Estimating the Absorbed Dose of Organs in Pediatric Imaging of ^{99m}Tc-DTPA Radiopharmaceutical using MIRDOSE Software

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ABSTRACT

Introduction: In this study, organ radiation doses were calculated for the renal agent ^{99m}Tc-DTPA in children. Bio-kinetic energy of ^{99m}Tc-DTPA was evaluated by scintigraphy and estimates for absorbed radiation dose were provided using standard medical internal radiation dosimetry (MIRD) techniques.

Material and Methods: In this applied research, fourteen children patients (6 males and 8 females) were imaged using a series of planar and SPECT images after injecting with technetium-99m diethylenetriaminepentaacetic acid (^{99m}Tc-DTPA). A hybrid planar/SPECT method was used to plot time-activity curves to obtain the residence time of the source organs and also MIRDOSE software was used to calculate the absorbed dose of every organ. P-values were calculated using t-tests in order to make a comparison between the adsorbed doses of male and female groups.

Results: Mean absorbed doses (µGy/MBq) for urinary bladder wall, kidneys, gonads, liver and adrenals were 213.5±47.8, 12.97±6.23, 12.0±2.5, 4.29±1.47, and 3.31±0.96, respectively. Furthermore, the mean effective dose was 17.5±3.7 µSv/MBq. There was not any significant difference in the mean absorbed dose of the two groups.

Conclusion: Bladder cumulated activity was the most contribution in the effective dose of patients scanned with ^{99m}Tc-DTPA. Using a hybrid planar/SPECT method can cause an increase in accumulated activity accuracy for the region of interest. Moreover, patient-specified internal dosimetry is recommended.

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Keywords

Internal Dosimetry, Hybrid Planar/SPECT Method, MIRDOSE Software, ^{99m}Tc-DTPA

Introduction

The biological effects of radioactive sources in the human body can be assessed through the physical quantity of the absorbed dose. For this reason, measuring the dose of various body organs is essential to make a judgment on the benefits of the radiopharmaceutical being used against the hazards of radiation for patients [1, 2]. In diagnostic imaging applications, including ionizing rays such as SPECT and PET, the exact measurement of absorbed dose is an important method in better analysis of risk-reward [3]. To reach this goal, the distribution of time-dependent activity in body requires the precise

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evaluation and quantitative analysis in nuclear medicine imaging. In general, activity data is placed into mathematical models describing radionuclide distribution in tissue, and then the energy deposited can be estimated in different parts of body [3, 4]. In order to calculate the absorbed dose in nuclear medicine, the time-activity kinetics of a radiopharmaceutical must be determined in the target organs [5]. Dose distribution varies according to the choice of radiopharmaceutical and radiation specifications. Therefore, examining internal dosimetry for each patient is the great importance of this method [6].

The collision of ionizing rays with biological systems causes ionization and the stimulation of atoms and molecules and creates abnormal and harmful products in the biological environment. The precise determinations of the prescribed amounts and the received radiation dose seem essential due to the side effects of ionizing rays from radionuclides so that patients are not subjected to unnecessary radiation [7, 8]. Exact calculation of radiation dose requires complete data on various types of radiopharmaceuticals, the physical decay and their distribution in body. On the other hand, the biological performance of body texture in the absorption and excretion of radiopharmaceuticals is a main factor in the absorbed dose of textures and varies among individuals [8]. Since the level of activity decreases in patient's body with time and eventually reaches zero.

Overall in nuclear medicine, two methods have been ruling to calculate absorbed dose of patient body, including the calculation using physical and biological data and specific mathematical equations. At the moment, the most common source of internal dosimetry in nuclear medicine (1960 to present) is the MIRD (Oak Ridge Institute for Science and Education, Oak Ridge, USA) system in which standard mathematical phantoms are used to calculate the internal absorbed dose [8, 9]. According to definition, the absorbed dose of every organ is the equal of the deposited energy in the mass unit of the organ. The deposited energy in each organ from radionuclide equals [10]:

deposited energy = the number of radionuclide decay in the volume of organ × the emitted energy of every collapse × the fraction of the energy absorbed in the mass of the given organ.

