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We have developed a stereoscopic mammography system using state-of-the-art digital technology that enables a mammographer to view the internal structure of the breast directly in depth. The primary aims of this project are to further develop and refine this system and then to evaluate its effectiveness in increasing the accuracy of diagnosis of breast cancer relative to the diagnostic accuracy afforded by standard, non-stereo film views. The expected increase in diagnostic accuracy could increase the yield of biopsy substantially by allowing the radiologist to more confidently recommend accelerated follow-up of truly benign disease and biopsy of truly malignant disease. Our accomplishments in Year 2 consist of progress in six areas: (1) further acceptance testing of the GE digital mammography system, (2) accrual of stereo mammographic images from enrolled patients, (3) development of methods for processing and storing stereo mammographic images, (4) improvements to the stereo display workstation, (5) design of a new stereo display workstation, and (6) identification of new stereo-based visual features.

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David J. Getty 7/11/98

PI - Signature Date

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INTRODUCTION

We have developed a stereoscopic mammography system using state-of-the-art digital technology that enables a mammographer to view the internal structure of the breast directly in depth. Stereo mammograms are obtained by taking two x-rays of the breast from viewpoints separated by about 6 degrees, each view captured by a digital CCD (charge-coupled-device) camera. The two digital images are viewed on a stereo display workstation by a radiologist wearing stereo-viewing eye-glasses. The system provides the user with control over many display parameters such as brightness, contrast, grayscale polarity, and inversion of depth.

The primary aims of this project are to further develop and refine this system and then to evaluate its effectiveness in increasing the accuracy of diagnosis of breast cancer relative to the diagnostic accuracy afforded by standard, non-stereo film views. The expected increase in diagnostic accuracy could increase the yield of biopsy substantially by allowing the radiologist to more confidently recommend accelerated follow-up of truly benign disease and biopsy of truly malignant disease.

One of two final goals in this project is to conduct a reading accuracy study with a group of mammographers. Each will rate the probability of malignancy for each of a set of cases acquired during the project, first reading only the conventional planar films, then reading the films supplemented by non-stereo viewing of the digital mammograms, and finally reading the films supplemented by stereo viewing of the digital mammograms. We will use ROC (receiver-operating-characteristic) methods (Swets, 1979, 1986a, 1988) to evaluate the increase in diagnostic accuracy due to the addition of the digital non-stereo views, and the increase due to addition of the stereoscopic view.

Our second goal is to determine the further improved accuracy that is attainable by use of a feature-based aiding system. In a second, separate study, readers will read each case and assign a numerical value to each of a set of stereo and non-stereo mammographic features on a checklist. A statistical prediction rule will be trained on those feature sets and evaluated, using ROC methods, as a diagnostic aid to further increase the accuracy attained by stereo mammography (Getty et al., 1988; Seltzer et al., 1996; Getty et al., 1997).

Three preliminary steps are necessary before conducting these studies: (1) to further develop and refine the user control interface of the stereo display system, (2) to acquire a large case set of standard films and digital stereo mammograms from consenting patients about to undergo breast biopsy, and (3) to identify new stereo features, and features that may be seen better in stereo, with the aid of expert mammographers and to develop quantitative rating scales for each.

Advantages of stereo mammography over standard non-stereo film mammography

Mammography is known to be one of the most difficult and demanding of the image-based examinations conducted by radiologists. Focal abnormalities are often difficult to detect because of obscuration by superimposed normal parenchymal tissue, particularly in the dense

breast. Moreover, once detected, a focal abnormality is often difficult to diagnose—first because of the difficulty of separating it perceptually from superimposed parenchymal tissue, and second because of the subtlety, even if unobscured, of the visual features distinguishing benign and malignant lesions. We believe that stereo mammography will significantly help with both of these problems, by providing the mammographer with much more precise information about the three-dimensional properties of each abnormality and by visually segregating the abnormality from the parenchymal context in which it resides.

With a conventional two-view mammographic study, the volumetric locus and the volumetric properties of a focal abnormality can only be determined through a rather demanding and imprecise cognitive process. The abnormality must first be localized, and its two-dimensional, planar properties assessed separately in two views. Then, to determine its volumetric locus and volumetric properties, the two sets of planar information have to be merged cognitively, into what can only be a rough impression of where the abnormality lies and how it would look if it could be seen in the volume. With the stereo display, the mammographer does not have to rely on such a demanding and imprecise process. He/she can look directly into the volume and, via a very natural and effortless perceptual process, see precisely where the abnormality is and what it looks like. Moreover, the perception is a global one that can reveal in a rich and precise way how the abnormality relates to the surrounding parenchymal structure as well as to other possible focal abnormalities. These gains in the richness, precision and global nature of the volumetric information that can be obtained from a stereo display have implications for potentially large improvement both in the detection and diagnosis of focal abnormalities. In this project, the focus is on improvements in accuracy of diagnosis.

