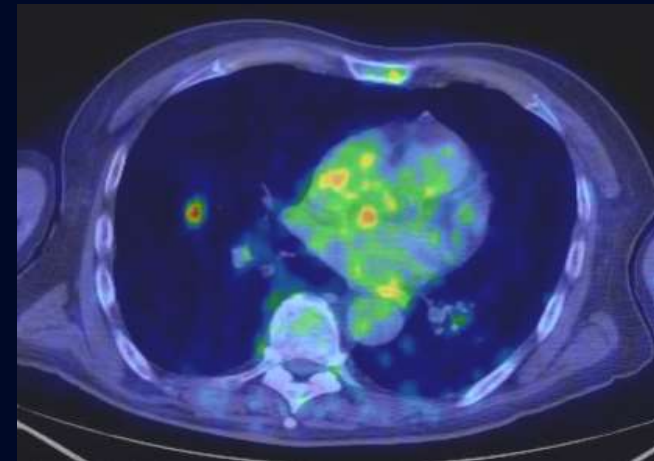


Medical-image Segmentation

Medical Imaging & Big Data | Data Science
Università degli studi di Milano-Bicocca

2019



Tumour

Complex biological object

Macroscopically

Heterogeneous shape, density, global metabolism

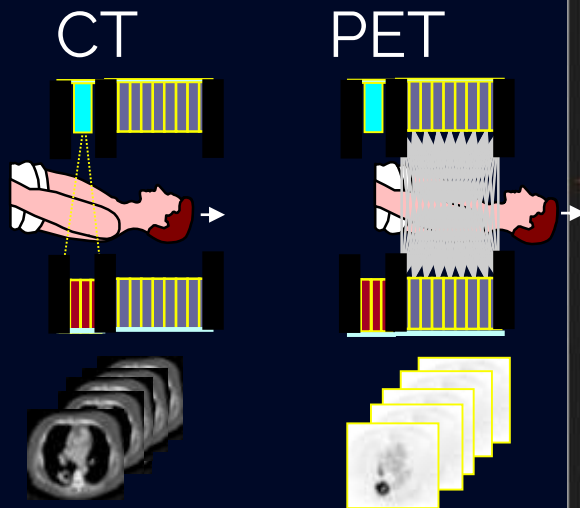
Microscopically

Cell proliferation, hypoxia, neoangiogenesis

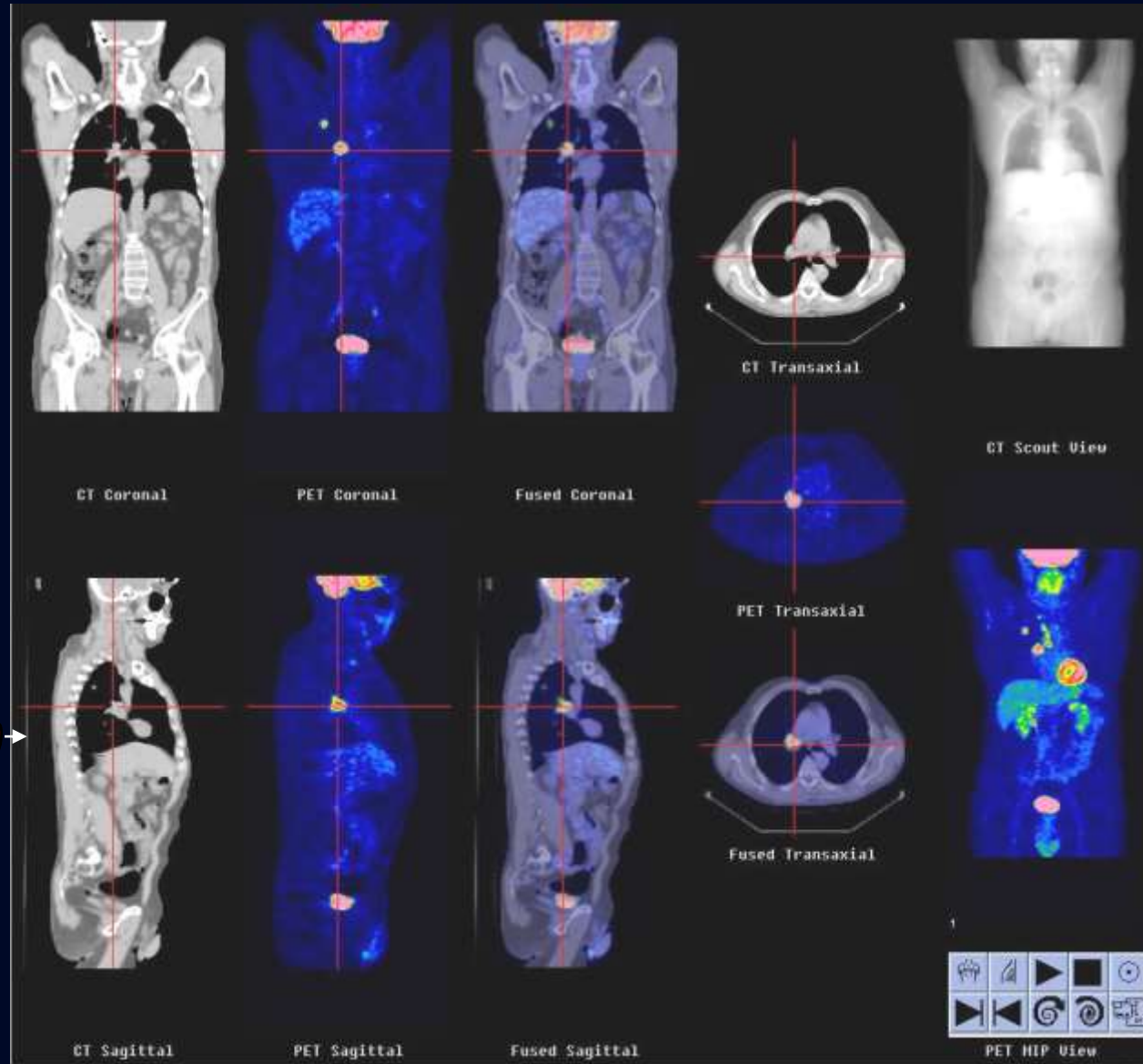
PET/CT in oncology



[¹⁸F]FDG PET-CT



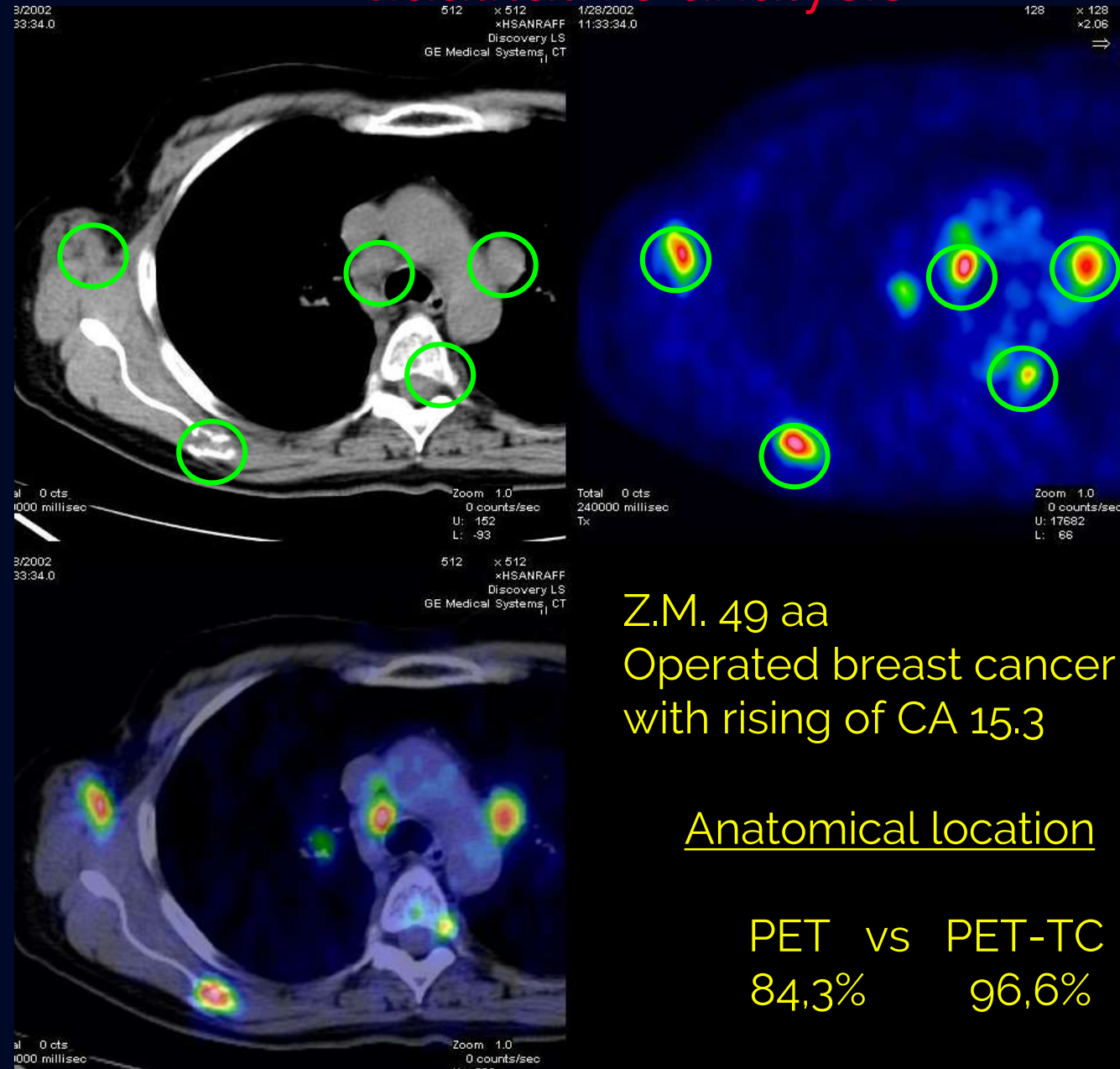
HSR Milan



PET/CT in oncology

- ANATOMICAL LOCATION
- CHARACTERIZATION
- CHOICE OF THERAPY
- THERAPY MONITORING

Qualitative analysis



Z.M. 49 aa
Operated breast cancer
with rising of CA 15.3

Anatomical location

PET	vs	PET-TC
84,3%		96,6%

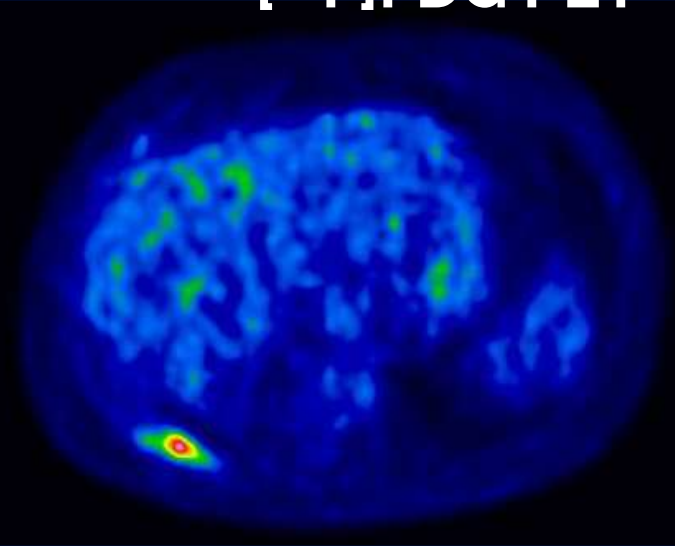
HSR Milan

Qualitative analysis

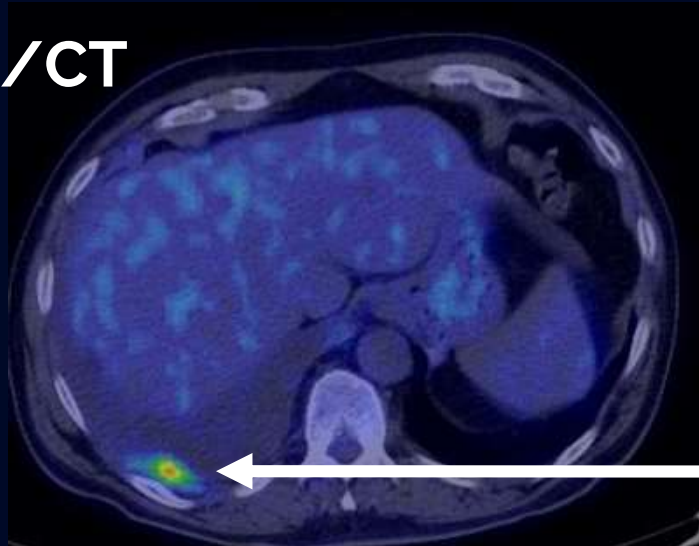
CT



[¹⁸F]FDG PET



PET/CT



**PET-CT Characterization:
Lung cancer**

M (Pleural mts)

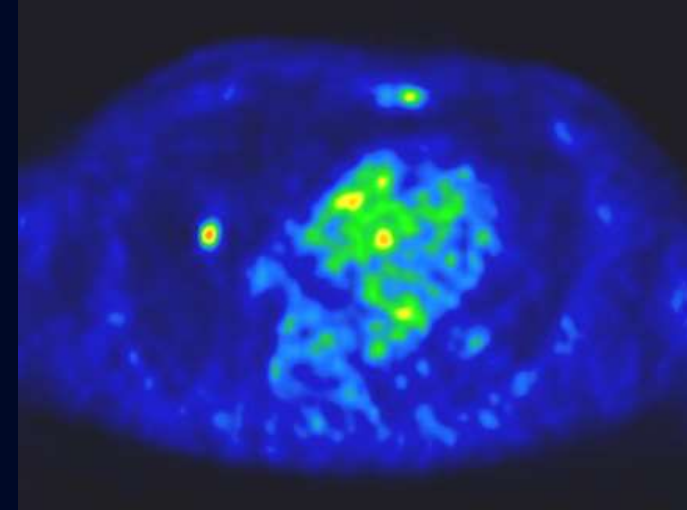
HSR Milan

Qualitative analysis

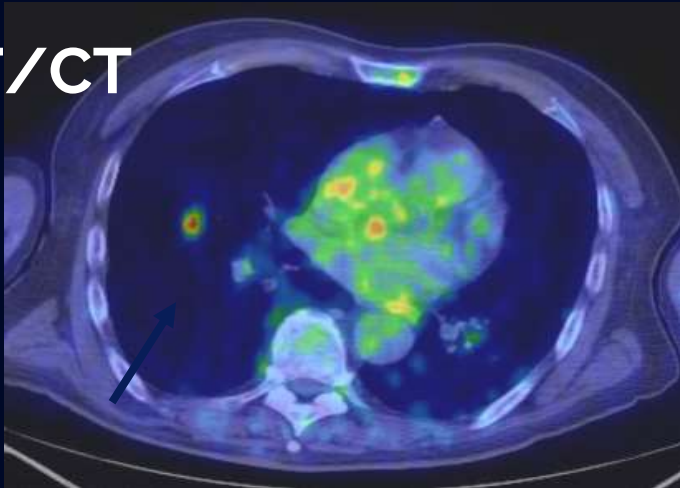
CT



[¹⁸F]FDG PET



PET/CT



**MF-50 yrs.
Exclusion from radiotherapy
treatment for presence of lung
metastasis**

HSR Milan

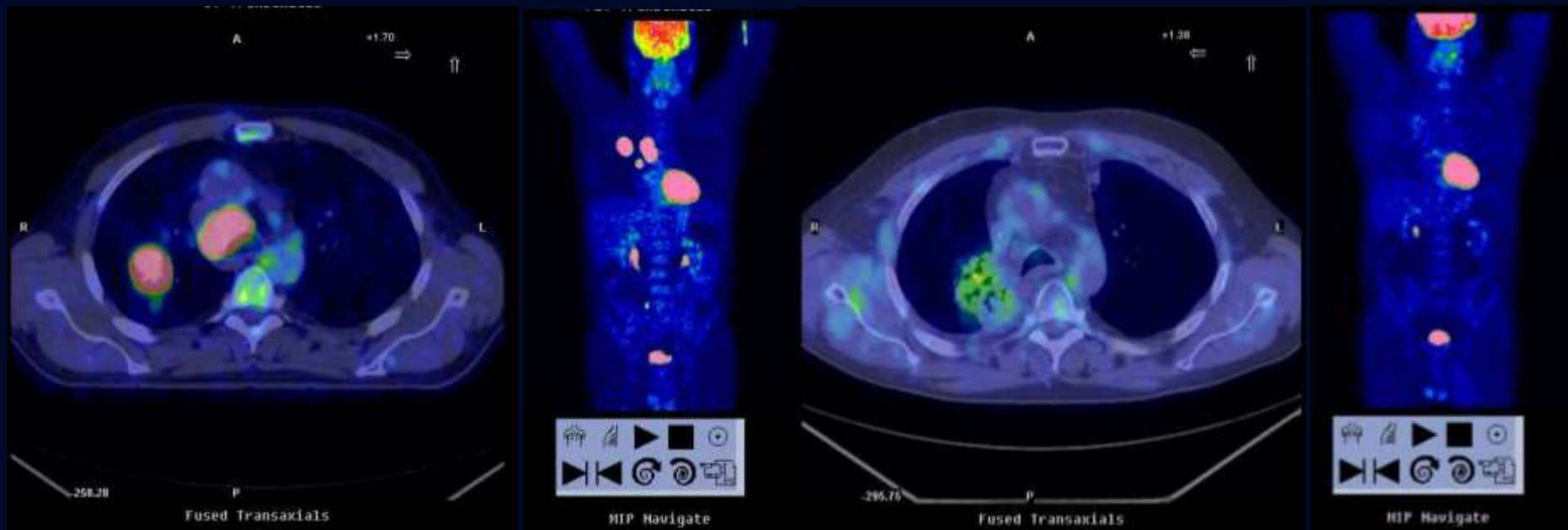
Qualitative analysis

[^{18}F]FDG PET/CT

Evaluation of residual mass

Evaluation of recurrence

Evaluation of therapy (early and at the end of treatment)



