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Techniques for imaging the breast continue to advance, but cost issues may limit their widespread use.

Recent Advances in Breast-Specific Imaging

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Background: *Imaging the breast is a vital component not only for breast cancer screening, but also for diagnosis, evaluation, treatment, and follow-up of patients with breast cancer.*

Methods: *The author reviews recent advances and also provides her personal experience in describing the status of digital mammography, computer-aided detection, dedicated magnetic resonance imaging (MRI), and positron-emission mammography for evaluating the breast.*

Results: *Full-field digital mammography is superior to standard mammography in women under 50 years of age and in those with dense breasts. Computer-aided detection assists inexperienced mammographers and enhances detection of microcalcifications in dense breasts. Breast MRI is useful in preoperative evaluation, clarification of indeterminate mammograms, and follow-up of BRCA mutation carriers. The specificity of MRI remains problematic, however. Positron-emission mammography promises enhanced detection of ductal carcinoma in situ (DCIS), even when not associated with microcalcifications, and should aid surgical planning.*

Conclusions: *These four significant advances in breast imaging have all improved the sensitivity of detecting breast abnormalities. Cost issues, however, may limit the widespread application of these advances.*

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Abbreviations used in this paper: FSM = film-screen mammography, FFDM = full-field digital mammography, CAD = computer-aided detection, PET = positron-emission tomography, PEM = positron-emission mammography, PPV = positive predictive value, DCIS = ductal carcinoma in situ.

Introduction

The increasingly early detection of breast cancer has resulted in significant improvements in the rate of cure in this disease. Major advances in the technologies of imaging provide improved detection and sensitivity with fewer unnecessary biopsies. This article discusses the most promising recent advances in breast cancer imaging, including digital mammography, computer-aided detection, magnetic resonance imaging, and positron-emission mammography.

Digital Mammography

Mammography is the standard of care for the detection of breast cancer in asymptomatic women. It is effective

in reducing breast cancer mortality rates in numerous studies. However, the success of any screening program of asymptomatic women depends on the detection of subtle and small lesions.

Standard film-screen mammography (FSM) has advantages in terms of cost and availability over the newer technology, full-field digital mammography (FFDM). Digital mammography is more expensive, at least at the onset. A digital mammography unit can cost about 10 times the cost of a standard unit (\$500,000 vs \$50,000). This is an important concern since screening mammography is poorly reimbursed and puts the interpreting physician at unusual risk for malpractice lawsuits. The American College of Radiology Imaging Network (ACRIN) study¹ showed that the cost of FFDM was 1.5 to 4 times greater than the cost of FSM. Another advantage of FSM is that it offers high spatial resolution. Image display is carried out with traditional view boxes that are convenient and widely available. It is possible to simultaneously display multiple images with as many images and studies as there are view boxes available. A recent study quantified the increased interpretation time required for FFDM compared to FSM.² The average time requirement for FFDM was 2.3 minutes compared with 1.4 minutes for FSM. This represents a significant differential time commitment in a busy screening practice.

The disadvantages of FSM are also clear. The images are immutable once acquired and cannot be adjusted or modified in any way. There is no way to correct technique that is over- or under-exposed. The only tools available to the mammographer are the hot light to view over exposed images and the skin surface, and the magnifying glass to observe fine detail and microcalcifications. Another disadvantage of FSM involves film reproduction and storage. Copied films are usually nondiagnostic as it is impossible to replicate the fine detail of the original images. This limits effective communication between the mammographer, patient, and surgeon. Hard-copy films must be stored, which requires an accessible film library with physical space and staff. Lost or misplaced films are irretrievable; this poses enormous problems in patient follow-up and in the advent of lawsuits.

The newer technology of FFDM, despite its cost, clearly offers major advances in mammographic practice. FFDM allows for the decoupling and optimization of the processes of image acquisition, display, and storage. The technologist can take images and almost instantaneously review them to assure proper positioning and technique. Once the quality of the exposures is assessed, the technologist can repeat any images deemed necessary. The processing time is reduced overall by at least 80%, which dramatically improves efficiency.³ Postprocessing of the images can reduce the number of recalls for technical reasons or for magnification.

Digital imaging is useful in performing and streamlining needle localization and stereotactic procedures. The time necessary for a patient to remain still and in compression for these procedures is greatly reduced when using digital imaging. It takes about 3 minutes for a technologist to chemically process traditional films; digital images are available within seconds.

Theoretically, the radiation dose employed with FFDM can be reduced compared to the dose incurred with FSM. However, this cannot be practically justified. The dose employed with FSM is already quite low. The dose necessary to achieve comparable or improved image resolution with FFDM is comparable to the dose employed with FSM.

An important advantage of digital imaging over the traditional approach involves image storage and transfer. Images can be viewed in soft copy on a workstation and stored in a digital format. The studies can be shared with the patient and surgeon by making hard film copies, or exact digital copies can be viewed through hospital or clinic archival systems or by downloading studies from compact disc. There is the potential to never lose or misplace films.

Digital imaging allows for tremendous flexibility in image evaluation to the mammographer. Soft-copy displays allow the mammographer to adjust contrast and window levels, magnify all the breast tissue as well as any focal areas of interest, and invert the color display. These digital techniques can improve visualization in dense breasts, cosmetically implanted breasts, processes involving the skin, and microcalcifications. Special computer algorithms have been developed to assist in the detection of suspicious findings such as spiculations and calcifications. Also, soft-copy or computer displays allow for the ready incorporation of computer-aided detection (CAD) and diagnosis programs that can further improve the sensitivity of cancer detection.

Digital imaging is necessary for the future utilization of telemammography. The most cost-effective approach to breast cancer screening may be achieved when digital images are taken at remote centers or on mobile units and transferred electronically to reading centers. This might streamline the process and allow for greater utilization of screening mammography, especially in remote, rural, and underserved areas.

The Colorado-Massachusetts Screening Trial⁴ undertaken between 1997 and 2000 was the first large clinical comparison of FFDM and FSM for the detection of breast cancer. There was no significant difference in the breast cancer detection rate when over 6,700 paired FSM and FFDM results were compared. Of the 42 cancers diagnosed, 18 were detected with both modalities, 9 with FFDM only, and 15 with FSM only. It is important to note that only prototype soft-copy display equipment was available, which effectively neutralized some of the greatest advantages of FFDM. This

study demonstrated a statistically lower recall rate with digital imaging (11.8% vs 14.9%).

