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Dose planning

Does enhanced CT influence the biological GTV measurement on FDG-PET images?

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ABSTRACT

Objectives: To test the influence of media injection in PET/CT on the functional or gross tumour volume measurement.

Patients and methods: Thirty-three patients (56 ± 19 years) with non-Hodgkin's lymphoma ($n = 22$) or Hodgkin's disease ($n = 11$) were prospectively studied at staging. PET/CTs were performed 60 min after injection of FDG. Iopamiron 300 (Iopamidol, 1.5 cc/kg) was injected immediately after, followed 50 s later by a second craniocaudal CT (CT+). PET images were successively reconstructed using the unenhanced CT (PET−) and the CT+ (PET+) for attenuation correction using iterative reconstruction (4 iterations, 8 subsets, 5 mm post-filtering). The SUV_{max}, SUV_{mean}, SUV_{peak} and functional tumoural volume were measured in tumoural lymphadenopathies or malignant tissues ($n = 56$ VOIs) using 5 3D-thresholding methods on PET− and PET+ images: absolute SUV value of 2.5; 40% of SUV_{max}, and 3 adaptative thresholding methods (Vauclin, Black and Schaefer methods).

Results: The SUV_{mean} and the volume measurement were significantly different ($p < 0.001$) for the five segmentation methods for PET− ($p < 0.001$) and PET+ ($p < 0.001$). The SUV_{max}, SUV_{mean} and SUV_{peak} increased significantly in PET+ compared to PET− (2–5%). The SUV_{peak} was not significantly different for the five segmentation methods. The functional volume measurements were significantly different between PET− and PET+ only for the 2.5 segmentation method (+3%; $p = 0.001$), but not for the 40%, Vauclin, Black and Schaefer methods.

Conclusion: The functional volume could be measured in PET/CT when CT was performed with enhanced media. Caution should be taken when using the volume delineation method. Volume delineation methods using absolute threshold may artefactually increase the functional volume when enhanced CT is used for attenuation correction. The delineation volume using the relative or adaptative method should be preferred when contrast media are used for PET/CT.

The ^{18}F-fluoro-2-deoxy-D-glucose (FDG) is the most widely used tracer in oncology for detection, staging, monitoring the therapeutic response and for target volume delineation in external radiotherapy [1–4]. The use of positron emission tomography (PET) images for gross tumour volume (GTV) delineation in radiotherapy and assessment of the therapeutic response requires delineation of the tumour boundaries [5–8]. Moreover, recent papers underlined a role for the functional volume measurement [9]. The integration of FDG-PET/CT into external beam radiation therapy planning and recommendations on methodological approaches has been proposed [10].

PET/CT is now widely used and has shown its superiority to PET and CT alone in the staging of cancer in most of solid tumours [11] and lymphomas [12]. Some authors propose the use of low-dose CT for anatomical localisation and attenuation correction of PET images, while others propose high-resolution CT using contrast-enhanced CT for a radiological interpretation [13–16]. Therefore, contrast media injection in PET/CT is a matter of debate. Many studies have demonstrated an increase in the Standard Uptake Value (SUV) from 3.6% to 8.4% when enhanced CT is used for attenuation correction [13,12,14,17,18]. Therefore, the volume measurement and the GTV delineation may be altered by the use of enhanced CT. Recently, Eccles et al. [19] defined GTV using 40% of the SUV_{max} on enhanced PET/CT images for locally advanced pancreatic cancer, but no data were available on the influence of enhanced CT on GTV delineation.

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Different segmentation methods have been proposed in the literature to define the functional volume in FDG-PET imaging. The most intuitive is the manual delineation by a physician [20,21]. The main approach proposed in the literature is the use of a threshold, mainly due to its ease of use. This threshold can be a fixed cut-off value of the SUV [22], a percentage of the SUV_{max} [23,24], or an adaptive threshold value defined by a semi-automatic algorithm taking into account different image parameters (SUV_{mean}, background activity level or tumour-background ratio) (Erdi et al. [25], Daisne et al. [26], Black et al. [27], Schaefer et al. [28], Vauclin et al. [29]). Multi-centre calibration of an adaptative thresholding method of tumour volumes in radiotherapy planning has been tested for lung cancer [30]. More complex algorithms have also been proposed based on random walk [31], watershed [32], fuzzy logic [33,34], and belief functions [35]. Due to a lack of consistency in tumour contour delineation on PET, interpretation of the available data is difficult, and how PET imaging should be integrated into planning treatment remains uncertain in the absence of a consensus method. The use of enhanced PET/CT for GTV delineation is a possible additional difficulty.

Our aim was to evaluate the influence of contrast media injection on PET/CT images for GTV delineation. Five thresholding methods were evaluated. PET images were successively corrected with enhanced and non-enhanced CT (paired data) to compare the volume delineation.