Before Therapy

After Therapy

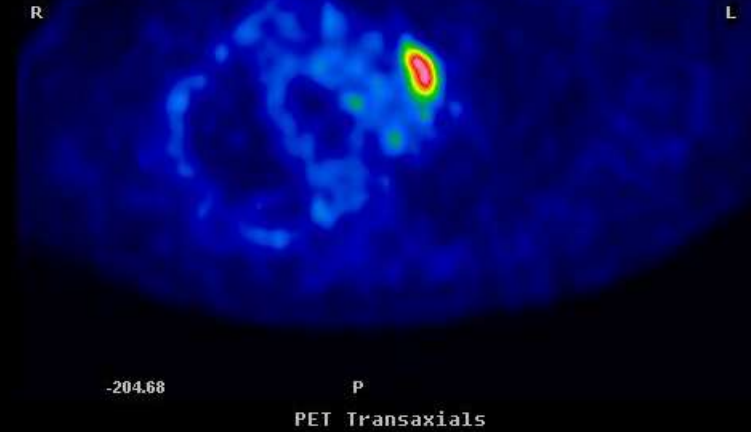
Qualitative analysis

Residual mass

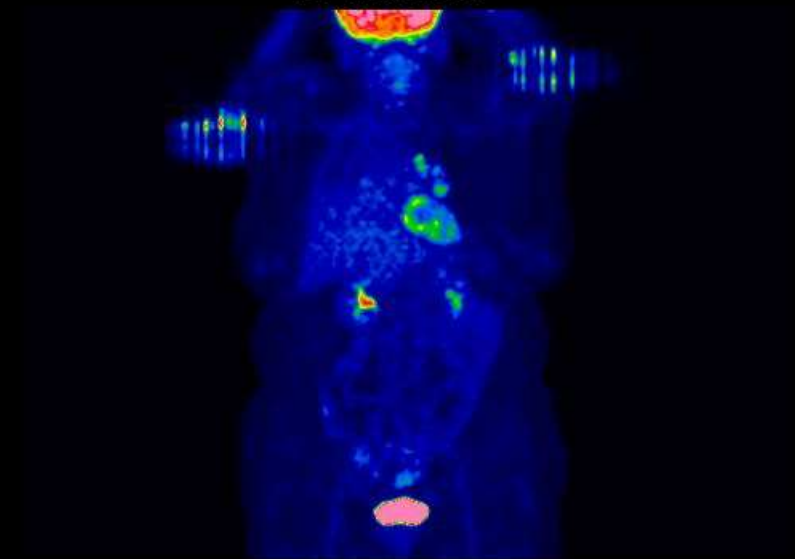
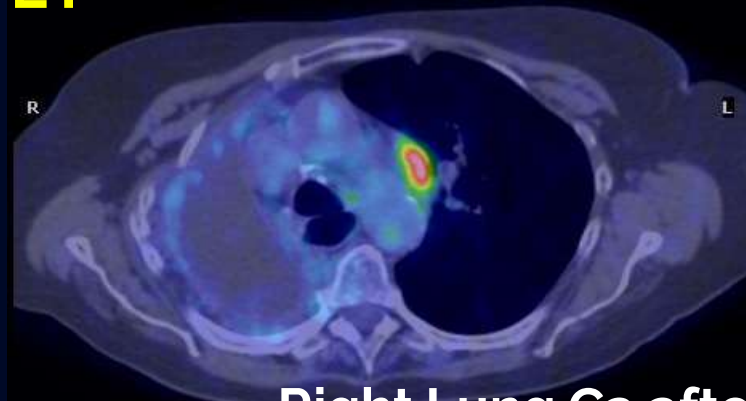
CT



[¹⁸F]FDG PET

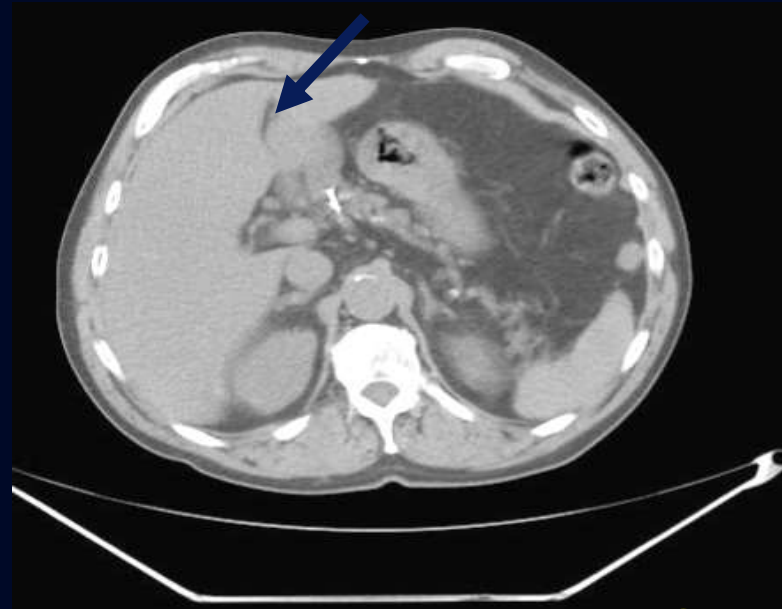


CT- PET

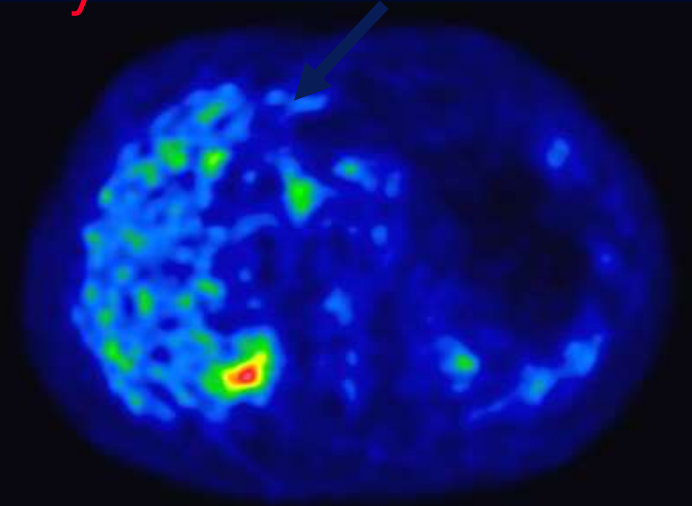


Right Lung Ca after pneumonectomy

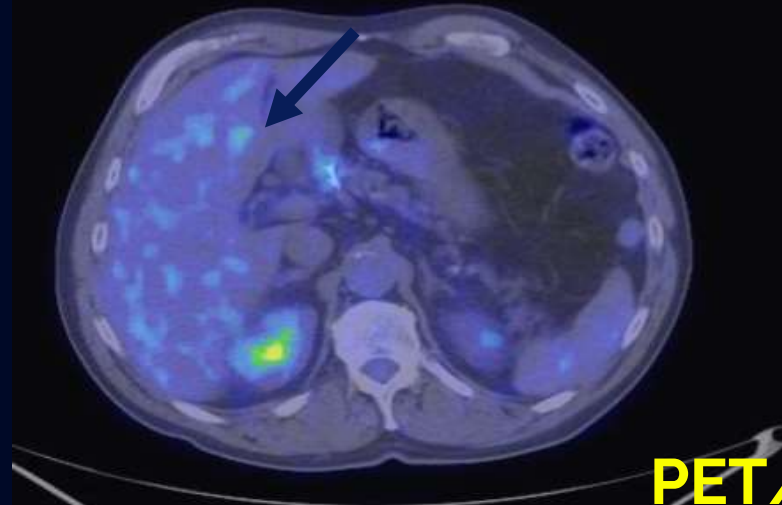
Qualitative analysis



CT



[18F]FDG-PET



PET/CT

E.B. 56 aa

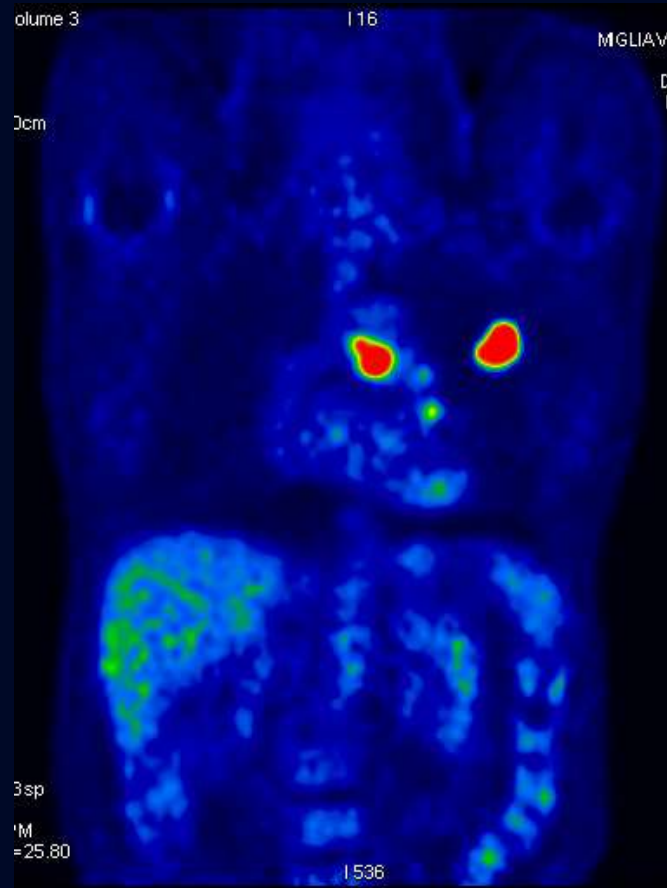
22/4/2002

**Pancreatic Ca after
surgery**

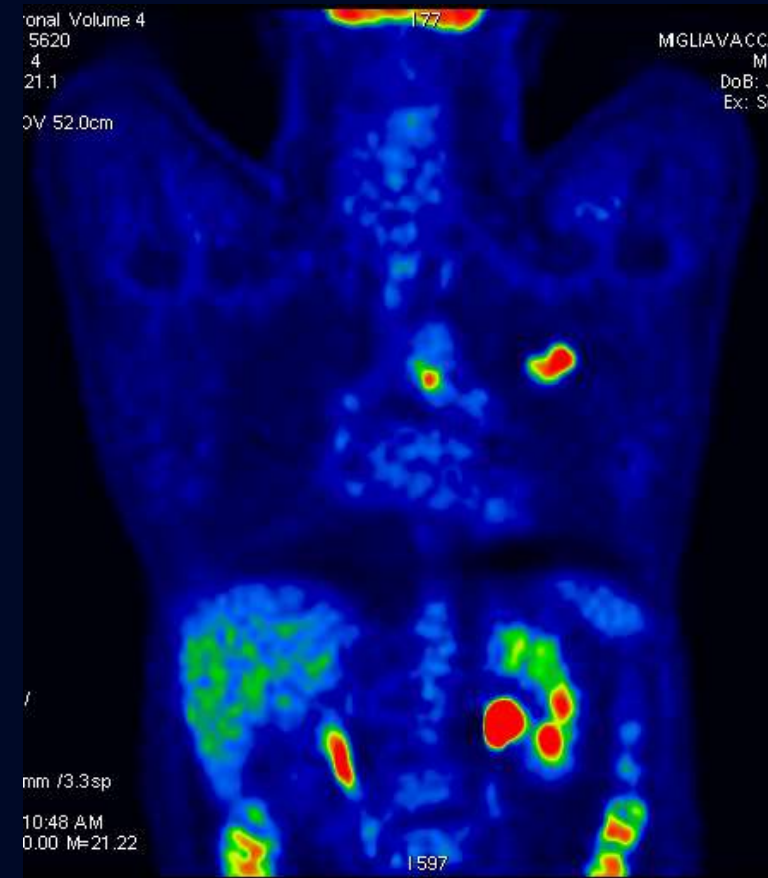
Recurrence

Qualitative analysis

Monitoring therapy response



Pre Chemotherapy Study
Apr 03 2007

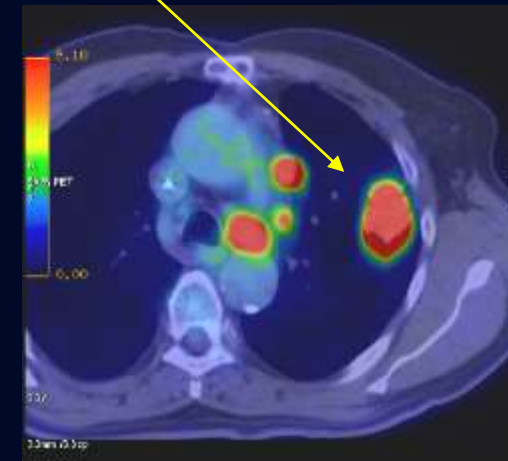
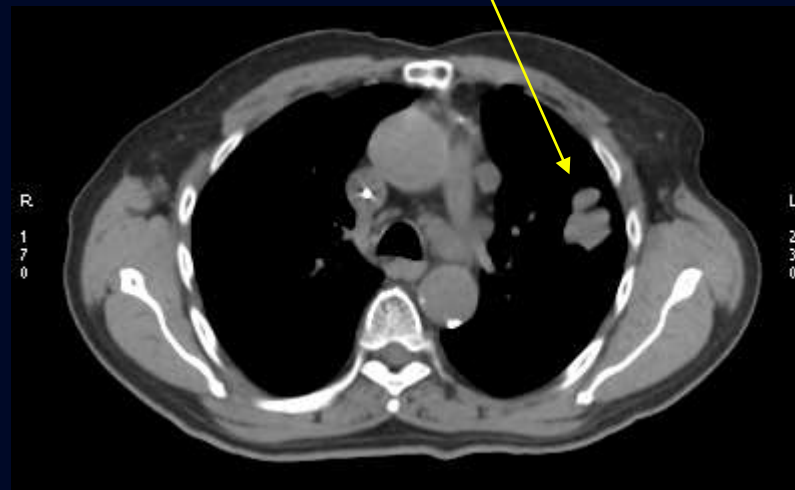


Post Chemotherapy Study
Sept 27 2007

PET/CT in oncology: quantitative analysis

Image-guided radiation therapy treatment planning

PTV: Planning Tumour Volume



PET-CT systems for radioterapy planning

- flat couch insert
- positioning system,
- respiratory gating
- dedicated software (e.g. virtual simulation, visualization and segmentation)
- tools, support of DICOM RT object definition, ...)



workflow for PET/CT-guided radiation therapy
treatment planning: strong collaboration between
nuclear medicine and radiation oncology

Indication for ^{18}F -FDG PET/CT-guided radiation therapy treatment planning

Well-established indications: head and neck cancer, lung cancer, gynaecological, oesophageal cancer

Experimental indications: colorectal cancer, breast cancer, lymphoma, malignant melanoma....

