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Metabolic volume measurement (physics and methods)

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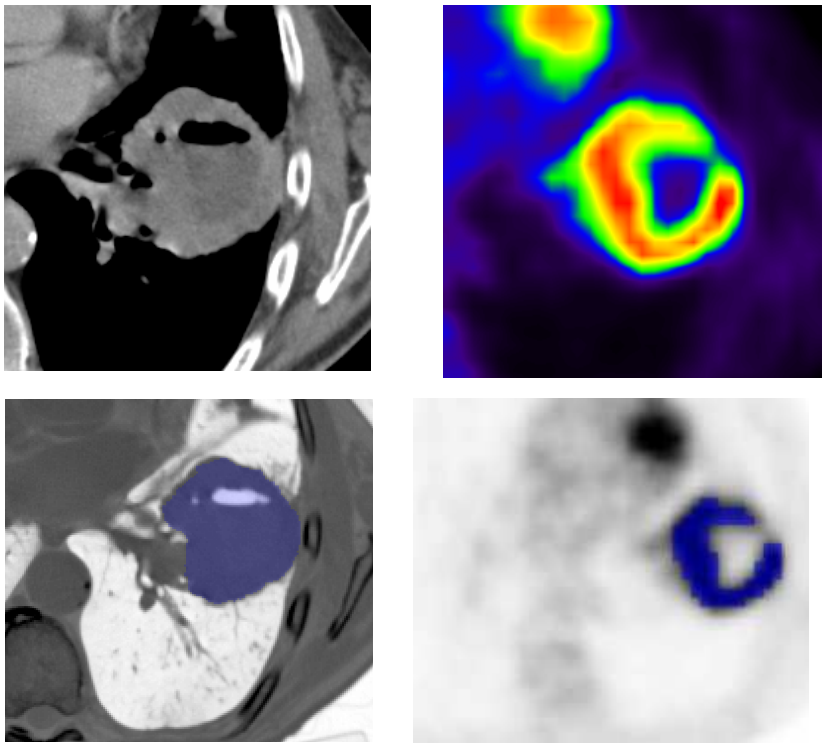
Metabolic volume vs tumor size



Metabolic volume ≠ tumor size !

Tumor size = 1D, 2D or 3D measurement of tumor size on structural (anatomical) images (CT or MR)

Metabolic volume = 3D measurement of the metabolically most active part of the tumor

Metabolic volume

- "Biological" target volume – RT
- Prognostic factor (Sasanelli M, *et al.* 2012)
- Predictive factor (residual or change in…)
- SUV x MVOL= TLG (or TLP for ^{18}F-FLT)

Aerts et al.

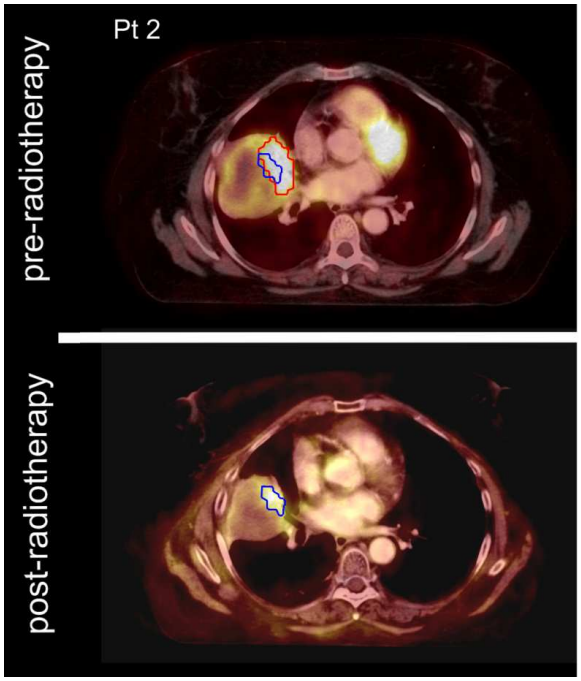


TABLE 2
Significant Differentiation of Prediction of PFS Using Different Quantitative Measurements for Metabolic Response After 1 Week of Treatment

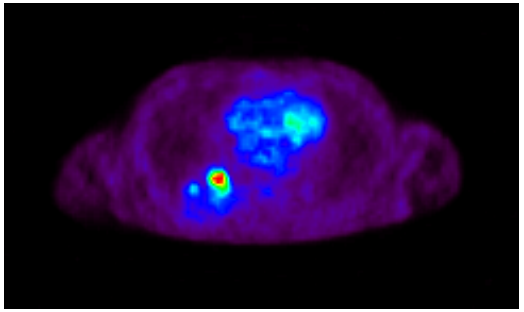
	^{18}F-FDG		^{18}F-FLT	
Parameter	Single	Sum	Single	Sum
SUV_{max}	0.003	0.002	NS	0.009
SUV_{2Dpeak}	0.006	NS	NS	NS
SUV_{3Dpeak}	0.018	0.006	NS	NS
SUV_{50}	0.003	0.002	0.026	0.031
SUV_{A50}	0.002	0.002	0.049	0.031
SUV_{A41}	0.003	0.002	0.015	0.020
SUV_{70}	NS	0.002	NS	NS
SUV_{A70}	0.002	0.004	NS	0.048
VOL_{50}	NS	NS	NS	0.042
TLG/TLP	NS	NS	0.014	0.039

Metabolic response according to PERCIST 1.0 (*16*). Metabolic tumor volume is given, based on isocontour at 50%, VOL_{50}. Significance level was set at $P < 0.05$.

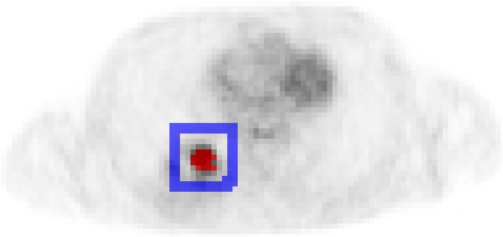
Quantitative Analysis of Response to Treatment with Erlotinib in Advanced Non–Small Cell Lung Cancer Using ^{18}F-FDG and 3′-Deoxy-3′-^{18}F-Fluorothymidine PET

Deniz Kahraman[1,2], Matthias Scheffler[2,3], Thomas Zander[2,3], Lucia Nogova[2,3], Adriaan A. Lammertsma[4], Ronald Boellaard[4], Bernd Neumaier[5], Roland T. Ullrich[2,3,5], Arne Holstein[1,2], Markus Dietlein[1,2], Jürgen Wolf[2,3], and Carsten Kobe[1,2]

Some automated metabolic volume methods



- Simple fixed thresholds (e.g.SUV=2.5)
  - PRO: widely available
  - CON: too simple, may fail for small lesions and low contrasts
- % thresholds (e.g. 42 or 50% of SUVmax)
  - PRO: widely available
  - CON: simple, may fail for small lesions and low contrasts



- Source-to-background or contrast oriented methods
  (e.g. Schaefer, Adaptive 42%, A50%)
  - PRO: better performance for small lesions and low contrasts
  - CON: less widely available
- Gradient(-watershed) based methods (Lee and Geets)
  - PRO: theoretically best method in case of uniform distributions
  - CON: almost not available
- Cluster based methods (e.g. fuzzy clustering, FLAB-Hatt *et al.*)
  - PRO: very promising results in literature, can deal with uptake heterogeneity
  - CON: not available, method hard to implement/reproduce, user interaction unclear
- All automated methods needs supervision (outliers/corrections)!

Definition of target volume with PET/CT: which method?

