PET/CT – Imaging in Radiooncology

Options – Limitations - Solutions

N.M. Blumstein
Department of Radiation Oncology,
University Bern, Inselspital, Bern, Switzerland

Role of imaging in Radiotherapy (1)

► Target volume definition

► Target volume delineation

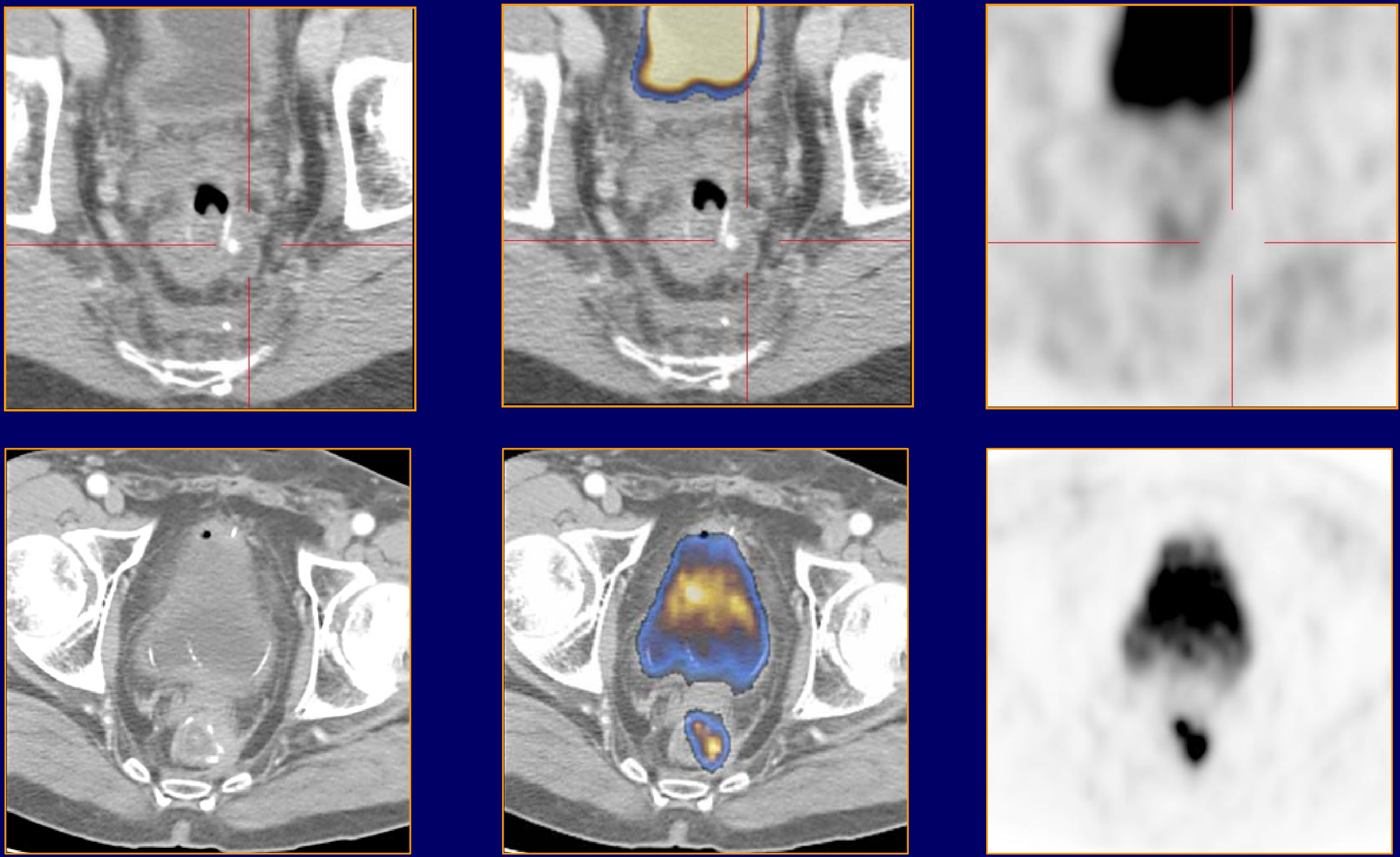
- delineation of the primary, delineation of the lymph nodes
- biologically relevant subvolumes

► Adaptive Image guided radiation

- tumor motion
- patients positioning and patient movement
- organ motion (e.g. bladder, rectum) in patients with prostate cancer undergoing radiotherapy
- Changes in biologically relevant subvolumes

PET/CT – Imaging in Radiooncology

Role of imaging in Radiotherapy (2)



Blumstein, Estro 2004

Schaefer,O.; Detection of recurrent rectal cancer with CT, MRI and PET/CT Eur Radiol. 2007 Aug;17(8):2044-54

PET/CT – Imaging in Radiooncology

Role of imaging in Radiotherapy (3)

► not a talk about role of PET/CT as a

- staging tool
- method for early response assessment
- possibility to visualize early disease recurrence

- few patients
- various sites
- sub-optimal segmentation methods
- no validation with „a gold standard“ in prospective trials

PET/CT – Imaging in Radiooncology

Target definition (1)

Comparison between CT (MRI) and FDG-PET for nodal staging

Comparison between CT and FDG-PET for nodal staging

Site	Sensitivity		Specificity	
	CT (%)	FDG-PET (%)	CT (%)	FDG-PET (%)
NSC lung cancer	45	80–90	85	85–100
Lymphoma	81	86–89	41	96–100
Esophageal cancer	11–87	30–78	28–99	86–98
Head and neck cancer	36–86	50–96	56–100	88–100

Gregoire V. Is there any future in radiotherapy planning without the use of PET? Radiother & Oncol, 2004

Antoch G, Accuracy of whole-body dual-modality fluorine-18-2-fluoro-2-deoxy-D-glucose positron emission tomography and computed tomography (FDG-PET/CT) for tumor staging in solid tumors: comparison with CT and PET, JCO 2004

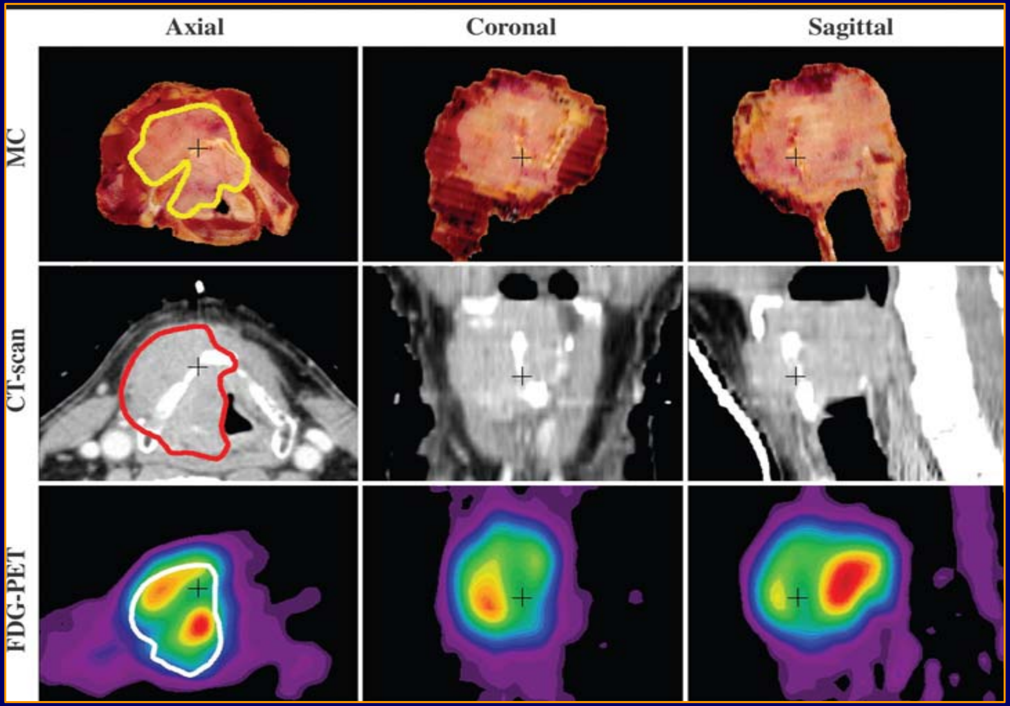
Target definition (2) Esophagus

Imaging methods	**lymph node regions (n)**	**pts. (n)**	**Influence of PET**	
CT/EUS (+) vs. FDG-PET (-)	9	8 (27%)	3 (10%)	smaller
CT/EUS (-) vs. FDG-PET (+)	8	6 (20%)	3 (10%)	larger

Vrieze et al. Radiother Oncol 2004

PET/CT – Imaging in Radiooncology

Target definition (3) Head and Neck



Imaging methods	**Vol**	**Mismatch**	**Mismatch**	**Mismatch**	**Mismatch**
n = 29 (larynx/hypophyrynx)	**ml**	**x/CT**	**x/MR**	**x/PET**	**x/Macro**
CT	20.8		28%	48%	18%
MR	23.8	45%		67%	107%
FDG-PET	16.3	17%	15%		47%
Macro	12.6	10%	9%	13%	

Daisne et al., Radiology 2004

p<0.05 (Wilcoxon rank test)

PET/CT – Imaging in Radiooncology

Clinical data (2002-2004)

	Jahr	Journal	Pat./Tier	Methode
Allgemein				
Macmanus	2004	Int J Radiat Oncol Biol Phys 1; 60(3):1005-6		PET
Bradley	2004	J Nucl Med 45 Suppl 1:96-101		PET
Yap	2004	Cancer 10(4): 221-33		PET
Delbeke	2004	Cancer 10(4): 201-13		PET
Paulino	2003	Semin Nucl Med 33 (3): 228-43		PET/SPECT
Schmucking	2003	Recent Results Cancer Res 162;195-202		PET
Ciernik	2003	Int J Radiat Oncol Biol Phys 11; 57(3):853-63		**PET/CT**
Perez	2002	Rays 27(3): 157-73		PET
Brachytherapie				
Mutic	2002	Int J Radiat Oncol Biol Phys 15; 52(4):1104-10		PET
IORT				
Antoch	2003	Radiology 230(3):753-60	Leber(pig)	**PET/CT**
SRS				
Levivier	2004	J Nucl Med 45 (7): 1146-54	57	PET
Grosu	2003	Int J Radiat Oncol Biol Phys 8; 56(5):1450-63	12	PET
Karger	2003	Phys Med Biol 21; 48(2): 211-21		PET/SPECT
Eubank	2002	Radiographics 22(1): 5-17		PET

PET/CT – Imaging in Radiooncology

Clinical data (2002-2004)

	Jahr	Journal	Pat.	Methode
NSCLC				
Bradley	2004	Int J Radiat Oncol Biol Phys 8; 22(16):3248-54	24	PET
Bradley	2004	Int J Radiat Oncol Biol Phys 5; 59(1):78-86	26	PET
Mah	2002	Int J Radiat Oncol Biol Phys 2; 52(2):339-50	30	PET
Erdi	2002	Radiother Oncol 62(1):51-60	11	PET
HNO				PET
Yao	2004	Int J Radiat Oncol Biol Phys 15; 59(4):1001-10		
Scarfone	2004	J Nucl Med 45(4):543-52	6	PET
Mamma				PET
Eubank	2002	Radiographicvs 22(1):5-17		PET
Cervix				
Tsai	2004	Int J Radiat Oncol Biol Phys 4; 58(5):1506-12	26	PET
Esthappan	2004	Int J Radiat Oncol Biol Phys 3; 58(4):1289-97	10	**PET/CT**
Mutic	2003	Int J Radiat Oncol Biol Phys 31; 55(1):28-35	4	PET
Pankreas				
Yoshioka	2004	J Gastroenterol 39(1): 50-5		
Rektum				
Delbeke	2004	Semin Nucl Med 34 (3): 209-23		**PET/CT**
Hocht	2004	Strahlenther Onkol 180(1):15-20	123	PET
Sarkome				
Johnson	2003	Clin Nucl Med 28(10): 815-20		PET
Dobrowolskij	2002	Orthopäde 31(9):921-9	79	PET
Lymphome				
Lavely	2003	Int J Radiat Oncol Biol Phys 10; 57(2):307-15	28	PET

PET/CT – Imaging in Radiooncology

Literature research (2005 - 08/2008)

PET/CT in Oncology n = 927

PET/CT and radiotherapy/ integration for treatment planning	2005	2006	2007	2008
General aspects/technical note	**9**	**8**	**17**	**11**
Lung cancer/Pleura mesothelioma	10	8	6	6
Head and Neck	3	10	7	9
brain tumours	0	1	1	2
thyroid cancer	0	0	1	2
breast cancer	0	1	0	2
Lymphoma	2	0	4	1
Esophagus cancer	1	3	0	0
Liver cancer/metastases	1	1	0	0
Rectal cancer	1	0	2	3
Cervix carcinoma	0	2	2	2
Prostate cancer	0	2	1	2
Anal cancer	0	1	0	1
Total	**27**	**37**	**41**	**42**

147/927 = 16%

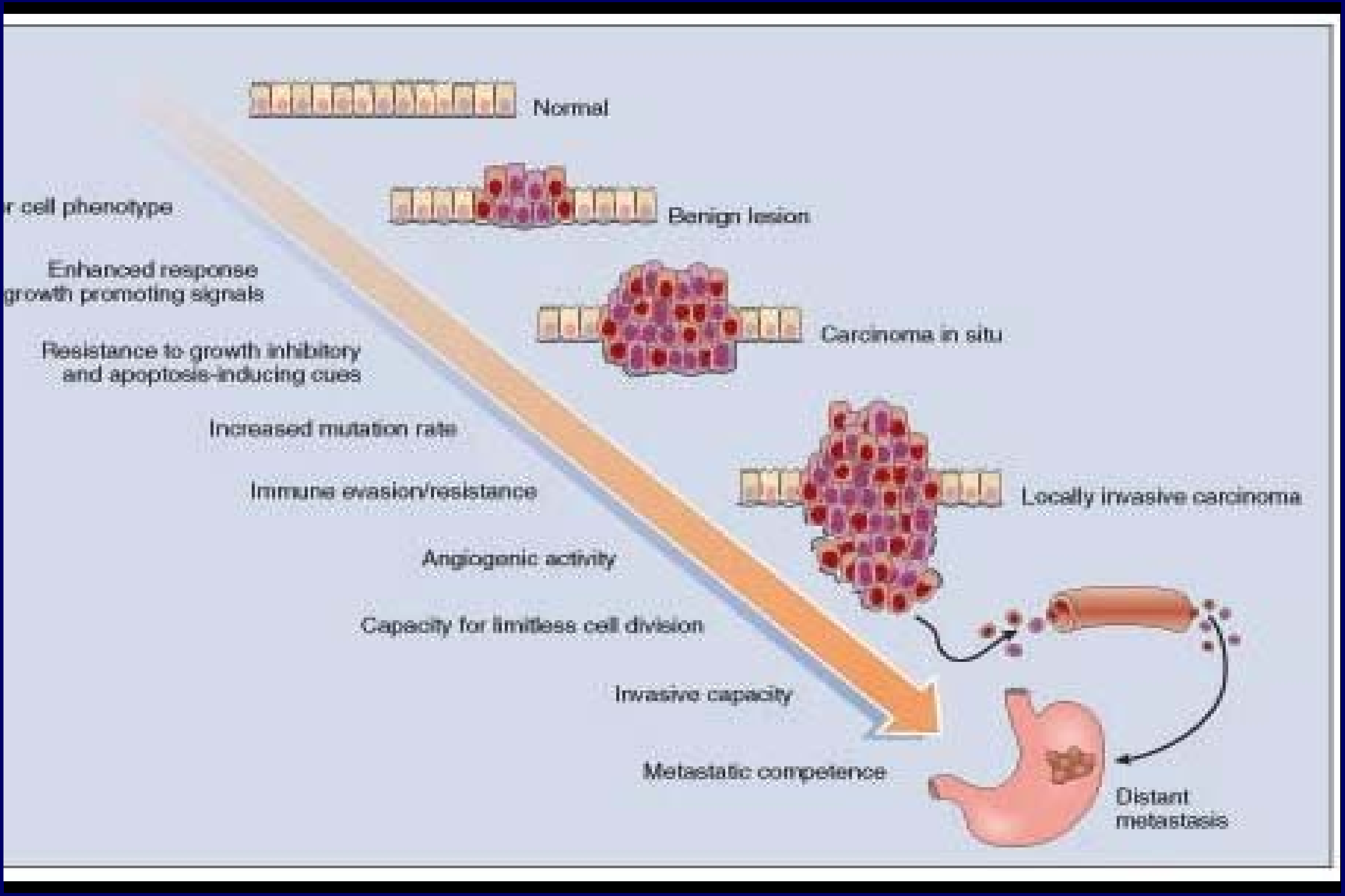
Ich sehe die Venusfliegenfalle, eine Schnecke, einen Hund,
einen Baum am Nagel, einen breiten, offenen Mund;
zwei Vieren, zwei Fledermäuse, vier fünfzackige Sterne,
eine große, grüne Raupe, das Fahrrad lenk' ich gerne.

Ich sehe die Venusfliegenfalle, eine Schnecke, einen Hund,
einen Baum am Nagel, einen breiten, offenen Mund;
zwei Vieren, zwei Fledermäuse, vier fünfzackige Sterne,
eine große, grüne Raupe, das Fahrrad lenk' ich gerne.

Ich sehe die Venusfliegenfalle, eine Schnecke, einen Hund,
einen Baum am Nagel, einen breiten, offenen Mund;
zwei Vieren, zwei Fledermäuse, vier fünfzackige Sterne,
eine große, grüne Raupe, das Fahrrad lenk' ich gerne.

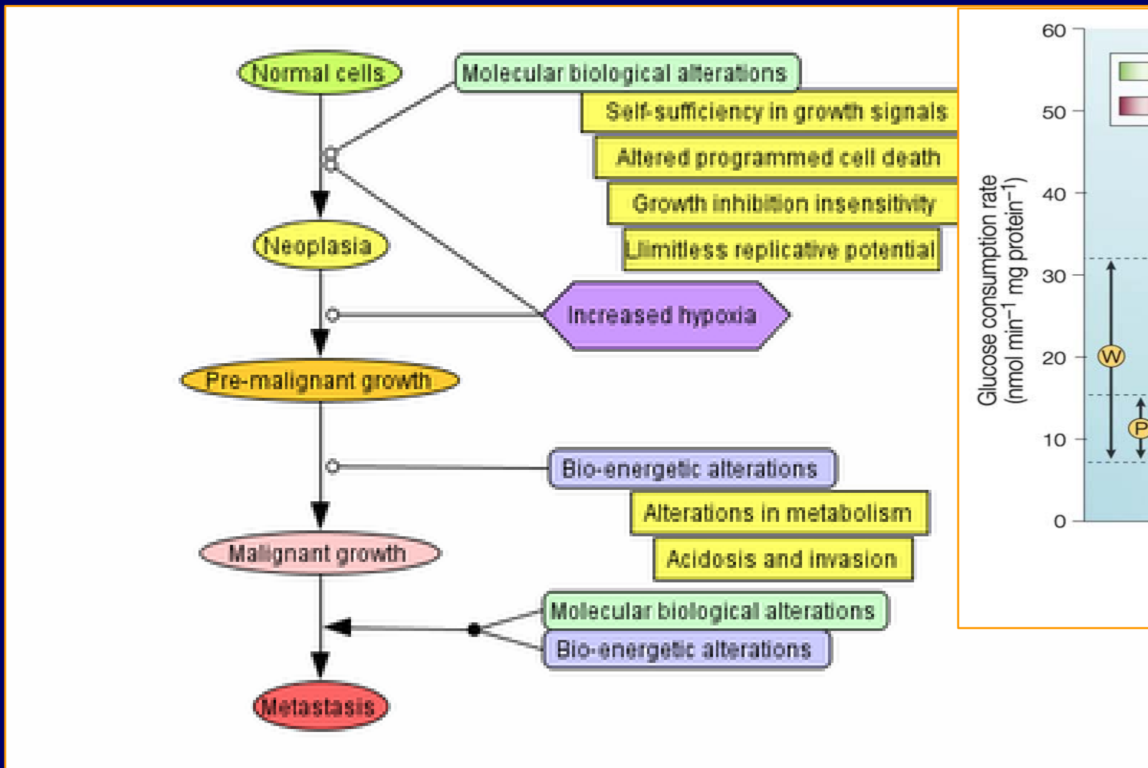
Ich sehe die Venusfliegenfalle, eine Schnecke, einen Hund,
einen Baum am Nagel, einen breiten, offenen Mund;

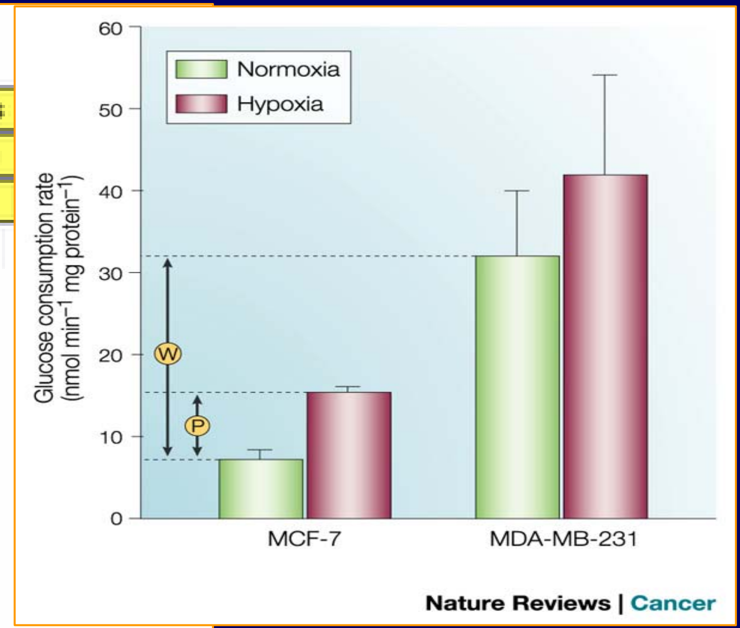
zwei Vieren, zwei Fledermäuse, vier fünfzackige Sterne,
eine große, grüne Raupe, das Fahrrad lenk' ich gerne.