Tumour

complex biological object

Macroscopically

shape, density, global metabolism

Microscopically

cell proliferation, hypoxia, neoangiogenesis

Problems during radioterapy
treatment:

Mispositioning of TV

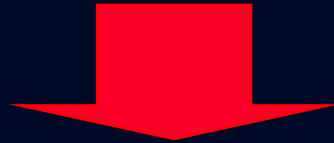
Changes of TV

PTV?

GTV (Gross tumor Volume)?

CTV (Clinical tumor volume)?

BTV (Biological tumour volume)?



International Commission on Radiation
Units and Measurements (ICRU)

PET/CT in oncology: quantitative analysis

SUV

**Standardized Uptake
Value**

“Standardized”?

$$\text{SUV} = \frac{\text{Decay corrected dose/ml of tumour}}{\text{Injected dose/patient weight in gr}}$$

- body-weight corrected

$$SUV_{bw} = \frac{\text{Tissue concentration [kBq ml}^{-1}\text{]}}{\text{Injected dose [MBq] / } W[\text{Kg}]}$$

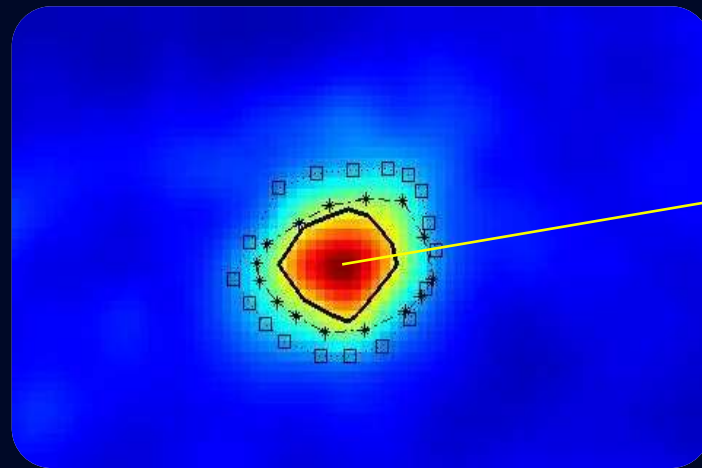
- body-surface-area corrected

$$SUV_{BSA} = \frac{\text{Tissue concentration [kBq ml}^{-1}\text{]}}{\text{Injected dose [MBq] / } 0.007184 \times W^{0.425} \times h^{0.725} [\text{Kg}]}$$

- lean body-mass corrected

$$SUV_{LBM} = \frac{\text{Decay corrected dose / ml of tumour}}{\text{Injected dose / } 48.0 + 1.06 \times (h - 152)}$$

Why SUV?



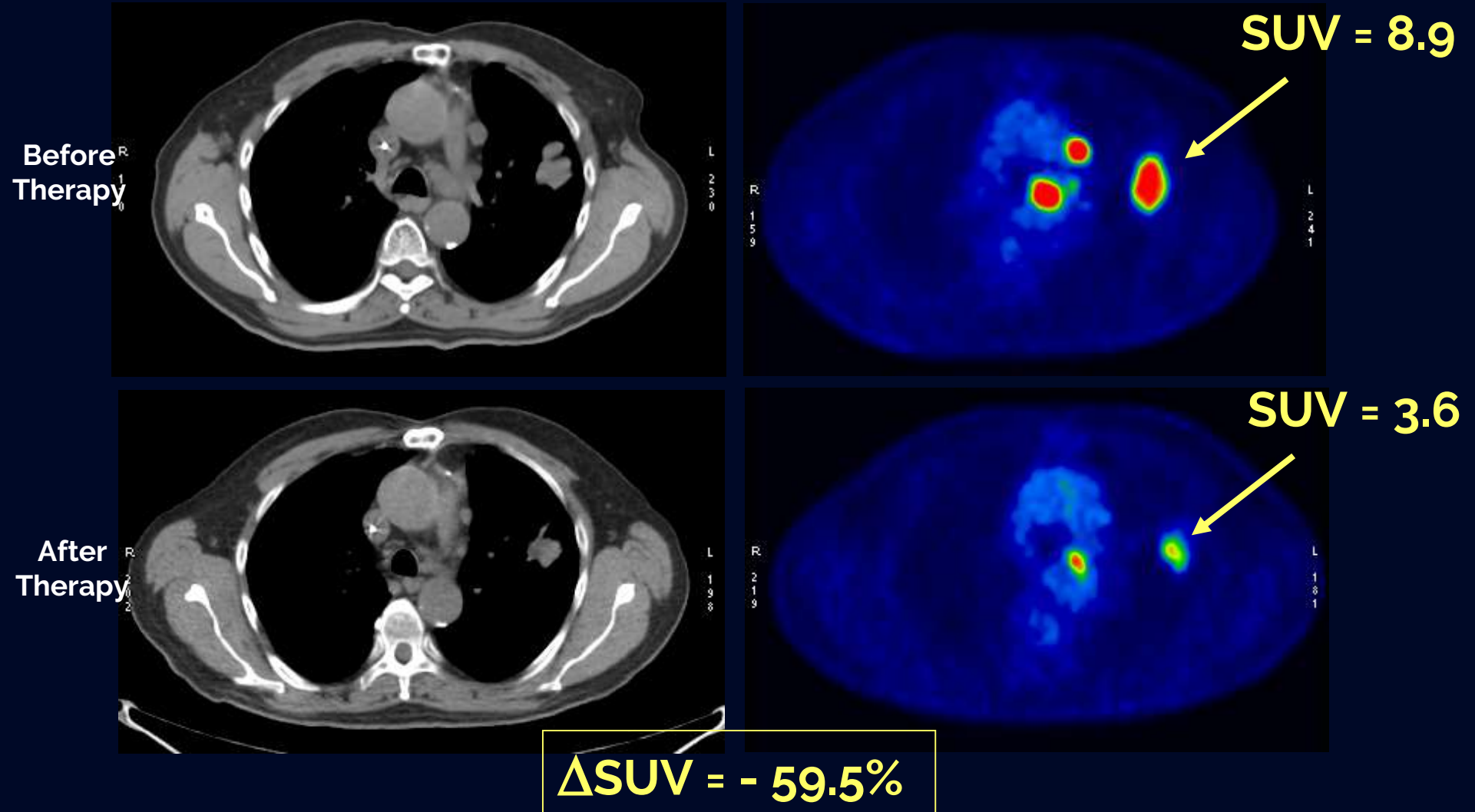
SUV=5.23


Metabolic response: EORTC Recommendations

Progressive metabolic disease (PD)	SUV > 25%↑ Visual increase of extent, new locations
Stable metabolic disease (SD)	SUV < 25% ↑, < 15%↓ No visible increase
Partial metabolic response (PR)	SUV > 15% ↓ one cycle CT SUV > 25% ↓ several cycles CT
Complete metabolic response (CR)	FDG uptake resolved

Young et al., European Journal of Cancer 1999

PET/CT Monitoring therapy response



PET (MRI-DWI)  BTV (SUV/ADC
can be derived)

CT, MRI  GTV



LESION SEGMENTATION

PET/MRI-DWI images

- Poor resolution
- Low signal
- High noise
- Low lesion-to-background contrast
- Movement
- Lesion heterogeneity
- Background heterogeneity

CT/MRI images

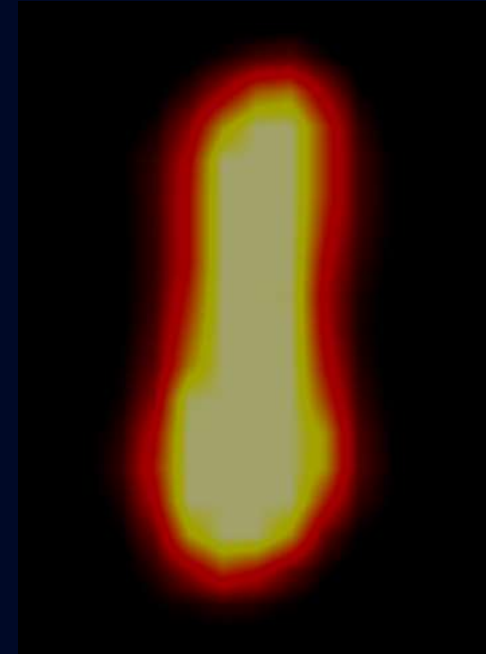
- High resolution
- High signal
- Medium noise
- Low/Medium lesion-to-background contrast
- Movement
- Lesion heterogeneity
- Background heterogeneity

Movement

STATIC TARGET

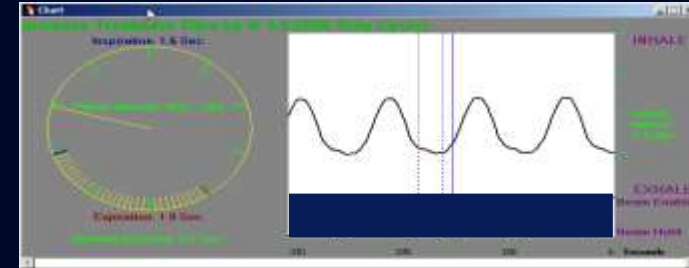


MOVING TARGET



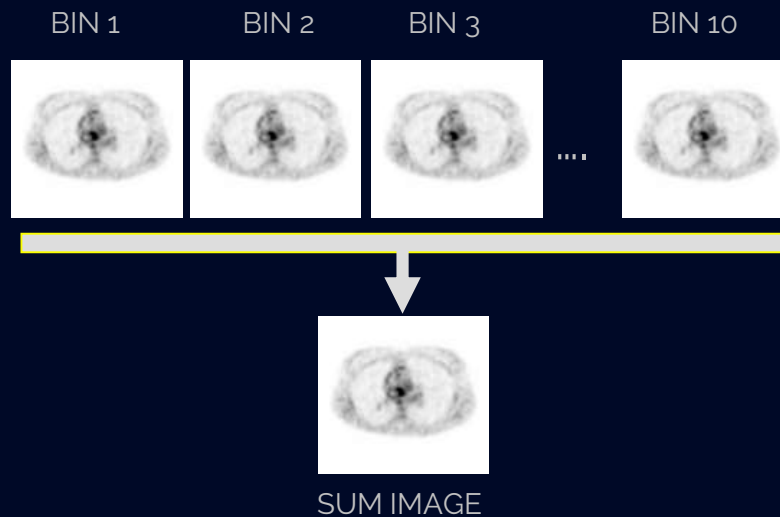
- apparent increase of lesion size
- apparent decrease of activity concentration
- lower threshold for a correct volume definition (10-20% Caldwell 2003)