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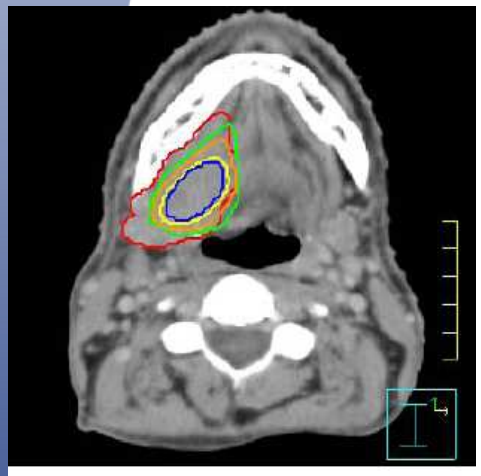
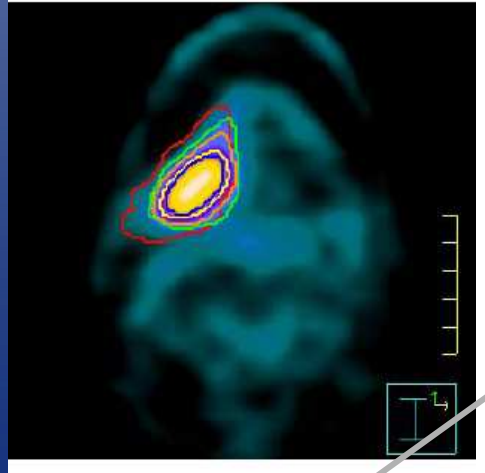
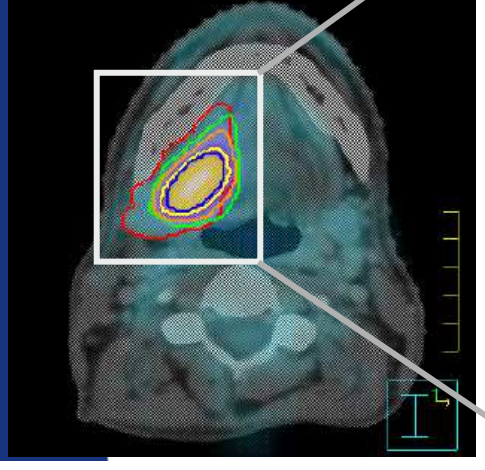






Results depend on segmentation method being used:

CT:

GTV - CT 47.5 cm^3 (**rood**)

PET:

GTV - visueel 43.8 cm^3 (**groen**)

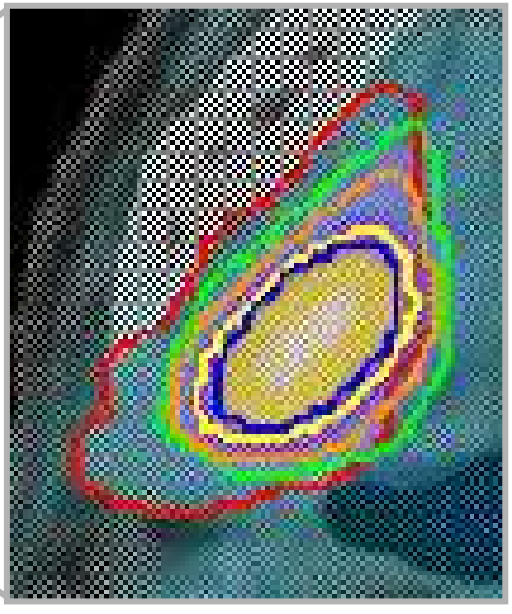
manual

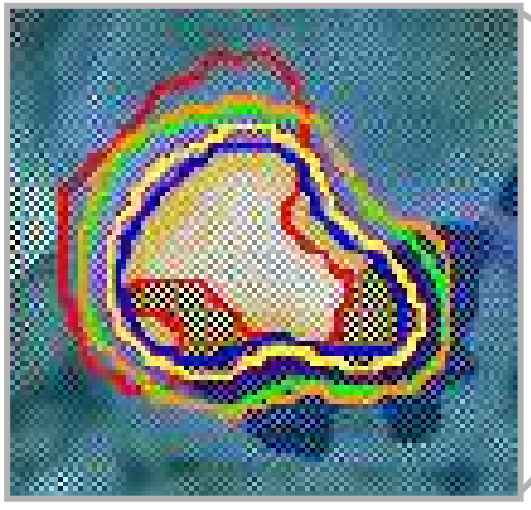
$GTV_{40\%}$ 20.1 cm^3 (**geel**)

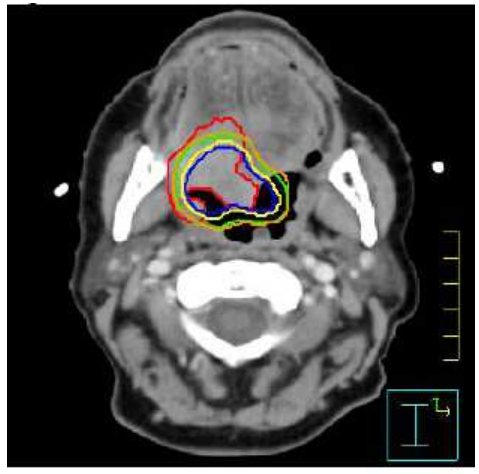
GTV_{SUV} 32.6 cm^3 (**oranje**)

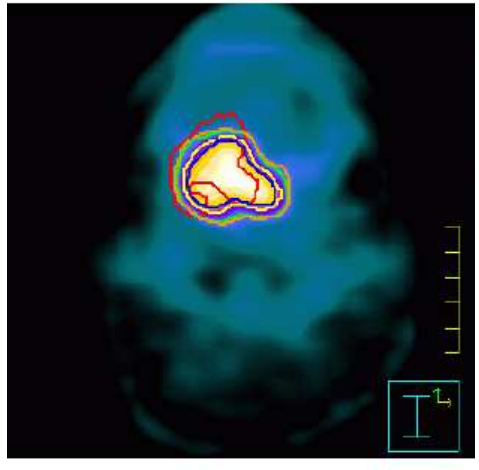
GTV_{SBR} 15.7 cm^3 (**blauw**)

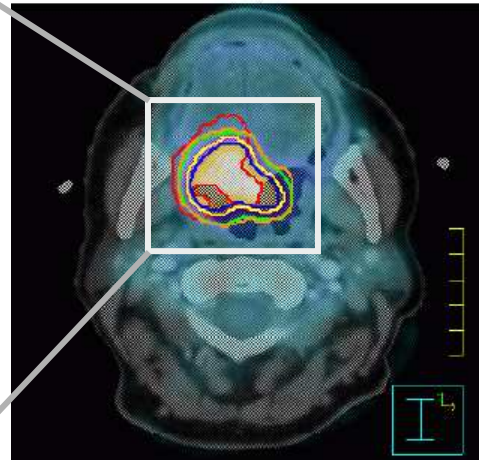
semi-automated











Theory of metabolic volume segmentation
Factors affecting metabolic volume measurements

1. Tumor characteristics
   - Tumor or metabolic volume size
   - Tumor to (local) background ratio – contrast

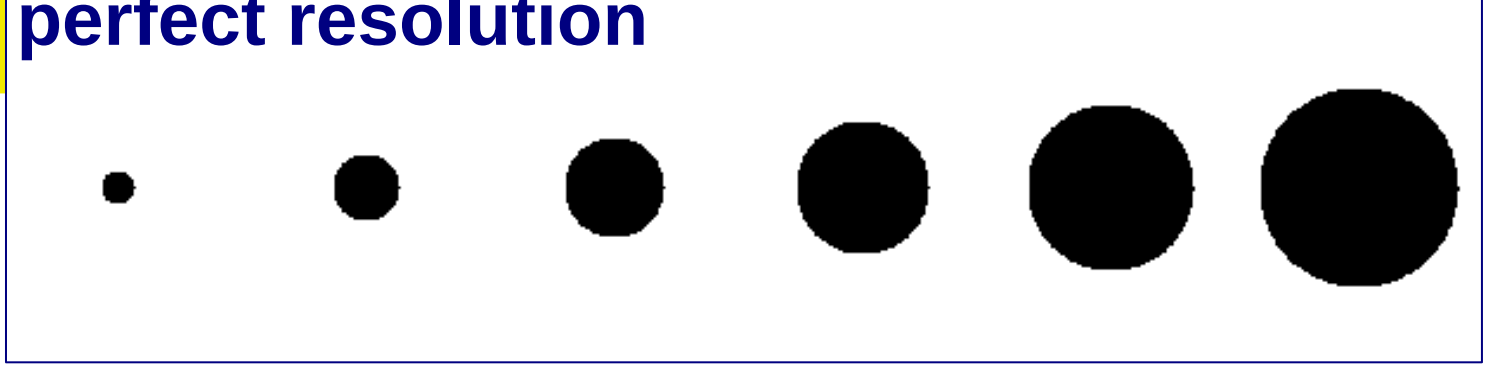
2. Image characteristics
   - Image resolution
   - Image noise