Normal
Benign lesion
Carcinoma in situ
Locally invasive carcinoma
Distant metastasis
r cell phenotype
Enhanced response
growth promoting signals
Resistance to growth inhibitory
and apoptosis-inducing cues
Increased mutation rate
Immune evasion/resistance
Angiogenic activity
Capacity for limitless cell division
Invasive capacity
Metastatic competence

PET/CT – Imaging in Radiooncology

Future begins in the past

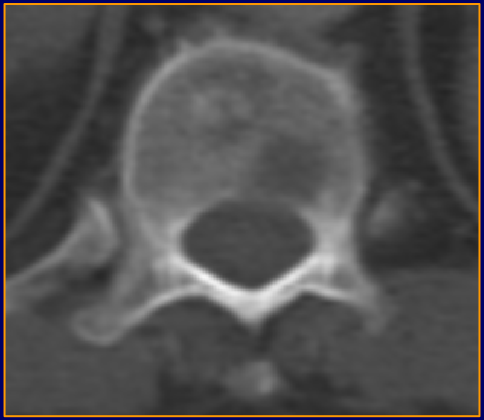


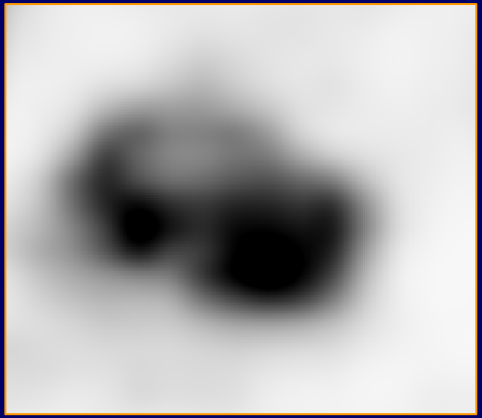


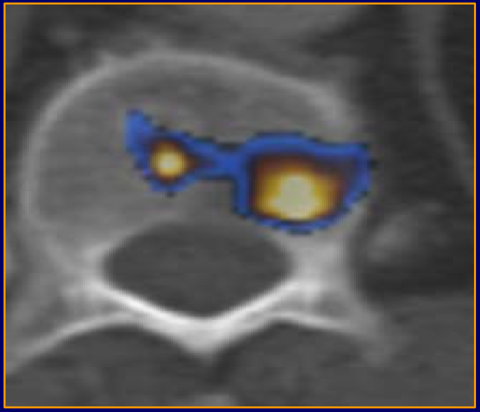
Warburg – effect (1920,1957)

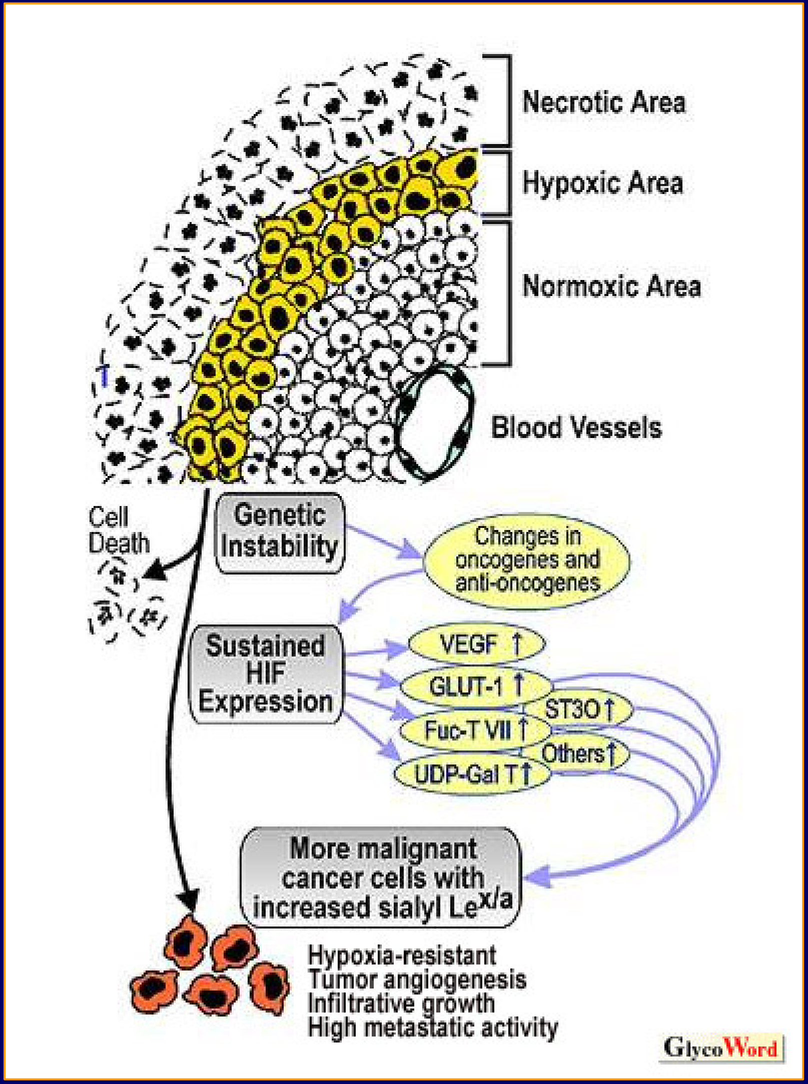
Robert A. Gatenby Robert J. Gillies
Why do cancers have high aerobic glycolysis?
Nature Reviews Cancer 4, 891-899 (November 2004)

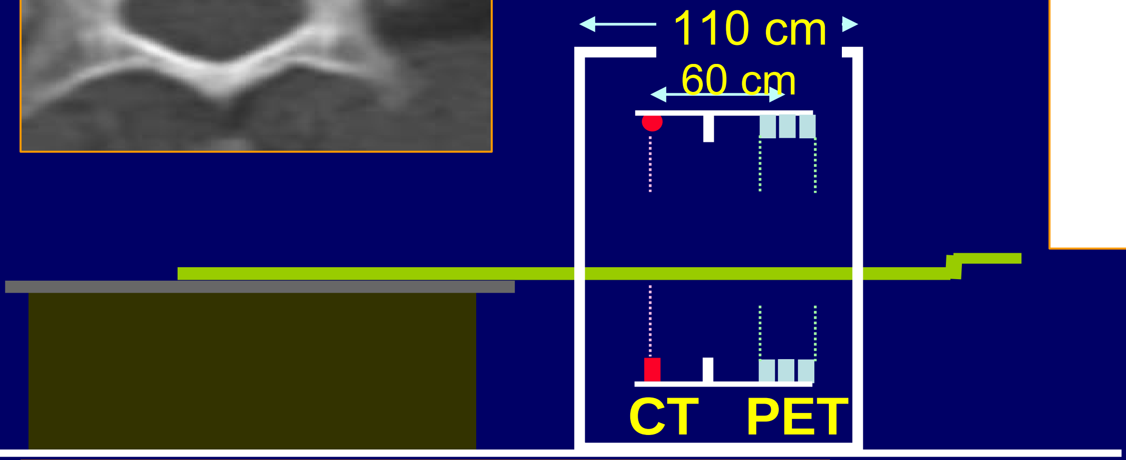
Christofk, H. R. *et al.*
Pyruvate kinase M2 is a phosphotyrosinebinding protein.
Nature 13 Mar 2008



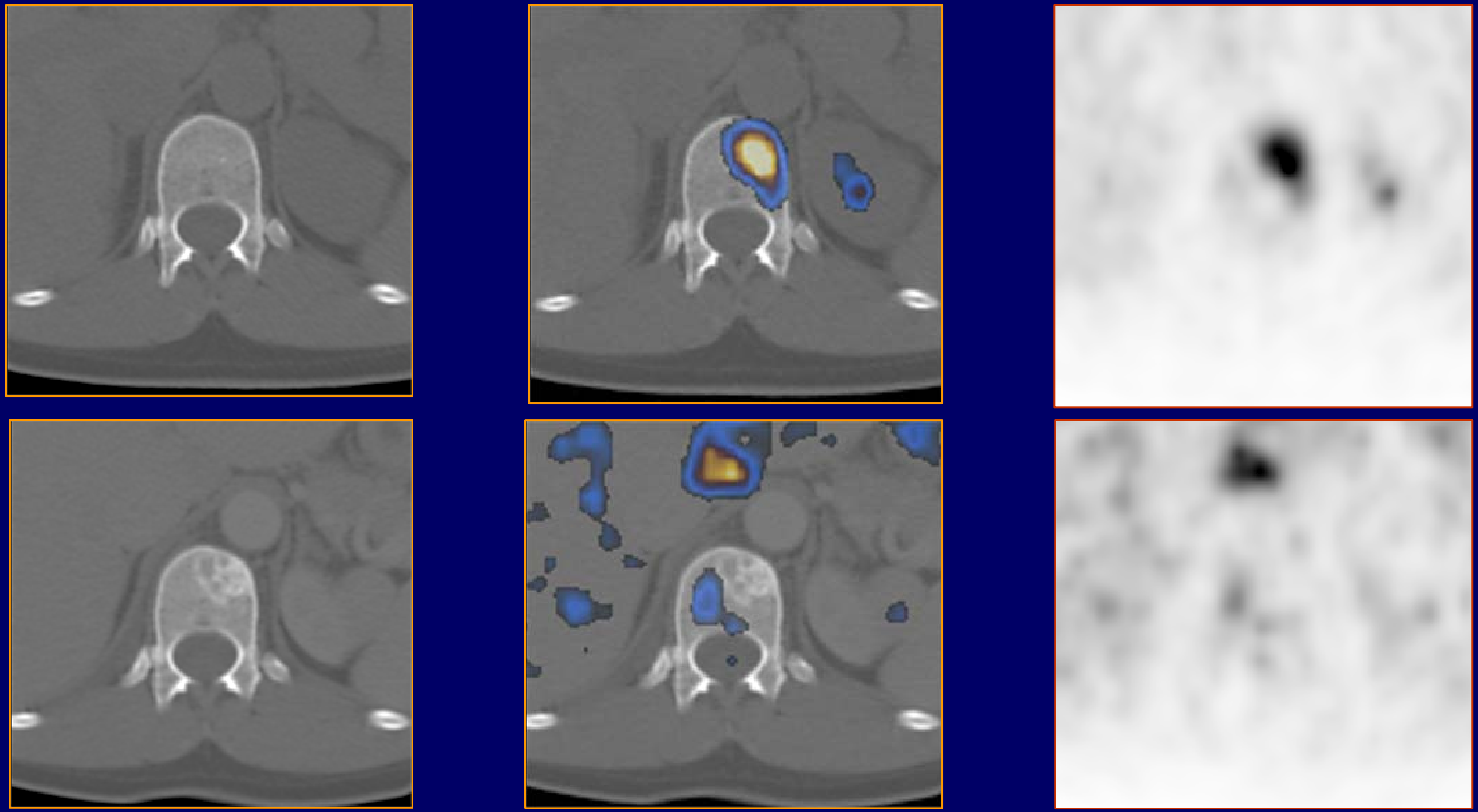








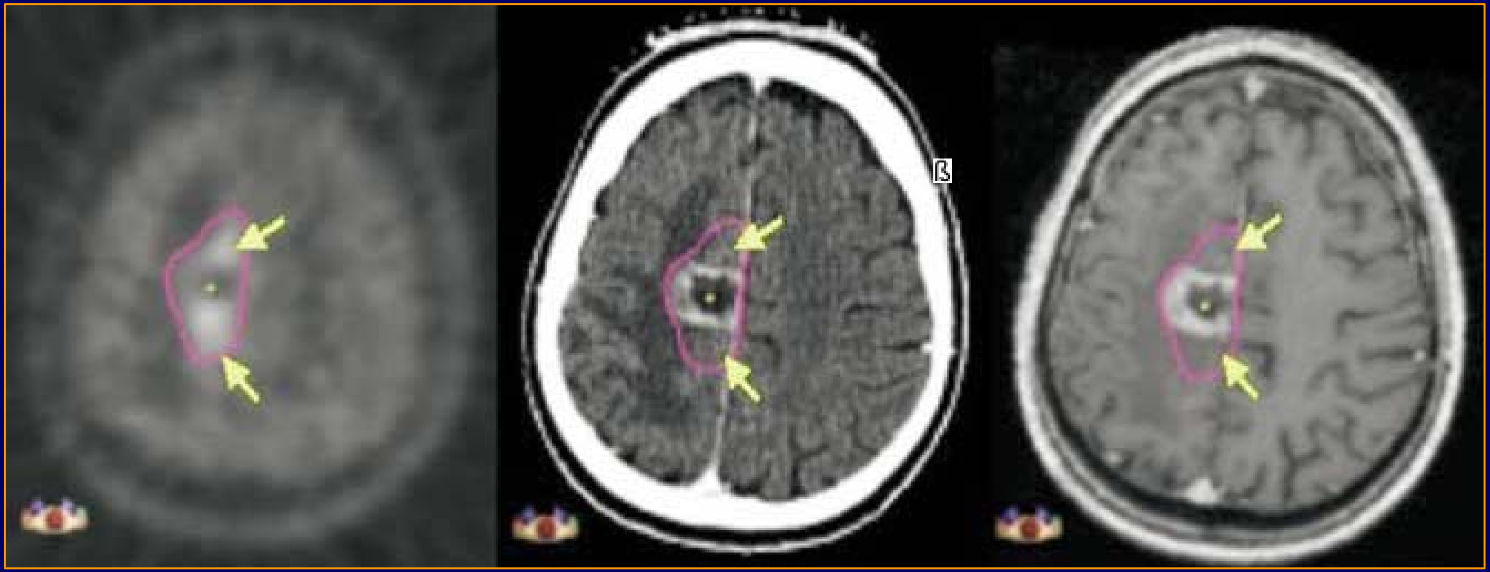
Dedicated PET/CT-Scanner



Radiation therapy (RT) of an osseous metastasis in men suffered from prostate cancer
Before RT and five month after RT (30 Gy)

PET/CT – Imaging in Radiooncology

tumor activity: visualization and detecting



Recurrent glioblastoma multiforme. ^{11}C-methionine positron emission tomography shows tumor infiltration in areas (arrows) located outside of the contrast enhancement on computed tomography and T1-magnetic resonance imaging.

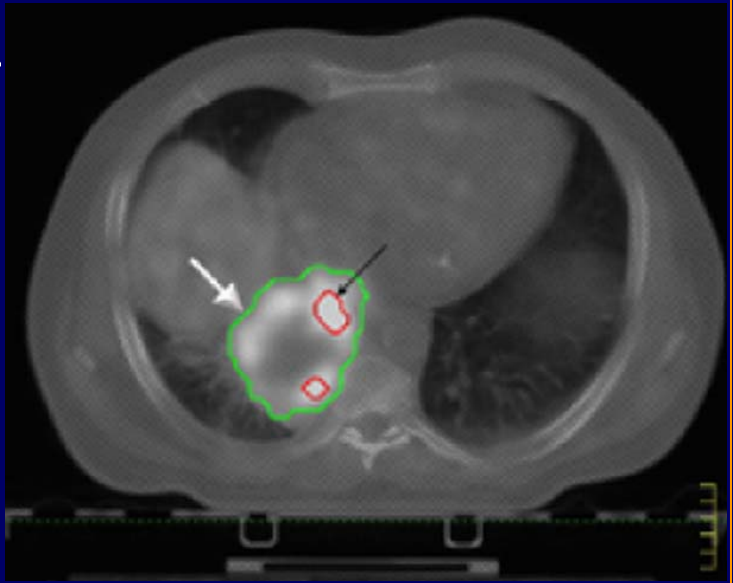
Grosu,A., Int. J. Radiation Oncology Biol. Phys., Vol. 63, No. 2, pp. 511–519, 2005

Plotkin,M, ^{18}F-FET PET for planning of thermotherapy using magnetic nanoparticles in recurrent glioblastoma. International Journal of Hyperthermia, Vol 22, Issue 4, 2006,p. 319-25

Ulrich, Clin Cancer res, 2008 (^{18}F-FLT)

Size of FDG-based GTV is influenced by the contouring method

N= 25, primary NSCLC, FDG based GTVs



Contouring methods:

- Visually
- Threshold = SUV 2.5
- 40% of maximum accumulation
- Contrast dependent algorithm

Significant differences correlating with

- SUV max
- Size of lesion
- Inhomogeneity of accumulation

Results of the use of different methods for contouring the GTV in a large inhomogeneous tumor.

Red (black arrow): isocontour comprising 40% of the maximum accumulation of the lesion. Green (white arrow): isocontour derived from source/background algorithm

Nestle U et al. J Nucl Med 2005 46: 1342-1348
Nestle U et al. Radiotherapy & Oncology 2006

PET/CT – Imaging in Radiooncology

FDG-PET/CT in lung cancer

Table 1

Literature reports on the impact of FDG-PET on radiotherapy planning in lung cancer

Author	Study	Patients	PET/CT image fusion	Method of GTV contouring (PET)	Change of GTV, PTV using PET	Increase of GTV, PTV using PET	Decrease of GTV, PTV using PET	Comment
Hebert et al. [46]	Prospective	20	Comparison X-ray, CT, PET	Visual evaluation of FDG-PET	GTV 7/20 P (35%)	GTV 3/20 P (15%)	GTV 4/20 P (20%)	PET may be useful for delineation of lung cancer
Kiffer et al. [54]	Retrospective	15	Graphical co-registration of coronal PET with AP simulator image	Visual evaluation of FDG-PET	GTV: 7/15 P(47%) PTV:4/15 P (27%)	GTV and PTV: 4/15 P (27%)		PET detects positive lymph nodes, not useful in tumor delineation
Munley et al. [63]	Retrospective	35	CT/PET co-registered manually using transmission PET	Visual evaluation of FDG-PET	PTV:12/35 P (34%)	PTV: 12/35 P (34%)	PET target smaller than CT not evaluated	PET complements CT information
Nestle et al. [69]	Retrospective	34	PET-portal compared to CT-portal	Visual evaluation of FDG-PET	change of field size in 12P(35%) Median19, 3% (cm2)	Increase of field size 9 P (26%)	Decrease of field size 3 P (9%)	Change of field size in patients with dys- or atelectasis
Vanuytsel et al. [92]	Retrospective	73 (N+)	CT-Naruke map compared with CT-PET-Naruke map and pathology	Visual evaluation of FDG-PET	GTV: 45/73P(62%)	GTV: 16/73P (22%) 11P = pathology 1P-unnecessary 4P-insufficient	GTV: 29/73P (40%) 25P = pathology 1P-inappropriate 3P-insufficient	PET data vs. pathology: 36 P(49%) = pathology 2 P(3%) inappropriate 7 P(10%) insufficient
MacManus et al. [61]	Prospective	153	PET results used for treatment planning, no image fusion	Visual evaluation of FDG-PET	GTV: 22/102 P(21%)	GTV: 22/102 P(21%) Inclusion of structures previously considered uninvolved by tumor	GTV: 16/102 P(15%) Exclusion of atelectasis and lymph nodes	Post-PET stage but not pre-PET stage was significant associated with survival
Kalff et al. [53]	Prospective	34	No image fusion	Visual evaluation	22/34 altered treatment delivery	n.e.	11/34 reduction of treatment volume	Part of a study on impact of FDG- PET on various endpoints (*n* = 105)
Giraud et al. [40]	Prospective	12	CT/PET image fusion	Visual evaluation of FDG-PET	GTV, PTV 5/12 P(42%)	n.e.	n.e.	4/12 P lymph nodes 1/12 atelectasis and distant meta
Mah et al. [62]	Prospective	30	Image coregistration CT-PET using external fiducial markers	50% intensity level of max. FDG uptake	GTV: 5/23 P (22%) FDG-avide lymphnodes	PTV: 30–76% of cases (varied between the 3 physicians)	PTV: 24–70% of cases (varied between the 3 physicians)	(a) Addition of PET does lower physician variation in PTV delineation

FDG-PET/CT in lung cancer

								(b) PET-significant alterations to patient management and PTV
Erdi et al. [34]	Prospective	11	Image fusion: manual method using transmission PET data compared with automated image registration based on mutual information	40% intensity level of max. FDG uptake	PTV: 11/11P (100%)	PTV: 7/11 P (36%) 19% (5–46%) cc detection of lymph nodes	PTV: 4/11 P 18%(2–48%) cc exclusion of atelectasis trimming the target vol. to spare critical structure	PET improves GTV and PTV definition
Ciernik et al. [23]	Prospective	6	Integrated PET/CT	manually	GTV: 6/6 P (100%)	GTV 1/6 (17%)	GTV 4/6 (67%)	PET/CT improves GTV delineation
Bradley et al. [13]	Prospective	26	Patient immobilization PET/CT fusion	40% intensity level of max. FDG uptake	PTV:14/24 P(58%)	11/24 P (46%) 10 lymph nodes, 1 tumor	3/24 P (12%) Tumor vs. atelectase	PET improves diagn. of lymph nodes and atelectasis
Van Der Wel et al. [89]	Prospective	21	PET/CT visual fusion technique		GTV and PTV: 12/21 P (57%)	0%	12/21 P (57%)	Nodal GTV decreased by PET dose escalation > increased TCP
Brianzoni et al. [14]	Retrospective	28	PET/CT	40% intensity level	GTV/CTV: 11/25 (56%)	6/11	5/11	
Ashamalla et al. [7]	Prospective	19	Integrated PET/CT Patient immobilization	Halo phenomenon	GTV: 10/19 P (52%) PTV: 8/19 P (42%)	GTV: 5/19 (26%) PTV: 4/19 (21%)	GTV: 5/19 (26%) PTV: 4/19 (21%)	Improvement of interobserver variability up to 84%
Deniaud-Alexandre et al. [29]	Retrospective	101	Image fusion using fiducial markers	50% intensity level of max FDG uptake integrated PET/CT	PTV: 43/101 (43%)	GTV: 24/101 (24%)	GTV: 21/101 (23%)	PET/CT has impact on treatment planning
Steenbakkers et al. [81]	Prospective	22	PET-CT	Integrated PET-CT standardized windowing	Significant reduction of mean GTV	n.e.	n.e.	Significant reduction of inter observer variation
De Ruysscher et al. [26]	Prospective	21	PET-CT simulator vs. CT-simulator	Identification of affected anatomical structures by FDG	14/21 (66%)	2/21 (10%)	12/21 (57%)	with PET simulator TCP signi. higher NTCP sign. lower

n.e.: not evaluated.

