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Time to enhancement derived from ultrafast breast MRI as a novel parameter to discriminate benign from malignant breast lesions

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ABSTRACT

Objectives: To investigate time to enhancement (TTE) as novel dynamic parameter for lesion classification in breast magnetic resonance imaging (MRI).
Methods: In this retrospective study, 157 women with 195 enhancing abnormalities (99 malignant and 96 benign) were included. All patients underwent a bi-temporal MRI protocol that included ultrafast time-resolved angiography with stochastic trajectory (TWIST) acquisitions ($1.0 \times 0.9 \times 2.5$ mm, temporal resolution 4.32 s), during the inflow of contrast agent. TTE derived from TWIST series and relative enhancement versus time curve type derived from volumetric interpolated breath-hold examination (VIBE) series were assessed and combined with basic morphological information to differentiate benign from malignant lesions. Receiver operating characteristic analysis and kappa statistics were applied.
Results: TTE had a significantly better discriminative ability than curve type ($p < 0.001$ and $p = 0.026$ for reader 1 and 2, respectively). Including morphology, sensitivity of TWIST and VIBE assessment was equivalent ($p = 0.549$ and $p = 0.344$, respectively). Specificity and diagnostic accuracy were significantly higher for TWIST than for VIBE assessment ($p < 0.001$). Inter-reader agreement in differentiating malignant from benign lesions was almost perfect for TWIST evaluation ($\kappa = 0.86$) and substantial for conventional assessment ($\kappa = 0.75$).
Conclusions: TTE derived from ultrafast TWIST acquisitions is a valuable parameter that allows robust differentiation between malignant and benign breast lesions with high accuracy.

1. Introduction

Breast magnetic resonance imaging (MRI) is the most sensitive of currently available imaging modalities to detect breast cancer. In a meta-analysis an overall sensitivity of 90% was reported, however, specificity was less accurate (72%) [1]. To improve specificity, recommendations for breast MRI state that the dynamic contrast-enhanced acquisition should be obtained at least three time points [2]. This allows evaluation of morphologic and kinetic features of breast lesions according to the breast imaging reporting and data system (BIRADS) lexicon. To further improve lesion classification, a high-resolution T2 sequence and diffusion-weighted sequences have been added to the state-of-art MRI protocol [2–4]. However, this makes breast MRI time-consuming, with reported investigation times between 20 and 40 min [5].

Based upon large screening studies in women at intermediate and high risk, the use of breast MRI as screening tool has increased as MRI largely outperforms mammography in terms of sensitivity [6–8]. However, despite its excellent diagnostic performance, cost-effectiveness analyses justify MRI screening only in women at very high risk [9], mainly those with BRCA1 or BRCA2 mutation. The use

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of MRI for screening in normal and intermediate risk groups is currently questioned because of high costs, limited availability, use of contrast agent and less than perfect specificity. Therefore, to align breast MRI to the requirements of a screening test, it is needed to focus on novel acquisition methods that can reduce costs and simultaneously increase the specificity, without sacrificing sensitivity.

It has been shown that new ultrafast view-sharing MRI sequences, such as time-resolved

angiography with stochastic trajectories (TWIST), time-resolved imaging of contrast kinetics (TRICKS) and 4-dimensional time-resolved magnetic resonance angiography with keyhole (4D-TRAK), can image the inflow of a contrast agent at both a high temporal and spatial resolution [10,11]. As reported recently [12], this novel approach allows detection and classification of breast lesions with high accuracy based upon morphology and the maximum slope of the contrast enhancement over time curve. The scan time can be reduced to less than 2 min, which in turn reduces the high costs, and increases the potential of breast MRI as a screening tool.

In movies of maximum-intensity projections, malignant lesions tend to enhance much earlier than benign lesions [12,13]. Evaluating whether a lesion enhances early or late after contrast has reached the descending aorta thus is a valid parameter for the differentiation of benign and malignant breast lesions. However, so far this 'time to enhancement (TTE)' has not been structurally investigated as a dynamic parameter for lesion classification in breast MRI. The aim of this study is to compare TTE to conventional curve type evaluation as a classifier to discriminate between malignant and benign breast lesions.

2. Materials and methods

2.1. Patient population

After institutional review board (IRB) approval was obtained, a review of our breast MRI database was performed to identify all patients with enhancing abnormalities scanned from January 2011 to December 2011. All patients had a clinical indication for breast MRI and were scanned using an IRB approved bi-temporal MRI protocol. The requirement for informed consent was waived because of the retrospective nature of this study.

