Optimization of a routine method for bone marrow dose estimation in ^{177}Lu-EDTMP therapy- Experience in Uruguay.

Teran. M[1], Paolino.A[2], Coppe.F[2], Nuñez M[2], Hermida J C[2], Gaudiano.J[2]

[1] Cátedra de Radioquímica-Facultad de Química. Av. Gral Flores 2124 CP 11800

[2] Centro de Medicina Nuclear-Hospital de Clínicas. Av.Italia s/n CP 11900

Montevideo - Uruguay

Abstract

Patients suffering from breast, lung and prostate cancer usually develop metastases or secondary cancerous lesions in bone. These lesions lead to pain and lack of mobility that conventional treatments not always give expected results. The use of systemic therapies with radionuclides is a good alternative to bone pain palliation to provide a higher quality of life. ^{177}Lu-EDTMP is an excellent alternative due to its radiopharmaceutical and nuclear decay characteristics (β^- , $t_{\frac{1}{2}}$ 6.73 d). Dosimetry estimations is mandatory to avoid haematological toxicity resulting from absorbed dose delivered to bone marrow.

As pre therapeutic dose estimation is gaining place in nuclear medicine this proposal intends to optimize dosimetric protocols to be used as reference methods to improve therapy and patient protection in Uruguay. To perform this work planar images of whole body of the patient were acquired. Regions of interest were drawn around lumbar spine or sacrum. Scatter and attenuation corrections were performed. Percentages of reminding activity in the same ROIs were plotted in OLINDA/EXM to determine the absorbed dose in red marrow and main lesions.

Key words

177Lu-EDTMP, pain palliation, dosimetry, bone.

Introduction

Radiotherapy is the most used mode of treatment of many cancers, it is usually given with external radiation sources but another option is to administer radiotherapy by specifically localizing radioisotopes emitting particulate radiation within the tumor tissue [1]. This targeted therapy has several potential advantages over external beam therapy, including the possibility of delivering doses more selectively to the tumor and treating widespread multiple metastases.

Patients suffering from breast, lung and prostate cancer usually develop metastases or secondary cancerous lesions in bone. These lesions lead to pain and lack of mobility that conventional treatments not always give expected results. The use of systemic therapies with radionuclides is a good alternative to bone pain palliation to provide a higher quality of life. ^{177}Lu-EDTMP is an

excellent alternative due to its radiopharmaceutical and nuclear decay characteristics (β⁻ , t ½ 6.73 d).

Dosimetry estimation is mandatory to avoid haematological toxicity resulting from absorbed dose delivered to bone marrow [2]. Bone marrow is the most radiosensitive tissue in the body and it is commonly considered the critical organ for radionuclide therapy. This tissue is spread throughout the skeleton, within the cavities of the bones. The total weight of the bone marrow is approximately 5.0% of the whole body weight [3]. Approximately one-third of the total bone marrow is red marrow which is the haematopoietically active tissue, and the rest is yellow marrow which mainly consists of fat and does not actively produce any blood cells [4].

The absorbed radiation dose from internally deposited radionuclides is a major factor in assessing risk and therapeutic utility when evaluating new radiopharmaceuticals for use in nuclear medicine. Absorbed dose, therefore, is a quantity that usually is estimated from the localized uptake and retention of administered radiopharmaceuticals. Response and toxicity prediction is essential to the rational implementation of cancer therapy [5,6]

The main goal of bone marrow dosimetry is to predict the level of toxicity caused by therapy with radiopharmaceuticlas. Thereby deliver the most efficient therapy with a minimal level of adverse effects for the patient. Toxicity can be predicted via the study of the relationships between absorbed dose and biological effect which must be established separately for each radiopharmaceutical and for each patient subgroup.

The mean absorbed dose to a target region (k) is calculated according to MIRD concept [7, 8] Eq 1. The total mean absorbed dose to a target region equals the sum of the contributions from all source regions:

$$\overline{D_k} = \sum_h \widetilde{A_k} \cdot S_{k \leftarrow h}$$

Equation 1.- Mean total absorbed dose

Objective

As pre therpeutical dose estimation is gaining place in nuclear medicine, the purpose of this work was to optimize an image quantification method to improve bone marrow and whole-body dosimetry in ^{177}Lu EDTMP to improve therapy and patient protection in Uruguay.

