An Approach of Modelling of Breast Lesions

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Abstract — **The goal of this study is to create and evaluate a methodology for generation of realistic three dimensional (3D) computational models of breast tumors with irregular shapes and import them into real mammographic images. These hybrid images are to be used for development of new breast cancer detection technologies.**

Keywords - **simulation, irregular masses, breast, tumor, mammography.**

I. INTRODUCTION

Breast cancer is the most common heterogeneous malignancy in women [1]. New technologies are constantly under development, which aim to detect and diagnose the findings during screening of the breast as earlier as possible. Development of new detection systems relies on the virtual clinical research, which insist availability of a large number of images with realistic looking pathologies. For this purpose, as realistic as possible models of the breast lesions are needed. Computerized modelling tools and simulation techniques could create data for these needs and replace expensive conventional clinical trials. The goal of this study is to create and evaluate a methodology for generation of realistic three dimensional (3D) computational models of breast tumors with irregular shapes and import them into real mammographic images. These hybrid images are intended for the development of new breast cancer detection technologies.

II. MATERIALS AND METHODS

The overall methodology of creation of mammograms with breast lesions is schematically shown in figure 1. Each part of the block diagram is presented in the following subsections.

A. Methodology for creation of breast lesions

The methodology for the creation of breast masses with irregular shapes consists of two major steps: (**a**) use of random walks to create the initial diffusive tumor shape, which is realized by either a Brownian motion or by nearest neighbor random walks, (**b**) creating of a solid tumor shape by applying a set of 3D filters, as well as morphological operations. In particular, the initial diffusive models were smoothed by applying the following image processing methods: averaging, repeated dilatations, morphological opening and closing and final smoothing, all utilized in 3D. Then, the originally created tumor shape is compared to the shapes generated after each step of the methodology, and consequently volumes were visually compared and analyzed. Thereafter, a technique for embedding of the simulated masses in real tissue mammography images was created and applied.

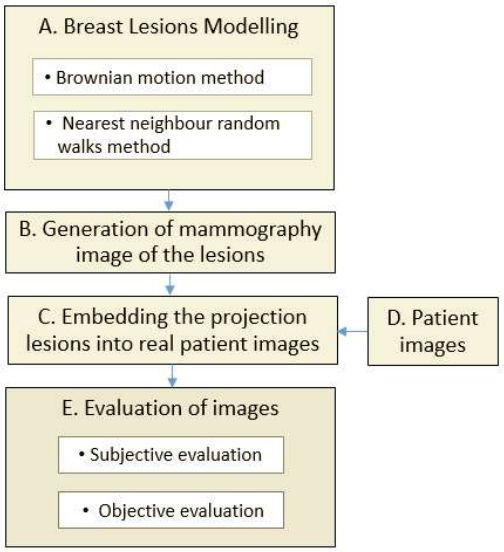


Figure 1: An outline of the process of creation of an x-ray mammogram with a breast lesion.

The *Brownian motion random walk* begins by assigning the central pixel of a 3D array, a value of 1 as a tumor pixel [2]. The tumor size is a function of the size of the voxel matrix and the voxel resolution, defined by the user. The user also assigns a number of random walks. Each random walking process stops either at the matrix boundaries or when the assigned number of steps is reached. The random walk starts from the center of the matrix and each step moves randomly to one of the neighbouring voxels, assigning it as the abnormality composition.

The resulting structure is converted to an abnormality with solid geometry by applying further processing with morphological operations: averaging, dilation, erosion. In these operations, the structuring element is a cube. For instance, the repeating dilation is made with a large cube size (5x5) followed by dilation with a smaller cube size (3x3), while averaging is reached with uniform averaging filter (arithmetic mean). Other morphological image processing methods, closing and smoothing have also cube as a structuring element. Size of the structuring element as well as its shape can be changed.

By changing the number of walks, number of steps per walk, degree of averaging, dilation and erosion, the shape of modelled

tumor is also changed as well the malignancy is also altered. Examples of generated abnormalities are shown in figure 3 a, b and c.

The Nearest neighbor random walk algorithm is based on the model used by Ruschin et.al. [3]. The random walk begins by assigning a value 1 to the center pixel of the 3D array. For each iteration, the nearest neighbor of the pixel chosen on the last iteration, are randomly selected from a uniform distribution and subsequently a non-zero value is assigned to them as a new tumor pixels. The walk is completed when the border of the 3D array is reached. [8] Examples of generated irregular abnormalities are shown on figure 3 d, e and f.

B. *Generation of mammography image of the lesions*

X-ray projection images of 3D breast lesions were generated by using an in-house developed XRAYImagingSimulator software application [2], capable to simulate the x-ray transport through the computational tumors. The geometry and the parameters of the simulated x-ray imaging are shown in figure 2.