Patients and methods

Patients

Patients with lymphoma were prospectively included (study TEP-TDM+; ClinicalTrial.gov observational study). They underwent PET/CT examination at baseline (before chemotherapy). The inclusion criteria were (1) age over 18 years, (2) lymphoma for which enhanced CT and PET were needed for pathology staging and (3) for which chemotherapy was recommended. The exclusion criteria were (1) uncontrolled diabetes (glycemia $\geqslant$10 mmol), (2) pregnancy or nursing, (3) allergy to iodine, (4) creatinine higher than 150 μmol/l, and (5) patients who had undergone previous diagnostic CT for the initial staging. The institutional review board for human studies approved the protocols and the consent form. All patients gave their written informed consent.

Image acquisition

The PET/CT protocol, described in Fig. 1, was performed on a Biograph® Sensation 16 Hi-Rez device (Siemens Medical Solutions, Hoffman Estates, USA). A total of 5 MBq/kg of FDG were injected after 30 min of rest. Sixty minutes later (±5 min), the acquisitions began with the non-injected CT (CT−) in the cranio-caudal direction. The scan parameters were set to 120 kV and 100–150 mAs (regarding the patient weight) using the dose reduction software (CareDose®, Siemens Medical Solutions). The arms were positioned over the head, and acquisition was performed during free breathing. A 0.75-mm collimation was considered. Then, the PET acquisition was performed in the caudo-cranial direction, using a whole-body protocol (3 min per bed position). The acquisition time was actually adapted as a function of the injected activity (regarding the standard 5 MBq/kg) and the delay between the injection and acquisition (standardised to 60 min) to keep a normalised count rate for all patients. Six to 8 bed positions per patient were acquired, knowing that the axial field of view for 1 bed position was 162 mm, with a bed overlap of 25% (plane spacing: 2 mm). The transverse spatial resolution reached 4.4 mm (centred point source in air). Immediately after the PET acquisition, 1.5 cc/kg of Iopamiron 300® (Iopamidol, Schering), containing 300 mg of iodine per ml, was automatically injected (Medrad© injector) at 2 ml/s. The contrast-enhanced CT (CT+) began automatically 50 s after the contrast agent injection to produce more informative venous phase images, as recommended [36]. The CT+ images were acquired in the cranio-caudal direction with a 0.75 mm collimation. The scan parameters were set to 120 kV and 200–250 mAs regarding the patient weight. The clinical dose reduction software (CareDose®) was used. All patients were breathing shallowly during the thoracic and abdominal acquisition.

Image reconstruction

All CT images were reconstructed in 512 × 512 matrices, and all PET images were reconstructed in 168 × 168 matrices.

- CT− images were successively reconstructed for attenuation correction and for anatomical localisation. For attenuation correction, the images were reconstructed in 5-mm contiguous slices. For anatomical localisation, the images were reconstructed in 3-mm slices every 2 mm.
- CT+ images were successively reconstructed for attenuation correction and radiological interpretation. For radiological analysis, the CT+ images were successively reconstructed as follows: (1) 1.5 mm slices every 1.1 mm for the whole body and (2) 1.0 mm slices every 0.75 mm at the pulmonary level. For the nuclear medicine analysis, the images were reconstructed in 3-mm slices every 2 mm (similar images than CT−).

The PET images were successively reconstructed for attenuation correction with the CT− (PET−) and the CT+ (PET+). The PET− and PET+ images were iteratively reconstructed using the Fourier Rebinning (FORE) and Attenuation Weighted Ordered Subset Expectation Maximisation (AWOSEM) clinical software, considering 4 iterations and 8 subsets. The images were corrected for random coincidences, scatter and attenuation using the CT− and CT+ data. The PET− and PET+ images were finally smoothed with a Gaussian filter (full width at half maximum = 5 mm).

Image segmentation and data analysis

All analyses were performed on a DOSIsoft Planet Oncology® workstation (Dosisoft, Cachan, France). The main pathological

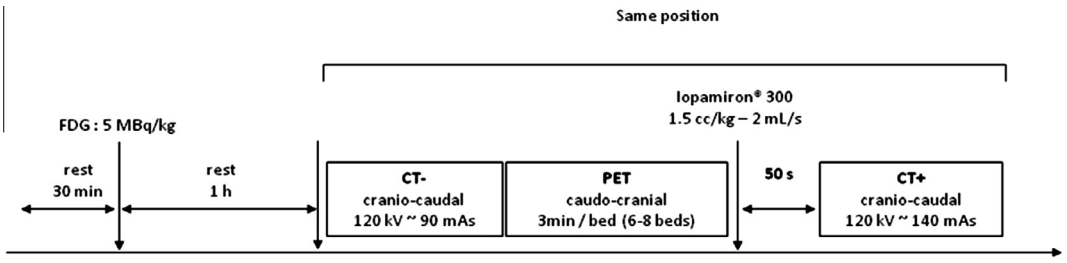

Fig. 1. Study protocol.