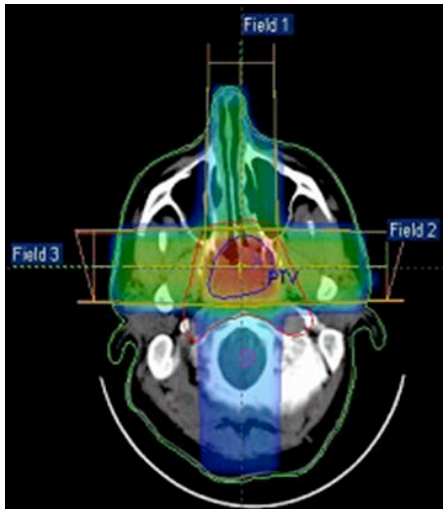
Combining PET/CT and RTP

David W. Townsend, PhD



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University of Tennessee, Knoxville, TN

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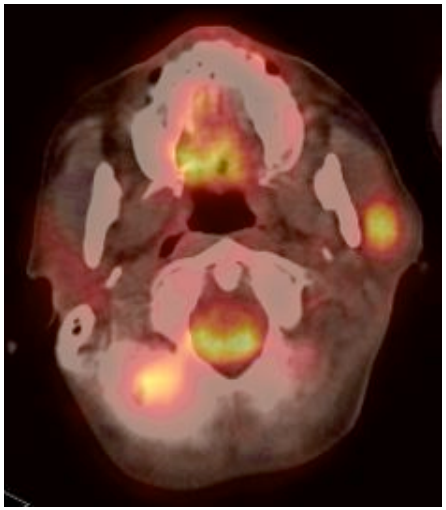


Advances in PET-SPECT/CT and RTP

Melbourne, Australia December 13th 2005

Topics

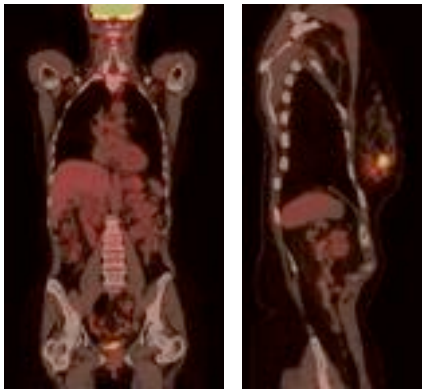
- PET/CT in Radiation Therapy Planning
- Monitoring response to therapy
- Imaging biomarkers: beyond FDG

PET/CT for image-guided radiation therapy

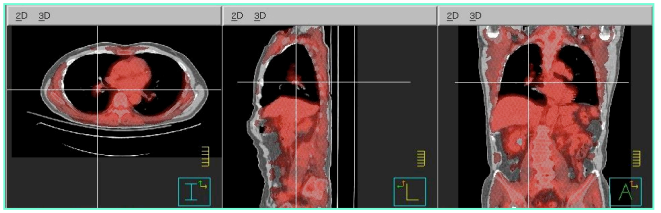
- define the appropriate target volume
  - functional changes precede, and do not necessarily match, structural changes
- define the optimal dose to deliver
  - PET can quantify basic tumor biological properties that can be used for determining target volumes and dose
- follow the response to radiation therapy
  - the same properties can be followed during and after therapy to assess treatment response

Integrating PET/CT in therapy planning

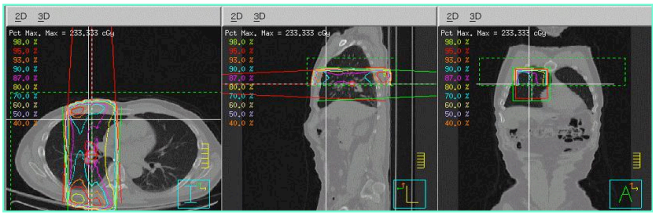
- *RT flat table top*
- *patient immobilization device*
- *laser positioning system*
- *70 cm patient port*



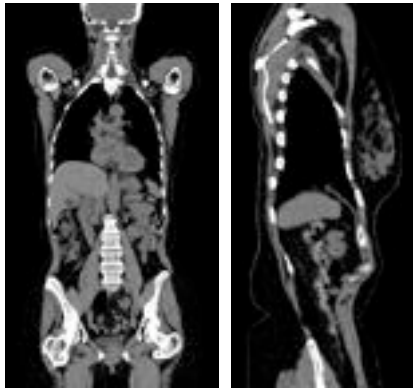
PET/CT scan



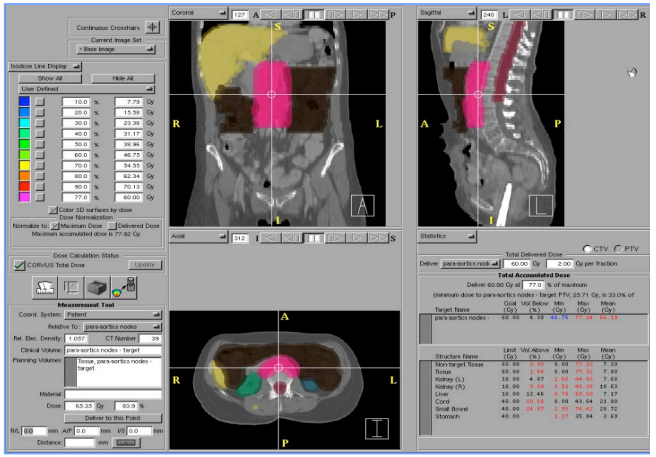
CT simulation, contouring



Fusion

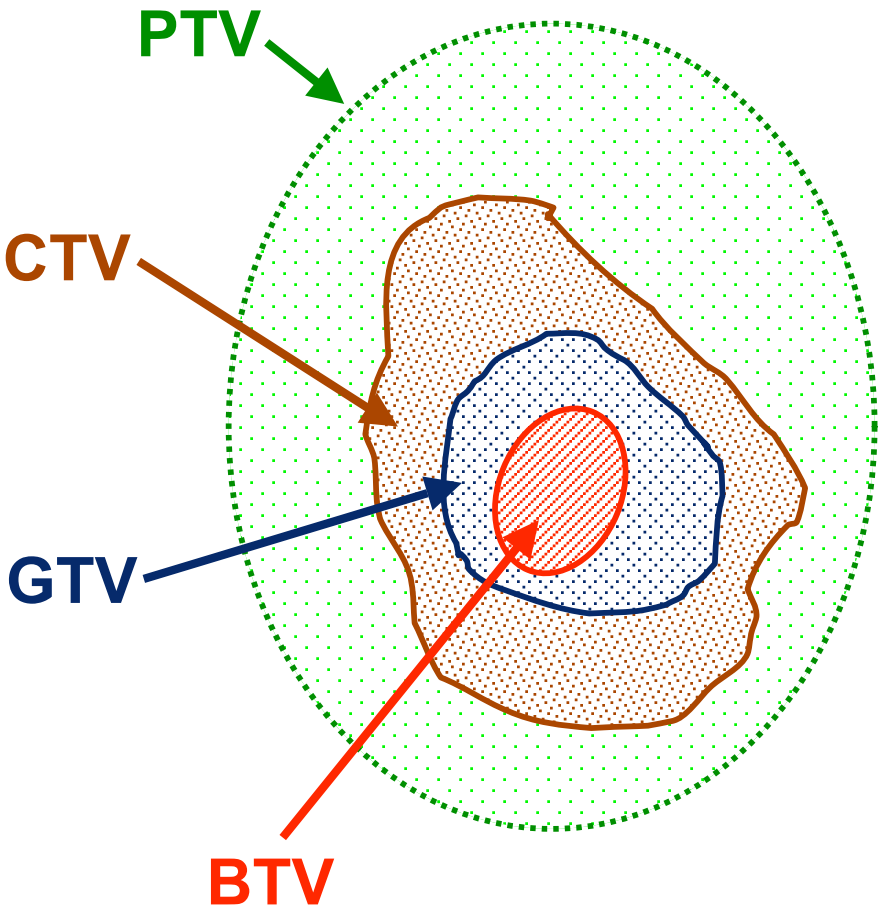


CT simulator



Treatment plan

Defining target volumes with molecular imaging



PTV: Planning target volume	physicist
CTV: Clinical target volume	clinician
GTV: Gross tumor volume	CT / MRI
BTV: Biological tumor volume	PET or SPEC

