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NSECT applied to the assessment of calcium deposition due to the presence of microcalcifications associated with breast cancer

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Abstract— **In this paper we presented an application of the Neutron Stimulated Emission Computed Tomography (NSECT) which uses a thin beam of fast neutrons to stimulate stable nuclei in a sample, emitting characteristic gamma radiation. The photon energy is unique and is used to identify the emitting nuclei. This technique was applied in evaluating the calcium isotopic composition changing due to the development of breast microcalcifications. A particular situation was simulated in which clustered microcalcifications were modeled with diameters less than 1.40 mm. In this case neutron beam breast spectroscopy was successful in detecting the counting changes in the photon emission spectra for energies which are characteristics of ^{40}Ca isotope in a low deposited dose rate.**

Keywords — **NSECT, microcalcifications, breast cancer, spectroscopy, diagnosis.**

I. Introduction

Breast cancer is the second most common cancer worldwide and the leading cause of death among women in Brazil. According to estimates for the year 2010 it is expected approximately 49,000 new diagnosed cases [1].

One of the main signs of breast cancer at an early diagnosis is the development of microcalcifications. Because of calcium radiological properties, microcalcifications are associated with non-palpable lesions that can be visualized on mammography, which makes it the primary mode of breast cancer diagnosis [2]. The importance of the detection of microcalcification formations in their early stages is well-known fact and according to the literature, the survival rate of patients who developed breast cancer is inversely proportional to the lesion size. Regardless of prognosis, women with invasive breast tumors with a diameter of 10 mm or even smaller die due to complications at diagnosis [3]. However, in early stages those microcalcifications are very small, becoming difficult to be detected by mammography.

The presence of isolated breast microcalcifications is not a decisive factor in the diagnosis of breast cancer but it is one of the first signs of metabolism disorder. In addition, the morphological changes caused by microcalcifications and visible on mammography screening occurs later on physiological changes due to increased calcium deposition.

In recent years, a new technique for *in vivo* spectrographic imaging of stable isotopes was presented as Neutron Stimulated Emission Computed Tomography (NSECT) [4]. In this technique, using multiple projections, a fast neutron beam interacts with the stable isotopes of the irradiated tissue, through inelastic scatterings, making them jump into an excited state. When they return to their ground state, they emit photons which energies are intrinsic to the emitting nuclei. The emitted gamma energy spectra can be used for two purposes: (a) reconstruction of the target tissue image and; (b) determination of the tissue elemental composition. Considering a clinical application, the spectroscopy of elements distribution in the body can be used in the study of the tissues metabolism. As the development of calcium deposits in the form of microcalcifications alter the abundance of this element in the breast, this spectrographic technique may be used to evaluate the calcium isotopic composition changing due to the development of microcalcifications.

In this present work the energy spectrum data obtained from the simulated spectroscopy of a healthy breast has been compared to those obtained from the simulated spectroscopy of a breast model with inserted microcalcifications with different diameters. Simulations have been done using the Monte Carlo code MCNP5. From these comparisons it was possible to establish a relationship between the microcalcifications sizes and the calcium emission photopeak intensities. A particular situation represented by clustered microcalcifications has been also analyzed. In this approach a mammography unit was simulated in order to relate the variation of calcium isotopic composition with the spatial distribution of microcalcifications.

II. Methodology

A. Monte Carlo code MCNP5

The Monte Carlo method can be described as a statistical method, which uses a sequence of random numbers to perform a simulation. In terms of radiation transport, the stochastic process can be seen as a family of particles moving randomly in each individual collision as they travel through matter. The average behavior of these particles is described in terms of macroscopic quantities such as flux or particle density. The expected value of these quantities corresponds to the deterministic solution of the Boltzman equation. Specific quantities such as

deposited energy or dose are derived from these quantities.

