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^{18}F-fluorocholine PET-guided target volume delineation techniques for partial prostate re-irradiation in local recurrent prostate cancer

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ABSTRACT

Background and purpose: We evaluate the contribution of ^{18}F-choline PET/CT in the delineation of gross tumour volume (GTV) in local recurrent prostate cancer after initial irradiation using various PET image segmentation techniques.

Materials and methods: Seventeen patients with local-only recurrent prostate cancer (median = 5.7 years) after initial irradiation were included in the study. Rebiopsies were performed in 10 patients that confirmed the local recurrence. Following injection of 300 MBq of ^{18}F-fluorocholine, dynamic PET frames (3 min each) were reconstructed from the list-mode acquisition. Five PET image segmentation techniques were used to delineate the ^{18}F-choline-based GTVs. These included manual delineation of contours (GTV_{man}) by two teams consisting of a radiation oncologist and a nuclear medicine physician each, a fixed threshold of 40% and 50% of the maximum signal intensity ($GTV_{40\%}$ and $GTV_{50\%}$), signal-to-background ratio-based adaptive thresholding (GTV_{SBR}), and a region growing (GTV_{RG}) algorithm. Geographic mismatches between the GTVs were also assessed using overlap analysis.

Results: Inter-observer variability for manual delineation of GTVs was high but not statistically significant ($p = 0.459$). In addition, the volumes and shapes of GTVs delineated using semi-automated techniques were significantly higher than those of GTVs defined manually.

Conclusions: Semi-automated segmentation techniques for ^{18}F-choline PET-guided GTV delineation resulted in substantially higher GTVs compared to manual delineation and might replace the latter for determination of recurrent prostate cancer for partial prostate re-irradiation. The selection of the most appropriate segmentation algorithm still needs to be determined.

A substantial number of prostate cancer patients develop biochemical recurrence within 10 years after curative radiotherapy (RT) [1,2]. Many of these patients will have local recurrence as the only site of disease [2]. Currently, there is no consensus regarding the optimal management of these patients. The most often considered strategy is androgen depression therapy which provides tumour control of limited duration [3]. Other treatment options are salvage prostatectomy, cryotherapy, brachytherapy, and high-intensity focused ultrasonography (HIFU) [4]. All of these local salvage treatment modalities have shown to be associated with a high rate of severe side effects [4].

Partial re-irradiation of the prostate might be an interesting alternative for the following reasons: (i) the rate of multifocal prostate cancer is substantially reduced in the case of local recurrence following external beam radiation therapy [5–8]; (ii) recent advances in molecular PET/CT imaging using ^{18}F-choline or ^{11}C-choline, along with many other recent probes [9], have shown its high potential in visualizing recurrent prostate cancer with high sensitivity and specificity [10,11]; (iii) intensity-modulated radiation therapy (IMRT), image-guided RT (IGRT), and brachytherapy allow highly precise and focused targeting with better sparing of surrounding healthy tissues such as the rectum and the urethra [12,13]. These advances in molecular imaging and radiation treatment planning and delivery give the opportunity to evaluate new indications such as partial prostate re-irradiation in local recurrent prostate cancer.

The delineation of gross tumour volume (GTV) in patients with local recurrent prostate cancer after initial irradiation using ^{18}F-choline PET/CT is very challenging [14]. Accurate delineation of target regions is crucial; however, vascular and urinary activity might disturb the exact determination of the recurrent tumour [15]. Various methods for PET-based target volume delineation have been

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suggested [16]. Despite the high intra- and inter-observer variability, time consuming manual delineation procedures by experienced radiation oncologists or nuclear medicine physicians are still the most widely used techniques in the clinic. Compared to manual delineation of target volumes, semi-automated or fully automated delineation using computer algorithms allows to achieve a higher reproducibility and to lower subjectivity [17,18]. The objective of this study is to assess the potential of this category of PET image segmentation techniques and to compare the GTVs delineated using various target delineation strategies for ^{18}F-fluorocholine PET-based radiation therapy treatment planning of recurrent prostate cancer.

