Award Number: DAMD17-99-1-9122

TITLE: A Method for Simulating Mammograms

PRINCIPAL INVESTIGATOR: Robert M. Nishikawa, Ph.D.

CONTRACTING ORGANIZATION: University of Chicago
Chicago, Illinois 60637

REPORT DATE: August 2000

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for public release;
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.
**REPORT DOCUMENTATION PAGE**

<table>
<thead>
<tr>
<th>1. AGENCY USE ONLY (Leave blank)</th>
<th>2. REPORT DATE</th>
<th>3. REPORT TYPE AND DATES COVERED</th>
<th>5. FUNDING NUMBERS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>August 2000</td>
<td>Annual (1 Aug 99 – 31 Jul 00)</td>
<td>DAMD17-99-1-9122</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>4. TITLE AND SUBTITLE</th>
<th>6. AUTHOR(S)</th>
<th>7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)</th>
<th>8. PERFORMING ORGANIZATION REPORT NUMBER</th>
<th>9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)</th>
<th>10. SPONSORING / MONITORING AGENCY REPORT NUMBER</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Method for Simulating Mammograms</td>
<td>Robert Nishikawa, Ph.D.</td>
<td>The University of Chicago</td>
<td>Chicago, Illinois 60637</td>
<td></td>
<td>U.S. Army Medical Research and Materiel Command</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>11. SUPPLEMENTARY NOTES</th>
<th>12a. DISTRIBUTION / AVAILABILITY STATEMENT</th>
<th>12b. DISTRIBUTION CODE</th>
<th>13. ABSTRACT (Maximum 200 Words)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Approved for public release; distribution unlimited</td>
<td></td>
<td>This project is to facilitate research in digital mammography and related technologies, in particular computer-aided diagnosis and image processing. A major limitation to the rapid development and subsequent clinical implementation of these technologies is the lack of a standardized set of mammograms to be used in development and evaluation. We are developing a method to produce simulated mammograms. The method relies on a model of image formation that takes into account the absorption of x-rays in the phosphor, subsequent conversion to light and the scattering of the light before escaping the phosphor. The model also takes into account the finite thickness of the phosphor, the divergence of the x-ray beam, scattered radiation, and noise due to film granularity and from the film digitizer. Almost all the components of the model are completed and computer code is being written. The model requires as input high fidelity images of breast tissue and of breast lesions. We have not started collecting samples because an essential piece of equipment is missing. Contingency plans are underway and image data collection will begin in year 2. In addition, early in year 2, we will test the model using x-ray phantoms.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>14. SUBJECT TERMS</th>
<th>15. NUMBER OF PAGES</th>
<th>16. PRICE CODE</th>
<th>17. SECURITY CLASSIFICATION OF REPORT</th>
<th>18. SECURITY CLASSIFICATION OF THIS PAGE</th>
<th>19. SECURITY CLASSIFICATION OF ABSTRACT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast Cancer, mammography, modeling, computer simulation</td>
<td>8</td>
<td></td>
<td>Unclassified</td>
<td>Unclassified</td>
<td>Unclassified</td>
</tr>
</tbody>
</table>
Table of Contents

Cover ......................................................................................................................... 1
SF 298 ......................................................................................................................... 2
Table of Contents ....................................................................................................... 3
Introduction .................................................................................................................. 4
Body ............................................................................................................................ 4
Key Research Accomplishments ................................................................................ 6
Reportable Outcomes ................................................................................................. 7
Conclusions ................................................................................................................ 7
References .................................................................................................................. 7
Appendices .................................................................................................................. 8
4. **INTRODUCTION**

This project is to facilitate research in digital mammography and related technologies, in particular computer-aided diagnosis and image processing. A major limitation to the rapid development and subsequent clinical implementation of these technologies is the lack of a standardized set of mammograms to be used in development and evaluation. We are developing a method to produce computer-simulated mammograms. The approach is to model the creation of the mammogram on the computer -- all steps from x rays exiting the breast to the image being displayed on a light box. This model, which we have developed previously, will be combined with accurate information of the appearance of normal breast anatomy and of benign and malignant breast lesions. These will be obtained from high quality images of mastectomy samples and biopsy specimens. We believe that this technique can produce simulated mammograms that appear to be actual mammograms. We will test this hypothesis by performing quantitative comparisons of simulated and real mammograms. We will also perform an observer study where radiologists choose the real mammogram from a pair of real and simulated mammograms shown side by side.

5. **BODY OF REPORT**

5.1 **Tasks**

There are four tasks in the Statement of Work, which are listed below.

1. To obtain radiographs of mastectomy and tissue specimens

   (a) radiograph 100 different mastectomy breast tissues at 2.0 times geometric magnification recording image on direct film (without intensifying screen) at five different orientations

   (b) radiograph 240 different tissue specimens at 4.0 times geometric magnification recording images on direct film (without intensifying screen) at five different orientations

   (c) segment lesions from specimen radiographs and measure their size, contrast, and shape metrics

2. To develop further a computer model of image formation

   (a) modify previously developed model for point source versus parallel beam

   (b) measure and model detector noise for film digitizer and screen-film system

   (c) measure scatter as a function of position in the image

   (d) measure beam intensity as a function of position in the image
3. To produce simulated mammograms
   (a) produce simulated mammograms with and without lesions
   (b) make preliminary comparison to actual mammograms
   (c) make adjustments to model, if necessary

4. To evaluate simulated images
   (a) collect real mammograms: normals and those with lesions
   (b) compare real and simulated mammograms based on quantitative measurements
   (c) conduct pilot observer study
   (d) conduct observer study comparing ROIs from real and simulated mammograms

5.1.1 Obtain radiographs of tissue specimens and mastectomy

   We have not collected any tissue samples as of yet. When the grant was submitted, our
   Department had budgeted to purchase a Faxitron, which would allow us to make high-resolution
   images of the samples. However, a new section head of mammography was hired and he diverted
   the funds to purchase other equipment. We plan to purchase a unit from our research funds. I
   expect to have the unit by October. An alternative approach, if necessary, is to record the images
   without geometric magnification and digitize them at high spatial resolution. A company,
   Retriever Technology, provides a service that we can use to digitize our films down to 10-micron
   pixel size.

