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4D PET/CT imaging in SBRT

Impact of 4D-^{18}FDG-PET/CT imaging on target volume delineation in SBRT patients with central versus peripheral lung tumors. Multi-reader comparative study

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ABSTRACT

Purpose: Evaluation of the effect of co-registered 4D-^{18}FDG-PET/CT for SBRT target delineation in patients with central versus peripheral lung tumors.
Methods: Analysis of internal target volume (ITV) delineation of central and peripheral lung lesions in 21 SBRT-patients. Manual delineation was performed by 4 observers in 2 contouring phases: on respiratory gated 4DCT with diagnostic 3DPET available aside (CT-ITV) and on co-registered 4DPET/CT (PET/CT-ITV). Comparative analysis of volumes and inter-reader agreement.
Results: 11 cases of peripheral and 10 central lesions were evaluated. In peripheral lesions, average CT-ITV was 6.2 cm^3 and PET/CT-ITV 8.6 cm^3, resembling a mean change in hypothetical radius of 2 mm. For both CT-ITVs and PET/CT-ITVs inter reader agreement was good and unchanged (0.733 and 0.716; $p = 0.58$). All PET/CT-ITVs stayed within the PTVs derived from CT-ITVs. In central lesions, average CT-ITVs were 42.1 cm^3, PET/CT-ITVs 44.2 cm^3, without significant overall volume changes. Inter-reader agreement improved significantly (0.665 and 0.750; $p < 0.05$). 2/10 PET/CT-ITVs exceeded the PTVs derived from CT-ITVs by >1 ml in average for all observers.
Conclusion: The addition of co-registered 4DPET data to 4DCT based target volume delineation for SBRT of centrally located lung tumors increases the inter-observer agreement and may help to avoid geographic misses.
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Stereotactic radiotherapy (SBRT) is increasingly regarded as the standard of care for patients with medically inoperable stage I lung cancer [1] and equivalent to surgery in terms of 2 year survival [2]. Excellent outcome data in peripheral lesions motivated that the method is currently tested as a feasible approach also for central tumors [3–5]. Due to the close proximity to centrally located organs at risk this treatment option remains challenging and requires elaborated imaging techniques for precise treatment planning. Taken the need for prospective research on SBRT [6,7], prospective trials, e.g. EORTC 22113-0113 [8] or RTOG 0813 [4] are under way to investigate, if this is a safe and effective approach.

The use of FDG-PET/CT has been shown to significantly influence radiotherapy treatment decisions and target volume delineation in the context of conventional radiotherapy of locally advanced lung cancer [9,10]. In SBRT, PET/CT is regarded as an indispensable staging procedure, but due to the need to cope with respiratory motion, for SBRT planning mainly 4DCT based target volume delineation is currently applied [11]. However, 4DCT imaging is restricted to 1–2 breathing phases and furthermore, the use of IV contrast in the 4D acquisition bears practical problems in bolus timing. Therefore, its routine use is not recommended by current guidelines [12], neither used in current SBRT clinical trial protocols [4,13]. To include the PET information, in some centers 3DPET/CT scans are co-registered to the 4D planning CTs. However, it has been shown that, other than assumed earlier [14], the 3DPET does not give reliable information on moving volumes [15].

As recently 4DPET/CT has become available, there may therefore be an added value to include this modality into the RT-planning process [16]. Phantom studies [14,17] have suggested that respiratory gated 4DPET/CT could address the above mentioned shortcomings, and subsequent clinical work has recognized

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a more accurate lung tumor depiction on respiratory gated PET [18,19]. Early reports [20,21] have shown diagnostic and target volume advantages by the additional use of co-registered 4DPET scans. However, due to workflow, storage capacity, manpower restrictions and lack of automatic contouring tools for 4D data, the full integration of 4DPET scans into the planning process would consume resources, why most centers do not routinely use this technique for SBRT target volume delineation. Furthermore, peripheral lung tumors are the mainstay of SBRT which can often be delineated accurately by 4DCT only. This is impacting negatively on the motivation to invest into the use of 4DPET scans.

Taking into account the growing interest for SBRT in central tumors, the current investigation explores the role of 4DPET/CT in target volume delineation for SBRT in peripheral and central lung tumors. With regard to current non-SBRT literature, the hypothesis was that in central tumors the addition of 4DPET might be beneficial and justify the increased workload in such cases.

