Radiography xxx (2018) 1–8

Contents lists available at ScienceDirect

Radiography

journal homepage: www.elsevier.com/locate/radi

Evaluation of an equilibrium phase free-breathing dynamic contrast-enhanced MRI prototype sequence compared to traditional breath-held MRI acquisition in liver oncology patients

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ARTICLE INFO

Article history:
Received 16 November 2017
Received in revised form
22 December 2017
Accepted 3 January 2018
Available online xxx

Keywords:
Magnetic Resonance Imaging
Free-breathing
Liver oncology
Radial sequence

ABSTRACT

Introduction: Magnetic Resonance Imaging (MRI) is a commonly used for diagnosing metastatic liver disease. When patients are unable to achieve the necessary arrested respiration required during image acquisition, image artefacts occur that affect image quality and diagnostic value. The main contribution of this study is the evaluation of a novel prototype technique that allows a specific sub-group of patients to breathe freely throughout the acquisition of dynamic contrast enhanced equilibrium phase MRI of the liver.

Methods: The study compared a traditional single phase of arrested respiration T1-weighted (T1W) fat saturated (FatSat) volumetric interpolated breath-hold sequence (VIBE) with a novel free-breathing T1W 3D Radial VIBE prototype sequence. A cohort of patients ($n = 30$) with known hepatic metastases who demonstrated difficulty in complying with the instructions for arrested inspiration were scanned. Both sets of data were compared for diagnostic quality using a Likert scale questionnaire by specialist Oncology Radiologists ($n = 2$).

Results: Higher scores for all image quality criteria, including the presence of artefact (2.6 ± 0.57; $p < 0.001$), lesion conspicuity (2.9 ± 0.35; $p < 0.001$) and visibility of intra-hepatic vessels (2.8 ± 0.37; $p < 0.001$) were found using the free-breathing sequence (13.5 ± 1.94; $p < 0.001$ $t = 13.31$; df 29; $p < 0.001$) than the breath hold phase (8.1 ± 2.06), confirmed with kappa (k-0.023; p-0.050).

Conclusions: The results demonstrated a 39.5% improvement in overall image quality using the T1W 3D Radial VIBE prototype sequence, and have the potential to improve patient experience and reduce image artefacts during MRI imaging of this sub-group of patients.

Introduction

Within oncology, it is essential that the imaging achieved is of the highest quality possible to ensure effective management and treatment options can be applied. The liver is the second most common site of metastatic disease from a primary breast, lung or a colorectal tumour.[1] The use of Magnetic Resonance Imaging (MRI) in hepatic metastatic disease has been evidenced in the United Kingdom (UK) by the Royal College of Radiologists[2] (RCR) and National Institute for Clinical Excellence[1] (NICE) guidelines as the reference standard examination to characterise small malignant liver lesions. Identifying or excluding malignancy is the primary aim, while the distinction between benign and malignant lesions contributes in determining disease severity/staging, and monitoring therapy/recurrence. If a malignant lesion is identified, it is important to distinguish between primary and secondary cancers as this will determine patient treatment options,[1] and establish the distribution of malignant lesions to adjacent vascular anatomy (for resection, radiofrequency ablation, or biopsy).[3–5]

The RCR guidelines[2] recommend contrast MRI oncology liver imaging with T1 and T2 weighted (W) sequences, in and out of phase for fatty tissue and focal lesion location, with diffusion-weighted imaging (DWI) to aid differential diagnosis of haemangiomas and benign cysts. The application of dynamic contrast-enhanced MRI (DCE-MRI) imaging can be a challenge in practice, as the duration of the scan is long compared to the physiological

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https://doi.org/10.1016/j.radi.2018.01.001
1078-8174/

processes of heart rate, blood flow rate and respiration cycles.[6] This may reduce temporal resolution and increases motion and reconstruction artefacts. Strategies such as breath-holding or respiratory compensation are routinely employed to reduce breathing artefacts.[7] Applying technological developments, such as parallel imaging, respiratory triggering, and partial-Fourier techniques to accelerate examinations, and allow periods of arrested respiration during the unenhanced, arterial, portal venous and equilibrium phases of DCE-MRI. With the potential to reduce each breath-hold examination to 23 s. This can be helpful when imaging children and adults with diminished respiratory capacity, or whose compliance may be complicated by communication difficulties (deafness or language barriers), or diminished cognitive ability.[7] Furthermore, protocols which employ hepato-biliary specific contrast can accentuate the number of breath holds required[8] increasing breathing artefacts resulting in repeat imaging and further intravenous (IV) contrast agents.

This study aimed to investigate whether a prototype (non-product) free-breathing DCE-MRI radial VIBE sequence could provide comparable diagnostic quality to a traditional arrested-respiration DCE-MRI sequence in patients who have difficulty in following breath-holding instructions. Comparing the equilibrium phase of imaging which is considered to be the 'standard' sequence for assessing metastatic pathology within the field of oncology imaging in the UK.[2]

Literature review

A literature search was performed to identify studies reporting performance data on MRI imaging (index test) and liver lesions (target conditions). The search used MEDLINE, PUBMED, Biomed Central databases, subject-specific electronic databases (Elsevier, ScienceDirect, Wiley, Springer and Sage), and manufacturer literature from 2005 to present. Manufacturer materials may introduce bias to the evidence, but it was also a source of technical data explaining pertinent physics, protocols, and data from early implementer sites.

