FDG-PET/CT in staging and treatment of esophageal cancer

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Chapter 4

Impact of 18-fluorodeoxyglucose positron emission tomography on computed tomography defined target volumes in radiation treatment planning of oesophageal cancer: Reduction in geographic misses with equal inter-observer variability

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Abstract

Background

Target volume definition in modern radiotherapy is based on planning computed tomography (CT). So far, 18-fluorodeoxyglucose positron emission tomography (FDG-PET) has not been included in planning modality in volume definition of esophageal cancer. This study evaluates fusion of FDG-PET and CT in patients with esophageal cancer in terms of geographic misses and inter-observer variability in volume definition.

Patients and Methods

In 28 esophageal cancer patients, gross, clinical and planning tumor volumes (GTV; CTV; PTV) were defined on planning CT by three radiation oncologists. After software-based positron emission tomography and computed tomography (PET/CT) fusion, tumor delineations were redefined by the same radiation-oncologists. Concordance indexes (CCI's) for CT and PET/CT based GTV, CTV and PTV were calculated for each pair of observers.

Results

Incorporation of PET/CT modified tumor delineation in 17/28 subjects (61%) in cranial and/or caudal direction. Mean concordance indexes for CT-based CTV and PTV were 72 (55–86)% and 77 (61–88)%, respectively, vs. 72 (47–99)% and 76 (54–87)% for PET/CT-based CTV and PTV. Paired analyses showed no significant difference in CCI between CT and PET/CT.

Conclusions

Combining FDG-PET and CT may improve target volume definition with less geographic misses, but without significant effects on inter-observer variability in esophageal cancer.

Introduction

In the treatment of esophageal cancer, radiotherapy is commonly used in combination with chemotherapy as neo-adjuvant treatment prior to surgery. Since there is no evidence of a survival benefit for patients getting surgery after chemoradiation compared with patients with chemoradiotherapy alone, it should be considered a valid alternative for treatment of esophageal cancer, especially in patients not fit enough for extensive surgery.1–3

Currently, modern radiotherapy includes target volume definition based on planning computed tomography (CT) scan. Target volume definition includes delineation of the gross tumor volume (GTV, i.e., the primary tumor and lymph node metastases); the clinical target volume (CTV, i.e., the GTV plus a safety margin in all directions and the elective nodal areas to cover potential microscopic disease); and planning target volume (PTV) to account for set-up inaccuracies and esophageal, cardiac and respiratory movements during radiation.

Until now, planning-CT based target volume definition is considered the gold standard. Limited depiction of pathologic changes in normal-sized structures and intrinsic lack of contrast between soft tissues may result in inter-observer variability in target volume delineation. Also, cranial and caudal tumor delineation can be complicated when the esophageal lumen has collapsed or the stomach is not totally expanded.4

Recently, applied dual-modality 18-fluorodeoxyglucose positron emission tomography and computed tomography (FDG-PET/CT) might have advantages to determine the GTV and the extent of its motion in several directions, as PET/CT imaging improves by reducing the PET scan time considerably from 45 to 60 min to 10–20 min for PET/CT using CT for attenuation correction.5 By combining two complementary techniques into one new imaging device, functional abnormalities can be visualized with high accuracy and facilitates the differentiation between physiological and pathological uptake, reducing the

incidence of both false positive and false negative outcomes.6–8 Therefore, PET/CT may play an important role in increasing the accuracy of tumor delineation and clinical outcome after radiotherapy. In several studies, PET/CT has a significant impact on the GTV, CTV and PTV and may result in a reduction of radiation-induced toxicity and improvement of loco-regional tumor control.9

The current study was initiated to test the hypothesis that the addition of FDG-PET to planning-CT results in a more accurate radiation planning with less inter-observer variability in the delineation of the GTV among patients with esophageal cancer as compared with planning-CT alone.

Patients and methods

This study is a retrospective radiotherapy (RT) planning study that utilizes diagnostic CT and FDG-PET images of patients with esophageal cancer from a prospective surgical study that looked at FDG-PET for staging. All patients had given informed consent and were entered between October 2002 and August 2004. They were staged by endoscopic ultrasonography (EUS), cervical/thoracic/abdominal CT, whole body FDG-PET, external ultrasound (US) of the neck, and fine needle aspiration biopsy (FNAB) or other additional investigations on indication. Tumors were staged according to the latest tumor-node-metastasis (TMN) system of the Union Internationale Contre le Cancer (UICC).10 Lymph node metastases within 1 cm of the celiac trunk were classified as M1a in case of distal esophageal cancer and as M1b in case of mid- or proximal esophageal cancer. Cervical metastases were graded as M1a in case of proximal cancer and as M1b when the tumor was located in the mid- or distal esophagus. Suspicious lymph nodes were verified by cytological or histological examination or otherwise by 12 months of radiological and clinical follow-up if pathological examination was not possible.