The MCNP code is a well-known and widely used Monte Carlo code for neutron, photon, and electron transport simulations [5]. The first MCNP version was released in the mid-1970s for neutron and photon transport, and was enhanced over the years to include generalized sources and tallies, electron physics and coupled electron-photon calculations, macrobody geometry, statistical convergence tests and other features. The present work utilized the last MCNP released version which is the version 5. The MCNP5 particle transport simulation requires an input file (inp), which allows the user to specify all the information about geometry modeling, source specifications, material compositions, and the specific quantities to be estimated (tallies).

B. Simulations

The simulated breast was modeled as a half of an ellipsoid placed in the x-y plane. The breast composition was taken from the literature [6]. Microcalcifications assume two distinct chemical compositions: calcium oxalate ($CaC_2O_4.2H_2O$) and hydroxyapatite ($Ca_{10}(PO_4).6H_2O$). Some morphological characteristics revealed that benign tumors have microcalcifications predominantly composed by calcium oxalate while microcalcifications composed by hydroxyapatite can be associated with both benign and malignant tumors [2]. The microcalcifications simulated in this work were modeled considering these two chemical compositions.

The NSECT is a spectrographic technique and the analysis of any sample is understood by both the spatial distribution of stable isotopes and the photon emission spectrum that characterizes the isotopic composition of irradiated medium. However, the approach proposed in this paper uses only the spectroscopic analysis of tissues under investigation.

First, the photon emission spectrum of the healthy breast was obtained and used as a reference assuming the existence of a normal [6] calcium concentration. Subsequently, the breast was modeled with the inclusion of microcalcifications of different diameters (1-14 mm) and using the two chemical compositions already described. The resultant spectra obtained from the simulations were compared with the reference spectrum with the aim of establishing a relationship between the diameters of the microcalcifications and the calcium emission photopeak intensities. Since the background is a common factor in all obtained spectra it was not necessary to adopt any suppression or background extraction procedure.

Two hyper-pure germanium (HPGe) detectors were modeled as cylinders of 5.32 g/cm^3 density with 12 cm diameter and 15 cm height. The detectors were separated 90° from each other and both forms 45° with the neutron beam axis. The neutron source was modeled in MCNP5 as a monoenergetic energy beam of 7 MeV and with a square section of 1 cm^2. 5x10^8 incident neutrons have been simulated and photons whose emission was stimulated by inelastic scattering of fast neutron beam were recorded on the surface of the detectors using the F2 superficial flux tally. This tally estimates the average particle scalar flux on a user-specified surface and it was associated with the E*n* card which allows separating the counting photons according to energy bins of interest. Using this MCNP5 tally resource it was possible to build the energy spectrum of the scattered photons arriving at the detectors. The configuration adopted of the spectrometric system is shown in Figure 1.

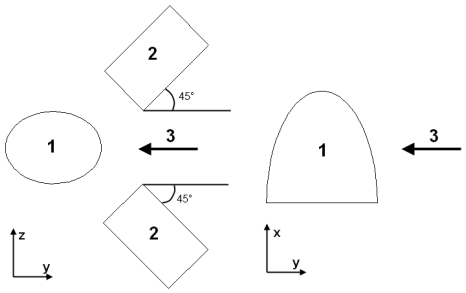

Fig.1 The MCNP5 spectrometric system setup: 1 Breast (1); HPGe detectors (2) and neutron beam (3).

Since 1913 when it was reported the first description of microcalcifications in a mammography, many studies were conducted to characterize and classify the types of microcalcifications [7]. Because microcalcifications are radiopaque structures, some researches show the importance of monitoring the development of calcifications mainly in the early diagnosis through mammography screening. Additionally, as hydroxyapatite can be found in both malignant and benign tumors, other parameters associated with microcalcifications should be evaluated such as shape, composition, quantity and distribution. However, the probability of malignancy is proportional to the number of calcifications [8]. Based on this fact, in order to simulate a more realistic case, using the spectrometric system setup showed in Figure 1, a randomized clustered hydroxyapatite microcalcifications with different diameters (0.15 - 1.40 mm) have been modeled for analysis. The spectrum obtained was compared with the reference spectrum of the healthy breast.

