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U.S. Public Health Service's
Office on Women's Health

In collaboration with the
National Cancer Institute
and the
Federal Multi-Agency Consortium on
Imaging Technologies to Improve Women's Health

U.S. Department of Health and Human Services

New Frontiers in Breast Cancer Imaging and Early Detection

From Missiles to Mammograms
A Capitol Hill Briefing

Sponsored by the
U.S. Public Health
Service's Office on
Women's Health,
Department of
Health and Human
Services

September 17, 1996
8:30 am - 1:00 pm
Hart Senate Office Building
Room 216

Imaging Exhibits
10:00 am - 6:00 pm
Hubert H. Humphrey Building
Great Hall

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Acknowledgements

The U.S. Public Health Service's Office on Women's Health would like to thank the following individuals for their contributions to this monograph:

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General Electric Company
Curtis R. Carlson, Ph.D.
National Information Display Laboratory
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The Federal Multi-Agency Consortium on Imaging Technologies to Improve Women's Health

Mission

This Consortium is fostering the identification, evaluation, and transfer of intelligence, space, defense, and other relevant technologies to advance the current state of the art in imaging to improve the early detection and diagnosis of diseases in women, including breast and ovarian cancer. Under the leadership of the U.S. Public Health Service's Office on Women's Health, many Federal agencies have been brought together to join their efforts, expertise, and resources in the area of imaging technologies to assess their potential application for improving women's health. The Consortium members include the following organizations:

- U.S. Public Health Service's Office on Women's Health, U.S. Department of Health and Human Services
- National Cancer Institute, U.S. Department of Health and Human Services
- Food and Drug Administration, U.S. Department of Health and Human Services
- Central Intelligence Agency
- Department of Defense
- National Aeronautics and Space Administration
- Department of Energy
- National Science Foundation
- Department of Commerce

The first meeting of the Consortium took place on March 29, 1996. Based on the Consortium recommendations, the U.S. Public Health Service's Office on Women's Health formulated and supported a new initiative devoted to the development of a comprehensive inventory of government-wide technology transfer opportunities that have the potential for improving the early detection, diagnosis, and treatment of diseases in women in such critical areas as digital image generation, display, analysis, three-dimensional processing, and transmission.

Planning Committee

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What Is Breast Cancer?

All women are at risk for developing breast cancer. Breast cancer is one of the most common forms of cancer, affecting 1 in 8 American women over a lifetime. During the decade of the 1990s, an estimated 1.5 million American women will be diagnosed with breast cancer and 500,000 will die of it. The disease not only has profound health consequences for women but also has a major psychological and socioeconomic impact on women and their families.

Breast Cancer Origins

Breast cancer growth occurs when breast cells become abnormal and divide without control or order. The specific events that trigger the transformation of a normal cell to a cancerous one are not fully understood, but the process seems to involve a complex interplay of genetics and environmental factors.

Breast cancer cells develop the ability to metastasize—to break off from the primary tumor and travel through the bloodstream or lymph system, spreading to other places in the body. Today, about half of women diagnosed with breast cancer die of metastatic disease. The likelihood of a breast cancer metastasizing is related to the size of the primary tumor. Small tumors (less than 1 cm) have a 20 percent or less chance of leading to metastasis. Early detection of the tumor, therefore, is vital to survival.

Metastatic cancer also is believed to be preceded by a process called angiogenesis—the development of new blood vessels in the primary tumor to support the tumor's growth. Recent studies have shown a direct relationship between the chance of metastasis and the extent of new blood vessel development in the primary breast tumor. This highlights the importance of developing new imaging techniques capable of detecting angiogenesis.

health issues across the agencies of the U.S. Public Health Service. The Office is working to redress the inequities in the health care system and in the conduct of research that have put the health of American women at risk.

The national leadership provided by the U.S. Public Health Service's Office on Women's Health, working collaboratively with the DHHS agencies and regions, has resulted in the establishment of initiatives and programs and the development of public/private partnerships across the Federal government and private sector to advance women's health nationwide and internationally.

Goals

The goals of the PHS Office on Women's Health include:

- Stimulating the development and implementation of effective women's health programs and policies, coordinated across the U.S. Department of Health and Human Services, with other Federal departments, and in partnership with public and private organizations at the national, State, and local levels.
- Stimulating and strengthening a broad range of research on the diseases and conditions that affect women.
- Promoting comprehensive and culturally sensitive diagnostic, treatment, and preventive health services for women.
- Supporting public and health care professional education, training, and information dissemination on women's health issues.
- Fostering the recruitment, retention, and promotion of women in research careers and in the health professions.

Initiatives

The PHS Office on Women's Health has fostered exciting collaborations within the DHHS, across other Federal agencies, and with health professional and consumer organizations, foundations, and academia.

Examples of PHS OWH initiatives include the following:

- Coordinating the implementation of the National Action Plan on Breast Cancer, an innovative public-private partnership (involving agencies of government, advocacy groups, and scientific and health care professional organizations) that is catalyzing new actions in research, service delivery, and education to eradicate breast cancer as a threat from the lives of American women.
- Initiating "From Missiles to Mammograms: New Frontiers in Breast Cancer Imaging and Early Detection," an innovative partnership among PHS OWH; NCI; academic radiologists; and imaging experts from DoD,

U.S. Public Health Service's Office on Women's Health U.S. Department of Health and Human Services

Mission

To improve the health of women across the life span by directing, developing, stimulating, and coordinating women's health research, health care services, and public and health professional education and training across the agencies and offices of the U.S. Department of Health and Human Services, and with other government agencies, public and private organizations, and consumer and health care professional groups.

