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At the start of this project in the clinical optimization of digital mammography systems, these systems had not been shown to have adequate quality for clinical use. In the first year of this project we worked on image processing optimization and demonstrated that additional developments were needed. During the second year we continued our testing and were able to produce images in geometric test objects that exceeded the conspicuity of small objects of conventional mammography. At the same time we were able to produce in a limited number of cases digital mammograms that appear to be equal to or better than conventional mammography. In the third year we will be testing these new methods in a clinical trial to demonstrate that they are likely equal to or perhaps better than conventional mammography in the detection of objects associated with small breast cancers.

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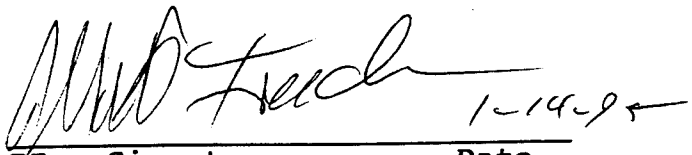

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CLINICAL OPTIMIZATION OF CURRENT DIGITAL MAMMOGRAPHY SYSTEMS

5 INTRODUCTION

5.1 STATUS AT TIME OF START OF PROJECT

As of the date of start of this project, January, 1993, there were two available, but experimental, methods for potential clinical use for digital mammography: film digitization and storage phosphor technology. Each of these methods had promise in that it could create digital images of the breast, but each also had potential limitations and neither had been shown to be adequate for clinical use. Work done by H.P. Chan (Invest. Radiol 1987; 22:581-589) and others had suggested that existing methods of film digitization would not be able to equal the conventional screen film methods in the detection of microcalcifications and major objections had been raised by M. Yaffe (Digital Mammography in Syllabus: A Categorical Course in Physics: Technical Aspects of Breast Imaging. Radiological Society of North America, 1992; 245-255.) and others that storage phosphor technology which had a minimum pixel size of 100 microns would not be sufficient either.

5.2 PROPOSED METHODOLOGY

The purpose of this project was to use mathematically based methods for optimization of image acquisition and image processing to provide incremental improvement in these methods that would allow them to equal screen film methods in diagnostic quality. This was based on the researchers experience with these methods and the improvements that we had achieved in imaging other parts of the body using these methods.

The procedure to be used was to experiment using geometric test objects to optimize the system and then to apply these methods in mammography in women. We had also proposed using anthropomorphic test objects, but found that these were of limited quality and not suitable for this purpose. We therefore used a combination of geometric test objects, biopsy specimen radiographs and stored digital mammograms.

We used response surface design methods to optimize the levels of exposure, both mAs and KVP and to optimize the methods of image processing. Much of this work was reported in the report we submitted at the end of the first year of the project. Additional tasks are underway as described below. These are to test two different mammographic films with different contrast scales, to test two different pixel sizes for film digitization and, in the final year of this project, to perform an ROC study of digitized film mammography on at least 50 cases comparing the original screen film mammogram, the digitized film displayed as a hard copy image and also as a soft copy image. The digitized film would be tested at two different digitization pixel sizes.

Tests of storage phosphor mammography tests would be performed in geometric test objects to be followed by clinical tests if existing methods were of sufficient quality.

6. BODY OF REPORT:

6.1 SUMMARY OF THE FIRST YEAR (1993) REPORT

The results of the first years work indicated to our satisfaction that, at least in geometric test objects, that digital mammography done with a 100 micron pixel combined with optimized image processing provided equivalent conspicuity of detail to what could be achieved with screen film mammography. In storage phosphor technology, this could be obtained only using new hardware and experimental software that had not been available at the start of the project.

