I SESSIONE

APPROPRIATEZZA DELL'IMAGING NEI TUMORI DELL'ESOFAGO

Moderatori: Luca Brunese - Renzo Corvo' - Felice Mucilli

L'IMAGING NEL PLANNING RADIOTERAPICO: IMAGING MORFOLOGICO O FUNZIONALE?

Luciana Caravatta

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lcaravatta@hotmail.com

Simulation:
- *CT + optical laser*

→

Treatment planning:
- *CT*
- *MRI-MRS*
- *PET*

→

Set-up verification:
- *US*
- *kV images*
- *CT on-rails*
- *kV or MV CBCT*

→

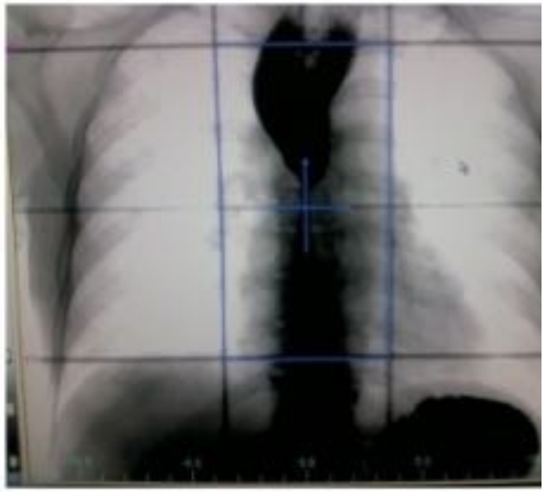
Dose delivering and organ motion:
- *4D imaging*
- *Fluoroscopy*
- *In-beam PET*

→

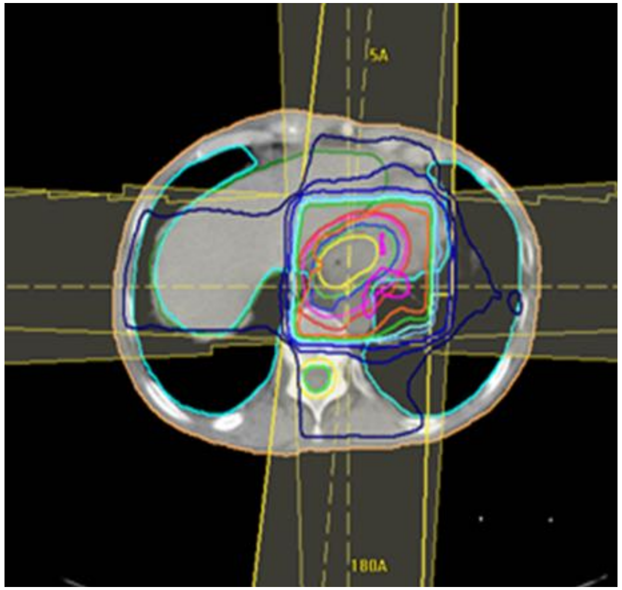
Response assessment:
- *CT*
- *MRI*
- *PET*
- *SPECT*

Lecchi M. Eur J Nucl Med Mol Imaging (2008) 35:821–837

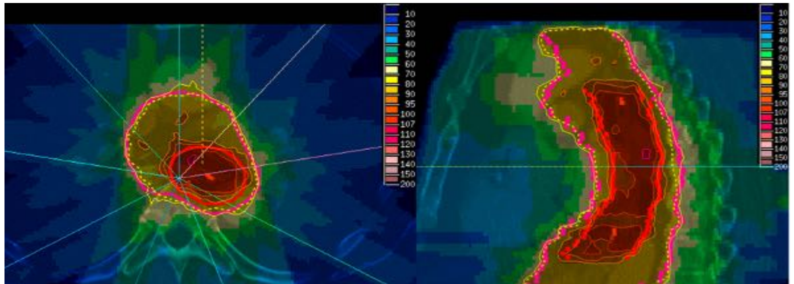
From 2D ...



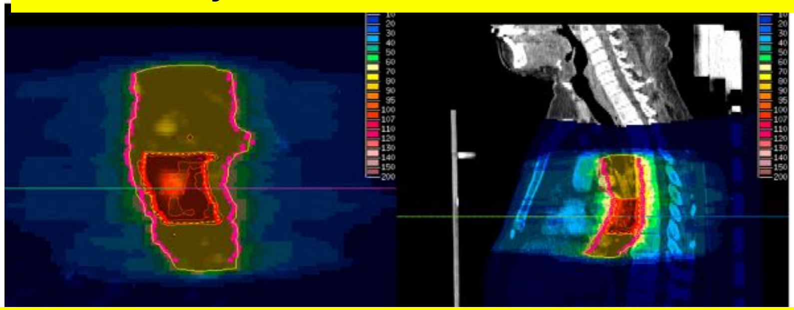
To 3D ...



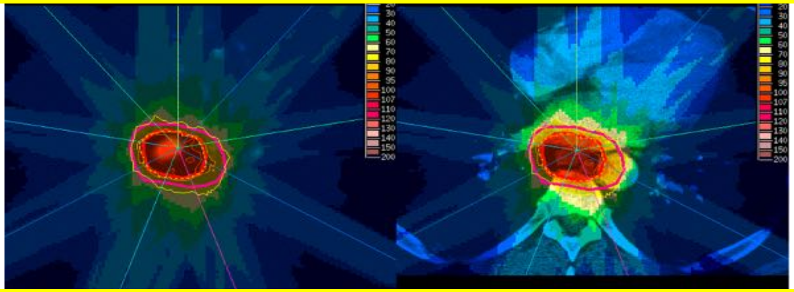
To IMRT, VMAT, IGRT



1-, 2- and 3-year-LRC rate= 77%, 65% and 48%.



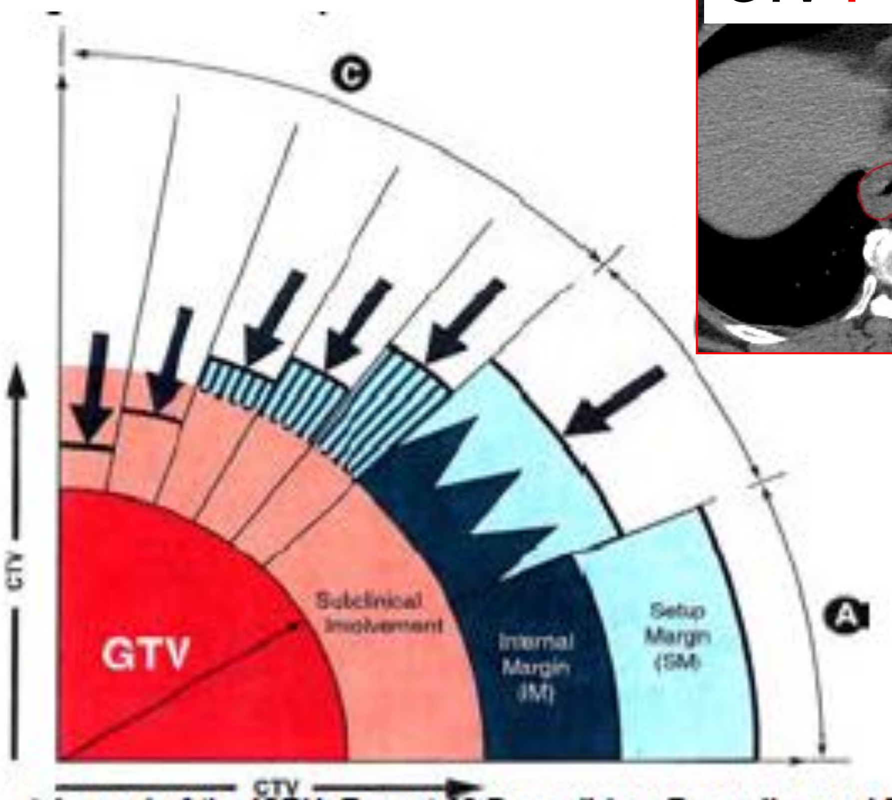
1-, 2- and 3-year-DFS rates=58%, 48% and 36%,



