# An innovative method for precise lymph node detection before surgical treatment in breast cancer

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## Abstract

**Objective:** To describe a new method of 3D interactive modeling which integrates images obtained by separate SPET and multi slice computed tomography (MSCT) modalities using an original software in order to better localize SNL in BC patients. **Subjects and Method:** We used technetium-99m-colloid rhenium sulphate for identifying SNL in seven patients with BC. Markers were made of lead pearls wrapped with cotton wool soaked in $^{99m}$Tc-pertechnetate and placed on the skin of the patients forming of a triangle. Using an original software, two separate 3D models were made after SPET and MSCT imaging and then merged into a hybrid 3D model which enabled precise visualization and localization of the SNL. **Results:** In all cases the position of the SNL established by our method was successfully verified using a gamma probe. Duration of SNL identification and extirpation were significantly reduced in less than 10 minutes per patient. The reproducibility of this method was confirmed by precise identification and biopsy of the SNL. **Conclusion:** We found this integrated SPET/MSCT 3D model to be much faster and easier to use as compared with the "classic" method, which was based on a radioactivity detection probe. In addition, our method was reproducible, accurate and of low cost. In other words, the method described in this paper could be very useful for health facilities with modest budget, because it obviates the need for buying expensive integrated SPET/MSCT hybrid imaging systems while detecting SNLs more accurately and in shorter time.

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## Introduction

Breast cancer (BC) is the most frequent malignant tumor among women, and second on the list of cancers in the world's population [1]. The incidence of BC is constantly increasing by an annual rate of 3.1%; e.g. The number of women with BC in USA in 2010 was about 2.5 million, and it increased in 2016 to 3.4 million [2]. However, the incidence rates could be falsely high due to diagnostic errors and "over diagnosing", especially of small tumors. As an example we can mention mammographic screening for breast cancer which resulted with 10% rate of over diagnoses [3]. In an another study, the authors found that one-quarter of breast cancers detected by mammography represented over diagnosis [4]. Nevertheless, mortality of patients with BC decreases due to earlier detection and improvement of treatment modalities [5].

Surgery is often used for the treatment of BC together with adjuvant treatments like chemotherapy, radiotherapy and/or hormonal therapy [6]. The extent of surgery depends on the site, histology, the grade of the tumor and the site and histology of the sentinel lymph nodes (SNL). If SNL are free from metastases, distal lymph nodes are also free and so no further dissection of axillary lymph nodes is necessary [7-9].

The simplest and the most used method for detection of SNLs is peritumoral injection of radio colloid and later intraoperative detection in of radioactivity in lymph nodes with special, narrow-collimated probe. The probe usually has scintillation, semi-conductor or rarely Geiger-Muller detector, which are all connected to a device which produces visual and sound signals in relation to the exposure dose of radioactivity. It is essential that intraoperative detection of SNLs is accomplished swiftly and precisely, so the anesthesia will not be unnecessarily prolonged. Numerous attempts were made in the past to decrease the operation time and increase sensitivity of the intraoperative detection of the SNLs. Good results were achieved with joint use of blue dye and radio colloid [10,11].

There are also numerous modifications of the detection and visualization methods used in clinical practice to identify SNLs, with variable efficiency. Certain authors use rou-

tine visualization of the SNLs preoperatively by gamma camera, which is then combined with intraoperative detection of SNLs by gamma probe [12].

Some of the methods are based on processing images from mammography or nuclear magnetic resonance (NMR) with the aim to create various phantoms, which will be used later like routine diagnostic tools [13, 14]. The most popular recent method is based on hybrid single-photon emission tomography/computed tomography (SPET/CT) system. Several studies were recently published describing such systems, and also 3D interactive modeling of SPET/CT hybrid systems which offer an insight into anatomical structures essential for localization of SNL [15-18].

However, hybrid SPET/CT systems are not available in many health facilities due to their high cost. Some authors [19] have created an inexpensive digital technique based on commercial software for fusing lymphoscintigraphic images with built-in anatomical reference profiles. This method allows easier recognition of the anatomical site and better lymph node dissection planning.

In order to obtain the same diagnostic yield without expen-sive technology, we describe a method which integrates images obtained by separate SPET and multi sliced computed CT (MSCT) modalities using original software.

## Description of our Method

### Patient preparation and data acquisition

For SNLs detection we used the radiopharmaceutical $^{99m}$Tc-nanocis (Cis bio international, Gif-sur-Yvette, Cedex, France). This is $^{99m}$Tc-colloid rhenium sulphate with particles size 50-200nm, which is rapidly transported from the injection site to the SNLs that become marked with radioctivity. The radiopharmaceutical was administered in doses of 100-160MBq per patient by 4-6 injections in close vicinity to the tumor and by 1-2 subcutaneous injections above the tumor. Volume and radioactivity of each injection were 0.1-0.2mL and 15-20MBq, respectively. Immediately after injecting the radiopharmaceutical, a physician gently massaged the injection site for about 1 minute to accelerate distribution of the radiopharmaceutical through the lymphatic system.