6.2 ACTIVITIES DURING THE SECOND YEAR OF THE PROJECT (1994)

6.2.1 IMAGE PROCESSING OPTIMIZATION

6.2.1.1 MINIMAL DETECTABLE OBJECT SIZE

Continued development of image processing optimization for digital mammography was undertaken. Experiments were performed both on storage phosphor and digitized film images. These experiments demonstrated that the conspicuity of small and larger details in geometric test objects could be improved with newer software methods. With newer software methods two effects were noted: first, that smaller objects could be detected than with conventional screen film methods and, second, that those smaller details that could be seen on both screen film and screen film systems were easier to see on the digital methods due to the improved contrast. As an example, in one geometric test object (Nuclear Associates CDMAM phantom), the screen film system could demonstrate the 130 micron object, but only at very low contrast. The newer methods allowed the digital system to clearly visualize the 100 micron objects, but resulted in an exaggeration of the heel effect on images so that they were not optimal for radiologists interpretation.

6.2.1.2 SOFTWARE INDUCED OBJECT ENLARGEMENT

An interesting property of digital imaging of object close to the pixel size was noted: that they increase in apparent size due to pixel overlap. Thus a 100 micron object processed for optimal visualization actually measures 200 x 200 microns because it usually will be superimposed on 4 pixels, partially covering each, rather than being exactly centered on one pixel. This enlargement, which results from high contrast image processing look up tables should improve its conspicuity. Once detected, however, altering the look up table to a lower contrast effect, restores the object toward its actual size. It is mathematically possible to use the effective contrast of an object being evaluated by a pixel based detector to calculate its approximate size and location. At the moment this does not seem to be clinically important.

6.2.1.3 DETRIMENTAL EFFECT OF UNSHARP MASKING IN DETECTION OF SMALL OBJECTS

We found that unsharp masking, which had been shown by us (SPIE: Medical Imaging, Vol. 2164. 1994; 537-554) and by Dr. HP Chan (Invest. Radiol 1987; 22:581-589) to be helpful in detecting larger objects, was detrimental in the detection of the smallest objects. Tests in the Nuclear Associates CDMAM phantom demonstrated that increasing the intensity of unsharp masking concealed the smallest objects in the phantom, objects that could be seen with a high contrast look up table.

6.2.1.4 USE OF A HIGH CONTRAST LOOK UP TABLE: HEEL EFFECT

While the high contrast look up tables appeared to offer advantages in the detection of objects close to the pixel size, they had the effect of exaggerating the heel effect from the x-ray tube, limiting their clinical applicability. The resulting images, while showing smaller details than conventional screen film mammography exceeded the optical density range of the film, requiring more than one image to display all of the image information. Parts of each image would therefore be clear or black.

6.2.1.5 NEW STORAGE PHOSPHOR EQUIPMENT: SOFTWARE

During the year we were approached by the manufacturer of new storage phosphor digital equipment to test their new hardware and software to help the company in obtaining FDA approval. Under their grant, we found that their experimental image processing allowed a form of low resolution histogram equalization that could partially correct for the problem we had experienced with the use of the high contrast look up table. The system as given to us, however, also caused small (4-5 mm) masses to be less visible.

We found in working with their software that we could alter it so that it could partially eliminate the detrimental heel effect of the x-ray tube and could preserve the visibility of all objects if set differently than the company had indicated. In running these optimization tests, however, we encountered a software defect that would shut our machine down if we tried to use the software as desired for our tests of digital mammography. This bug does not affect the operations of the machine for the uses the company designed it for, but only affects our work in digital mammography optimization. So far, despite 6 months of negotiations between us and the company, we have been unable to convince the company to make the software modifications to eliminate this bug and to allow us to proceed with our tests. The company also

will not, currently, allow us to test this software on digitized film images. We are currently working to write software that will accomplish the same type of result, without infringing on the company's patent and are continuing to negotiate with the company to convince them that this new software would be even better with this bug removed.