Prior Work Developing a Prototype Stereoscopic Digital Mammography System

In earlier work, we developed a prototype stereoscopic digital mammography system which consists of two components: the first, a mammography unit modified to capture stereo direct-digital mammograms, and the second, a workstation to display the stereo mammograms.

The system for capturing direct-digital mammograms was developed by team members in the Department of Radiology at the University of Massachusetts Medical Center (UMMC). The prototype laboratory system consisted of a standard GE Senographe, Model 500TS, as the x-ray source. The film tray of the unit was replaced with a high resolution fluorescent screen to which was attached an experimental CCD camera, developed by Dr. Andrew Karellas (Karellas et al., 1989, 1992a). We designed and built a special mounting system to hold the compression table, fluorescent screen and camera fixed while the gantry and x-ray tube were allowed to rotate, enabling the capture of correctly imaged stereo pairs.

At BBN, we developed a stereo display workstation that permits the radiologist to view a pair of images stereoscopically and to control various aspects of their presentation. Left and right eye views are presented alternately at 120 Hz, in non-interlaced mode, on a single, high resolution monitor. The viewer's two eyes are alternately occluded in synchrony with successive images displayed on the monitor by a pair of StereoGraphics liquid crystal shutters mounted as eyeglasses. By synchronizing the shuttering of the glasses to the display, the left eye always sees the appropriate left-eye-image and the right eye the right-eye-image. We developed software that

gives the user control over the brightness and contrast of the displayed stereo image, the ability to move a cursor in depth within the displayed volume, and the ability to invert the displayed grayscale and the displayed depth.

Using this prototype system, we collected a set of stereo images of 39 breast biopsy specimens. For many of these specimens, we were able to obtain multiple images spaced apart at 2-degree angular increments. From those multiple images, we determined that the optimal angular separation for stereoscopic viewing of the specimen tissue was about 6-degrees. We expect that the optimal separation for stereo views of the compressed, intact breast will be no greater than 6-degrees, and possibly slightly less. This will be determined from cases imaged early in this project and then fixed for the remainder of the project.

We also conducted a diagnostic reading study using 27 of the 39 cases for which we had complete materials, including digital stereo images of the specimen, localization films, specimen radiographs, and pathology reports. The cases were read blind, in a random order, by one expert mammographer, who first rated the probability of malignancy after viewing the two orthogonal localization mammograms, and then re-rated the probability of malignancy after being shown the stereo mammogram. We conducted an ROC analysis of these data and obtained an accuracy measure, Az, of 0.725 when the mammographer viewed the standard pair of nonstereo views. Accuracy increased dramatically to 0.939 when the stereo mammogram was added.

BODY OF REPORT

In this report, we discuss progress during Year 2 of this project in six major areas: (1) further acceptance testing and stereo acquisition trials with the new GE full-field-of-view digital mammography unit at the University of Massachusetts Medical Center (UMMC), (2) accrual of stereo mammographic images from patients enrolled in this project, (3) development of methods for processing and storing stereo images, (4) improvements to the stereo display workstation, (5) work on the design of a new stereo display system, and (6) work on identifying and understanding the new featural information available to the mammographer in the stereo view of the breast.

1. Acceptance Testing and Stereo Acquisition Trials

Installation of the new General Electric full-field-of-view digital mammography imaging unit was completed towards the end of Year 1 of the project. Initial testing of the physical characteristics of the new full-field imager have revealed that the radiation dose with this device can be even lower than with typical small-field CCDs, and the contrast resolution and overall detectability are outstanding. Further acceptance testing was conducted over the first few months of Year 2 of the project. Both objective and subjective evaluations of the images produced by the unit continue to confirm the very high contrast resolution attainable with the unit.

2. Accrual of Stereo Mammographic Images from Patients Enrolled in this Project (Task 4)

To date, we have obtained stereo mammographic images of 106 lesions from 101 patients enrolled in this project. This number is close to the 125 lesions we had hoped to acquire during Year 2. We did experience several periods during the first few months of Year 2 when the digital mammography unit was unavailable for use in this study due to further acceptance and evaluation testing. Since those first few months, the unit has been available for full-time clinical use.

The breakdown of stereo-imaged lesions is shown below in Table 1 for 99 of the 106 imaged lesions. (We have not received the pathology reports yet on the remaining 7 lesions.) Of the 99 lesions with known pathology, 25 of them are malignant and 74 are benign. With respect to mammographic appearance of the lesion, 50 of the lesions are seen as a mass, 44 as clustered microcalcifications, and 5 are seen as architectural distortion.

Table 1. Distribution of imaged lesions by type and pathology.

