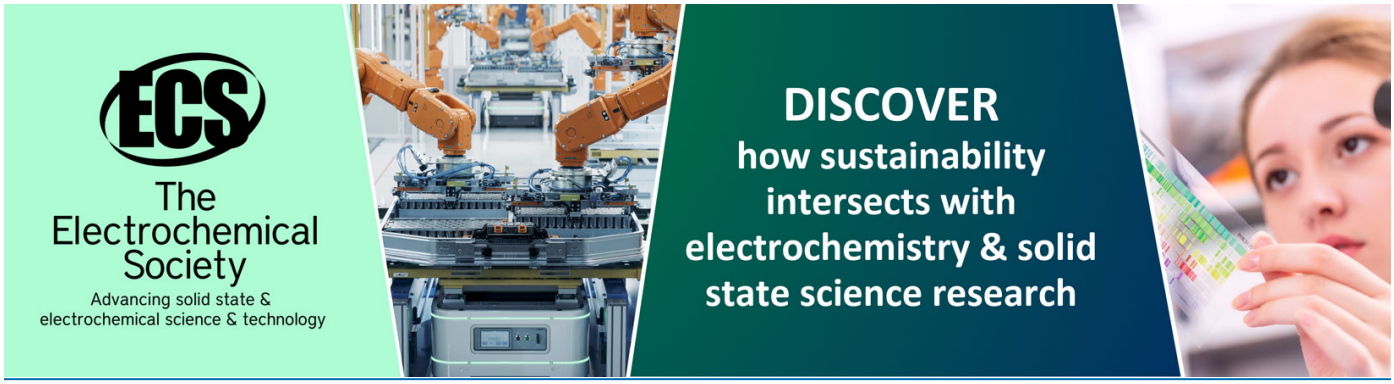
Lu-177 DOTATATE dosimetry for neuroendocrine tumor: single center experience



Lu-177 DOTATATE dosimetry for neuroendocrine tumor: single center experience

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Abstract. Lu-177 labelled with DOTATE is widely acceptable to treat Neuroendocrine Tumor (NET) disease and it better improvement of quality of patients' life since few years ago. However, the radionuclide toxicity becomes the main limitation of the (NET) treatment. Therefore, we performed a pilot study aimed to estimate radiation absorbed doses to dose-limiting organs to develop a systemic therapy with Lu-177 in NET patients. In this study, five set of planar whole body images was acquired every 0.5 hour, 4 hours, 24 hours, 48 hours and 72 hours after Lu-177 administrations. The planar image acquisition was done using Philip Brightview X with Medium Energy General Purpose Collimator (MEGP) collimator. All patients' images in Conjugate View (CV) format were transferred into PMOD 3.7 Software for Region of Interest (ROI) analysis. The ROI were drawn at selected organs such as kidneys, liver, spleen and bladder. This study found that the mean absorbed dose for kidneys 0.62 ± 0.26 Gy/GBq, liver 0.63 ± 0.28 Gy/GBq, spleen 0.83 ± 0.73 Gy/GBq and bladder 0.14 ± 0.07 Gy/GBq. The radionuclide kinetic for the whole body 99.7 ± 0.1 percent at 0.5 hours, 79.5 ± 10.7 percent at 4 hours, 56.6 ± 10.3 percent at 24 hours, 43.2 ± 7.9 percent at 48 hours and 37.1 ± 9.0 percent at 72 hours. This study verifies that this planar quantitative method able to determine organ at risk and the result line with other published data.