RESPIRATORY GATING



Varian patent 6,279,579
Varian Medical System: GatingSchool

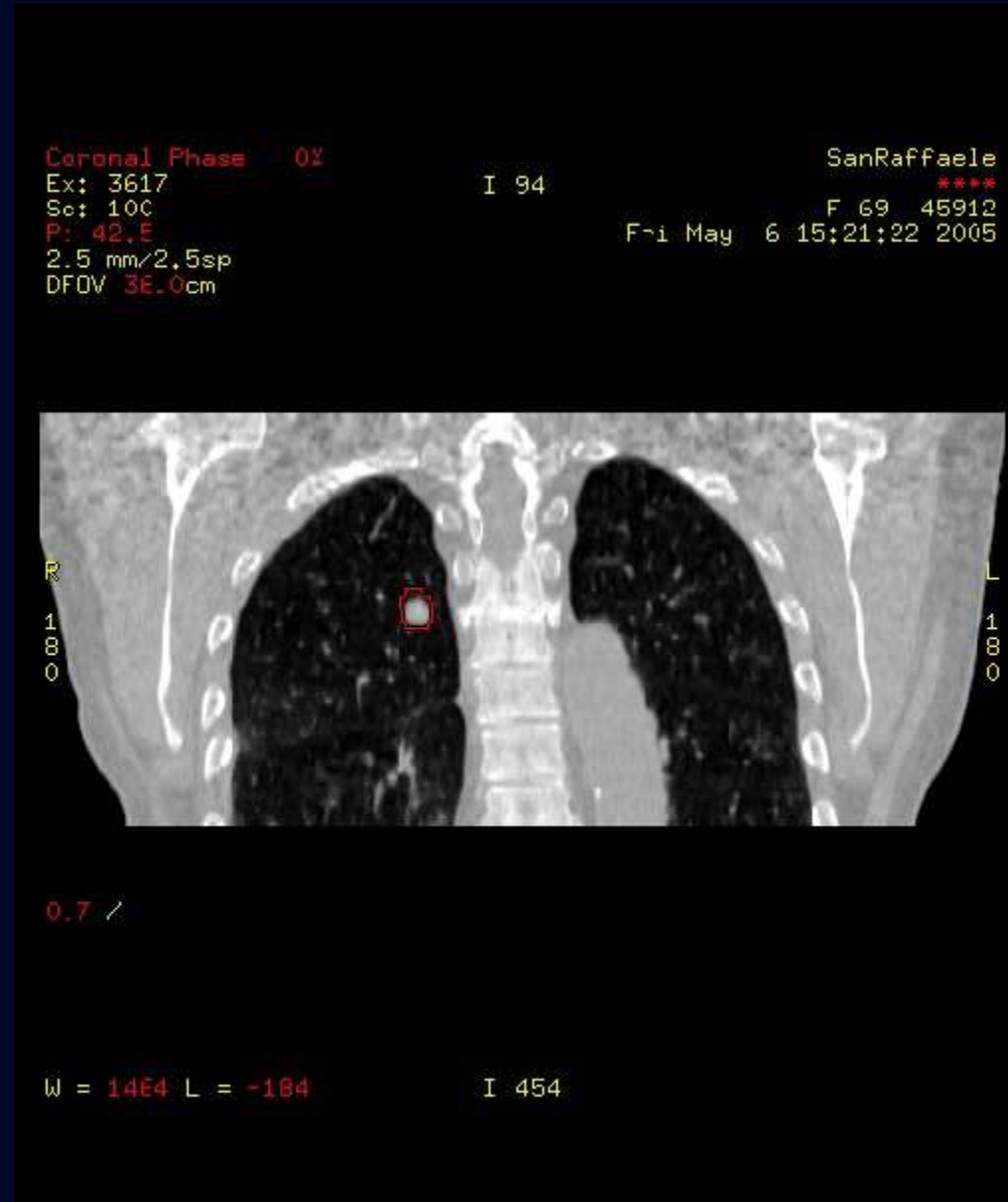
4D PET



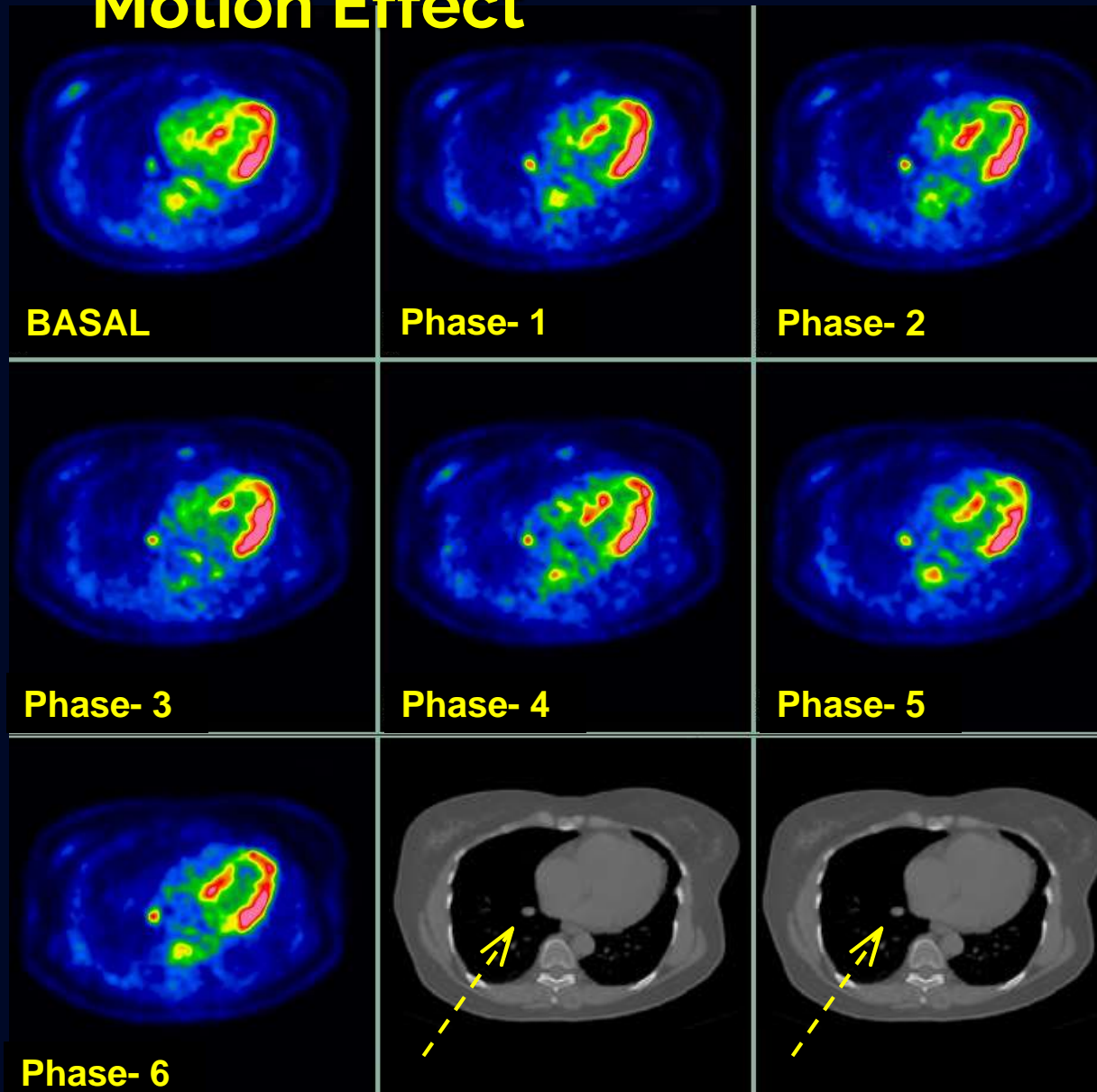
4D CT



4D PET/CT: IMPROVED DEFINITION



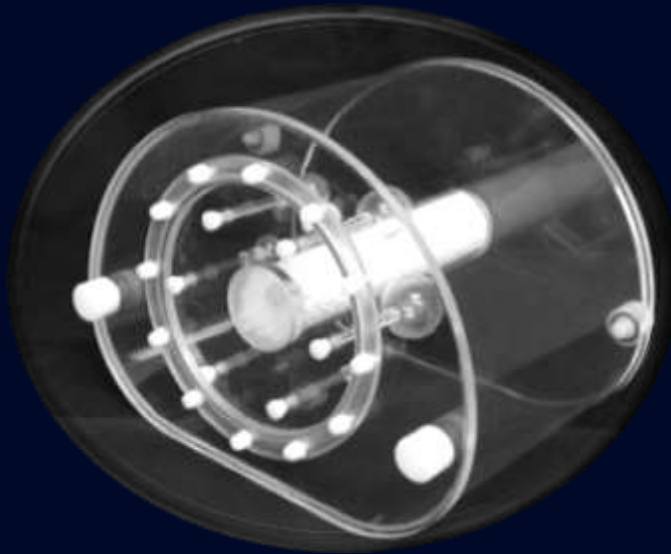
Motion Effect



PET SUV max	
BASAL:	2.2
Ph-1:	2.9
Ph-2:	3.1
Ph-3:	3.3
Ph-4:	3.4
Ph-5:	2.9
Ph-6:	3.5

HSR Milan

SUV estimation during movement

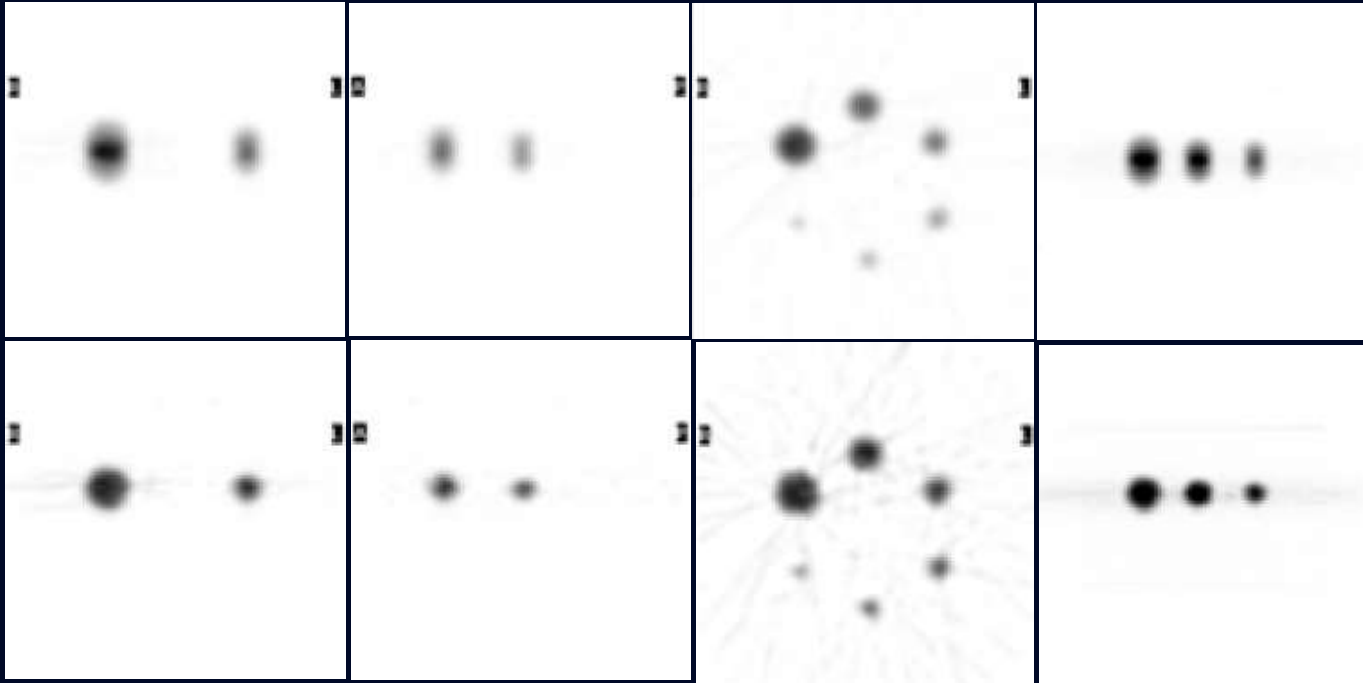


NEMA IQ phantom

Sphere diameter:

10 mm, 13 mm, 17 mm, 22 mm, 28 mm, 37 mm

Motion Effect



Coronal

Sagittal

Axial

Mip

<i>spheres</i>	<i>static</i>	<i>gated</i>	<i>% error</i>
37 mm	33546	31624	-6.1
28 mm	21872	31316	+30.2
22 mm	20607	29919	+31.1
17 mm	13643	22857	+40.3
13 mm	8264	19087	+56.7
10 mm	5143	11897	+56.8

Mawlawi et al.

PARTIAL VOLUME EFFECT

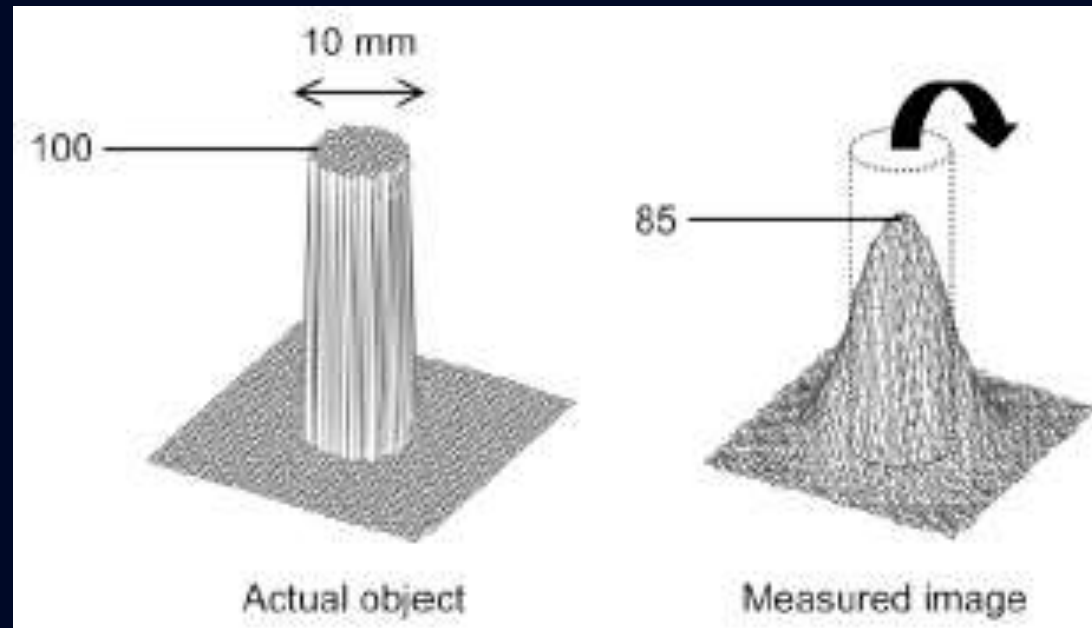
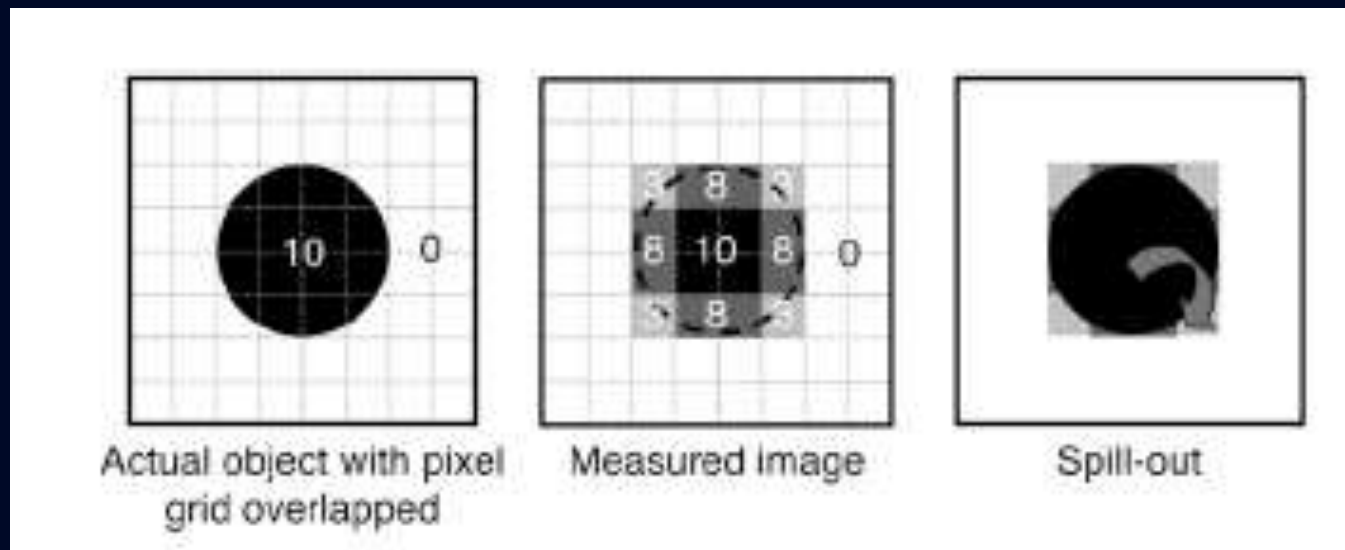


IMAGE BLURRING introduced by the finite spatial resolution of the imaging system
The image is formed by the convolution of the source with the 3D PSF
spill over: part of the signal is seen outside the actual source
reduction of maximum activity

Soret JNM 2007

PARTIAL VOLUME EFFECT

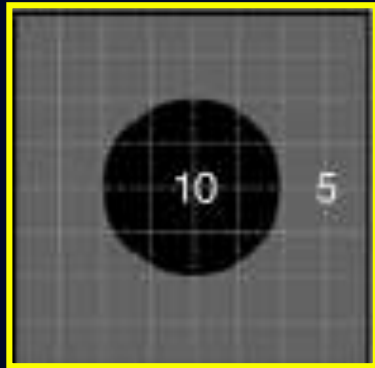


2. **TISSUE FRACTION EFFECT** introduced by **IMAGE SAMPLING**
the contours of the voxels do not match the contours of the tracer distribution
most voxels include different types of tissues

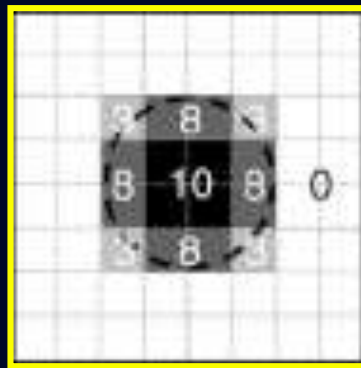
Soret JNM 2007

PARTIAL VOLUME EFFECT

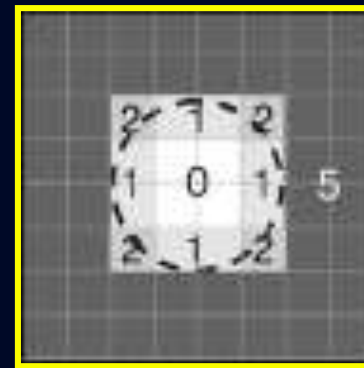
- **SPILL IN and SPILL OUT**



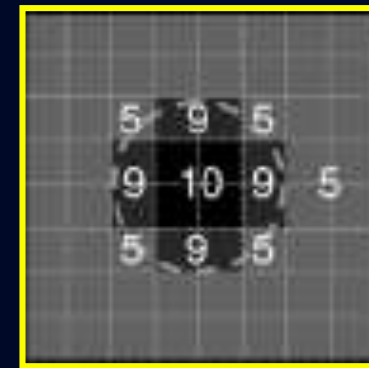
Actual activity distribution



Spill - out

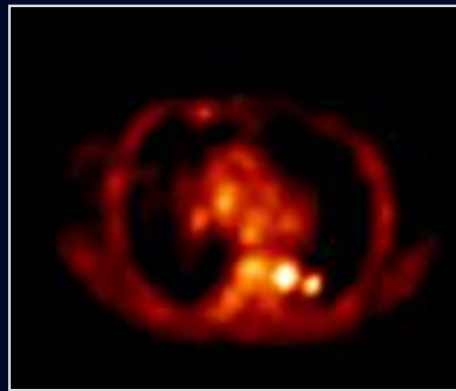


Spill in



Measured image

- **apparent LESION SIZE**

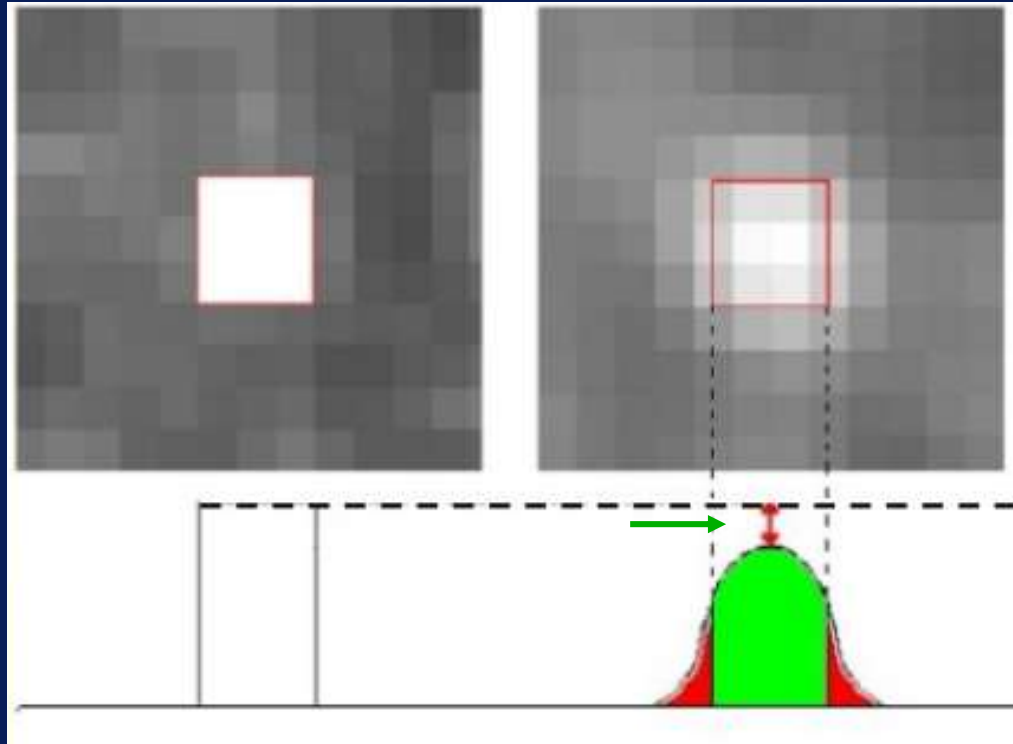


Soret JNM 2007

How to correct SUV for PVE?