PTV: tumor motion and setup errors

CTV: includes microscopic disease

GTV: from high resolution anatomy

BTV: from molecular imaging

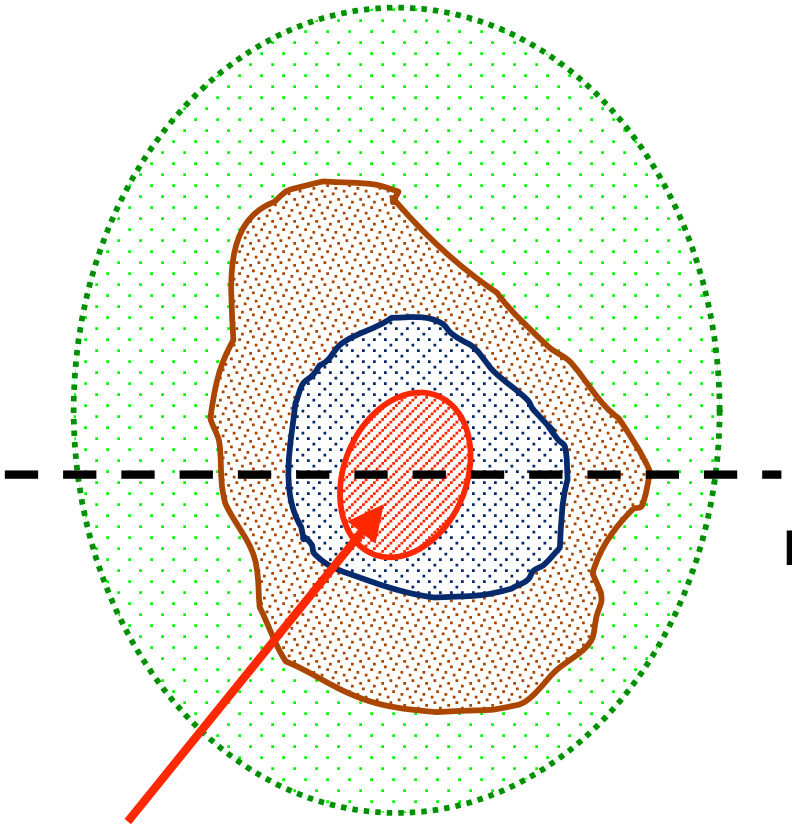
Issue #1

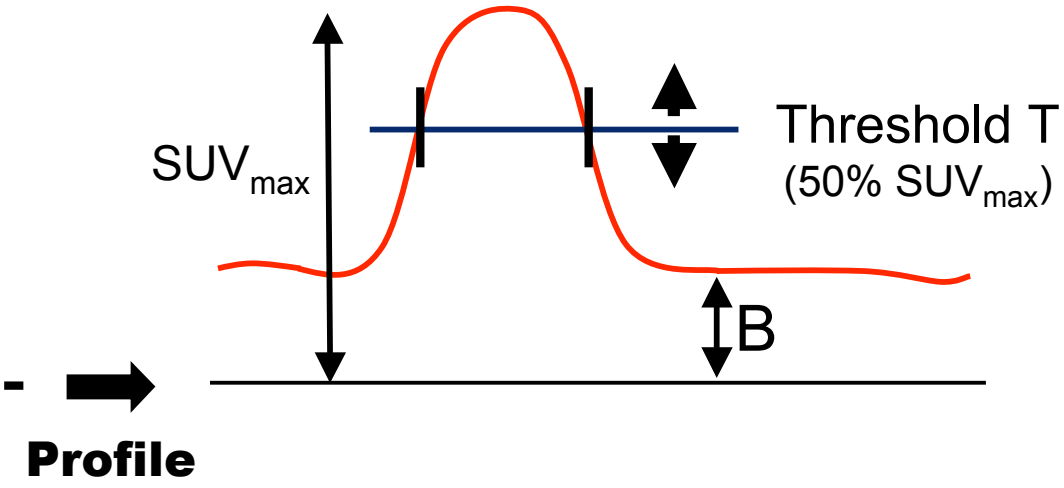
- Defining the Biological Tumor Volume

Defining BTV based on Standardized Uptake Value

$$SUV = \frac{a_{ROI}(\mu Ci/ml)}{A\ (mCi) / W(kg)}$$

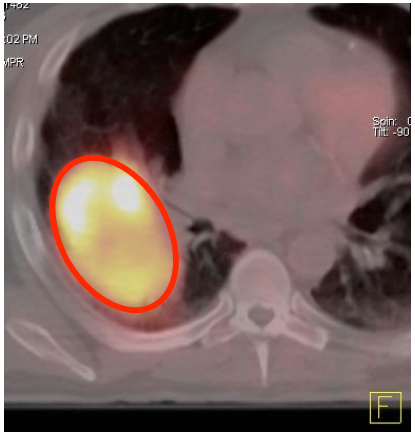
- Choice of threshold (T) affects BTV
- T varies with size and background





- SUV_{max} may depend on B but not T
- SUV_{mean} and contour (BTV) depend on T
- SUV depends on BMI

Factors affecting apparent tumor ^{18}FDG uptake



- lesion size and partial volume effects
- tumor heterogeneity
- cellular avidity for glucose
- image reconstruction parameters
- definition of region-of-interest
- patient blood glucose levels
- time after injection of FDG
- difference between FDG and glucose (LC)

