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Original paper

Radiation dosimetry of ^{18}F-flurocholine PET/CT studies in prostate cancer patients

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ABSTRACT

Purpose: We aimed to evaluate the Equivalent Doses (H_{Ts}) to highly exposed organs as well as the Effective Dose (ED) for ^{18}F-fluorocholine PET/CT scan in the follow-up of prostate cancer patients.
Methods: Fifty patients were administered with ^{18}F-fluorocholine. The activities in organs with the highest uptake were derived by region-of-interest (ROI) analysis. OLINDA/EXM1.0 and Impact software were used to assess ED for the administered ^{18}F-fluorocholine and CT scan, respectively, and the ^{18}F-fluorocholine and CT-scan EDs summed to yield the total ED for the PET/CT procedure.
Results: The calculated ^{18}F-fluorocholine and CT scans EDs based on ICRP Publication 103 were 5.2 mSv/300 MBq and 6.7 mSv, respectively. The ^{18}F-fluorocholine H_{Ts} to the liver, kidneys, spleen and pancreas were about threefold higher than those from the CT, which contributed a greater proportion of the total ED than the ^{18}F-fluorocholine did.
Conclusions: For ^{18}F-fluorocholine PET/CT procedures, about 40% of the ED is contributed by administered ^{18}F-fluorocholine and 60% by the CT scan. The kidneys and liver were the highly exposed organs. Considering the large number of diagnostic procedures oncology patients undergo, radiation dosimetry is important in relation to the stochastic risk of such procedures.

Introduction

Administration of radiotracers to human subjects exposes them to a stochastic risk that needs to be carefully evaluated. The International Commission on Radiological Protection (ICRP) Recommendations take into account the detriment from the exposure of different organs to low doses of radiation through tissue weighting factors (w_{Ts}) that represent the relative contributions of individual organs and tissues to total detriment. The ICRP103 Recommendations [1] replaced the weighting factors published in ICRP60 [2] with substantially modified values and introduced the official computational models representing the adult Reference Male and Reference Female used in establishing radiation protection guidance [3].

Research protocols involving the clinical use of new radiotracers, such as ^{18}F-fluorocholine, should include estimation of normal organ absorbed doses (particularly for high-uptake organs) and of the ED.

In Europe, although there is no dose limit for research purposes, the ED must be evaluated and justified with respect to the calculated risk for the patient. On the other hand, the USA Food and Drug Administration for certain types of clinical research studies places limits per organ per study (generally 50 mSv, with the exception of red marrow, gonads and lens of the eye, for which 30 mSv are recommended). Moreover, while hybrid imaging techniques such as SPECT/CT and PET/CT scans allow a better diagnostic evaluation based on functional and morphological information, they deliver an ED to the patient due to internal energy deposition from radiopharmaceutical administration and external irradiation from CT X-rays. In order to optimally balance the

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stochastic risk of diagnostic procedures [4–6] with the medical information being sought, it is important to optimize such procedures in terms of the CT parameters as well as the administered activity of the radiopharmaceutical.

It should be noted that the ED is defined by ICRP for a generic reference individual and in practice it cannot actually be evaluated for individual patients.

Our work contributes dosimetric data for ^{18}F-fluorocholine used for the detection of local and distant recurrence of prostate cancer and focuses on the absorbed dose to normal organs with higher uptakes.

Materials and methods

Patients

The ^{18}F-fluorocholine PET/CT studies were approved by the local Ethics Committee and activated in our institute in October 2011. To date about 200 patients with prostate cancer have been enrolled in the study, of whom 50 were included in the dosimetric evaluations. Patients had previously undergone prostatectomy or radiotherapy with curative intent and a ^{18}F-fluorocholine PET/CT scan was scheduled to screen for local and distant recurrence after an increase in prostate specific antigen (PSA $>$ 1 ng/ml). Patients were injected with about 4 MBq/kg of ^{18}F-fluorocholine (Advanced Accelerator Applications S.A., Saint Genis Pouilly, France).

Imaging: acquisition, reconstruction and elaboration

Imaging was performed in 2D-mode using a Discovery LS PET/CT scanner (General Electric Medical System, Milwaukee, WI), with well-counter calibration updated every three months. The full-width at half maximum (FWHM) spatial resolution was 5 mm in each direction and 2D-mode sensitivity was 7.1 cps/Bq/cc, determined according to NEMA NU 2-1994 [7]. The volumetric computed tomography dose index (CTDIv) of the clinical protocol visible on the screen of the CT console was compared with the measured CTDIv by specific phantom tests; the agreement was good, with a percentage difference of less than 4%.

