Les Sables-d'Olonne
Octobre 2015

« Radiomics » et analyse de textures en imagerie TEP/TDM : potentiel et limites

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EPU Traitements d'images en physique médicale

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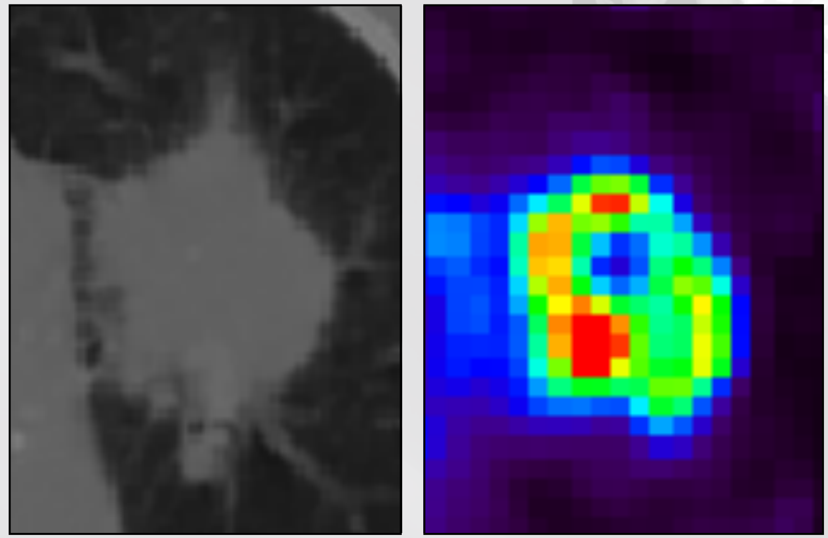
Introduction

Characterization of tumors in oncology: rationale

Research:



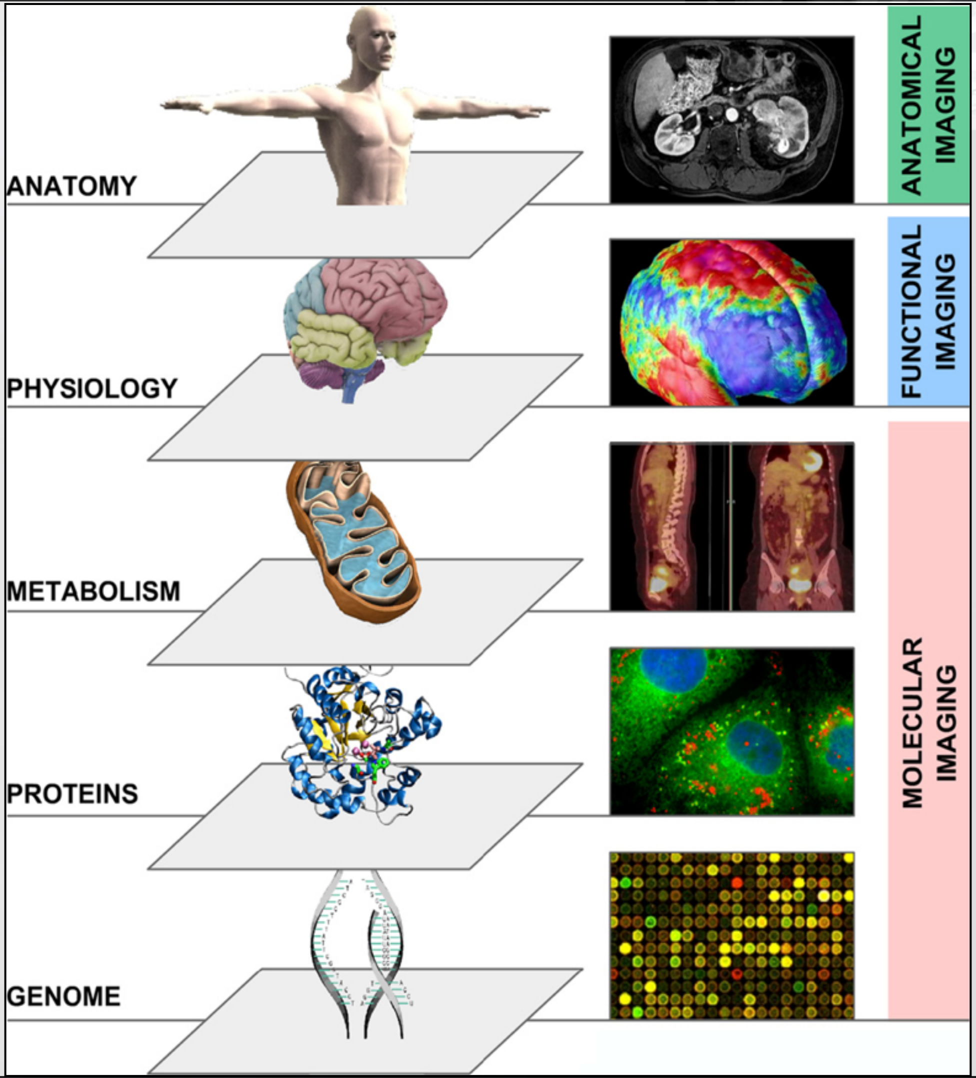
CT FDG PET

- ❑ (Semi)Automatic
- ❑ Robust
- ❑ Reproducible
- ❑ Quantitative
- ❑ Prognostic / predictive

Pre-processing → Segmentation → Characterization → Imaging signature Clinical value?

Introduction

Radiomics



P Lambin, *et al*. Radiomics: extracting more information from medical images using advanced feature analysis. *Eur J Cancer* 2012

Introduction

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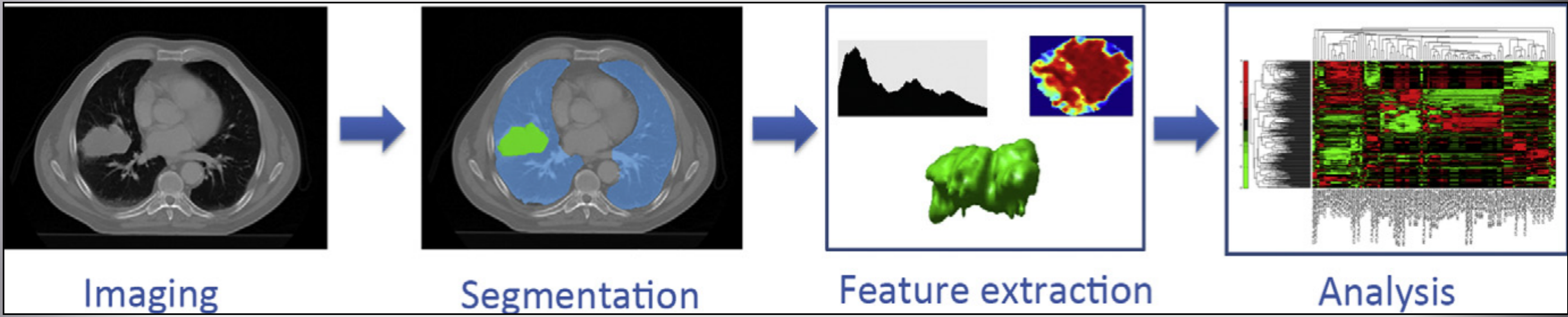

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Introduction

Radiomics

nature COMMUNICATIONS

ARTICLE

Received 25 Nov 2013 | Accepted 29 Apr 2014 | Published 3 Jun 2014

DOI: 10.1038/ncomms5006

OPEN

Decoding tumour phenotype by noninvasive imaging using a quantitative radiomics approach

Hugo J.W.L. Aerts[1,2,3,4,*], Emmanuel Rios Velazquez[1,2,*], Ralph T.H. Leijenaar[1], Chintan Parmar[1,2], Patrick Grossmann[2], Sara Cavalho[1], Johan Bussink[5], René Monshouwer[5], Benjamin Haibe-Kains[6], Derek Rietveld[7], Frank Hoebers[1], Michelle M. Rietbergen[8], C. René Leemans[8], Andre Dekker[1], John Quackenbush[4], Robert J. Gillies[9] & Philippe Lambin[1]

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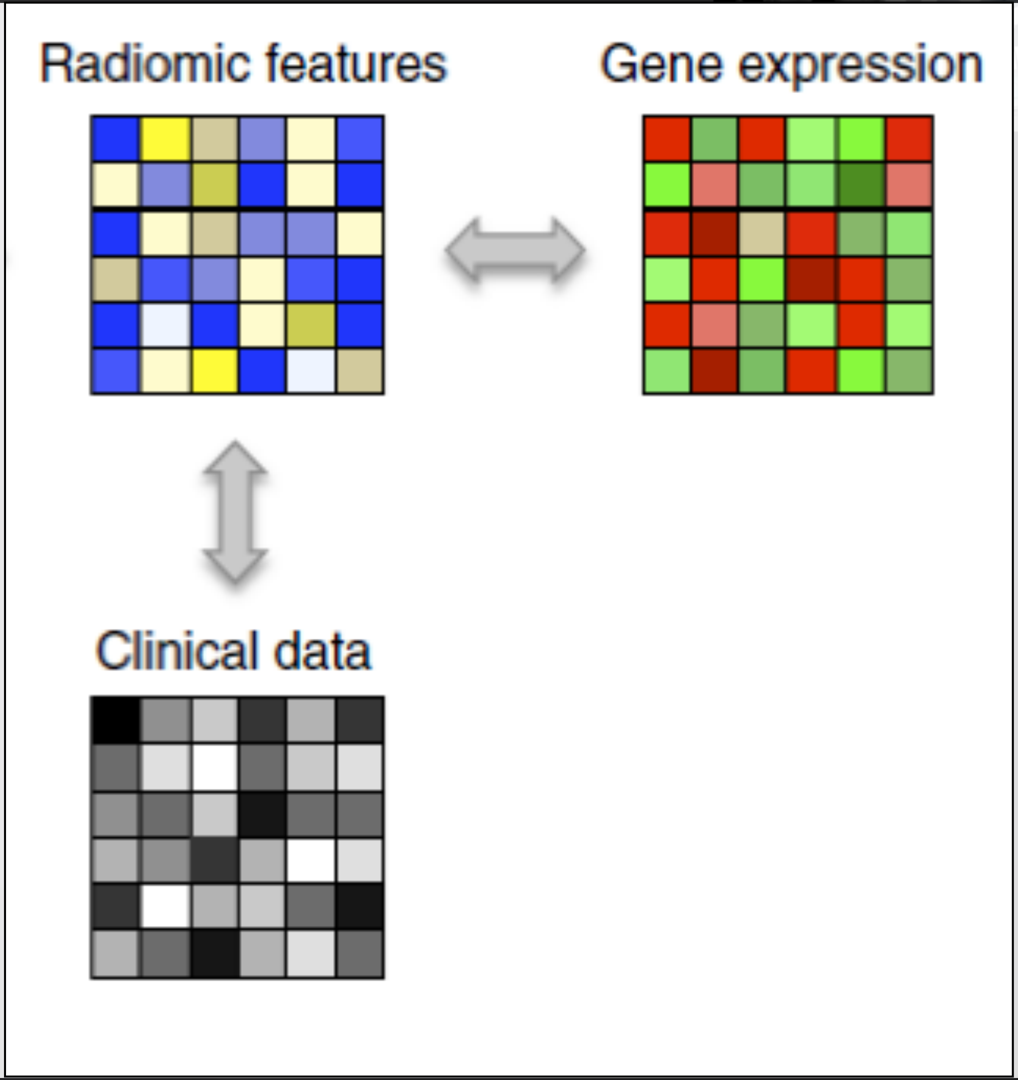

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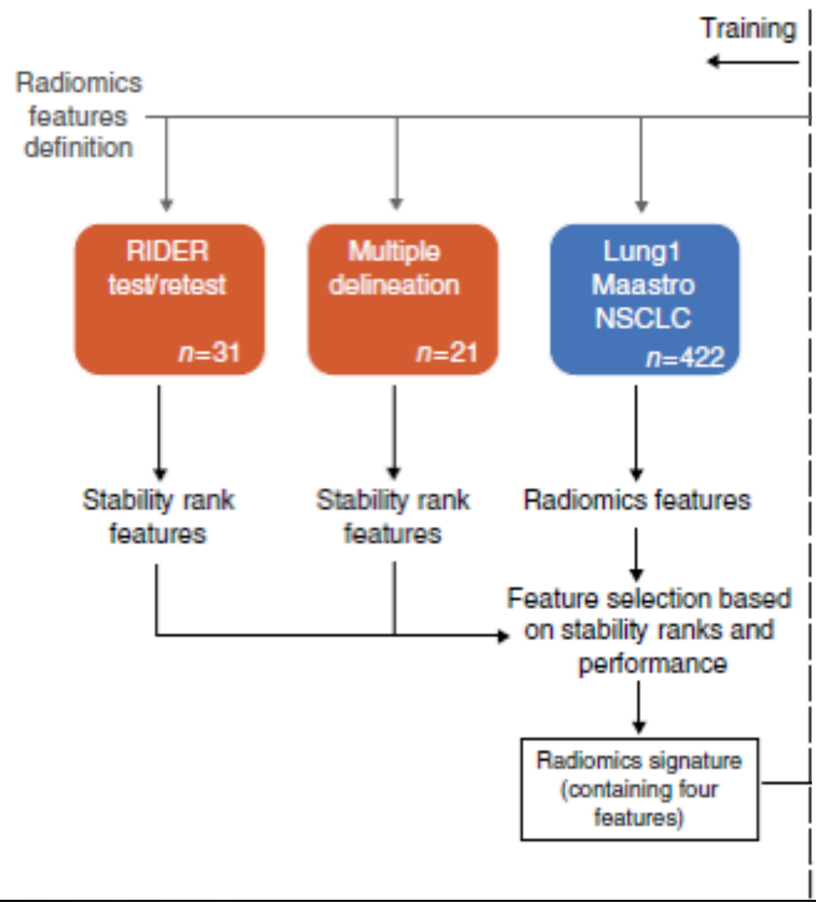

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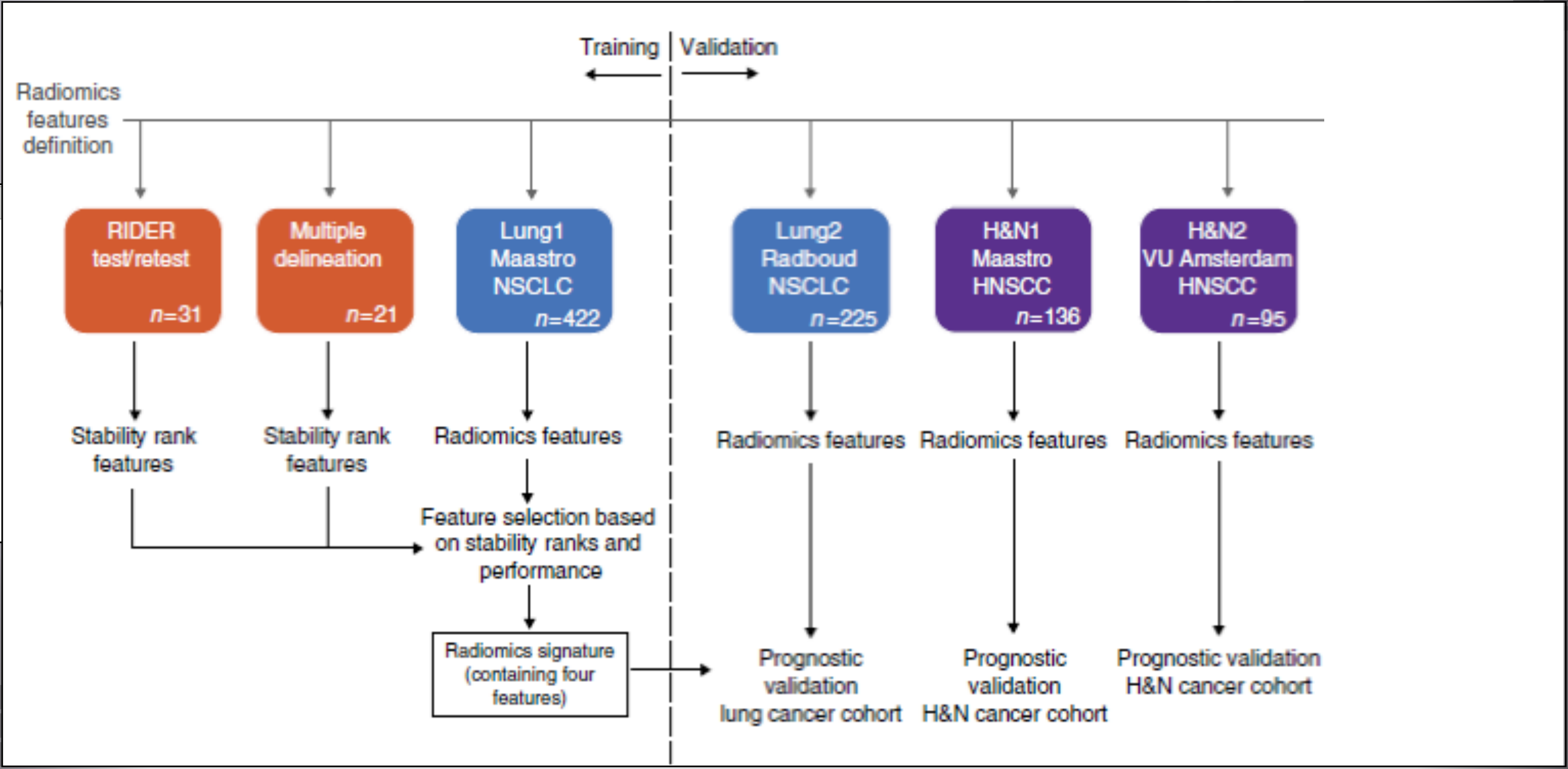

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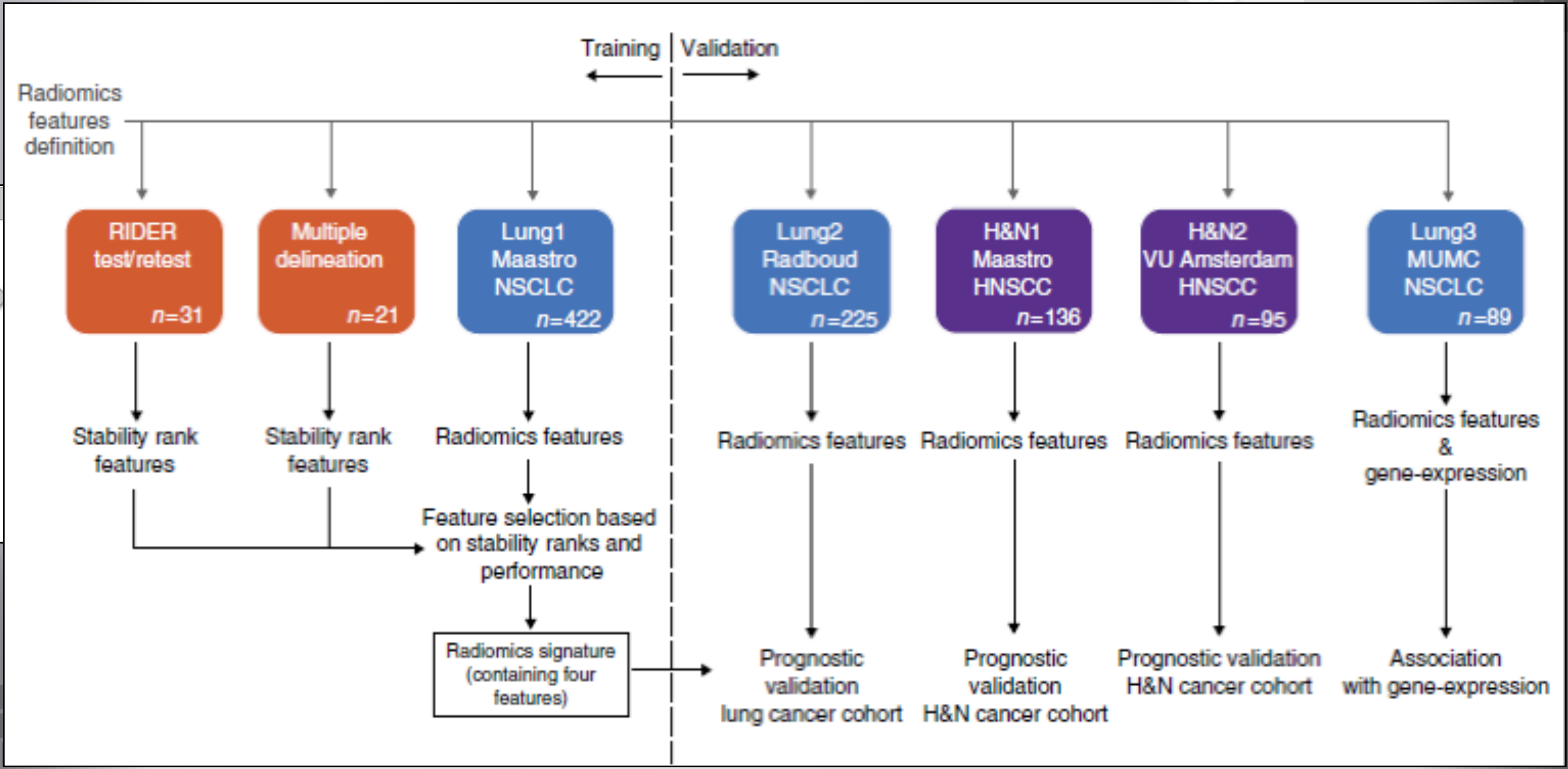

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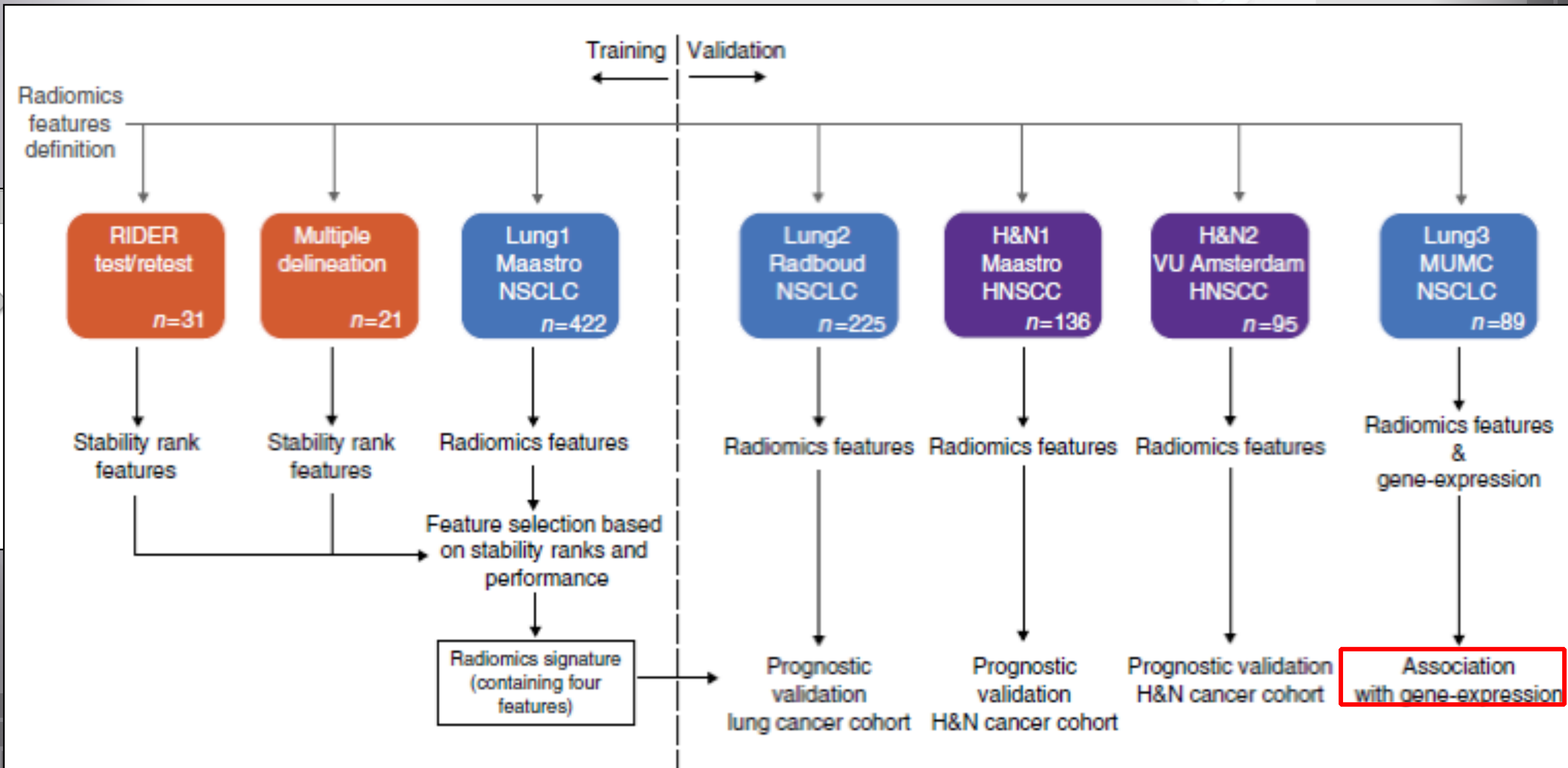

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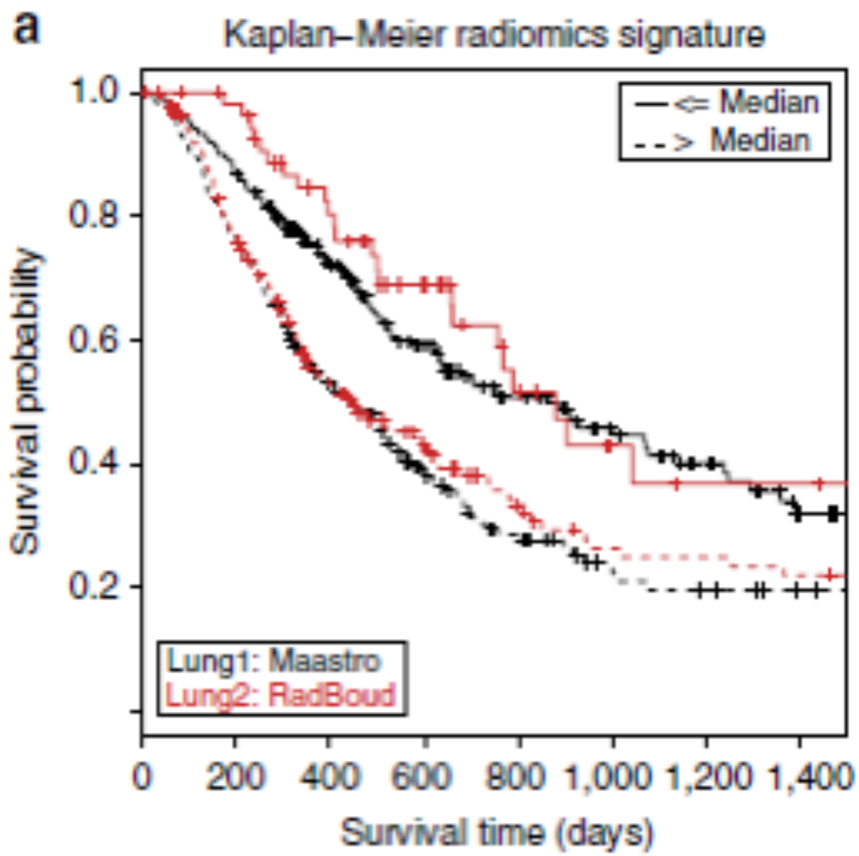

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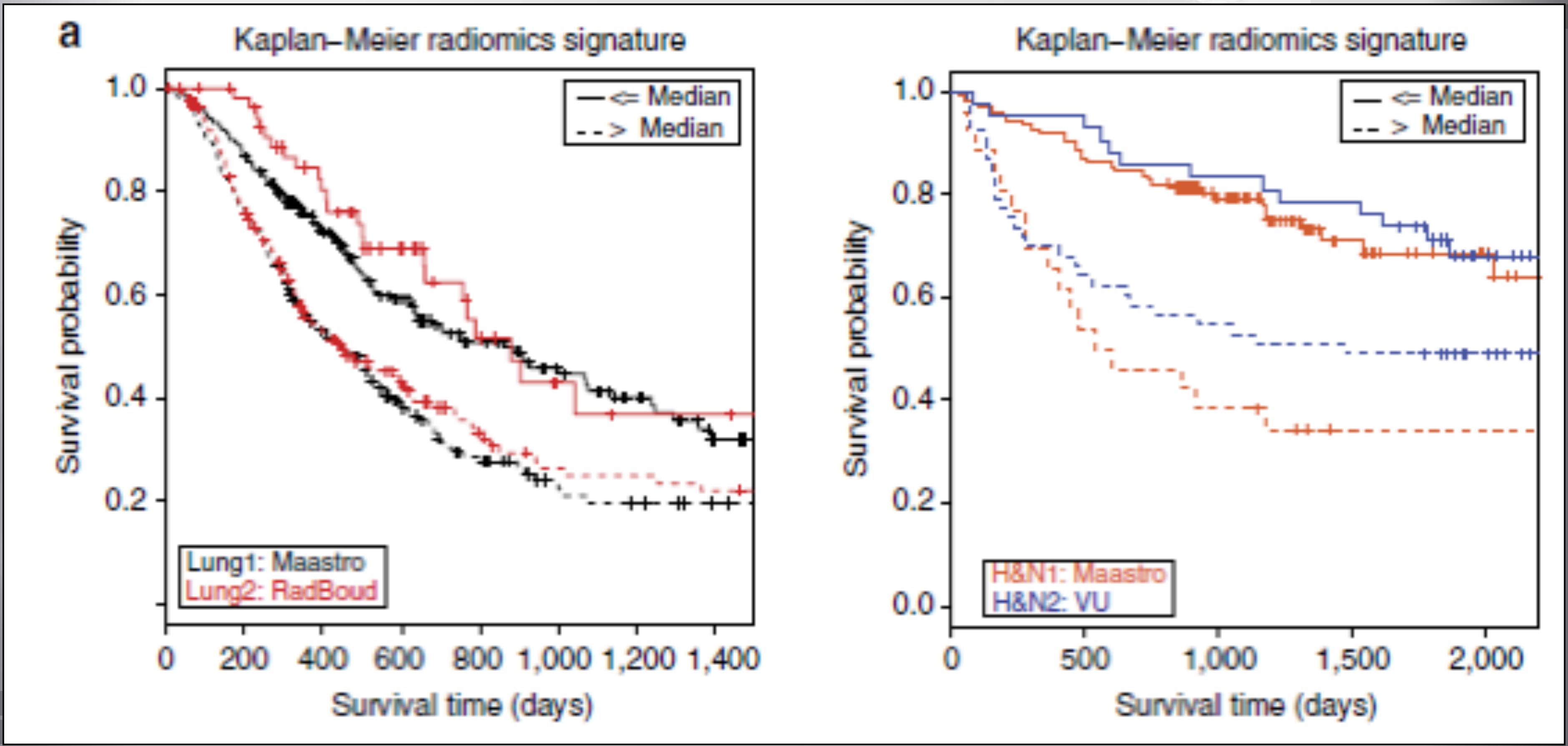

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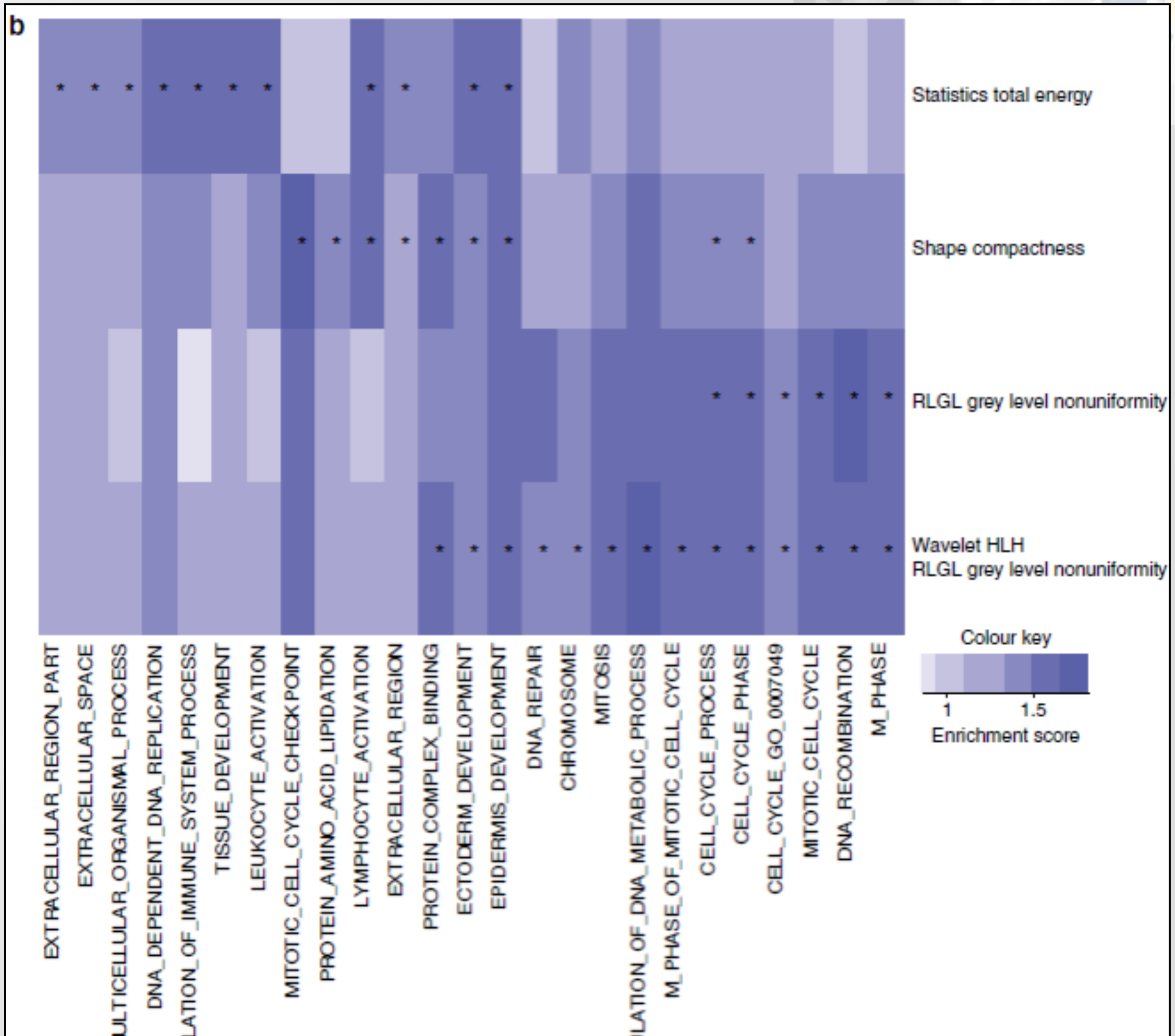

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Institut national de la santé et de la recherche médicale

HJ. Aerts, *et al*. Decoding tumour phenotype by noninvasive imaging using a quantitative radiomics approach. *Nat Commun*. 2014

Introduction

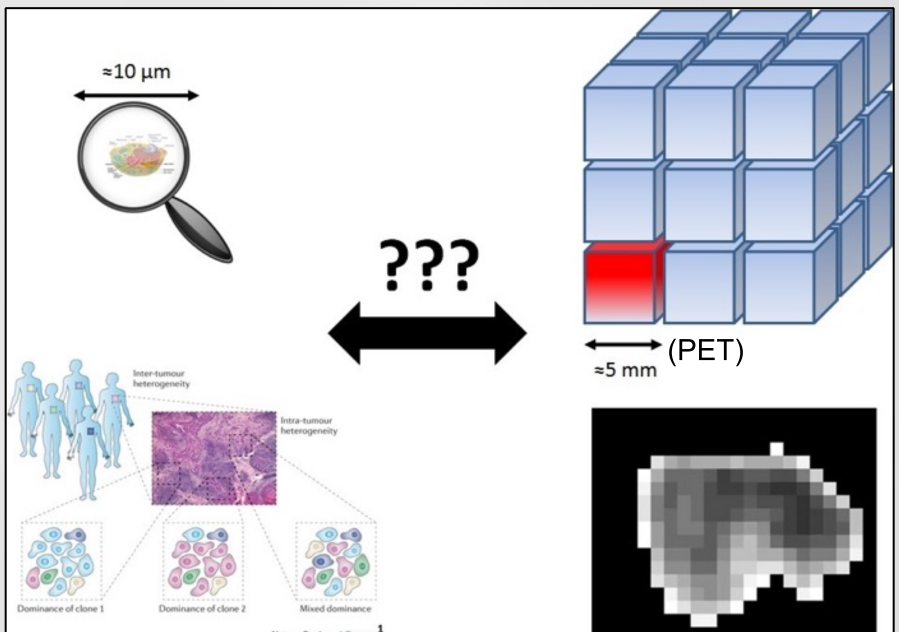
Rationale behind the use of textural features in PET imaging

Introduction

Rationale behind the use of textural features in PET imaging

Heterogeneity:

- Tumors are heterogeneous [1] at various scales
  - Genetic, cellular, tissues (macroscopic)
  - <u>Hypothesis</u>: heterogeneity in medical images of tumors reflects (partly) heterogeneity in lower scales [2]



1. Gerlinger, *et al*. Intratumor heterogeneity and branched evolution revealed by multiregion sequencing. *N Engl J Med*. 2012
2. Segal, *et al*. Decoding global gene expression programs in liver cancer by noninvasive imaging. *Nat Biotechnol*. 2007

Introduction

Textural features

- Objective: quantify heterogeneity
  - Texture analysis can quantify different patterns of spatial arrangements and/or intensity variations

Jensen. Introductory Image Processing 3rd ed. Upper Saddle River, NJ: Prentice-Hall 2005

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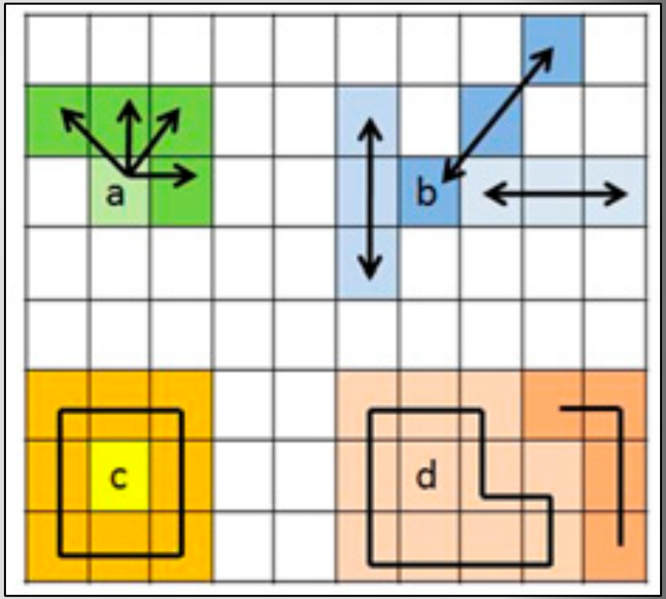
- Texture analysis can quantify different patterns of spatial arrangements and/or intensity variations
- Has been used since the 1970's in image processing applications (classification, data mining, pattern recognition, segmentation…)
- May quantify differences in
  - Intensities (contrast)
  - Sizes of voxels' groups
  - Directionality or lack of it



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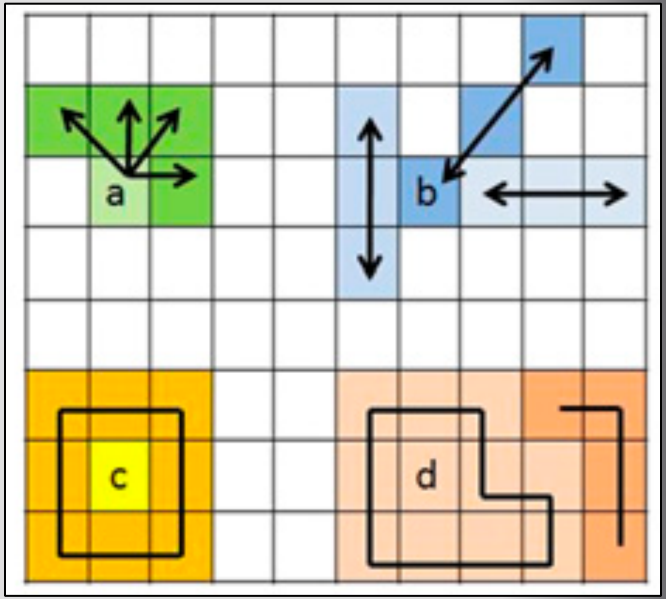
  - Directionality or lack of it
- Main idea for medical imaging:

May quantify tissues properties



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Introduction

Textural features in PET: quantify uptake heterogeneity

Numerous types of features exist

Increasing complexity and difficulty of interpretation

Versatility and potential

Order of textural feature	Description		Examples
First	Grey level frequency distribution from histogram analysis	Global	Minimum, mean and maximum intensity Standard deviation Skewness Kurtosis

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Second	From spatial grey level dependence matrices	Local	Entropy Energy Contrast Homogeneity Dissimilarity Uniformity Correlation

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Co-occurrence matrix
Local spatial info

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Second	From spatial grey level dependence matrices	Local	Entropy Energy Contrast Homogeneity Dissimilarity Uniformity Correlation
Higher	From neighbourhood grey-tone difference matrices	Local	Coarseness Contrast Busyness Complexity
	From voxel alignment matrices	Regional	Run-length and emphasis Run-length variability
	From grey level size zone matrices	Regional	Zone emphasis Size-zone variability

Histogram analysis
No spatial info

Co-occurrence matrix
Local spatial info

Size-zone matrix
Regional spatial info

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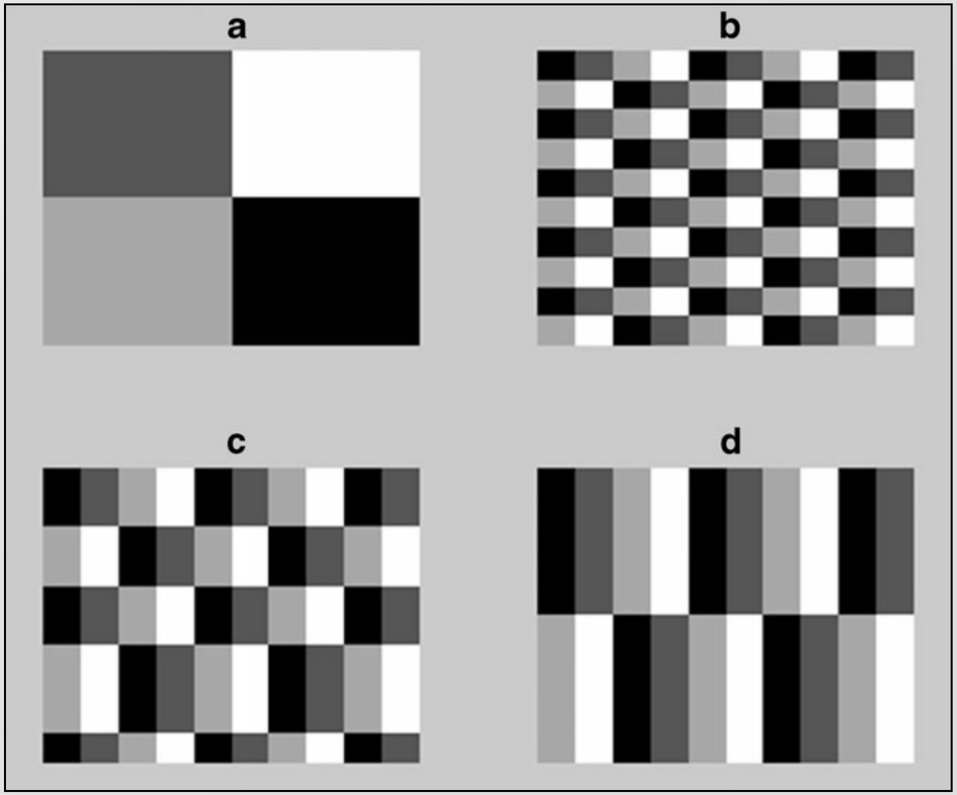
Textural features in PET: quantify uptake heterogeneity

Potential of 1st and higher order features



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The GLCM tutorial page http://www.fp.ucalgary.ca/mhallbey/tutorial.htm

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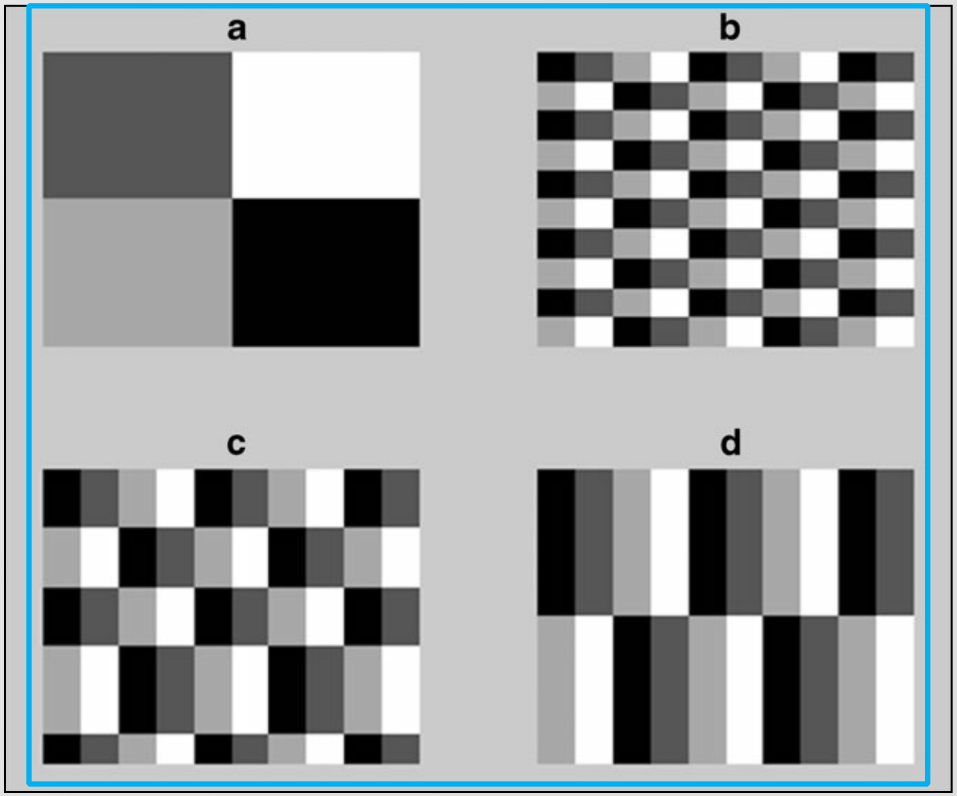
Potential of 1st and higher order features

1st order:

a = b = c = d



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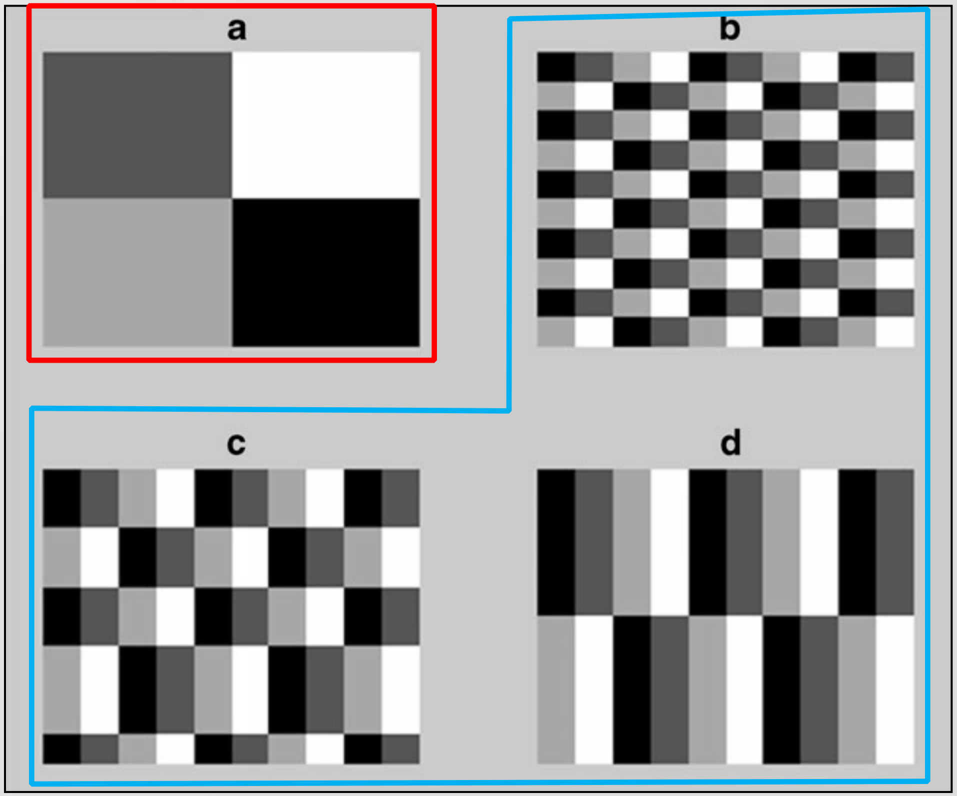
2^{nd} order:

a # (b = c = d)



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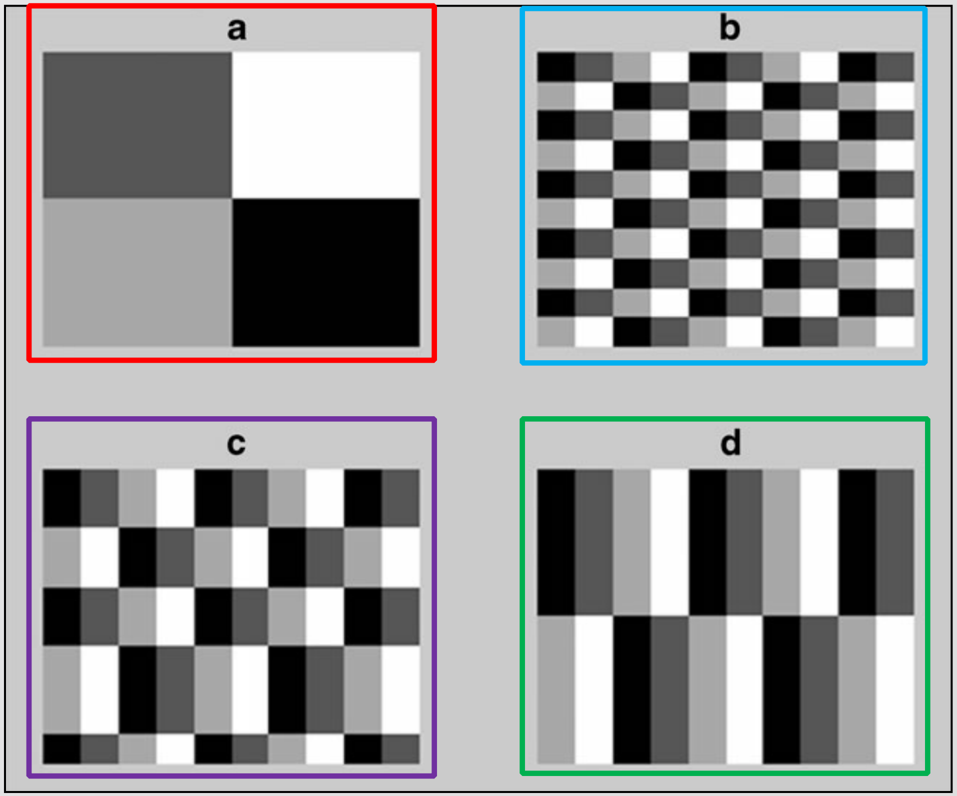
3rd order:
a # b # c # d



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Textural features in PET

The past: the early beginnings

- Textural features applied to PET imaging
  - Much later than MRI or CT (in the 90's[1,2])

1. Schad LR, *et al*. MR tissue characterization of intracranial tumors by means of texture analysis. *Magn Reson Imaging* 1993.
2. Mir AH, *et al*. Texture analysis of CT-images for early detection of liver malignancy. *Biomed Sci Instrum.* 1995.

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- Issues still exist (SUV quantification, standardization..), however:
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  - Time-of-flight capabilities
  - Improved iterative reconstruction algorithms
  - New applications beyond diagnosis (therapy monitoring, radiotherapy dosimetry) gaining interest for PET

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Textural features in PET

The past: the early beginnings

First papers

NIH Public Access

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Pattern Recognit. Author manuscript; available in PMC 2010 June 1.

Published in final edited form as:

Pattern Recognit. 2009 June 1; 42(6): 1162–1171. doi:10.1016/j.patcog.2008.08.011.

Exploring feature-based approaches in PET images for predicting cancer treatment outcomes

I. El Naqa, Ph.D.[a], **P. Grigsby, M.D.**[a], **A. Apte, M.Sc**[a], **E. Kidd, M.D.**[a], **E. Donnelly, M.D.**[a], **D. Khullar, M.Sc**[a], **S. Chaudhari, B.Sc**[a], **D. Yang, Ph.D.**[a], **M. Schmitt, B.Sc**[b], **Richard Laforest, Ph.D.**[b], **W. Thorstad, M.D.**[a], and **J. O. Deasy, Ph.D.**[a]

[1]Department of Radiation Oncology, Washington University School of Medicine St. Louis, MO, USA

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Textural features in PET

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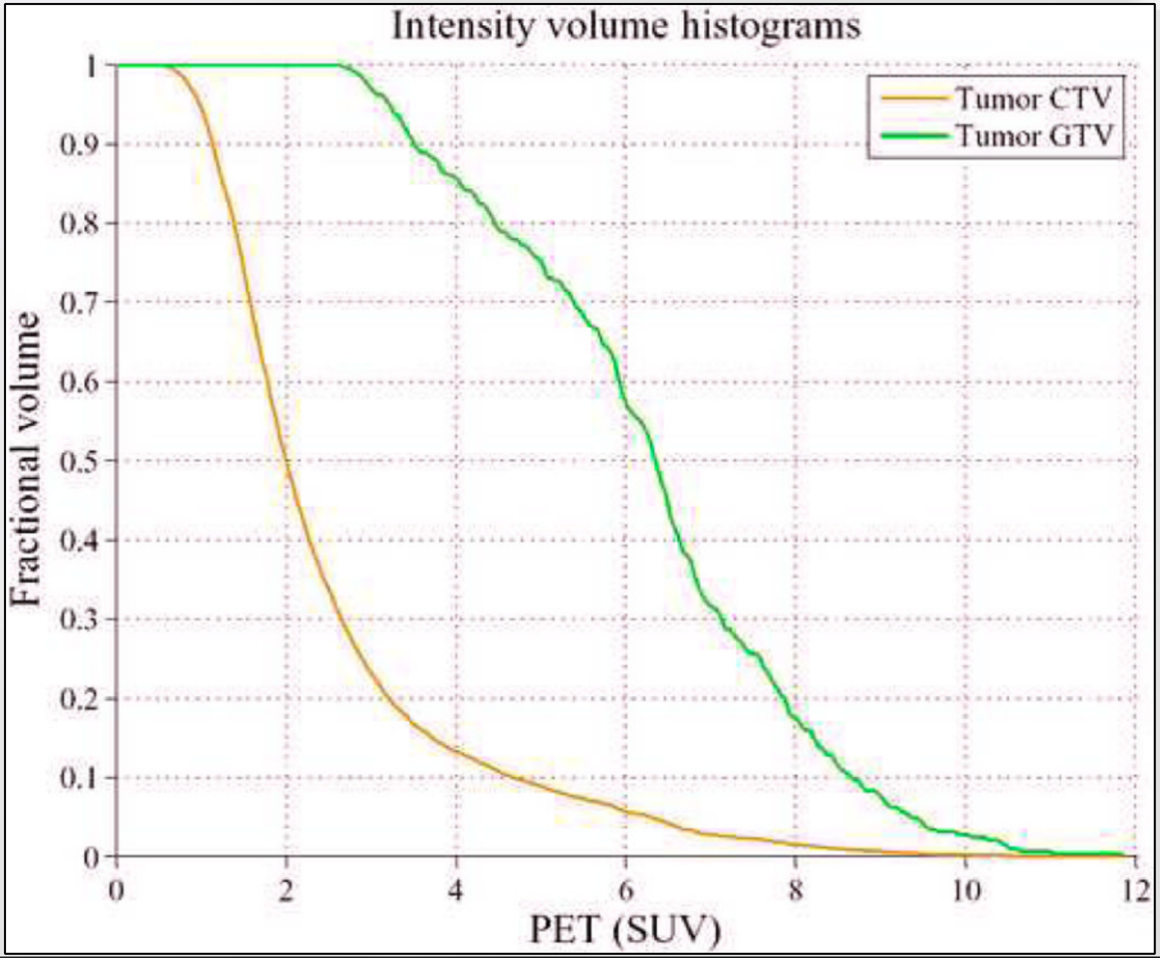
First papers



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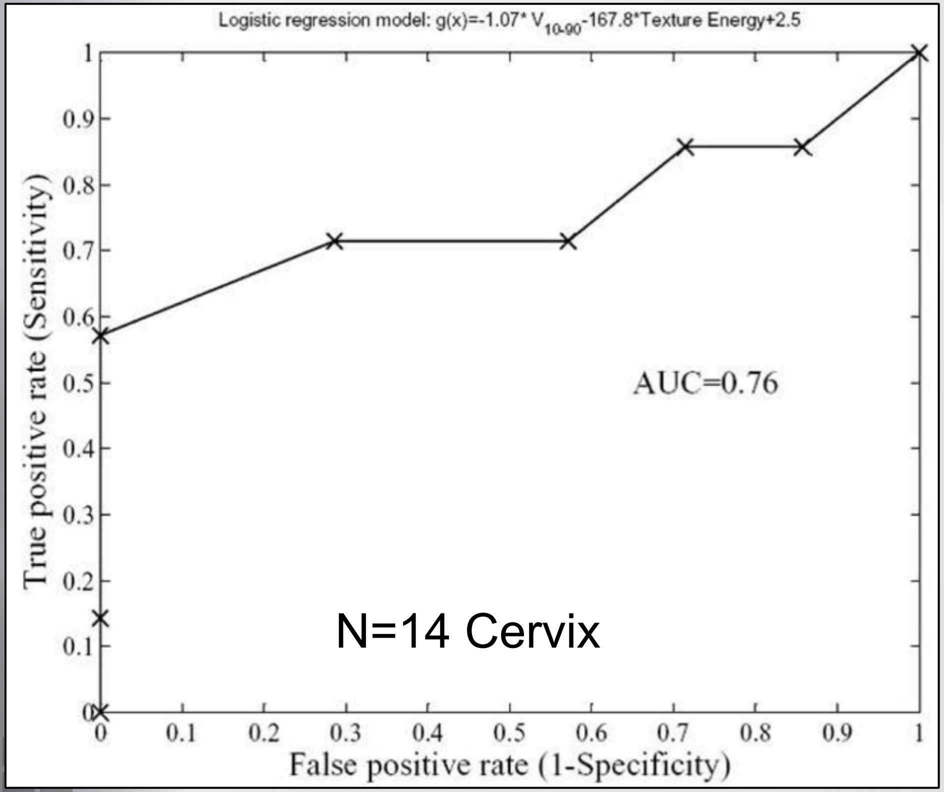
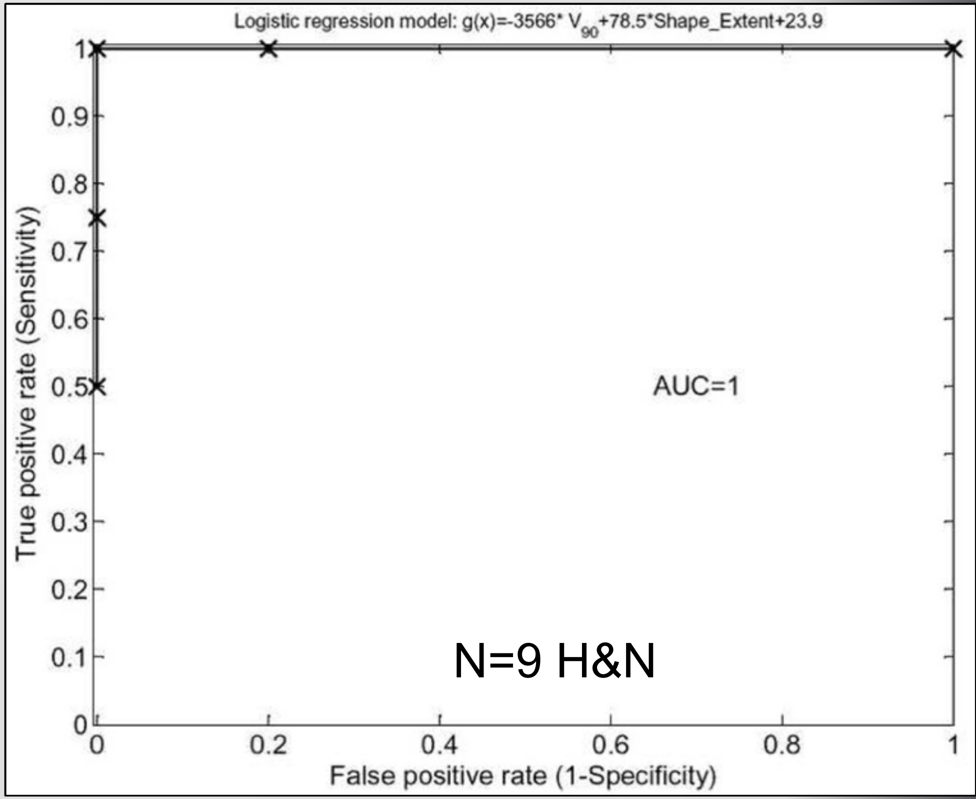




Textural features in PET

The past: the early beginnings

First papers

Acta Oncologica, 2010; 49: 1012–1016

informa healthcare

ORIGINAL ARTICLE

Variability of textural features in FDG PET images due to different acquisition modes and reconstruction parameters

PAULINA E. GALAVIS[1], CHRISTIAN HOLLENSEN[2,3], NGONEH JALLOW[1], BHUDATT PALIWAL[1,4] & ROBERT JERAJ[1,4]

[1]*Department of Medical Physics, University of Wisconsin, Madison, WI, USA,* [2]*Department of Informatics and Mathematical Models, Technical University of Denmark, Copenhagen, Denmark,* [3]*Department of Radiation Oncology, Copenhagen University Hospital-Rigshospitalet, Denmark and* [4]*Department of Human Oncology, University of Wisconsin, Madison, WI, USA*

Textural features in PET

The past: the early beginnings

First papers

Image #	Acq. Mode	Grid-Size	Recon. Alg	Iter. number	Post-filter width (mm)	Legend
1	2D	128×128	OSEM	2	3	2D-128-OSEM2-3mm
2	2D	128×128	OSEM	2	5	2D-128-OSEM2-5mm
3	2D	128×128	OSEM	4	5	2D-128-OSEM4-5mm
4	2D	256×256	OSEM	2	3	2D-256-OSEM2-3mm
5	2D	256×256	OSEM	2	5	2D-256-OSEM2-5mm
6	3D	128×128	ITER	2	3	3D-128-ITER2-3mm
7	3D	128×128	ITER	2	6	3D-128-ITER2-6mm
8	3D	128×128	ITER	4	6	3D-128-ITER4-6mm
9	3D	256×256	ITER	2	3	3D-256-ITER2-3mm
10	3D	256×256	ITER	2	6	3D-256-ITER2-6mm

Acq. Mode = acquisition mode; Recon. Alg = reconstruction algorithm; Iter = iteration.