Found literature evidenced improved quality using free-breathing DCE-MRI[9–11] and controlled aliasing DCE-MRI[12] in 3 T[7–11] imaging. The novelty of this study is the application of a 1.5 T MRI scanner, which due to the lower field strength than the published studies would gain new clinical results. Previous studies applied 3 T[7–11] strength which would inherently result in different data due to different signal to noise ratios, contrast to noise ratios, spatial and temporal resolution quality.[13] Furthermore, the published studies concentrated on arterial and portal-venous sequences acquired with a high IV flow rate (2 ml/s[7,9,10]). This study will review data acquired post contrast after a lower IV flow rate (1 ml/s) in the equilibrium phase, potentially resulting in different imaging outcomes.

Methods

The institutional ethics board approved this study. The sample population were selected from the prospective worklist of the MRI department within the study setting (specialist oncology centre). The eligibility criteria consisted of adults (>18 years) referred with known secondary liver malignancy to assess on-going treatment and management. All patients recruited from the prospective worklist demonstrated difficulty complying with pre-MRI examination breath hold instructions and pre-scan arrested respiration exercises. All patients provided informed consent to participate in the study. The minimum recruitment sample size required was calculated using a priori power analysis to allow reasonable detection of effect using G-power (v.3.1.9.2, Universität Kiel, Deutschland) software. Applying a *t*-test (two-tails) of difference between two independent means (two groups), with an error probability (α) of 0.05, power (1-β probability of error) of 0.80, and an effect size (ρ) of 0.8 (large). The sample size calculated required $n = 26$ participants (Table 1).

The DCE-MRI protocol consisted of an unenhanced, arterial, portal venous (using a liver-specific contrast agent) and equilibrium phases (Table 2). The department's protocol contra-indicated IV contrast more than once within 24 h due to documented risks associated in patients with healthy and impaired renal function.[14–16] Furthermore, it would be unethical to delay patient's treatment to undertake additional imaging on two separate occasions. Likewise, it is unrealistic to compare the new technique with standard historical imaging as the patient condition can change between attendances. In this study, a compromise was reached by obtaining imaging with a prototype T1W 3D radial (non-product) free-breathing work-in-progress (WIP) novel sequence and a breath-held T1W Volumetric Interpolated Breath-hold Examination (VIBE) sequence in the equilibrium (contrast washout) phase of imaging. The investigation employed the free-breathing sequence (#528 radial VIBE WIP sequence, Siemens Healthineers, Erlangen, Deutschland), similar to the commercially available StarVIBE sequence (FREEZEit package, Siemens Healthineers, Erlangen, Deutschland). This sequence allows DCE-MRI of the liver to be acquired during free respiration, which was achieved by filing k-space in a radial stack of stars sampling fashion with 2016 radial views, to reduce the susceptibility of breathing motion artefacts.[17] Additionally, K-space weighted image contrast (KWIC, Siemens Healthineers, Erlangen, Deutschland), and golden angle view-sharing reconstruction were applied to make further use of redundant data and thereby increase the temporal resolution. The view angle was incremented by the golden angle (111.246°) after all partitions of a particular view were measured and view sharing reconstruction applied.[18] The view sharing used with golden angle sampling is most similar (but not identical) with the work of Winkelmann et al.[18] The interventional free-breathing sequence took approximately 6 min 30 s to acquire data, with a temporal spacing of 4.2 s with 21 spokes on the inner k-space ring. The traditional breath-held imaging took approximately 23 s; both sequences were acquired on a Siemens MAGNETOM Aera1.5 T (Siemens Healthineers, Erlangen, Deutschland, Tables 2 and 3).

Both imaging datasets were reviewed using a Likert scale questionnaire. A bias of using Likert scoring is the subjective nature of the scoring. This study adopted a forced choice method as 'undecided' and 'neutral' options were removed[19] to reduce central tendency and acquiescence bias. Both sequences were reviewed by two Consultant Radiologists specialising in both MRI and liver oncology on Picture Archiving and Communications (PACs) workstations (Sectra, Linköping, Sweden). The datasets were separated, anonymised and presented in a randomised order. The Radiologists (blinded to the original results) graded both sequences against diagnostic image quality criteria that were considered essential by the Radiologists. The study reviewed sharpness of the liver capsule; visibility of the intra-hepatic vessels; and conspicuity of lesions smaller than 1 cm and larger than 1 cm. Against grading of (1) major blurring, not clearly visible; (2) some blurring, visible but not clear; and (3) no blurring, visible and clear. Additionally, the presence of artefacts was graded with a scale of (1) major artefact, non-diagnostic; (2) some artefact, remains diagnostic; or (3) no artefact, and diagnostic.

This study represented a two-sample comparison with the null hypothesis of no statistical difference between the two samples (equal). The alternative hypothesis was the free-breathing sequence is inferior/or superior in diagnostic quality to the breath-held phase. Statistical analysis applied a paired two sample

Please cite this article in press as: Hopkinson G, et al., Evaluation of an equilibrium phase free-breathing dynamic contrast-enhanced MRI prototype sequence compared to traditional breath-held MRI acquisition in liver oncology patients, Radiography (2018), https://doi.org/10.1016/j.radi.2018.01.001