Radiology

Preoperative MRI Improves Surgical Planning and Outcomes for Ductal Carcinoma in Situ

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Ductal carcinoma in situ (DCIS) is a heterogeneous group of lesions that differ with regard to histopathologic features, biologic markers, and genetic and molecular abnormalities. It is defined as "a neoplastic proliferation of epithelial cells confined to the ductal-lobular system and characterized by subtle to marked cytological atypia and an inherent but not necessarily obligatory tendency for progression to invasive breast cancer" (1). Whereas some DCIS may not or may only progress slowly to non–high-grade invasive breast cancer, some DCIS will progress rapidly to high-grade invasive breast cancer. Surgery is the most common treatment for DCIS, but it is also controversial and may be overtreatment. There is no current diagnostic means that can determine which DCIS will develop into invasive breast cancer.

DCIS was traditionally a "mammographic disease." DCIS initially accounted for only 1%–2% of breast cancers, but there has been a significant increase in incidence particularly in women of screening age with the implementation of population-based screening programs (2). Approximately 20% of all screen-detected breast cancers are DCIS that typically manifest with suspicious microcalcifications or less often as masses or architectural distortions at screening mammography (3). Nevertheless, although mammography for DCIS is a success story, DCIS remains a diagnostic challenge. The adequate assessment of calcifications is only possible with invasive tissue sampling (ie, vacuum-assisted core biopsy). However, vacuum-assisted core biopsy is often unnecessary due to false-positive diagnoses, showing a positive predictive value for suspicious calcifications ranging from 25%–40%. In addition, high-grade DCIS clustered calcifications in particular are often a poor indicator of actual lesion extent (known as the "tip of iceberg" phenomenon), leading to inadequate presurgical localization and subsequent re-excision for negative margins.

Pathologists note that the vast majority of breast cancers evolve through the ductal stage. Yet even in women who attend annual screening with mammography, 80% of breast cancers are diagnosed at the invasive stage, indicating that screening mammography fails to help diagnose the majority of DCIS stages. Moreover, more than half of invasive breast cancers are not associated with calcifications. In summary, there is an overdiagnosis of biologically inert DCIS and an underdiagnosis of prognostically relevant DCIS.

The European Society of Breast Cancer Specialists recommendations for breast MRI that date from 2010 (4) state that the acceptable indications for preoperative MRI are limited to the following indications: *(a)* patients newly diagnosed with an invasive lobular cancer (level of evidence [LoE], 2a; degree of recommendation [DoR], B) by using the methodology defined by the Centre for Evidence-based Medicine, Oxford, England); *(b)* patients at high risk for breast cancer (LoE, 2b; DoR, B); *(c)* patients younger than 60 years with discrepancy in size greater than 1 cm between mammography and breast US with an expected impact on treatment decision (LoE, 2b; DoR, B); and *(d)* patients eligible for partial breast irradiation on the basis of clinical breast examination and conventional imaging with mammography and sonography (LoE, 3b; DoR, B). Most of the evidence to support these indications stems from the era when the possibilities to perform MRI-guided biopsies to verify the MRI findings were not widely available (comparative effectiveness of MRI in breast cancer [COMICE] trial, ISRCTN number 57474502) or important methodologic biases were overlooked (MR mammography of nonpalpable breast tumors [MONET] trial, NCT00302120).

To date, there is a compelling body of evidence that breast MRI is the method with the highest diagnostic accuracy for the detection and staging of breast cancer. Breast MRI is the most sensitive modality currently available for identifying DCIS. Breast MRI is more

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Conflicts of interest are listed at the end of this article.

See also the article by Yoon et al in this issue.

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accurate than is mammography in evaluating the extent of DCIS (92% vs 56%) and is particularly sensitive for identifying high-grade and intermediate-grade DCIS (3). DCIS depicted with MRI has a higher likelihood to progress to invasive cancer than does DCIS depicted with mammography (5). Nevertheless, the role of MRI in determining surgical outcomes remains controversial, with diverging results published in different studies.

