



Journal of Medical Sciences

ISSN 1682-4474

science
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JMS (ISSN 1682-4474) is an International, peer-reviewed scientific journal that publishes original article in experimental & clinical medicine and related disciplines such as molecular biology, biochemistry, genetics, biophysics, bio-and medical technology. JMS is issued eight times per year on paper and in electronic format.

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J. Med. Sci., 14 (5): 210-216
1st July, 2014
DOI: 10.3923/jms.2014.210.216

Liver Bremsstrahlung Imaging with Pure Beta Emitter

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Pure beta emitters have application in treatment of the patients with the malignant diseases. Imaging of pure beta emitters is possible through bremsstrahlung imaging. If the presently available imaging devices are to be used the main problem will be setting of the energy windows and selection suitable collimator. In this study we determined the optimum energy window for bremsstrahlung imaging of P32 in liver imaging using Monte Carlo simulation. Gate Monte Carlo code was used to image the Zubal digital phantom. Activity was assumed uniformly distributed in the liver of phantom and attenuation properties of organs were defined using ICRU data. The pure spectrum of bremsstrahlung radiation from liver was simulated. The changes to this spectrum due to photoelectric and Compton interaction were determined. The useful range of bremsstrahlung radiation was determined and imaging was performed at 20 keV steps. The SNR and FWHM of the images were calculated and the optimum energy window was determined for LEGP and MEGP collimators. Analyses of energy spectrum showed the useful range of energy for bremsstrahlung images is 20-400 keV. Further analyses using the SNR and FWHM of acquired images showed that the optimum energy for both LEGP and MEGP collimators.

Key words: Bremsstrahlung imaging, GATE, Monte-Carlo simulation, liver, energy windows

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INTRODUCTION

Until recently nuclear medicine was mainly considered as a diagnostic modality. However, radionuclide therapy is changing dynamically and the therapeutic procedures are now constitute an imperative part of the nuclear medicine disciplines (Stabin, 2008). The basis of radionuclide therapy is simply the placement of radioisotopes in close contact to the target cells (Zimmermann, 2012). Depending upon the type and the range of particles, absorbed dose to the target tissue can be very high compared to non-target tissues. Radionuclides are being used as palliative and/or curative agents for the patients who suffer from malignant diseases (Eary and Brenner, 2007).

Radionuclide therapy can be extremely useful for the treatment of wide-spread lesions where application of external beam radiation is problematic (Stigbrand *et al.*, 2008). The type and the average energy of particles emitting from radionuclide is extremely important (O'Donoghue *et al.*, 1995). Radionuclides used for the therapeutic applications are mainly beta emitters of medium energy. Beta decay is generally followed by emission of gamma and/or X-rays (e.g., ^{64}Cu , ^{131}I , ^{186}Re). However in some cases there is no extra emission or extra emissions are negligible (e.g., ^{32}P , ^{90}Y , ^{165}Dy). Handling and application of these two types of beta emitters are somehow different.

When working with the pure beta emitters, radiation safety is primarily concerns with the handling of the excreta and body fluids from the administrated patients. However, when radiations include energetic photons, exposure to the public is also an important issue in the safety concerns (Eary and Brenner, 2007). From the therapeutic point of view, some knowledge about the kinetic and distribution of radionuclide is essential for the treatment planning of the patient (Stabin, 2006). The required information can only be obtained using nuclear medicine imaging devices. However very few beta emitters have photon emission that are suitable for imaging (Clarke *et al.*, 1992; Cipriani *et al.*, 1997).

A technique for tracking of the pure beta emitters radionuclides inside the body is through the bremsstrahlung radiation (Bayouth and Macey, 1994; Shen *et al.*, 1994). This radiation is produced during inelastic interaction of beta electrons with the nuclei of the atoms in the media (Balachandran *et al.*, 1985). Though the idea to use the bremsstrahlung radiation for imaging and dose estimation goes back to 1955 (Liden and Starfelt, 1955), application of the technique is thus far very limited and is still the subject of research by

many scientists over the world (Rong and Frey, 2013; Rong *et al.*, 2012a, b; Minarik *et al.*, 2010).