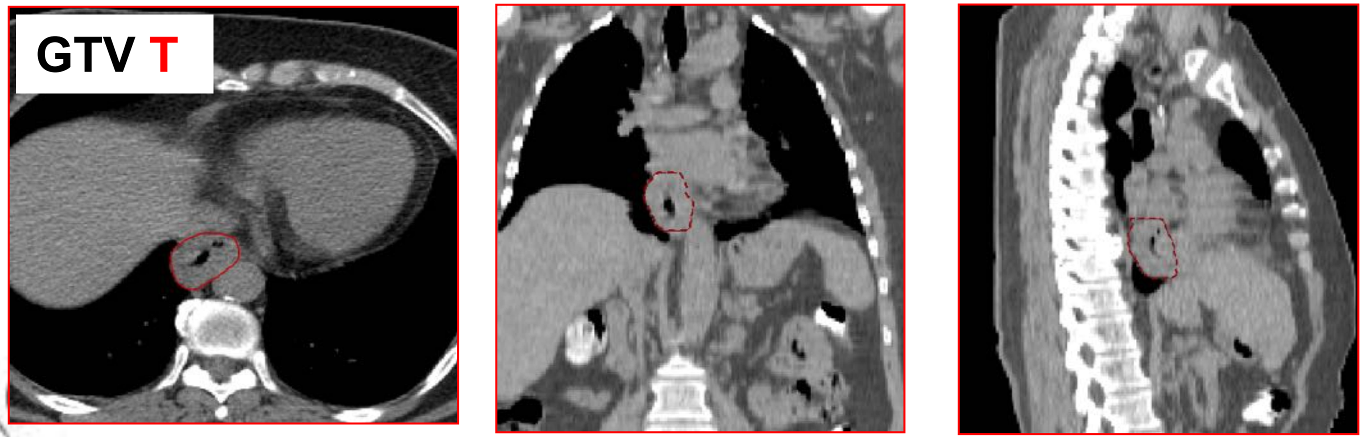
1-, 2- and 3-year-OS rates =82%, 61% and 56%.

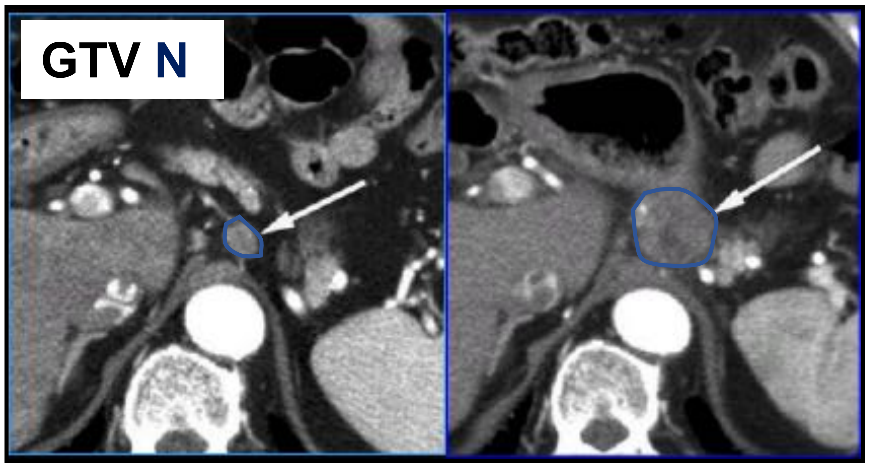
Roeder 2014, Nguyen 2014, Yang 2009

CTV 1: GTV T & N site with margins, by using information from endoscopic examination , barium swallowing x-ray and DIAGNOSTIC IMAGING

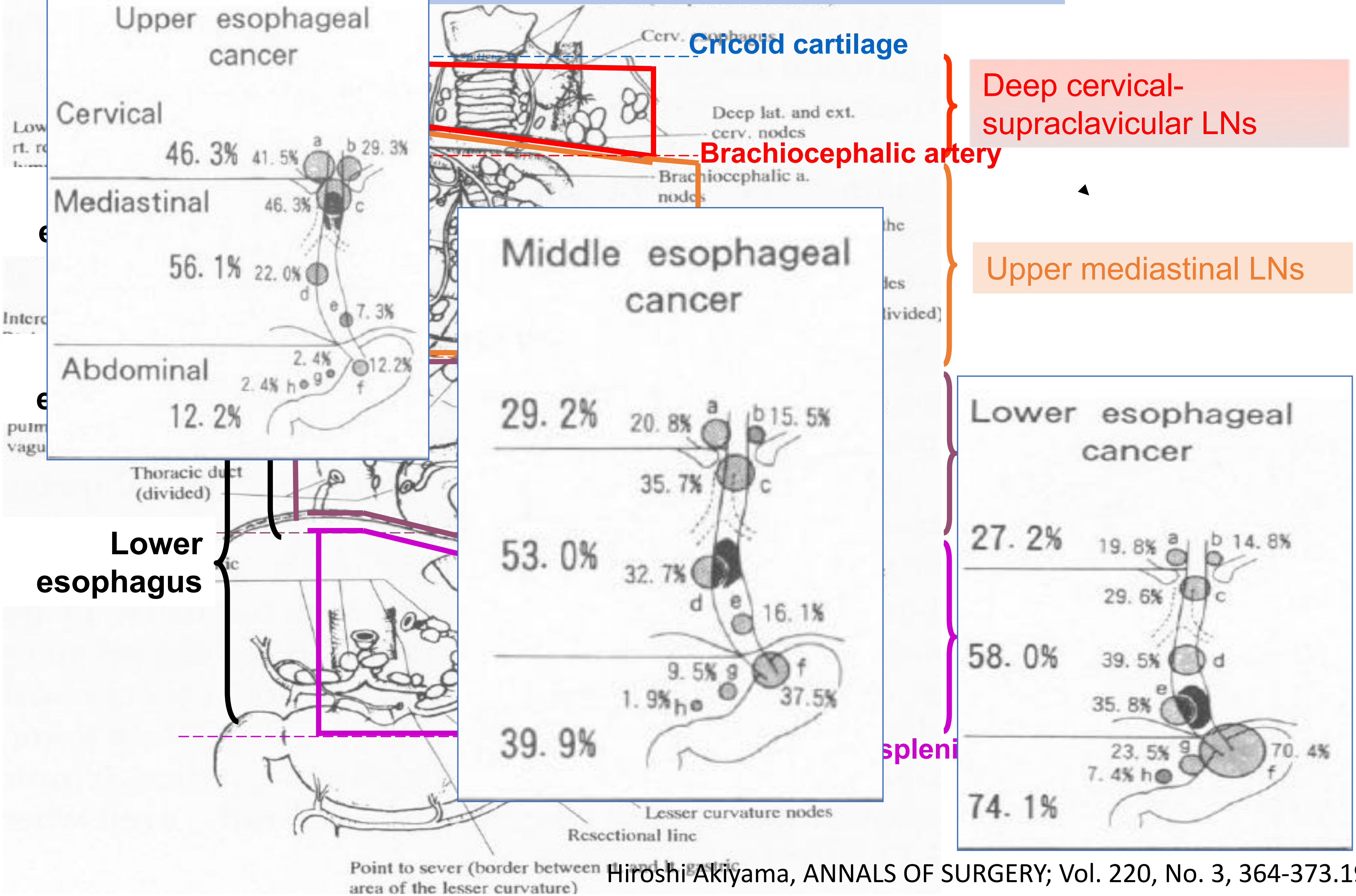


©Journal of the ICRU. Report 62 Prescribing, Recording and Reporting Photon Beam Therapy (Supplement to ICRU Report 50) 1999, Figure 2.16 from p 16.