As already described, mammography is the primary mode of diagnosis of breast cancer and currently is in constant technological development. To confirm the change in the calcium abundance due to clustered microcalcifications development, a mammography unit was modeled considering a 23 keV photon beam focusing on a molybdenum target at a distance of 15 cm of the rhodium filter 25 μm thick and 45 cm of the compressor plate. It was considered 10 cm compression thick and a decrease in breast volume by 10%. Using the resources

available in MCNP5, the mammography screening was simulated using the FIR tally which property reproduces a radiographic image of the photon flux that goes through a user-specified image grid.

In any diagnostic techniques with ionizing radiation, the absorbed dose in patients during the procedure requires special attention, and all intrinsic parameters to the diagnosis should ensure that the ALARA principle be satisfied. Therefore, the absorbed dose rate on neutron spectroscopy of the breast with clustered microcalcifications was estimated and compared with the allowed limits for the average glandular dose for mammography.

III. Results and Discussion

Simulations were performed on a Linux environment at Ubuntu operating system on a 2.67 GHz Intel® Core™ i7 and 6 GB RAM desktop in an average CPU time of five days. All results presented in this section were obtained considering a maximum standard deviation of 3%.

As described in the methodology section, in the first approach, the emission spectrum of the healthy breast and also the spectrum of the breast with the inclusion of microcalcifications of different diameters have been simulated. Comparing both calculated spectra it was possible to observe the change of the breast isotopic composition in function of breast calcium concentration. Figure 2 shows the behavior of the normalized counts by emission spectrum of the healthy breast for different photopeak energies characteristics of ^{40}Ca isotope due to the increase in the microcalcifications diameter.

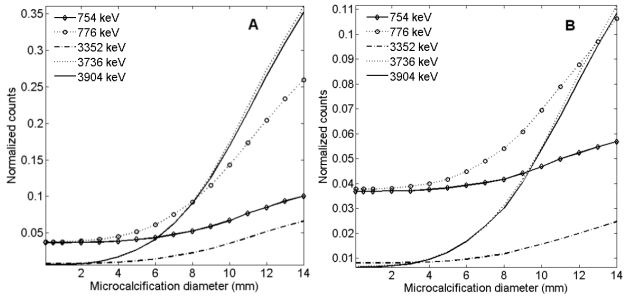

Fig.2 Change of normalized counts in accordance with the increase in diameter of microcalcifications of different chemical compositions: hydroxyapatite (A) and calcium oxalate (B).

The first feature that can be observed is the difference in the range of normalized counts relative to differences in the microcalcification compositions. This behavior is justified by the number of calcium atoms in hydroxyapatite and calcium oxalate molecules which has a ratio of 10-1. According to the literature the recognition of lesion malignancy by invasive methods is determined by physical, chemical and morphological characteristics of the lesion sample, and the most used noninvasive procedure is the analysis of mammographic findings. However, noninvasive methods like mammography for diagnosis of breast cancer are limited to a minimum detectable size of the microcalcification itself. As an example we can mention the use of high-frequency ultrasound [9].

With the obtained spectra, it is possible to verify the sensitivity of the presented spectrometric technique to distinguish the composition of microcalcifications as a function of the amplitude of the normalized counts once calcium oxalate microcalcifications are strictly associated with benign tumors. Another favorable factor for the diagnosis is associated with the possibility of evaluation of 2 mm diameter microcalcifications and even smaller.

The second approach proposed is to model a breast with clustered microcalcifications and obtain spectroscopy and mammography in order to verify the change in the isotopic composition of calcium through the presence of microcalcifications. To achieve this purpose sixteen hydroxyapatite microcalcifications with diameters ranging from 0.15 to 1.40 mm were simulated. Figure 3 shows the energy spectrum of the healthy breast and breast with clustered microcalcifications in a range from 50 to 4000 keV with the detail of the energy range of interest.