Role

The U.S. Public Health Service's Office on Women's Health (PHS OWH) within the Department of Health and Human Services (DHHS), established in 1991, is the champion and focal point for women's health activities within the Department of Health and Human Services. The Office coordinates and stimulates research, service delivery, and education programs and activities across the agencies and regions of the DHHS, including the National Institutes of Health, Centers for Disease Control and Prevention, Agency for Health Care Policy and Research, Food and Drug Administration, Health Resources and Services Administration, Indian Health Service, and Substance Abuse and Mental Health Services Administration. The PHS OWH also collaborates with other governmental organizations and consumer and health care professional groups to advance women's health. The Office advises the Assistant Secretary for Health and the Secretary on scientific, medical, and policy issues relating to women's health issues. The Office serves as a catalyst for women's health programs, initiatives, and policies across the agencies, offices, and regions of the DHHS, providing the structure throughout DHHS for addressing crosscutting women's health issues that require the combined resources, blending of programs, and activities administered by the respective DHHS agencies, offices, and regions.

In 1994, a new senior-level position, Deputy Assistant Secretary for Health (Women's Health), was established within the Department of Health and Human Services to direct the U.S. Public Health Service's Office on Women's Health and to provide leadership and to give greater emphasis to women's

Current Statistics

In 1996, an estimated 184,300 women will develop breast cancer and 44,560 will die of the disease. Breast cancer is the second leading cause of cancer death in American women. Men also can develop breast cancer, but to a much lesser extent. In 1996, an estimated 1,400 men will develop breast cancer and 260 will die of it.

While the disease affects women of all races, it is more prevalent in non-Hispanic white women than in African-American, Hispanic, or Native-American women. The exception is Native-Hawaiian women, whose breast cancer rate is almost as high as it is in white women.

According to Government statistics, the rate of breast cancer in women increased by 25.3 percent between 1973 and 1992. However, despite the increasing incidence of breast cancer since 1940, the overall death rate (mortality rate) in American women has been declining in the 1990s. Among white women, the mortality rate has dropped approximately 6 percent between 1989 and 1993. For African-American women, increases in mortality persist, especially among older women, but the overall increase has slowed significantly. From 1989 to 1993, the mortality rate rose about 1 percent in African-American women. By comparison, from 1980 to 1989, mortality increased 3 percent in white women and 16 percent in African-American women.

Experts believe that the recent overall decline in breast cancer death rates is partly a result of mammography screening, which rapidly increased in the United States during the 1980s, and resulted in a shift toward the detection of breast cancer at earlier stages, when treatment can be most effective and survival rates are higher.

African-American and Hispanic women have poorer 5-year survival rates from breast cancer than do non-Hispanic white women. Part of the reason for poorer survival in minority populations is the more advanced stage of disease at the time of diagnosis. It is anticipated, therefore, that improvements in imaging technology, better education, and increased access to mammography screening for early detection will have an important impact on decreasing mortality rates and increasing survival rates from breast cancer for all women, particularly minority populations.

Risk Factors

There is an increased risk for breast cancer among women of higher socioeconomic status, married women, women living in urban versus rural areas, and women living in northern States. But the most important risk factor for breast cancer is increasing age. Eighty percent of breast cancers occur in women older than age 50. Other known risk factors include:

- Family history of the disease
- Early onset of menstruation and/or late menopause

development in breast cancer imaging technologies and provide a glimpse of several "new frontiers," in which technologies from fields outside of medicine, such as those used in the defense, space, and intelligence communities and the computer graphics industry, are being applied to improve breast cancer imaging. Some of the technologies described are in use today; others are more distant visions. All are being pursued in the hope of reducing the toll of breast cancer on the lives of American women.

FIGURE 1. EVOLUTION OF MAMMOGRAPHY

A. General-purpose x-ray equipment was used for this 1939 mammogram. Image quality was limited, and the radiation dose was high.

B. This 1992 screening image, taken with dedicated mammography equipment, provides excellent detail of breast tissue. The arrow points to a tiny, star-shaped mass, which biopsy found to be a cancer that had not spread to the lymph nodes.

(Photos courtesy of Lawrence Bassett, M.D., University of California at Los Angeles School of Medicine)

From a patient's perspective, the advantages of "virtual colonoscopy" are substantial. It is considerably less expensive than traditional colonoscopy ($500 versus $1,500) and reduces the examination time dramatically (30 seconds versus 20 minutes for a barium enema and most of a day for colonoscopy).

"Virtual colonoscopy," an example of computer graphics developed by the entertainment industry for movie special effects, is now being tested for its usefulness in cancer screening.

FIGURE 14. Three-dimensional colon created from a spiral CT scan.

FIGURE 15. Inside the colon looking at its internal surface.

FIGURE 16. Color-enhanced images (red zones) indicating areas of potential tumor in the colon.

(Photos courtesy of David Vining, M.D., Bowman Gray School of Medicine of Wake Forest University)

Cancer Detection Using Interactive Computer Graphics

The results of interactive computer graphic simulations such as virtual reality are currently being applied to the detection of colon cancer. These techniques also suggest intriguing possibilities for wider adaptation to screening for and diagnosing breast cancer.

It is thought that most colon cancers develop from preexisting polyps and that removal of these polyps can prevent the development or spread of cancer, thus reducing the high mortality from this disease. Conventional screening examinations for colorectal cancer—barium enema and colonoscopy—involve a certain degree of discomfort and inconvenience; for this reason, most people avoid them. "Virtual colonoscopy," the application of interactive three-dimensional (3-D) computer graphics to this problem, offers an easier way to examine the colon. The technique involves inflating the patient's colon with air, performing a 30-second spiral computed tomography scan of the abdomen, and constructing a 3-D virtual reality simulation of the colon for visual inspection. With "virtual colonoscopy," a physician can visualize internal structures of the colon—"flying through" the colon on a computer workstation to search for polyps and suspicious masses (see Figs. 14, 15). In a recent advance, scientists are using computer-aided diagnosis to color-enhance suspicious bowel lesions (Fig. 16), a technique similar to computer-assisted detection of breast microcalcifications on mammograms.