Theoretical radiation dose escalation with PET/CT planning

<u>Atelectasis in PET/CT</u>

Significant potential benefit by FDG - PET: Reduction radiation volumes

but:

False positive uptake in postobstructive inflammation is possible

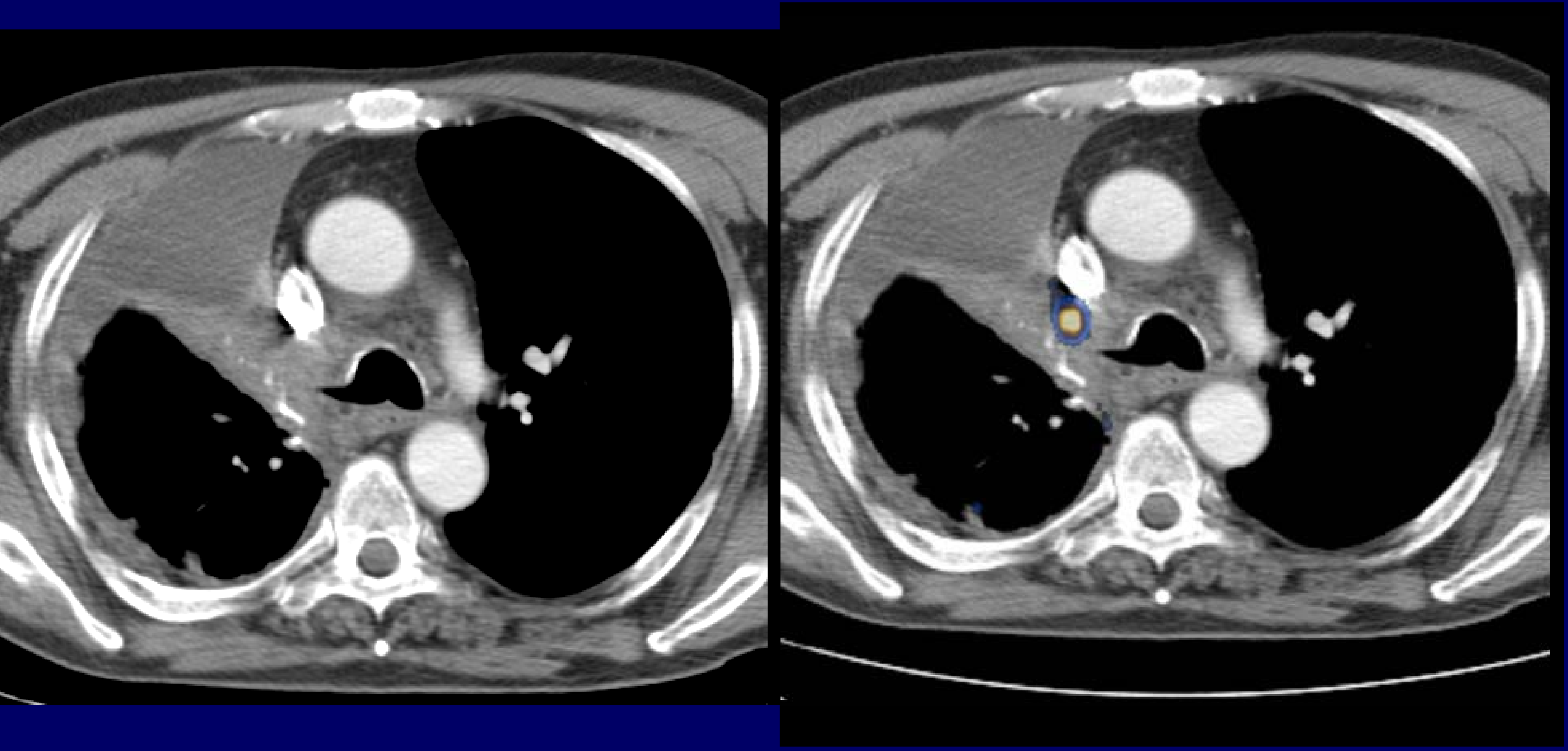
Histological correlation of PET - findings with pathology are lacking

Van der Welt et al, Int J Radiat Oncol Biol Phys, 2005

De Ruysscher et al Radiother Oncol 2005

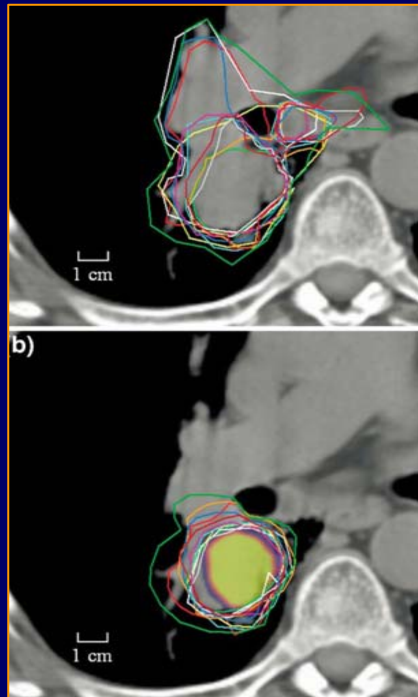
PET/CT – Imaging in Radiooncology

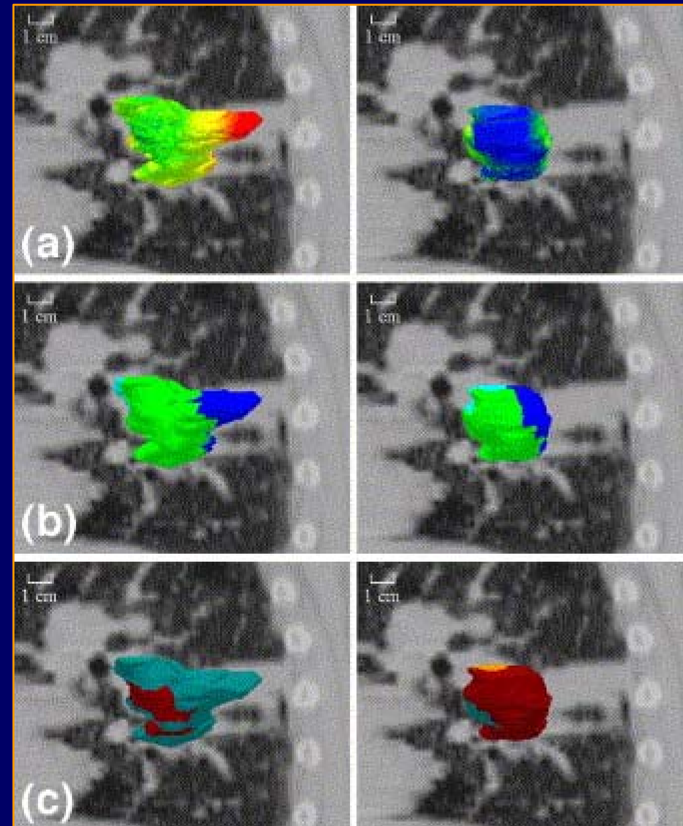
Theoretical radiation dose escalation with PET/CT planning (2)



PET/CT – Imaging in Radiooncology

Reduction of interobserver variation and delineation



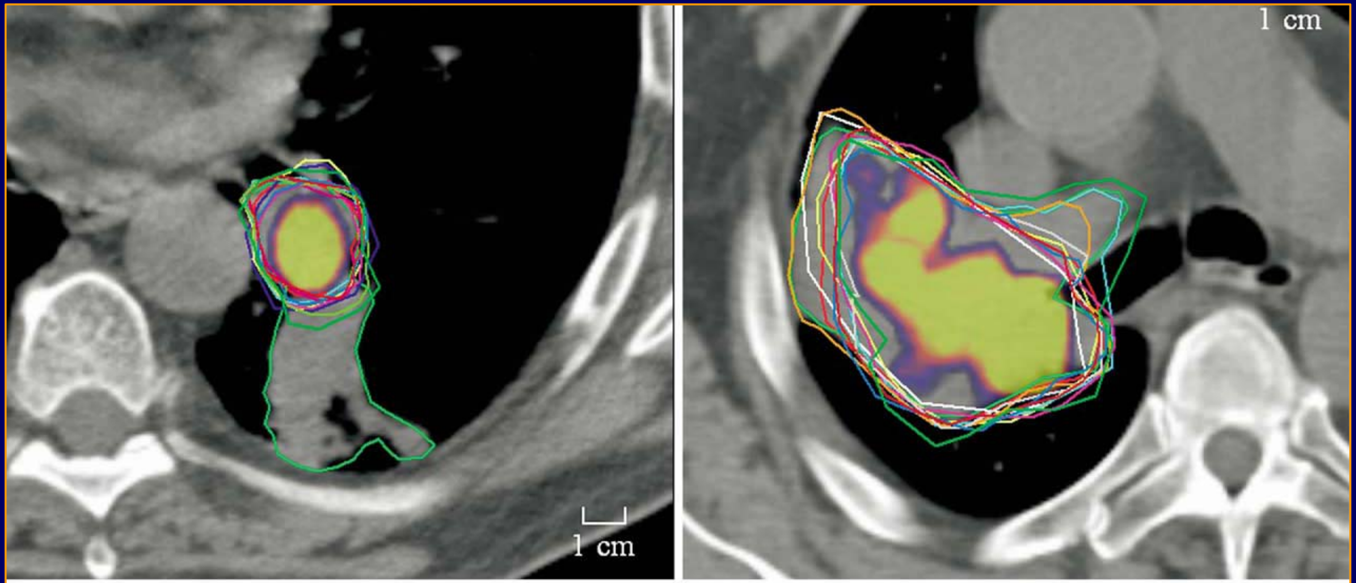


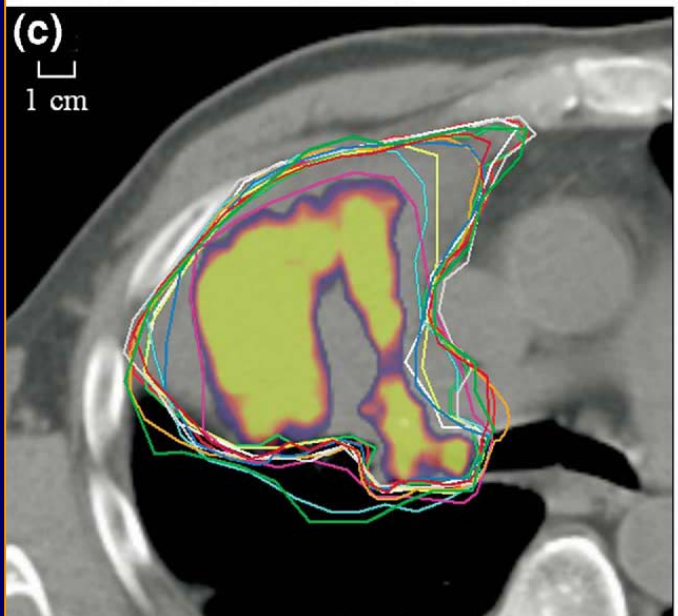
Steenbakkers R. et al.
Int. J. Radiation Oncology Biol. Phys., Vol. 64, No. 2, pp. 435–448, 2006

Computed tomography image with the contours made by all 11 radiation oncologists. blue labeled as disagreement region (i.e., <9 of 11 radiation oncologists agreed).

PET/CT – Imaging in Radiooncology

Further reduction of the interobserver variability with automatic contouring





All patients had some form of atelectasis.

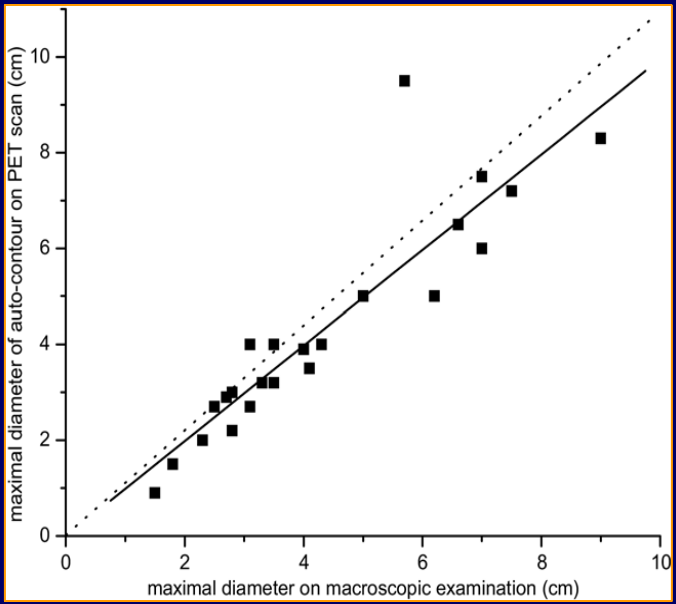
Color wash represents overlay of matched 2-[18F]fluoro-2-deoxy-D-glucose positron emission tomography.

PET/CT – Imaging in Radiooncology

Further reduction of the interobserver variability with automatic contouring (2)

Table 5. For all anatomic regions, theoretical PTV margin for upper and lower lobe tumor with motion amplitude (peak–peak) of 0.2 cm and 1.2 cm, respectively, and delineation based on CT only (first phase) and matched CT–FDG-PET (second phase)

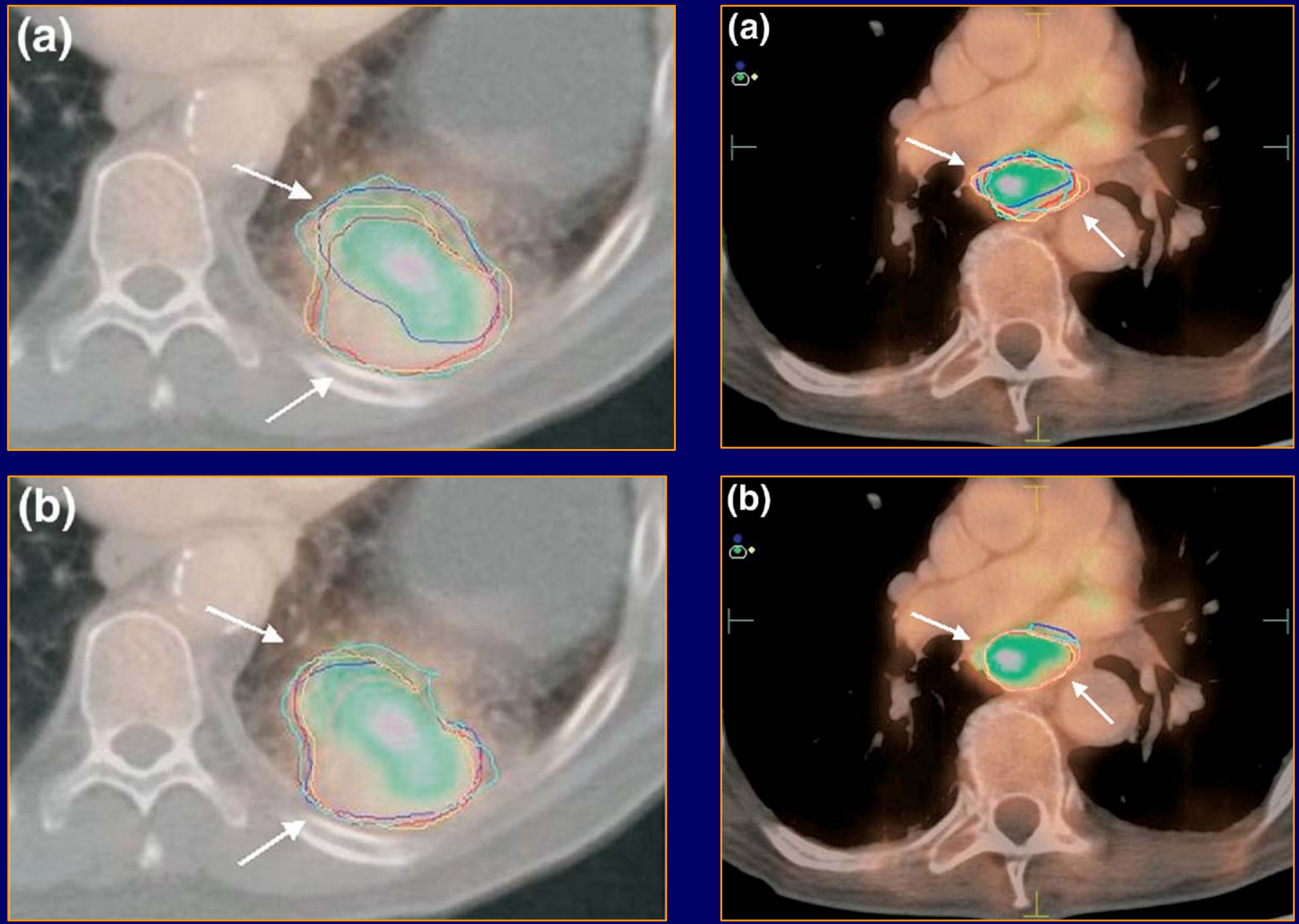
	PTV margin (cm)*			
	Upper lobe tumor		Lower lobe tumor	
Anatomic region	First phase	Second phase	First phase	Second phase
Tumor–lung	1.4	0.8	1.8	1.4
Tumor–mediastinum	1.8	1.1	2.2	1.6
Tumor–chest wall	1.0	0.9	1.5	1.4
Lymph nodes	3.6	2.0	3.8	2.3
Tumor–atelectasis	4.7	1.2	4.9	1.6
All	2.5	1.0	2.8	1.5



Van Barardewijk A. et al. Int J Radiat Oncol Biiol Phys, 2007

PET/CT – Imaging in Radiooncology

Further reduction of the interobserver variability with automatic contouring (3)



Example of (a) manual and (b) auto-contour– based delineation of a primary tumor (Gross Tumor Volume 1, and lymph node volume, Volume 2) delineated by the five observers. Arrows indicate changes in interobserver variation in delineation between the two methods.

PET/CT – Imaging in Radiooncology

FDG-PET based RT planning in NSCLC

Table 2. Patterns of recurrence

Recurrences	No. of patients (%)
None	26 (59)
In-field	10 (23)
Exclusively in-field	5
In-field and distant	5
Isolated nodal	1 (2)
Nodal (outside of CTV) along with local or distant failure	2 (4.5)
Distant only	7 (16)
Brain only	1

Abbreviation: CTV = clinical target volume.

De Ruysscher D et al. Int J Radiat Oncol Biol phys 2005, 62;998-994 FDG-PET based RT planning in NSCLC

N = 44, NSCLC I - III

10/44 mediastinal downstaging by PET

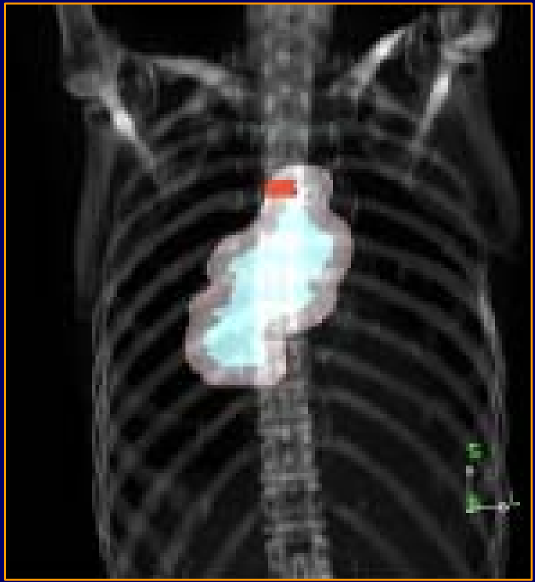
Dose escalation to 64,8 Gy/1,8 Gy b.i.d.

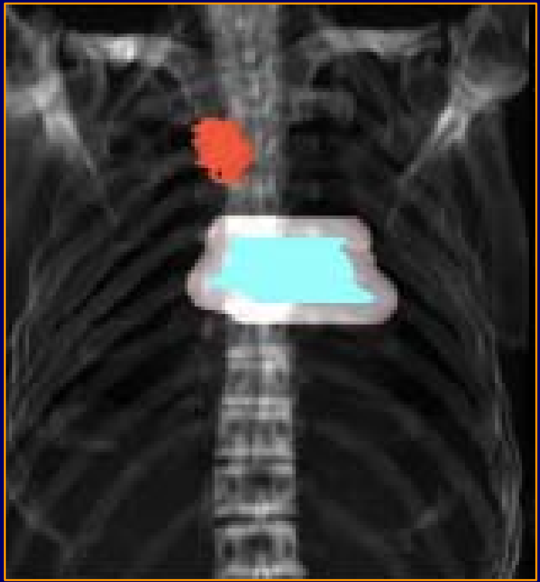
GTV= tumor + FDG-PET positive LN - stations

After median follow-up of 16 months 1 isolated out field recurrence at LN pre-treatment cN0 in CT and PET

PET/CT – Imaging in Radiooncology

Risk of marginal miss after FDG based RT planning with visual aids





Dose	Local failure pattern (n = 26): Within GTV/PTV	Within GTV/PTV and outward	Marginal miss (within PTV and outward)	Geographic miss (outside but within 1 cm of PTV)
D_{95} <60 Gy	6	2	0	0
D_{prescr} <60 Gy	6	2	0	0
D_{95} ≥60 Gy	6	11	1	0
D_{prescr} ≥60 Gy	6	11	1	0

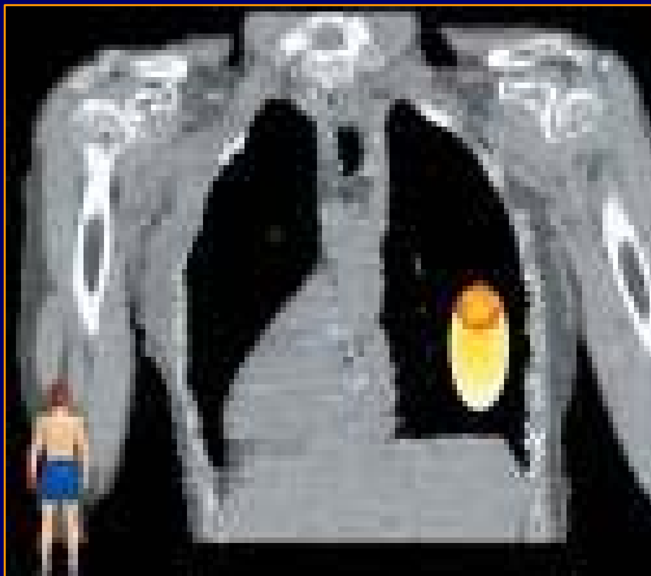
Sura S et al. Int J Radiat Oncol Biol Phys 2008 70; 1397-1402

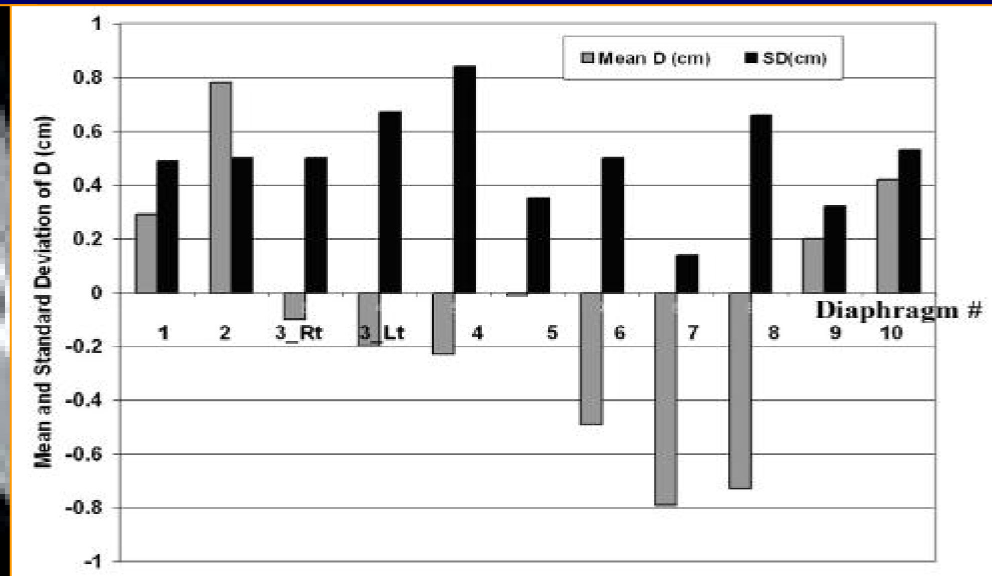
26 local recurrences after FDG-based RT planning in advanced NSCLC

after doses > 60 Gy 12/18 recurrences located at margin of GTV or PTV

PET/CT – Imaging in Radiooncology

Body in motion

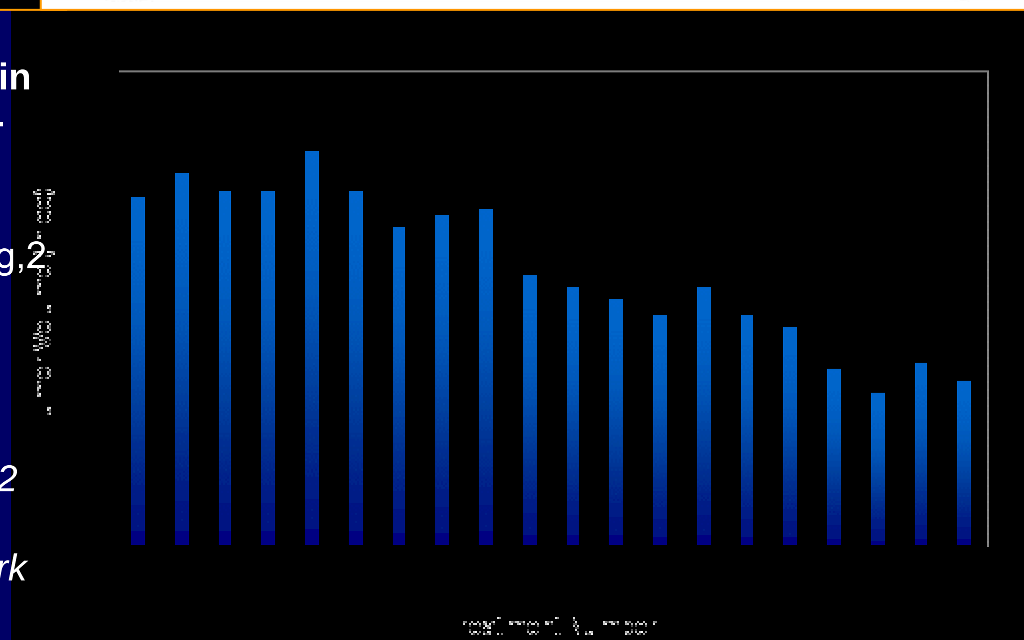




Interfractional anatomic variation in patients treated with respiration-gated radiotherapy