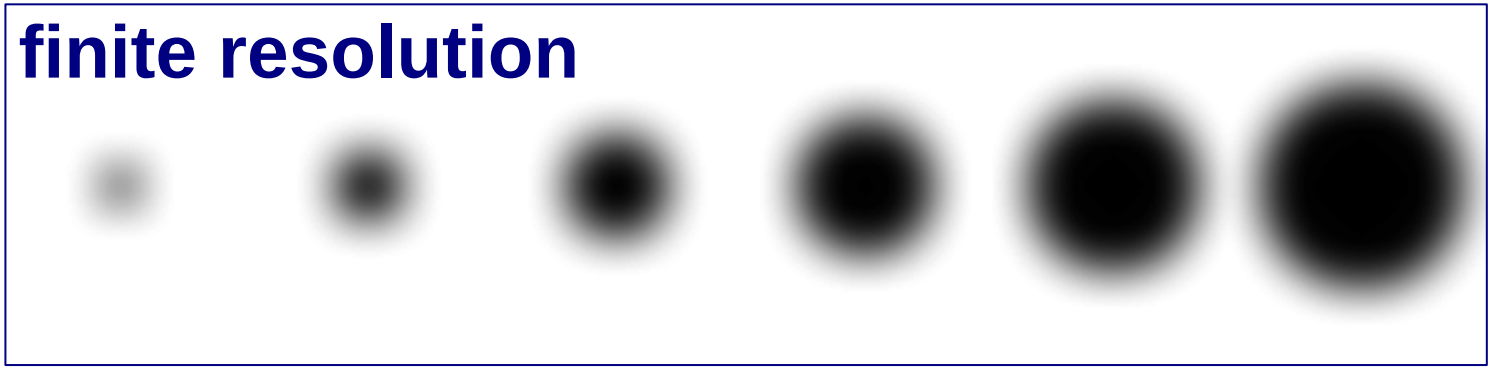
3. VOI method

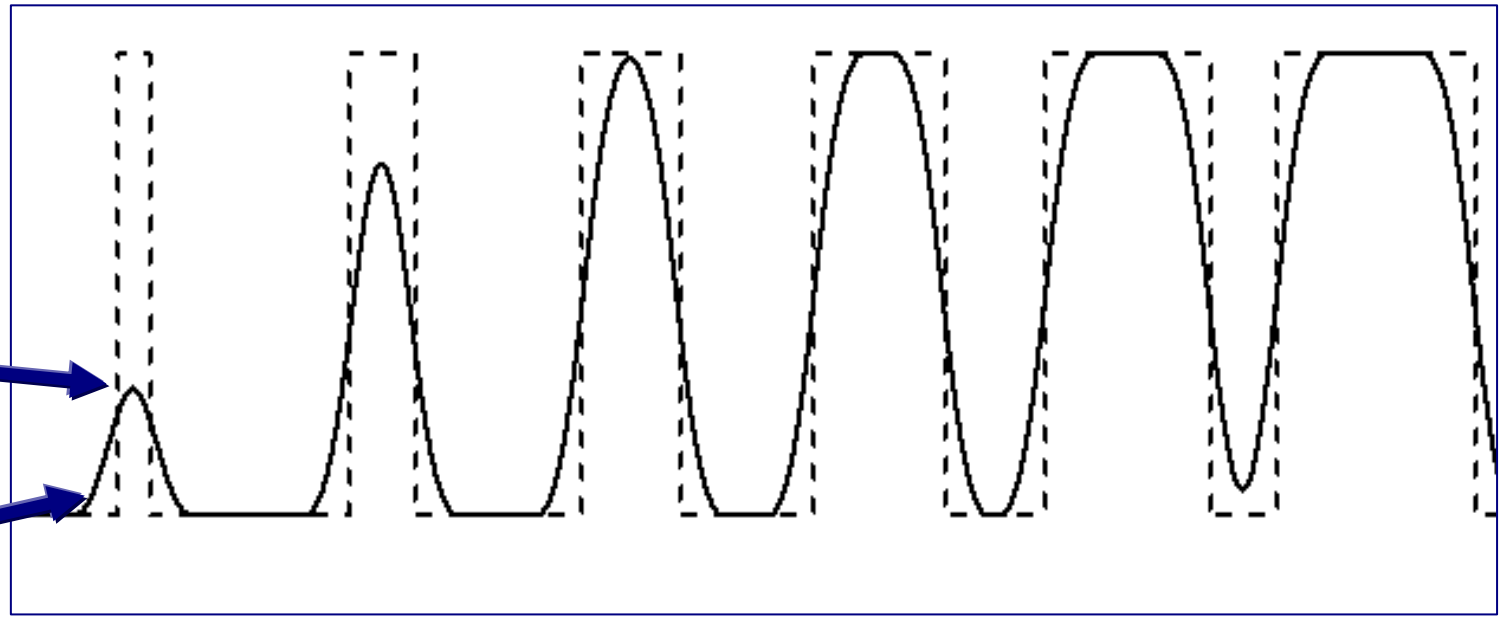
Partial volume

constant concentration

finite resolution

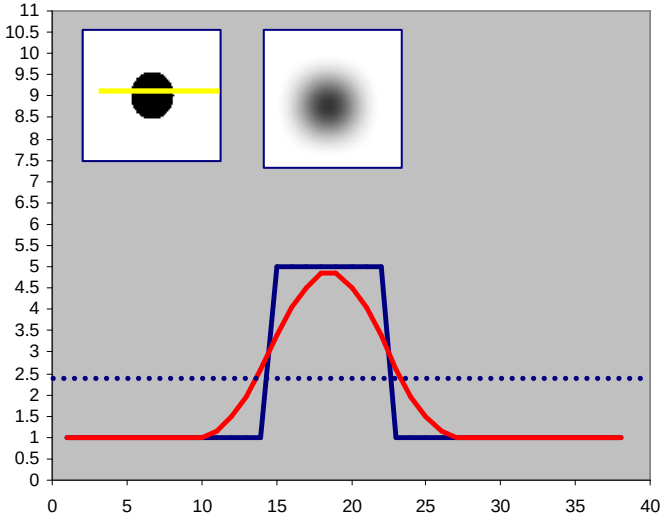






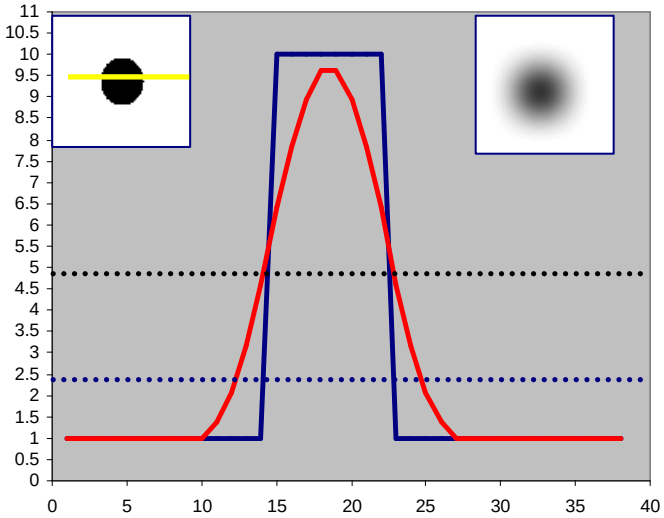
Courtesy of J. Nuyts

Theory of metabolic volume segmentation (1)



In this example:
SUV2.5=50% of max : only slight overestimation

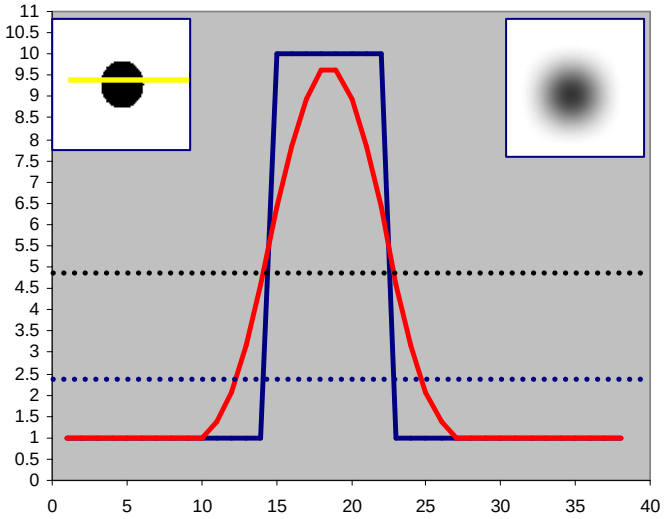
…… SUV=2.5



…… SUV=2.5
……. 50% of max

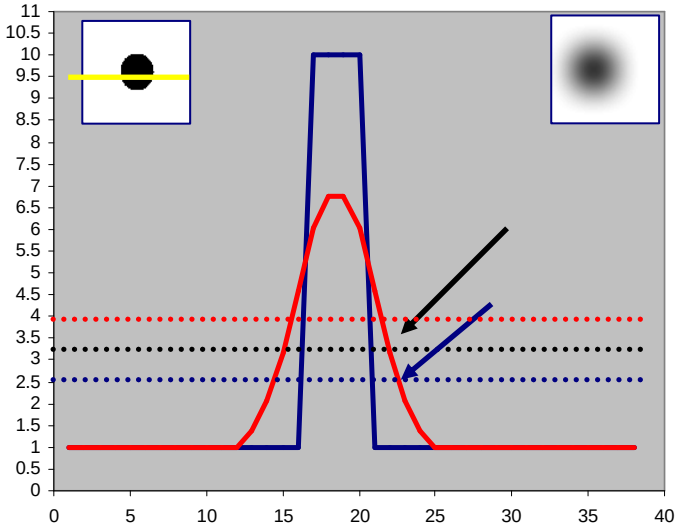
Now, same metab.volume but higher uptake
SUV2.5 > 50% of max: large m.volume overestimation