Textural features in PET

The past: the early beginnings

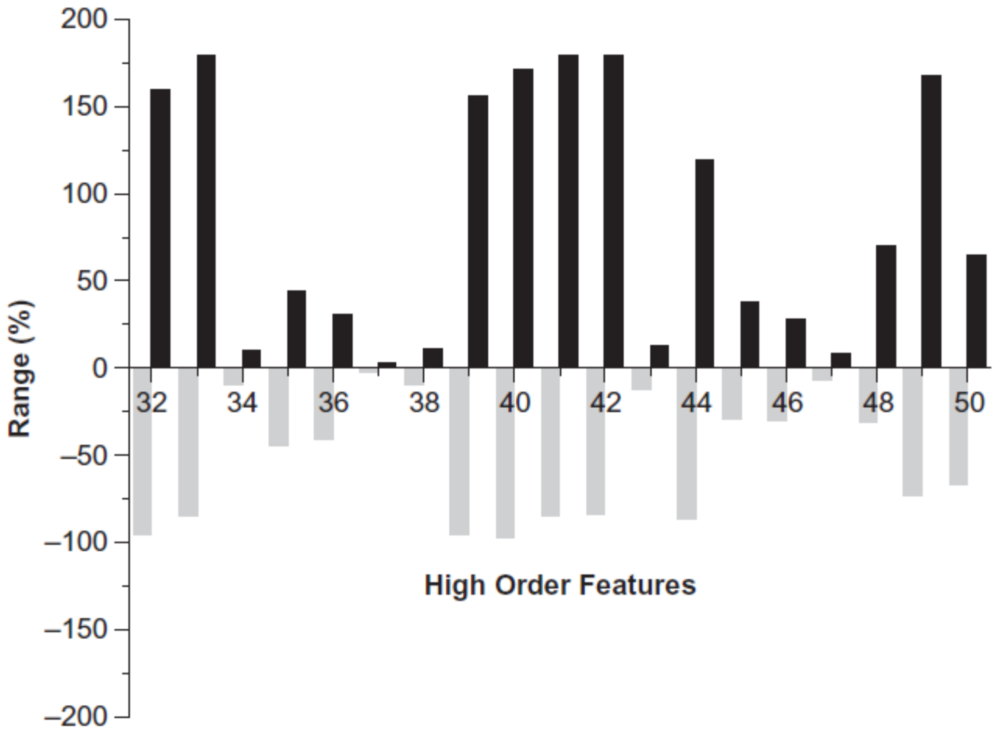
First papers

First-order features:
1: Mean
2: Median
3: Variance
4: Coefficient of variance
5: Skewness
6: Kurtosis
7: Energy
8: Entropy
Second-order features:
9: Homogeneity
10: Contrast-GLCM
11: Correlation
12: Sum of squares
14: Sum average
15: Sum variance
16: Sum entropy
17: Entropy-GLCM
18: Difference variance
19: Difference entropy
20: Information measure of correlation
21-22: Maximal correlation coefficient
23: Maximal probability
24: Diagonal moment
25: Dissimilarity
26: Difference energy
27: Inertia
28: Inverse difference moment
29: Sum energy
30: Cluster shade
31: Cluster prominence

Textural features in PET

The past: the early beginnings

First papers



High Order Features (GLRL)
32: Short run emphasis
33: Long run emphasis
34: Gray-level nonuniformity
35: Run length nonuniformity
36: Run Percent
37: Low gray-level run emphasis
38: High gray-level run emphasis
39: Short run low gray-level emphasis
40: Short run high gray-level emphasis
41: Long run low gray-level emphasis
42: Long run high gray-level emphasis
High Order Features (NGL)
43: Small number emphasis
44: Large number emphasis
45: Number nonuniformity
46: Second moment
47: Entropy-NGL
High Order Features (NGTD)
48: Coarseness
49: Contrast-NGL
50: Busyness

Textural features in PET

The past: the early beginnings

First papers

Intratumor Heterogeneity Characterized by Textural Features on Baseline ^{18}F-FDG PET Images Predicts Response to Concomitant Radiochemotherapy in Esophageal Cancer

Florent Tixier[1], Catherine Cheze Le Rest[1,2], Mathieu Hatt[1], Nidal Albarghach[1,3], Olivier Pradier[1,3], Jean-Philippe Metges[3,4], Laurent Corcos[4], and Dimitris Visvikis[1]

[1]INSERM, U650, LaTIM, CHU Morvan, Brest, France; [2]Department of Nuclear Medicine, CHU Morvan, Brest, France; [3]Institute of Oncology, CHU Morvan, Brest, France; and [4]INSERM, U613, Faculty of Medicine, Brest, France

Textural features in PET

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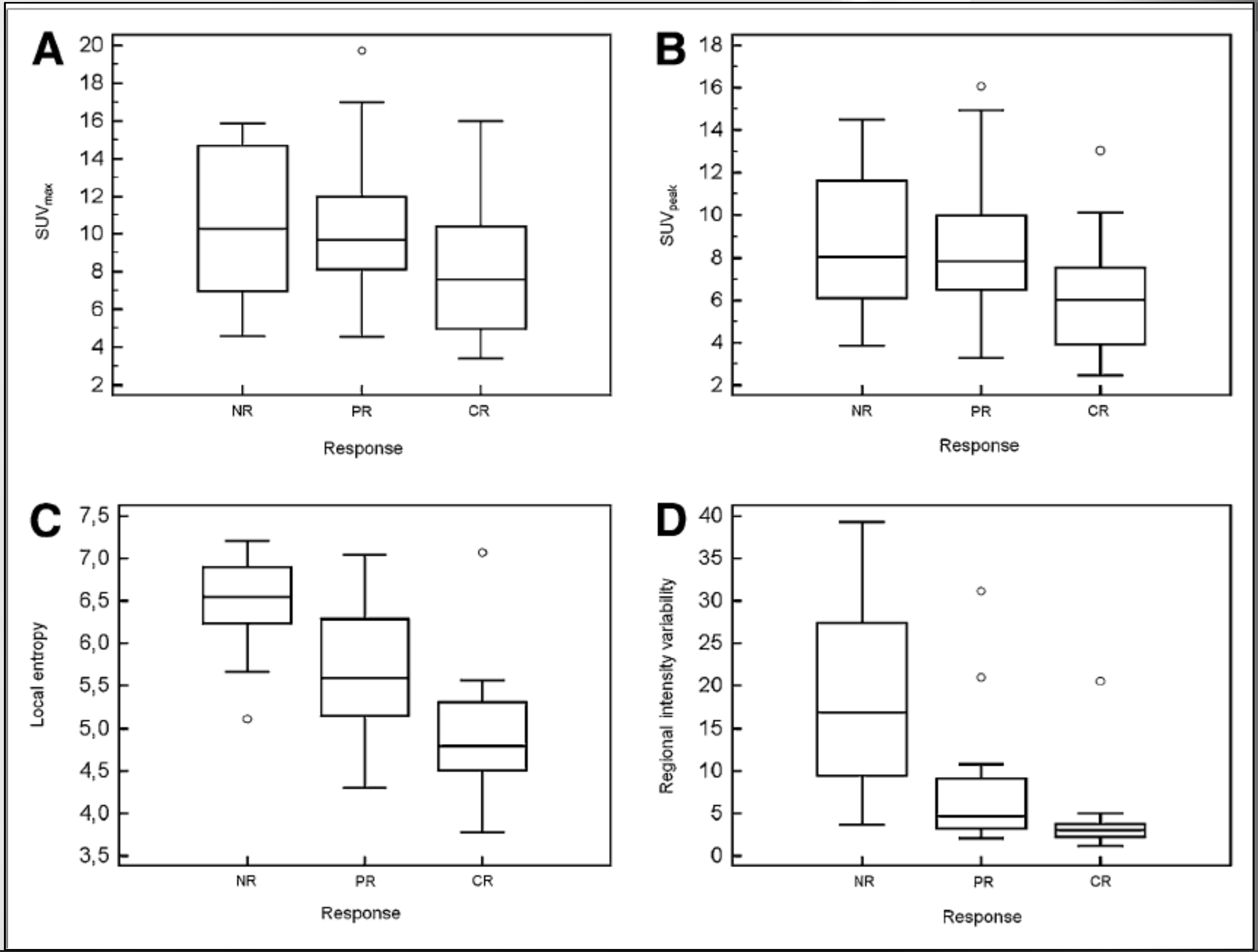
First papers

N=41 esophageal cancer



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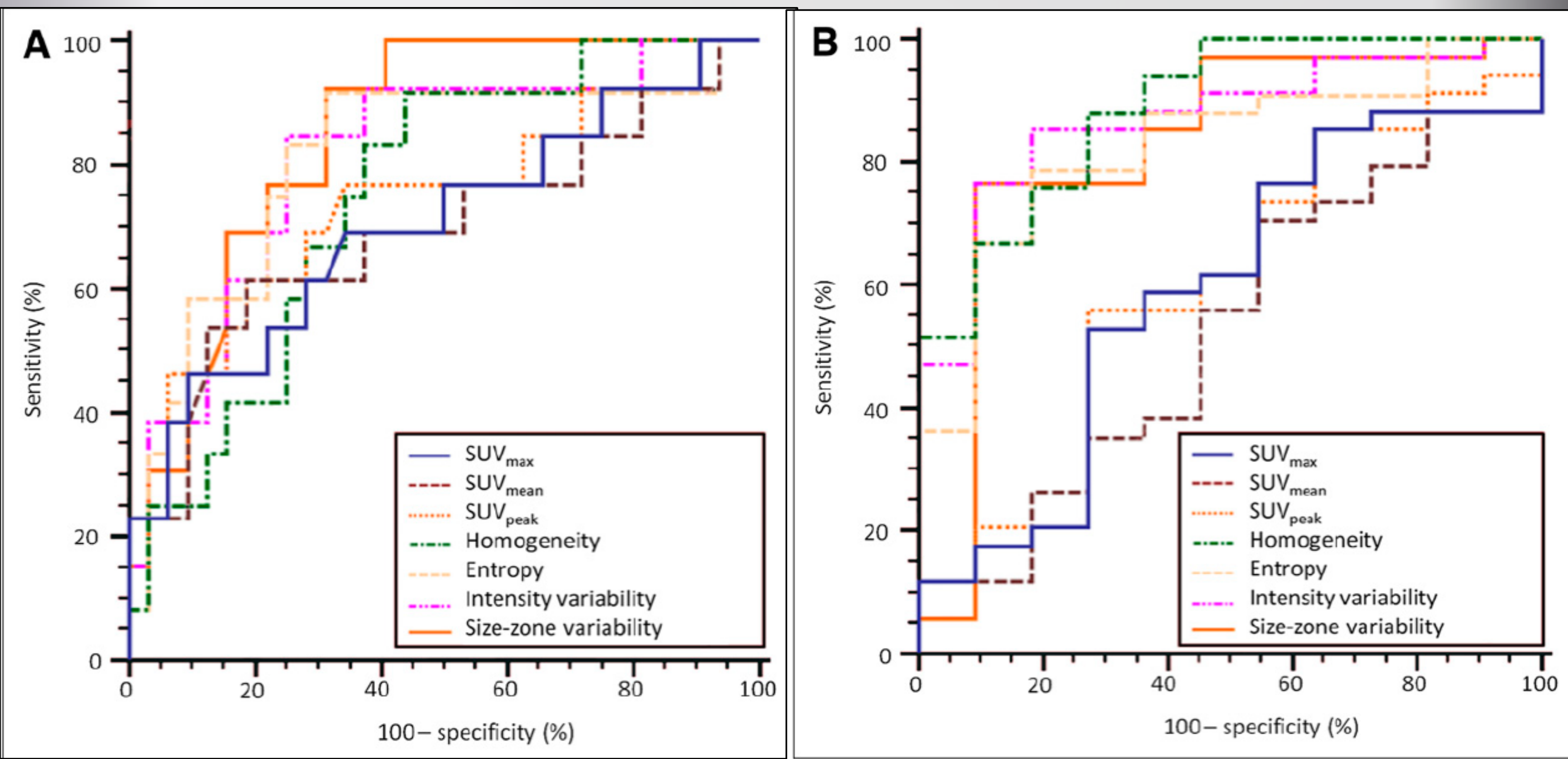

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- Increasing visibility: number of citations to date

NIH Public Access
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PAULINA E. GALAVIS[1], CHRISTIAN HOLLENSEN[2,3], NGONEH JALLOW[1], BHUDATT PALIWAL[1,4] & ROBERT JERAJ[1,4]
[1]Department of Medical Physics, University of Wisconsin, Madison, WI, USA, [2]Department of Informatics and Mathematical Models, Technical University of Denmark, Copenhagen, Denmark, [3]Department of Radiation Oncology, Copenhagen University Hospital-Rigshospitalet, Denmark and [4]Department of Human Oncology, University of Wisconsin, Madison, WI, USA

Intratumor Heterogeneity Characterized by Textural Features on Baseline ^{18}F-FDG PET Images Predicts Response to Concomitant Radiochemotherapy in Esophageal Cancer

Florent Tixier[1], Catherine Cheze Le Rest[1,2], Mathieu Hatt[1], Nidal Albarghach[1,3], Olivier Pradier[1,3], Jean-Philippe Metges[3,4], Laurent Corcos[4], and Dimitris Visvikis[1]
[1]INSERM, U650, LaTIM, CHU Morvan, Brest, France; [2]Department of Nuclear Medicine, CHU Morvan, Brest, France; [3]Institute of Oncology, CHU Morvan, Brest, France; and [4]INSERM, U613, Faculty of Medicine, Brest, France

Textural features in PET

The past: the early beginnings

First papers

- Increasing visibility: number of citations to date

NIH Public Access

Author Manuscript

Pattern Recognit. Author manuscript; available in PMC 2010 June 1.

Published in final edited form as:

Pattern Recognit. 2009 June 1; 42(6): 1162–1171. doi:10.1016/j.patcog.2008.08.011.

Exploring feature-based approaches in PET images for predicting cancer treatment outcomes

I. El Naqa, Ph.D.[a], P. Grigsby, M.D.[a], A. Apte, M.Sc[a], E. Kidd, M.D.[a], E. Donnelly, M.D.[a], D. Khullar, M.Sc[a], S. Chaudhari, B.Sc[a], D. Yang, Ph.D.[a], M. Schmitt, B.Sc[b], Richard Laforest, Ph.D.[b], W. Thorstad, M.D.[a], and J. O. Deasy, Ph.D.[a]

[1]Department of Radiation Oncology, Washington University School of Medicine St. Louis, MO, USA

[2]Department of Radiology, Washington University School of Medicine, St. Louis, MO, USA

Cited 138 times since 2009

Acta Oncologica, 2010; 49: 1012–1016

informa healthcare

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Cited 162 times since 2011

Textural features in PET

The past: optimism and naïveté

- >2011: numerous other papers
  - Dozens, in several pathologies
    - Breast, Lung, Head and neck, rectum, sarcoma, lymphoma…

Textural features in PET

The past: optimism and naïveté

- >2011: numerous other papers
  - Dozens, in several pathologies
    - Breast, Lung, Head and neck, rectum, sarcoma, lymphoma…
  - Use of textural features or different quantification approaches
    - Different types of textural features
    - Area under the curve of the cumulative histogram
    - Simpler metrics (heterogeneity factor, SUV_{COV} or SUV_{SD})

Textural features in PET

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- Use of textural features or different quantification approaches
  - Different types of textural features
  - Area under the curve of the cumulative histogram
  - Simpler metrics (heterogeneity factor, SUV_{COV} or SUV_{SD})
- As many issues as there are papers…
  - Small cohorts, no external validation
  - Use of unreliable/unreproducible features
  - Lack of rigorous statistical analysis
  - Lack of redundancy analysis
  - …

Textural features in PET

The past: alternative measurements

- Other heterogeneity measurements
  - SUVcov (SD/mean)
  - Area under the curve of the cumulative histogram
  - « Heterogeneity factor »
- Shape
  - Asphericity
  - Others (solidity, rectangularity, eccentricity…)

Other heterogeneity measurements

- Area under the curve of the cumulative histogram

Ann Nucl Med (2012) 26:222–227
DOI 10.1007/s12149-011-0562-3

ORIGINAL ARTICLE

Intratumoral heterogeneity of F-18 FDG uptake differentiates between gastrointestinal stromal tumors and abdominal malignant lymphomas on PET/CT

Tadashi Watabe · Mitsuaki Tatsumi · Hiroshi Watabe · Kayako Isohashi · Hiroki Kato · Masahiro Yanagawa · Eku Shimosegawa · Jun Hatazawa

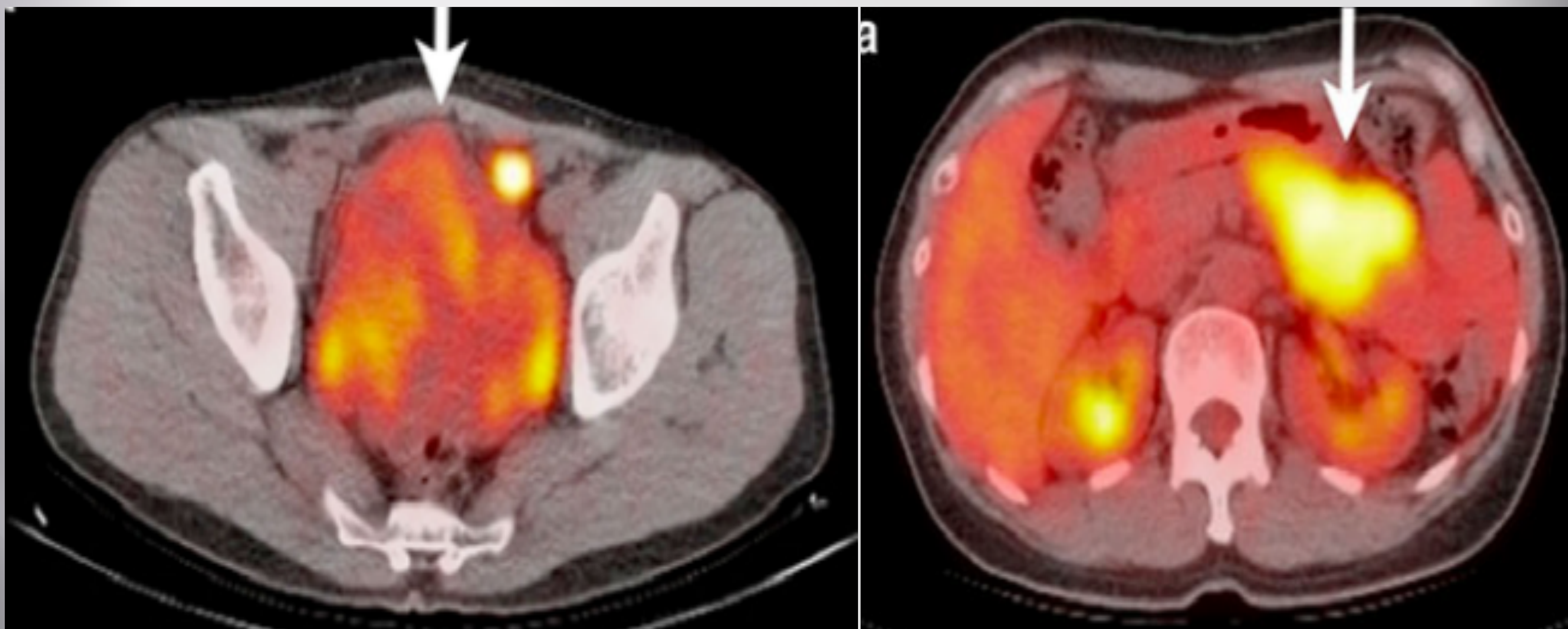
T. Watabe, *et al*. Intratumoral heterogeneity of F-18 FDG uptake differentiates between gastrointestinal stromal tumors and abdominal malignant lymphomas on PET/CT. *Ann Nucl Med* 2012

Textural features in PET

The past: alternative measurements

Other heterogeneity measurements

- Area under the curve of the cumulative histogram



T. Watabe, *et al*. Intratumoral heterogeneity of F-18 FDG uptake differentiates between gastrointestinal stromal tumors and abdominal malignant lymphomas on PET/CT. *Ann Nucl Med* 2012

Textural features in PET

The past: alternative measurements

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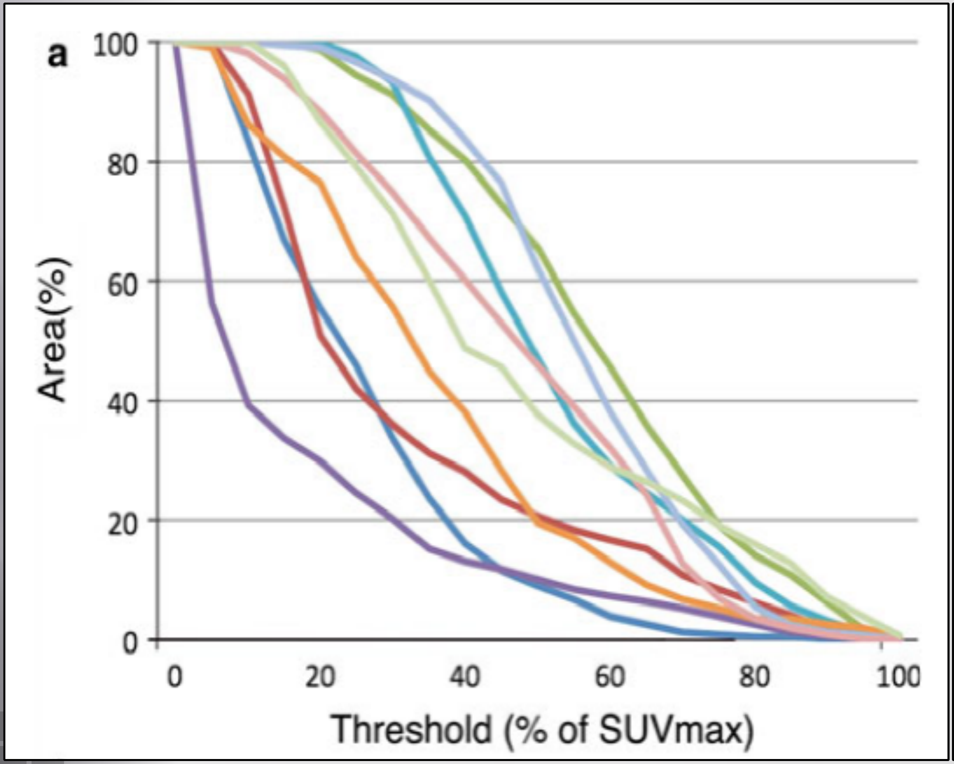
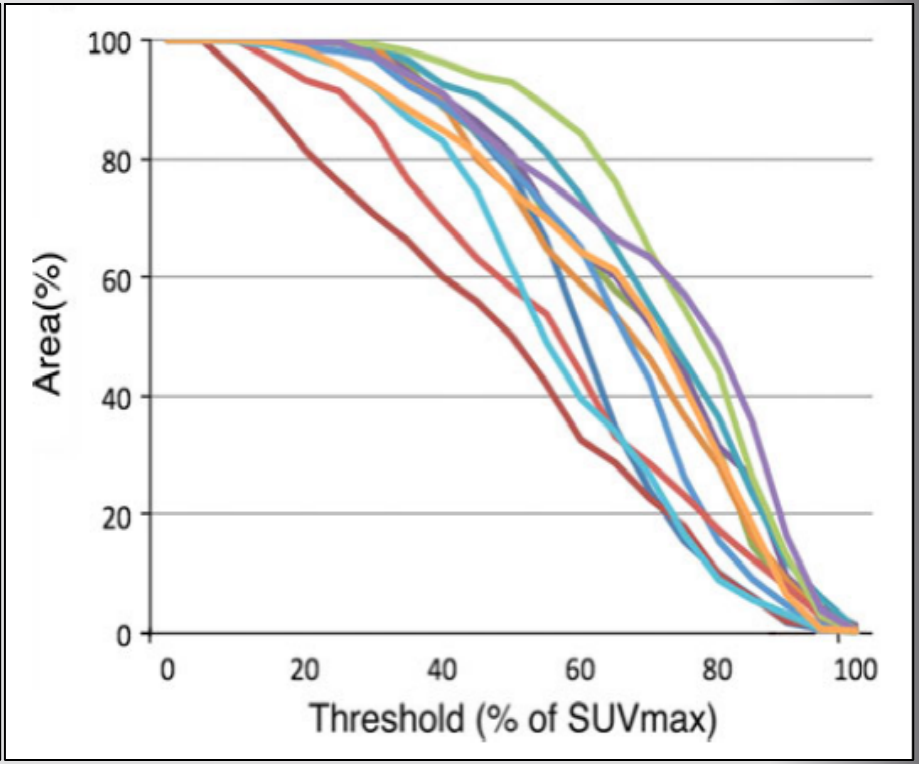




T. Watabe, *et al*. Intratumoral heterogeneity of F-18 FDG uptake differentiates between gastrointestinal stromal tumors and abdominal malignant lymphomas on PET/CT. *Ann Nucl Med* 2012

Textural features in PET

The past: alternative measurements

Other heterogeneity measurements

- Area under the curve of the cumulative histogram

Table 2 Results of visual and ROI analysis of the GIST and ML groups

	GIST N=9	ML N=12	*p* value
Visual score	2.67 ± 0.50	0.58 ± 0.79	<0.001*
2D-SUV_{max}	7.4 ± 2.6	11.0 ± 6.4	0.219
3D-SUV_{max}	9.0 ± 3.6	12.6 ± 6.0	0.169
CV	0.58 ± 0.30	0.31 ± 0.09	0.001*
AUC-CSH	0.41 ± 0.14	0.64 ± 0.08	0.001*
Tumor area (cm^2)	118.6 ± 102.1	40.1 ± 31.6	0.034†

Mean ± SD

* $p < 0.01$, † $p < 0.05$

T. Watabe, *et al*. Intratumoral heterogeneity of F-18 FDG uptake differentiates between gastrointestinal stromal tumors and abdominal malignant lymphomas on PET/CT. *Ann Nucl Med* 2012

Textural features in PET

The past: alternative measurements

Other heterogeneity measurements

- "Heterogeneity factor"

Son *et al. BMC Cancer* 2014, **14**:585
http://www.biomedcentral.com/1471-2407/14/585

BMC Cancer

RESEARCH ARTICLE **Open Access**

Prognostic implication of intratumoral metabolic heterogeneity in invasive ductal carcinoma of the breast

Seung Hyun Son, Do-Hoon Kim, Chae Moon Hong, Choon-Young Kim, Shin Young Jeong, Sang-Woo Lee, Jaetae Lee and Byeong-Cheol Ahn*

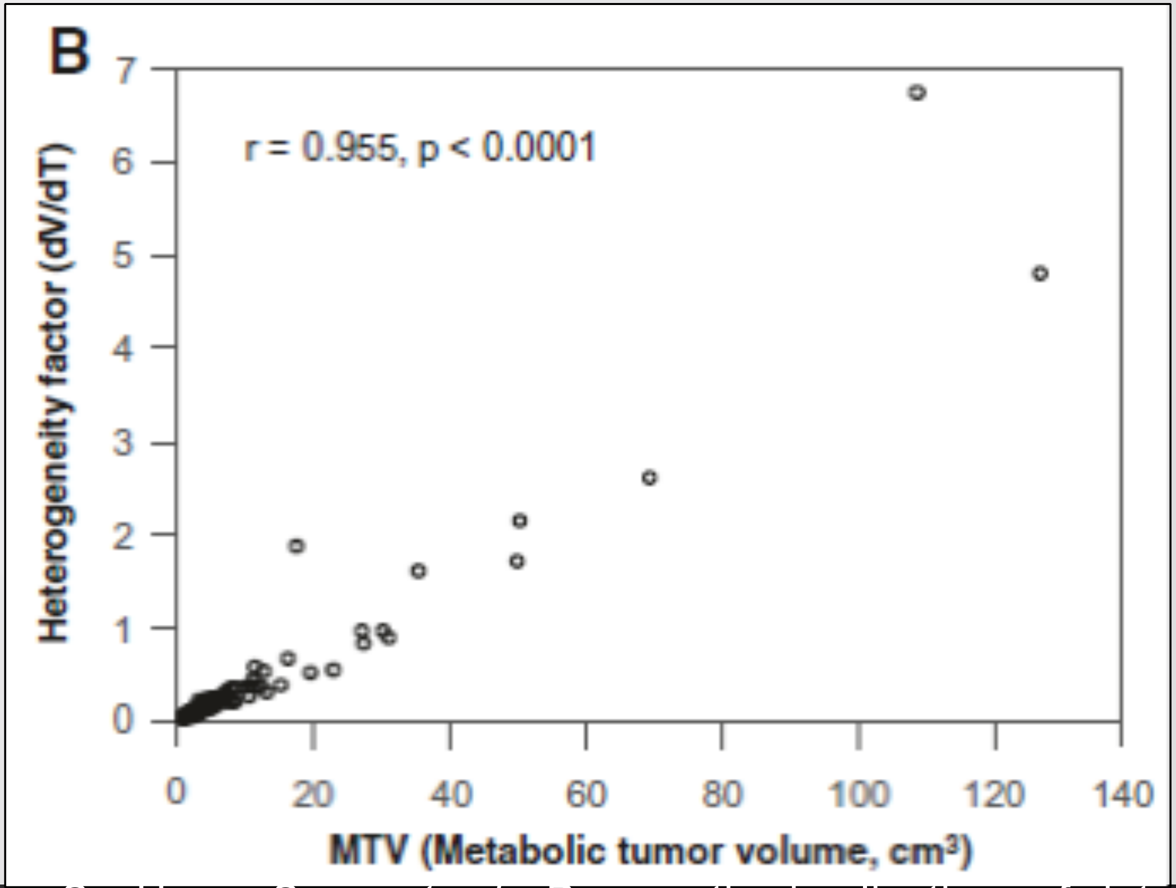
S. Hyun Son, *et al*. Prognostic implication of intratumoral metabolic heterogeneity in invasive ductal carcinoma of the breast. *BMC Cancer*. 2014

Textural features in PET

The past: alternative measurements

Other heterogeneity measurements

- "Heterogeneity factor"



S. Hyun Son, *et al*. Prognostic implication of intratumoral metabolic heterogeneity in invasive ductal carcinoma of the breast. *BMC Cancer*. 2014

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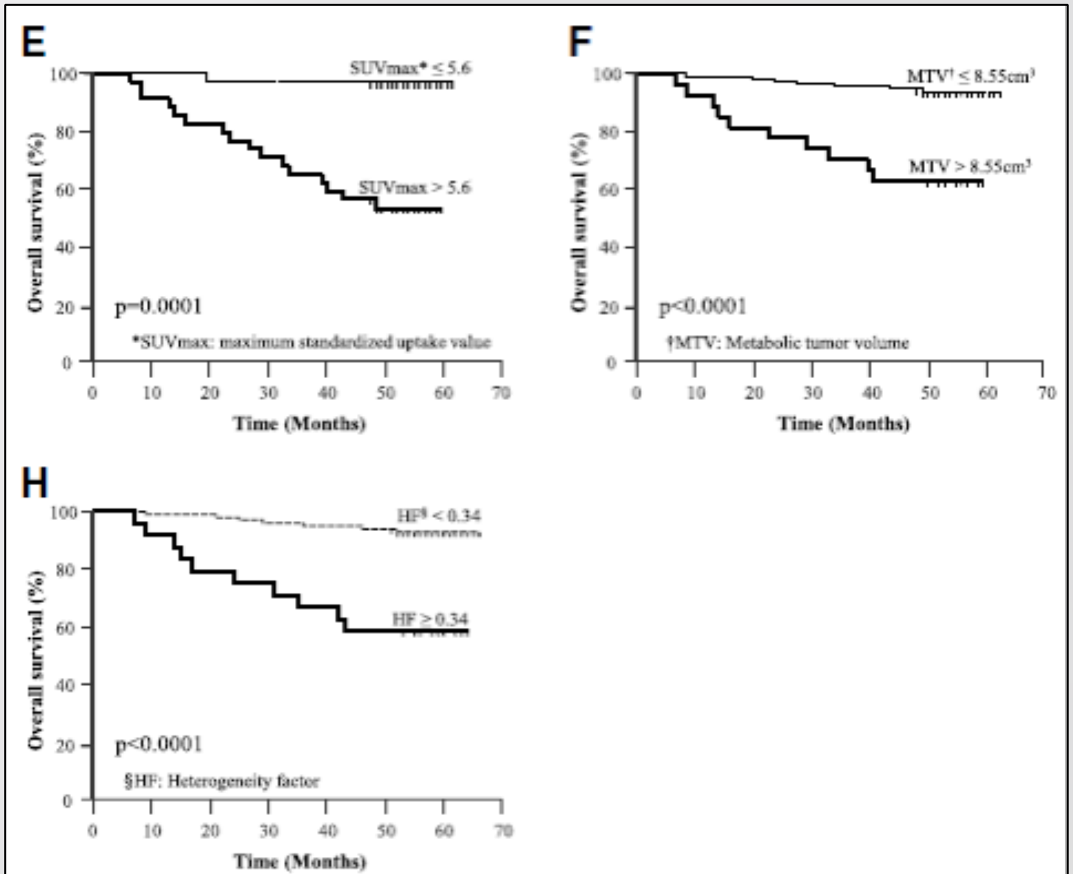

S. Hyun Son, *et al*. Prognostic implication of intratumoral metabolic heterogeneity in invasive ductal carcinoma of the breast. *BMC Cancer*. 2014

Textural features in PET

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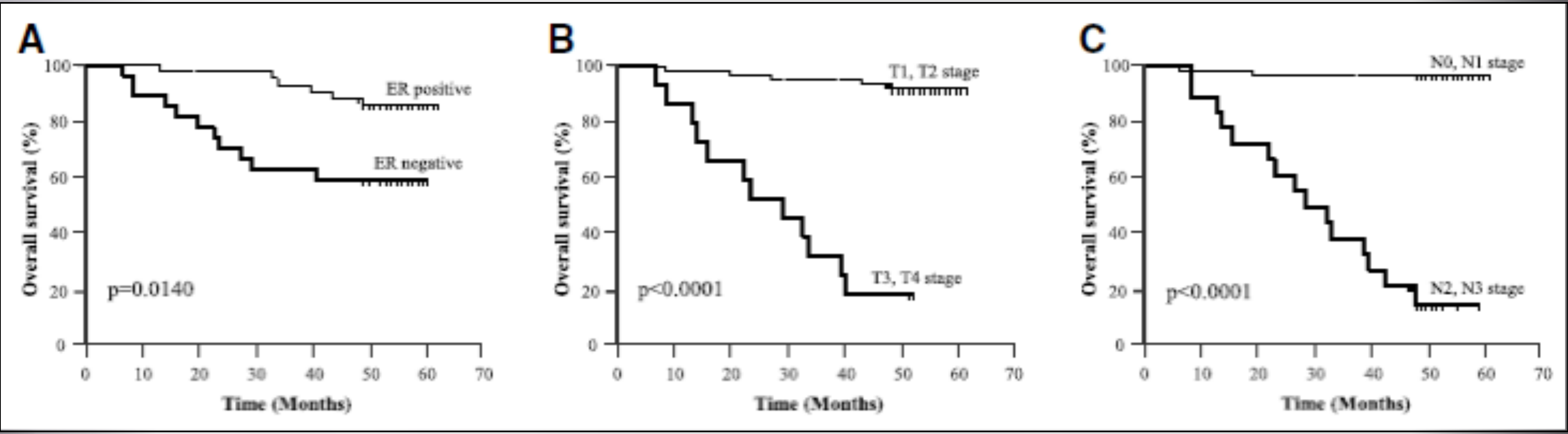
- "Heterogeneity factor"



S. Hyun Son, *et al*. Prognostic implication of intratumoral metabolic heterogeneity in invasive ductal carcinoma of the breast. *BMC Cancer*. 2014

Textural features in PET

The present: issues galore

- Did we go too fast? [1,2]
  - No thorough technical validation
  - Little to no consideration of volume interaction, and redundancy among features
  - (Very) small cohorts
  - Loose statistical analysis, only surrogate of endpoints/outcome, no gold-standard
  - Use of unreliable features, no acknowledgment of previous publications
  - …

1. Cheng NM, *et al*. The promise and limits of PET texture analysis. *Ann Nucl Med*. 2013
2. Brooks FJ. On some misconceptions about tumor heterogeneity quantification. *Eur J Nucl Med Mol Imaging*. 2013

Controversies

Eur J Nucl Med Mol Imaging
DOI 10.1007/s00259-013-2381-3

LETTER TO THE EDITOR

Area under the cumulative SUV-volume histogram is not a viable metric of intratumoral metabolic heterogeneity

Frank J. Brooks

Textural features in PET

The present: issues galore

Controversies

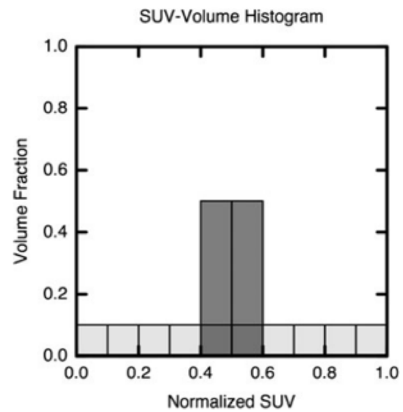


Fig. 1 Two distinct intensity histograms

by a precipitous drop. Still, that CSH is, overall, decreasing. From Fig. 2, it is readily seen that the AUC for each CSH is 5.5. Thus, the AUC for the nearly homogeneous histogram equals the AUC for the maximally heterogeneous histogram. In this context, it is difficult to see how the AUC can be used as a distinguishing quantifier of nonspatial heterogeneity.

There are two simple explanations as to why some researchers have reported statistically significant results after employing the AUC as a heterogeneity metric. First, both the SUV and volume themselves are inherently noisy measurements [4, 5]. Thus, any measure based jointly upon them has an increased uncertainty and is therefore particularly sensitive to the fundamental experimental concerns such as sample size, significant digits, and reproducibility.

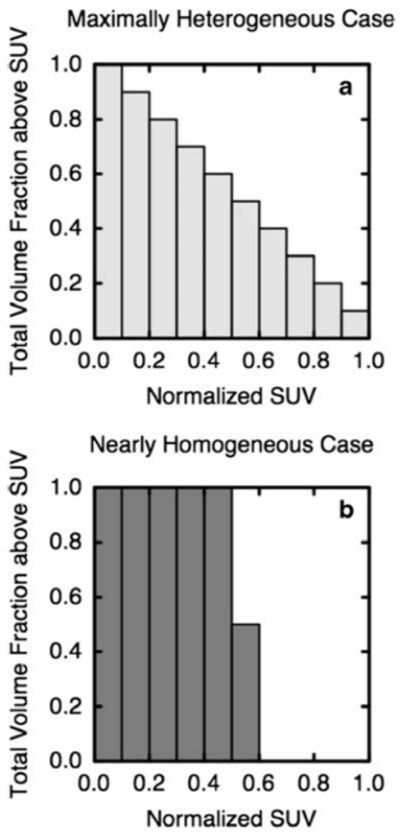


Fig. 2 **a** CSH for the maximally heterogeneous histogram. **b** CSH for the more homogeneous histogram

Textural features in PET

The present: issues galore

Controversies

Eur J Nucl Med Mol Imaging (2013) 40:1469–1470
DOI 10.1007/s00259-013-2474-z

LETTER TO THE EDITOR

Reply to: Area under the cumulative SUV-volume histogram is not a viable metric of intratumoral metabolic heterogeneity

Floris H. P. van Velden • Ronald Boellaard

Textural features in PET

The present: issues galore

Controversies

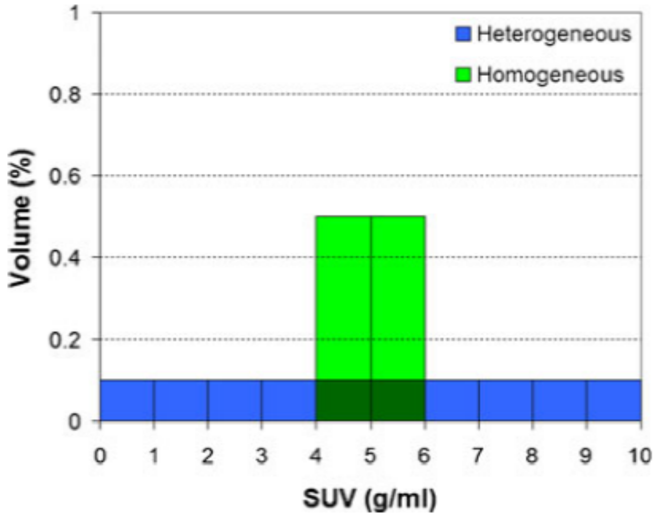


Fig. 1 Two distinct intensity histograms derived from the example discussed by Brooks [1]. Only ten different SUV levels have been chosen. The tumour with maximally heterogeneous tracer uptake has SUV_{max} 10 g/ml, while the tumour with more homogeneous tracer uptake has SUV_{max} 6 g/ml

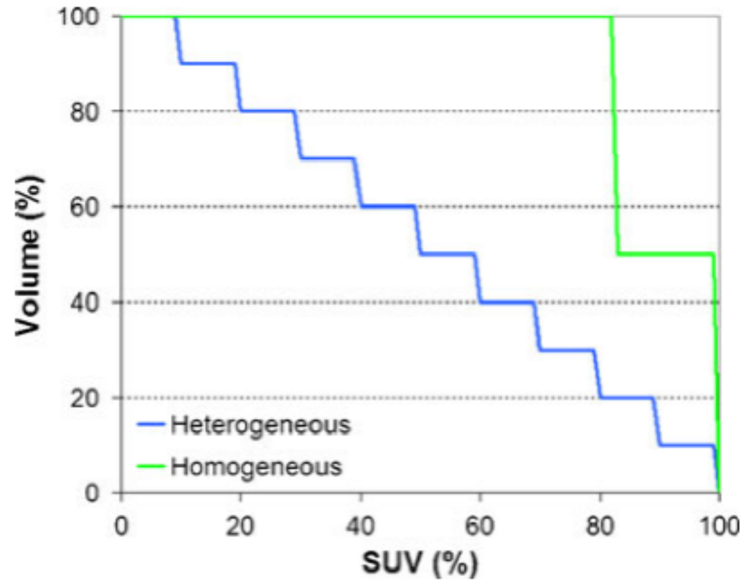


Fig. 2 CSHs for two example tumours, one with more homogeneous tracer uptake and the other with maximally heterogeneous tracer uptake

Textural features in PET

The present: issues galore

Controversies

Eur J Nucl Med Mol Imaging (2013) 40:1926–1927
DOI 10.1007/s00259-013-2572-y

LETTER TO THE EDITOR

Area under the cumulative SUV-volume histogram is not a viable metric of intratumoral metabolic heterogeneity: further comments

Frank J. Brooks

Textural features in PET

The present: issues galore

Controversies

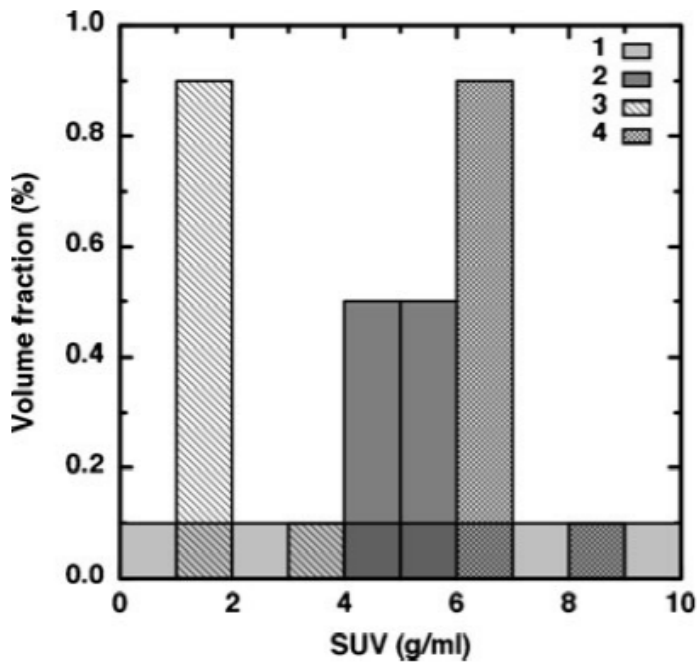


Fig. 1 Four distinct histograms are given. The first (*lightly shaded*) corresponds to a maximally heterogeneous volume. The other three correspond to virtually homogeneous tumor volumes

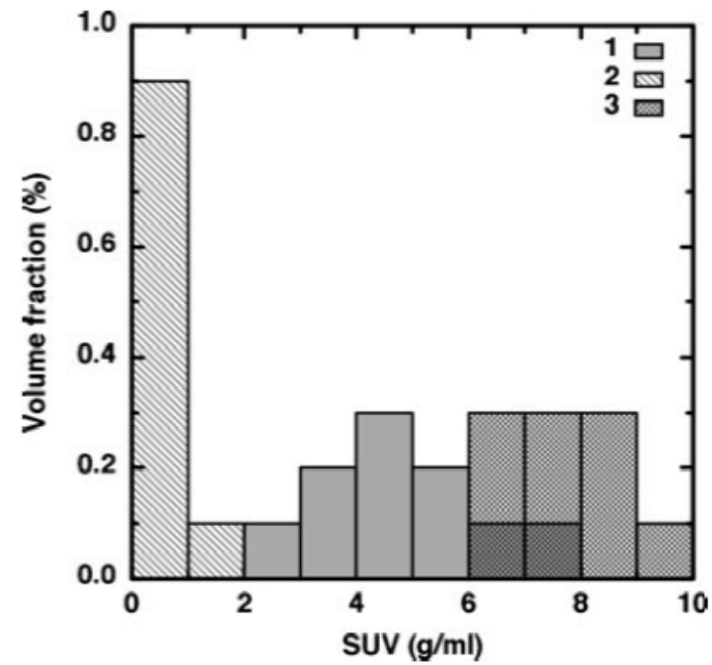


Fig. 2 Three distinct histograms are given. The second (*hatched*) clearly represents a nearly homogeneous tumor volume. Because more SUVs occur with greater probability in the other two histograms, those correspond to more heterogeneous tumor volumes

Textural features in PET

The present: issues galore

Overoptimistic results / negative results

OPEN ACCESS Freely available online PLOS ONE

Relationship between Tumor Heterogeneity Measured on FDG-PET/CT and Pathological Prognostic Factors in Invasive Breast Cancer

Michael Soussan[1,2,3*], Fanny Orlhac[3], Marouane Boubaya[4], Laurent Zelek[1,5], Marianne Ziol[1,6], Véronique Eder[1,2], Irène Buvat[7]

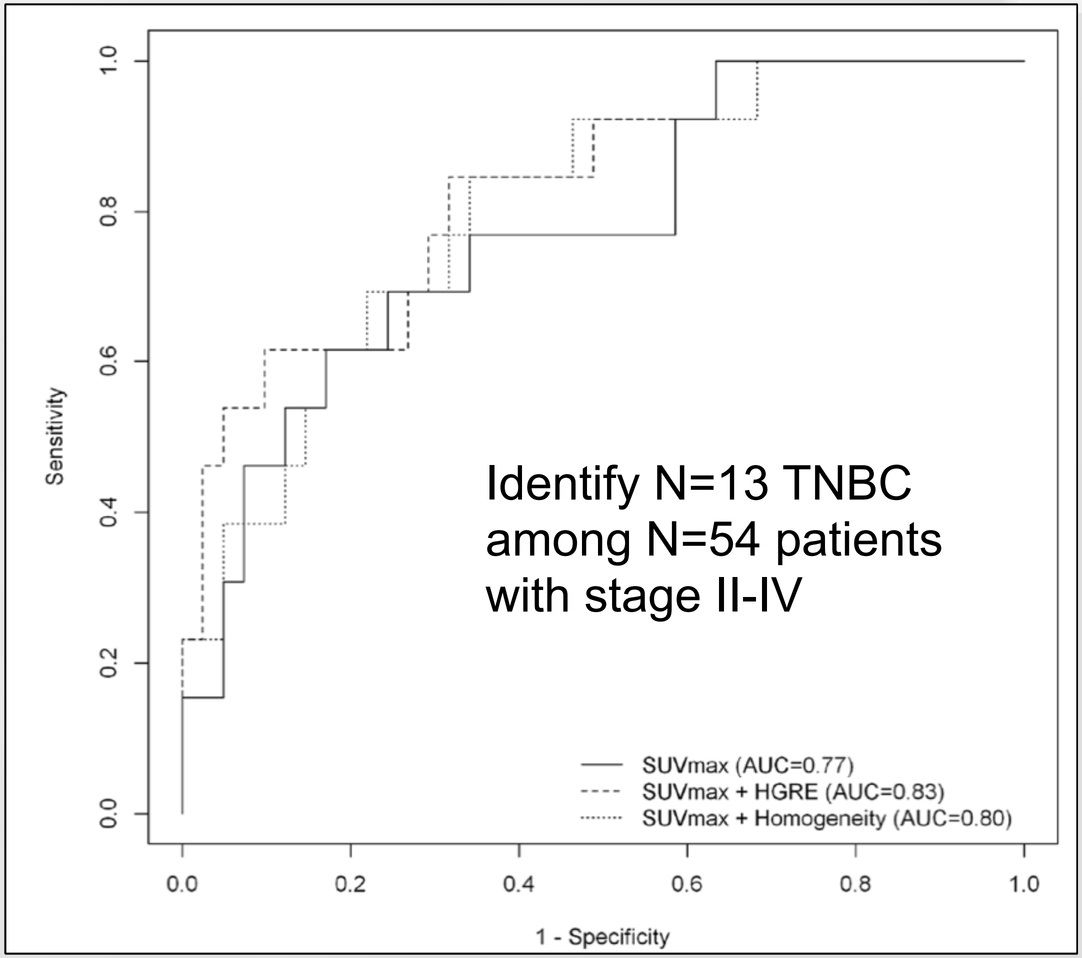
1 Paris 13 University, Sorbonne Paris Cité, Bobigny, France, **2** Department of Nuclear Medicine, AP-HP, Avicenne University Hospital, Bobigny, France, **3** IMNC - UMR 8165 CNRS - Paris 7 and Paris 11 Universities, Orsay, France, **4** Clinical Research Unit, AP-HP, Avicenne University Hospital, Bobigny, France, **5** Department of Oncology, AP-HP, Avicenne University Hospital, Bobigny, France, **6** Department of Pathology, AP-HP, Jean Verdier Hospital, Bondy, France, **7** CEA-SHFJ, Orsay, France

M. Soussan, *et al*. Relationship between tumor heterogeneity measured on FDG PET/CT and pathological prognostic factors in invasive breast cancer. *PLOS ONE*. 2014

Textural features in PET

The present: issues galore

- Overoptimistic results / negative results



M. Soussan, *et al*. Relationship between tumor heterogeneity measured on FDG PET/CT and pathological prognostic factors in invasive breast cancer. *PLOS ONE*. 2014

Textural features in PET

The present: issues galore

Overoptimistic results / negative results

Eur J Nucl Med Mol Imaging
DOI 10.1007/s00259-015-3110-x

CrossMark

ORIGINAL ARTICLE

Do clinical, histological or immunohistochemical primary tumour characteristics translate into different ^{18}F-FDG PET/CT volumetric and heterogeneity features in stage II/III breast cancer?

David Groheux[1] • Mohamed Majdoub[2] • Florent Tixier[3] • Catherine Cheze Le Rest[3] • Antoine Martineau[1] • Pascal Merlet[1] • Marc Espié[4] • Anne de Roquancourt[5] • Elif Hindié[6] • Mathieu Hatt[2] • Dimitris Visvikis[2]

Instituts thématiques Inserm Institut national de la santé et de la recherche médicale

D. Groheux, *et al*. Do clinical, histological or immunohistochemical primary tumour characteristics translate into different 18F-FDG PET/CT volumetric and heterogeneity features in stage II/III breast cancer? *Eur J Nucl Med Mol Imaging* 2015

Textural features in PET

The present: issues galore

Overoptimistic results / negative results

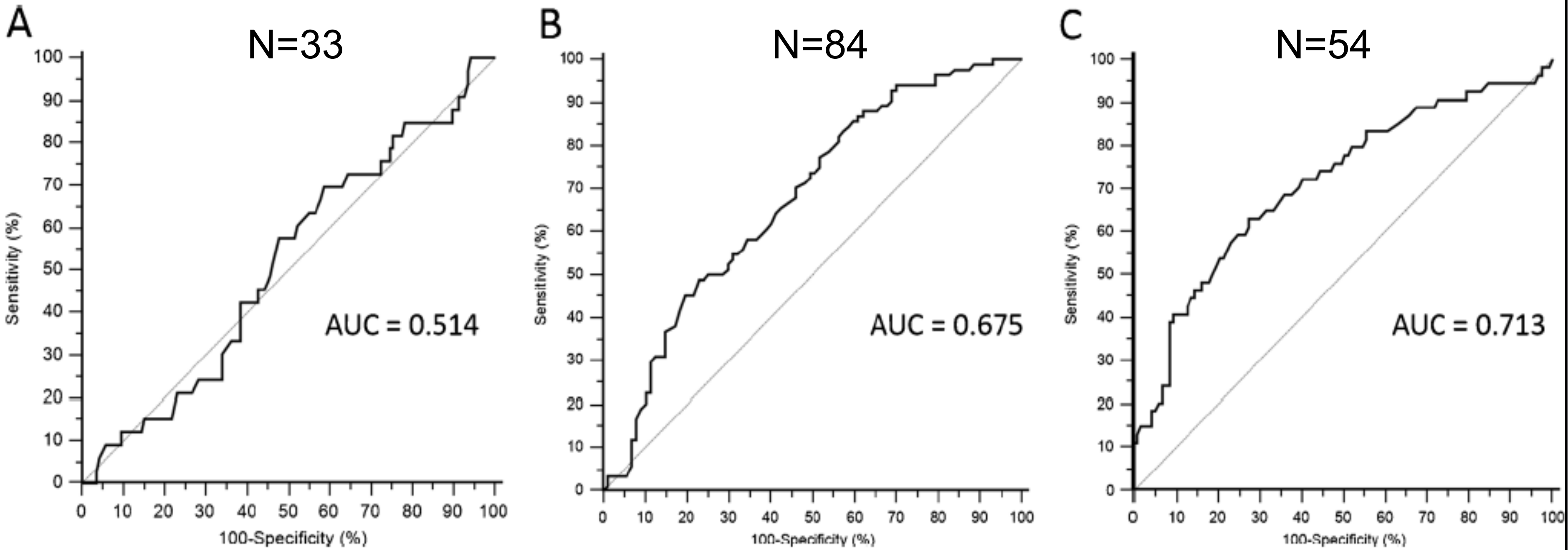


Fig. 4 ROC curves for the identification of patients with the different subtypes of BC using SUV_{max}: **a** HER2-positive BC, **b** ER-positive/HER2-negative BC, and **c** triple-negative BC N=171

D. Groheux, *et al*. Do clinical, histological or immunohistochemical primary tumour characteristics translate into different 18F-FDG PET/CT volumetric and heterogeneity features in stage II/III breast cancer? *Eur J Nucl Med Mol Imaging* 2015

Textural features in PET

The present: issues galore

- Overoptimistic results / negative results

erogeneity. Oestrogen and progesterone receptor expression were associated with several heterogeneity patterns, but the discriminative power was limited. Finally, the three different BC subgroups (ER-positive/HER2-negative, HER2-positive and triple-negative) did not show any significant and measurable differences in levels of heterogeneity.