1. Introduction

Lu-177 label with DOTATOC is widely acceptable to treat Neuroendocrine Tumor (NET) disease and showing patients increase of quality of life since few years ago due to its properties able to emitted Beta particle and Gamma rays simultaneously. This radionuclide also good for dosimetry assessment [1-4]. In current clinical practice, Lu-177 DOTATATE treatment is normally infused between 5.55 to 7.4 GBq per cycle with time interval between per cycle about 6–16 weeks apart two to six number of cycle together with kidney protection agents [4-5]. The radionuclide toxicity to the kidneys become the main limitation of the (NET) treatment. The role of radionuclide dosimetry is to assess of optimum radionuclide therapy to administered to the patients and assess the organs at risk condition. The dose-limiting organs for NET therapy are the kidney less than 23-28 Gy[1-3]. In order to avoid toxicity the amount of radiation dose given to these dose-limiting organs has to be estimated. Recently, the dosimetry technique used in nuclear medicine was proven to assess the absorbed dose for the critical organ such as kidneys [2, 3, 5]. In general the dose estimates by using MIRD scheme, with the basic equation (1)

$$D=\tilde{A}S \quad (1)$$

Where Ã is the integral activity in the organ and S is a dose conversion factor of the radionuclide and the target [6]. The value of S should be corrected for the actual organ volume and mass of the organ. However, there are limited data regarding the radiation absorbed dose given to the normal tissues for systemic therapy with Lu-177 for this region. Therefore, we aimed a pilot study to estimate radiation absorbed doses to dose-limiting organs in order to develop a systemic therapy with Lu-177 with suitable NET patients.

2. Methods

In this study, five set of planar whole body images from patients was acquire every 0.5 hour, 4 hour, 24 hour, 48 hour and 72 hour post Lu-177 administrations as shown at Figure 1. The planar image acquisition was done by using Philip Brightview X with MEGP collimator and window energy was set at 208 keV (20%) and 111 keV (20%) at 12 cm/min [2], [7]. The (Ant-Post) planar images were convert into conjugate view (CV) by using Philip Jetpack 2.0 software for every each patient's scanning acquisitions hours. All Patients images in Conjugate View (CV) format were transfer into PMOD 3.7 Software for Region of Interest (ROI) analysis. The ROI were drawn at selected organs such as Kidneys, liver, spleen and bladder. The ROI's were draw starting 24 hour, 0.5 hour, 4 hour, 48 hour and 72 hour. All the ROI's data was transfer in MS Excel spreadsheet. The time activity curve (TAC) is obtained by using fractionation factor (f-factor) for every ROI's count for every organ. The resident time for every each organ obtained from Area under curve (AUC) graph fitting obtained from bi or three exponential fit by using MS EXCEL worksheet. The estimation of Absorbed Dose (S-Value) to the organ were based resident time from each organ. The actual kidney weight was obtained from Radiotherapy Planning System, MONACO and patient's body weight is compulsory for accurate result by using OLINDA-EXM 1.1 software.