CTV2: Elective Nodal CTV

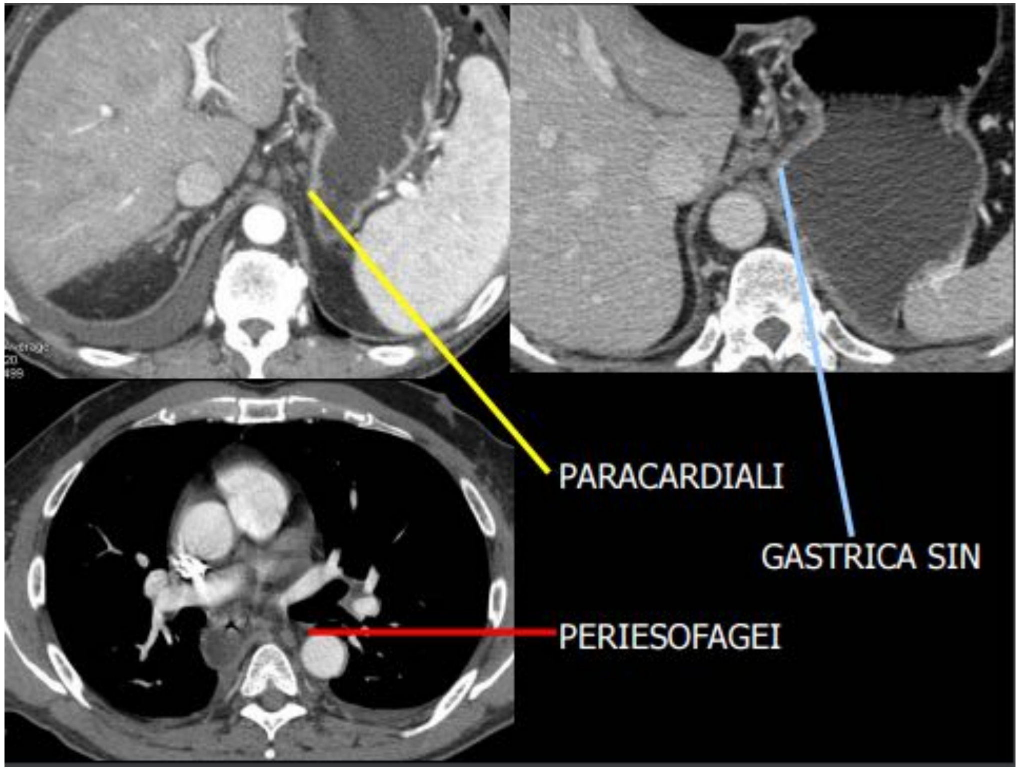


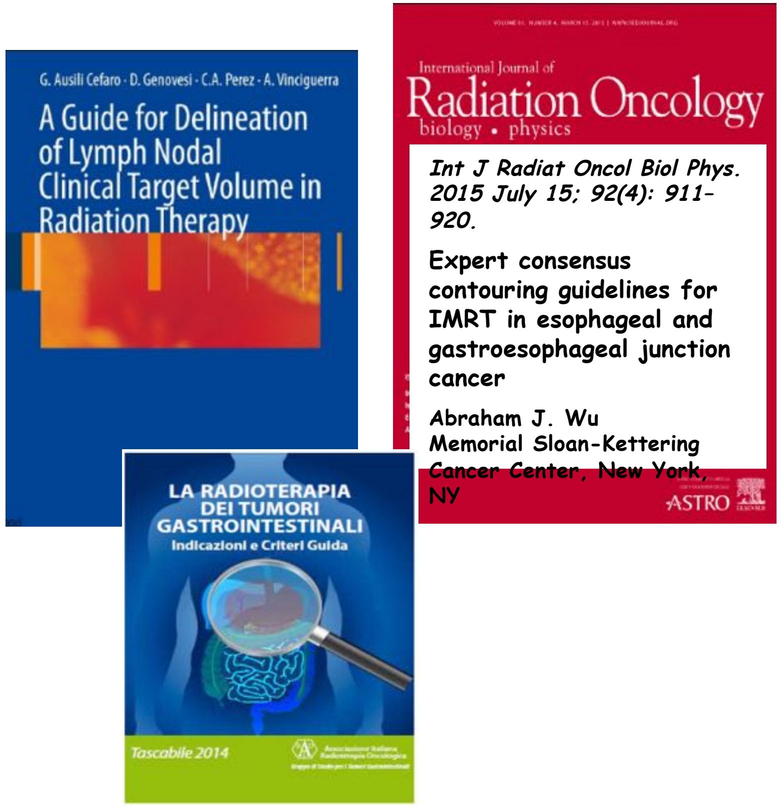
Hiroshi Akiyama, ANNALS OF SURGERY; Vol. 220, No. 3, 364-373.1994

WHICH IMAGING?

CTV2: Elective Nodal CTV

CT has traditionally been used to aid in radiation therapy planning, giving information regarding mediastinal & abdominal lymphadenopathy.





The use of <u>contrast agent does not significantly influence dose calculation</u> of PTV, lung and spinal cord. However, it does have influence on dose accuracy for heart.

Hong-Sheng Li et al. Asian Pacific Journal of Cancer Prevention, Vol 14, 2013

CTV 1: GTV T & N

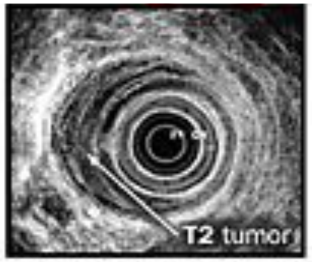
CT scan

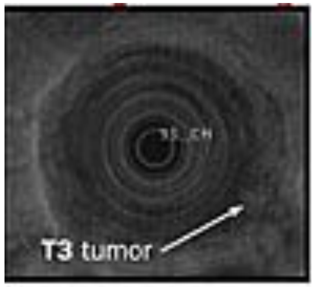
Accuracy	Limitations
Pathological T stage = 80%	T1 from T2
staging the depth of the tumor=49% to 60%	Microscopic infiltration of the periesophageal fat (T3)
N stage = 60-80 %	morpho-dimensional criterion
	tumor extention

Kavita U. Vaishnav, GUJARAT MEDICAL JOURNAL ,2014 Vol. 69 No. 1

CTV 1: GTV T & N

Esophageal US





Benefit	Limitations
Pathological T stage = 76% to 92%	obstructing lesion (failure rate of 14–25 %)
N stage sensitivity =80 % and specificity = 70 %	experience dependent
	difficult to translate in radiation treatment planning

Kavita U. Vaishnav, GUJARAT MEDICAL JOURNAL ,2014 Vol. 69 No. 1

WHAT'S THE ROLE OF FDG-PET/CT?

1. ability of FDG-PET(/CT) to detect the T and/or pathologic N;
2. Does the addition of FDG-PET change target volume delineation?
3. validity of FDG-PET/CT with regard to GTV delineation;
4. Does the addition of FDG-PET improve inter-observer and intra-observer variability in target volume delineation;
5. what consequences for radiotherapy treatment planning with regard to either target volumes or OARS?

J.M. Wilson, Clinical Oncology 26 (2014) 581e596
C.T. Muijs et al. Radiotherapy and Oncology 97 (2010) 165–171

1. Ability of FDG-PET(/CT) to detect the T

FDG-avidity of the primary tumour: increased uptake of FDG was seen in 68– 100%

Undetected tumours are mostly stages T1 and T2 tumours.