D. Groheux, *et al*. Do clinical, histological or immunohistochemical primary tumour characteristics translate into different 18F-FDG PET/CT volumetric and heterogeneity features in stage II/III breast cancer? *Eur J Nucl Med Mol Imaging* 2015

Textural features in PET

The present: issues galore

Volume confounding effect

The Effect of Small Tumor Volumes on Studies of Intratumoral Heterogeneity of Tracer Uptake

Frank J. Brooks[1] and Perry W. Grigsby[1–4]

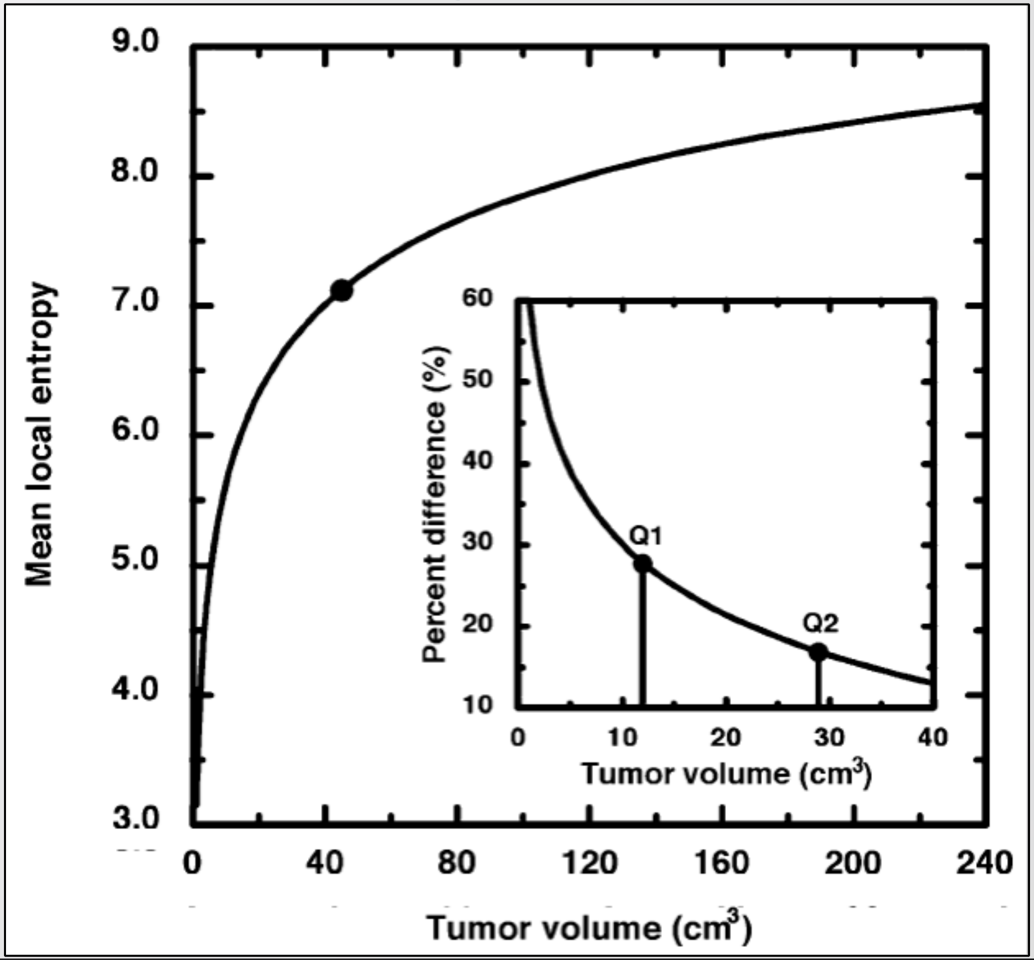
[1]*Department of Radiation Oncology, Washington University School of Medicine, St. Louis, Missouri;* [2]*Division of Nuclear Medicine, Mallinckrodt Institute of Radiology, Medical Center, St. Louis, Missouri;* [3]*Department of Obstetrics and Gynecology, Washington University Medical Center, St. Louis, Missouri; and* [4]*Alvin J. Siteman Cancer Center, Washington University Medical Center, St. Louis, Missouri*

FJ. Brooks, *et al*. The effect of small tumor volumes on studies of intratumoral heterogeneity of tracer uptake. *J Nucl Med.* 2014

Textural features in PET

The present: issues galore

Volume confounding effect



FJ. Brooks, *et al*. The effect of small tumor volumes on studies of intratumoral heterogeneity of tracer uptake. *J Nucl Med.* 2014

Textural features in PET

The present: issues galore

- Volume confounding effect

Example Heterogeneity Statistic

We computed the local information entropy of a 2-dimensional image as described by Haralick et al. (*13*). In brief, the cooccurrence matrix describes the probability p that a pixel of a shade i occurs next to a pixel of shade j. This matrix can be computed for various directions, pixel separations, and bit depths. We computed the horizontal and vertical cooccurrence matrices for the nearest pixel neighbors of 8-bit gray-scale images. From each of these matrices, the local entropy

$$h = -\sum_{j=103}^{255} \sum_{i=103}^{255} p(i,j) \ln p(i,j) \qquad \text{Eq. 1}$$

was computed for each direction and then root-mean-square–averaged to obtain a single local entropy value. The limits on the summations reflect the 40% clinical threshold within the 8-bit (0–255) color scale.

FJ. Brooks, *et al*. The effect of small tumor volumes on studies of intratumoral heterogeneity of tracer uptake. *J Nucl Med.* 2014

Textural features in PET

The present: issues galore

Volume confounding effect

^{18}F-FDG PET Uptake Characterization Through Texture Analysis: Investigating the Complementary Nature of Heterogeneity and Functional Tumor Volume in a Multi–Cancer Site Patient Cohort

Mathieu Hatt[1], Mohamed Majdoub*[1], Martin Vallières*[2], Florent Tixier[1,3], Catherine Cheze Le Rest[1,3], David Groheux[4], Elif Hindié[4], Antoine Martineau[4], Olivier Pradier[1,5], Roland Hustinx[6], Remy Perdrisot[3], Remy Guillevin[7], Issam El Naqa[2], and Dimitris Visvikis[1]

[1]INSERM, UMR 1101 LaTIM, Brest, FRANCE; [2]Department of Oncology, McGill University, Montreal, Canada; [3]Nuclear Medicine, CHU Milétrie, Poitiers, France; [4]Nuclear Medicine, CHU Saint Louis, Paris, France; [5]Radiotherapy, CHRU Morvan, Brest, France; [6]Nuclear Medicine, CHU Liège, Liège, Belgium; and [7]Radiology, CHU Milétrie, Poitiers, France

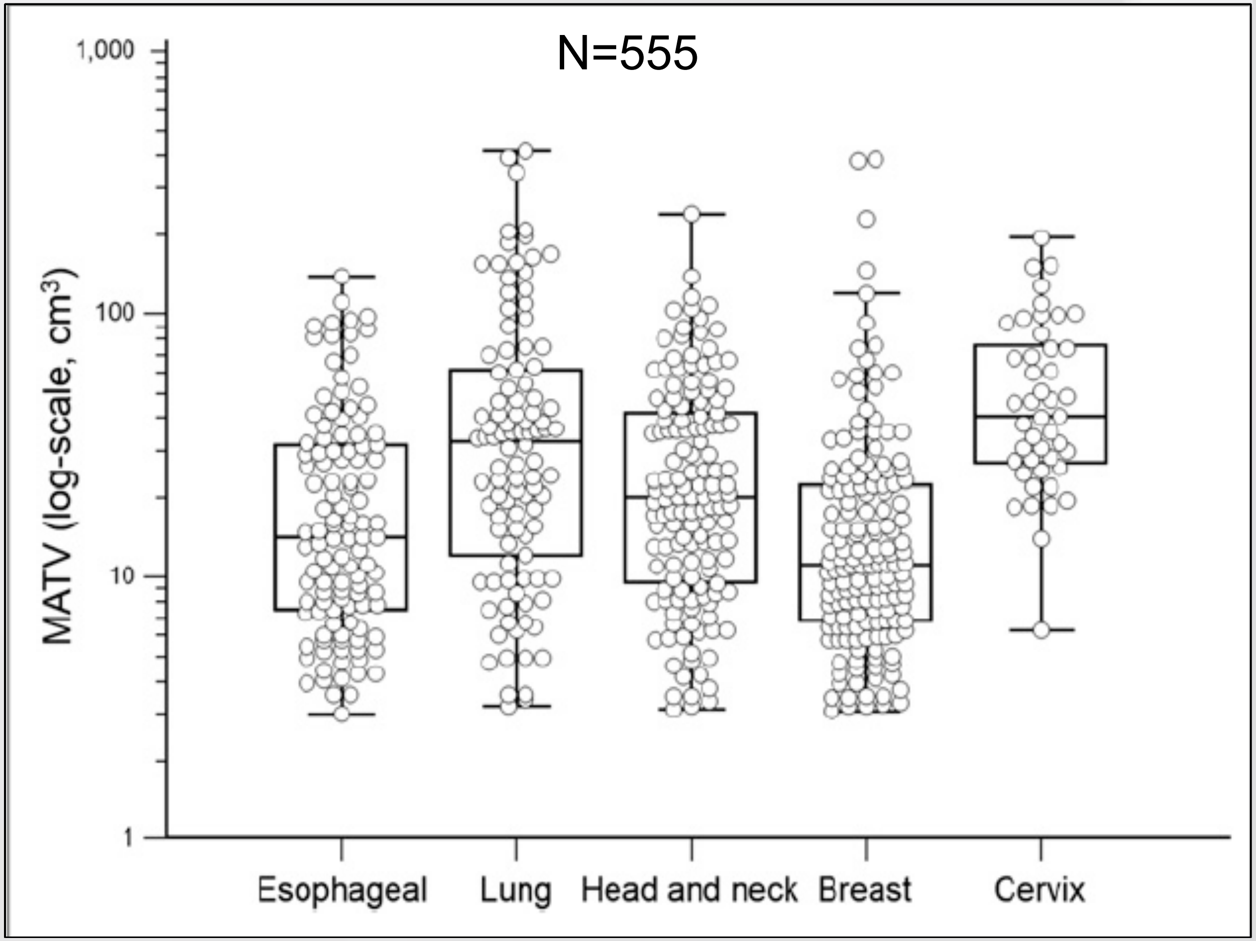
Instituts thématiques Inserm Institut national de la santé et de la recherche médicale

M. Hatt, *et al*. 18F-FDG PET uptake characterization through texture analysis: investigating the complementary nature of heterogeneity and functional tumor volume in a multi-cancer site patient cohort. *J Nucl Med 2015*

Textural features in PET

The present: issues galore

- Volume confounding effect



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The present: issues galore

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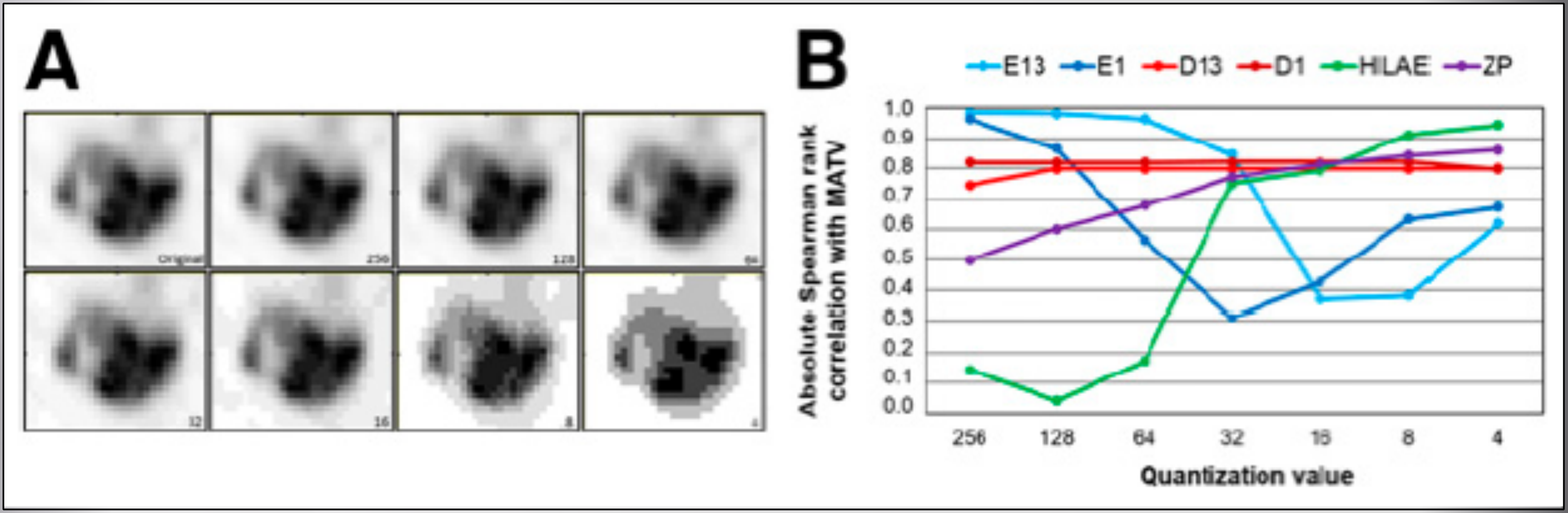

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Textural features in PET

The present

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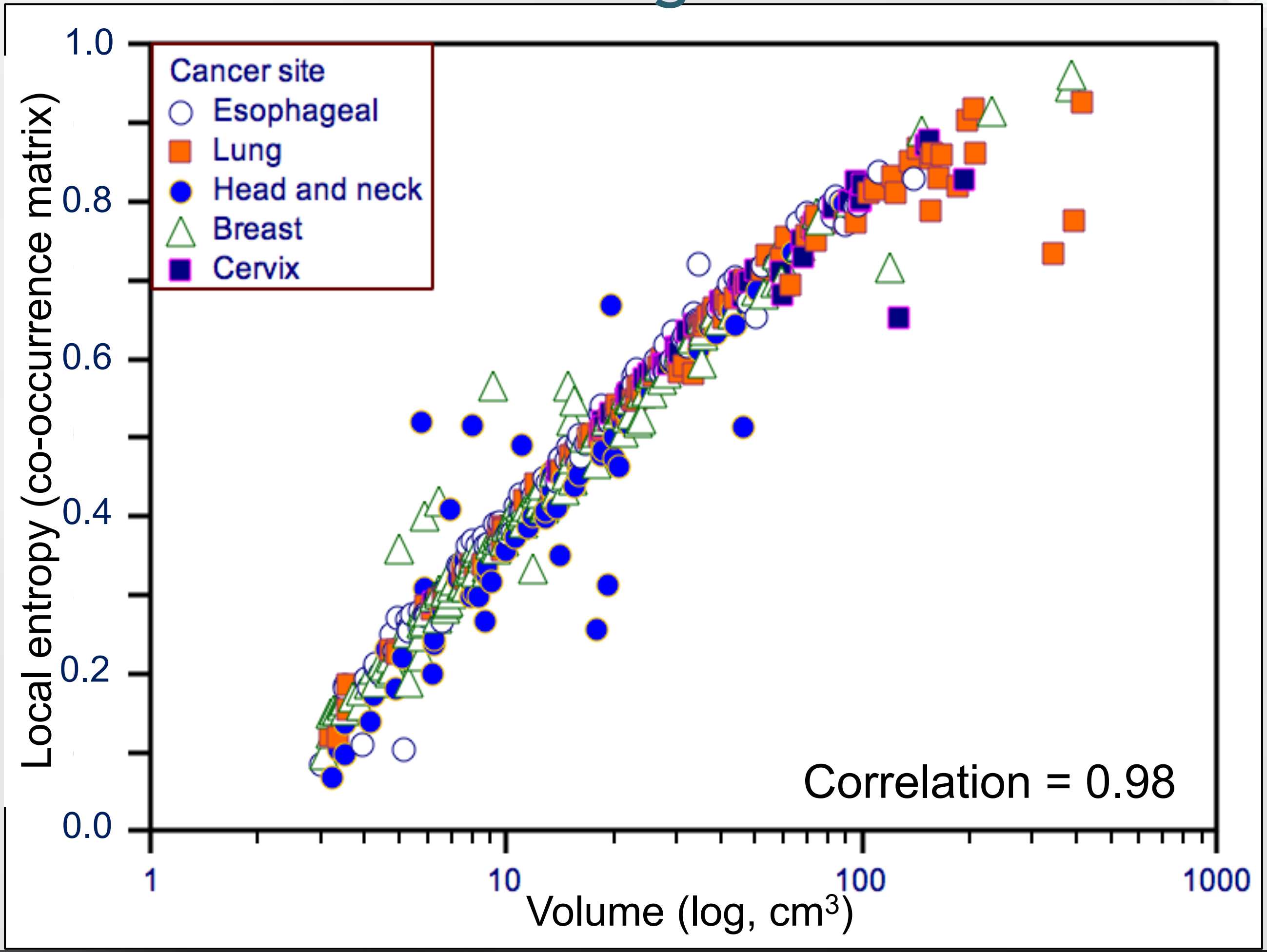


Quantization = 128

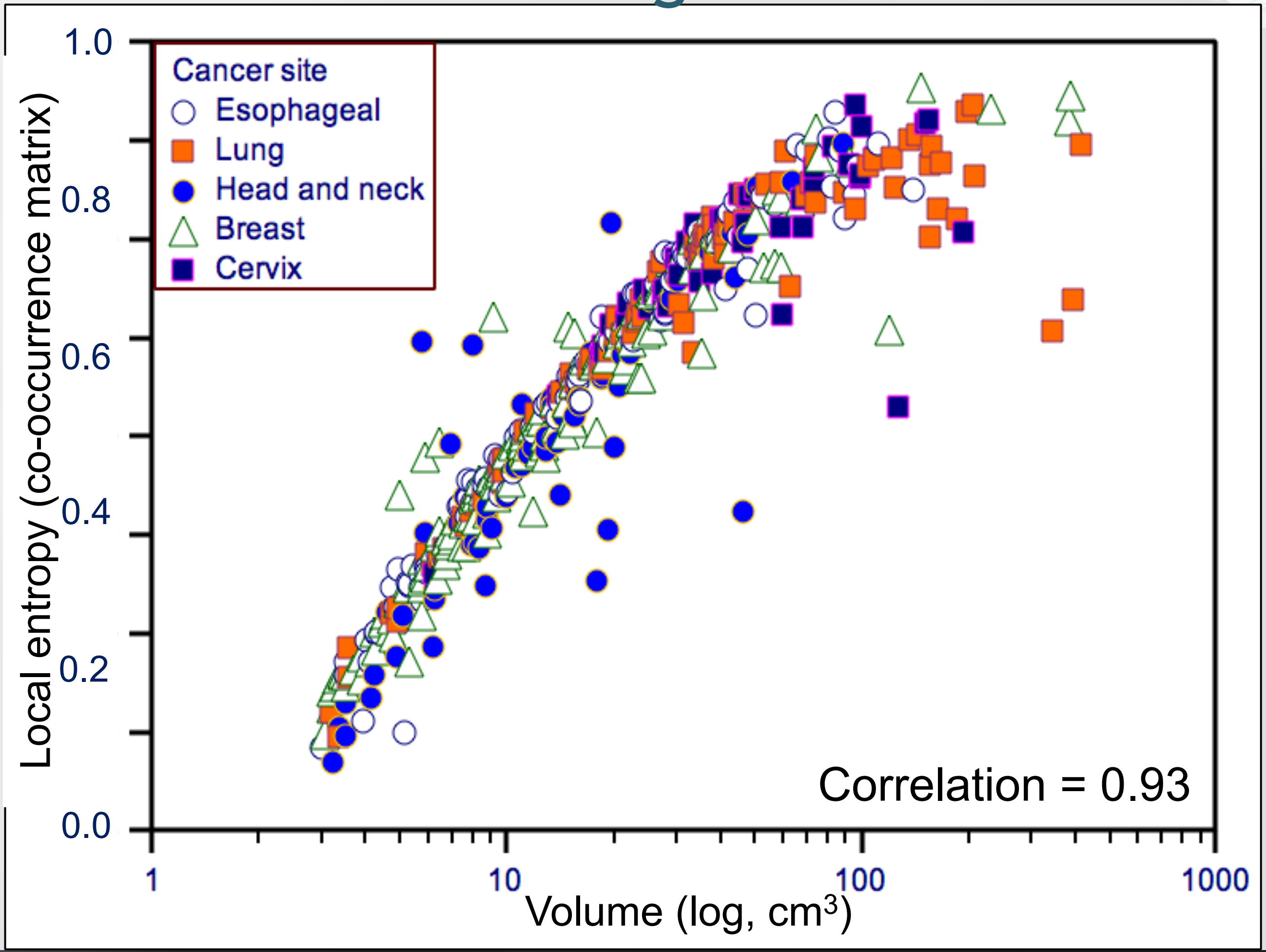
13 matrices + averaging

M. Hatt, *et al*. 18F-FDG PET uptake characterization through texture analysis: investigating the complementary nature of heterogeneity and functional tumor volume in a multi-cancer site patient cohort. *J Nucl Med 2015*

Textural features in PET

The present

Volume confounding effect



Quantization = 64

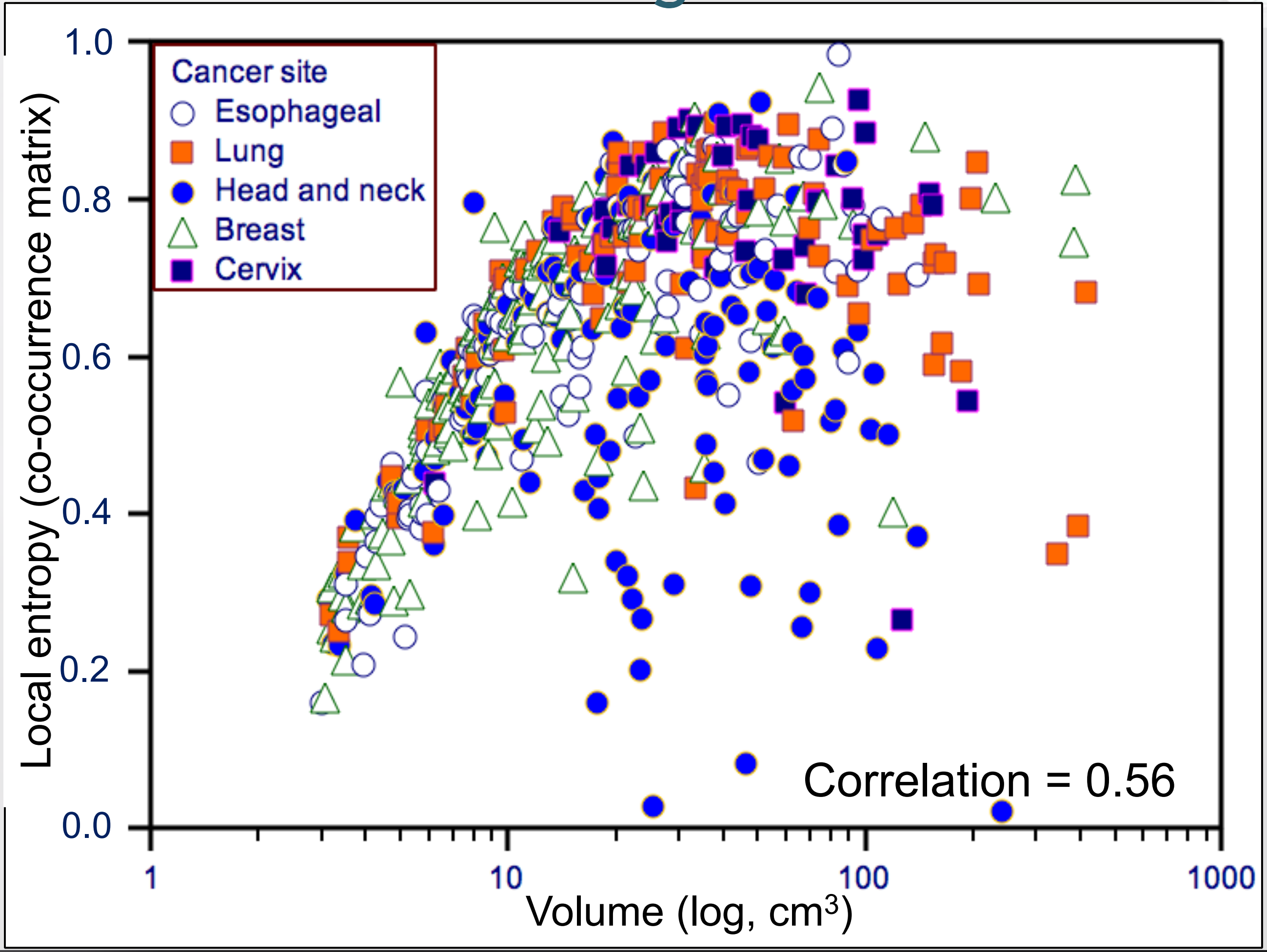
13 matrices + averaging

M. Hatt, *et al.* 18F-FDG PET uptake characterization through texture analysis: investigating the complementary nature of heterogeneity and functional tumor volume in a multi-cancer site patient cohort. *J Nucl Med 2015*

Textural features in PET

The present

Volume confounding effect



Quantization = 64

1 matrix

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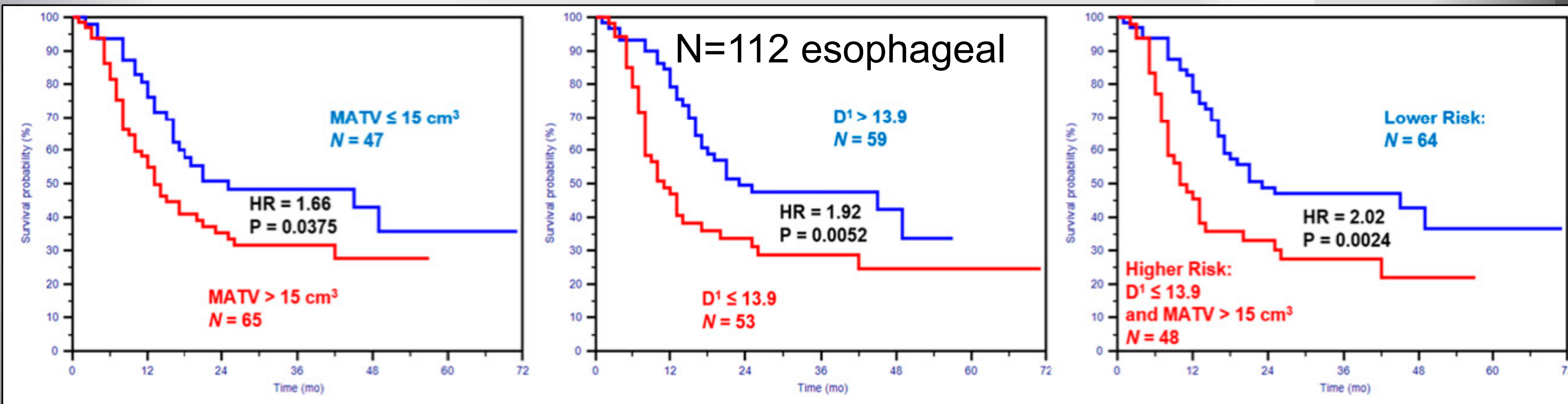
M. Hatt, *et al.* 18F-FDG PET uptake characterization through texture analysis: investigating the complementary nature of heterogeneity and functional tumor volume in a multi-cancer site patient cohort. *J Nucl Med 2015*

Textural features in PET

The present

Volume confounding effect



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The present

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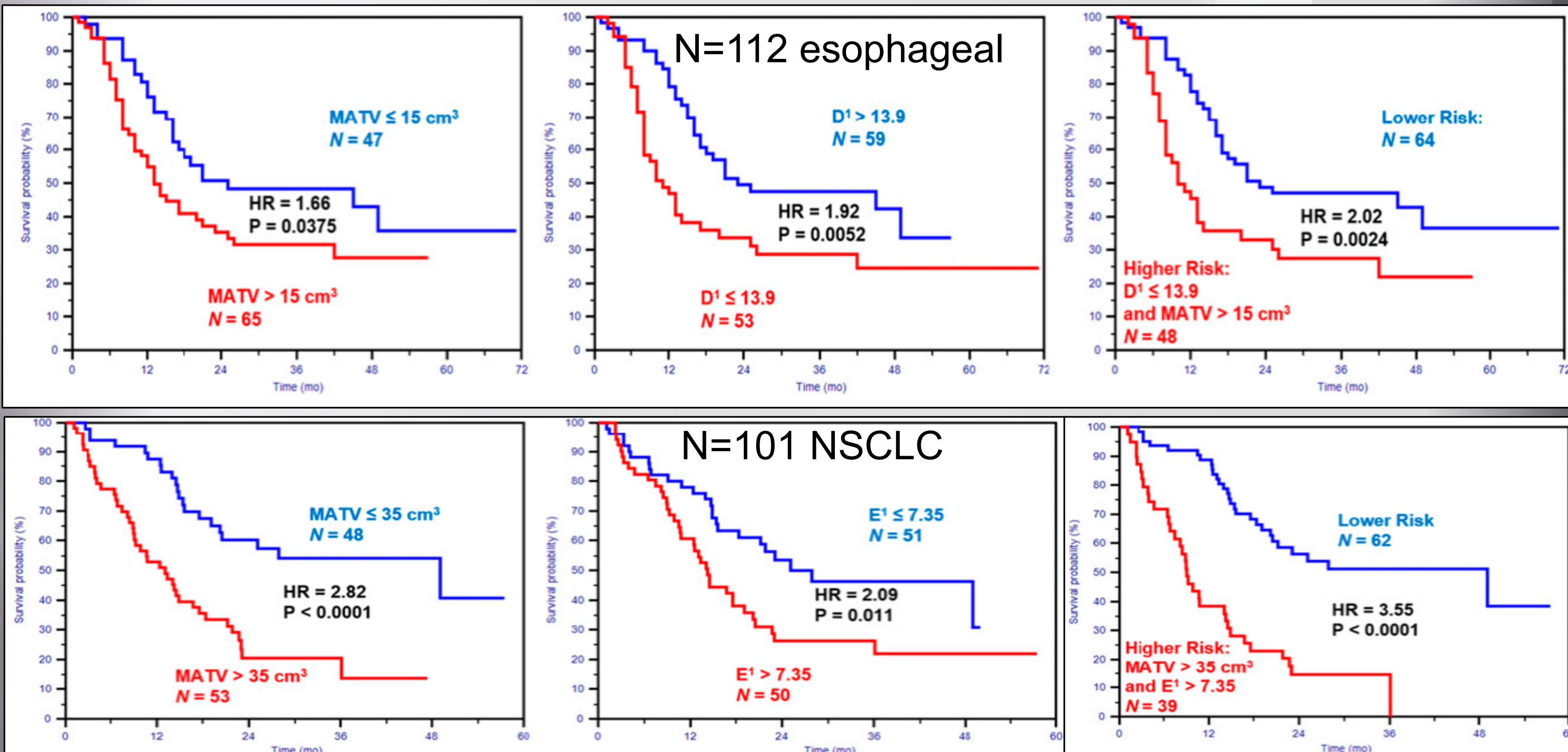

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Statistics related issues

PLOS | ONE

RESEARCH ARTICLE

False Discovery Rates in PET and CT Studies with Texture Features: A Systematic Review

Anastasia Chalkidou*, Michael J. O'Doherty, Paul K. Marsden

Division of Imaging Sciences and Biomedical Engineering, Kings College London 4th Floor, Lambeth Wing, St. Thomas Hospital, SE1 7EH, London, United Kingdom

* anastasia.chalkidou@kcl.ac.uk

Textural features in PET

The present: issues galore

Statistics related issues

Table 1. Statistical characteristics of the selected studies divided in three categories: A) Studies with multiple hypotheses testing only, B) studies employing both multiple hypothesis testing and the optimum cut-off approach and C) studies with multiple hypothesis testing, with or without the optimum cut-off approach, but with validation analysis.

Category	Study	Multivariate analysis included volume	Optimum cut-off	Type I error adjustment	Validation dataset	cross correlation reported	Sample size	Hypotheses tested
A	Willaime [19]	Not applicable	No/Mean	No	No	Yes	12	68
	El Naqa [31]	NI*	Not clear	No	No	No	14/9	19
	Tixier [33]	NI	Not clear	No	No	Yes	41	54
	Yip [41]	No	No/Median	Yes#	No	No	36	90
B	Miles [30]	No	Yes	No	No	No	48	10
	Goh [32]	No	Yes	No	No	No	39	24
	Cook [29]	No	Yes	No	No	Yes	53	30
	Ganeshan [28]	No	Yes	No	No	Yes	21	15
	Ganeshan [34]	No	Yes	No	No	No	54	8
	Ng [36]	No	Yes	No	No	Yes	55	25
	Zhang [40]	Yes	Yes	No	No	No	72	40
	Cheng [39]	Yes	Yes	No	No	Yes	70	59‡
C	Vaidya [35]	Yes	No	No	LOOCV†	No	27	102
	Win [37]	No	Yes	No	Yes	No	66	12
	Ravanelli [38]	No	No/Median	No	LOOCV	No	53	16

* No information provided

#For multiple hypotheses tested

†Leave one out cross validation

‡ Number is a conservative approximation due to the difficulty establishing the exact number of hypotheses tested

Instituts thématiques Inserm

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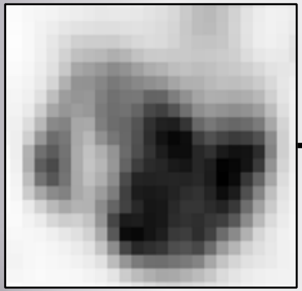
Textural features in PET

The present: technical and practical issues

- How we think it works *vs.* how it **actually** works

Image



« Calculate textural features »

Useful heterogeneity quantification

Textural features in PET

The present: technical and practical issues

- How we think it works *vs.* how it **actually** works

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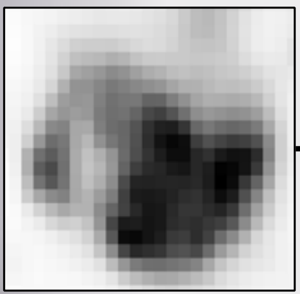

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Textural features in PET

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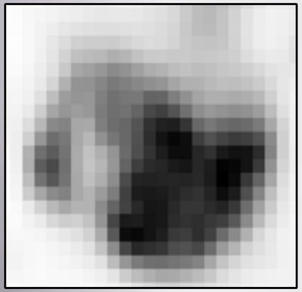

Textural features in PET

The present: technical and practical issues

- How we think it works *vs.* how it **actually** works

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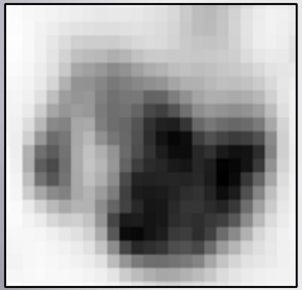

PET or CT?
Acquisition protocol? Gating?
Reconstruction process?
Post-reconstruction processing?

Textural features in PET

The present: technical and practical issues

- How we think it works *vs.* how it **actually** works

Denoising?
Contrast-enhancement?

Pre-processing

Image

PET or CT?
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Textural features in PET

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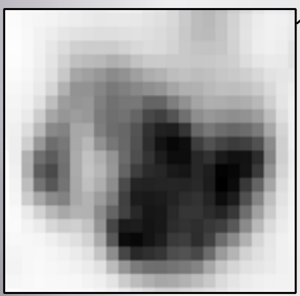

Defining region of analysis

2D? 3D?
Segmentation method?

PET or CT?
Acquisition protocol? Gating?
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Textural features in PET

The present: technical and practical issues

- How we think it works *vs.* how it **actually** works

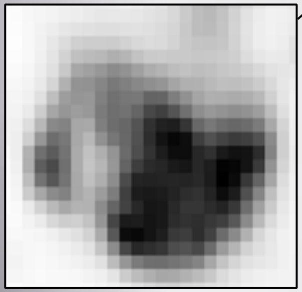
Denoising?
Contrast-enhancement?

Pre-processing

Image

Quantization

4? … 256?
Equalization? Uniform?



Defining region of analysis

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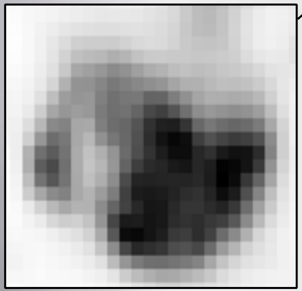
How we think it works *vs.* how it **actually** works

Image



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4? … 256?
Equalization? Uniform?

Matrices

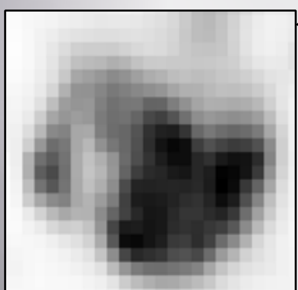
1 … 13 directions?
Averaging?

Textural features in PET

The present: technical and practical issues

- How we think it works *vs.* how it **actually** works

Image



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Parameters

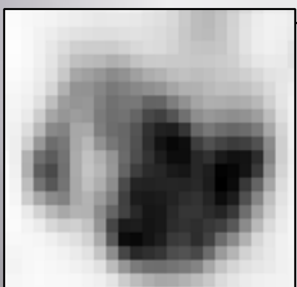
Hundreds of features:
Evaluation + choice
Statistics + machine learning

Textural features in PET

The present: technical and practical issues

- How we think it works *vs.* how it **actually** works

Image



Pre-processing

Denoising?
Contrast-enhancement?

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Quantization

4? … 256?
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Matrices

1 … 13 directions?
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Parameters

Hundreds of features:
Evaluation + choice
Statistics + machine learning

Potentially useful heterogeneity quantification

PET or CT?
Acquisition protocol? Gating?
Reconstruction process?
Post-reconstruction processing?

Textural features in PET

The present: technical and practical issues

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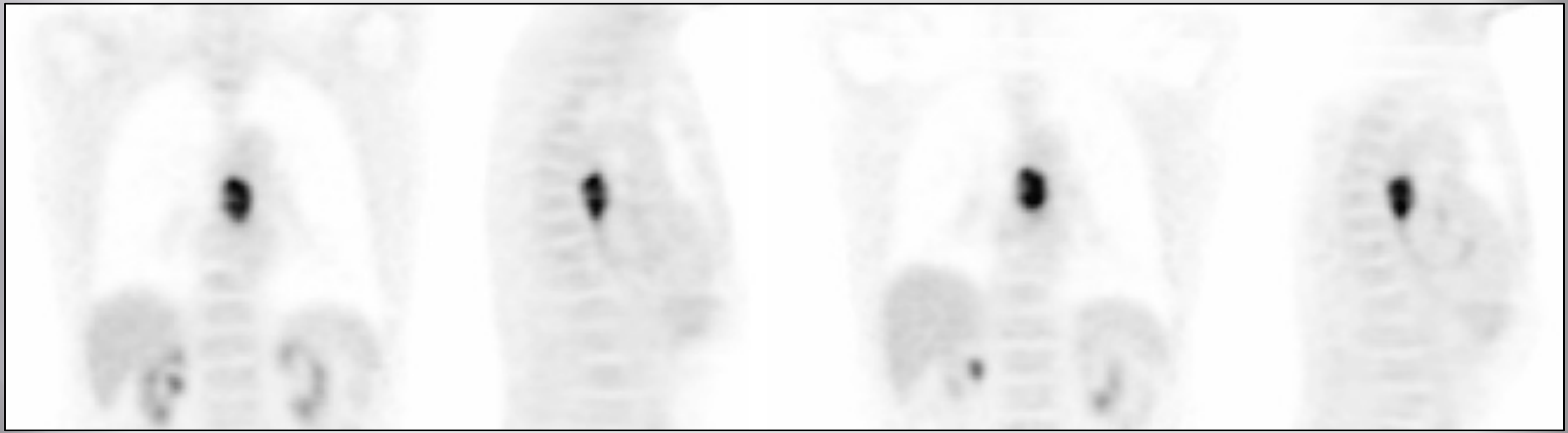
Textural features in PET

The present: technical and practical issues

Selection and validation of parameters

- Before investigating any potential clinical value
- Evaluate their reproducibility
  - Test-retest (double baseline) images[1,2,3]



1. Tixier F, *et al*. Reproducibility of Tumor Uptake Heterogeneity Characterization Through Textural Feature Analysis in FDG PET. *J Nuc Med* 2012
2. Leijenaar RT, *et al*. Stability of FDG-PET Radiomics features: an integrated analysis of test-retest and inter-observer variability. *Acta Oncol* 2014
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Textural features in PET

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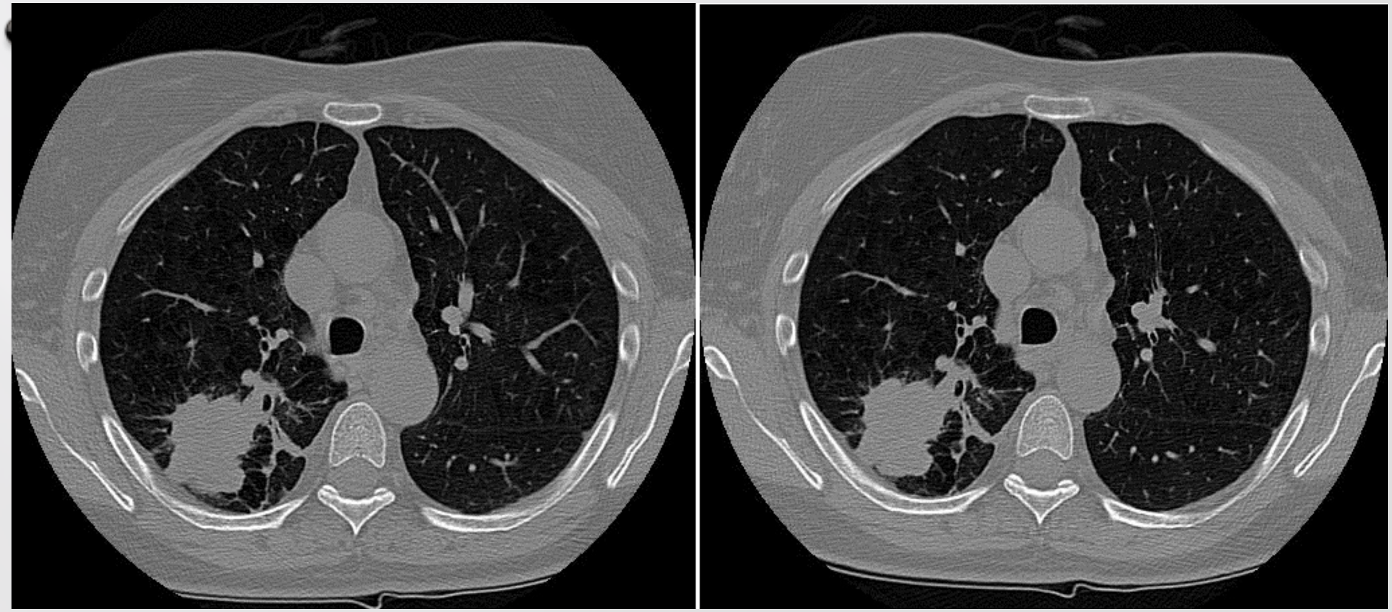

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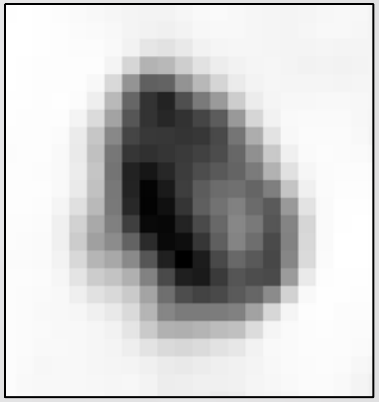
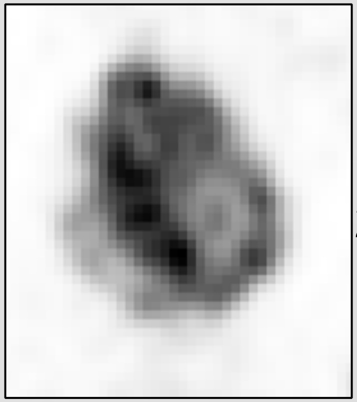
  - Reconstruction algorithms and parameters[4]
  - Processing and analysis workflow[5]

4×4×4 mm^3





2×2×2 mm^3

4. Galavis P, *et al*. Variability of textural features in FDG PET images due to different acquisition modes and reconstruction parameters. *Acta Onco* 2010
5. Hatt M, *et al*. Robustness of intra-tumor ^{18}F-FDG PET uptake heterogeneity quantification for therapy response prediction in esophageal carcinoma. *Eur J Nuc Med* 2013

Textural features in PET

The present: technical and practical issues

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- ❑ Features very sensitive to small intensity variations
- ❑ Features quantifying regions of small size and/or low intensity

  → Not robust / reproducible

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- ❑ Features quantifying regions of small size and/or low intensity

  → Not robust / reproducible

→ Among dozens of parameters, only a handful are sufficiently reliable (robust+reproducible)

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Textural features in PET

The present: technical and practical issues

Reproducibility/variability/robustness

Journal of Nuclear Medicine, published on March 27, 2012 as doi:10.2967/jnumed.111.099127

Reproducibility of Tumor Uptake Heterogeneity Characterization Through Textural Feature Analysis in ^{18}F-FDG PET

Florent Tixier[1,2], Mathieu Hatt[1], Catherine Cheze Le Rest[1], Adrien Le Pogam[1], Laurent Corcos[2], and Dimitris Visvikis[1]

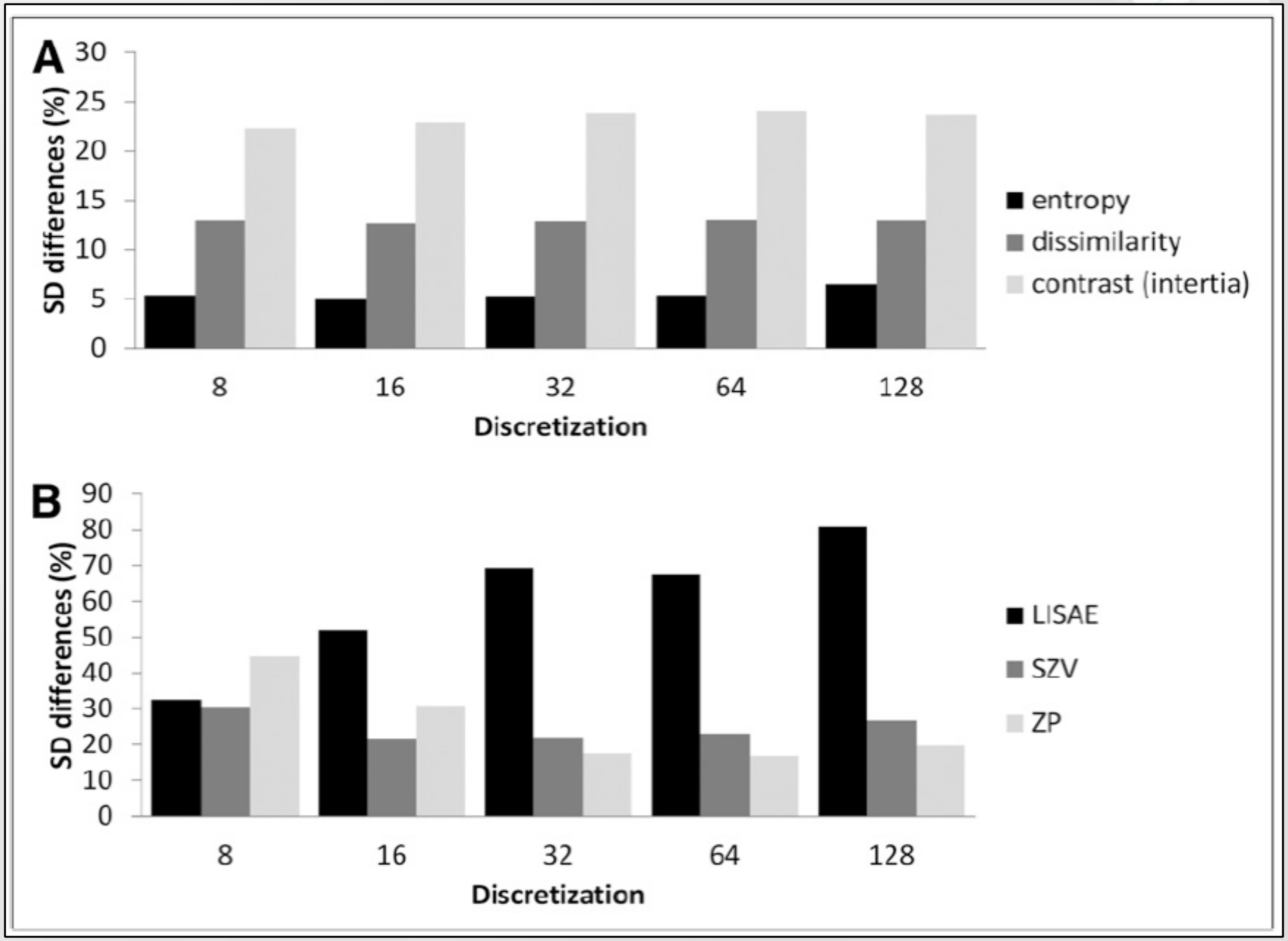
[1]LaTIM, INSERM UMR1101, CHRU Morvan, Brest, France; and [2]INSERM UMR1078, Faculty of Medicine, Brest, France

F. Tixier, *et al*. Reproducibility of tumor uptake heterogeneity characterization through textural feature analysis in 18F-FDG PET. *J Nucl Med 2012*

Textural features in PET

The present: technical and practical issues

Reproducibility/variability/robustness



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Textural features in PET

The present: technical and practical issues

Reproducibility/variability/robustness

TABLE 3

Reproducibility Results for All Image-Derived Parameters, Including SUVs and Textural Features (Calculated Using Downsampling Range of 64 Values)

Texture	Feature	Mean ± SD	95% CI	LRL	95% CI for LRL	URL	95% CI for URL
Global	Minimum SUV	6.3 ± 26.5	−7.8 to 20.4	−45.6	−70.2 to −20.9	58.2	33.6 to 82.8
	SUV_{max}	4.7 ± 19.5	−5.7 to 15.0	−33.5	−51.7 to −15.4	42.9	24.7 to 61.0
	SUV_{mean}	5.5 ± 21.2	−5.8 to 16.8	−36.1	−55.8 to 16.4	47.1	27.3 to 66.8
	SD	1.2 ± 23.2	−11.1 to 13.6	−44.18	−65.7 to −22.6	46.6	25.1 to 68.2
	Skewness	−0.3 ± 27.5	−15.0 to 14.3	−54.2	−79.8 to −28.6	53.6	28.0 to 79.2
	Kurtosis	2.1 ± 18.0	−7.4 to 11.7	−33.1	−49.8 to −16.4	37.3	20.6 to 54.0
	Mean/SD	4.1 ± 24.1	−8.8 to 16.9	−43.2	−65.6 to −20.7	51.3	28.9 to 73.7
Local	Second angular moment	10.9 ± 26.4	−3.2 to 25.0	−40.9	−65.5 to −16.3	62.7	38.1 to 87.3
	Contrast (inertia)	5.4 ± 24.0	−18.1 to 7.4	−52.3	−74.6 to −30.0	41.6	19.3 to 63.9
	Entropy	−2.0 ± 5.4	−4.9 to 0.9	−12.6	−17.7 to −7.6	8.7	3.6 to 13.8
	Correlation	−0.6 ± 27.7	−15.3 to 14.1	−54.8	−15.3 to 14.1	53.6	27.9 to 79.3
	Homogeneity	1.8 ± 11.5	−4.4 to 7.9	−20.8	−31.5 to −10.1	24.4	13.6 to 35.1
	Dissimilarity	−2.1 ± 13.0	−9.0 to 4.9	−27.6	−39.7 to −15.5	23.5	11.4 to 35.6
Regional	Small-area emphasis	−6.0 ± 54.3	−35.0 to 22.9	−112.5	−163.0 to −62.0	100.4	49.9 to 150.9
	Large-area emphasis	3.6 ± 30.0	−12.4 to 19.6	−55.2	−83.1 to −27.3	62.4	34.5 to 90.3
	Intensity variability	−9.7 ± 24.0	−22.5 to 3.1	−56.7	−79.0 to −34.4	37.3	15.0 to 59.6
	Size–zone variability	11.2 ± 23.1	−1.1 to 23.5	−34.1	−55.6 to −12.6	56.5	35.0 to 78.0
	Zone percentage	−2.7 ± 16.9	−11.7 to 6.2	−35.8	−51.5 to −20.1	30.3	14.6 to 46.0
	Low-intensity emphasis	−4.0 ± 55.3	−33.5 to 25.4	−112.4	−163.9 to −61.0	104.4	525.9 to 155.8
	High-intensity emphasis	3.9 ± 20.4	−7.0 to 14.8	−36.1	−55.1 to −17.1	44.0	24.9 to 63.0
	Low-intensity small-area emphasis	−7.0 ± 67.6	−43.1 to 29.0	−139.5	−202.4 to −76.6	125.4	62.5 to 188.3
	High-intensity small-area emphasis	1.0 ± 31.2	−15.6 to 17.6	−60.1	−89.1 to −31.1	62.0	33.0 to 91.0
	Low-intensity large-area emphasis	1.8 ± 28.9	−13.6 to 17.2	−54.9	−81.8 to 28.0	58.5	31.6 to 85.4
	High-intensity large-area emphasis	3.5 ± 35.8	−15.6 to 22.6	−66.7	−100.1 to −33.4	73.7	40.4 to 107.1

LRL and URL = lower and upper reproducibility limits, respectively.

F. Tixier, *et al*. Reproducibility of tumor uptake heterogeneity characterization through textural feature analysis in 18F-FDG PET. *J Nucl Med 2012*

Textural features in PET

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	Size–zone variability	11.2 ± 23.1	−1.1 to 23.5	−34.1	−55.6 to −12.6	56.5	35.0 to 78.0
	Zone percentage	−2.7 ± 16.9	−11.7 to 6.2	−35.8	−51.5 to −20.1	30.3	14.6 to 46.0
	Low-intensity emphasis	−4.0 ± 55.3	−33.5 to 25.4	−112.4	−163.9 to −61.0	104.4	525.9 to 155.8
	High-intensity emphasis	3.9 ± 20.4	−7.0 to 14.8	−36.1	−55.1 to −17.1	44.0	24.9 to 63.0
	Low-intensity small-area emphasis	−7.0 ± 67.6	−43.1 to 29.0	−139.5	−202.4 to −76.6	125.4	62.5 to 188.3
	High-intensity small-area emphasis	1.0 ± 31.2	−15.6 to 17.6	−60.1	−89.1 to −31.1	62.0	33.0 to 91.0
	Low-intensity large-area emphasis	1.8 ± 28.9	−13.6 to 17.2	−54.9	−81.8 to 28.0	58.5	31.6 to 85.4
	High-intensity large-area emphasis	3.5 ± 35.8	−15.6 to 22.6	−66.7	−100.1 to −33.4	73.7	40.4 to 107.1

LRL and URL = lower and upper reproducibility limits, respectively.

F. Tixier, *et al*. Reproducibility of tumor uptake heterogeneity characterization through textural feature analysis in 18F-FDG PET. *J Nucl Med 2012*

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Textural features in PET

The present: technical and practical issues

Reproducibility/variability/robustness

TABLE 3
Reproducibility Results for All Image-Derived Parameters, Including SUVs and Textural Features (Calculated Using Downsampling Range of 64 Values)

Texture	Feature	Mean ± SD	95% CI	LRL	95% CI for LRL	URL	95% CI for URL
Global	Minimum SUV	6.3 ± 26.5	−7.8 to 20.4	−45.6	−70.2 to −20.9	58.2	33.6 to 82.8
	SUV_{max}	4.7 ± 19.5	−5.7 to 15.0	−33.5	−51.7 to −15.4	42.9	24.7 to 61.0
	SUV_{mean}	5.5 ± 21.2	−5.8 to 16.8	−36.1	−55.8 to 16.4	47.1	27.3 to 66.8
	SD	1.2 ± 23.2	−11.1 to 13.6	−44.18	−65.7 to −22.6	46.6	25.1 to 68.2
	Skewness	−0.3 ± 27.5	−15.0 to 14.3	−54.2	−79.8 to −28.6	53.6	28.0 to 79.2
	Kurtosis	2.1 ± 18.0	−7.4 to 11.7	−33.1	−49.8 to −16.4	37.3	20.6 to 54.0
	Mean/SD	4.1 ± 24.1	−8.8 to 16.9	−43.2	−65.6 to −20.7	51.3	28.9 to 73.7
Local	Second angular moment	10.9 ± 26.4	−3.2 to 25.0	−40.9	−65.5 to −16.3	62.7	38.1 to 87.3
	Contrast (inertia)	5.4 ± 24.0	−18.1 to 7.4	−52.3	−74.6 to −30.0	41.6	19.3 to 63.9
	Entropy	−2.0 ± 5.4	−4.9 to 0.9	−12.6	−17.7 to −7.6	8.7	3.6 to 13.8
	Correlation	−0.6 ± 27.7	−15.3 to 14.1	−54.8	−15.3 to 14.1	53.6	27.9 to 79.3
	Homogeneity	1.8 ± 11.5	−4.4 to 7.9	−20.8	−31.5 to −10.1	24.4	13.6 to 35.1
	Dissimilarity	−2.1 ± 13.0	−9.0 to 4.9	−27.6	−39.7 to −15.5	23.5	11.4 to 35.6
Regional	Small-area emphasis	−6.0 ± 54.3	−35.0 to 22.9	−112.5	−163.0 to −62.0	100.4	49.9 to 150.9
	Large-area emphasis	3.6 ± 30.0	−12.4 to 19.6	−55.2	−83.1 to −27.3	62.4	34.5 to 90.3
	Intensity variability	−9.7 ± 24.0	−22.5 to 3.1	−56.7	−79.0 to −34.4	37.3	15.0 to 59.6
	Size–zone variability	11.2 ± 23.1	−1.1 to 23.5	−34.1	−55.6 to −12.6	56.5	35.0 to 78.0
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Challenges to address

- Standardization
  - Pre-processing, delineation
  - Textural features definitions, implementations, optimization and parametrization

Textural features in PET

… any future? : challenges

Challenges to address

- Standardization
  - Pre-processing, delineation
  - Textural features definitions, implementations, optimization and parametrization
- Investigating complementary value with respect to standard features/biomarkers
  - Need large cohorts
  - In each cancer type
  - Prospective studies, external validation
  - Combination with clinical variables + other –omics!

Textural features in PET

Conclusions and perspectives

- Applying textural features in PET:
  - Feasible but much more complex than anticipated

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  - Potential to provide complementary clinical value to standard metrics, but previous results may be over-optimistic
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  - Large, multi-centric prospective studies
  - Additional technical knowledge (impact of various factors, methodological and implementation choices…)
  - Standardization and benchmarking
  - Open access code/datasets
  - Combining genetics (and other –omics) with imaging

Multimodal characterization of tumors

Characterization: clinical value?

