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13. ABSTRACT *(Maximum 200 words)*

The Georgetown University research team has four separate but related grants to address key components of a digital mammography system that includes image data acquisition, image processing, image display and communication. A core grant serves as administrative support to the four related interactive grants on digital mammography. This report of the core grant summarizes the progresses of all four related projects throughout the entire period of the funded research in a concise format. Detailed reports on each individual projects can be found in the individual final reports that have been submitted to USAMRMC.

The project for clinical optimization of current mammography systems has produced very promising results that are shown in our demonstrations and publications. This study has guided manufacturers to develop the necessary tools for acceptable digital mammography. A computer based method for evaluation and quality control of image quality of digital mammograms has been developed. A new storage based CR system with image quality that meets the requirements of mammography has been evaluated. We have demonstrated the feasibility of telemammography. Significant progresses have been made in the development and implementation of computer-aided diagnosis (CADx) algorithms.

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Coordinated Approach to Breast Cancer Diagnosis and Treatment for the Military (Core Program)

1.0 Introduction

There are three components required for the successful development of a digital mammography system: image data acquisition, image processing, and image display and communication. The Georgetown radiology research team has five separate but related grants on digital mammography to address technical issues in a coordinated manner. One of the five grants deals with administrative support functions to four related interactive grants on digital mammography. Detailed individual reports have been submitted to the Army. This report will summarize all four related projects in a concise format. Readers are encouraged to refer to the individual reports for the detailed information.

2.0 Summary of Tasks

- Clinical Optimization of Current Digital Mammography Systems
- Digital Mammography Based on Novel Photo Detector
- Computer Assisted Quality Control and Telemammography
- Implementation of Computer Aided Breast Cancer Diagnosis

3.0 Coordinated Project Summaries

3.1 Clinical Optimization of Current Digital Mammography Systems

Army grant DAMD17-93-J-3008 was initiated in December 1992 for completion in December 1995. This was extended to a completion date of December 1996. This represents the final report for this project.

The original purpose of this project was to test existing methods for digital mammography. We discovered in this process that the methods current in 1992 were not sufficient for digital mammography and that we needed to encourage and cajole manufacturers into modifying and/or making the devices we needed. This resulted in delays in the progress of the project. In this process we have had to work directly with Fuji Photo Film Corporation in the US and with their development facilities in Japan, with DBA, Inc. in Florida, with Analogic Corporation in Peabody, MA, with 3M in St. Paul, MN, and with Polaroid in Newton, MA, as well as develop our own software. One of our outside suppliers was unable to meet equipment specifications for the film digitizer (this supplier was replaced). Another supplier delayed the delivery of equipment for six months and the software provided needed to be rewritten to eliminate bugs that resulted in equipment crashes (with a six month additional delay). We also found that a key component of printer server software that we needed did not exist in the commercial market. We have worked with our current suppliers over the last two years and now have a successful print server for acceptable quality mammographic images, but are continuing to encourage the development of a better hard copy display device as we believe that this will further enhance the image quality of these digital mammograms.

3.1.1 Introduction

During this project we have investigated optimization of methods for image acquisition, image processing and image display. Each of these represented major challenges and it was only by the close working relationship established between the research team and our commercial suppliers that the goal of acceptable digital mammography was reached. We are currently engaged in the performance of a ROC study to validate our results. The results from the first reader have been calculated and indicate ROC areas of Az screen film = 0.7373Az digital = 0.7646 when tested for detection of cancer. When tested as a method of discrimination between cancer and benign lesions that were detected, the Az of screen film = 0.5743. The Az of the digital system = 0.7412 . We do not know how the other 6 readers will perform in the ROC study, but are encouraged by the results of this first reader.

The purpose of this project is to determine whether or not digital mammography is feasible with existing

equipment either by using digitized film or by using direct digital acquisition using storage phosphor technology. The brief answer is that it was not feasible with the equipment available at the initiation of the grant. There has been substantial development over the past three years and we believe our data from the ROC analysis will show that digital mammography is feasible using direct acquisition, but not using digitized film. It is adequate using hard copy display, but not with soft copy display at this time. This project has, based on our findings and advice, we believe, guided manufacturers to develop the necessary tools for acceptable digital mammography. We believe that our presentations and publications have helped push the agenda for the development of still better digital mammography systems because our results were so promising.

3.1.1.1 Digitized Film Mammography

The evaluation of digitized film required a process of quality control of the digitization equipment and display equipment that has been completed and a preclinical trial of proven cases, the first phase of which has been completed. This first phase demonstrated that digitized film mammography at 100 micron pixel size was considered clearly inferior to the original films by each of the five radiologists who reviewed its display on a workstation and that this lower quality would decrease the detectability of breast cancer. Digitization of a small sample of two different film screen systems of different latitudes demonstrated that they both were of sufficient contrast that information close to the skin line and within the dense portions of the breast could not be adequately demonstrated with either system. Initial laser prints of 50 micron digitized film mammography in June 1993, were of poor quality because of the lack of an appropriate print server with correct image processing. We have been unable to produce adequate images based on digitizing conventional screen film mammograms either printed as hard copy or displayed soft copy. Both methods produced artifacts that could be easily confused with microcalcifications, and both methods obscured microcalcifications so that they could not be recognized. This is a problem we are continuing to work on as we believe that a solution to this would be most important both for further developments in digital mammography and that it may represent one of the problems limiting advances in the computer aided detection of microcalcifications.

3.1.1.2 Storage Phosphor Digital Mammography

The evaluation of direct digital mammography using storage phosphor technology required machine and software optimization. In order to accomplish this it was necessary to perform a long optimization procedure that has been detailed in the two prior annual summaries. Briefly, a multivariate analysis was performed using response surface experimental design methods to define the optimal exposure and image processing factors for digital mammography. The results of this, summarized below and in the attached paper demonstrated that storage phosphor digital mammography using a 100 micron pixel and proper exposure and image processing optimization could result in images of standard mammographic phantoms that showed objects equal in size or smaller than those shown in standard screen film mammography and that the resulting images were highly pleasing to viewers. Additionally, we found that digital mammography may prove to be especially useful for the detection of cancer in the radiodense breast. These findings are detailed below.

TABLE OF SMALLEST OBJECT SEEN

Test Object	Screen Film	100 micron phosphor	50 micron CCD
CDMAM	130micron 100 at 5x mag	100 at 1 micron thick	100 at 0.8 microns thick
CIRS Detail	240	160	160
RMI 156	240 (3/6)	240 (3/6))	240 (3/6)
Steel Fleck	100	50 (noisy, high contrast)	100
CIRS Half Round	160	160	160

This table demonstrates that in two of the test objects, the 100 micron storage phosphor allowed detection of smaller objects than screen film mammography and that in the other two standard geometric test objects,

that it provided the same object visibility as screen film mammography. The steel fleck phantom is a home-made system and showed that if a 50 micron object were of sufficient radiodensity, it could be identified on a 100 micron system, though it would measure larger than its true size. (From Freedman, 1995 A)

A comparison of a 50 micron digital spot device based on CCD technology and a 100 micron whole breast system using storage phosphor technology was performed and reported in February 1995, and demonstrated that the 50 micron system provided higher contrast, but did not allow smaller objects to be detected, and that the 50 micron system needed 1.5 to 3 times the exposure of the 100 micron system. In the above table, the improved contrast from the 50 micron system is demonstrated for the CDMAM phantom for which a thinner object could be seen with the 50 as compared to the 100 micron system. Both were superior in resolution to screen film mammography. These results were specific to the devices tested and cannot be generalized however.

We have also reported on the classification of microcalcifications comparing screen film mammography with digital mammography (in a version earlier than the one used in our current ROC test). In this study, we selected 20 patients who had gone to biopsy. Half had benign calcifications and half had calcifications associated with malignancy. In each case, the region of the calcifications was outlined by Post-it Notes and the biopsy specimen radiograph was also provided as a measure of truth. The study showed that the four radiologists involved were split in their preferences for screen film vs. digital images both on individual cases and on the cases grouped together. In general, the radiologists preferred the conspicuity of the microcalcifications on the digital system. They were divided on preference between the digital and screen film systems for counting the number of microcalcifications and defining their shape. Whichever system the radiologists preferred, they were unable to use this information to make better decisions between benign and malignant calcifications on the two systems. Since that time we have improved the printing system for digital mammography and are using a better printing system in our ROC study. As previously stated, the first ROC reader in our multi-reader study was better at classifying benign vs. malignant on the digital compared to the conventional screen film system and the other results are not yet available.

3.1.1.3 Collaborative Relationship with Army Medical Centers

Our original intention of working with Madigan Army Medical Center (MAMC) and Brooke Army Medical Center (BAMC) has been modified so that we are now working with Col Robert Shah, MD at BAMC and Col Ted Raia's designee, (Major Morgan Williamson, MD) at Walter Reed Army Medical Center (WRAMC). We also consult with and obtain advice from by Major Donald Smith, MD at Madigan. Two WRAMC radiologists are participating in the ROC reading study. We have had discussions with radiologists at WRAMC, Bethesda Naval Medical Center, Mike Freckleton, MD at Wilford Hall AFMC, and Anna Chacko, MD at BAMC regarding our findings on digital mammography as well as discussions at special meetings with General Russ Zajtchuk, MD and his assistant Major Paul Zimnick, MD about the appropriate utilization of digital mammography.

3.1.1.4 Presentations for other Federal Agencies

Our material on digital mammography has been presented to Lillian Yin PhD, Director, Division of Reproductive, Abdominal, ENT and Radiological Devices at the FDA, and her colleagues in a special meeting, Florence Houn, MD, MPH and her colleagues as an invited speaker at the Mammography Quality Standards Board meeting on Digital Mammography Quality Control July 10, 1996, to Faina Shtern, MD and her colleagues at their invitation at NIH. We have also presented material to Susan Blumenthal, MD, Deputy Assistant Secretary of Health for Women's Health, Health and Human Services (HHS) and have participated with exhibits at two meetings held for informing Congress of work in improving breast cancer detection and diagnosis.

3.1.2 Methods

Our work has involved system analysis, system development and clinical trials. We will briefly summarize our previous reports.

3.1.2.1 System Analysis

At the time of the initiation of this project, many parameters of requirements for digital analysis were incompletely understood. Work by our group and others has greatly extended knowledge in this field.

Required exposure: Digital radiography systems currently under development represent a different tradeoff in image quality than screen film images. In screen film images, one chooses a screen film combination based on three considerations: film granularity, system resolution, and image optical density. The choice of a desired exposure dictates which screen film system one uses. In general, one can consider that a decrease in dose requires a decrease in resolution. In digital radiography, exposure in any specific digital system is related to the resulting signal to noise ratio (SNR). In any specific system, dose does not dictate the resolution of the system. SNR however determines the visibility (conspicuity) of low contrast objects. Test objects of resolution are usually designed to measure high contrast resolution which can give a false representation of the likely value of different systems required for mammography. In mammography, the objects one wishes to detect are usually low contrast objects.

There are two components of exposure: energy distribution (usually measured as KVP) and exposure (often measured as mAs). In addition, it can be helpful to divide mAs into its components: exposure intensity and time. KVP affects the contrast of the resulting image, but higher KVP allows one to decrease the time of exposure limiting any motion that may occur. For any specific digital system, one needs to determine the best exposure range, both in terms of KVP and mAs. We did these measurements and reported our results in 1995 in a paper relating the visibility of objects in selected geometric test objects to both KVP and mAs. We showed, for the system we used, where the tradeoffs were. We showed that image processing could not recapture information on images obtained at 36 KVP because the use of image processing increased both the visibility of noise as well as the object contrast and that, in our tests, these two balanced out. If one used high contrast image processing to correct for the loss of contrast resulting from higher KVP, that one then had problems because of the varying thickness and composition of the breast. Certain regions became all black or all white as we applied corrective imaging processing. Between 22 and 28 KVP, no differences were encountered.

We also showed that there was a region of lesser exposure where the digital system still recorded information, while the screen film system resulted in a clear film. We have used this to develop experimental image processing for the radiodense breast. This is described below. We reported this in 1996.

Our experiments in exposure indicated that for the system we used, that standard mammographic exposures were sufficient to demonstrate the same sized objects as conventional mammography, but that decreases in exposure would likely result in some loss of information.

Image Processing Optimization: A large amount of our work was related to the optimization of image processing of digital mammography. Prior to the start of our work, published articles on digital mammography usually assumed that the best image processing for a digital mammogram would be a screen film look-alike image. Some work has suggested that edge enhancement using unsharp masking might improve the detection of microcalcifications, but this had not been fully explored. We began work by deciphering the meaning and image appearance effect of the image processing available on the digital imaging system available to us (the Fuji AC-1). Fuji was, at that time, not willing to make available to its customers detailed information of its system and was not and still is not our partner in the work we are doing in digital mammography. We therefore proceeded to test each of the image processing parameters in selected combinations using partial factorial design to gain understanding of the system. These results were published and since that time Fuji has begun to release increasing amounts of information about their system.

The effect of different image processing parameters on breast images and on breast geometric test objects had not been previously systematically explored. We tested selected combinations of the Fuji parameters on several geometric test objects and reported our results in 1994. We showed that there was a tradeoff (influenced by exposure) of the effect of image processing on the visibility of details in the test objects with

kernel size and enhancement intensity and that the enhancement factors that best showed details could result in digital mammograms that were so distorted as to be uninterpretable for subtle signs of disease. As our concepts developed, we realized that any edge enhancement (using the available kernel sizes in the Fuji system) resulted in some loss of conspicuity of the smallest details in geometric test objects.