Materials and methods

This retrospective data analysis was approved by the Ethical Committee of Geneva University Hospital and performed in conformance with the Swiss legislation regarding patient confidentiality and data protection. All patients provided their written informed consent to the use of ^{18}F-fluorocholine as an unregistered radiopharmaceutical that was authorized for each patient by the Swiss federal authorities (Swissmedic and Federal Office of Public Health, section of radiation protection).

Patients

Between April 2006 and February 2008, 30 patients with biochemical recurrent prostate cancer after curative RT were evaluated with ^{18}F-fluorocholine PET/CT in our institution. Seventeen of these patients presenting with local-only recurrent prostate cancer were selected for this retrospective evaluation. Thirteen of these patients presented with biochemical recurrence >4 years after initial RT. Initial combined hormone and radiation therapy was performed in 9 patients and RT alone in 8 patients. Three of these patients (3/8) received a brachytherapy boost. The median time between RT treatment and the PET study was 5.7 years. None of the patients was under hormonal therapy when PET scanning was performed. The clinical characteristics and referral patterns of the patient population are summarized in Table 1. The relatively small number of clinical studies included in this study is mainly due to financial constraints, given that ^{18}F-choline PET studies are not reimbursed in Switzerland. It should be emphasized, however, that the number is sufficient for reliable statistical analysis thus allowing to achieve the objectives set.

Table 1
Clinical characteristics and referral patterns of the patient population (n = 17).

Characteristics	Median (range)	Number (%)
Age at recurrence (y)	76 (63–86)	
Initial stage		
cT1c		2 (12)
cT2		4 (23)
cT3		11 (65)
cN0		16 (94)
cN1		1 (6)
Initial PSA (ng/ml)	12.2 (5.2–73.0)	
Initial Gleason score		
5–6		10 (59)
7		4 (23)
8–9		3 (18)
Total dose of RT (Gy)	74.4 (70.0–78.4)	
Pelvis irradiation		7 (41)
Brachytherapy boost		3 (18)
Hormonal therapy		9 (53)
Nadir PSA (ng/ml)	0.38 (0.08–2.13)	
Recurrence time (y)	5.71 (2.17–8.47)	
PSA at PET-CT (ng/ml)	5.14 (2.47–16.05)	
PSADT (month)	9.0 (2.9–25.8)	
Biopsy at recurrence		10 (59)
Endorectal IRM		16 (94)
Bone scan		17 (100)

Abbreviations: PSA, prostate-specific antigen; RT, radiation therapy; PSADT, prostate-specific antigen doubling time.

^{18}F-fluorocholine synthesis

^{18}F-fluorocholine (fluorocholinefluoromethyl-dimethyl-2-hydroxyethylammonium) was prepared according to GMP conditions at the Centre of Radiopharmacy, University Hospital of Zürich, Switzerland [19]. All patients received a standard activity of 300 MBq of ^{18}F-fluorocholine resulting in an average effective dose of 8.2 mSv [20].

PET/CT scanning protocol

PET/CT studies were performed on two commercial LSO-based PET/CT scanners, namely the Biograph 16 and Biograph 64, equipped with utilities for PET/CT-guided radiation therapy treatment planning (Siemens Medical Solutions, Erlangen, Germany). All patients were fasted for at least 4 h before the ^{18}F-fluorocholine PET study. After bladder voiding, patients underwent an initial low dose CT scan from the mid thigh to the skull. Following the CT scan, patients underwent a continuous list-mode PET data acquisition of the pelvis for 10 min starting immediately at the time of tracer injection. Three dynamic frames (3×3 min) were then binned from the list-mode file. Following the list-mode acquisition, a standard whole-body static PET study was performed from the mid thigh to the skull over 7–8 bed positions of 3–4 min each, depending on patient size and weight. An additional late image (5 min) of prostate bed was acquired after whole-body PET ($\sim$40 min after tracer injection). Careful assessment of PET images generated using this protocol allowed to conclude that the second dynamic frame (4–6 min post injection) is the most reliable for accurate target delineation owing to better discrimination of blood pool and urinary activity from recurrent cancer [15].

PET/CT interpretation

PET/CT interpretation was performed by two experienced nuclear medicine physicians. A multimodality computer platform (Syngo Multimodality Workplace, Siemens Medical Solutions, Erlangen, Germany) was used for image review and interpretation. All PET/CT studies showing at least one site of abnormal ^{18}F-fluorocholine uptake in the prostate were characterized as recurrent cancer.