Especially T1a tumours, remaining within the submucosa, are difficult to detect by FDGPET

Author	N	Primary tumour: Detection rate on CT (%)	Primary tumour: Detection rate on PET (%)	Lymph node metastases: Sensitivity of PET for LN (%)	Specificity of PET for LN (%)	Sensitivity of CT for LN (%)	Specificity of CT for LN (%)	Sensitivity of PET/CT for LN (%)	Specificity of PET/CT for LN (%)	Remarks
Pfau et al. [28]	44	80	92	–	–	–	–	–	–	4 of 5 undetected were T1–T2
Rankin et al. [29]	19	95	100	–	–	–	–			
Salahudeen et al. [30]	25	–	100	–	–	–	–			
Wren et al. [43]	21	–	–	71	86	57	71			
Kato et al. [17]	149		80	32	99	23	97			Most undetected were T1
Kato et al. [16]	32	–	78	78	93	61	71			The not visible tumours were T1
Flamen et al. [10]	39		95	33	89	0	100			All false negative on PET were T1
Himeno et al. [13]	22	–	68	42	100	38	96			All undetected tumours were T1
Block et al. [3]	58	–	94	52	79	29	79			2 undetected lesions were T1a
Kato et al. [15]	167	–	74	33	99	27	98			Most undetected were T1–2
Kim et al. [18]	52	98	94	52	94	42	97	–	–	False negative on PET was T1 tumour
Meltzer et al. [23]	47	97	87	35–41	90	63–87	14–43	–	–	
Yoon et al. [44]	79	82	92	30	90	11	95	–	–	All undetected tumours were T1
Kole et al. [19]	26	81	96	92	88	38	100	–	–	
Sihvo et al. [33]	55	69	82	35	100	42	82	50	100	Of the false negative 7 T1 tumours and 3 T2 tumours
Yuan et al. [46]	45	–	–	82	87	–	–	94	92	
Schreurs et al. [32]	85	–	–	–	–	–	–	87	87	

The sensitivity increases with increasing depth of invasion, the value being 83% for T2 tumors, 97% for T3, and 100% for T4 tumors.

C.T. Muijs et al. Radiotherapy and Oncology 97 (2010) 165–171

1. Ability of FDG-PET(/CT) to detect the pathologic N;

sensitivity of CT and FDG-PET varied widely; 11–93% vs. 30– 93%.
specificity of CT and FDG-PET: 71–100% vs. 79–100%, respectively

Author	N	Primary tumour: Detection rate on CT (%)	Primary tumour: Detection rate on PET (%)	Lymph node metastases: Sensitivity of PET for LN (%)	Specificity of PET for LN (%)	Sensitivity of CT for LN (%)	Specificity of CT for LN (%)	Sensitivity of PET/CT for LN (%)	Specificity of PET/CT for LN (%)	Remarks
Pfau et al. [28]	44	80	92	–	–	–	–	–	–	4 of 5 undetected were T1–T2
Rankin et al. [29]	19	95	100	–	–	–	–	–	–	
Salahudeen et al. [30]	25	–	100	–	–	–	–	–	–	
Wren et al. [43]	21	–	–	71	86	57	71	–	–	
Kato et al. [17]	149		80	32	99	23	97	–	–	Most undetected were T1
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Yoon et al. [44]	79	82	92	30	90	11	95	–	–	All undetected tumours were T1
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Sihvo et al. [33]	55	69	82	35	100	42	82	50	100	Of the false negative 7 T1 tumours and 3 T2 tumours
Yuan et al. [46]	45	–	–	82	87	–	–	94	92	
Schreurs et al. [32]	85	–	–	–	–	–	–	87	87	

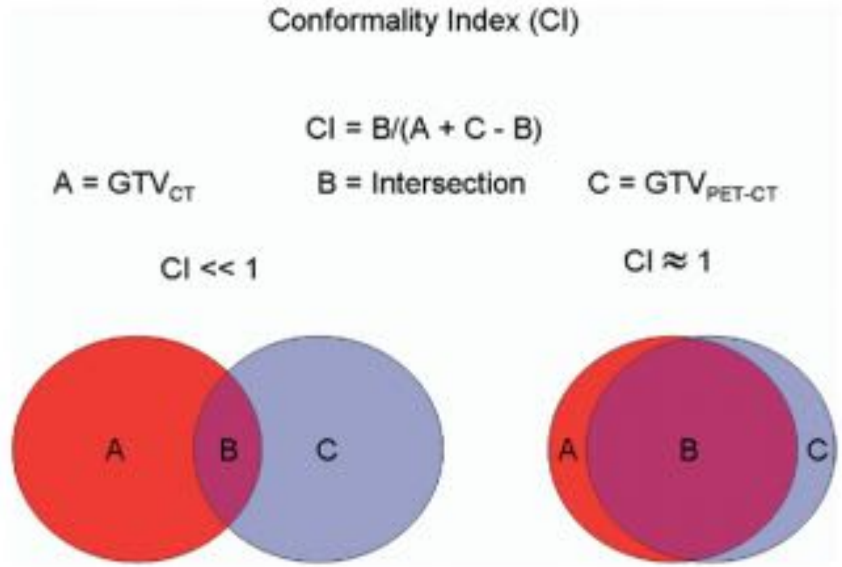
NPV (98%)

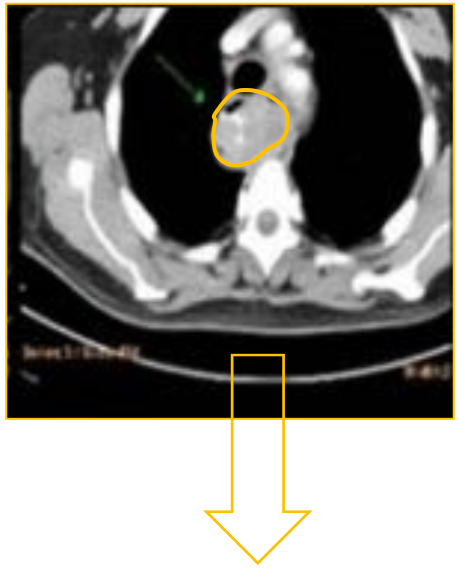
Although FDG-PET/CT improved the sensitivity, it remained significantly lower than that for EUS (p = 0.001).

C.T. Muijs et al. Radiotherapy and Oncology 97 (2010) 165–171

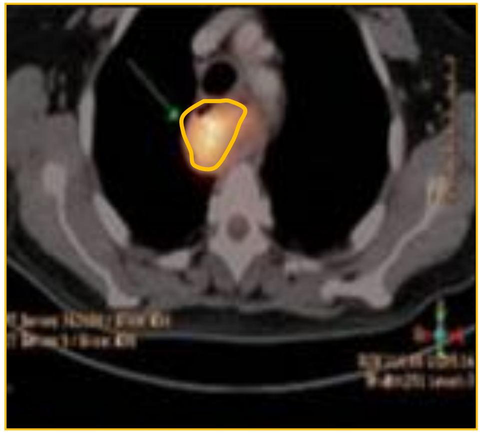
2. Target volume modifications

Author
Tumour delineation
Gondi et al. [11]
Konski et al. [20]
Vrieze et al. [40]
Hong et al. [14]
Moureau-Zabotto et al. [25]
Leong et al. [21]
Vesprini et al. [39]
Schreurs et al. [31]
Muijs et al. [26]





Smaller **62.5%**



Conformality Index of GTVs derived from computed tomography and computed tomography co-registered with FDG-PET
0.46-0.68

