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Patient specific computer automated dosimetry calculations during therapy with ^{111}In Octreotide

Ioannis Vamvakas, Nefeli Logopati, Maria Andreou, Marios Sotiropoulos, Athanasios Gatzis, George Limouris, Christos Antypas, Maria Lyra.

Abstract— **The aim of this study was to calculate the absorbed dose of 22 patients that were diagnosed for neuroendocrine tumours in liver and had received therapeutic dose of ^{111}In octreotide. In-111 Octreotide infusion, via intrahepatic catheterization is well established technique in our Institution in hepatocellular carcinoma and neuroendocrine tumours treatments. The patient specific dosimetry calculations, for this way of treatment, were based on anterior and posterior scintigraphy images that were acquired immediately after radiopharmaceutical infusion, through hepatic arterial port and at 24 and 48 hours post-infusion. Gamma – camera was calibrated in order to estimate source organ activity considering count rate, patient's body diameter and source organ size. The results showed that the tumour absorbed dose ranged from 2.5 to 18.4 mGy/ MBq, depending on the lesion size. Patient specific dosimetry calculations helps the physician to optimize the planning of the treatment, avoid side effects to healthy tissue and assign administered dose to treatment results.**

Index Terms— *internal dosimetry, In-111, planar scintigraphy, dose calculation*

I. INTRODUCTION

THE radiopharmaceutical In-111-DTPA-D-Phe-1 octreotide is a peptide composed of 8 amino acids and is an analogue of the active part of the peptide hormone somatostatin [1]. Somatostatin is an endogenous neuropeptide that acts as a regulator of growth hormone secretion [2]. Somatostatin is present in many neurons and endocrine cells, mainly in the brain and in the GI tract, and has an inhibitory effect on growth hormone secretion. ^{111}In – Pentetreotide specifically binds to receptors for tissues where, as a consequence of disease, the cell – surfaces contain these receptors in higher than physiological density[3]. Till now, it has been indicated mainly for use in diagnosis of somatostatin receptor bearing tumours, such as neuroblastoma, some types of endocrine gastro –enteric – pancreatic (GEP) tumours, small cell lung cancer and breast cancer, by aiding in their localization. Tumours that bearn either somatostatin receptors nor sufficient receptors density are not visualized [4]. In palliative treatment use,the radiopharmaceutical entrance into the tumor cell and itsdestructive effect to DNA by emission of Auger and internal conversion electrons is exploited. The aim of this study was to estimate absorbed dose by tumour and healthy tissue using anterior and posterior planar scintigraphs [5] – [7], (fig.1, fig2). This method gives fast and accurate patient specific dosimetry calculations. Calibration measurements of the gamma - camera that obtained the planar scintigraphy images were performed in order to convert count rate to activity at patient organs. Radiation absorption through patient body and source organ, gamma - camera dead time and sensitivity must be considered in order to convert count rate to activity accurately [8], [19]. The infusion of the radiopharmaceutical was performed directly to patient liver through a port that was attached to the hepatic artery. This is proved to be the best method to give better uptake of the radiopharmaceutical by the tumour. Patient specific dose estimation for the tumour and healthy tissue is very important for radiopharmaceutical therapeutic applications as this is the most accurate way to assign an administered dose to the best therapeutic result. It is also assistance to the physician in order to avoid side effects of the therapy and compare the treatment results to other related therapies as external radiotherapy.

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II. MATERIALS AND METHOD

A. Patients

In this study, 22 patients with histologically confirmed neuroendocrine tumours lesions located in liver and normal kidney function were infused with mean activity of 4500 MBq ^{111}In - octreotide. The infusion was performed through a port attached to the hepatic artery. The hepatic artery port makes the therapy more comfortable for the patient as in this way the hepatic artery angiography catheterization, at each therapeutic session, is avoided.

B. Scintigraphy

Scintigraphy was performed immediately after radiopharmaceutical infusion and at 24 and at 48 hours post-infusion. Anterior and posterior planar images were obtained using an APEX SPX4 ElScint gamma - camera. The parameters that were used during imaging were medium energy all-purpose collimator, 20 % energy window centred at 247 KeV ^{111}In photo peak and 1 minute time to acquire an image.

C. Gamma - camera calibration.

A set of measurements were performed in order to convert count rate that was measured from planar images to activity. A cubic tank 0.1 m x 0.3 m x 0.3 m was filled with water and was placed on the examination bed and simulated patient's body [19]. 10 ml vials were placed at the center of the cubic phantom consecutively, filled with ^{111}In radionuclide.

Planar scintigrams of each vial were obtained with $_{111}$In activity varying from 200 to 2000 MBq. A linear fit function was applied to correlate measured count rate with source organ activity. R= 0.019 A + 0.41 where R : count rate, A : activity.