Transrectal multiple bilateral biopsies were performed in 10 patients which confirmed local recurrence. Recurrent cancer was diagnosed in at least one biopsy cylinder and no biopsy showed prostate cancer in a side of the prostate which was not displayed by the ^{18}F-fluorocholine PET/CT study. Owing to the absence of an indication for salvage local treatment, biopsy was not performed for seven patients who had severe comorbidities or were very old at the time of recurrence. Eight of the 17 patients have been followed with simple observation, whereas 4 patients received hormonal therapy. Five patients received a local salvage treatment, one of them was treated with a radical prostatectomy and 4 patients were treated with a combined hormonal radiotherapy using IMRT and a salvage irradiation dose of 63–70 Gy. An additional evaluation by bone scintigraphy was performed in all patients and was interpreted as negative.

PET-guided gross tumour volume (GTV) delineation

We used the second dynamic time frame (4–6 min after injection of ^{18}F-choline) for the delineation of GTVs reported in this

study. Disturbance by vascular and urinary activity could thereby be minimized, and enabled better target definition. As reported earlier, this timeframe was chosen as optimal following careful assessment of various dynamic sequences [15].

Manual GTV delineation

The TrueD software (Siemens Medical Solutions, Erlangen, Germany) was used for manual delineation of the GTV. The GTV (GTV_{man}) was delineated manually by two teams (GTV_{man1} and GTV_{man2}) consisting of an experienced radiation oncologist and a nuclear medicine physician (HW/MW and HV/CS). Besides the dynamic information extracted from the list-mode PET series, the whole-body and late PET/CT studies as well as all clinical history and previous imaging studies were provided.

Semi-automated PET image segmentation techniques

GTVs were also delineated using four semi-automated PET image segmentation techniques by means of the *RT_Image* software [21] as described in our previous work [22]. The assessed image segmentation techniques included: a fixed threshold of 40% and 50% of the maximum signal intensity to delineate $GTV_{40\%}$ and $GTV_{50\%}$, respectively, GTV delineation based on the region growing (GTV_{RG}) segmentation algorithm [21], and the signal-to-background ratio (SBR)-based adaptive thresholding technique (GTV_{SBR}) [23]. The scanner-specific parameters required for derivation of the adaptive threshold calibration curve were obtained through a phantom experiment with various signal-to-background ratios [22]. For GTV_{SBR} delineation, the maximum signal intensity of the tumour was defined as the mean activity of the hottest voxel and its eight surrounding voxels in a transversal slice, whereas the mean background activity was obtained from the mean of three manually drawn ROIs far away from the tumour. The GTVs obtained using semi-automated delineation algorithms were checked visually by an experienced radiation oncologist before approval.

Statistical analysis of GTVs

Quantitative evaluation of the difference between the obtained GTVs was performed using statistical analysis. Student's *t*-test values and the corresponding significance levels associated to Student's analysis (two-tailed test) were calculated for the volumes obtained using the different GTV delineation techniques. In addition, the geographic mismatch between the GTVs delineated using the different segmentation techniques was assessed through overlap volume analysis as described in our previous work [22]: the overlap volume of GTV_{man1} and five other remaining PET-based GTVs (GTV_{man2}, GTV_{SBR}, GTV_{RG}, $GTV_{40\%}$, and $GTV_{50\%}$) for which overlap was expressed as the overlap volume of GTV_{man1} and each of the remaining five GTV_{PET} relative to GTV_{man1} (overlap fraction (OF) man1 [OF_{man1}]). The same applies to GTVs defined using the other techniques to yield overlap fractions [OF_{man2}], [OF_{SBR}], etc. Statistical analyses and curve fitting were performed using SPSS® (version 15.0, SPSS Inc., Chicago, IL, USA). Regression analyses were used to evaluate differences between calculated volumes and overlap between GTVs when using the different segmentation algorithms.

Results

Table 2 summarizes the comparative evaluation of the various ^{18}F-choline PET-guided GTV delineation techniques for the 17 patients included in this study protocol. Nineteen lesions in total were assessed given that two lesions were detected on the PET scans of two patients. All semi-automated image segmentation techniques were able to technically achieve successful target volume delineation. This is in contrast with the gradient find and 2.5 SUV cut-off image segmentation techniques which might fail in case of low and inhomogeneous tumour uptake as reported in [22].