5.1.2 Further development of computer simulation method

   The theoretical basis for the model has been developed previously by the PI, but with a
   number of simplifying assumptions [1]. For this project, we need to check these assumptions
   and include other relevant factors particular to our application. In addition, we need to cover the
   theory into a computer program that can produce a simulated image. Our efforts in these areas
   are described below.

5.1.2.a Modify model from parallel beam of x rays to x rays from a point source.

   We have calculated the difference in energy deposition in the detector assuming a parallel
   beam of x rays and a diverging beam of x rays. If the x rays are parallel and are incident at 90
   degrees to the detector, then each pixel at the output has a one-to-one correspondence to a point
   at the input, in terms of energy deposition (ignoring scattered x rays). If the beam diverges
   however, depending on the depth of interaction of the x ray in the detector, a pixel at the output
   can have contributions from x rays that enter the detector at several different points at the input
   surface. Standard patient geometry is a focal-film distance of 65 cm and maximum detector size
   of 24x30 cm, with the central axis of the beam at one edge of the detector, centered in the other
direction). Then assuming a phosphor thickness of 85 microns, we have calculated that the maximum energy spread because of a diverging beam is 30 microns (i.e., the difference between parallel and non-parallel beam assumptions is a 30-micron difference in point at which the x-ray is absorbed). Since we will initially use a 25-micron pixel size at the output to form the image, and subsequently form larger pixels by averaging, we need to take the beam divergence into account to be absolutely accurate. However, for pixels within 10 cm of the central axis, the maximum spread is 14 microns. Therefore, for any breast whose area projects to less than 20x10-cm, the assumption of a parallel beam of x-rays will produce a negligible error. Because of the added complexity a non-parallel beam introduces, we will initially assume a parallel beam in our calculations. If we find that this assumption produces poor results, we will modify our calculations for a diverging beam.

5.1.2.b Model detector noise for film digitizer and screen-film system.

Based on published noise power spectra of film [2], we integrated the spectra, weighted by the Fourier spectrum of a 50-micron scanning aperture. This gives us the standard deviation (square root of the integral) as a function of film density (see Figure 1). This was done for different film optical densities. Then assuming the noise on the film follows Gaussian statistics, we can use a random number generator to produce a noise pattern that will be added to the simulated image. That is, given a pixel with a certain film density, we will generate a random number that is from a Gaussian distribution with zero mean and a standard deviation corresponding to that film density, and then add the number to the pixel value.

We have also data on the noise of the film digitizer as a function of film density that we have measured in our laboratory (see Figure 2). To obtain these data, we digitized a calibration strip that had near-noiseless squares of constant optical densities from 0.10 to 4.0. Again, assuming Gaussian statistics, a random number generator will be used to produce a noise pattern that will be added to the simulated image. This information is necessary because we propose to use digital data for our comparison (simulated versus real) observer study, so we need to model digitization noise. We are using digital data because, if we printed the simulated images on film and used film for comparison, it would be obvious which images were simulated because they would look pixilated.

5.1.2.c Measure scatter as a function of position in the image

This will be done using mastectomy samples, which we will do next year.

5.1.2.d Measure beam intensity as a function of position in the image

This has not been done yet but it is straightforward to do. We will produce a “uniform” air exposure on film. This will be digitized to determine the x-ray intensity distribution incident on the detector.

5.1.3 Produce simulated mammogram

This will be done after tissue samples have been collected. However, as a first step, we will image an ACR accreditation phantom on plain x-ray film (Kodak XV), digitize the film, and calculate a simulated image for a Kodak Min-R E system. We will then compare the simulated
image to one recorded on the Min-R E system. We are currently writing the code to produce the simulated image.

5.1.4 Evaluation of simulated mammograms

The observer study is planned for year three. It is dependent on completion of 5.1.3.

5.2 Recommendations in relation to the Statement of Work

We do not anticipate making any changes to the Statement of Work.

6. KEY RESEARCH ACCOMPLISHMENTS

- Computer model is being developed.
- Corrections to the noise properties of simulated image due to digitizer and film noise have been determined.

7. REPORTABLE OUTCOMES

None so far.

8. CONCLUSIONS

Progress has been made in developing the computer model. We, however, have not yet imaged any tissue samples, because the planned purchase of a Faxitron was cancelled. We will either purchase a unit from our research funds or farm out high-resolution digitization (down to 10-micron pixel size) to a third party (Retriever Technology).

9. REFERENCES

11. APPENDICES

Figure 1. Standard deviation in the mean pixel value as a function of film optical density due to film granularity for mammographic x-ray film exposed to light.

Figure 2. Standard deviation in the mean pixel value as a function of film optical density (or pixel value) due to digitization noise.