In a given clinical method, the images obtained over sequential times after the injection of the radiopharmaceutical are used to estimate the accumulated activity in a certain volume. The activity obtained at sequential times after the injection is plotted versus time and the time-activity is obtained for a given volume or organ. The integral or the area under the curve provides the total number of decays or collective activity in that area. The total activity for each patient has to be determined separately. To calculate absorbed dose on the internal organ level normally, MIRDOSE program is used [11]. Using MIRDOSE software, the user enters the residence times into the program and the program calculates the absorbed dose for every organ. Estimated doses are based on pre-calculated S values on the organ level, S (source => target) using standard man, woman, or child phantoms [12].

Radioisotope scan of kidneys is a common procedure in nuclear medicine which involves imaging structural abnormalities as well as estimating the quantitative half of profusion and kidney performance. The ^{99m}Tc-DTPA radiopharmaceutical is used to evaluate the performance of kidneys [13]. This radiopharmaceutical is commonly used in assessing kidney perfusion, imaging kidneys and the urinary system. Nearly 90 percent of injected ^{99m}Tc-DTPA leaves body after 4 hours through simple- exchange or dispersion into urine. Thus, by taking consecutive images using a gamma camera, it will be possible to calculate the performance of kidney in passing urine [14]. This study aims to estimate the absorbed dose reaching various organs in kidney scan using

the ^{99m}Tc-DTPA radiopharmaceutical, MIRDOSE software and the compound Planar/SPECT method to determine total activity and the residence of source organs in every patient.

Material and Methods

The ^{99m}Tc-DTPA radiopharmaceutical known as the DTPA commercial kit produced by Pars Isotope Co. was used for scintigraphy on patients. The activity level injected into patients using the dose calibrator device (Capintec, Inc., Ramsey, New Jersey, USA) was presented in the ward. The limitation of activity injected into patients was 95-188 MBq depending on the height and weight of patients.

In this study, 14 pediatric patients were chosen, including 9 female and 5 male patients referred to the nuclear medicine ward of Tehran's Shohada-e-Tajrish hospital. The personal information of each patient, including age, gender, weight, height as well as the injected activity is given in Table 1. Sampling was non-random and done among children referring to Shohada-e-Tajrish hospital, the nuclear medicine ward, who needed to have kidney perfusion scans with ^{99m}Tc-DTPA radiopharmaceutical , and whose parents agreed to sign a consent form. The size of the sample was determined according to the similar articles of the internal dosimetry and sample size determination formula (15-18).

All of the imaging was done after the injection of ^{99m}Tc-DTPA to the patients, by a dual headed gamma camera (Philips ADAC, forte, Netherlands) with a low energy, high resolution (LEHR) collimator. The three energy windows technique (TEW) was utilized to estimate photon scattering. The width of photopic window was chosen at 15 percent and the width of scattered upper and lower photopic windows were chosen at 7 percent. During a period of 1 to 12 hours after the injection of ^{99m}Tc-DTPA radiopharmaceutical, 4 planar scans of the thigh up to the chest area from anterior and posterior views were made 30 minutes, 1 hour, 3 and 12 hours after the injection, and a tomographic scan (SPECT) was made of each patient 2 hours after the injection. Other areas did not have noticeable levels of activity. The protocol for obtaining the anterior and posterior views from the abdominal and pelvic regions included a 256*256 matrix with a pixel size of 1.25mm. The SPECT data was gathered in a 360 degree rotation in a circle around the patient with 64 projections and a duration of 30 seconds in each frame in a matrix size of 128*128. The reconstruction of tomographic images for all patients was made using the filter back projection method. In accordance with recommendation of MIRD pamphlet No. 16, the effective attenuation coefficient of 0.15 cm-1 was used to modify attenuation extinction in the target mass [15]. Absolute activity in tumors and healthy organs was calculated according to the following equation through count correction in the intended volumes and divided it to the calibration factor of the camera.