Histogram equalization: In 1994, Fuji selected the PI of this project to be one of two US research sites for a new method for histogram equalization to be used for digital chest radiographs. We attempted to apply this method for low resolution histogram equalization to digitally acquired mammograms. After a period of trials of different parameter settings, we arrived at a usable system. The use of this system presents problems because if the parameters are incorrectly selected, small masses in geometric test objects become of very low conspicuity and may not be seen. We have determined usable settings that we believe will prove useful in the imaging of microcalcifications in the radiodense breast. We have reported our findings. This topic is discussed below in clinical trials.

New directions in image processing: We have been working to develop better look-up tables (LUTs) for digital mammography. These newer concepts are not yet fully developed and are only partially implemented. The goal is to create a contrast linearized look-up table optimized for the detection of microcalcifications and masses in the complex pattern and radiodense breast. In concept, one would expect low object (microcalcification and masses) contrast in areas of the breast containing fibroglandular tissue and high object contrast for microcalcifications and masses in fatty regions of the breast. One should therefore have a high contrast LUT in the low optical density regions and a low contrast LUT in the high optical density regions of the breast. We have partially implemented this and are looking toward further improvements of this method over the next 6 months. We reported on the conceptual basis for this in 1996.

Image display: The third major component we have been working with is image display. We have worked on both soft copy display and hard copy display. With soft copy display, we have encountered many problems and do not consider this to be currently adequate for clinical mammography. We have done progressive optimization of hard copy display and consider current systems adequate, but not optimal, and have been advising manufacturers on methods that could be used to improve the hard copy displays.

Soft copy display: At the current state of available technology, soft copy display of digital mammograms results in many problems. We have worked to define clinical scenarios of how soft copy display might be used and will discuss why soft copy display is not now suitable. Current soft copy displays have the following limitations: (1) Limited number of pixels: displays are limited to 2 K by 2.5 K. To have adequate demonstration of microcalcifications this resolution is required for each mammogram -- four mammograms in a study of each woman. In addition, comparison of old and new images is necessary to detect subtle changes. Thus one would need eight monitors for effective display. As a radiologist interpreting mammograms, I go back and forth between images: right-left, new-old, craniocaudal-mediolateral oblique (CC-MLO). The pattern varies with what I see on an image. Because of the limited number of pixels, displaying two breasts on one monitor works only if a woman has small breasts. (2) Display luminance: The limited luminance limits resolution in darker portions of the image. We have previously evaluated the ability of one high quality monitor to respond to changes in luminance and found that the characteristic curve was distorted in the blacker regions of the image. In effect the blacks are not black enough probably secondary to internal reflections in the CRT. Because of the wide variation of breast density that results in wide variations of exposure information, one needs the same range of output OD that one would have on a screen film or laser print image. (3) Bloom: In high brightness regions of an image, image bloom can occur decreasing the sharpness of small bright objects such as microcalcifications. In our study of digitized film we found that microcalcifications were less visible on monitors, which we believe is, at least in part, due to bloom effects. Center-edge-corner variations in focus: All CRT displays vary in focus between the center and the edge and the corners of the monitor face. This is because of the radius of curvature of the CRT face is such that the distance from the CRT gun to the tube face varies. Because microcalcifications can occur anywhere in the breast, this may result in lesser degrees of detection.

Hard copy display: Quite early in our work we realized that the laser film printers available to us were not optimized for use in digital mammography. There are several reasons for this:

(1) Radiologists interpreting mammography usually use a magnifying lens to better see microcalcifications. Until quite recently, laser imagers were not designed with this need in mind and therefore, with magnification, the scan lines became visible. In the same way that grid lines interfere with the ability to see microcalcifications on screen film mammograms, scan lines decrease the visibility and degree of certainty of detection of microcalcifications. There are several potential solutions to this problem but each requires equipment modification and development. We have been monitoring this and believe that there are two current systems that are adequate (but not optimal), and a third that we will be testing in the near future. Improvements in the scanning mechanism of traditional laser printers to decrease the visibility of scan lines can occur in three ways: improved alignment control allowing a larger spot size without overlap, overlapping scanning, and increasing the number of pixels used for each pixel in the original image. We have found that the 3M 969 laser printer provides much less visible scan lines without affecting apparent conspicuity of microcalcifications. We have used this printer to print the images used in our ROC study. We are about to acquire a new Fuji laser printer that uses 4 pixels in the print for each pixel at acquisition and will be testing this once it arrives. In addition, a newer method for producing a laser print: creating a digital representation of digital data, as is done in the Polaroid Helios printer, provides very high quality dry prints. We have tested this, but have not yet done a formal comparison study of it.

(2) Look-up table: The look-up tables available for laser printing of digital mammograms are not optimal. We have been working with Polaroid to develop new look-up tables to improve image quality for their printer. Look-up tables for digital mammography will probably have to be optimized to each individual laser printer.

(3) Display size: Digital mammograms are acquired at a specific pixel size. Laser printers print with a specific pixel size. Current digital mammography systems and current laser printers are not matched in pixel size. This results in images that are not life-size. Since minor enlargement of a mass may indicate that it is malignant, accurate measurement of the size of a mass is important. Correcting for differences in size is time consuming and can result in errors of interpretation.

(4) Electronic accuracy: Microcalcifications can result in quite subtle differences in optical density. Variations induced by scanning speed variations and ripples in the power system can result in visible variations in scan line optical density that can be confused with microcalcifications. The control requirements for this are higher than in laser imagers used for other purposes. Some laser images appear to have problems with the degree of scanning control needed.

Of the systems we have tested, we believe that the 3M 969 laser printer is appropriate for use and that the Polaroid Helios printer is probably appropriate for use. Better laser printers such improve the conspicuity of lesions on digital mammograms. These systems must be optimized for digital mammography prior to use.

3.1.2.2 Clinical Case Series

We have been collecting a set of cases in which we have in each case the original screen film mammogram, the storage phosphor 100 micron direct digital mammogram obtained on the latest update of equipment and software, and the biopsy specimen radiograph. We currently have over 130 cases containing more than 30 proven cancers. The data for the direct digital mammograms is stored electronically and each of the original screen film mammograms has been digitized and is available in 50 micron and 100 micron formats. As of November 1995, we have sufficient cases of adequate quality to perform an ROC study. Because of an important update in software that resulted in improved digital mammography acquisition, an earlier dataset was not used; the current dataset has been collected since March 1995. We delayed starting our ROC study because the laser imagers available to us were not considered adequate. We received our new 3M 969 laser and created with the aid of Analogic Corporation an adequate interface during the Summer of 1996 and are currently performing our ROC analysis.

We have also digitized 100 cases in which we can compare wider and narrower latitude films. The prior film system was the Dupont Mammography screen film system. The newer higher contrast system is the

Fuji IM Fine mammographic system and has moderately higher contrast. We still do not have an adequate method of printing high quality images from this dataset.

3.1.2.3 Digitized Film Methodology

Our initial choice of film digitizer (DBA, Inc.) proved unstable and despite many attempts by the manufacturer to improve the product, remained unstable. Eventually we decided that the system would not be able to provide the quality we needed. In 1995, we switched to the Lumisys 50/100 micron system. We have digitized approximately 2000 mammogram films with this system. The system still shows intermittent instability, but is adequate for our experiments.

3.1.2.4 Digitized Film Mammography Display

We have developed display parameters for the soft copy display of digitized film mammograms on the Vicom display system. This Sun computer based system using Megascan monitors provides sufficient flexibility to allow us to test soft copy display. We have performed a reader comparison study in which 25 cancer images, 25 benign biopsy cases and 50 normal images were compared by 5 radiologists who evaluated the image preference looking at the visibility of microcalcifications, masses, and asymmetric densities on the original screen film mammogram and on the soft copy display. The radiologists were allowed to adjust the window level and width on the displayed images. All 5 radiologists expressed strong preference of the hard copy display for microcalcifications. In some cases the microcalcifications could not be seen on the soft copy display and in some cases dust and pick artifacts appeared on the soft copy display with an appearance that could not be distinguished from the appearance of microcalcifications, whereas on the hard copy display they could be easily determined to represent dust or pick artifacts.

So far we have assessed only 100 micron pixel digitized film images. We will evaluate a smaller sample of 50 micron digitized film images in the near future. We do not have a clinically usable method for the display of 50 micron digitized film images on soft copy displays since the pixel size exceeds that of available monitors. Thus one ends up looking at images in segments -- 1/4 of the image displayed at a time. This therefore would not be clinically practical. Our original concept was that one could assess the image with the pixels combined to produce 100 micron pixel size and zoom into the full dataset when a suspicious region was found. What we have found is that we cannot identify many of the regions containing suspect calcifications on the 2K matrix-100 micron pixel images and therefore would not know where to zoom the image. We consider zooming the entire image impractical for clinical use. We are unaware of any 4K display with sufficient luminance for clinical radiography.

3.1.2.5 Digitized Film Mammography: Hard Copy Display

Our first hard copy display of digitized film mammography was in June 1993. The initial system did not provide adequate control of contrast and unsharp masking. It was clear from this initial work that the image processing capabilities of our available print server system were not sufficient for adequate display of mammography. Over the past 15 months we have been working with a supplier of print servers (Analogic Corp.) to have them build into their system adequate capabilities for us to obtain proper control of the digitized film mammography printing to assure high quality images with our existing laser printers. We are still working towards an appropriate image print system with adequate image parameter control for digitized film images. We expect to have a working system in late October or November, 1996. At present, we do not consider the hard copy images of digitized film mammography adequate for clinical diagnosis. We do not know if this is caused by the digitization process or by the printing process, since we know that the printing process is still not optimal.

3.1.2.6 Direct Digital Method

Images are currently acquired using Fuji HR-V imaging plates and a Fuji 9000 Computed Radiography system. Based on problems we identified during beta testing of this system, it was modified and appears adequate for digital mammography. Images are automatically processed using Fuji's standard parameters and the unprocessed data is then stored on the Fuji 954 workstation. We reprocess the image data sets to meet our optimized image processing standards. The image data sets are then transferred for permanent storage to a Fuji optical disk drive to provide for long term optical disk storage. This image data can be

transferred through an Analogic DASM to an Analogic experimental workstation which serves both as a print server and a method of transferring the images over our internal network. The Analogic print server can (as recently developed) mimic the Fuji print parameters (except for DRC) printing to a 3M laser printer. It can also send processed images for printing as TIFF files to other printers.

Image processing for the direct digital system can be performed using the standard Fuji parameter settings. We have also found it of value to use specially designed dynamic range control curves for printing digital mammography in the radiodense breast. Our previous Annual Reports to the Army documented the procedures used to optimize image appearance.

3.1.2.7 Direct Digital Images: Hard Copy Display

We have found that the standard Fuji laser printer supplied with the original Fuji 9000 was acceptable, but less than optimal. We have printed some of these images on a Polaroid Helios Printer and other images on a 3M 969 Laser Printer and have found the image quality of these prints superior to that of the Fuji laser printer. The main reason for this is that when the images are magnified with a hand lens, the scanning lines from the printer are sufficiently wide that they interfere with the detection of microcalcifications. We expect to receive an updated Fuji laser printer by December 1996 or January 1997 for testing. The other two printers have less apparent scan lines (3M) or inapparent scan lines (Polaroid) resulting in images that radiologists prefer. At this time, we believe that the Polaroid Helios Printer will prove to be optimal, but we do not currently have funds to purchase this printer and therefore must work through Polaroid's generosity and willingness to print these images for us in their research laboratory. Polaroid placed a Helios printer at Georgetown in October 1996 and we are currently developing the interface to this system for testing.

3.1.2.8 Direct Digital Images: Viewer Acceptance of Hard Copy Display

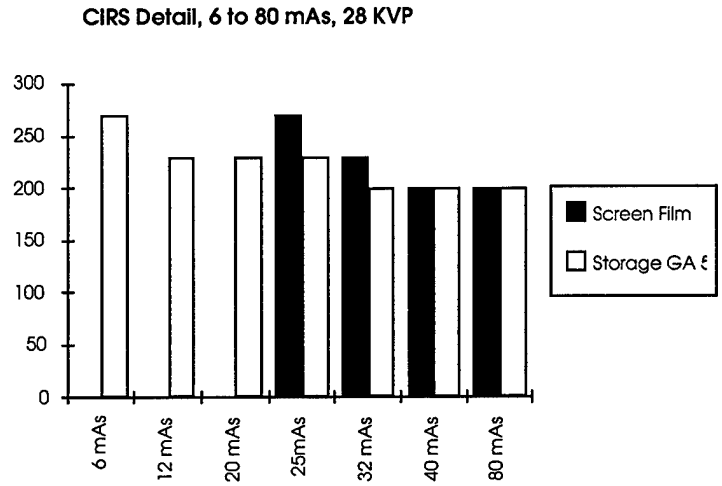
We have displayed comparison images from the Fuji computed radiography digital system and conventional screen film images in several meetings. The acceptability of these images has been considered high by many of those viewing the images at meetings. At the RSNA Annual Meeting, 1994, we demonstrated with a backlit display the original screen film images and CR digital images of the standard breast geometric test objects, three cancers (5, 6, and 15 mm) manifested by microcalcifications, one 8mm cancer manifested by spiculated mass, and two microcalcification cases that on biopsy showed benign findings. We provided magnifying glasses and asked those who wished to indicate which images they preferred. Ninety-four percent of those who responded preferred the digital images of the test objects, 83% preferred the clinical microcalcification cases, and 57% preferred the one mass case we showed. We have shown a similar exhibit at the American Roentgen Ray Meeting in May 1995, where the exhibit received a bronze medal. The direct digital images appear to be acceptable to many of those viewing them.

3.1.2.9 ROC Study of Direct Digital Images

This study was delayed because improvements of hardware and software that occurred in March 1995 were of sufficient magnitude that we decided not to use our prior data, but only the newest data. We have selected from our collected set of digitally acquired mammograms 24 biopsy proven cancer cases, 24 benign biopsy cases and 50 cases selected by radiologists as being normals for incorporation in our ROC study. In each case we have both conventional and digital mammograms. These cases have been randomized and radiologists are now providing interpretations of these comparing (in separate reading sessions one month apart or greater) interpretations of screen film and digital mammograms. The first radiologists results have been calculated and showed an Az screen film = 0.7373 and Az digital = 0.7646 when tested for detection of cancer. When tested as a method of discrimination between cancer and benign lesions that were detected, the Az of screen film = 0.5743. The Az of the digital system = 0.7412.