Patients

Eligible patients presented with a curatively resectable tumor, except for T1N0, of the thoracic esophagus. Patients with non-resectable T4 tumors invading into vital structures or with distant metastases (M1b), either lymphatic or hematogenous, were excluded from this study. Also excluded were patients who underwent recent thoracic surgery and/or stent placement. Twenty-eight patients fulfilled the eligibility criteria and were included in the study. The median age was 63 years (range: 48–80). Patient and tumor characteristics are listed in Table 1.

Table 1. Patient characteristics

Characteristics	*n = 28 (%)*
Sex	
Male	23 (82)
Female	5 (18)
Age (years)	
Mean (range)	63
Range	48 - 80
Histology	
AC	24 (86)
SC	4 (14)
Localization	
High	3 (11)
Low	21 (75)
GEJ	4 (14)
Clinical stage	
T2N0M0	4 (14)
T2N1M0	1 (4)
T3N0M0	8 (29)
T3N1M0	12 (43)
T3N1M1a	2 (7)
T4N1M0	1 (4)

AC, adenocarcinoma; clinical stage, staging based on clinical examination, endoscopic ultrasound, computed tomography, positron emission tomography, additional investigations when necessary but without FDG-PET/CT fusion; GEJ, gastroesophageal junction; SC, squamous cell carcinoma.

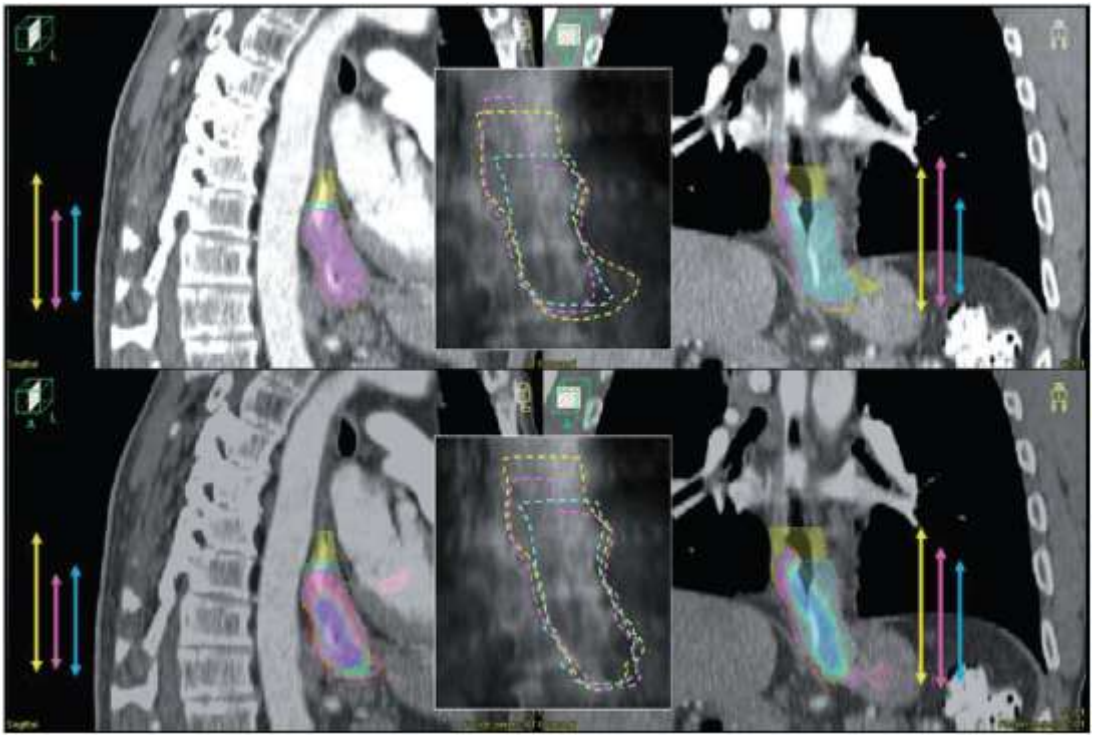
Imaging protocol

CT scans and whole body FDG-PET scans were performed within 2 weeks after the initial diagnosis. CT scans were performed with a 16 or 64 multidetector row spiral CT scanner (Somatom Sensation, Siemens Medical Systems, Erlangen, Germany). Patients had to drink 500 mL of oral contrast fluid directly before the scanning process. CT scans were obtained in cranial-caudal direction from the lower neck to the upper abdomen, including the liver, 70–90 seconds after an intravenous injection of 120 mL iodixanol contrast (Vispaque, GE Healthcare