➢ **These factors will also affect the SUV**

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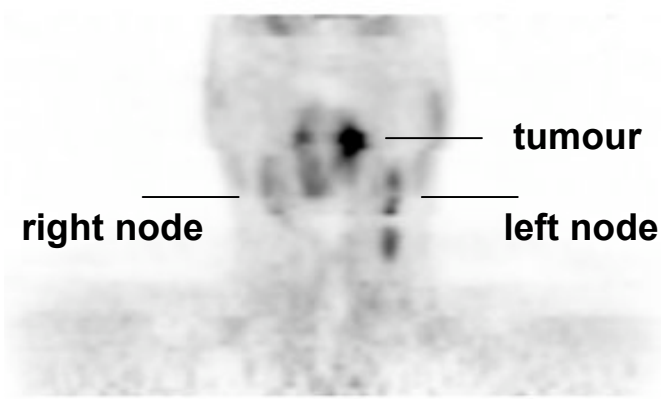
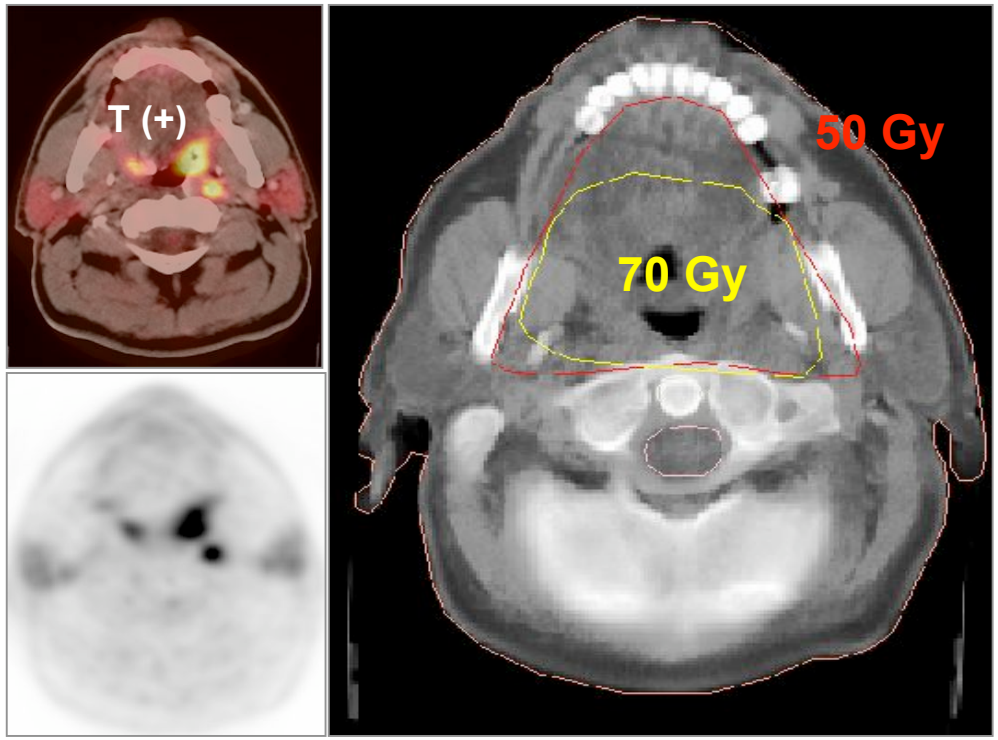
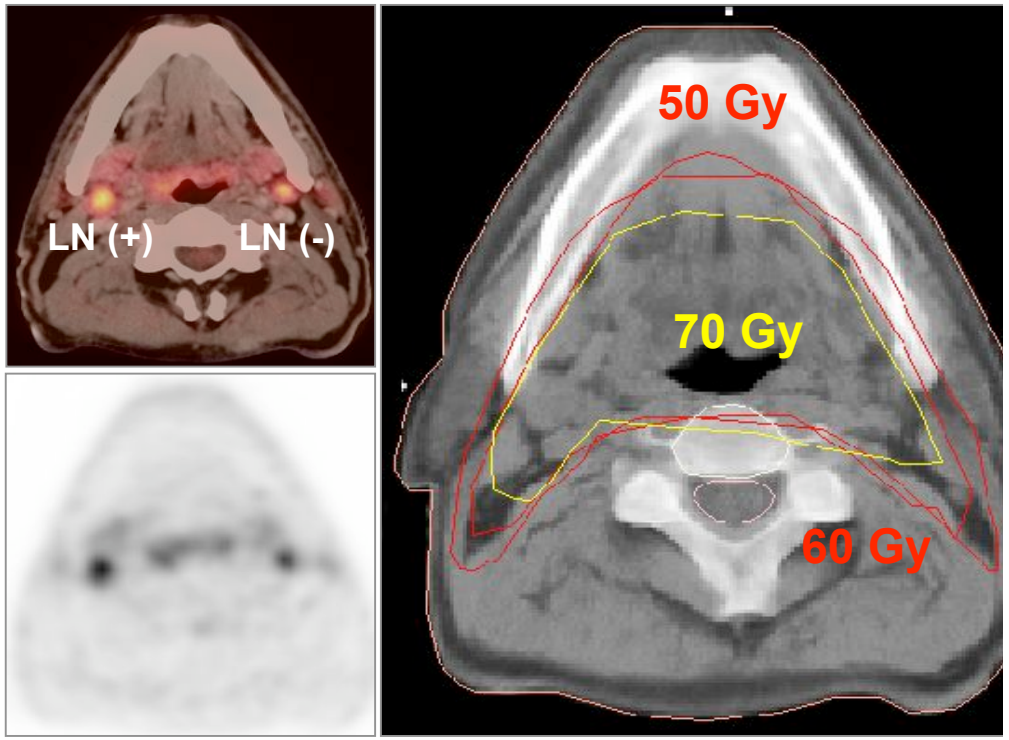
PET/CT in RTP

Courtesy Dr Sara Grehl, University Hospital Essen



58 year old male with oro/naso-pharyngeal cancer crossing the midline (T4) with unilateral lymph node involvement on CT. Left lymph node negative on CT but positive on PET/CT (N2). Modified boost-PTV (70 Gy) includes left lymph node.

