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DIGITAL SYNTHESIS OF MICROCALCIFICATIONS ON DIGITAL MAMMOGRAMS

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Abstract: We propose a model to simulate clustered microcalcifications on digital mammograms. The simulation model is based on the gray-level, size and number of microcalcifications per cluster. All the parameters describing the individual microcalcifications and clusters were randomly sampled within a wide range of values, the exception being the center of the cluster; this was interactively positioned to ensure the location of all the microcalcifications inside the breast. Subsequently, a database of clustered microcalcifications was created. These clusters of microcalcifications from this database were tested from indistinguishability from real ones. Two radiologists and one physicist were asked to indicate whether the microcalcifications were either real or simulated. Results (χ^2 test) indicate that there was not statistical and significant difference between real and simulated clustered microcalcifications.

Keywords: Computer-aided diagnosis, microcalcifications, digital radiography, simulation, mammography.

1. INTRODUCTION

Several studies have proven that isolated clusters of microcalcifications is the most frequent radiological feature of asymptomatic breast cancer [1]. Observer-performance studies and computerized methods for mammography are being developed to alert radiologists to focus their attention on suspicious regions [2, 3].

Microcalcifications are relevant radiologic signs which are frequently missed in mammographic exploration. These frequently appear as small sized-low contrast radiopacities. Microcalcifications detection has been a primary focus of attention for the radiology community. They are ideal targets for computer detection, because of their clinical relevance and their potential subtlety [4]. However, its small size and low contrast make them difficult to detect.

To evaluate techniques for improving detection of clustered microcalcifications, a set of images must be used in which the presence or absence of microcalcifications has been established. Lefebvre et al [5] have proposed a simulation model of clustered microcalcifications superimposed on normal mammographic backgrounds. We have also developed a simulation model of clusters of microcalcifications on digital mammograms and validated the model by superimposing the clusters on mammograms in which the presence of real microcalcifications was proven and had led to surgical removal.

2. MATERIALS AND METHODS

2.1. Acquisition of digital mammograms

Thirty-five craniocaudal and lateral digital mammograms were obtained using a Konica KFDR-S laser scanner (Konica Corp, Tokyo, Japan). Images were digitized at a resolution of 2000 horizontal x 2600 vertical pixels (87.5 $\mu\text{m}/\text{pixel}$).

The optical density range from zero to four was transformed to 1024 gray levels, resulting in a 10 MBytes/image. A DEC VAX Computer (Digital Equipment Corp, Maynard, MA) running VMS operating system was used for all calculations. The computer programs were written in DT-IDL. Digitized images were stored on magnetic disk. Hardcopies of the images were produced by an Agfa Matrix Compact L laser printer (Agfa Gevaert N. V., Morstel, Belgium) interfaced to the VAX.

2.2. Simulation model

The simulation model of clustered microcalcifications is a three-step process: (1) creation of a binary image, (2) assignment of grey level values to the pixels of the binary microcalcification, and (3) background correction.

To create a cluster of microcalcifications its global features were introduced by the user. The center was manually positioned to ensure that all microcalcifications belonging to the cluster were totally inside the breast region. After the center was located, the number of microcalcifications, the mean area, the shape appearance of each microcalcification, and the mean contrast (c_g) between the cluster and the background were introduced. The individual parameters of each microcalcification, such as size and location within the cluster, were randomly sampled from a wide set of values centered on the corresponding values introduced. The shape of the microcalcification was determined by the shape appearance r_a , defined as the relation between the size of the microcalcification and the bounding rectangle surrounding it.

The average gray level value of the microcalcification was calculated from the contrast value of the microcalcification and the background, and from the gray level value of the neighbor pixels. Each binary microcalcification and the surrounding pixels were divided into concentric rings. Only the two first outer rings were considered. Average gray level value of the pixels belonging to the second ring outer to the microcalcification was computed on the original mammogram. The average gray level value of both the microcalcification (l_m) and the first surrounding outer ring (l_n) was calculated from the contrast value between the microcalcification and this first outer ring to the microcalcification (c_m), and from the contrast between the microcalcification and the second outer ring (c_n); c_m was randomly sampled from c_g , and c_n was calculated from its relation with c_m . Both l_m and l_n were distributed, assigning a different gray level value to each

concentric ring, taking into account that gray level values decreased on sucesive rings. Finally, to obtain a uniform distribution of gray level values between the microcalcification and its surrounding pixels, a lowpass filtering over the clustered microcalcifications region was applied.

2.3. Testing of simulated clustered microcalcifications

Testing of the simulated clustered microcalcifications was performed as follows: 35 mammograms with 42 real clustered microcalcifications were digitized. A total of 42 computer-generated clusters from the clustered microcalcifications database were added to this set of mammograms. Hardcopies of all the mammograms were obtained and the location of each cluster was marked with a numeric label. No image processing was performed. The set of images was presented to two experienced radiologists and one physicist. The order of case presentation was varied for each of the three readers, who were asked to indicate whether each cluster of microcalcifications was either real or simulated in accordance with a three level decision scale, (1) simulated, (2) unsure, (3) real. No time constraints were imposed on the observers. Statistical analysis was performed on each set of responses, comparing results of real and simulated microcalcifications by using a χ^2 test (figure 1).