Worldwide, Buckinghamshire, UK). Arms were positioned upward above the head and the examination was performed at maximal inspiration. Image slices had a 3-mm reconstructed thickness with a 1.5-mm effective section thickness (collimation 16 × 1.5 mm). Lymph nodes measuring 10 mm or more were considered malignant as well as round hypo-dense lymph nodes measuring >5 mm.

FDG-PET scans were performed with an ECAT 951/31 or an ECAT HR+ positron camera (Siemens/CTI, Knoxville, TN, USA). The 951/31 acquires 31 planes over 10.9 cm, while the HR+ acquires 63 planes over a 15.8 cm axial field of view. Patients had to fast for at least 4 hours before 190–810 MBq FDG (mean dose 396 MBq, s.e. 7.5 MBq, depending on body weight) was administered intravenously. Ninety minutes after contrast injection, emission scans were performed for 5 min per bed position from the skull base to mid-femur, arms beside the body. Transmission scans were performed for 3 min per bed position allowing attenuation correction. Scans were corrected for decay, scatter and randoms, while ordered subset expected maximization (OSEM) with two iterations and 16 subsets was used for reconstruction. A Gaussian filter of 5 mm full width at half maximum was used for post smoothing of the reconstructed images.11 FDG-uptake was scored by two nuclear medicine physicians on a four-point scale of intensity: 'normal' (physiological), 'slightly increased,"moderate increased' and 'intense increased.' Interpretation of intensity was scored on a five-point scale: 'absolutely benign,"probable benign,"indeterminate,"probably malignant' and 'definitely malignant.' All 'indeterminate,"probably malignant' and 'definitely malignant' lesions were defined as hotspot. Suspect lesions (scores 3–5) were verified by FNAB, pathological examination during or after surgery, or otherwise by radiological and clinical follow-up to one year.

Figure 1. Sagittal and coronal cross-sections of a tumor located at the gastro-esophageal junction



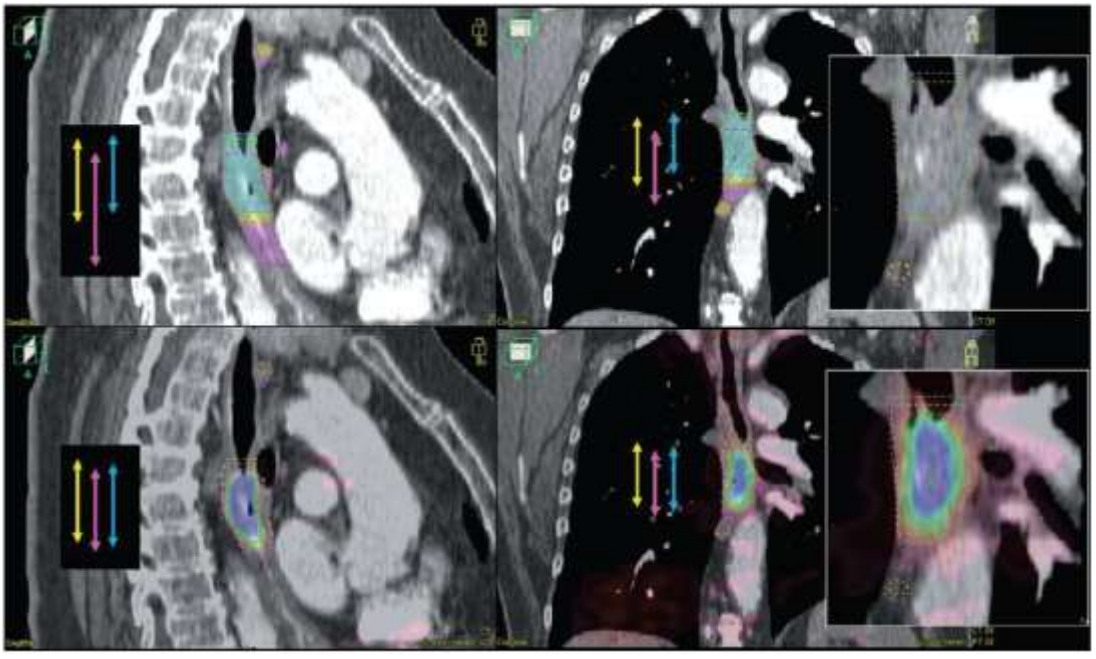
Especially the tumor's extension into the stomach is vague. PET/CT imaging decreased the inter-observer variability (Patient 6; mean CCI of CT-GTV: 57% vs. mean CCI of PET/CT-avid GTV: 64%). Left-side: sagittal cross-sections; right-side: coronal cross-sections; on top: CT-images; beneath: PET/CT images; in the middle: transmission scans with CT structures (above) and PET/CT-avid structures (below); pink and blue and yellow structures: three different delineations of three different observers.