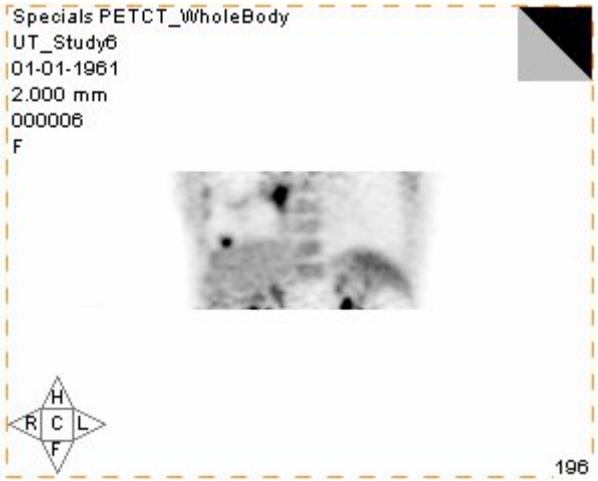


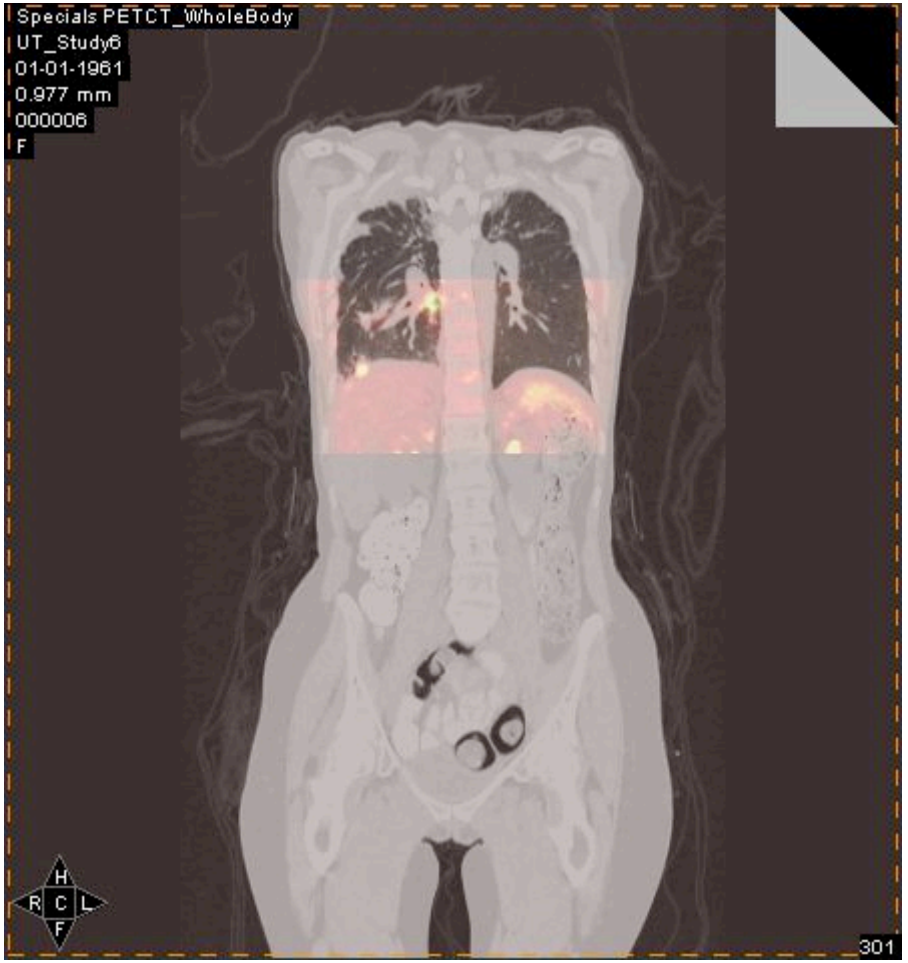


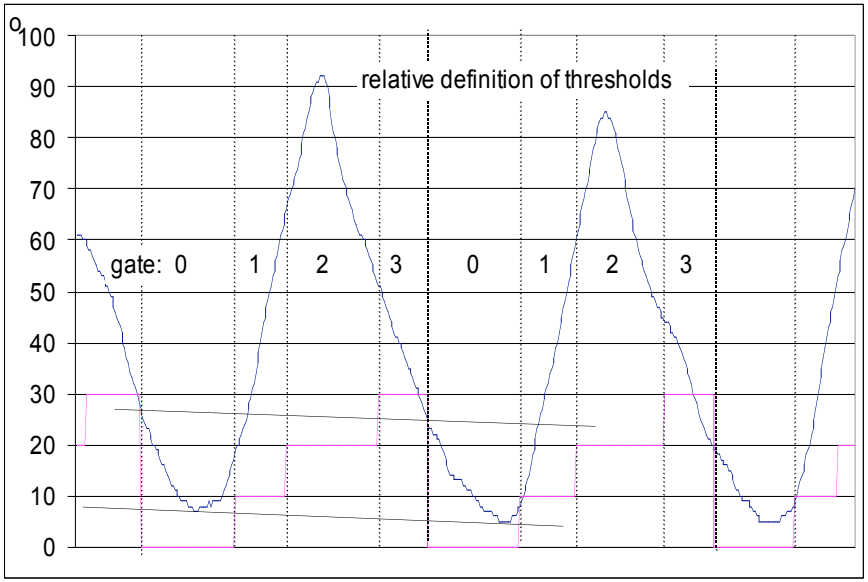
Issue #2

- Monitoring respiration (lung cancer)

PET respiratory gating







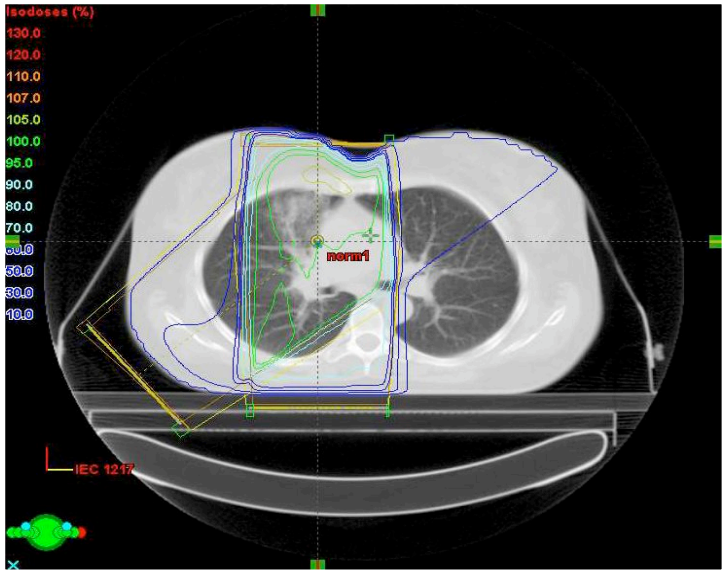
Results

- 9 out of 22 lung lesion patients exhibited lesions with significant motion
- 6 of those with sufficient statistics and regular breathing pattern to evaluate 4-gate studie

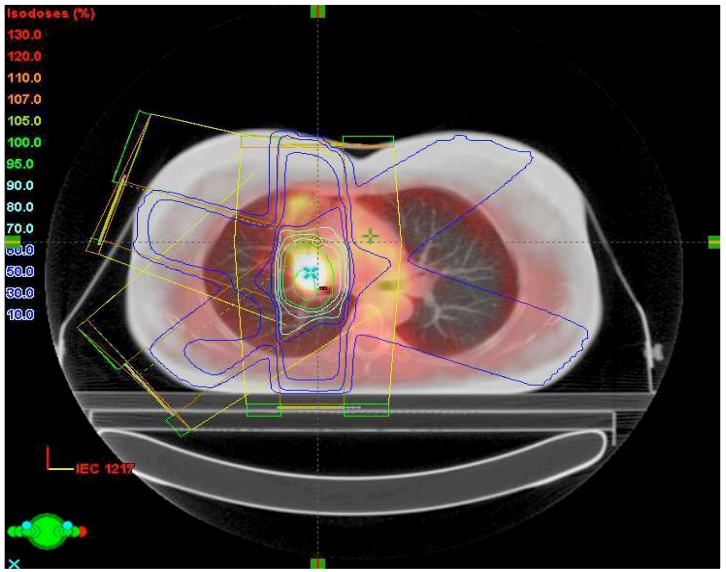
Gates	2 (11 lesions)	4 (8 lesions)
Average increase [SUV]	**14%**	**17%**
Max increase [SUV]	65%	39%
Duty cycle per gate	15-80% typical: 30-60%	10-50% typical: 20-30%
SUV range	2.1 – 35	2.3 - 35

Non-small cell lung cancer

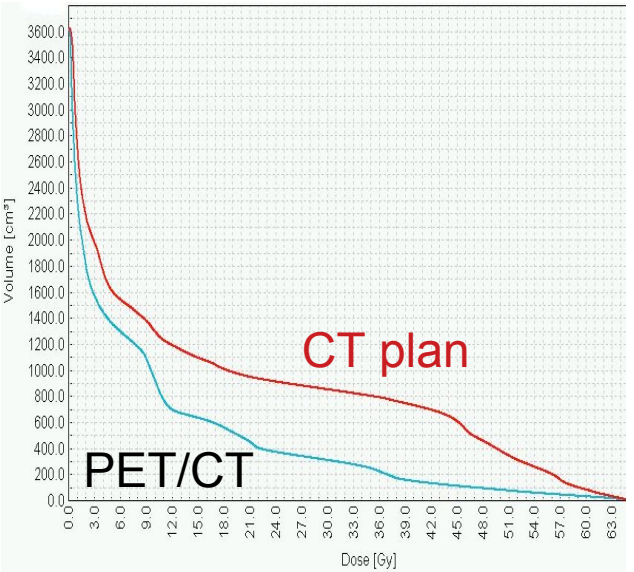
University Hospital Essen, Germany



CT plan



PET/CT plan



Dose-Volume Histogran

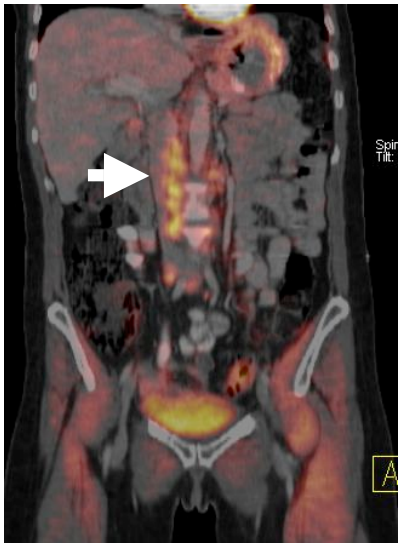
46 year-old female with NSCLC: cT2pN2 diagnosed 01/04 post 3 x CTX; PET/CT for RTP.