Table 2
Summary of gross tumour volumes (cc) derived using the different PET image segmentation techniques.

Pt. No	GTV_{SBR}	GTV_{RG}	$GTV_{40\%}$	$GTV_{50\%}$	GTV_{man1}	GTV_{man2}
1	14.3	15.9	17.8	8.8	4.0	3.9
2	11.3	11.4	11.7	8.2	3.3	5.9
3	14.2	12.9	14.8	7.8	18.3	14.5
4	4.2	5.5	5.5	4.1	7.4	5.2
5	2.0	1.5	2.3	1.5	0.6	1.6
	3.0	3.2	3.9	2.8	1.3	1.3
6	24.1	37.0	29.3	18.6	11.6	9.3
7	2.2	1.7	2.9	1.3	1.2	0.6
8	4.2	7.5	7.1	4.6	2.4	2.9
	3.4	4.1	4.3	3.5	0.3	0.3
9	22.3	29.1	21.7	11.0	25.5	18.4
10	1.7	2.4	1.5	0.6	0.5	0.3
11	5.9	7.2	7.6	5.3	2.0	0.9
12	6.9	3.8	7.2	3.6	3.4	3.0
13	18.7	16.3	18.1	10.9	8.2	12.5
14	14.7	17.6	18.3	13.0	9.2	6.7
15	9.4	10.5	15.1	11.9	1.6	1.3
16	14.2	20.5	20.4	13.3	6.0	7.3
17	3.2	7.5	3.4	2.7	3.4	6.0
Median	6.9	7.5	7.6	5.3	3.4	3.9
Range	1.7–24.1	1.5–37.0	1.5–29.3	0.6–18.6	0.3–25.5	0.3–18.4

Abbreviations: GTV, gross tumour volumes; SBR, signal-to-background ratio; RG, region growing; 40%, threshold of 40% of the maximum signal intensity; 50%, threshold of 50% of the maximum signal intensity; man, manual delineation of contours.

Fig. 1A–D shows CT, PET and fused PET/CT images of a 66-year-old patient with stage cT2b (patient 7 in Table 2) with PSA relapse 5.5 y after radical RT. The prostate-specific antigen doubling time (PSADT) was 9 months with a PSA of 6.76 ng/ml in the PET/CT study. The ^{18}F-choline PET study allowed to pinpoint the local recurrence (Fig. 1B), whereas the fused PET/CT image aided to accurately localize the lesion on the left side of the seminal vesicles (Fig. 1C). Notwithstanding, the volumes of the delineated GTVs varied between 0.6 and 2.9 cc, depending on the technique used, the centre of gravity of the target volumes did not vary too much (Fig. 1D).

Another case is shown in Fig. 1E–H where PET/CT images are depicted for an 86-year-old patient with stage cT3a, with PSA relapse 8 y after radical RT. The PSADT was 14 months with a PSA of 3.94 ng/ml in the PET/CT exam. Likewise, despite the enormous variability of the delineated PET-guided GTVs (between 6.7 and 18.3 cc), they were all concentric (Fig. 1H) leading one to expect virtually little dosimetric effect on the quality of an IMRT plan.

Fig. 2 compares the mean tumour volumes for the 17 patients (19 lesions) included in this study protocol when using manual delineation, thresholding using 40% and 50% of the maximum intensity, as well as RG and SBR techniques. Error bars indicate SD on the mean. Inter-observer variability for manual delineation of GTVs by the two teams was high but not statistically significant ($p = 0.459$). The same applies to GTV_{man} when compared to $GTV_{50\%}$. However, there were statistically significant differences ($p < 0.01$) between manually delineated techniques (GTV_{man1} and GTV_{man2}) and the remaining three semi-automated segmentation methods ($GTV_{40\%}$, GTV_{RG}, and GTV_{SBR}). Overall, GTV_{SBR} was higher than $GTV_{50\%}$ ($p < 0.01$) and smaller than $GTV_{40\%}$ ($p < 0.005$).