The Oslo I study⁵ attempted to compare FFDM with soft-copy reading and FSM in a large screening population. This study also showed no significant difference in detection rates when about 3,700 paired examinations results were reviewed. The cancer detection rates were 0.76% with FSM and 0.62% with FFDM. Twenty cancers were detected on both modalities, 8 with FSM only, and 3 with FFDM only. The recall rates were comparable: 3.5% for FSM and 4.6% for FFDM. However, a retrospective analysis of the images from this study showed that inexperience using the digital equipment and soft-copy reading might have led to interpretation errors that could be overcome with experience. Viewing conditions, reader experience, imaging processing, and detection algorithms were not optimized for the FFDM.

The Oslo II study⁶ assessed the results of over 25,000 paired screening studies in breast cancer detection and found that FFDM and soft-copy reading is equivalent to FSM and is suitable for screening.

More recently, the National Cancer Institute and ACIN evaluated nearly 50,000 women in a trial comparing these modalities.¹ The results showed that although FFDM and FSM are equivalent for the entire population, FFDM is significantly better for breast cancer detection in women younger than 50 years (regardless of breast tissue density), women with heterogeneously dense or extremely dense breasts (regardless of age), and in pre- or peri-menopausal women. Sixty-five percent of the participants fit into one of these subsets showing benefit from digital imaging. No benefit was seen in women over 50 years of age, in those with fatty breasts, or in those who were postmenopausal. Callbacks were 8.4% with both modalities.

In summary, FFDM provides the mammographer with an effective way of performing large-scale screening for breast cancer. It has been shown to confer an advantage in diagnosing breast cancer in young women, women with dense breasts, and women who are pre- or peri-menopausal. The callback rates are at least equivalent to traditional FSM. Also, the digital format offers better transfer and storage of images and the ability to use other digital techniques such as CAD in concert.

Computer-Aided Detection

The false-negative rate for mammography has been reported to be between 10% and 30%.^{3,7,9} Although many cancers are occult mammographically, especially in radiographically dense breasts, the largest portion of false-negative cancers are visible in retrospect. Blinded reviews of prior mammograms showed that 25% to 41% of cancers seen with screening mammography

could be seen retrospectively.⁷⁻¹⁰ These cancers are either overlooked or not perceived as worrisome by the imager, both of which need to improve in order to increase cancer detection rates.

Perceptual oversights can be reduced through the use of double reading. Sensitivity can be improved by 4.6% to 15% when two radiologists are used rather than one.^{7,11} Cancers detected through double reading are detected at an earlier stage of development. However, the additional costs incurred from double reading are prohibitive.

CAD programs are commercially available systems that use computer software to assist the mammographer in detecting or identifying potentially suspicious abnormalities on a mammogram. The CAD program identifies potential abnormalities on the images and marks areas on the study that the computer considers to be suspicious. The radiologist reviews the flagged areas to assure that nothing was missed. FFDM readily provides images that can be used with CAD. FSM has to be digitized in order for CAD to be performed. The digitization process is time consuming, but the results of CAD from digitized FSM and FFDM are equivalent.¹²

CAD systems have proven to be quite sensitive in detecting breast cancers on screening mammograms. Studies have shown that CAD correctly flagged 98% of microcalcifications, 86% to 88% of masses, and 90% of all cancers.^{3,13} The detection rates tend to increase with the level of mammographic suspicion.¹² Specificity, however, proves to be a problem with CAD. The number of false prompts varies with the level of sensitivity, and one false prompt per image is allowed. CAD tends to falsely mark benign calcifications (ie, vascular calcifications) and overlapping breast tissue. Experienced mammographers learn to ignore false-positive prompts without an increase in callbacks.

The use of CAD in screening mammography has reportedly improved cancer detection. A 19.5% increase in cancer detection, from 3.2 to 3.8 cancers per 1,000, was reported in a high-volume screening study of about 13,000 women.¹⁴ Seven of the 8 additional cancers detected were microcalcifications, which seem prone to oversight error. Most importantly, the proportion of early-stage cancers increased from 73% to 78%. The recall rate increased from 6.5% to 7.7%, or by about 19%. The positive predictive value (PPV) at biopsy was unchanged at 38%.

Morton et al⁷ prospectively evaluated the impact of CAD on screening mammography and found that CAD improved cancer detection with mild increases in recall rate and benign biopsies. A total of 21,349 screening mammograms of 18,096 women were reviewed with and without the use of CAD. The preliminary evaluation resulted in 2,101 patients being called back for further evaluation, and 256 biopsies were performed yielding 105 cancers for a breast can-

cer detection rate of 4.92 per 1,000. An additional 199 patients were recalled following the application of CAD. Eight more cancers were recovered after an additional 21 biopsies. CAD resulted in a relative increase of 7.62% in cancers detected, improving a rate of 4.92 per 1,000 without CAD to 5.92 per 1,000 with CAD. The recall rate pre-CAD was 9.84% and increased to 10.77%. The pre-CAD PPV of biopsy was 41.0% and the PPV for CAD was 38.0%. The mammographers in this study found 105 (92.9%) of 113 cancers while CAD identified 86 (76.1%) of 113 cancers. The 8 cancers not perceived by mammographers were microcalcifications (62%), noncalcified masses (25%), and architectural distortion (12%). The 27 cancers not flagged by CAD were mass or density (93%) and architectural distortion (7%). No cases of microcalcifications were missed using CAD.

The impact of CAD on the false-negative rate was explored following a review of 1,083 screening mammograms with biopsy-proven breast cancer on the most recent mammogram in 427 cases.¹⁰ A retrospective review by a panel of 5 radiologists of the prior mammograms of these biopsy-proven breast cancer cases showed that 286 (67%) of 427 were visible and that 115 (27%) of 427 of these warranted recall. CAD flagged 89 (77%) of these 115 cases. Utilization of CAD could have decreased the false-negative rate of 21% by 77%. There was no significant increase in recall rate prior to and following the use of CAD (8.3% and 7.6%, respectively).