Digital Mammography

During the past two decades, conventional mammography practice and interpretation have improved dramatically through advances in film and x-ray technology as well as education of physicians, other health care professionals, and patients. Despite these advances, mammography still has room for improvement. Limitations arise primarily from the dual functions that radiographic film performs in conventional mammography, namely, the detection of x-rays and the final display of the radiographic image. In order to perform each of these separate functions, compromises in

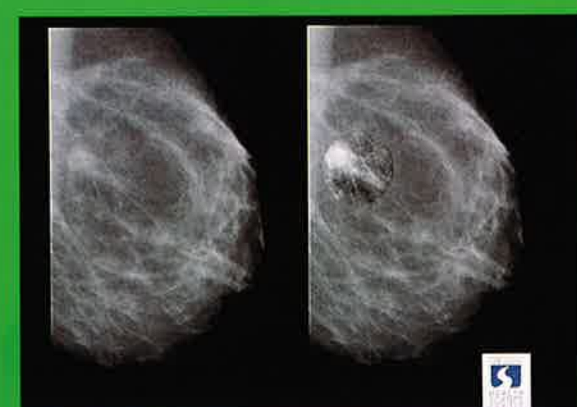


FIGURE 2.
A digital mammogram of a patient with breast cancer. Computer enhancement of the mammogram improves the visualization of a small breast lesion.

(Photo courtesy of Donald B. Plewes, Ph.D., University of Toronto) system performance occur. Furthermore, once a film is processed, no further manipulation of the image characteristics is possible. This is particularly troublesome in patients with "dense" breasts, for whom optimal contrast between normal tissues and tumors throughout the mammogram is often impossible.

Digital mammography promises to overcome these limitations through the use of a dedicated electronic detector system that captures and displays the x-ray information on computers. The digital data can then be used for image analysis, review in the form of computer-enhanced images, transmission for expert consultation (telemammography), and electronic patient records for improved storage and retrieval. Processing of digital images can substantially improve the visualization of the presence and extent of breast cancer. This is shown in Figure 2, where a small cancer is seen on digital mammography. The figure clearly illustrates the ability to improve cancer visualization through computer enhancement.

While women with dense breasts may derive the greatest advantage from digital mammography, all women are likely to benefit from better physician/radiologist consultation and coordination allowed by rapid transmission of images to major medical centers through digital information networks (telemammography). This feature will be of particular value for women in more isolated and/or underserved communities by providing them access to experts nationwide for interpretation of their mammograms.

Advancing digital mammography is the focus of the National Digital Mammography Development Group (NDMDG), a research consortium of five academic and two industrial laboratories formed by the National Cancer Institute and cosponsored by industry. The consortium is working to develop clinical systems for digital mammography through joint university/industrial research. In addition, the NDMDG is conducting research in computer enhancement of digital mammograms, telemammography, and computer-aided detection and diagnosis. Its ultimate aim is to conduct and stimulate research in these areas and to measure the impact of digital technology on the diagnosis of breast cancer through a series of coordinated clinical evaluations in major university hospital centers.

can be done on exactly the same image, which then provides a continuous record of the patient's health care from diagnosis to treatment and follow-up. The 3-D image becomes the permanent electronic medical record.

Many of these imaging modalities and sophisticated 3-D computer visualizations are current prototype devices for the management of battlefield injuries and other military applications, which also will be applicable to civilian needs (Fig. 13).

FIGURE 11. 3-D visualization of a virtual nerve of the intestines (celiac ganglion).

FIGURE 12. High-resolution ultrasound image showing cross-section anatomy of the leg.

FIGURE 13. Portable 3-D tele-ultrasound unit in backpack currently deployed in Bosnia.

(Photos courtesy of Richard M. Satava, M.D., Defense Advanced Research Projects Agency)

Virtual Reality Applications in Women's Health

Advanced imaging technologies and three-dimensional (3-D) visualization are the cornerstone of virtual reality. As a medical application, virtual reality takes a previously acquired image from any method, such as a CT scan, MRI scan, or ultrasound, and uses a high-performance computer to create a full 3-D volume image (Fig. 11).

This 3-D image is now the "information equivalent" of the organ or tissue (such as the breast). It contains all the normal anatomy and disease in the form of "bits and bytes," permitting the physician to regenerate the image on a computer monitor and interact with the image as if the breast were actually there. Interaction includes rotating, slicing into various planes (Fig. 12), making layers transparent, fusing multiple images (e.g., MRI and ultrasound), and eventually even taking a miniaturized view and "flying through" the ducts and glands, looking for disease and cancer.

This diagnosis is but the first step. The same 3-D computer image can then be used to explain the problem to the patient, to plan an operation and to practice the surgery (using a virtual reality surgical simulator), as a guide or navigational tool during the operation (such as stereotactic breast biopsy), and finally in postoperative follow-up to compare with subsequent images for outcomes analysis. The important factor is that all of this

Computer-Aided Diagnosis

Computer-aided diagnosis (CAD) involves the use of sophisticated computer programs to assist radiologists in analyzing medical images. Much of the activity in CAD has concentrated on digital mammography. The computer completely searches a digital mammogram for questionable areas that may contain cancer and flags them for the radiologist for further examination (Fig. 3). The radiologist uses this

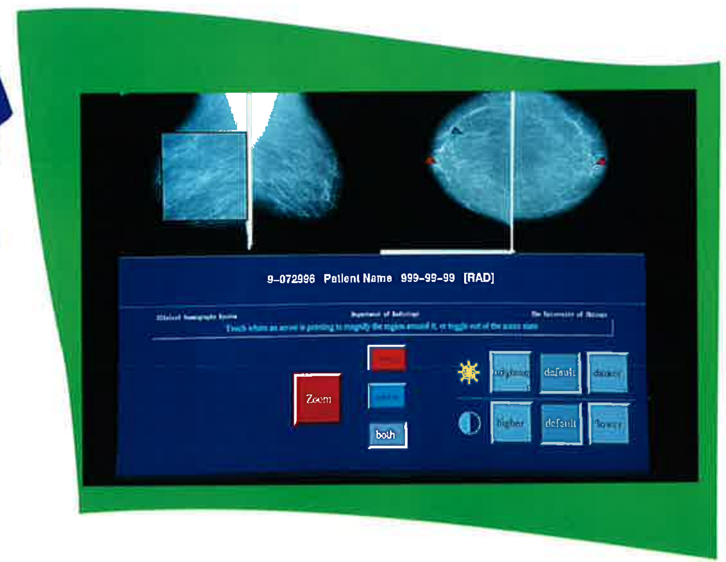


FIGURE 3. Touchscreen display of CAD results on a clinical workstation. The red arrow on the right image of the breast shows a small cancerous mass detected by the computer. The other red arrow is normal tissue, and the blue arrow points to an area containing possible microcalcifications. With digital images, areas in question can be magnified, as in the left mammogram image.