Ideal lesion

Real lesion

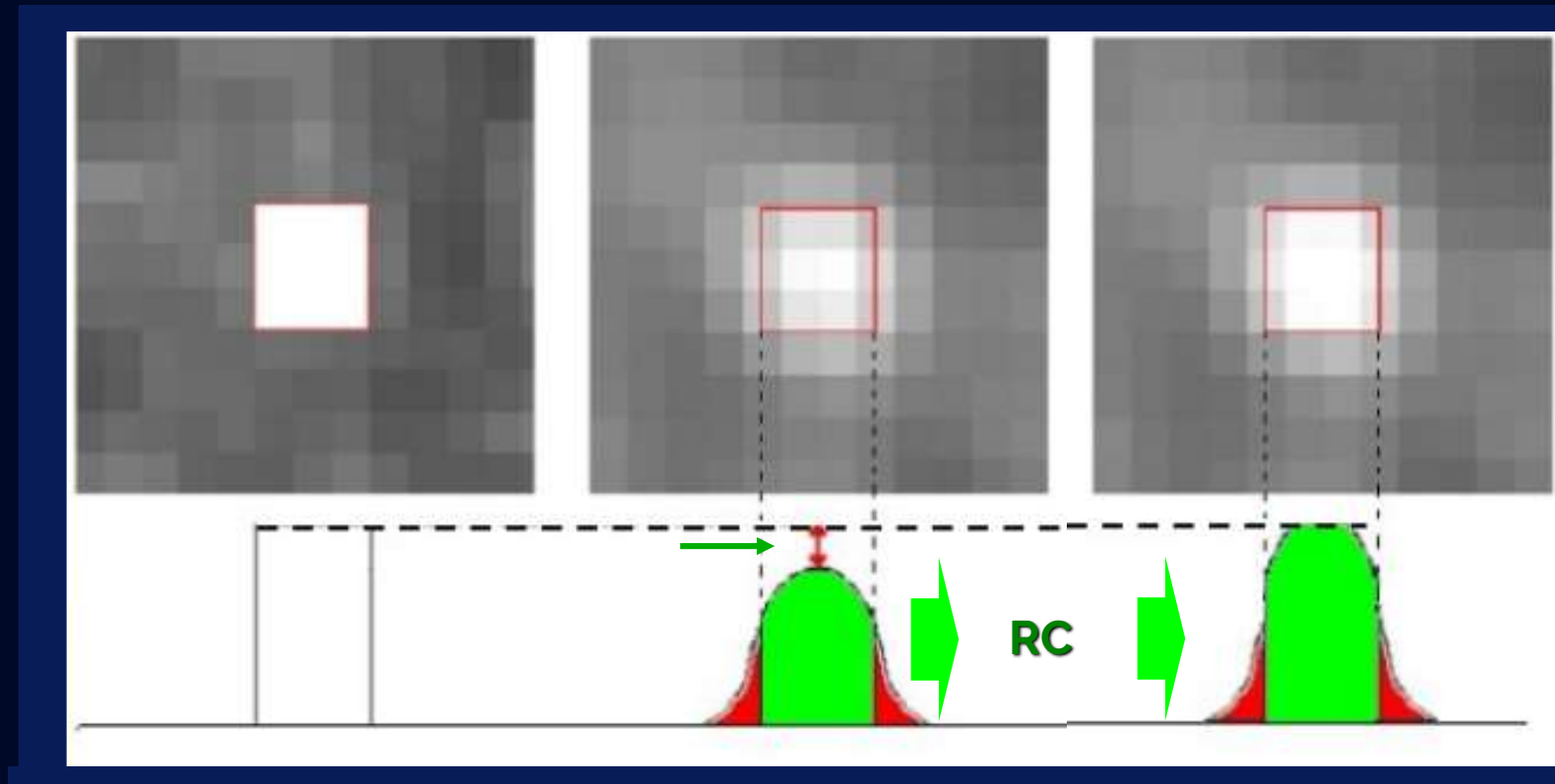


How to correct SUV for PVE?

Ideal lesion

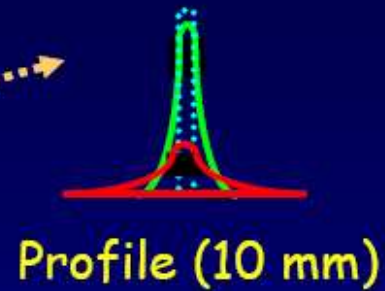
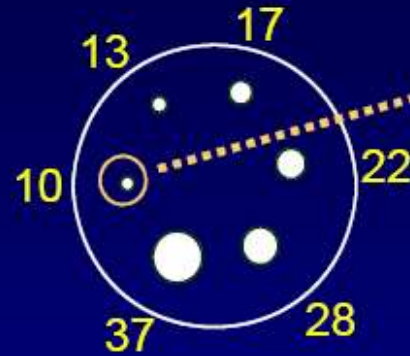
Real lesion

Corrected lesion



Partial volume

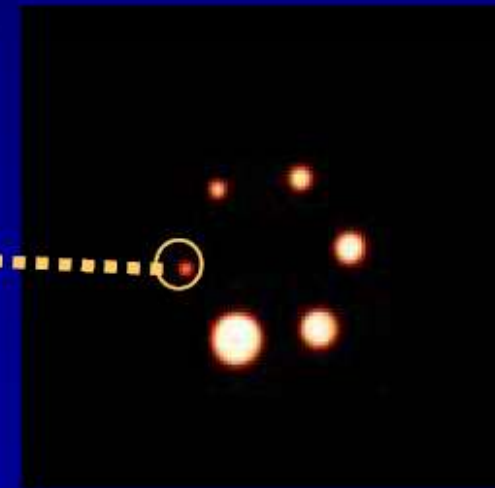
All spheres contain the same activity concentration



**Standard
8 x 8 detector**

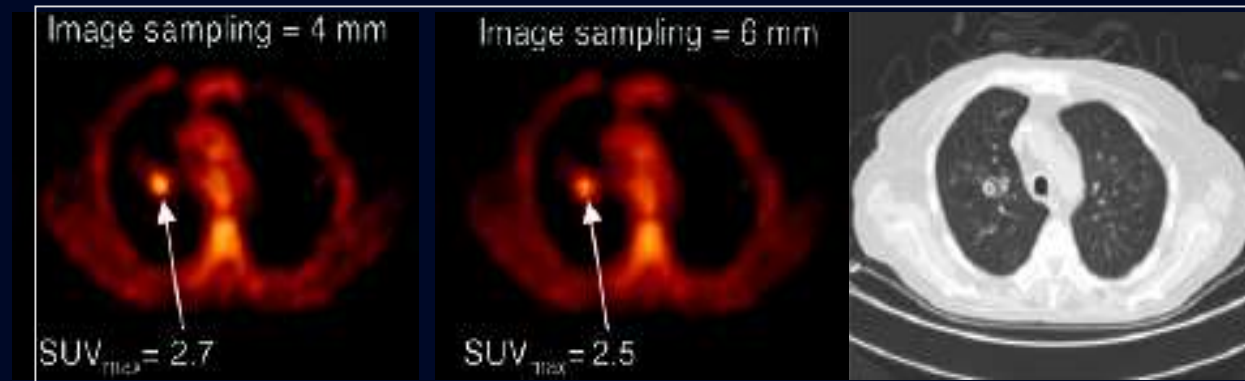


Recovery coefficients



**HI-REZ
13 x 13 detector**

- Image Sampling



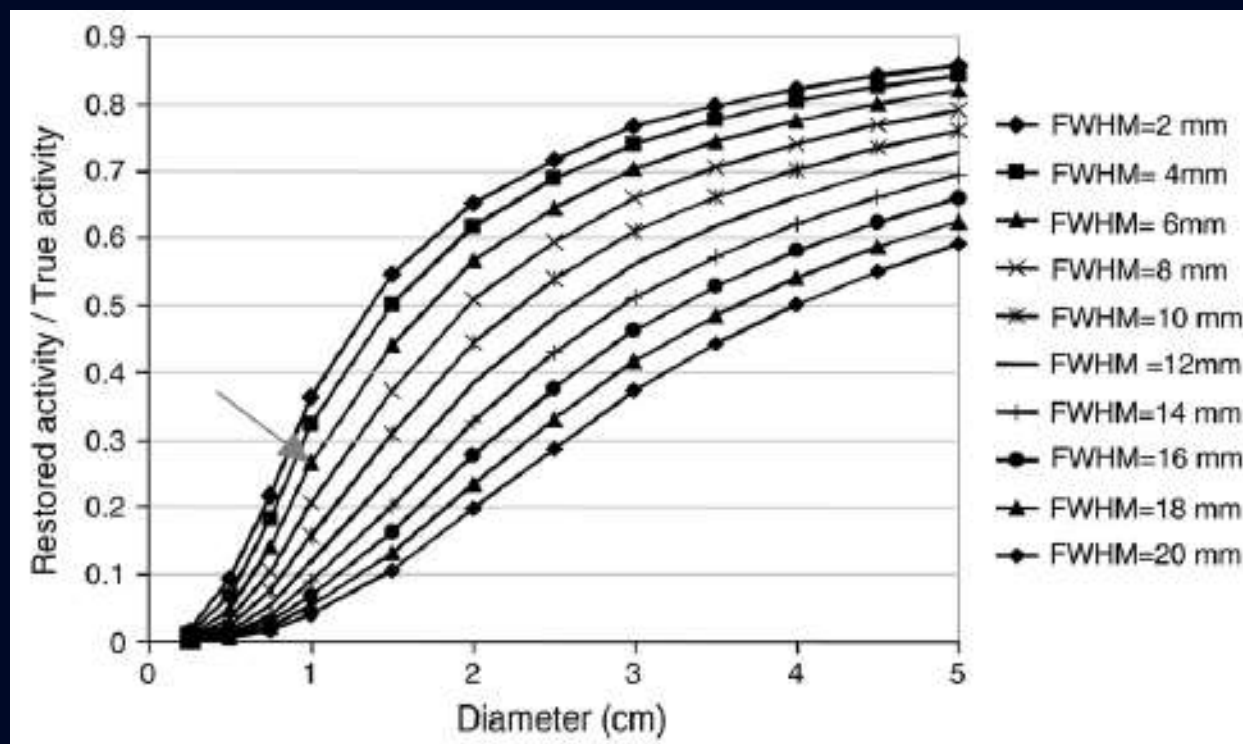
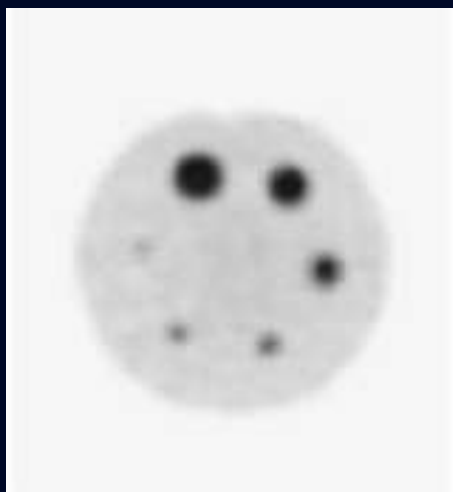
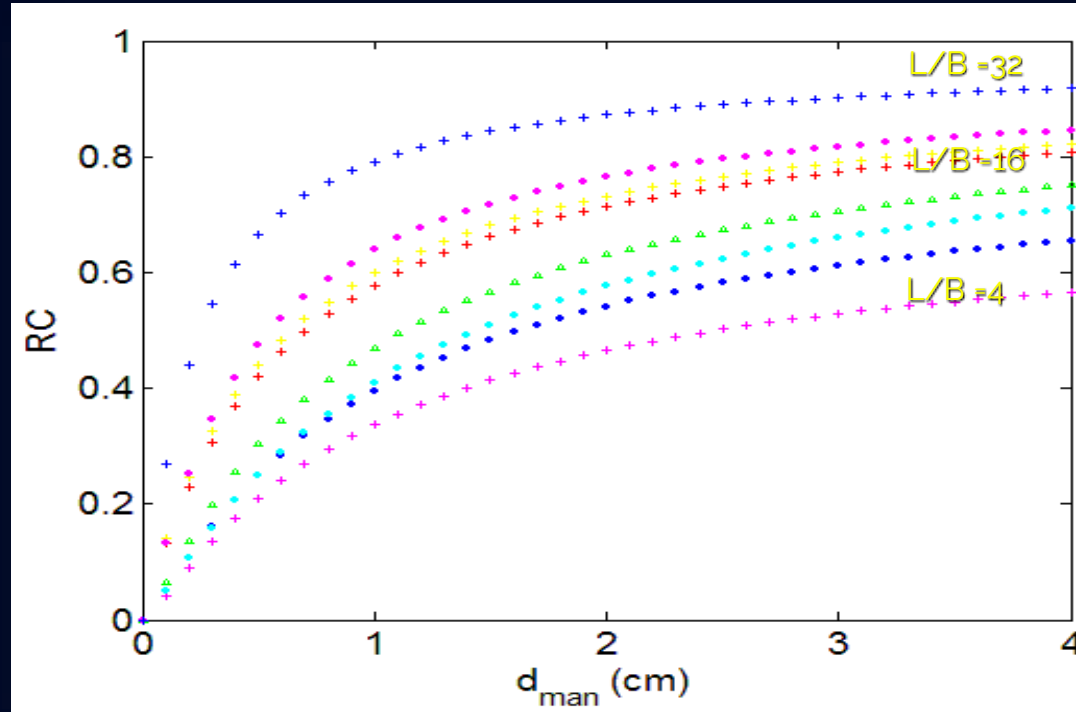


FIGURE 10. Restored activity measured in actual contour of spheres in cold background as function of sphere diameter and spatial resolution of imaging system.