A prospective study by Dean and Ilvento¹⁵ looked at the impact of CAD on the interpretations of nearly 10,000 consecutive mammograms. Ten (9.6%) of 104 cancers were detected only with CAD assistance. CAD assistance increased screening-detected cancers by 13.3%. CAD had the greatest effect on ductal carcinoma in situ (DCIS) by increasing detection by 14.2% (3 cancers in addition 21 already detected). Here again, the additional CAD-detected cancers were significantly smaller. The recall rate increased from 6.2% to 7.8% following the introduction of CAD. CAD resulted in a decrease in biopsy rate with a nonsignificant increase in PPV of 26.3% from 21.9%.

CAD systems show excellent sensitivity for malignancies associated with microcalcifications. In a study of 273 breast cancers, CAD correctly flagged 84% of masses, 98% of microcalcification cases, and 89% of mixed mass/microcalcification lesions.¹⁶ The sensitivity for identifying invasive cancers with calcifications was 100%, and the system showed a high sensitivity for the detection of DCIS (95%), invasive lobular cancer (95%), and invasive ductal carcinoma (85%).

The addition of CAD was shown to improve the detection rate of breast cancers in a screening population from 90% to 94%. Ko et al¹⁷ reviewed about 5,000 studies, yielding 48 malignancies. Eight of 48 cancers were missed with CAD but detected by the radiologist.

These included 3 cases of architectural distortion, 4 irregular masses, and 1 circumscribed mass. Two faint clusters of microcalcifications were detected only with CAD and proved to represent DCIS. CAD flagged a mass that was dismissed by the imager. The sensitivity of screening studies increased from 90% to 94% with CAD. The specificity of screening studies with and without CAD was 99%. The recall rate with the addition of CAD increased from 12% to 14%.

Increased breast density has a major adverse impact on conspicuity of lesions on mammography. In a small CAD study, Ho et al¹⁸ found a significant decrease in sensitivity with increasing breast density among 15 cancers in a series of 264 mammograms. A sensitivity of 93.3% was achieved along with 1.3 false prompts per image in totally fatty breasts. In breasts with a scattered fibroglandular pattern, the sensitivity was 93.9% with 1.6 false-positive prompts. In heterogeneously dense breast tissue, the sensitivity was 84.8% with 1.6 false-positive prompts. Markedly dense breasts showed a sensitivity of only 64.3% at a specificity of 1.2 false-positive prompts.

In a larger study, Brem et al¹⁹ analyzed 906 mammographically detected breast cancers along with 147 normal studies and did not find a decrease in overall sensitivity with CAD with increasing breast density. Of 906 cancers, 90% of cancers were detected with CAD in nondense breasts and 88% in dense breasts and 90% overall. They identified excellent sensitivity for microcalcifications in dense breasts using CAD: 95% vs 93% in nondense breasts. However, they also found that increased breast density diminished detection of masses, as the detection rate dropped from 89% in nondense breasts to 83% in dense breasts. Mirroring the experience of Ho and colleagues noted above, these investigators found that breast density also affected the number of false-positive prompts with more prompts in denser breasts.^{16,19}

While CAD can improve the performance of seasoned mammographers as well as the less experienced, it seems to be most helpful in situations where the mammographer is less experienced or reads fewer studies. A study by Chu et al²⁰ involving symptomatic Asian women showed a 7.4% increase in the number of masses and 10.4% increase in microcalcification clusters identified by experienced mammographers reading with CAD compared to increases of 13.7% for masses and 27.3% for microcalcifications identified by less experienced readers using CAD.

In summary, numerous studies have demonstrated the positive effects of CAD on breast cancer detection rates in screening mammography. CAD does not seem to significantly increase recall rates, although the algorithms allow for many false-positive prompts. CAD has the greatest potential impact on finding microcalcifications, particularly in dense breasts, that might otherwise be overlooked by radiologists. CAD can also have

false-negative results; therefore, the absence of CAD detection of an otherwise suspicious mammographic finding should not preclude a diagnostic workup.

Breast Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) of the breast proves to be a valuable adjunct to the more traditional means of evaluating for breast cancer along with mammography, the physical examination, and sonography. Studies have shown nearly 100% sensitivity in detecting invasive breast carcinomas, although most show poor specificity.²¹

Performing diagnostic breast MRI requires dedication and attention to detail. Most breast imagers prefer studies performed on a high-field strength (>1.5 Tesla) magnet with a dedicated breast radiofrequency coil. A standard imaging protocol should be developed to optimize imaging breast tissue prior to and following the dynamic administration of ferromagnetic contrast with gadopentate dimeglumine (Gd-DTPA). Additional image series should be performed to optimize visual-

ization of silicone and to further differentiate benign from malignant findings.

Contrast enhancement with Gd-DTPA is essential in identifying breast cancers and distinguishing malignancies from benign findings.^{22,23} Cancers have a tendency to enhance briskly and vividly. Kaiser and Zeitler²⁴ found a 100% increase in signal intensity within the first 2 minutes of contrast enhancement. Kuhl et al²⁵ evaluated contrast kinetics and contrast wash-out curves to distinguish benign from malignant lesions. The cancers were found to have rapid wash-in of contrast and either a rapid wash-out of contrast or a leveling off of contrast. These two patterns of dynamic contrast enhancement yielded 91% sensitivity and 83% specificity for malignancy detection. Slow, progressive enhancement was seen in 137 (83%) of 165 benign lesions and in 9 (6%) of 146 malignant lesions. Three different patterns of dynamic contrast enhancement were described. The type I pattern (persistent) shows slow, progressive contrast uptake over time and is suggestive of benignity (Fig 1). The type II contrast pattern (plateau) shows a rapid uptake in contrast and then a plateau or leveling off of uptake. This pattern is suggestive of malignancy (Fig 2). The type III curve shows rapid uptake of contrast and then a sudden complete wash-out of contrast. The type III pattern (wash-out) is indicative of malignancy (Fig 3). Therefore, it is necessary for imaging protocols to include rapid temporal sampling. Normal lymph nodes often show early, brisk enhancement and the type III pattern (wash-out) kinetics.

An evaluation of contrast kinetics should be made. Several software programs are commercially available that assess the degree of contrast enhancement, speed of uptake, and elimination of contrast. Kinetic curves can be generated and lesions can be color-coded based on kinetics.

