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ORIGINAL ARTICLE – BREAST ONCOLOGY

MRI Versus Breast-Specific Gamma Imaging (BSGI) in Newly Diagnosed Ductal Cell Carcinoma-in-situ: A Prospective Head-to-Head Trial

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ABSTRACT

Background. Mammography remains the standard imaging technique for the diagnosis of ductal carcinoma-in-situ (DCIS). Functional breast imaging, including breast magnetic resonance imaging (MRI), has known limitations in evaluating DCIS. To date, there are limited data on the utility of breast-specific gamma imaging (BSGI) in DCIS. We sought to prospectively compare the sensitivity of BSGI to MRI in newly diagnosed DCIS patients.

Methods. Patients with newly diagnosed DCIS from June 1, 2009, through May 31, 2010, underwent a protocol with both breast MRI and BSGI. Each imaging study was read by a separate dedicated breast radiologist. Patients were excluded if excisional biopsy was performed for diagnosis, if their MRI was performed at an outside facility, or if final pathology revealed invasive carcinoma.

Results. There were 18 patients enrolled onto the study that had both MRI and BSGI for newly diagnosed DCIS. The sensitivity for MRI was 94% and for BSGI was 89% ($P > 0.5$, NS). There was one index tumor not seen on either MRI or BSGI, and one index tumor seen on MRI but not visualized on BSGI.

Discussion. Although BSGI has previously been shown to be as sensitive as MRI for detecting known invasive breast carcinoma, this study shows that BSGI is equally as sensitive as MRI at detecting newly diagnosed DCIS. As a result of the limited number of patients enrolled onto the study, larger prospective studies need to be performed to determine the true sensitivity and specificity of BSGI.

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Breast cancer remains the most common cancer in women. In 2010, an estimated 207,000 new cases of breast cancer will be diagnosed in women.[1] Ductal carcinoma-in-situ (DCIS) currently accounts for approximately 20% of all breast cancer and 30% of all imaging diagnosed breast cancer.[2] The proportion of DCIS has been steadily rising, due in large part to widespread screening mammography.[3] Mammography remains the gold standard for the diagnosis and evaluation of DCIS. The vast majority of cases (90%) present as coarse, heterogeneous, or fine pleomorphic calcifications in branching patterns.[2] However, not all DCIS is calcified, leading to variable reported mammographic sensitivities for DCIS (27–86%).[4–9]

Breast magnetic resonance imaging (MRI) is a well established functional breast imaging modality. MRI relies on gadolinium contrast characteristic enhancement patterns of vascularized lesions within the breast for the identification of malignancies. Although DCIS typically does not show evidence of neovascularization, DCIS can be identified by clumped enhancement on images. This has been thought to be due to permeability of the ductal basement membranes when DCIS is present, leading to uptake of the contrast.[10] Early studies evaluating MRI in DCIS found the sensitivity to be limited as well as a high false-positive rate. However, more recent data have shown improvement in MRI identification of DCIS.[6,7] Despite this, known limitations of MRI in the setting of DCIS exist.

Breast-specific gamma imaging (BSGI) has emerged as an alternative functional imaging study. BSGI measures mitochondrial density, a marker of cellular proliferation. High cytoplasmic density of mitochondria is identified in

cells with marked hyperproliferation (invasive and in situ cancers as well as lesions with marked atypia). Thus, by using technetium-99m sestamibi as a tracer, mitochondria on a cellular level are tagged and density measured using optimized breast-specific image detectors.[11] Current data do not show any statistically significant difference in the sensitivity of MRI and BSGI in the identification of index tumors in invasive breast cancer.[12] However, limited data exist regarding the utility of BSGI in DCIS. We sought to prospectively compare the sensitivity of BSGI to MRI in newly diagnosed DCIS patients.

METHODS

Patients with newly diagnosed DCIS from June 1, 2009, through May 31, 2010, were enrolled onto an institutional review board–approved prospective protocol in which they underwent both breast MRI and BSGI. Each imaging study was read by a dedicated breast radiologist, with one radiologist reading all MRI studies and another reading all BSGI studies.

For the BSGI scan, patients received an intravenous injection of 25 mCi of ^{99m}Tc sestamibi. A 10-minute delay time was provided before obtaining images. Craniocaudal and mediolateral views were performed of both breasts using a high-resolution, small field-of-view gamma camera optimized for breast imaging (Dilon 6800 Gamma Camera; Dilon Technologies, Newport News, VA). Evaluation was then performed in conjunction with mammography by a dedicated breast imager.