Bremsstrahlung radiation has a wide spectrum of energy from zero to a maximum, equal to the maximum energy of beta particles. Though energy spectrum of bremsstrahlung is not uniform however, it does not have a distinct peak of radiation (Siegel, 1994). The atomic composition of the medium has considerable effect on the shape of the spectrum due to interaction of bremsstrahlung photons with the atoms in media (Manjunatha and Rudraswamy, 2009). This makes a big challenge to set the energy window of a gamma camera for optimum bremsstrahlung imaging (Rong *et al.*, 2013).

Nuclear medicine imaging devices are generally optimized for photons of certain range of energies (100-200 keV). Collimators are also designed for different range of energies that are low, medium and high energies (Gunter, 2004). Lack of flexible imaging devices for bremsstrahlung range of energy is probably the main reason for the slow progress in this field of investigation.

Up to when more suitable imaging devices are available, the investigations on the bremsstrahlung imaging are confined to the use of presently available imaging systems therefore, for the time being, the problem is to determine the optimum energy window for imaging and selecting the more suitable collimator for this purpose.

In this study, we investigated the optimum windows for the bremsstrahlung imaging. We also compared two types of collimators generally available in nuclear medicine department that is, Low-Energy General-Purpose (LEGP) and Medium-Energy General-Purpose (MEGP) collimators. Due to importance of P32 microsphere in the treatment of hepatic cancer, this investigation was performed on P32 bremsstrahlung imaging of liver. Leakage of P32 microspheres outside the liver may cause serious complications, such as ulceration and bleeding (Sadeghi *et al.*, 2007; Elschot *et al.*, 2013). Bremsstrahlung imaging is very helpful in detection of leakages of P32 outside the liver. Malignant cells have a tendency to accumulate more phosphate than their normal counterparts.

Due to practical difficulties in such studies, we performed Monte Carlo simulation as the first step for an excremental study. Monte Carlo simulation provides the opportunities to investigate different aspects of bremsstrahlung imaging that is almost impossible in experimental studies (Ljungberg *et al.*, 1998). In this study we used Zubal phantom to represent a typical human body and Gate Monte Carlo code (version 6.2) to simulate a gamma camera system.

MATERIALS AND METHODS

Beta spectrum of P32 radiation: Phosphorus-32 is a pure beta emitter that decays in a single step. The average energy of beta particles is 695 keV (maximum beta particles energy 1.71 keV). The energy spectrum of P32 beta particles was derived using the Murphy equation:

$$N_0(E)dE = k \{A_0 + A_1E + A_2E^2\} \times \{E_0 - E\}^2$$

where, E_0 is the maximum energy of beta particles (1.71 keV) and k , A_0 , A_1 ,... are constant values (Murthy, 1971).

Monte Carlo gate simulator: The GATE/GEANT Monte Carlo package (version 6.2) was used to determine the spectrum of bremsstrahlung radiation from P32 inside the liver (Jan *et al.*, 2004, 2011; Visvikis *et al.*, 2006). Using this package a gamma camera (Infinia Hawkeye GE Healthcare with LEGP and MEGP collimators) was simulated and the simulation was validated using characteristic, published by manufacturer. This version of GATE/GEANT was developed over GEANT4 version 9.5.1.p01. Bremsstrahlung interaction, ionization and multiple scattering were considered for the electron interactions. For photons, photoelectric absorption, Compton interaction, Rayleigh scattering and characteristic X-ray production were also considered to have more genuine results. X-rays and bremsstrahlung radiations were tracked down to 1 keV, below that was assumed to be absorbed at the location (voxel) of interaction in the phantom. The cut-off range applied on the secondary electrons was 1 mm. Each voxel in the phantoms was linked to the table describing the attenuation properties of tissues based on ICRU tissue composition data (Jan *et al.*, 2004).

Human Zubal phantom: The voxel-based anthropomorphic Zubal phantom was used to model a typical adult male (Zubal *et al.*, 1994). The phantom included head and body torso (no arms or legs) segmented into 56 different tissue types. Phantom was in $128 \times 128 \times 246$ voxels of $4 \times 4 \times 4$ mm dimensions. Activity was considered uniformly distributed in the liver. Attenuation properties of the tissue (atomic constitution) were derived from ICRU report 44 (ICRU, 1989).

Bremsstrahlung radiation spectrum: The attenuation properties of all tissues except liver were set to zero (vacuum) and activity (P32) was considered uniformly

distributed inside the liver. The photoelectric and Compton scattering were inactivated and a simulation was performed (1.0×10^8 photon history) to obtain the pure spectrum of the bremsstrahlung radiation.