Data interpretation and analyses

Cervical/thoracic/abdominal CT images were reviewed by two experienced radiologists and FDG-PET images were reviewed independently by two experienced nuclear physicians. The GTVs of the primary tumor (GTV-pt) and suspicious lymph nodes (GTV-ln) visible on CT were defined independently and blinded to each other by three experienced radiation-oncologists (observers A, B and C), using additional information of the EUS (including tumor length, location, extension, and suspicious nodes) FNAB, physical examination and knowledge of clinical tumor behavior. The CTV was defined as the CTVs of the

primary tumor (CTV-pt) and lymph node metastases (CTV-ln) as far as they did not overlap each other. The CTV-pt was delineated as the GTV-pt plus a margin of 10 mm in the transversal plane and a 20-mm margin in caudal direction if the tumor was expanded into the stomach or otherwise a 30 mm margin in cranial-caudal direction, following the curves of esophagus with exclusion of bony structures. For lymph nodes, a 10-mm margin in the whole circumference in the transversal plane was added to the GTV-ln. The PTV was automatically generated by adding a 3D-margin of 10 mm around the CTV.

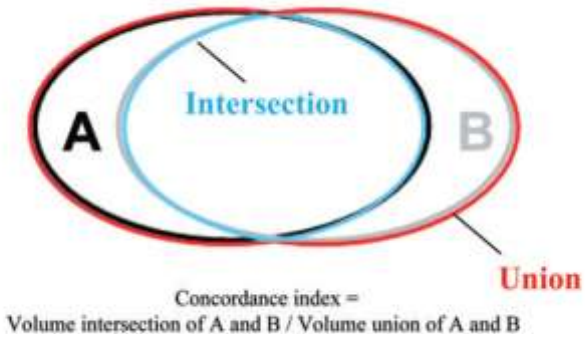
Figure 2. Sagittal and coronal cross-sections of a tumor located in the distal part of the esophagus, with major differences in cranial-caudal delineation



Incorporation of FDG-PET imaging decreased both tumor length and inter-observer variability (Patient 10; mean CCI of CT-GTV: 56%, vs. mean CCI of PET/CT-avid GTV: 76%, tumor length on CT: 52 mm vs. 48 mm on PET/CT). Left-side: sagittal cross-sections; right-side: coronal cross-sections with enlargements of the tumor delineations; on top: CT-images, beneath: PET/CT images, coronal images of the CT structures (above) and PET/CT-avid structures (below); yellow, pink and blue structures: three different delineations of three different observers.

Software-based PET/CT fusion was accomplished on a Siemens Workstation using the Oncentra MasterPlan software program. An experienced physician carried out or supervised the fusion process. To differentiate tumor from normal tissue, we did not estimate a rigid standard uptake value (SUV), but we used the method which is described as superior by Nestle.12 In this method, FDG-uptake in the liver tissue is used as reference tissue for FDG-uptake under fasting conditions. The diameter of an FDG hot spot consisted with the CT tumor diameter on one slice with maximal tumor size. After software-based PET/CT fusion, tumor delineations were redefined independently and blinded by the same radiation oncologists (Figures 1 and 2).