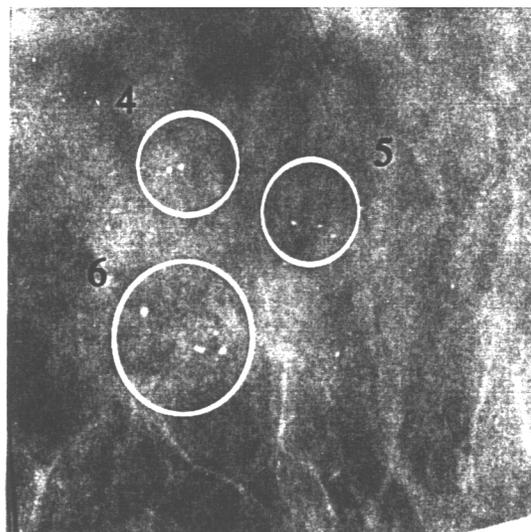


Figure 1. Example of real and simulated clustered microcalcifications. (4) Real; (5) Simulated; (6) Simulated.

3. RESULTS

The results of the observer testing of simulated vs. real clustered microcalcifications were as follows: 52.38% of the simulated clusters were called simulated and 39.68% were called real, the rest (7.94%) being classified as uncertain. Of the real clusters, 43.65% were called simulated and 46.83% were called real, the rest (9.52%) being classified as uncertain. Individual results for each observer are shown in Table I. The χ^2 test performed for each reader was not statistically significant, which demonstrates that neither of them were able to distinguish between real and simulated clustered microcalcifications, with a significant degree of accuracy for this test set. These almost identical results prove the validity of employing computer-generated simulated clustered microcalcifications in investigations such as that being reported here.

	Observer 1	Observer 2	Observer 3
<i>Simulated clusters called simulated</i>	54.76%	50.00%	52.38%
<i>Simulated clusters called real</i>	38.09%	45.24%	35.71%
<i>Simulated clusters called uncertain</i>	7.14%	9.52%	11.90%
<i>Real clusters called simulated</i>	52.38%	42.86%	35.71%
<i>Real clusters called real</i>	42.86%	40.48%	57.14%
<i>Real clusters called uncertain</i>	4.76%	11.90%	7.14%

Table I. Results obtained for each observer.

4. DISCUSSION

The results of the observer testing show that there was no statistically significant difference between real and simulated clustered microcalcifications. Detection of microcalcifications is a critical factor in screening and diagnosing breast cancer. In evaluation of techniques for improved detection of microcalcifications a set of images must be used, in

which the presence or absence of microcalcifications has been established. Investigators have used dried human bone pulverized into specks and aluminum oxide specks and superimposed them on breast phantoms [6]. Others [7] have used microcalcifications from biopsy material and randomly superimposed them on a preserved human breast specimen. However, these studies are of limited value because the appearance of the microcalcifications was unrealistic and the phantoms presented only one background.

Digital technology allows for the generation of clusters of microcalcifications by means of a computer. This approach is compatible with the use of images initially acquired on film and subsequently digitized. It allows for the creation of a set of images in which the presence or absence of microcalcifications, or the truth, is unambiguously known. It also allows for the creation of simulated microcalcifications that are virtually indistinguishable from real microcalcifications. Of interest of our approach is the relative ease with which a variety of realistic microcalcifications with different structures and sizes can be created. Lefebvre et al [5] have also created a model for simulation of clustered microcalcifications. The differences with our approach are: (1) In their study the distribution of the position and contrast between the microcalcification and the first outer ring was assumed to be gaussian. We did not consider a gaussian distribution. The values were randomly sampled within a broad range of values, centered on the mean value introduced by the user. (2) We have obtained the shape of our microcalcifications by subtracting the pixels of the bounding rectangle that contained the microcalcification, that exceeded its area, while they obtained it by randomly sampling, according to its size, from their real database. (3) Lefebvre et al validated their simulation model by presenting the images of the test set one by one to two radiologists; that is, in each of their cases the reader was in front of either a real or a simulated case. We consider this of a more limited value than ours, because the reader cannot compare the simulated and real at the same time, thus, is not forced to choose. In each of our cases there was at least one real cluster and one simulated cluster, the three observers of our study being forced to decide between the two possibilities. As a consequence, we believe that the simulated clusters of microcalcifications from our database can be used for testing the visual perception of clustered microcalcifications and for evaluation of image processing techniques designed to improve microcalcifications detection rate. Our software allows simulation of enough number of clinical

situations to achieve statistically valid tests of observer performance.

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