The attenuation properties of all tissues were set as normal and activity was considered uniformly distributed inside the liver. The photoelectric interaction was activated and the simulation performed (1.0×10^9 photon history). The procedure was repeated while photoelectric interaction was inactivated but Compton scattering activated. The same procedure was repeated (1.0×10^9 photon history) while both photoelectric and Compton scattering activated. These simulations were performed to obtain the partial effects of photoelectric absorption, Compton scattering and the both interactions on the bremsstrahlung radiation emitting from the body. In all the cases full spectrum of radiation (0-2 MeV at 10 keV interval) were determined using the corresponding actor in the Gate package.

Simulation: The attenuation properties of the tissues were set normal and P32 uniformly distributed inside the liver. Zubal phantom was imaged using the Gate package (all interactions were activated). The energy window width were set at 20-40, 40-60, ... 380-400 keV and the images of liver were acquired (1.0×10^7 photon history for each simulation). Imaging was performed using LEGP and MEGP collimators independently. In order to evaluate the pure effect of collimators crystal blurring was inactivated. To acquire the reference image simulation (imaging) was performed using parallel photons without collimator and crystal blurring (1.0×10^9 photon history). Due to limited resolution of Zubal phantom ($4 \times 4 \times 4$ mm), resolution of images were at 4×4 mm in 128×128 matrix size. In order to determine the resolution of images for each imaging condition one point source was also imaged.

Statistical analyses: The energy spectra were compared and analysed to determine the part of bremsstrahlung radiation spectrum is at least affected inside the body due to photoelectric and Compton interactions.

The simulated images were analysed to determine signal-to-noise ratio and resolution of images. All images were normalized to the corresponding reference images and signal-to-noise ratio and resolution were calculated. We used deconvolution technique to calculate the response function of collimators at different energy. The response functions were compared to determine the best window width for bremsstrahlung imaging.

RESULTS

The general geometry used in the simulations is presented in Fig. 1. The figure shows Zubal phantom, beta particles in the liver of phantom, bremsstrahlung radiation emitted from body. The collimator and detector are also shown in Fig. 1.

Bremsstrahlung spectrum analysis: The results of spectrum analysis are shown in Fig. 2 in semi logarithmic scale. There are 4 curves in this figure. The first curve represents the original spectrum of bremsstrahlung radiation produced in the liver. To create this graph all type of interactions except bremsstrahlung were inactivated. Except the liver the attenuation properties of all tissues were considered zero (vacuum). Second curve

shows the spectrum of this radiation after attenuation inside the body due to photoelectric absorption. For simulation of this curve, all the interactions excluding Compton were activated and tissue properties were as reported in ICRU-44. The third represents the effect of Compton scattering on the bremsstrahlung radiation emitting from liver. This curve was obtained as the second curve but photoelectric interaction was inactivated. The last curve (curve-4) represents the actual bremsstrahlung radiation emerging from the body due to P32 inside the kidney. For generation of this curve all the interactions were activated and all tissue properties were normal (ICRU tissue properties).

To evaluate the effect of collimator to the bremsstrahlung energy spectrum, a collimator was between the Zubal phantom (representative a typical