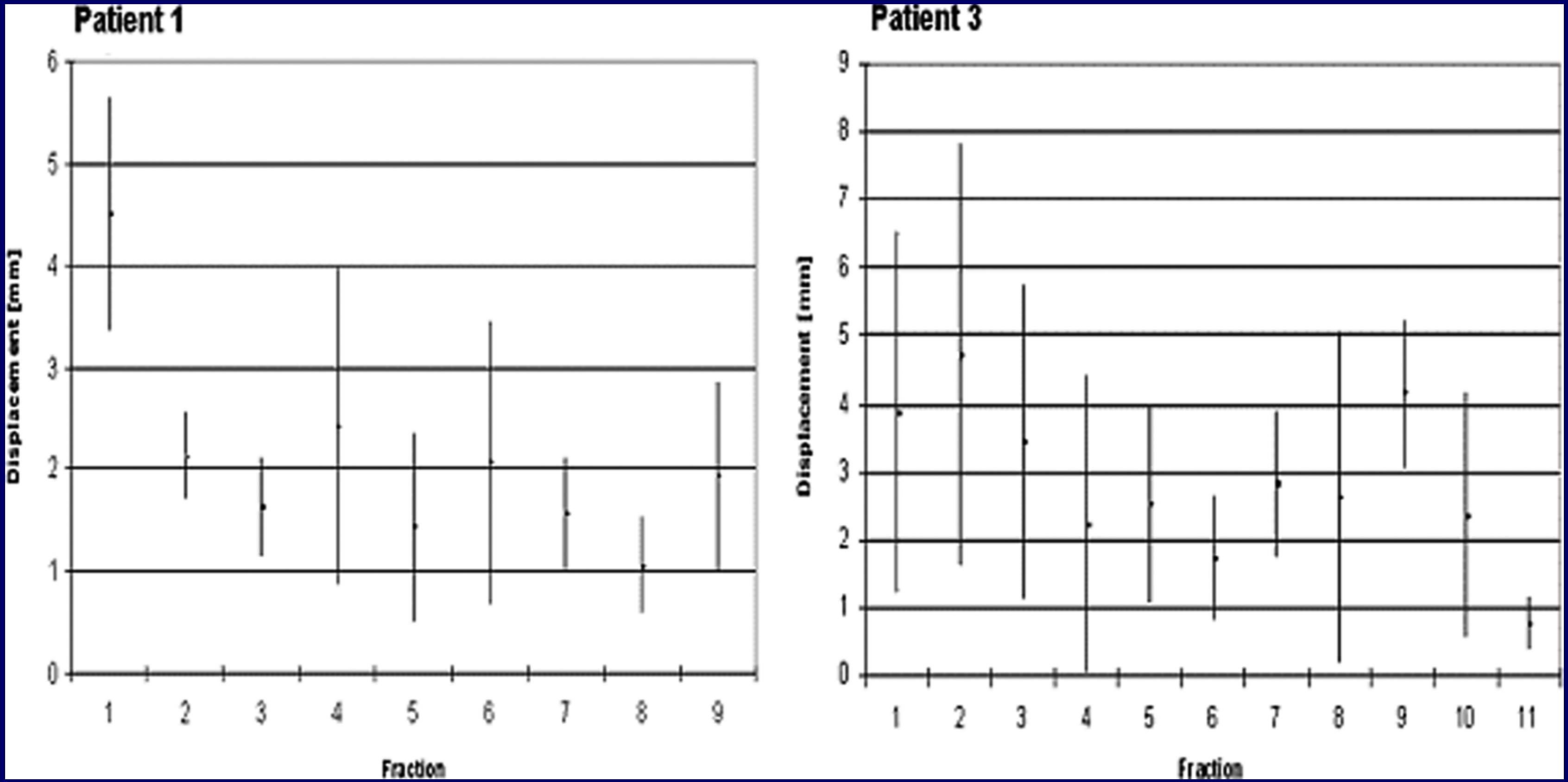
Ellen Yorke,1 Kenneth E. Rosenzweig,2 Raquel Wagman,2 and Gikas S. Mageras1

Department of Medical Physics1, Department of Radiation Oncology,2 Memorial Sloan Kettering Cancer Center, 1275 York Avenue, New York City, New York 10021 U.S.A.

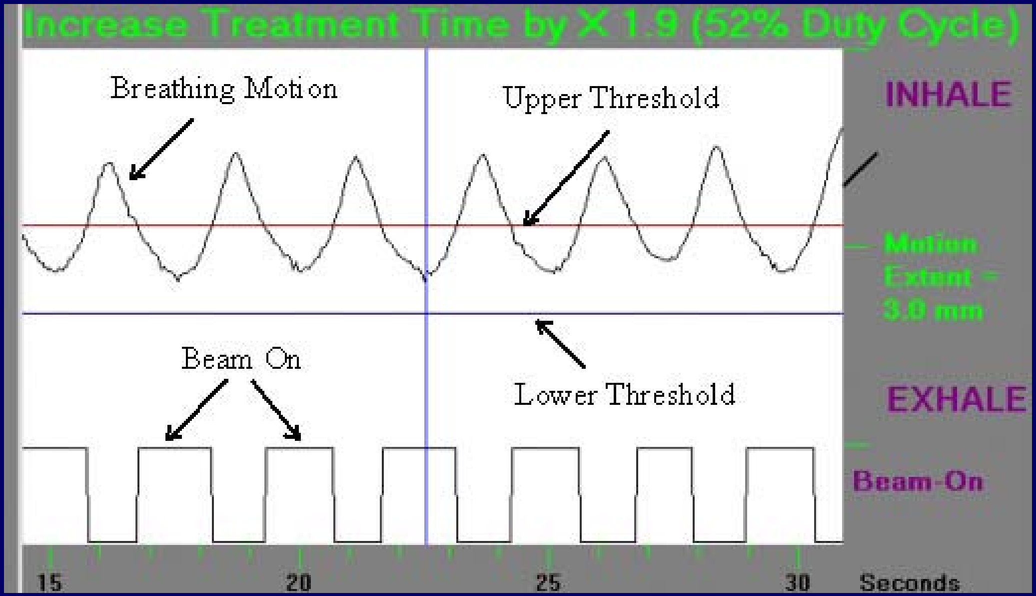


Body in motion caused by diaphragma (2)

Intrafractional average marker displacement ± SD and interfractional variation of on target verification for all fractions for patient 1 with a lung and patient 3 with a liver tumor.



Tumor in motion (3)



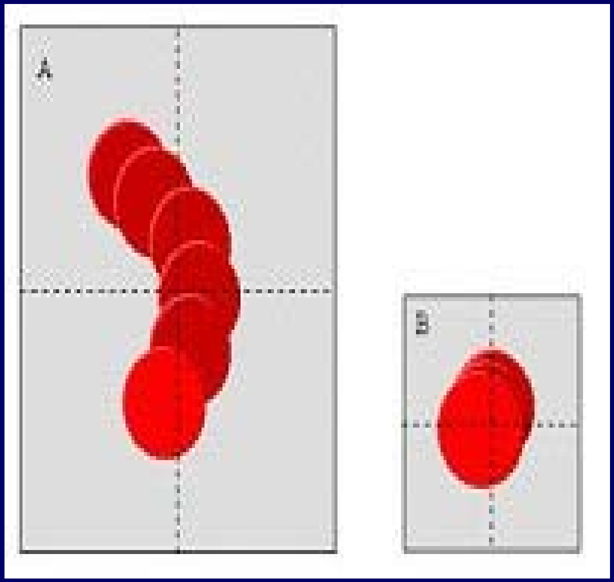
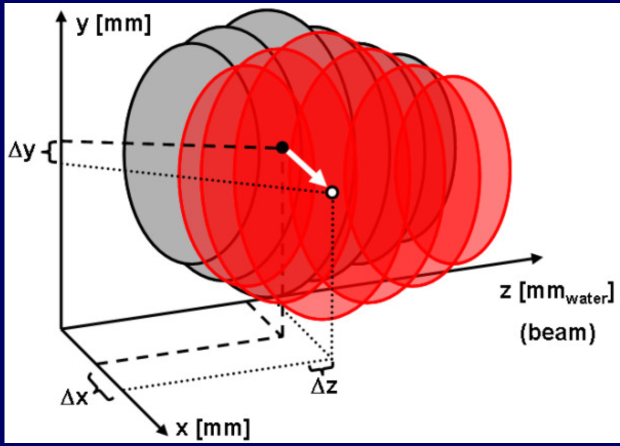


Illustration of yumor motion during treatment (a) without respiratory gating, and (b) with gating technology



Bert and Rietzel *Radiation Oncology* 2007 **2**:24

Juhler-Nottrup et al., Acta Oncol, 2008

Interfractional changes in tumour volume and position during entire radiotherapy courses for lung cancer with respiratory gating and image guidance

N= 10; 60 Gy/ED 2.0 Gy

Lung tumours reduction: 19%

mediastinal tumours/Lnn: 34 %

Mobility vector: 0.51 cm (+/- 0.21) for matching bony landmarks
0.85 cm (+/- 0.54) for matching skin tattoos

0.55 cm (+/- 0.19) for matching bony landmarks
0.72 cm (+/- 0.43) for matching skin tatoos

interfractional overlap (lung tumor): 80%-87% for using bony landmarks
70%-76% for using skin tattoos

overlap (mediastinal tumors): 60%-65% for using bony landmarks
41%-47% for using skin tattoos

PET/CT – Imaging in Radiooncology

Why 4D-imaging ?

- ► Radiation treatment planning for lung is mostly based on CT and PET images
- ► Different acquisition times for CT (fast) and PET (slow) improved tumor volume delineation
- ► 4D-Imaging improved SUV determination
- ► 4D-Imaging improved (automatic tumor) contouring
- ► 3D CT is used for attenuation correction of PET (in PET/CT-scanners)
  This can lead to geographical errors and false positive lesions

De Ruysscher, Radiology, 2003; 226:906-910

Chest belt + pressure sensor (Siemens – (Phillips)

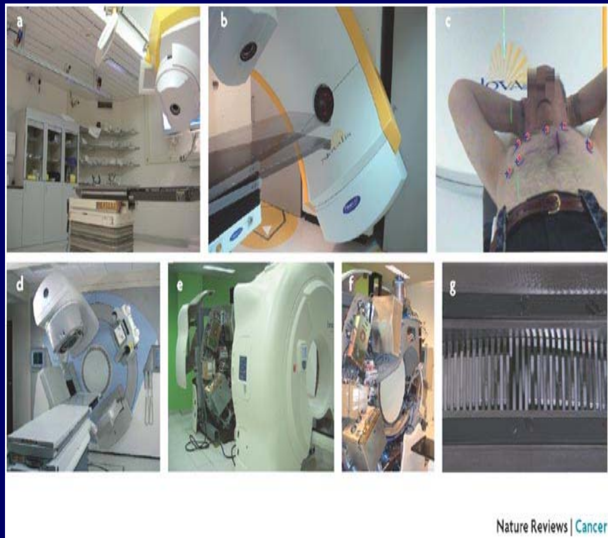
Infrared reflective markers + infrared camera (GE-Varian)

Respiration correlated PET:

Why is 4D CT attenuation correction is needed for 4D PET ?

► Up to 196% overestimation SUV without respiratory correlation

Hamill JJ et al, Med.Phys. 2008

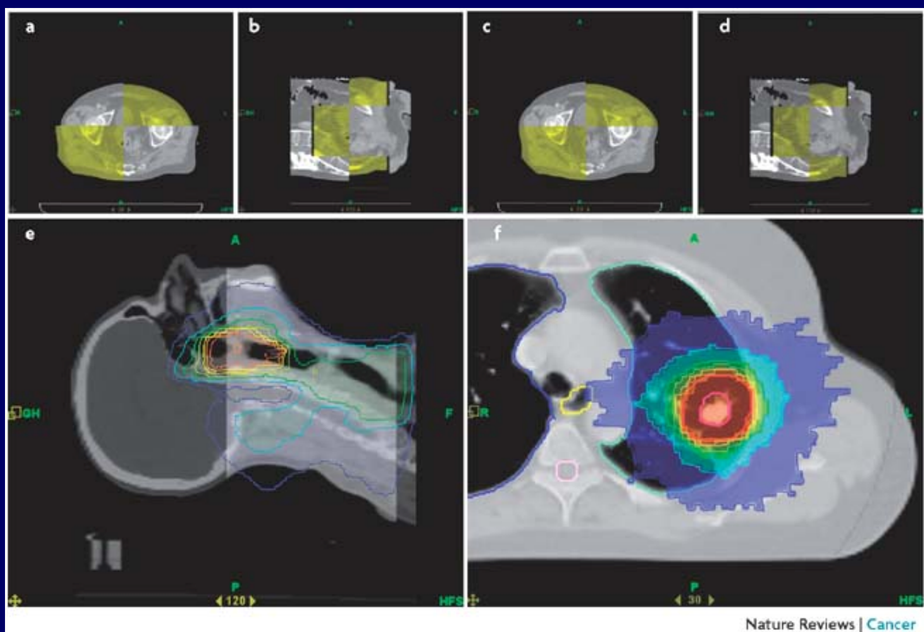


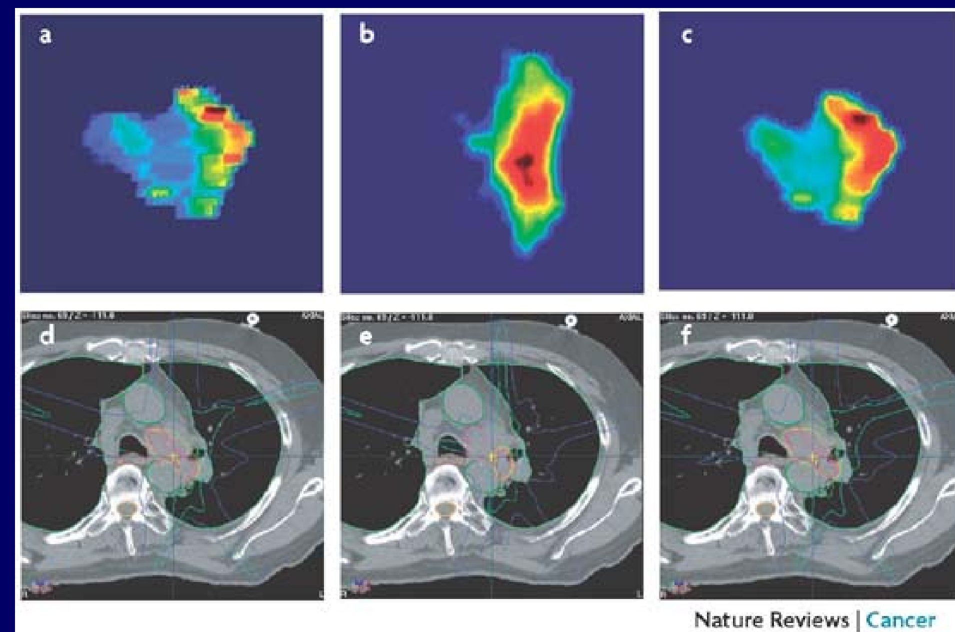
Influence of margins on volume

Innovation in image-guided radiotherapy

Dirk Verellen, Mark De Ridder, Nadine Linthout, Koen Tournel, Guy Soete & Guy Storme

Nature Reviews Cancer 7, 949-960 (December 2007)





PET/CT – Imaging in Radiooncology

Respiration correlated PET – 4D autodelineation

- ► Autodelineation across all PET phases
- ► Ability to adapt contouring threshold per phase
- ► Ability to detect necrotic or hypoxic areas using 4D PET
- ► Overall, 4D PET SUV contour will be more realistic due to better SUV estimation

Active Breathing Control (ABC)

Mean organ movement as studied with 2 CT scans

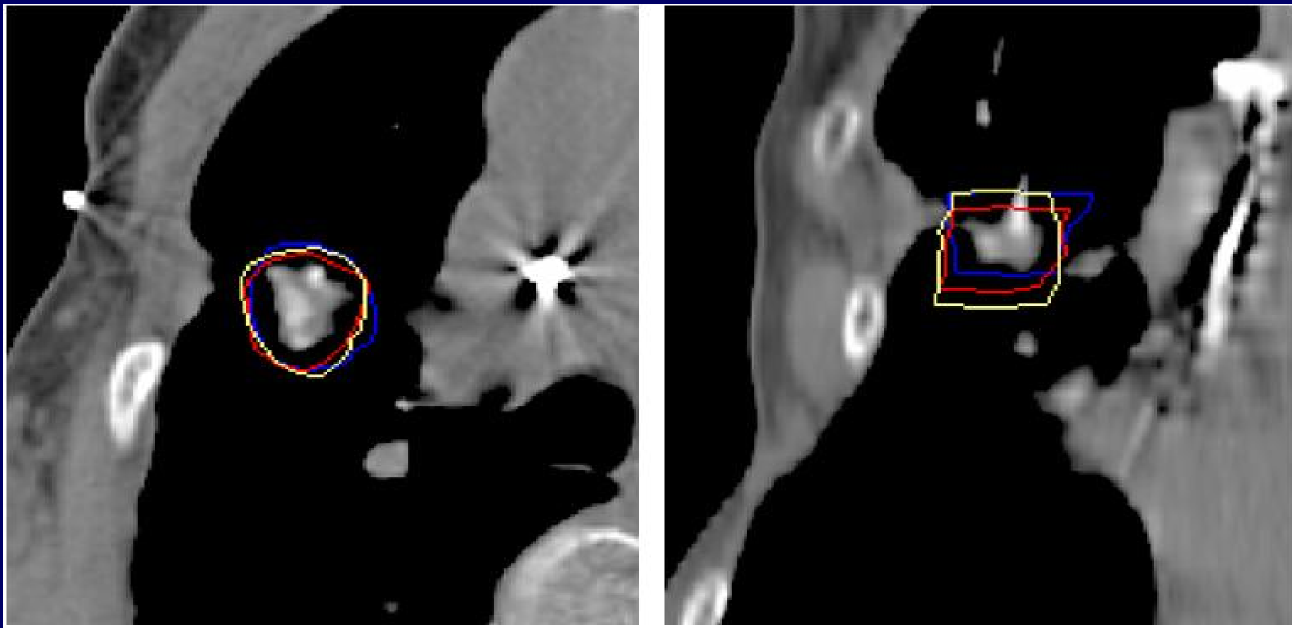
Structure	Intra-fraction	Inter-fraction
Diaphragm	1.5 +/- 1.8 mm	4.0 +/- 3.3 mm
Mid-thorax	2.1 +/- 1.7 mm	3.9 +/- 3.1 mm
Apex lung	2.6 +/- 2.0 mm	2.0 +/- 2.2 mm

Wong, et al., Int J Radiat Oncol Biol Phys 44, 1999

Do we need any margins ? (INT)

PET/CT – Imaging in Radiooncology

Body and tumor motion in motion (4)



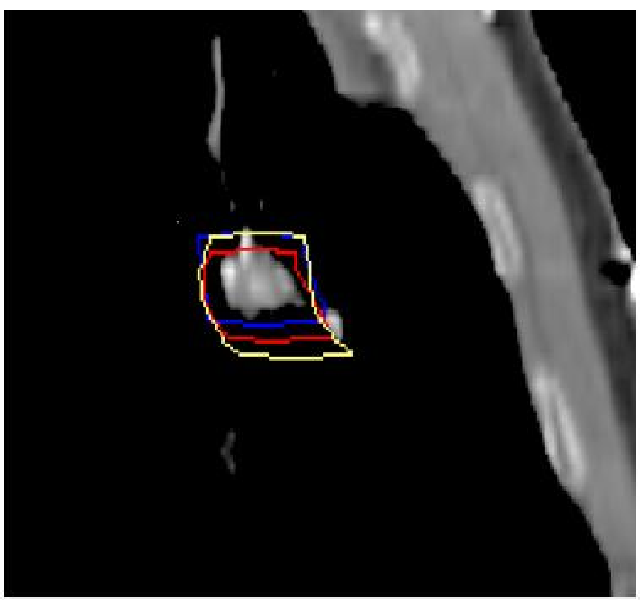
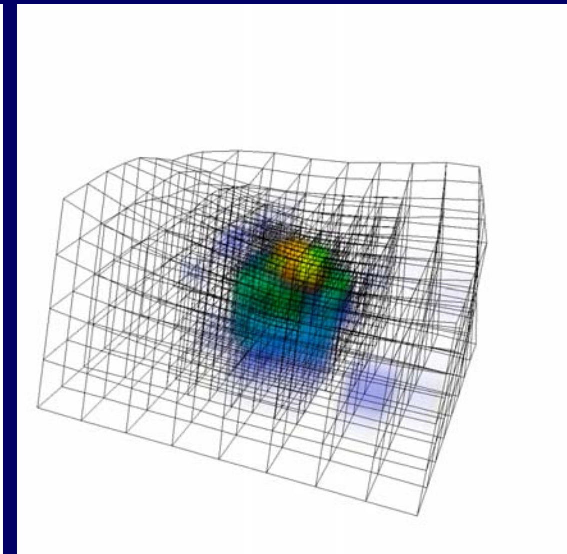
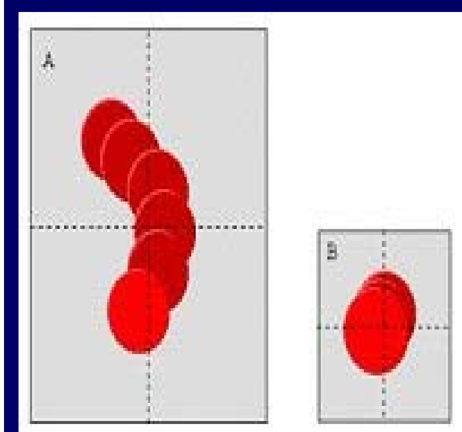


Figure 2. Example of "4D Gated CT" images in a patient with a peripheral lung tumor demonstrating axial (top left), sagittal (top right), coronal (bottom left) views of tumor location at full expiration (blue outline) and inspiration (yellow outline) as well as at 50% inspiration (red outline). Note that the tumor moves with breathing in all three dimensions in a non-uniform manner.





