Clinically Feasible Quantitative Breast DCE-MRI Protocol with High Spatial and Temporal Resolutions

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Introduction: Dynamic contrast-enhanced (DCE) MRI is a critical part of a clinical breast MRI protocol, providing both morphology and contrast kinetics assessments. DCE images are generally acquired with conventional gradient-echo (GRE) pulse sequence, which employs full k-space sampling strategy. The trade-off between spatial and temporal resolution (sRes and tRes) in such an acquisition scheme and the preference for high sRes in a clinical protocol result in a typical tRes of 1-2 min. This precludes meaningful quantitative pharmacokinetic analysis of DCE-MRI time-course data, which requires high tRes. Consequently clinical breast DCE-MRI data are usually processed with qualitative or semiquantitative approach. The results are strongly dependent on data acquisition details, leading to limited specificity and lack of reproducibility (1). Quantitative clinical imaging is the future. DCE-MRI time-course data must be subjected to pharmacokinetic analysis to obtain quantitative properties of tumor biology. Thus, for breast DCE-MRI there is genuine need to acquire images with high sRes and tRes simultaneously: the former for precise tumor morphology evaluation and the latter for accurate quantitative analysis.

The commercially available, GRE-based TWIST (Time-resolved angiography WIth Stochastic Trajectories) pulse sequence employs k-space undersampling and data sharing strategy and is originally intended for time-resolved high spatiotemporal resolution MR angiography (2). Combined with parallel imaging method, the TWIST sequence can achieve up to 10-fold faster imaging speed while maintaining nominal sRes and signal-to-noise ratio (SNR). In this study, we sought to investigate the feasibility of using the TWIST sequence for high sRes and tRes breast DCE-MRI in a pre-biopsy patient cohort with suspicious lesions.

Methods: 31 patients with 36 mammography- and/or sonography-detected suspicious lesions (three patients with 2 lesions each and one patient with 3 lesions) consented to research DCE-MRI studies prior to standard care biopsy procedures. Axial bilateral DCE-MRI images with fat-saturation and full breast coverage were

Fig. 1

acquired with a 3D TWIST sequence using a 3T Siemens scanner with the body transmit and a 4-channel phased-array breast receive RF coils. The TWIST sequence relies on partial k-space undersampling, with emphasis on more frequent sampling of the k-space center, which governs signal intensity and contrast, relative to the k-space periphery, which governs image fine detail. **Fig. 1** shows 2D k-space TWIST coverage with each dot representing a read-out line in the 3rd dimension. The TWIST scheme divides k-space into a center disk **A** and an outer ring **B**. After a full k-space scan for the very first image set, each following dynamic scan acquires all of **A** and a fraction of **B**. For image reconstruction, the missing points in **B** are copied from the previous or subsequent images. For this study, the fractions of **A** (relative to full k-space) and **B** were set at 0.15 and 0.2, respectively. Other acquisition parameters included 10^0 flip angle, 2.9/6.2 ms TE/TR, a parallel imaging acceleration factor of two, 30-34 cm FOV, 320x320 matrix size, and 120 or 128 slices with 1.4 mm slice thickness, resulting in ~ 1.0x1.0x1.4 mm^3 sRes. The DCE-MRI tRes was 18 or 20 s with ~ 10 min total acquisition time. Gd contrast agent (Prohance®) IV injection (0.1 mmol/kg at 2 mL/s) was carried out following acquisition of two baseline image volumes. A one-frame DCE-MRI image volume

Fig. 2a   2b

with matching spatial coverage was acquired immediately after TWIST DCE-MRI, using a conventional full-k-space-sampling GRE sequence with matching acquisition parameters and a tRes of ~ 60 s.
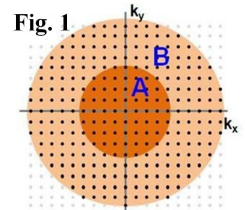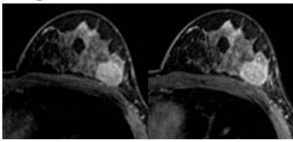
To determine whether TWIST DCE-MRI provides tumor morphology characterization equivalent to conventional DCE-MRI, three breast radiologists compared the last TWIST DCE-MRI image set with the conventional GRE images in multiple morphology categories (including enhancement type, shape, margin, internal enhancement pattern, tissue density, background enhancement, and lesion size) based on ACR BIRADS MRI Lexicon (3), and gave yes/no decisions. One pre- and five post-contrast image sets were selected from the DCE series to form a new dynamic series with an effective tRes of 72 s, imitating the institutional clinical DCE-MRI protocol. These images were submitted to a CAD system (DynaCad®) for qualitative kinetics evaluations. The radiologists gave BIRADS scores based on both morphology and qualitative kinetics assessments (3). In addition, the lesion ROI TWIST DCE time-course data were subjected to Shutter-Speed model (SSM) pharmacokinetic analyses (4-6).

