

Magnetic Resonance Imaging in the Evaluation of Ductal Carcinoma In Situ

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Before 2000, breast magnetic resonance imaging (MRI) was considered a relatively poor imaging tool for ductal carcinoma in situ (DCIS), as a high percentage of false-negative magnetic resonance examinations were cases of DCIS. Three specific shifts in breast MRI occurred, which changed this assessment: 1) a shift from high temporal to high spatial imaging, revealing specific morphological features on MRI suspicious for DCIS; 2) a shift from diagnostic studies of patients with cancers identified on mammography to screening studies of high-risk patients, allowing more accurate comparisons of mammography vs MRI in detecting the full spectrum of breast cancers regardless of appearance on mammography; and 3) a shift from emphasis on masses to improved understanding of features of non-mass-like malignant lesions, distinct from benign background parenchymal enhancement patterns. Over the last decade, research has confirmed that of all imaging tools, MRI has the highest sensitivity in detection of DCIS (compared with mammography and ultrasound). Future studies are needed to clarify how best to use this tool for improved patient outcomes.

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Breast Magnetic Resonance Imaging in the Evaluation of DCIS

The role of magnetic resonance imaging (MRI) in the evaluation of ductal carcinoma in situ (DCIS) has focused on two specific clinical applications. The first is the performance of MRI in the evaluation of the extent of the disease in patients with a diagnosis of DCIS, before therapeutic planning. The second application is early detection of DCIS in breast cancer screening programs. These studies have focused on patients at high risk for breast cancer in whom both mammography and MRI are recommended for screening.

The intention of the studies to date was to clarify the potential of MRI in select patient populations to reduce the morbidity of breast cancer treatment by 1) allowing more targeted and accurate surgical approaches to remove DCIS, with fewer surgeries required to achieve negative margins, and 2) supporting earlier detection of breast cancer in high-risk patients by detecting cancer at a preinvasive stage. In addition, some have hypothesized that MRI may allow more sensitive detection of the DCIS lesions more likely to progress to invasive disease while allowing less aggressive treatment approaches to those DCIS lesions highly unlikely to progress to invasive disease.

Historically, MRI was considered a poor imaging tool to assess DCIS. In fact, numerous investigators claimed that although MRI had high sensitivity in the detection of invasive cancer, it was a poor imaging tool to identify DCIS. Many urged caution in relying on MRI to evaluate DCIS, claiming that mammography, by detecting calcifications associated with DCIS, was the preferred imaging method for DCIS detection and that MRI was not sensitive in detecting DCIS (1–4). Based on the literature available at the time, the American College of Radiology's

Breast MRI Practice Guidelines specifically excluded the detection of DCIS as an indication for MRI (5). MRI high-risk screening trials provided added support to this limitation of MRI by reporting DCIS cases identified by mammography but occult to MRI (6–9).

At the same time, investigators shifted attention from MRI acquisition techniques of lower spatial resolution (with thicker slice acquisitions) and higher temporal resolution (with rapid acquisition of images) to techniques of higher spatial resolution. Using these higher spatial resolution techniques, investigators reported improved detection of DCIS with MRI. In 2004, Berg et al. (10) reported that MRI was the preferred method of detecting DCIS in patients with known breast cancer. In her study, all patients with a diagnosis of cancer, whether invasive or in situ, were evaluated with mammography, ultrasound, and MRI to assess the extent of disease before treatment planning. As expected, MRI significantly improved the assessment of invasive lobular carcinoma compared with mammography and ultrasound. What was more surprising at the time was the finding that MRI was far superior to either mammography or ultrasound in the assessment of extent of disease of DCIS. MRI sensitivity for accurate assessment of DCIS extent was 89% compared with only 55% and 47% for mammography and ultrasound, respectively.

In 2007, the American College of Radiology 6667 trial (C. D. Lehman, Principal Investigator) reported results of MRI of the contralateral breast in 969 women recently diagnosed with breast cancer (11). A total of 196 (20.2%) of these 969 women entered the study with an index cancer diagnosis of DCIS. MRI of the contralateral breast identified an additional 30 cancers not detected by mammography or clinical breast examination. Twelve

of these 30 cancers (40%) were pure DCIS. Three false-negative magnetic resonance examinations were reported, all cases of DCIS. These cases of DCIS were also occult to mammography. The same year, Kuhl et al. (12) published a large study of patients with pure DCIS, showing that the sensitivity of MRI far surpassed that of mammography in the detection of DCIS. In that study of 7319 women who underwent both MRI and mammography, pure DCIS was diagnosed in 167 patients. The sensitivity of MRI was 92% for DCIS compared with only 56% by mammography. Of interest, MRI sensitivity was particularly strong in women with high-grade DCIS. In patients with high-grade or comedo-type DCIS, the sensitivity of MRI was 98% compared with only 52% for mammography. The majority (87%) of cases of DCIS not identified by MRI were low-grade DCIS. Age, menopausal status, personal or family history of breast cancer or of benign breast disease, and breast density did not differ in women with MRI-only diagnosed DCIS compared with those with mammography-diagnosed DCIS.

Investigators found that the classic patterns of invasive carcinoma on MRI were not present in the majority of cases of DCIS, and techniques focused on high spatial resolution with thin slices seemed to produce improved results in the detection and diagnosis of DCIS compared with techniques emphasizing high temporal resolution. Patterns of contrast enhancement over time, central to the effectiveness of high temporal resolution imaging, did not appear to distinguish DCIS lesions from normal tissue. In a large multicenter study by the International Breast MRI Consortium (M. D. Schnall, Principal Investigator), the specific feature of a washout pattern identified only 20% of the cases of DCIS. The sensitivity increased to 60% when plateau enhancement was also included (13). Other investigators confirmed these findings and clarified that DCIS relies on morphological features more heavily than on kinetic features and typically presents as non-mass-like enhancement with delayed peak enhancement profiles (14–16).

A recent study (17) in a mouse model of DCIS lesions demonstrated that gadolinium contrast diffuses from the vessels into the surrounding tissue, across the basement membrane, and into the ducts within the breast effected by DCIS. This understanding may provide further information to clarify the mechanisms by which DCIS can be visible on MRI and suggests MRI may also provide information regarding the permeability of the basement membrane of DCIS lesions (18).

In summary, the ability of MRI to detect the presence and extent of DCIS unequivocally significantly exceeds that of mammography or ultrasound and is associated with acceptable specificity. This improved sensitivity is particularly robust for high-grade DCIS lesions. How this improved diagnostic accuracy will affect outcomes in patients at risk for and with breast cancer warrants careful investigation.

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