Subtraction images are especially helpful with lower-field-strength magnets. The images of the breast prior to the administration of contrast are digitally superimposed over and subtracted from the contrast-enhanced images. Any areas of contrast enhancement are “subtracted out” and become quite visible to the interpreter. Any motion during the MRI will degrade the quality and usefulness of the images.

The diagnostic evaluation must also include the assessment of lesion morphology, which requires high-resolution imaging. The border of the lesion is the most important feature of lesion evaluation. Spiculated and irregular margins have a PPV for malignancy ranging from 76% to 91%.^{21,26,27} Most benign masses have smooth borders with a negative predictive value for malignancy of 90%. Morphologic enhancement patterns also yield information about the lesion. Irregular rim enhancement has a PPV for malignancy of 79% to 92%. Heterogeneous enhancement of a mass has been shown to have a PPV for malignancy of 84%.²⁸

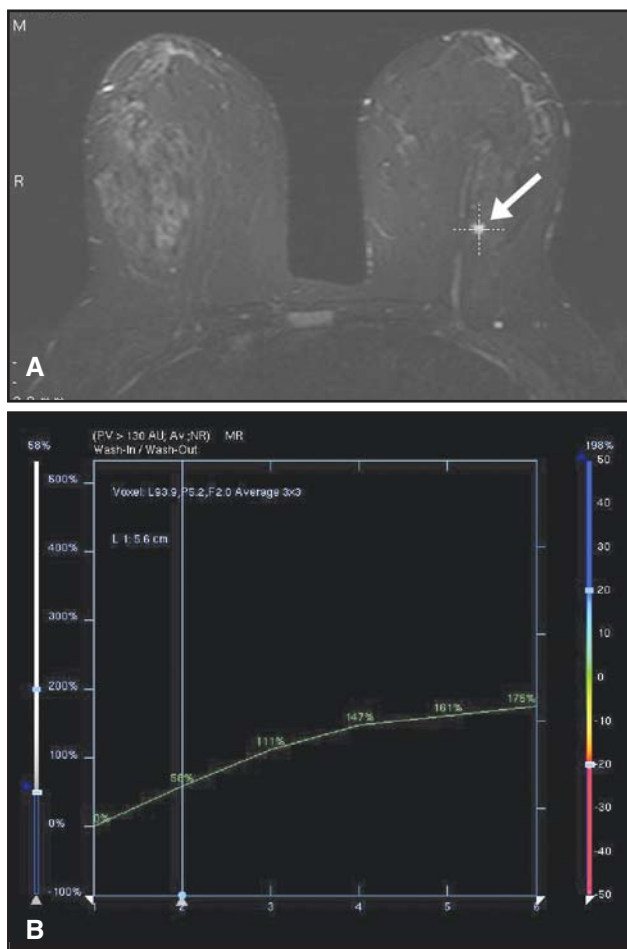


Fig 1A-B. — (A) A well-circumscribed enhancing lesion in the central left breast (arrow). (B) Type I, slow, progressive, persistent enhancement curve suggestive of a benign nature for in this fibroadenoma.

Confluent areas of uniform enhancement are associated with benign tissue, as are multiple, focal, tiny stippled areas of enhancement separated by normal tissue. Malignancy (especially DCIS) is suggested by small, clumped foci that are within a segment or duct. The PPV for malignancy in the presence of ductal enhancement is 80% to 85%.^{21,29}

The precise role of MRI is evolving. One of the most widely used indications for imaging is to preoperatively evaluate known tumors for size of tumor, extent of disease, multicentricity, and multifocality. As such, MRI can have a huge impact on the surgical approach.

Boetes et al³⁰ correlated the pathologic size of 61 breast cancers with mammography, sonography, and MRI. The pathologically determined tumor size correlated well with the size of the tumor identified by MRI. Tumor size relative to pathologic measurements was found to be 14% smaller on mammograms and 18%

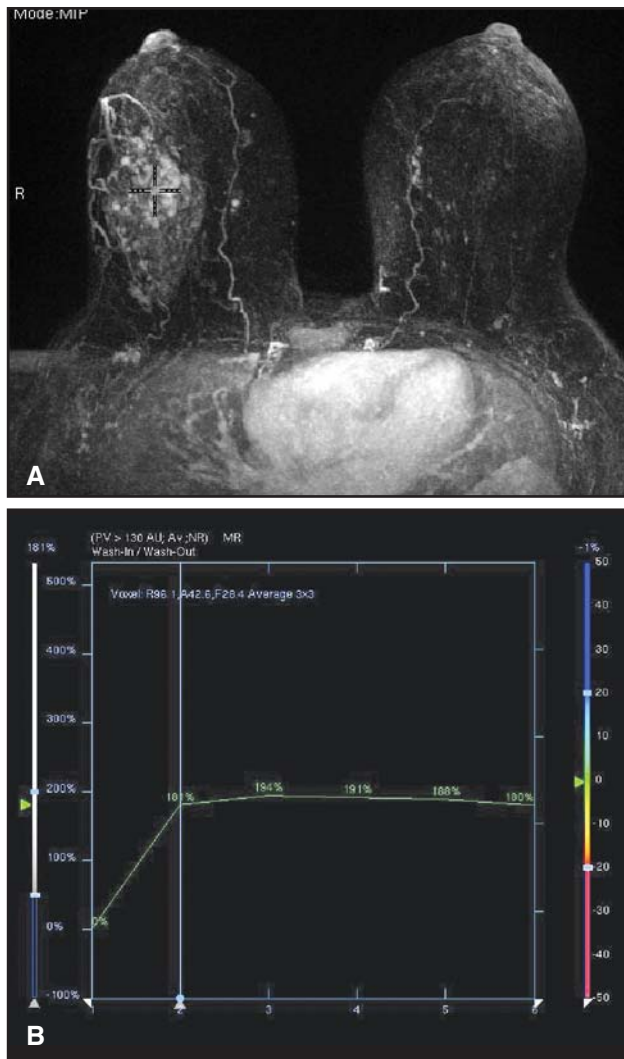


Fig 2A-B. — (A) Maximum intensity projection (MIP) image or volume rendered subtraction image that shows clumped, small foci of enhancement in a regional distribution involving the lateral right breast in a patient with DCIS. (B) Type II curve with rapid uptake of contrast enhancement and a plateau of uptake suggestive of a malignant process.

smaller on sonograms. However, enhancement in the region of a tumor may be related to benign findings and should be evaluated carefully.