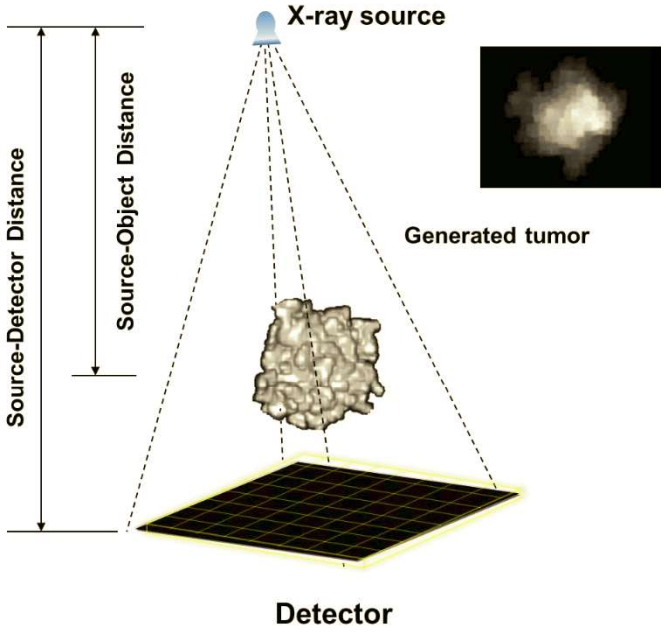


Figure 2: Scanning geometry and parameters. Three acquisitions at 0° (CC), 60° (MLO), 90° (ML) were simulated. Source to detector distance is 800 mm, while source to patient table distance is 600 mm. The insert of this figure shows the simulated projection image of the breast lesion.

X-ray images were simulated for monochromatic x-ray beams with energy of 20 keV. Distances from the source to the isocentre point, where the centre of the tumour was placed and to the detector surface were 600 mm and 800 mm, respectively. The size of the images was 500 x 500 pixels, while the pixel resolution was 0.1 x 0.1 mm. Analytical relationship between the initial intensity of the x-rays and the intensity registered at the detector is exploited. The transmitted intensity reaching the detector pixel is calculated using the Beer's law:

$$I = I_0 * \exp\left(-\int_{ll} \mu(x, y, z) dl \right) \quad (1)$$

where μ(x, y, z) is the spatially dependent linear attenuation coefficient, l is the path length through the object and I_0 is the intensity of radiation at the source segment that emits to the area of the detector. The generated images are free of scatter, since they exploit the analytical relationships for x-ray matter interaction.

A more complex level of simulation of the radiation interaction at the absorber and the detector includes Monte Carlo techniques. These are used to calculate the photon transport by sampling the interactions with the matter and the distances that x-rays travel until the next interaction. Since these techniques are time consuming, the use of powerful multi-core computers or cloud computing.

Three mammography views were simulated: mediolateral-oblique (MLO), cranio-caudal (CC), and mediolateral (ML) views, which correspond to 60°, 0° and 90°.

C. *Embeding the projection of the lesions within the patient projection images*

Anonymized planar and free of breast abnormalities patient images obtained with Giotto Tomo IMS system, were used[5]. The pixel size of the images is 100 μm x 100 μm. The created projection image of the breast tumor is then added to the patient image by using the following approach. Initially, patient and lesion images were normalized to their maximal values. Then, the values of the lesion pixels are transferred to the patient images at a position defined by the medical doctors. No further image processing is applied at this stage. The program script implementing the embedding procedure was written in Matlab [5]. Images are then stored in a database and used in the subjective assessment and research and educational activities.

D. *Evaluation of images*

The realism of the projected breast masses on 2D projection images was evaluated both subjectively and quantitatively. Subjectively, images with embedded projection lesions were visually assessed by a medical doctor involved in screening and diagnosing of mammography images. The focus of the evaluation is the realism of the lesions: brightness, shape, size and location on patient mammogram. For the objective evaluation, the recently developed software application for quantitative assessment of x-ray images was used [6]. Specifically, the tool is used to compute a set of features from x-ray images such as standard deviation, skewness and kurtosis, fractal and spectrum analysis. These features are then compared to features extracted from real patient images with breast lesions.

[5] All images were acquired with ethical approval and with written consent from women undergoing regular mammography screening.

III. RESULTS AND DISCUSSION

A. Created breast lesions

Thirty irregular masses with different sizes and shapes were generated with the proposed two methodology: 15 irregular masses by using the Brownian motion method and 15 such by using the Nearest-neighbour random walks method. The parameters used for their generation are summarized in table 1 (A and B). Each voxel of the three-dimensional array represents an elemental composition, which can be either air (no abnormality) or water. Water was chosen as an elemental composition to represent the mass abnormality, since their x-ray properties are very similar [7].