(Photo courtesy of Robert Nishikawa, Ph.D., The University of Chicago) computerized analysis as a tool in detecting lesions. These computer programs also may help the radiologist decide whether lesions are cancerous.

CAD generally works in four steps: (1) Possible abnormalities are enhanced visually through image-processing techniques, and comparison of images of both breasts (or comparison of images of the same breast taken at different times) is conducted; (2) abnormal regions are isolated from the rest of the image; (3) various features of the abnormal region, such as size and shape, are used to classify normal, benign, and cancerous regions; and (4) sophisticated neural network techniques are used for further analysis of the areas classified as abnormal.

In preliminary studies, CAD has been shown to improve radiologists' ability to detect breast cancer and to distinguish benign from cancerous lesions. Research studies indicate that a computer can identify approximately half of the breast cancer lesions that a radiologist has overlooked in a routine clinical setting.

However, the computer may tend to question too many areas that eventually prove to be normal. Collaboration with the intelligence community has produced a method for improving the accuracy of early breast cancer detection with CAD by nearly a factor of two.

Current research is directed toward translating this technology into the clinical arena, which includes developing display modalities to present the computer information to radiologists reading the mammogram studies (Fig. 4) and proving that CAD can actually improve their ability to identify breast cancer. The collaboration of industrial and academic partners should result in the introduction of a clinical prototype CAD unit within the next year. There is great promise for the combination of improved digital mammographic images and computer-generated analysis of these images to enhance our ability to reliably detect earlier, curable breast cancers.

recognition tools used to detect missiles and targets to the problem of finding microcalcifications in mammograms.

In one of the projects, scientists from the intelligence community, working in close collaboration with leading medical researchers, applied a neural network, modeled after human brain cells (neurons) and developed to find targets in military surveillance images, to the problem of detecting microcalcifications in mammograms. Preliminary results generated by this joint team of scientists found that this neural network technology could be used to improve the accuracy of breast cancer detection by nearly a factor of two compared with the state-of-the-art computer-aided diagnosis (CAD) currently available in radiology (see Fig. 10). Medical scientists believe that this is a significant improvement that could potentially facilitate the acceptance of CAD tools by the radiological community. Given the promise of this initial effort, the U.S. Public Health Service's Office on Women's Health is supporting a comprehensive clinical evaluation of this technology transfer project to assess its effectiveness in improving the accuracy of breast cancer detection.

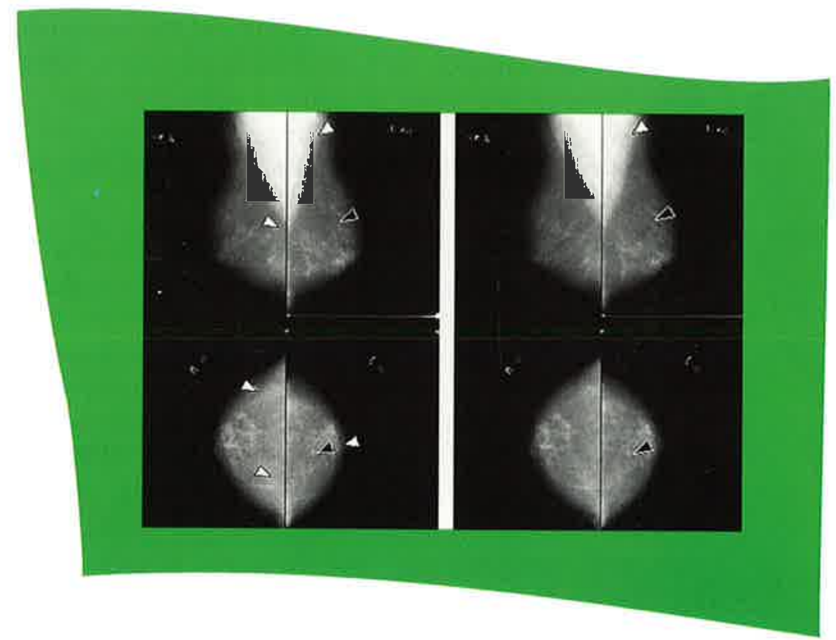


FIGURE 10. Results of CAD computer output before (left) and after (right) applying the intelligence community neural network for finding microcalcifications. True cancer detections are shown with black arrows and false identification with white arrows. When the intelligence community neural network was added to the state-of-the-art radiologic CAD system, four of five lesions that were falsely identified as cancers were eliminated, with no loss in detecting true cancers, substantially increasing accuracy.

(Photos courtesy of Robert Nishikawa, Ph.D., The University of Chicago, and Paul Sajda, Ph.D., National Information Display Laboratory)

Transferring Technologies from the Intelligence Community to the Medical Community

The medical and intelligence communities share some challenging information processing, display, and image transmission needs. For example, radiologists and intelligence analysts must look for very small objects or targets while rapidly scanning a large number of high-resolution, information-intensive images. Incorrect analysis—a missed cancer or a missed military target—can have profound consequences.