MRI can show the extent of disease and is particularly valuable, at least in comparison to the other available modalities, in invasive lobular cancers and tumors with an extensive intraductal component.^{31,32} Multifocal tumors (multiple lesions confined to one quadrant) and multicentric tumors (multiple lesions arising in different quadrants) are better imaged by MRI than by conventional methods.^{33,34} Multifocal and multicentric cancers were found in 27 (26%) of 104 women in a study by Hlawatsch et al.³⁵ Mammography showed 48%, sonography and mammography 63% and MRI with mammography 81% of additional ipsilateral tumors.

Additional sites of cancer in the ipsilateral breast were present on MRI in 19 (27%) of 70 women studied at Memorial Sloan-Kettering Cancer Center.³⁴ Of these 19 women, 8 (42%) had DCIS and 11 (58%) had infiltrating cancer. Of the 70 women studied, multifocal cancer was present in 14 (20%), multicentric cancer in 3 (4%), and multifocal and multicentric cancer in 2 (3%).

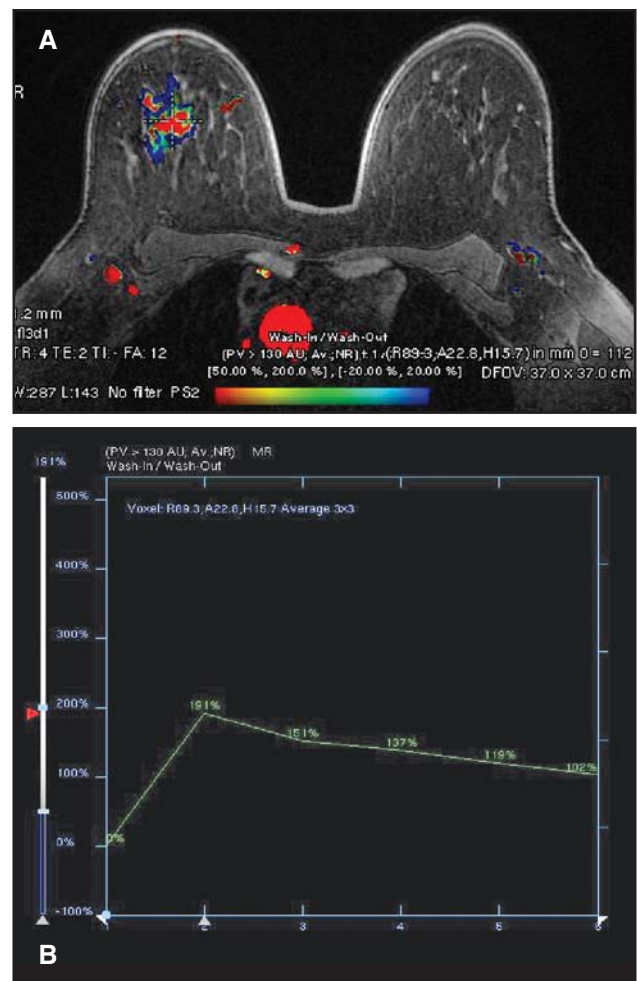


Fig 3A-B. — (A) Brightly colored focus in the central right breast representing a cancer identified with a CAD program. (B) Type III pattern with rapid uptake and wash-out of contrast consistent with a malignancy.

Therefore, about three fourths of the additional ipsilateral cancer was within the same quadrant. Seventeen (24%) had MRI-detected benign ipsilateral lesions.

A study by Fischer et al³⁵ showed that as many as 6% of patients undergoing preoperative breast MRI had synchronous cancers and that there were additional relevant findings in 16% of the patients.

Occult contralateral breast cancers can be found with MRI in 4% to 9% of patients. In a study performed at Memorial Sloan-Kettering Cancer Center,³⁶ MRI detected contralateral breast cancer that was occult mammographically and by physical examination in 5% of women with a known breast cancer. This capacity of MRI for detecting breast cancer in the apparently uninvolved contralateral breast of women with recently diagnosed breast cancer has been further described in a multi-institutional study of 969 women.³⁷ Biopsy-appropriate lesions were identified in the apparently benign contralateral breast in 12.5% of these women. Approximately 25% of these biopsies contained malignancy (3.1% of the entire group), of which over half were invasive. Also notable was the negative predictive value of MRI at 1 year, 99%.

In a recent noteworthy study,³⁸ investigators from Germany obtained confirmed diagnoses of DCIS in 167 women from a screening population of 7,000 women. Mammography and breast MRI were both utilized. Ninety-two percent of DCIS lesions were identified on MRI compared to 56% on mammography. For the high-risk subgroup with high-grade DCIS, 98% were identified on MRI vs 52% on mammography. While encouraging, these data do not yet constitute a justification for the standard use of MRI, given the lack of protocol standardization, concerns about the negative impact of false-positive studies, and the question of cost.

Re-excision of margins is performed in patients who have close or positive surgical margins to minimize the chances of local recurrence. Enhancing granulation tissue cannot be reliably distinguished from residual tumor using MRI until 28 to 35 days following biopsy.³⁹ This may limit the usefulness of MRI in directing re-excision.

The largest randomized trials show that recurrence rates following breast conservation therapy are 8.8% to 14.3% at 20 years of follow-up.^{40,41} The breast is often difficult to follow with mammography or physical examination after treatment due to increased firmness from scar tissue, fibrosis, and fat necrosis.

Scar tissue becomes less vascular after 9 to 18 months and enhances minimally or not at all. Fat necrosis can be problematic not only on MRI, which can show solid brisk enhancement, but also on mammogram and physical examination. MRI can distinguish mature scar at the site of lumpectomy from recurrence with sensitivities of 93% to 100% and specificities of 88% to 100%.⁴²

Breast MRI is being used increasingly as a problem-solving tool or for indeterminate findings on a mammogram. There is a negative predictive value of 97% to 100% for mammographic abnormalities that lack Gd-DTPA enhancement.^{26,43} A study by Lee et al⁴⁴ showed the utility of breast MRI when a mammogram shows indeterminate findings. Negative histology and/or stable follow-up mammography was found on 60 of 89 mammographically indeterminate cases that showed no abnormal contrast with MRI. All of the lesions that lacked contrast enhancement proved to be benign, and 35% of the enhancing lesions proved to be malignant.