3.1.2.10 Direct Digital Mammography and the Radiodense Breast

In 1993, we determined that the wider exposure latitude of the storage phosphor plate system did indeed allow the recording of useful information in mammographic test objects over a wider range of exposures than did standard mammographic film screen systems. This information was included in our Annual Report to the U.S. Army in 1994. This was determined by our systematic response surface optimization experiments and was reported in 1995.



This chart demonstrates that at mAs less than 25, while the storage phosphor system could demonstrate objects, the screen film failed to demonstrate any of the objects. At 25 and 32 mAs, the storage phosphor demonstrated smaller objects than screen film. At 32, 40, and 80 mAs, the two systems performed equivalently. (Storage = Storage Phosphor Radiography. GA = gradient angle of the look up table.) These results indicate that there is information available that can be captured by the storage phosphor plate that correlates to those regions seen in mammograms as radiodense (clear or almost clear) regions of the image. (From Freedman, 1995 B)

Although we knew of this phenomenon in 1993, we did not have a clinically useful method of retrieving this information for display in a clinical setting. If we attempted to include the full range of information in a single image, the resulting image was of low contrast and not clinically useful. If we attempted to post-process the images so that one image reflected the high exposure image and another the low exposure image, the Fuji PRIEF prevented it. In June 1994, I requested Fuji to modify their software so that I could test a system for bypassing the PRIEF effect using the Dynamic Range Control (DRC) system software with special DRC curves. These curves were provided in the Spring of 1995 but resulted in system crashes. The modified software became available in the Summer of 1995. The effect of DRC using these new curves was to provide images that contain both levels of exposure data in a single image. Examples of the new processing are attached to this report.

Although the math is more complex, the easiest way to understand the effect of DRC in mammography is to consider it a complex form of image processing. In this image processing, the image is separated into two images: a low frequency mask and an original image. Histogram equalization is then performed on the low frequency mask and this mask is then subtracted from the original image. This final image shows a decreased range grayscale of pixel values that covers large regions of the image, but leaves intact the pixel values of high spatial frequency regions. Since the high frequency regions represent the microcalcifications and edges of most masses, the resulting image provides the ability to see the high frequency structures of the breast potentially from the skin line to the most dense regions of the breast (as shown in figure 1) while preserving the visibility of microcalcifications (as shown in figures 2 a and b).

Three types of modification of the look-up table are possible. These are explained in a paper presented at the SPIE Medical Imaging 1996 meeting.

The Fuji software still imposes limits so that we cannot produce the optimal image automatically and some cases show the effect better than others. Currently, we cannot reprocess images retrieved from the optical disk drive, but only those still stored as original data on the Fuji 254 workstation hard disk, but have requested a software modification from Fuji Japan to allow this. We have, however, been able to partially mimic this effect using wavelet transforms and are working to improve this. We are also working with Fuji

to better define the applications of this algorithm. We believe that this will allow us to better image the radiodense breast allowing us to see microcalcifications and possibly masses better than on screen film mammography. If we are correct in our analysis, this new form of digital mammography may improve the sensitivity of mammography for the detection of breast cancer in women under the age of 50. Since 37% of the breast cancer new cases seen at Georgetown occur in this age group and the current sensitivity of mammography in this age group is 60-68% (compared to 90% in women over the age of 50), we consider this a most important development.

3.1.2.11 Digital Mammography and The Shape of Microcalcifications

Concern has been expressed that digital mammography at 100 micron pixel size will not allow sufficient information about the shape of microcalcifications to be seen. Based on this concern, we have recently performed an experiment in which we compared the original screen film mammogram, the 100 micron pixel storage phosphor mammogram and the biopsy specimen radiograph in 10 randomly selected cancer cases and 10 randomly selected benign biopsy proved cases. All cases contained microcalcifications. Four radiologists indicated their preferences between the screen film and digital images. Four radiologists expressed preference in the majority of cases for the digital system in microcalcification conspicuity. One of the four preferred the digital images for shape and number of microcalcifications, one considered each system preferable in an equal number of cases, and two preferred the screen film system. Whatever the radiologists' preferences, the radiologists were unable to distinguish benign and malignant cases on either the digital or conventional systems. Thus, although there may be a slight preference for evaluation of shape on the conventional system, this preference did not appear to be of clinical importance since it did not help the radiologists to better classify the benign or malignant features associated with the calcifications.

The improved conspicuity of microcalcifications found by the radiologists with the digital systems suggests that these systems may prove to be better than screen film mammography in a screening setting. We are working to obtain funds for such a full scale screening test.

3.1.2.12 Current Recommendations for the Implementation of Digitized Film Mammography

We have been unable to define an adequate system for acquisition, image processing, and display for digitized film mammography that is diagnostically equivalent to conventional screen film mammography. We continue to work on this problem.

3.1.2.13 Current Recommendations for the Implementation of Direct Digital Mammography

Image Acquisition

Image acquisition with either the Fuji 9000 or Fuji AC-3 with the images printed on a 3M 969 laser printer appears adequate for diagnostic mammography. Our ROC study is expected to confirm this. This ROC study will, we expect, provide preliminary data supporting the use of this system for screening mammography. The Fuji AC-1 provides a lower quality image than the Fuji 9000 and the AC-3 and in our studies is not adequate. The lower signal to noise ratio of the AC-1 results in noisier images. It is possible that using higher exposures with the AC-1 could provide adequate images, but we have not tested that hypothesis since we would then have to exceed the standard dose used for conventional screen film mammography. The Fuji system is not FDA approved for mammography. The FDA published draft guidelines for those seeking approval of digital mammography systems. We submitted comments on their proposal. The final guidelines are still subject to comment. The guidelines resulted from a meeting the FDA held March 6, 1995. The PI of this project was one of the experts testifying at the FDA hearing.

The Fuji systems use a 100 micron pixel size which appears adequate. Tests of a commercially available 50 micron pixel small field system showed that that the 50 micron system required a higher radiation exposure and while it provided higher contrast, it did not allow the detection of smaller objects. We believe that the 50 micron system we tested can be improved upon and that the eventual 50 micron system may prove to be superior to the 100 micron system we currently use.

Image Processing

Fuji image processing modified to the following parameters appears to provide adequate display for hard copy direct digital mammography. An ROC study is in process to confirm this statistically. Application of special DRC methods appears potentially to provide improved imaging of the radiodense breast. Additional investigation of this new image processing method is underway.

GA=1.2, GT=G, GS=0.6, GC=0.3 RN=7, RT=R, RE=0.0

ABBREVIATIONS
GA, gradient angle; GC, gradient center; GS, gradient shift;
GT gradient type; RN, frequency number; RT, frequency type.

Image Display

Hard Copy Display: Display with the Fuji FL-IM3543 printer appears adequate, but not optimal. Display on the Polaroid Helios printer and 3M 969 printers result in better image appearance, but it is not yet shown that they affect diagnostic accuracy. The newest Fuji printer FL-IM D has not yet been tested by us, but in images of digital mammograms we have seen from other sites appears very promising. This system will be available for our testing late in 1996 or early 1997.

Soft Copy Display: We have not been able to produce images that we consider adequate on soft copy display systems.

3.1.3 Current Status of Items in Statement of Work

3.1.3.1 Recommended resolution size for digitized film mammography

Using existing technology, we have been unable to define a system configuration that will provide diagnostic information equivalent to conventional screen film mammography. We have more extensively tested 100 micron digitization and have shown it to be inferior to screen film in the display of microcalcifications. We have been unable to come up with a reasonable clinical scenario for the display of 50 micron digitized film.

3.1.3.2 Coordinating the testing of these parameters with the associate military sites

At various stages in the process of this project we have worked with Major Donald Smith MD, MAMC, Col Robert Shah, MD, BAMC, Col Ted Raia, MD, Major Robert Leckie, MD, and Major Morgan Williamson, all of WRAMC. We have also presented our results to Colonel Anna Chacko, MD of BAMC and General Russ Zajtchuk, MD, at MATMO. Two radiologists have participated in the ROC study of digital mammography; others were asked and declined. We are currently working with Major Michael Freckleton, MD, Wilford Hall AFMC on a related project.

3.1.3.3 Implementation document for direct digital mammography

We have defined the image acquisition parameters, image processing parameters and factors for display of direct digital mammography. Col Ted Raia, MD at WRAMC agreed prior to his retirement to have WRAMC serve as a test site for direct digital mammography to be managed by Major Morgan Williamson, MD. We are working with them towards a prospective clinical trial of direct digital mammography to be performed at WRAMC and Fort Belvoir, Virginia. The purpose of this trial will be to compile the data for FDA approval. We are currently awaiting the FDA response to comments on their draft recommendations on the performance of digital mammography clinical trials and for the FDA's final recommendations.

3.1.5 Bibliography

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3.2 Computer Assisted Quality Control and Telemammography

3.2.1 Introduction

This project, DAMD17-93-J-3015, started in December, 1992 and with a one year no cost extension is to end in December 1996. The purpose of this project was to develop systems to enable the integration of mammography into MDIS, to allow the acquisition of mammograms in facilities remote from the radiologist who will interpret the images, to develop automated methods of quality control of image quality and to develop methods for the teletransmission of digital mammograms.

This project contains five components.

A. The evaluation of the feasibility of interpreting mammograms on a soft copy viewing station.

B. Investigation of methods for digital storage and retrieval of mammograms.

C. The identification of mammograms that are of substandard quality.

D. The identification of mammograms that require additional views prior to the release of the patient.

E. The demonstration of the effectiveness of telemammography.

As we complete this project, we have learned that digitized film mammograms displayed soft copy are not of sufficient diagnostic quality for primary interpretation of microcalcifications, that digital storage and retrieval of both digitized film and digitally acquired mammograms is feasible and that those acquired digitally are of probable diagnostic quality. We have developed methods of identifying mammograms that are of substandard quality and have demonstrated the effectiveness of telemammography when used with direct digital capture of breast images. We were unable to create a system that, at this time, is capable of automatically identifying women who need additional images.

We will discuss the work done on each of these sub-projects and indicate the portions that succeeded and those that did not succeed. After these discussions, we will describe a working system for telemammography and quality control suitable for obtaining mammograms at remote sites, their transmission and the remote interpretation of mammograms.

3.2.2 Collaborative Relationship with Army Medical Centers

Our original intention of working with Madigan Army Medical Center (MAMC) and Brooke Army Medical Center (BAMC) has been modified so that we are now working with Colonel Robert Shah, MD at BAMC and Colonel Ted Raia's designee, (Major Morgan Williamson, MD) at Walter Reed Army Medical Center (WRAMC). We also consult with and obtain advice from Major Donald Smith, MD at MAMC. Two WRAMC radiologists are participating in the receiver operating characteristic (ROC) reading study of digitally stored and transmitted mammograms. We have had discussions with radiologists at WRAMC, Bethesda Naval Medical Center, Major Mike Freckleton, MD at Wilford Hall AFMC, and Colonel Anna Chacko, MD at BAMC regarding our findings on digital mammography and teledigital mammography. We have also discussed at special meetings with General Russ Zajtchuk, MD and his assistant Major Paul Zimnick, MD the appropriate utilization of digital telemammography for incorporation into the mammography van that they are currently working to develop. We have had discussions of the implementation of a clinical trial of digital telemammography at WRAMC and Ft Belvoir.

3.2.3 Overview

3.2.3.1 The evaluation of the feasibility of interpreting mammograms on a soft copy viewing

station

An evaluation of digitized film mammograms displayed on a workstation showed that radiologists had great difficulty in identifying microcalcifications and also misidentified film defects as microcalcifications.

3.2.3.2 Investigation of methods for digital storage and retrieval of mammograms

We have digitized and stored several thousand digitized mammograms and approximately 250 digitally acquired breast images. The retrieval of these images has been accomplished. The digitally acquired and retrieved images are of high quality and are probably of diagnostic quality. We are currently performing an ROC study to prove this. The digitized screen film mammograms are of lesser quality and do not appear adequate for primary diagnosis. They are clearly not acceptable when displayed soft copy.

3.2.3.3 The identification of mammograms that are of substandard quality

1. A set of training cases has been assembled.

A. Set A is a set of images of geometric test objects that are available in direct digital form as well as digitized film. The accuracy of diagnosis of microcalcifications on these varies with the signal to noise ratio which is related to exposure. From this data, the exposure level at which information loss occurs has been calculated allowing one to determine whether there are regions within mammograms in which full information has not been captured. Data from this project was reported to SPIE Medical Imaging 1995. (Freedman 1995)

B. A program has been written to determine cases that are under- and overexposed. A set of 181 selected clinical mammograms were obtained from clinical files and digitized. While all of these were considered clinically acceptable originally, the radiologist interpreting them considered some of them somewhat overexposed or underexposed and listed them in a record book. Thirty images were underexposed, 83 normally exposed and 58 overexposed based on clinical criteria. In this set, the automatic program provided clear classification. Of the 83 with normal exposure, 76 were so classified. Of the 30 underexposed images all were classified as underexposed. Of the 58 overexposed images all were classified as overexposed.

2. We have developed segmentation algorithms for digitized screen film mammography that divide the image into regions of different pixel values. This will enable us to determine the average pixel value for under- and overexposed regions of the image.

3. Quality control procedures for the acquisition of digital images including mammograms using Fuji equipment have been established. Manuals for the Fuji AC-1, AC-3 and Fuji 9000 have been prepared. These manuals provide methods for quality control of data acquisition.