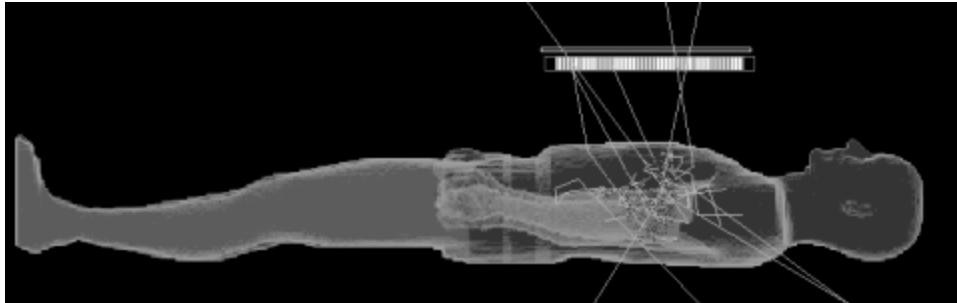


Fig. 1: General form of the geometry used in this study

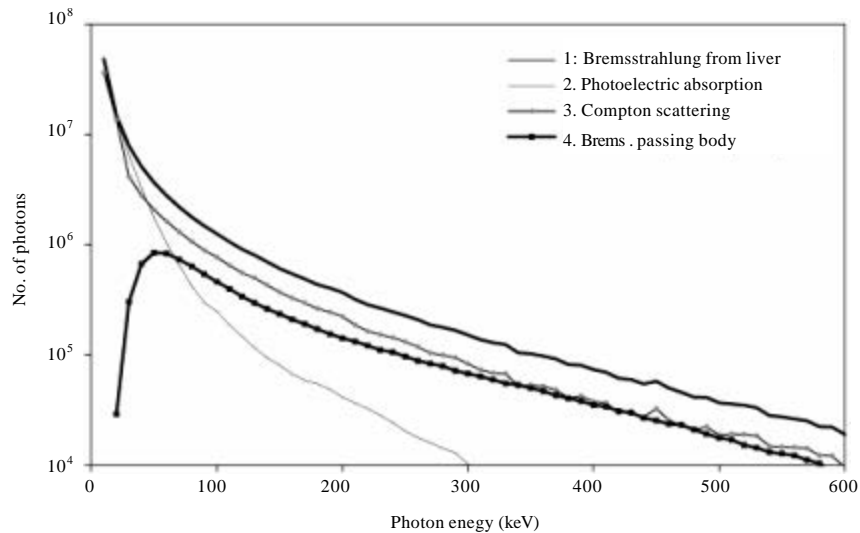


Fig. 2: Simulated spectra of the bremsstrahlung radiations. 1: Pure radiations produced in the liver, 2: Spectrum of radiation affected by photoelectric absorption, 3: Spectrum of radiation affected by compton scattering after passing through the LEGP collimator and 4: Spectrum that is actually emitting from the body. The spectra are taken at 10 keV resolution

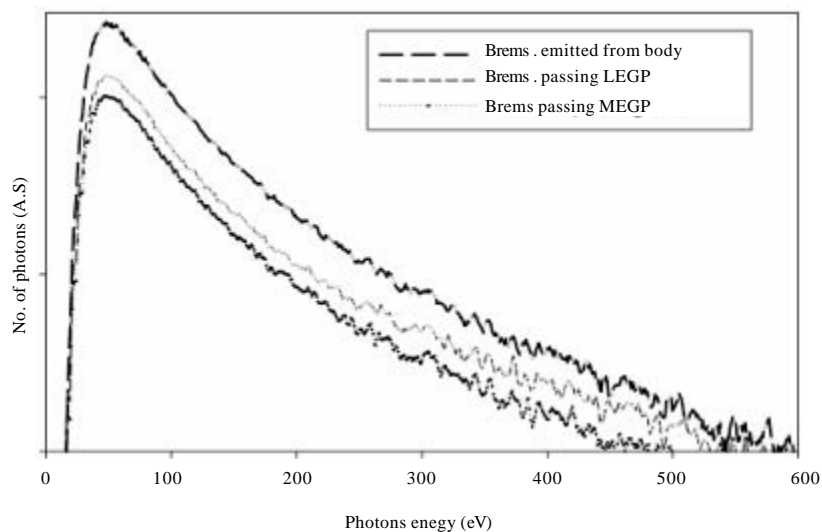


Fig. 3: Comparison of the bresmstrahlung after passing through LEGP and MEGP collimators. The spectrum of bresmstrahlung radiation is not considerably affected. The spectra are taken at 1 keV resolution

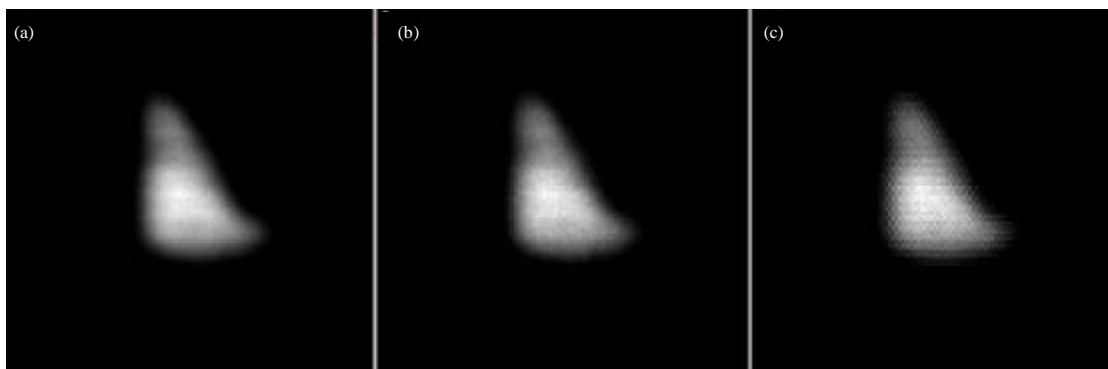


Fig. 4(a-c): Simulated images of bresmstrahlung radiation from P32 (a) Reference image containing very high counts, (b) Optimum image using LEGP collimator and (c) Optimum image using MEGP collimator