- Example: NSCLC stage I-III
- Previous studies in NSCLC:
  - Either on FDG PET or CT, rarely both
  - Often contrast-enhanced CT, dosimetry CT or diagnostic CT, rather than the CT component from routine PET/CT acquisitions

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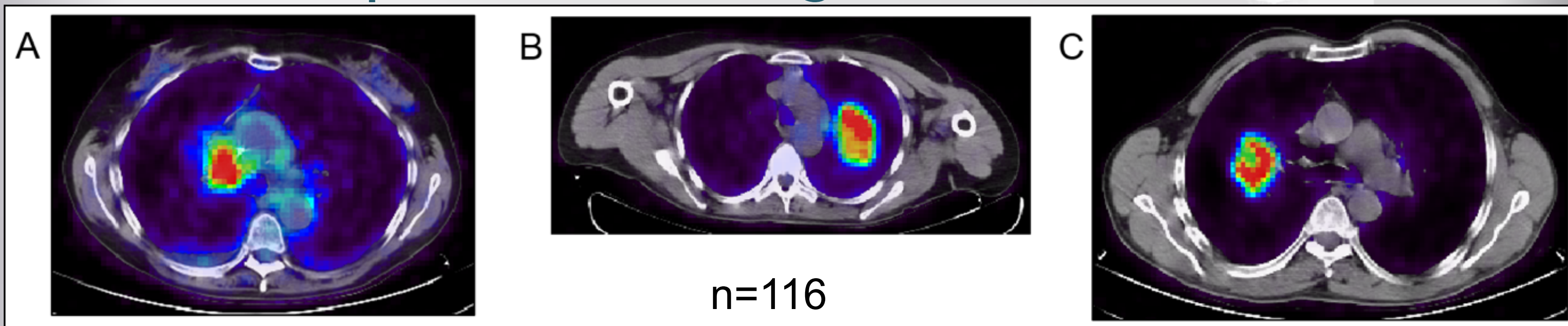

- Stage I (N=29), II (N=30), III (N=57)
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Desseroit MC, *et al*. Development of a nomogram combining clinical staging with 18F-FDG PET/CT image features in Non-Small Cell Lung Cancer stage I-III, *under submission 2015*

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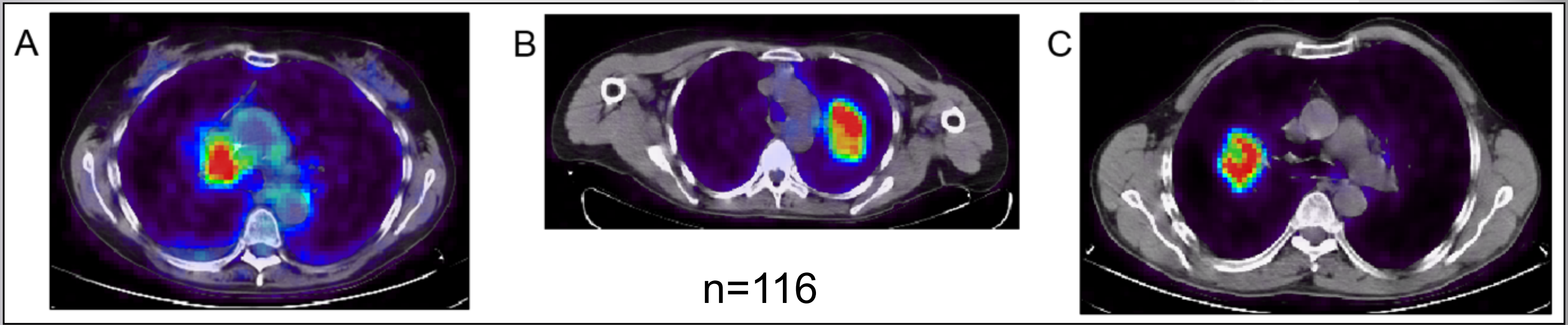

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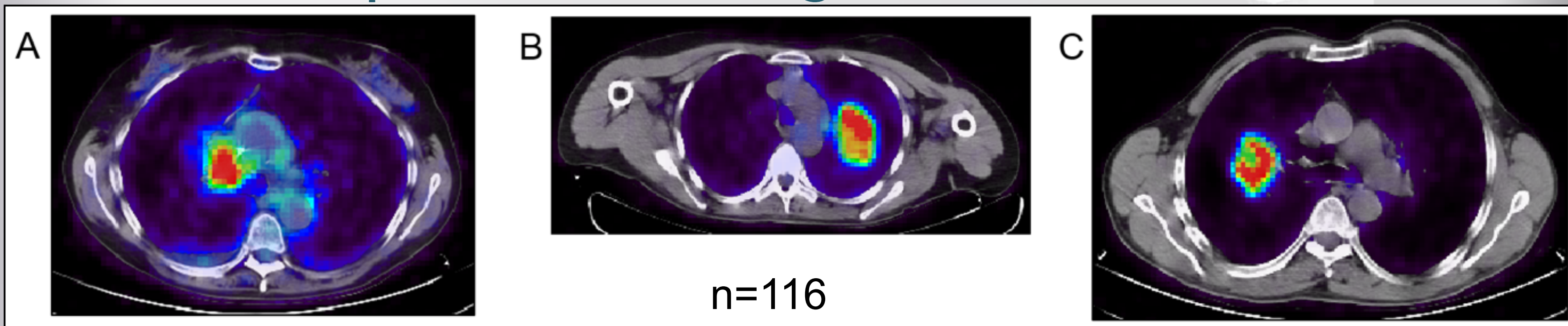

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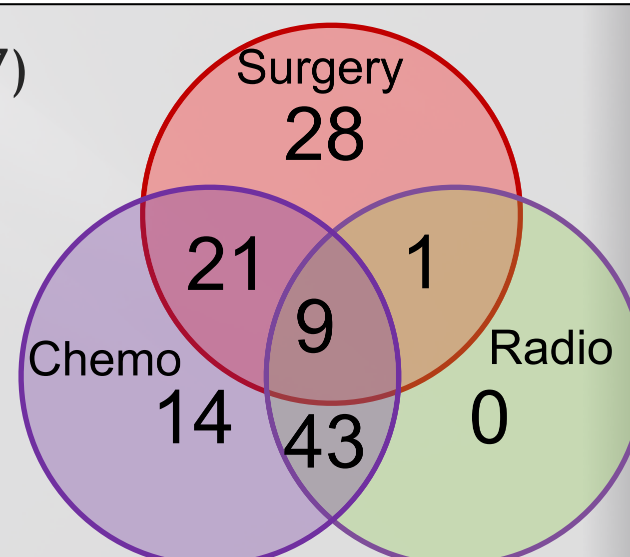

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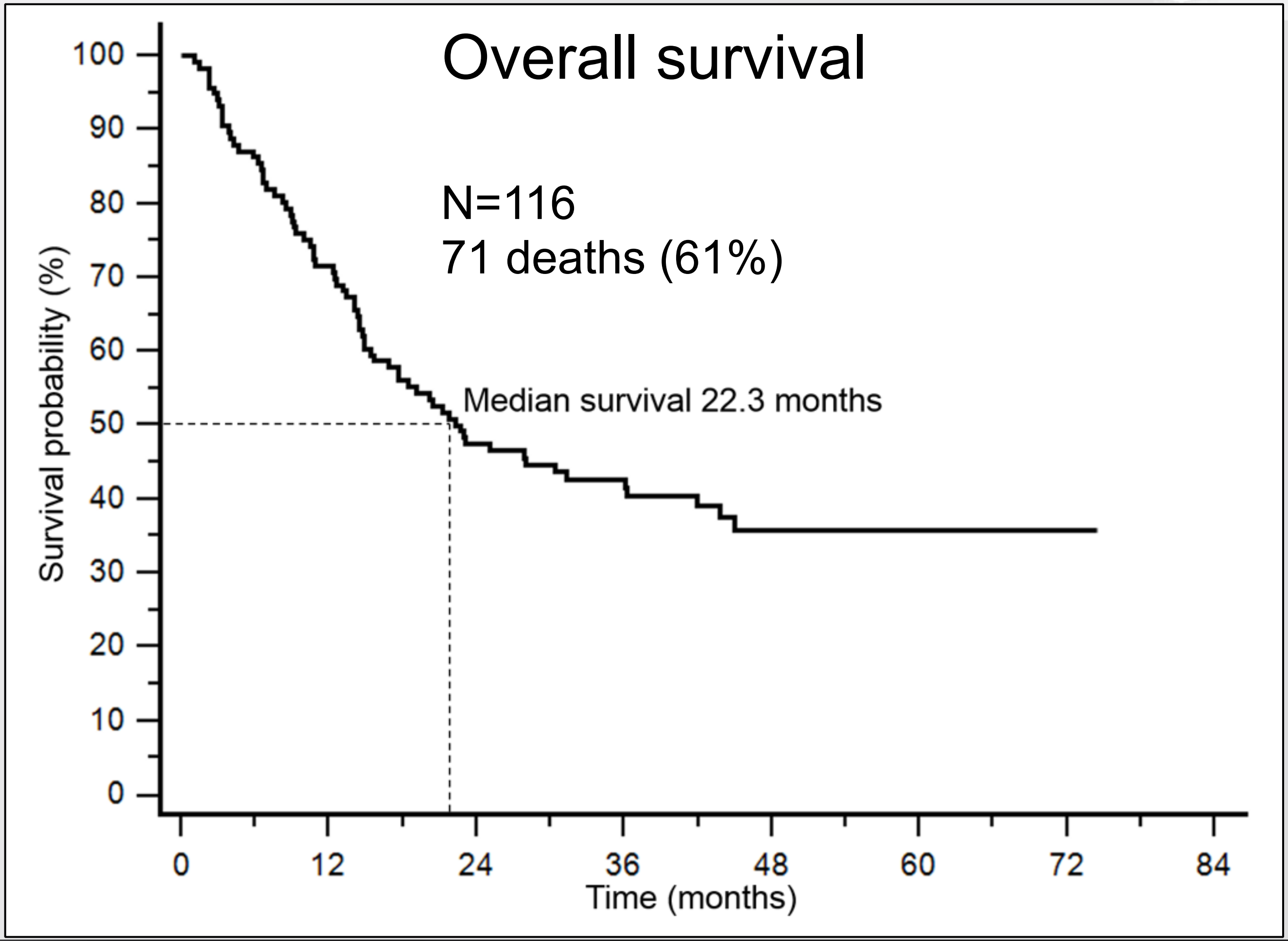

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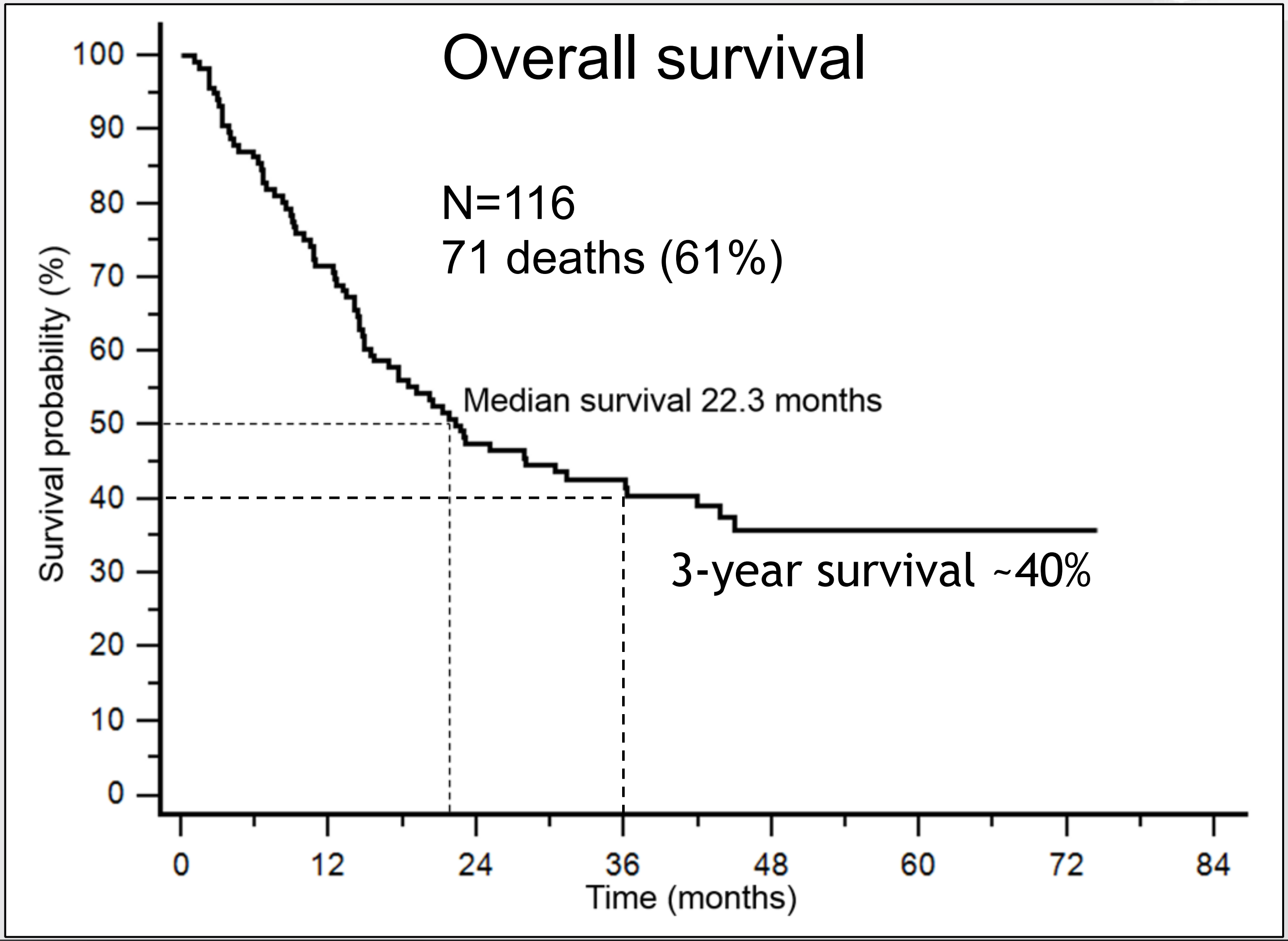

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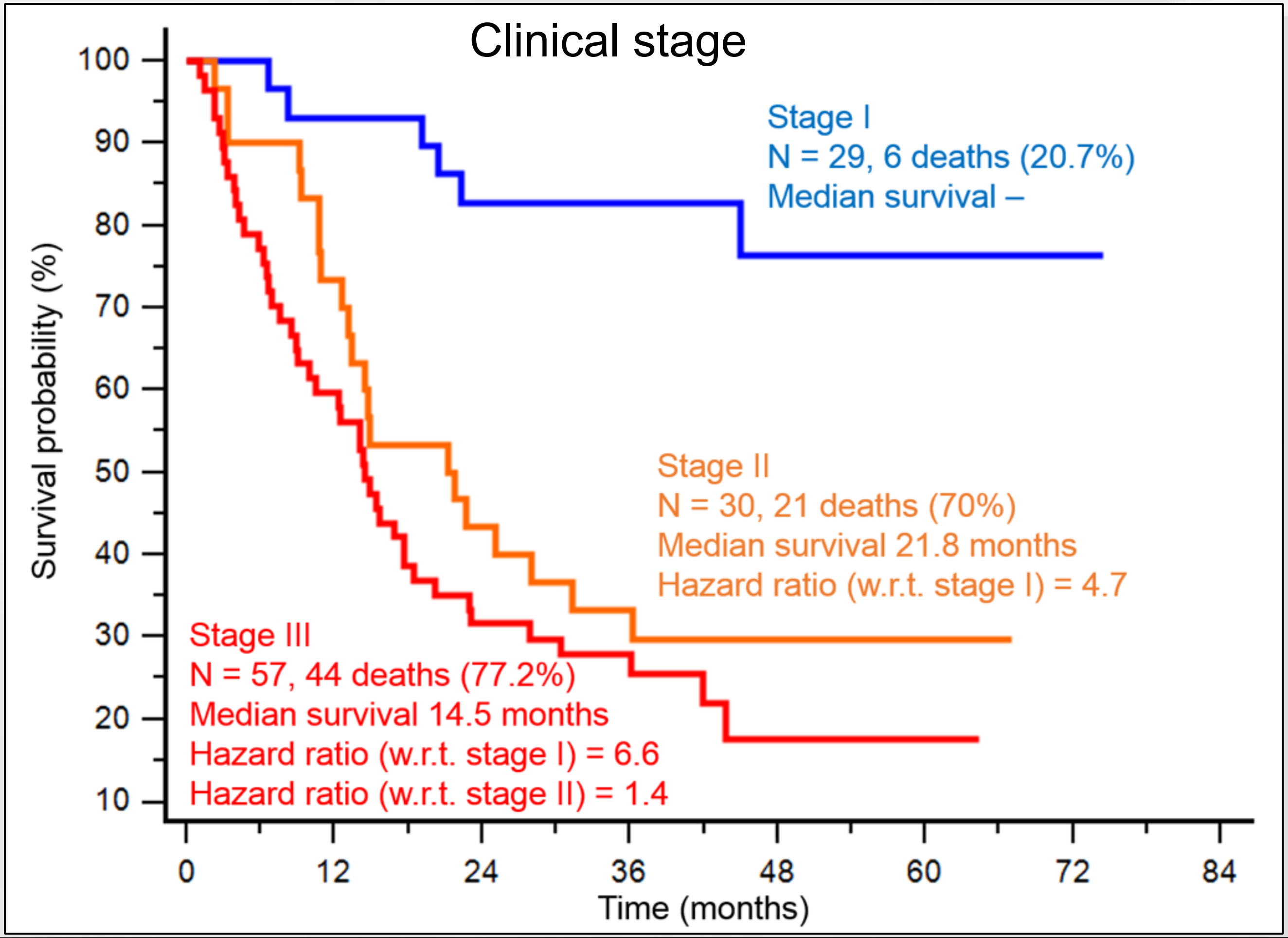

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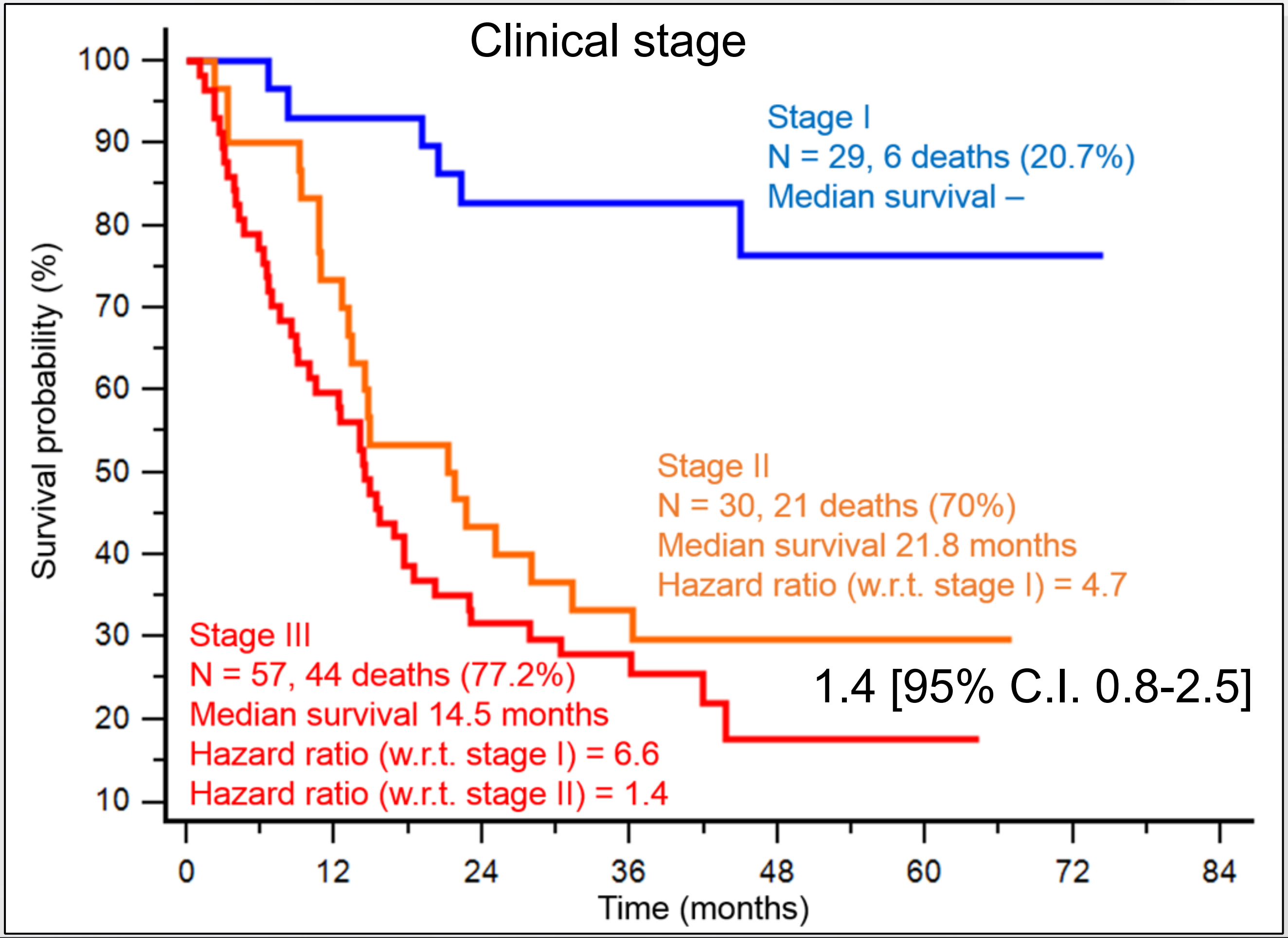

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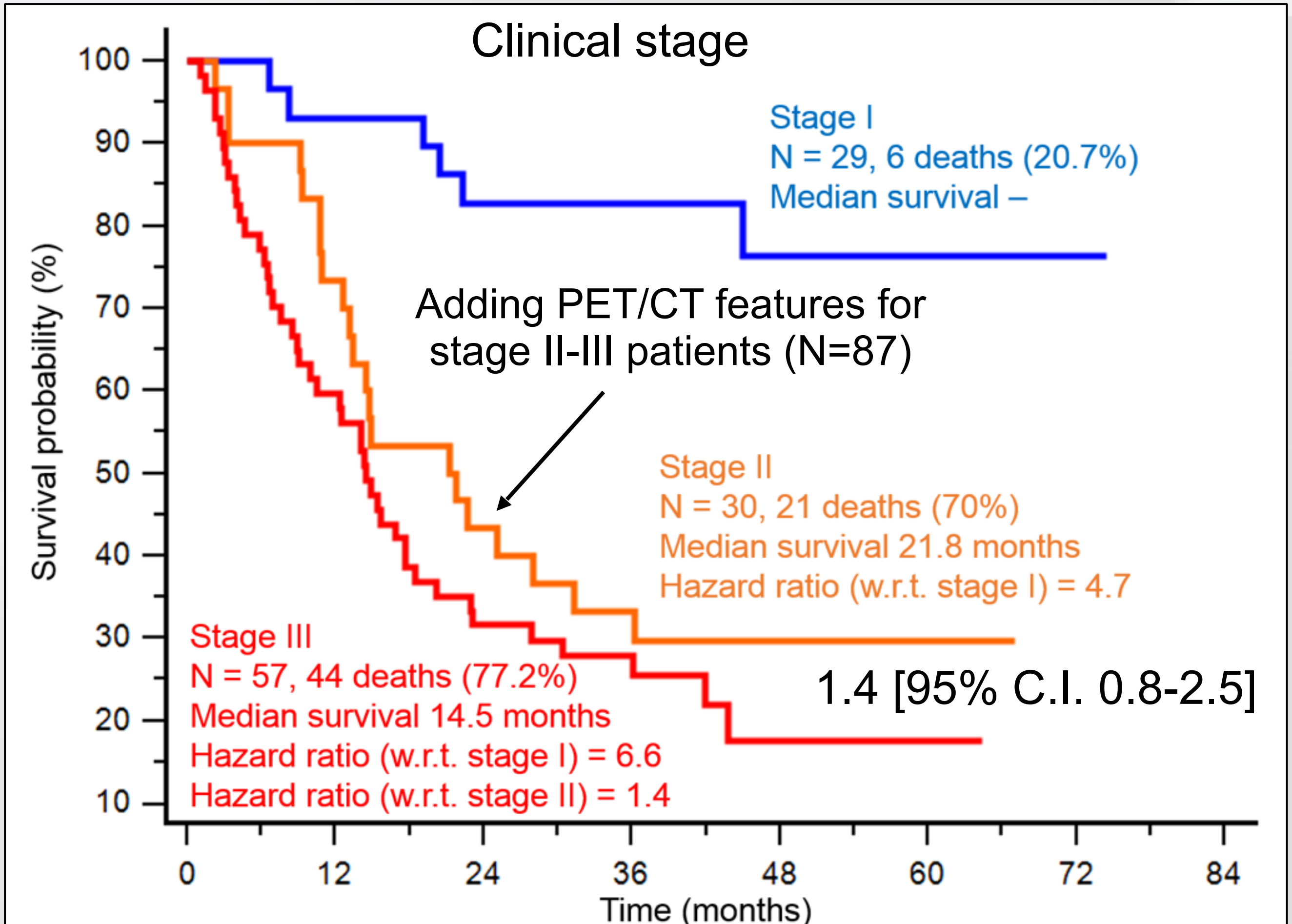

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  - Combine them in a multiparametric model
- Multivariate analysis (Cox), taking into account:
  - Clinical variables (treatment modality, gender…)
  - Standard features (SUV_{max}…)
  - Novel features (heterogeneity)
    - Only robust and reproducible features

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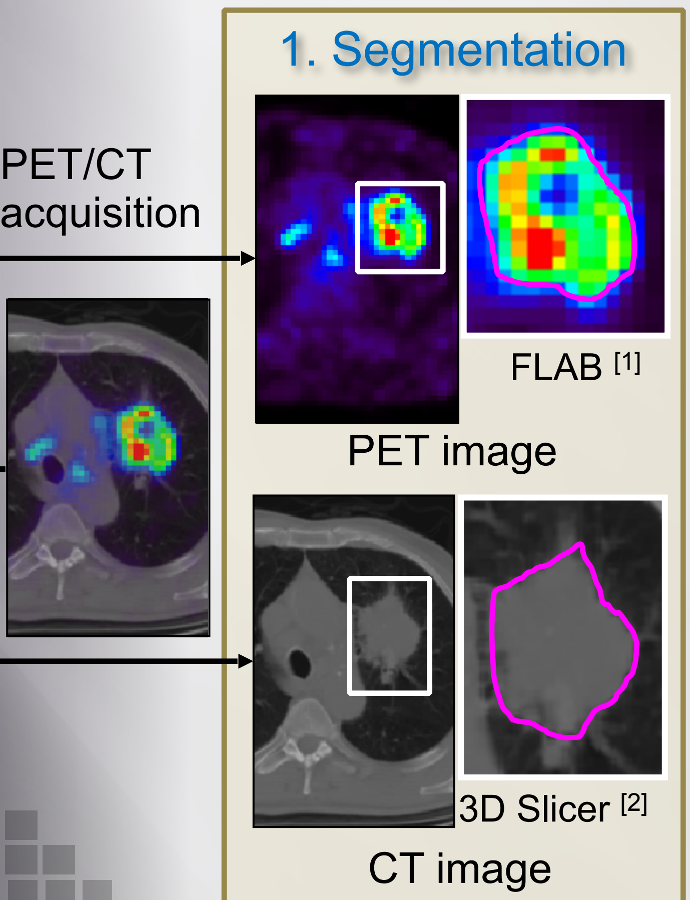
Material & methods

Workflow: image analysis

PET and CT features extraction



1. Hatt, *et al*. A fuzzy locally adaptive Bayesian segmentation approach for volume determination in PET. *IEEE Trans Med Imaging*. 2009
2. Velazquez, *et al*. Volumetric CT-based segmentation of NSCLC using 3D-Slicer. *Sci Rep*. 2013

Material & methods

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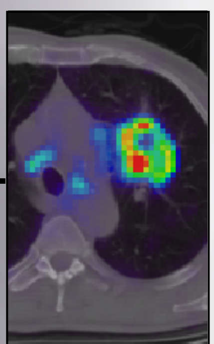
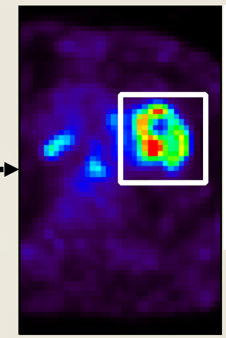
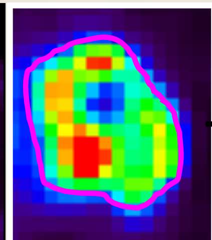


1. Segmentation





FLAB [1]

PET image

3D Slicer [2]

CT image

2. Quantification

- ✓ Standard metrics (functional volume (MATV), mean and max SUVs…)
- ✓ Heterogeneity metrics (texture analysis)

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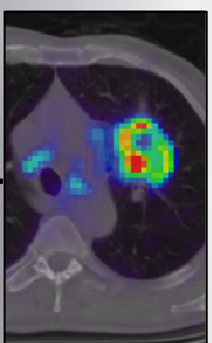

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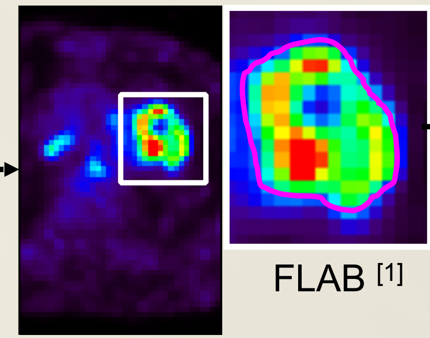

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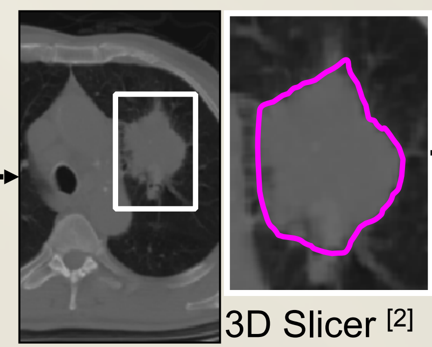

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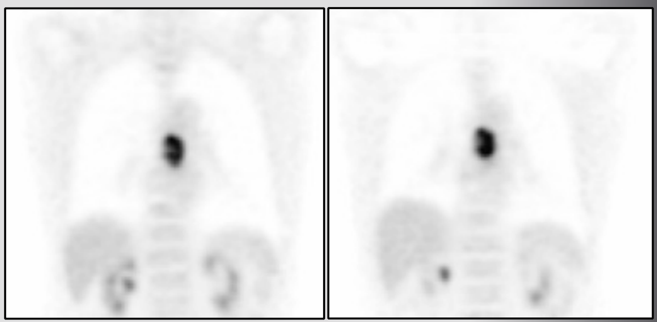
Test-retest PET [3,4]



3. Tixier, *et al*. Reproducibility of Tumor Uptake Heterogeneity Characterization Through Textural Feature Analysis in FDG PET. *J Nuc Med* 2012
4. Leijenaar, *et al*. Stability of FDG-PET Radiomics features: an integrated analysis of test-retest and inter-observer variability. *Acta Oncol* 2014

Material & methods

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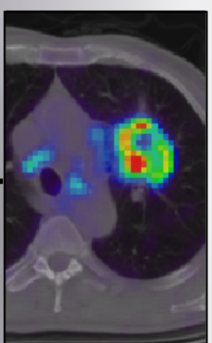

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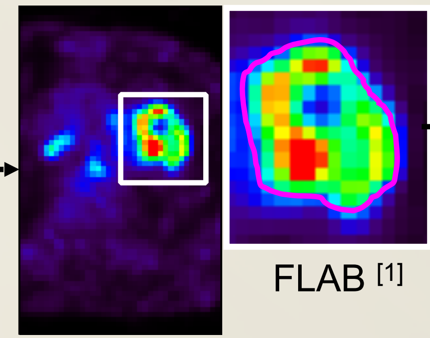

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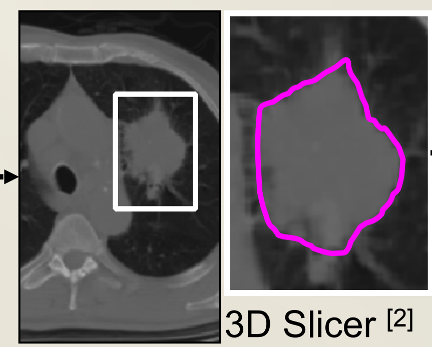

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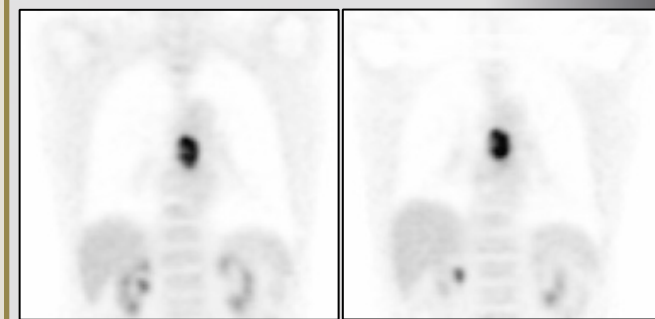

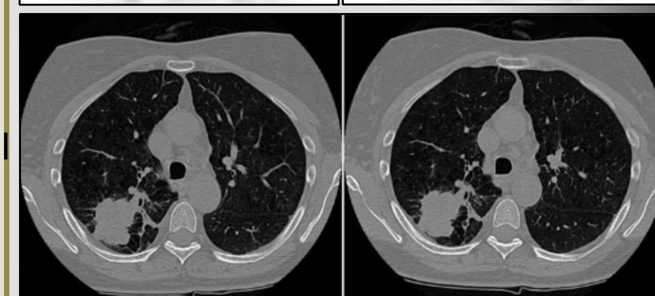

Test-retest CT [5,6]

5. Fried, *et al*. Prognostic value and reproducibility of pretreatment CT texture features in stage III non-small cell lung cancer. *Int J Radiat Oncol Biol Phys*. 2014
6. Desseroit, *et al*. Complementary Prognostic Value of CT and 18F-FDG PET Non-Small Cell Lung Cancer Tumor Heterogeneity Features Quantified Trough Texture Analysis, *Med Phys*. 2014

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Material & methods

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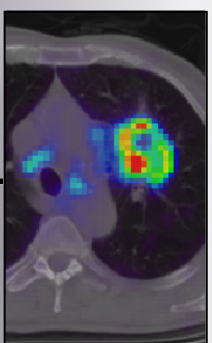

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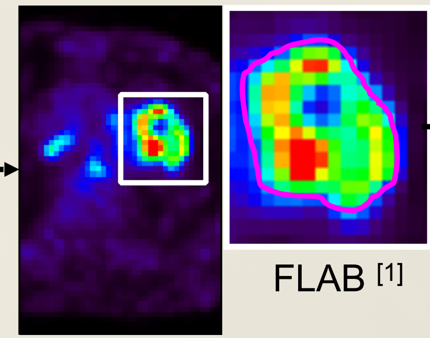

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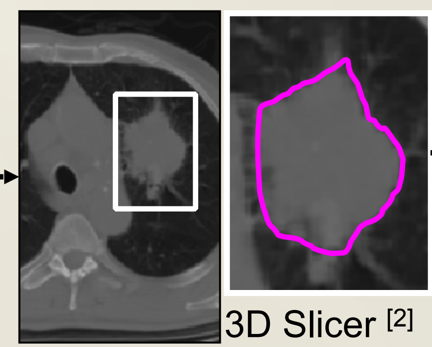

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❖ Robustness [7,8]

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- ✓ Image reconstruction [7]
- ✓ Segmentation [8]
- ✓ Pre-processing [8]

7. Galavis, *et al*. Variability of textural features in FDG PET images due to different acquisition modes and reconstruction parameters. *Acta Onco* 2010
8. Hatt, *et al*. Robustness of intra-tumor ^{18}F-FDG PET uptake heterogeneity quantification for therapy response prediction in esophageal carcinoma. *Eur J Nuc Med* 2013

Results

Features selection, prognostic value

Features selection

- CT textures: only 7/34 features were reproducible
  - variability < twice the anatomical volume (±10%)
- High redundancy [1]: most parameters were correlated (r>0.7)

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Univariate / Multivariate analysis

- Factors associated with poor prognosis

Parameters	**Univariate analysis**	**Multivariate analysis**
Clinical	*Age, gender, treatment*	
Imaging (PET)	*Volume, SUV, heterogeneity*	
Imaging (CT)	*Volume, HU*, heterogeneity (8 textural features)*	

* HU = Hounsfield units

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Univariate / Multivariate analysis

- Factors associated with poor prognosis

Parameters	Univariate analysis	Multivariate analysis
Clinical	*Age, gender, treatment*	*Stage III***
Imaging (PET)	*Volume, SUV, heterogeneity*	*Large volume*
Imaging (CT)	*Volume, HU*, heterogeneity (8 textural features)*	*Low heterogeneity (Zone percentage)*

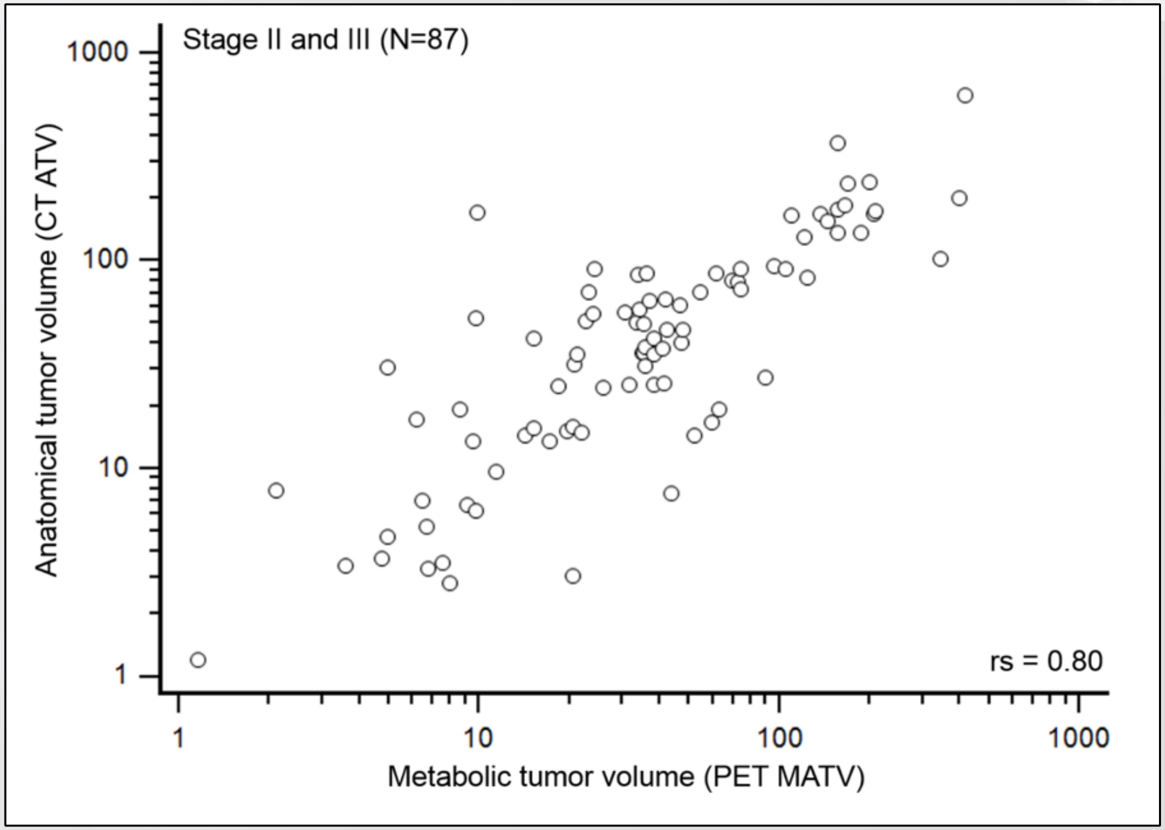
* HU = Hounsfield units

** Surgery was highly correlated with stage: 86% stage I patients
73% stage II patients
21% stage III patients

Results

Correlation between features

Tumor volume: Functional (PET) *vs.* Anatomical (CT) volume



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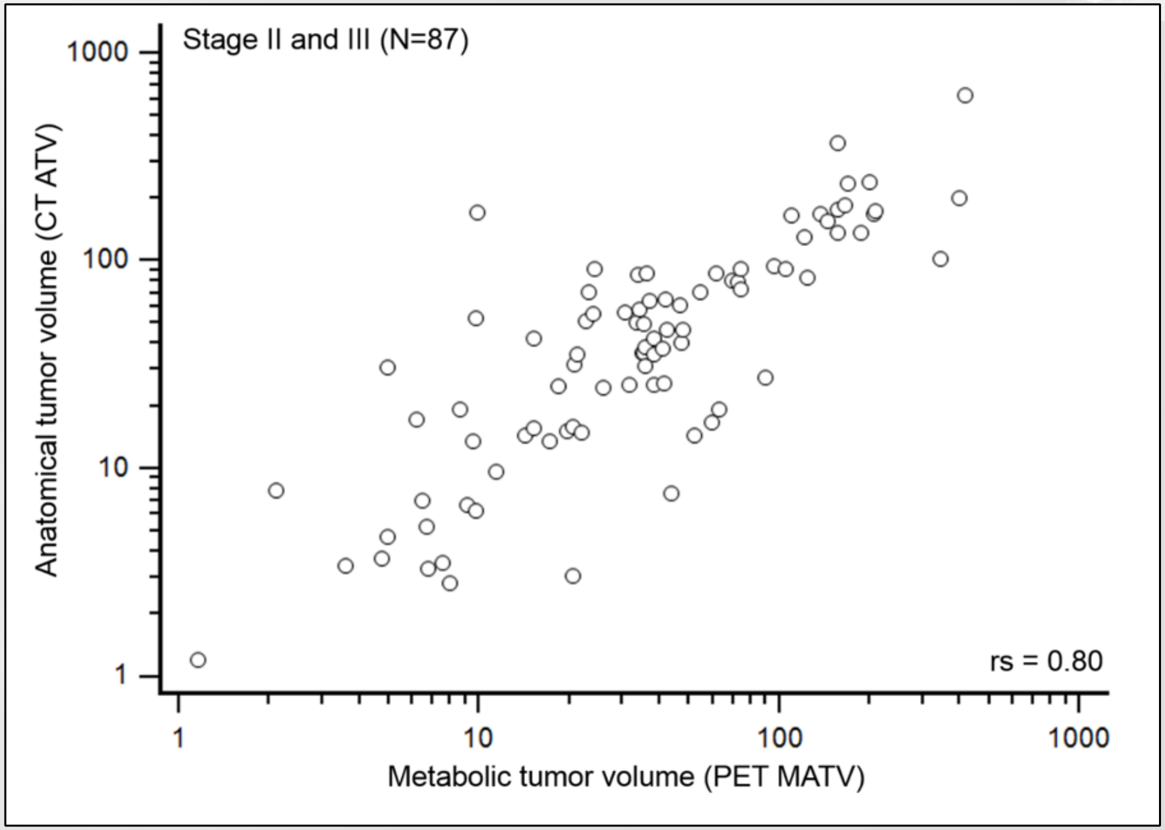


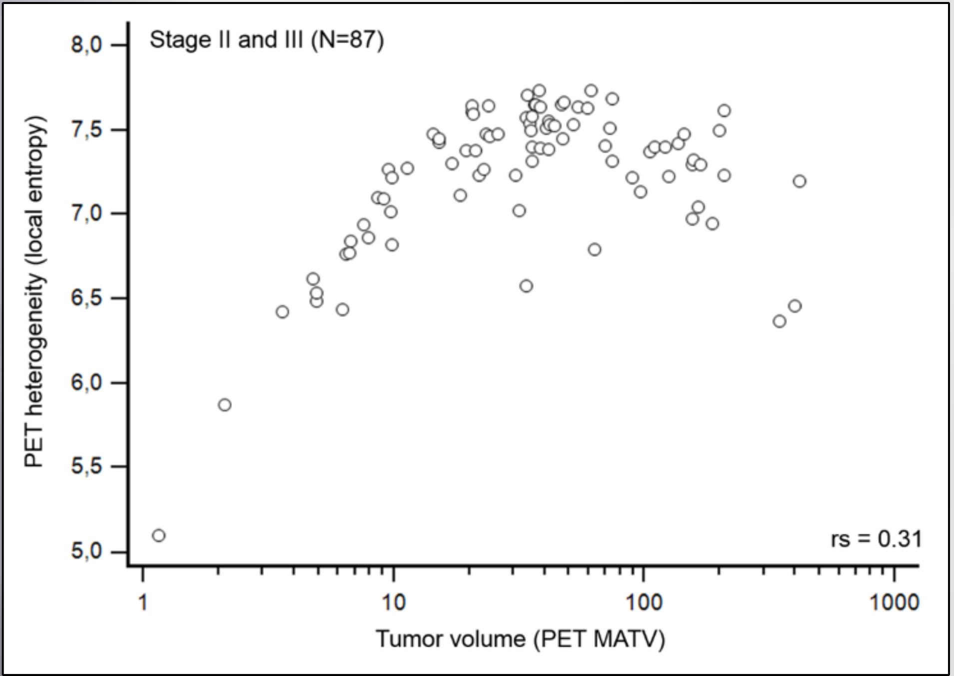
Functional (PET) volume had higher prognostic value:
Hazard ratio 2.5 *vs.* 1.9

Desseroit MC, *et al*. Development of a nomogram combining clinical staging with 18F-FDG PET/CT image features in Non-Small Cell Lung Cancer stage I-III, *under submission 2015*

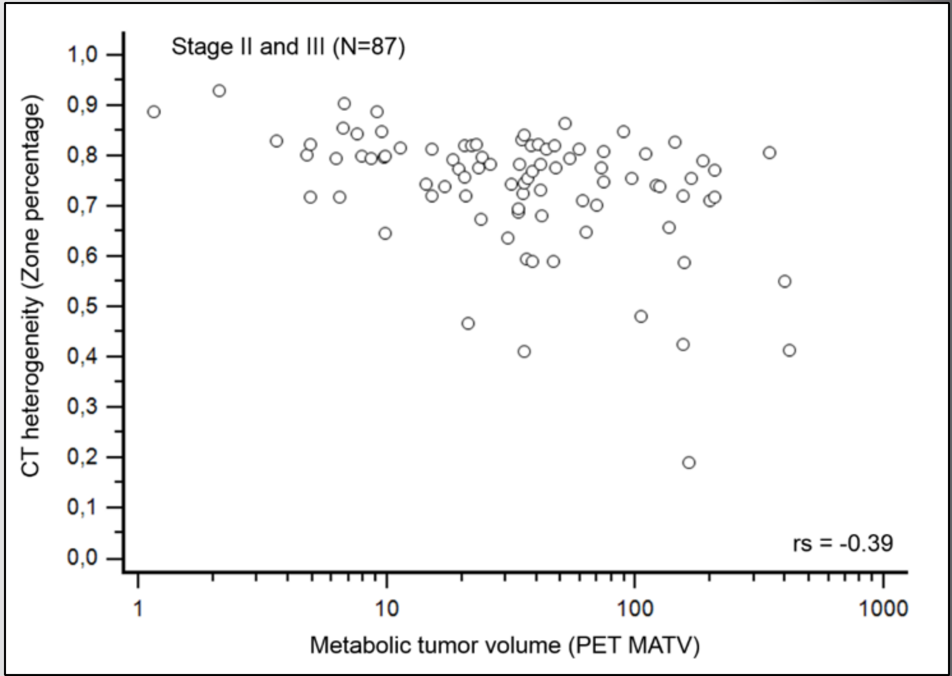
Results

Correlation between features

Tumor volume *vs.* PET heterogeneity



Tumor volume *vs.* CT heterogeneity



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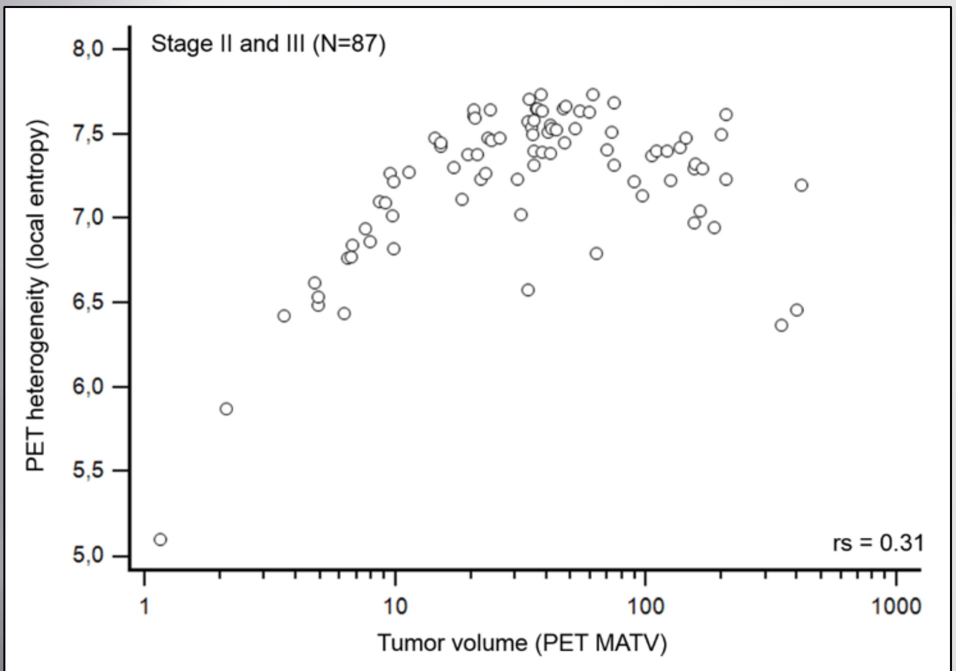
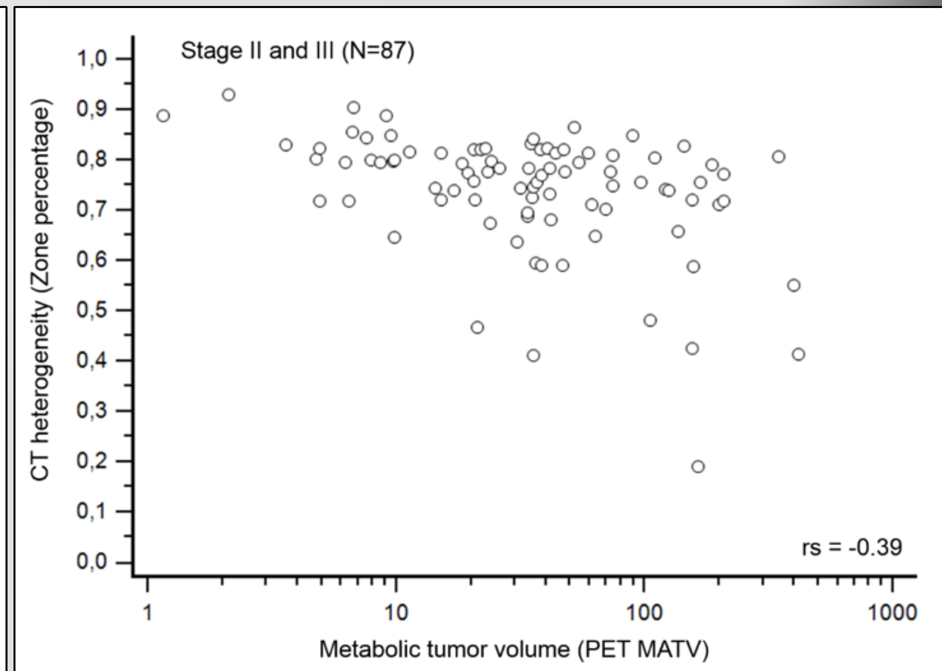


Hazard ratio = 1.9

Tumor volume *vs.* CT heterogeneity



Hazard ratio = 2.1

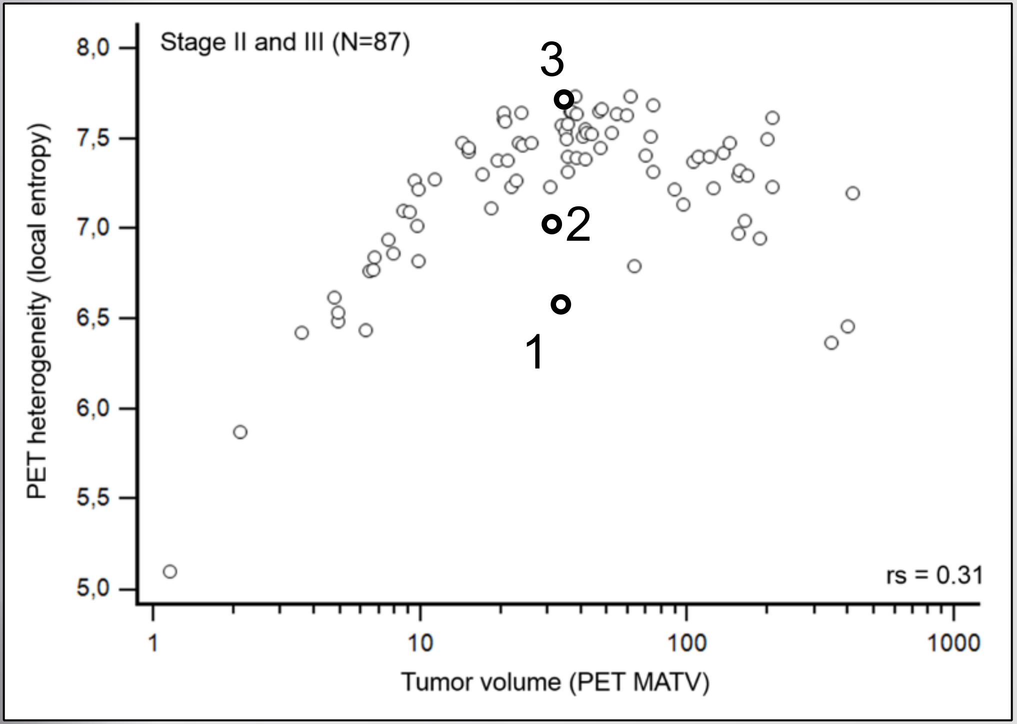
Desseroit MC, *et al*. Development of a nomogram combining clinical staging with 18F-FDG PET/CT image features in Non-Small Cell Lung Cancer stage I-III, *under submission 2015*

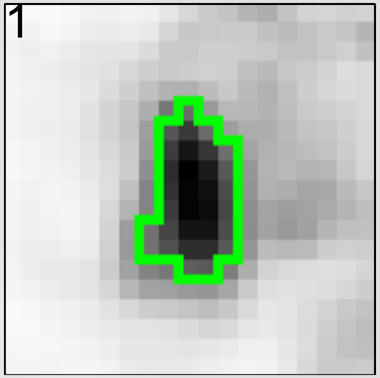
Multimodal characterization of tumors

Characterization: clinical value?

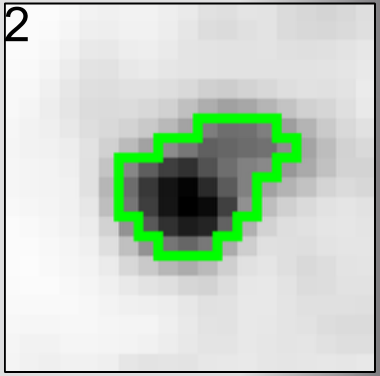
Example: NSCLC stage I-III

- PET heterogeneity *vs.* volume?

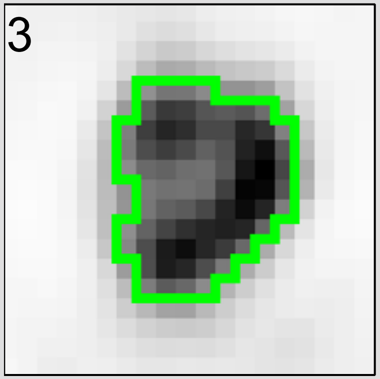




$V = 34\ cm^3$ $E = 6.5$



$V = 32\ cm^3$ $E = 7.0$



$V = 35\ cm^3$ $E = 7.7$

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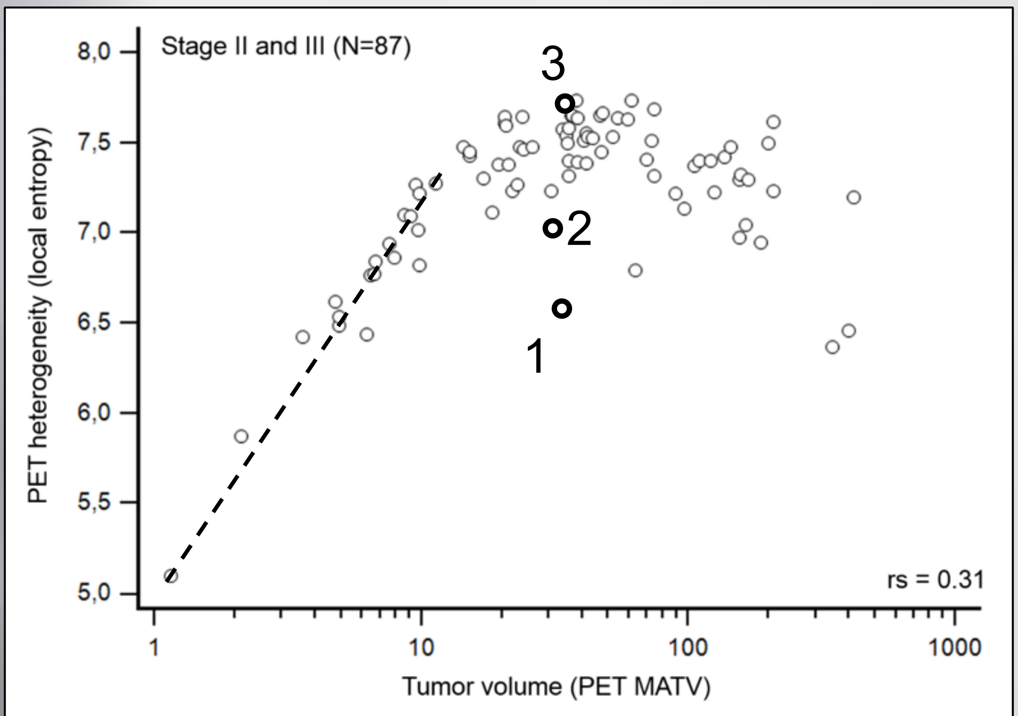

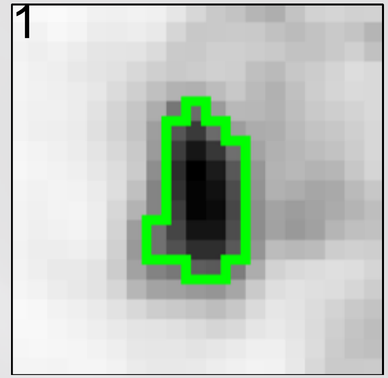

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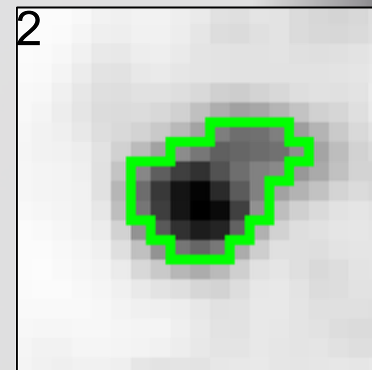

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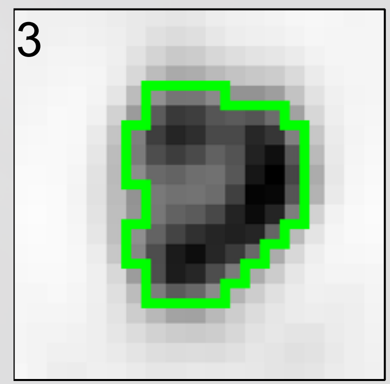

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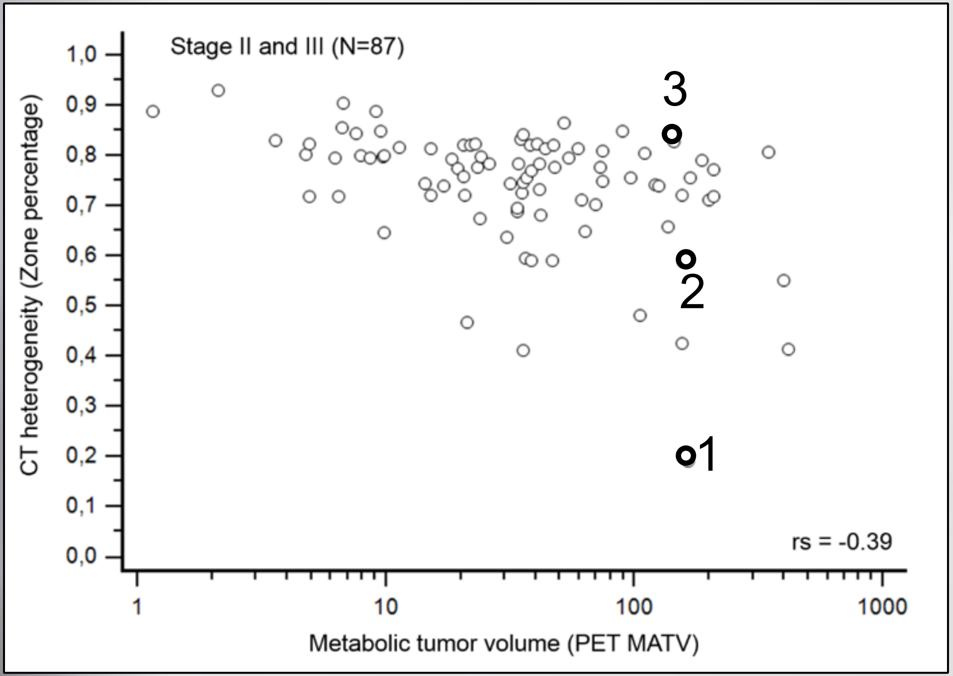
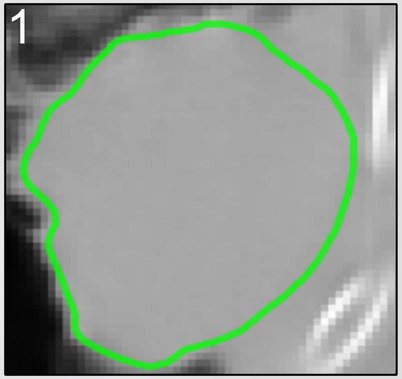
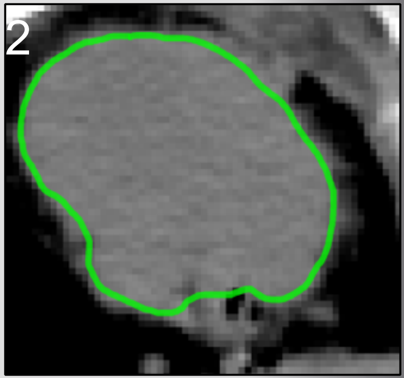
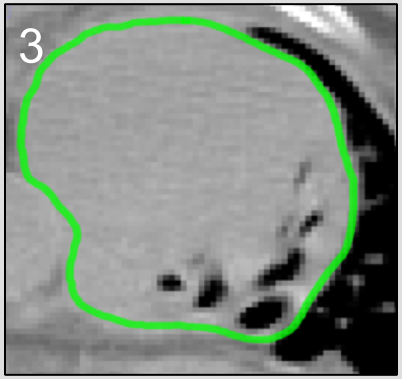




V = 156 cm³ ZP = 0.2



V = 144 cm³ ZP = 0.55



V = 156 cm³ ZP = 0.85

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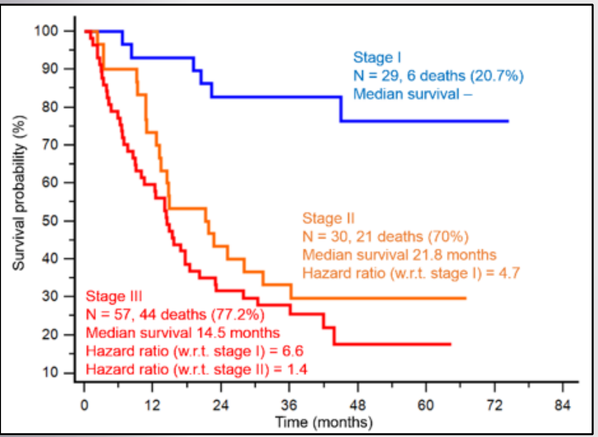
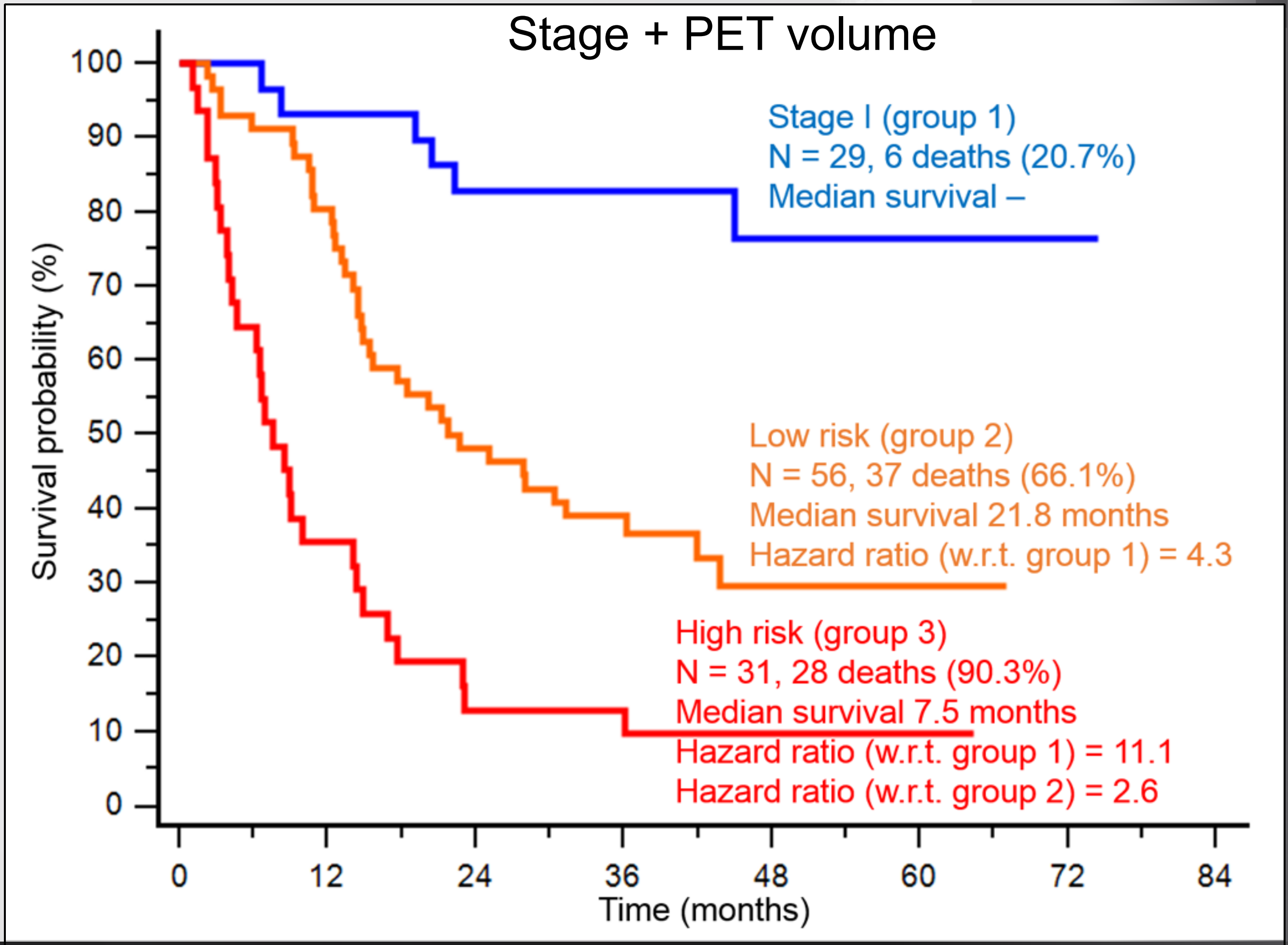
Multimodal characterization of tumors

Characterization: clinical value?