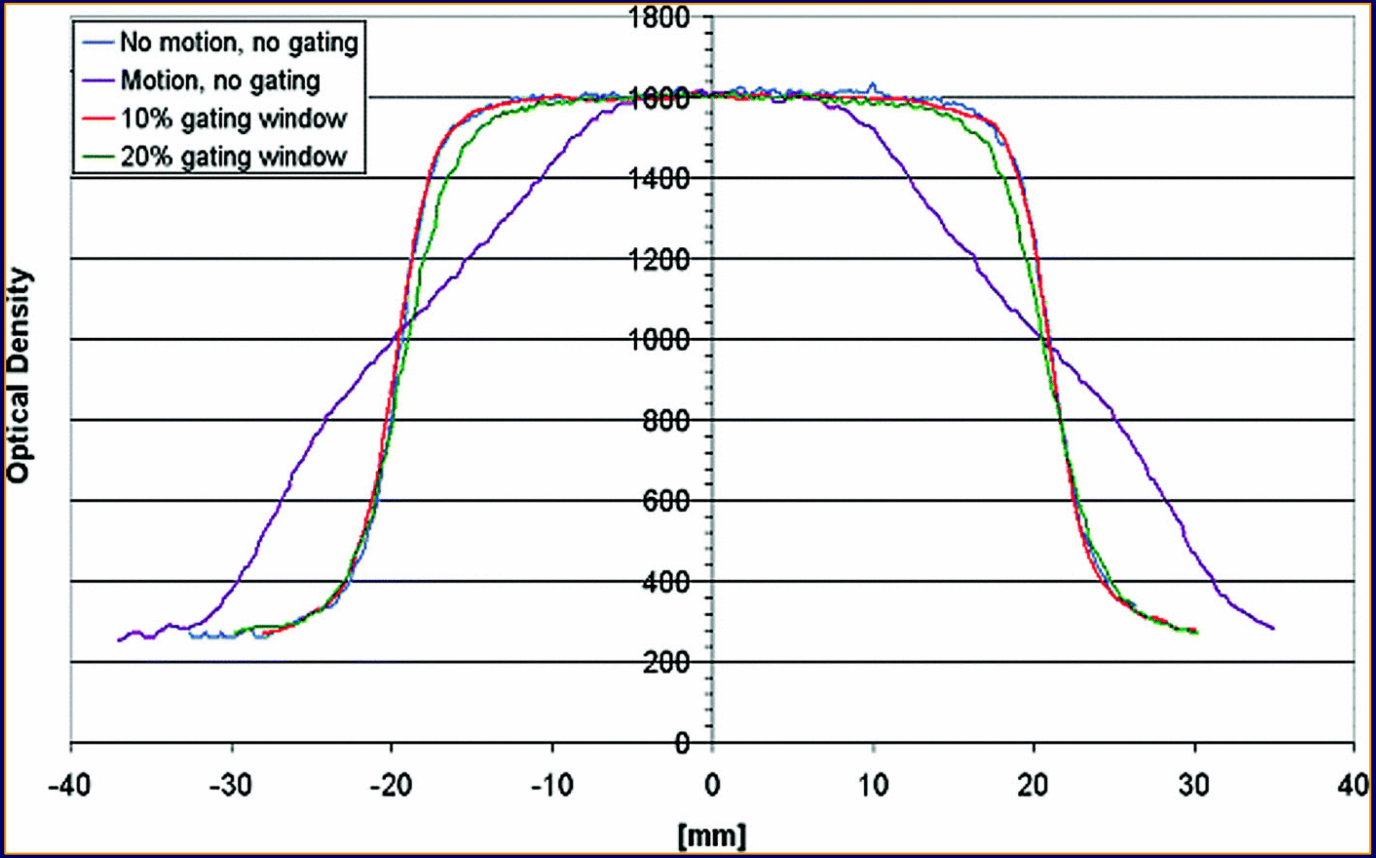


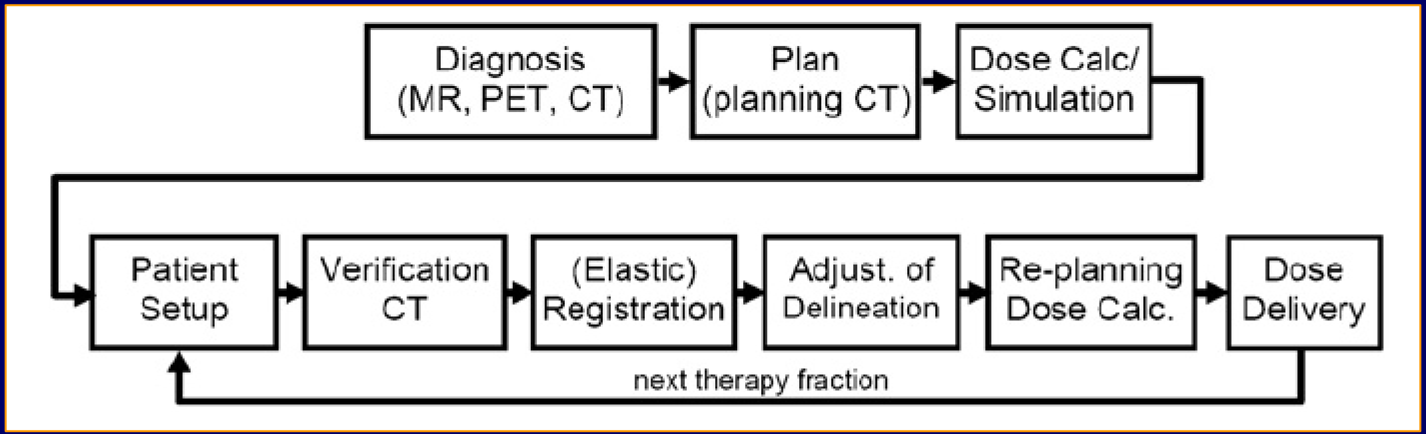
Image guided respiratory gated hypofractionated Stereotactic Body Radiation Therapy (H-SBRT) for liver and lung tumors: Initial experience

Authors: R. E. Wurm [a]; F. Gum [a]; S. Erbel [a]; L. Schlenger [a]; D. Scheffler [a]; D. Agaoglu [a]; R. Schild [a]; B. Gebauer [b]; P. Rogalla [c]; M. Plotkin [b]; K. Ocran [d]; V. Budach [a]

Acta Oncologica, Volume 45, Issue 7 September 2006 , pages 881 - 889

PET/CT – Imaging in Radiooncology

Adaptive Radiotherapie

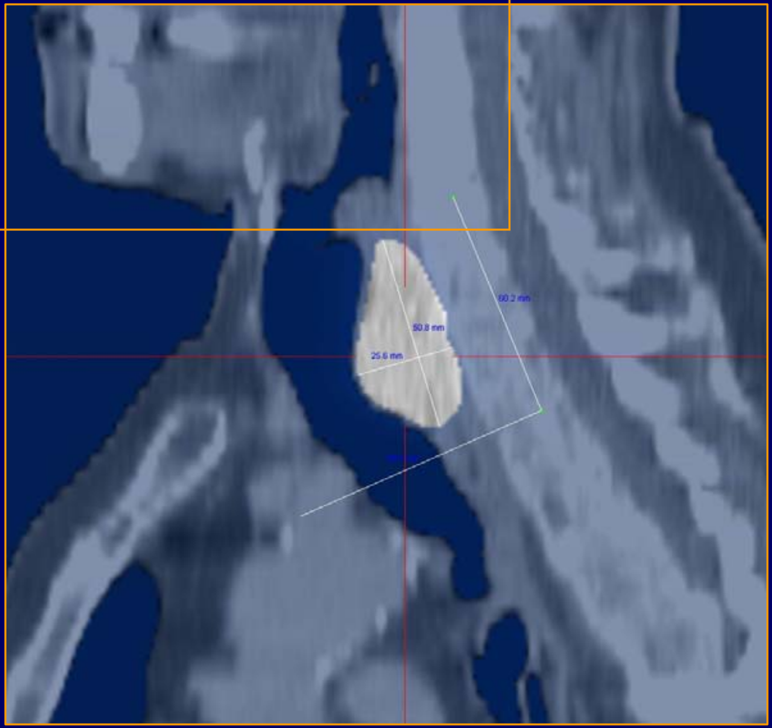


(a) (b) (c)

PET/CT – Imaging in Radiooncology

Hypoxia imaging in lung cancer

- Hypoxia imaging in lung cancer reported e.g. with ^{18}F-MISO and ^{60}Cu-ATSM
- Possible prognostic value (hig hypoxia = bad prognosis)
- Value for treatment planning unclear



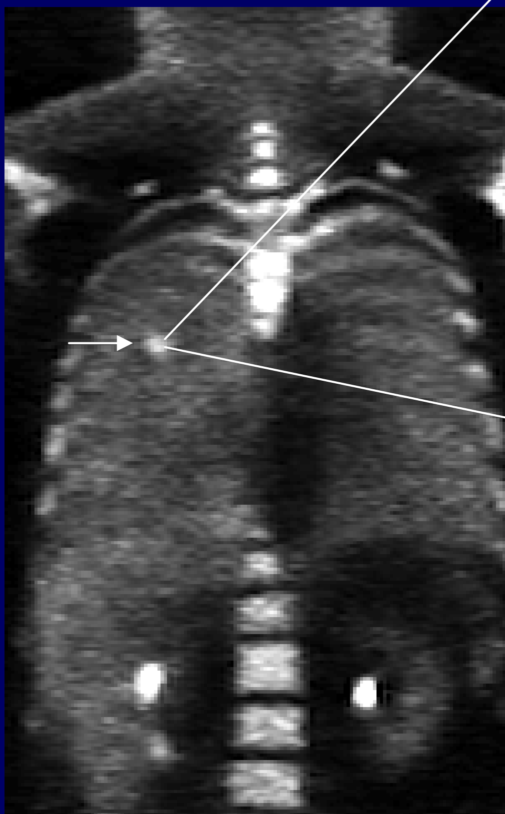
Imaging of proliferation (FLT)

- ► FLT-uptake correlates with proliferation
- ► Evaluation as diagnostic tracer for lung cancer
- ► FLT-uptake lower compared to FDG-uptake
- ► Unspecific uptake possible
- ► Diagnostic use unclear, no clear advantage over FDG
- ► No studies on integration in RT planning

PET/CT – Imaging in Radioonkology

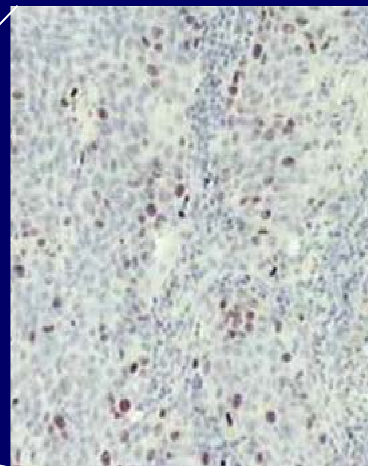
Imaging of proliferation (FLT)

NSCLC, niedrige Proliferationsrate

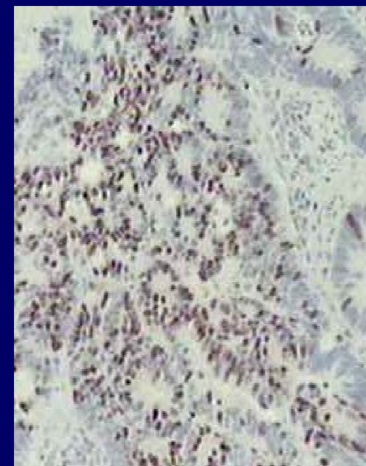


FLT-SUV 2,1

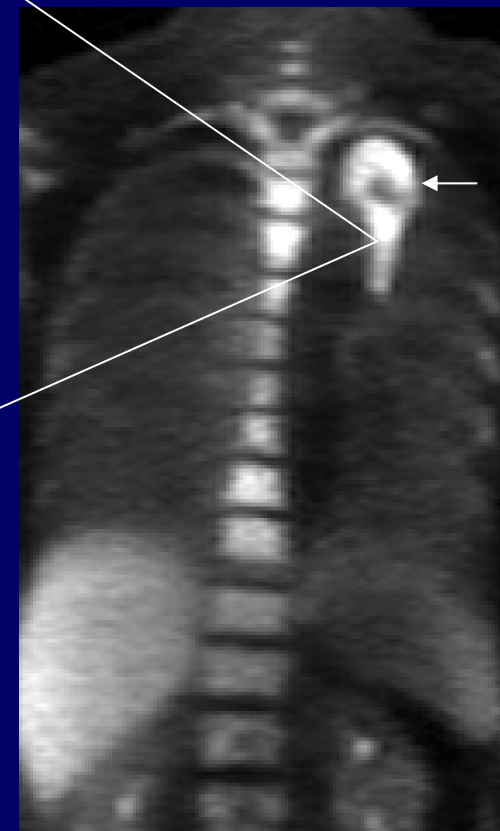
proliferation 25%



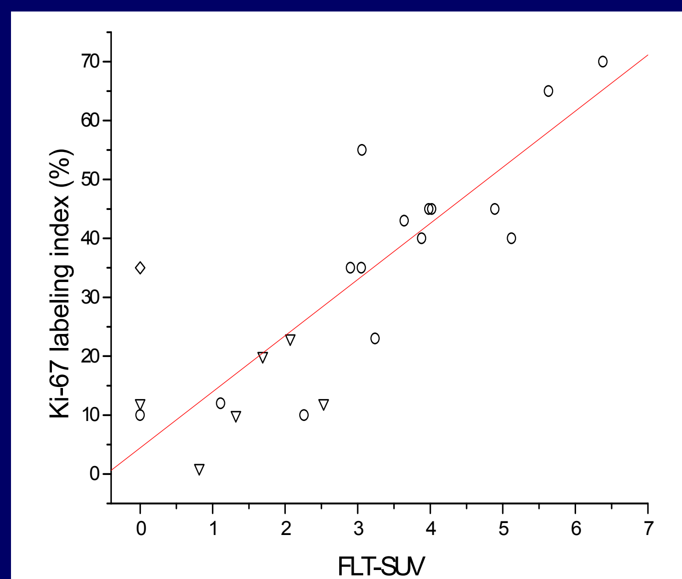
proliferation 56%



NSCLC, hohe Proliferationsrate



FLT-SUV 4,8



Buck et al., Cancer Res 2002

Future possibilities

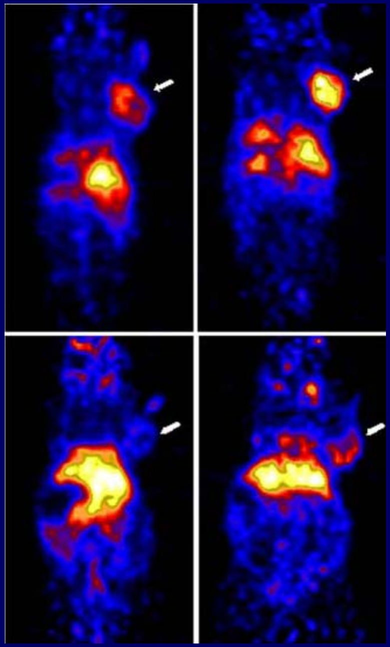
PET imaging with

89 Zr-Cetuximab for

identification of radioresistant

areas within the tumor

(Epidermal growth factor receptor status in Imaging and for treatment)

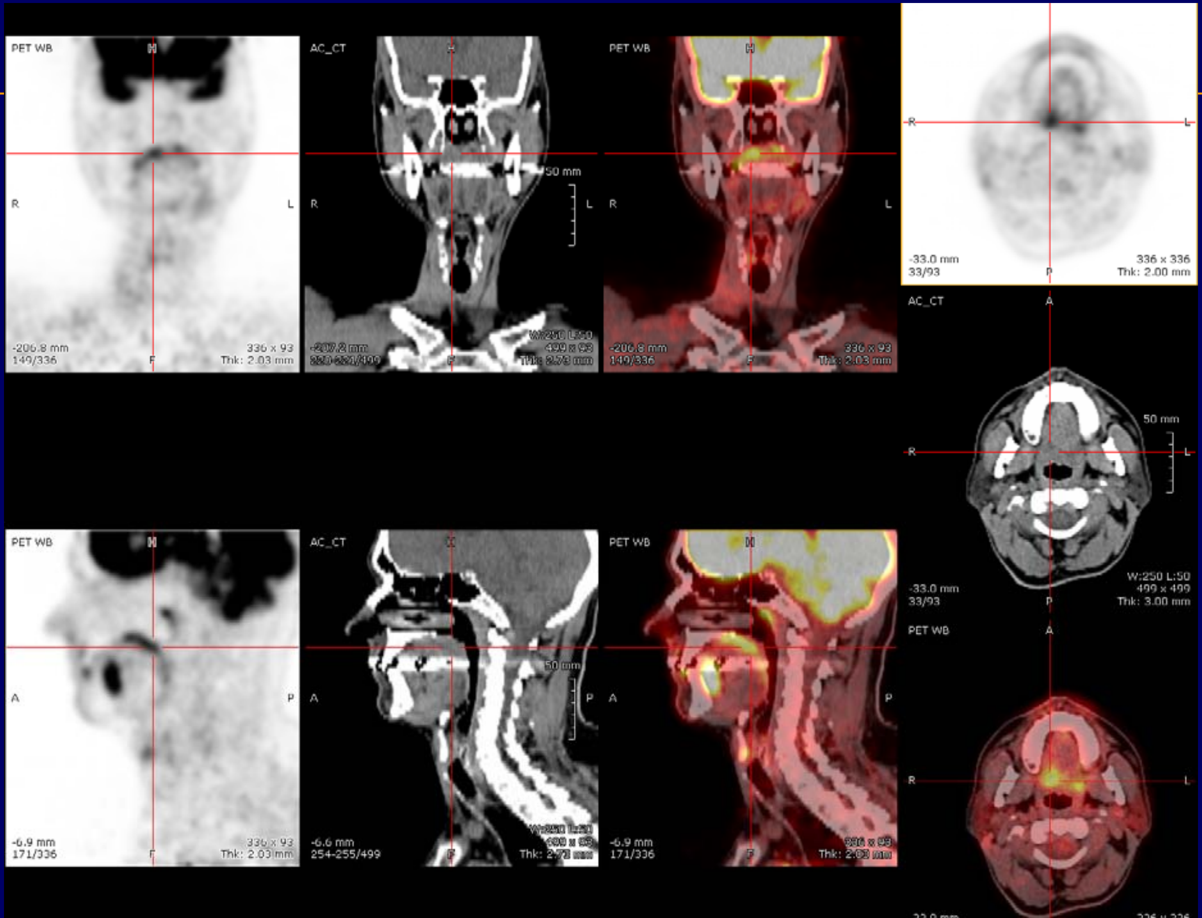


^{64}Cu-DOTA-Cetuximab, a PET-Imaging Agent for Epidermal Growth-Factor Receptor-Positive Tumors Receptor-Binding,

Biodistribution, and Metabolism Studies of ^{64}Cu-DOTA-Cetuximab, a PET-Imaging Agent for Epidermal Growth-Factor Receptor-Positive Tumors

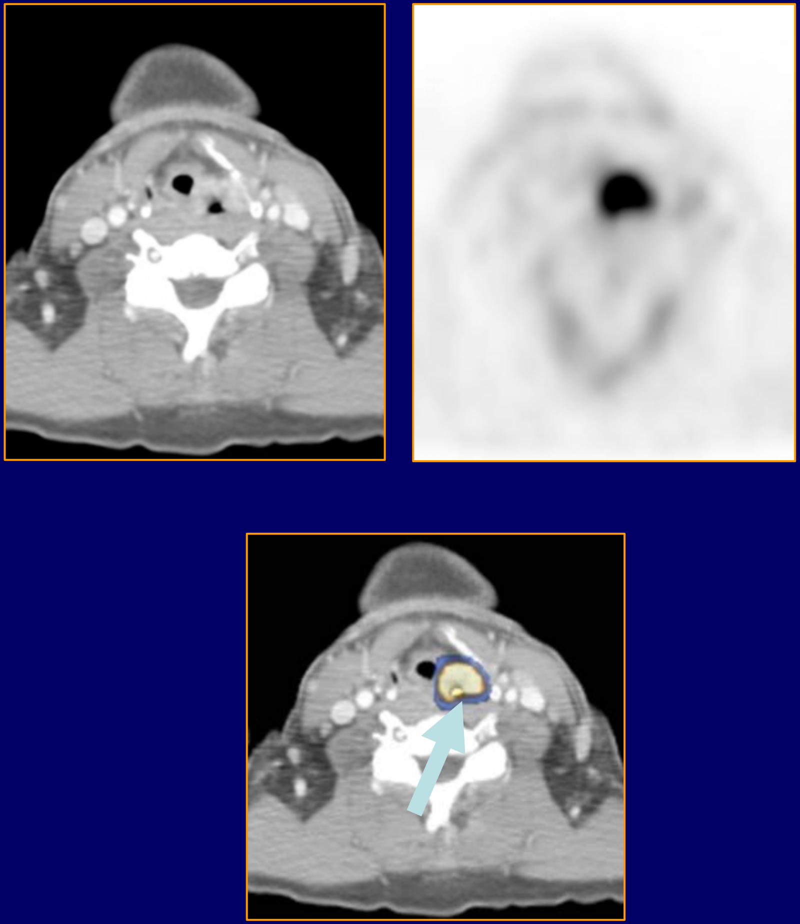
Wen Ping Li, Laura A. Meyer, David A. Capretto, Christopher D. Sherman, Carolyn J. Anderson. Cancer Biotherapy & Radiopharmaceuticals. April 1, 2008, 23(2): 158-171.

In addition to FDG other PET radiopharmaceuticals are avaiable that image specific biological tumour characteristics involved in radiation resistance, such as hypoxia, proliferative activity and tyrosine kinase receptor expression



PET/CT – Imaging in Radiooncology

Head and neck (2)



- ^{18}F-FAZA
- ^{18}F-Miso
- ^{18}F-FDG
- ^{18}F-Annexin ?
- ^{11}C-Methionin no

Heron et al., IJROBP, 2004

Koshy, Head and Neck, 2005

Schwartz et al., IJROBP, 2005

Paulino, IJROBP, 2005

Wang, IJROBP, 2006

Geets, 2006

Deantonio, Radiation Oncology, 2008

Rischkin, JCO 2008

Head and neck (3)

PET/CT and treatment with IMRT (n = 45) improved cure rates compared to patients without PET/CT and IMRT.