patient) and the energy spectrum was obtained after passing the collimators. The considered collimators were Low-Energy General Purpose (LEGP) and medium energy general purpose. The results of this part are presented in Fig. 3. As can be seen the changes in energy spectrum are negligible however sensitivities of collimators are different.

Image analyses: We acquired several images of the liver (Zubal phantom) at different energy window widths for both LEGP and MEGP collimators. The window widths were 20-40, 40-60 380-400 keV energy (19 images for each collimator). We made several combination of the images (sum of 2, sum of three,...) and the Signal-to-Noise

Ratio (SNR) and the resolution of images (FWHM of corresponding point source) were calculated. Figure 4 shows three images from this investigation. Figure 4a represents the reference image acquired using 1.0×10^9 photon histories. The optimum images acquired using LEGP and MEGP are shown in Fig. 4b and c, respectively. The criterion for optimization was the maximum value for the ratio of SNR to FWHM.

DISCUSSION

Knowledge about the spatial distribution of radioisotopes inside the body is essential for dosimetry and treatment planning of the patients with malignant

disease. It is possible to include a gamma emitter along with beta emitter however, it requires some extra preparation. Miss match between the half-lives of the two radionuclides can be problematic and except Tc99m almost all gamma emitters also essentially beta emitters. The other option for tracking pure beta emitters is through the bremsstrahlung radiation. One big advantages of bremsstrahlung imaging is the direct relation between the absorbed dose and the intensity of bremsstrahlung radiation emitting from the tissues. High cross section for the bremsstrahlung interaction means high atomic number that has high probability of photoelectric interaction. The biological effects of radiation are directly depended upon the ionization in the tissues.

An important example of pure beta emitter is P32 that is largely used in treatment of liver cancer. In the present paper we investigated the optimum width of energy window for gamma camera imaging of the bremsstrahlung radiation. Timeliness of LEGP and MEGP collimators for this type of imaging were also compared.

Obviously such investigation is very hard or almost impossible to be performed experimentally. However, high resolution digital phantoms representing accurate anatomy of human and the dedicated Monte Carlo package for nuclear medicine imaging provided the opportunity to perform very accurate simulations in this objective.

In the first step we analyzed the spectrum of bremsstrahlung radiation in order to determine the suitable range of energy for gamma camera imaging. As Fig. 1 shows, the spectrum of bremsstrahlung produced in liver is almost in the form of an exponential function. As theoretically expected, the number of photons monotonically decreases with increasing the photon energy (first curve). Almost all the low energy bremsstrahlung photons are absorbed in the body via photoelectric interaction (second curve). By increasing the photon energy the probability of photoelectric interaction rapidly decreases (second curve) and the relative probability of Compton interaction increases. The variation of Compton scattering do not considerable changes with increase the energy however, it shifts the energy spectrum towards the left (third curve). Scattered photons lost their spatial information. The overall effect is shifting of the spectrum to the left (Compton effect) and absorption of low energy photons (photoelectric effect). It is clear that the higher part of the energy spectrum is less affected by the interaction of bremsstrahlung photons inside the body however the intensity of photons decreases very rapidly therefore SNR in the image decreases.

After that images acquired at the energy width of 20 keV were combined in different ways and for each combination the SNRs were calculated. The corresponding point images were also analyzed in order to determine FWHM. Among all the possible combination of images the optimum window width was 20-200 keV for both collimators however the ratio of SNR to FWHM was higher for LEGP than MEGP collimator.

CONCLUSION

Based on the results of this study the optimum energy window for bremsstrahlung imaging is 20-200 keV. This result was based on the Monte Carlo simulation using Zubal phantom. Though Zubal phantom is representative of a real human body however, the results may be somehow different if other phantom were used.

ACKNOWLEDGMENT

This study was supported by a grant from Tarbiat Modares University.

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