The absence of MRI enhancement excludes most cancers, but the presence of enhancing lesions can be nonspecific as Gd-DTPA enhancement can be found with normal tissue, hormonal stimulation, fibrocystic disease, inflammatory processes, hyperplasia, and dysplasia. Fibroadenomas can be especially problematic for MRI diagnosis. In one series, overlapping features with malignancy were present in 20% of fibroadenomas with MRI.⁴⁵

False-negative studies can occur with invasive lobular cancers and DCIS, which does not always show rapid or intense enhancement. The overall accuracy of MRI in a study of 62 women with microcalcifications was 56%.⁴⁶ Any mammographically indeterminate calcifications should be sampled.

Occult primary breast cancers presenting as metastatic disease in axillary lymph nodes are unusual. MRI can be helpful since identifying a primary tumor can direct the surgeon and allow for lumpectomy rather than mastectomy. MRI found the occult tumor with axillary lymph node metastases and no palpable or mammographic findings in 75% of 12 women, 86% of 22 women and 70% of 40 women in various studies.⁴⁷⁻⁴⁹

Spontaneous unilateral serosanguineous or bloody discharge can be evaluated with MRI assistance. MRI was able to correctly identify all 8 women with invasive cancers in a study of 48 women with nipple discharge.⁵⁰ Orel et al⁵¹ found that MRI could identify the underlying lesion in 73% of 15 women with discharge who underwent surgery. This included all 7 women who had carcinomas. MRI also can be helpful in demonstrating a poor response to chemotherapy. This allows the oncologist the option of changing regimens. MRI does not appear to be reliable in determining the extent of disease following chemotherapy and can overestimate or underestimate the extent of residual disease. Granulation tissue associated with tumor regression can enhance vividly, making it indistinguishable from viable tumor. Also, chemotherapy can decrease tumor enhancement, making the evaluation of contrast kinetics unreliable.⁵²

The value of MRI screening in patients at high risk for developing breast cancer such as those with *BRCA* mutations has been studied. Occult cancer has been

detected in these women at rates between 2% and 7%. However, additional follow-up and benign biopsies will be generated when patients are screened.

A meta-analysis by Morris et al⁵³ that included 1,305 women at high risk for developing breast cancer who were studied with breast MRI showed mammographically occult cancer in 4% (range: 2% to 7%) of the women screened. The PPV of biopsy was 34%, which is commensurate with mammographically detected lesions in a general population. About one third of the cancers were DCIS and two thirds were invasive carcinomas. Biopsy was recommended in about 14% of patients (range: 7% to 18%). Benign biopsies were performed on about 9% (range: 1% to 15%) of the women screened. High-risk lesions such as radial scar, atypical hyperplasia, and lobular carcinoma in situ were found in 22% of women undergoing biopsy and in 4% of women screened.

The American Cancer Society guidelines for breast cancer screening with MRI as an adjunct to mammography have recently been updated.⁵⁴ However, only limited guidance is provided. The panel recommends that MRI be included in women with a 20% to 25% or greater lifetime breast cancer risk. This group is composed of those with strong family history of breast or ovarian cancer (including those with *BRCA* mutations) and those treated for Hodgkin's disease with chest radiation. No guidance is available for the many subgroups at risk who constitute the overwhelming majority of patients in clinical practice. Among these are women with a history of prior invasive and noninvasive breast cancers, with atypical hyperplasia, and with extremely dense breasts.

MRI has been used to evaluate the integrity of saline and silicone implants, to discern intracapsular from extracapsular rupture, and to identify silicone within the breast parenchyma. Using silicone selective sequences, Monticciolo et al⁵⁵ evaluated 38 implants in 28 women. These sequences found 20 (95%) of 21 intact implants at surgery and correctly identified 17 leaky implants. The MRI agreed with mammography in 30 (88%) of 34 cases, with MRI being correct in 3 of 4 of the disagreements.

Berg et al⁵⁶ found that MRI was superior to sonography in detecting implant ruptures in patients with both double and single lumen implants. Sonography had a sensitivity of 65% and a specificity of 57% in 122 women with single lumen implants compared with 98% sensitivity and 91% specificity for MRI. The sensitivity was 20% and specificity 20% in the 22 women with double lumen implants using sonography compared to 80% sensitivity and 90% specificity seen with MRI.

In summary, breast MRI promises to be a useful adjunct to mammography, sonography, and physical examination in the preoperative evaluation of patients with known breast cancer. MRI can be used to follow patients after lumpectomy and those with problematic

or indeterminate mammograms. Women with occult primary breast cancers and those with nipple discharge can benefit from MRI examination. The role for MRI in screening high-risk patients appears promising. MRI is the most accurate means of ascertaining breast implant integrity. However, the poor specificity of MRI can lead to many benign biopsies. MRI must be performed and interpreted under rigorous conditions.

Dedicated Breast Positron-Emission Tomography or Positron-Emission Mammography

Most breast malignancies have greater metabolism than normal tissues and concentrate 18F-fluorodeoxyglucose (FDG), the agent most widely used in clinical positron-emission tomography (PET) scanning. Whole-body PET is expensive, and although whole-body PET has shown good specificity for breast cancers, spatial resolution is poor and there is volume averaging of small lesions. This results in poor sensitivity, especially in the smaller tumors found in a screening population.

Several small, compact dedicated PET scanners have been developed that are easily incorporated into a breast imaging program. These dedicated scanners improve spatial resolution and geometric sensitivity for the detection of the emitted radiation and reduce photon attenuation. In some instances a dose of FDG as low as 2.0 mCi can be employed, which reduces radiation exposure to the patient and staff. These units are similar in size and configuration to either a traditional mammography gantry system or a prone biopsy table. Gentle compression is used providing the advantages of spreading out the breast tissue for imaging and making the images comparable to standard mammographic views. The images can also be reconstructed into three dimensions for localization of abnormalities.