Figure 3. Concordance index



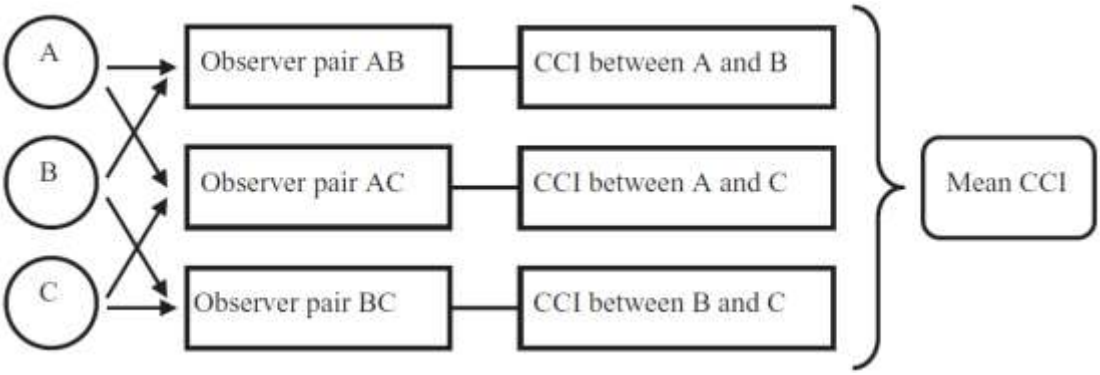
A: volume delineated by observer A (grey**),** B: volume delineated by observer B (black)**,** Volume intersection (blue), volume union (red)

The length of the esophageal tumor was measured in cranial-caudal direction both on CT and PET/CT by all three observers. Mean tumor length and target volumes were calculated per patient for statistical analysis. Volume intersections (Vi) and volume unions (Vu) of GTV, CTV and PTV were calculated for all three pairs of observers. Inter-observer concordance indexes (CCI) were computed by dividing the Vi of one observer pair by the Vu of that observer pair (Figure 3). Mean CCIs were calculated per subject. These calculations were executed for both

CT-based volumes and PET/CT based volumes. Finally, the volume intersections of CT and PET/CT-based GTV, CTV and PTV were calculated per observer. With this, the volume percentages of PET/CT-avid target volumes situated outside the CT volumes were computed by dividing the PET/CT volumes by the volume intersections of CT and PET/CT volumes. These percentages were also averaged per patient (Figure 4).

Both target volumes and CCIs in CT and PET/CT-based target volume definition were compared in nonparametric paired analysis using the Wilcoxon test. *P*-values <0.05 were considered statistically significant (SPSS 16.0 for Windows).

Figure 4. Stream flow per patient



CCI, concordance index. The mean CCI was calculated from the CCIs of all three observer pairs. This was done for both CT and PET/CT-based target volume definition.

Results

Tumor length and target volumes

The mean tumor length on CT was 58.1 mm (range: 18.0–97.5; 95% CI: 49.9–66.4) vs. 57.1 mm (range: 33.0–99.7; 95% CI: 50.0–64.2) on PET/CT. In 15 out of 28 patients (54%), the mean observed PET/CT-based tumor length was significantly smaller than the mean observed CT-based length (mean decrease in tumor length: 7.2 mm; P= 0.001), and in nine cases it was significantly larger (mean increase in tumor length: 9.2 mm; P= 0.008). However, these changes by PET/CT were not significant when decreases and increases in tumor length were taken together (P= 0.639). The mean difference between CT and PET/CT-avid tumor length was 1.1 mm (range: −24.0–27.0).

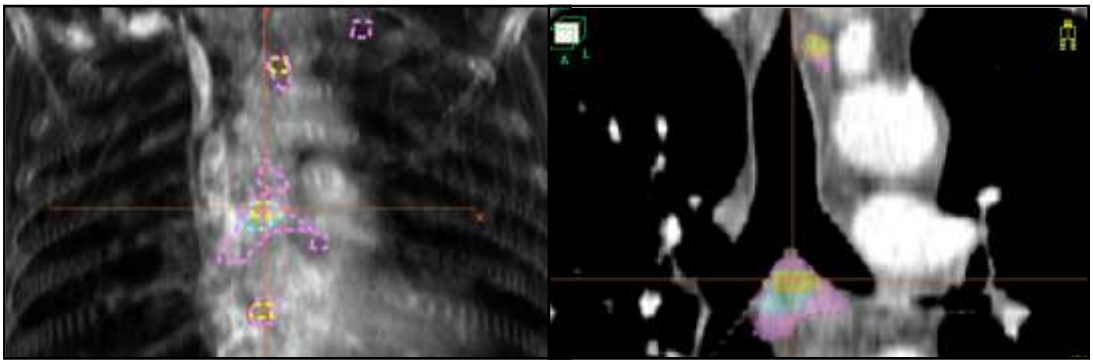
The mean GTV-pt increased after PET/CT fusion from 46.2 cm3 (range: 4.8–116.5; 95% CI: 34.4–58.0 cm3, Table 2) to 48.8 cm3 (range: 8.1–138.0; 95% CI: 36.1–61.6 cm3), which was not statistically significant (P= 0.785). In 11 out of 28 patients (39%), FDG-PET information led to an increase in the GTV-pt (mean increase: 13.3 cm3; range: 0.1–33.1 cm3) and in 17 patients (61%) to a decrease (mean decrease: 4.3 cm3; range: 0.3–9.4 cm3). Sixteen patients (57%) had suspicious lymph nodes as assessed by conventional staging techniques without FDG-PET. Especially regarding lymph node involvement, there was a major difference between observers, both in number as in localization of the nodes (Fig. 5). Delineation of suspicious lymph nodes was not altered by the addition of PET/CT. The PTV increased from 578.0 cm3 (range: 225.2–1015.7; 95% CI: 505.4–650.5) to 581.8 cm3 (range: 279.3–1011.8; 95% CI: 509.87–653.79), which was also not significantly different (P= 0.399).