6.2.2 DISPLAY

6.2.2.1 SOFT COPY DISPLAY

Work in developing image processing methods for the display of digitized film mammography has been underway for the past 9 months. The current system allows for the soft copy display of high quality images on 2 x 2.5 K monitors. The system we are working on contains four 2 x 2.5 K monitors and is designed with the concept that a screening mammography workstation would have to be designed differently than the existing MDIS workstation to allow the rapid throughput of these images. Major Donald Smith, MD of Madigan Army medical center has worked closely with us on the conceptual design of this workstation. At its current state of development, the research mammography workstation can display a single full breast image in 0.5 seconds at 2 x 2.5 K. The system provides unsharp masking, high/low and band pass filtering, and windowing capability. We are currently working on improved human interface programs for this soft copy mammography display system. In addition to working on soft copy display, we have printed a few images as laser prints to show its feasibility, but have not yet fully optimized the laser print parameters for digitized film mammography.

Some of the results from this project were presented at the Annual Meeting of the Radiologic Society of North America, December, 1994. Others will be presented at SPIE Medical Imaging Conference in February, 1995, and published in their proceedings.

6.2.3 TESTS OF FILM DIGITIZERS

After an analysis of available film digitizers we decided that a prototype film scanner made by DBA would provide the quality of images that we needed for our experiments based on film digitization. We ran tests on the prototype at DBA and reviewed their specification document. Once we had received the production model we ran tests on gray scale response, resolution and signal to noise ratio. Unfortunately the scanner failed to meet the specifications. After multiple discussions with the manufacturer, several modifications, repeat tests and more discussions, we decided that this scanner was still too unreliable for our experiments. We reevaluated available scanners and have acquired a new scanner which in our preliminary tests of gray scale response, resolution and signal to noise ratio has sufficient quality for the experiments planned for the third year of this project.

6.2.4 TESTS OF FILMS OF TWO DIFFERENT CONTRAST SCALES FOR FILM DIGITIZATION

The signal to noise ratio and gray scale response of film scanners is dependent on the optical density of the film to be digitized. As part of the project, we indicated that we would test films with two different contrast scales. We have accumulated in a logbook listing approximately 200 cases in which we have breast images obtained with films of two different contrast scales. We will be selecting from these 25 cases for this comparison once the new film digitizer has been tested and is ready.

6.2.5 ACQUISITION OF DATASET OF PROVEN MAMMOGRAMS FOR ROC PROJECTS

During 1994, 46 proven documented cases (including 14 cancers) were obtained for the project in evaluating the value of film digitization for digital mammography. These cases are kept in a separate file so that they are easily available. Our original research plan had to be modified when we discovered during this year that there were objects seen in these digitized film images of conventional mammograms that could not be seen in conventional screen film mammograms. Initially it was presumed that these were artifacts of the digitization process, but when we compared these to the biopsy specimen radiograph, these objects could in some cases be identified in the specimens indicating that the digitized film mammograms were detecting details not otherwise visible in the original mammogram. To compile the data set for the ROC study and

to have a proper "gold standard" of proof, it became necessary to acquire only cases that had high quality specimen radiographs. While this made gathering data more difficult, we now have almost the required number of cases needed for the ROC studies and expect that by April, 1995, we will have sufficient cases with subtle findings to conduct the study.

6.2.6 TESTS OF THE SUITABILITY OF MDIS TYPE DISPLAY FOR DIGITAL MAMMOGRAPHY

Tests done of the monitor display of digital mammograms and geometric test objects were performed on two different systems, a 1.5 x 2K and a 2 x 2.5 K system. We were unable to create images on the 1.5 x 2K monitor that equaled the conspicuity we could obtain on laser prints of the same data. At this point in time is seems likely that 1.5 x 2K display will not be adequate without zooming the image. We consider zooming to be unacceptable for high volume screening mammography and therefore a large matrix method of display will be necessary. In paragraph 2 we described the characteristics of the display system we are developing. Display on the 2 x 2.5 K system is still at a preliminary stage of testing at our site, but at this time appears likely to be sufficient. We expect to be ready to start the soft copy reading tests of digitized film mammography this summer.

6.2.7 COLLABORATIVE RELATIONSHIPS WITH DOD SITES

We have had extensive oral and written communications with Major Donald Smith, MD at Madigan Army Medical Center concerning the requirements for soft copy display of mammography and he is collaborating with us in the work on digital mammography. Major Smith brings to the project his extensive knowledge both of breast imaging and his knowledge of soft copy display on the MDIS system.