C.T. Muijs et al. Radiotherapy and Oncology 97 (2010) 165–171

2. Target volume modifications

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Tumour delineation
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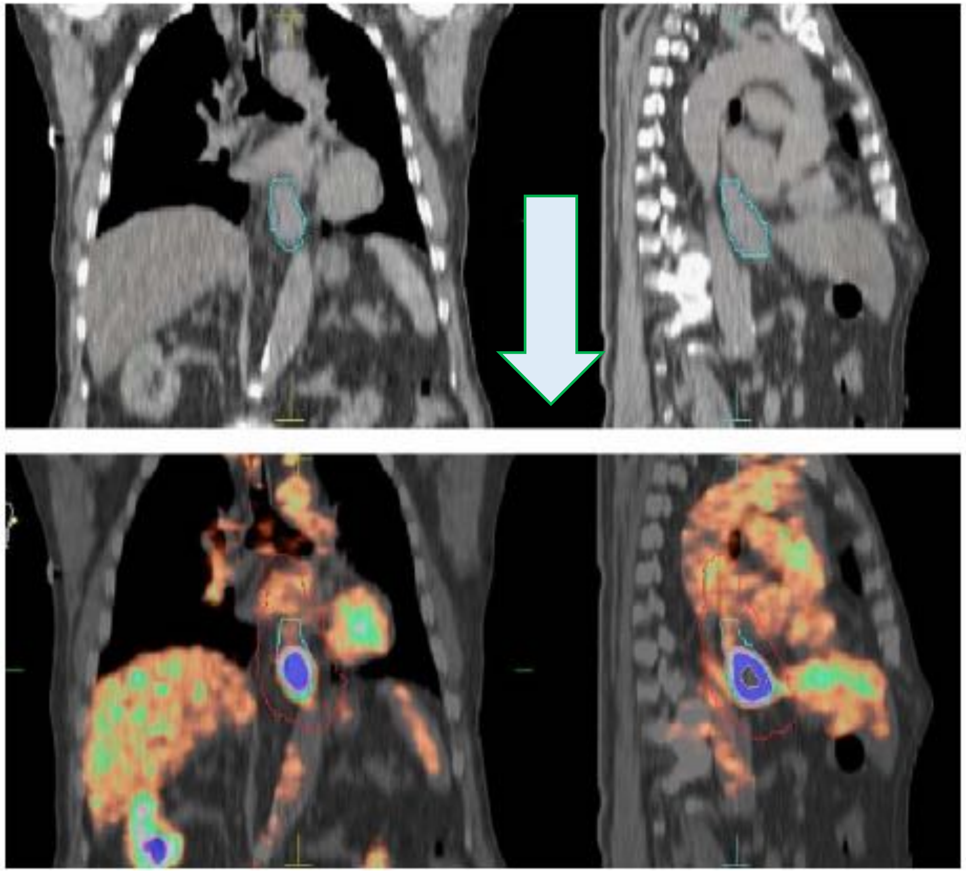
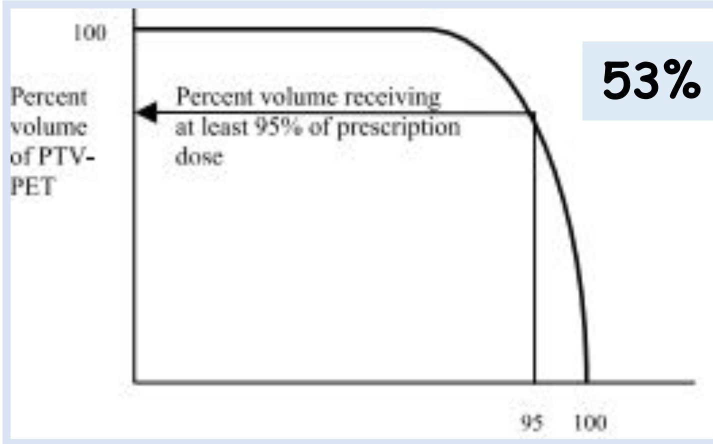


shorter in 22%, longer in 20 %

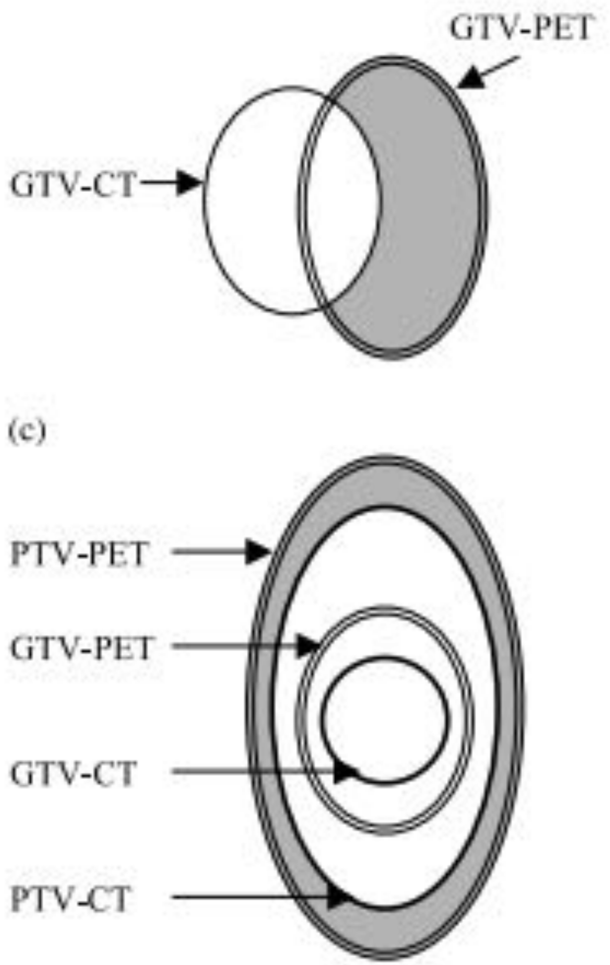


the addition of FDG-PET/CT resulted in changes in the delineation of target volumes in a considerable proportion of patients (20–94%).

C.T. Muijs et al. Radiotherapy and Oncology 97 (2010) 165–171

2. Target volume modifications

21 esophageal carcinoma patients



PET-CT detected disease in 8 patients (34%) that was not detected by CT scan:

The GTV based on CT information alone excluded PET-avid disease in 11 patients (69%)

in 5patients (31%) this would have resulted in a geographic miss of gross tumour.

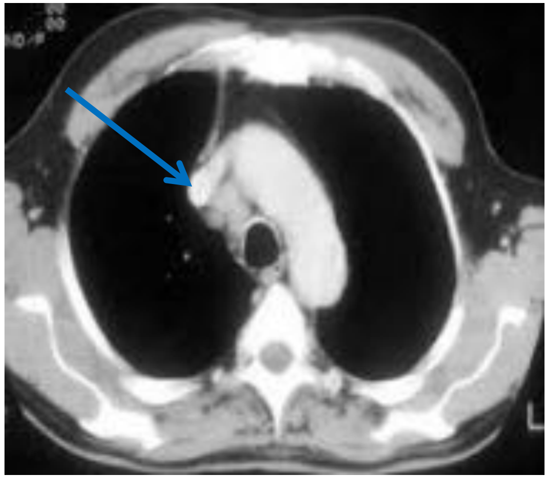
The cranial extent of the primary tumour as defined by CT vs PET/CT differed in 75% of cases, while the caudal extent differed in 81%.

Leong et al. Radiother Oncol 78:254– 261, 2006 15.

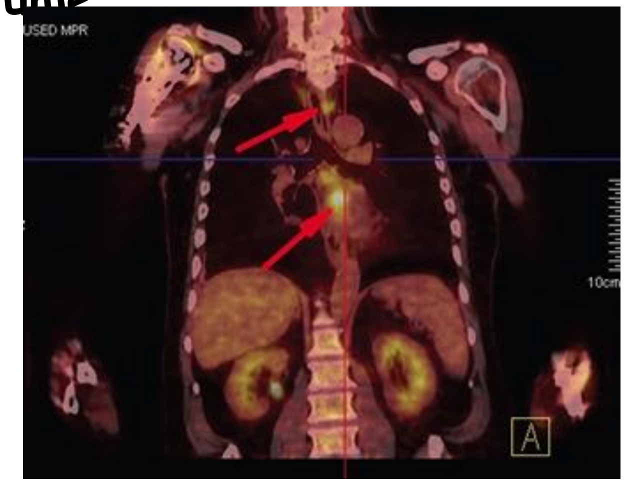
2. Target volume modifications

30 patients with advanced esophageal carcinoma

lymph node involvement by CT, EUS, and FDG-PET: discrepancy **47%**



- FDG-PET **failed to detect 9 nodes in 8 patients** that were detected by CT/ EUS.
- In 3 of these 8 patients, failure of FDG-PET to detect CT/EUS-detected disease would have led to a reduction in the irradiated volume



- **8 nodes in 6 patients** were detected by FDG-PET that were not detected by CT/ EUS.
- In 3 of these 6 patients, disease detected by FDG-PET would have resulted in an increase in the irradiated volume.