Compared to pre-CTX, the bronchial tumor is reduced both in size and metabolic activity (SUV_{max} reduced from 14 to 4.6). Atelectasis was sufficiently differentiated on PET/CT. PET/CT-based conformal treatment plan yields a cumulative mean lung dose of 8 Gy compared to 15 Gy with an assumed CT-based conventional treatment plan. Thus, PET/CT allowed for dose escalated treatment of this NSCLC.

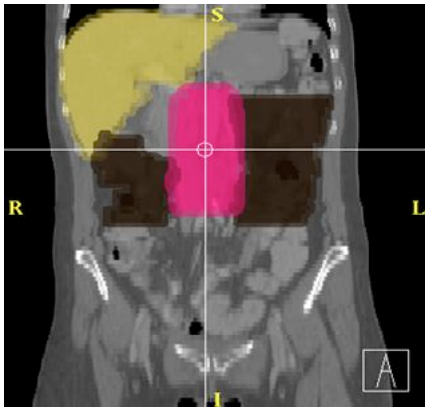
BGO-PET: 320 MBq ^{18}F-FDG, 80 min pi, 3.5 min per bed, 3 beds

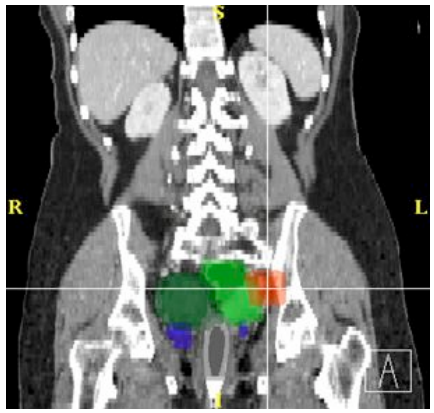
Dual-row CT: 110 mAs, 130 kVp, IV and water-based oral contrast, 4 mm slices

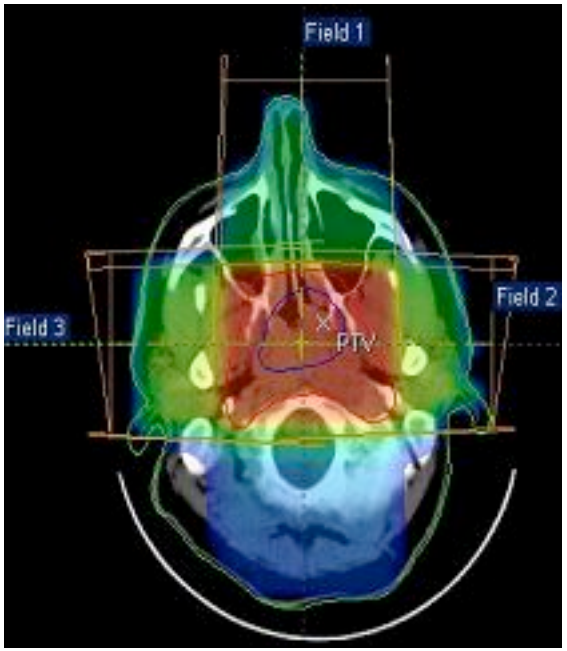
Change of treatment volume

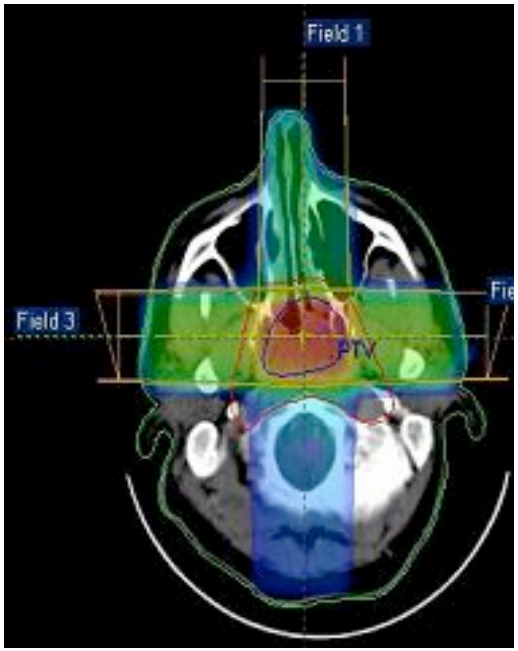


Increase in PTV









PTV from CT PTV from PET/CT

Decrease in treatment volume

Erdi et al: 11 patients: 7/11 PTV ⬆ (19% ave)
4/11 PTV ⬇ (18% ave)

Schmucking et al:
27 patients: 2/27 PTV ⬆
25/27 PTV ⬇ (12% ave)

PET/CT in radiation therapy

Total of 39 patients for radiation treatment

	head and neck	lung	pelvis
GTV ▲> 25%	**17%**	**17%**	**33%**
GTV ▼> 25%	**33%**	**67%**	**19%**

- GTV changed in 56% of cases
- PTV change >20% in 46% of cases
- decreased GTV differences between oncologists

I.F. Ciernik et al., Int. J. Radiation Biol. Phys. 2003; 57(3): 853-863

Response to therapy

Assessment measures:

- Kinetic analysis from dynamic scan: CMRGlu
- Patlak-Gjedde analysis: K_i, net rate of FDG trapping
- Standardized Uptake Value (SUV)
- Visual inspection

Issues for assessing response:

- requires at least 20% change in SUV between studies
- valid for tumors with sufficient baseline metabolic activity
- wait 4-6 weeks after completion of radiation therapy
- radiation-induced inflammatory response or tumor

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Response to therapy: Lymphoma

biograph 16

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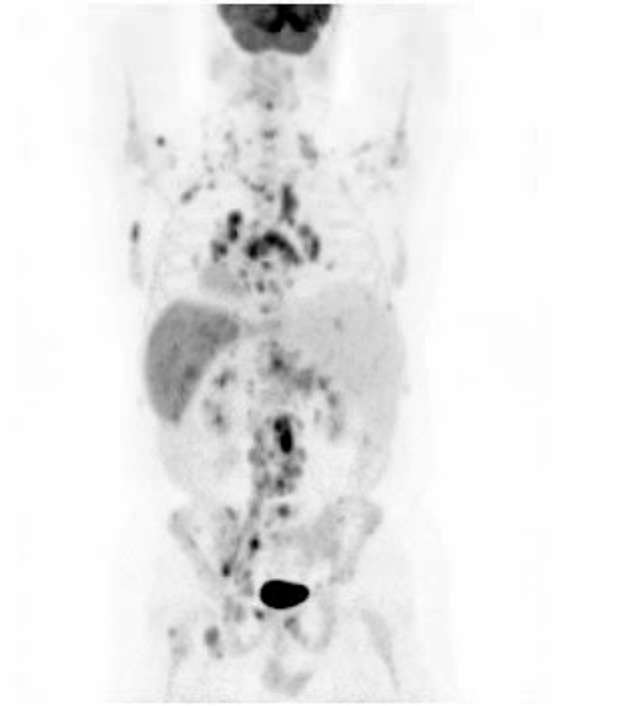
PET/CT fused image