A preliminary study was undertaken by Rosen et al⁵⁷ from Duke University to assess the value of dedicated positron-emission mammography (PEM). They studied 23 women with 23 lesions for which definitive histology was subsequently available. All lesions were identified as being highly suggestive of malignancy on mammography and/or sonography (BI-RADS 5⁵⁸). PEM was performed approximately 1 hour after the intravenous administration of 2.0 to 2.5 mCi FDG with the patient gently compressed in the craniocaudal position. Five-minute acquisitions were processed and reconstructed in the transverse craniocaudal and coronal planes. Core needle biopsy was performed following imaging. Given the small numbers of patients and the exclusion of true negative cases, useful statistics cannot be derived from this study. PEM failed to detect 3 of the 20 mammographically identified malignant lesions. These were located in the posterior third of the breast,

which is more difficult to image with the current equipment due to technical and positioning factors. Improvements in equipment design should yield better results. Also, there were instances of false-positive PEM results in 2 cases of benign fat necrosis and 1 case of benign microcalcifications within fibrocystic disease.

A prospective pilot study of PEM conducted by Taft et al⁵⁹ blindly evaluated images from 44 women with a confirmed diagnosis of malignancy. The median size of the index or presenting tumor was 22 mm (range: 1 to 100 mm) on pathology. Thirty-one (70%) of 44 index lesions were nonpalpable. Seven (54%) of 13 palpable lesions were found in mammographically

dense tissue (Fig 4). PEM demonstrated 39 (89%) of 44 of the presenting or index cancers. In 3 cases, extensive DCIS was found only with PEM. Multifocal disease was correctly ruled out in 17 of 17 (100%) suspected cases but accurately predicted in only 9 (64%) of 14 cases. However, it was the retrospective opinion of the surgeons that PEM would have been helpful in 6 cases with positive margins had the findings been available to them preoperatively. The cancers missed on PEM included a tumor in a very posterior position, a 1-mm lymphoma, a 6-mm low-grade tubular carcinoma, and 3-mm intermediate-grade and 10-mm low-grade infiltrating ductal carcinomas. Also missed were incidental cases of Paget's disease and DCIS in contralateral breasts.

A study by Berg et al⁶⁰ involved PEM examination of 77 women with 77 index lesions and 15 incidentally discovered lesions that were all histologically proven. Of the patients enrolled, suspicious findings on core biopsy were found prior to PEM in 33 cases, 6 had suspicious clinical breast examinations, and 38 had abnormal mammograms. PEM was positive in 39 (93%) of 42 index cancers. When incidental cancers were included, PEM was positive in 43 (90%) of 48 malignancies. Thirty-three (92%) of 37 invasive cancers and 10 (91%) of 11 cases of DCIS were PEM positive. Three intermediate-grade foci of DCIS were seen only with PEM (Fig 5).

Berg et al⁶¹ reported that the use of sonography and magnetic resonance imaging (MRI) contributed to the detection of additional malignant foci unsuspected clinically or mammographically in 27% to 48% of women in their study. However, overestimation of disease extent can be attributed to 21% of MRI and 12% of ultrasound cases. The authors found that PEM combined with mammography and sonography yielded 47 (98%) of 48 cancers, improving sensitivity without reducing accuracy (Fig 6). Indeed, it was the retro-

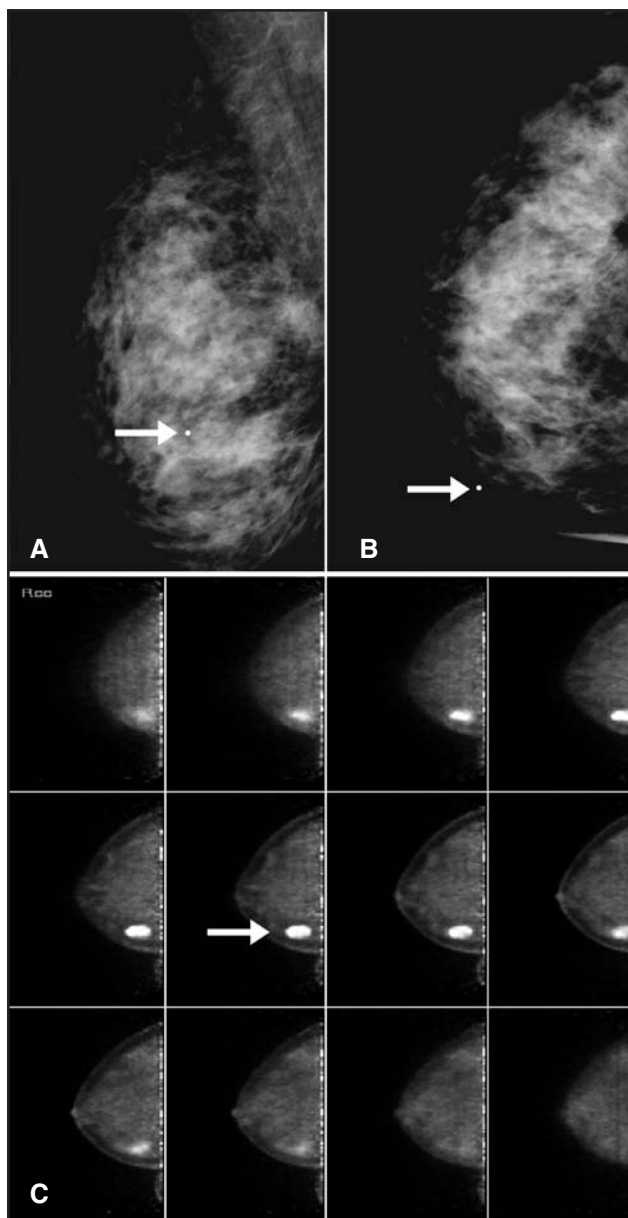


Fig 4A-C. — (A) Mediolateral oblique and (B) craniocaudal mammographic views of the right breast showing dense tissue that obscures the palpable cancer, which is noted by the placement of radiodense markers and arrows. (C) The cancer is clearly seen in the inferior right breast (arrow) on PEM images. (Courtesy Naviscan PET Systems, Inc.)

