

## Magnetic Resonance Imaging Facilitates Breast Conservation for Occult Breast Cancer

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**Introduction:** Occult primary breast cancer, i.e., isolated axillary adenocarcinoma without detectable tumor in the breast by either physical exam or mammography, represents up to 1% of operable breast cancer. Modified radical mastectomy (MRM) is generally the accepted treatment for this condition although tumor is identified in only two-thirds of mastectomy specimens. Breast magnetic resonance imaging (MRI) can identify occult breast carcinoma and may direct therapy. This study examined the ability of breast MRI to detect occult breast cancer and to facilitate breast conservation therapy.

**Methods:** Forty women with biopsy-proven metastatic adenocarcinoma to an axillary lymph node and no evidence of primary cancer were studied. All patients had a physical examination, mammography, and MRI of the breast. Using a dedicated breast coil, MRI imaging was performed with and without gadolinium enhancement. Positive MRI scans were compared with histopathologic findings at the time of operation (n = 21).

**Results:** MRI identified the primary breast lesion in 28 of 40 women (70%). Of these 28 patients, 11 had MRM, 11 had lumpectomy/axillary lymph node dissection (ALND)/radiotherapy (XRT), 2 had ALND/XRT alone, and 4 had no local treatment secondary to stage IV disease. Two women initially treated with lumpectomy/ALND subsequently had mastectomy for positive margins. Of the women with positive MRI who had breast surgery, 21 of 22 (95%) had tumor within the surgical specimen. Twelve women had negative MRI of the breast. Five of these 12 underwent MRM, of whom 4 had no tumor in the mastectomy specimen. The remaining 7 patients had ALND and whole breast radiation (ALND/XRT) (n = 5), or were observed (n = 2). Overall, 18 of 34 women surgically treated had MRM, while 16 (47%) preserved their breast. Tumor yield for patients having breast surgery was 81%.

**Conclusions:** MRI of the breast can identify occult breast cancer in many patients and may facilitate breast conservation in select women. Negative breast MRI predicts low tumor yield at mastectomy.

**Key Words:** Occult breast cancer—Axillary adenopathy—Breast MRI.

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Occult breast cancer, i.e. breast cancer discovered in isolated axillary lymph nodes of women without a primary tumor evident in the breast (T0, N1, M0) represents up to 1% of operable breast cancer.<sup>1–3</sup> Women with this presentation of stage II breast cancer are most often treated with modified radical mastectomy (MRM) fol-

lowed by systemic chemotherapy and can expect equivalent survival to women with non-occult stage II breast cancer.<sup>4,1,5</sup>

Although MRM effectively treats occult breast cancer, pathological examination of mastectomy specimens identifies a primary tumor in only two-thirds of these patients.<sup>6</sup> This has led some investigators to question whether breast-preserving therapy can be offered to women with occult cancer of the breast.<sup>7</sup> Limited resection or radiotherapy (XRT) alone in women with clinically and mammographically occult breast cancer have been associated with high rates of local recurrence, although overall survival at 10–15 years is unaffected.<sup>8,9</sup>

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In principle, breast conservation for these patients could be facilitated in two ways: (1) by improved identification of small tumors amenable to lumpectomy and (2) by identifying women without detectable tumors who may be treated adequately by XRT alone.

Breast MRI using contrast enhancement is a relatively new imaging modality for assessing the breast.<sup>10-12</sup> Several studies have demonstrated high (86-100%) sensitivity with this technique, but with a comparatively lower (37-97%) specificity.<sup>13,14</sup> Breast MRI is thus an attractive option to identify lesions that have evaded detection by mammography and physical exam. Small series of patients from Memorial Sloan-Kettering Cancer Center (MSKCC) and elsewhere have demonstrated previously that MRI can identify occult breast cancer.<sup>15,16</sup> This study was performed to evaluate the impact of breast MRI on the management of a relatively large cohort of patients with occult breast cancer.