Pre-therapy: 9/04

203 lbs
12.3 mCi
90 min uptake
120 kVp; 159 mAs
7 beds; 4 min per bed

Post-therapy: 1/05

219 lbs
11.7 mCi
98 min uptake
120 kVp; 193 mAs
7 beds; 4 min per bed

31 year-old male with lymphoma. Status pre and post chemotherapy

Response to therapy: head and neck

biograph 16

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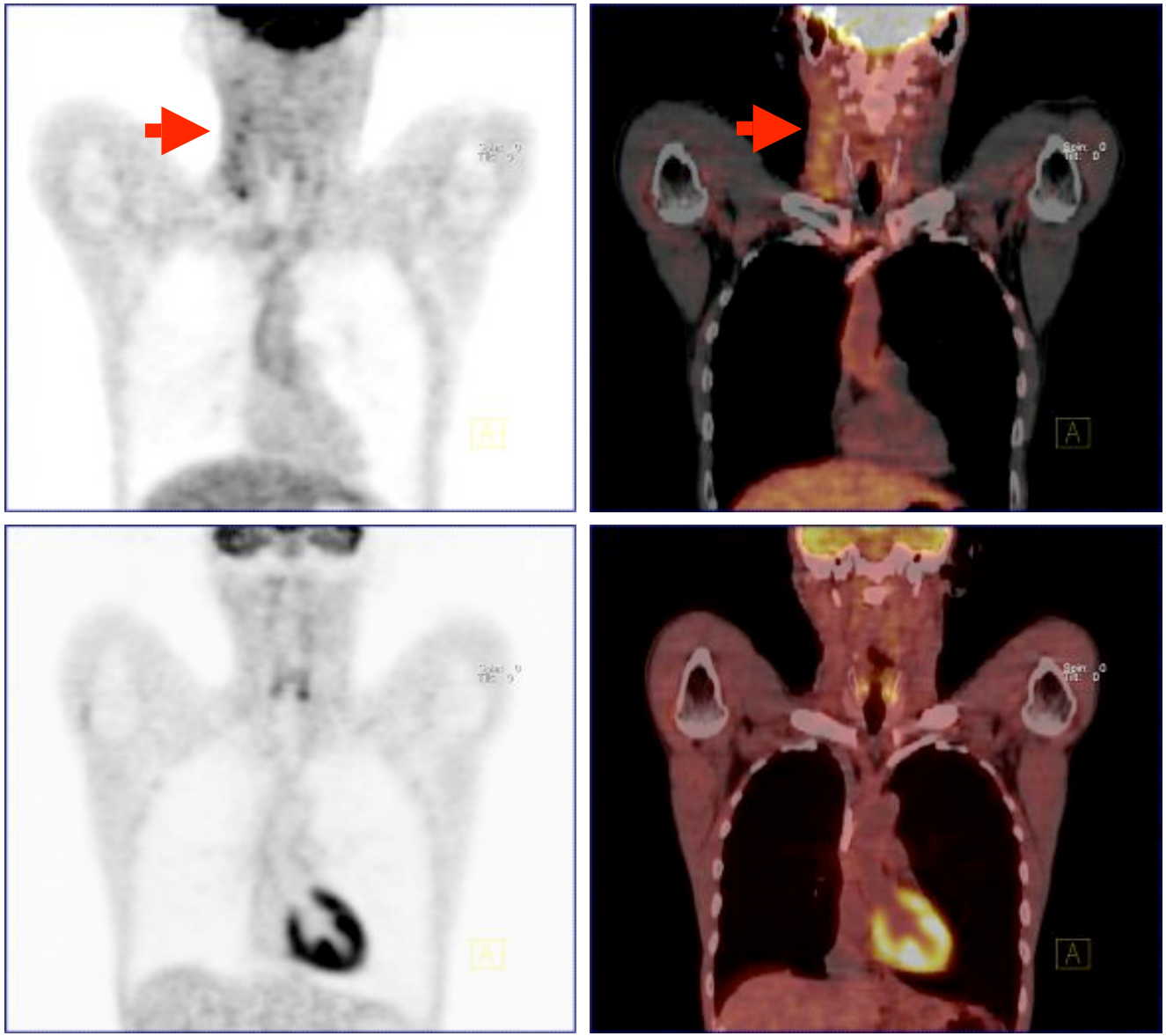
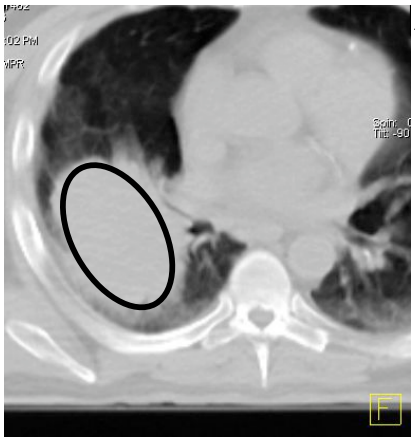


Multiple 2-8 mm hyper-metabolic lymph nodes

1 month post-chemotherapy and radiation

Quantitation of response to therapy: size and SUV



Anatomy (CT)

Size (d)

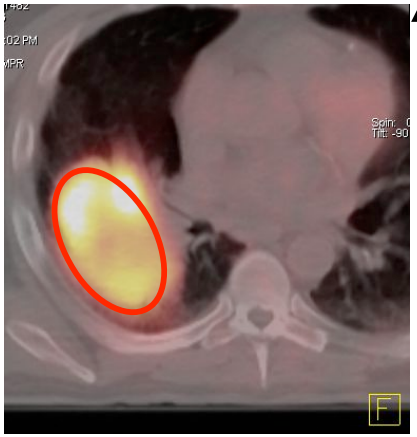
Anatomical response:
30% decrease in d

Anatomical ROI

d

1 2 3 4 5 Time (weeks)

SUV (ROI) = a_{ROI} (μCi/ml) / (**A** (mCi) / **W** (kg))



Function (PET)

Functional ROI

Metabolic response:
25% decrease in SU

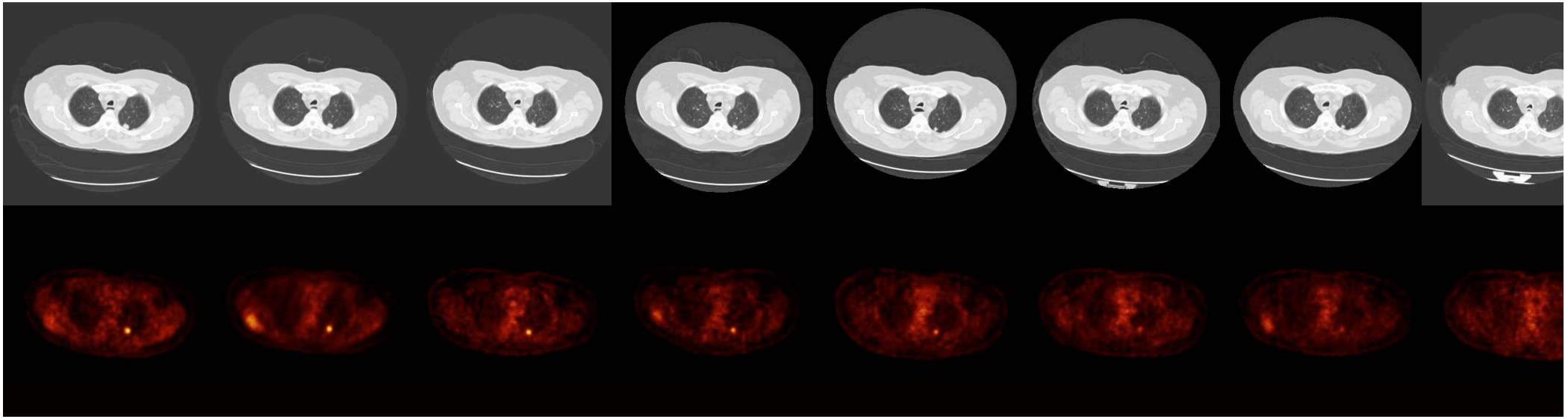
1 2 3 4 5 Time (weeks)