Equation 1: $$A(j)=\frac{R_0(j)}{K}=\frac{R_{Corr}(j)}{K\,T}f$$

In this equation, $R_{Corr}(j)$ is the corrected count rate in the intended volume, f is the self-absorption correction factor in the source or-

Table 1: Shows information of the age, gender, weight, height, and injected activity

Patient number	1	2	3	4	5	6	7	8	9	10	11	12	13	14
gender	M	M	F	M	F	F	F	M	M	F	M	F	F	F
Age (y)	3	5	4	6	8	3	9	6	8	10	12	7	3	4
Weight (Kg)	12	14	13	16	19	14	21	18	19	30	32	20	14	16
Height (Cm)	97	105	100	110	122	98	130	125	134	128	140	125	90	95
Injected activity (MBq)	110	120	105	150	170	100	150	160	169	170	188	140	95	145

gan [16]. ($f = [(\mu_j d_j/2)/\sinh(\mu_j d_j/2)]$)

(μ_j & d_j are the attenuation coefficient of the source area and the thickness of the source, respectively). T represents the transmission factor and can be calculated for the diameter of patient body and the linear absorption coefficient of water in the energy field of the radionuclide being used. The calibration factor (K) (titled the count rate in activity unit) was determined through SPECT imaging from a point spot source with a certain activity level in the air and with a 15 cm distance from the surface of each detector [9].

To plot the time-activity curves, the compound Planar/SPECT imaging protocol was used [12]. After choosing a series of images from the whole body of each patient, an area was drawn manually around the organs with absorption such as kidneys, liver, bladder, and the rest of the body. Then, the 2 dimensional areas drawn were matched and applied manually to all image series of the whole body to obtain the count pertaining to each organ. The correction related to scattering was made using the TEW method [17] and background correction was used through drawing the areas surrounding each organ and subtracting it from the count relating to that organ [6]. After background and scatter correction, the corrected counts were done based on time. At this stage, attenuation correction was not applied to planar images because this factor has been obtained for all planar image series and is constant at different times [18]. For each source region, an exponential curve was fitted into the planar data to obtain the effective elimination constant (λ_{eff}) related to that region. In the next step, through scaling each curve based on measured activity from the SPECT (A_{spect}) image at the time of imaging (tSPECT), accumulated activity ($\tilde{A}$) was measured according to the following equation [19]:

Equation 2: $$\tilde{A} = \tilde{A}_{SPECT} \cdot \frac{e^{\lambda_{eff}\, t_{SPECT}}}{\lambda_{SPECT}}$$

To calculate the absorbed dose on the level of the organ, we need a quantity called residence time; this quantity can also be calculated by dividing collective activity to injected activity ($\tilde{A}/A_{inj}$). The residence time related to the rest of the body can also be determined by subtracting calculated residence times from the overall body residences time for every segmented organ. The segmentation of the images was carried out using ITK-snap software version 3.4.0-rc1. Plotting, fitting, and obtaining residence times for source organs were done using MATLAB software version R2013.

Calculating absorbed dose on organ level is a method of estimating absorbed dose of patients' organs based on residence times obtained from scintigraphic images, which are approved by the MIRD committee of nuclear medicine association. In this method, the absorbed dose is calculated based on pre-calculated S values for standard phantoms. S value equals the average absorbed dose in the target organ corresponding to the dissociation taking place in the source organ. Therefore, the absorbed dose of target organ can simply be calculated by multiplying S value by the number of dissociation taking place in the source organ (i.e. collective activity of $\tilde{A}$) [20]. To this end, the MIRDOSE program was used to calculate the average absorbed dose for various organs of patient based on μGy/MBq.

Finally, the P-values were calculated using independent samples T-test in order to make comparison between the adsorbed doses of male and female groups. It should be noted that $P<0.05$ considered to be statistically significant.