In the summer of 1994, the Central Intelligence Agency (CIA) was asked by the U.S. Public Health Service's Office on Women's Health, within the Department of Health and Human Services (DHHS), whether there were intelligence imaging technologies that could be applied to improve the early detection of breast cancer. Several existing technical programs that focused on image analysis and display in the intelligence community were identified as potentially having a high and near-term impact on saving women's lives. A working group of scientists from the intelligence community and medical experts was formed to foster technology transfer efforts.

In 1995, the intelligence community identified four projects for initial consideration. Two of the projects applied intelligence community-developed image registration technology to the problems of detecting changes in mammograms and MRI images of the breast. A third technical project applied assisted-search/pattern

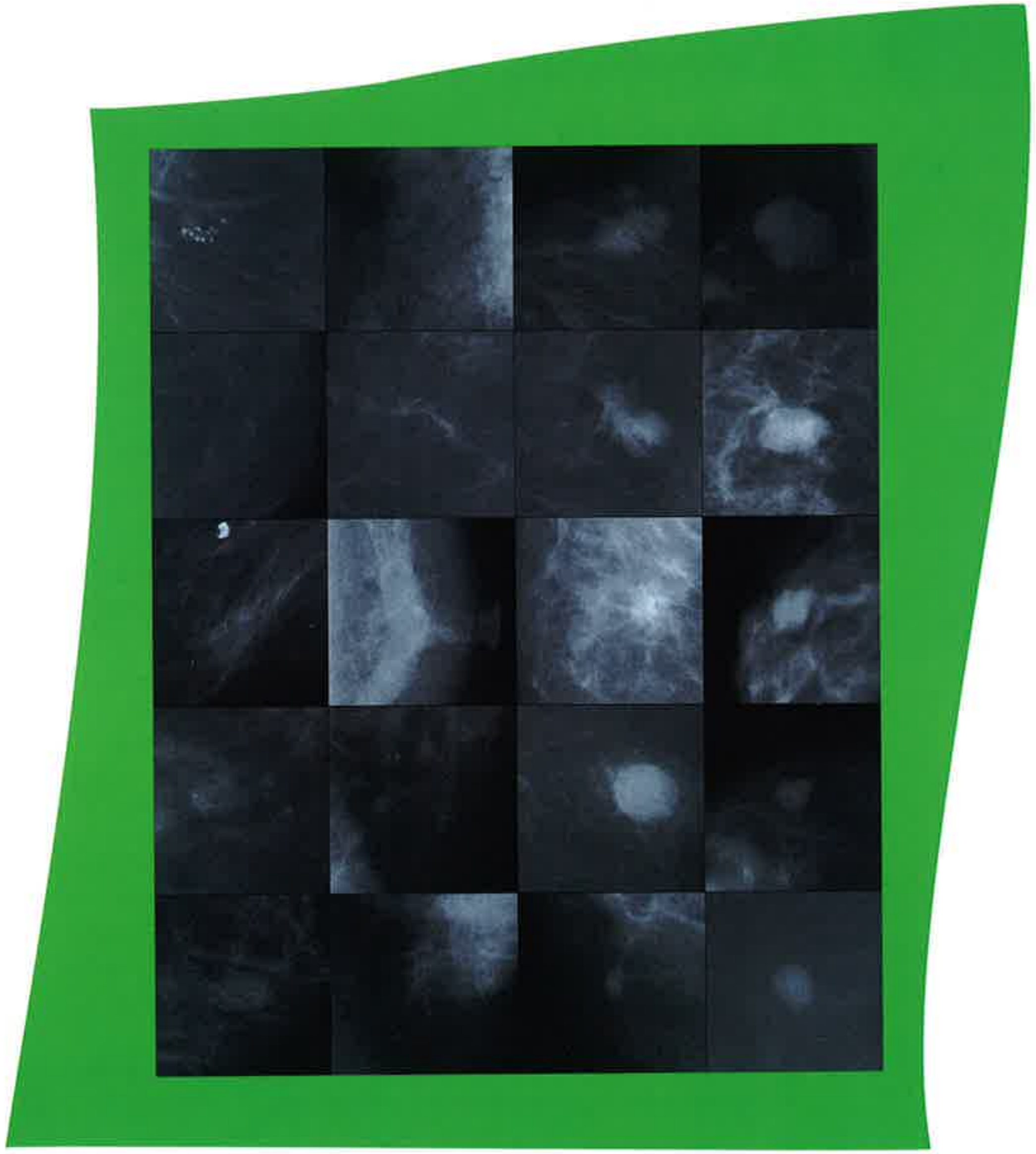


FIGURE 4. Digital collage of breast lesions extracted from mammograms by the computer. The right column contains five benign masses; the left column contains five benign microcalcification clusters. The two middle columns contain malignant microcalcifications and masses, respectively. Presentation of lesions in this fashion with documented pathology may help radiologists improve the accuracy of diagnosis.

(Photo courtesy of Robert A. Schmidt, M.D., The University of Chicago)

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) is the creation of images from signals generated by the excitation—the gain and loss of energy—of nuclear particles in a magnetic field. In sharp contrast to conventional and digital mammography, MRI examination is free of ionizing radiation. Although MRI is still under investigation for the diagnosis of breast cancer, it shows particular promise in detecting and staging cancers in dense breasts, where mammography is not as effective.

Currently, breast MRI is performed with conventional whole-body MRI units that have been specially adapted for breast imaging. A contrast dye injected into the bloodstream gives additional information about blood supply to tissues and new blood vessel formation in cancerous lesions. MRI is performed both before and after infusion of a contrast medium (see Fig. 5). Currently, breast MRI takes 35 to 40 minutes to complete.

At the current stage of development, MRI, using pre- and post-contrast scanning, has promise for breast cancer detection and staging. MRI is capable of detecting most cancers, including small lesions that are not detectable by clinical breast examination or mammography. Current results indicate that breast MRI is also valuable for defining tumor extent, or staging, which is important for selection of the most effective treatments.