In order to create hybrid 3D image from the images obtained from separate SPET and MSCT modalities, it was necessary to mark at least three reference points on the patient's skin, clearly visualized by both imaging techniques. The reference points were marked by lead pearls 3mm in diameter, previously covered with thin layer of cotton wool (Figure 1) and soaked in solution of $^{99m}$Tc pertechnetate ($^{99m}$TcP) with specific activity 37MBq/mL. Average radioactivity per pearl was only a few MBq. The lead of the pearls was a complete X-rays absorber and a good marker for MSCT imaging, while $^{99m}$TcP in the cotton wool was an excellent marker for SPET imaging. The pearls were fixed on a patient's skin, forming a triangle and were later used for overlay and reconstruction (Figure 2).

**Figure 1.** Lead pearls (left) coated with thin layer of cotton wool (right).

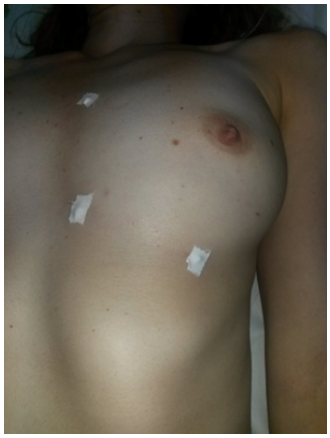

**Figure 2.** Lead pearls coated with thin layer of cotton wool, soaked in $^{99m}$Tc-pertechnetate and fixed on the patient's skin.

One to two hours after the markers were placed on the skin of the patient and the radiopharmaceutical injected, SPET imaging was made using gamma camera. We used Siemens e-cam Dual Head equipped with LEHR collimator. Acquisition was made with rotation of both heads for 180˚, 60 views, 30sec per view in a matrix of 128x128x16 and zoom 1.45. If a SNL had been displayed, its position was marked with a water-proof marker on the patient's skin to help the surgeon to identify its position, i.e. he followed the "classic" procedure using gamma probe for the detection of radioactivity of the SNL. If a SNL was not located, the SPET scan was repeated six hours after administration of the radiopharmaceutical under the same conditions.

After the SPET imaging, the patient was subjected to the MSCT study. We used Toshiba Aquilion 64, voltage 120kV, current 102mA, tube rotation time 0.5s, 27mm/rotation, matrix 512x512x16 and slices 5mmx64. Both diagnostic methods produced images in DICOM format, which were later processed and analyzed.

### 3D image reconstruction

Using our own "in house" software that overlaps data from SPET and MSCT DICOM images we created an accurate 3D model representing tumor location, SNL as well as all other visualized anatomical structures. Hybridization of SPET and MSCT DICOM images was made in 3D environment, by overlapping positions of corresponding markers from SPET and MSCT images. In order to achieve this, the SPET and MSCT images were at first transformed to 3D object. This proedure

is known as "voxelization". It is a method which creates 3D voxels from 2D pixels. The algorithm is well known, and already used in practice for many years [20]. Using this method we first created slice images from the MSCT DICOM images, and then reconstructed 3D model of a breast skin surface with objects of interest such as lead pearl markers and also anatomical structures of interest (lymph nodes and bones around) (Figure 3). Then, we created the other 3D reconstruction using SPET data gathered from the gamma camera. However, for this reconstruction we could not use the above-mentioned algorithm (used with the MSCT), since previous back projection to SPET introduced additional "noise", and made more difficult precise identification of objects of interest and their later segmentation at DICOM images. Therefore we had to made segmentation of objects at source SPET images first, and then by "back projection" algorithm to transform SPET raw images with already segmented objects of interest to series of slice images. For this purpose we used our original, home-made software.

Here we will briefly explain our method. When a gamma camera rotates around the patient's body, obtains images by rotation for the angle α which depends on the predefined study settings. The value of this angle could be found at the DICOM image header and in our case it was 360/128. In order to create 3D model it is necessary to transform these images into series of parallel images. For this purpose we developed the software in the C++ language, which uses raw DICOM images obtained from the gamma camera. In Figure 4 the selected objects of interest are shown, such as lead pearls as markers, tumor and SNL. The algorithm transforms the images, rotated for the corresponding angle α, into the spatial matrix, which is then cut with parallel planes that are shifted for the appropriate distance between the slices and are perpendicular to the axis of rotation of the gamma camera. The objects of interest (white objects) are projected along the planes. In this way, at the intersection of the projections on each plane, the image of the object is obtained (indicated by yellow color in Figure 5). From this series of parallel images, by lifting the pixels, the voxels are created and by linking them the complete 3D model is obtained (Figure 6).

