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PET/CT target delineation

Multiple training interventions significantly improve reproducibility of PET/CT-based lung cancer radiotherapy target volume delineation using an IAEA study protocol

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ABSTRACT

Background and purpose: To assess the impact of a standardized delineation protocol and training interventions on PET/CT-based target volume delineation (TVD) in NSCLC in a multicenter setting.
Material and methods: Over a one-year period, 11 pairs, comprised each of a radiation oncologist and nuclear medicine physician with limited experience in PET/CT-based TVD for NSCLC from nine different countries took part in a training program through an International Atomic Energy Agency (IAEA) study (NCT02247713). Teams delineated gross tumor volume of the primary tumor, during and after training interventions, according to a provided delineation protocol. In-house developed software recorded the performed delineations, to allow visual inspection of strategies and to assess delineation accuracy.
Results: Following the first training, overall concordance indices for 3 repetitive cases increased from 0.57 ± 0.07 to 0.66 ± 0.07. The overall mean surface distance between observer and expert contours decreased from -0.40 ± 0.03 cm to -0.01 ± 0.33 cm. After further training overall concordance indices for another 3 repetitive cases further increased from 0.64 ± 0.06 to 0.80 ± 0.05 ($p = 0.01$). Mean surface distances decreased from -0.34 ± 0.16 cm to -0.05 ± 0.20 cm ($p = 0.01$).
Conclusion: Multiple training interventions improve PET/CT-based TVD delineation accuracy in NSCLC and reduce interobserver variation.
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Lung cancer is the most common cause of death from cancer worldwide, estimated to be responsible for nearly 17% of the total [1] and it is estimated that more than 80% of patients in low and middle income countries are diagnosed with lung cancer in an advanced stage (III and IV) [2,3]. The use of fused ^{18}F-fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (FDG-PET/CT) imaging is now the standard method of acquiring FDG-PET images for the purpose of baseline staging and RT treatment preparation [4], since it has been shown to be superior to either PET or CT alone [5,6]. The number of PET/CT scanners has increased in low and middle income countries in the last decade [7] and additional training in the use of PET/CT in radiotherapy planning (RTP) is vital to ensure appropriate interpretation of PET/CT with the hope, that the use of PET/CT will improve outcomes for patients treated with radiotherapy.

Due to advancements in radiotherapy techniques, accuracy in treatment delivery is improving and precise target volume definition has become more important, particularly in the era of dose escalation [8,9]. However, gross tumor volume (GTV) delineation is very sensitive to observer variation [10] and hence there is a potential risk of geographic miss of tumor [11]. PET has been shown to have a significant impact when used in the radiation treatment planning process and in particular when used for target volume delineation (TVD), where a significant reduction in interobserver variability (IOV) has been noted [11–15]. It is recommended that a radiation oncologist (RO) and a nuclear medicine physician (NMP)/PET radiologist should be both involved where PET is used for TVD [16,17]. Complex cases of GTV delineation in lung cancer patients should always be discussed in a multi-disciplinary quality control meeting. Most clinical studies have used a visual interpretation technique, while others have reported the use of a range of

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automated segmentation techniques to either guide or generate the relevant target volume [18–21]. There is no clear consensus on which method most closely approximates to the tumor position and tumor edge, and pathological correlation has proven difficult [22]. Preoperative PET imaging shows a remarkably good correlation with resected pathological specimens [23], although it is acknowledged that those specimens are affected by processing artifacts. Most recent guidance advises the use of visual interpretation of the PET signal when drawing the final contour, even in cases where auto-contouring is used to generate an initial draft for editing, if PET is to be used to inform the target volume [17].

Factors causing IOV in TVD are variable interpretation of guidelines, lack of differentiation between normal structures and tumor, incorrect interpretation of radiological images, lack of knowledge in cross sectional radiological anatomy, and suboptimal imaging techniques e.g. lack of IV contrast [24–26]. The use of a rigorous contouring protocol in which clinicians follow a detailed set of instructions and the use of a teaching intervention may help in minimizing IOV [21,31,32,34,35]. To ensure adequate and reproducible visual interpretation and application of PET images for RTP, this procedure should be standardized. A recent publication provided guidance on the use and role of PET/CT imaging for RTP in NSCLC patient [17]. This study evaluates the impact on the use of these practical guidelines through active teaching using multiple training interventions involving multiple centers with minimal experience in PET/CT-based TVD.