Vrieze et al. Radiother Oncol 73:269–275, 2004

2. Target volume modifications

Nodal Diameter and PET+	Action	Comment
< 1 cm (0.6 cm mediastinal) PET+ve	Include in GTV	Although FDG-PET/CT improved the sensitivity, it remained significantly lower than that for EUS (p = 0.001). → include EUS +ve
< 1 cm (0.6 cm mediastinal) PET-ve	Exclude from GTV	
> 1 cm (0.6 cm mediastinal) PET-ve	Include in GTV	

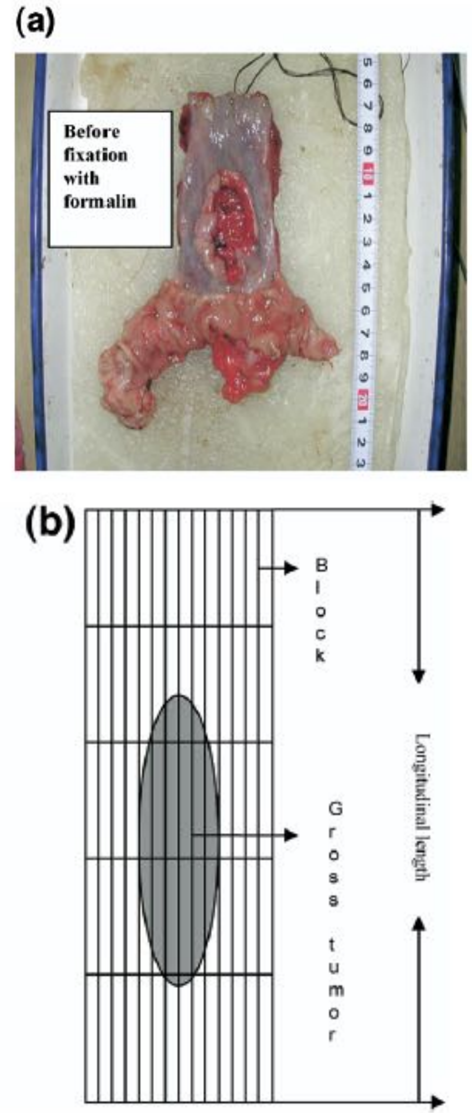
Vrieze et al. Radiother Oncol 73:269–275, 2004

3. Pathological validation of FDG-PET findings

Surgical specimens of esophageal SCC (n 34) and
GEJ adenocarcinoma (n 32)

	Proximal margin	Distal margin
Esophageal SCC	**30 mm** *	**30 mm** *
GEJ adenocarcinoma	**30 mm** *	**50 mm** *

***margin beyond the gross tumor that appeared to be adequate for negative microscopic spread in more than 94% of cases.**



to cover both submucosal tumour spread and lymphatics along the oesophagus, enlarged longitudinal safety margins

X.-S. GAO *et al.* Int. J. Radiation Oncology Biol. Phys., 2007

3. Pathological validation of FDG-PET findings

Correlation between diagnostic image and pathologic length of gross disease

	Endoscopic examination+/- Esophageal US	*CT scan*
Esophageal SCC	**Accurate**	Not always accurate (*Overestimates*)
GEJ adenocarcinoma	**Accurate**	**Accurate**

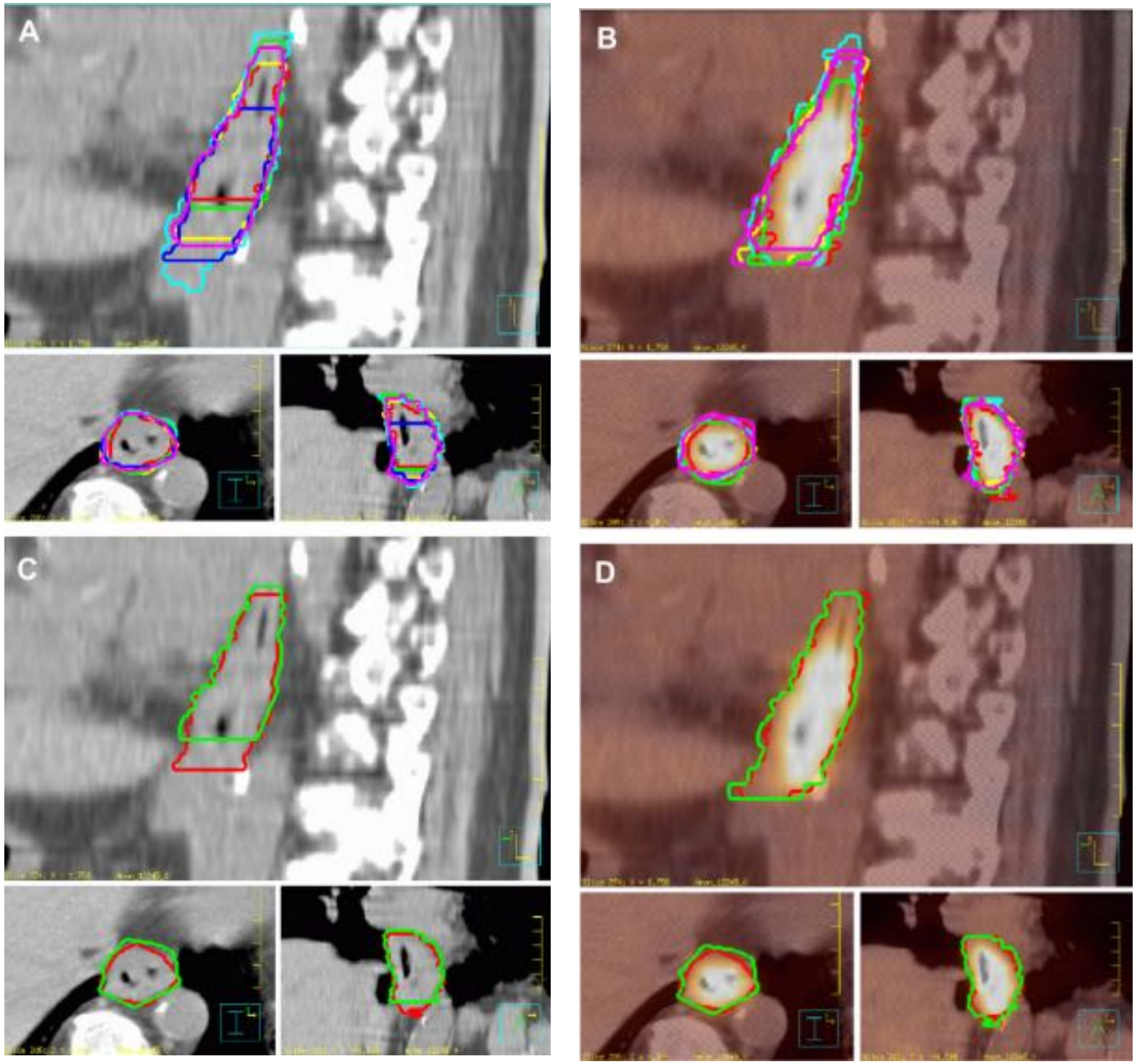
Table 1. Mean length of the esophageal tumor as measured by PET, EUS, and CT

p =0.0063

Tumor location	PET 2.0 SUV	PET 2.5 SUV	PET 3.0 SUV	EUS	CT
Upper/middle n = 8	5.5 cm (3.7, 7.4)	5.4 cm (3.5, 7.3)	5.1 cm (3.2, 7.1)	5.4 cm (2.9, 8.0)	7.6 cm (5.2, 10)
Lower n = 8	5.6 cm (4.4, 8.1)	6.7 cm (5.6, 7.8)	6.4 cm (5.3, 7.6)	5.5 cm (4.1, 6.9)	7.6 cm (5.8, 9.5)
GE junction n = 9	4.5 cm (2.6, 6.3)	4.0 cm (2.1, 5.9)	3.6 cm (1.7, 5.6)	4.4 cm (2.9, 6.0)	5.8 cm (4.1, 7.6)

Konski et al. Int J Radiat Oncol Biol Phys 61:1123–1128, 2005

4. interobserver variability in target delineation



intraobserver agreement with the mean standard deviation in tumour length reducing from 5.3 mm to 1.8 mm (P =0.001),

improvement in Conformity Index = 0.73 for PET/CT versus 0.69 for computed tomography (P=0.05)

J.M. Wilson, Clinical Oncology 26 (2014) 581e596
C.T. Muijs et al. Radiotherapy and Oncology 97 (2010) 165–171

Great potential for optimizing (RT) treatment planning.