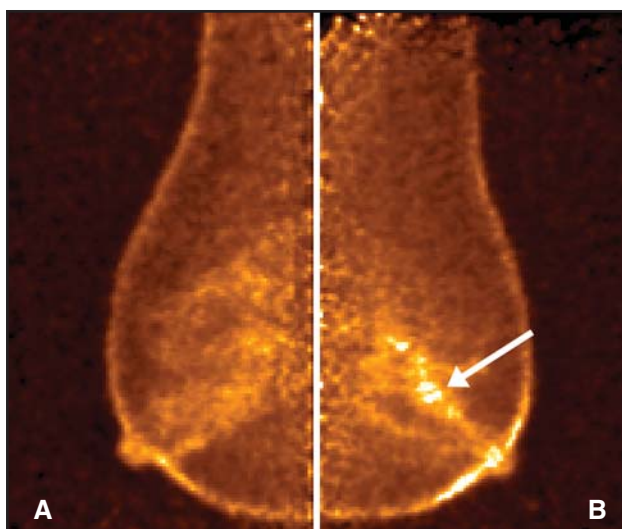


Fig 5A-B. — (A) Mediolateral PEM images of the normal right breast and (B) DCIS (arrow) extending in a linear fashion from the nipple toward the chest wall. (Courtesy Naviscan PET Systems, Inc.)

spective opinion of surgeons that in 6 of 8 unsuccessful lumpectomies, definitive surgery would have been more likely had PEM information been used preoperatively. It should be noted that the method of calculating standardized uptake value (SUV) in this study is nonstandard. Quantification of the degree of glucose metabolism was made by comparing the degree of uptake within the tumor relative to breast fat or glandular tissue. This is not comparable to the standard method, which is based on variables such as lean body mass and injected dose. The SUV information provided and the deductions from it are therefore not strictly comparable to whole-body PET values.

In summary, dense breasts are problematic in mammography, and sensitivity can be reduced to 30% to 48%. In the limited data available, the sensitivity of PEM was not degraded by increased breast density. Also, disease extent was more accurately assessed with PEM than with conventional means. Those tumors missed with PEM tend to be lower grade. It is not possible to visualize and evaluate the axilla and posterior tissue with current technology.

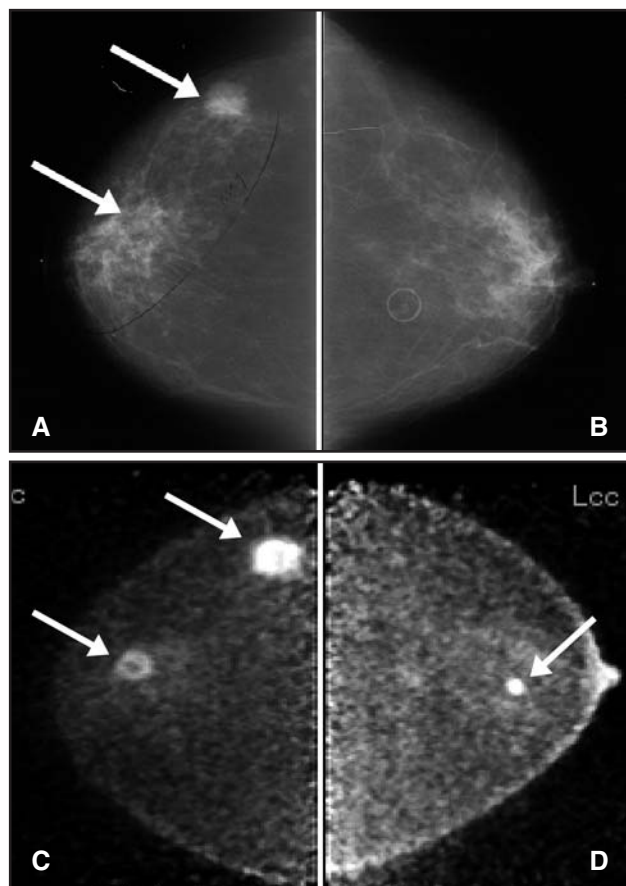


Fig 6A-D. — Craniocaudal mammographic views showing (A) a mass in the lateral right breast and spiculated density behind the nipple (arrows) and (B) a normal left breast. (C) The right craniocaudal PEM showing abnormal uptake to correspond with the mammographically identified malignant lesions (arrows). (D) An otherwise occult infiltrating ductal cancer (arrow) discovered in the left breast with PEM. (Courtesy Naviscan PET Systems, Inc.)

These studies suggest that PEM will be more than a useful adjunct to conventional breast imaging. The units are compact and well suited to a breast imaging suite. The images can be acquired comfortably with gentle compression and in a short period of time. Improvement in design could alleviate problems in visualizing the posterior breast tissue.

Size of tumor does not appear to be a problem with PEM. In fact, small foci of DCIS otherwise occult have been discovered. Complementary to and unlike mammography, PEM does not depend on the presence of microcalcifications for DCIS identification. This provides a dramatic improvement in the sensitivity of detection when combined with standard imaging without a decrease in accuracy.

PEM could have a dramatic impact on surgical planning, size of resection, and re-excision rates as it has the potential to accurately establish the extent of disease. PEM shows promise of major improvement over mammography in uncovering DCIS. Methods to guide the biopsy of lesions seen only on PEM are needed and are currently being developed.

Conclusions

Each of the four modalities discussed above offers specific benefits. FFDM provides the mammographer with an effective way of performing large-scale screening for breast cancer. It has been shown to confer an advantage in diagnosing breast cancer in young women, women with dense breasts, and women who are pre- or peri-menopausal. Also, FFDM offers better transfer and storage of images and the ability to use other digital techniques such as CAD in concert. CAD has the greatest potential impact on finding microcalcifications, particularly in dense breasts, that might otherwise be overlooked by radiologists. Breast MRI promises to be a useful adjunct to mammography, sonography, and physical examination in the preoperative evaluation of patients with known breast cancer. MRI can be used to follow patients after lumpectomy and patients with problematic or indeterminate mammograms. Women with occult primary breast cancers and those with nipple discharge can benefit from MRI examination. However, the poor specificity of MRI can lead to many benign biopsies. MRI must be performed and interpreted under rigorous conditions. In the limited data available, the sensitivity of PEM was not degraded by increased breast density. Also, disease extent was more accurately assessed with PEM than with conventional means.

The field of breast-specific imaging has undergone robust change in recent years. Advances and ongoing improvements in imaging technologies such as FFDM, CAD, MRI, and PEM have improved the sen-

sitivity of breast cancer detection and diagnosis, but each modality is most beneficial when utilized according to individual traits such as age, risk, and breast density. The clinician needs to be aware of the benefits and weaknesses of each technology in order to apply them appropriately in evaluating their patients with breast problems.

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