Material and methods

Patients

In this analysis 21 cases with lung lesions treated with SBRT between 2011 and 2012 were included from a prospectively kept database. Ten consecutive patients with centrally located tumors (according to the definition of EORTC 22113-08113 [5]: any tumor within 2 cm or touching the zone of the proximal bronchial tree or tumor that is immediately adjacent to the mediastinal or pericardial pleura, with a PTV expected to touch or include the pleura) and eleven representative patients with peripheral (i.e. not central to the above definition) lung lesions and acceptable imaging quality, treated within the same period of time, were selected, who had undergone 3D and 4DPET/CT imaging for SBRT planning. Details on patients' demographics, tumor staging, location, histology and treatment are provided in Table 1. Retrospective evaluation of SBRT associated imaging in these prospectively recorded patients has been approved by the institutional Medical Ethics Committee.

Table 1
Patient, tumour and treatment characteristics ($n = 21$).

Age (years)		
Median	73	
Range	57–84	
	No.	Frequency (%)
Gender		
Male	18	85.7
Female	3	14.3
Histology		
Unknown	14	66.7
SCC	5	23.8
Other NSCLC	2	9.5
Tumour location		
RUL	7	33.3
RML	1	4.8
RLL	3	14.3
LUL	6	28.6
LLL	4	19
Centrally	10	47.6
Peripherally	11	52.4
cT-stage		
rT1a	1	4.8
rT1b	0	0
rT2a	2	9.5
T1a	6	28.6
T1b	3	14.4
T2a	1	4.8
T2b	0	0
T3	1	4.8
T4	1	4.8
cN-stage		
N0	21	100
cM-stage		
M0	15	71.4
M1	6	28.6
UICC stage (7th edition)		
I	12	57.1
II	2	9.5
III	1	4.8
IV	6	28.6
SBRT – total dose		
26	1	4.8
30	2	9.5
32.5	1	4.8
35	7	33.3
37.5	9	42.9
52.5	1	4.8

PET/CT protocol

After a fasting period of at least 4 h (glucose level less than 150 mg/dl), the patients underwent a diagnostic whole-body ^{18}F-FDG PET/CT scan at approximately 60 min (±15), following weight adjusted ^{18}F-FDG intravenous injection (average 331 MBq, range 172–427 MBq). The diagnostic CT scans were acquired with IV contrast agent in 16 patients and without in 5 patients, due to contraindications as kidney problems, hyperthyreosis or previous allergic reactions. Imaging was performed on a Philips GEMINI TF PET/CT scanner (Gemini TF BigBore 16, Philips Medical Systems, Cleveland, OH), with 3D time-of-flight list mode acquisition. After correction for dead time, random events, scatter and photon attenuation the data were reconstructed with a fully 3D list mode LOR BLOB-OS-TF algorithm in 288×288 matrix and $2 \times 2 \times 2\ mm^3$ voxel size. Non-contrast CT used for attenuation had 512×512 matrix and $1.17 \times 1.17 \times 2\ mm^3$ voxel size. From approximately 100 min (±16) after FDG injection, all patients underwent a chest limited 4DPET/CT scan (one bed position, 15 min acquisition duration time). Imaging was performed on the same scanner system with patients in radiotherapy (RT) planning positioning on a vacuum mattress with integrated markers [22]. Breathing motion was monitored with a belt (Mayo Clinic Respiratory feedback system) and the respiratory curve was synchronized with the acquisition time of scanner. The data were reconstructed in 10 respiratory phases, resulting in 10 PET and 10 CT sets, which were correspondingly hardware co-registered [23]. The summation of all respiratory gated 4D data represented the ungated PET and ungated CT, respectively. 4DPET was reconstructed with BLOB-OS-TF algorithm in a 144×144 matrix and $4 \times 4 \times 4\ mm^3$ voxel size and the 4DCT with 512×512 matrix and $1.17 \times 1.17 \times 2\ mm^3$ voxel size. Attenuation correction of 4DPET was based on the corresponding respiratory-phase 4DCT. Correction for dead time, scatter, random events and decay was applied and the standard uptake value (SUV) was calculated with body weight.

Lesion segmentation

Anonymized PET/CT data were displayed in ARTIVIEW™ on an AQUILAB workstation with institutional standard window-level settings (WLS). Visual contouring was performed by 4 independent observers (two physicians in radiation oncology with 7–8 years of clinical experience including PET/CT, one Nuclear Medicine physician with 2 years of PET/CT training and one medical student) in two distinct contouring phases. Before contouring, the hardware co-registration of 4DPET and 4DCT was visually evaluated using specific anatomic landmarks [24], successfully passed by all datasets without any further adjustment. The CT as well as the PET