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Improving malignancy prediction in breast lesions with the combination of apparent diffusion coefficient and dynamic contrast-enhanced kinetic descriptors

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AIM: To assess how the joint use of apparent diffusion coefficient (ADC) and kinetic parameters (uptake phase and delayed enhancement characteristics) from dynamic contrast-enhanced (DCE) can boost the ability to predict breast lesion malignancy.

MATERIALS AND METHODS: Breast magnetic resonance examinations including DCE and diffusion-weighted imaging (DWI) were performed on 51 women. The association between kinetic parameters and ADC were evaluated and compared between lesion types. Models with binary outcome of malignancy were studied using generalized estimating equations (GEE), (GEE), and using kinetic parameters and ADC values as malignancy predictors. Model accuracy was assessed using the corrected maximum quasi-likelihood under the independence confidence criterion (QICC). Predicted probability of malignancy was estimated for the best model.

RESULTS: ADC values were significantly associated with kinetic parameters: medium and rapid uptake phase ($p<0.001$) and plateau and washout curve types ($p=0.004$). Comparison between lesion type showed significant differences for ADC ($p=0.001$), early phase ($p<0.001$), and curve type ($p<0.001$). The predicted probabilities of malignancy for the first ADC quartile ($\leq 1.17\times10^{-3}$ mm^2/s) and persistent, plateau and washout curves, were 54.6%, 86.9%, and 97.8%, respectively, and for the third ADC quartile ($\geq 1.51\times10^{-3}$ mm^2/s) were 3.2%, 15.5%, and 54.8%, respectively. The predicted probability of malignancy was less than 5% for 18.8% of the lesions and greater than 33% for 50.7% of the lesions (24/35 lesions, corresponding to a malignancy rate of 68.6%).

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CONCLUSION: The best malignancy predictors were low ADCs and washout curves. ADC and kinetic parameters provide differentiated information on the microenvironment of the lesion, with joint models displaying improved predictive performance.

Introduction

Breast magnetic resonance imaging (MRI) is the most sensitive imaging method to detect breast cancer.[1–3] Previous studies have shown its advantages in lesion detection and characterization when compared to mammography and ultrasound.[4–6] Moreover, guidelines and recommendations based on previous single and multicentre studies[7,8] were established for its use in the clinical practice.[3,9–11]

Breast MRI protocols include dynamic contrast-enhanced (DCE) images with high spatial and temporal resolution.[12] Interpretation of those images integrates morphological and kinetic descriptors from the breast imaging report and data system (BIRADS)-MRI lexicon, allowing lesion classification and appropriate recommendations for patient management.[13]

The relevant information regarding DCE lesion kinetics was previously studied.[14–18] The kinetic descriptors rely on tracking the signal intensity (SI) over time, during two phases following a bolus injection of contrast medium: the early phase (wash in) and the delayed phase (washout). Both provide physiological information on lesion vascularity. Kuhl *et al.*[19] reported that the kinetic predictors most associated with malignancy were rapid early enhancement followed by a washout curve in the delayed phase.

A recent meta-analysis by Peters *et al.*[20] including 44 studies, assessed the diagnostic performance of DCE in breast cancer, with an overall sensitivity and specificity of 90% and 72%, respectively. The moderate specificity reflects some overlap in the morphological and kinetic features between benign and malignant lesions, which lead to false-positive cases. The direct consequence of a false-positive diagnosis is that it could result in unnecessary biopsy.

To increase breast MRI specificity, other sources of image contrast should be explored. Diffusion-weighted imaging (DWI) is a promising method. The apparent diffusion coefficient (ADC) quantifies the restriction to the random motion of water molecules within tissues, probing their properties at the cellular level.[21] The ADC is estimated from the SI decay between two or more diffusion-weighting factors (b-values).[22] Increased cellularity restricts the diffusivity of water molecules within tissues, leading to low ADC values.[23] Previous studies have demonstrated the role of DWI in breast lesion detection and characterization.[24–26]

Considering that DWI and DCE kinetics reveal distinct physiological and functional characteristics of the lesion environment, it is likely that combining both may improve lesion characterization. Studies exploring DWI and DCE together have recently been performed,[27–30] suggesting that the specificity and accuracy can be increased. Based on those results, it is important to evaluate the ability of the two combined parameters to predict lesion malignancy. Therefore, the purpose of the present study was to explore the relationship between ADC and kinetic parameters, and to determine their ability to predict malignancy.

Materials and methods

Patients and lesions

A prospective study focusing on breast lesion characterization using DWI-MRI at 3 T was conducted between 2009 and 2012. The study was approved by the Institutional Ethics Committee (protocol: CES 276/13). Women with clinical indications for breast MRI gave their written informed consent.

During 2011, breast MRI examinations were performed in 82 consecutive patients. Clinical indications included unknown primary malignancy, suspicious lesions on mammography and/or ultrasound, preoperative staging, breast cancer screening in women at high-risk, therapeutic monitoring, follow-up after surgery, breast cancer recurrence, and evaluation of implant integrity.

For all pre-menopausal women, breast MRI was performed between the 7th and 14th day of the menstrual cycle to reduce hormonal variations and minimize the enhancement on the fibroglandular tissue.[31,32]

For the purpose of this study, exclusion criteria were applied to patients (1) who had lesions that were biopsied before the MRI examination (n=7); (2) subjected to breast surgery within <6 months (n=6); (3) undergoing radiotherapy and/or chemotherapy within the previous 48 months (n=5); (4) with only simple cystic lesions (n=6); (5) who had completed hormone-replacement therapy within <24 months (n=3); (6) with breast implants (n=1); and (7) whose images had motion artefacts (n=3).

Lesions were included in the analysis if: (1) they were solid; (2) the histological results or a minimum of 2-year follow-up with mammography, ultrasound, or breast MRI were available[33]; (3) their size was ≥7 mm; and (4) they were classified as 3 to 5 in the BIRADS-MRI lexicon and were not biopsy-proven prior to breast MRI examination to exclude the influence of haematoma and/or oedema in the ADC estimates.

Acquisition protocol

All the examinations were performed using a 3 T MRI system (Magnetom® Tim Trio, Siemens Medical Solutions, Erlangen, Germany) using a four-channel phased-array coil