Overall survival with PET/CT and IMRT	97% and 91% at 1 and 2 years
vs.	74% and 54% (p=0.002)

The event-free survival rate of the patients on the PET/CT group was

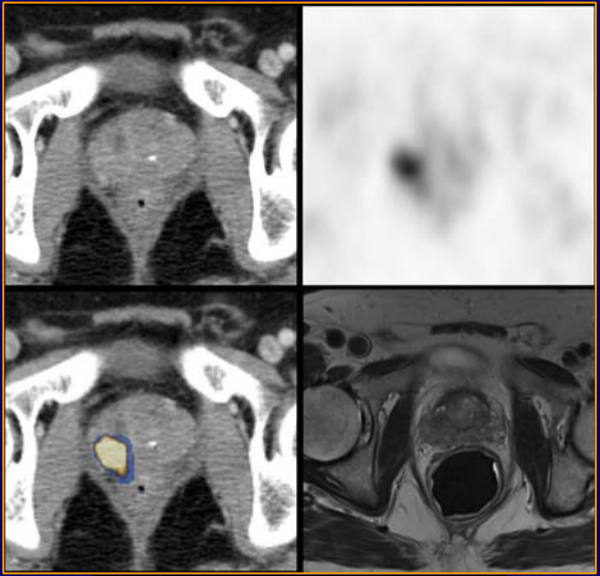
	90% and 80% at 1 and 2 years
compared to	72% and 56% in the control group (p=0.005)

^{18}F-FDG-PET/CT Staging followed by Intensity-modulated Radiotherapy (IMRT) improves treatment outcome of locally advanced pharyngeal Carcinoma: a matched-pair comparison

Rothschild S et al., Radiation Oncology 2007, 2:22

^{11}C-Cholin PET/CT in prostate cancer

F-18 Fluordesoxyglukose
C-11 Acetate
C-11 Choline
F-18 Fluormethylcholine
Ga-68 Bombesin



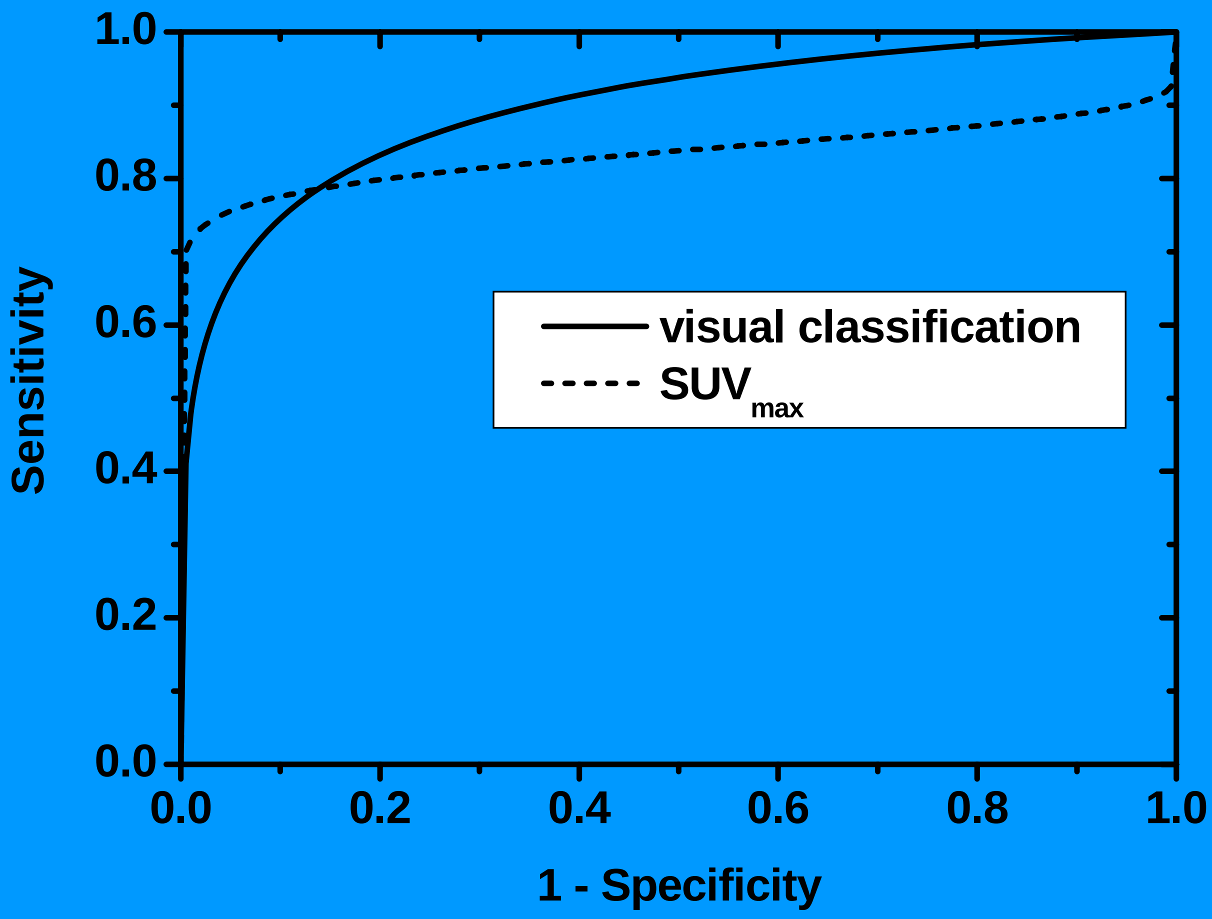
Imaging Prostate Cancer with ^{11}C-Choline PET/CT

Sven N. Reske[1], Norbert M. Blumstein[1], Bernd Neumaier[1], Hans-Werner Gottfried[2], Frank Finsterbusch[1], Darius Kocot[1], Peter Möller[3], Gerhard Glatting[1], and Sven Perner[3]

J Nucl Med 2006; 47:1249–1254

n= 26, SUV > 2,6	
Sens	82%
Spez	86%
PPV	84%
NPV	84%
ACC	84%

^{11}C-Cholin PET/CT in prostate cancer (2)



PET/CT – Imaging in Radiooncology

^{11}C-Cholin PET/CT in prostate cancer (3)

Figure 2

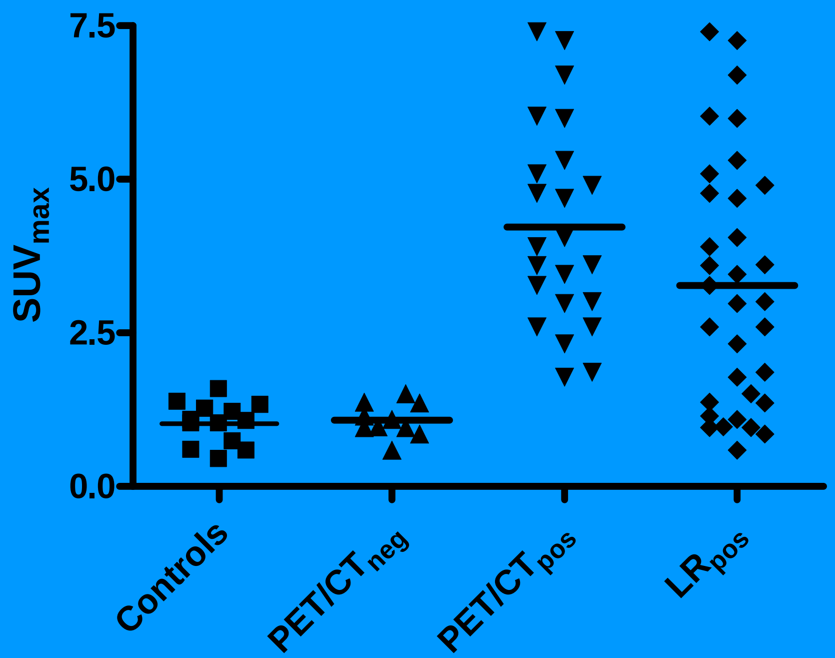
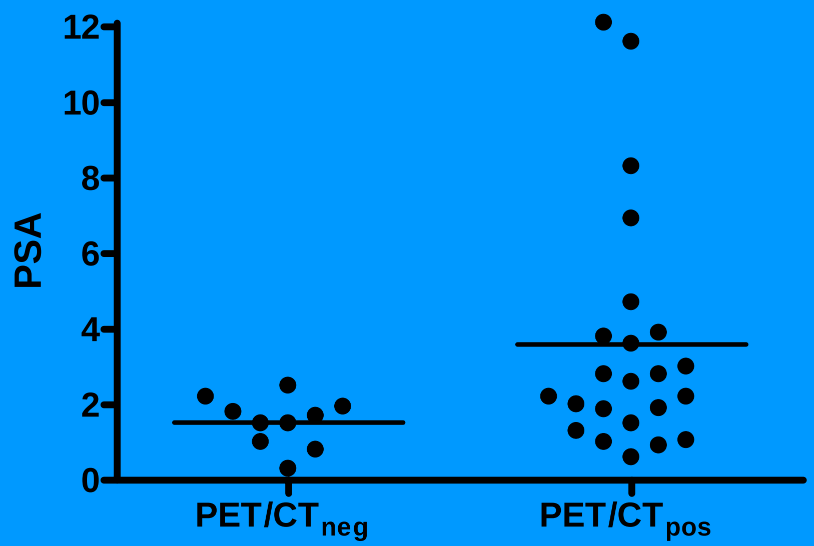
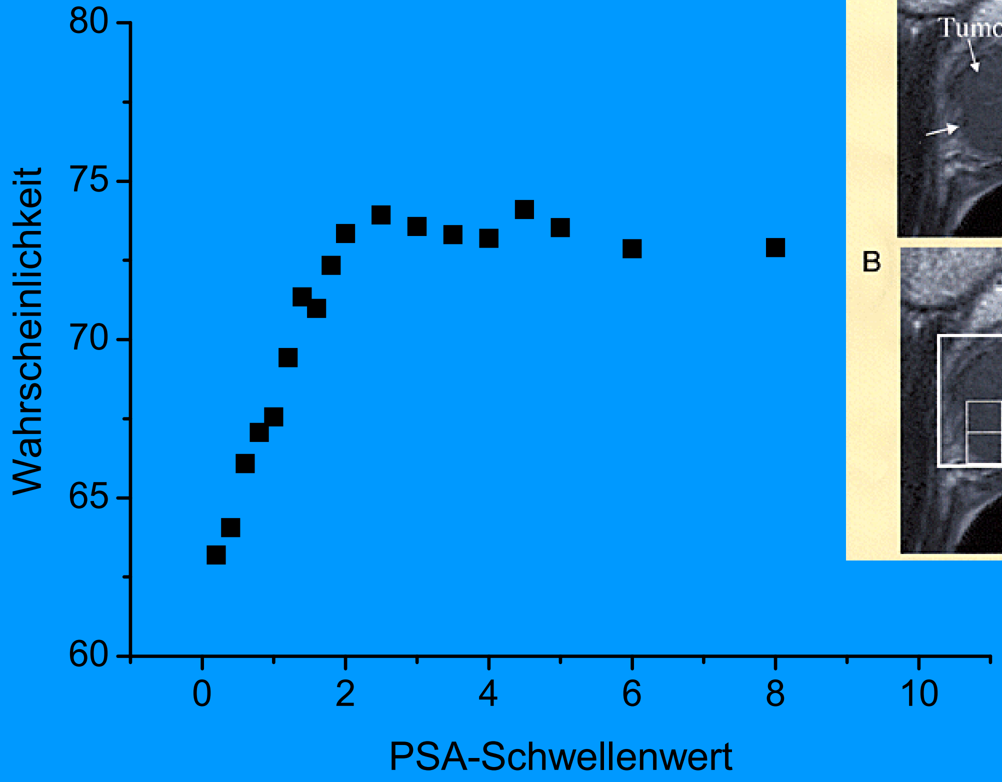


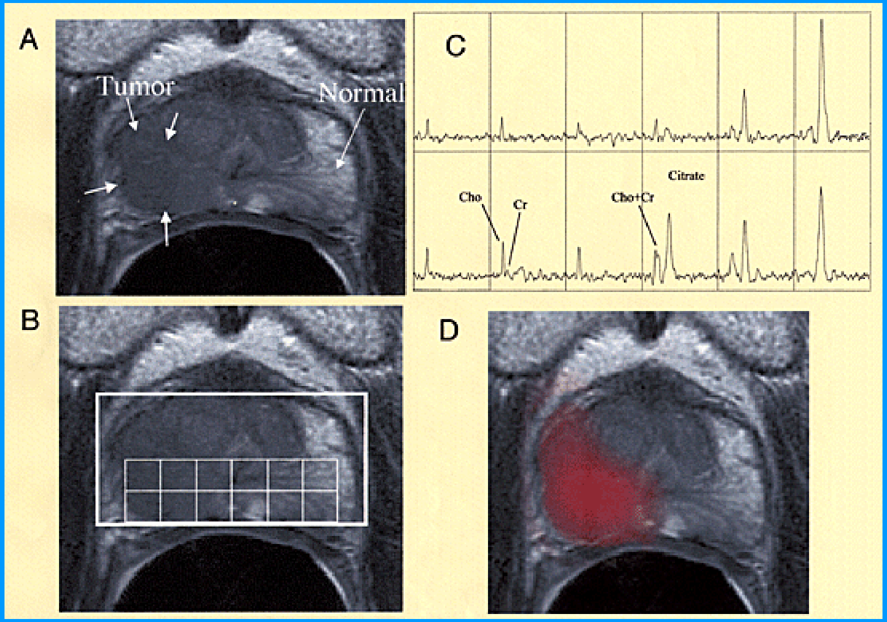
Figure 4



PET/CT – Imaging in Radiooncology

Local relapse and detection rate by PSA-level

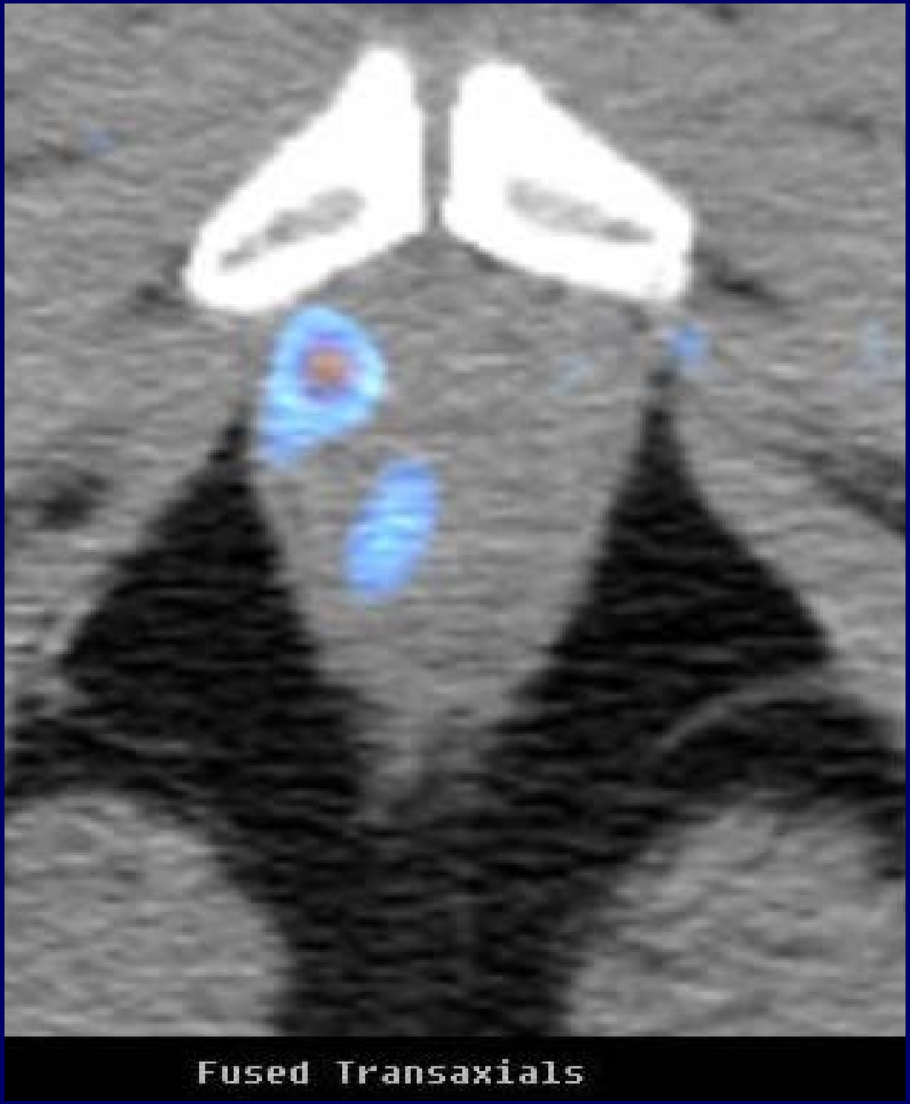


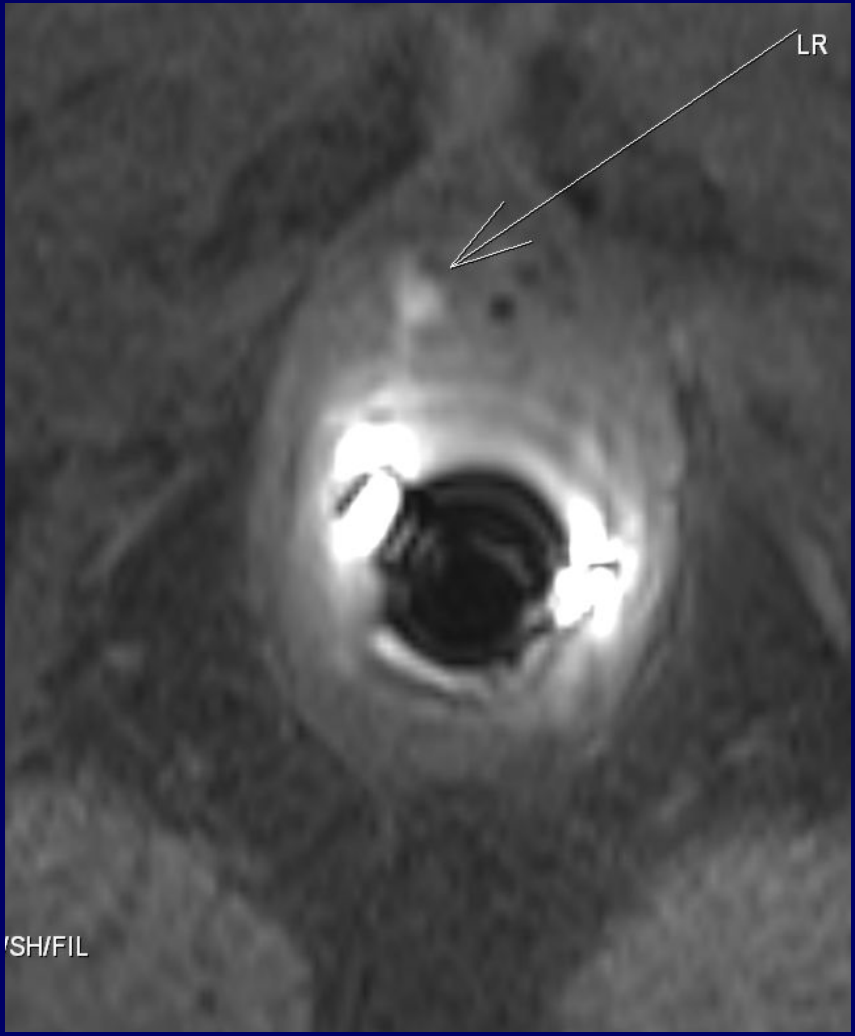


Reske SN, Blumstein NM et al.
Eur J Nucl Med Mol Imaging. 2008 Jan;35(1):9-17.
[(11)C]choline PET/CT imaging in occult local relapse of prostate cancer after radical prostatectomy.

PET/CT – Imaging in Radiooncology

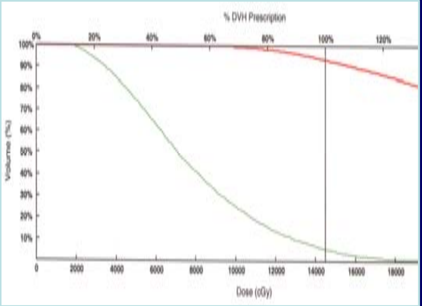
Local recurrence after RPX



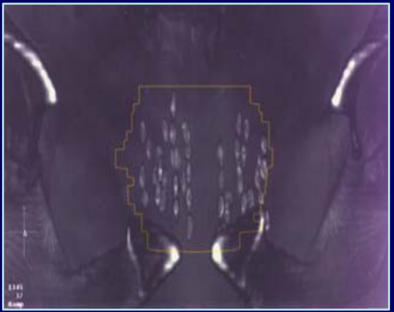


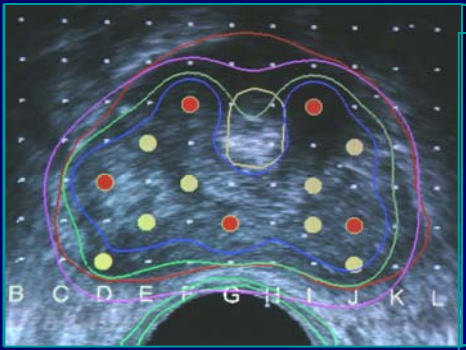
PET/CT – Imaging in Radiooncology

^{11}C-Choline in prostate cancer (4)



D 90: 159.2 Gy





ONLINE PLANNING

Abb.1: Zustand nach Brachytherapie der Prostata mit J-125 Seeds eines low risk-Patienten

Abb. 2

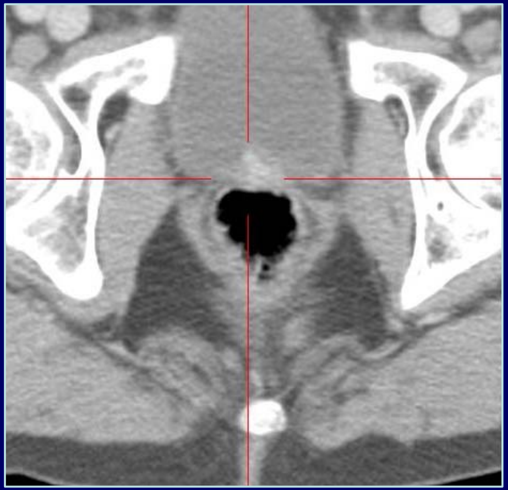
Abb.2: Zustand nach Brachytherapie der Prostata mit J-125 Seeds (Lokalrezidiv)

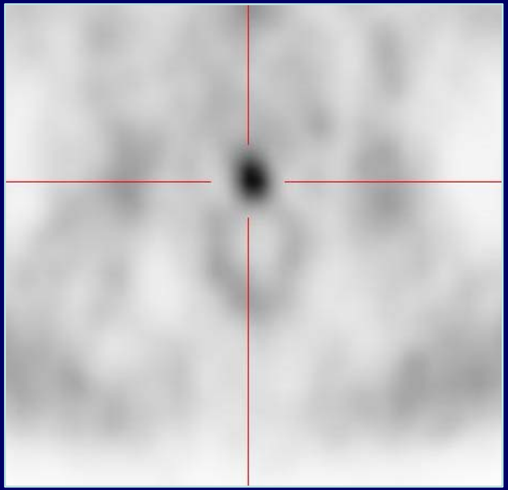
seeds

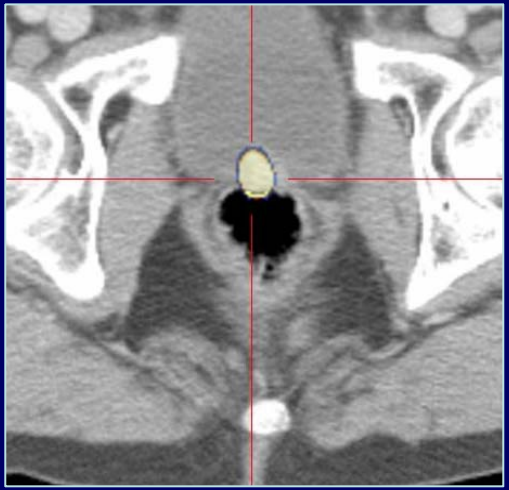
Operationspräparat

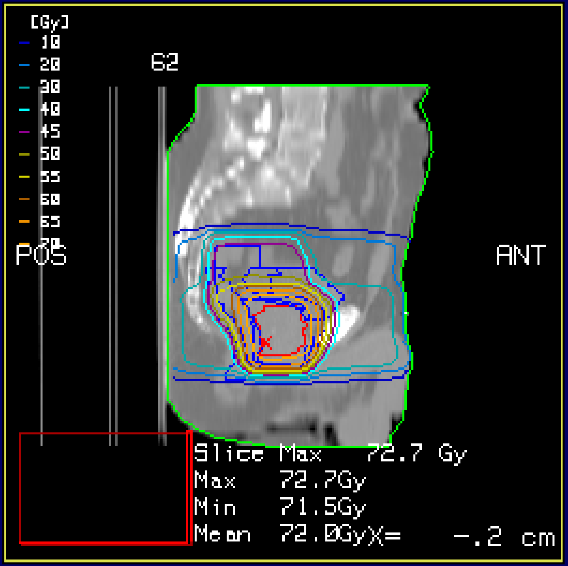
PET/CT – Imaging in Radiooncology

^{11}C-Choline in prostate cancer (5)