Table 2. Mean target volumes of three independent observers

Patient number (n=28)	*Mean $GTV_{pt\text{-}CT}$ (cm^3)*	*Mean $GTV_{pt\text{-}PET/CT}$ (cm^3)*	*Mean CTV-CT (cm^3)*	*Mean CTV-PET/CT (cm^3)*	*Mean PTV-CT (cm^3)*	*Mean PTV-PET/CT (cm^3)*
1	8,43	8,10	104,37	101,60	283,63	279,33
2	41,07	39,83	234,47	232,80	517,37	515,17
3	102,37	92,93	493,03	468,00	1015,67	978,03
4	70,43	67,20	352,70	336,47	744,53	700,23
5	33,97	29,80	237,37	224,60	553,83	524,17
6	44,43	49,53	263,37	262,17	582,67	572,60
7	36,70	31,83	279,13	265,80	680,63	658,47
8	22,10	21,23	203,10	205,50	467,60	474,47
9	31,07	29,70	180,40	178,30	417,60	413,00
10	21,27	20,50	184,73	174,00	460,17	438,40
11	116,47	137,20	450,30	505,93	905,97	1011,77
12	20,47	21,07	144,67	147,00	356,13	360,57
13	86,43	80,60	341,37	333,20	700,33	695,43
14	33,73	28,80	293,37	287,53	676,53	670,43
15	57,17	53,23	277,57	255,90	601,03	559,03
16	67,70	59,27	366,00	334,83	790,80	727,90
17	31,03	32,70	217,27	220,93	509,43	505,33
18	107,67	138,00	405,87	467,50	844,73	945,67
19	35,67	31,57	205,20	178,90	491,47	452,70
20	4,77	37,90	79,93	204,37	225,17	457,13
21	36,47	46,63	248,43	268,60	566,43	589,27
22	14,67	11,83	123,00	111,70	311,83	287,00
23	26,93	59,40	216,20	278,53	529,37	609,87
24	54,10	58,30	292,93	301,90	611,17	646,60
25	31,13	42,97	219,80	254,33	491,77	555,07
26	28,93	23,17	190,40	172,50	465,47	436,57
27	92,43	83,60	381,43	358,30	785,23	736,93
28	35,50	30,03	267,53	202,80	596,27	490,17
Mean	**46,18**	**48,82**	**259,07**	**261,93**	**577,96**	**581,83**
95%	**34.4-58.0**	**36.1-61.6**	**220.0-298.1**	**222.6-301.2**	**505.4-650.5**	**509.9-653.8**

CT, computed tomography; CTV, clinical target volume; GTV-pt, gross target volume of the primary tumor; PET/CT, fusion of positron emission tomography and computed tomography; PTV, planned target volume; 95%, 95% confidence interval.

Figure 5. Gross tumor volume of affected lymph nodes



Large differences in number and size of suspicious nodes were seen between different observers. Observer A (pink): 5 small and medium-sized nodes and one large conglomerate, observer B (blue): one medium-sized node, observer C (yellow): three small to medium-sized nodes. Leftside: transmission scan with involved nodes; rightside: coronal cross-section through the largest node.

Geographic misses

In 17 out of 28 patients (61%), addition of FDG-PET to the planning-CT led to cranial and/or caudal adjustment of the original tumor demarcation on the planning-CT; in three patients, both borders of the primary tumor on PET/CT were outside the CT-based CTV; in three patients, the cranial border was above the CT delineation; and in 11 patients, the caudal border was beneath the original delineation. Mean difference in cranial direction was 1.0 cm (range: 0.3–3.0) and in caudal direction 1.1 cm (range: 0.1–5.4). On average, 11% of the volume (three-dimensionally) of the PET/CT-avid CTV was located outside the planning-CT based CTV (range 1–72%, 95% CI: 5–17%).