Theory of metabolic volume segmentation (1)



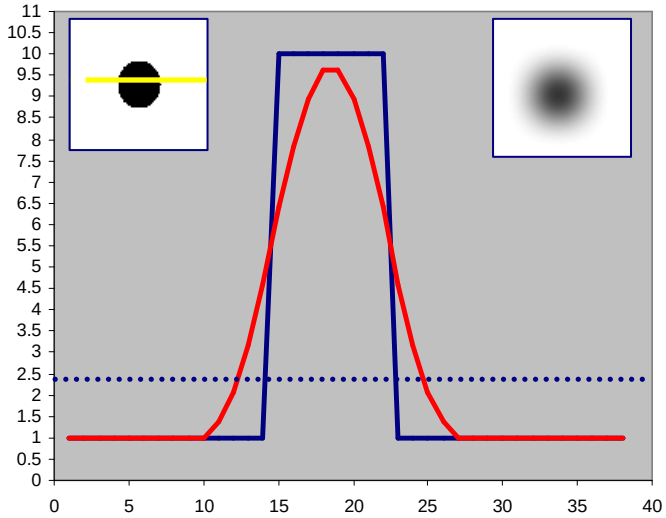
SUV2.5 > 50% of max: large m.volume overestimation

..... SUV=2.5
..... 50% of Max
..... SBR-50%



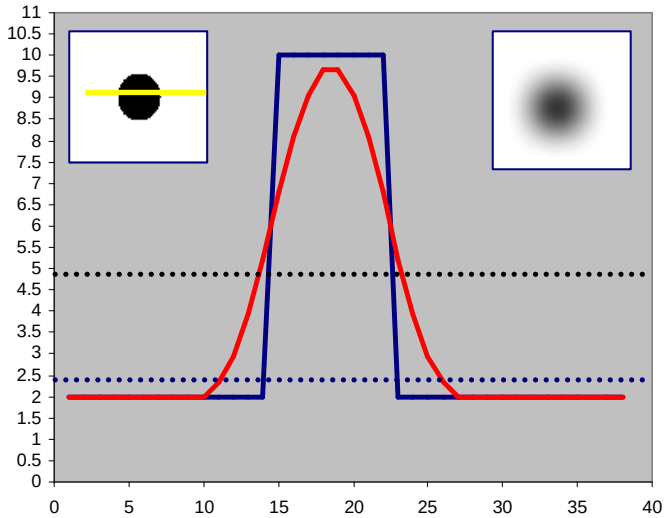
Same uptake, smaller volume
SUV2.5 and 50% of Max overestimage metab.volume

Theory of metabolic volume segmentation (1)



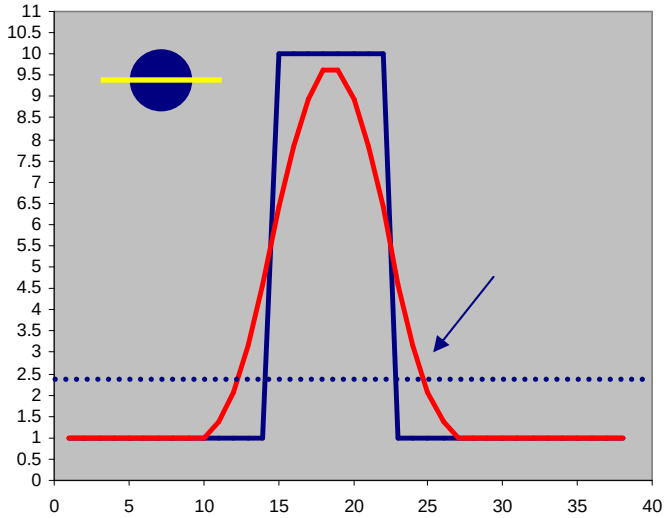
SUV2.5 > 50% of max: large m.volume overestimation

Same volume, same uptake, higher background



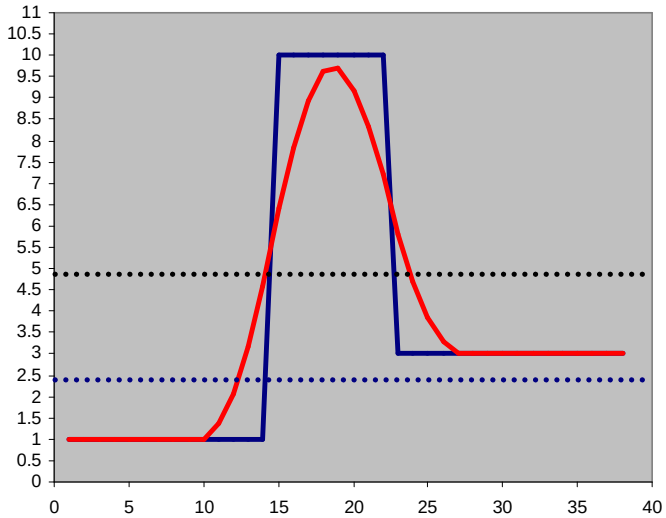
- SUV2.5 overestimates..
- 50% of Max seems OK again….

Theory of metabolic volume segmentation (1)



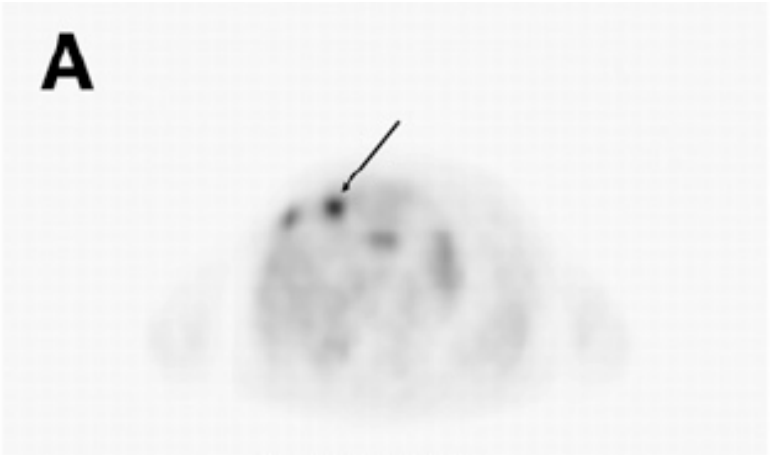
SUV2.5 > 50% of max: large m.volume overestimation

Same volume, same uptake, heterogeneous background
Basically only gradient may work…..



Clinical example

Both the measured SUV_{max} and tumour volume depends image characteristic settings



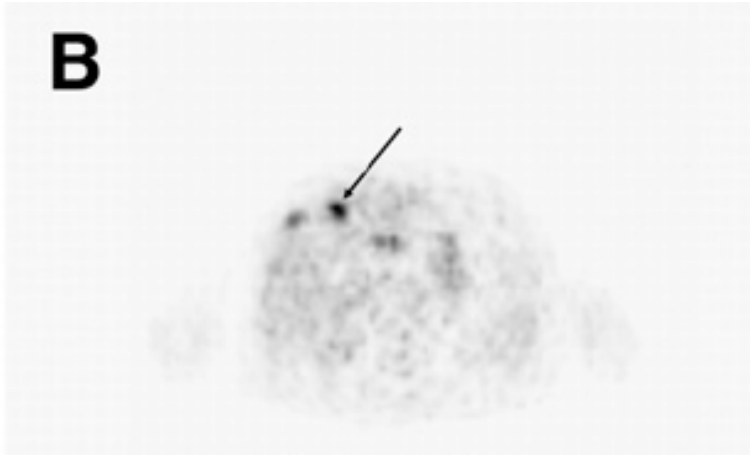


Image resolution (FWHM):	11 mm	7 mm
Estimated volume:	4.5 mL	1.5 mL
SUV_{max} :	3.3	5.5

Boellaard R. *J. Nucl Med.* 2009; 50:11S-20S.