Example: NSCLC stage I-III





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Multimodal characterization of tumors

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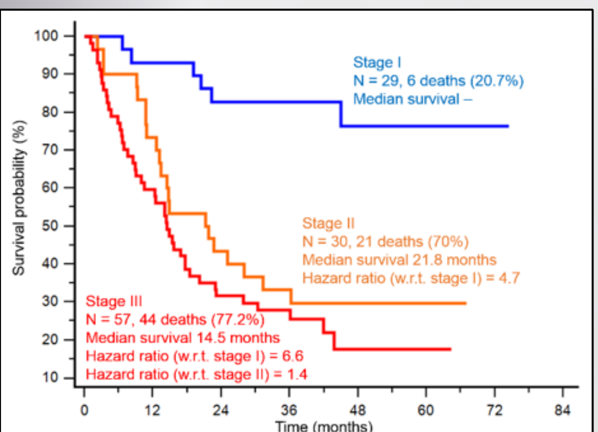

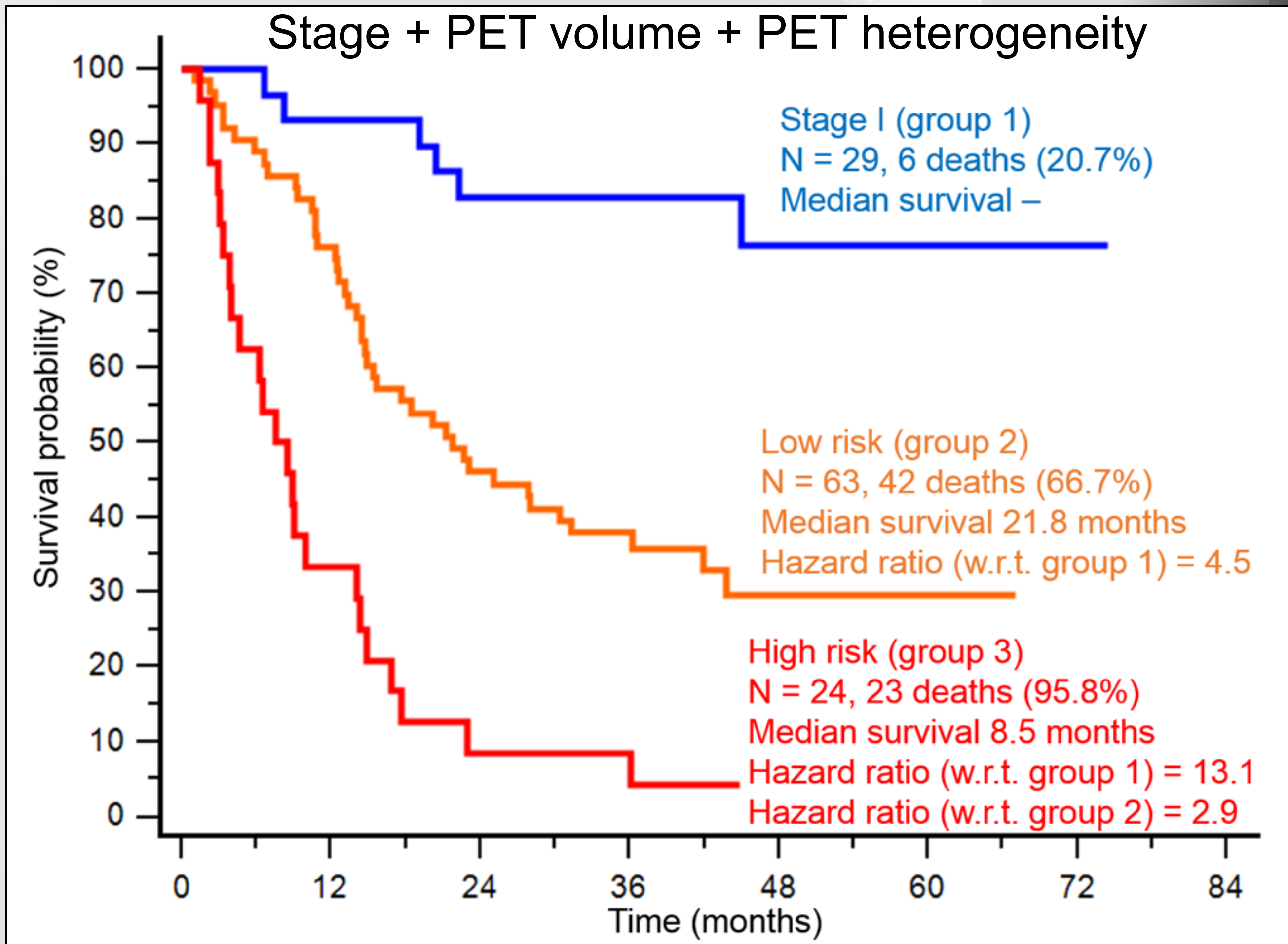

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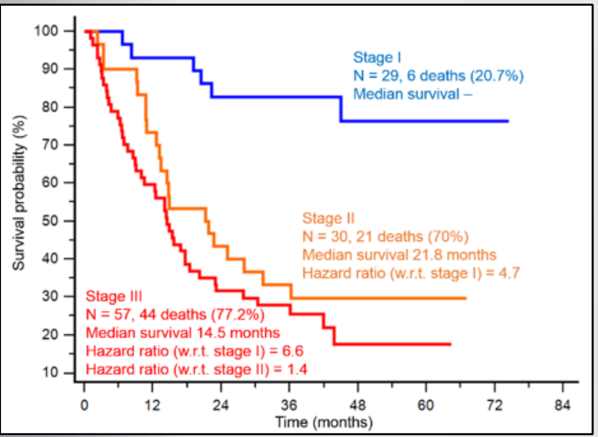

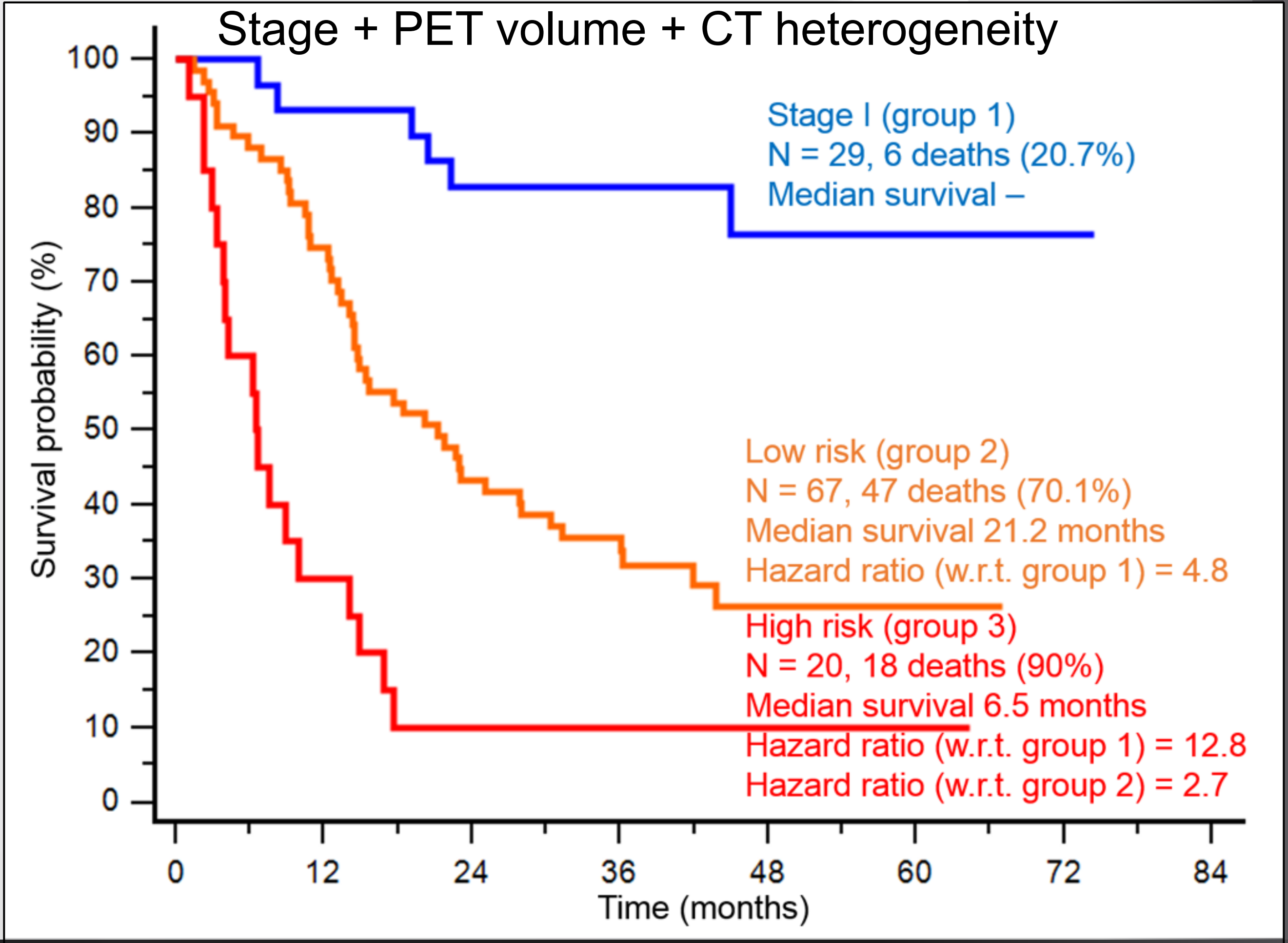

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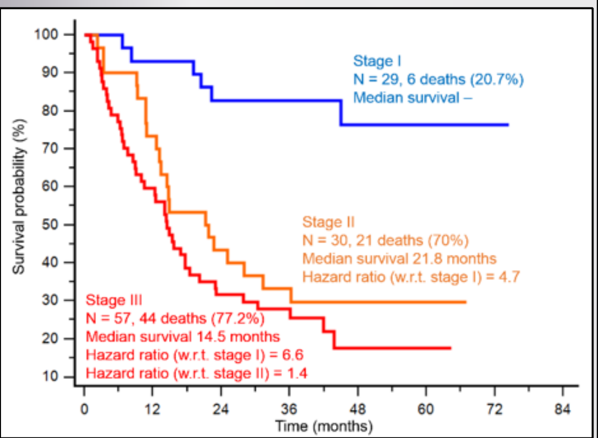

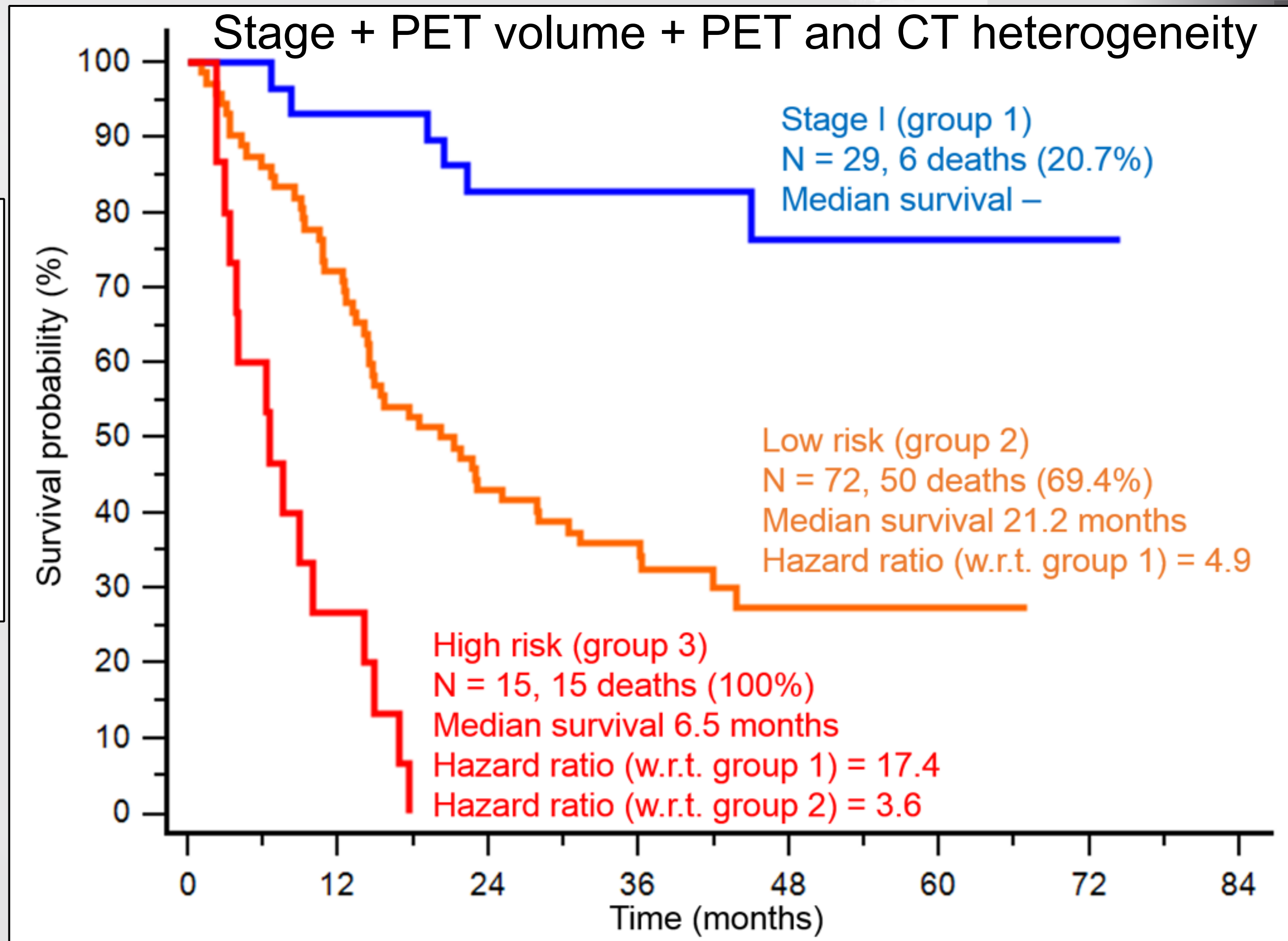

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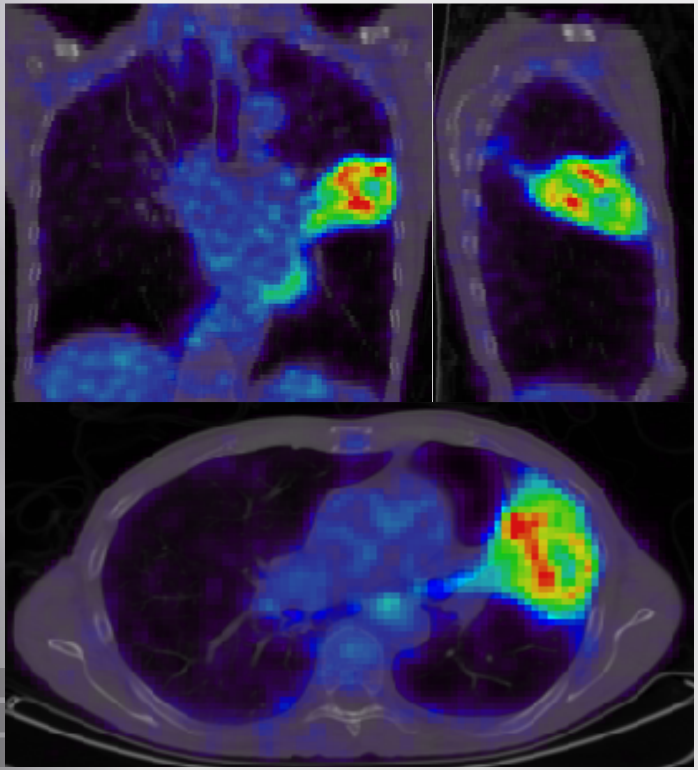
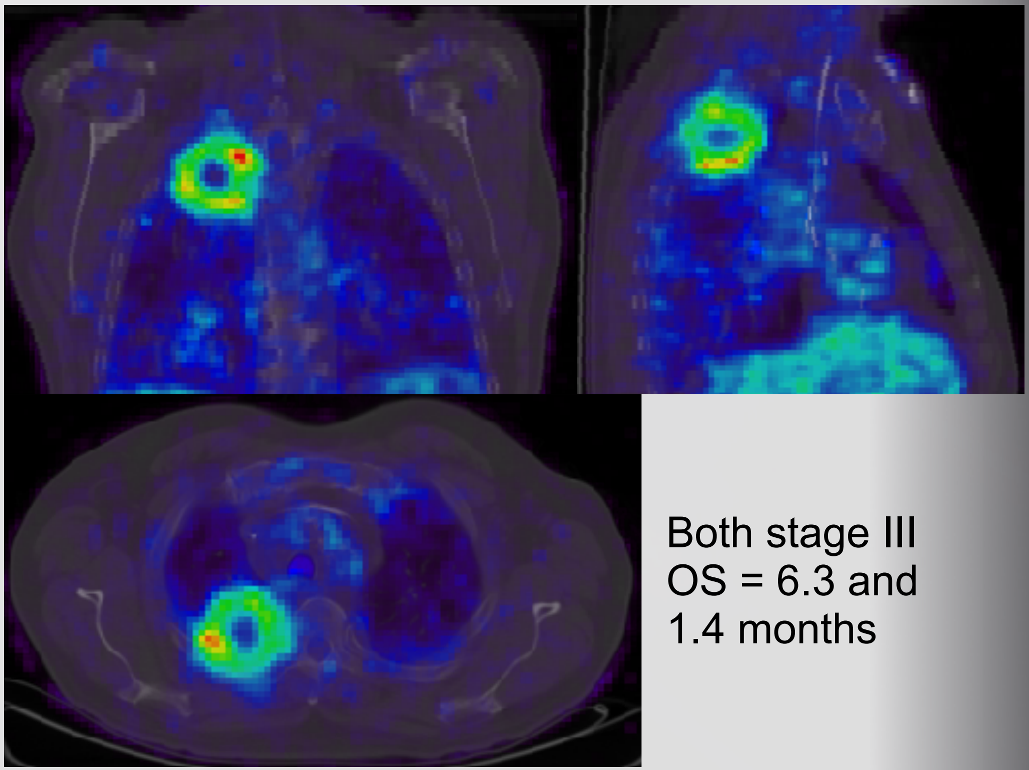
- PET/CT based prognostic model combining:
  - Clinical stage, PET volume, PET & CT heterogeneities





Both stage III
OS = 6.3 and
1.4 months

Desseroit MC, *et al*. Development of a nomogram combining clinical staging with 18F-FDG PET/CT image features in Non-Small Cell Lung Cancer stage I-III, *under submission 2015*

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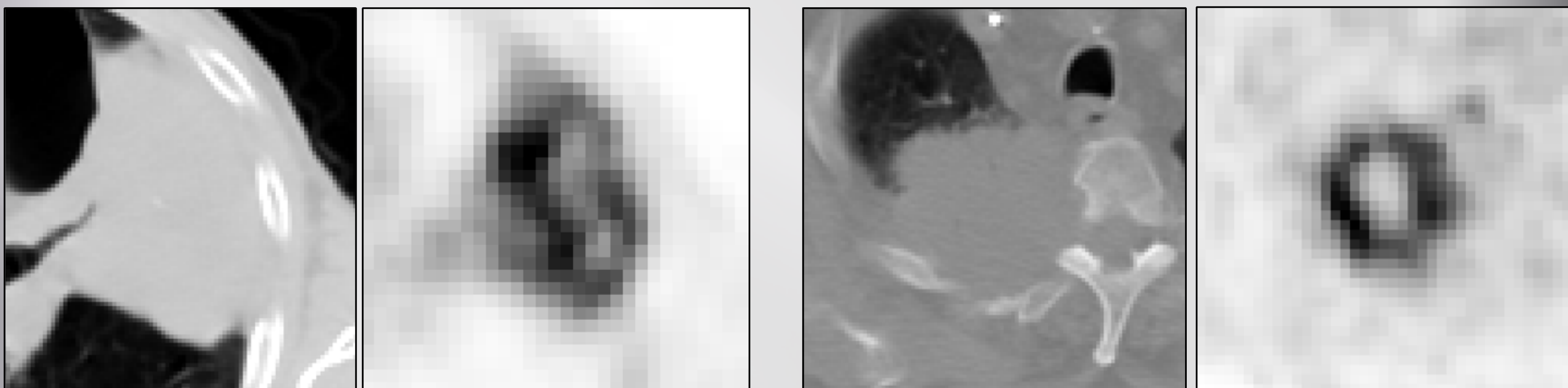

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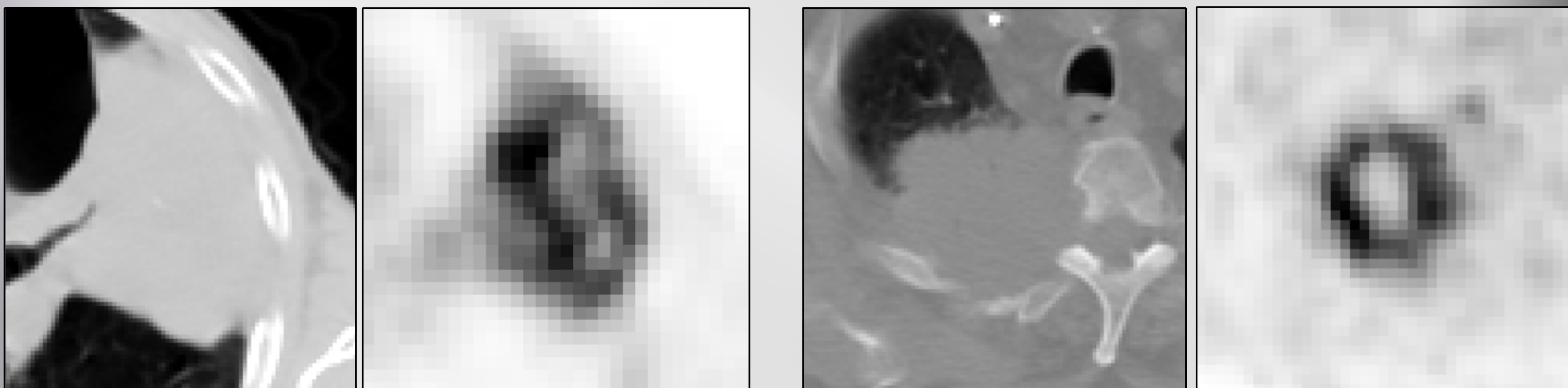


For comparison, higher CT H values:

Desseroit MC, *et al*. Development of a nomogram combining clinical staging with 18F-FDG PET/CT image features in Non-Small Cell Lung Cancer stage I-III, *under submission 2015*

Acknowledgments

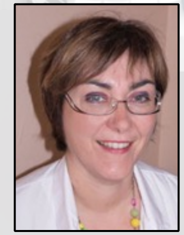
LaTIM team

Team leader

D. Visvikis

Associated clinicians

O. Pradier



C. Cheze Le Rest

Post-doc

F. Tixier

Medical physicist

N. Boussion

PhD students

M. Majdoub

M-C. Desseroit

T. Upadhaya

Thank your for your attention

La pointe Saint-Mathieu, Finistère, Bretagne, France

Additional material

3D geometrical shape:

- Hypotheses: associated with growth rate, metastatic potential, aggressiveness…

Multimodal characterization of tumors

Characterization: geometrical shape

3D geometrical shape:

- Hypotheses: associated with growth rate, metastatic potential, aggressiveness…
- Morphological, functional and/or morpho-functional:
- Shape descriptors
  - (a)sphericity, solidity, convexity, rectangularity, excentricity…

Multimodal characterization of tumors

Characterization: geometrical shape

- 3D geometrical shape:
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    - (a)sphericity, solidity, convexity, rectangularity, excentricity…
    - Shape of PET uptake: independent prognostic value demonstrated in:
      - Head and neck cancer[1]
      - Lung cancer[2]

1. Apostolova I, *et al*. Quantitative assessment of the asphericity of pretherapeutic FDG uptake as an independent predictor of outcome in NSCLC. *BMC Cancer*. 2014
2. Hofheinz F, *et al*. Increased evidence for the prognostic value of primary tumor asphericity in pretherapeutic FDG PET for risk stratification in patients with head and neck cancer. *Eur J Nucl Med Mol Imaging*. 2015

Textural features in PET

The past: alternative measurements

Shape

- Asphericity

Eur Radiol (2014) 24:2077–2087
DOI 10.1007/s00330-014-3269-8

HEAD AND NECK

Asphericity of pretherapeutic tumour FDG uptake provides independent prognostic value in head-and-neck cancer

Ivayla Apostolova • Ingo G. Steffen • Florian Wedel • Alexandr Lougovski • Simone Marnitz • Thorsten Derlin • Holger Amthauer • Ralph Buchert • Frank Hofheinz • Winfried Brenner

Textural features in PET

The past: alternative measurements

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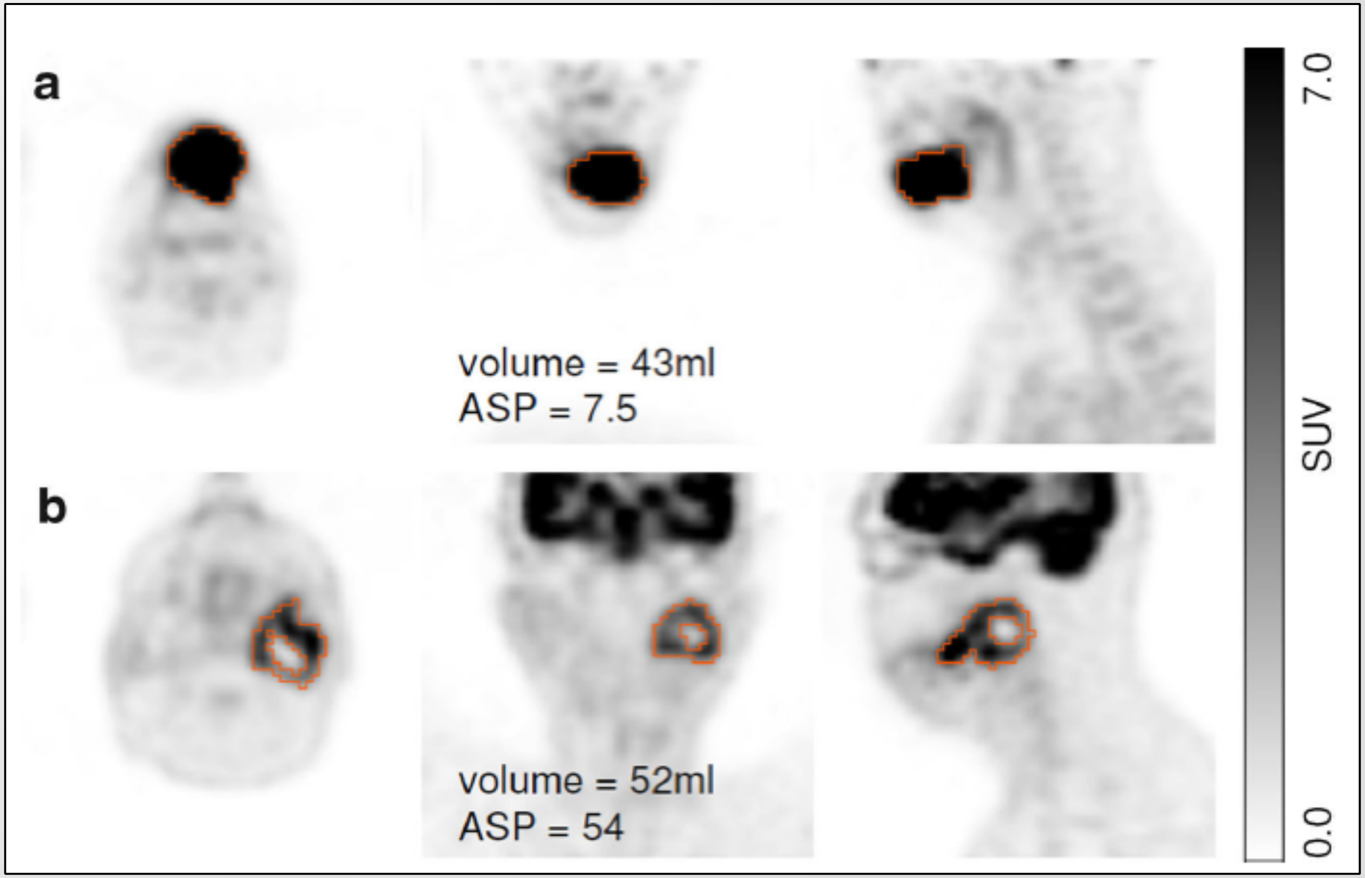

Textural features in PET

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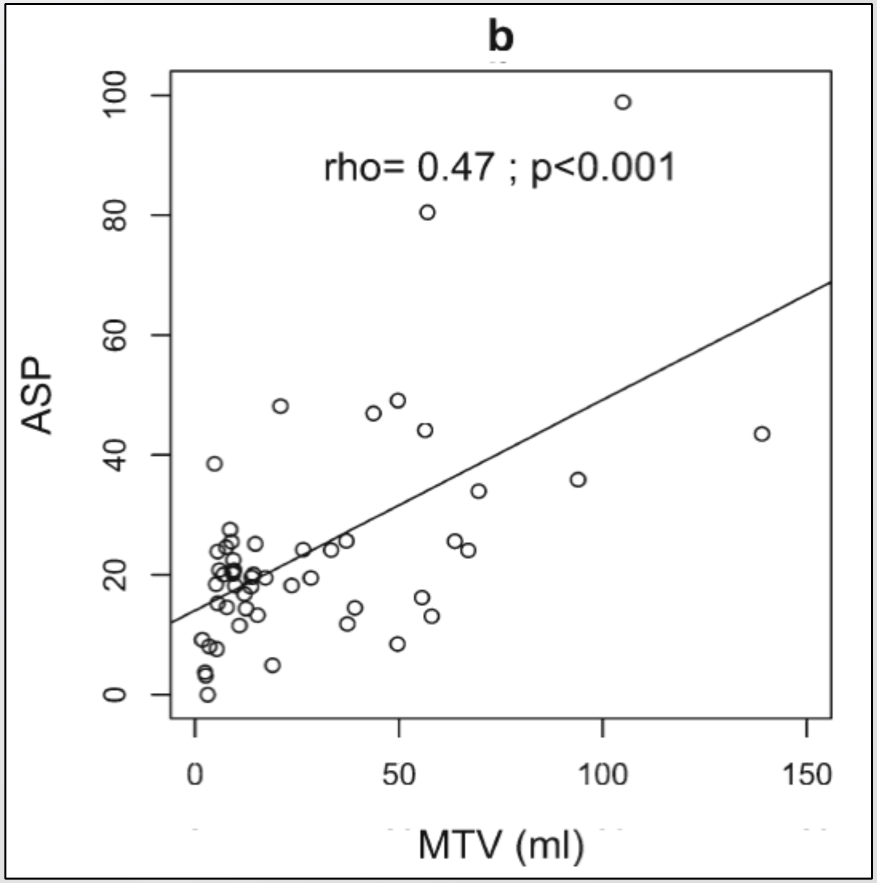

Textural features in PET

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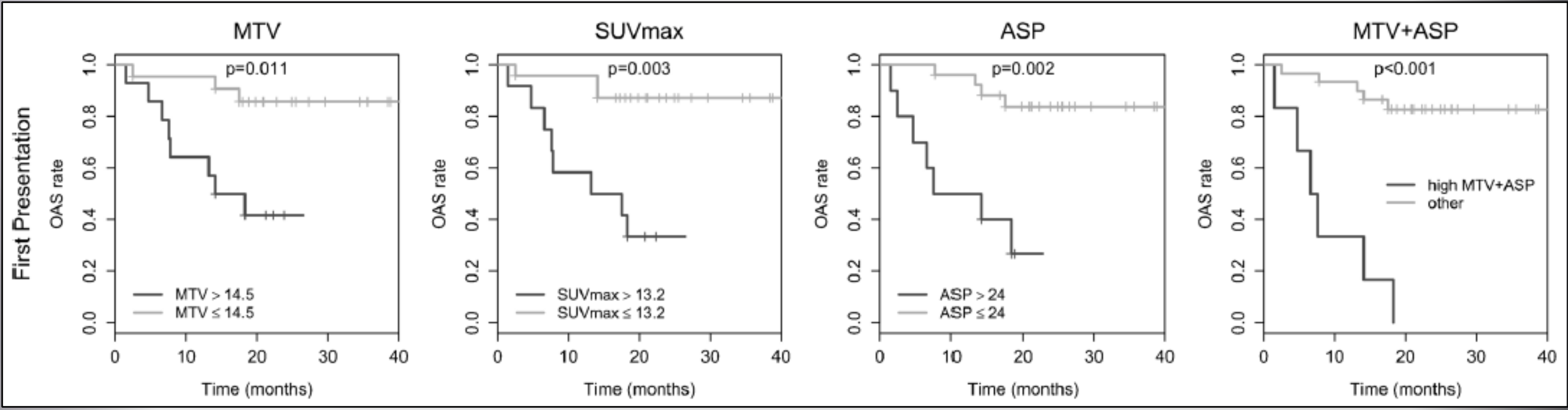

Textural features in PET

The past: alternative measurements

Shape

- Asphericity

Eur J Nucl Med Mol Imaging (2015) 42:429–437
DOI 10.1007/s00259-014-2953-x

ORIGINAL ARTICLE

Increased evidence for the prognostic value of primary tumor asphericity in pretherapeutic FDG PET for risk stratification in patients with head and neck cancer

Frank Hofheinz · Alexandr Lougovski · Klaus Zöphel · Maria Hentschel · Ingo G. Steffen · Ivayla Apostolova · Florian Wedel · Ralph Buchert · Michael Baumann · Winfried Brenner · Jörg Kotzerke · Jörg van den Hoff

Textural features in PET

The past: alternative measurements

Shape

- Asphericity

Apostolova *et al. BMC Cancer* 2014, **14**:896
http://www.biomedcentral.com/1471-2407/14/896

BMC Cancer

RESEARCH ARTICLE Open Access

Quantitative assessment of the asphericity of pretherapeutic FDG uptake as an independent predictor of outcome in NSCLC

Ivayla Apostolova[1*], Julian Rogasch[1], Ralph Buchert[2], Heinz Wertzel[3], H Jost Achenbach[3], Jens Schreiber[4], Sandra Riedel[4], Christian Furth[1], Alexandr Lougovski[5], Georg Schramm[5], Frank Hofheinz[5], Holger Amthauer[1] and Ingo G Steffen[1]

Textural features in PET

The past: alternative measurements

Shape

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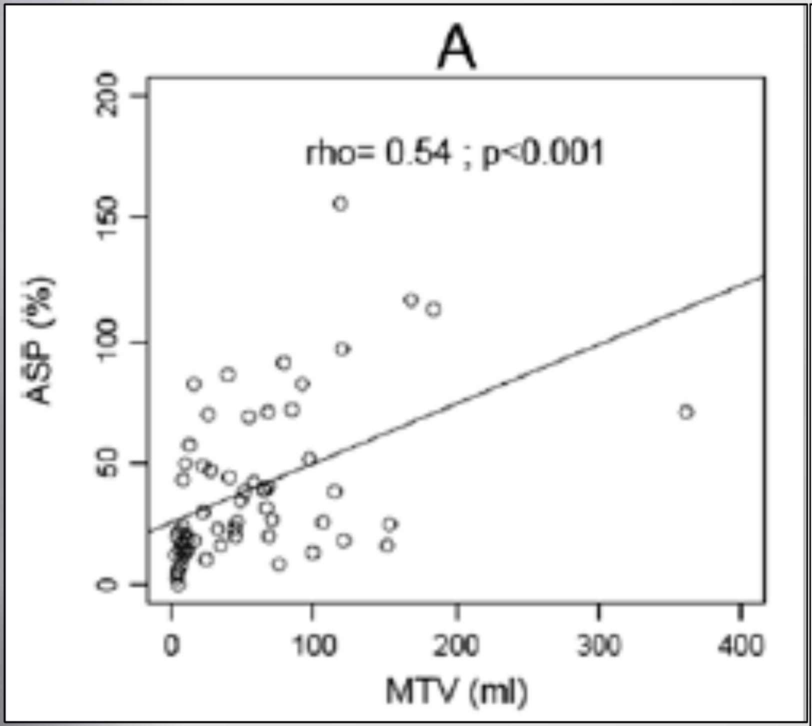

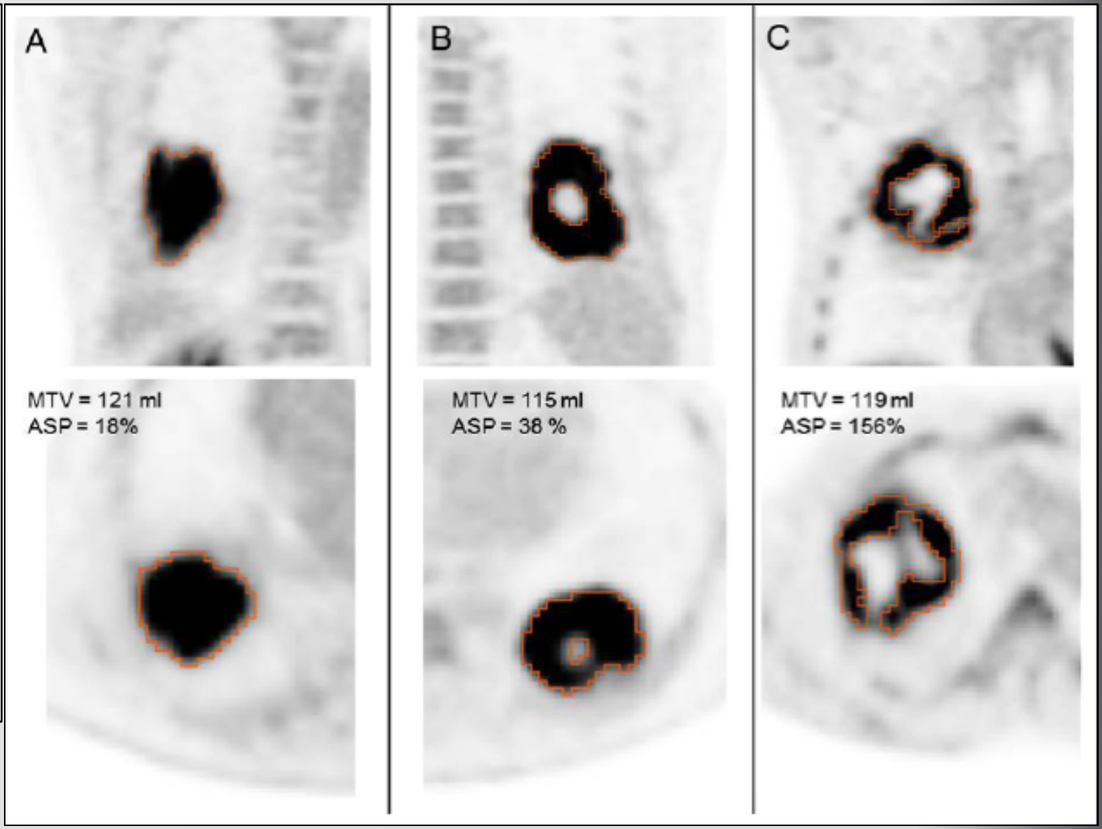

Textural features in PET

The past: alternative measurements

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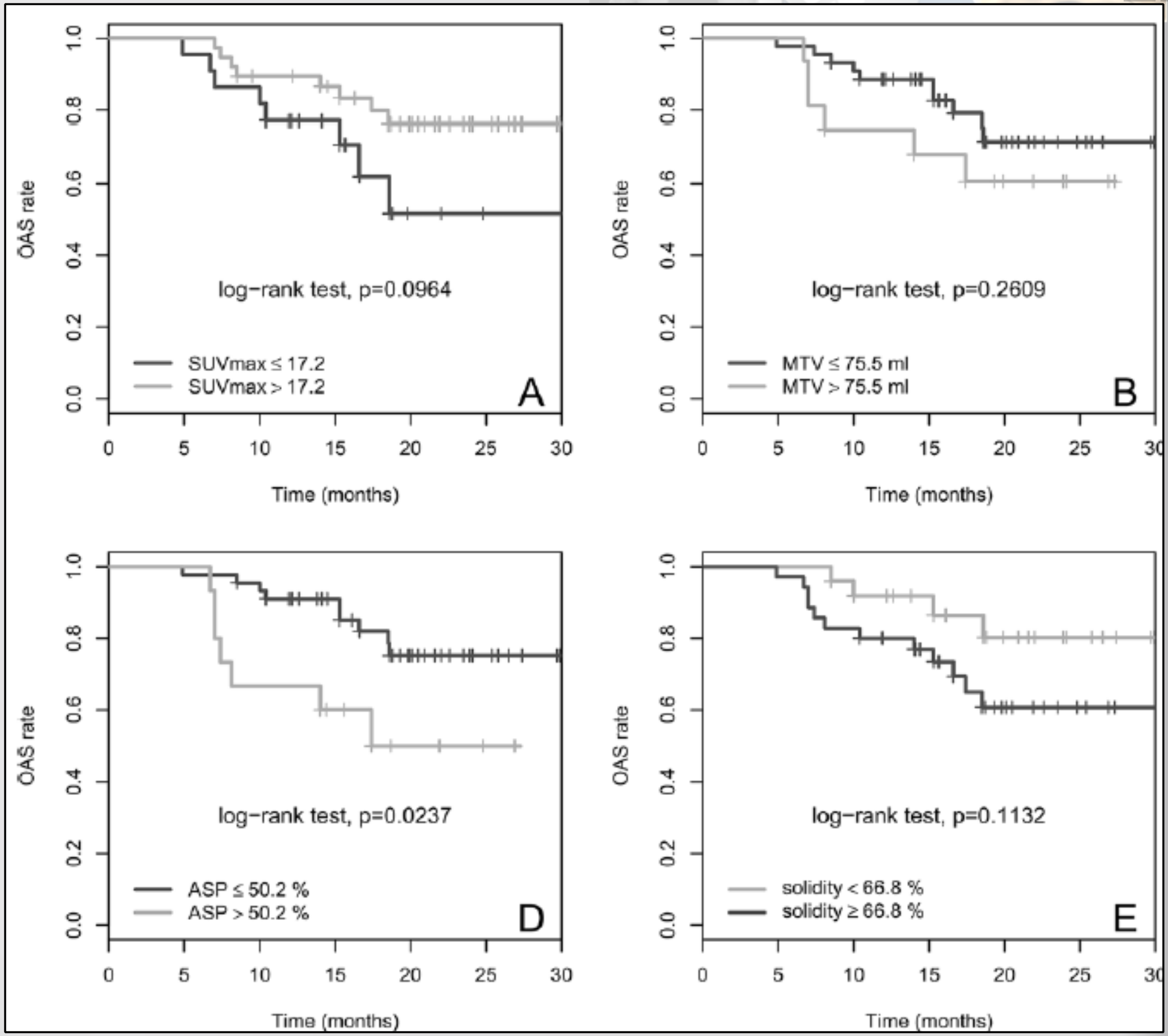
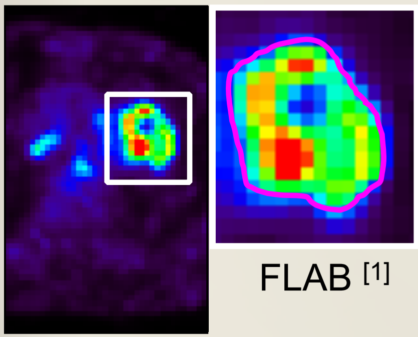
  - Asphericity



3D geometrical shape:

1. Segmentation



FLAB [1]

Solidity = Volume/Convex Hull volume

$$Rectangularity = Volume/Min\ bounding\ box\ volume$$

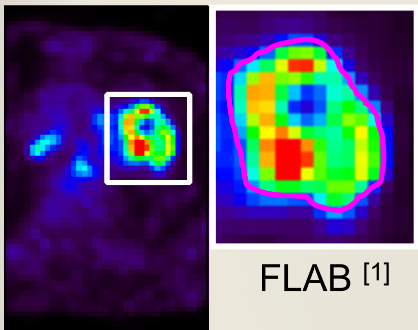
$$Sphericity = \sqrt[3]{36\pi\, Volume^2}/Surface$$

Multimodal characterization of tumors

Characterization: geometrical shape

3D geometrical shape:

1. Segmentation



FLAB [1]

2. Quantification

- ✓ Standard metrics (functional volume, mean and max SUVs…)
- ✓ Shape metrics [2]

❖ Reproducibility ?

❖ Robustness ?

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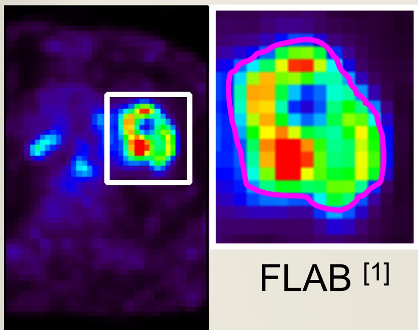

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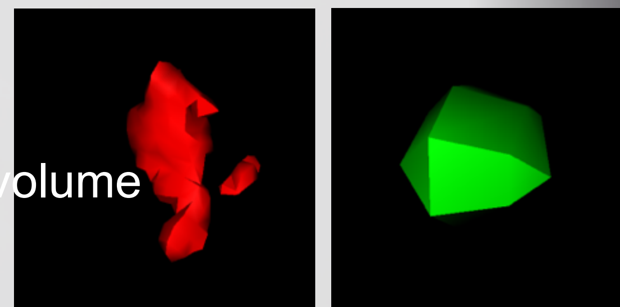
Low High



Institut thématiques Inserm Institut national de la santé et de la recherche médicale

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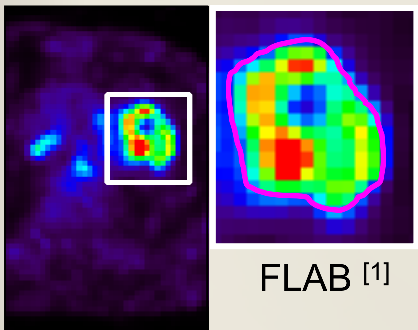

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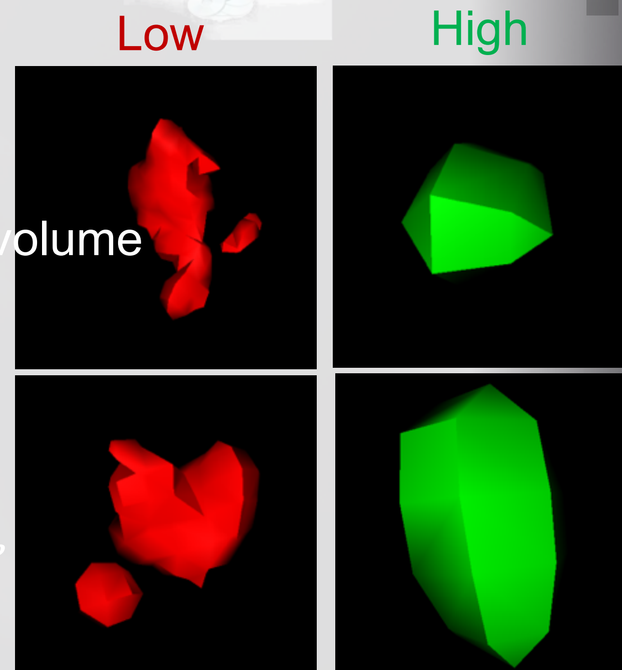

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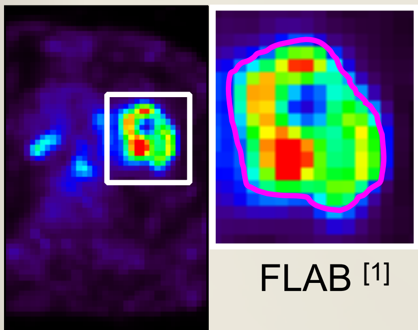

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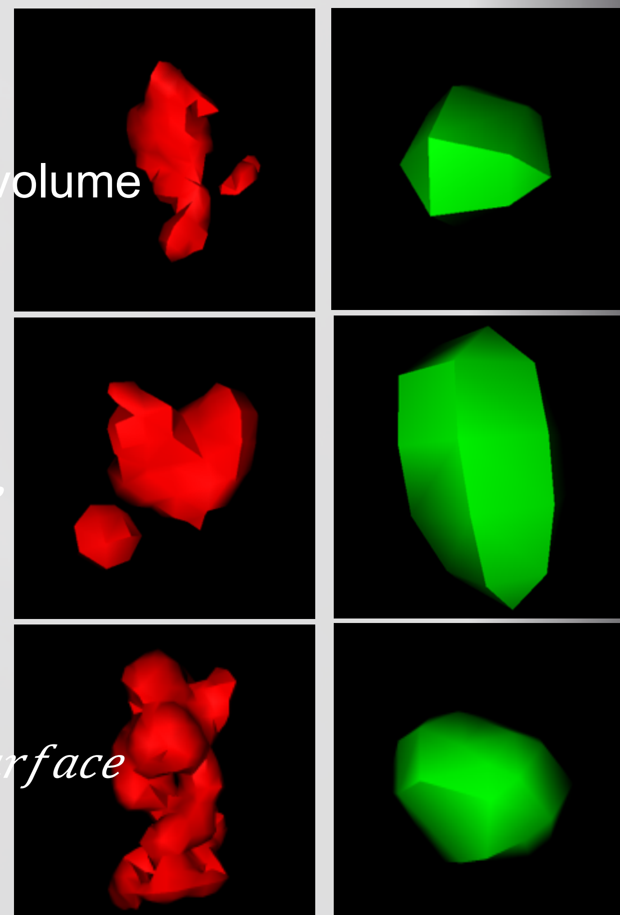
❖ Robustness ?