RC depends from:

- **Lesion volume**
- **Lesion concentration/lesion background (L/B)**

Tumour

complex biological object

Macroscopically

shape, density, global metabolism

Microscopically

cell proliferation, hypoxia, neoangiogenesis

Lesion heterogeneity different in CT vs PET

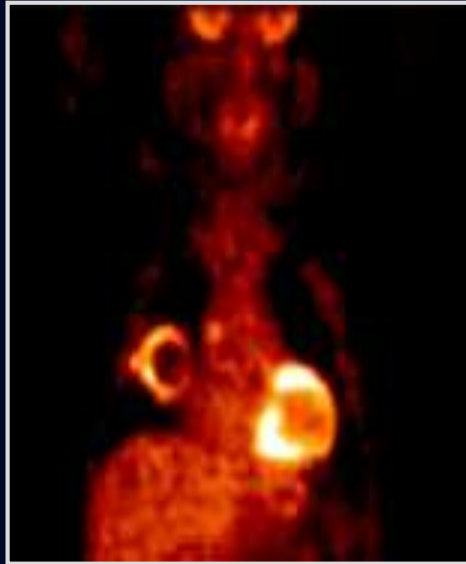
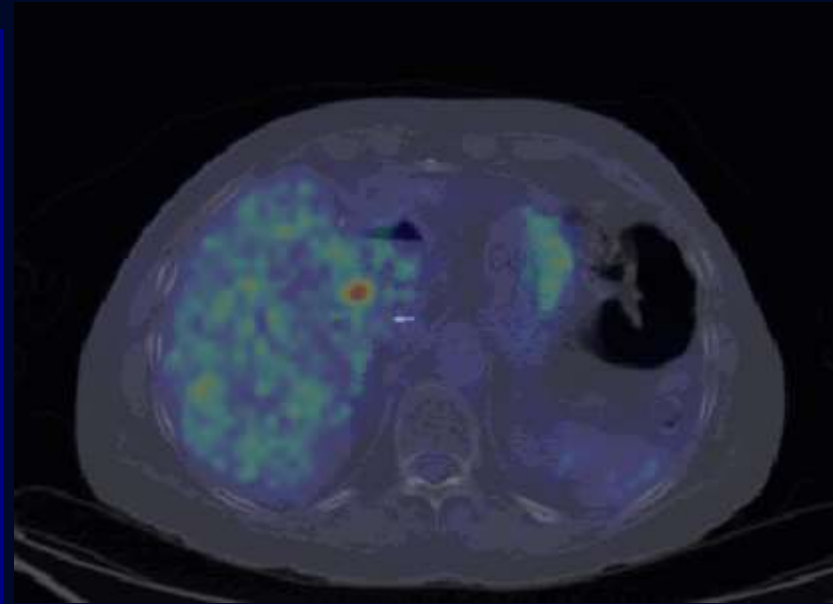
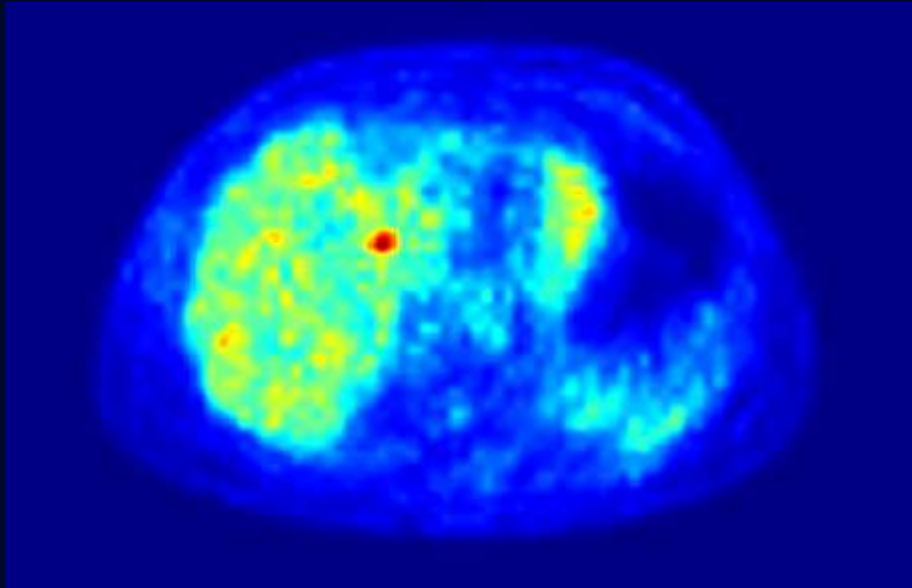


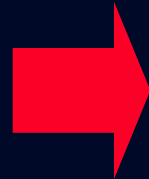
FIGURE 12. CT image (left), corresponding PET image (middle), and PET/CT image (right) of tumor with no uptake in center. Delineation of tumor from CT image would yield inappropriate definition of metabolically active part of tumor.

Background heterogeneity different in CT vs PET



LESION SEGMENTATION

Qualitative methods



Visually inspection,
manual contouring

Quantitative methods

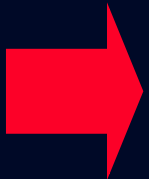


Image processing,
semi-auto/autocontouring

Segmentation : partitioning of an image I
into different subregions S



classes

$$I = \sum_i S_i$$

$$I = 1, \dots, n$$

$$S_i \subset I$$

$$S_i \cap S_j = \emptyset$$

Manual methods

- Image modality-dependence
- Operator-dependence
- Window level-dependence (colorbar)

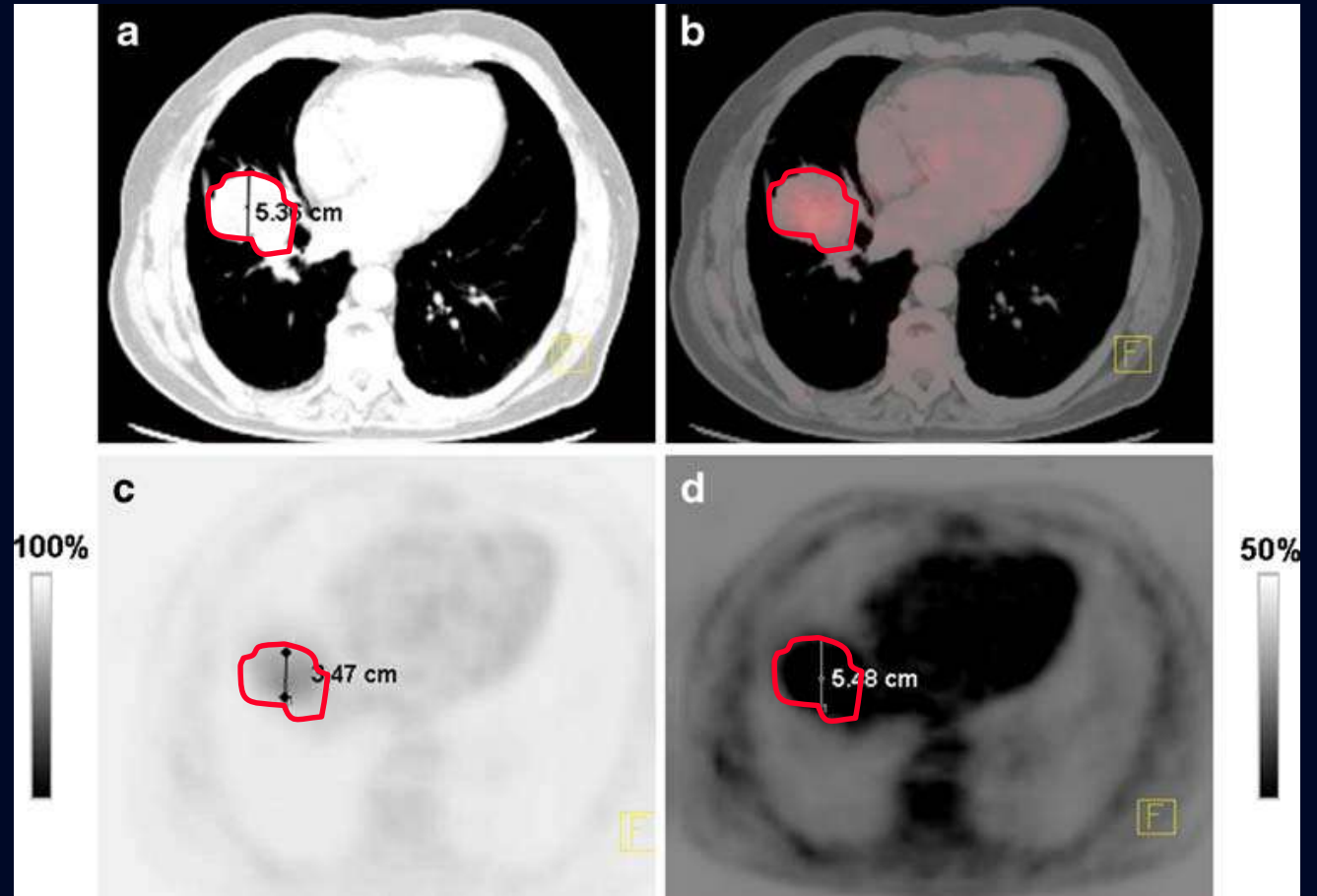
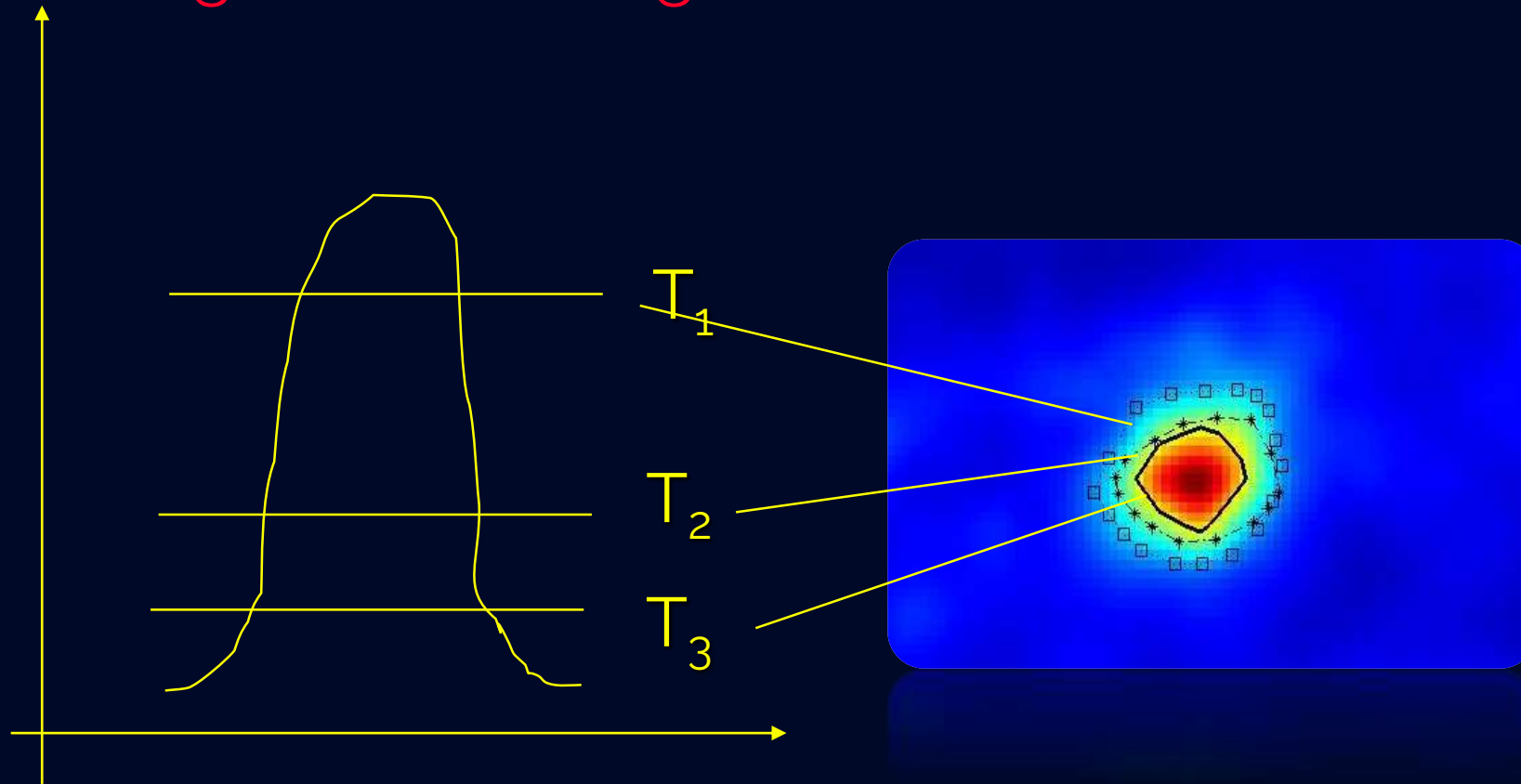


Image thresholding methods



$$\text{lesion} = T[I(\mathbf{x})] = \begin{cases} 1, & I(\mathbf{x}) \geq T \\ 0, & I(\mathbf{x}) < T \end{cases}$$

Image thresholding methods

2a) with respect to lesion uptake (fixed)

%T = 40, 50, 60% of the maximum uptake

2b) with respect to lesion volume

$$\%T = a + b \times \log_{10}(\text{BTV}) + q$$

a = 59.1

b = -18.5

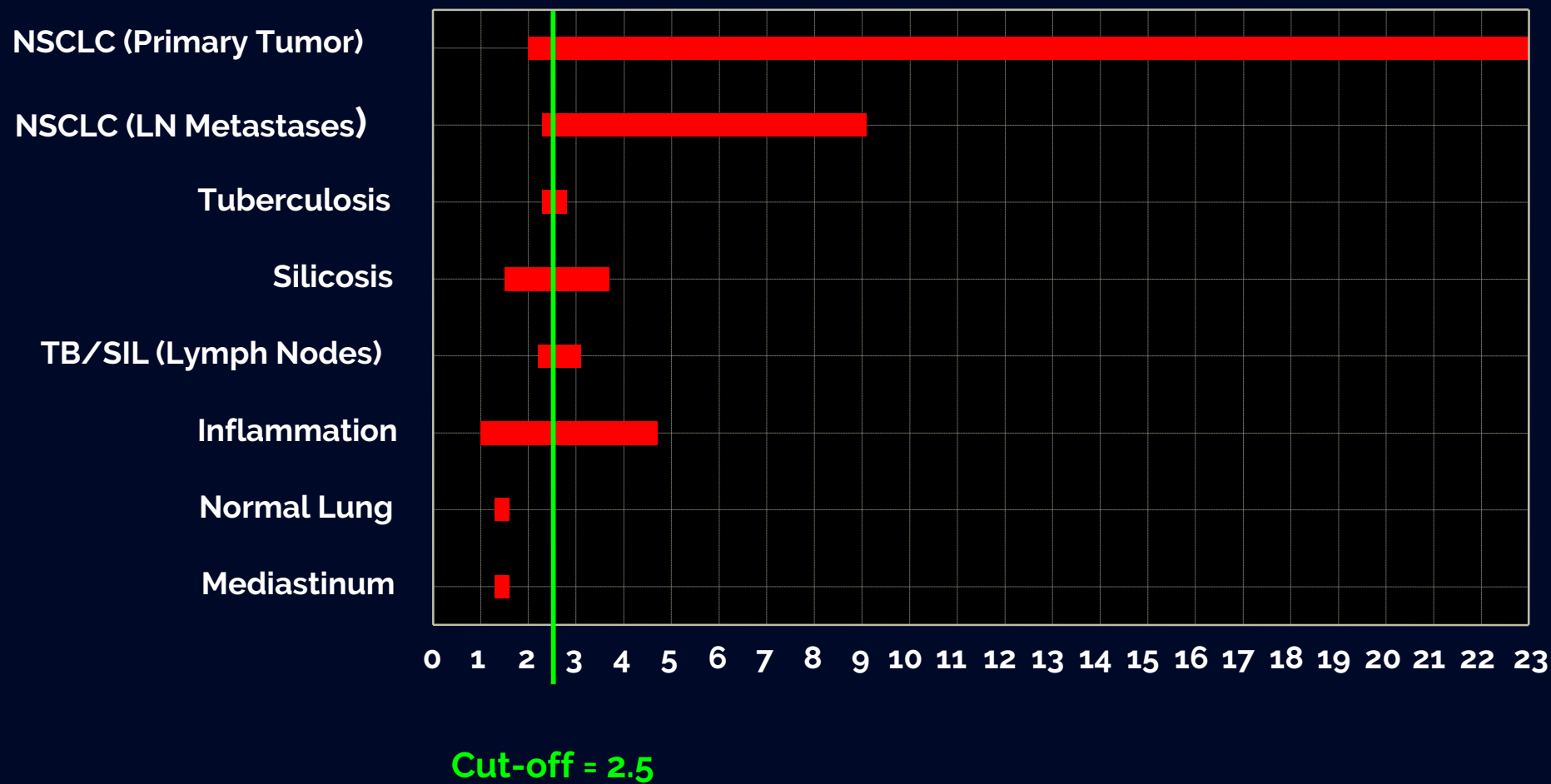


a priori knowledge of the lesion volume

2c) absolute

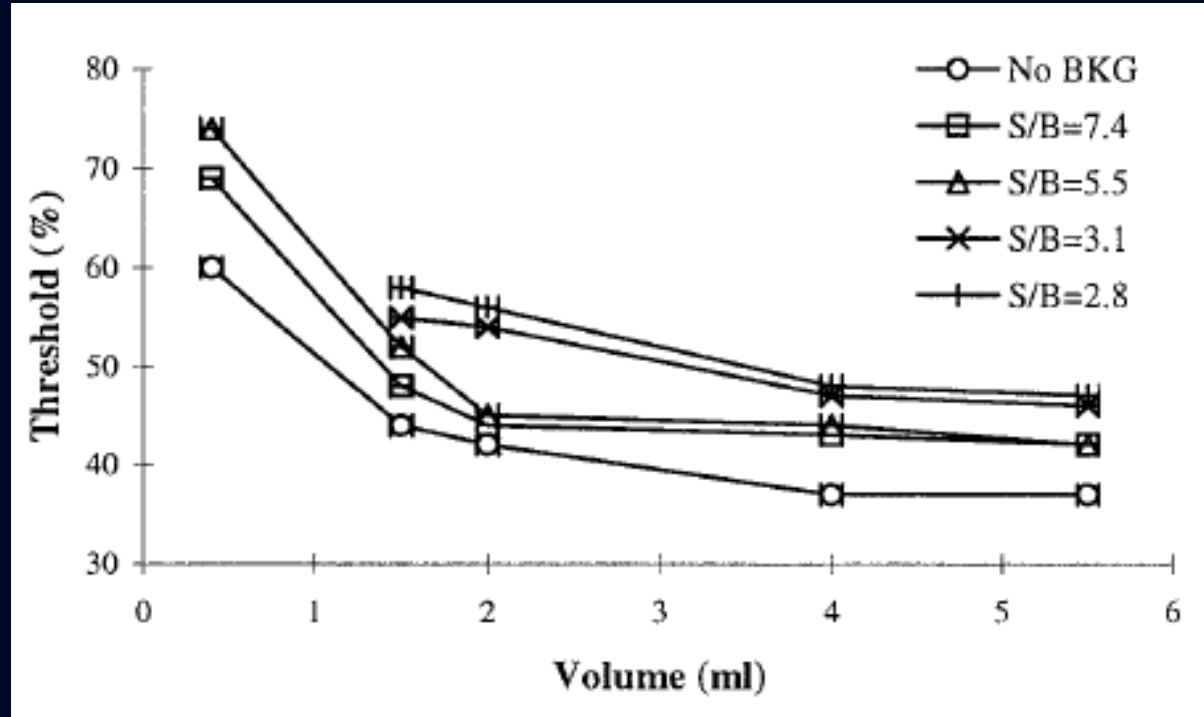
T = 2,5 cut off

SUV in oncological and not-oncological diseases



2d) with respect to lesion-to-background ratio (LB)