Results

After the injection of ^{99m}Tc-DTPA radiopharmaceutical and imaging, the organs with the highest radiopharmaceutical absorption were determined as bladder, kidneys, liver and the rest of organs, respectively in the imaging areas of abdomen and pelvis. The collective activity in source organs was obtained by drawing time-activity curve for source organs

and other organs and then calculating the area under each curve. Then, the residence time of the radiopharmaceutical for each source organ and other organs were obtained by dividing collective activity by the injected activity. Figure 1 as a sample that shows time-activity curve of the bladder for third patient number (4-year old female) that regression factor for fitted formula of the curve was more than 95%. The residence times for source organs and the rest of organs for each patient are shown in Table 2. As can be seen from the this table, the average residence time for bladder, kidneys and liver were 2.19 ± 0.15, 0.11 ± 0.05, 0.10 ± 0.05 hours, respectively, and the residence time for rest of organs was obtained at 1.43 ± 0.22 hours.

The results related to the amounts of calculated absorbed dose using MIRDOSE software for each patient's various organ have been reported in Table 3. Among organs, bladder wall has the highest absorbed dose with 213.5 ± 47.8 (μGy/MBq) followed by kidneys, gonads, liver and adrenals with the absorbed doses of 12.97 ± 6.23, 12.00 ± 2.50, 4.29±1.47, and 3.31 ± 0.96, respectively. Besides, the mean

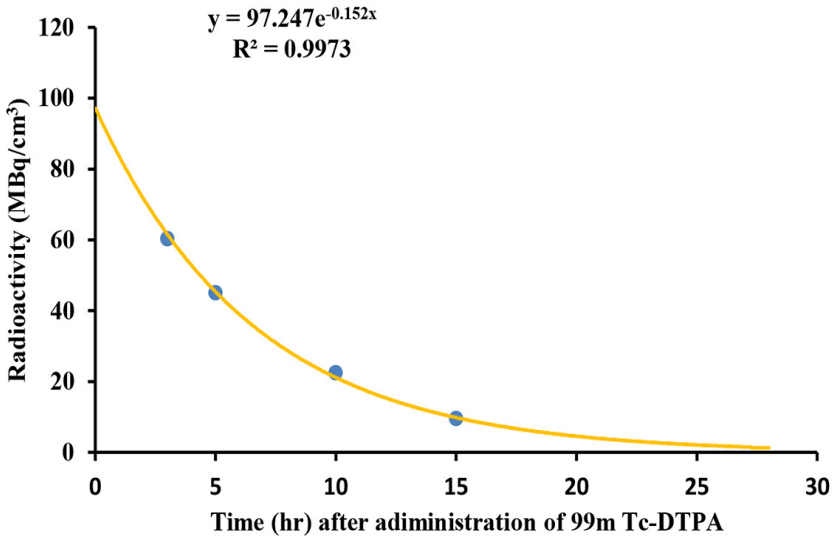

Figure 1: Time-activity curve of the bladder for third patient number (4-year old female)

Table 2: The residence time ^{99m}Tc-DTPA for source organs and the rest of the body (MBq h/MBq)

Patient number	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Kidneys	0.09	0.08	0.11	0.03	0.12	0.18	0.07	0.21	0.11	0.14	0.05	0.08	0.13	0.08
Bladder	2.3	2.19	2.41	2.22	1.98	1.9	2.33	2.41	2.25	2.16	2.02	2.2	2.29	2.08
Liver	0.08	0.11	0.05	0.04	0.1	0.09	0.13	0.19	0.15	0.17	0.03	0.07	0.1	0.04
Rest of the body	1.24	1.51	1.88	1.33	1.31	1.19	1.55	1.17	1.6	1.08	1.61	1.58	1.51	1.45
Injected activity (MBq)	110	120	105	150	170	100	150	160	169	170	188	140	95	145

Table 3: Absorbed dose (µGy/MBq) and effective dose (µSv/MBq) for each patient activity for ^{99m}Tc-DTPA