PET scans that are not recent or were acquired without proper patient positioning should be repeated for RT planning.

The best available approach employs integrated PET/CT images, acquired on a dual scanner in the radiotherapy treatment position after administration of tracer according to a standardized protocol, with careful optimization of images within the RT planning system

carefully considered rules for contouring tumor volumes.

MacManus M. Radiother Oncol. 2009

Co-registered PET and CT in radiation treatment planning

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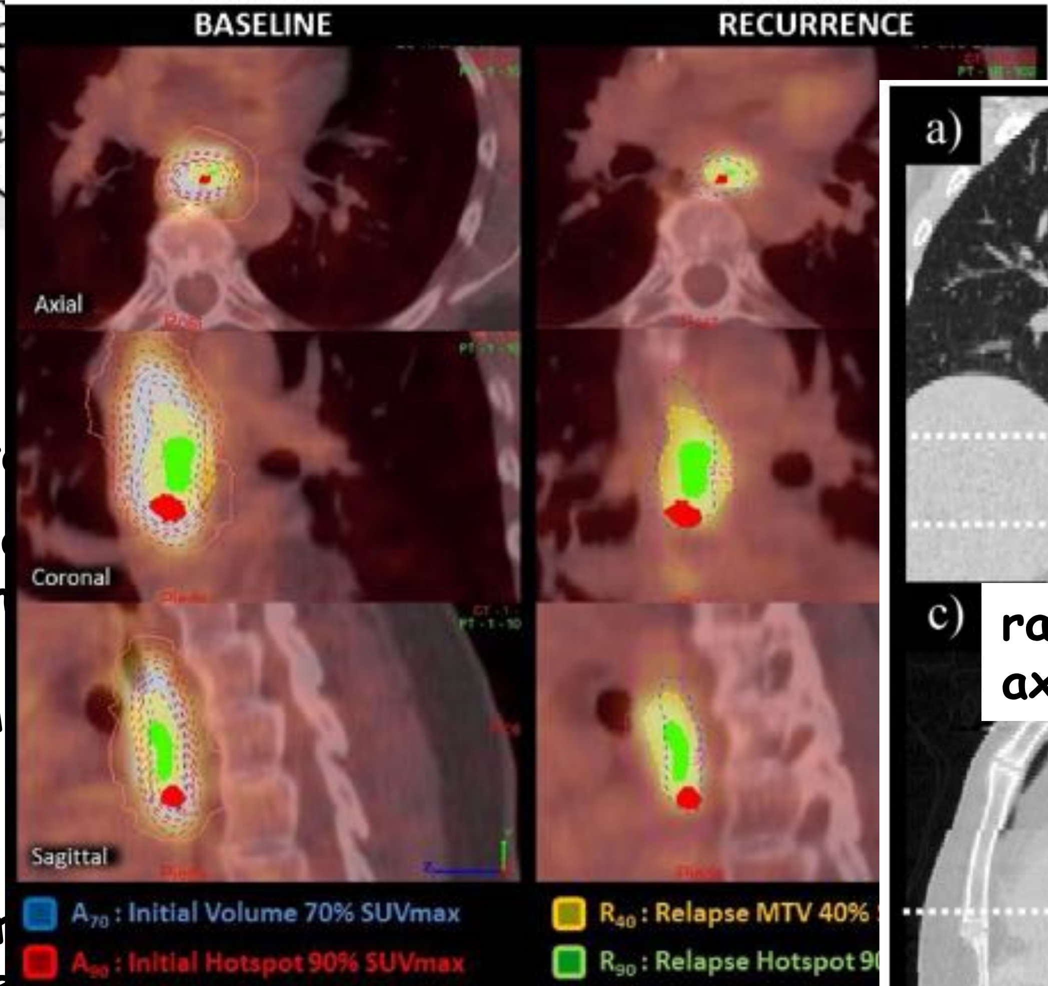
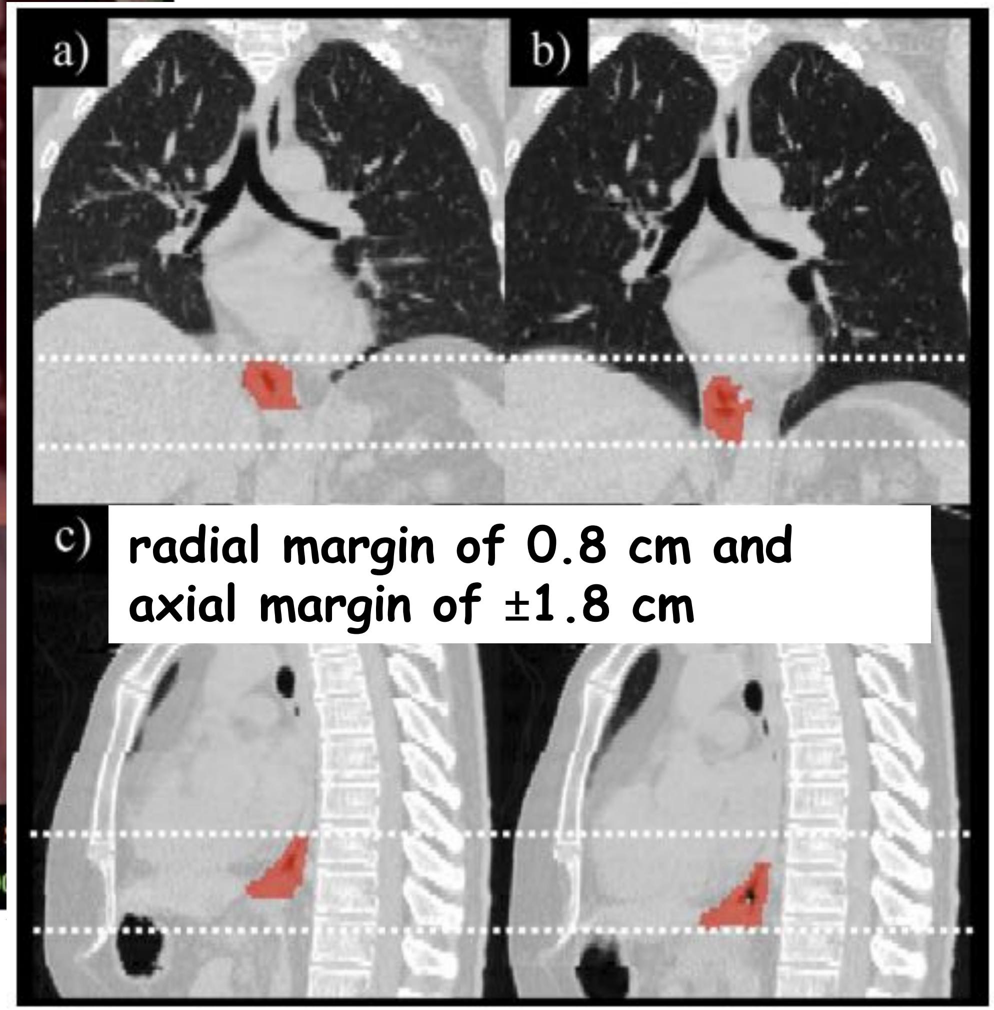




J.M. Wilson, Clinical Oncology 26 (2014) 581e596

BRIAN P. YAREMKO, Int. J. Radiation Oncology Biol. Phys., Vol. 70, No. 1, pp. 145–153, 2008