$$T = a + b \times 1/LB$$

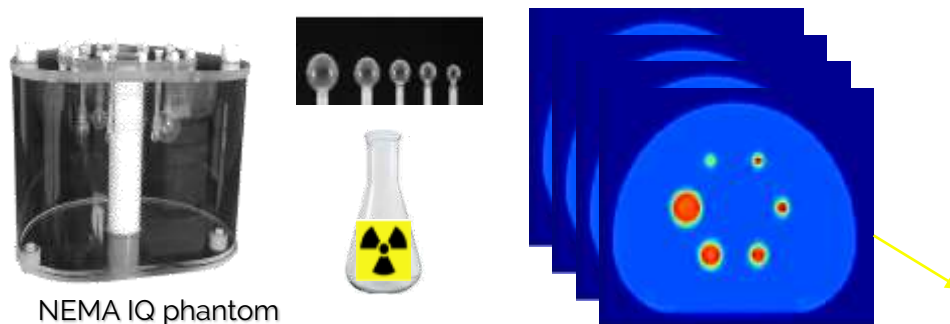


precalibration of LB vs lesion volume is necessary

a priori knowledge of the lesion volume

Erdi et al.,1997

Solutions (Repeatable/Reproducible/Accurate)



NEMA IQ phantom

Automatic segmentation of lesion volume

070-1-4708-0034-A-130021-02-00213-0002

Adaptive threshold method based on PET measured lesion-to-background ratio for the estimation of Metabolic Target Volume from ^{18}F -FDG PET images

Francesca Gallivanone, Federico Padoa, Luca Provenzi, Member, IEEE, Mario C. Gilardi, Carlo Canevari, Isabella Castiglioni

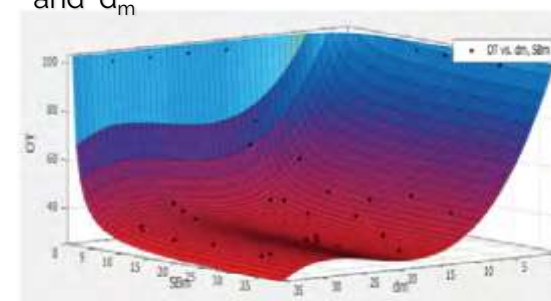
Elsevier Publishing Corporation
Computational and Mathematical Methods in Medicine
Volume 20, Issue 1, 2017, 12 pages
<http://dx.doi.org/10.1016/j.cmm.2017.07.001>

Research Article

An Adaptive Thresholding Method for BTV Estimation Incorporating PET Reconstruction Parameters: A Multicenter Study of the Robustness and the Reliability

M. Brunzella,¹ E. Marfisi,¹ C. Bello,¹ C. Boscon,¹ I. Castiglioni,¹ C. Cavadas,¹ M. Cazzanese,² S. Morroni,² F. Harimi,² M. Gini,² F. Betta,² F. Gallivanone,¹ E. Grassi,³ M. Facilio,³ E. De Ponti,³ M. Stasi,³ S. Pasotto,³ S. Valzania,³ and D. Zanzi⁴

Adaptative Threshold = function of L/B_m and d_m



Automatic Partial Volume correction

Elsevier Publishing Corporation
BioMed Research International
Volume 2017, Article ID 790456, 12 pages
<http://dx.doi.org/10.1155/2017/790456>

Research Article

A Partial Volume Effect Correction Tailored for ^{18}F -FDG-PET Oncological Studies

F. Gallivanone,¹ C. Canevari,² L. Gianolli,² C. Salvatore,³ P. A. Della Rosa,¹ M. C. Gilardi,¹ and I. Castiglioni¹

¹ IRCC-CNR, Via Eli Gerli 93, 20090 Segrate, Milan, Italy

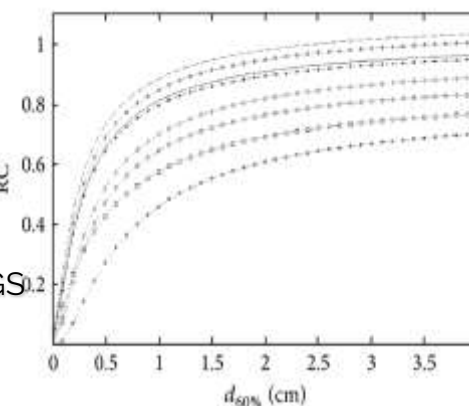
² IF San Raffaele, Via Olgettina 62, 20090 Segrate, Milan, Italy

³ University of Milan-Brescia, Milan, Italy

PVE Correction in PET-CT Whole-Body Oncological Studies From PVE-Affected Images

Francesca Gallivanone, Alessandro Seifino, Eleonora Grasso, Carlo Canevari, Luigi Gianolli, Cristina Mena, Maria Carla Gilardi, and Isabella Castiglioni

$$RC = \frac{L/B_m}{L/B_{GS}}$$



--- $L/B_m = 28-29$ $L/B_m = 8-11$
 \cdots $L/B_m = 25-27$ $L/B_m = 6-7$
 — $L/B_m = 17-19$ $L/B_m = 4-6$
 \cdots $L/B_m = 14-16$ $L/B_m = 2-3$

$$T = a + b \times SUV_{\text{mean}}$$

Black et al., 1990

$$a = 0.588 \quad b = 0.307$$

$$T = \text{Contrast level} \times (L_{\text{max}} - B_{\text{mean}}) + B_{\text{mean}}$$

Drever et al., 2006

$$T = \beta L_{\text{mean-70\%}} + B_{\text{mean}}$$

Nestle et al., 2005

$$\beta = 0.15$$

$$T = (a \times SUV_{\text{mean-70\%}} + b \times B_{\text{mean}}) / SUV_{\text{max}}$$

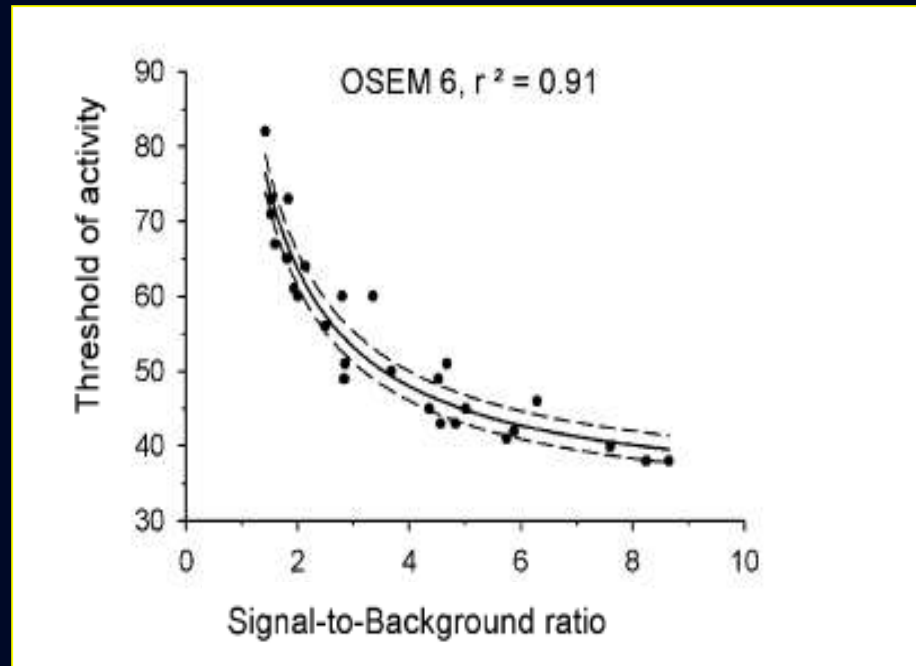
Schaefer et al., 2008

$$a = 0.50 \quad b = 0.50 \quad \text{for } d > 3\text{cm}$$

$$a = 0.67 \quad b = 0.60 \quad \text{for } d < 3\text{cm (Ecat ART)}$$

$$\%T = b \times B/L + c$$

Daisne et al. , 2003



2d) iterative

$$\%T = a/V_l + b \times B/L + c$$

Jentzen et al., 2007

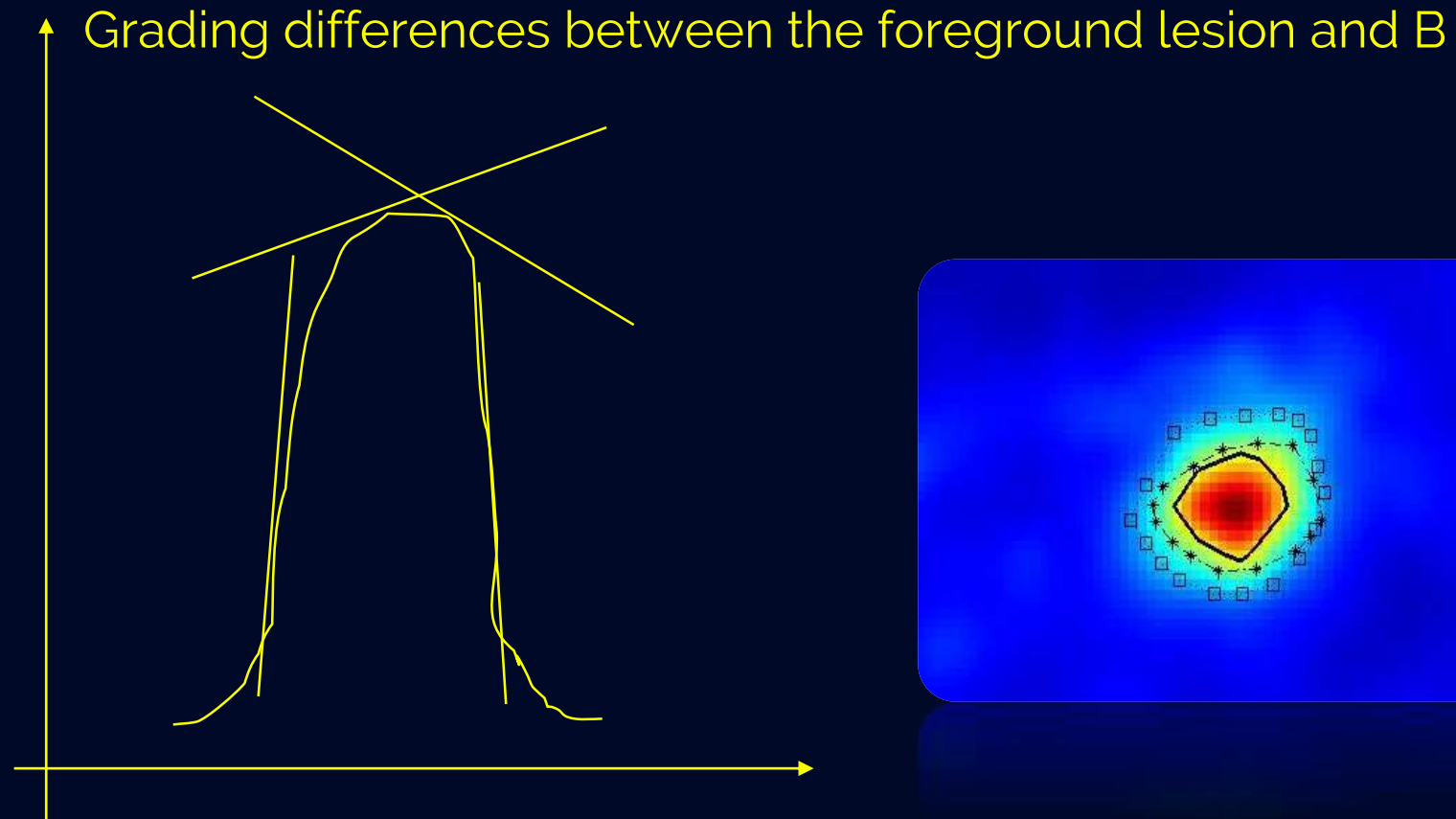
$$a = 7.8\% \quad b = 61.7\% \quad c = 31.6\%$$

$$\%T = a_0 + \exp[a + b/V_l + c \log V_l]$$

Nehmeh et al., 2009

$$a_0 = 5 \quad a = 3.568 \quad b = 0.197 \quad c = -0.1069$$

(3) variational



3a) edge detectors (Sobel operator)

3b) ridge detectors (Watershed Transform)

3c) deformable active contour models

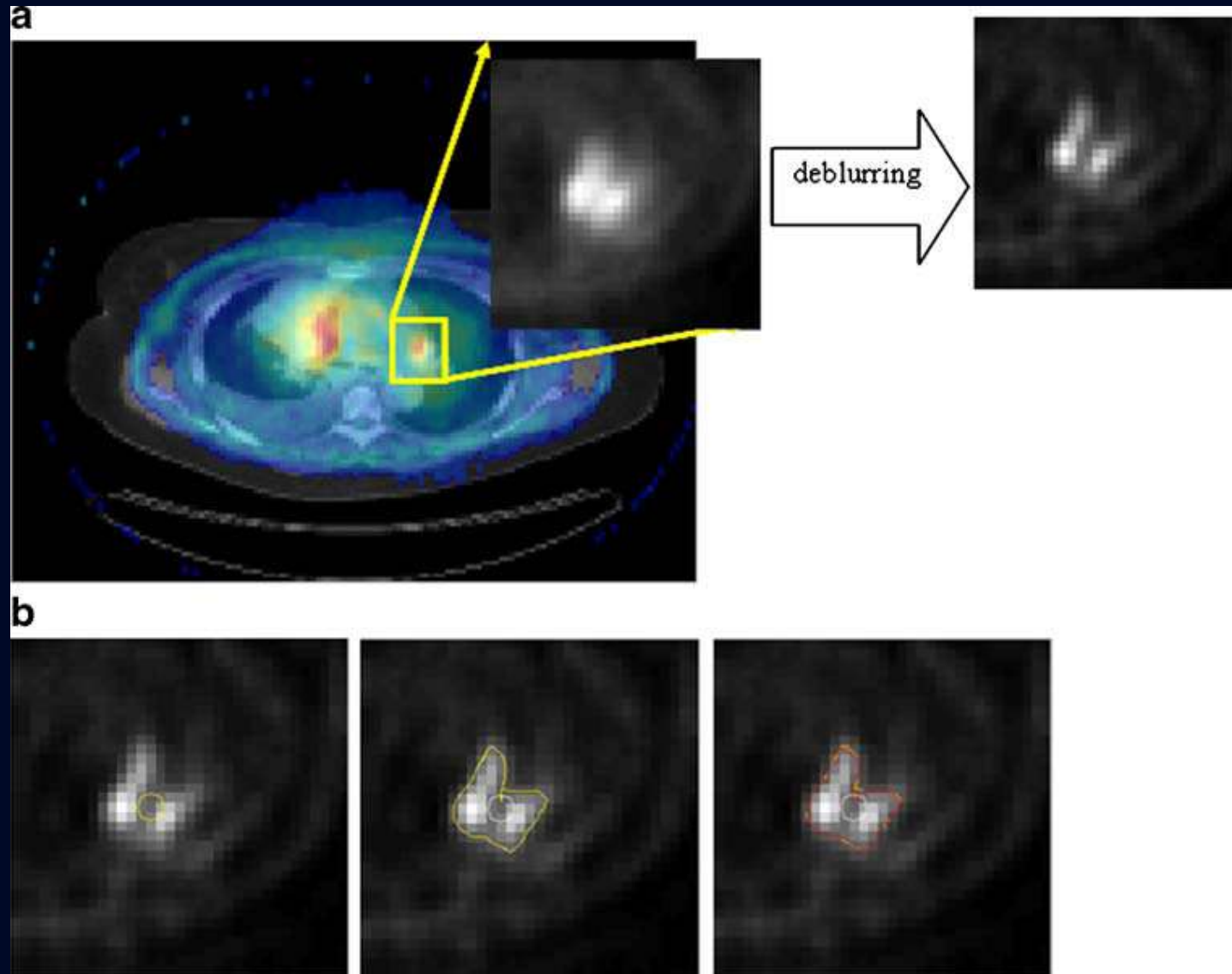
Geometric function of surface deforming under internal (surface bending characteristics) and external (directional gradients) forces