Table 3 summarizes the average GTVs delineated and OFs between the different segmentation techniques. As can be seen, the

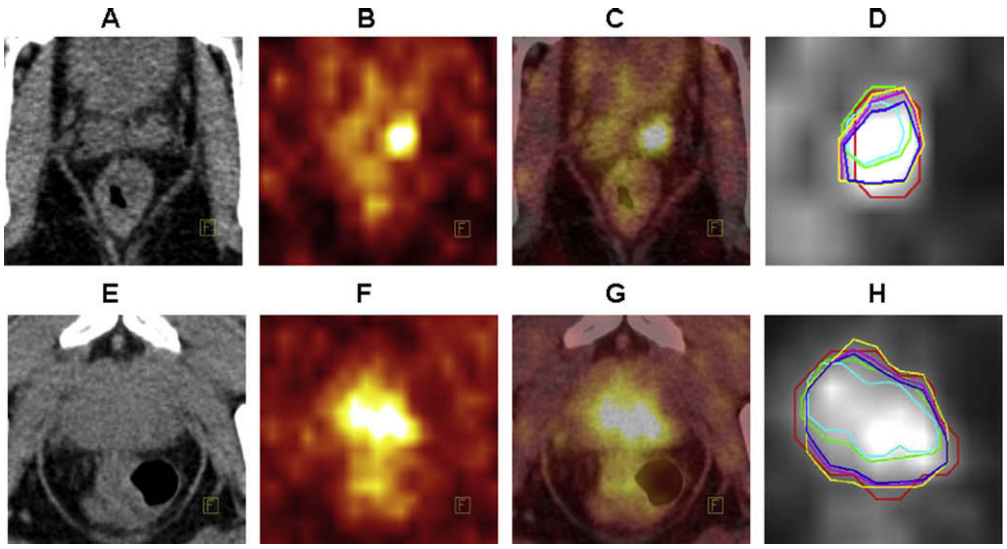

Fig. 1. Illustration of a clinical PET/CT study showing the CT image (A), ^{18}F-choline PET image (B), and the fused PET/CT (C) of an isolated recurrence in the left seminal vesicle. The enhanced details of PET-based GTVs (D) obtained by manual delineation of contours (GTV_{man1}: green, GTV_{man2}: cyan), region growing (GTV_{RG}: red), a fixed threshold of 40% ($GTV_{40\%}$: yellow) and 50% ($GTV_{50\%}$: blue) of the maximum signal intensity, and the signal-to-background ratio (SBR)-based adaptive thresholding technique (GTV_{SBR}: purple). (E and F) Same as (A–D) for another clinical study with two recurrent lesions in the left and right prostate lobes.

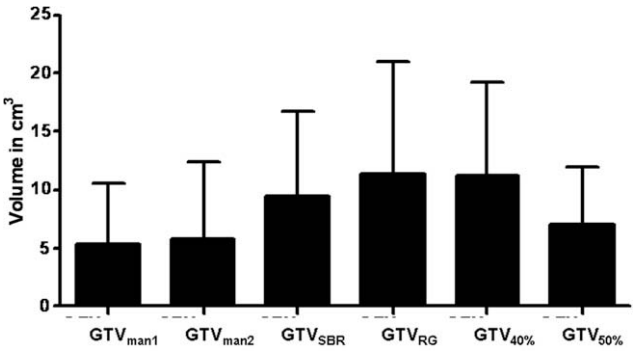

Fig. 2. Comparison of mean tumour volumes for 17 patients and 19 lesions where manual delineation, thresholding using 40% and 50% of the maximum intensity, as well as RG and SBR techniques were able to adequately delineate the tumour volume. Error bars indicate SD on the mean. Results are shown for the gross tumour volume (GTV) delineated on PET-based GTVs obtained by manual delineation of contours (GTV_{man1} and GTV_{man2}), an isocontour obtained using a fixed threshold of 40% (GTV_{Th40}) and 50% (GTV_{Th50}) of the maximum signal intensity, signal-to-background ratio (SBR)-based adaptive thresholding (GTV_{SBR}), and region growing (GTV_{RG}) segmentation algorithms.

average OF_{SRB} varies between 0.48 and 0.99. GTV_{SBR} was well enclosed in $GTV_{40\%}$; however, GTV_{RG} encloses GTV_{SBR} well but to a lesser extent compared to $GTV_{40\%}$. Although the average of manually defined GTVs were less than those defined using semi-automated methods, the corresponding OFs (OF_{man1} and OF_{man2}) were very close to unity (0.85 and 0.9, respectively). These results suggest that manually defined GTVs might underestimate the target volumes with respect to semi-automated techniques. More importantly, a small fraction of manually defined volumes encompassed tissues located outside the GTVs delineated using semi-automated techniques. The *p* values are for manual OFs relative to OF of SBR (OF_{SBR}) obtained by linear regression analysis.