Patient number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Mean
Adrenals	3.45	3.89	2.56	2.98	2.49	4.02	2.6	4.67	2.91	2.56	2.26	2.51	4.27	3.53	3.19 ± 0.77
Kidneys	12.8	11.9	15.7	5.75	11.2	23.1	7.4	27.1	10.7	12.9	5.6	8.1	17.8	11.6	12.97 ± 6.23
Liver	4.38	5.43	4.03	3.04	3.41	4.75	4.15	8.02	4.68	4.89	1.9	2.85	5.29	3.21	4.28 ± 1.47
Bladder wall	260	245	273	251	150	215	176	271	170	163	153	167	259	235	213.42 ± 47.75
Gonads	13.7	13.5	16.1	13.4	8.9	12.2	10.3	14.2	10.1	9.2	8.22	9.88	14.7	13.4	11.98 ± 2.49
Effective dose	20.7	20.3	22.6	20	12.5	17.6	14.6	22	14.3	13.4	12.8	13.9	21.2	19.2	17.50 ± 3.74

effective dose resulting from the injection of ^{99m}Tc-DTPA radiopharmaceutical on patients was obtained at 17.5 ± 3.7 (µSv/MBq), where the activity present in the bladder has the biggest share in this effective dose.

Figure 2 demonstrates the mean absorbed dose of different organs in the male and female groups. It was found that the mean absorbed dose in these two groups for kidneys, gonads, liver, adrenals and bladder wall did not have any significant differences (P-value>0.05).

Discussion

The precision of internal dosimetry calculations is largely dependent upon the precision of activity quantification and obtaining collective activity in patient's body; therefore, choosing a method that, while being simple and effective, does not create disturbances to the workload of the busy nuclear medicine working environments and enjoys sufficient precision for the quantification of activity in the body seems essential [18]. In this study, unlike the quanti-

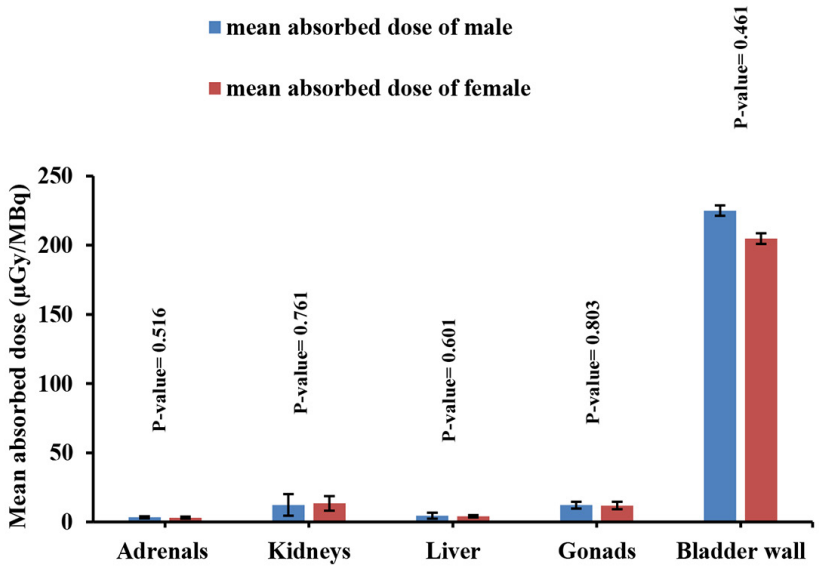

Figure 2: Mean absorbed dose in the male and female groups

fication method employed in previous studies [14, 21] (the image integration method), the compound Planar/SPECT method [22] was employed to determine the time distribution of the radiopharmaceutical in patient's body. In this method, using tomographic images, the errors resulting from the texture interference effect are eliminated, and the correction of activity quantifying errors such as attenuation effect is more precise. Above all, to correct for the scattering, the TEW method was employed enjoying a higher exactness in comparison with the single energy window method [17].