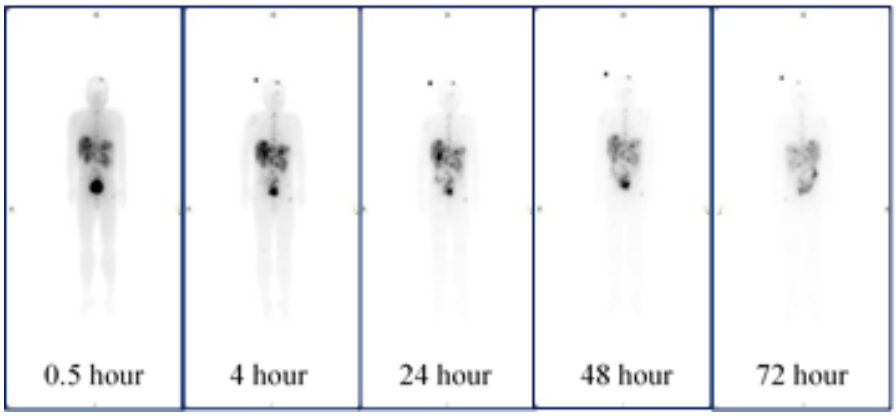

Figure 1. Five data point's for Lu-177 planar images

3. Results

The results of the organ dosimetry S-Value absorbed doses for kidneys, spleen liver and bladder of all six patients are presented in Figure 1. Mean absorbed dose for kidneys is 0.64 ± 0.41 Gy/GBq, liver 0.76 ± 0.32 Gy/GBq, spleen 1.23 ± 0.59 Gy/GBq and bladder 0.17 ± 0.11 Gy/GBq. The kinetics of Lu-177 DOTATE at patient's whole body are also shown in Graph 2. The IA kinetic for the whole body is 99.7 ± 0.1 percent at 0.5 hours, 79.5 ± 10.7 percent at 4 hours, 56.6 ± 10.3 percent at 24 hours, 43.2 ± 7.9 percent at 48 hours and 37.1 ± 9.0 percent at 72 hours.