Clinical example: a TRT study

- **Patient studies:**

- **10 NSCLC patients in dynamic FDG TRT study**
  - 51±5 y, weight 76±10 kg, 388±71 MBq
  - Blood glucose level were obtained
  - All patients fasted >6 h before scanning
  - Retest scan was acquired the next day

Cheebsumon et al. JNM 2011, EJNMMI 2011

Materials and methods

- **Two different contrasts were used by summing the last 3 (45-60 min p.i.) and last 6 (30-60 min p.i.) frames**
- **Data were reconstructed using OSEM with 2 iterations and 16 subsets followed by post-smoothing using a Hanning filter**
- **Additional Gaussian smoothing was performed, resulting in resolutions of 6.5, 8.3 or 10.2 mm FWHM**

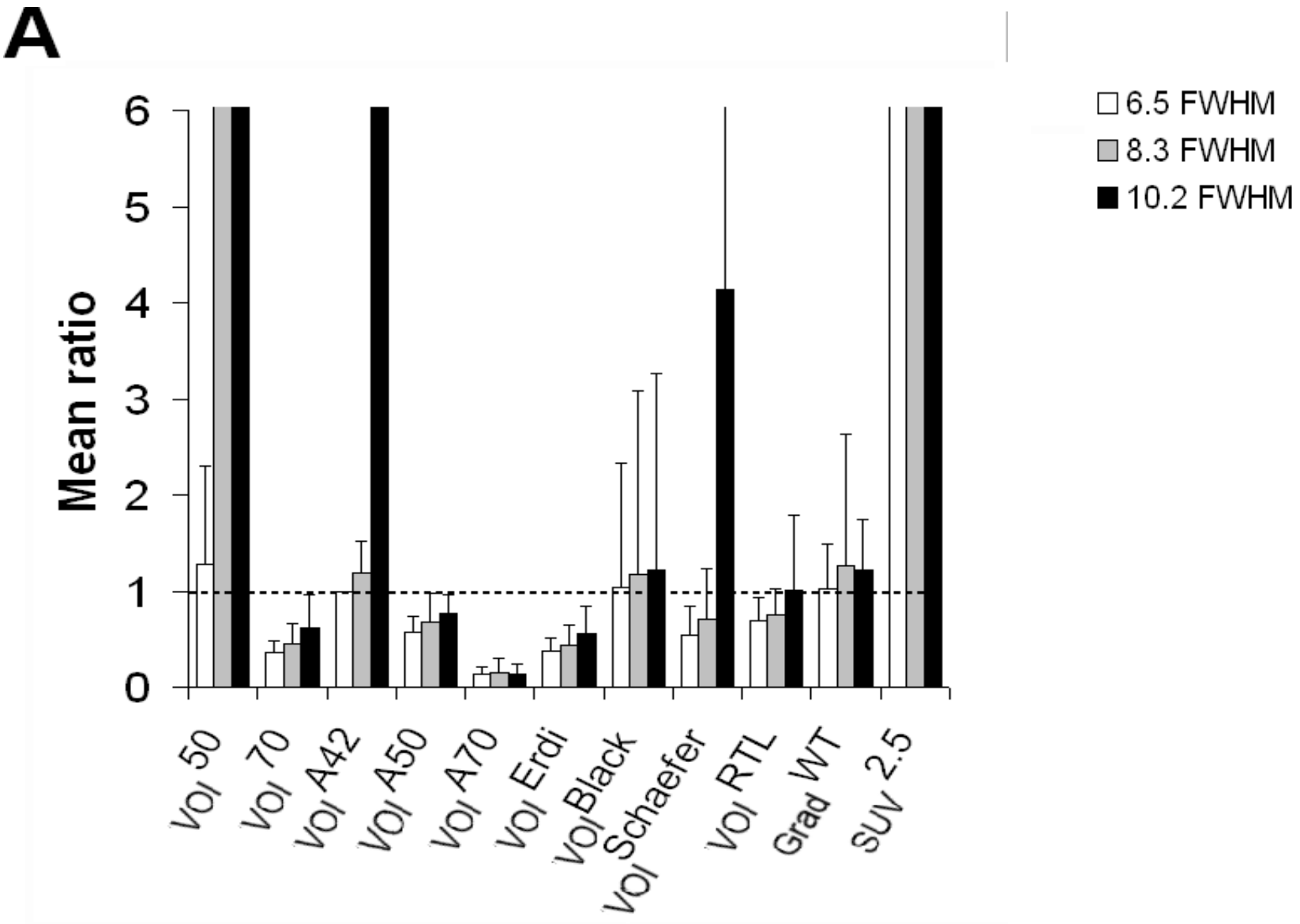
Frings et al. JNM 2010

VOI methods….

- **9 different tumour delineation methods were used:**
  - Absolute SUV (i.e. $SUV^{2.5}$)
  - Fixed or adaptive threshold of the maximum pixel value[(1)] i.e. 50% (VOI^{50}) or A50% (VOI^{A50})
  - Relative threshold level (RTL) method[(2)] (VOI^{RTL})
  - Adaptive threshold methods[(3-5)] (VOI^{Nestle}, VOI^{Erdi}, $VOI^{Schaefer}$)
  - Iterative threshold method[(6)] (VOI^{Black})
  - Gradient-based segmentation method that applied the Watershed transform (WT) algorithm ($Grad^{WT}$)

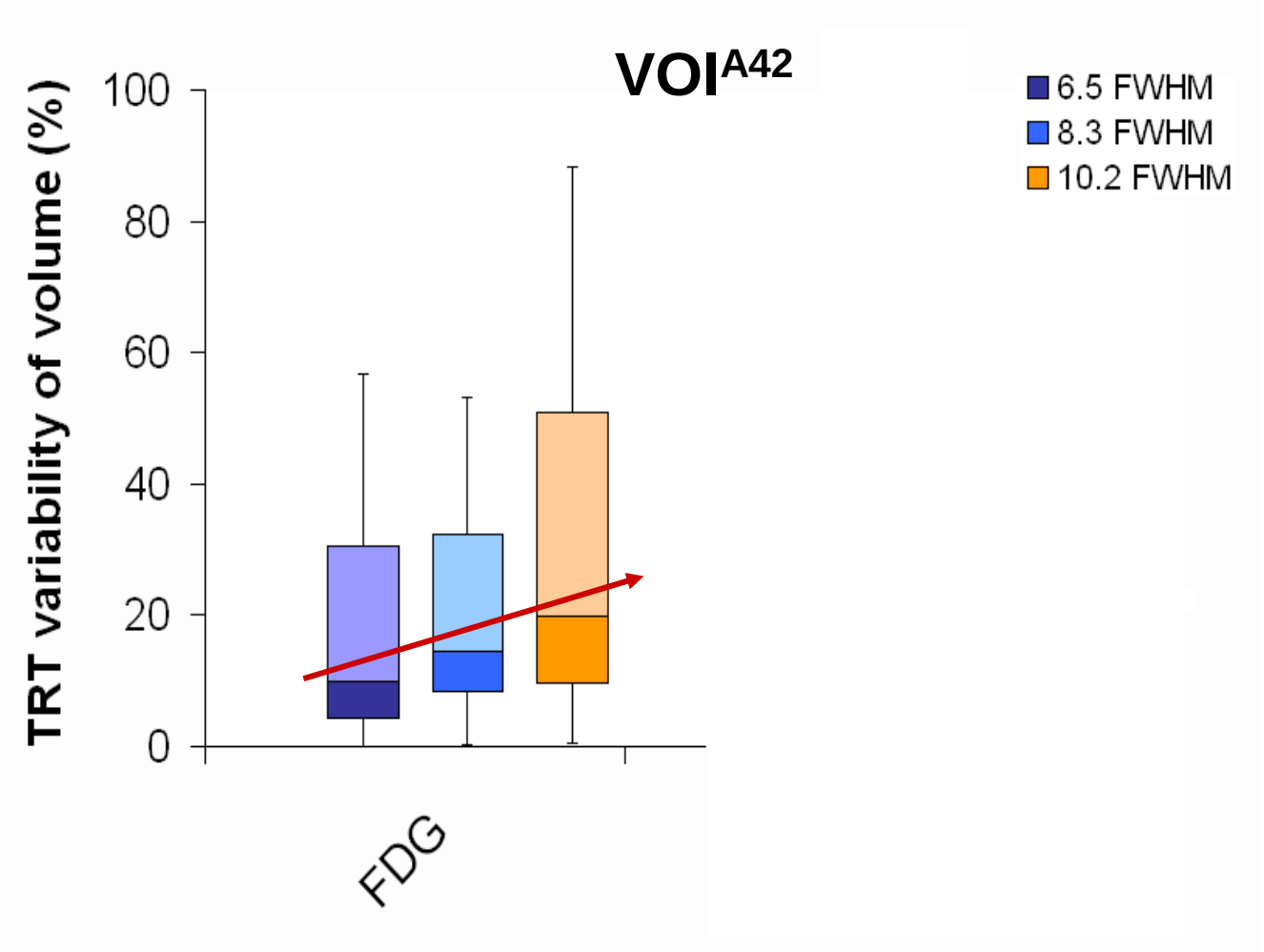
(1) Boellaard R, 2004, (2) van Dalen JA, 2007, (3) Erdi YE, 1997,
(4) Nestle U, 2005, (5) Schaefer A, 2008, (6) Black QC, 2004