3.2.3.4 The identification of mammograms that require additional views prior to the release of the patient

Our computer aided diagnosis program for microcalcifications has undergone further development. It can now identify 97% of microcalcification clusters in our test set. We are currently developing a user friendly interface so that this data can be easily displayed. We are currently performing a preclinical test of this system with the goal of determining the cause of false positive detections. Currently the system still has too many false positive detections to be of clinical use as an aid to the technologist for determining whether or not additional views will be necessary. The detection program, however, should be of use in aiding the radiologist in detection suspicious clusters of microcalcifications. Once we have completed our local preclinical trial, we expect to work with Major Morgan Williamson, MD at WRAMC and with Col Robert Shah, MD at BAMC in a larger clinical test of this algorithm.

We are concurrently working on a system for microcalcification classification--into calcification clusters that are associated with benign disease and those associated with malignancy. This work which was started in 1994 was substantially delayed because of instability with our high resolution film digitizer. We have replaced that system. Automated classification combined with computer aided diagnosis of

microcalcifications would aid the technologist not only to know where there were clusters of microcalcifications that might benefit from magnification views, but would also allow her to eliminate obtaining the magnification views in some of those patients where the computer could clearly indicate that the microcalcifications were benign. At this stage in the development of these algorithms, it is still to early to implement them for use by technologists.

3.2.3.5 The demonstration of the effectiveness of telemammography.

In June 1994, we first demonstrated teledigital mammography using digitized film and sending the image from Washington, DC to St. Paul, Minnesota to be printed. The quality was not adequate for diagnosis. In 1995, we were co-developers of a system that could transmit Fuji direct digital mammograms with what we believe to be adequate quality. Digital mammograms obtained at Georgetown were stored on a hard disk, transferred to a WORM optical disk, recalled to the hard disk, transferred to another hard disk, transferred via push over T-1 to another hard disk and then sent over the Internet to be stored on another hard disk and then laser printed. We believe that the quality is now appropriate, and will be spending the next few months optimizing the final image quality. We are currently performing an ROC study comparing digitally stored and locally transmitted mammographic images to the original screen film image.

In November 1995, at the Radiologic Society of North America (RSNA) annual meeting, we provided Internet access to our digital mammograms through the Inforad booth of our industrial collaborator, Analogic. At the recent presentation for Congress on Breast Cancer Imaging Improvements, we continuously transmitted images from Georgetown to the Hubert H. Humphrey Building of the Department of Health and Human Services (HHS), printing them on-line using a Polaroid Helios Printer. The quality is quite high and we believe it is suitable for diagnosis. An ROC study based on the Polaroid dry printing technology is planned for the near future. The ROC study using the 3M 969 wet laser is currently in process. This method has been demonstrated to General Russ Zajtchuk and Susan Blumenthal, MD, Assistant Secretary of Health for Women's Health, HHS.

3.2.4 Details of Research Performed

3.2.4.1 The evaluation of the feasibility of interpreting mammograms on a soft copy viewing station.

An evaluation of digitized film mammograms displayed on a workstation showed that radiologists had great difficulty in identifying microcalcifications and also misidentifed film defects as microcalcifications. For this project we collected 50 cases of cancerous and non- cancerous mammograms with screen film, direct digital and digitized film images. Digitization was performed at both 50 and 100 microns. Detailed testing of the 100 micron digitized screen film images showed that the four radiologists had a high degree of preference for the hard copy images.

3.2.4.2 Investigation of methods for digital storage and retrieval of mammograms.

We have digitized and stored several thousand digitized mammograms and approximately 250 digitally acquired breast images. The retrieval of these images has been accomplished. The digitally acquired and retrieved images are of high quality and are probably of diagnostic quality.

We have been collecting a set of cases in which we have in each case the original screen film mammogram, the storage phosphor 100 micron direct digital mammogram obtained on the latest update of equipment and software, and the biopsy specimen radiograph. We currently have over 130 cases containing more than 30 proven cancers. The data for the direct digital mammograms is stored electronically, and each of the original screen film mammograms has been digitized and is available in 50 micron and 100 micron formats. Because of an important update in software that resulted in improved digital mammography acquisition, an earlier dataset was not used; the current dataset has been collected since March 1995. We delayed starting our ROC study because the laser imagers available to us were not considered adequate. We received our new 3M 969 laser and created with the aid of Analogic Corporation an adequate interface during the Summer of 1996 and are currently performing our ROC analysis.

Images are currently acquired using Fuji HR-V imaging plates and a Fuji 9000 Computed Radiography system. Based on problems we identified during beta testing of this system, it was modified and appears adequate for digital mammography. Images are automatically processed using Fuji's standard parameters and the unprocessed data is then stored on the Fuji 954 workstation. We reprocess the image data sets to meet our optimized image processing standards. The image data sets are then transferred for permanent storage to a Fuji optical disk drive to provide for long term optical disk storage. This image data can be transferred through an Analogic Data Acquisition System Manager (DASM) to an Analogic experimental workstation which serves both as a print server and a method of transferring the images over our internal network. The Analogic print server can (as recently developed) mimic the Fuji print parameters (except for Dynamic Range Control (DRC)) printing to a 3M laser printer. It can also send processed images for printing as TIFF files to other printers.

Direct Digital Images: Viewer Acceptance of Hard Copy Display
We have displayed comparison images from the Fuji computed radiography digital system and conventional screen film images in several meetings. The acceptability of these images has been considered high by many of those viewing the images at meetings. At the RSNA Annual Meeting, 1994, we demonstrated with a backlit display the original screen film images and CR digital images of the standard breast geometric test objects, three cancers (5, 6, and 15 mm) manifested by microcalcifications, one 8mm cancer manifested by spiculated mass, and two microcalcification cases that on biopsy showed benign findings. We provided magnifying glasses and asked those who wished to indicate which images they preferred. Ninety-four percent of those who responded preferred the digital images of the test objects, 83% preferred the clinical microcalcification cases, and 57% preferred the one mass case we showed. We have shown a similar exhibit at the American Roentgen Ray Meeting in May 1995, where the exhibit received a bronze medal. The direct digital images appear to be acceptable to many of those viewing them.

ROC Study of Direct Digital Images
We have selected from our collected set of digitally acquired mammograms 24 biopsy proven cancer cases, 24 benign biopsy cases and 50 cases selected by radiologists as being normals for incorporation in our ROC study. In each case we have both conventional and digital mammograms. These cases have been randomized and radiologists are now providing interpretations of these comparing (in separate reading sessions one month apart or greater) interpretations of screen film and digital mammograms. The first readers results are available and showed Az screen film = 0.7373; Az digital = 0.7646 when tested for detection of cancer. When tested as a method of discrimination between cancer and benign lesions that were detected, the Az of screen film = 0.5743. The Az of the digital system = 0.7412. We believe that when this ROC study is completed in November 1996 that it will show that digitally acquired, stored, and retrieved mammograms are equivalent to screen film mammograms.

3.2.4.3 Identification of mammograms that are of substandard quality.

1. A set of training cases has been assembled.

Set A is a set of images of geometric test objects that are available in direct digital form as well as digitized film. The accuracy of diagnosis of microcalcifications on these varies with the signal to noise ratio which is related to exposure. From this data, the signal to noise ratio (SNR) at which information loss occurs can be calculated allowing one to determine whether there are regions within mammograms in which full information has not been captured. Data from this project was reported to SPIE 1995 Medical Imaging.

This report demonstrated that as one decreased the exposure, that the ability to detect the smallest microcalcifications was decreased. This is summarized in the following chart:

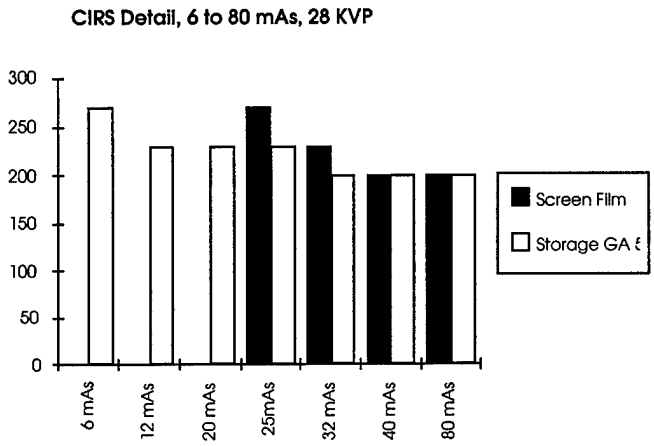


Chart 1: This chart demonstrates the smallest sized test details visible on the CIRS Detail Phantom as exposure is varied, comparing two systems: conventional screen film mammography and Fuji Digital Storage Phosphor radiography, processed in Sensitivity Mode. At low exposure levels, the digital system allows the detection of simulated microcalcifications that cannot be seen in the conventional system. This is analogous to detecting microcalcifications in radiodense regions of the breast.

The major factors affecting the detectability of small details in a geometric test object are signal to noise ratio and contrast. Image processing can be used to change the contrast scale, but increasing the contrast also increases the contrast and visibility of the image noise. By calculating the signal to noise ratio in these images, one can determine whether or not full information about small microcalcifications has been obtained. Because SNR is an easily calculated quantity, one will then be able to use a computer to look at regions of the mammogram, segmented as discussed below, to determine whether or not exposure parameters are appropriate.

A program has been written to determine cases that are under-exposed and overexposed. A set of 181 selected clinical images was obtained from clinical files and these mammograms were digitized. While all of these were considered clinically acceptable originally, the radiologist interpreting them considered some of them somewhat overexposed or underexposed and listed them in a record book. Thirty were under exposed, 83 normally exposed and 58 over exposed based on clinical criteria. In this set, the automatic program provided clear classification. Of the 83 with normal exposure, 76 were so classified. Of the 30 underexposed images all were classified as underexposed. Of the 58 overexposed images all were classified as overexposed. In this study, the program detected all under- and overexposed images correctly, but did assign 7 of the 83 normal images to the overexposed category. Since all of these images were considered within the acceptable range at the time of initial reading, though noted to be a little dark or a little light, the system is both sensitive and relatively specific. It should be able to serve as a good guide for the automated assessment of mammograms obtained at remote sites.

We have developed segmentation algorithms for digitized screen film mammography that divide the image into regions of different pixel values. This will enable us to determine the average pixel value for different regions of the image. The segmentation system is adjustable and can use different thresholds. It works by looking at regional pixel values to determine margins within an image.

As our work with digitized film progressed, it became clear that teletransmission of digitized screen film obtained mammograms would be of limited utility because of the introduction of artifacts simulating microcalcifications and the obscuration of microcalcifications that can occur. Successful teletransmission of mammograms would require the use of digitally acquired mammograms. The system we chose to use for development is a storage phosphor based system -- the Fuji 9000. We discovered that if this machine were not maintained at a high level of quality, that artifacts could result resembling calcifications. A very high

level of quality control was therefore necessary. We sent one of the faculty scientists to the Fuji factory training course to learn everything that he could about the machine and had him come back to write a quality control manual for use with this system.

Quality control procedures for the acquisition of digital images including mammograms using Fuji equipment have been established. Manuals for the Fuji AC-1, AC-3 and Fuji 9000 have been prepared. The manual for the AC-3 is attached. These manuals provide methods for quality control of data acquisition. If one is to produce high quality digital mammograms, one must have methods for assuring that the quality of image acquisition is high and that the machine used for this acquisition is properly maintained. Our experience in using storage phosphor mammography is that it requires very careful attention to machine cleanliness and that the functions of the machine must be checked on a regular basis. Attached are two articles related to QC of storage phosphor devices that we have recently published. (Appendices 11,12) The more complete manual for machine QC is also attached.

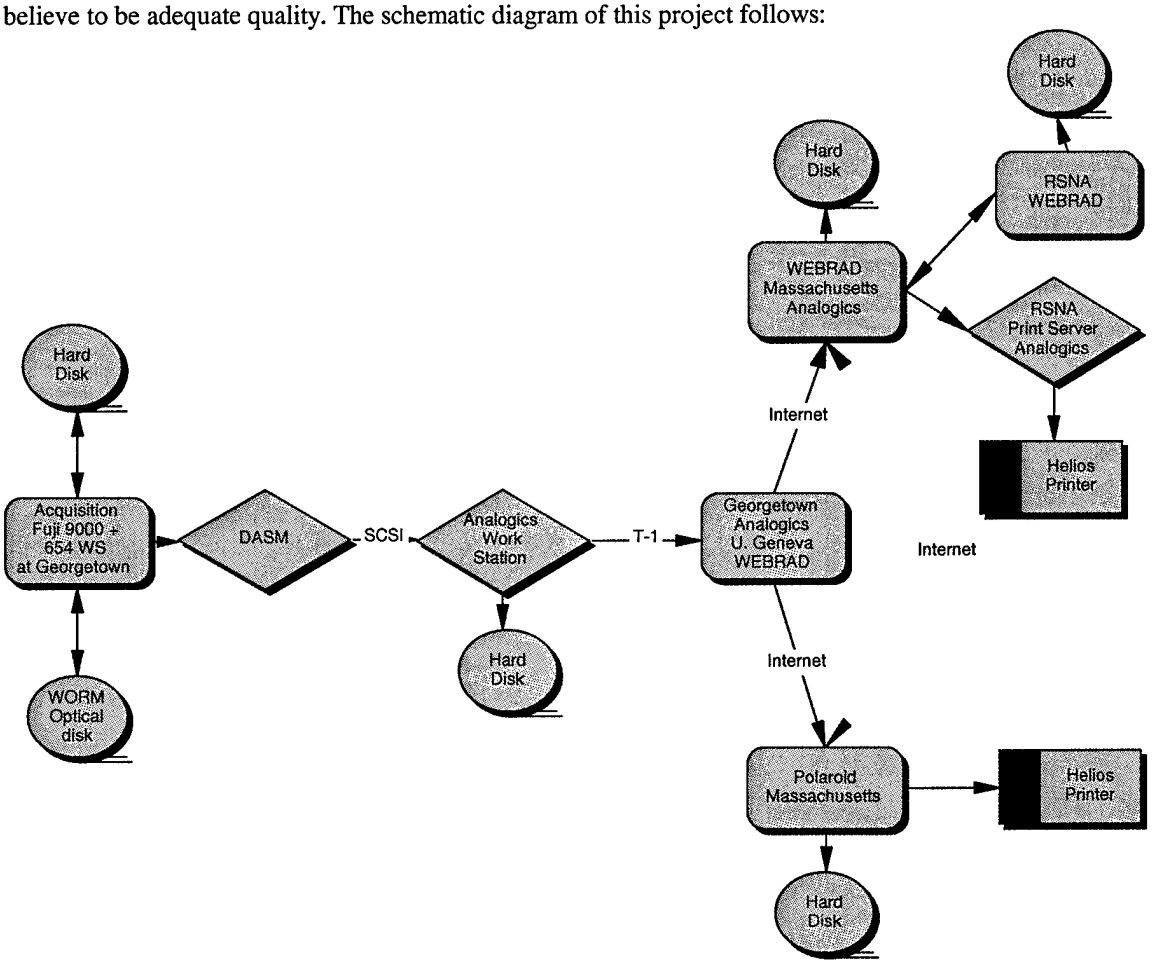
3.2.4.4 Identification of mammograms that require additional views prior to the release of the patient.