For the MRI, T1- and T2-weighed axial images were obtained at 2-mm slice thickness before and after administration of intravenous gadolinium (GE 1.5T System, General Electric Healthcare, Milwaukee, Wisconsin). Delayed postcontrast sagittal images were performed. Postprocessing subtraction and maximum intensity projection images were evaluated, the latter obtained with a Dynacad workstation, which was also used to evaluated enhancement kinetics.

All subsequent findings were evaluated and percutaneously sampled using image guidance. Patients were excluded if excisional biopsy was performed for diagnosis or if their MRI was performed at an outside facility. Patients with invasive carcinoma were also excluded. The sensitivity for each modality was calculated.

RESULTS

Eighteen patients with newly diagnosed DCIS that had both MRI and BSGI were identified. The average patient age at diagnosis was 51 years. Table 1 details the clinical characteristics of the patients. Of the 18 patients, MRI identified 17 of the index DCIS lesions and BSGI identified 16 of the index DCIS lesions (Table 2, Fig. 1). The extent of DCIS ranged from 0.2 cm to extensive multicentric disease. One index cancer was not observed on either MRI or BSGI, a low-grade, 0.2-cm estrogen- and progesterone-positive lesion in a premenopausal woman. One index DCIS lesion was visualized on MRI but not on BSGI, a mixed intermediate- to high-grade estrogen receptor-positive, progesterone receptor–negative cancer, also in a premenopausal woman. The sensitivity for MRI was 94% and for BSGI was 89% ($P > 0.5$, ns).

DISCUSSION

DCIS today accounts for approximately 30% of all imaging detected breast cancers. Over 90% of DCIS is diagnosed by visualizing abnormal calcifications on screening mammography.[2] However, the sensitivity of mammography has wide variability throughout the literature, anywhere from 27–86%.[7,8] This variability in sensitivities may be related to mammography's reliance on visualizing calcifications for the diagnosis of DCIS. These calcifications may in fact be a late finding in DCIS. For this reason, functional imaging has been investigated in an attempt to identify mammographically occult DCIS or disease more extensive than that which is estimated by microcalcifications.

MRI has been the most widely studied functional imaging modality in DCIS. Initial data showed limited sensitivity of MRI in the detection of DCIS.[13,14] As MRI technology evolved, techniques focusing on high spatial resolution with thin slices have resulted in improvement in the ability to detect DCIS on MRI.[5] In addition, enhancement patterns specific to DCIS have been described. In a review of MRI findings in patients with DCIS, Rosen et al.

TABLE 1 Patient characteristics

Characteristic	*n*	%
Menopausal status		
Premenopausal	9	50
Perimenopausal	1	6
Postmenopausal	8	44
Receptor status		
ER positive	16	89
ER negative	2	11
PR positive	12	67
PR negative	6	33
Grade		
Low	3	17
Intermediate	7	39
Mixed intermediate/high	3	17
High	5	27

ER estrogen receptor, *PR* progesterone receptor

TABLE 2 Index DCIS detected by imaging

Imaging modality	Detected, *n* (%)	Not detected, *n* (%)
MRI	17 (94)	1 (6)
BSGI	16 (89)	2 (11)

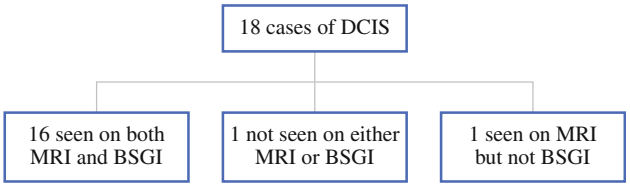

FIG. 1 Index DCIS detected by imaging

found that 59% of patients had non-mass-like enhancement patterns and 12% had a focus of enhancement. In their series, 97% of patients with DCIS had their lesions identified on MRI.[9]

With improved imaging techniques as well as the understanding of enhancement patterns in DCIS, the sensitivity of MRI in DCIS has greatly improved. Berg et al. were among the first to show MRI exceeded mammography and ultrasonography in the sensitivity of evaluating the extent of DCIS (89% vs. 55% and 47% respectively).[4] A report of 39 patients with pure DCIS evaluated with MRI from Memorial Sloan-Kettering Cancer Center found that 64% of their patients' DCIS lesions were visualized only by MRI and that the sensitivity of MRI far exceeded that of mammography (88% vs. 27%).[7] Subsequent series have found the sensitivity of MRI in DCIS to be as high as 92% and 98% in patients with high-grade DCIS.[6]

However, MRI is not without limitations. MRI has been criticized for lower specificity, leading to increased numbers of biopsies of benign lesions. The use of MRI may also be limited by patient-related factors including gadolinium allergies, pacemakers, and other metal implants. Finally, MRI is found by some patients to be a difficult examination, a result of the prone positioning as well as issues of claustrophobia.