Mammographic Lesion Type	Pathology	
	Benign	Malignant
Mass	32	18
Clustered Calcifications	39	5
Architectural Distortion	3	2

In addition to the pair of digital stereo images obtained for each enrolled patient, we are also collecting three documents: (1) a study form filled out by the mammographer indicating the radiographic nature of the biopsied lesion and its locus in the cranio-caudal view (the point-of-view of the stereo mammogram), the full mammographic report that led to the biopsy, and the final pathology report. A copy of the study form is attached to this report as Appendix A.

We are currently in the process of developing a case database for the project. The database will contain fields of relevant information for each case, including case study number, breast biopsied, mammographic lesion type, lesion locus, pathology truth, and several stereo image transformation parameters. When the reading studies begin later in the project, fields will be added to contain the reading data obtained from the mammographers. We note that case records and stereo images are being identified only by sequential case study number—not related to any UMMC hospital ID number. To maintain patient confidentiality, only the study administrator at UMMC and the PI for the project have access to information relating study number to patient identification information.

3. Development of Methods for Processing and Storing Stereo Images (Task 4)

During Year 2, we have developed methods for processing and storing the stereo pairs of images captured at UMMC and subsequently displayed on the stereo display workstation located at BBN Technologies. Captured digital images are moved from the mammography unit to a laboratory computer at UMMC where they are stored as 16-bit TIFF-format files and burned onto a CD-ROM. The CD-ROM is then mailed to BBN where the images are processed and displayed.

Each digital mammographic image captured on the GE mammographic unit is 2304 pixels wide by 1800 pixels high, with a grayscale resolution of 16 bits stored in a 16-bit word. When used in the stereo display mode, the Matrox image processing card in the stereo display workstation is able to store a stereo pair of images, each of which is 1024 by 1024 pixels with 8 bits of grayscale resolution. The smaller image size and reduced grayscale resolution of the display necessitate processing of the original images to meet these requirements. We tried out and evaluated a number of different image processing programs, including OSIRIS, Scion Image, and Image Tool, to find one that would meet our processing needs. The only satisfactory program was a relatively expensive commercial piece of software, Image-Pro Plus, from Media Cybernetics.

A number of steps are involved in preparing a stereo pair of images for display from the raw images. First, the left-eye image of a pair is opened and visually examined to judge the adequacy of the image. Then, a grayscale-windowing control is used to determine lower and upper bounds within the 16-bit range such that all of the breast tissue, with the possible exception of the skin and subcutaneous fat, is imaged within the specified range. These upper and lower bounds are recorded and then used in a 16-bit to 8-bit conversion of the image grayscale through a piece-wise linear transformation such that all 16-bit values less than the lower bound are mapped to 0, all grayscale values between the two bounds are linearly mapped between 0 and 255 (8-bits), and all values greater than the upper bound are mapped to 255. This transformed

version of the entire image is saved as an 8-bit TIFF file. A 1024 by 1024 region-of-interest window is then introduced into the image and moved around within the larger image until the lesion and surrounding tissue are appropriately enclosed within the window. The coordinates of the window are recorded, and the region-of-interest is then extracted and saved as a 1024 x 1024 8-bit TIFF file.

This process is repeated for the right-eye image, except that the coordinates used for positioning the 1024 x 1024 window in the image are the same ones determined from the left-eye image. We had expected that we would also be able to use the same grayscale mapping bounds as determined from the left-eye image, but we have discovered that the grayscale range representing breast tissue is not necessarily identical between the two images. Consequently, we must re-determine the bounds for the right-eye image independently. We are currently trying to understand why this is occurring; it is counter-intuitive that the ranges would differ significantly since both images are acquired with the same x-ray exposure parameters, with the only difference being the six-degree rotation of the x-ray source between exposures.

Processed images are currently being stored on SyQuest SyJet removable cartridge disks. We will soon acquire a CD-R recorder that will enable us to write out the processed images on CD-ROM's for permanent storage. CD-ROM's will also provide a convenient way ultimately for us to send image sets to other investigators. We are currently in the process of writing macros for the image processing program that will allow us to automate as much of the process described above as possible. We have encountered several bugs in Image-Pro's macro language that must be resolved by Media Cybernetics before we will be able to complete this task.

4. Studies of User Control of the Stereo Display Workstation (Task 3)

During Year 2, we conducted several informal human factors' studies to compare different ways for the user to control various aspects of the stereo display. Four different control methods were explored: (1) pointing and clicking with a mouse on controls displayed on the system monitor (not the image display monitor), (2) speech-enabled control using spoken commands, (3) control of particular functions using an independent joystick, and (4) control of particular functions using an independent mouse. From these studies, we have reached several conclusions. We describe the strengths and weaknesses of each method of control below.