Results: effect of changes in resolution



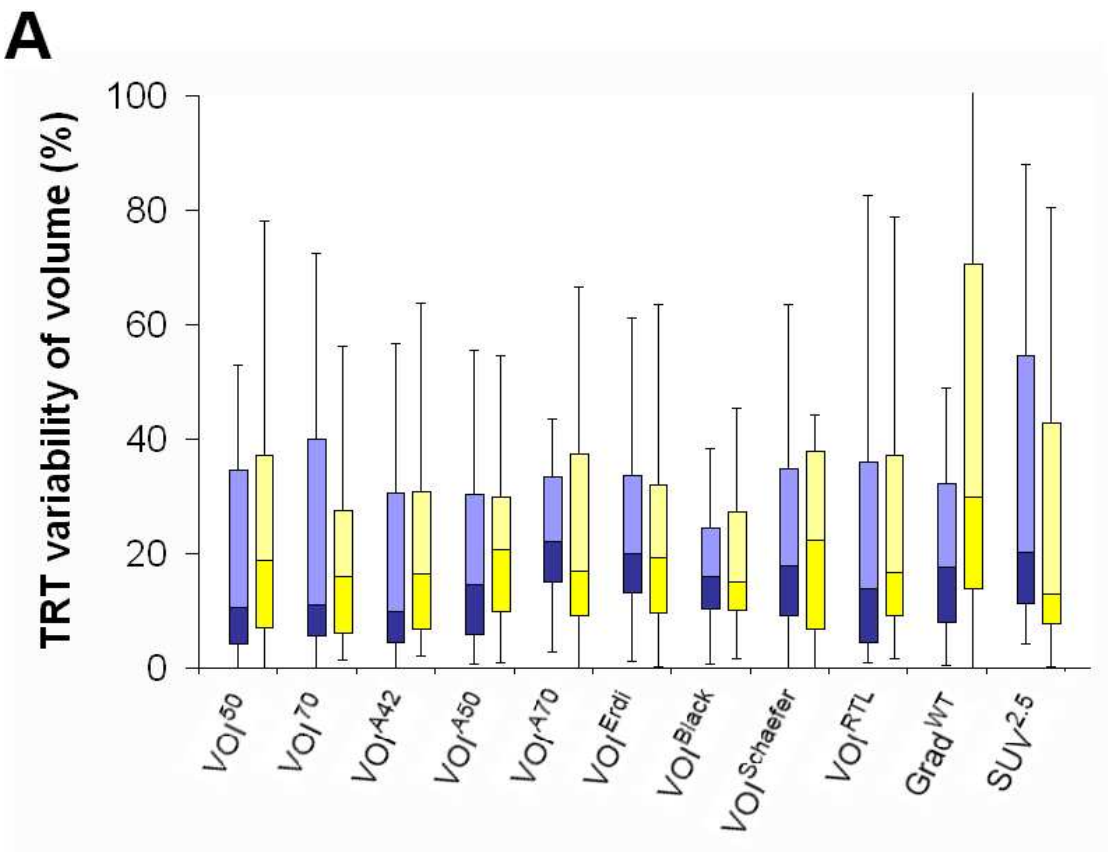
Metabolic volume depends strongly on the resolution & VOI method being used

TRT results: effect of changes in resolution



- Volume TRT depends on the resolution & VOI method being used (up to 20%)

TRT results: effect of changes in contrast

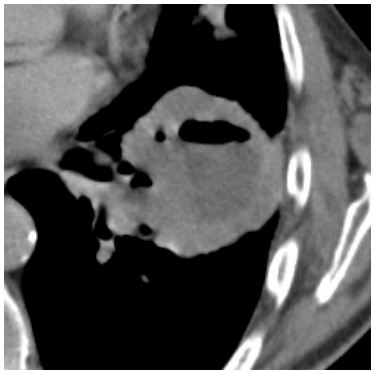


- FDG: for most VOI methods TRT worsens with lower contrast

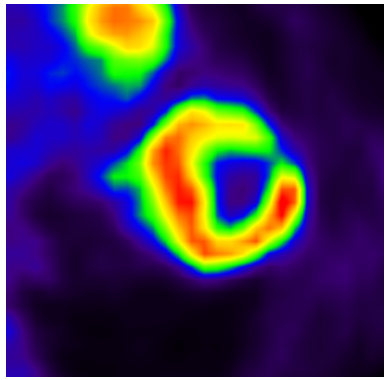
Cheebsumon et al. JNM 2011, EJNMMI 2011

A clinical example: validation study

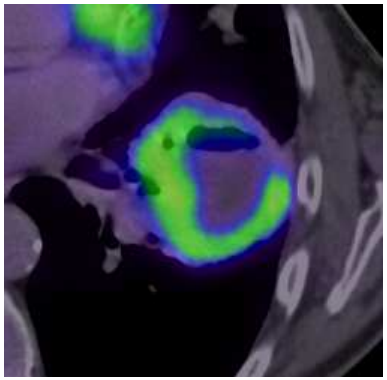
CT



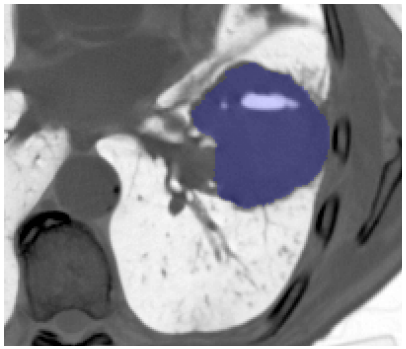
PET



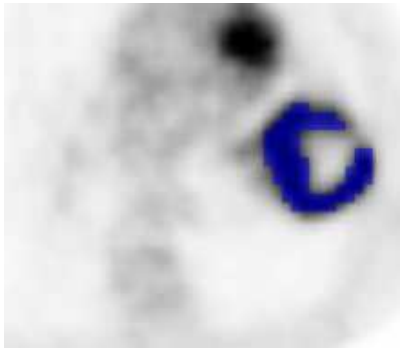
PET/CT



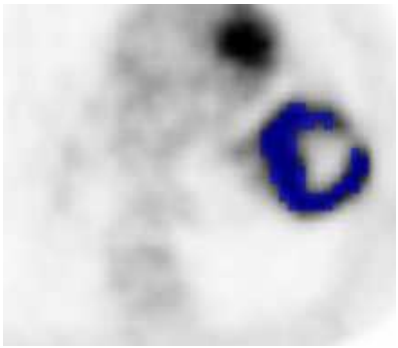
This example clearly shows difference between anatomical (CT) and metabolic (PET) tumor volumes, illustrating the potential of PET to identify regions within a tumor that show different metabolic activity. In this case PET-based volume was closer to pathology-derived volume than the CT-based volume.