Discussion

Endorectal MRI and MR spectroscopy are well established diagnostic tools for visualizing recurrent prostate cancer [24]. However, their use for target volume determination is limited. The endorectal coil provokes a deformation and displacement of the prostate and the seminal vesicles which make the coregistration with a RT planning CT challenging. MRI and PET/CT showed a good correlation concerning the recurrent prostate cancer.

Novel diagnostic imaging tools such as PET/CT using various tracers [9] have shown promising results in the detection of recurrent prostate cancer with high sensitivity and specificity [25]. ^{18}F-choline PET has particularly shown promising results in revealing recurrent prostate cancer with a high sensitivity and specificity after initial RT [10,11]. The exploitation of additional information available through dynamic PET imaging might help to exclude vascular and urinary activity artefacts, thus enabling precise target volume definition [15]. In particular, restricting the target volume

Table 3
Summary of gross tumour volumes delineated using the different methods and overlap fractions (OFs) between various segmentation techniques. The mean volumes are for the 17 patients and 19 lesions. OF_{SBR} is the overlap fraction of various GTVs with respect to GTV_{SBR}. The *p* values are reported for OFs of each manual segmentation technique relative to GTV_{SBR} obtained by linear regression analysis.

Segmentation method	Mean tumour volume in cc (95% CI)	Mean OF_{SBR} (95% CI)	Mean OF_{man1} (95% CI)	*P* value	Mean OF_{man2} (95% CI)	*P* value
GTV_{man1}	5.4 (2.9–7.8)	0.53 (0.41–0.65)	–	–	0.76 (0.68–0.85)	0.664
GTV_{man2}	5.8 (2.7–9.0)	0.48 (0.37–0.59)	0.80 (0.72–0.88)	0.144	–	–
GTV_{SBR}	9.5 (6.1–12.9)	–	0.85 (0.78–0.91)	–	0.86 (0.79–0.94)	–
GTV_{RG}	11.4 (6.8–16.0)	0.93 (0.88–0.98)	0.86 (0.80–0.92)	<0.001	0.86 (0.79–0.94)	<0.001
GTV_{Th40}	11.2 (7.4–15.1)	0.99 (0.98–1.0)	0.88 (0.82–0.95)	<0.001	0.90 (0.83–0.97)	<0.001
GTV_{Th50}	7.0 (4.7–9.4)	0.77 (0.68–0.85)	0.76 (0.67–0.84)	<0.001	0.77 (0.68–0.86)	<0.001

to only a small part of the prostate can help to reduce toxicity to critical organs, including the urethra, bladder, and rectum.

PET-guided GTV delineation was addressed for various applications, particularly for lung and head and neck cancers and more recently for brain tumours, rectal cancer, as well as breast cancer and lymphoma [14]. However, there is a lack of reports on the use and impact of PET-guided GTV delineation in prostate cancer using the plethora of tracers available today [9]. This study has shown the feasibility of determining the extent of the target volume for recurrent prostate cancer using ^{18}F-choline PET/CT. Semi-automated target volume determination using ^{18}F-choline PET/CT has the advantage of improved standardization and reduced inter-observer variability. A volumetric correlation was not carried out owing to the lack of a reliable non-rigid PET/MRI registration technique suitable for this task.