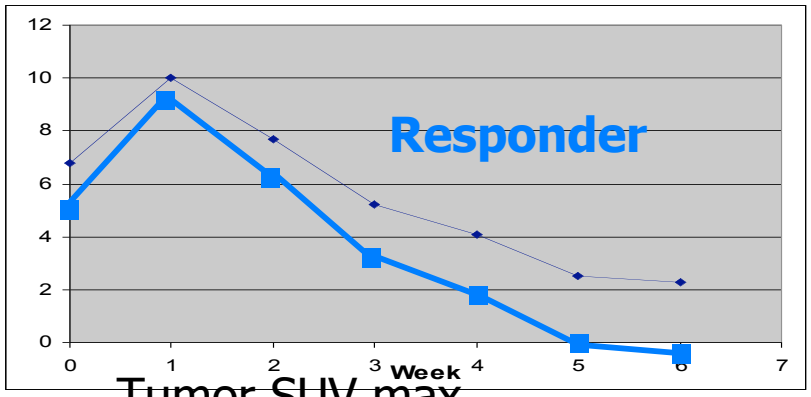
First cycle of chemotherapy

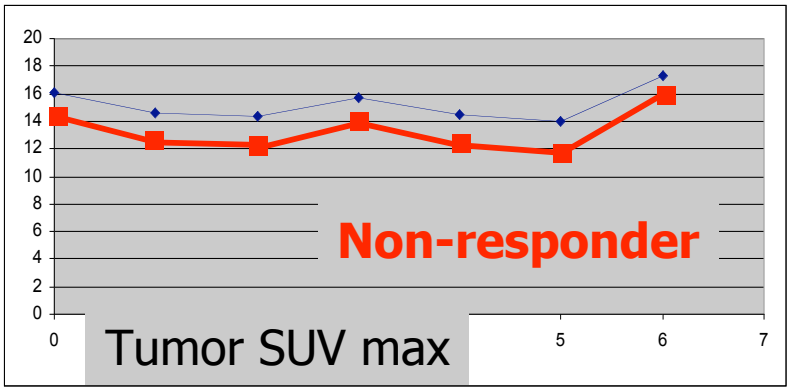
Second cycle of chemotherapy

Cancer Imaging and Tracer Development

Week 0 **Week 1** **Week 2** **Week 3** **Week 4** **Week 5** **Week 6** **Week 19**





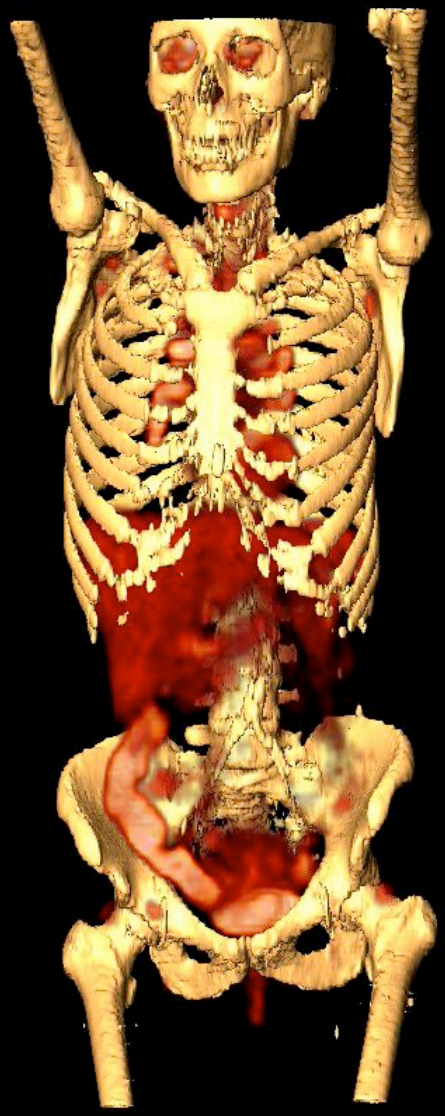


Summary: response to therapy

Tumor	No. of Patients	Criterion (% SUV)	Median survival (months)	
			Responders	Non responders
Lymphoma	30	Visual	>24	5
Esophagus	37	35	>48	20
	22	30	>38	18
Stomach	35	35	>48	17
Head and Neck	47	50	>120	40
Lung	57	20	9	5

Weber W. JNM 2005

Combined PET/CT imaging for RTP: outcome



The use of PET(/CT) can result in a change of treatment plan in more than 50% of cases.

Does this change improve outcome?

Grosu AL, Weber WA, Franz M, et al. Re-irradiation of recurrent high-grade gliomas using amino acid PET(SPECT)/CT/MRI image fusion to determine gross tumor volume for stereotactic fractionated radio-therapy. Int J Radiat Oncol Biol 2005 (In press)

^{11}C-methionine PET with CT/MRI fusion
Defining GTV with molecular imaging improved mean survival from 5 months to 9 months.