BSGI has emerged as an alternative functional breast imaging modality. Enhancement with technetium-99m sestamibi allows for the measurement of mitochondrial density, a marker for cellular proliferation. Therefore, the technique is not reliant on vascular enhancement characteristics of lesions, which may be lacking in DCIS. Because BSGI measures mitochondrial density, the imaging technique is not limited by the density of the surrounding breast tissue. In addition, the gamma cameras of BSGI obtain images similar to mammography, mediolateral oblique views as well as craniocaudal views, allowing for direct comparison to mammogram images. Finally, BSGI obtains images with the patients in an upright seated position, which is more comfortable for patients.

Reports have shown that BSGI can identify index cancers as well as mammographically occult lesions.[15] BSGI has previously been compared with MRI in small retrospective series with comparable sensitivity and improved specificity over MRI.[16] In a recent abstract prospectively comparing BSGI to MRI in newly diagnosed invasive breast cancers, no difference in sensitivity was found between the two functional modalities.[12] However, data evaluating BSGI in DCIS are limited.

Khalkhali et al. initially reported a sensitivity of 100% in detecting DCIS by scintimammography using traditional gamma cameras.[17] However, the sensitivity decreased to 46% in a subsequent multicenter trial.[18] Using an alternative radiotracer, 99m dimercaptosuccinic acid, Papantoniou et al. found a sensitivity of 75% for pure DCIS.[19]

BSGI, with the superior resolution of breast specific gamma cameras, has improved accuracy over traditional scintimammography. In 2007, Brem et al. reported a sensitivity of 91% in BSGI in 22 patients with biopsy-proven DCIS, superior to that of mammography (82%).[20] Seven of the 22 patients also had an MRI performed, with a sensitivity of 88%.

Our results (sensitivity of 89%) of BSGI in DCIS are comparable to those of Brem et al.[20] The one lesion that was not demonstrated by either modality was 0.2 cm at final pathology. However, both MRI and BSGI identified an index DCIS lesion 0.45 cm in size. In addition, by prospectively evaluating each patient with both MRI and BSGI, no statistically significant difference in sensitivity found between the two modalities. To our knowledge, this is the first prospective direct comparison of the two functional imaging modalities in patients with diagnosed DCIS.

Although BSGI has many of the previously stated advantages compared to MRI, one disadvantage is the associated radiation dose from the technetium-99m. Clinical trials evaluating decreased technetium-99m doses in BSGI are currently being performed to address this concern.[21,22] A second disadvantage of the BSGI pertains to its limited use in the delineation of adjacent lesions. As our current study and other recent data show, BSGI allows for the identification of index invasive and in situ lesions as well as potential other findings in the ipsilateral and contralateral breast.[23] However, the gamma imagers as a functional study do not allow for distinction of adjacent lesions, with two adjacent lesions appearing as one larger lesion.

Our data add to a growing body of literature that supports the use of diagnostic BSGI as an alternative functional breast-imaging modality. BSGI is a useful modality when patients are unable to undergo a breast MRI as a result of contrast allergies, metal implants, or

claustrophobia. In addition, BSGI may be a more comfortable test for patients with positioning issues.

Our findings are limited by the small number of patients enrolled onto the study. However, our results confirm the improving sensitivity of MRI in the detection of DCIS. In addition, our current data do not allow for the calculation of specificity and positive predictive value. Further data are expected to outline these issues in BSGI compared with MRI, as MRI has been limited by a lower specificity.

In conclusion, in a prospective comparison of MRI and BSGI in the detection of index DCIS lesions, the sensitivities of the two modalities were found to be comparable. Data continue to emerge suggesting comparable sensitivities of BSGI and MRI. Larger prospective studies need to be performed to determine the true sensitivity and specificity of BSGI.

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