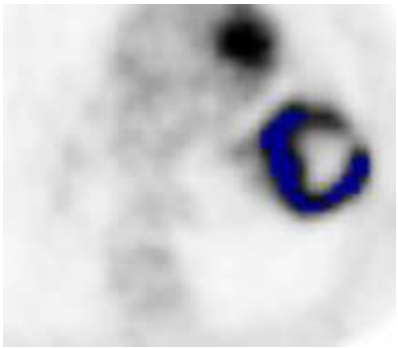
CT



VOI^{A41}



VOI^{50}



VOI^{RTL}

Materials and methods

- **Patients and pathology**
  - 21 whole body FDG PET/CT (Biograph, CTI/Siemens) studies were acquired for primary NSCLC patients (77±14 kg)
  - Patients fasted for >6 h before scanning
  - Mean blood glucose levels were normal (5.7±2.0 $mmol \cdot L^{-1}$)
  - Data were reconstructed using OSEM (4i, 18s), having an image resolution of ~6.5 mm FWHM
  - After scanning, the primary tumour was surgically resected and the maximum diameter of this tumour was measured

Van Baardwijk et al. Int J Radiat Oncol Biol Phys 2007

Materials and methods

- **8 different automatic PET-based delineation methods were used:**
  - Absolute SUV threshold (e.g. $SUV^{2.5}$)
  - Fixed or adaptive threshold of the maximum pixel value(1) i.e. 50% (VOI^{50}) or A50% (VOI^{A50})
  - Relative threshold level (RTL) method(2) (VOI^{RTL})
  - Adaptive threshold methods (e.g. $VOI^{Erdi\ (3)}$ and $VOI^{Schaefer\ (4)}$)
  - Iterative threshold method (e.g. $VOI^{Black\ (5)}$)
  - Gradient-based segmentation method in combination with a Watershed algorithm ($Grad^{WT}$)

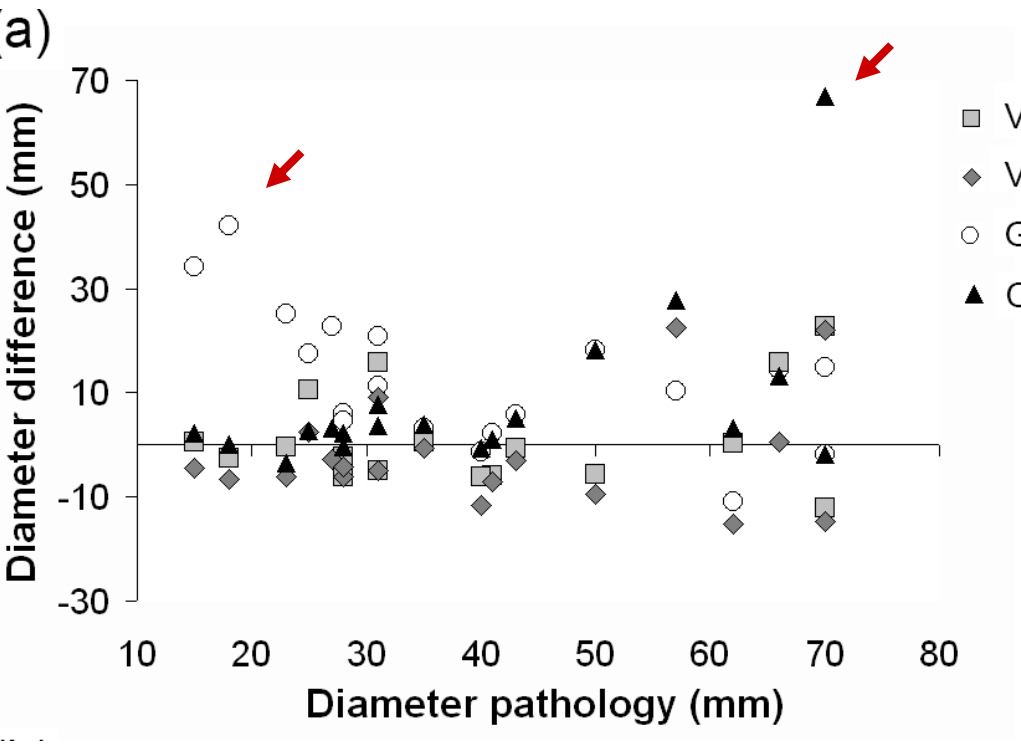
- Manual CT-based delineation by expert physician

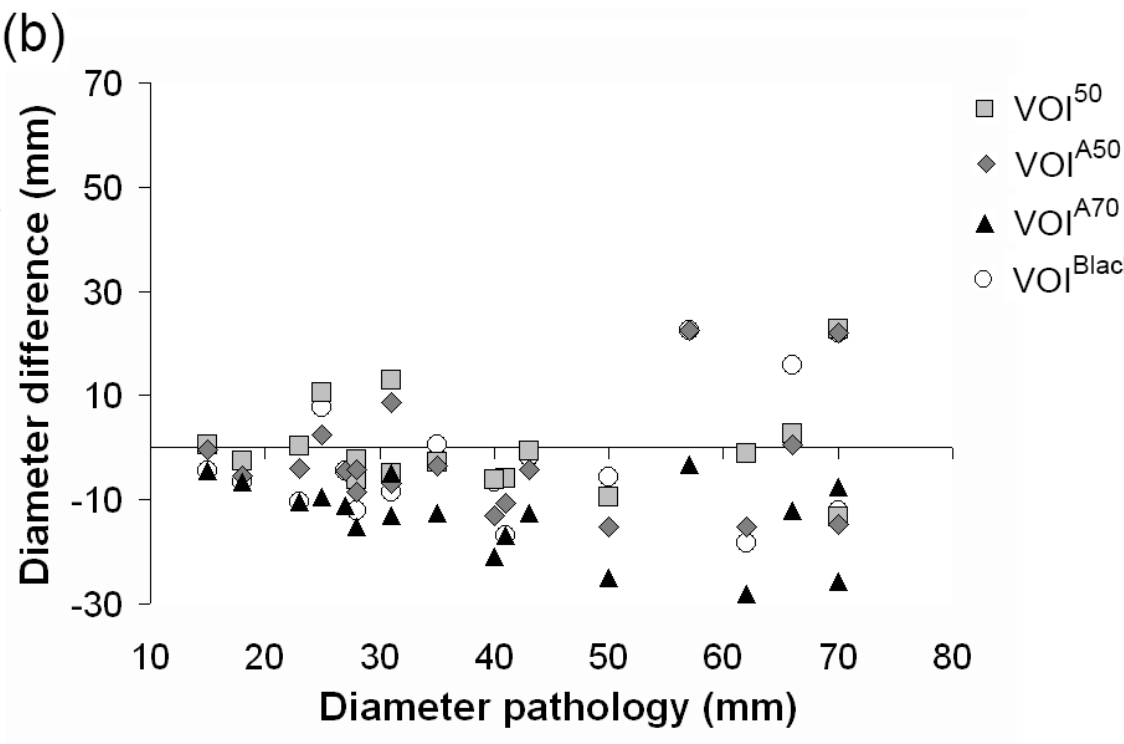
(1) Boellaard R, 2004, (2) van Dalen JA, 2007, (3) Erdi YE, 1997,
(4) Schaefer A, 2008, (5) Black QC, 2004

Materials and methods

- Data analysis
  - Comparison of PET and CT derived volumes (volume difference, slope and R^2)
  - Comparison of maximum tumour diameter from PET- and CT-based methods to that obtained from pathology (diameter difference, slope and R^2)