Contours are identified by sharp variations (“snakes”)

Gradient Vector Flow (GVF), iterative evolutionary Poisson Differential Equation (up to the balance between internal and external forces) (e.g. level set method,)

level set method



Minimum contours

40 it

(4) learning methods

learning task aims to discriminate signals in the lesion voxels from surrounding normal tissue voxels based on a set of extracted features from these images



supervised

unsupervised

Supervised learning is used to estimate an unknown (input, output) mapping from known labelled samples called the training set (e.g. classification of lesions given a certain number of example images)

In unsupervised learning, only input samples are given to the learning system (e.g. clustering)

Classifiers:

k-nearest neighbour (KNN)

support vector machine (SVM)

artificial neural network (ANN)

Clustering:

k-means algorithm

fuzzy C-means (FCM) algorithm

Expectation maximization (EM) algorithm

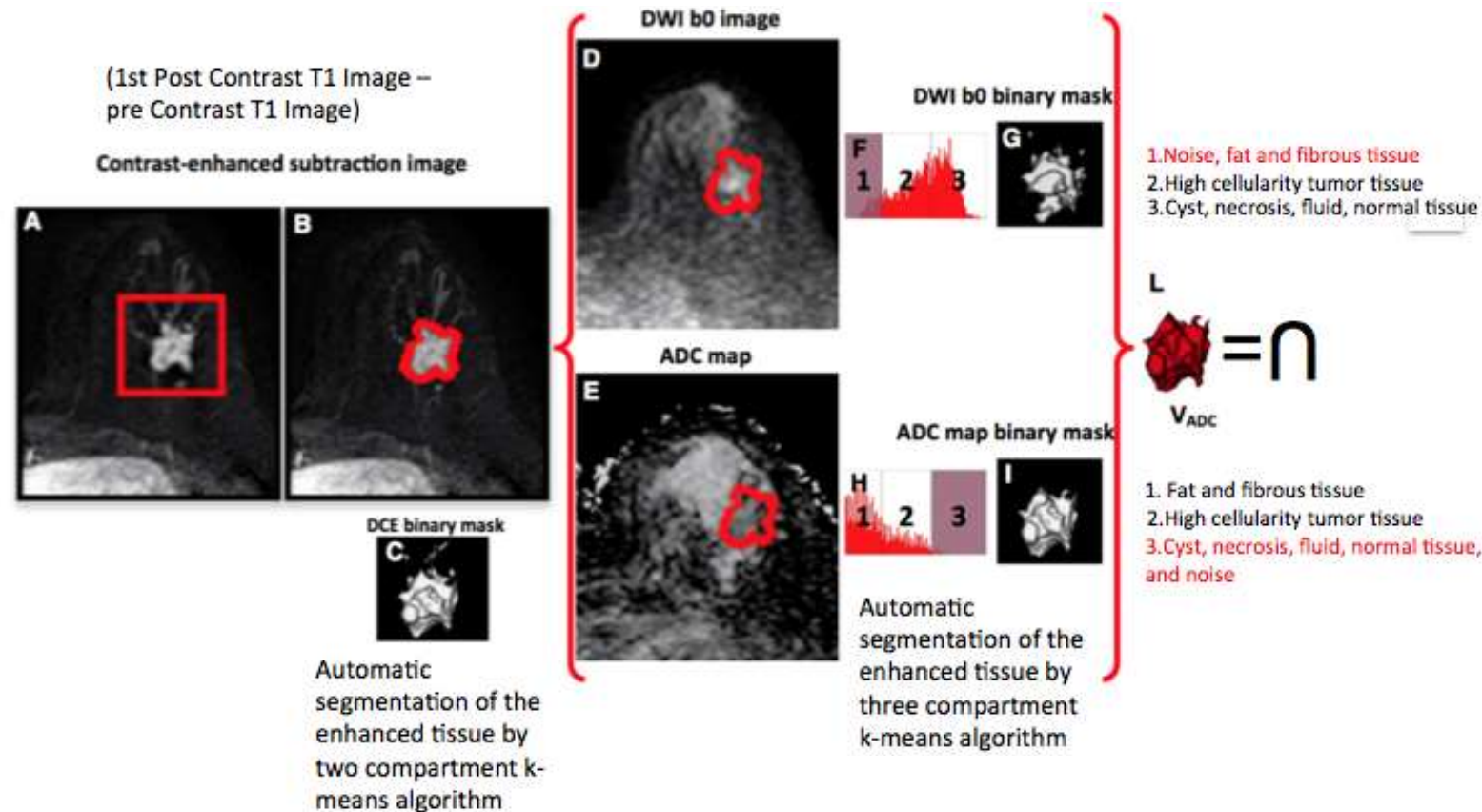
Solutions (Accurate/Repeatable/Reproducible)

- Automatic segmentation of lesion volume on MRI images

An Automatic Segmentation Method for the Measurement of the Functional Volume of Oncological Lesions on MR ADC Maps

Francesca Gallivanone, Marta Maria Panzeri, Carla Canevari, Interleghi Matteo, Claudio Lania, Luca Gianoli, Francesco De Cobelli, and Castiglioni Isabella

978-1-5090-1642-6/16/\$31.00 ©2016 IEEE

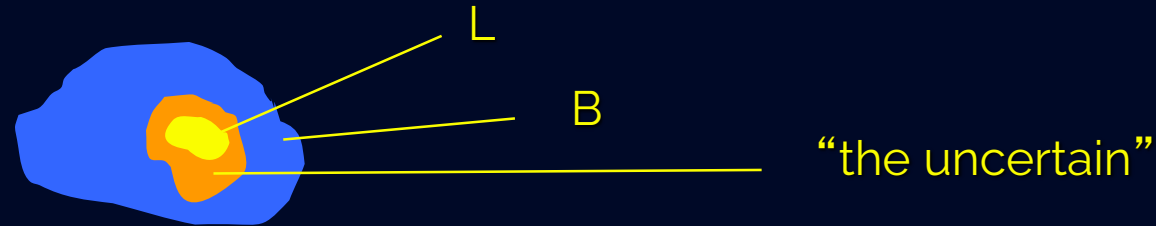


(4) Stochastic modeling

The intensity distribution of tumour and B are statistically different

4a) Gaussian mixture model (GMM)

3 classes:



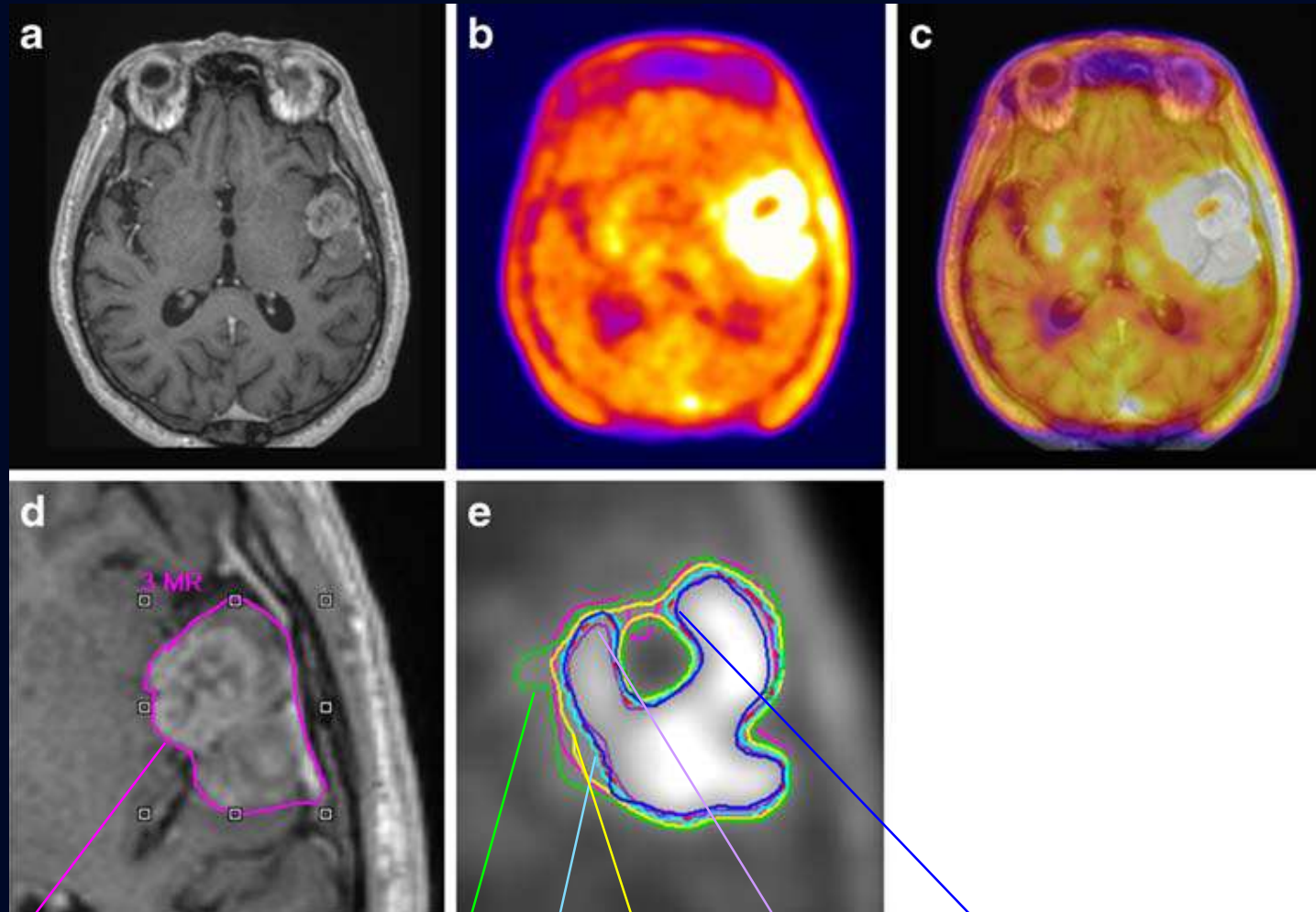
The maximum likelihood estimates the unknown parameters by the probability of voxel x_i belonging to class k p_{ik}

Markov models, wavelet-based multiscale decomposition, Fuzzy locally adaptive Bayesian (FLAB)

MRI

 ^{18}F -FET PET

MRI-PET

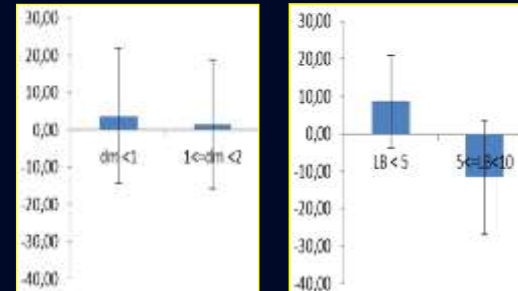
 GTV_{MRI} $\text{GTV}_{40\%}$ GTV_{man} GTV_{LB} $\text{GTV}_{2,5}$ GTV_{grd}

Vees et al., 2009

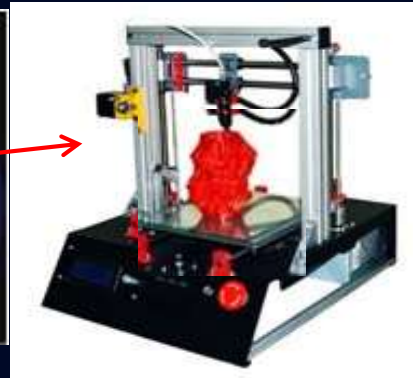
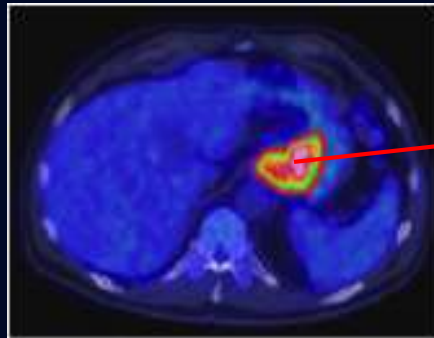
Validation on small, heterogeneous, non-spherical lesions



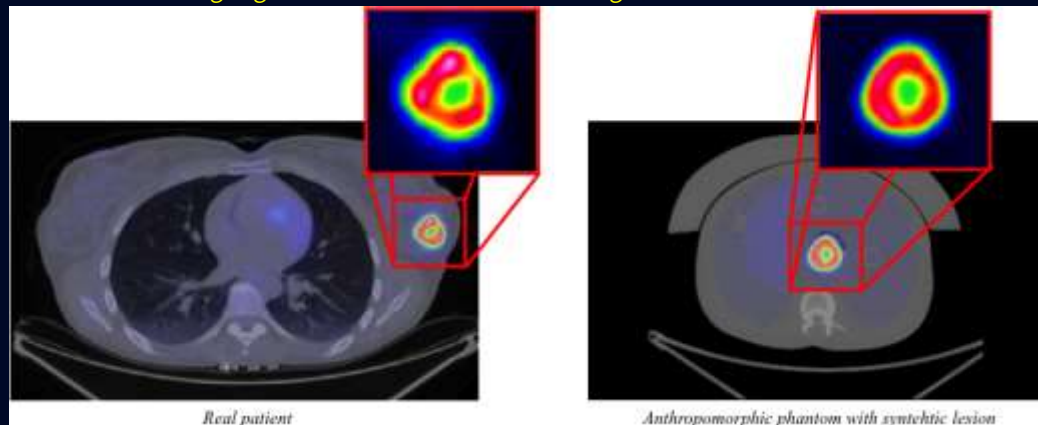
% residual error in V_m



d (mm)	% residual error after PVE correction
9.8	0.26 ± 0.12
12.3	0.13 ± 0.06
15.6	0.002 ± 0.002
25.8	0.09 ± 0.03
31.3	0.10 ± 0.01



Selected as highlight at IEEE NSS MIC, Strasburgh, November 2016



		$V_{GS} (cc) \ 29.4$			$V_{GS} (cc) \ 11.7$
		$L/B_{GS} \ 24$			$L/B_{GS} \ 25$
		$V_{GS} (cc) \ 10.0$			$V_{GS} (cc) \ 6.8$
		$L/B_{GS} \ 11$			$L/B_{GS} \ 10$
		$V_{GS} (cc) \ 0.9$			$V_{GS} (cc) \ 7.4$
		$L/B_{GS} \ 4$			$L/B_{GS} \ 4$

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IN CONCLUSION

- Lesion segmentation is a key challenge in medical imaging
- Respiratory gated acquisitions is mandatory to improve lesion definition when respiration is involved (thorax)
- Partial volume correction is recommended to improve lesion definition when lesion is small and image has low LB (PET, MRI-DWI)
- Segmentation methods can be used to extract lesion volume but should be defined taking into account for lesion complexity and on different image modalities