In the future, advanced MRI technologies are expected to provide improved biologic information about the detected abnormalities that may assist with evaluation of clinical prognosis as well as prediction and early assessment of tumor response to treatment. Ultimately, MRI-based biologic information may be useful for "customization" of breast cancer treatment for individual patients.

Current needs include improved three-dimensional computer-aided image analysis, MRI-compatible biopsy equipment, and development of optimal, cost-effective which investments in the space, defense, and intelligence communities can be used to save the lives of women. The U.S. Public Health Service's Office on Women's Health is fostering new initiatives to facilitate collaboration among these experts to develop new imaging technologies for breast cancer detection.

FIGURE 9. SPACE TECHNOLOGY APPLIED TO DIAGNOSTIC IMAGING

(Photos courtesy of Joan Vernikos, Ph.D., National Aeronautics and Space Administration)

Digital Imaging: Space Technology Supporting Women's Health

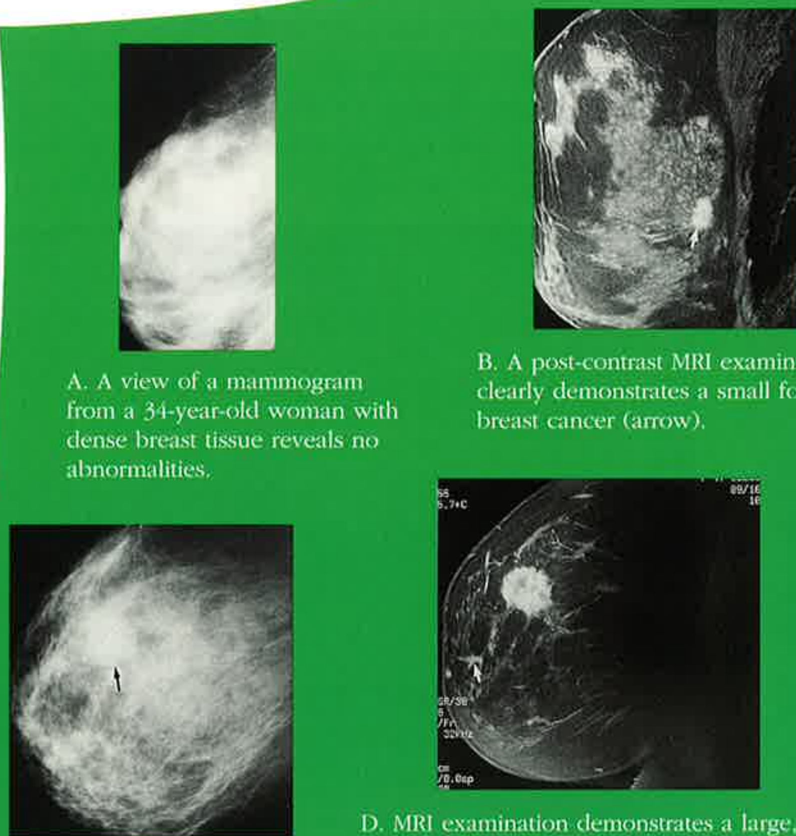
Scientists and engineers of the National Aeronautics and Space Administration (NASA) develop advanced imaging devices and innovative image-processing tools to meet the requirements of space exploration and earth remote-sensing applications. Over the years, these developments have been applied to medical diagnostic imaging (see Fig. 9).

For the past 5 years, NASA has worked with the National Cancer Institute (NCI) to apply the latest in advanced imaging technologies to the development of digital mammography systems. This initiative investigated 43 different aerospace and defense imaging technologies with the potential for improving image quality, computer-aided diagnosis of breast cancer, and telemammography. Now NASA and NCI are jointly supporting six research projects that should, in the next 1 to 2 years, yield the next generation of high-resolution, high-contrast digital mammography systems, which are expected to find smaller breast cancers. For example, a charge-coupled device (CCD) detector developed for the Hubble Space Telescope is now used in a high-precision digital mammography-guided (stereotactic) needle biopsy system for the diagnosis of breast cancer.

In recent years, scientists and other experts from a variety of fields have come together to discuss ways in which advances in imaging technologies in nonmedical fields can be applied to the early detection of breast cancer. They have found that there are a number of ways in approaches to generating breast images. While breast MRI is expensive today, development of dedicated breast MRI units may permit major cost reductions for the procedure in the future.

Several potential applications of breast MRI may increase our ability to detect the disease: assisting in diagnosis for women at high risk of breast cancer with hard-to-interpret mammograms; clarifying how much breast tissue is involved to aid in treatment planning for women with known cancer; evaluating response to treatment; and detecting recurrent cancer in the breast after breast-conserving therapy and/or plastic surgery (e.g., breast implants).