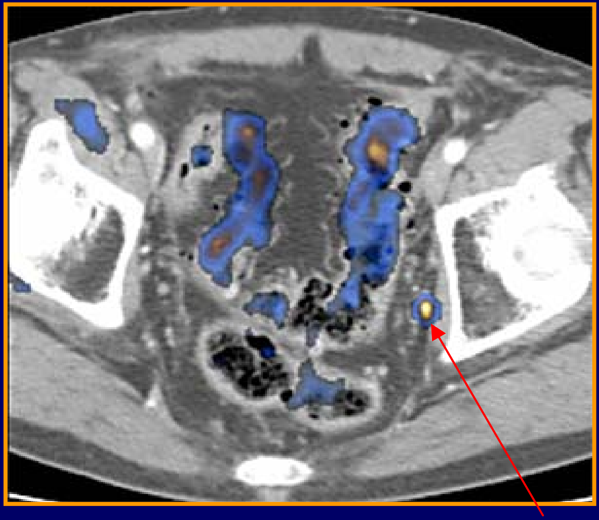


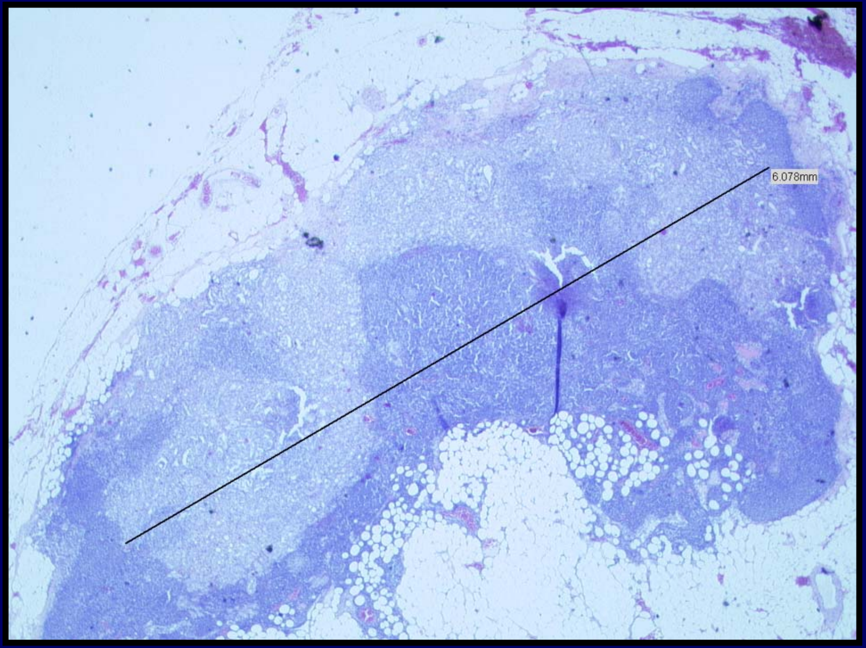


PET/CT – Imaging in Radiooncology

^{11}C-Choline in prostate cancer (6)

Rinnab L, Mottaghy FM, Simon J, Volkmer BG, de Petriconi R, Hautmann RE, Wittbrodt M, Egghart G, Moeller P, Blumstein N, Reske S, Kuefer R.
[11C]Choline PET/CT for targeted salvage lymph node dissection in patients with biochemical recurrence after primary curative therapy for prostate cancer. Preliminary results of a prospective study.
Urol Int. 2008;81(2):191-7





De Neve, Estro 2008 (Ghent)

Dose-volume characteristics and acute toxicity of hypofractionated intensity-modulated arc therapy (IMAT) and androgen deprivation (AD) as primary therapy for lymph node metastasized prostate cancer

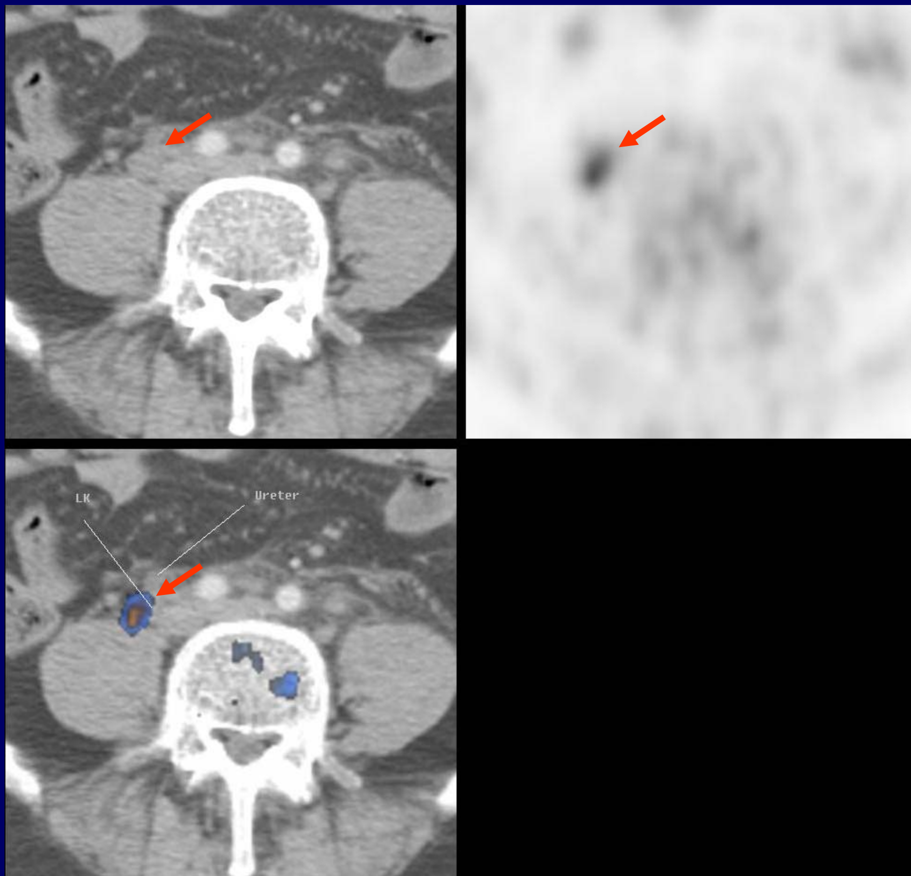
PET/CT – Imaging in Radiooncology

Impact of PET/CT to radiotherapy planning considerations

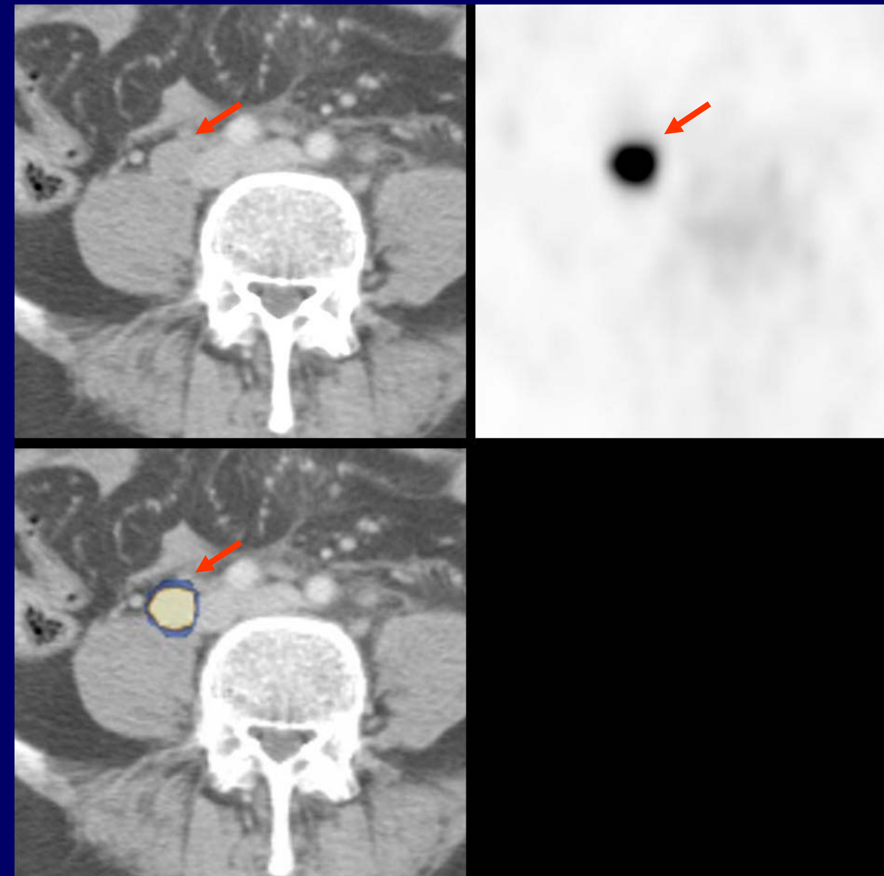
Predictive Value of Whole Body ^{18}F-FDG PET for Post-Treatment Evaluation in HD

Authors	Median Follow-Up (Months)	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Accuracy
de Wit et al (33)	26	100% (10/10)	78% (18/23)	67% (10/15)	100% (18/18)	85% (28/33)
Dittmann et al (34)	6	87% (7/8)	94% (17/18)	87% (7/8)	94% (17/18)	92% (24/26)
Spaepen et al (35)	32	50% (5/10)	100% (50/50)	100% (5/5)	91% (50/55)	92% (55/60)
Weihrauch et al (36)	28	67% (6/9)	80% (16/20)	60% (6/10)	84% (16/19)	76% (22/29)
Guay et al (37)	16	79% (11/14)	97% (33/34)	92% (11/12)	92% (33/36)	92% (44/48)
Friedberg et al (38)	24	80% (4/5)	85% (23/27)	50% (4/8)	96% (23/24%)	84% (87/32)
Panizo et al (39)	28	100% (9/9)	85% (17/20)	75% (9/12)	100% (17/17)	90% (26/29)
Overall		80% (52/65)	91% (174/192)	74% (52/70)	93% (174/187)	88% (226/257)

Juweid ME, Wiseman GA, Vose JM, Ritchie JM, Menda Y, Wooldridge JE, Mottaghy FM, Rohren EM, Blumstein NM, Stolpen A, Link BK, Reske SN, Graham MM, Cheson BD
Response assessment of aggressive non-Hodgkin's lymphoma by integrated International Workshop Criteria and fluorine-18-fluorodeoxyglucose positron emission tomography.
J Clin Oncol. 2005 Jul 20;23(21):4652-61



Occult nodal
Residual
mass

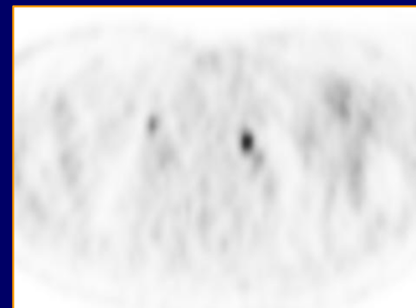


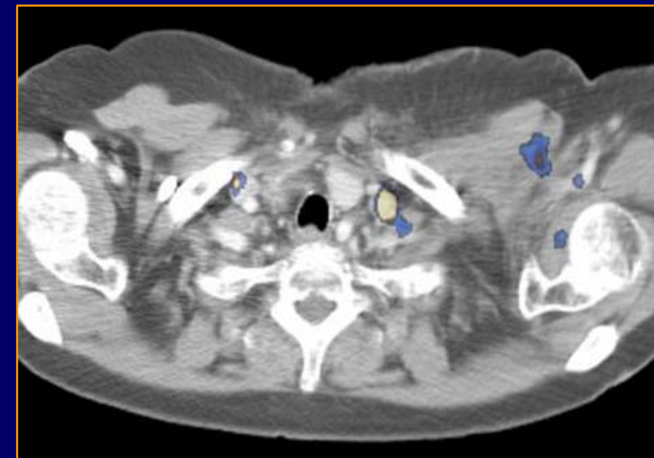
Follow up after 4 weeks:
Rapid progress

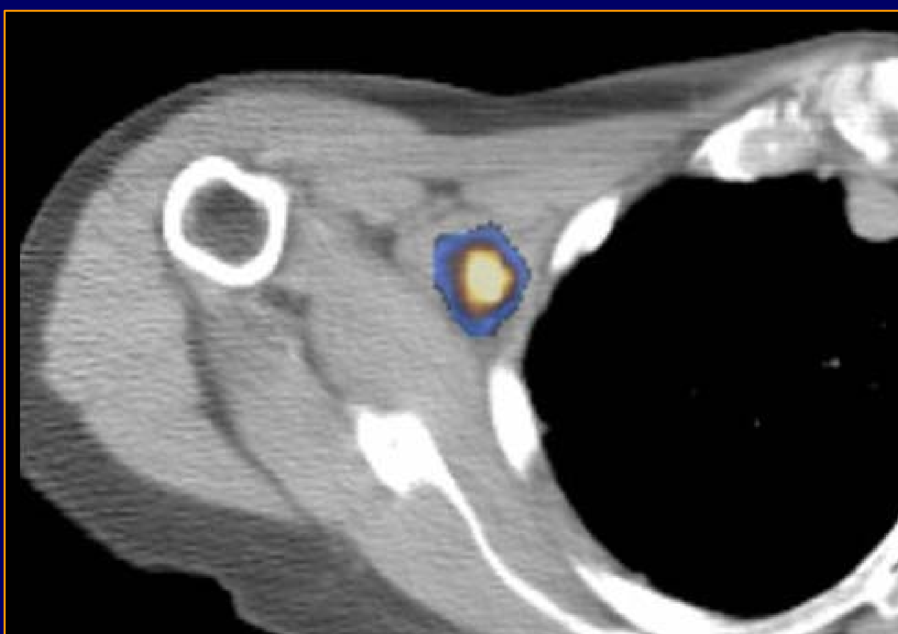
FDG PET/CT of a residual occult viable NHL 8 weeks after completion of chemotherapy. Rapid progression at 4 week follow-up.