## MATERIALS AND METHODS

Forty women with metastatic axillary adenocarcinoma from an unknown primary site were studied. These women were referred to the Breast Service at Memorial Sloan-Kettering Cancer Center (MSKCC) during the period from October 1994 to October 1998. Clinical data were obtained from the MSKCC Breast Center prospective database, chart review, and by contact with patients and their oncologists.

All patients had a physical examination by a breast surgeon and mammography performed at MSKCC within 6 weeks of MRI. No patient had palpable or mammographic evidence of primary breast cancer at that time. Biopsy was performed before definitive breast treatment in all patients, and all patients had adenocarcinoma with features diagnostic or suspicious of breast origin. Estrogen and progesterone receptor status from axillary lymph node (LN) biopsy specimens was available for 19 patients with an overall positivity rate (ER, PR, or both) of (7/19) 37%. Any patient with evidence of a non-breast primary tumor was excluded from the study.

Mammograms were reviewed independently by one breast radiologist (EAM) before MRI to confirm absence of cancer or to note suspicious lesions. Breast MRI was performed at MSKCC using a 1.5-T commercially available system (Signa; GE Medical Systems, Milwaukee, WI) as previously described.<sup>15</sup> Patients underwent imaging in the prone position with the use of a dedicated breast coil. Sagittal fat-suppressed T2-weighted fast-spin echo images were obtained of the entire breast at: 4000/105 (repetition time, msec/echo time, msec), 30 flip angle, 16 cm field of view (range, 16-20 cm), 2-mm

section thickness without gap, and 256 × 192 matrix. Images were obtained before and after rapid bolus injection of gadopentetate dimeglumine. Total acquisition time was 5-10 minutes. Baseline images were subtracted from contrast-enhanced images on a pixel-by-pixel basis using a GE Advantage Windows workstation (GE Medical Systems). Ultrasound was employed selectively based on MRI findings, and ultrasound (US)-guided needle localization of MRI-detected lesions was subsequently performed in selected cases.

## RESULTS

### Patient Characteristics

The median age of patients in this study was 58 (range, 37-78 years). Axillary adenopathy was left-sided in 22 cases (54%) and right-sided in 18 (45%). Five women (13%) had a history of carcinoma of the contralateral breast, treated from 1-23 years previously. Follow-up was current at a mean of 21 months and a median of 19 months (range, 4-52 months).

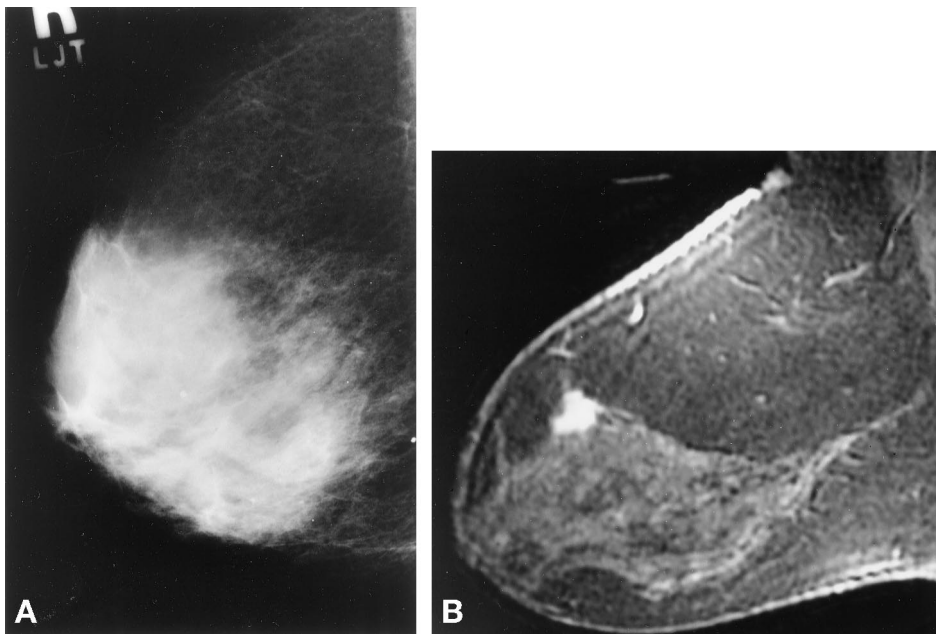
### Imaging

Mammograms were negative in 23 patients, showed enlarged axillary lymph nodes alone in 11 patients, and were indeterminate for malignancy (BiRads 3, or less) in 6 patients. Four patients had negative breast ultrasound before referral for MRI. No patient had findings diagnostic of malignancy on either mammography or ultrasound alone.