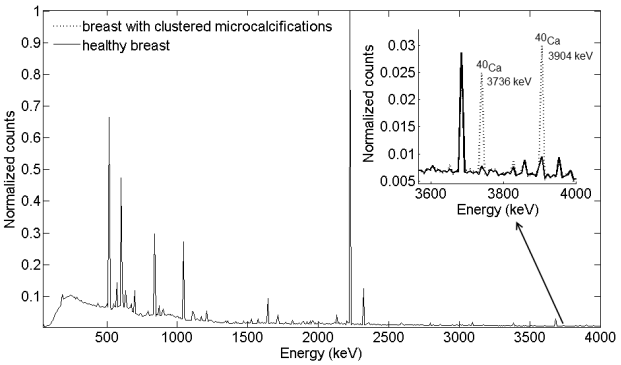

Fig.3 Photon emission spectra of the healthy breast and breast with clustered microcalcifications.

Even for clustered microcalcifications with diameters smaller than 1.40 mm is possible to observe the increased calcium isotopic composition, altering the normalized counts of the emission spectrum for the 3736 keV and 3904 keV energies. In a clinical application, this result confirms the ability of NSECT spectroscopy mode in detecting the change in calcium abundance due to the development of microcalcifications or even other conditions that would be associated with the disorder in the calcium production.

Using the same microcalcifications arrangement, the mammography screening was performed using the MCNP5 FIR tally to simulate the radiographic image of the photon on a high-resolution matrix array over a 16 x 16 cm field with 0.1 mm resolution discrimination per pixel. Figure 4 shows the radiographic image

obtained where it is possible to visualize some clustered radiopaque structures. In a hypothetical clinical case, this image could represent the first indication of breast physiology disorder.

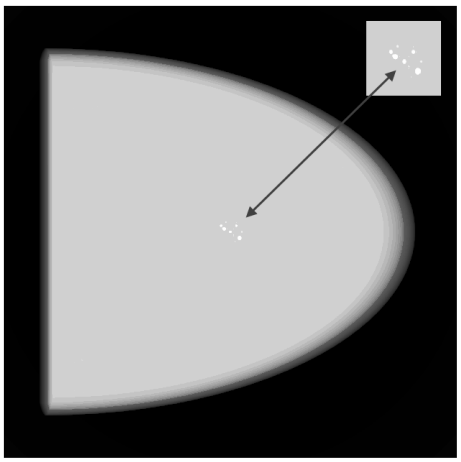

Fig.4 Mammography screening performed with 0.1 mm resolution discrimination per pixel of breast with clustered microcalcifications.

A. Neutron radiation dose

Using the resources available in MCNP5, the average energy deposited by each 7 MeV neutron that interacts in breast was estimated to be 2.92 MeV. As the results provided by MCNP5 are normalized by the number of simulated particles, to obtain the absolute absorbed dose is necessary to assume that the neutron source intensity is known. For the calculation purpose it was adopted the standard intensity of an Am-Be sealed natural source with the intensity of 10^8 neutrons emitted per second on a single projection. Assuming that the fast neutron beam has been simulated with this intensity, the absorbed dose rate obtained in the breast spectroscopy is 0.074 mGy/s.

According to the American College of Radiology [10], the tolerated limit for the breast average glandular dose is 3 mGy in a single exposure. Whereas the exposure times are low, the absorbed dose rate in mammography is superior to that of neutron spectroscopy.

IV. Conclusion

It was demonstrated the ability of NSECT spectroscopy mode in detecting the change in calcium deposition due to the development of hydroxyapatite and calcium oxalate microcalcifications. The results obtained where microcalcifications with different diameters were inserted on the healthy breast revealed the change of the breast isotopic composition in function of the increasing calcium abundance through normalized counts of photopeak energies of this element.

In a clustered microcalcifications situation, even considering microcalcifications with diameters less than 1.40 mm, the breast spectroscopy was able to detect the isotopic composition changing, and this task was achieved under a low deposited dose rate if compared with the average glandular dose limit for mammography.

Considering a compromise between deposited dose and the counting efficiency of the detectors, the factors that could have prevented the application NSECT spectroscopy mode on breast isotopic composition analysis are exposure time and neutron source intensity.

Acknowledgment

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