All consecutive patients with enhancing lesions with a histological confirmed diagnosis or at least 24 months follow-up with unchanged MRI morphology and enhancement characteristics, indicating the benign nature of the lesion, were included.

2.2. MR imaging acquisition

All patients were scanned in the prone position using a 3T MRI scanner (Siemens Magnetom Trio/Skyra), with a 16-channel bilateral breast coil (Siemens, Erlangen, Germany). For contrast administration, an intravenous cannula was inserted in the antecubital vein just before the investigation. During the examination the contrast agent (Dotarem®, Guerbet, France) was injected at a dose of 0.1 mmol/Kg using a power injector (Medrad, Warrendale, PA) at a flow rate of 2.5 mL/s, followed by a 20 mL saline flush.

The MRI protocol has been published before [11,12], but in short, all MRI scans included two dynamic series to evaluate contrast behavior in breast lesions. A conventional high-resolution T1-weighted non-fat saturated volume interpolated breath-hold examination (VIBE) was obtained before and four times after contrast administration. This was interleaved with a series of 20 ultrafast TWIST acquisitions acquired immediately before and during the inflow of the contrast agent. Each repetition of the TWIST sequence updates only a small cylindrical part of the central k-space (zone A), and semi-randomly samples a percentage of the peripheral k-space (zone B). In our protocol zone A covers only the central 15% of k-space. In zone B 10% of points are updated for each TWIST repetition. The initial TWIST sequence, obtained before contrast administration, populates the full k-space and takes 18.4 s. The subsequent 19 TWIST series, performed during inflow of contrast agent, have a temporal resolution of 4.32 s each. Despite the very high temporal resolution the TWIST images have a spatial resolution of $1.0 \times 0.9 \times 2.5$ mm, and therefore meet the requirements for diagnostic breast MRI [2]. The total acquisition time of the TWIST sequence was 102 s. Since the VIBE acquisitions are sampled in a 3D centric fashion (which means that the center of k-space is filled first), the contrast timing of the latest TWIST acquisition only differs about 5 s with the VIBE acquisition and both sequences thus provide comparable morphological information at this time point. The dynamic sequences were preceded by diffusion-weighted images and followed by a T2-weighted TSE acquisition. Details of the MRI technique are listed in Table 1.

2.3. Image interpretation

Two readers with different levels of experience independently evaluated all MRI examinations. The first reader (XX) was an experienced breast radiologist with 20 years of experience in breast MRI (reader 1). The second reader (XX) was a senior radiology resident with 3 years of experience in breast MRI (reader 2).

Both readers were aware of the quadrant in which the lesion was located but had no further patient information or information on lesion histology.

Evaluation of all examinations was performed on a dedicated breast MRI workstation (DynaCAD, InVivo, Philips, The Netherlands). This workstation performs 3D registration of dynamic series, provides T1-weighted and subtracted images, maximum-intensity projections (MIPs) of subtracted images, multiplanar reformatted images (MPRs), color parametric maps, and

Table 1
Scan parameters of the bi-temporal breast MRI protocol.

Sequences parameters	DWI	TWIST (T1)	VIBE (T1)	T2
Spatial resolution	$1.5 \times 1.5 \times 4.0$ mm	$1.0 \times 0.9 \times 2.5$ mm	$0.9 \times 0.8 \times 1.0$ mm	$1.3 \times 1.1 \times 2.5$ mm
Temporal resolution	186 s	4.32 s	80 s	88 s
N. of dynamics	1	20	5	1
FOV	340 mm	360 mm	360 mm	340 mm
TE/TR	60 ms/6400 ms	2.02 ms/3.96 ms	1.71 ms/5.50 ms	143 ms/3220 ms
FA	NA	20°	20°	80°
b value	50, 800	NA	NA	NA
Parallel imaging factor(GRAPPA)	2	3	3	3
Reordering	Standard	Standard	3D centric	Standard
Central zone	NA	15%	NA	NA
Sampling density outer zone	NA	10%	NA	NA

TWIST, time-resolved angiography with stochastic trajectory; VIBE, volumetric interpolated breath-hold examination; DWI, diffusion-weighted imaging; FOV, field of view; TE/TR, echo time/repetition time; FA, flip angle; GRAPPA, generalized auto-calibrating partially parallel acquisition; NA, not applicable.