The data format used for this representation is 16bit unsigned integer. The size of the three-dimensional arrays varied between 100 x 100 x 100 voxels to 200 x 200 x 200 voxels, which corresponded to approximately 15 and 30 MB, respectively. Number of walks and steps varied between 500 to 2000 and 1000 to 5000. These numbers were found to reflect the variety of the shapes which can be obtained with the discussed algorithms.

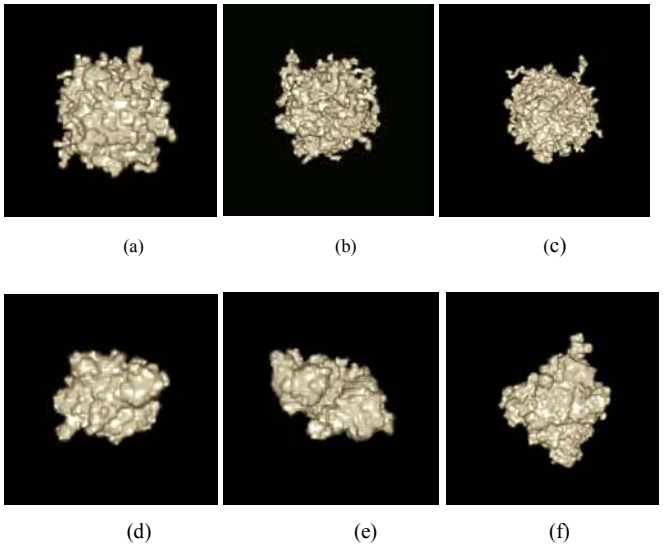
TABLE XII. A. PARAMETERS OF THE TUMORS GENERATED USING BROWNIAN MOTION METHOD

No	Parameters		
	Tumor size, pixel	*No of walks*	*No of steps*
1	100x100x100	500	1000
2	100x100x100	500	2000
3	100x100x100	500	3000
4	100x100x100	500	4000
5	100x100x100	1000	1000
6	100x100x100	1000	3000
7	100x100x100	1000	4000
8	100x100x100	1500	3000
9	100x100x100	1500	5000
10	100x100x100	2000	4000
11	200x200x200	500	1000
12	200x200x200	500	3000
13	200x200x200	1000	1000
14	200x200x200	1500	1000
15	200x200x200	2000	1000

TABELE II. B. PARAMETERS OF THE TUMORS GENERATED USING NEAREST NEIGHBOUR RANDOM WALKS METHOD

No	Parameters		
	Tumor size, pixel	*No of walks*	*No of steps*
1	100x100x100	500	1000
2	100x100x100	500	2000
3	100x100x100	500	3000
4	100x100x100	1000	1000
5	100x100x100	1000	2000
6	100x100x100	1500	2000
7	100x100x100	1500	4000
8	100x100x100	2000	1000
9	100x100x100	2000	2000
10	100x100x100	2000	4000
11	100x100x100	2000	5000
12	200x200x200	500	3000
13	200x200x200	1000	1000
14	200x200x200	1500	1000
15	200x200x200	2000	1000

1 pixel = 0.1 mm



(a) (b) (c)

(d) (e) (f)

Figure 3: Breast lesion models, generated by (a, b, c) the Brownian motion method; and (d, e, f) by the Nearest neighbour random walks method. Specifically, the lesions in (a-c) correspond to lesions 2, 11 and 14 from Table 1, while lesions in (d-f) correspond to lesions 3, 9 and 14 from Table 2.

Examples of generated models of tumors are shown in Figure 3. As was already mentioned, variation of the parameters in tumor-modeling affects the irregularity of the mass. As shown in the figure 3, examples of masses simulated with nearest neighbor random walk look smoother and more benign, whereas those generated with Brownian motion method look speculated and malignant.

The computational time for the generation of the lesions by the two algorithms was similar. For a tumor array of size 100 x 100 x 100 pixels and 500 walks, the needed computational time was around 5 min., while for a tumor array of 200 x 200 x 200 pixels and 2000 walks this time was approximately 15 min. All simulations ran on a laptop configuration RAM 8GB, Processor Intel(R) Core(TM) i5-32320M CPU @ 2.60 GHz, 64-bit operating system.

The biggest generated mass created with the Nearest-neighbour method was 50mm x 50mm x 50mm, and this process took about 11 hours. This tumor-model is shown in figure 4.