Breast MRI subsequently identified abnormalities within the breast in 28 of 40 women (70%) (Table 1). These abnormalities included single masses in 19 cases and multiple masses in 9. All lesions demonstrated suspicious enhancement and were readily detected on contrast-enhanced images (Fig. 1). The sizes of the masses ranged from 6 to 20 mm. Breast MRI identified enhancing lesions in 4 of the 6 patients with low suspicion mammograms. Sixteen patients had ultrasound to investigate MRI-discovered lesions. Ten examinations were negative, whereas 6 patients had a lesion identified within the breast.

**TABLE 1.** MRI findings in patients with occult breast cancer (N = 40)

MRI result	No. %
Positive	28 (70)
Single mass	19
Multiple masses	9
Assoc. w/indeterminate mammogram	4
Negative	12 (30)



**FIG. 1.** Representative mammogram and breast MRI in occult breast cancer.

### Wire Localization

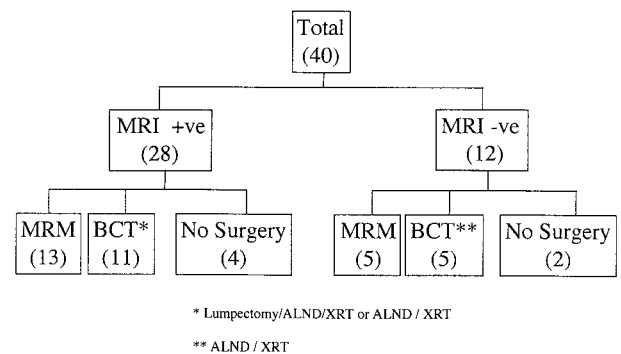
Three of 6 patients, with tumor seen by MRI-directed US, had US-guided needle localization as part of breast conservation therapy (BCT). The remaining 3 patients had MRM ( $n = 2$ ) or excision of tumor in the axillary tail without localization ( $n = 1$ ). Wire localization for breast conservation was performed by mammographic guidance in two patients. Tumors localized mammographically required MRI-directed review of mammograms that were initially read as normal. At the time of this study, MRI-guided wire localization was not clinically available at our institution.

### Surgery

Thirty-four women underwent additional surgery after axillary lymph node biopsy. All had completion ALND and 27 had further surgery to the ipsilateral breast. Eighteen patients ultimately had MRM, 11 of whom had lesions detected by breast MRI. Lumpectomy and XRT were initially performed on 11 patients, all of whom had enhancing masses on MRI. Localization of these masses was accomplished in 3 cases by US-guided needle localization and in 2 cases by mammogram-guided needle localization. In these 5 cases, MRI findings directed the radiologist to areas of abnormality within the breast. The remaining 6 patients had excisional biopsies of areas of MRI abnormality without localization and all had a primary breast cancer identified within the lumpectomy specimen. Two patients initially treated with lumpectomy required completion total mastectomy for inability to obtain negative margins.

Seven patients had ALND and breast XRT alone as primary treatment of the breast. Five of these women were offered this approach based upon negative MRI. Two women with suspicious but non-enhancing small masses on MRI elected ALND and breast XRT alone. Overall, 16 (47%) of 34 women in this series preserved their breast.

Six patients in this series had no surgical treatment other than the initial axillary lymph node biopsy. Two of these women with negative MRI and a history of contralateral MRM for breast cancer were presumed to have metastatic disease from the opposite breast. Four other women with positive MRI and distant metastases had systemic therapy alone. Treatment of all patients in this series is summarized in Fig. 2.