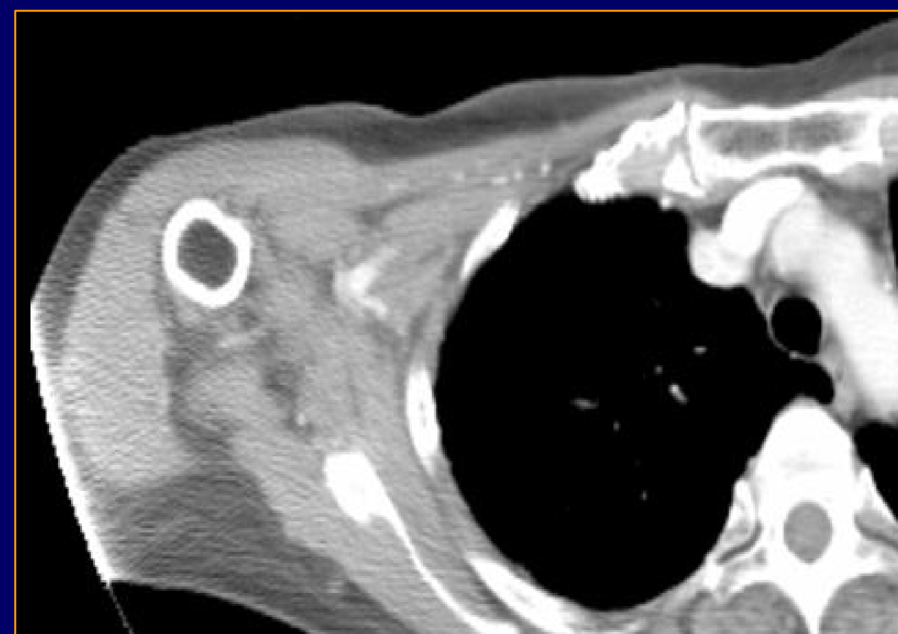
PET/CT – Imaging in Radiooncology

Breast cancer



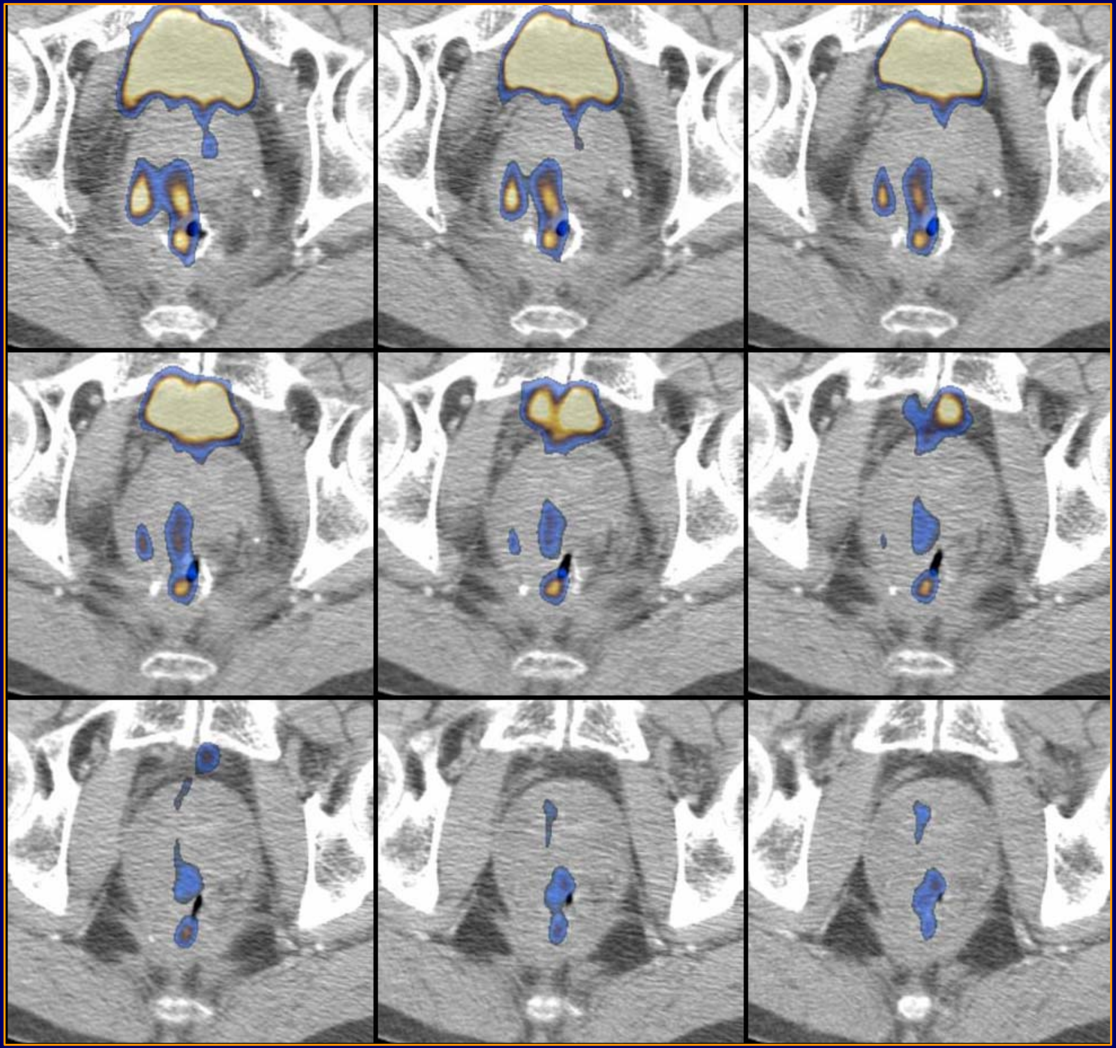


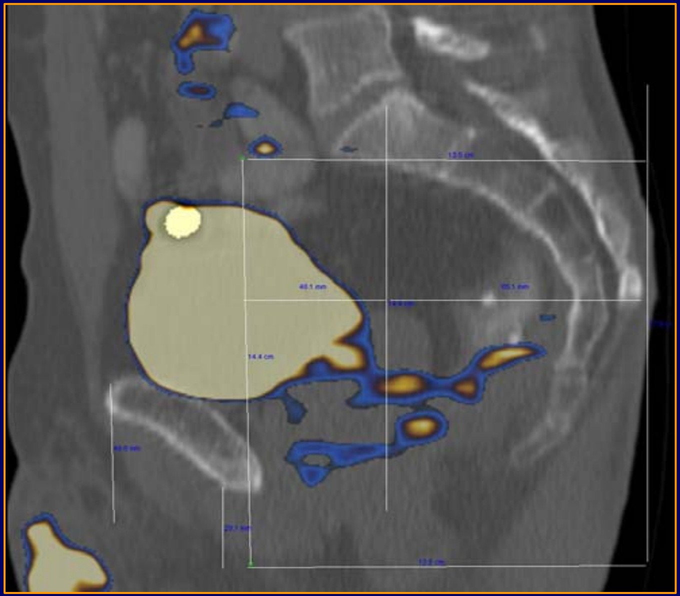


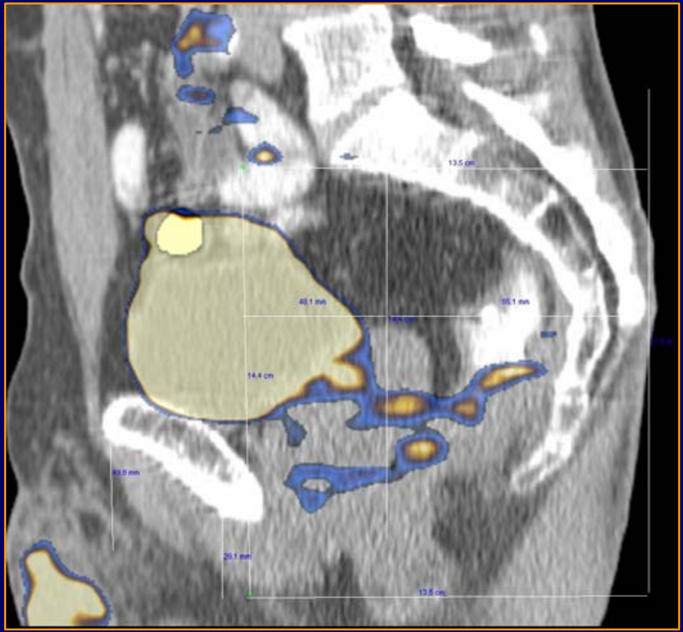


PET/CT – Imaging in Radiooncology

Rectal cancer

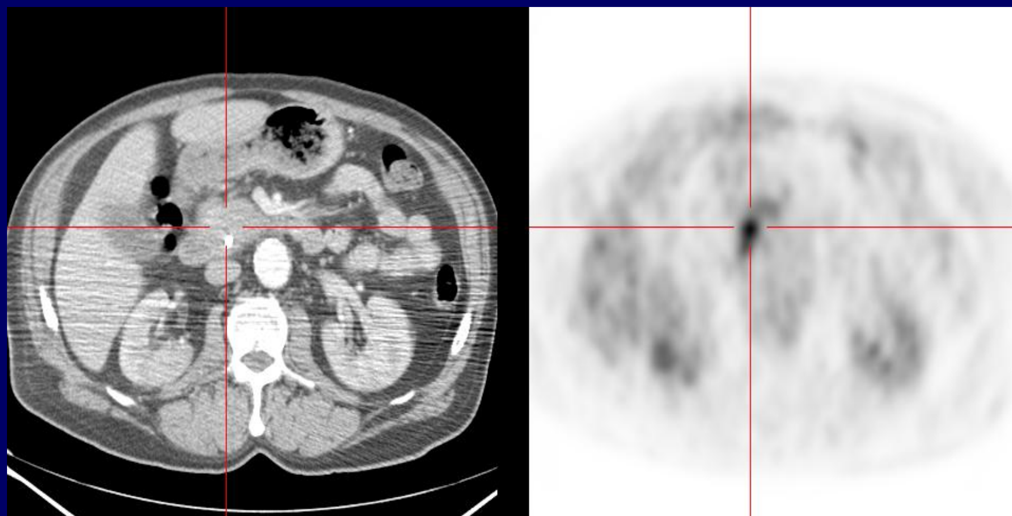


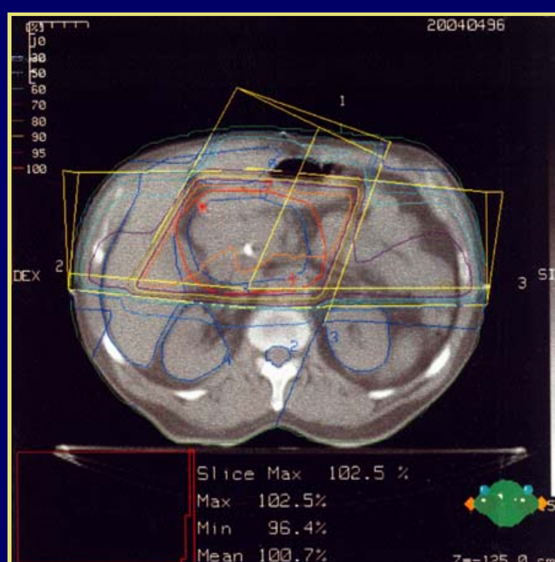


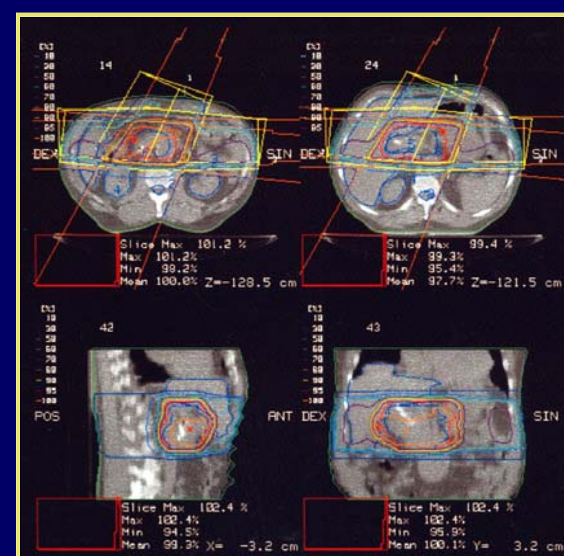


PET/CT – Imaging in Radiooncology

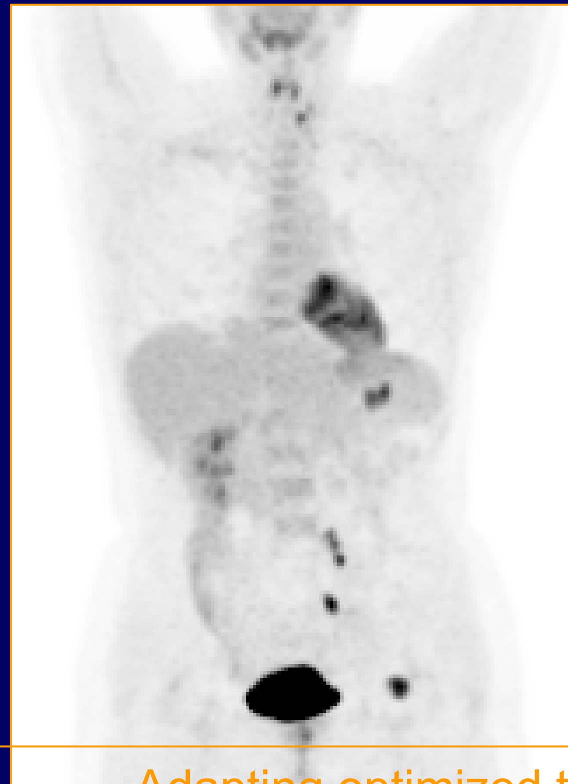
Pancreatic cancer







Cervical cancer



Adapting optimized therapy

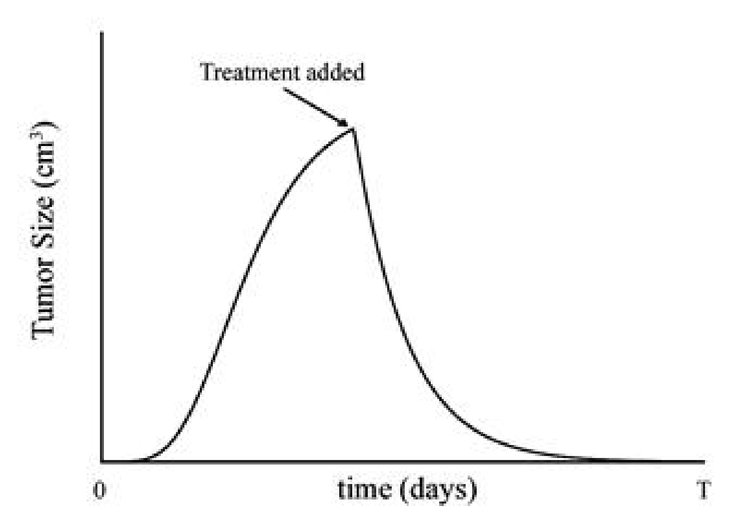
Cozzi, L. et al.

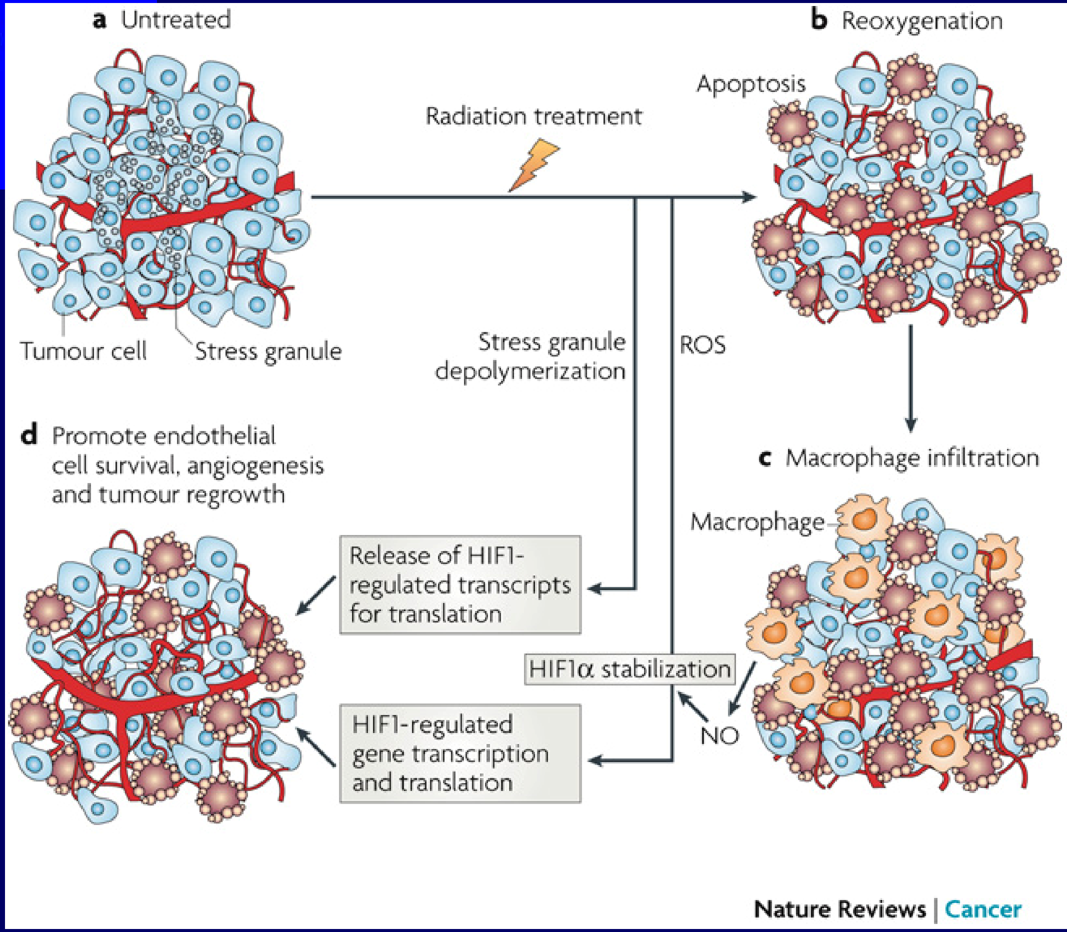
A treatment planning study comparing volumetric arc modultion with RapidArc and fixed field IMRT for cervix uteri radiotherapy

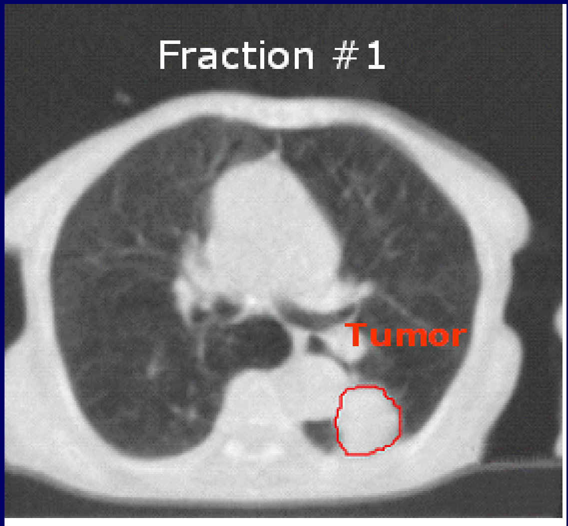
Radiation and Oncology, 2008 (in press)

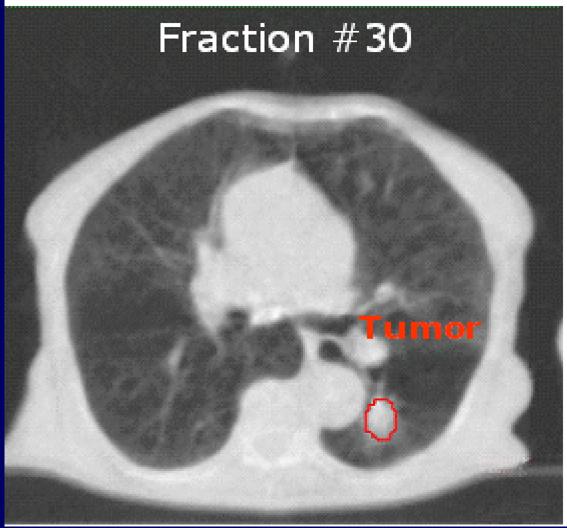
Response to Therapy

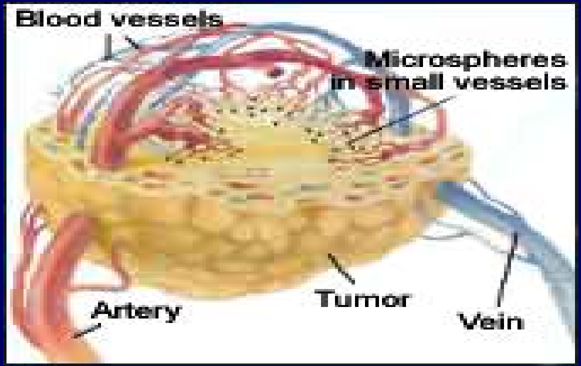
Hypothesis: A measure of metabolism such as FDG PET should be a sensitive way to detect response to therapy.

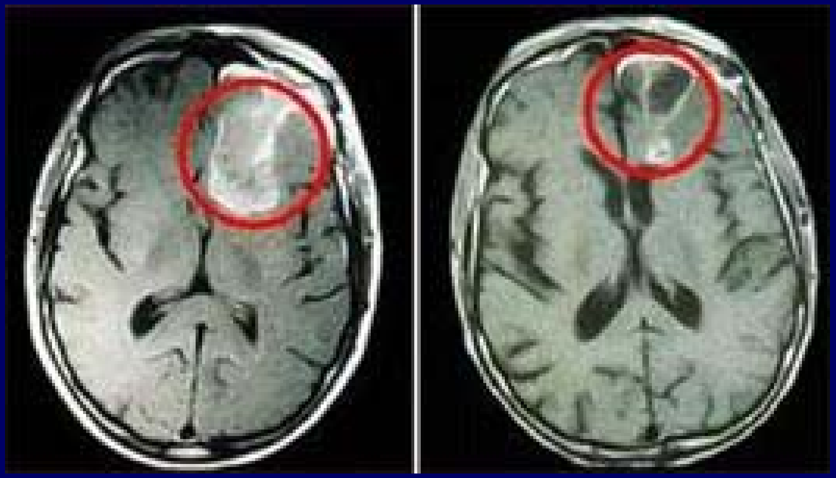


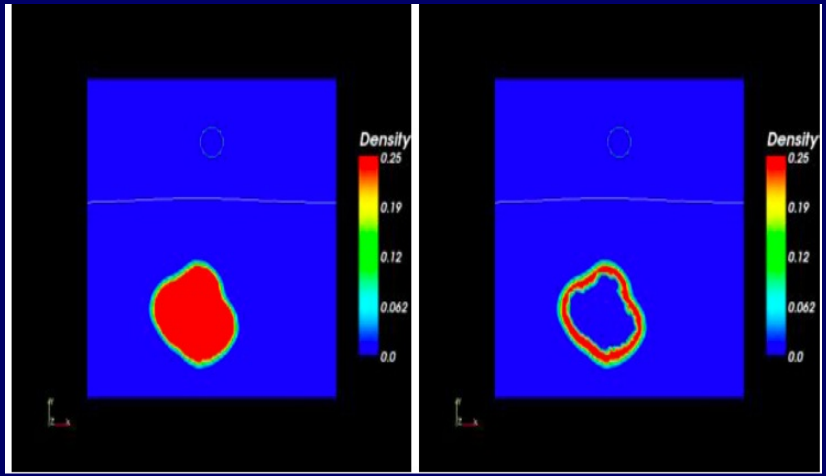


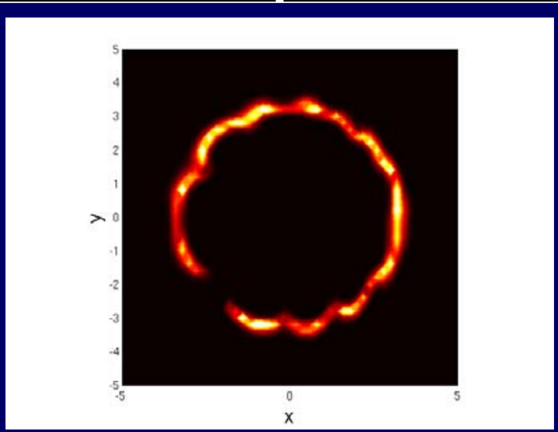

Fraction #1
Tumor


Fraction #30
Tumor


Blood vessels
Microspheres
in small vessels
Artery
Tumor
Vein




Density
0.25
0.19
0.12
0.062
0.0
Density
0.25
0.19
0.12
0.062
0.0


y
x
5
4
3
2
1
0
-1
-2
-3
-4
-5
-5
0
5

The technological basis of in-beam PET is a double head positron camera integrated into the therapy unit

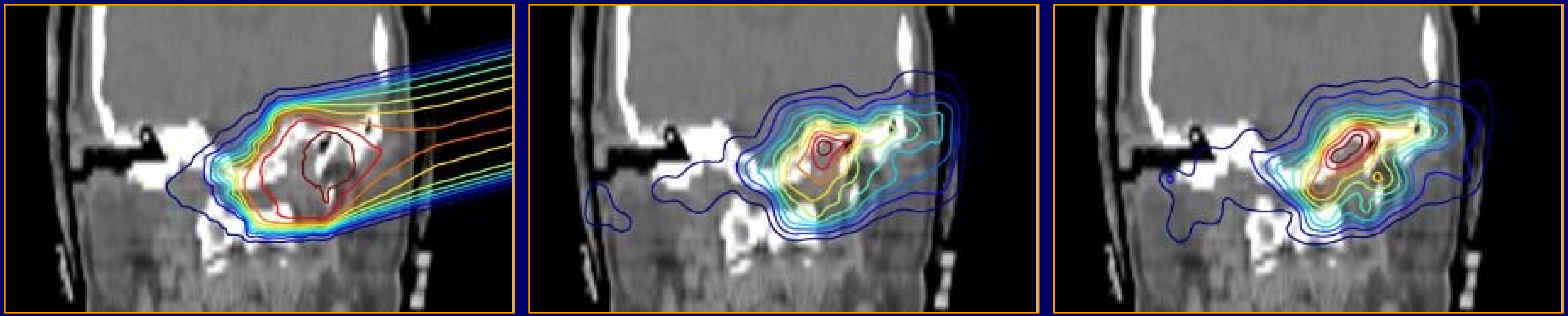
The horizontal carbon ion beam leaves the beam pipe visible through a 20´20 cm^2 window in the centre of the picture. To provide sufficient space for patient positioning, the PET scanner can be moved on rails parallel to the beam between the measuring position displayed and the parking position upbeam.

Double head positron camera developed by FZD at the treatment site of GSI Darmstadt.

Charged hadron tumour therapy monitoring by means of PET, W. Enghardt, P. Crespo, F. Fiedler, R. Hinz, K. Parodi, J. Pawelke, F. Pönisch, Nuclear Instruments and Methods in Physics Research A525, 284 (2004)

PET/CT – Imaging in Radiooncology

In-beam PET for radiotherapy monitoring (1)



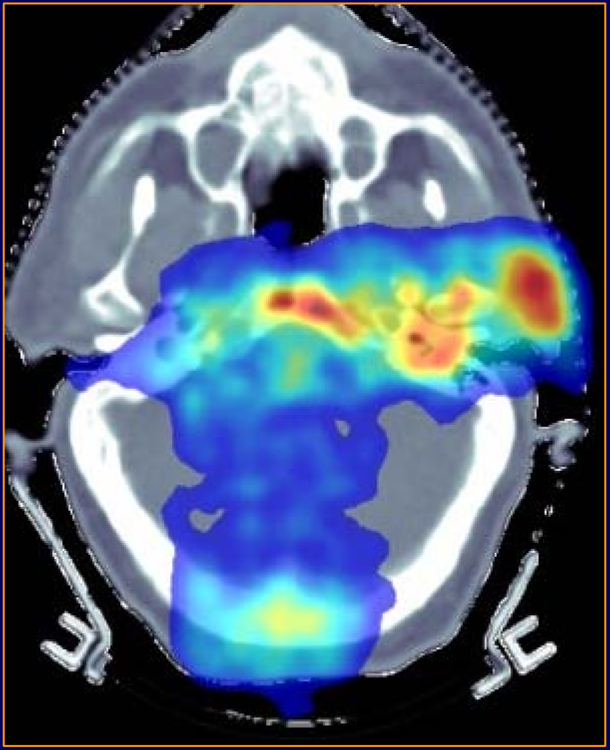
Clinical application of in-beam PET at the carbon ion therapy facility at GSI Darmstadt.

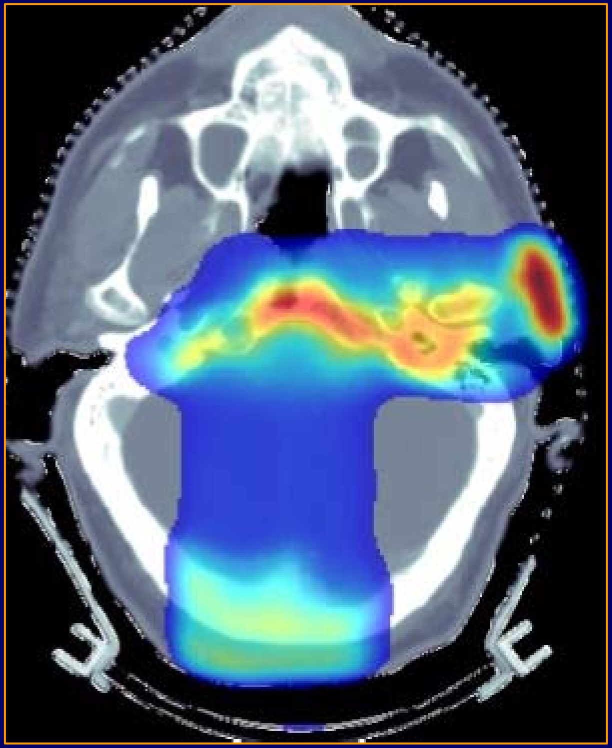
As an example, the irradiation of a chondrosarcoma of the skull base with a lateral portal coming from the left side of the patient, i.e. right side in the picture, (maximal dose: 0.63 Gy) is displayed.

As indicated by the dose distribution superimposed onto the computed tomogram (left), the carbon ions must not penetrate the brain stem as an organ at risk. The comparison of the predicted (middle) with the measured (right) b+-activity distributions shows that this was fulfilled during the treatment. The isodose and isoactivity lines are decoded in rainbow colours and denote 5, 15 … 95 % of the maxima.

PET/CT – Imaging in Radiooncology

In-beam PET for radiotherapy monitoring (2)





Monte Carlo calculated (left) and measured (right) activity distribution after proton irradiation of a clivus chordoma patient at Massachusetts General Hospital, Boston. Images by courtesy of K. Parodi and T. Bortfeld

Patient study on in-vivo verification of beam delivery and range using PET/CT imaging after proton therapy, K. Parodi, H. Paganetti, H. Shih, S. Michaud, J. Loeffler, T. DeLaney, N. Liebsch, J. Munzenrider, A. Fischman, A. Knopf and T. Bortfeld, International Journal of Radiation Oncology, Biology, Physics, in press

PET/CT – Imaging in Radiooncology

Last image (nearly)

- PET- tracer (s)
- PET- images and reconstruction
- PET/CT vs. gated PET/CT
- PET and real tumor extension ?
- PET - imaging: when ?
- Image fusion ? Which images ?

PET/CT – Imaging in Radiooncology

Many options – known limitations – solutions are possible