When the user is wearing the CrystalEyes stereo glasses, viewing of the system monitor can be problematic. The glasses and the stereo display refresh at a 120 Hz rate, while the system monitor is typically constrained to run at a lower refresh rate. As a result, the system monitor screen appears to the user with alternating bright and dark bands whose phase shifts continuously in time, depending on the frequency difference in refresh rates. The simplest solution to the problem is to locate the system monitor display screen at a position that requires the user to turn his/her head to view it. If the angle of head turn is sufficient (greater than about 45 degrees), the CrystalEyes glasses no longer "see" the infrared synchronization beam coming from the emitter located above the stereo display and automatically switch out of stereo shuttering mode, thereby eliminating the problem. We believe that all aspects of control of the stereo display should always be available to the user by point and click operations with a mouse on displayed controls.

However, many control functions are better served through one of the alternate methods described below.

We have gained experience over this past year with speech control of the display system. We had implemented the speech recognition system in Year 1. A primary drawback to the use of speech to control the display is the need to tether the mammographer to the workstation with a headset or dictation-style microphone. In either case, a push-to-talk button is needed to exclude incidental conversation from being presented to the recognition system. One conclusion we have reached is that speech control is appropriate and convenient for categorical commands (for example, "invert brightness", "invert depth", "zoom in", "zoom out", "cursor on", "cursor off"). On the other hand, we have also found that speech control is not optimal for controlling continuous adjustments such as adjusting brightness and contrast in the displayed image. A command to "increase brightness" can be used to initiate an increase in brightness at a particular rate which can then be halted with a "stop" command. But, in order to give the user fine enough control, the rate of change of brightness has to be made quite slow, which can be irritating if the desired change is large—and overshooting occurs frequently because of time lag in the speech recognition process.

It is clear to us that control over continuous adjustments is far better implemented by giving the user fine motor control using a physical device such as a mouse or trackball, although not a joystick. We have conducted experiments using both a mouse and a joystick. The mouse was implemented as an direct controller of brightness (movements along the x-axis) and contrast (movements along the y-axis). By direct control, we mean that position of the mouse maps directly to values of brightness and contrast. In contrast, the joystick was necessarily implemented as a rate controller of brightness (x-axis) and contrast (y-axis), where movement of the joystick away from its spring-loaded neutral central position determines rate and direction of change of brightness and/or contrast. The results of our study indicate that the mouse, using direct control, is a much more intuitive control of brightness and contrast. The user quickly develops the appropriate cognitive model of a square in which low brightness is at the left edge, high brightness at the right edge, low contrast at the bottom edge and high contrast at the top edge. It is easy for the user to make large rapid changes in brightness or contrast by making rapid movements of the mouse towards the appropriate region of the square, and then to make small, fine movements for precise adjustment. By contrast, the control of rate of change of brightness and/or contrast provided by the joystick is much less intuitive to the user. It takes longer, and is more difficult, to achieve a desired brightness and contrast level.

5. Design of a New Stereo Display Workstation (new task)

We have begun the task of designing a new stereo display workstation. The current system is based on a Matrox Image-1280 display card which is no longer manufactured by Matrox, and requires an EISA-bus PC which is now obsolete. More recent image display cards introduced by Matrox do not directly support stereo display. However, several other companies manufacturing high-end display cards have begun including direct support for stereo displays in one or more of their PC display controller cards. We are currently examining the specifications for several such cards: (1) Gloria-XXL (ELSA AG), (2) Oxygen 3D (Dynamic Pictures, Inc.),

and (3) Fire GL Pro (Diamond). The goal is to configure a new system that will duplicate the current system's functionality with minimal rewriting of our software. Our interest in developing this alternative display workstation is both to provide a backup for our current system and to make a stereo display system available to the mammographers at UMMC where the stereo images are being acquired.

6. Identification and Development of Stereo-based Visual Features (Task 5)

The primary activity of this task is to conduct intensive visual examinations of the stereo-images of cases as they accrue, and the primary goal is to identify new features for discriminating between benign and malignant lesions. The general approach has been for the perception scientists, presumably less constrained in their speculations by formal training and extensive prior experience in conventional mammography, to do their own explorations of the stereo images first, and then to sit with the mammography consultants to examine the images and merge both points of view. To date, we have worked only with our primary mammography consultant, Dr. Carl D'Orsi, awaiting accrual of more cases to bring in the other two consultants.

Our explorations of the images have followed a general course first of visually assessing the overall quality of the images, their resolution and fidelity in delivering the new sources of information in depth that one would logically expect. Our conclusions in that regard are that the images appear to be very sharp and clear and to deliver strong impressions in fine detail of the structure of the breast in depth. A somewhat surprising finding is that these images provide an astoundingly rich and fine sense of the parenchymal structure of the breast, showing in subtle detail the interweaving strands and sheets of glandular and connective tissue of the breast. In fact, we see this now as such an important new basis for discriminating lesions of interest, i.e., with regard to how they are situated in the parenchyma and how they relate to specific neighboring strands or sheets of tissue, that we have added to the work of Task 5 a review of sources of histopathology information on the global structure of the breast and how lesions occur within that structure. We have also looked at the extensive work in conventional mammography aimed at discerning and interpreting the global structure of the breast as a breast cancer risk factor (Wolfe, 1976; Wellings et al., 1975; Moffat & Going, 1995; Ohtake et al., 1996).