Our computer aided diagnosis program for microcalcifications has undergone further development. It can now identify 97% of microcalcification clusters in our test set. We are currently developing a user friendly interface so that this data can be easily displayed. We are preparing to test this system in a preclinical setting working with Col Ted Raia, MD at Walter Reed Army Medical Center and with Col Robert Shah, MD at Brooke Army Medical Center. Our original goal was to develop a program that would enable the technologist to know when a magnification view was needed. Currently, the computer aided diagnosis system has been tuned for screen film mammograms digitized at 100 micron pixel size. While our current program has a high true positive detection rate, it still has an average of 1 false positive detection per image. We are currently doing a careful analysis of the types of findings that are causing the false positives and have submitted an abstract to present a paper at SPIE Medical Imaging 97. A copy of this abstract is attached. What we are finding in our review, so far, of more than 200 images, is that real findings are causing the false detections. These include groups of several film defects, benign microcalcifications, grid artifacts, film scratches, and what we believe are dilated terminal ductal units in the breast. These dilated terminal ductal units are a common site of benign calcification formation and closely resemble the appearance of calcification clusters. We believe that improving our knowledge of the causes of false positives will enable us to develop improved algorithms and improved quality of our screen film mammograms that will help us avoid these problems. At present, the system would result in too many extra films if technologists were to use it as a guide.

It is clear that a system that identifies calcifications that radiologists can easily classify as being benign would, in the end, not be useful in telemammography. We therefore have been working on systems to aid in microcalcification classification--into calcification clusters that are associated with benign disease and those associated with malignancy. This work which was started in 1994 was substantially delayed because of instability with our high resolution film digitizer. We have replaced that system. Automated classification combined with computer aided diagnosis of microcalcifications would aid the technologist not only to know where there were clusters of microcalcifications that might benefit from magnification views, but would also allow her to eliminate obtaining the magnification views in some of those patients where the computer could clearly indicate that the microcalcifications were benign. We have run two different datasets through our developing program. In the first dataset of biopsy specimen radiographs, the system performed moderately well in distinguishing benign and malignant cases. This has been previously reported. We have just completed testing a second, more difficult dataset of digitized screen film mammograms. In this set the radiologists were not able to distinguish benign from malignant (all had gone to biopsy as suspicious lesions after diagnostic workup). The computer program was not able to distinguish benign from malignant in these cases either. This was presented in 1996. We are now working to test a set of cases that radiologists performing screening mammography considered suspicious, but which were then classified into benign or malignant categories by diagnostic mammograms. These results have been submitted for presentation in February 1997, but we do not know yet whether the paper has been accepted.

3.2.4.5 Teledigital Mammography

In June 1994, we first demonstrated teledigital mammography using digitized film and sending the image from Washington, DC to St. Paul, Minnesota to be printed. The quality was not adequate for diagnosis. In 1995, we were co-developers of a system that could transmit Fuji direct digital mammograms with what we believe to be adequate quality. The schematic diagram of this project follows:



Digital mammograms obtained at Georgetown were stored on a hard disk, transferred to a WORM optical disk, recalled to the hard disk, transferred to another hard disk, transferred via push over T-1 to another hard disk and then sent for over Internet to be stored on another hard disk and then laser printed. During the annual meeting of the Radiological Society of North American, November 1995, we demonstrated teledigital mammography over the Internet transmitting images from Boston to the Radiologic Society of North America and printing the images in the Inforad booth of our industrial collaborator, Analogic. We believe the quality is now appropriate and will be spending the next few months optimizing the final image quality. Once image quality is optimized, we will perform an ROC analysis comparing the original mammogram obtained with screen film to the direct digital mammogram teletransmitted images in a set of proven cases. The final images resulted from a combination of technology developed by Fuji, Georgetown, Analogic Corp. and Polaroid.

In October 1996, with further developments, we were able to demonstrate on-line digital teledigital mammography from Georgetown to the Hubert H. Humphrey Building of HHS in Washington, DC, printing images pulled over the Internet. The image quality appears to be of diagnostic quality.

The system that we designed and helped to build now transmits 100 micron pixel digital mammograms, but could be easily converted to a 50 micron system should that become the standard for digital mammography and should the problems of image display be solved.

3.2.5 Summary

The goal of this project was to develop methods to improve the ability of mammograms to be obtained at remote sites and to develop methods for their teletransmission to a central site of excellence in the interpretation of mammography. We were unable to accomplish this using digitized screen film mammograms, but have succeeded in doing this with direct digital mammograms. The ROC study that will prove this is currently underway with the results of the initial reader being favorable with Az screen film = 0.7373. Az digital = 0.7646 when tested for detection of cancer. When tested as a method of discrimination between cancer and benign lesions that were detected, the Az of screen film = 0.5743. The Az of the digital system = 0.7412. We have demonstrated the effectiveness of digital storage and retrieval for which the same ROC study will provide the proof. We have demonstrated the feasibility of teletransmission of images transmitting them over the Internet from Georgetown to Boston to the Radiologic Society of North America annual meeting in Chicago and separately from Georgetown over the Internet to the Hubert H. Humphrey Building of the HHS in Washington, DC. We have defined quality control procedures for this system. We have been able to build a system that identifies under- and overexposed mammograms based on digitization of the mammographic films. We have been unable to develop a clinically useful method of directing technologists as to which patients need additional images during their mammogram based on the detection of microcalcifications. This still remains a human rather than a computer based task.

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3.3 CLINICAL EVALUATION OF A DIGITAL MAMMOGRAPHY BASED ON MICRO-LITHOGRAPHY *(US Army Grant No. DAMD17-93-J03012)*

3.3.1 INTRODUCTION

The incidence of breast cancer is increasing. Each year more than 182,000 women will be diagnosed with breast cancer and 46,000 will die of breast cancer in the United States of America.[1] Breast cancer is a major health problem in the U.S. and is the second most frequent cause of cancer death among women after lung cancer.[2-4] Unlike lung cancer, however, the causes of breast cancer have not yet been identified, and until then a formal methodology for preventing and curing breast cancer remains unknown.

The goal of mammography is the reduction of mortality by the detection of breast cancer at the earliest possible stage. X-ray mammography is acknowledged to be the most sensitive and specific technique for detection of breast cancer in its earliest and most curable stages. The NCI-NASA Working Group Digital Mammography Technology Transfer Workshop held in May 1993 identified digital mammography as the most promising novel technology for improving mammographic performance. Despite its status as the method of choice in breast cancer detection, it is clear that significant improvements in mammographic performance are possible. Kopans and Plewes, at the National Cancer Institute Consensus Conference "Breast Imaging; State-of-the-Art and Technologies of the Future," stated that "While there is room for continued development with conventional methods, it is believed that advances in digital acquisition and manipulation of breast images represent the most fertile territory for major advances in the x-ray detection and diagnosis of minimal breast cancers."[5] While digital technology offers many benefits, its full potential will be realized only when it is carefully integrated into the overall design of mammography systems.

One potential advantage of digital over screen-film mammography is higher detector efficiency, since detectors, in principle at least, are subject to noise limitations such as that associated with film granularity in screen-film mammography. A second advantage of digital mammography is much higher detector dynamic range, which would permit significantly improved recording of information in areas of the image exposed to radiation levels significantly lower or higher than the optimal level. Maidment et al.[6] estimate that dynamic ranges of well over three orders of magnitude will be produced in digital mammography. Wagner[7] has shown that if dynamic range is defined by the high and low exposures that correspond to degradation of detector detective quantum efficiency (DQE) to ten percent of its maximal value, the dynamic range of screen-film systems is barely one order of magnitude, rather than the two to three orders of magnitude that might be inferred from considering film only as a display medium. A third major advantage of digital mammography is that it permits consideration of display characteristics independent of the image capture requirements of the system. The recent work of Sabol et al.[8] on scanning equalization mammography includes a striking demonstration of the combined effects of non-optimal display and limited dynamic range, in a DQE sense, in conventional mammography. Additional advantages of digital mammography are related to the fact that direct digital acquisition of the image greatly facilitates image processing, computer-aided diagnosis, and image transmission.

Small calcifications are one of the earliest and most reliable, although nonspecific, findings of early and minimally invasive breast cancer.[9] Detection of such lesions truly tests the ability of the present digital systems caompared to the conventional screen-film system which has a far lower spatial resolution.[10,11] Even digitization of conventional mammographic films with fine pixel size (100 x 100 μm) degrades the detectability of microcalcifications. High quality mammography images require excellent spatial resolution in order to detect fine and subtle microcalcifications within the breast. At the same time excellent contrast sensitivity is needed for seeing the subtle differences in x-ray attenuation coefficient between normal and malignant tissues.[12]

Up to the present time, the only commercially available technology that has been used to perform digital full

breast studies is based on the storage phosphor computed radiography (CR) system developed by Fuji. Both digital and screen-film systems have been improved significantly, but the characteristic of the systems (i.e., spatial resolutions and contrast detectability for detection of microcalcifications) remained the same. Technologies which may produce digital detectors with both a higher resolution and a field of view needed for mammography are now in the development stage by many radiographic industries. 3M Corporation has offered Georgetown University their new technology which we expected to have significant advantages over the existing conventional and digital technologies. This new system is expected to have both a wider dynamic range and a higher spatial resolution than the conventional screen-film and Fuji CR system.

The new digital system developed by 3M[13,14], uses a detector system based on a multilayer structure containing a photo-conductor. The latent image produced at the photo-conductor surface is then read out by scanning the plate with a laser beam. After the laser read out, the image will be processed digitally. The resulting image will be processed and viewed as a soft copy display or a hard copy film as needed. The prototype device operates with a wide dynamic range and produces linear x-ray signal response for clinically reasonable x-ray exposure. Clinical image quality can be obtained at x-ray exposures that are comparable to those used in a conventional screen-film system.

Before conducting the clinical study in a mammography energy range, the system was evaluated for imaging body parts which are less radio-sensitive than breast images. First, phantom study was performed on extremities, the hip, and the shoulder. The physical characteristics of the system such as image quality and radiation dose were studied. In that evaluation the radiation dose was optimized for extremities and the system was improved significantly, mainly by redesigning the detector and using image processing to enhance the contrast and spatial frequency for better image quality. The phantom study's evaluation was divided into two parts. In the first part, the performance of the system was evaluated in high kVp on the study of extremities, hip and shoulder. In the second part, system optimization was performed in order to minimize the patient dose on the extremities. Then in the second study, a very limited patient study was performed for extremities to conclude that if the new system is ready for clinical study in mammography.

3.3.2 METHODS

The 3M imaging system is a new technology that has not yet been established as suitable for clinical mammography examination. Therefore, a sequence of experiments was performed to study the system's physical characteristics, image quality, and image sensitivity. The study also include radiation dose optimization for good image quality. The experiments were performed on body parts that are less radio-sensitive than the breast. The physical characteristics of the system such as image quality and radiation dose were studied in a energy range higher than mammography energy range. The study was performed in three years:

Year 1
The first year we concentrated on the initial tests of the 3M system on the extremities phantoms for a range of kVp and mAs. The results showed that the machine did not have sufficient image quality to proceed with a clinical trial in mammography energy range (Reference to the Report on the First Year Project).

Year 2
Image optimization was performed on body parts that are less radio-dense than the breast. Several major adjustments were made to improve the image quality of the system. The system was improved mainly by redesigning the detector structure and using image processing parameter settings. By the completion of the second year, the radiation exposure was optimized and the image quality was improved. The study concentrated on the extremities, hip, and shoulder phantoms (Reference to the Report on the Second Year Project).

Year 3
In the final year, we have concentrated on thin and medium size anatomy such as hand, foot, ankle, elbow, knee, and shoulder. We have also made some study on a high resolution plate made specifically for

mammography. The mammography images were performed on an ACR phantom, a CD MAM contrast detail phantom and CIRS detailed and curved phantoms. A 3M 18 x 24 cm Imaging Plate (IP) was used. The study was based on the comparison of 3M images and those taken from a screen-film system, and also the storage phosphor imaging plate taken from a Fuji 9000 computed radiography (CR) system. The evaluation of the system was divided into two categories: self evaluation (image evaluation based on the 3M plate itself) and comparison with the screen-film and Fuji 9000 CR systems. The categories for evaluation were based on the noise, contrast, sharpness, overall image quality, and overall diagnostic content. A scale of 1-5 was applied in which 1 was unacceptable performance and 5 was excellent performance. The comparisons of the results are listed in the appropriate tables.