FIGURE 5. MRI SCANS



A. A view of a mammogram from a 34-year-old woman with dense breast tissue reveals no abnormalities.

B. A post-contrast MRI examination clearly demonstrates a small focus of breast cancer (arrow).

C. A mammographic view demonstrates a focal area of increased density that was later shown to be cancer (arrow).

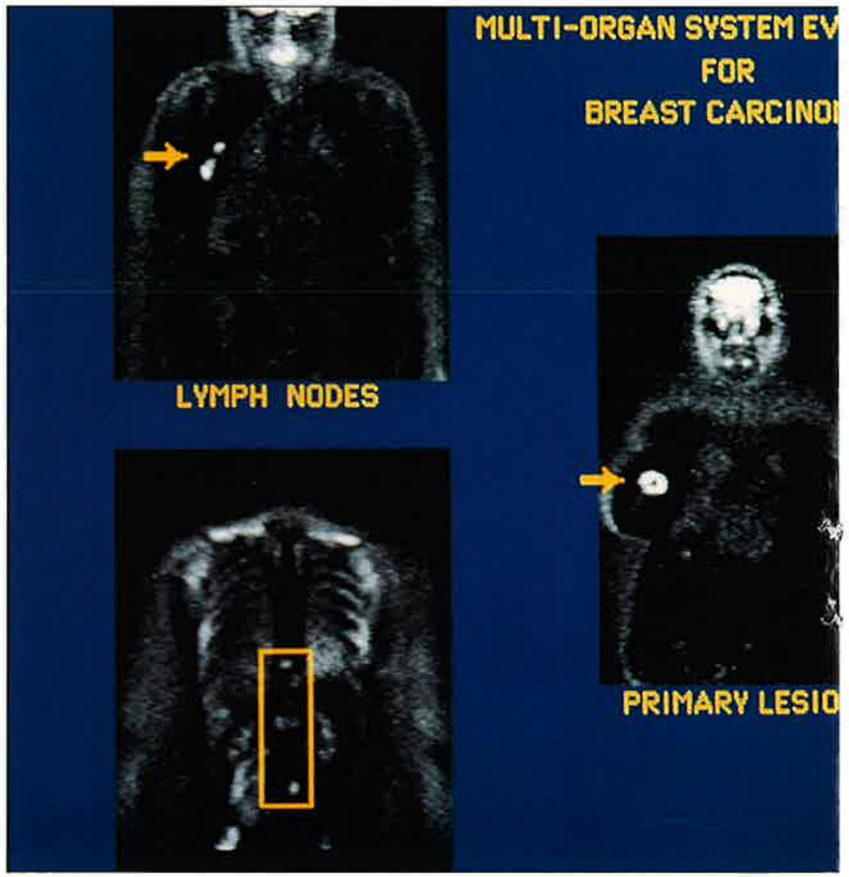
D. MRI examination demonstrates a large, irregularly shaped enhancing mass representing the same cancer seen in the mammogram. However, MRI detects an additional small, 1.5-mm diameter focus of cancer (arrow) missed by a mammogram.

(Photos courtesy of Mitchell D. Schnall, M.D., Ph.D., University of Pennsylvania)

Nuclear Medicine

Nuclear medicine imaging techniques include positron-emission tomography (PET) and gamma camera methods, which produce images of biochemical and physiological processes in the body.

The most widely available PET scan method employs a radioactive form of sugar to produce images of glucose utilization in tumors as well as in the rest of the body.



recently has been the enormous size of the digital file needed to encode a complete mammogram. In order to have the high resolution needed in a mammogram, an image would contain 4,000 pixels in one direction by 5,000 in the other and have about 12 bits of gray scale, for a total of about 240,000,000 bytes (240 megabytes) of information. In contrast, a standard video image contains only approximately 180,000 bytes of information. Over the past few years, the ability to transmit the file size needed for mammography has improved significantly. The National Digital Mammography Development Group funded by the National Cancer Institute that allied an industrial group with an academic medical center demonstrated that a digitized mammogram can be sent from one part of the country to another by a satellite relay in less than 4 minutes without an error. These preliminary data indicate that screening telemammography is feasible using today's telecommunications technologies.

The development of telemammography will permit experts in breast imaging to evaluate images from anywhere in the country or even the world. Underserved women in rural areas and inner cities who do not have access to high-quality breast cancer screening could be visited by a mobile mammography unit. A digital mammogram could be obtained and immediately transmitted by satellite to a breast screening center, where a radiologist could immediately interpret the images and relay any need for additional evaluation back to the mobile unit so that the follow-up could be undertaken while the patient was still at the screening site. The mobile unit would also facilitate the evaluation of lesions found at screening and reduce the likelihood that, if a significant problem was identified, the individual might not be properly evaluated because she would not avail herself of follow-up services that were too far away.

FIGURE 8. TELEMAMMOGRAPHY SYSTEM

(Photo courtesy of Aiman Abdel-Malek, Ph.D., General Electric Company)

Telemammography

Enormous advances are being made in the field of telecommunications. These have resulted in the ability to transmit information virtually instantaneously, anywhere in the world. Remote medical evaluation using standard television video images (telemedicine) has been used for many years and continues to improve and expand so that patients may be evaluated and even receive treatment instituted by physicians hundreds or thousands of miles away.

Television images, however, have significant limitations. Since they are relatively low in resolution, they are not useful for sending breast images that must contain a lot of detail.

Every image can be thought of as a composite of numerous small spots called picture elements (pixels) arrayed in rows and columns. The resolution of the image depends on the size of the spots, and the contrast of the structures in the image depends on the degree of blackness or whiteness of each spot (gray scale). Dividing an image into spots allows a number to be assigned that represents the location and gray scale of each pixel. This converts the image into a "digital" image, since it can be completely represented by a matrix of specific numbers. An image that is in digital form becomes a fixed record that can be transmitted as an electrical signal by telephone lines, dedicated telecommunication lines, or satellite. The transmitted image will be a perfect reproduction of the original when it is sent as a string of numbers. Furthermore, use of numbers to send an image allows carefully devised techniques to correct any mistakes that may occur in the transmission so that the image that is received is exactly identical with the image that was transmitted.

The development of digital mammography will permit more widespread use of telemammography, a technology that will allow mammographic images to be sent anywhere in the world. One of the limitations preventing the transmission of high-quality mammograms until

Like many tumors, breast cancers have higher glucose metabolic rates compared with normal tissues, making it possible to detect primary tumors as well as spread of breast cancer to lymph nodes and other regions of the body with PET (see Fig. 6). Additionally, because PET employs isotopes of carbon, nitrogen, oxygen, and fluorine, among others, many molecules of biological and medical importance can be appropriately "labeled" with these isotopes and imaged with PET. Other examples of relevance to breast cancer include PET imaging of estrogen receptors and chemotherapeutic agents.

Gamma camera methods can be used to detect primary breast cancers and to map the potential spread of disease to lymph nodes.

The major strength of "molecular imaging" with PET and other nuclear medicine techniques is the ability of these methods to detect disease when it may not be visible with other imaging methods, particularly in lymph nodes. Additionally, new research with these methods promises to produce specific biochemical methods for predicting and monitoring the effects of treatment of breast cancer.