In this project, after repeated imaging of patients with the ^{99m}Tc-DTPA radiopharmaceutical and drawing time-activity curve and then calculating residence times for the organs having noticeable activity, bladder was found to have the highest residence time, followed by kidneys and liver, and the other organs were considered as rest of organs body. Since the absorbed dose of organs results from two main causes of the existing activity in the organ itself (self-absorption) and the proximity of the organ to source organs (other-absorption) [19, 23]; for this reason, the bladder wall contained the highest level of absorption dose in all patients. Kidneys, gonads, and adrenals were other organs with noticeable absorbed dose. In addition, the high variation in the absorbed dose of different organs for each patient is the result of the differences in accumulated activities and consequently differing residence times in various organs of each patient in a way that the dose resulting from self-absorption has the highest share in the absorbed dose of each source organ [12]. Moreover, the variations in the absorbed dose in various organs of different patients are due to differences in the biological distribution of the radiopharmaceutical [5]. In a study, by Pirdamooie et al. [14], was remarked that the significant difference in the cumulated activity and absorbed doses among the kidneys, spleen and liver can be due to the biological variation of the functionalized radiopharmaceutic. In another study, Razaq et al. [24] investigated the possible alteration in the bio-distribution of ^{99m}Tc-DTPA when given in combination with doxorubicin (DOX) in rats. They showed that the percent total retained dose significantly decreased in urinary tract while significantly increased in liver and biliary tree as compared to the experimental group (DOX with prior ^{99m}Tc-DTPA).

The ^{99m}Tc-DTPA radiopharmaceutical bonds with blood plasma proteins to some extent (about 5 percent) and thus leaves body only through glomerular filtration. The amount ^{99m}Tc-DTPA absorbed into the kidney is limited since only 20 percent of kidney's blood stream is refined through glomerular filtration. This mere 20 percent share causes a decrease in the proportion of ^{99m}Tc-DTPA absorption to background and thus reduces the whole absorption of the kidneys [21].

The ^{99m}Tc-DTPA radiopharmaceutical accumulates in the bladder to a high degree. The high concentration of the radiopharmaceutical causes the high bladder absorption rate and more uptake by kidneys and leads to a higher absorption rate of this organ in patients being scanned using this radiopharmaceutical. The high concentration of activity in bladder can be the main cause of the high dose reaching the ovaries among patients scanned using ^{99m}Tc-DTPA. Regarding the results obtained in this study and other studies, scanning the kidneys using the ^{99m}Tc-DTPA radiopharmaceutical can be concluded since the most of the injected radiopharmaceutical is concentrated in the bladder; this organ acts as the main source organ and the other surrounding organs act as target organs. Frequent emptying of the bladder and recommending it to the patients referring to a kidneys scanned part can contribute towards reducing the amount of dose reaching neighboring organs especially gonads regarding their high sensitivity [21, 25].

We showed that there was not any significant difference in the mean absorbed dose of the male and female groups for kidneys, gonads, liver, adrenals and bladder wall organs (Figure

2).

The calculated dose levels in this study were comparable with amounts reported in previous studies [14, 26]. The factors causing difference and indeed the sources of error in this and the previous studies are attributable to internal dosimetry, including the inherent limitations of devices used in each study in differentiating energy, and lost data due to scattering and attenuation [15]. In addition, the background correction method used, the calibration agent and anatomical differences between human body and phantoms, can be the causes of error and variations between studies.

Conclusion

The basis of this study was the estimation of the absorbed dose reaching kidneys, liver, adernals, bladder wall and gonads in the scans of kidneys and urinary tracts (urethras) using ^{99m}Tc-DTPA in pediatric patients referring to the nuclear medicine ward of Shohada-e-Tajrish Hospital, Tehran, Iran, and using MIRDOSE software. Various studies have shown there are noticeable differences between the anatomy of every patient and phantoms used in the general dosimetry method. Therefore, it is recommended that for internal dosimetry calculations, methods based on patients' images and the Monte-Carlo method be employed. The differences between patients' effective doses and the absorbed dose of various organs represent the difference in spatial and temporal distribution of the radiopharmaceutical in the bodies of various patients that it indicates the specific calculation of the internal dose for each individual.

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Conflict of Interest

None

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