Fig. 3

Descriptive statistic analysis was used to assess intra-radiologist reader agreement in morphology evaluations between the TWIST and the conventional GRE images, with "1" implying complete agreement for all the lesions and "0" no agreement for any lesion. Cohen's κ statistics was used to assess inter-reader agreement in morphology comparison, qualitative kinetics curve shape description and BIRADS score, with κ = 1 indicating full agreement and κ = 0 agreement only by chance. Two-sided z-test was used to test whether the inter-reader agreement was statistically significantly greater than that by chance.

Results: The SNR measured from an ROI of normal appearing breast parenchyma in the last TWIST image sets (mean ± SD: 20.4 ± 10.5) was not significantly different (P = 0.84, paired t test) from that measured from the same ROI in the conventional GRE images (20.0 ± 11.2), indicating that the TWIST acquisition strategy preserves DCE-MRI SNR from a full-k-space-sampling scheme. **Fig. 2** shows an example of morphology comparison: a TWIST image from the last image set of a DCE series (2a) and a GRE image at the same location (2b). The images were zoomed to show a contrast-enhanced tumor in the left breast. The intra-reader agreement in morphology assessments based on the two types of images ranged from 0.88 for enhancement type to 0.94 for lesion size. The Cohen's κ ranged from 0.77 for qualitative kinetics description to 1 for background enhancement. The κ test results for inter-reader agreement were statistically significant (P < 0.0001) in all categories.

Pathology analyses revealed 13 malignant and 23 benign lesions. Based on MRI BIRADS scores with BIRADS 4 or 5 indicating positive finding, all three readers attained 100% sensitivity with specificities at 69%, 69%, and 65%, respectively. Using SSM pharmacokinetic analyses of the TWIST DCE-MRI data and a cut-off K^{trans} (contrast agent plasma/interstitium transfer rate constant) value of 0.08 min^{-1} (**Fig. 3**), the diagnostic specificity was improved to 83% at 100% sensitivity.

Discussion: High tRes is crucial for accurate pharmacokinetic analysis of DCE-MRI time-course data. Recent simulation studies show that low tRes is detrimental to breast cancer diagnostic accuracy, whether a quantitative (7) or a semiquantitative (8) approach is used. The results from this study suggest that the agreement in morphology evaluation between the TWIST and conventional GRE images is excellent. Thus, it is feasible to achieve, without sacrificing high sRes and precise morphology assessment, high tRes for breast DCE-MRI using the TWIST sequence, potentially making quantitative breast DCE-MRI a reality in clinical settings. Though sophisticated acquisition methods have been explored to improve breast DCE-MRI tRes, the impact on clinical practice would be more immediate and robust if a commercially available sequence could achieve this goal. Therefore, it may be beneficial to investigate the feasibility of using time-resolved MR angiography sequences from other major vendors, such as TRICKS (9) from GE and 4D-TRAK (10) from Philips, for high spatiotemporal resolution breast DCE-MRI. In this study, the fractions of k-space regions **A** and **B** were set at the fixed values. It has been shown in a kidney study (2) that errors in a TWIST DCE-MRI signal intensity time-course are less than 5% compared to a full-k-space-sampling GRE acquisition when the fractions of **A** and **B** are both set at 0.2. The optimization of the combined **A** and **B** fractions through simulations is warranted in future research to ensure the reliability of TWIST DCE signal intensity time-course while minimizing image artifact. Furthermore, with 16-channel phased-array breast RF coil commercially available and thus higher parallel imaging acceleration factors possible, it is likely that sub-10s tRes can be achieved for TWIST breast DCE-MRI along with high sRes.

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