Methods

To perform this work a Mediso Gamma Cammera of 2 heads was used. A 185 MBq (5 mCi) tracer dose of the radiopharmaceutical of interest was administered to patients, both anterior and posterior whole body images were acquired at 1, 6, 24 hours post administration according to the following conditions:

- 3/8 ", rectangular field,
- medium energy collimator
- window centered in the peak of energy (±15%)
- matrix 128 x 128

The first images at 1 h were acquired without patient micturition and these counts were considered as 100% of injected activity. The other images were acquired after patient micturition.

Scattering corrections were performed using triple-energy-window (TEW) method ($\pm$ 10%).

In order to correct for individual patient attenuation, a ^{57}Co flood source was used according to the following conditions:

- A complete image of the flood source was acquired without the patient
- WB image was acquired with the patient previous radiopharmaceutical administration on the flood source.
- WB images of the patient after radiopharmaceutical administration at different times without flood source.
- ROIs were drown around the organs of main interest and with these data attenuation factors of the organs were calculated.
- Activity concentration in ROIs were calculated using equation Eq 2 that considers AP and PA scatter corrected counts and S attenuation factor [6]:

$$C = \sqrt{\frac{I_a \ I_p}{e^{-\mu d}}} \ x \frac{1}{S}$$

Equation 2.- Siegel et al

The number of disintegrations in red marrow were determined by drawing regions of interest (ROI) over the lumbar spine or sacrum, as large proportions of the red marrow are situated in these regions. Fig 1.a &b
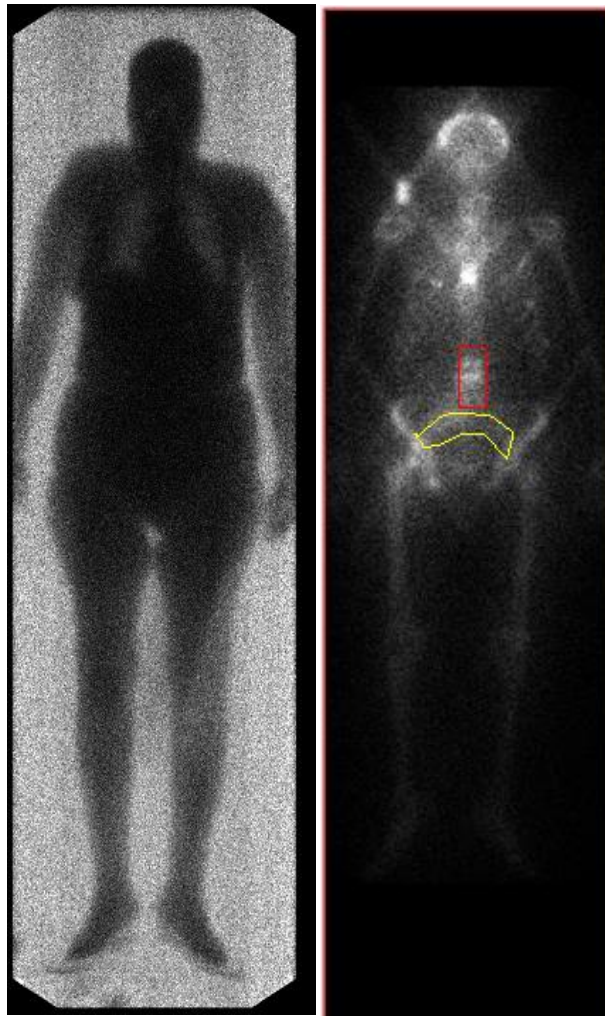
Figure 1: a) Transmition image with cobalt flood b) ROIsin spine and sacrum

Percentages of reminding activity in the same ROIs were plotted at each time point in OLINDA/EXM to determine the absorbed dose in red marrow and main lesions.

Discussion

Mean bone marrow dose was 0.95 ± 0.2 mGy/MBq and mean whole body doses were 0.19 ± 0.07 mGy/MBq. These results are explained because of the rapid urinary elimination of the radiopharmaceutical. There is still too much work to be done, more cases to get statistically relevant data and get more time points to clearly establish the uptake and elimination phases This method revealed to be efficient, easy to implement in routine and reliable to guarantee adequate bone marrow dose estimation before therapy with radionuclides.

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