Whole-body PET images were acquired 50 min post-injection (p.i.) from the nose to the mid-thigh (6–7 bed positions, 3–3.5 min/bed). CT acquisition parameters were as follows: 120 kV, 90 mA, 0.75–1.5 pitch, 0.8 s/rot, 20 mm collimation, 5 mm slice thickness. PET data were corrected for scatter, randoms, dead time and decay and images were reconstructed using a 2D Ordered-Subsets-Expectation Maximization (OSEM) iterative reconstruction algorithm (2 iterations, 28 subsets). Image analysis was carried out using Xeleris1 GE software. In particular, ROIs of 2 cm in diameter were drawn within each source organ on three/four slices selected at the top, in the middle and at the bottom of the organ and the mean value of the Standard Uptake Value calculated with body weight (SUV_{bw}) on the three/four slices of each organ was calculated. The source regions were bone, fat, kidneys, liver, lungs, muscle, pancreas, salivary glands (parotids and submandibular glands), spleen, small intestine and testes.

Moreover, in a group of 18 patients we performed also an early acquisition (within 5 min p.i.) in order to evaluate the uptake kinetics in the highly exposed organs (kidneys, liver and spleen).

Biodistribution and dosimetric study

The mean activity concentration (kBq/ml) and the percentage of injected activity (%IA) for all 50 patients were obtained for each organ at 50 min p.i. The time integrated-activity coefficients [8], $\tilde{a}(r_S, T_D)$, were calculated assuming no biologic removal, $t_b = \infty$ (equation (1)) according to data from a number of studies [9,10] wherein, a very fast distribution of the radiotracer was reported in organs and lesions (by 10 min p.i.), confirming the imaging acquisition at 50 min as representative of the near-steady state distribution of the radiotracer.

$$\tilde{a}(r_S, T_D) = 1.44 * t_{1/2p} * \frac{\text{Organ}(r_S)\text{total activity}}{\text{Injected activity}} \quad (1)$$

where

r_s = source organ
$t_{1/2p}$ = physical half time
$T_D = \infty$

Furthermore, for the 18 patients with acquisitions at 5 and 50 min p.i. the time integrated-activity coefficients were calculated in kidneys, spleen and liver by applying the trapezoidal rule [11] and with physical decay only assumed for integration from 50 min on. The above values were compared in term of percentage difference with those obtained by assuming no biological removal.

The calculation of the total organ activity was determined taking into account the organ reference masses and the standard-man total body mass of the reference male and the standard uptake value [12].

We used OLINDA/EXM1.0 software to calculate the equivalent doses, H_{Ts} (mSv/MBq), entering the $\tilde{a}(r_S, T_D)$ of each source organ (liver, lungs, kidneys, muscle, pancreas, small intestine, spleen, testes, red marrow, urinary content and remainder-of-body) and using the sphere model to obtain the H_T for salivary glands. The mass of the parotid glands was assumed equal to 50 g and the mass of the submandibular glands 25 g [13]. The $\tilde{a}(r_S, T_D)$ of blood and urinary bladder contents reported in the literature [14,15] was used to calculate the H_T for red marrow and urinary bladder wall, respectively, since it was not possible to collect and count samples of blood and urine.

A bladder voiding interval of 1 h was assumed [14,15] and because of the absence of specific uptake in the bones and red marrow, red marrow time integrated-activity coefficient was calculated by the blood-based method (which assumes a linear relation between the blood and red marrow time integrated-activity coefficient). The proportionality factor was the ratio between standard-man red marrow mass and standard-man blood mass.

ED (mSv/MBq) was calculated by summing the products of the organ equivalent doses H_{Ts} and their respective organ weighting factors and adding the remainder-of-body ED contribution according to the different calculation algorithms and w_{Ts} proposed in ICRP60 [2] and ICRP103 Recommendations [1]. In particular, to determine the remainder-of-body ED contribution as stated in ICRP103, the remainder tissues mean H_T was multiplied for the relative w_T equal to 0.12 [2]. Instead, to obtain the remainder-of-body ED contribution according to the ICRP Publication 60, in those exceptional cases in which one single organ of the remainder (in our specific case the kidney) receives an equivalent dose in excess of the highest dose in any of the twelve organs (or tissues) for which a w_T is specified [1], a weighting factor of 0.025 was applied to that organ (kidney) and a weighting factor of 0.025 to the average dose calculated among the other organs of the remainder.

The comparison was performed in order to evaluate possible significant differences, in terms of percentage differences, calculated as showed in equation (2), between the ED values based on ICRP Recommendations 103 and 60 [1,2].

$$\%\text{DIFF}(\text{ED}_{\text{ICRP60}} \text{vs } \text{ED}_{\text{ICRP103}}) = \frac{\text{ED}_{\text{ICRP60}} - \text{ED}_{\text{ICRP103}}}{\text{ED}_{\text{ICRP103}}} * 100 \quad (2)$$