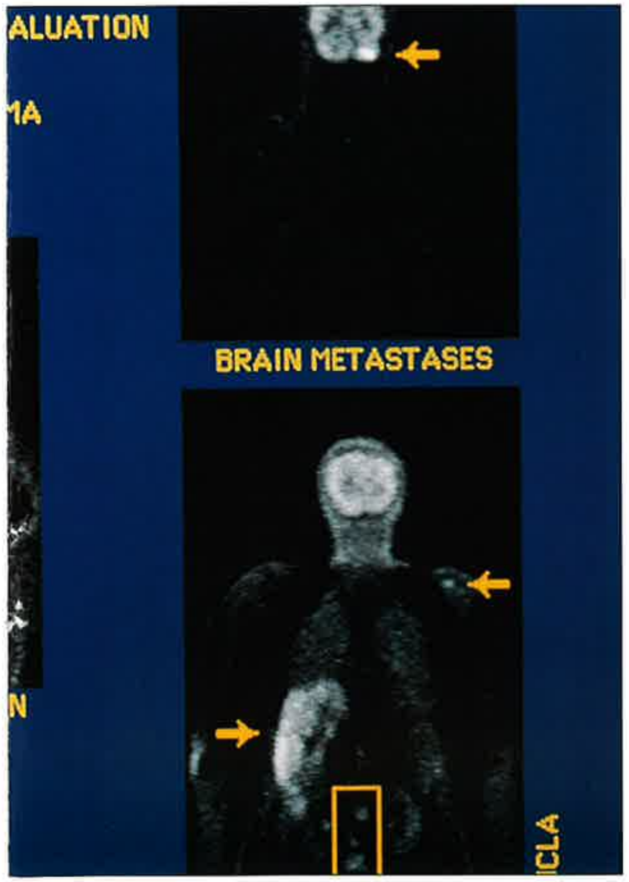


FIGURE 6. Whole-body PET scans with glucose analog FDG. In the center is a primary breast cancer; the other images show metastatic disease elsewhere in the body.

(Photo courtesy of Randall A. Hawkins, M.D., Ph.D., University of California at San Francisco Medical Center)

Ultrasound

Breast ultrasound, unlike other innovative imaging techniques described in this booklet, already has an established role in the diagnosis and management of breast disease. High-resolution, hand-held breast ultrasound is used to determine whether masses found on mammography or clinical examination are benign cysts or solid lesions. The features of solid masses can be further analyzed with high-resolution ultrasound to help differentiate those that are most likely to be benign from those that have malignant characteristics. Ultrasound can then be used to guide procedures such as aspiration of cysts and needle biopsy of suspicious solid masses. Because approximately 50 percent of well-circumscribed masses are benign cysts, reliable ultrasound recognition of their fluid-filled nature is cost-effective in avoiding unnecessary surgical biopsies for ruling out cancer (see Fig. 7).

Ultrasound is not currently used to screen for breast cancer because it often misses microcalcifications, which are important in diagnosing cancer. It is, however, used for the following:

- Characterization of masses as fluid filled or solid, where mammographic diagnosis is uncertain, to avoid unnecessary biopsies.
- Guidance of procedures such as aspiration of cysts, needle biopsies, and, potentially, local tumor treatment.
- First imaging of palpable masses in women who are younger than age 30, pregnant, or lactating.
- Evaluation of an asymmetrical density shown on a mammogram where the cause is suspected to be an underlying mass.
- Confirmation and better imaging of an abnormality spotted on a mammogram but not seen completely.

Sonographic evaluation of breast lesions after administration of enhancing contrast agents is being studied. These agents may help highlight areas of cancer angiogenesis described earlier. Also under investigation are other features that can help identify cancers, such as tissue elasticity (tumors tend to have less elasticity than normal tissue); three-dimensional ultrasound; and computer-aided diagnosis to facilitate image interpretation.

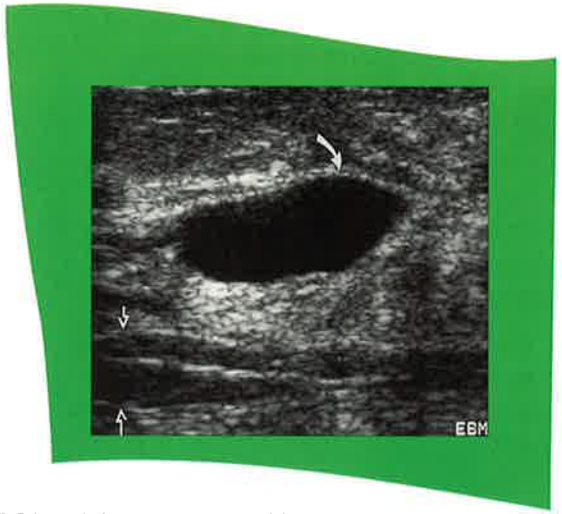


FIGURE 7A. SIMPLE CYST
Four criteria are fulfilled to permit diagnosis of this palpable mass (curved arrow) as a fluid-filled benign cyst. The walls are smooth; the shape is oval; no "echoes" (small white dots of sound) are seen within it; and the acoustic beam travels easily through it, leaving a bright white column behind. Chest muscle (arrow) is at the bottom of the image. The skin is at the top of the image and the cyst is approximately 1.5 cm deep.

FIGURE 7B. COMPLEX CYST
Looking very similar is a fluid-filled mass, although it contains a nodule (arrow) against one wall. Although rare, this was a small cancer that was easily seen within the fluid-containing mass. The mass was removed, and the patient has been doing well.

FIGURE 7C. BREAST CANCER
This irregular mass with indistinct margins (arrows) and a fuzzy rim around it is one of many typical appearances of breast cancer.

(Photos courtesy of Ellen Mendelson, M.D., University of Pittsburgh School of Medicine)