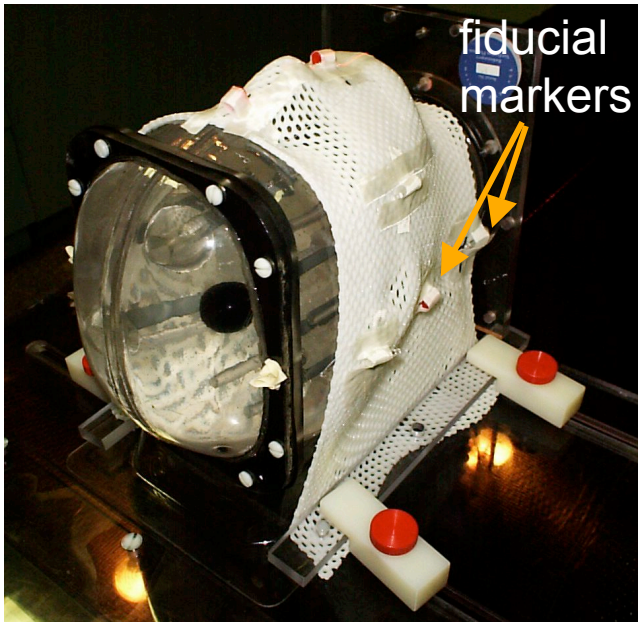
Issue #3

- Automated synthesis of radiotracers

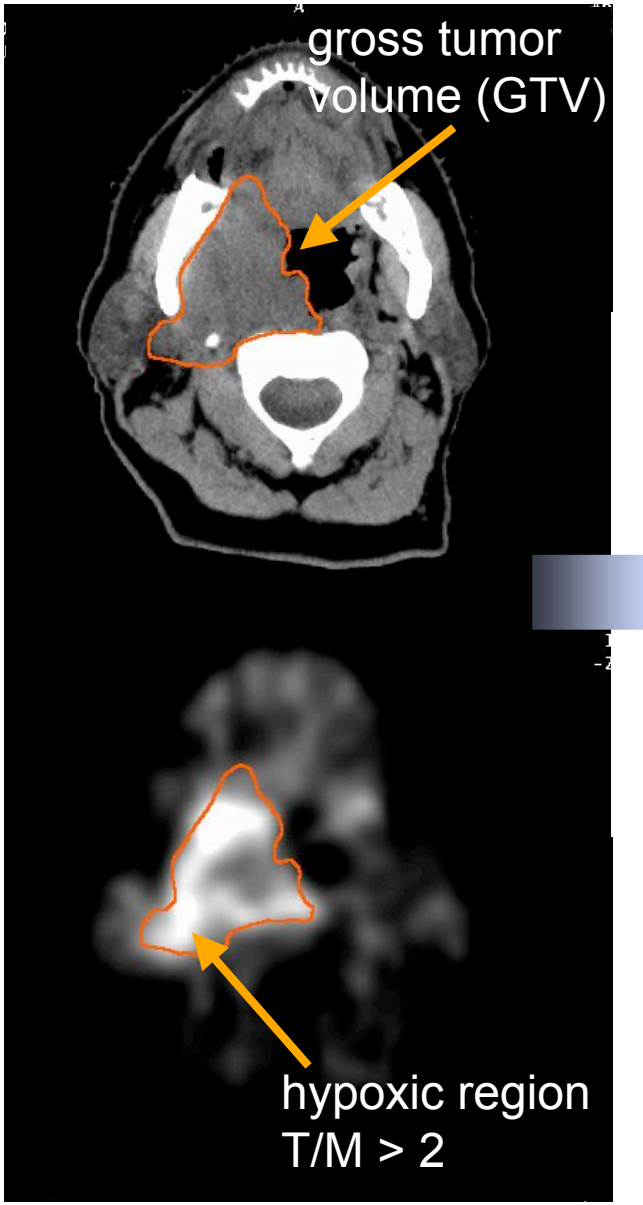
PET tracers for tumor imaging

• blood flow	[^{15}O] water
• glucose transport/utilization	[^{18}F] FDG
• tumor hypoxia	[^{64}Cu] ATSM
• angiogenesis	[^{18}F] RGD
• amino acid synthesis	[^{11}C] methionine
• cell replication (analog)	[^{18}F] FLT
• apoptosis	[^{18}F] annexin-V
• somatostatin receptors	[^{68}Ga] DOTATOC
• chemotherapy drugs	[^{18}F] fluorouracil
• prostate cancer	[^{18}F] fluorocholine

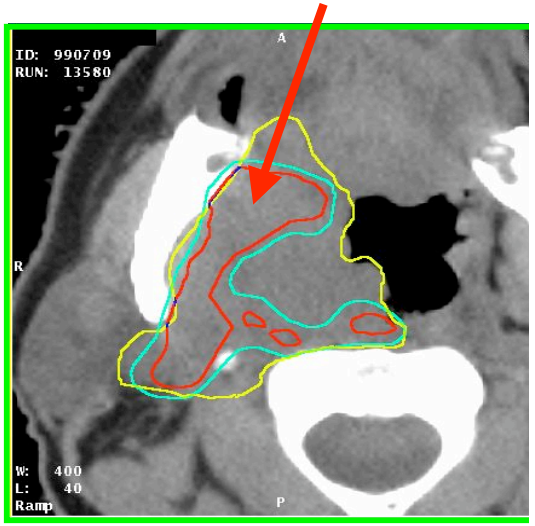
Hypoxia (^{60}Cu-ATSM)-guided RTP



Head phantom and face mask showing fiducial markers for CT and PET registration; with a PET/CT scanner, registration would be automatic.



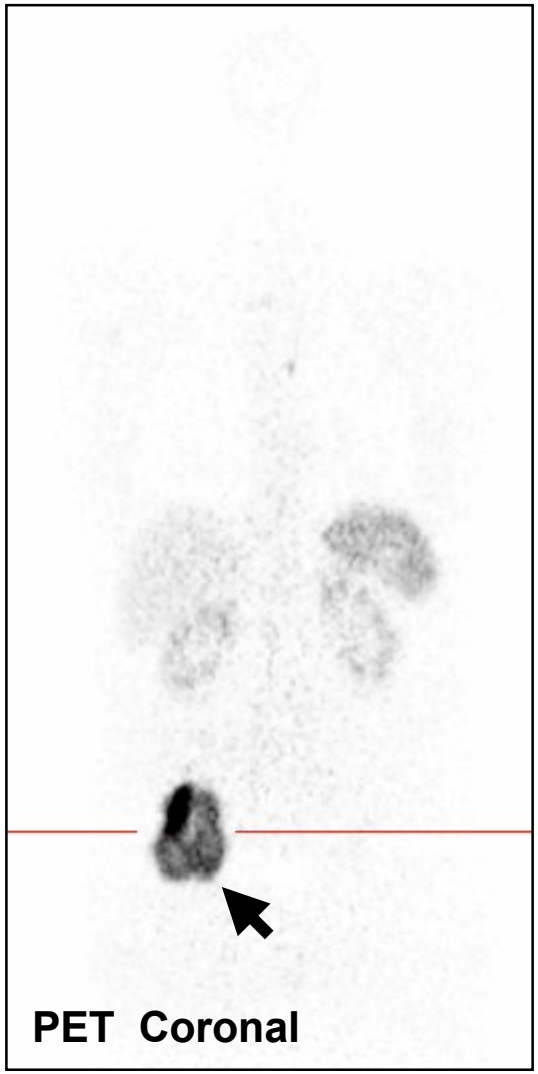
hypoxic tumor volume (*hGTV*)

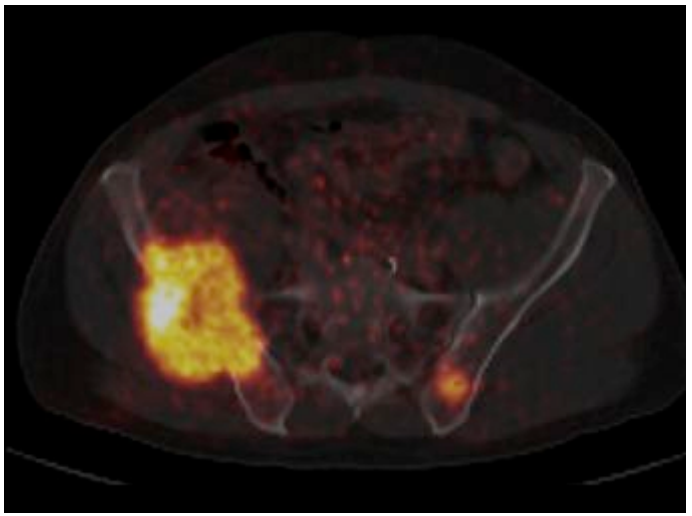


GTV and *hGTV*

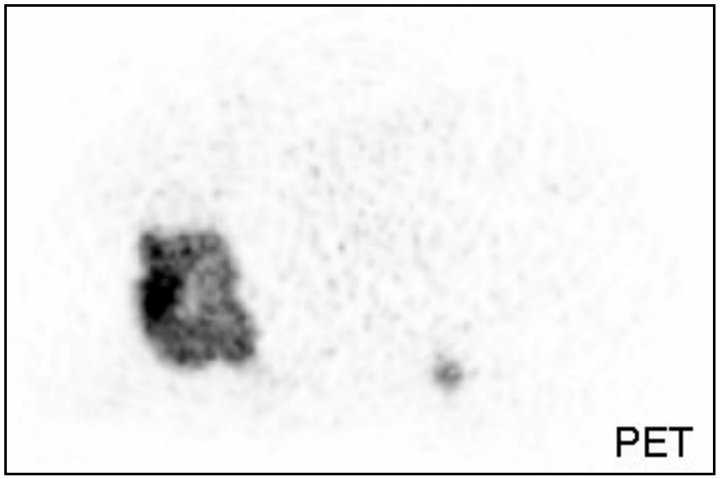
K.S Clifford Chao et al., Int. J. Radiation Biol. Phys. 2001; 49(4): 1171-1182

PET/CT imaging with ^{68}Ga-DOTATOC





Fused PET/CT image



Imaging tumors that express somatostatin receptors

M Hofmann and A. Bockisch
University of Bern and University of Essen

130 kV, 100 mAs, 5 mm
6 min/bed, 8 beds, 6i/16s, 2 mm, 256

Cancer Imaging and Tracer Development Research Program

University of Tennessee, Knoxville

Cancer Imaging an
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