Concordance indexes

Mean inter-observer CCIs are listed in Table 3. The mean inter-observer CCI among observer pairs in CT-CTVs varied from 55 to 86% (mean: 72%; 95% CI:

69–75%) vs. 47 to 83% in PET/CT-avid CTVs (mean: 72%; 95% CI: 68–75%). Mean concordance indexes in CT- PTVs varied from 61 to 88% (mean: 77%; 95% CI: 74–79%) vs. 54 to 87% in PET/CT-avid PTVs (mean: 76%; 95% CI: 73–80%). These differences were not statistically significant (P= 0.891 and 0.802, respectively).

Table 3. Mean concordance indexes in percentages

Patient number (n=28)	*Mean CCI GTVpt-CT (%)*	*Mean CCI GTVpt-PET/CT (%)*	*Mean CCI CTV-CT (%)*	*Mean CCI CTV-PET/CT (%)*	*Mean CCI PTV-CT (%)*	*Mean CCI PTV-PET/CT (%)*
1	40	46	62	67	69	74
2	81	79	82	82	86	86
3	63	66	68	70	73	76
4	63	77	74	77	79	80
5	64	75	68	75	77	77
6	57	64	72	76	76	81
7	53	52	67	62	73	72
8	68	62	82	82	86	85
9	76	71	72	71	79	79
10	56	76	63	71	67	74
11	68	71	74	74	76	77
12	56	53	70	67	75	72
13	83	82	82	79	86	82
14	75	69	68	64	76	72
15	70	76	76	80	79	83
16	72	66	72	66	79	72
17	73	68	81	78	87	85
18	48	79	55	70	61	73
19	82	74	86	83	88	87
20	48	58	65	69	74	75
21	52	52	73	62	76	68
22	70	69	78	82	82	86
23	66	34	69	47	71	54

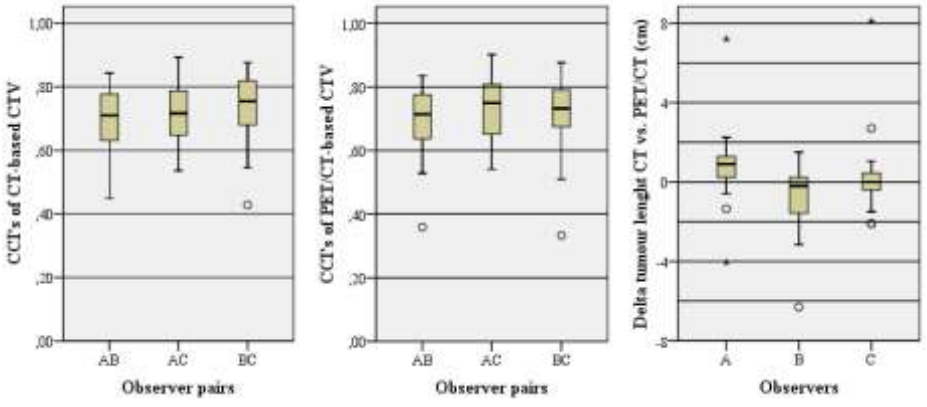
24	67	72	69	67	75	72
25	31	59	57	75	65	80
26	65	53	77	76	79	82
27	86	81	79	75	84	78
28	62	53	63	55	71	59
Mean	**64**	**66**	**72**	**72**	**77**	**76**
95%	**59-69**	**61-70**	**69-75**	**68-75**	**74-79**	**73-79**

Mean concordance indexes in percentages (%). CCI= concordance index, GTVpt= gross target volume of the primary tumour, CTV= clinical target volume, PTV= planned target volume. CT= computed tomography, PET/CT= fusion of positron emission tomography and computed tomography, 95%=95% confidence interval.

Observer dependent differences

Grouped by each observer pair, there were modest differences between CCIs of different pairs, both for CT as PET/CT delineation (Fig. 6). These differences were not statistically significant. The mean difference in tumor length, grouped by observer, was nearly zero after application of PET/CT imaging, and therefore, was not observer-dependent.

Figure 6. Box plots of concordance indexes between observer pairs for CT-based CTV and PET/CT-based CTV (on top) and delta tumor lengths for each observer (below)



CCI, concordance indexes between observer pairs, delta tumor length, tumor length on CT minus tumor length on PET/CT. Differences between observers are visible, as observer B altered his delineation much more than A and C.

Discussion

Radiation oncologists determine the various radiation volumes on all clinical and radiographic examinations as all results are complementary to each other with different contributions to give. Although logical, the additional value of FDG-PET to current CT-based radiotherapy planning still is unclear.

