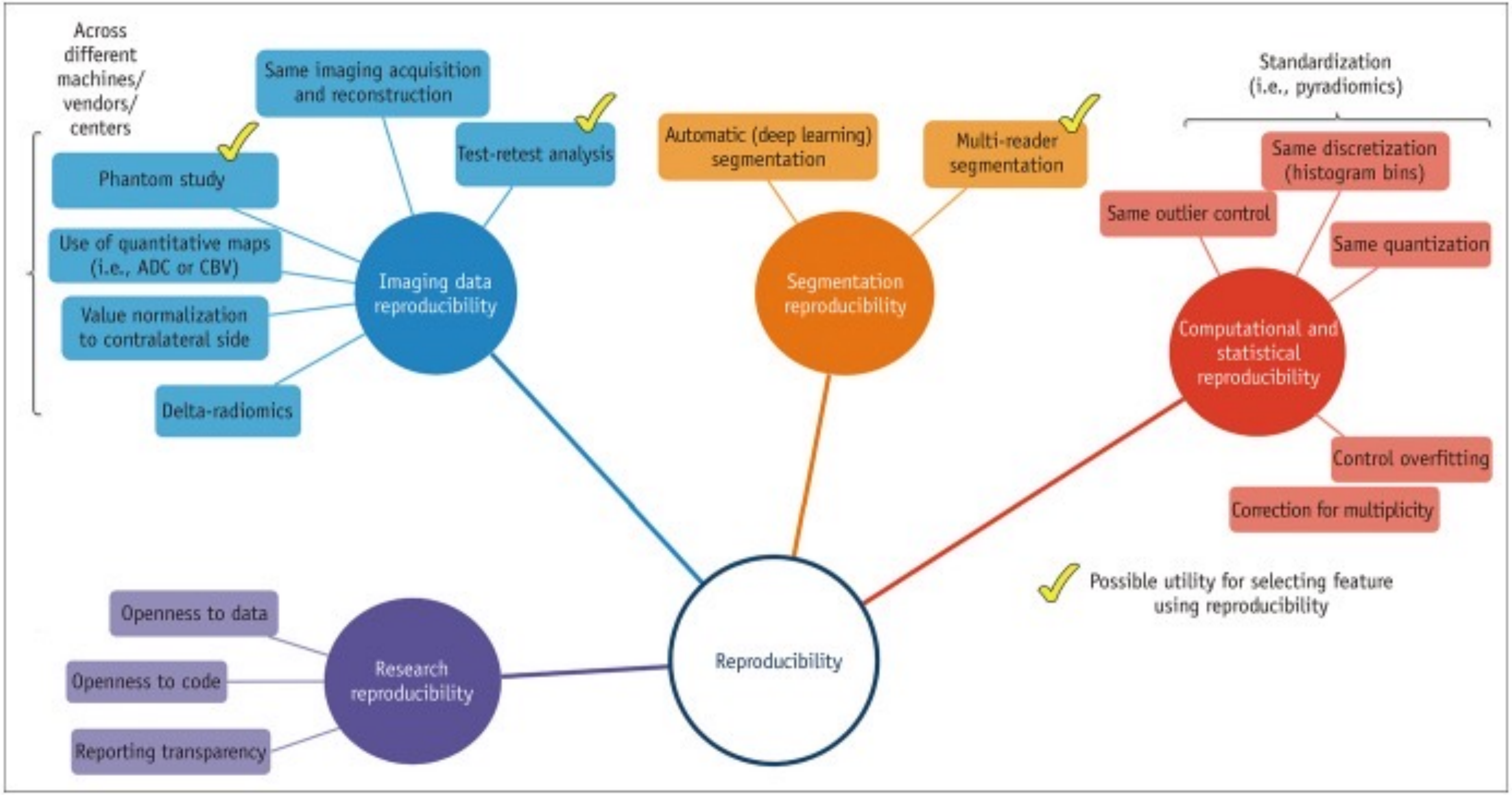


Image acquisition → ROI Segmentation → Feature Extraction → Analysis Methods

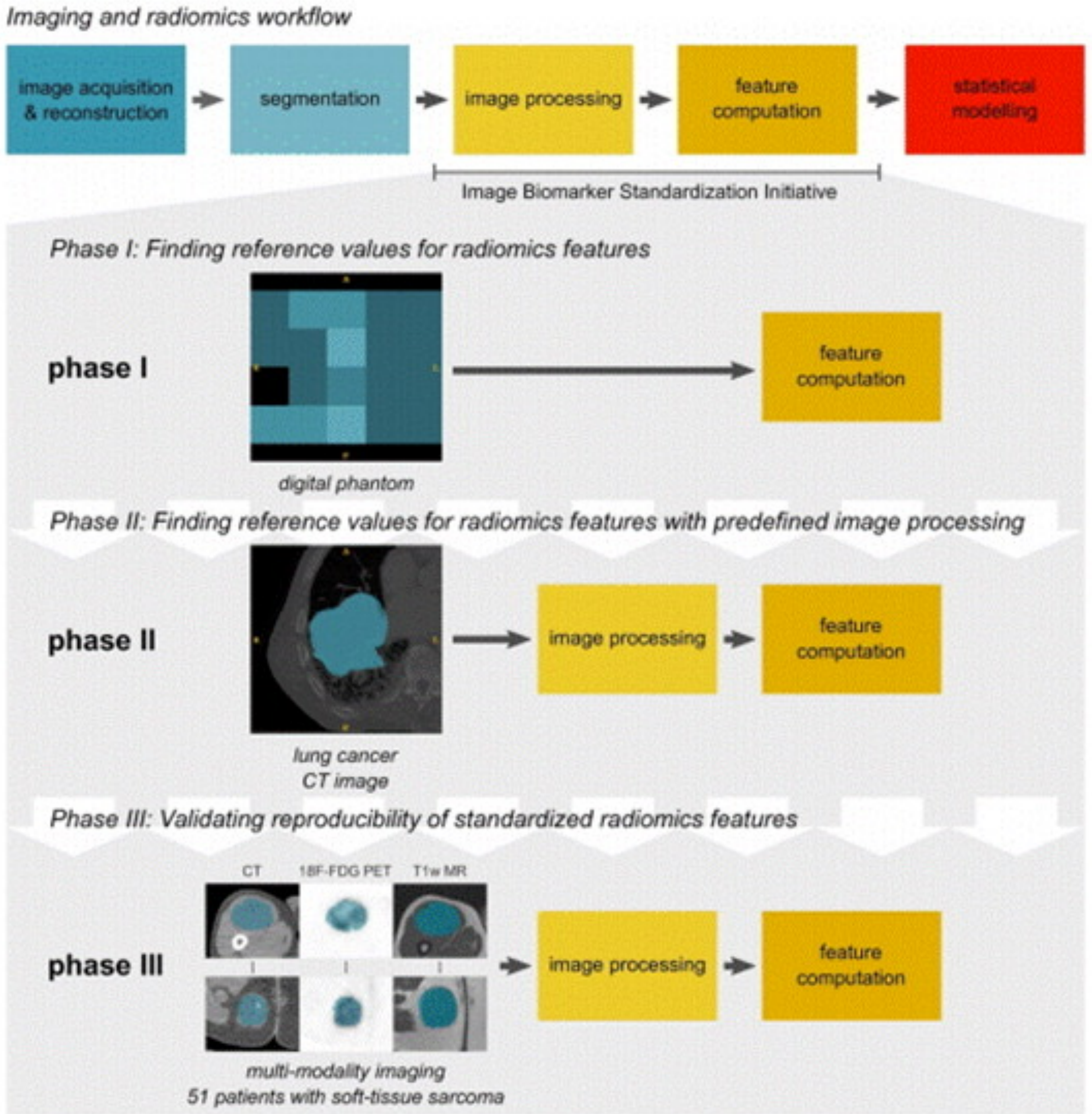
LIMITI

- Small Sample Sizes (Overfitting)
- Variability in Image Quality
- Lack of Validation



Park JE. et al. Reproducibility and Generalizability in Radiomics Modeling: Possible Strategies in Radiologic and Statistical Perspectives. Korean J Radiol. 2019 Jul;20(7):1124-1137. doi: 10.3348/kjr.2018.0070

The Image Biomarker Standardization Initiative: Standardized Quantitative Radiomics for High-Throughput Image-based Phenotyping



- Twenty-five research teams found agreement for calculation of 169 radiomics features derived from a digital phantom and a human lung cancer on CT scans
- Among these 169 candidate radiomics features, good to excellent reproducibility was achieved for 167 radiomics features by using MRI, fluorine 18 fluorodeoxyglucose PET, and CT images obtained in 51 patients with soft-tissue sarcoma

Zwanenburg A et al. Published Online: March 10, 2020
https://doi.org/10.1148/radiol.2020191145
Radiology

CONCLUSIONI

Potenzialità della Radiomica	Criticità della Radiomica
- Utilizzo di dati non invasivi, non richiede biopsie o altre procedure invasive.	- Il processo di estrazione dei dati radiomici richiede competenze tecniche avanzate.
- Possibilità di ottenere informazioni dettagliate sulla struttura e la funzione dei tessuti e dei tumori.	- Variabilità nelle modalità di acquisizione delle immagini radiologiche, che possono influire sulla qualità dei dati e sulla loro utilità per l'analisi radiomica.
- Capacità di identificare caratteristiche e pattern nascosti nelle immagini radiologiche che non sono visibili ad occhio nudo o che sono difficili da individuare con altri metodi.	- Bisogno di grandi quantità di dati per ottenere risultati affidabili e generalizzabili.
- Potenziale per aiutare nella diagnosi precoce, nella valutazione della gravità della malattia e nella scelta del trattamento più efficace per il paziente.	- Il rischio di overfitting, ovvero di adattare il modello di radiomica ai dati di addestramento, senza riuscire a generalizzare i risultati su nuovi pazienti.
- Possibilità di integrare l'analisi radiomica con altri dati clinici e molecolari per una valutazione più completa e personalizzata della malattia.	- Validare i risultati in studi clinici su larga scala prima di poterli utilizzare nella pratica clinica.

Grazie per l'attenzione!

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