Results – Diameter difference: vs pathology





Results – Slope and R^2 of maximum diameter

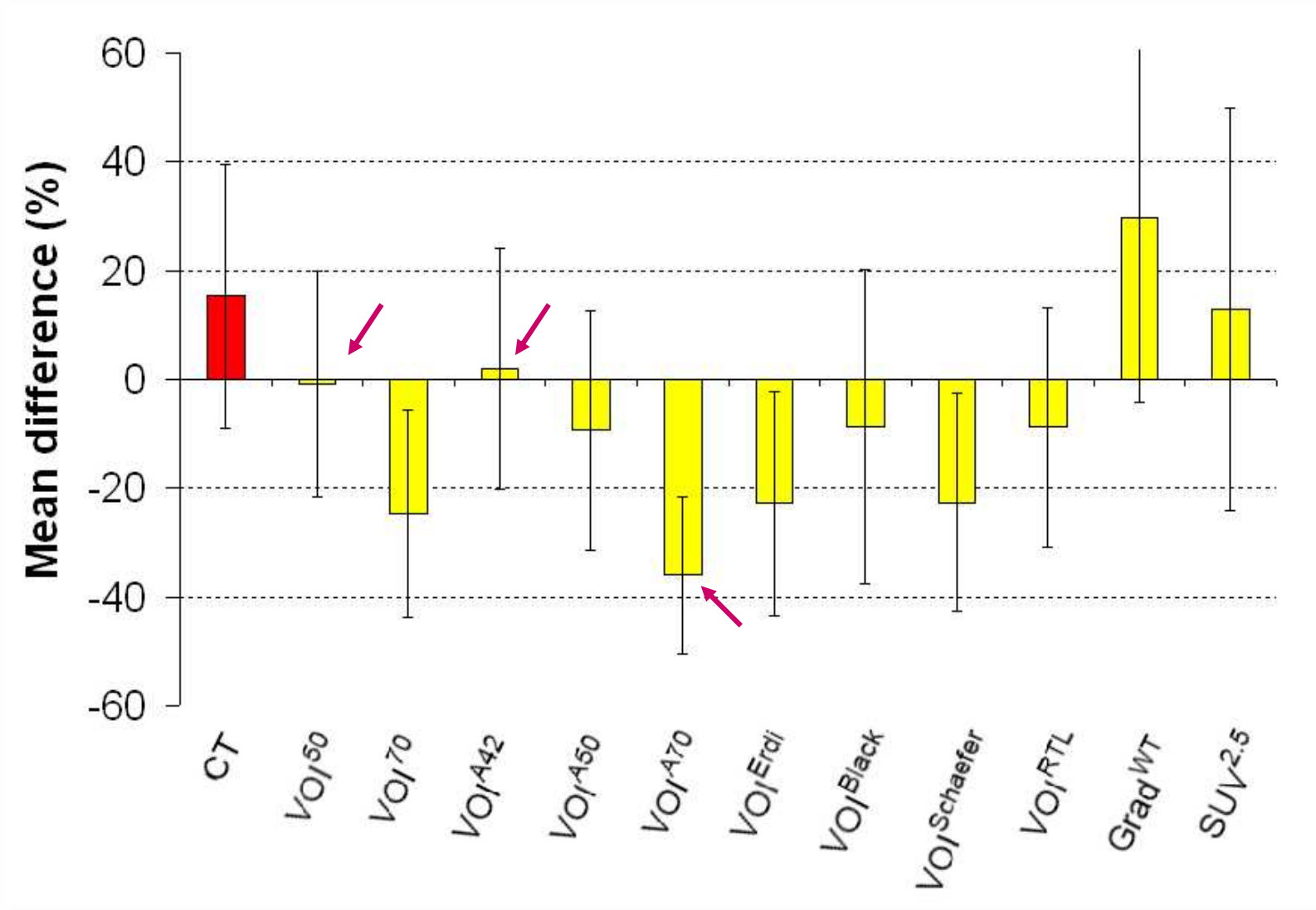
Intercept set to 0

	R^2	Slope
CT-based delineation	**0.77**	**1.25**
PET delineation methods		
VOI^{50} *	**0.82**	**1.00**
VOI^{70}	**0.73**	**0.79**
VOI^{A42} *	**0.82**	**1.04**
VOI^{A50}	**0.75**	**0.95**
VOI^{A70}	**0.81**	**0.69**
VOI^{Erdi}	**0.71**	**0.81**
VOI^{Black}	**0.74**	**1.00**
$VOI^{Schaefer}$ *	**0.75**	**0.85**
VOI^{RTL}	**0.78**	**0.97**
$Grad^{WT}$ *	**0.48**	**1.17**
$SUV^{2.5}$ *	**0.79**	**1.16**

Slope and R^2 of maximum diameter obtained from PET-based delineation methods or CT delineation against maximum diameter obtained from pathology

* Without outliers:
- 2 outliers for VOI^{50}, VOI^{A42}, $VOI^{Schaefer}$ and $Grad^{WT}$
- 5 outliers for $SUV^{2.5}$

Results – Diameter mean difference vs pathology



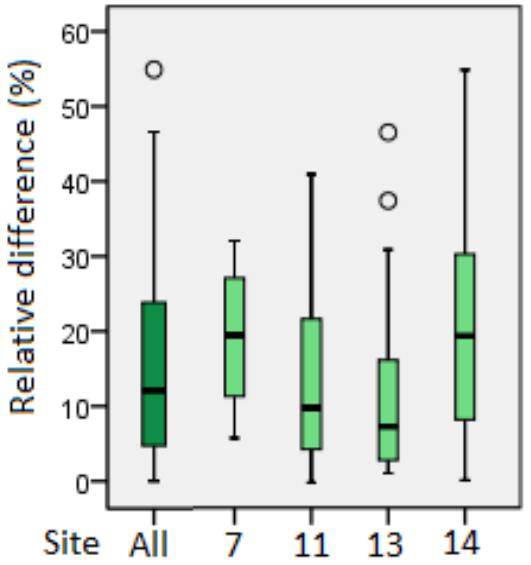
Cheebsumon, EJNMMI Research (in press)

Preliminary multi-center TRT results

TRT FDG PET/CT data from 4 sites (Velasquez *et al.* JNM)
Advanced GI malignancies
No standardisation in place

Table 5a - Mean & RC of relative difference in volume

Base parameter	Method / threshold	n	Mean relative difference (%)	RC (%)
	GradWT	85	23.4	38.5
SUV_{max}	A50%	87	20.2	37.0
	Schaefer	89	15.9	25.7
	RTL	87	14.9	25.2
SUV_{peak}	A50%	87	16.9	25.5
	Schaefer	81	11.9	24.9
	RTL	79	13.2	23.5
$SUV_{local\ peak}$	A50%	77	12.1	22.7
	Schaefer	86	13.2	26.9
	RTL	86	17.1	28.0
SUV_{star}	A50%	86	17.4	28.9
	Schaefer	86	17.3	29.0
	RTL	86	17.4	28.9



Use of $SUV_{peak,3D}$ and SBR based thresholds result in improved metabolic volume measurement repeatability (SUVpeak is less sensitive to noise)

Some automated metabolic volume methods

- Simple fixed thresholds (e.g.SUV=2.5)
  - Many outliers, not able to provide reproducible (TRT) results for small lesions (<5mL) and at low TBR (<4)
- % thresholds (e.g. 42 or 50% of SUVmax)
  - May work reasonable well for NSCLC (high contrast, low background)
- Source-to-background or contrast oriented methods (e.g. Schaefer, Adaptive 42%, A50%)
  - Reasonably good performance, available in some display stations, if not then can be applied with more user interaction
  - Use of SUVpeak rather than SUVmax improves TRT performance considerably
- Gradient(-watershed) based methods (Lee and Geets)
  - Theoretically best method in case of uniform distributions
  - Sensitive to noise
- Cluster based methods (e.g. fuzzy clustering, FLAB)
  - Not tested, not easy to implement and not available
- All automated methods needs supervision (outliers/corrections)!

Theory of metabolic volume segmentation
Factors affecting metabolic volume measurements

- Tumor or metabolic volume size
- Tumor to (local) background ratio – contrast
- Image resolution
- Image noise
- Automated VOI method being used

Eur J Nucl Med Mol Imaging (2011) 38:2136–2144
DOI 10.1007/s00259-011-1899-5

ORIGINAL ARTICLE

Impact of [^{18}F]FDG PET imaging parameters on automatic tumour delineation: need for improved tumour delineation methodology

Patsuree Cheebsumon · Maqsood Yaqub · Floris H. P. van Velden · Otto S. Hoekstra · Adriaan A. Lammertsma · Ronald Boellaard

- For both SUV and metabolic volume assessments standardisation is required
- With STD and optimization: good TRT repeatability

Cheebsumon et al. JNM 2011, EJNMMI 2011, EJNMMI Res 2011, EJNMMI Res 2012

EANM STD/Guideline

- Interpretation, image quality and quantification depends on the combination of many factors (biological, technical, physics)*
- FDG PET/CT guideline* – imaging procedure
  - Feasibility of following GL shown in several trials/studies
- NB it is a harmonizing guideline/standard aiming at minimizing difference in quantitative performance between centers
- GL is optimized for use of SUVmax for quantification !
- EARL accreditation- PET/CT system calibration/perf.harmonization
  - About 70 sites across EU, likely 100 in 2013
  - Options to arrive at harmonized image quality and quantification:
    - Acquire and reconstruct data such to meet harmonizing std (preferred)
    - 2 reconstructions, one that meets std (danger of mixing up)
    - Postproces data to generate second image dataset that meets std (online or during analysis)

Uniformity of Protocols In Clinical Trials: UPICT

FDG PET/CT consensus guideline

- EANM/EARL (GL & accreditation)
- SNM & SNM-CTN
- ACR
- RSNA
- QIBA
- PET/CT Vendors

UPICT FDG PET/CT consensus GL – imaging procedure GL

UPICT GL available for external review/comment Q4/2012

Thank you for your attention