In this issue of *Radiology,* Yoon and colleagues (6) investigated the associations between preoperative breast MRI and surgical outcomes in women with DCIS and evaluated the clinical-pathologic variables associated with a benefit from MRI. The authors demonstrate that preoperative breast MRI depicted additional malignancy in US-guided biopsy-confirmed DCIS, reducing positive surgical margins and repeat surgery rates without affecting the mastectomy rate. Patients with DCIS confirmed by using US-guided core-needle biopsy between January 2012 and December 2016 were included in this retrospective study. Propensity score matching with 18 confounding covariates matched groups with MRI (n = 430) and without MRI (n = 111). Surgical outcomes were compared. Clinical-pathologic variables covering demographics, tumor characteristics, and clinical features were evaluated to determine women who benefited from MRI.

In the current study by Yoon et al, among the 430 women, preoperative breast MRI depicted an additional 67 lesions (16%), with 25 (37%) of these being malignant. In 57 of 430 (13%) women who underwent preoperative MRI, there was a subsequent change in surgical treatment that was deemed appropriate in 31 of 57 (54%) women. Preoperative breast MRI was associated with a reduction in the rates of positive resection margin (odds ratio [OR], 0.39; P = .03) and repeat surgery (OR, 0.33; P = .03) compared with the non-MRI group. There was no evidence of different initial (OR, 1.2; P = .59) or overall mastectomy rates (OR, 0.93; P = .79).

In contrast, a recent meta-analysis that included nine studies with 1077 patients with and 2175 patients without preoperative MRI did not find significant differences between the proportion of women with positive margins (7) and also showed that patients undergoing preoperative MRI were significantly more likely to have initial mastectomy. However, several of the prior studies included in the meta-analysis did not use image-guided biopsy or image-guided localization to translate the imaging findings into surgical approaches. In the current study, there were also unnecessary changes in surgical plan such as wider excision, conversion from breast-conserving surgery to mastectomy, and contralateral breast excision. This can be explained in part by the fact that 19 of the additional suspicious lesions were surgically excised upfront without preoperative biopsy. In addition, other additional lesions confirmed to be high risk by using MRI-directed US and biopsy without subsequent upgrade at surgery were also included in the unnecessary change group.

This highlights the importance of presurgical histopathologic verification of additional depicted suspicious lesions to maximize the benefits of pretreatment MRI. This is in line with a recent study (8) that investigated surgical outcomes in patients with breast cancer presenting with and without DCIS components who underwent preoperative breast MRI and subsequent MRI-guided biopsy and/or MRI-guided preoperative localization. It is also debatable whether a change in surgical management due to a high-risk lesion is inappropriate. After all, high-risk lesions diagnosed as standalone lesions would also be recommended for excision per standard of care.

In the current study, preoperative MRI was also associated with an improvement in surgical outcomes for achieving upfront successful breast conservation. This is in agreement with the results from a recently published randomized phase III trial by Balleyguier et al (9) showing that preoperative MRI resulted in a lower repeat surgery rate without a higher mastectomy rate in the per-protocol analysis, but not in the intention-to-treat analysis.

Interestingly, Yoon and colleagues also found that preoperative MRI was particularly helpful in the surgical planning of patients with low nuclear grade, progesterone receptor–positive, and human epidermal growth factor receptor–negative DCIS. The results contradict previous reports in the literature, where it has been suggested that MRI is more sensitive in prognostically relevant DCIS (5). Nevertheless, the results are in agreement with a recent study by Bae et al (10), who found a lower sensitivity with nuclear grade. Therefore, further research to elucidate whether breast MRI can provide an imaging marker for prognostically relevant DCIS is warranted.

A limitation of the current study was the imbalance between patients with and patients without preoperative MRI. The propensity score matching method using clinical-pathologic covariates to reduce potential confounding factors can only control for factors included in the matching process. Thus, some uncontrolled factors (eg, patient and surgeon preferences) may remain. There was also a possible selection bias because only data for which matching was possible were modeled.

In conclusion, preoperative breast MRI in patients with DCIS is beneficial for surgical planning by depicting additional malignancy, and it improves surgical outcomes by reducing the rates of positive resection margin and repeat surgery without increasing mastectomy rates. In this study, Yoon and colleagues provide further evidence that the role of breast MRI needs to be revised and the idea that it has no value in the preoperative work-up of DCIS must be challenged.

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