3.3.2.1 Dosimetry

The exam rooms at Georgetown University Medical Center were again tested, using the dosimeter for consistency of x-ray exposure. The new sets of dosimetry were performed. The Radcal Model 9010MS Radiation Monitor with 90x5-6M and 90x5-180 ion chambers was used for dose measurement. The entrance dose was measured for the primary beam at the center of the phantoms. The results of exposure were consistent for different kVp and mAs.

3.3.2.2 Clinical Evaluation for Thin and Medium Sized Anatomy

After some experience with physics and anthropomorphic phantoms and optimizing the exposure technique the system was evaluated based on system performance in the clinical environment. During the phantom study the system was adjusted and recalibrated for better performance and for different generations of the plate. We believe that the 3M system is now ready for at least thin and medium size anatomy. In this phase the 3M system was evaluated based on different patients' anatomy such as:

1- **Hand (PA)**
2- **Foot (AP)**
3- **Ankle (AP, Lateral)**
4- **Elbow (Lateral)**
5- **Knee (Lateral)**
6- **Shoulder (AP)**

The study was performed using the standard exposure technique used at Georgetown University Medical Center (GUMC) for a range of kVp, mA, and exposure time, depending on the application of the individual anatomy. Source to Detector Distance (SDD) is fixed at 40 inches (102 cm). The exposures are fixed for screen-film and storage phosphor Fuji computed radiography (FCR) 9000 systems, but vary for the 3M system for preliminary image optimization. The standard techniques used for screen-film system are listed in Table I:

Table I. Standard Techniques For Different Anatomical Regions

Anatomy	kVp	mA	sec.	mAs	SDD	Bucky	Tabletop	AFS(large)	AFS(small)
Hand (Ext. Cassette)	60	250	.02	5	40"		x		x
Foot (Ext. Cassette)	63	250	.02	5	40"		x		x
Foot (LAT) (Ext. Cassette)	63	250	.02	5	40"		x		x
Ankle (Ext. Cassette)	63	250	.02	5	40"		x		x
Knee	66	250	.025	6.3	40"	x		x	
Elbow	63	250	.025	6.3	40"		x		x
Shoulder	70	250	.04	10	40"	x			x

Note : standard technique refers to the one used in screen-film radiography
SDD Source to Detector Distance
AFS Focal Spot Size

3.3.2.3 Patient Recruitment

Patients who are male or female coming into the main radiology department for routine exams will be asked to give written informed consent for one additional image on the 3M imaging plate. The original image will be on screen-film system or Fuji 9000 computed radiography (CR) system. The informed consent will be obtained by a member of the Georgetown University Hospital staff. The form will be kept at GUMC. The patient demographic information will be kept confidential from 3M personnel. The identification of each patient in the 3M database will be based on a three digit number and the first initial of the patient's first name and the first 3 letters of the patient's last name (e.g., KINR 001). The data collection form has information about demographic data, exam type, clinical information (exam, view, exposure technique, etc.), and signature section for Principal Investigator, and an RT's initial from both GUMC and 3M resident technical personnel.

3.3.3 RESULTS

After the data collection, the images are evaluated by our radiologist and the results are tabulated in appropriate appendices. In the third year of the study, we have carried out 18 patient exams for hand, foot, ankle, knee, elbow and shoulder. The number of patients in each category is listed in Table II. The 3M images were compared to 10 screen-film images and 8 FCR 9000 images. During that time the 3M system had some deficiency in image quality and we had to wait until the system was fixed, which delayed the whole process. The patients' ages ranged from 19 to 84 years old, and the sex coincidentally was distributed such that half of them were male and half female. For the comparison, ten images were made with screen-film system and eight images with FCR 9000. The clinical log of the patients are listed in Tables III and IV. The tables include enrollment number, date of exam, sex, age, exam, view, and exposure technique, along with the 3M plate ID number and read out voltage, as well as plate reader scanning criteria and the comparison with screen-film or storage phosphor FCR 9000 systems.

Table II. The Distribution of Patients in Selected Exams

Exam	No. of Exam
Hand	5
Foot	6
Elbow	1
Knee	1
Ankle	2
Shoulder	3

Table III. Patient Demographic Information and Exposure Technique

Enrollment	Date	Sex	Age	Exam	View	kVp	mAs	Grid	Room
KINR 001	15-Sep-94	F	73	Hand	PA	60	5	N	10
CHUE 002	21-Sep-94	M	19	Foot	AP	63	6.3	N	10
MATR 003	21-Sep-94	M	71	Hand	PA	61.5	3.2	N	Gorman
BAZS 004	22-Sep-94	F	55	Foot	AP	63	5	N	Gorman
MCMM 005	26-Sep-94	F	55	Hand	PA	60	5	N	Gorman
HERJ 006	26-Sep-94	M	38	Ankle	Lateral	63	6.3	N	Gorman
GERL 007	29-Sep-94	F	42	Ankle	AP	60	5	N	Gorman
WDGD 008	29-Sep-94	M	57	Shoulder	AP	77	20	Y	16
STEJ 009	5-Oct-94	M	30	Elbow	Lateral	63	6.3	N	Gorman
MYLE 010	5-Oct-94	M	19	Foot	AP	63	5	N	Gorman
BARL 011	10-Oct-94	F	34	Hand	PA	60	5	N	Gorman
COOP 012	10-Oct-94	M	31	Hand	PA	60	5	N	Gorman
TYRS 013	12-Oct-94	F	46	Foot	AP	63	5	N	Gorman
DELJ 014	12-Oct-94	M	21	Foot	AP	63	5	N	10
HOLL 015	14-Oct-94	F	47	Foot	AP	66	6.3	N	Gorman
HARL 016	13-Apr-95	M	84	Shoulder	AP	70	20	Y	16
SUDA 017	13-Apr-95	F	45	Knee	Lateral	63	5	N	16
PEEM 018	14-Apr-95	F	40	Shoulder	AP	70	20	Y	16

Table IV. Plate Reader Information and Control Device

Enrollment	Date	Plate ID	Plate V(x)	Reading V(r)	Scan	Control
KINR 001	15-Sep-94	H0146	8	2.5	Hi Res	FCR HR-V
CHUE 002	21-Sep-94	H1024	8	3	Hi Res	FCR HR-V
MATR 003	21-Sep-94	H1024	8	3	Hi Res	SF System
BAZS 004	22-Sep-94	H1024	8	3	Hi Res	SF System
MCMM 005	26-Sep-94	H1024	8	3	Hi Res	SF System
HERJ 006	26-Sep-94	H1024	8	3	Hi Res	SF System
GERL 007	29-Sep-94	H1034	8	3	Hi Res	FCR HR-V
WDGD 008	29-Sep-94	H1024	8	3	Hi Res	SF System
STEJ 009	5-Oct-94	H1036	8	3	Hi Res	SF System
MYLE 010	5-Oct-94	H1034	8	3	Hi Res	SF System
BARL 011	10-Oct-94	H0146	8	3	Hi Res	SF System
COOP 012	10-Oct-94	H1034	8	3	Hi Res	SF System
TYRS 013	12-Oct-94	H1036	8	3	Hi Res	SF System
DELJ 014	12-Oct-94	H1146	8	3	Hi Res	FCR HR-V
HOLL 015	14-Oct-94	H1136	8	3	Hi Res	SF System
HARL 016	13-Apr-95	H1167	8	3	Hybrid	FCR HR-V
SUDA 017	13-Apr-95	H1148	8	3	Hybrid	FCR HR-V
PEEM 018	14-Apr-95	H1148	8	3	Hybrid	FCR HR-V

Note:

- FCR HR-V is related to Fuji Computed Radiography 9000 System with High Resolution Plate.
- SF System is Screen-Film System using Fuji HR-G 50 speed film system.

In order to evaluate the 3M imaging system in a clinical environment, the number of patients were selected based on thin and medium size anatomy. The system was evaluated for noise, contrast, sharpness, overall image quality, and overall diagnostic information. The evaluation was also based on two categories: self evaluation and comparison against two controls: one to screen-film (SF) system and the other to FCR 9000 system.

3.3.4 DISCUSSIONS

A series of limited patient studies were performed on thin and medium sized anatomy. The focus was on the extremities (hand, foot) and the shoulder in order to determine the 3M system performance in the clinical environment for mammography. The optimized (accepted image) images from conventional screen-film (SF) system were compared with the 3M images. Image processing was performed on the 3M images in order to find the preliminary optimum image for comparison with SF images. The images were compared to those taken from SF images and evaluated for clinical studies. The evaluation was performed in the following two ways:

3.3.4.1 3M Self Evaluation

The 3M images were self evaluated based on five categories: noise, contrast, sharpness, overall image quality, and overall diagnostic information. The rating was between 1 (unacceptable) to 5 (excellent).

Noise

The noise was the most important problem of the 3M system. Through different generations of the imaging plate, the noise was reduced. The images are rated from unacceptable to marginal and in few foot exams are considered good.

Contrast

The contrast also varied from marginal to very good in rating. Most medium size anatomy has marginal contrast whereas hand and foot images have good or very good contrast.

Sharpness

The system resolution is rated as good to very good and in a few cases even excellent. Only in one case the system did not perform well.

Overall Image Quality

The overall system image quality varies between marginal to very good in rating. Most of our hand and foot images are showing very good image quality.

Overall Diagnostic Content

The overall diagnostic information are rated from marginal to excellent. In two cases such as hand (PA) and shoulder (AP) the rating was unacceptable. Most of the exam ratings are good or better.

3.3.4.2 3M Versus Control

The 3M images were compared to those images taken from two modalities: one screen-film system and the other FCR 9000 system. The comparison was similar to the self evaluation and was based on five categories: noise, contrast, sharpness, overall image quality, and overall diagnostic information. The rating was between 1 (Strong Control Preference) to 5 (Strong 3M Preference).

Noise

3M images were compared to SF and FCR 9000 images. In terms of noises, SF images are only slightly better over than the 3M images, whereas FCR images in most cases are strong preferred to the 3M images. In one of the shoulder studies there was no preference between 3M and FCR images.

Contrast

The contrast also varies from mild control preference in 6 cases to mild 3M preference in 6 cases. In some of the exams such as ankle, knee, and hand, the contrast of the 3M images and control images are similar/equal. In one shoulder study, the FCR image is better than the 3M image.

Sharpness

In the self evaluation rating, the 3M system has better resolution than both control systems. In 11 cases 3M images have a slight advantage over the two control system images and in 2 cases the 3M images have a stronger advantage over SF and FCR images.

Overall Image Quality
The overall system image quality varies between mild control preference to no preference and in some cases to 3M mild preference.

Overall Diagnostic Content
The rating for the overall diagnostic information of the 3M system varies between mild control preference to mild 3M preference. In cases such as ankle (SF) and shoulder (FCR) exams the control has a strong performance than the 3M system.

3.3.5 CONCLUSIONS

In the evaluation of the 3M digital mammography based on micro-lithography, the feasibility of the system was studied. The focus was on the imaging of body parts (e.g., extremities) less radio-sensitive than the breast. A series of exams were performed on the hand, foot, ankle, elbow, knee and shoulder in order to evaluate the 3M digital radiography system's performance under the standard technique(s). The optimized base line (accepted image) images are those taken from the conventional screen-film (SF) system and the Fuji 9000 storage phosphor (SP) based computed radiography system. Image processing was performed on the 3M images as little as possible in order to find the optimum images for comparison with SF and SP images. KHOROS, the image processing software developed by the University of New Mexico, was used for this study.

Noise reduction was achieved for most exams through image processing. In some of our studies the elimination of complete noise also eliminated the fine structure of the image. We observed that the noise is more visible on the darker side of the image. Limited image processing and elimination of pattern noise will produce better image quality.

During the study period several imaging plates were made by acquiring different plate structures in order to study the performance of the 3M digital radiography system. Each generation performed better than the previous one in terms of noise reduction.

In the final phase of the 3M digital radiography system study and after a series of extensive experiments, we came to the following conclusions and recommendations:

1- The 3M system has shown for some cases the capability of operating in the lower kVp with lower exposure dose as compared to the screen-film system with as little image processing as possible to enhance the images.

2- The variation of mA in the applicable range of radiography has little effect on the images for foot and hand.

3- Noise should be reduced in order to get better image quality. This was shown in our last few clinical studies when a new plate was manufactured. In those studies, because of the new plate's structure, very little image processing was used to enhance the images. This issue should be carefully studied.

4- The standard exposure technique system is capable of producing better images for thin parts of the anatomy than for the thick parts. In order to achieve better resolution and better contrast for thick body parts, the 3M system needs to operate at a higher exposure dose than the conventional technique. Hopefully the dose can be reduced through mathematical image optimization and image processing.

5- We still need to determine what or how much will be gained from image processing.

6- What are the characteristics of the noise? (Shape, pattern, etc.). The types of noise influencing

images can result from quantum noise (x-ray quantum noise and light photon noise) and fixed noise (imaging plate structure noise, electrical system noise, quantization noise, and other noise). This should be addressed if future study is needed. Some of the fixed noise can be reduced as the new generation of the imaging plate is manufactured. The noise reduction improvement was seen when the latest generation of the imaging plate was used.

The overall conclusions based on patient study and comparison with SF and FCR 9000 systems are as follows:

7- In most of our patient studies the image noise reduction is the most important factor that gives SF and FCR 9000 systems advantages over the 3M system.

8- The contrast in some of 3M images is better than that of the SF images, but not as good as the FCR 9000 images.

9- In most cases, 3M system resolution is better than SF and FCR 9000 systems.

10- In most cases there is no preference of overall image quality are between the 3M system and the other two modalities.

11- The overall diagnostic content does not differ significantly among the 3M and other systems.

12- In terms of overall system performance, with the exception of noise, the 3M system has better performance compared to the screen-film system, but not as good as the FCR 9000 system.