There was a small difference between the two teams of observers with average volumes of 5.4 and 5.8 cc for GTV_{man1} and GTV_{man2}, respectively (Fig. 2). The mean difference for all patients is 1.7 cc (range 0–7.1 cc). On the other hand, the average OFs between the GTVs defined by the two teams of observers are high (the OF of GTV_{man1} relative to that of GTV_{man2} is 0.80 ± 0.19, whereas the OF of GTV_{man2} relative to that of GTV_{man1} is 0.76 ± 0.20). At least three rationales could explain this trend. First, these results are in agreement with observations reported in the literature, confirming that the inclusion of PET information for target volume delineation allows to reduce inter- and intra-observer variability [26,27]. The average ratio between the largest and smallest GTV_{man} was only 1.48 which is also in agreement with the results reported by [26] for NSCLC (1.56 for FDG-PET compared to 2.31 for CT). Second, the GTVs were delineated by two teams, each consisting of a radiation oncologist and a nuclear medicine physician who did their best to reach consensus. Third, although the CT was not helpful for lesion delineation, it helped achieving an easy localization of the prostatic gland thus allowing to exclude normal tracer uptake in some soft tissues and organs such as the rectum and bulbs of penis.

The median GTVs (Table 2) are larger than typical lesion volumes reported in two related anatomo-pathologic studies following salvage radical prostatectomy. Huang et al. [7] studied the pathological data of 47 patients where the average tumour volume was 0.68 cc (range 0.31–1.63 cc). Likewise, the study by Pucar et al. [8] involving nine patients reported a median tumour volume of 1 cc (range 0.22–8.63). However, these results do not necessarily suggest that our delineated GTVs overestimate the actual volumes since candidates for prostatectomy were adequately chosen. In [7], 94% of the patients had stages cT1c and cT2, with a median PSA of 4.26. In contrary, Ward et al. [28] assessed pathologic tumour volumes in 121 patients with salvage radical prostatectomy where the mean (median) tumour volume was 8.6 cc (5.0 cc). The $GTV_{50\%}$ and GTV_{SBR} reported in our study were very close to these estimates.

Manual delineation revealed the smallest volumes in all cases. According to our analysis, the hypothesis of a systematic error was discarded and the most plausible explanation is that subjective visual analysis fails to provide a reliable delineation for two reasons: (i) According to our experience the GTV delineated by radiologists/physicians alone is usually smaller than the GTV delineated by radiation oncologists. This was also demonstrated in the literature (e.g. [29]). (ii) Re-irradiation of parts of the prostate might lead to complications to nearby soft tissues. This combined with prior knowledge of prostate cancer pathology (suggesting that the tumour volume is relatively small) has likely influenced the team which was instinctively prudent during the GTV definition process and tended to delineate small volumes, thus underestimating the tumour volume.

The SBR-based adaptive thresholding technique was successfully used by many investigators [22,23,30], and it is the only one thoroughly validated using histologic data obtained from microscopic specimen [31]. In our study, the estimated thresholds required by the SBR technique varied between 38% and 57% (median ~44%). These thresholds resulted in GTVs being very close to those reported in the above-referenced anatomo-pathologic studies, including a large number of patients with radical prostatectomy [32,33]. It should be emphasized that in the absence of gold standard, a comparative study of imaging results with anatomo-pathologic data is necessary to validate this segmentation technique. The results seem to suggest that PET/CT scanning allows to localize accurately the site of local recurrence; however, the choice of the optimal GTV delineation technique remains an open question that requires further research and development efforts.

Currently, partial irradiation of the prostate is only used to boost dose escalation protocols for prostate cancer [13,34]. It was concluded that dose escalation did not increase the toxicity. Nowadays, recent advances in IGRT are allowing to further decrease the margin for PTV delineation and thus to reduce toxicity. Therefore, considering the situation of local recurrent prostate cancer, we suggest partial re-irradiation of the tumour to leave the opportunity open for other therapeutic strategies.

Conclusion

Re-Irradiation of parts of the prostate in case of recurrence after primary radiotherapy is still controversial and should be performed and evaluated in clinical trials only. The contribution of ^{18}F-choline PET/CT in the delineation of gross tumour volume (GTV) in local recurrent prostate cancer after initial irradiation was evaluated through comparison of various PET image segmentation techniques. Even though PET/CT-guided manual volume segmentation reduces the inter-observer variability, it is likely that the tumour volumes are underestimated. Validated semi-automated segmentation techniques for ^{18}F-choline PET-guided GTV delineation allow to lower inter-observer variability compared to manual techniques and can help to determine recurrent prostate cancer for partial prostate re-irradiation. The selection of the most appropriate segmentation algorithm for clinical use still needs to be determined.

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