Solidity = Volume/Convex Hull volume

$$Rectangularity = Volume/Min\ bounding\ box\ volume$$

$$Sphericity = \sqrt[3]{36\pi\, Volume^2}/Surface$$



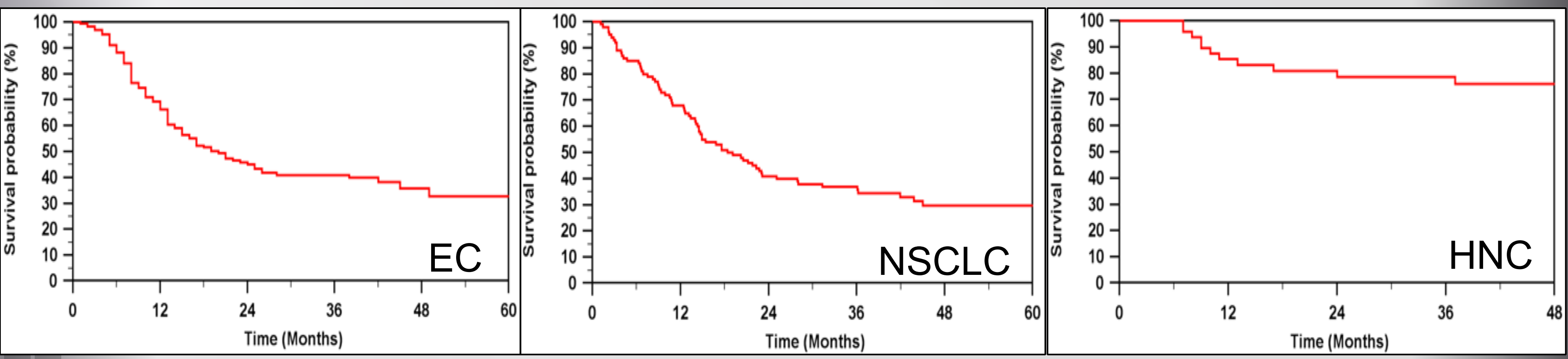
1. Hatt, *et al*. A fuzzy locally adaptive Bayesian segmentation approach for volume determination in PET. *IEEE Trans Med Imaging*. 2009
2. El Naqa, *et al*. Exploring feature-based approaches in PET images for predicting cancer treatment outcomes. *Pattern Recognit*. 2009

Multimodal characterization of tumors

Characterization: geometrical shape

3D geometrical shape:

Pathology	Tracer	Acquisitions	N	Centers	Endpoint	Events	Median, mean ± std (months)
EC	FDG	Baseline	170	3	Overall survival (OS)	98 (57%)	15, 21±16
NSCLC	FDG	Baseline	100	1	Overall survival (OS)	68 (68%)	18, 25±19
HNC	FLT	Baseline + during treatment	48	1	Disease-free survival (DFS)	11 (23%)	42, 36±15



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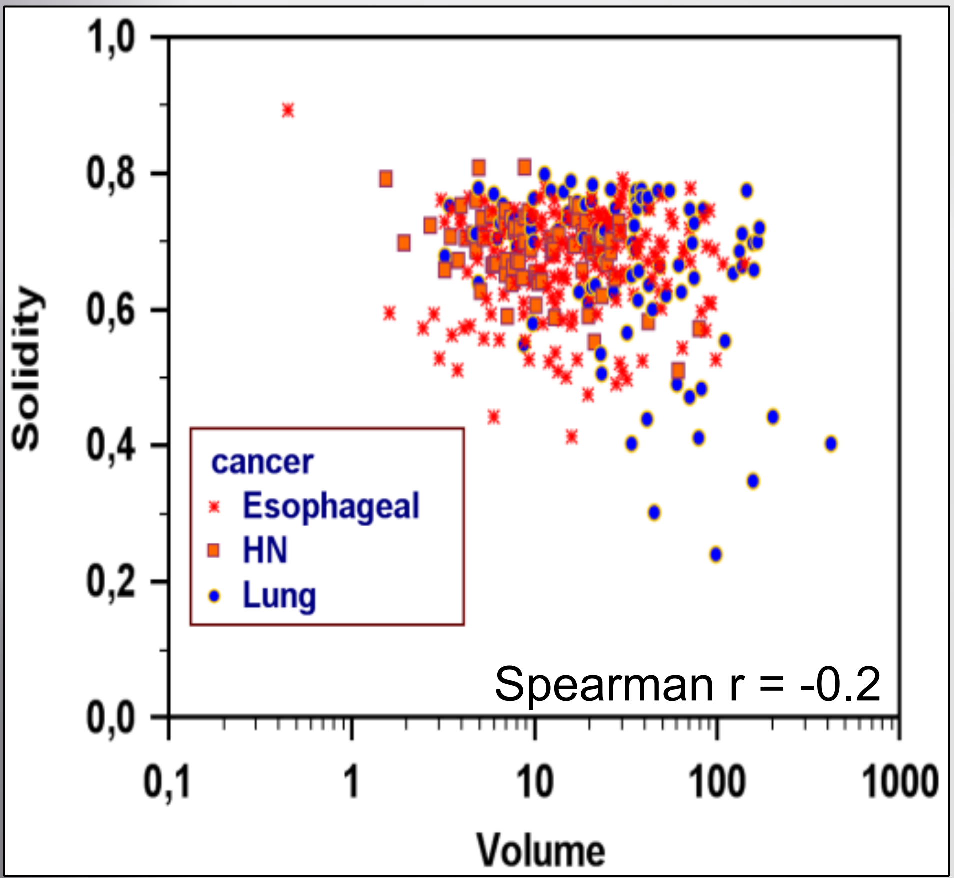
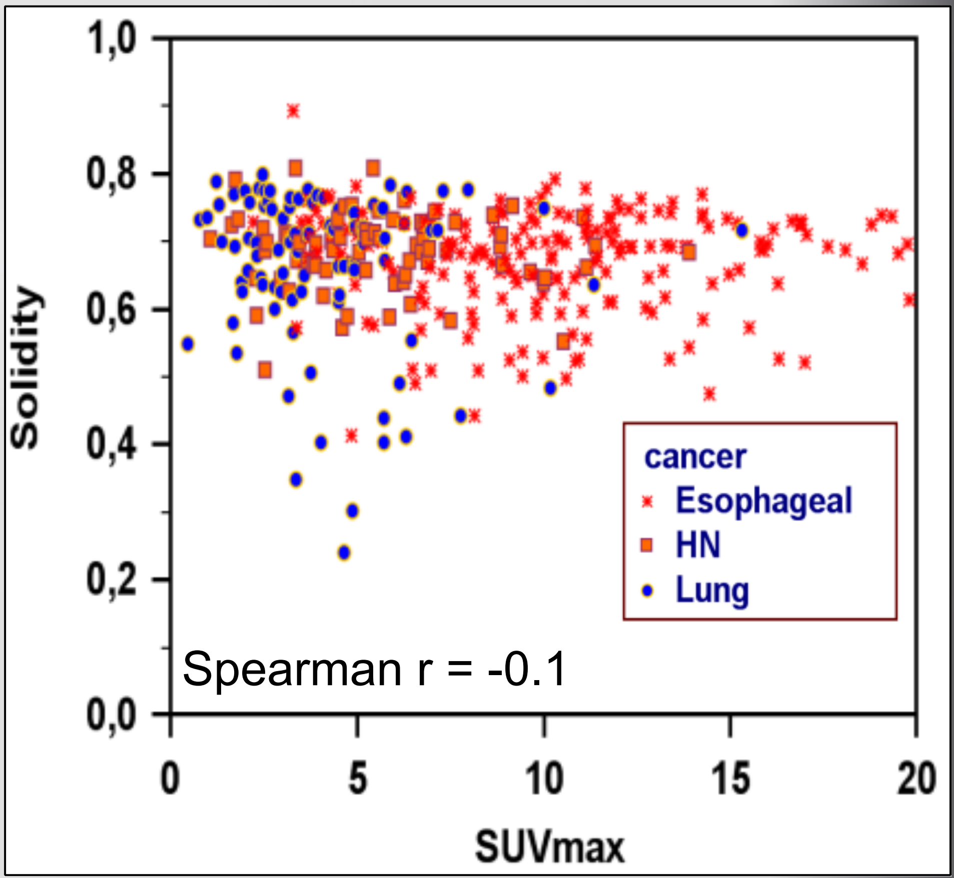
Multimodal characterization of tumors

Characterization: geometrical shape

3D geometrical shape:

Solidity





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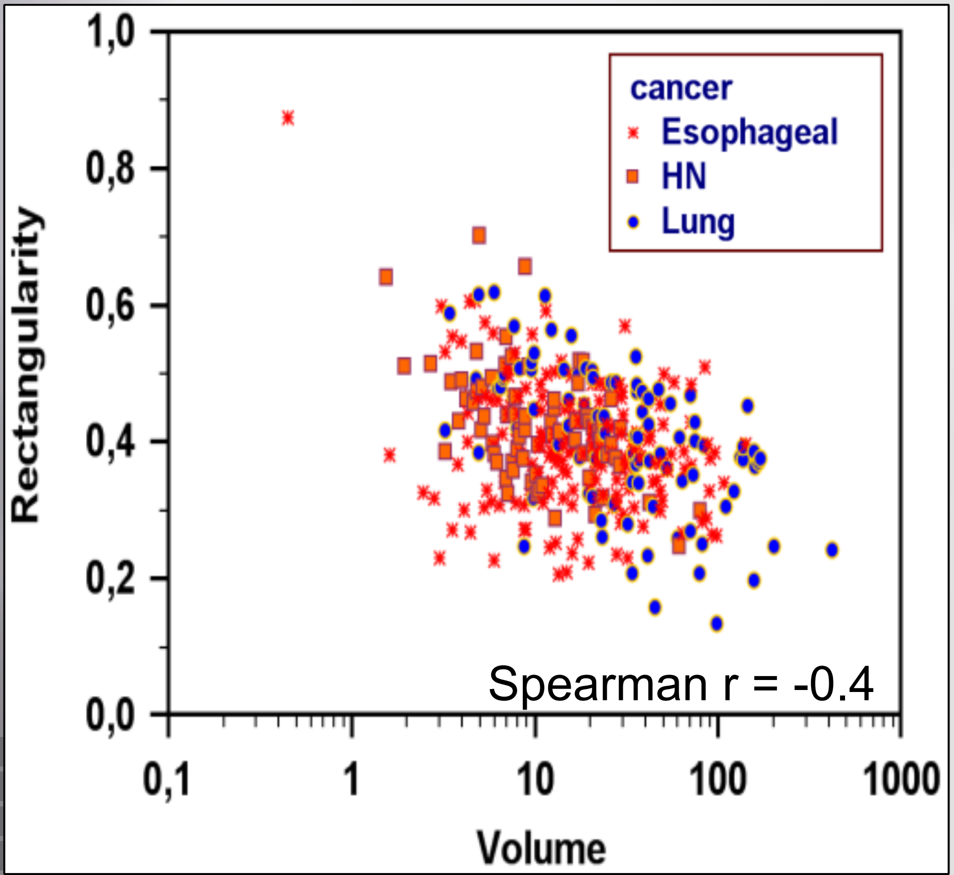
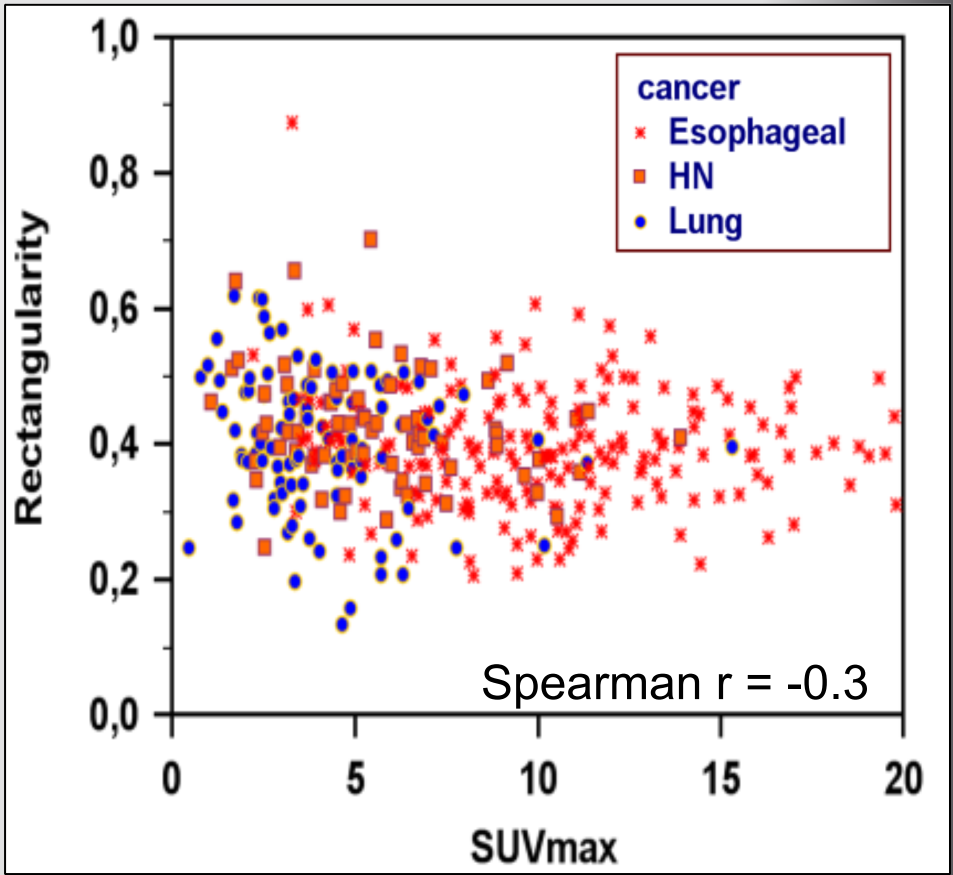
3D geometrical shape:

Rectangularity





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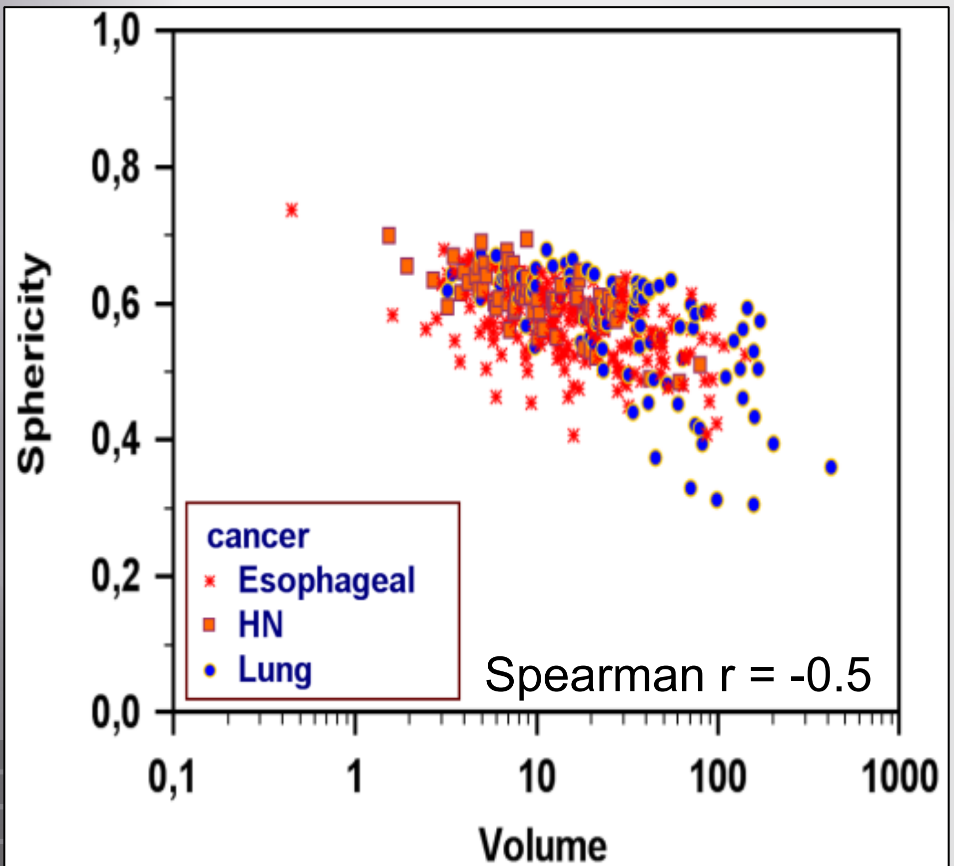
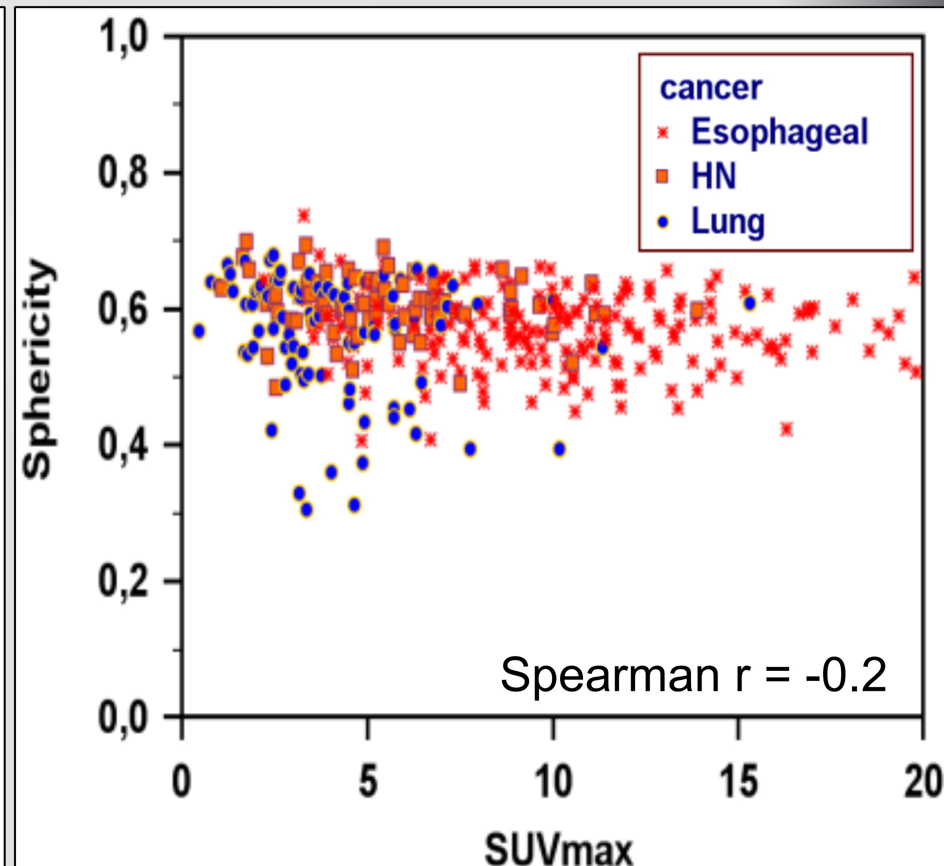
Multimodal characterization of tumors

Characterization: geometrical shape

3D geometrical shape:

Sphericity





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Multimodal characterization of tumors

Characterization: geometrical shape

3D geometrical shape:

Pathology (endpoint)	Univariate analysis			Multivariate features selection
	Feature	P-value	Hazard ratio	
EC (OS)	Clinical stage	0.03	1.3	0.8 × Length + 1.1 × Rectangularity
	Volume	0.0003	2.3	
	Length	<0.0001	2.6	
	Sphericity	0.0003	2.8	
	Rectangularity	<0.0001	3.6	
	Solidity	<0.0001	3.5	
NSCLC (OS)				
HNC (DFS)	ΔSUV_{max}	0.03	4	SUV_{mean}2 - Sphericity2
	Sphericity2	0.01	4.2	

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	Length	<0.0001	2.6	
	Sphericity	0.0003	2.8	
	Rectangularity	<0.0001	3.6	
	Solidity	<0.0001	3.5	
NSCLC (OS)	Clinical stage	0.006	1.8	0.9 × Volume – 0.4 × Sphericity
	Volume	<0.0001	3.2	
	Sphericity	0.0004	2.3	
HNC (DFS)	ΔSUV_{max}	0.03	4	SUV_{mean}2 - Sphericity2
	Sphericity2	0.01	4.2	

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Multimodal characterization of tumors

Characterization: geometrical shape

3D geometrical shape:

Pathology (endpoint)	Univariate analysis			Multivariate features selection
	Feature	P-value	Hazard ratio	
EC (OS)	Clinical stage	0.03	1.3	0.8 × Length + 1.1 × Rectangularity
	Volume	0.0002	2.3	
	Length	<0.0001	2.6	
	Sphericity	0.0003	2.8	
	Rectangularity	<0.0001	3.6	
	Solidity	<0.0001	3.5	
NSCLC (OS)	Clinical stage	0.006	1.8	0.9 × Volume – 0.4 × Sphericity
	Volume	<0.0001	3.2	
	Sphericity	0.0004	2.3	
	Rectangularity	0.001	2.1	
HNC (DFS)	$SUV_{mean}2$	0.02	4.1	$SUV_{mean}2$ - Sphericity2
	ΔSUV_{max}	0.03	4	
	Sphericity2	0.01	4.2	

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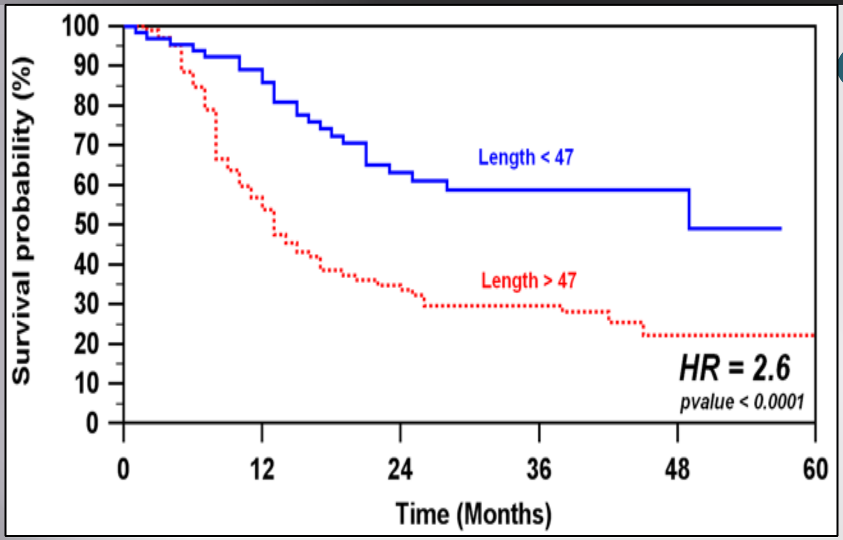
Multimodal characterization of tumors

Characterization: geometrical shape

e 3D:



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Multimodal characterization of tumors

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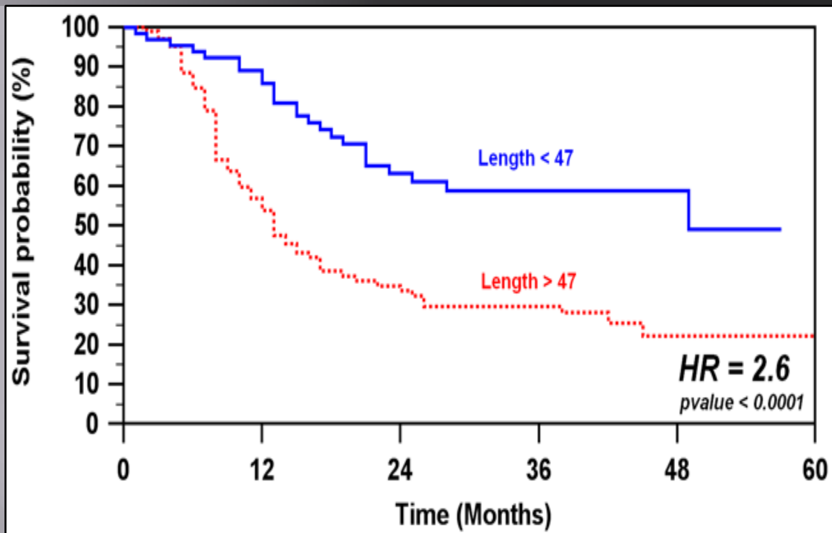

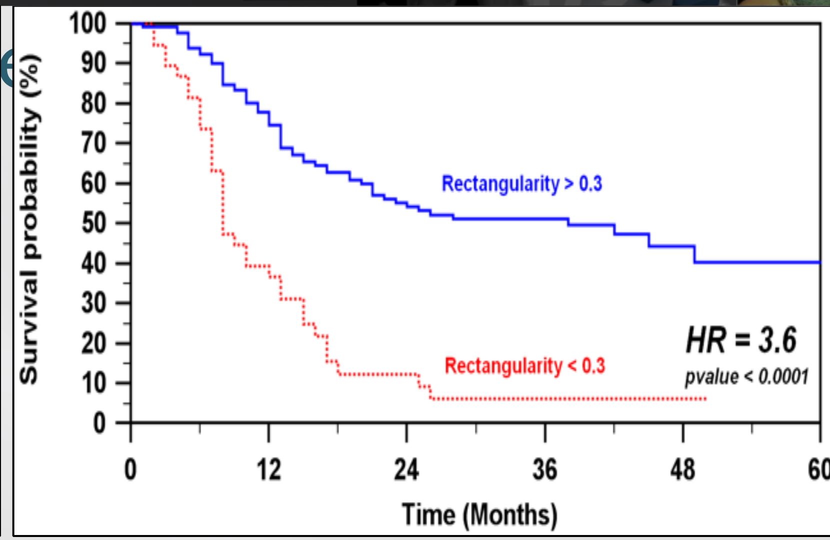

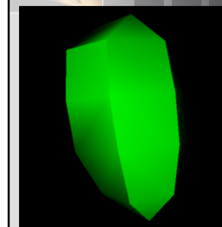

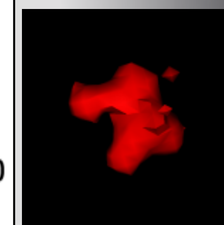

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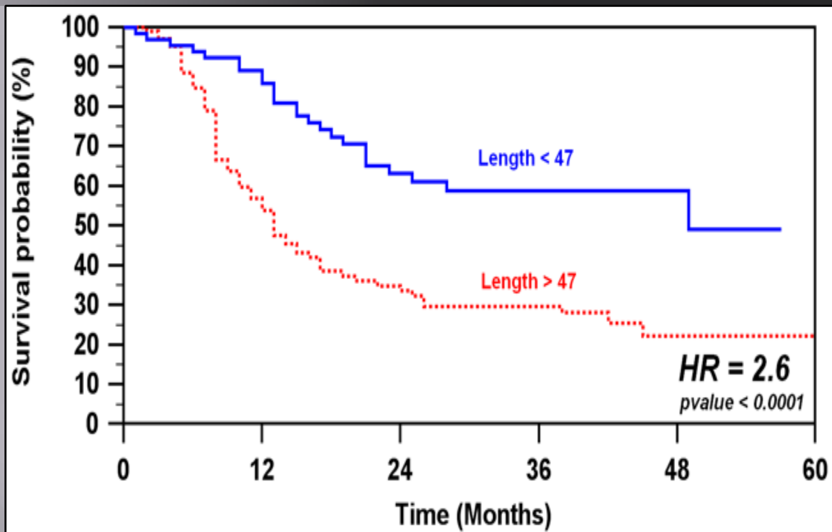

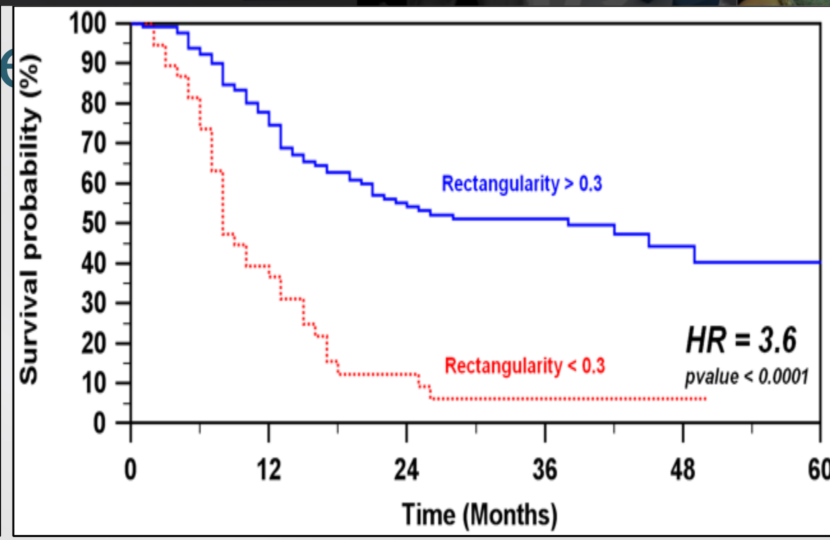

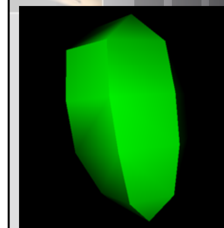

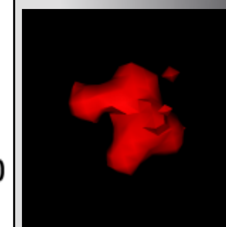

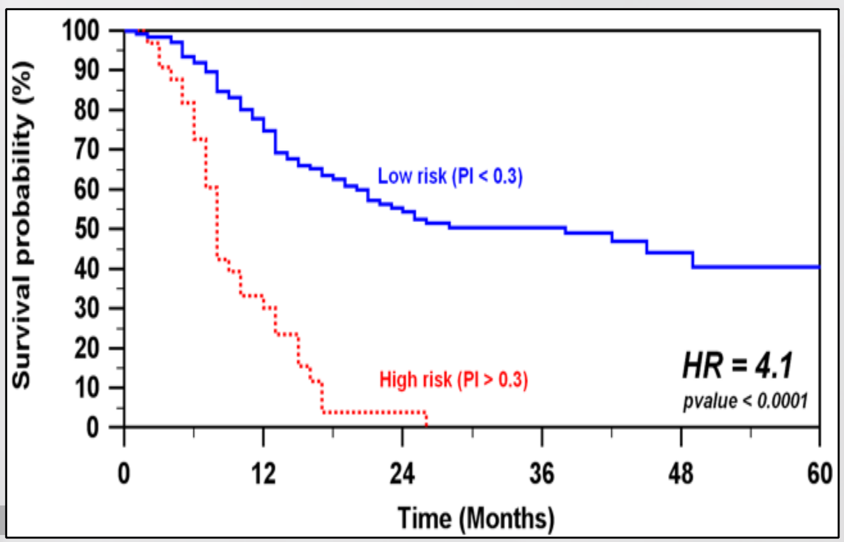

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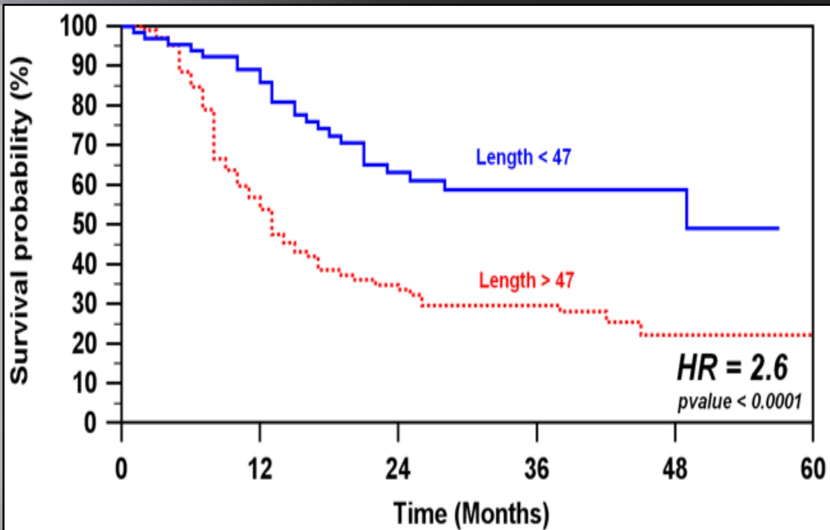

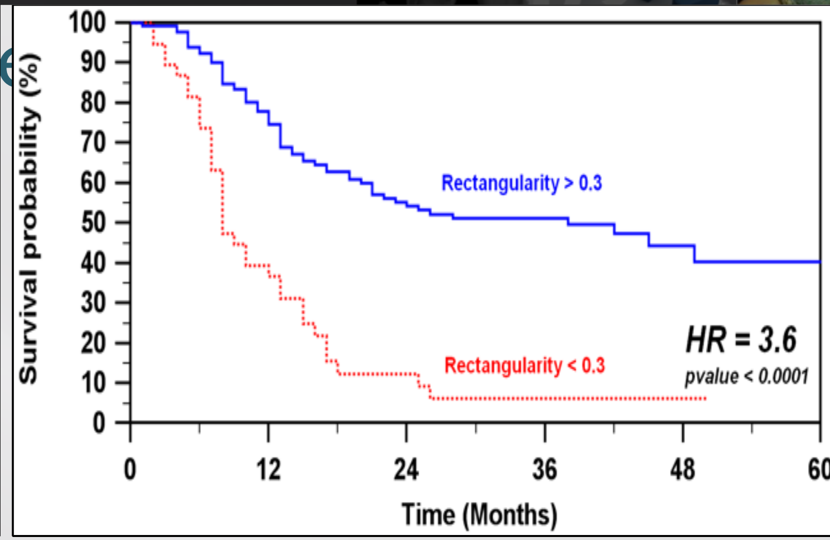

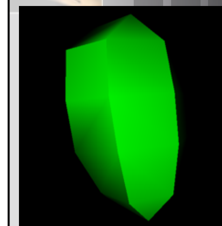

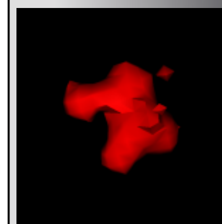

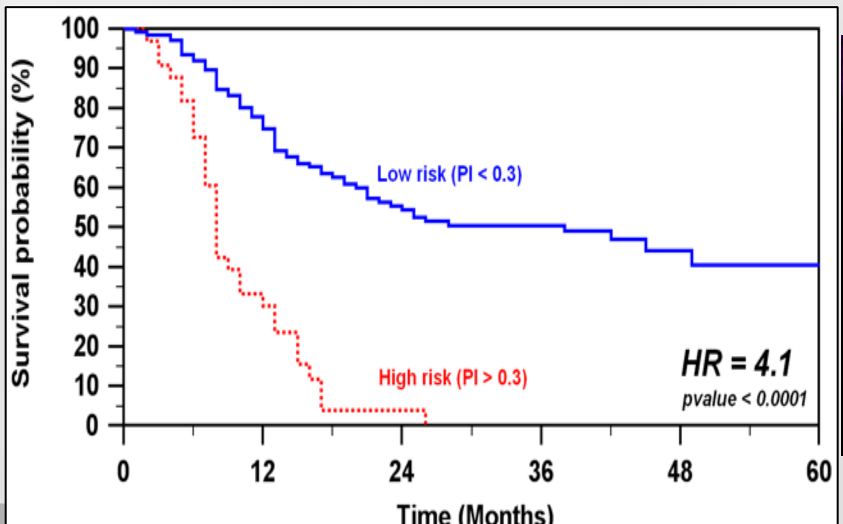

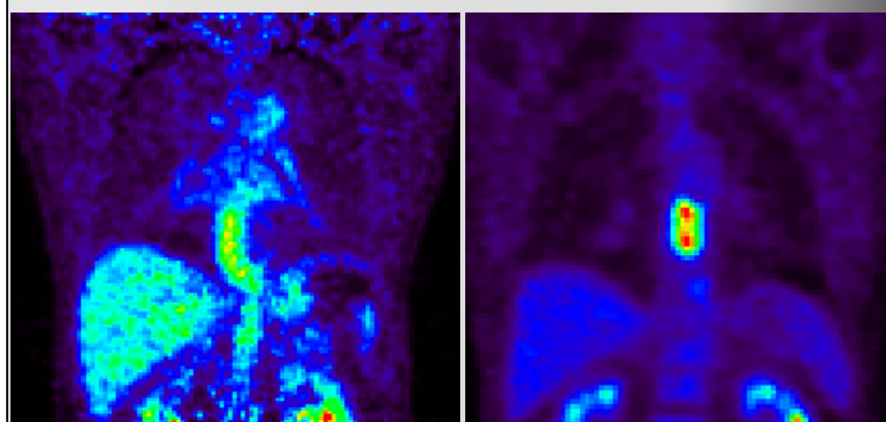

High risk Low risk

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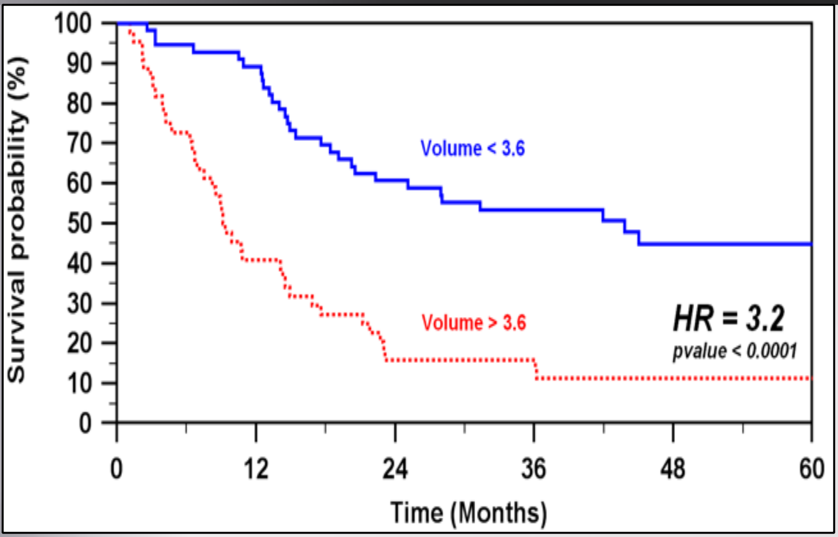
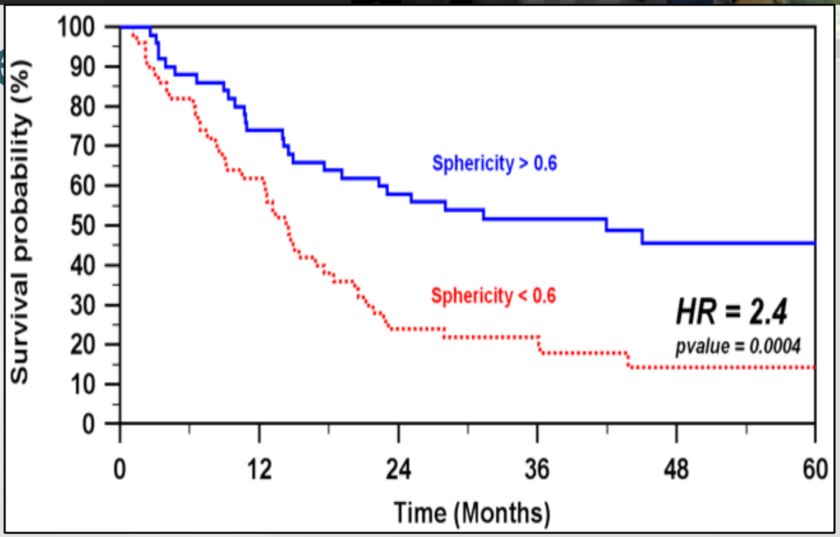
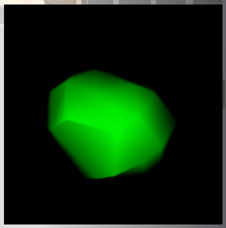
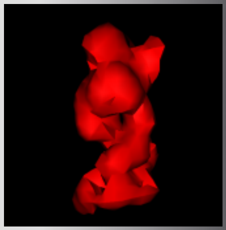
Characterization: geometrical shape









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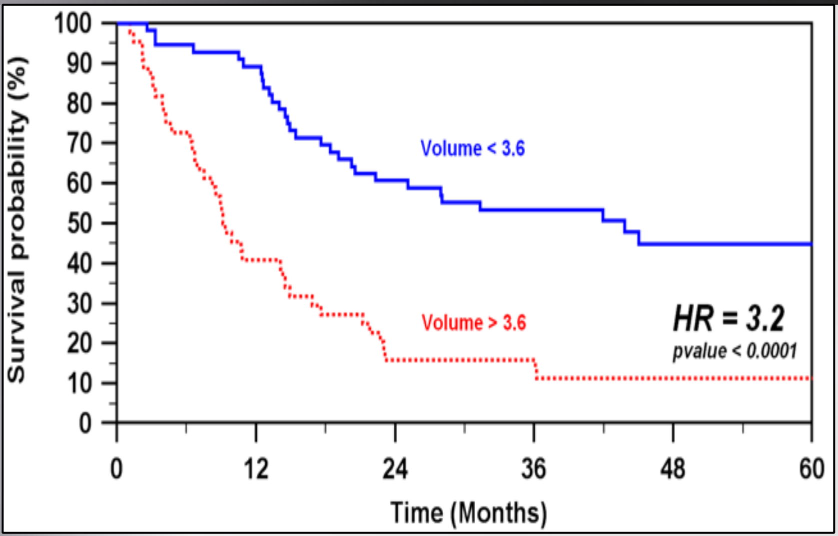

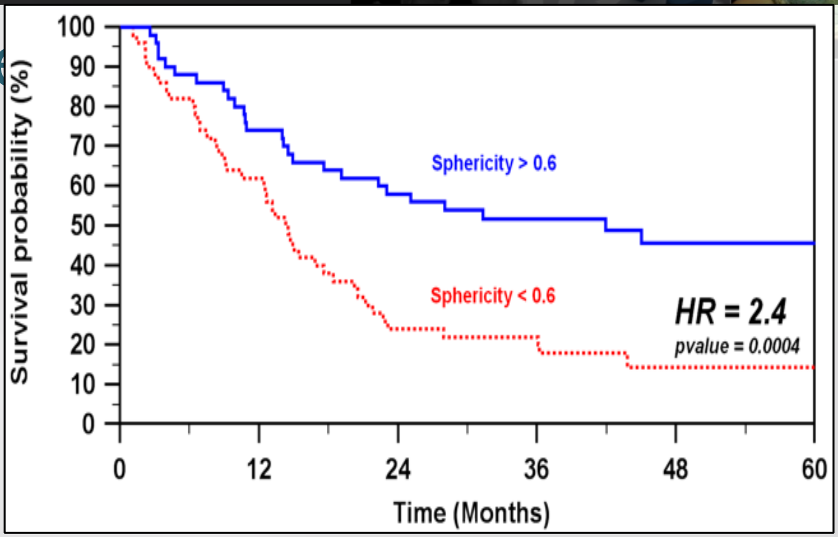

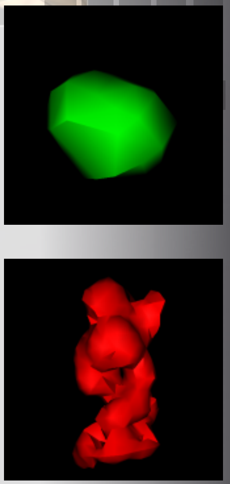

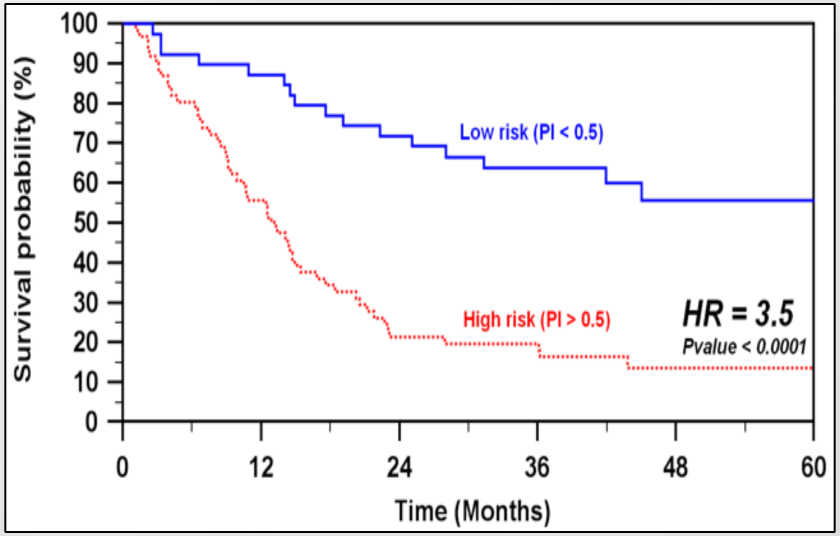

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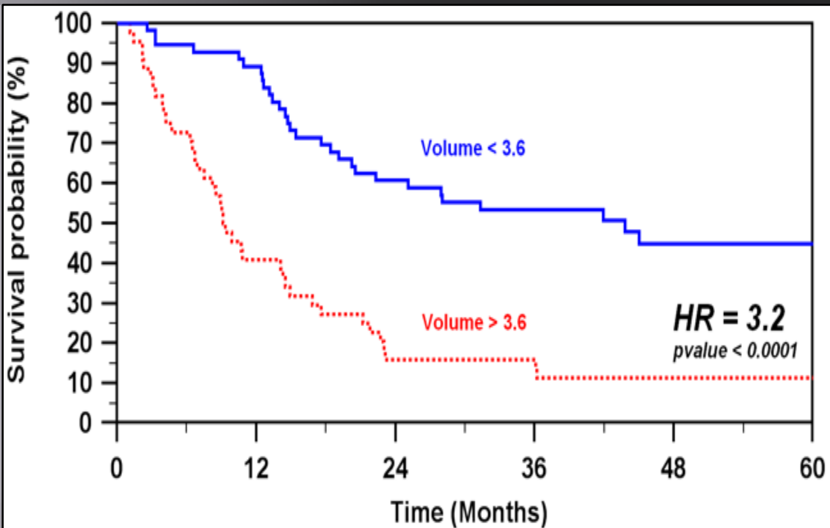

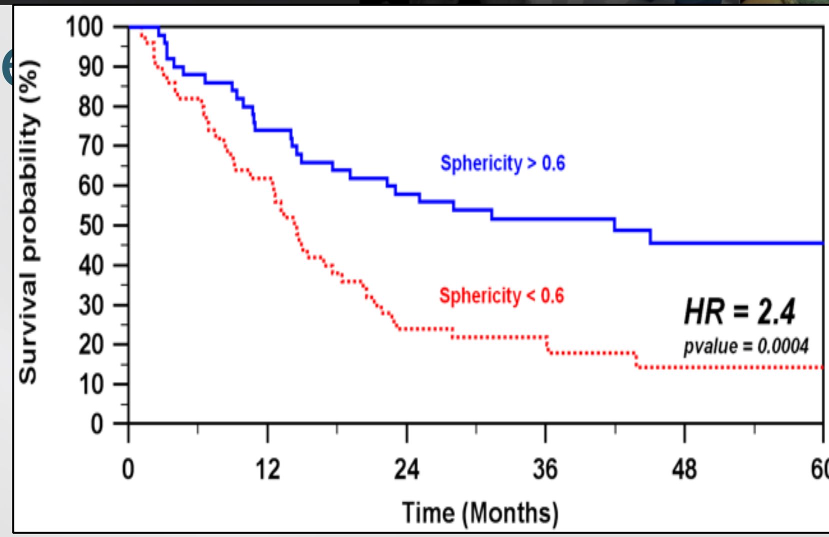

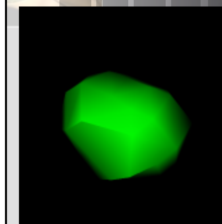

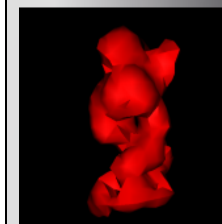

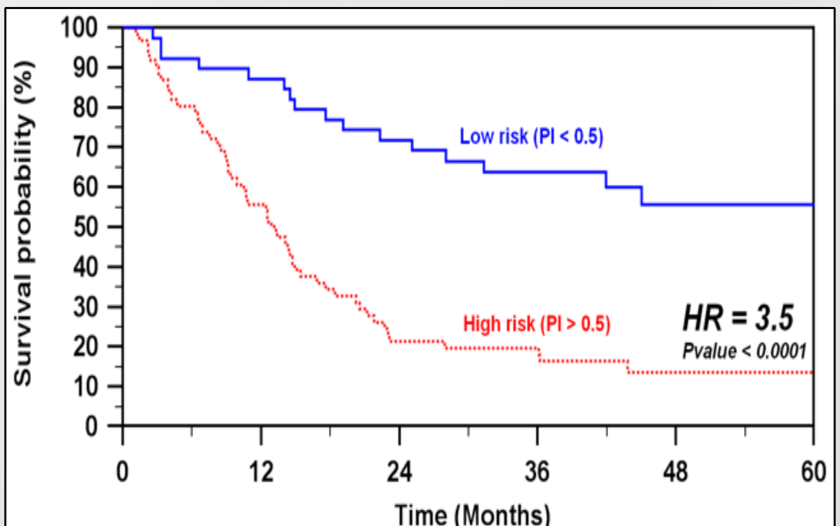

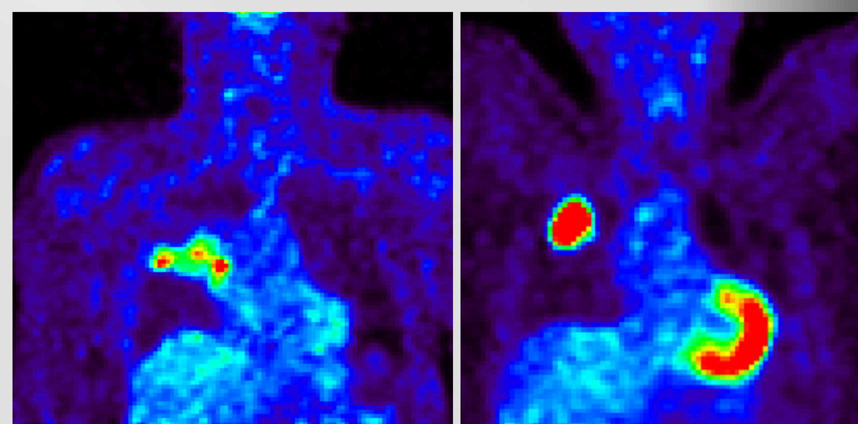

High risk Low risk

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Multimodal characterization of tumors

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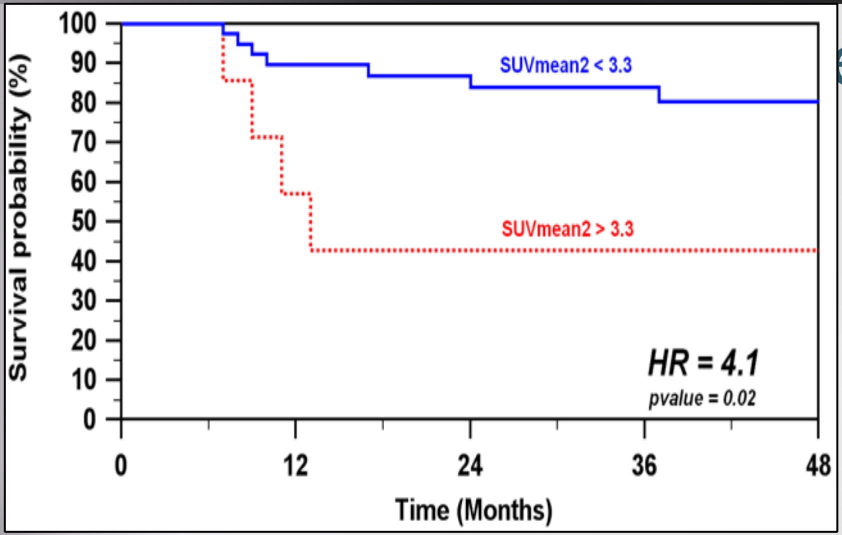

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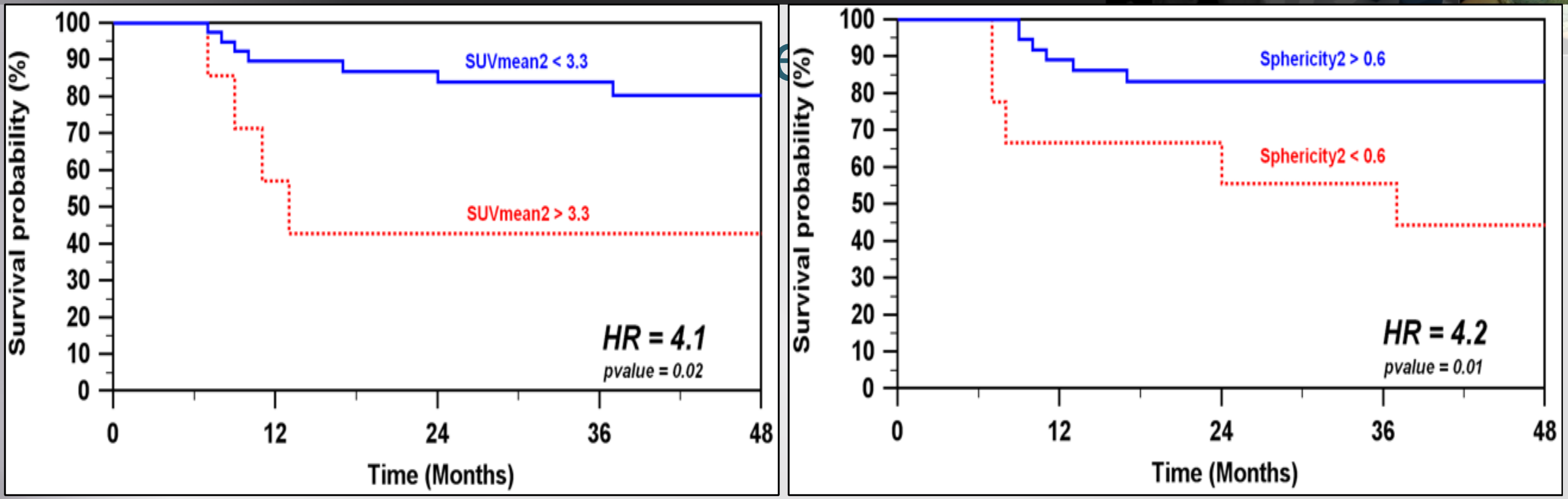

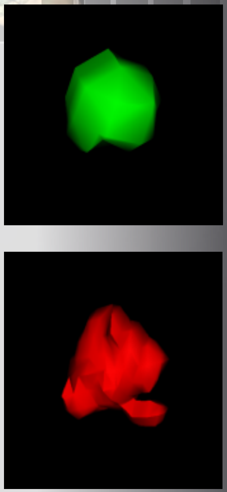

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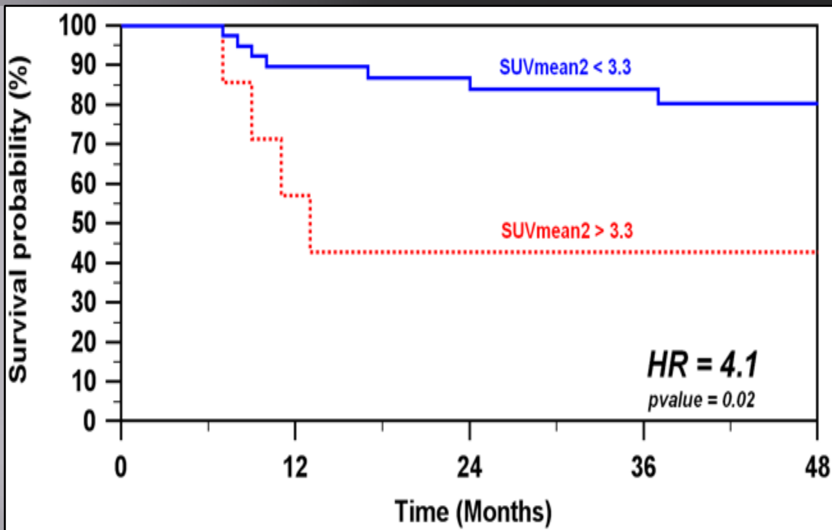

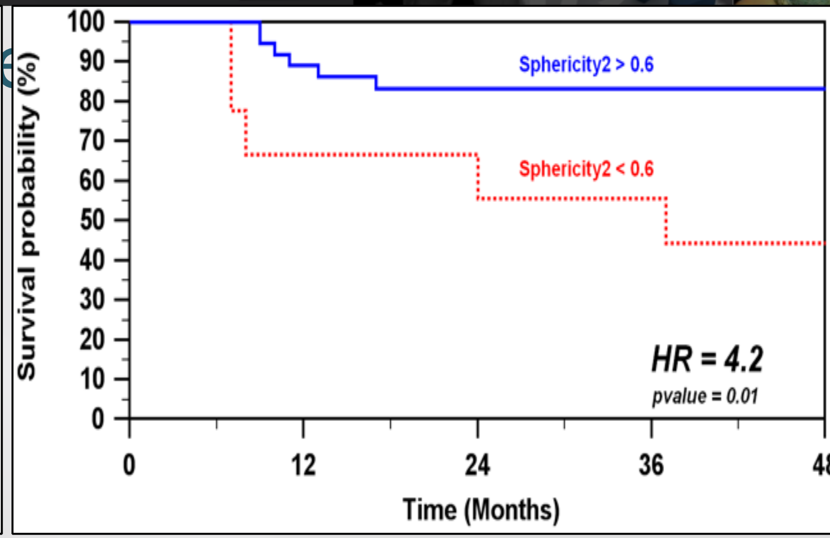

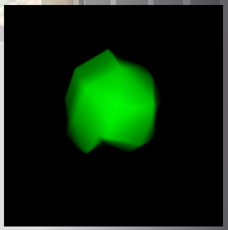

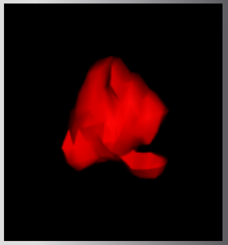

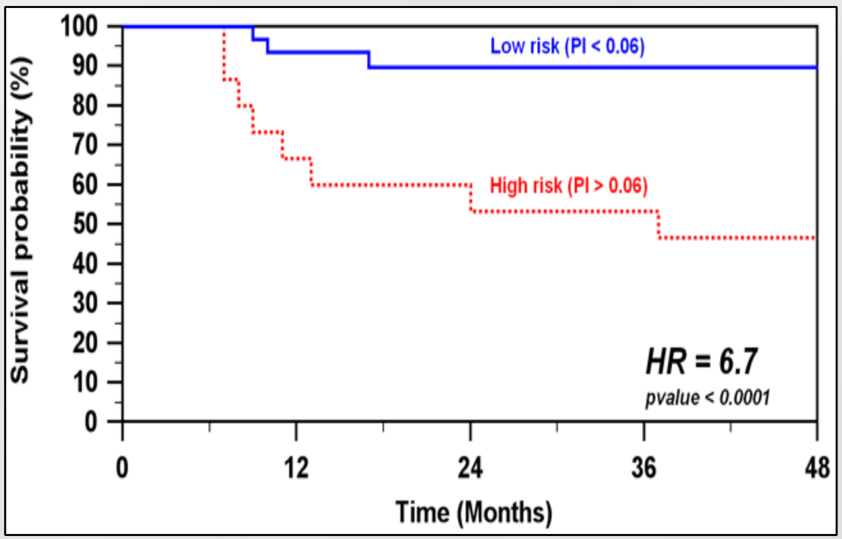

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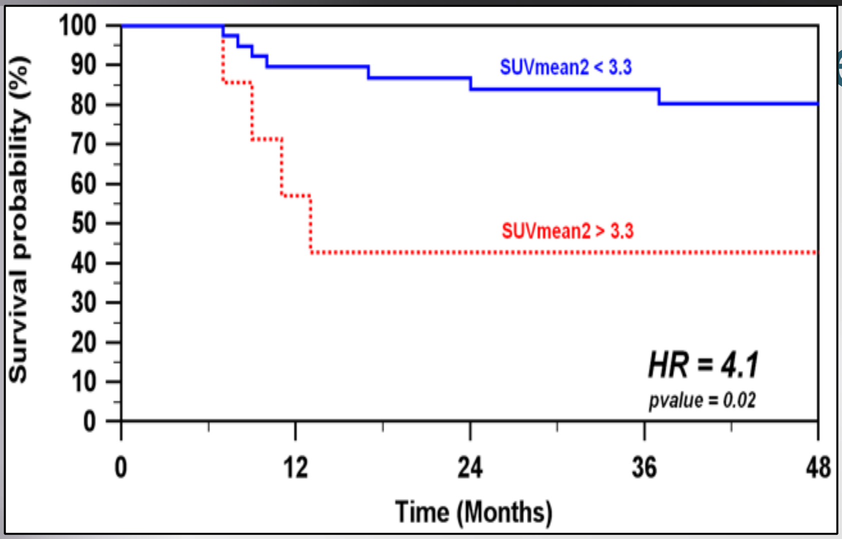

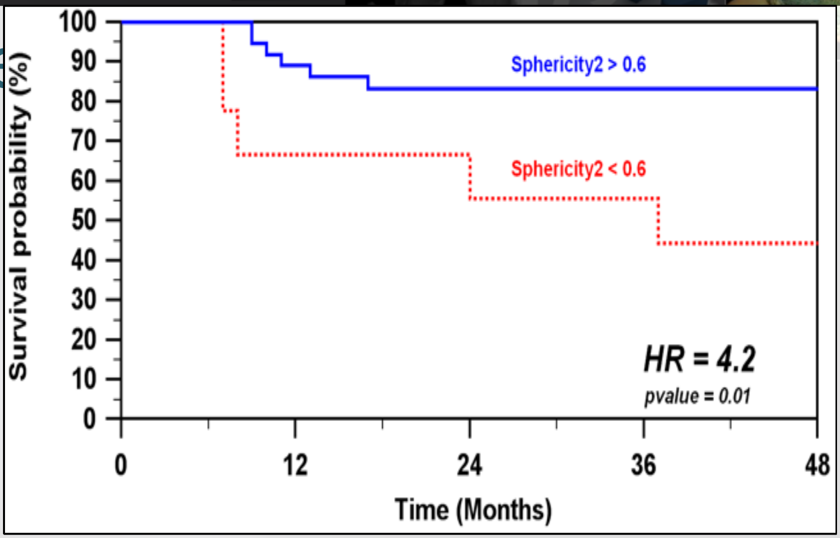

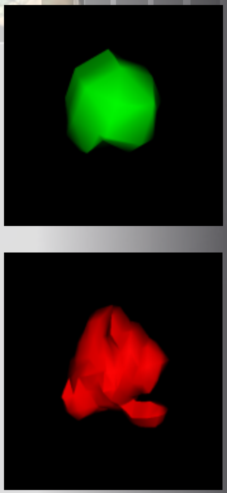

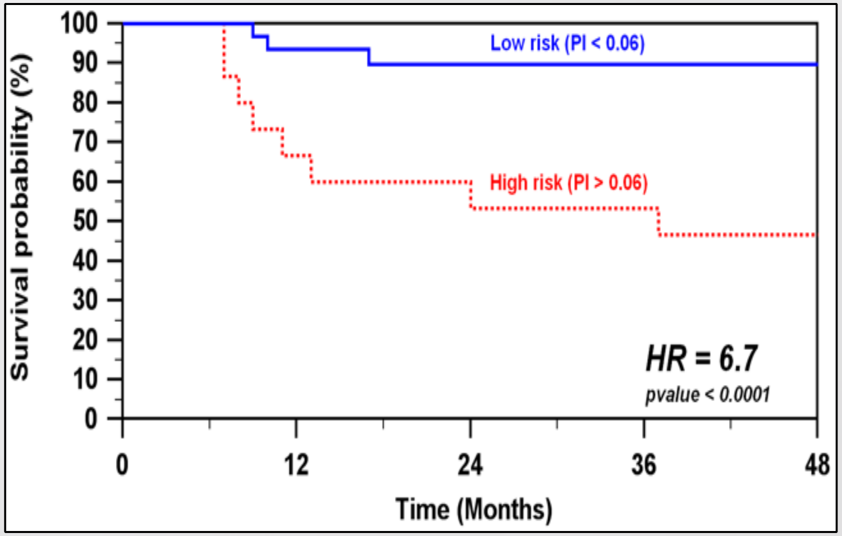

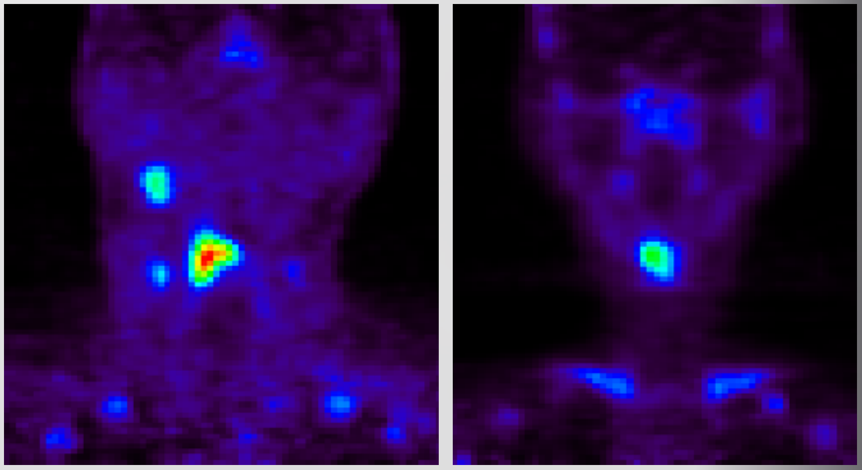

High risk Low risk

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Textural features in PET

The present: technical and practical issues

Reproducibility/variability/robustness

Acta Oncologica, 2013; 52: 1391–1397

informa healthcare

ORIGINAL ARTICLE

Stability of FDG-PET Radiomics features: An integrated analysis of test-retest and inter-observer variability

RALPH T. H. LEIJENAAR[1]*, SARA CARVALHO[1]*, EMMANUEL RIOS VELAZQUEZ[1], WOUTER J. C. VAN ELMPT[1], CHINTAN PARMAR[1], OTTO S. HOEKSTRA[2], CORNELINE J. HOEKSTRA[3], RONALD BOELLAARD[2], ANDRÉ L. A. J. DEKKER[1], ROBERT J. GILLIES[4], HUGO J. W. L. AERTS[1,5] & PHILIPPE LAMBIN[1]

[1]*Department of Radiation Oncology (MAASTRO), GROW-School for Oncology and Developmental Biology, Maastricht University Medical Center (MUMC+), Maastricht, The Netherlands, [2]Department of Radiology and Nuclear Medicine, VU University Medical Center, Amsterdam, The Netherlands, [3]Department of Nuclear Medicine, Jeroen Bosch Medical Center, 's-Hertogenbosch, The Netherlands, [4]Department of Cancer Imaging and Metabolism, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA, and [5]Departments of Radiation Oncology and Radiology, Dana-Farber Cancer Institute, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA*