III. D. DOSE CALCULATIONS

Radiation emitted from organ source is absorbed by patient's body. It is necessary to correct measured count rate with the transmission factor. Transmission factor T can be calculated if we know patient's body diameter, using the function

$$T = e^{-\mu L} \quad (1),$$

where L is patient's body diameter and μ is linear absorbent coefficient for water. The value for L can be obtained by patient's computed tomography study because scintigraphic images do not provide any anatomical data [9], [10]. Also radiation is absorbed by the source organ. A correction factor f is applied due to this phenomenon. Factor f can be calculated from the function

$$f = [(\mu d/2)/\sinh(\mu d/2)] \quad (2)$$

where d is anterior-posterior size of the source target [11]. Considering the factors T, f and gamma – camera sensitivity E due to collimator and dead time, measured count rate was converted to activity A according to the function

$$A = (R_{ant} R_{post} / T)^{1/2} (f / E) \quad (3)$$

where Rant is the measured count rate from anterior image and Rpost is the measured count rate from the posterior image [12]. The count rates were measured with manually drawn regions of interest for liver, spleen, kidneys and tumour. Background count rate was measured close to regions of interest and a simple background subtraction method was performed. Activity was calculated from the planar anterior and posterior images immediately after radiopharmaceutical infusion, at 24 and 48 hours later. Activity was calculated for the tumour, liver, kidneys and spleen. Curves of activity as a function of time were drawn for each source organ. The area between each curve and time axis is the cumulative activity [13]. Cumulative activity A_c is measured in MBq hr and was calculated for each source organ. The residence time t was calculated for each source organ using the function

$$t = A_c / A_0 \quad (4)$$

where A_0 is the total infused activity. This method is appropriate for patient specific dosimetric calculations as residence times are calculated from patient's scintigraphic image. The MIRD schema, proposed by the Medical Internal Radiation Dose (MIRD) Committee, is widely accepted for absorbed dose calculations in the scale of human organs (i.e. greater than a centimeter) [7], [14]. The MIRD schema attempts to calculate the mean absorbed dose, assuming an average tissue deposition of energy and a uniform distribution of the radiopharmaceutical. The dose is calculated for the target region (T), by summing up the contribution of each source region (S) to the target and the contribution of the target region itself. Any region containing activity greater than the average concentration of activity in the total body is accepted as source region. It is assumed that non - penetrating radiation (beta particles, Auger electrons, internal conversion electrons and photons below 13 keV) is absorbed only if it is emitted within the target region [15]. On the other hand, penetrating radiation emitted by all source regions, including radiation emitted by the target region itself, contributes to the absorbed dose to the target region. The mean absorbed dose can be roughly estimated, due to major limitations in absorbed dose calculations; these come from the inherent difficulty in measuring radioactivity inside the body, as well as from the use of standard generalized biokinetic models, that may deviate considerably from the suitable for certain patient's size and physiology [16]. We have used the MIRDOSE3 program to calculate patient absorbed dose. MIRDOSE3 is a tool for calculating doses using standard models once the kinetic data are established. MIRDOSE3 software calculates absorbed dose per cumulative activity (S values) using anthropomorphic phantoms. The calculation is fast; dose estimation is accurate and patient specific, as residence times are calculated separately for each patient from his own planar images. A Microsoft Excel calculation sheet is developed so that count rate was converted to activity in a simple way. Measured count rate, patient's body diameter, administered activity and source organ size is entered to the program and cumulative activity is automatically calculated. Cumulative activity curves were then automatically drawn (fig 3, fig 4). Cumulative activity was then measured for tumour, kidneys, spleen and pancreas. Residence times were then calculated for each organ. Residence times were the inputs for MIRDOSE3. Finally absorbed doses for each organ were calculated with MIRDOSE3 in mGy/MBq.

IV. RESULTS

The residence times for source organs liver, spleen, kidneys and tumour was calculated and the mean values were 3.4 hr for liver, 2.85 hr for kidneys, 4.72 hr for spleen and 11.2 hr

for the tumour. Mean absorbed dose was estimated at 0.35 mGy/ MBq for kidneys, 0.15 mGy/ MBq for liver, 1.1 mGy/ MBq for spleen and 10.2 mGy/ MBq for the tumour. Minimum and maximum estimated absorbed dose values were 0.1 mGy/ MBq and 0.25 mGy/ MBq for liver, 0.2 mGy /MBq and 1.2 mGy/ MBq for kidneys, 0.2 mGy/ MBq and 1.9 mGy/ MBq for spleen, 2.5 mGy/ MBq and 18.4 mGy/ MBq for the tumour (fig 5).