To a lesser extent, Brooke Army Medical Center is also involved in our projects. This has been a less active affiliation than originally envisioned, since it has become clear that newer storage phosphor equipment is necessary for the best digital mammography image and BAMC does not have this newer equipment and software. A radiologic technologist has been placed at BAMC to assist in the research efforts at that site and to help acquire images for research. MAMC has indicated that such a person is not needed at this time.

We are in the process of working to develop a research relationship with Tripler Army Medical Center, with Major Jay Cook, MD, since TAMC has installed the equipment that could acquire images of sufficient quality that we could process with the experimental software that we are testing at Georgetown. TAMC has requested that discussion of such a research relationship in digital mammography be postponed until the Summer because the current Director of Breast Imaging will be rotated to a new assignment at that time and that the research relationship should be developed with the new Director.

6.2.8 CLINICAL TEST OF STORAGE PHOSPHOR MAMMOGRAPHY

In the original proposal, we indicated that we would test existing storage phosphor technology in geometric test objects and if it was found to be sufficient, would perform clinical tests. Our tests showed that the technology existing at the time of the proposal was not sufficient to justify clinical testing. Based on our findings, we would be unlikely to be able to get approval from the Georgetown IRB to test this inferior equipment and could not ethically justify performing it.

During this year we acquired a contract from the manufacturer of an experimental storage phosphor digital system to test this system to help them acquire FDA approval of their system for digital mammography. This system provides a higher signal to noise ratio that previous systems. These improvements were achieved by improved phosphor chemistry in the imaging plates and improved laser and readout electronics. The image processing software allows a higher contrast look up table than this company's prior methods and also provides a low resolution histogram equalization image processing program. Working under the research protocol for this product we have been obtaining digital mammograms.

We demonstrated images from this machine at the Annual Meeting of the Radiological Society of North American in November-December, 1994, and asked those who wished to give their impression of the quality of the images. We showed comparison images obtained with both conventional and digital methods, using the same exposure levels and in all but one case showing the original conventional mammogram film (one case had an outside initial mammogram and we showed a first copy). 74 people responded. 94% thought that the digital images of the test objects were better, 97% thought they were equal or better. 83% thought the demonstration of microcalcifications was better with the digital method, 88% thought the digital was equal or better. 52% thought the mass demonstration was better with digital method, 77% thought is was equal or better with the digital method. This preference study does not indicate that the system will improve the detection of cancer, but it is a promising preliminary impression of its potential value.

We identified significant problems with the machine both with the durability of the new formulation imaging plates and with the new software as applied to digital mammography. Based on our findings, the company has redesigned the imaging plates and cassettes for improved durability. So far they have been resistant to making the modifications needed in the software.

7. CONCLUSIONS:

The project as originally proposed continues to progress with positive findings supporting the expectation that digital mammography will be able to be clinically implemented at DoD sites by the conclusion of the process. If one reviews the original proposed schedule of activities, those activities not dependent on film digitization are on schedule. Because of the unexpected delays in the delivery of the film digitizer and its unanticipated instability, those projects requiring the large volume digitization of film have been delayed. The acquisition of clinical cases for the tests of digitized film digital mammography are on schedule and it is thought that the delays introduced by the lack of a proper film digitizer will be rapidly corrected now that the replacement digitizer is on site.

As anticipated in the project proposal, we demonstrated that the storage phosphor devices existing at the time of the proposal were not suitable for digital mammography. A newer device using experimental software is currently undergoing tests for the manufacturer and is expected to be sufficient for digital mammography. The hardware for this has recently been made available in the US market and has been installed at TAMC. The software we are using is still experimental and is not commercially available. We expect, based on the experiments that we and others are doing on this experimental software, that it will become FDA approved and available within the next 18 months. We will include information on our findings on this experimental device in our final report.

Although the collaborative relationship with DoD Radiologists is different that originally proposed, it is an active relationship that has been modified to meet changes in equipment and personnel needs.

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