13- The image quality for mammography phantoms (e.g., CIRS, CD MAM, and ACR) are not good in comparison to screen-film mammography system. 3M images are noisy in mammography energy range. The images also do not have enough contrast.

14- The final conclusion is that, the 3M system is not suitable at this time to conduct clinical trial for mammography. The system is noisy and does not have enough contrast to go to mammography energy range. In order to get reasonable image quality, we have to increase the dose level which will not be acceptable in clinical settings.

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3.4 Implementation of Computer Assisted Breast Cancer Diagnosis (US Army Grant No. DAMD17-93-J-3007)

Army grant DAMD17-93-J-3007 was initiated in December 1992 for completion in December 1995. This was extended to a completion date of June 1996. This represents the final report for this project.

3.4.1 Introduction

Recently, several investigators have proposed a number of methods for the automatic detection of microcalcifications and masses on mammograms. Significant improvements in accuracy have been made since the initial attempt [Chan 1987; 1988] to apply the computer algorithms for the detection of microcalcifications. We believe that it is important to implement the program into a high speed workstation and conduct a large scale clinical trial in order to evaluate its clinical practicability and limitations. Although the false-positive rate for the detection of masses is still very high, we have been using an artificial neural network to classify malignant and benign masses. We believe that the creation of a computer program to analyze features of suspected masses will give rise to a more useful and fundamental approach to computer-aided diagnosis.

Because digital mammography produces a large data volume for its high-resolution imaging, data compression is an important means to facilitate the mammographic image transmission and storage. We have studied characteristics of the mammograms and developed compression methods specifically for mammograms using gray value splitting in conjunction with wavelet and full-frame discrete cosine transform (DCT) techniques. Effects of applying the data compression to the proposed computer aided diagnosis (CADx) scheme in the detection of microcalcifications were also tested during this reporting period.

3.4.2 Research in the Detection of Microcalcifications

3.4.2.1 Detection of Suspected Microcalcifications

Microcalcifications in breast cancer are reported to occur with five or more microcalcifications as a cluster in a $1cm^2$ area [Black 1965, Fisher 1975]. When the digitization pixel size is 50 μm (using a Lumiscan 150), there are 40,000 pixels in a $1cm^2$ area. To have five detections or pixels (0.0125%) possessing high intensity in the area means that one should set a threshold on pixel intensity of approximately 3.61σ (σ: standard deviation). In one experiment, we used 3.02σ as the threshold corresponding to a maximum of 50 pixels (0.125% as indicated in Figure 1) due to a potentially larger microcalcification containing several detected pixels together. Note that a background trend correction was applied to each image block prior to the statistical calculation. The previously detected suspected areas (i.e., 50 pixels) were masked with the mean value in this detecting procedure. This procedure was performed with a $1cm^2$ template (200× 200 pixels) by moving 190 pixels per step for each operation and by scanning through the mammogram horizontally and then vertically.

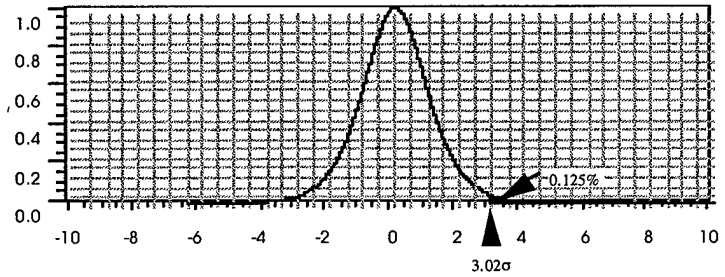

Figure 1. Assuming the noise spectrum fits Gaussian distribution, only 0.125% of pixels have an intensity higher than 3.02σ.

After carefully evaluating twenty-two mammograms containing subtle microcalcifications (only three

clustered microcalcifications on three mammograms were associated with malignant process), we found that the use of 3.02σ for the threshold value was fine except for radiolucent regions (OD > 2.3) where a threshold value should be set at 2.75σ corresponding to 120 pixels (0.3%) in a 1 cm^2 area. In addition, when a large area was detected (> 30 pixels) then additional pixels corresponding to the area would be granted in the local operation. Our results indicated that all microcalcifications (27 clusters confirmed by biopsy and 126 singles were confirmed by an experienced radiologist) were detected through the above procedure. However, an average of 858 suspected areas per mammogram was obtained (i.e., 99.5% false-positive rate for 100% true-positive detection). This procedure is equivalent to a pre-scan process of a computer-aided diagnosis in the detection of microcalcifications [Chan 1987; 1990]. The important point here is that we have developed an effective computer program that can detect all microcalcifications. It takes 5-7 seconds on a DEC Alpha computer to run a digital mammogram of 4,096× 5,120 pixels. The suspected areas will be used for the further evaluation of CADx using more stringent criteria and in the mammographic image compression for error handling in the next section.

3.4.3 Adaptive Lossless Mammographic Image Compression

We have also developed an adaptive lossless compression scheme for mammograms by combining a high compression method and techniques involving the detection of all suspected microcalcifications to ensure data accuracy in the clinically significant areas. In the previous section, we described how to detect suspected microcalcifications. It is no a big task to handle 858 suspected areas when compared to the compression of a 4K× 5K mammogram. However, we can preserve the maximum data accuracy on clinically significant areas. This type of error control should be used in any medical image compression scheme when possible.

3.4.3.1 Mammographic Image Compression via Wavelet Decomposition

Recently, we have used a wavelet transform for mammographic image compression [Daubechies 1988, Mallat 1989, Cody 1992, Atonini 1992]. Before the wavelet transform, the boundary of the breast was outlined. Only the area within the boundary was the area to be compressed. Figure 2 shows a typical multi-level wavelet transform and the associated compression procedure. The larger the image, the more levels of wavelet transform can be applied. In general, "A" contains a much smaller computer space than "B" and "A" space + "B" space is about 4K× 5K× 3 bit (a compression ratio of 4:1). If the air region is included in the compression process, the average error-free compression ratio is 2.5:1.

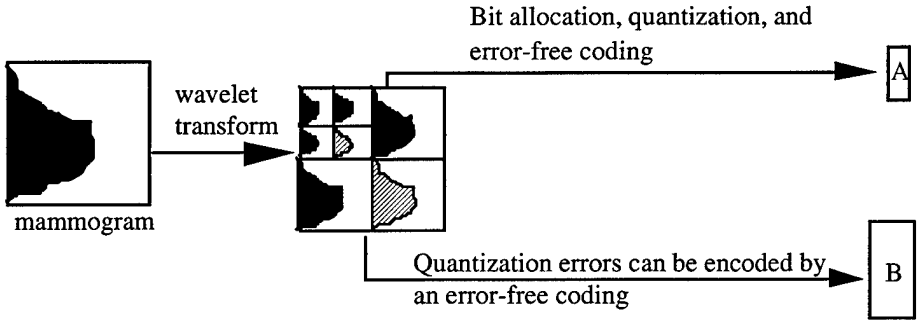

Figure 2. A typical wavelet decomposition and associated compression procedure for a mammogram.

(Note: only a two-level decomposition is shown.)

In this study, we decomposed each image with 7-level wavelet transform; hence, the smallest size image will be a matrix of 128× 160 pixels. The lowest resolution subimage will be further decomposed by an operation called deferential pulse code modulation (DPCM). The entropy of the all-decomposed subimages will be calculated to determine the best wavelet kernel for the mammographic image compression.

3.4.3.2 Error-Controlled Compression for Digital Mammograms

We believe that an accurate error-control procedure is an innovative solution to make a compression scheme clinically useful. A computer scheme for the compression was tested and is described as follows:
(a) Detect all suspected microcalcifications (clusters and singles) based on the method described in Section 3.4.2.
(b) Perform an error-free compression using DPCM and arithmetic coding on the detected areas. Replace the area with surrounding intensity using cubic spline interpolation.
(c) Perform multi-level wavelet transform for the mammogram.
(d) Perform quantization on the wavelet domain (For the higher level of low resolution subimages the less destructive quantization should be applied.)
(e) Perform an entropy coding on quantized subimages to get file "A" indicated in Figure 2. (arithmetic coding [Witten 1987] for uncorrelated coefficients and L-Z coding [Ziv 1978] for correlated data sequence).

3.4.3.3 Experimental Results

The unique point of this work is to add the error-free feature for the suspected disease areas to a compression scheme. No compression artifact shall be observed by an experienced breast radiologist. One must realize that there is no need to digitize a resolution as high as 50μm/pixel except those areas containing subtle microcalcifications. However, the error control feature reduced some degrees of the entire compression efficiency (ratio). Equation (1) provides a formula to calculate the effective compression ratio when the error-control feature is added into the compression system:

$$R_t = \frac{R \times R_e \times T}{(R - R_e) \times N \times S + R_e T} \qquad ...(1)$$

where T is the total number of pixels in the original mammogram, S is the number of pixels in the suspected area for error-free coding, N denotes the number of suspected areas, R is the compression ratio obtained by performing a transform (wavelet) coding, R_e is the average compression ratio to encode microcalcification areas losslessly, and R_t is the total effective compression ratio.
We tested the same twenty-two mammograms as used in Section 3. We calculated the effective compression ratio by providing values:

N = 858;
S = 640 (25× 25 pixels) which was averaged from 81% tiny suspects requiring 20× 20 pixels (i.e., 1mm× 1mm area) and 19% medium-sized suspects requiring 40× 40 pixels;
T = 20,971,520 (4,096× 5,120);
R_e = 2.5;
R = 40:1 (estimated acceptable compression ratio) which is partly due to the fact that 50% of mammogram contains air space.
Substituting the above values into Equation (1), we received R_t = 29 which also indicates that an additional 40% of the compressed data was increased when the error-free feature was added to the compression scheme. Since each 12-bit datum is stored in a 16-bit computer space, R_t was 38 for current commercial data systems. Because the suspected areas may contain significant clinical information, we believe that the error control feature is necessary and is a cost-effective approach for mammography data reduction.

3.4.4 Recognition of Mammographic Microcalcifications with an Artificial Neural Network

3.4.4.1 Detection of Clustered Microcalcifications

We have developed a computer-aided diagnosis (CADx) program for automated detection of clustered microcalcifications in digital mammograms. In this study, we investigated the use of a convolution neural network (CNN) in conjunction with the CASx program to reduce false-positive (FP) detections.

Screen-film mammograms containing subtle microcalcifications were digitized with a laser film scanner. After signal-to-noise ratio (SNR) enhancement and background removal with a spatial filter, potential signal sites were detected with a locally adaptive gray-level thresholding technique. The size and contrast were used to discriminate false signals from true microcalcifications. The remaining signals were then inspected by the CNN. Image blocks containing individual microcalcifications in the SNR-enhanced images were input to the CNN. The CNN consisted of nodes organized in groups and the weights connecting the nodes were organized by convolution kernels. These weights integrated neighborhood information for recognition of the true signals. After training, we found that a CNN with two hidden layers, both containing 10 groups of nodes, was effective in the classification of true and false signals. The output signals from the CNN further underwent a regional clustering algorithm for detection of clustered microcalcifications. We found that the CNN could classify individual microcalcifications with the area under the ROC curve, Az, of 0.88. Free-response ROC (i.e., FROC) analysis showed that the addition of CNN classification to the CADx program reduced the false-positive cluster detection by 60-70% for a given true-positive (TP) rate. After adding a criterion regarding a minimum of three calcifications in one cluster for a detection, the Az was increased to 0.96. These results indicate that the CNN can significantly increase the accuracy of the CADx program.

3.4.4.2 Classification of Malignant and Benign Clustered Microcalcifications

We have developed computer vision methods for classification of malignant and benign clustered microcalcifications. Mammograms are digitized at a pixel size of 35 mm × 35 mm. The program operates locally in regions of interest (ROIs) containing clusters of microcalcifications on the mammograms. Morphological features characterizing the microcalcifications and texture features characterizing textural changes in the tissue region surrounding the cluster are extracted from the ROIs. For extraction of texture features, we first employ a distance-weighted interpolation technique to estimate the low-frequency background of the ROI using a band of pixels around its perimeter. The spatial gray level dependence (SGLD) matrices ´ of the background-corrected ROI are determined at various pixel pair distances. Thirteen texture features that characterize the ROI, such as correlation, energy, inertia, inverse difference moment, and entropy, are calculated from the SGLD matrices.

For extraction of morphological features, a segmentation method is used similar to that in the detection program except that segmentation is applied to an unfiltered image in order to avoid distortion of its shape due to signal-to-noise ratio (SNR) enhancement. An ROI containing a microcalcification is background-corrected and the signal is extracted based on the local SNR using a region growing technique. We calculate visibility descriptors such as the SNR, mean density, and size of the microcalcifications, shape descriptors such as the second moments, the ratio of the second moments, the eccentricity and the ratio of major and minor axes of an effective ellipse, and determine cluster features such as the standard deviation, the maximum, and the coefficient of variations of the visibility descriptors, shape descriptors, and the number of microcalcifications within the cluster. We have trained a linear discriminant classifier (LDA) to classify the input features. The performance of the trained classifier has been tested both with a jackknife method and a cross-validation method. Both methods yielded similar test results. The discriminant scores of the LDA were analyzed with Receiver Operating Characteristic (ROC) methodology and the area under the ROC curve (Az) was used as a performance index. In the texture feature space, the LDA classifier achieved an Az of 0.88 for training and 0.84 for testing. In the morphological feature space, the LDA classifier achieved an Az of 0.84 for training and 0.79 for testing. In the combined texture and morphological features, the Azs were improved to 0.94 and 0.89, respectively, for training and testing. We have also trained a non-linear classifier, a back-propagation neural network (BPN), to classify the malignant and benign microcalcifications. In the texture feature space, the BPN classifier achieved an Az of 0.88 for training and 0.86 for testing. In the morphological feature space, the BPN classifier achieved an Az of 0.84 for training and 0.80 for testing. In the combined texture and morphological features, the Az's were improved to 0.94 and 0.91, respectively, for training and testing. These results demonstrate the feasibility of our approach to classification of malignant and benign microcalcifications.