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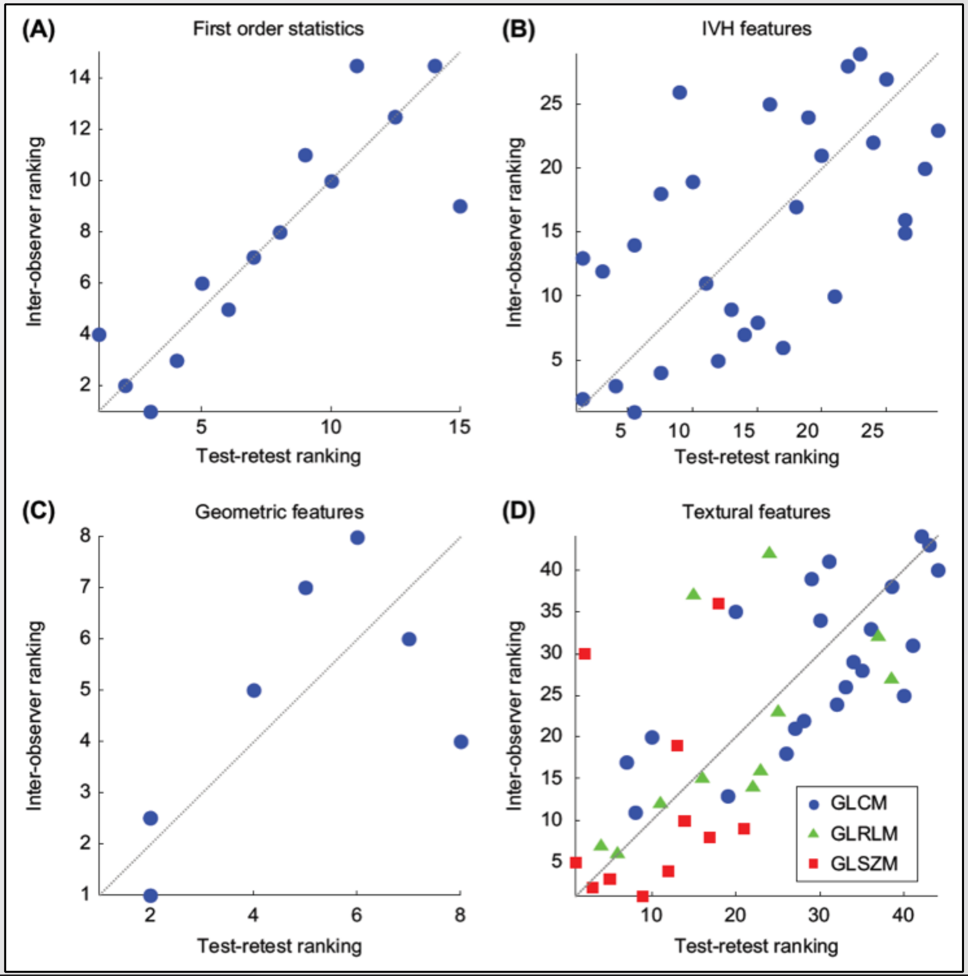

Textural features in PET

The present

Reproducibility/variability/robustness

SCIENTIFIC REPORTS

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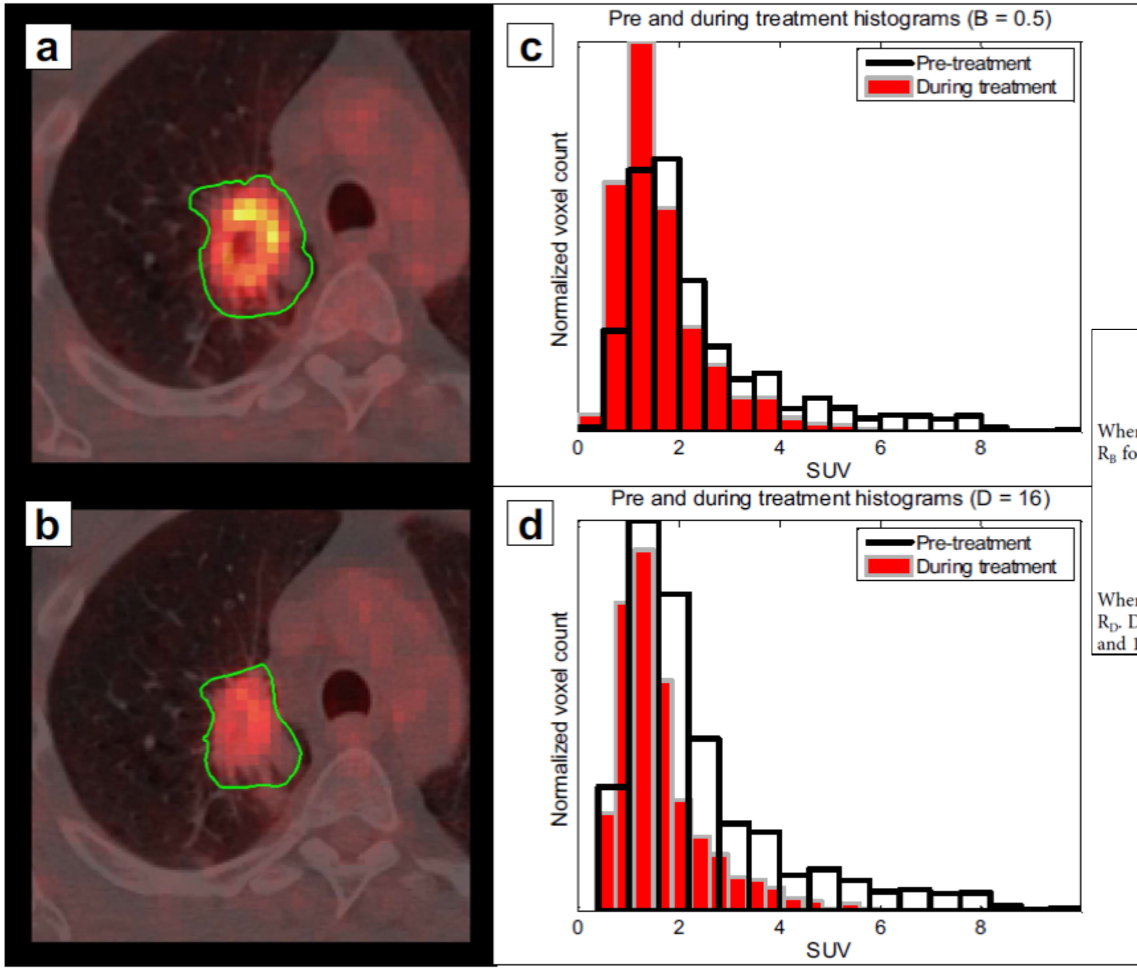
The effect of SUV discretization in quantitative FDG-PET Radiomics: the need for standardized methodology in tumor texture analysis

Ralph T.H. Leijenaar[1], Georgi Nalbantov[1], Sara Carvalho[1], Wouter J.C. van Elmpt[1], Esther G.C. Troost[1], Ronald Boellaard[2], Hugo J.W.L Aerts[1,3], Robert J. Gillies[4] & Philippe Lambin[1]

Textural features in PET

The present

Reproducibility/variability/robustness



$$I_B(x) = \left\lceil \frac{I(x)}{B} \right\rceil - \min\left(\left\lceil \frac{I(x)}{B} \right\rceil\right) + 1 \qquad (1)$$

Where term $[\min(I(x)/B) + 1]$ ensures that the bin count starts at 1. We use the shorthand notation R_B for this resampling method. Resampling SUVs into D bins was performed using:

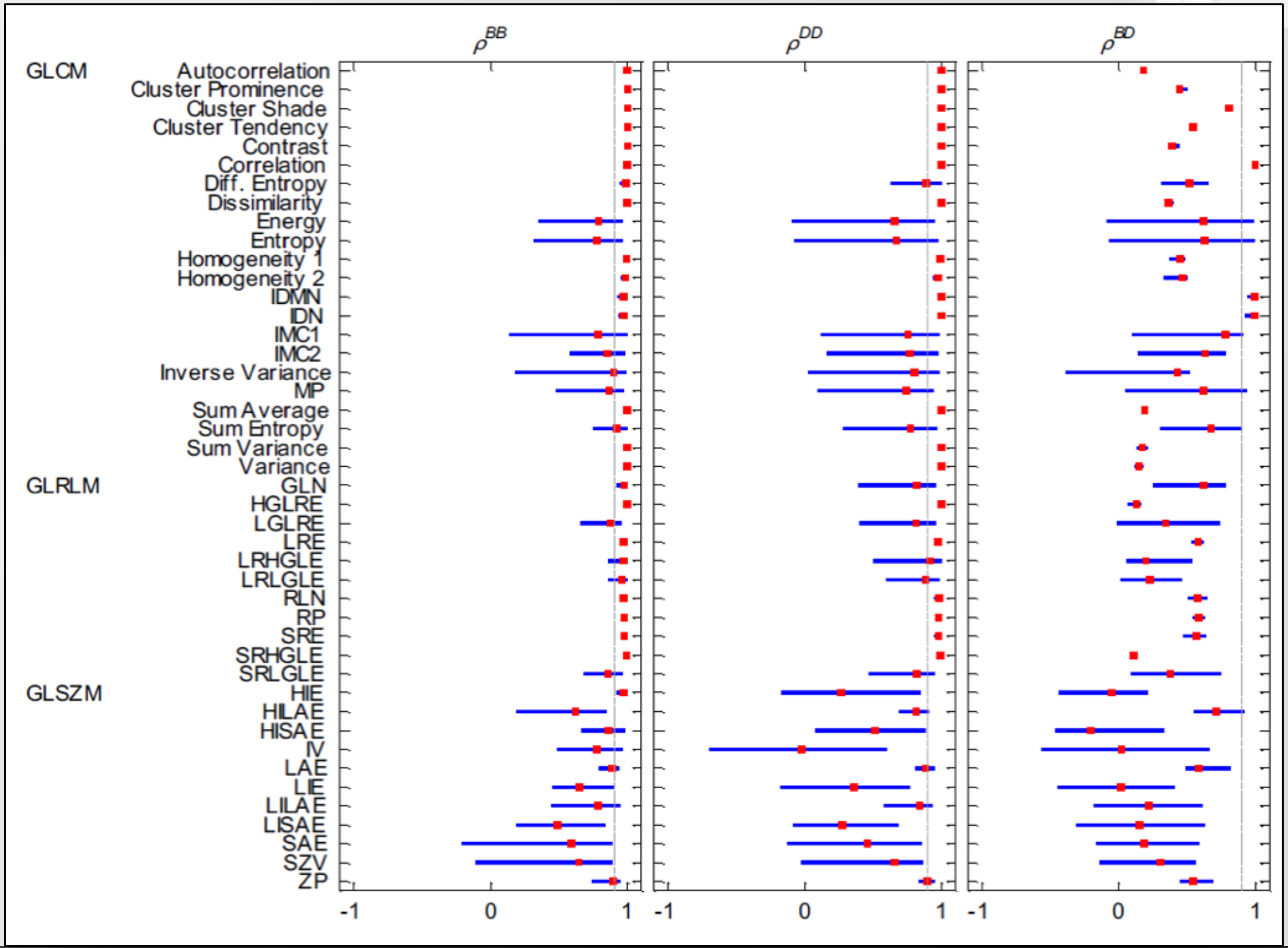
$$I_D(x) = \begin{cases} 1 & I(x) = SUV_{min} \\ \left\lceil D \times \dfrac{I(x) - SUV_{min}}{SUV_{max} - SUV_{min}} \right\rceil & \text{otherwise} \end{cases} \qquad (2)$$

Where the intensity resolution equals $(SUV_{max} - SUV_{min})/D$. This resampling method is denoted by R_D. Discretization using R_B and R_D was performed for different discretization values B (0.05, 0.1, 0.2, 0.5 and 1 [SUV]) and D (8, 16, 32, 64 and 128), respectively.

Textural features in PET

The present

- Reproducibility/variability/robustness



Textural features in PET

The present

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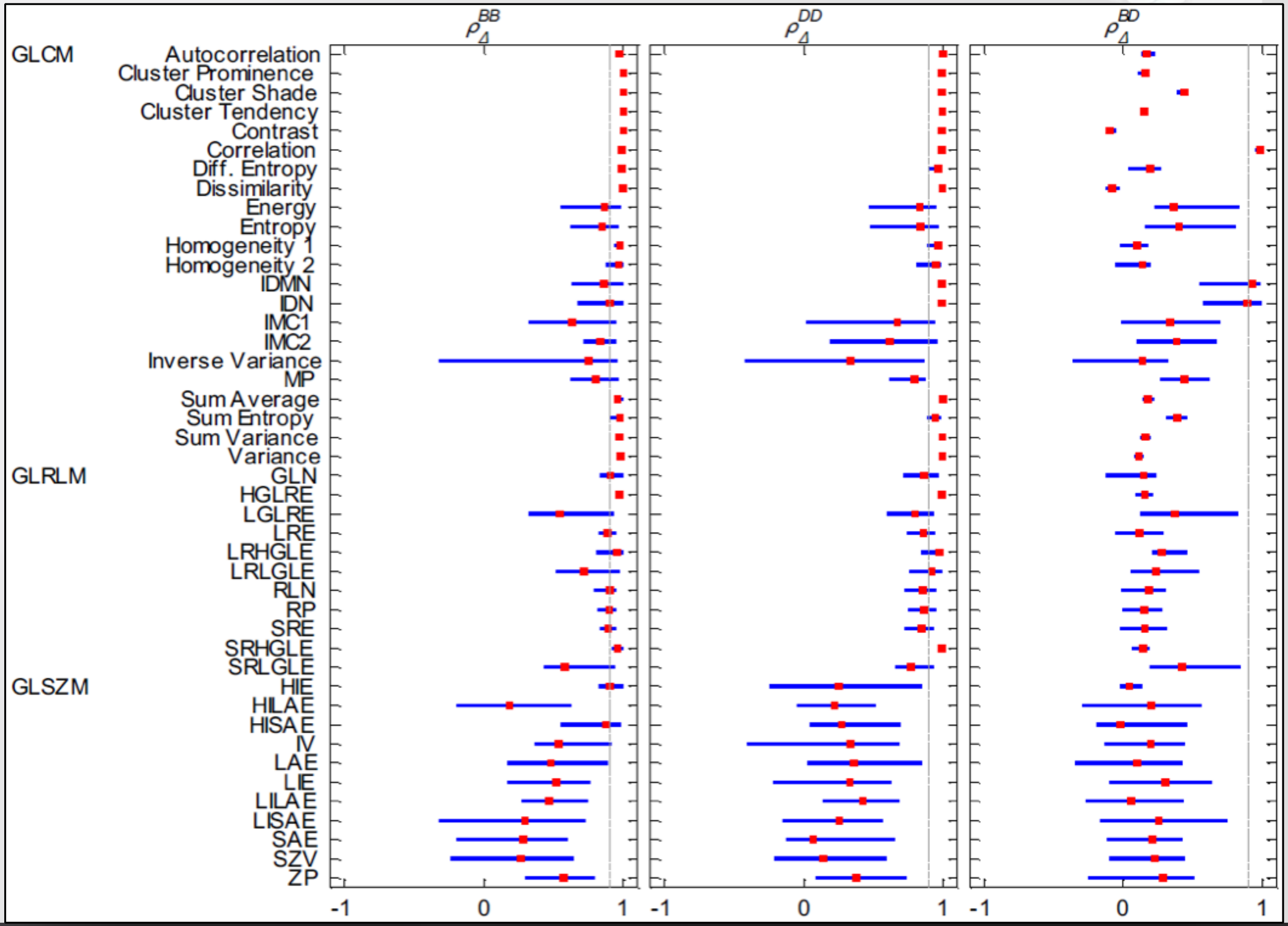


Textural features in PET

The present: technical and practical issues

Reproducibility/variability/robustness

Impact of image reconstruction settings on Texture Features in ^{18}F-FDG PET

Jianhua Yan, Jason Chu-Shern Lim, Hoi Yin Loi, Lih Kin Khor, Arvind Kumar Sinha, Swee Tian Quek, Ivan WK Tham and David William Townsend

J Nucl Med.
Published online: July 30, 2015.
Doi: 10.2967/jnumed.115.156927

Textural features in PET

The present: technical and practical issues

Reproducibility/variability/robustness

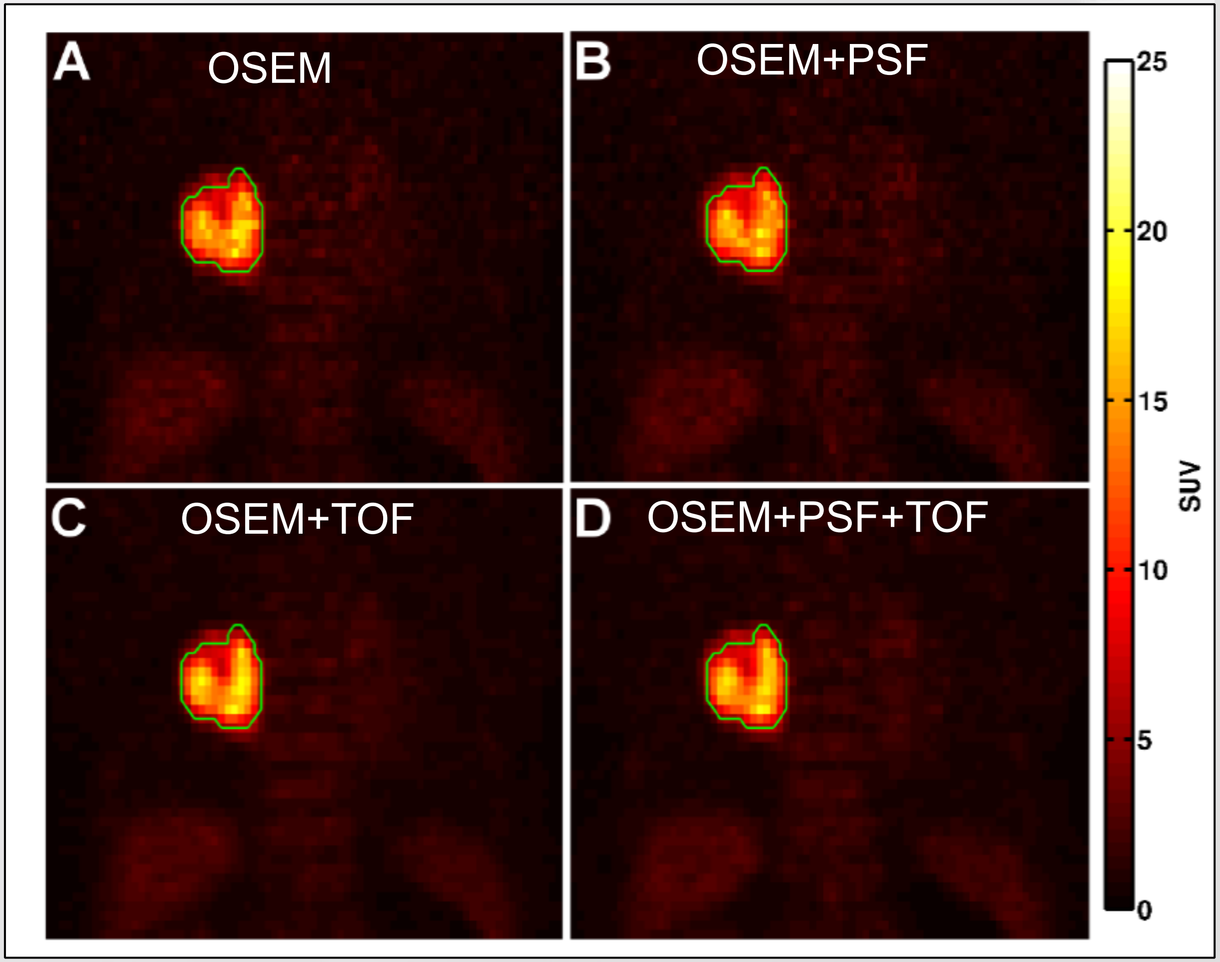
TABLE 1
List of reconstruction settings

Reconstruction algorithm	**Variation over the default reconstruction settings**	**Impact of iteration number on image features** FWHM: 2.5 mm; Grid size: 256 × 256	**Impact of FWHM on image features** iteration: 2; Grid size: 256 × 256	**Impact of grid size on image features** iteration: 2; FWHM: 2.5mm
OSEM	iteration: 2 FWHM: 2.5 mm; Grid size: 256 × 256	iteration: 1, 2, 3	FWHM: 2.5, 3.5, 4.5, 5.5 mm;	Grid size: 256 × 256 128 × 128
OSEM+PSF	iteration: 2 FWHM: 2.5 mm; Grid size: 256 × 256	iteration: 1, 2, 3	FWHM: 2.5, 3.5, 4.5, 5.5 mm;	Grid size: 256 × 256 128 × 128
OSEM+TOF	iteration: 2 FWHM: 2.5 mm; Grid size: 256 × 256	iteration: 1, 2, 3	FWHM: 2.5, 3.5, 4.5, 5.5 mm;	Grid size: 256 × 256 128 × 128
OSEM+PSF+TOF	iteration: 2 FWHM: 2.5 mm; Grid size: 256 × 256	iteration: 1, 2, 3	FWHM: 2.5, 3.5, 4.5, 5.5 mm;	Grid size: 256 × 256 128 × 128

Textural features in PET

The present: technical and practical issues

Reproducibility/variability/robustness



Textural features in PET

The present: technical and practical issues

Reproducibility/variability/robustness

TABLE 2

Change of image features over the default reconstruction settings

	COV≤5%	5%<COV≤10%	10%<COV≤20%	COV>20%
SUV	SUVmean, SUVpeak	SUVmax		
FOS	Entropy	COV, Kurtosis, Energy	Variance	Skewness
GLCM	Dissimilarity, Energy, Entropy, ID,SE, DE, IMC, IDM, IDMN, DM, SDN	Contrast, Correlation, Homogeneity, MP, SA, DV	Autocorrelation, SOS, SV	CS
GLRLM	GLNr, RP,LGRE, HGRE		SRE, LRE, RLN, SRLGE, SRHGE, LRLGE, LRHGE	
GLSZM	GLNz, LGZE	ZLN, HGZE, WVGLZ_S	SZE, LZE, SZLGE, SZHGE, LZLGE, LZHGE, WVGLZ_N	ZP
NGLDM	Entropy	SNE, NN, SM	LNE	
NGTDM		Coarseness, Busyness, Complexity, TS	Contrast	

Textural features in PET

The present: technical and practical issues

Reproducibility/variability/robustness

TABLE 5

Impact of grid size on image features

	COV≤5%	5%<COV≤10%	10%<COV≤20%	COV>20%
SUV		SUVmean, SUVpeak	SUVmax	
FOS	Entropy		Kurtosis, Variance, COV, Energy	Skewness
GLCM	DE, IDM, IDMN	SA, SE	Autocorrelation, Entropy, ID, SOS, SV	Contrast, Correlation, CS, Dissimilarity, Energy, Homogeneity, MP, DV, IMC, DM, SDN
GLRLM	LGRE, HGRE			LRE, SRE, GLNr, RLN, RP, SRLGE, SRHGE , LRLGE ,LRHGE
GLSZM	LGZE		SZE, LZE, LZLGE, HGZE, SZLGE, LZHGE	GLNz, ZLN, ZP, SZHGE, WVGLZ_N, WVGLZ_S
NGLDM			SNE	LNE, NN, SM, Entropy
NGTDM				Coarseness, Contrast, Busyness, Complexity, TS

Reproducibility/variability/robustness

Journal of Medical Imaging 2(4), 041002 (Oct–Dec 2015)

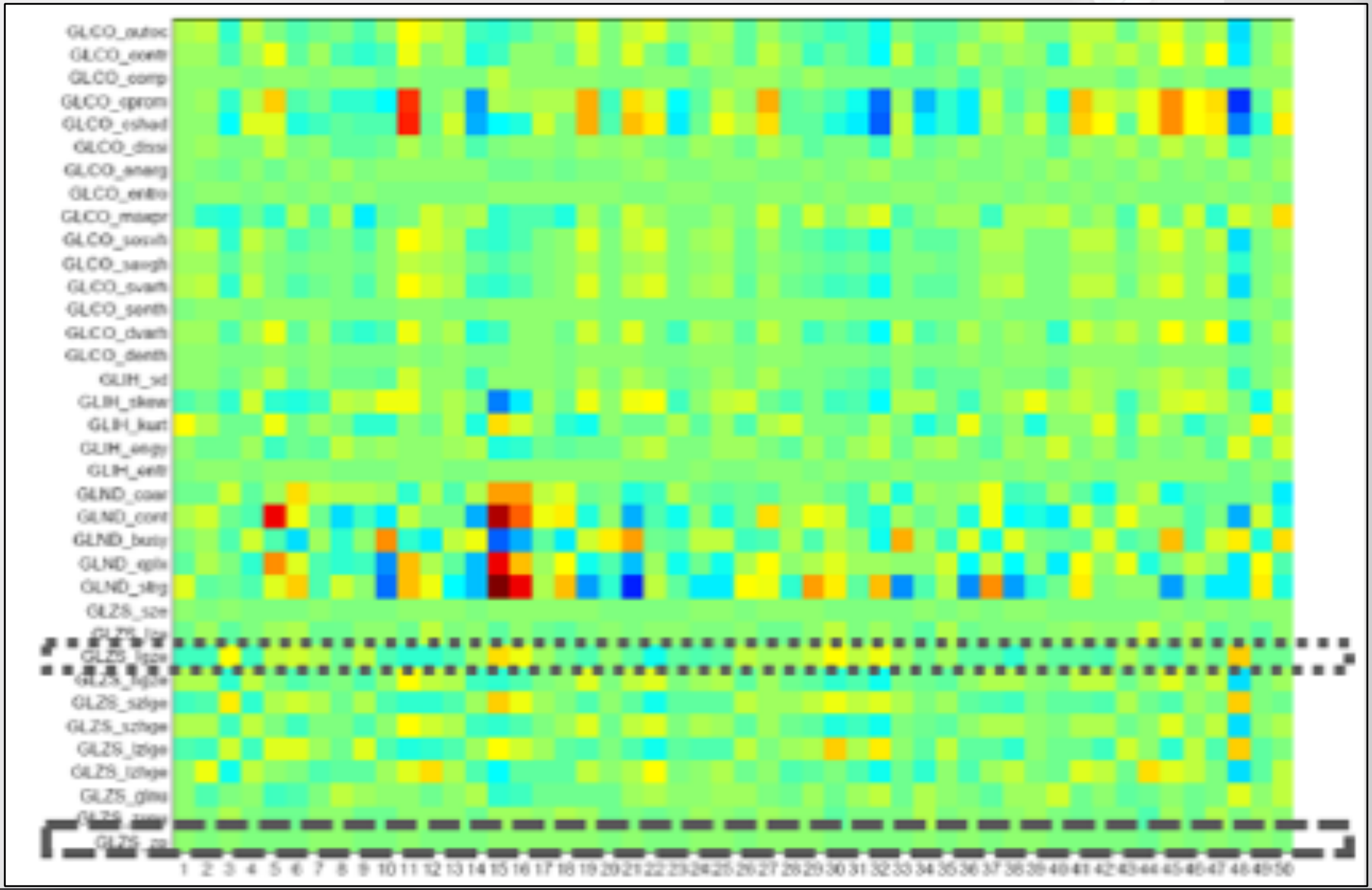
Quantitative radiomics: impact of stochastic effects on textural feature analysis implies the need for standards

Matthew J. Nyflot,[a,*] Fei Yang,[a] Darrin Byrd,[b] Stephen R. Bowen,[a,b] George A. Sandison,[a] and Paul E. Kinahan[b]
[a]University of Washington, Department of Radiation Oncology, 1959 NE Pacific Street, Box 356043, Seattle, Washington 98195-6043, United States
[b]University of Washington, Department of Radiology, 1959 NE Pacific Street, Box 356043, Seattle, Washington 98195-6043, United States

Textural features in PET

The present: technical and practical issues

Reproducibility/variability/robustness



Textural features in PET

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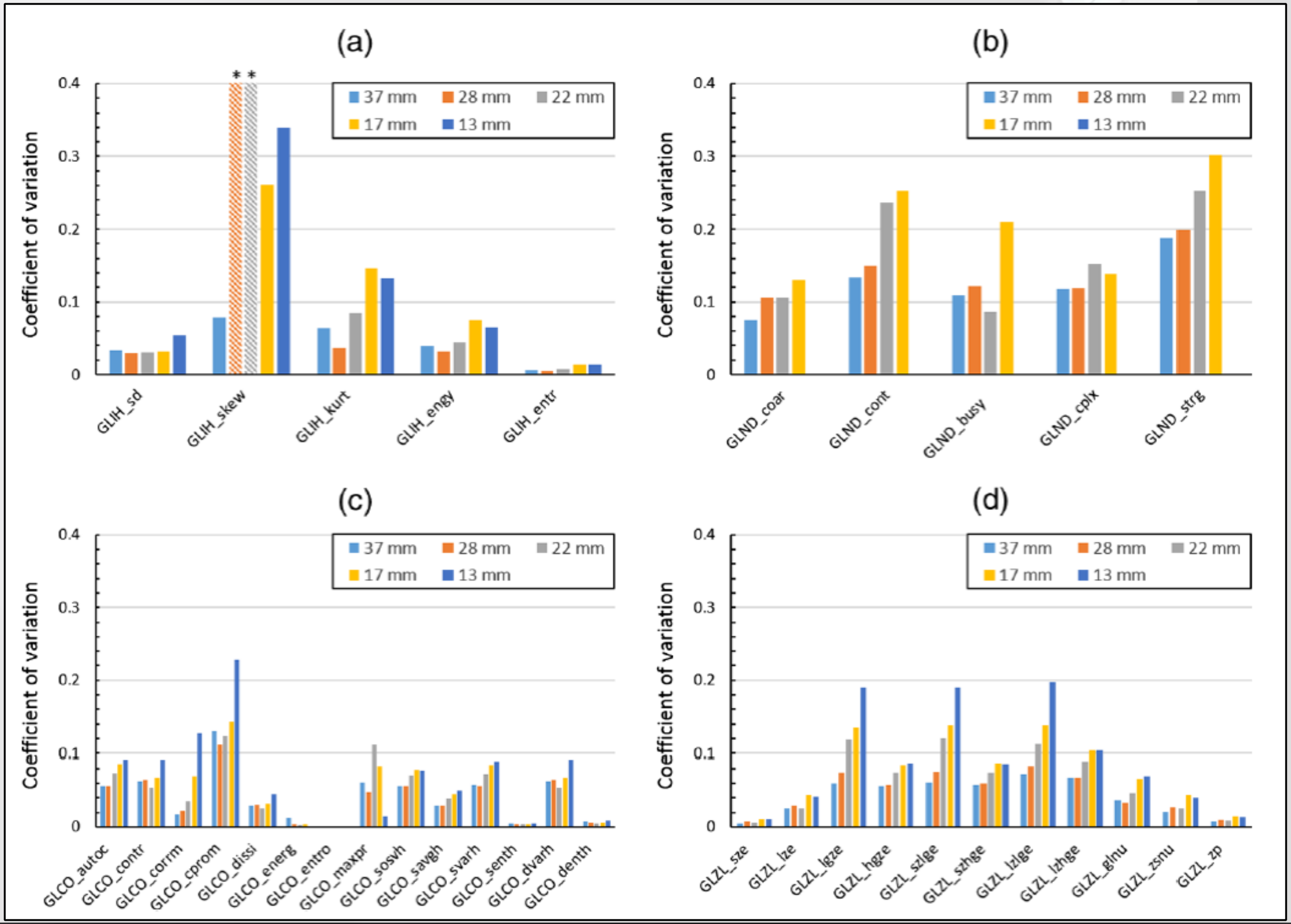

Textural features in PET

… any future? : an example

Challenges

- A recent example

IOP Publishing | Institute of Physics and Engineering in Medicine   Physics in Medicine & Biology

Phys. Med. Biol. **60** (2015) 5471–5496   doi:10.1088/0031-9155/60/14/5471

A radiomics model from joint FDG-PET and MRI texture features for the prediction of lung metastases in soft-tissue sarcomas of the extremities

M Vallières[1], C R Freeman[2], S R Skamene[2] and I El Naqa[1,2]

[1] Medical Physics Unit, McGill University, 845 Rue Sherbrooke O, Montreal QC H3A 0G4, Canada
[2] Radiation Oncology, McGill University Health Centre, 1547 Pine Avenue West, Montreal Qc H3G 1B3, Canada

Textural features in PET

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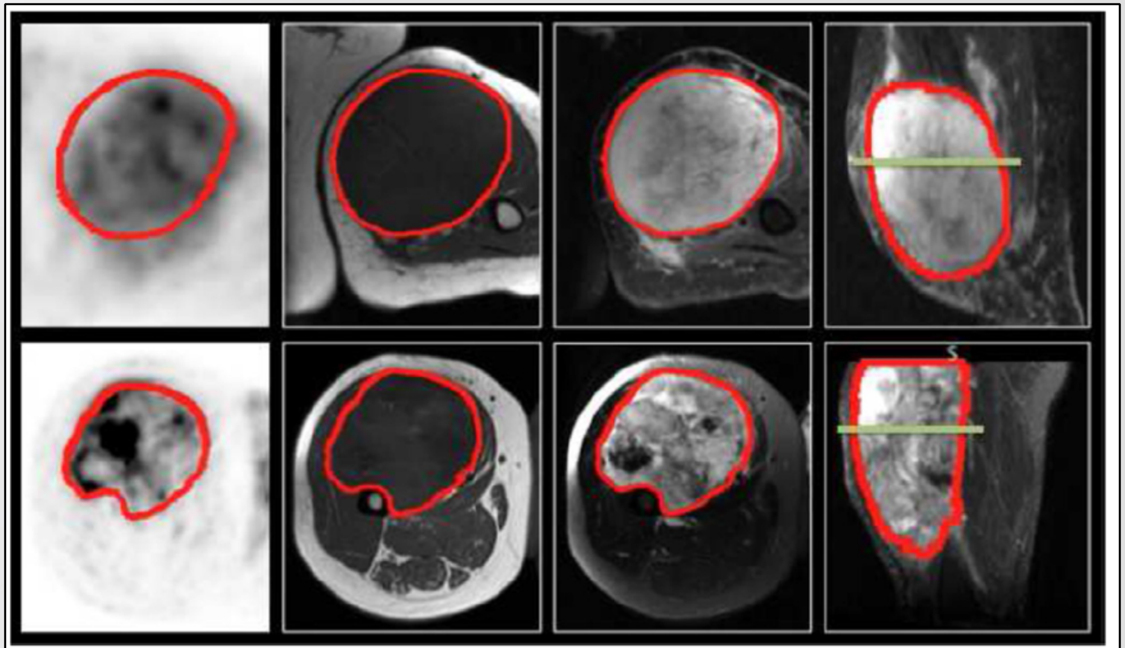
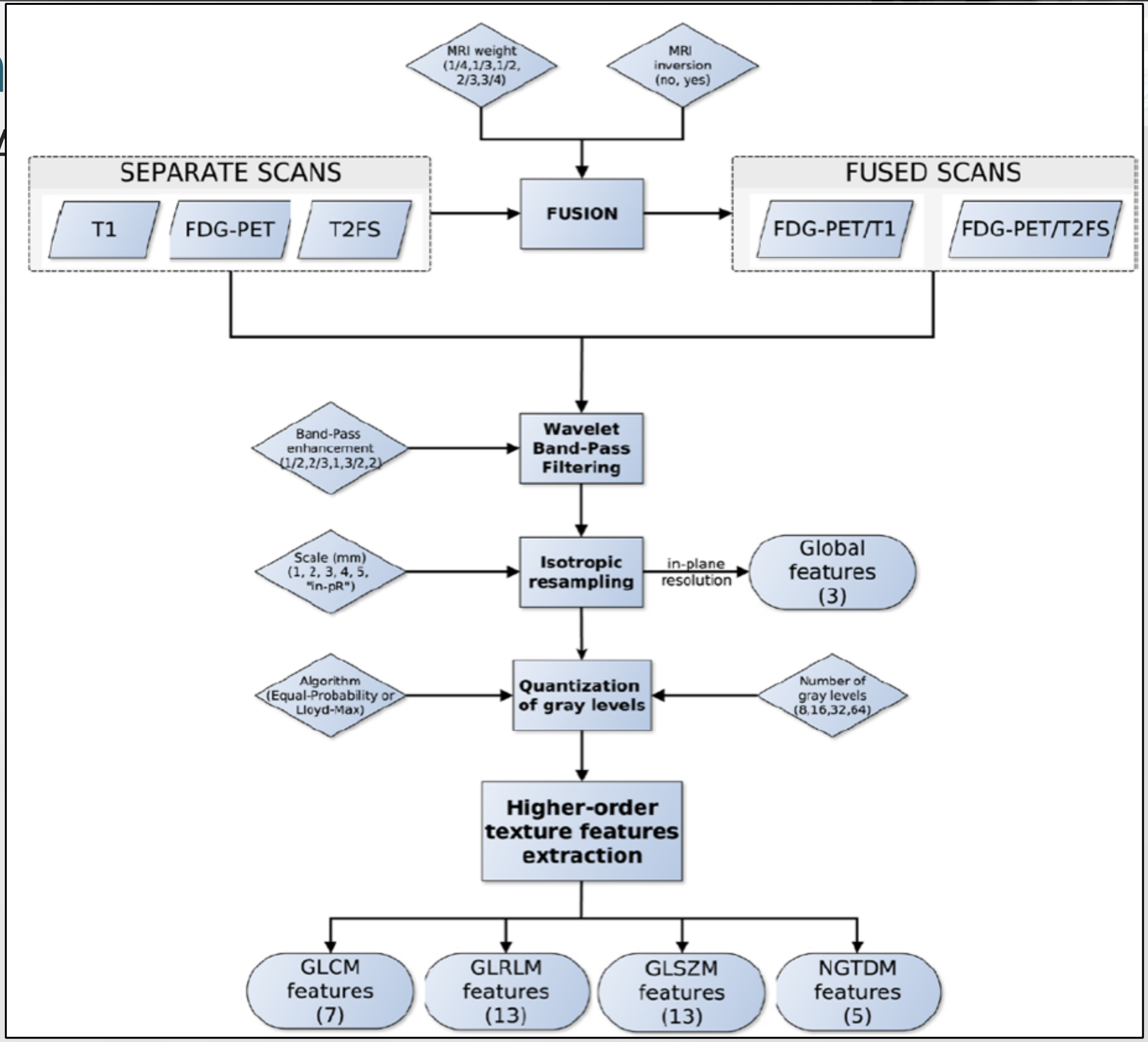


Figure 1. FDG-PET and MRI diagnostic images of two patients with soft-tissue sarcomas of the extremities. Top row: patient that did not develop lung metastases. Bottom row: patient that eventually developed lung metastases. 1st column: FDG-PET images, axial plane. 2nd column: T1-weighted images, axial plane. 3rd column: T2-weighted fat-saturated images, axial plane. 4th column: short tau inversion recovery images, sagittal plane. The green lines in the two images of the 4th column correspond to the plane shown in the three other respective images.

Textural features in PET

… any future? : an example

- Ch
  - A



Textural features in PET

… any future? : an example

Challenges

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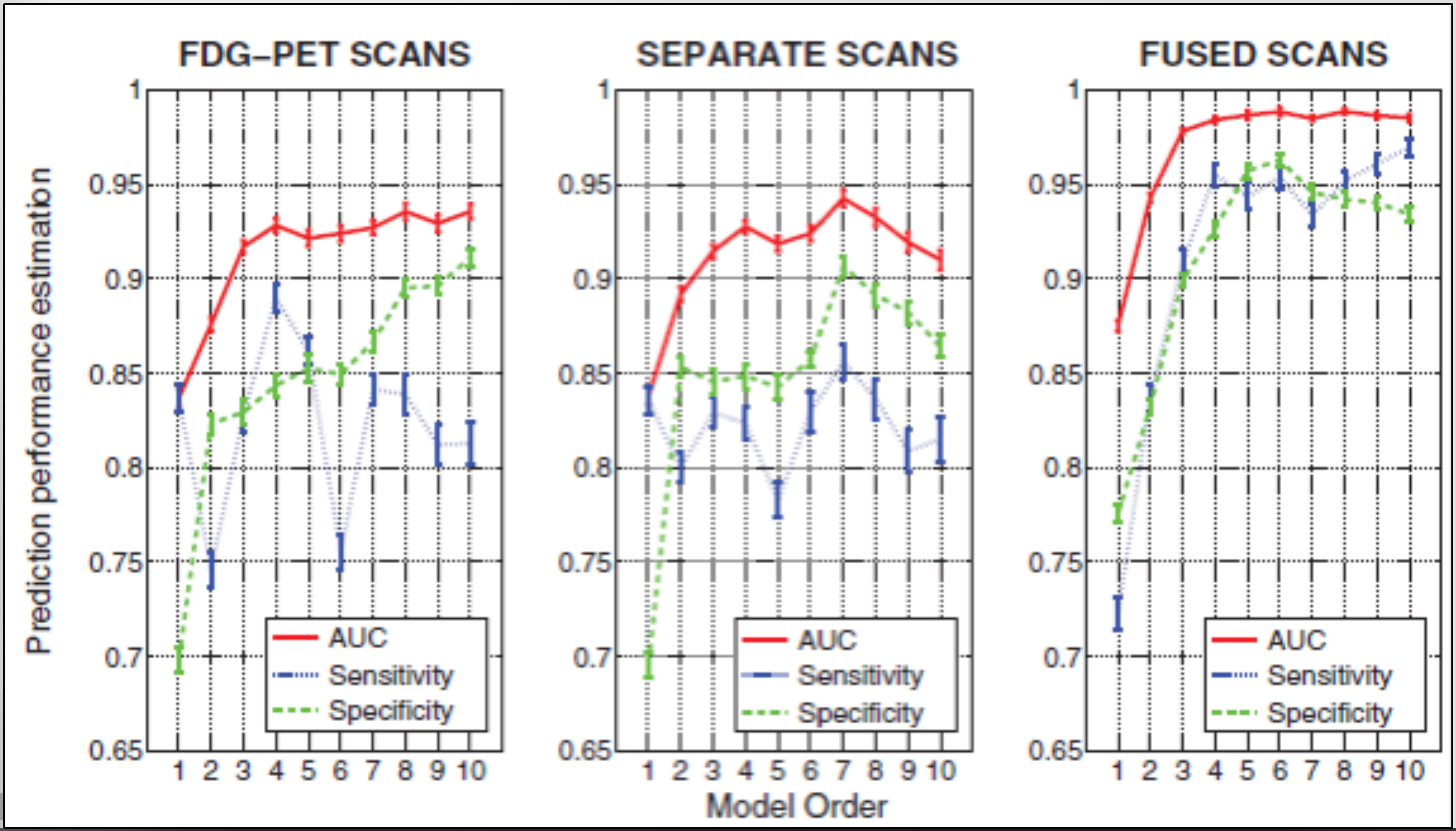

Textural features in PET

… any future? : an example

Challenges

- A recent example

$$
\begin{aligned}
g(\mathbf{x}_i) = \; & -256 \times \text{FDG-PET/T2FS}(\textit{MRI Inv.} = \text{No Inv.}, \textit{MRI weight} = 1/2, R = 3/2, \textit{Scale} = 3\,\text{mm}, \textit{Quant. algo.} = \text{Lloyd-Max}, \textit{Ng} = 64) -- \text{GLSZM/SZE} \\
& + 5360 \times \text{FDG-PET/T1}(\textit{MRI Inv.} = \text{Inv.}, \textit{MRI weight} = 1/2, R = 1/2, \textit{Scale} = \textit{in-pR}, \textit{Quant. algo.} = \text{Lloyd-Max}, \textit{Ng} = 16) -- \text{GLSZM/ZSV} \\
& + 1.75 \times \text{FDG-PET/T1}(\textit{MRI Inv.} = \text{Inv.}, \textit{MRI weight} = 3/4, R = 1, \textit{Scale} = 2\,\text{mm}, \textit{Quant. algo.} = \text{Lloyd-Max}, \textit{Ng} = 8) -- \text{GLSZM/HGZE} \\
& + 3.16 \times \text{FDG-PET/T2FS}(\textit{MRI Inv.} = \text{Inv.}, \textit{MRI weight} = 3/4, R = 2, \textit{Scale} = 1\,\text{mm}, \textit{Quant. algo.} = \text{Equal}, \textit{Ng} = 8) -- \text{GLRLM/HGRE} \\
& + 26.7 \qquad (7)
\end{aligned}
$$

Introduction
Textural features in PET: quantify uptake heterogeneity

- Methodological choices have a strong impact
  - Required steps
    - Pre-processing (noise, PVE, segmentation…)

Haralick, et al. Textural Features for Image Classification. IEEE Transactions on Systems, Man and Cybernetics. 1973
The GLCM tutorial page http://www.fp.ucalgary.ca/mhallbey/tutorial.htm

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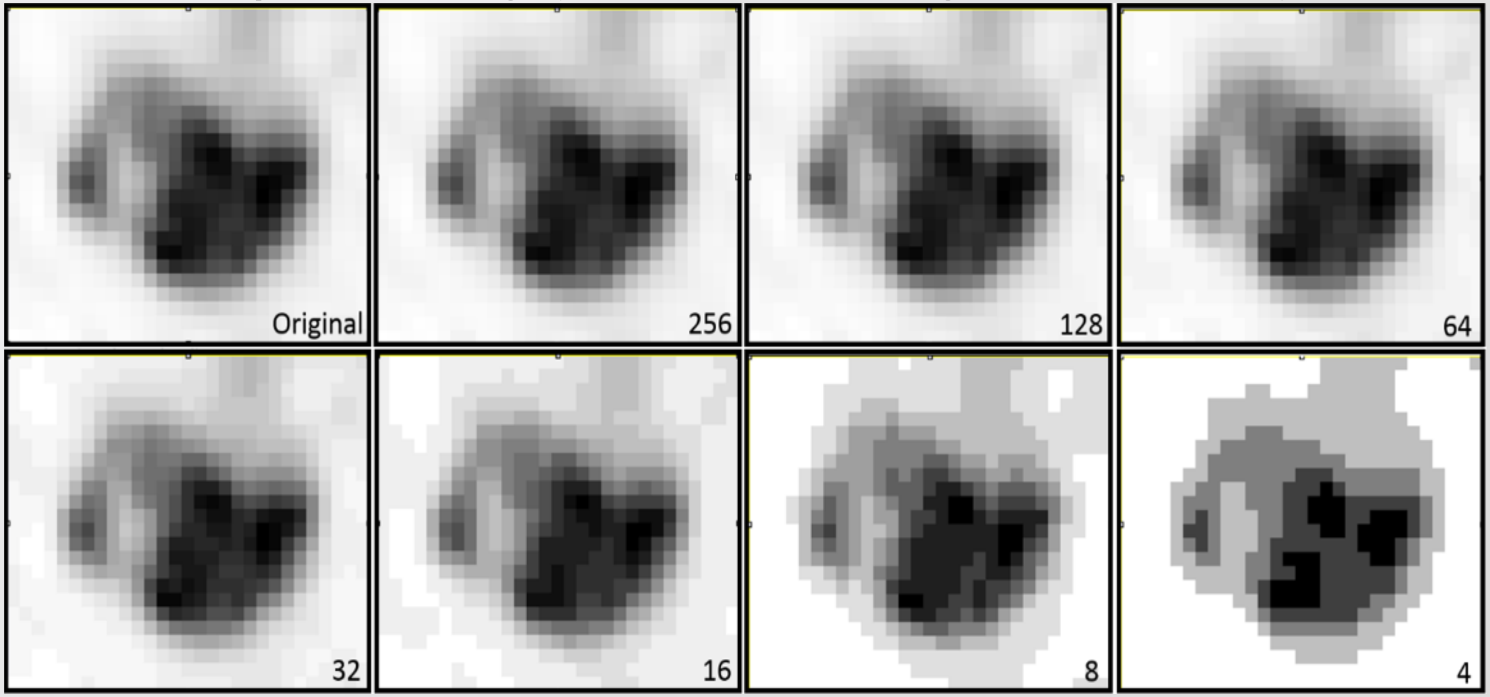

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      - One matrix taking into account all directions
    - Choice of parameters
      - Robust / reproducible?
      - Clinical value?

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Multimodal characterization of tumors

Characterization: heterogeneity

- How we think it works *vs.* how it **actually** works

Multimodal characterization of tumors

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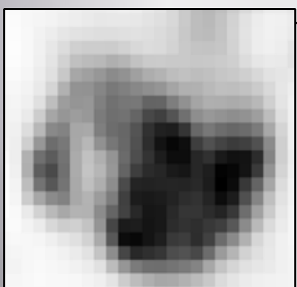
Image



PET or CT?
Acquisition protocol? Gating?
Reconstruction process?
Post-reconstruction processing?

Pre-processing

Denoising?
Contrast-enhancement?

Defining region of analysis

2D? 3D?
Segmentation method?

Quantization

4? … 256?
Equalization? Uniform?

Matrices

1 … 13 directions?
Averaging?

Parameters

Hundreds of features:
Evaluation + choice
Statistics + machine learning

<u>Potentially</u> useful heterogeneity quantification

Multimodal characterization of tumors

Characterization: heterogeneity

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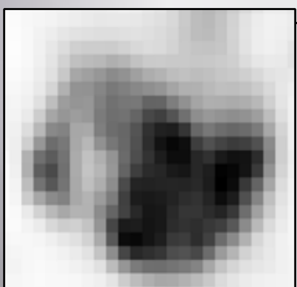

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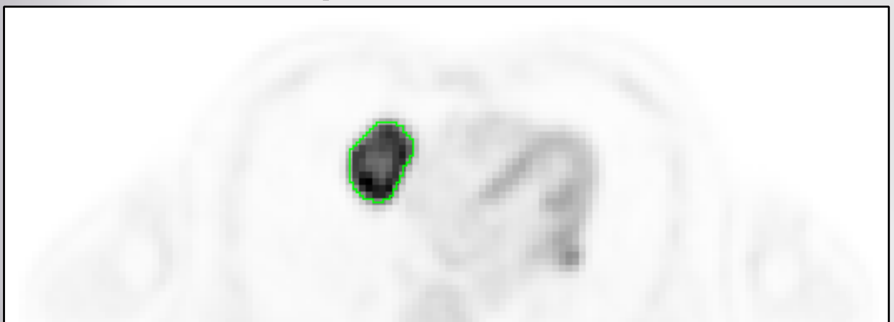
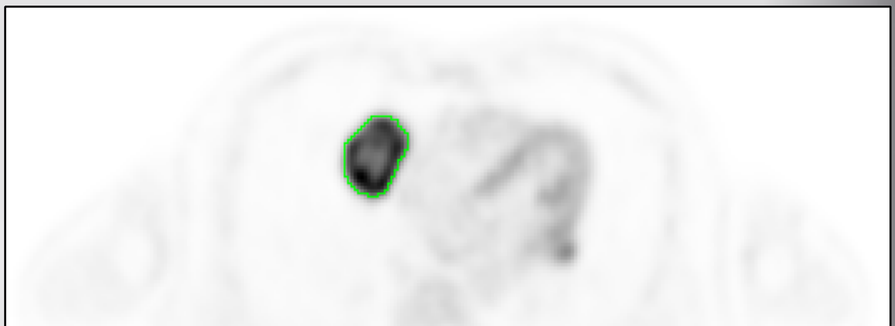
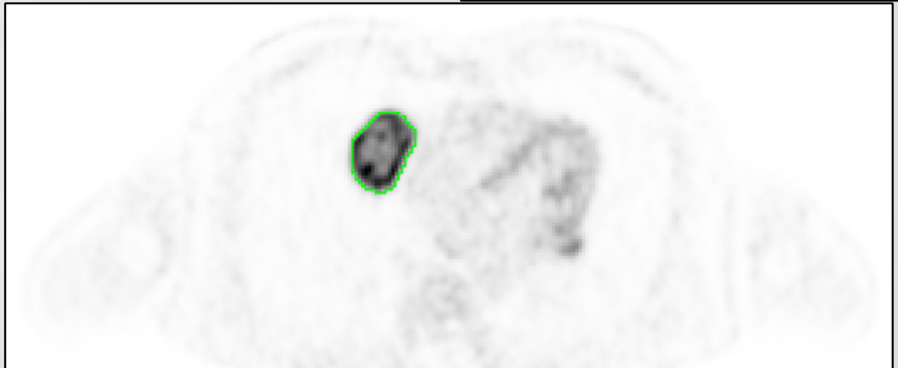
- Objective: quantify heterogeneity
  - Acquisition, reconstruction



128×128 (4×4×4 mm^3)
Upsampled using nearest neighbors



128×128 (4×4×4 mm^3)
Upsampled using quintic B-splines



Native 256×256 (2×2×2 mm^3)

Unpublished results

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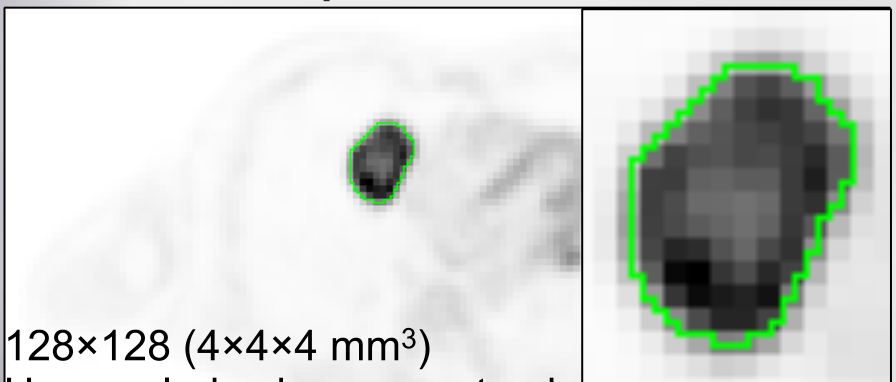

128×128 (4×4×4 mm³)
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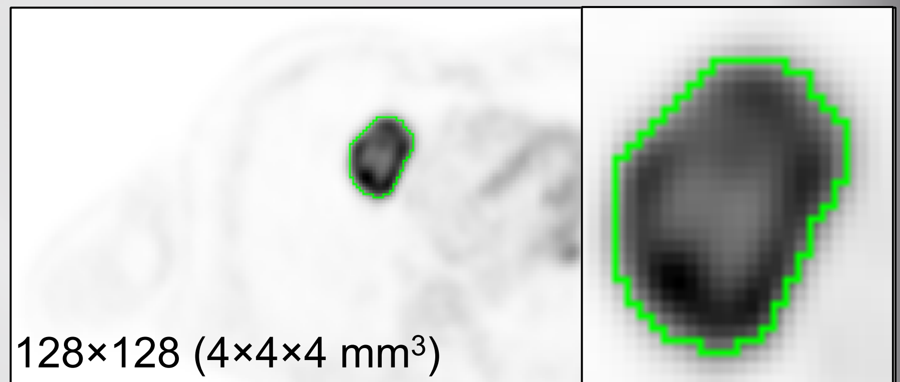

128×128 (4×4×4 mm³)
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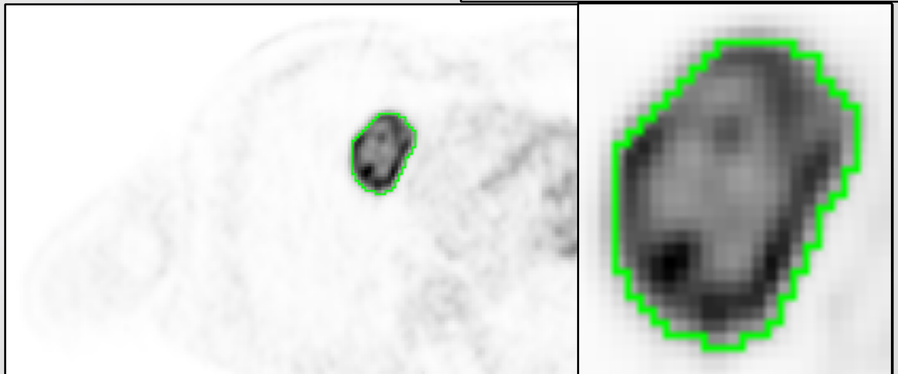

Native 256×256 (2×2×2 mm³)

Unpublished results

Multimodal characterization of tumors

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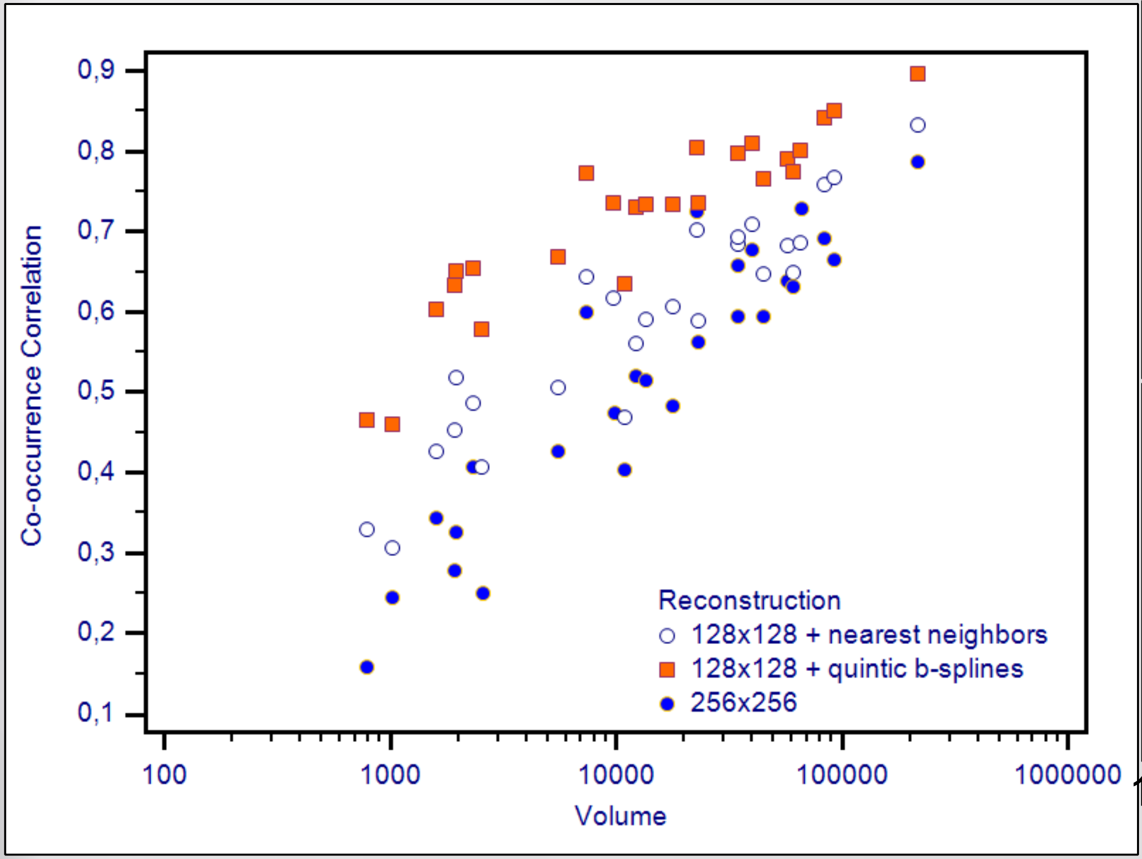
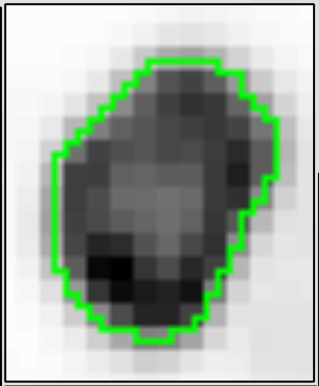
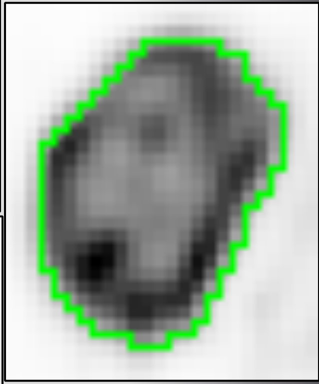
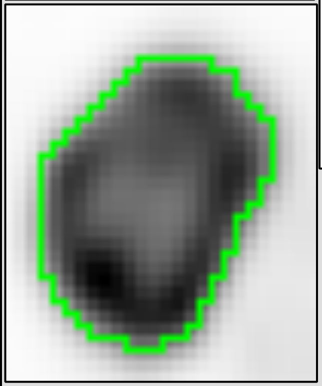