The main purpose for successful irradiation is delivery of an optimal radiation dose on tumor tissue with a minimum of geographic misses on the one side and a minimum of irradiation injury of healthy tissue on the other side. However, a major clinical issue still remains unresolved; target volume delineation itself remains uncertain as it is prone to a large inter-observer variability.13,14 In this study, we showed that incorporation of FDG-PET in CT-based radiation planning for esophageal tumors may be important, as software-based PET/CT had major effects on target volume definition in 61% of the subjects (17/28) with a rate of 11% of the volume of the PET/CT based CTVs situated outside the CT-based target volumes. In this way, PET/CT has the potential to avoid geographical misses. With concordance indexes of 63–76% for different target volumes, observer variation remains one major determinant of target delineations. We observed neither significant improvement nor deterioration by PET/CT on the inter-observer variability.

Incorporation of FDG-PET in radiotherapy planning has been mainly investigated in non-small-cell lung cancer and head and neck cancer and an increasing number of studies in esophageal cancer demonstrate its significant impact on target definition as well.15,16 Recently, Hong et al. compared two different PET/CT-based techniques with CT-only based esophageal tumor definition. Both manual and semiautomatic contouring on specific thresholds affected target definition, though the two PET/CT-based techniques produced significantly different tumor volumes in 15 patients (56%).17 Another study reported a substantial reduction of target volumes by using PET/CT in treatment planning in a large majority of patients (63% of esophageal patients

vs. 86% of lung cancer patients).18 Konski et al. also found a significant smaller tumor length of 5.4 cm (95% CI: 4.4–6.1 cm) on PET/CT compared with 6.8 cm on CT (95% CI: 5.6–7.9 cm).19 Leong et al. reported that the CT-based GTV excluded PET-avid disease in 11/21 patients (69%), and a geographic miss of gross tumor in 5/21 patients (31%). The discordance between CT and PET/CT was due mainly to differences in defining the longitudinal extent of disease in the esophagus.4 In the study of Moureau-Zabotto et al., PET/CT fusion appeared to decrease the GTV in 12 (37%) of the 43 patients, owing to a reduction in tumor length. However, PET/CT fusion also appeared to increase the GTV in 21% (n= 7), owing to an increased tumor and the detection of occult lymph node metastases.20

Spatial resolution of an FDG-PET is limited to at least 5 mm. Therefore, small suspicious lymph nodes may be missed on FDG-PET. Difficult decisions may occur when there is no consensus regarding lymph node metastases between FDG-PET and CT/EUS. Not including suspicious lymph nodes on CT or EUS in the target volume based on negative FDG-PET imaging would be incorrect and may have serious consequences. However, the radiobiological significance of FDG-negative tumor margins remains unclear until the longer-term outcomes data come through to show that FDG-based definition of treatment volumes really does improve the therapeutic index. Conversely, including false positive nodes in the target volume may lead to an increased radiation field with the possibility of late radiation toxicity.

In this study, we chose for tumor delineation the method which is described as superior by Nestle et al. using the mean activity of the liver as reference value for physiological soft tissue uptake of FDG under fasting conditions. Other semi-quantitative methods used for tumor contour definition by FDG-PET are visually correlation, the use of an FDG intensity level with a threshold of 40% of the maximum SUV, and the use of an isocontour of SUV = 2.5 around the tumor.21 Of these three different techniques, a cut-off value of 2.5 SUV

provided the closest estimation in radiotherapy planning. Since other studies measured substantially different volumes with these techniques, especially in inhomogeneous tumors, they appeared to be less accurate and less reproducible than the method which uses liver FDG-uptake as cut-off value.12,22

In software fusion, time and patient positions are different for CT and PET scanning. Because difference in patient positions, i.e., arms above the head for CT and arms beside the body for PET and respiratory activity between the CT plan and PET/CT, it is difficult to compare tumor volumes and lengths, particularly when the differences are small. CT imaging is usually performed in maximum inspiration in several seconds and FDG-PET imaging is completed in half an hour of moderate respiration. In the last few years, hybrid PET/CT scanners together with respiration-gated acquisition are more and more used for staging properties, but not yet in radiotherapy planning. This study indicates what could be the impact of hybrid PET/CT on target volume planning and inter-observer variability. Further investigations, including pathological examination on resected specimen are needed for a standard use of hybrid PET/CT in the radiation planning of esophageal tumors.

In conclusion, incorporation of FDG-PET imaging in CT-assisted volume definition seems to have a great impact on target volume definition with the potential to reduce geographical misses, though without significant interference of the inter-observer variability.

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