Our detailed explorations of the images have been guided by a systematic consideration of the potential impact on diagnosis of the information in depth provided by the images at all conceivable levels of visual analysis of a lesion —at the level of the elemental constituents of the lesion, at the level of its overall pattern or configuration, and at the level of how it relates to other lesions or structures in its neighborhood, including the parenchymal structure in which it is situated. We see this as a framework useful in guiding our reviews with the mammography consultants, as we consider at each level of analysis what specific features might be diagnostically informative and how they might be described and assessed.

Many, perhaps most, of those features now recognized and assessed in conventional mammography could be usefully, if not better, assessed in stereo. Whether the ultimate master list of relevant features for stereo analysis should include them would depend, of course, on whether stereo would be used in combination with conventional mammography, or as a stand-

alone system. It is probably safe to assume for the foreseeable future that it would be used in combination, and that stereo mammography would be used to assess features for which it is particularly informative. In any event, the primary approach has been to concentrate first on those sources of information in the stereo images that take mammography into a new regime – either of greatly improved accuracy of conventionally assessed features, or of accessibility to entirely new features. The following summary of our results to date reflects that focus. For each of the three main forms of presentation that worrisome lesions can take—clustered calcifications, mass and architectural distortion—we review the nature of the three-dimensional information provided at each level of analysis and consider just the critically new or more powerful diagnostic information that the stereo display promises to provide. The goal in our consultations with the mammography consultants will be to consider how that information might contribute to discriminating benign from malignant lesions and how to translate that understanding into specific features for visual assessment.

6.1 Stereo-based information on lesions that present as clusters of calcifications.

Information in the locus, shape and orientation of individual elements of calcification. The stereo display provides a powerful new basis for perceiving the locus, shape and orientation in depth of individual calcifications. The characteristic size and shape of elements comprising the cluster are now recognized as critically important in diagnostic analysis, so this is a critically important gain in information.

Information in the locus, shape and orientation of sub-clusters. The improved localization of individual elements in depth will also permit much more valid and accurate perceptions of the position, shape and orientation in depth of sub-clusters. Linear arrangements of elements are of particular diagnostic significance because they can suggest conformance of the lesion to a ductal structure. Stereo viewing seems to aid detection of linearity immensely, regardless of the 3D orientation of the line of elements. Also, the added information that stereo provides for improved sensing of the shapes and orientations of the individual elements comprising the sub-cluster may permit even sharper diagnostic distinctions, helping, for example, to distinguish between less virulent (cribriform) and more aggressive (comedo) types of malignant tumor.

Information in the configuration of the cluster as a whole. Importantly, stereo viewing can tell the mammographer whether a collection of elements truly occupy a small volume in depth—and thus qualify as a related cluster—or are actually dispersed in depth and only appear to be clustered from the imaged point-of-view. Being able to see better the positions in depth of individual elements as well as the position, shape and orientation of its sub-clusters, will enable improved perception of the overall configuration in depth of the cluster as a whole. This can be additionally important in determining the type of lesion spawning those calcifications. If, for example, it is comprised of two or more linear sub-clusters, telling whether or not they point to a common nexus would be an important further consideration of its ductal conformance.

Information in the locus and orientation of the cluster relative to other visible structures in the breast. Perception in depth of the locus and configuration of the cluster in relation to the

configurations and locations in depth of other breast structures opens many new possible bases for diagnosis. Of first interest in this regard are relationships between the cluster in different configurations or orientations and how it relates to the surrounding parenchymal structure. The potential for critical new diagnostic information is probably greater in this regard with respect to lesions that present as masses, but well worth exploring here as well. The refined information that the stereo display will provide about the overall configuration of the cluster will potentially provide bench marks for characterizing its orientation, and how it, in turn, relates to the surrounding parenchymal structure. One might expect, for example, that a branching configuration would be oriented appropriately relative to the ductal system whether visually evident or posited. Also intriguing, for those lesions that present both as a cluster of calcifications and a mass, are the possibilities of relating configuration of the cluster to configuration of the mass. So far, we have not accrued such dual presentation cases to begin exploring that possibility.

6.2 Stereo-based information on lesions that present as masses.

Information in the locus, size, shape and orientation of individual lobulations. A critical consideration in the diagnosis of masses is the nature of the surface of the mass. Telling whether and how it is lobulated is an important consideration, and that can only be crudely determined in conventional mammography from inspection of the border seen only in profile. There is no way to tell where any individual lobe originates on the surface of the mass, the angle at which it protrudes from the surface, or its true length or shape. Stereo can potentially provide all of that information. Indeed, in one case we have examined, a large lobe that does not protrude out from the mass profile at all can be seen in its full extent in depth against the frontal surface of the mass. In conventional mammography, that lobe would be seen, if at all, just as a meaningless variation in density in the interior of the mass.