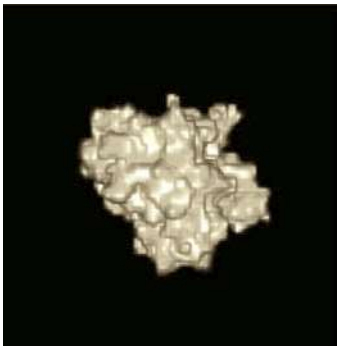
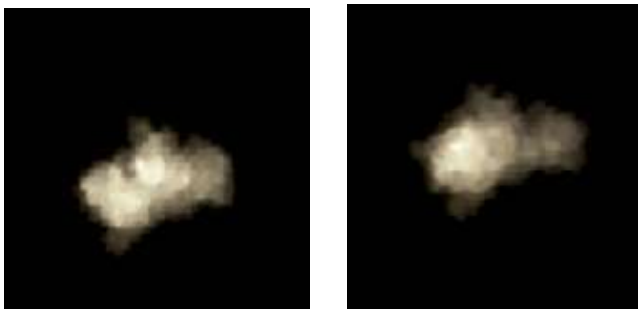


Figure 4: The biggest model 50mm x 50mm x 50mm generated by using the nearest-neighbour random walks method with 500 walks and 1000 steps in each walk.

B. Mammography images

The created three-dimensional lesions were processed with the *XRAYImagingSimulator*, developed in our Laboratory[2] and mammography images at three different mammographic views (60^o, 0^o and 90^o) were received. Two such examples are shown in Figure 5a, b.

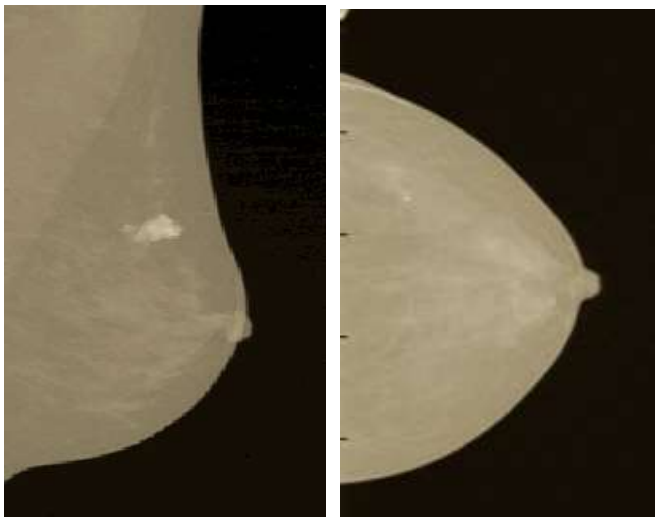


(a) **(b)**

Figure 5: Projection images of two of the generated tumors: (a) Tumor generated with Brownian motion random walk 200x200 pixels, 500 walks and 1000 steps; and (b) Tumor generated with Nearest-neighbour random walks motion random walk 100x100 pixels, 500 walks and 2000 steps.

By using a Matlab script [5], the projection images of the created tumor were mapped to the real mammography images, which are free of lesions. Images are then stored in a database and used in the subjective assessment and research and educational activities.

Mammograms with the inserted projections of the abnormalities are shown in figure 6a, b. In figure 6a, the projection image of the lesion is inserted into a patient MLO view projection, while in figure 6b the projection image of a small abnormality is inserted into a patient CC view.



(a) **(b)**

Figure 6: Real patient images with inserted lesions in (a) MLO view and (b) CC view.

C. Evaluation

The generated thirty mammographic projection of tumour images were visually inspected by a medical doctor with experience in mammography imaging. While the realism of the shapes on the image is quite promising, the comments were mainly to improve the contrast appearance of the abnormality as well as to smooth the tumor outlines. Another limitation of the proposed approaches is the long computational time when high-resolution models are to be generated. This limitation may be overcome with parallel implementation of these algorithms or by using cloud technology.

Objectively, four parameters: skewness, kurtosis, fractal dimension and the power spectrum parameter β were evaluated from these images. The skewness and kurtosis were 0.14 ± 0.30 and 2.55 ± 0.29, while the evaluated fractal dimension was 2.60 ± 0.08. The power spectrum parameter β was 2.79 ± 0.15. These values are well within the ranges of values for these parameters, reported by other researchers [9, 10]. Currently, we are collecting patient images with breast lesions which will be used to evaluate these parameters precisely and perform the comparison with the simulations correctly.

IV. CONCLUSIONS

The methodology for the creation of breast masses with irregular shapes will be used to generate unique and at the same time realistic in shape and size computational models of breast adenoma, intraductal papilloma, cysts and duct hyperplasia. These computational models are powerful tool in the hands of all professionals working toward the creation of new technology for screening and diagnosing of the breast.

ACKNOWLEDGMENT

This work is supported by the Bulgarian National Science Fund under grant agreement DN17/2. It is also supported by MaXIMA project, which has received funding from the

European Union's Horizon 2020 research and innovation program under grant agreement No 692097.

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