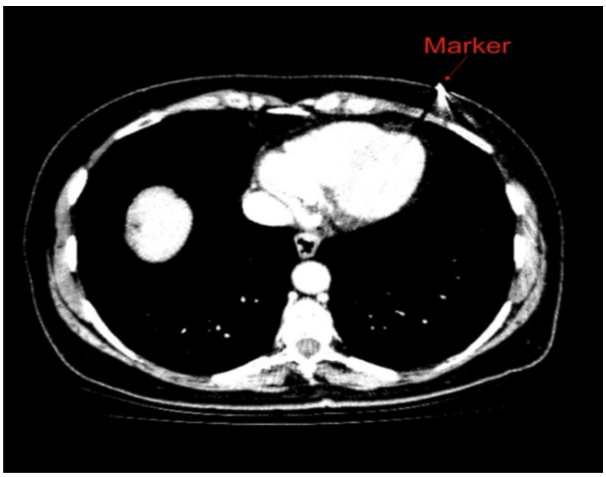


**Figure 3.** Multi slice CT scanner DICOM with lead pearl as marker on the skin surface.

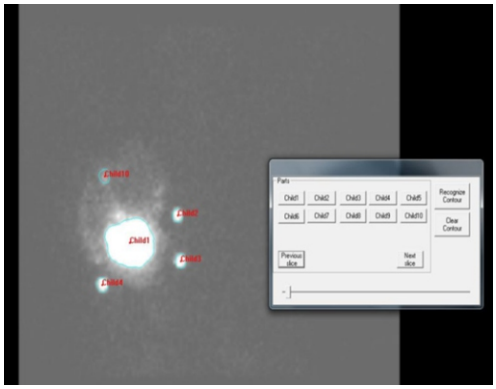

**Figure 4.** Automatic segmentation for each of the DICOM slices.

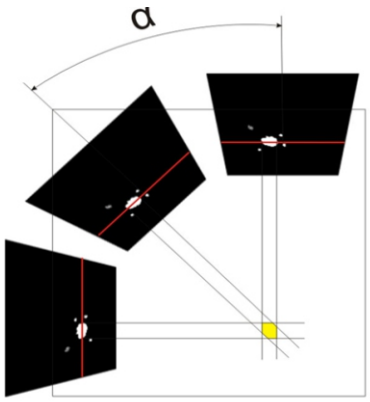


**Figure 5.** Transformation of the gamma camera images to the parallel slices.

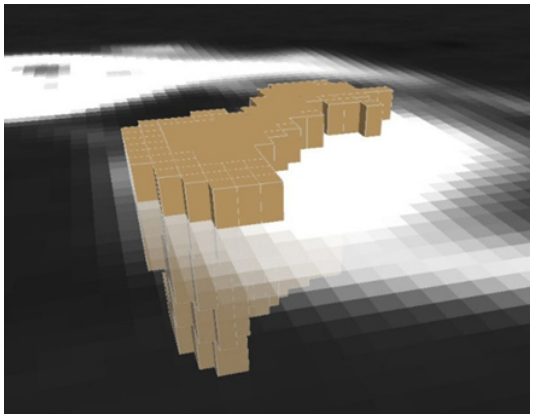

**Figure 6.** Creation of the 3D image from parallel slices.

Final step is overlapping of these two 3D models, generated on SPET and MSCT systems, into one hybrid model. In this way we obtain a hybrid model that contains integrated data from both diagnostic systems. Two models are merged together according to the three marked referent points on the chest surface that are recognized by both MSCT and SPET systems (Figure 7). Examples of 3D hybrid models created with the described method are shown in Figures 8-10. The 3D hybrid model is interactive, precisely showing all anatomical structures of interest, and it can be rotated and viewed from different angles, zoomed in and out, allowing marking of anatomic structures. It faithfully shows normal anatomic structures like bones, blood vessels, muscles, as

well as tumor and all lymph nodes in the axilla with clearly distinguished SNL that has absorbed the radioactive colloid. The model contains an option to easily measure the distance between the tumor and lymph nodes, and precise identification of their relationship to normal anatomic structures.

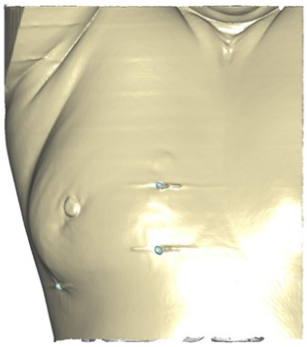

**Figure 7.** Reconstructed surface of the breast skin with markers.

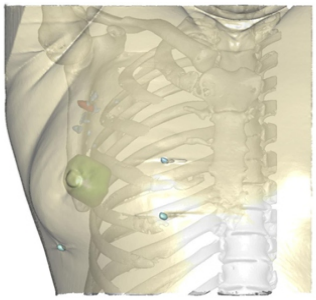

**Figure 8.** A hybrid image of markers on the surface of breast skin, the point of peritumoral injections, lymph nodes in axilla and marked SNL.