Information in the distribution and arrangement of lobulations. With the ability to distinguish the wholes of individual lobulations comes the potential assessing characteristics of them in combination—how they are arranged, how nested, etc. Such distributional characteristics may be informative of the glandular structure in which the tumor is growing, e.g., in some type of lobular structure.

Information in the origin, length, configuration and path of individual spicules. Determining whether the mass shows any evidence of spiculation is also critical to diagnosis, and, for the same reasons that apply in checking for lobulation, the conventional display provides very limited information, while the stereo display is very informative. Our experience is that where an individual spicule emerges from the mass can often be clearly pinpointed, and its path, from beginning to end, even if twisting, clearly traced in depth. This provides remarkably complete views of individual spicules probably never previously seen, not even in the most intensive pathology examinations, limited as they are to slice-by-slice viewing of specimens.

Information in the locus and orientation of the mass relative to other visible structures in the breast. Again, the stereo display promises to supply much more information about the overall configuration of the lesion, here the shape of the mass and the arrangement of variations

in its surface, possibly to provide bench marks for determining its orientation relative to the surrounding parenchymal structure. If the mass appears to be lobular, where and how the lobulation varies over its surface may be discernible enough to suggest how it ought to be oriented and how it ought to fit into the parenchymal structure. When the mass exhibits clear spicules, that provides sufficient evidence to confidently call it malignant. But seeing how those spicules extend into the parenchyma and interact with other structures, may be important for guiding treatment and prognosis. It might also contribute to understanding the disease process. We have one example where two spicules extending from a large mass end up connected to two smaller masses. That poses an intriguing puzzle about how the three tumors are related.

6.3 Stereo-based information on lesions that present as architectural distortion.

Information in the locus of the origin of the defining spicules and in their radiating paths. The stereo display will provide the same richness of information here as with the spicules emanating from visible masses, ensuring much more accurate identification of architectural distortion. Being able to pinpoint precisely where the origin lies relative to the parenchyma may contribute to improved understanding of the disease process. We have one case in which the visible mass, appears to be but a dense collection of spicules all emanating from the center of the mass. This poses a very interesting question about whether some masses might be but dense collections of processes that when seen individually as just a few spokes emanating from a point are called architectural distortion. The stereo display will also provide a powerful source of information for distinguishing between normal striations in the parenchyma that in a particular two-dimensional view just happen to line up in depth into a purely illusory spoke pattern. We have one clear case so far where in conventional mammography there appeared to be architectural distortion, but where the stereo display showed that not to be the case.

7. Presentations of Research During Year 2

Dr. Getty participated, both as a poster presenter and as an invited platform speaker in the "Era of Hope" meeting held in Washington, DC from October 31 to November 4, 1997. The meeting was organized by the U.S. Army Medical Research and Materiel Command as part of the DoD Breast Cancer Research Program. He presented the research efforts of this project to the meeting, in a talk entitled "Stereoscopic Digital Mammography: Improving Diagnostic Accuracy." Textual slides from this talk are included as Appendix B of this report. Dr. Getty also presented a demonstration of stereoscopic mammography to individual participants, in the form of sample stereo mammograms captured on 35mm slides and viewed in hand-held stereoscopic viewers.

Dr. Getty also participated as a speaker in a Working Group on Digital Mammography at the invitation of Drs. Faina Shtern from the PHS Office on Women's Health, and Dan Sullivan from the National Cancer Institute. This meeting was held in Bethesda, MD on March 9-10, 1998. The goal was to set the future national research agenda for digital mammography. As a member of the panel on Digital Displays and Workstation Design, Dr. Getty described the promise of digital stereo mammography, as well as the ongoing evaluation research occurring in this project.

8. Schedule and Level of Effort

The project ran at a level of effort and expenditure through Year 2 of close to 100% of budget. All staff and consultants continue with the project as planned, with the exception of one of our three mammography consultants, Dr. Thomas Frenna. Dr. Frenna left his position on the mammography staff of Brigham and Women's Hospital (BWH) in Boston during this past year and has moved to a practice in New York city. We have arranged with Dr. Darrell Smith, newly appointed Director of Mammography Service at BWH, to take Dr. Frenna's place on this project as expert consultant on mammography.

Because of the delays in acquisition and installation of the GE full-field-of-view digital mammography unit that occurred in Year 1, we remain somewhat behind our original schedule regarding accrual of imaged cases. We have been able to compensate for the delay, at least in part, by carrying out other tasks that did not require an extensive case database and which we could begin earlier than originally planned. Consequently, we are proposing to modify the timeline as shown below. The work to be completed within the set of project tasks remains as originally proposed; only the timeline for when tasks begin and end is modified.