128×128 + NN



256×256



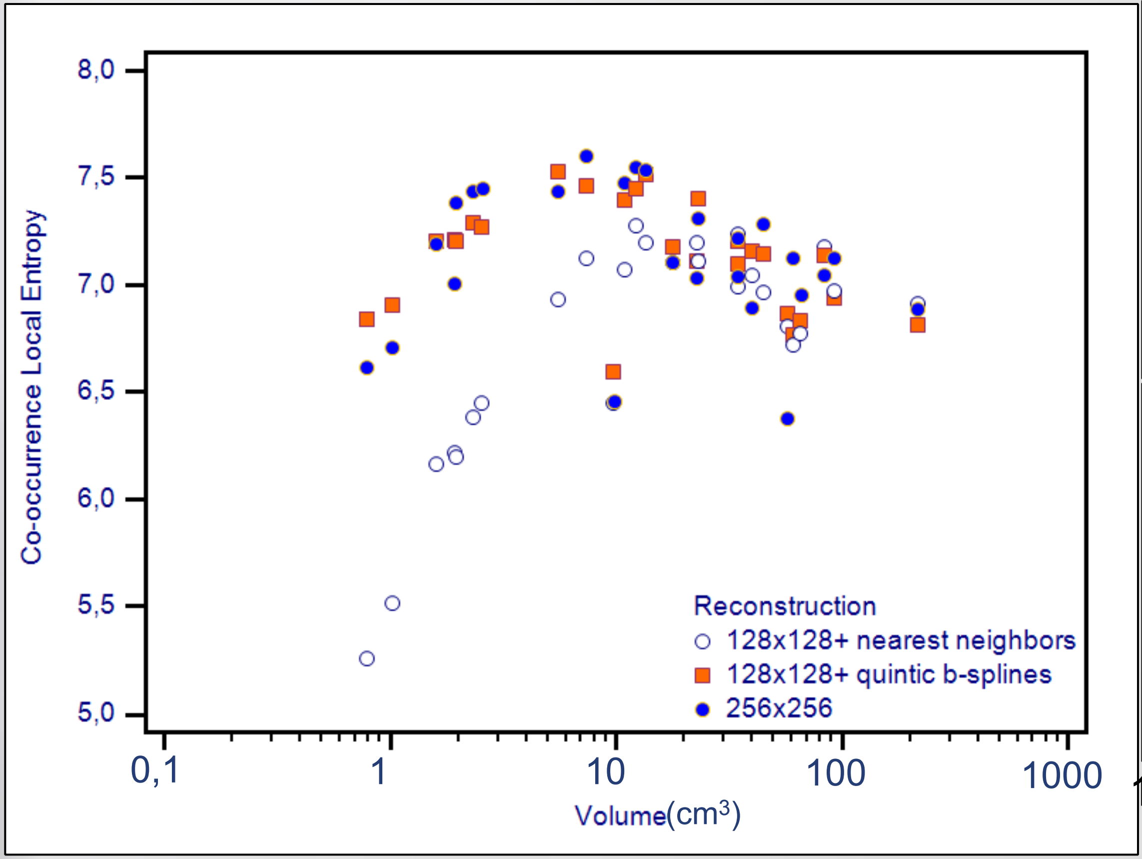


128×128 + qB-S

Unpublished results

Objective: quantify heterogeneity

- Acquisition, reconstruction

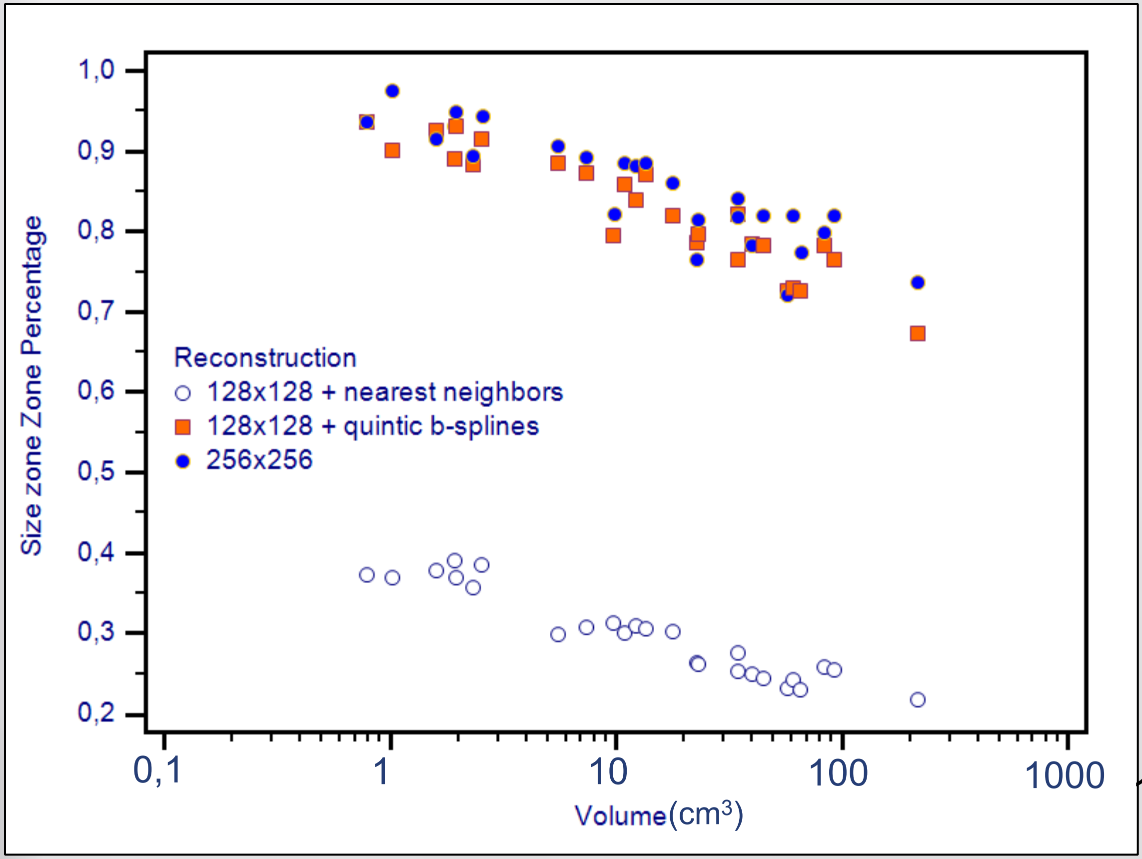


Unpublished results

Multimodal characterization of tumors

Characterization: heterogeneity

- **Objective: quantify heterogeneity**
  - Acquisition, reconstruction

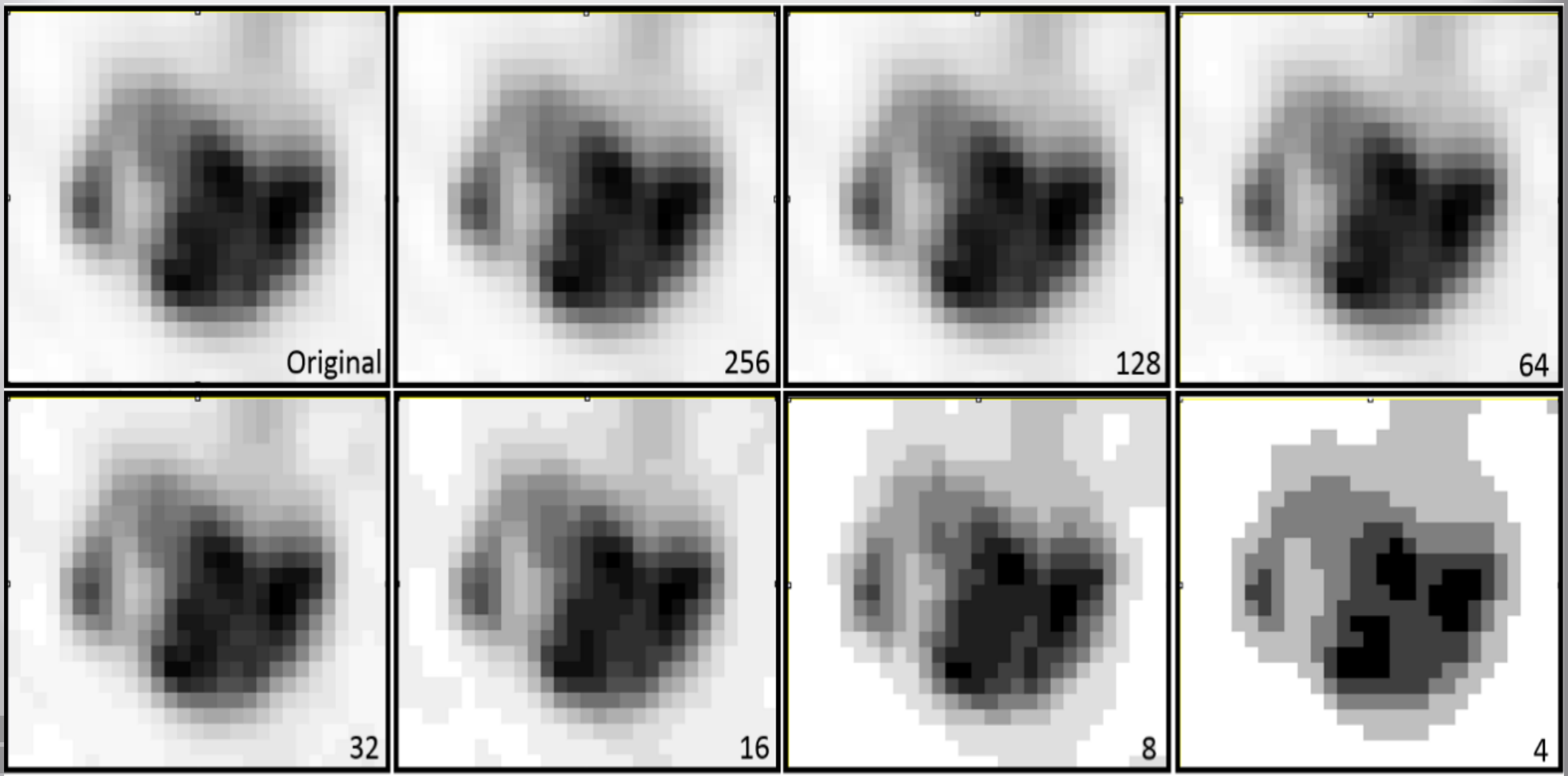


Unpublished results

Multimodal characterization of tumors

Characterization: heterogeneity

- Objective: quantify heterogeneity
  - Quantization: choice of value (usually 4 - 256)



Unpublished results

Instituts thématiques Inserm
Institut national de la santé et de la recherche médicale

Multimodal characterization of tumors

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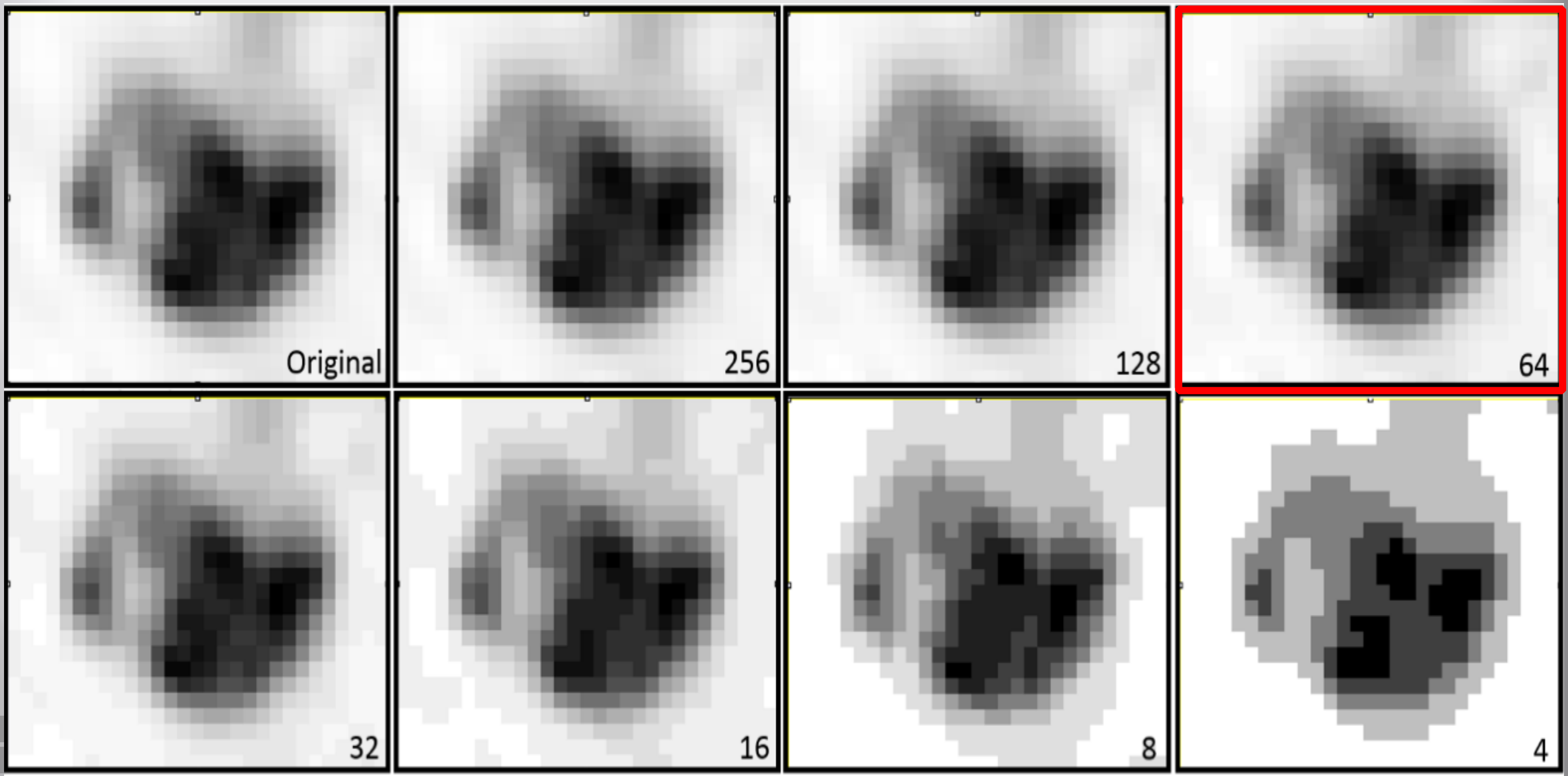
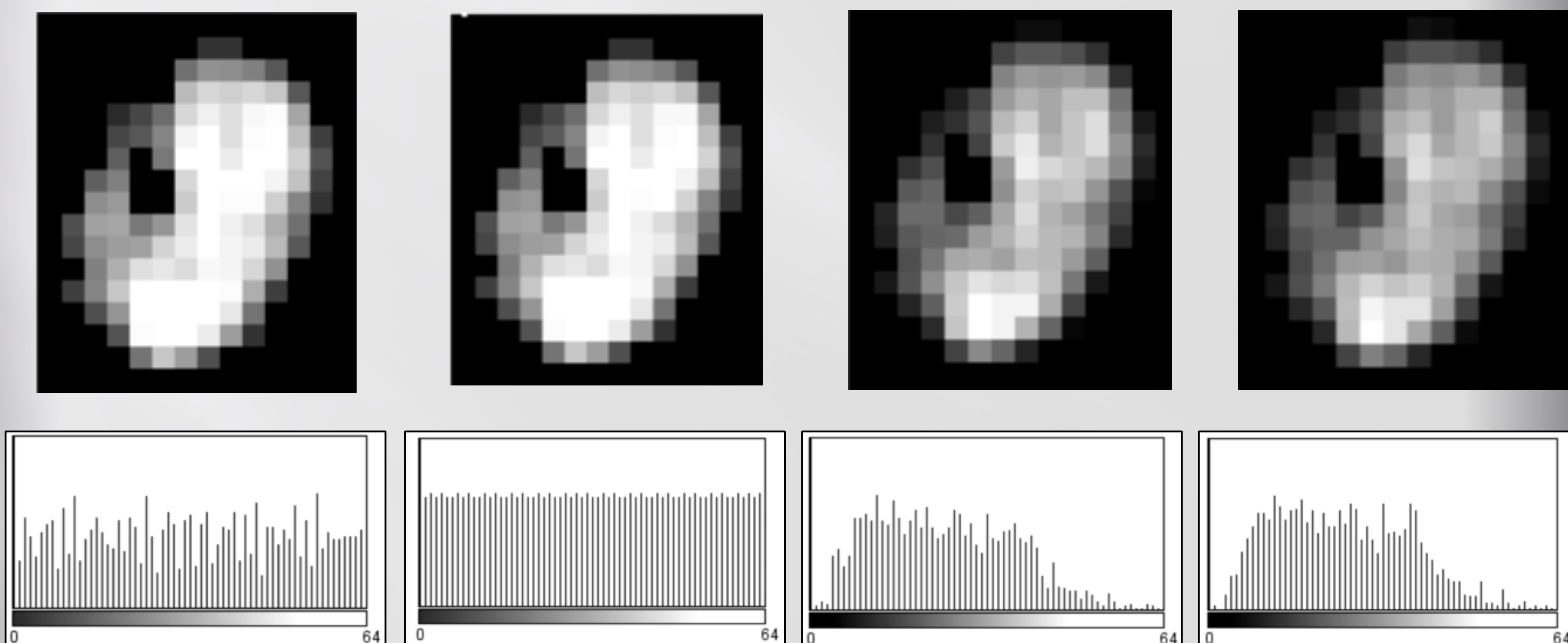


Unpublished results

Multimodal characterization of tumors

Characterization: heterogeneity

Equalization | Equalization | Lloyd's | Uniform



Unpublished results

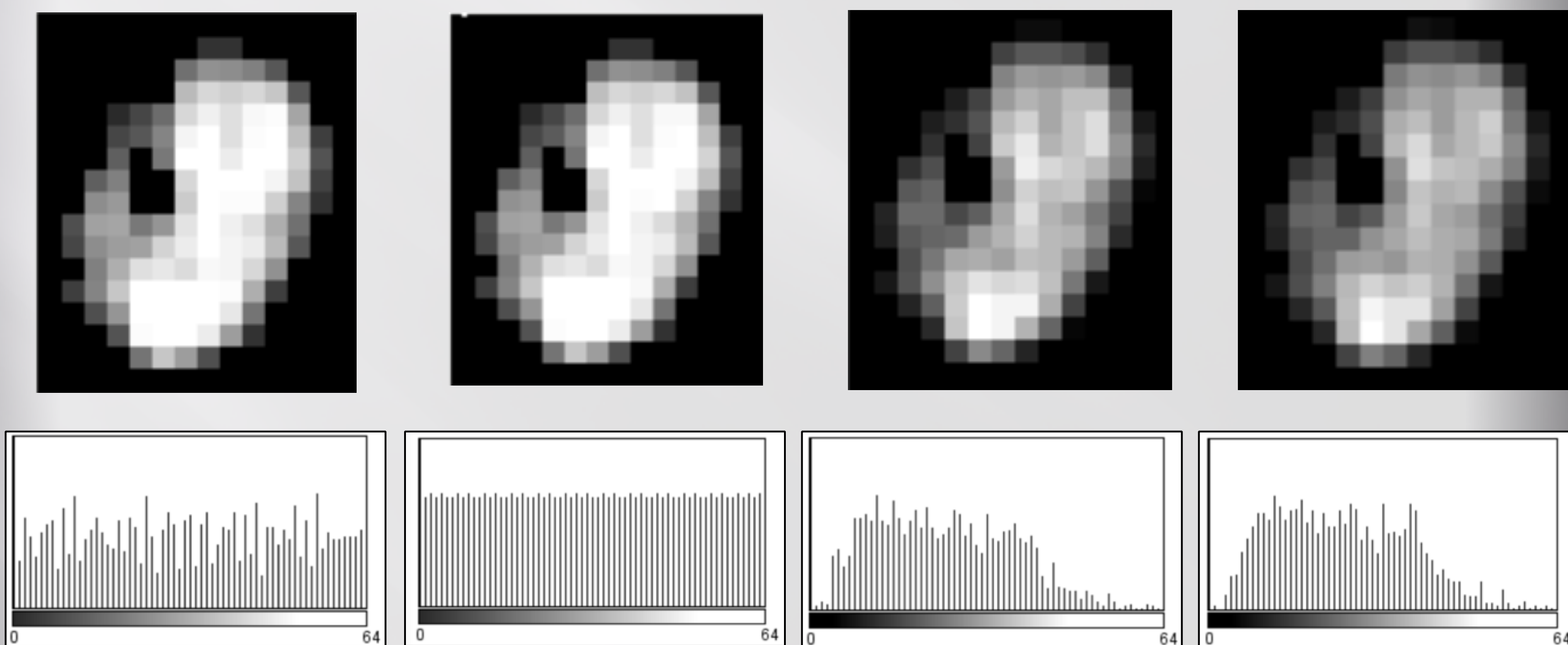
Multimodal characterization of tumors

Characterization: heterogeneity

Objective: quantify heterogeneity

- Quantization: choice of method

Equalization | Equalization | Lloyd's | Uniform



Unpublished results

Multimodal characterization of tumors

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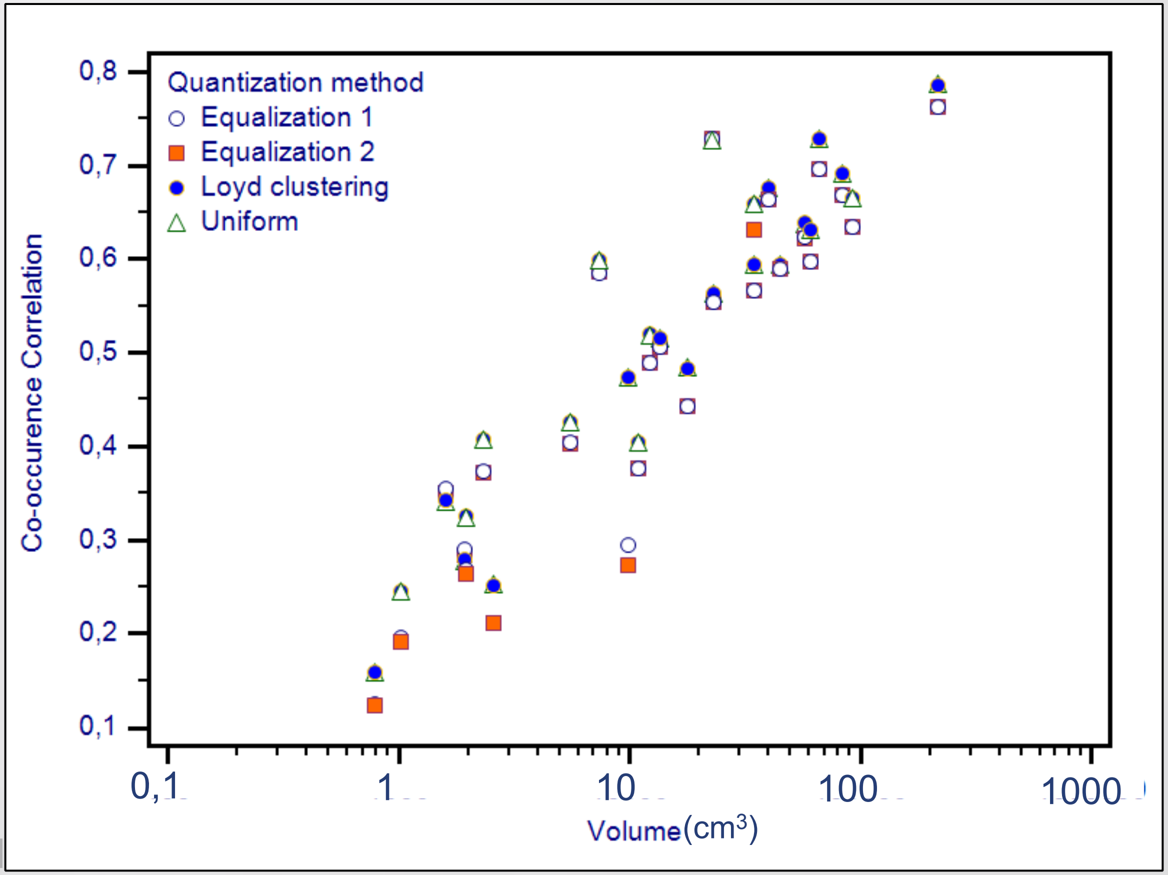
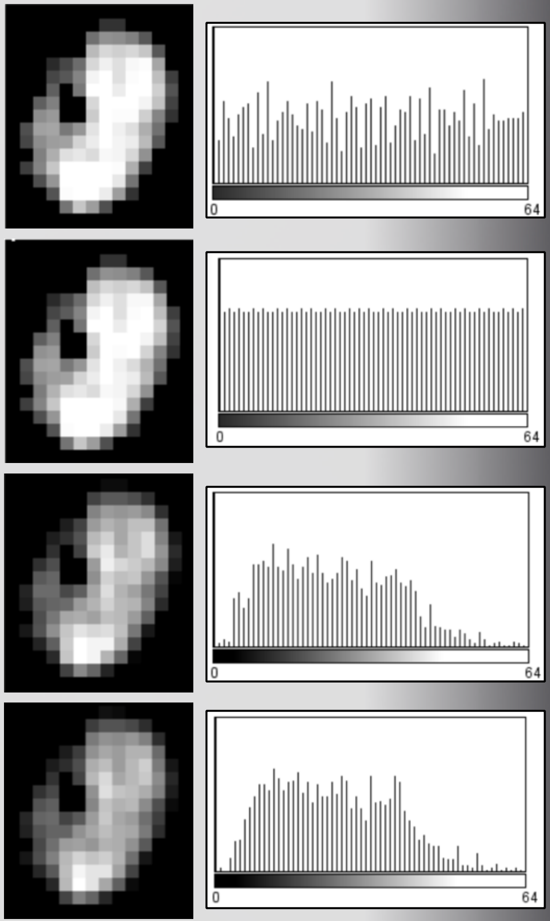




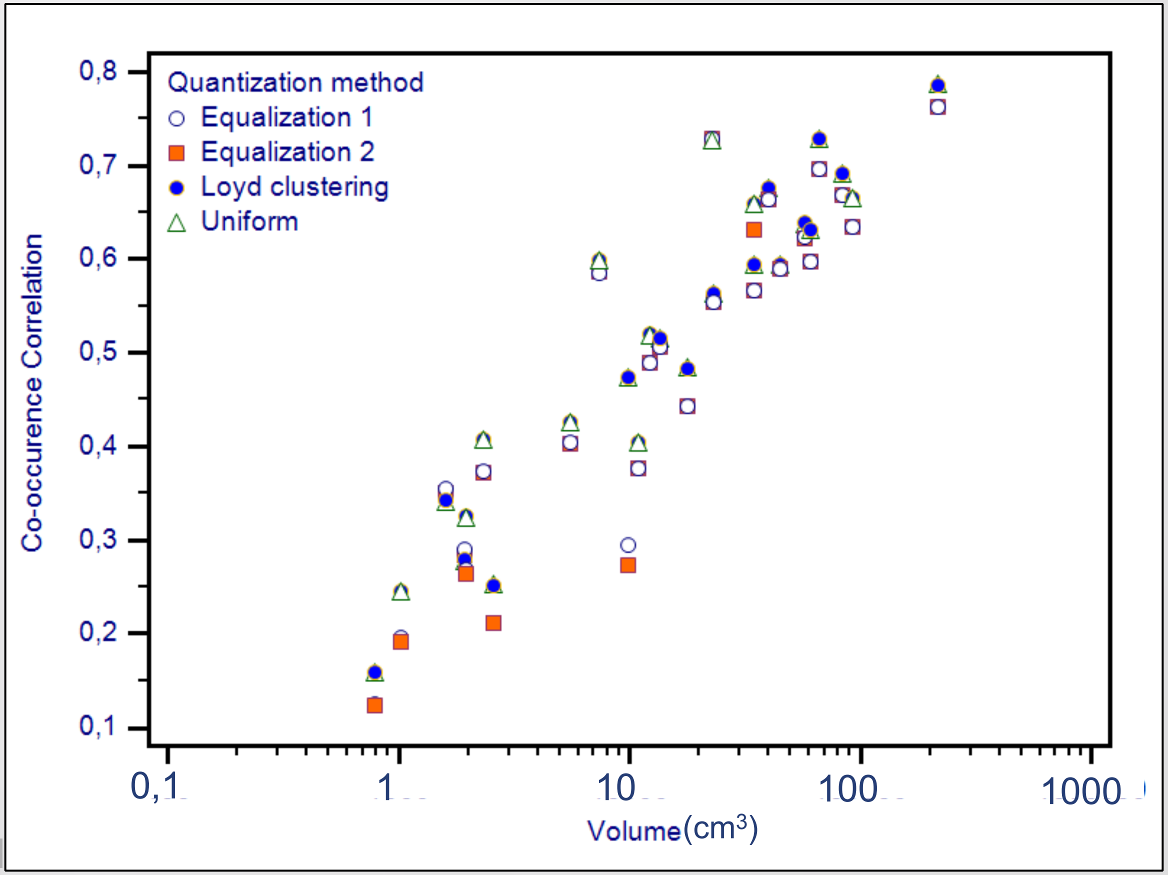
Unpublished results

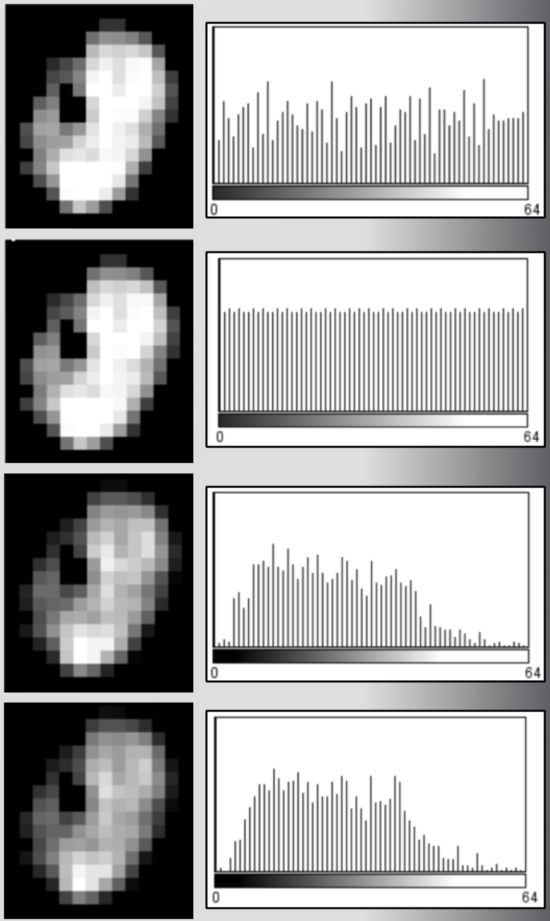
Multimodal characterization of tumors

Characterization: heterogeneity

Objective: quantify heterogeneity

- Quantization





Unpublished results

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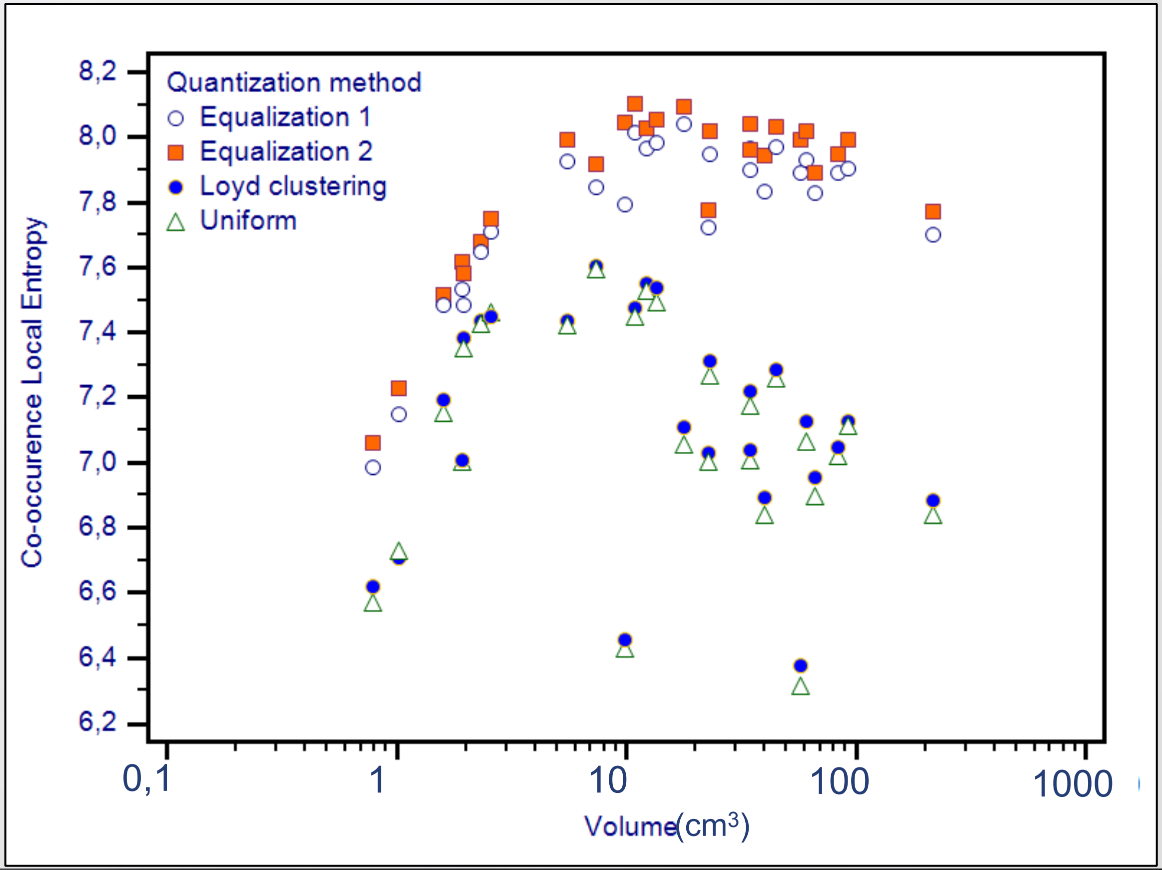

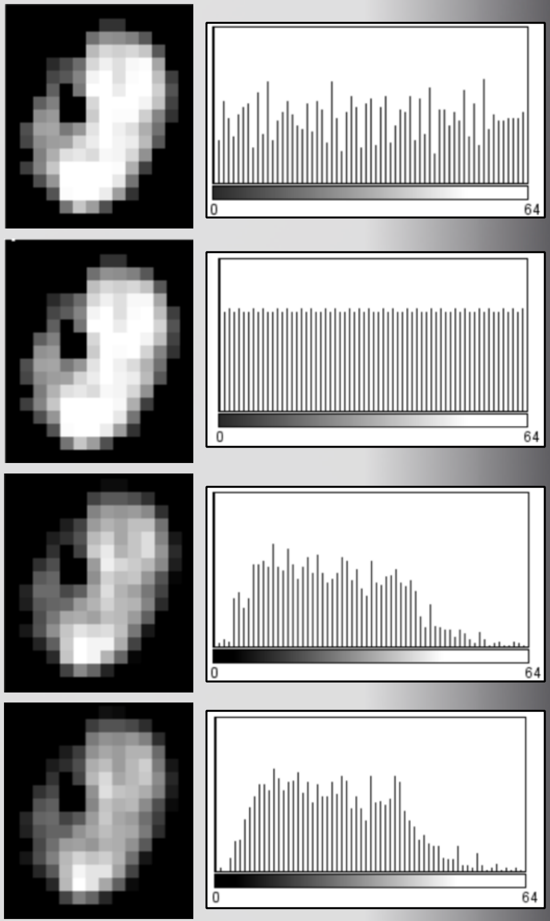

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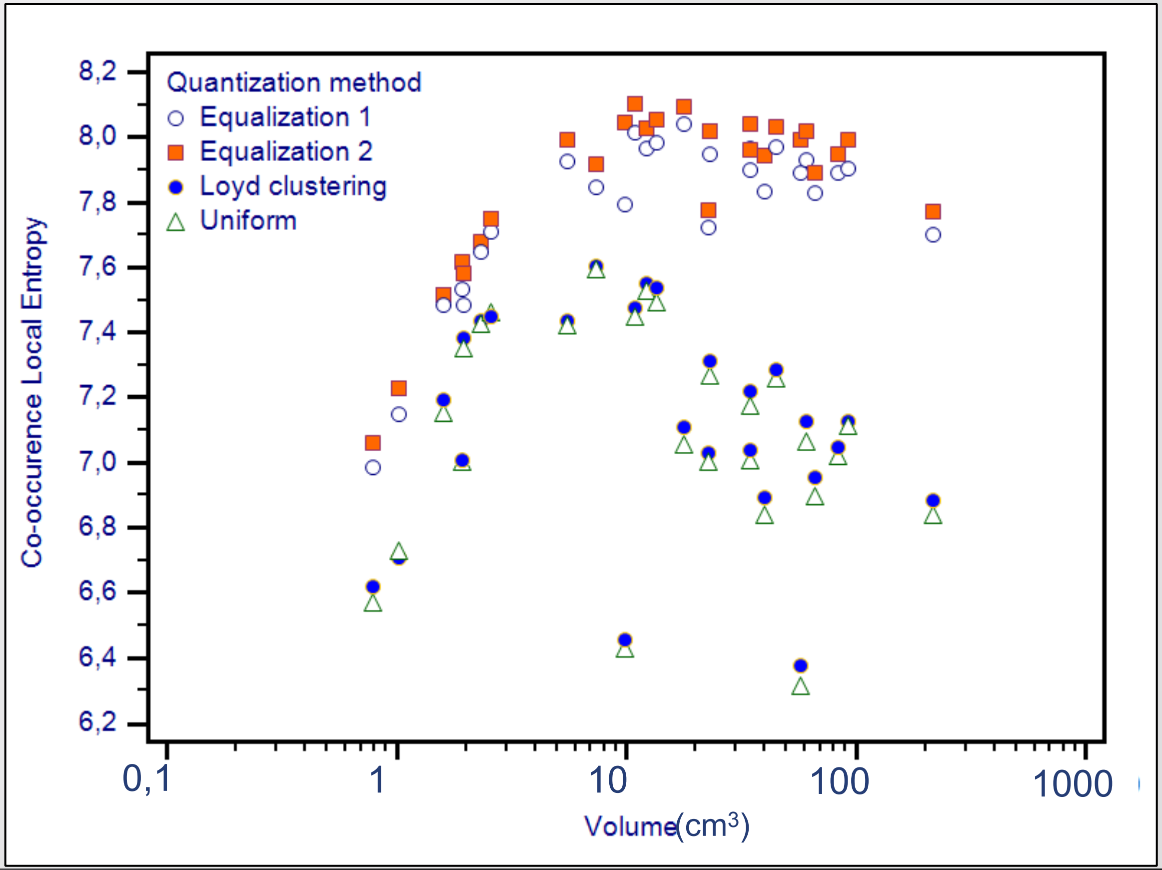
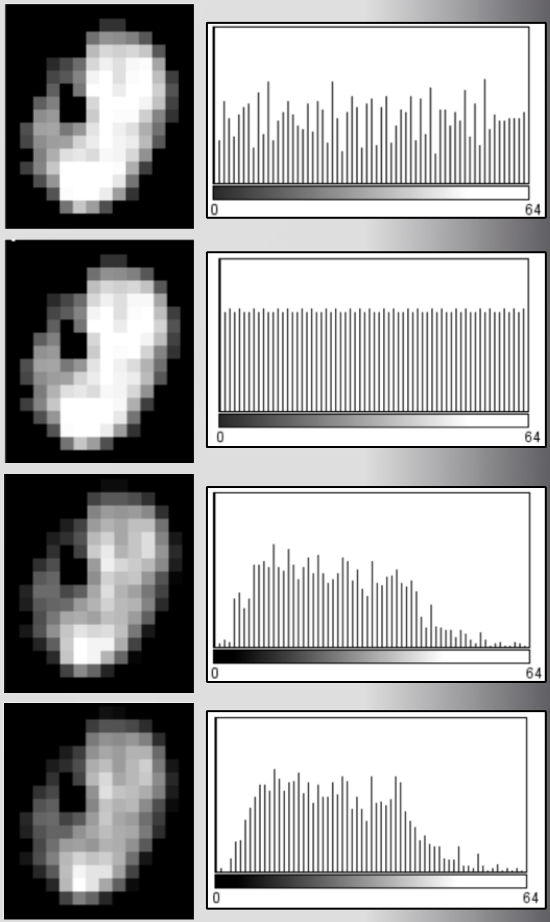
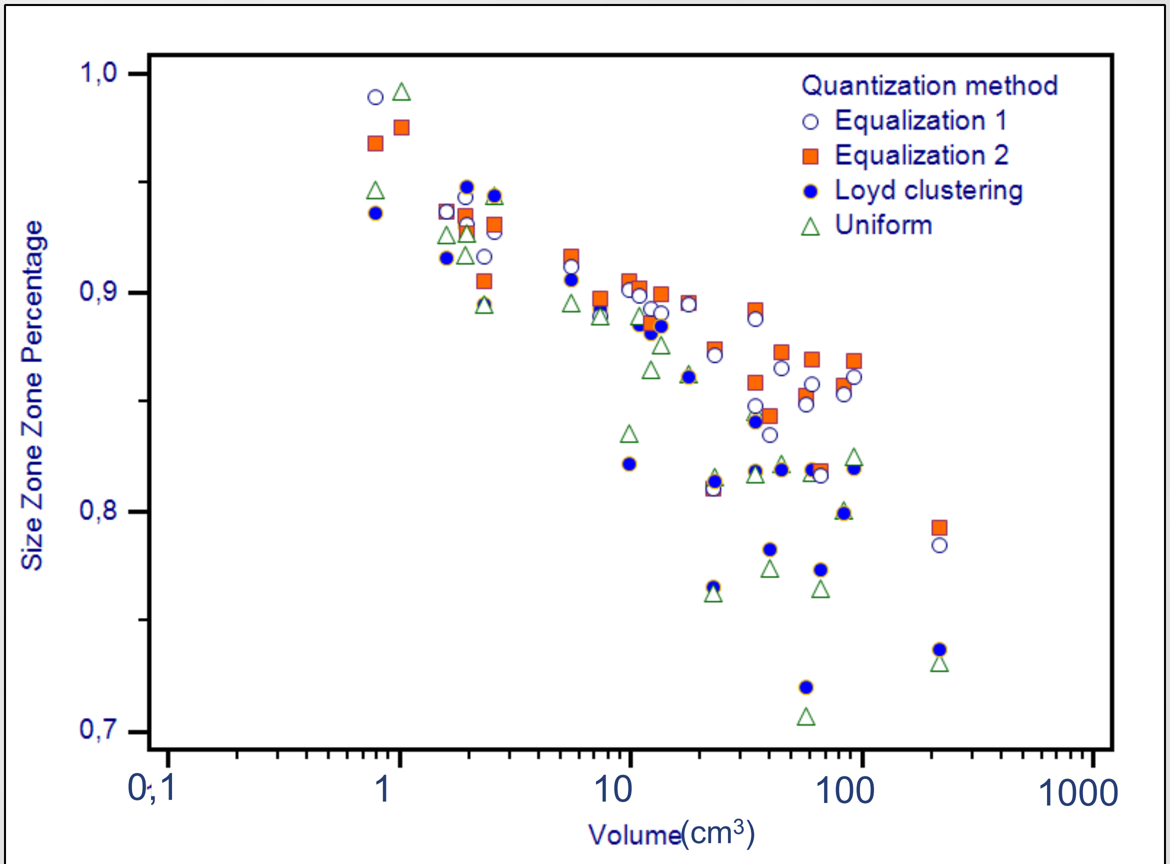


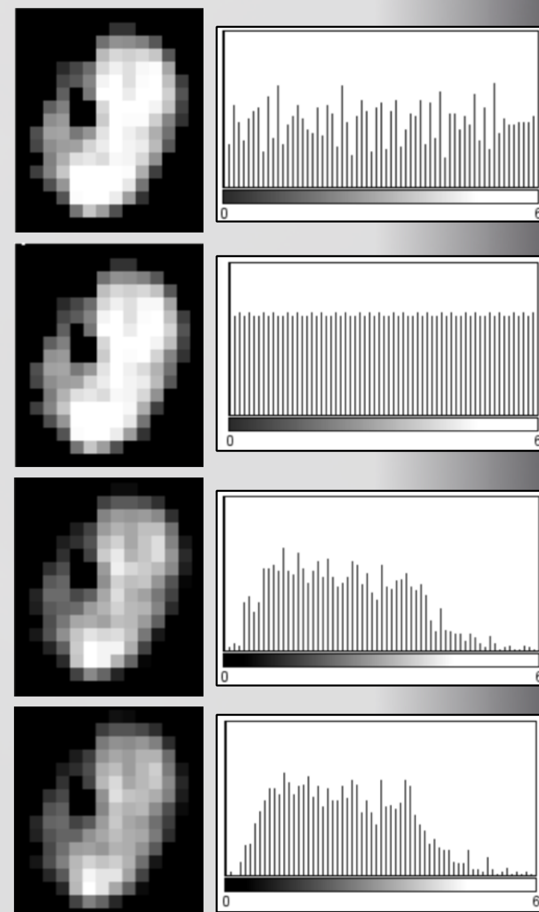


Unpublished results

Multimodal characterization of tumors

Characterization: heterogeneity





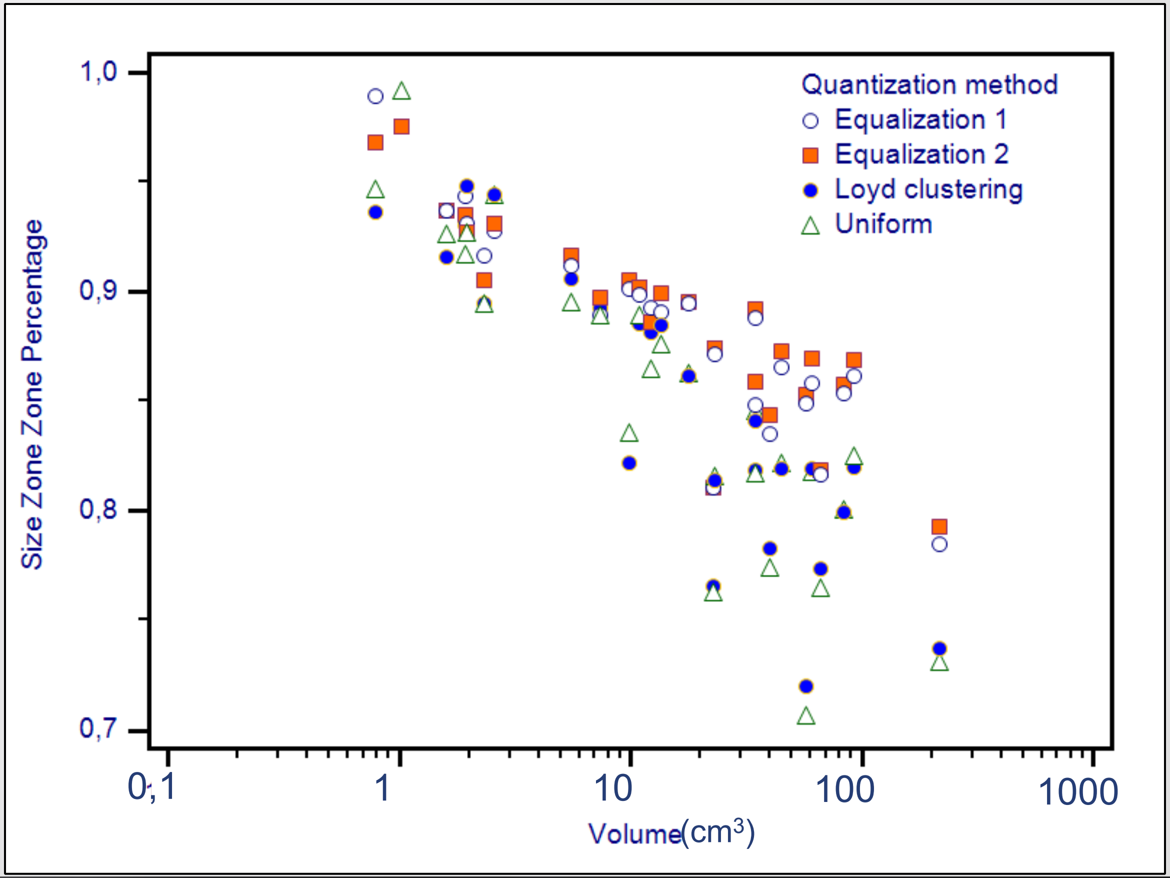
Unpublished results

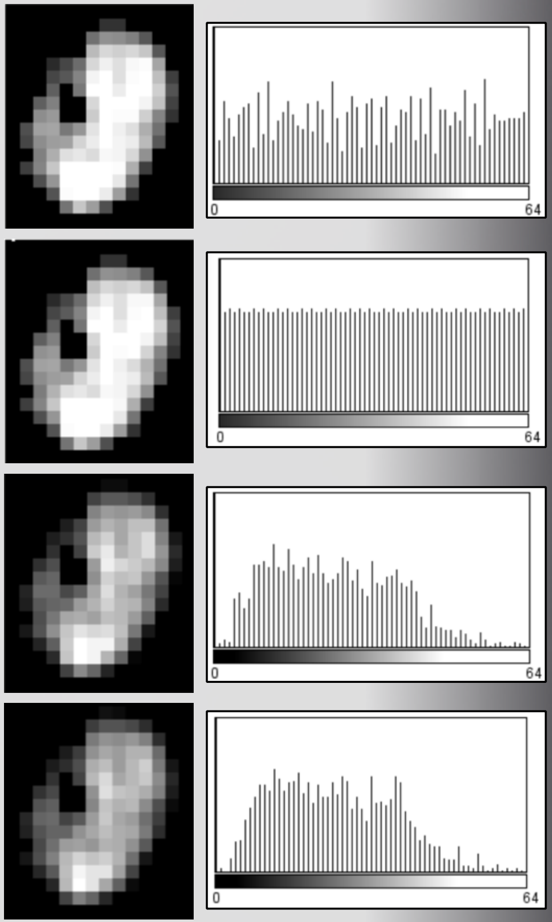
Multimodal characterization of tumors

Characterization: heterogeneity

Objective: quantify heterogeneity

- Quantization





Unpublished results

Reproducibility/variability/robustness

Eur J Nucl Med Mol Imaging
DOI 10.1007/s00259-013-2486-8

ORIGINAL ARTICLE

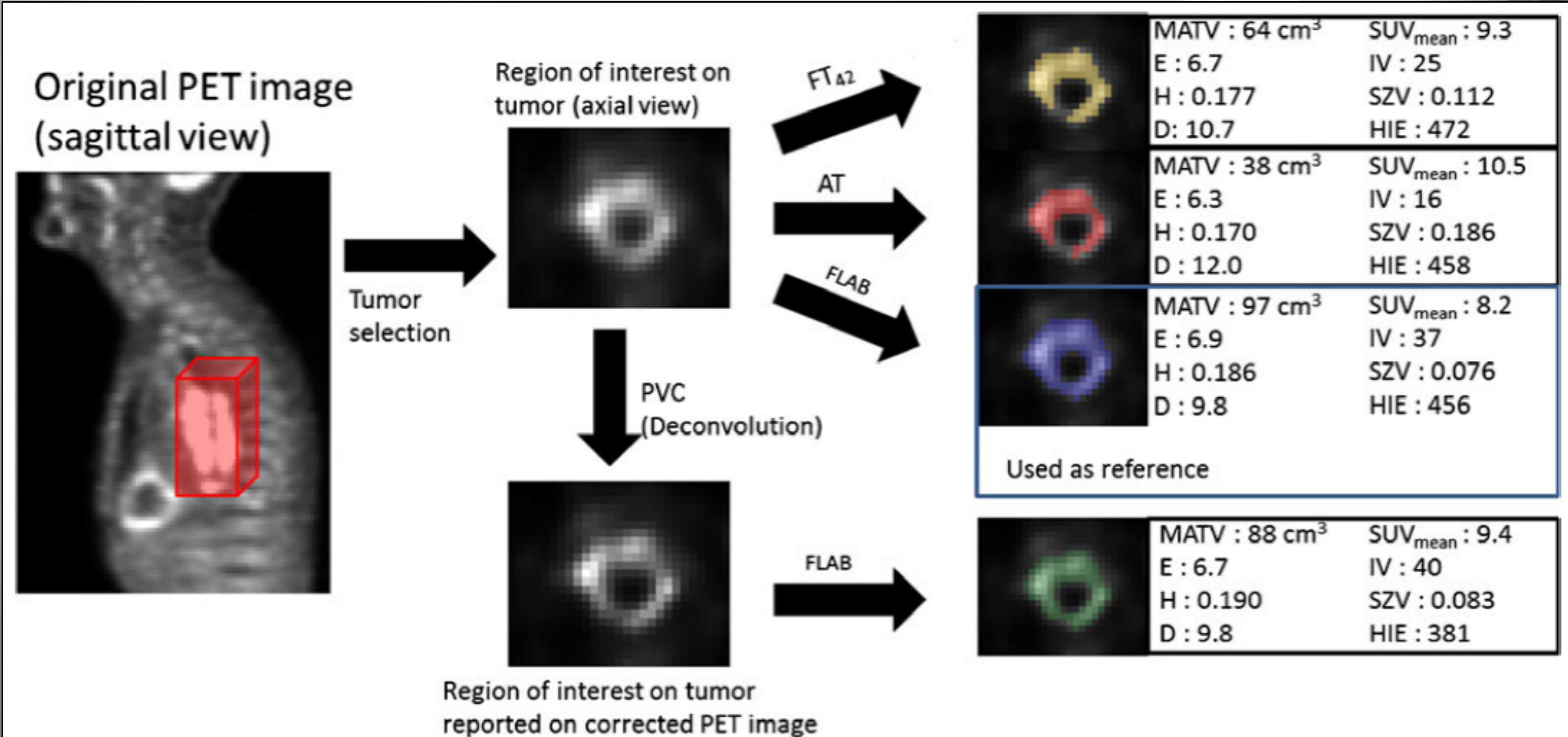
Robustness of intratumour ^{18}F-FDG PET uptake heterogeneity quantification for therapy response prediction in oesophageal carcinoma

Mathieu Hatt • Florent Tixier • Catherine Cheze Le Rest • Olivier Pradier • Dimitris Visvikis

Textural features in PET

The present: technical and practical issues

Reproducibility/variability/robustness



Instituts thématiques Inserm

Institut national de la santé et de la recherche médicale

Textural features in PET

The present: technical and practical issues

Reproducibility/variability/robustness

Parameter			Difference with respect to FLAB delineation on noncorrected images								
			FT42%			AT			PVC		
			Mean ± SD (%)	LRL (%)	URL (%)	Mean ± SD (%)	LRL (%)	URL (%)	Mean ± SD (%)	LRL (%)	URL (%)
Standard		SUV_{mean}	−1±20.7	−41.5	39.6	5.2±21.1	−36.2	46.7	16.9±8.7	−0.2	34
		MATV	7.1±52	−94.9	109.1	−18.4±49.4	−115.1	78.3	−14.4±19.2	−32.0	23.2
Heterogeneity quantification	Local	Entropy	1.5±9.4	−16.9	19.9	−4.3±12.6	−28.9	20.3	−4.6±5.3	−15.0	5.7
		Homogeneity	4.7±22.1	−38.7	48	−3.7±19.9	−42.8	35.4	4.2±10.9	−17.1	25.5
		Dissimilarity	−5.3±28	−60.1	49.5	4.9±22.6	−39.3	49.1	−3.2±11.4	−25.5	19.1
	Regional	Intensity variability	7±50.1	−91.1	105.1	−16.2±47	−108.4	76	0.2±19.9	−38.8	39.2
		Size-zone variability	−6.5±48.9	−102.3	89.4	17.8±46.9	−74.2	109.8	3.3±47.9	−90.7	97.3
		Zone percentage	−2.4±20.4	−42.3	37.5	5.3±14.1	−22.4	32.9	10.3±11.6	−12.5	33
		High intensity emphasis	−4.6±19.8	−43.5	34.3	3.7±24.7	−44.6	52.1	−20.6±18.8	−57.5	16.3
	Global	Area under the curve of the cumulative histogram	1.2±4.1	−6.8	9.2	−1.1±6	−12.8	10.6	5±5.6	−5.9	15.9

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Textual features in PET

… any future? : machine learning

Challenges

- Machine learning

SCIENTIFIC REPORTS

OPEN

Machine Learning methods for Quantitative Radiomic Biomarkers

Chintan Parmar[1,3,4,*], Patrick Grossmann[1,5,*], Johan Bussink[6], Philippe Lambin[3] & Hugo J. W. L. Aerts[1,2,5]

Received: 02 April 2015

Textural features in PET

… any future? : machine learning

Challenges

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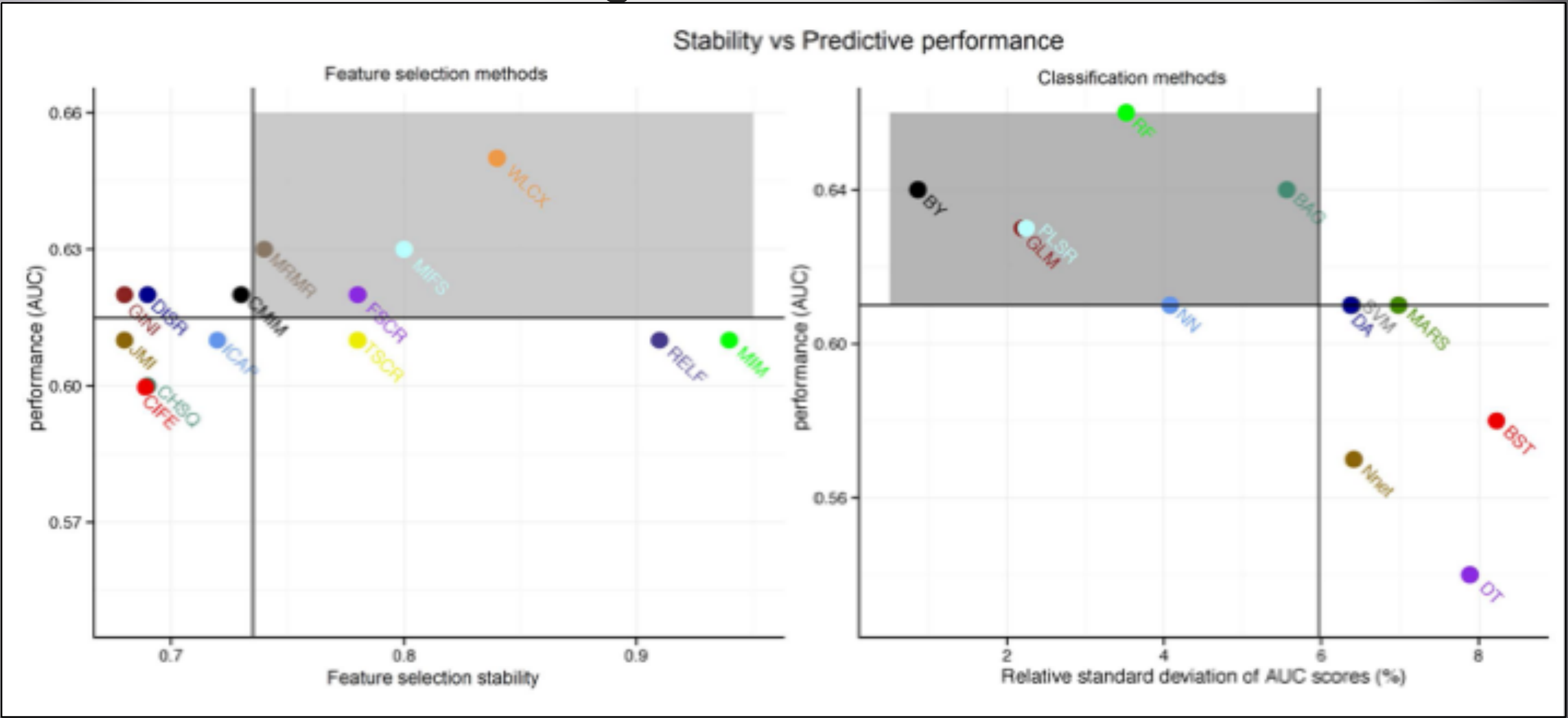
Classification method acronym	Classification method name	Feature Selection method acronym	Feature selection method name
Nnet	Neural network	RELF	Relief
DT	Decision Tree	FSCR	Fisher score
BST	Boosting	GINI	Gini index
BY	Bayesian	CHSQ	Chi-square score
BAG	Bagging	JMI	Joint mutual information
RF	Random Forset	CIFE	Conditional infomax feature extraction
MARS	Multi adaptive regression splines	DISR	Double input symmetric relevance
SVM	Support vector machines	MIM	Mutual information maximization
DA	Discriminant analysis	CMIM	Conditional mutual information maximization
NN	Neirest neighbour	ICAP	Interaction capping
GLM	Generalized linear models	TSCR	T-test score
PLSR	Partial least squares and prinicipal componenet regression	MRMR	Minimum redundancy maximum relevance
—	—	MIFS	Mutual information feature selection
—	—	WLCX	Wilcoxon

Textural features in PET

… any future? : machine learning

Challenges

- Machine learning



Textural features in PET
… any future? : machine learning

Challenges

- Machine learning