Methods

Target volume delineation assignments

PET/CT-based TVD was assessed through the use of repeated delineation assignments. In all contouring assignments a team consisting of a RO and a NMP were asked to delineate tumor volumes of primary tumor (GTV). Before the training, participants were asked to delineate as per their local delineation protocol and then again after the first training intervention according to a standardized delineation protocol [17]. Fully anonymized patient cases were used, including three dimensional FDG-PET and CT image data sets acquired for the purpose of radiotherapy planning. No intravenous contrast agent was used. Comprehensive case specific medical reports were included in all assignments to avoid bias due to incorrect diagnosis. An overview of the patient cases used during this training program is given in Table 1. In each case two senior ROs and a senior NMP delineated one reference 'expert' contour (GTV_{exp}) in agreement in the absence of a histopathologically proven gold standard.

Participants

The participants in this study were from eleven medical centers from nine different countries (Brazil, Estonia, India, Jordan, Pakistan, Poland, Turkey, Uruguay, and Vietnam). Each center was represented by a RO and a NMP. Before the training program centers were asked if they already performed PET/CT-based RTP. Five out of eleven centers already had limited experience in TVD with PET/CT. Other centers used PET/CT imaging for diagnostic and staging purposes only. Participants were not able to see delineations of other centers.

Big Brother target volume delineation software

Software developed in the Netherlands Cancer Institute, called Big Brother, was used throughout this multicenter study as platform for image viewing and analysis, and TVD in FDG PET/CT imaging [10]. As soon as the observer starts the Big Brother software and initiates TVD, any interaction with the software is recorded such as mouse motion, window/level and use of delineation tools. This feature allows visual inspection of strategies and comparison with expert contours to assess delineation accuracy.

Target volume delineation training program

The training program consisted of four contouring assignments, two training events and three additional clinical cases for practice (see Fig. 1). Contouring assignments 1 and 2 were performed before the first training event without the use of a standardized delineation protocol and were used as a baseline measurement. The first training event was face-to-face over a three-day period and included various lectures about relevant topics in nuclear medicine and radiation oncology and a delineation workshop on the use of PET/CT for RTP in NSCLC. The delineation workshop contained three more clinical cases which were again performed without the IAEA delineation protocol. The delineation protocol as described in the IAEA consensus document was introduced during the workshop [17]. The differences between the results and the IAEA protocol constituted the basis for a teaching discussion, consequentially clarifying protocol ambiguities. More contouring assignments followed after this training to evaluate its impact on delineation accuracy and IOV. Contouring assignment 3 was performed three months after contouring assignment 2 and contained the same clinical cases. To allow the participants to practice more with the delineation protocol three additional clinical cases were added.

After results were obtained from the above described assignments, an interim analysis was performed with the aim of identifying difficult areas in TVD and to ensure delineation occurred

Table 1
Sequence of events and characteristics of the included patients. Abbreviations: T = Primary tumor, N = Regional Lymph Nodes according to the 7th edition TNM classification.

	Case number	T	N	M	Stage	Lymph nodes
Contouring Assignment 1	1	2	1	0	IIB	11L
	2	2	2	0	IIIA	10R, 7, 8, 4R
Contouring Assignment 2	3	3	0	0	IIB	
	4	2	0	0	IIA	
	5	4	2	0	IIIB	7, 4R, 2R
Training 1	6	3	2	0	IIIA	4R, 2R
	7	3	0	0	IIB	
	8	1	2	0	IIIA	10R, 4R
Contouring Assignment 3	Consisting of cases 3, 4 and 5 (repeat assignment)					
Practice	9	2	2	0	IIIA	10R, 7, 4R
	10	2	2	0	IIIA	10R, 7
	11	2	2	0	IIIA	7, 4R
Training 2	Webinar/feedback reports					
Contouring Assignment 4	Consisting of cases 1, 6 and 7 (repeat assignment)					

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