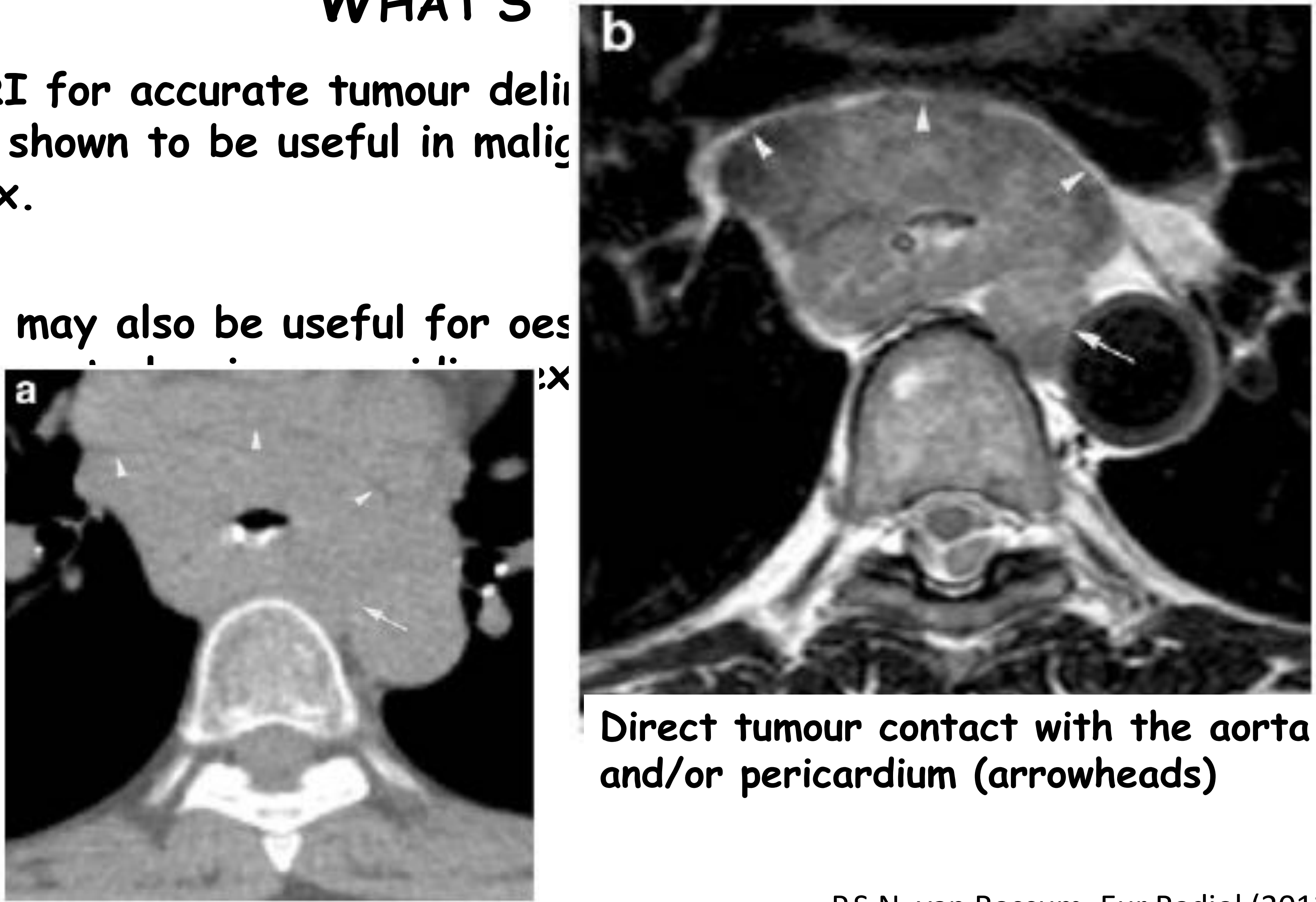
WHICH IMAGING?

CTV 1: GTV T & N

WHAT'S THE ROLE OF MRI?

• MRI for accurate tumour deli… …as already been shown to be useful in malig… …tate and cervix.

•MRI may also be useful for oes… …liation treat… …x…



Direct tumour contact with the aorta (arrow) and/or pericardium (arrowheads)

P.S.N. van Rossum, Eur Radiol (2013) 23:1753–1765

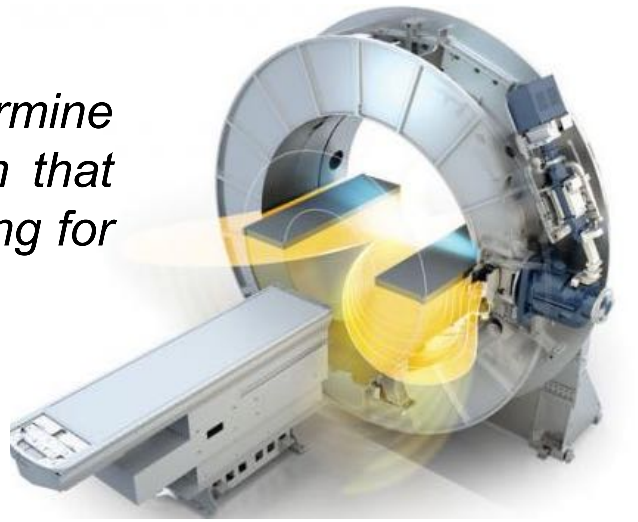
CTV 1: GTV T & N

investigational

WHAT'S THE ROLE OF MRI? where we are going ….

- **Limited data.**
- **More studies are required to clarify the potential role of high-resolution MRI including DWI for this purpose before any firm recommendations can be made.**
- **DWI displays esophageal <u>SCC lengths</u> most precisely when compared with CT or regular MRI. DWI scans fused with CT images can be used to improve accuracy to delineate GTV in esophageal SCC.**

Future clinical studies in oesophageal cancer should aim to determine the potential value of the recently developed MRI-linac system that integrates an MRI system with a radiotherapy accelerator, allowing for simultaneous irradiation and real-time MRI



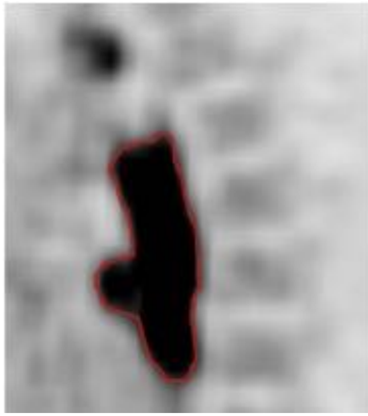
P.S.N. van Rossum, Clinical Radiology 70 (2015) 81e95

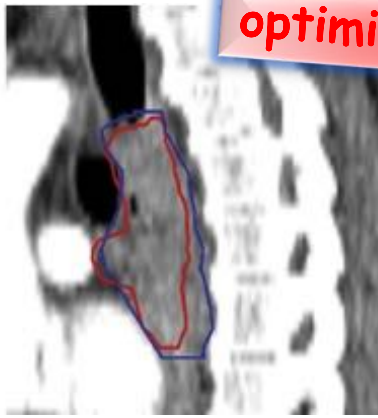
CONCLUSIONS

Delineation of the GTV on contrast-enhanced CT

standard

Corresponding PET may help to determine the shape and volume of the GTV and the biologically active volume



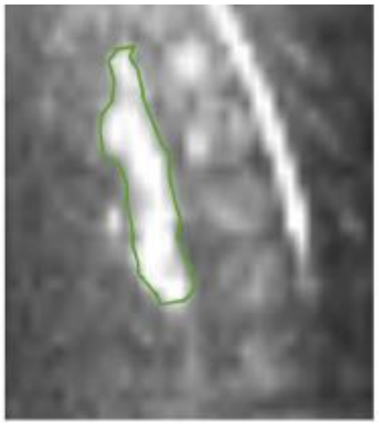


optimization

T2-weighted MRI provides higher soft-tissue contrast resolution compared to CT and may allow for further target definition improvement

investigational

Similar to PET, DWI may provide a better reflection of the true (functional) malignant volume and cranio-caudal length



investigational

thank for your attention

Luciana Caravatta

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