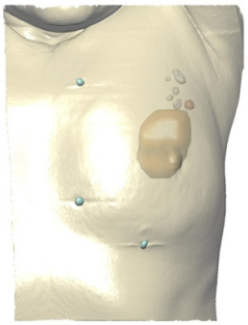

**Figure 9.** A hybrid image: markers on the surface of breast skin, the point of peritumoral injections, lymph nodes in axilla and marked SNL.

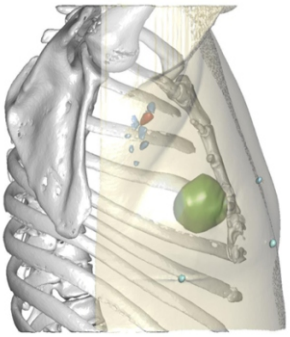

**Figure 10.** Hybrid image lateral view: markers on the surface of breast skin, the points of peritumoral injection, lymph nodes in axilla and marked sentinel lymph node.

All models are in WRL file format and commercial software can be used to view and analyze the models.

## Results

This method was performed on 7 female BC patients without significant comorbidity. All patients signed a written consent for this type of diagnostic investigation. During surgery, we presented the 3D SPET/MSCT hybrid model to the surgeons in a personal computer, which helped them to identify the sentinel lymph nodes quickly and precisely. In all cases the position of the sentinel lymph nodes established by our method was successfully verified using manual gamma probe.

Duration of surgery was significantly reduced whenever generated 3D SPET/MSCT hybrid model was used. When "classic" method is used alone, identification and SNL extirpation often lasts over 15 minutes per patient. With our method this process was significantly shortened in less than 10 minutes per patient.

## Discussion

Accurate detection of SNL avoids unnecessary surgical manipulations, supports the correct diagnosis and treatment and specifically may avoid lymphedema [21, 22]. Our method offers to the surgeon an opportunity to more easily and accurately identify and extirpate only sentinel lymph nodes, without damaging other tissues, what is very difficult to perform in usual way using gamma probes. In five cases the SNL were negative and we didn't perform axillary dissection, but in the other two of the SNL were positive and mastectomy with axillary dissection was performed. Conventional imaging modalities like X-ray mammography, US, computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET) scanning all provide critical information for clinicians during diagnosis and staging of breast cancer. However, the latter three methods are associated with relatively large running costs. Therefore, it is obvious that the new diagnostic tool is necessary [23]. Hybrid SPET/CT devices are beneficial in several ways, because special computer software and external fusion landmarks are redundant. Also, position of the patient does not change, so possible errors in image alignment caused by movements of the patient can be avoided [24].

Nowadays there are already commercially available hybrid machines that combine features of both CT and SPET, but they are not yet used in routine practice in our country, and even in developed countries they are limited to a small number of highly equipped medical centers. Anatomical accuracy of SPET/CT fusion images is still a challenge [25].

Some authors tried to acquire additional transmission images via a backlighting 57Co sheet source in order to facilitate the anatomic localization of the nodes seen on the sci-

ntigraphy image. Backlighting imaging technique created an outline of the patient's body, but fusion of backlighted scintigrams and CT images remained complicated [26].

Model that we present is based on a very simple marking reference points system recognized by our software, common to both scintigraphy and MSCT, which serve as the basis for creating three-dimensional hybrid model allowing a clear and precise identification of sentinel lymph nodes and corresponding normal anatomic structures. Also, our system does not require special hardware support; it is enough to have a personal computer and appropriate software. Advantages are simplicity, lower cost and certainly improved safety.

Reconstruction of SPET and MSCT 3D images by our method is of acceptable duration. Only framing the objects of interset at raw DICOM images takes a couple of minutes on average, while the rest of the procedure is authomatized, so total time of recostruction and creation of 3D hybrid model is only a few minutes long. However, since critical moment (in regard to the duration) is intraoperative idantification, extirpation and histological analysis of the SNLs, which should be as short as possible to decrease total duration of anesthesia, preoperative preparation, imaging and processing of the acquired images are not adding significantly to the total time spent.

*In conclusion*, based on our experience from pilot clinical testing of our system, we can conclude that precise identification and biopsy of sentinel lymph nodes are faster and easier for the surgeon in comparison with the "classic" method, based on just radioactivity detection probe. The method described in this paper could be very useful for health facilities with modest budget, because it obviates the need for buying expensive integrated SPECT/MSCT hybrid imaging systems while detecting SNLs more accurately and in less time.

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