3.4.5 Recognition of Mammographic Masses

3.4.5.1 Detection of Mammographic Masses

(A) Computerized detection of masses on mammograms

We have developed a new approach for segmentation of suspicious mass regions on digitized mammograms using an adaptive Density-Weighted Contrast Enhancement (DWCE) filter in conjunction with Laplacian-Gaussian (LG) edge detection. The DWCE filter can enhance masses of a wide range of intensities and sizes, and suppress background intensity variations. The algorithm processes a mammogram in two stages. In the first stage the entire mammogram is filtered globally using a DWCE adaptive filter which enhances the local contrast of the image based on its local mean pixel values. The enhanced image is then segmented with an LG edge detector into isolated objects. A feature classifier using morphological or texture features is used to reduce the number of FPs. In the second stage of processing, the DWCE adaptive filter and the edge detector are applied locally to each of the segmented object regions detected in the first stage. The local operation allows more precise extraction of the features of the objects. The number of objects is further reduced based on these features. ROIs are extracted from the image based on the remaining object set. The selected ROIs are input to either an LDA classifier or a convolution neural network to further differentiate TPs and FPs as described below. Using a cross-validation test method with two partitions, our results indicated that the current algorithm achieved an average test TP rate of 80% at about 2.1 FPs/image and a TP rate of 90% at 4.7 FPs/image. This accuracy may not be adequate in clinical practice, however, it demonstrates the feasibility of detecting masses on mammograms with the new DWCE technique. We therefore propose to evaluate the performance of the algorithm in a preclinical trial using a large number of randomly selected clinical cases. The causes of FP detections in such a test will be analyzed, and more effective FP reduction methods will be developed in order to improve the detection accuracy.

(B) Multiresolution wavelet decomposition and texture analysis

We have developed a new method to distinguish abnormal from normal tissue for CAD algorithms using texture analysis. An ROI containing mass or normal breast tissue is input to the program. The wavelet transform is used to decompose the ROI into several scales. Global multiresolution texture features are calculated from the SGLD matrices of the low-pass wavelet coefficients up to a certain scale and then at variable distances between the pixel pairs. Texture features in the suspicious object sub-region and their differences with features in the peripheral sub-regions of the ROI are also calculated to form a local texture feature space. Stepwise linear discriminant analysis is used to select effective features from the combined global-local feature space to maximize the separation of mass and normal tissue ROIs. To evaluate the accuracy of this method, we used 168 ROIs containing a biopsy-proven mass and 508 ROIs with normal dense, mixed dense/fatty, or fatty tissues extracted from digitized mammograms by radiologists. The ROIs were randomly and equally divided into a training and a test group. It was found that, using the global multiresolution feature space alone, the Az was 0.89 and 0.87 for the training and test groups, respectively. Using local features only, the Az was 0.88 and 0.85 for the training and test groups, respectively. With the combined global and local feature spaces, the Az reached 0.95 and 0.91 for the training and test groups, respectively. When this classification method was applied to the false-positives detected by the automated mass detection program using the DWCE approach described above, the classification accuracy in terms of Az reached 0.97 during training and 0.96 during testing in the combined global and local feature space. The results demonstrate that an LDA using a combination of the global and the local texture features can effectively classify masses from normal tissue on mammograms. This classifier will be incorporated into the automated mass detection program as one of the steps to reduce FP detections in the preclinical trial.

(C) Artificial neural network

We have investigated the use of a convolution neural network (CNN) and a backpropagation neural network (BPN) for classification of ROIs on mammograms as either masses or normal tissue. A CNN is a BPN with two-dimensional weight kernels that operate on images. A generalized, fast and stable implementation of the CNN has been developed. ROIs containing masses and normal breast tissue are first segmented with an automated detection program. The CNN input images are obtained from the ROIs using (i) averaging and subsampling, and (ii) texture feature extraction from SGLD matrices and gray level difference statistics (GLDS) vectors on smaller sub-regions inside the ROI. In (ii), features computed over different sub-regions were arranged as texture-images, and subsequently used as inputs to the CNN. Input features to the BPN

are obtained from SGLD matrices at multiple resolutions. Using 168 ROIs containing masses and 504 ROIs containing normal tissue, we found that the test Az reached 0.83 for the CNN using spatial input images, 0.87 using spatial and texture images, 0.88 for the BPN using SGLD texture features, and 0.91 for a combination of the CNN and BPN outputs. Our results indicate that the CNN performance may be improved by using additional texture information and that the overall performance may be improved by combining CNN and BPN classifiers.

(D) Feature selection

The performance of a feature classifier in a CAD scheme depends strongly on feature selection. For the LDA, we use a stepwise LDA procedure to select significant feature variables for the classification tasks. In order to have a general feature selection method that can be applied to both linear and non-linear classifiers, we have investigated the application of a genetic algorithm (GA) for feature selection. One of our applications is to select features for the classification of masses and normal breast tissue. ROIs containing biopsy-proven masses and normal ROIs containing breast parenchyma are first segmented from mammograms. A total of 587 texture and morphological features are automatically extracted from each ROI. Multiple regression is applied to the features selected by the GA to form a discriminant function with the training set. The presence/absence of a feature in the regression is coded by a 1 or 0 at the appropriate gene in a chromosome in the GA. The fitness and survival rate of a chromosome are determined by Az. The chromosomes are allowed to crossover, mutate, and evolve for a number of generations in a training procedure. The final selected features are used for classification of the test set. To evaluate the effectiveness of this GA, we used 168 ROIs with masses and 504 ROIs with normal tissue as our data set. We randomly divided the data set into 10 partitions of training and test subsets. The GA selected an average of 20 features from the 587 input features for each training process. It was found that the average training and test Az values reached 0.93 and 0.89, respectively. This accuracy is superior to that obtained with the entire feature set input to the classifier without feature selection, or that with features selected individually based on their distributions. We also compared the results to feature selection using the stepwise LDA method. Using the same cross-validation test technique, the test Az's obtained with both methods were similar, indicating that the GA and stepwise LDA approaches can provide near-optimal feature selection for linear classifiers.

3.4.5.2 Classification Of Malignant And Benign Mammographic Masses

We have investigated the classification of malignant and benign masses on mammograms. After ROIs containing suspicious masses are located by the automated mass detection program on the mammogram, segmentation and feature extraction are performed locally in each ROI. A new segmentation method has been developed by the research team based on a migrating mean clustering algorithm. An ROI is first corrected for the low-frequency structured background. This method then separates the mass from the surrounding background based on clustering of pixels with similar gray level and edge gradient information. The two groups of pixels are coded as a binary image so that a simple edge tracking algorithm can define the boundary. We extract morphological features such as the fuzziness or spiculation of the mass margin which is quantified by the root-mean-square (RMS) variation around a smoothed version of the edge, the perimeter-to-area ratio, and shape features such as circularity, rectangularity, ratio of its axes, and shape features derived from the normalized radial length. We also extract texture features in a 40-pixel-wide boundary region surrounding the mass from the SGLD matrices. The features are then input to an LDA or a BPN classifier to distinguish the malignant and benign masses. The results indicated that the migrating mean clustering method could extract mass margins more closely than other edge detection techniques that we tested. With the morphological features and texture features derived from the boundary regions surrounding the mass, we obtained a training Az of 0.86 and a test Az of 0.82 for a group of 85 malignant and 83 benign masses. The Az was 0.86 by a radiologist's visual evaluation in the same set of mammograms. This result is encouraging although improved methods still need to be developed to further increase the classification accuracy before clinical implementation.

3.4.6 Status Report in the Implementation of CADx for the Detection of Clustered Microcalcifications

We continue to work on the CADx program with a DEC Alpha workstation. The basic user interface is complete. The user interface can select a mammogram and display it on the workstation. Several image

functions have been implemented: (1) "window and level" for the adjustment of the brightness and contrast, (2) pan, (3) a cursor box for the user to select the area of interest, (4) print the image with CADx marks on high quality paper or a laser film. Initial clinical trial began January 15, 1996 at the Breast Imaging Division of Georgetown University Hospital. The results of this study will be presented at the 1997 SPIE Medical Imaging Conference at Newport Beach, California.

3.4.7 Contractual (SOW) Issues

Dr. R.V. Shah, chief breast radiologist at Brooke Army Medical Center and Dr. Don Smith, attendant breast radiologist at Madigan Army Medical Center have sent us some proven cases (in the Spring of 1995) associated with mammographic microcalcifications for inclusion in our test database [Private Communication]. We are in the process of installing our software for evaluation at Army Hospitals. The CADx clinical trial can be started anytime when they are ready for the experiment. At present, radiologists would like to have an integrated viewing system so that thay can evaluate the effects of CADx in a clinical setting. We are currently negotiating with R2 Technology Inc. who have a product that synchronizes soft copy images on small monitors mounted under the bench of the mammography viewing alternator using a bar code system. We plan to miniturize the mammograms and provide marks indicated by our CADx. The images will be interfaced to the R2 monitors to facilitate the clinical use of this development. Dr. R.V. Shah can be reached at (210)916-4062. R2 Technology's phone number is (415)254-8988.

3.4.8 References

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1. Sahiner B, Chan HP, Petrick N, Wei D, Helvie MA, Adler DD, Goodsitt MM. "Classification of mass and normal breast tissue: A convolution neural network classifier with spatial domain and texture images," IEEE Trans. Medical Imaging.

2. Chan HP, Lo SCB, Niklason LT, Ikeda DM, Lam KL. "Image compression in digital mammography: Effects on computerized detection of subtle microcalcifications." Medical Physics.

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3. Sahiner B, Chan HP, Petrick N, Wei D, Helvie MA, Adler DD, Goodsitt MM, "Image feature selection by a genetic algorithm: Application to classification of mass and normal breast tissue on mammograms," Medical Physics

4. Petrick N, Chan HP, Wei D, Sahiner B, Helvie MA, Adler DD, "Automated detection of breast masses on mammograms using adaptive contrast enhancement and tissue classification," Medical Physics

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4.0 Conclusions

Work to optimize the appearance of digitized film mammography and digital mammography using storage phosphor technology is nearly complete. The attached report and its appendices indicate that digitized film mammography (digitized at 100 micron pixel size) is insufficient for clinical interpretation with soft copy display. Hard copy display is still insufficient. Digital mammography using storage phosphor methods has been optimized and an ROC analysis of this method using our current data set is underway. This ROC study compares matched conventional and digital images using six radiologists. Each of the cancer and benign finding cases is pathologically proven. We are also exploring special image processing methods for the radiodense breast and these are discussed in this report. An analysis of the shape of microcalcifications comparing conventional and digital mammography using a 100 micron pixel size has been completed and shows that there is general preference for the conspicuity of microcalcifications on digital mammography. Analyses of shape and number of microcalcifications resulted in varying opinions from the four radiologists doing the comparisons. Whichever system the radiologists preferred, they were unable to differentiate benign from malignant in this series so any slight differences in shape visibility did not seem to affect classification.

The development of methods to improve the ability of mammograms to be obtained at remote sites and to tele-transmit them to a central site of excellence in the interpretation of mammography. We were unable to accomplish this using digitized screen film mammograms, but have succeeded in doing this with direct digital mammograms. The ROC study that will prove this is currently underway with the results of the initial reader being favorable with Az screen film = 0.7373. Az digital = 0.7646 when tested for detection of cancer. When tested as a method of discrimination between cancer and benign lesions that were detected, the Az of screen film = 0.5743. The Az of the digital system = 0.7412. We have demonstrated the effectiveness of digital storage and retrieval for which the same ROC study will provide the proof. We have demonstrated the feasibility of teletransmission of images transmitting them over the Internet from Georgetown to Boston to the Radiologic Society of North America annual meeting in Chicago and separately from Georgetown over the Internet to the Hubert H. Humphrey Building of the HHS in Washington, DC. We have defined quality control procedures for this system. We have been able to build a system that identifies under- and overexposed mammograms based on digitization of the mammographic films. We have been unable to develop a clinically useful method of directing technologists as to which patients need additional images during their mammogram based on the detection of microcalcifications. This still remains a human rather than a computer based task.

In the evaluation of the 3M digital mammography based on micro-lithography, the feasibility of the system was studied. The focus was on the imaging of body parts (e.g., extremities) less radio-sensitive than the breast. A series of exams were performed on the hand, foot, ankle, elbow, knee and shoulder in order to evaluate the 3M digital radiography system's performance under the standard technique(s). The optimized base line (accepted image) images are those taken from the conventional screen-film (SF) system and the Fuji 9000 storage phosphor (SP) based computed radiography system. Image processing was performed on the 3M images as little as possible in order to find the optimum images for comparison with SF and SP images. KHOROS, the image processing software developed by the University of New Mexico, was used for this study.

Noise reduction was achieved for most exams through image processing. In some of our studies the elimination of complete noise also eliminated the fine structure of the image. We observed that the noise is more visible on the darker side of the image. Limited image processing and elimination of pattern noise will produce better image quality. During the study period several imaging plates were made by acquiring different plate structures in order to study the performance of the 3M digital radiography system. Each generation performed better than the previous one in terms of noise reduction.

During the past three years, we have spent our effort not only in algorithm improvement but also in merging our newly developed algorithm in C and useful codes previously developed by Dr. Chan and her colleagues. At this point, we have completed our mammographical image compression and CADx research in terms of

algorithm improvement and computer speed. Database collection is underway and will continue in the clinical tests to be conducted. Several basic functions and user interface have been implemented in the workstation. The CADx clinical trial has been undertaken at Georgetown University Medical Center. We will report the results of the clinical test in a future paper.