Table 2. Revised Timeline and Status of Project Tasks

Task #	Original Period	Revised Period	Status	Task Description
Task 1	Months 1-8	Months 1-12	Completed *	Reorganize user interface
Task 2	Months 9-18	Months 1-18	Completed *	Add new functionality to control software
Task 3	Months 1-18	Months 1-24	Completed *	Explore joystick and speech control
Task 4	Months 1-36	Months 11-39	Ongoing	Acquire stereo-imaged cases
Task 5	Months 6-11	Months 18-29	Initiated	Interviews and studies with mammo. experts
Task 6	Month 12	Month 30	To be done	Consensus meeting with mammo. experts
Task 7	Months 13-18	Months 30-36	To be done	Develop checklist of stereo features
Task 8	Months 19-24	Months 19-30	Initiated	Explore stereo display modes with experts
Task 9	Months 25-30	Months 25-36	To be done	Modify display software for new modes
Task 10	Months 25-30	Months 34-39	To be done	Prepare case set and reading study materials
Task 11	Months 31-42	Months 40-45	To be done	Conduct reading studies
Task 12	Months 43-48	Months 43-48	To be done	Analyze reading study results
Task 13	Months 43-48	Months 46-48	To be done	Train statistical prediction rules on feature data and measure accuracies

* Work originally proposed within these tasks has been completed; however, we will continue to work on them as needs arise within the project.

9. Plans for Year 3

As indicated by the proposed timeline shown above, we will continue accruing cases (Task 4) throughout Year 3, as well as through the first quarter of Year 4. In Year 3, we expect to image at least another 100 to 125 lesions.

Over the early months of Year 3, we will continue the interviews begun this past year with our three mammography experts, to identify new information available in the stereo images (Task 5). This activity will culminate in a consensus meeting with the three experts in Month 30 to arrive at a master feature list (Task 6). Then, over the last half of Year 3, we will develop descriptions and quantitative scales for each of the identified features (Task 7).

During our interactions with the mammography experts during the first half of Year 3, we will also continue to explore new or better ways of displaying the stereo images to optimize their presentation, and the user's control over that presentation (Task 8). As we identify new methods, we will modify the display software to incorporate these functions (Task 9).

Finally, in the last quarter of Year 3, we will initiate the process of preparing the cases and other supporting materials needed for the evaluative reading studies that will take place in Year 4 (Task 10).

CONCLUSIONS

Our conclusions arising from this second year of work on the project fall into two general categories: (1) conclusions regarding the usability and functionality of the stereo display workstation, and (2) conclusions arising from our close study of the stereo mammograms collected over this past year.

Much of our effort on the stereo display workstation has addressed development and a human factors evaluation of alternative methods by which the user may exercise control over various aspects of the stereo display. The alternatives examined during the year included point-and-click control using the system monitor, control by spoken command, and use of independent pointing devices (a second mouse or joystick). The conclusion we have reached is that no single method is best for everything. Commands that are categorical by nature—such as turning things on or off—can be effectively given either by speech or using point-and-click methods. On the other hand, commands that are continuous by nature—such as controlling display brightness or contrast—are most sensitively and effectively controlled by use of a second, non-system, mouse. As we gain more experience with mammographers actually using the system, we will continue to refine its organization and control structure.

With regard to our study of the collected stereo mammograms, we remain impressed by the high quality of the stereo images, and increasingly excited by what we can see in the images. The images are highly informative—sharp images of the fine features of lesions that have to be discriminated for diagnosis, and all perceived with remarkably strong impressions of position, separation and orientation in depth. Our explorations of cases this year suggests that the display does indeed provide rich new sources of diagnostic information. We have found that the stereo images provide an astoundingly rich and fine sense of the parenchymal structure of the breast, and of the spatial relationship between a lesion and that surrounding structure. We believe that the stereo images will contribute diagnostic information at three levels of analysis: understanding the elemental constituents of a lesion, understanding the overall pattern or structure of the lesion, and understanding how the lesion relates to surrounding tissue. From these early findings, we remain very optimistic about the promise of stereo mammography to improve diagnostic accuracy.

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STEREOSCOPIC DIGITAL MAMMOGRAPHY

Date:

Patient Name:

Date of Birth:

ID Number

Clinical Information:

Projection:

kVp

MAS

Filter

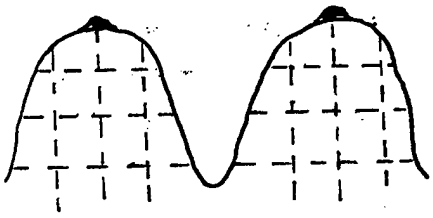
SID

METAL BB POSITION:

Bottom-Lateral (receptor) Yes / No

Top-Medial (breast) Yes / No

Left Right



Legend:
Calcifications
Mass

Date sent to Getty: _____

Stereoscopic Digital Mammography

Improving Detection and Diagnosis of Breast Cancer

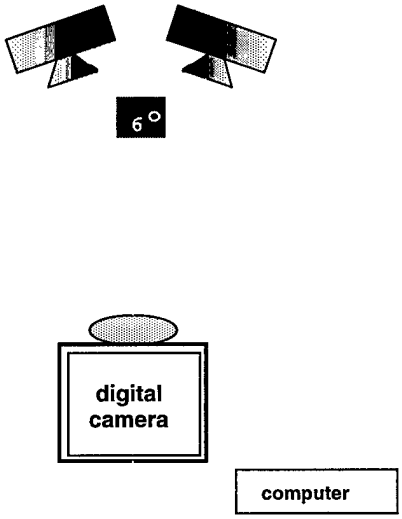
David J. Getty, Ph.D.

BBN Technologies

Why Stereo Mammography?

- Potential to improve detection of early, subtle breast lesions.
- Potential to improve the ability to distinguish malignant from benign lesions.
- Potential to lead to new insights about 3-D lesion structure and development.

Stereo Image Acquisition



A Significant Problem with Standard Mammography

- Difficult to integrate information from a pair of 2-D views to mentally construct the 3-D structure of the breast.
- In stereo, one can directly see the internal 3-D structure.

Gains in Detection from Stereo

- Problems with Standard Mammography
  - Layers of normal glandular tissue at different depths can mask detection of subtle lesions, or can superimpose by chance to resemble a focal density.
  - Often difficult to be certain that a suspected density in one view corresponds to a particular suspected density in the other view.
- Solutions with Stereo Mammography
  - In stereo, layers of glandular tissue lying at different depths are directly seen as separated in depth.
  - A true focal lesion is directly seen as a lump of tissue at a location in the breast volume.

Gains in Diagnostic Accuracy from Stereo

- Masses
  - Easier to see a mass because of the separation in depth of nearby overlying and underlying glandular tissue.
  - Easier to judge characteristics of the surface of the mass because it is seen as a 3-D shape.
- Calcifications
  - One can directly see the 3-D shapes of individual elements of calcium.
  - One can directly see the 3-D geometric distribution of a cluster of calcifications.

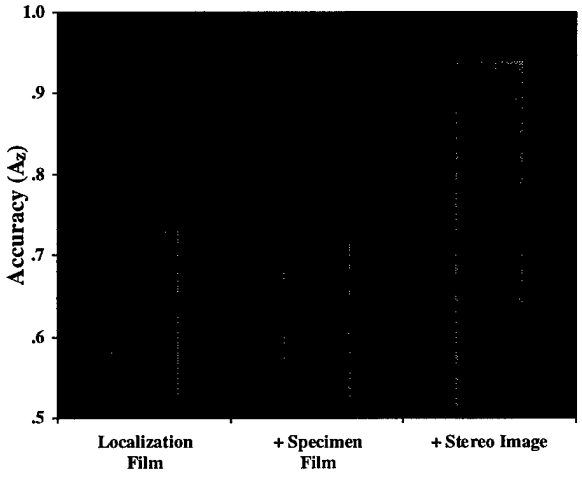
Potential Gains in Understanding of Lesion Structure and Development

- Stereo may stimulate new insights about gross structure and development of lesions in the breast.
- One can see the 3-D structure of the breast, and of lesions within the breast, in a way not possible using any other technique.

Why Stereo Now?

- Earlier attempts to use stereoscopic viewing in radiology were technically weak and often flawed.
- We now have a better understanding of the optical and psychophysical principles underlying stereoscopic perception.
- Computer-based, high-resolution digital display systems provide precise control of stereo image presentation.
- High-quality stereo display hardware now exists.

Diagnostic Accuracy
Under Three Viewing Conditions



Project
Stereoscopic Digital Mammography: Improving Diagnostic Accuracy

- BBN Technologies
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  - Ronald M. Pickett, Ph.D.
  - John A. Swets, Ph.D.
- University of Massachusetts Medical Center
  - Carl J. D'Orsi, M.D.
  - Andrew Karellas, Ph.D.

Supported by funding from the Breast Cancer Research Program of the Department of Defense, managed by the U.S. Army Medical Research and Materiel Command

Goals of the Project

- Focus on improving diagnostic accuracy.
- Acquire stereo mammograms from about 300 women patients scheduled for biopsy of a focal breast lesion.
- Develop understanding of new stereo-based visual features.
- Using ROC methods, compare the diagnostic accuracy attained with:
  - 1. Standard films
  - 2. Non-stereo viewing of digital images + standard films
  - 3. Stereo viewing of digital images + standard films

Demonstration of Stereoscopic Digital Mammography

- Stereo mammograms of 4 cases, illustrating stereo views of masses and clustered calcifications.
- Images presented in hand-held stereo viewers, each containing a stereo pair of 35mm slides of one case.