V. DISCUSSION

From the dosimetric point of view, radiopharmaceutical therapy dosimetry differs significantly of the diagnostic applications' dosimetry. The organ absorbed dose is high at radiopharmaceutical therapy and there is a much greater risk for the healthy tissues. MIRD schema calculations give a satisfying precision at dose estimation for diagnostic applications but it is not the same for therapeutic dose estimations. For radiopharmaceutical therapy patient, specific dose calculation is essential because each patient has different pharmacokinetic and his anatomy deviates from anatomic averages [17]. Measured absorbed doses for tumour and kidneys are in good agreement with absorbed doses measured by Kontogergakos et al, 10.8 mGy/MBqfor tumour and 0.41 mGy/MBq for Kidneys. At this study high deviations of absorbed dose between patients were observed. This proves that patient specific dosimetry must be introduced in radiopharmaceutical therapy department, routinely, as a tool for the determination of the therapeutic activity dose that will have maximum biological effect to the tumour and avoid great risks for the healthy tissue [6], [18].

VI. CONCLUSION

Great differences of crucial organ absorbed dose during ^{111}In octreotide therapy are measured. Patient specific dosimetry is a necessary calculations technique that guides for optimum therapeutic activity dose to the tumour and keeps low risk for healthy tissue.

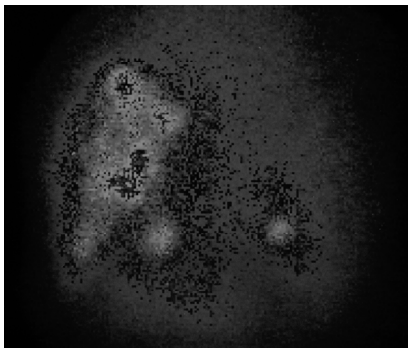

Fig.1. Planar anterior image immediately after In-111-octreotide infusion.

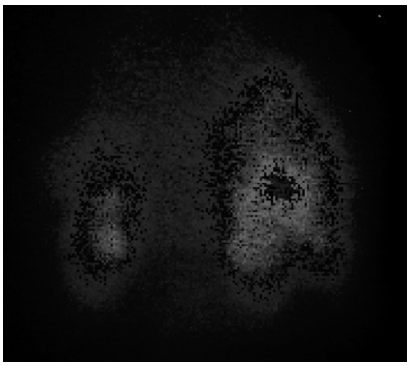

Fig.2. Planar posterior image immediately after In-111-octreotide infusion (same patient).

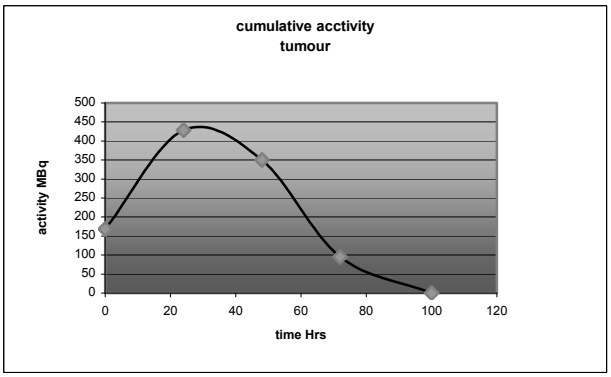

Fig.3. Tumour cumulative activity curve extrapolated to 100 hours (smooth line fit).

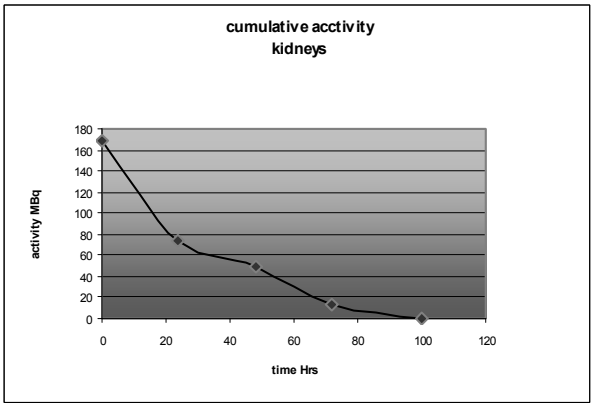

Fig.4. Kidneys cumulative activity curve extrapolated to 100 hours (smooth line fit).

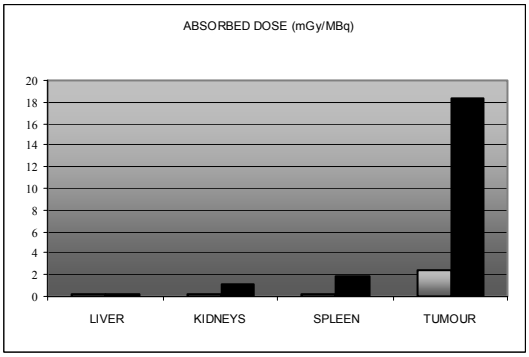

Fig.5. Minimum and maximum estimated absorbed doses for tumour and source organs.

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