**FIG. 2.** Treatment of patients with occult breast cancer.

### MRI and Results of Surgery

A total of 22 tumors were identified in the breasts of 27 patients who had breast surgery. Of these cancers, 19 were infiltrating ductal carcinomas and 3 were infiltrating lobular carcinomas. Tumors ranged from 2 mm to 3 cm in size.

Pathological findings were used to determine the accuracy of breast MRI (Table 2). A positive breast MRI facilitated removal of an occult breast cancer in 21 of 22 cases (95%). No tumor was identified in one MRI-positive patient. This patient had nodular enhancement on MRI that corresponded to an area of low suspicion on mammography. Needle localized biopsy of this area revealed fibrous mammary tissue and a cyst but no cancer. The patient desired breast preservation and two subsequent MRI examinations have revealed no suspicious lesions.

One patient with a negative MRI who underwent MRM was subsequently found to have a 3 cm ductal carcinoma within the mastectomy specimen. This patient was obese with large breasts that did not fit completely within the MRI coil. The tumor was located deep within the breast in an area not visualized by the MRI scan. This case was the single false negative among the 5 MRI negative patients who underwent surgery.

The overall tumor yield for patients who had surgery to the breast was 22 of 27 (81%). At a median follow-up of 19 months, no patient who had either lumpectomy/ALND/XRT or ALND/XRT has had a recurrence locally in the breast. No patient has subsequently demonstrated a non-breast malignancy.

### DISCUSSION

This study demonstrates that MRI can reliably identify breast cancers that have evaded detection by mammography and physical examination. A significant proportion of women with previously occult breast cancer successfully underwent BCT based upon MRI findings. Positive MRI findings were associated with a high (21 of 22, 95%) tumor yield, whereas negative MRI was asso-

ciated with a relatively poor (1 of 5, 20%) tumor yield following surgery. The overall tumor yield of 81% exceeds that reported for other series of occult breast cancer.<sup>1,9,17</sup>

Breast MRI has the potential to greatly simplify the management of up to 70% of patients with occult breast cancer. Patients with MRI-identified breast tumors can be offered BCT if the lesion can be needle-localized by ultrasound or by re-review of the mammogram. MRI-guided needle localization is currently available under a study protocol at our institution and promises to increase the proportion of MRI-visualized tumors amenable to needle localization.<sup>18</sup> Up to 11 additional MRI-positive patients in this series could have had BCT if their tumors could have been localized.

Patients with negative MRI results pose a more difficult problem. These patients either have microscopic disease in the breast or have a non-breast primary. The former possibility is unproven but seems more likely because no MRI-negative patient in this study has developed a non-breast primary tumor. Conversely, we cannot prove that the MRI-negative patients who had XRT/ALND alone did not have undetectable microscopic tumor within the breast. None of these patients have subsequently developed a breast primary tumor which suggests that MRI-negative patients with presumably microscopic disease may be suitable for radiotherapy alone. Recent trials that demonstrated a high rate of local recurrence in women with occult breast cancer treated with radiotherapy alone may have included women with MRI-identifiable tumors.<sup>8,9</sup> These women would probably benefit from MRI-directed surgery to the breast. If women with negative MRI elect MRM, our data suggest a low likelihood of finding the tumor.

Modified radical mastectomy is traditionally thought to provide the best local control for women with occult breast cancer. This study demonstrates that breast MRI increases the proportion of patients appropriate for BCT by identifying cancers not seen on physical examination, mammography, or ultrasound. Results from MRI can be used not only to offer breast conservation to selected women, but also to prepare women who choose MRM for the possibility of negative pathological findings after mastectomy. A randomized trial that compares MRM with MRI-directed BCT in women with occult breast cancer would validate this approach.

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**TABLE 2.** Tumor yield following surgery for occult breast cancer (N = 34)

	MRM	BCT*	Tumor yield
MRI positive N = 24	13	9	21/22 (95%)
MRI negative N = 10	5	0	1/5 (20%)
Total	18	9	22/27 (81%)

\* Lumpectomy + ALND.

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