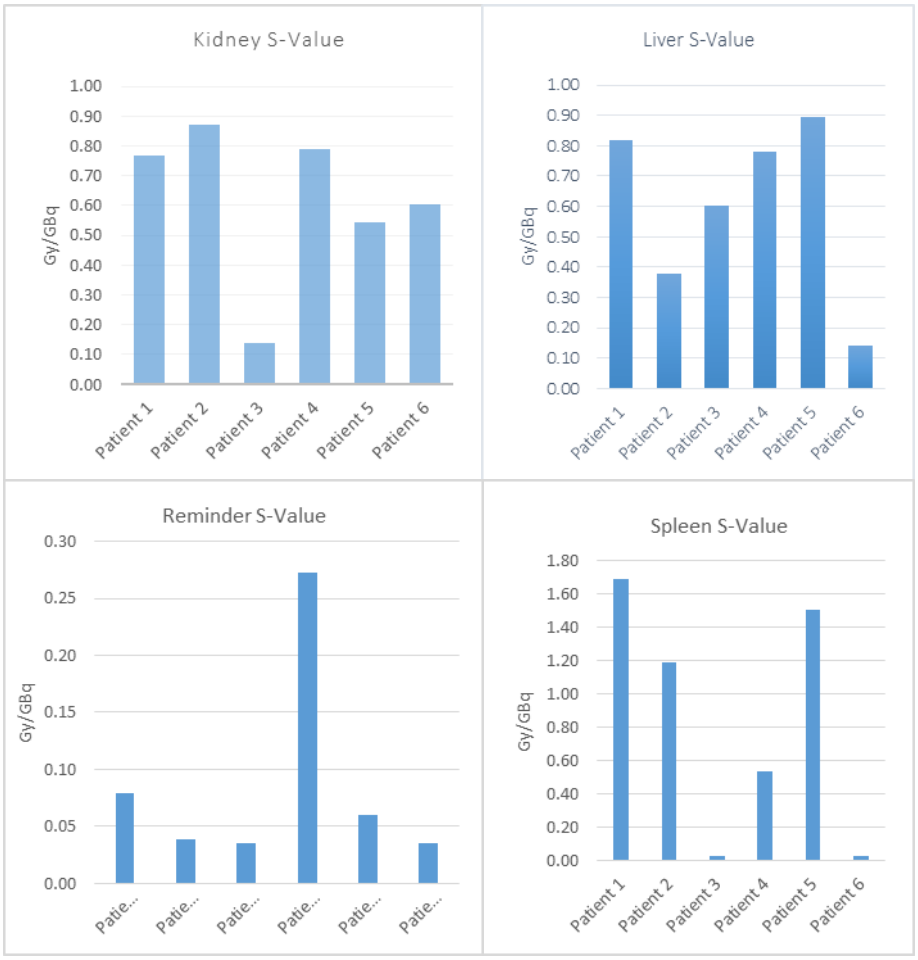

Figure 2. S Value Lu-177 for kidney, liver, spleen and reminder

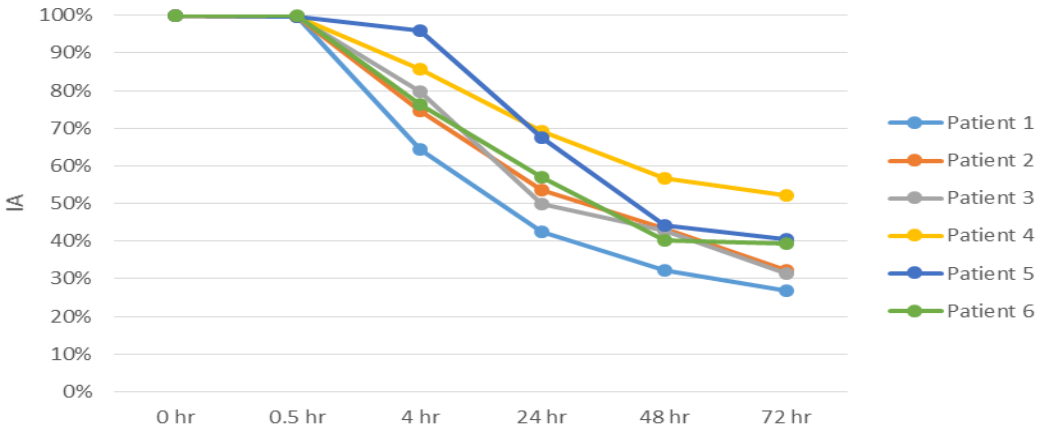

Figure 3. The whole body Lu-177 DOTATATE kinetic.

4. Discussions

In Lu-177 DOTATATE therapy, patient specific dose calculation is important technique to determine organ absorbed dose due to different pharmacokinetic for every each patients and organ weight. The general equations for absorbed dose (D) is defined in Equation (2):

$$D=d\varepsilon/dm \quad (2)$$

Where D is the mean energy imparted by ionising radiation to matter of mass *dm*. The units of absorbed dose are typically J/kg and refer as Gray (Gy) as SI unit. In radionuclide therapy with specific peptides receptor such as 177-Lu DOTATATE, kidneys and bone marrow highly sensitive with radionuclide toxicity [4-10]. Agreed with previous works, the absorbed radiation dose to the kidneys varies widely between patients treated with 177Lu-DOTATATE [2], [4], [7], [11-15]. Our current result for kidney range between 0.15 to 1.27 Gy/GBq, Liver 0.34 to 1.28 Gy/GBq, spleen 0.55 to 2.14 Gy/GBq and reminder 0.07 to 0.14 Gy/GBq. The maximum limit absorbed dose to the kidneys in our center is 27 Gy and in average it's would be reached with a total cumulative administered dose up to 46 GBq. Agreed with [7], bone marrow dosimetry in previous studies had shown that the absorbed dose to the bone marrow is usually low by others researchers. The difference in calculated absorbed doses to the kidneys depending on the dosimetry method used and the administration of amino acids has proven to decrease the doses to the kidney effectively and improved the toxicity profile of the treatment [13]. Although the calculation method at our institution is different with previous works [3], [5-6], but the dosimetry concept still similar. In our works, the actual organ weight measurement were done in radiotherapy planning software will make the absorbed dose to the critical organ more realistic approach. Our works are not covering the planar lesion dose study to the tumour due to the accuracy issues [2].

Current measured absorbed doses for kidneys are in good agreement with absorbed doses measured by other published works [13-15]. The residence time of Lu-177 in the whole body in our works is 0.5 to 5.6 days and longer compared with other published data (range 0.89 – 3.0 days) [10]. In this work, all the patients result show the absorbed dose to the critical organ are below the maximum limit.

5. Conclusions

The patient-specific dosimetry procedure were introduced here helps optimise the planning of administered radionuclide therapy. The patients' self-assessed quality of life increases significantly after treatment with 177Lu-DOTATOC. This procedure is highly recommend to the patients would go for the radionuclide therapy and also to optimise the treatment.

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