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MRI protocol optimization for quantitative DCE-MRI of the spine

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ABSTRACT

Purpose: In this study we systematically investigated different Dynamic Contrast Enhancement (DCE)-MRI protocols in the spine, with the goal of finding an optimal protocol that provides data suitable for quantitative pharmacokinetic modelling (PKM).

Materials and methods: In 13 patients referred for MRI of the spine, DCE-MRI of the spine was performed with 2D and 3D MRI protocols on a 3T Philips Ingenuity MR system. A standard bolus of contrast agent (Dotarem - 0.2 ml/kg body weight) was injected intravenously at a speed of 3 ml/s. Different techniques for acceleration and motion compensation were tested: parallel imaging, partial-Fourier imaging and flow compensation. The quality of the DCE MRI images was scored on the basis of SNR, motion artefacts due to flow and respiration, signal enhancement, quality of the T_1 map and of the arterial input function, and quality of pharmacokinetic model fitting to the extended Tofts model.

Results: Sagittal 3D sequences are to be preferred for PKM of the spine. Acceleration techniques were unsuccessful due to increased flow or motion artefacts. Motion compensating gradients failed to improve the DCE scans due to the longer echo time and the T_2* decay which becomes more dominant and leads to signal loss, especially in the aorta. The quality scoring revealed that the best method was a conventional 3D gradient–echo acquisition without any acceleration or motion compensation technique. The priority in the choice of sequence parameters should be given to reducing echo time and keeping the dynamic temporal resolution below 5 s. Increasing the number of acquisition, when possible, helps towards reducing flow artefacts. In our setting we achieved this with a sagittal 3D slab with 5 slices with a thickness of 4.5 mm and two acquisitions.

Conclusion: The proposed DCE protocol, encompassing the spine and the descending aorta, produces a realistic arterial input function and dynamic data suitable for PKM.

1. Introduction

Dynamic contrast enhanced (DCE) MRI has found broad application in radiology, and established itself as a valuable technique used in the staging of cancer and assessment of arthritis, and in the monitoring of their treatment [1]. While a large amount of literature presents DCE–MRI data for many anatomical regions (such as brain, breast, prostate, upper and lower joints) DCE-MRI application in spine imaging remains limited. DCE-MRI in the upper and lower spine is used in multiple myeloma [2–6], assessment of metastases [7–10], differentiation between multiple myeloma and metastases [3], (compression) fractures [11–13], Osteoporosis [14–16], Leukaemia [17,18] and Paget's disease [19].

In addition to the limited amount of DCE-MRI studies in this region, there is also a lack of data presenting a true quantitative pharmacokinetic (PK) analysis.

Quantification using Pharmacokinetic models, (e.g. Tofts' model [20] has become the gold standard in DCE-MRI analysis: quantification not only offers physiology-related parameters (instead of scan-related parameters), but it also allows for an inter-patient, inter-study or inter-group comparison, something particularly useful in multi-centre studies where absolute values are needed to compare outcomes. The application of pharmacokinetic analysis, however, puts extra requirements on the data acquisition protocol. For the extraction of absolute PK parameters such as the transfer constants K^{trans} [20] or flow, knowledge of the absolute contrast agent concentrations is required, the signal-to-noise ratio (SNR) should be sufficient to allow pixel-by-pixel non-linear fitting, and the MRI protocol should include scans (e.g. a pre-contrast T_1 measurement) to allow the contrast agent concentration measurement. Furthermore, as most models require de-convolution with the arterial input function (AIF), the scan field of view (FOV) should include an artery from where the contrast agent (arterial) input function can be extracted. Though quantitative analysis is common in many studies in other anatomical areas, the existing literature does not provide

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evidence on how to set up a DCE-MRI protocol of the spine that provides at the same time a good arterial AIF, high SNR in the vertebral bodies and a reliable T_1 quantification.

Our quest is therefore to find a reliable DCE-MRI protocol for the imaging of the whole spine which would be suitable for analysis with PK models. The challenge is manifold. On the one hand it is essential to obtain large FOV DCE-MRI images in problem areas such as the thoracic spine, avoiding breathing artefacts and artefacts caused by the beating heart, while providing a high SNR in the spine. On the other hand, the signal in the aorta, the only visible artery in these scans, is hampered by the high flow and the high concentration of contrast agent (CA). While high sampling frequency and minimization of flow and T2* saturation effects are required to correctly sample the contrast agent (CA) bolus peak in the aorta, imaging of the spine requires longer acquisition times, while breathing and heartbeat hamper the use of parallel imaging. We have so far found no published viable protocol fulfilling all these conditions.

In this work we have investigated different DCE-MRI protocols covering the whole spine, and assessed them for their capacity to provide robust qualitative and quantitative analysis. We analysed the protocols in terms of SNR, contrast-to-noise ratios (CNR), contrast enhancement, motion artefacts, ability to provide a reliable AIF, and reliability of the pre-contrast T_1 measurement using a variable flip angle (VFA) scheme with the same sequence used for the DCE-MRI. This last was used as a mirror of the reliability of the contrast agent concentration measurements. We investigated both 2D and 3D imaging schemes.

From this evaluation of protocol parameters, we have come to a recommendation for the optimal DCE-MRI protocol that suits the needs for PKM modelling. Finally, we have also applied a qualitative analysis of the time-intensity curves (TICs), which has resulted in a characterisation of the TICs in unaffected vertebral bodies, muscle and the spinal cord.

2. Methods

2.1. Subjects

In total thirteen patients undergoing a DCE-MRI of the spine as part of clinical care or a clinical study were enrolled in this study. Nine patients were scanned because of lower back pain or radicular complaints, two of which had a history of non-small cell lung carcinoma. One patient was scanned because of TB spondylodiscitis, one as follow up after resection of an intradural mass and two in the context of a study investigating spine metastases in prostate cancer. All patients received an additional dynamic acquisition during and after the injection of the contrast agent. This study was reviewed by the Medical Ethical Review Committee of the VU University Medical Center and they concluded that the Medical Research Involving Human Subject act (WMO) did not apply. The scans were obtained at the VU University Medical Center and all subjects gave written informed consent.

2.2. Image acquisition

Patients were scanned on a 3.0 Tesla Philips Ingenuity PET/MRI scanner, Release 3.2.2.0 2015-08-05 (Philips, The Netherlands). We tested different DCE-MRI protocols, which were performed using Dotarem® (Guerbet Netherlands) as contrast agent, injected at a speed of 3 ml/s, 0.2 ml/kg body weight using a 20 gauge cannula. Contrast bolus was followed by a flush of 15 ml saline water injected at 3 ml/s.

All the tested DCE protocols were based on a Spoiled Gradient Echo sequence. The sequence used for the DCE-MRI protocol was also used prior to the DCE-MRI scan with different flip angles (each using only 1 dynamic scan), in order to extract pre-contrast T_1 values [21].

The DCE-MRI protocols were constructed starting from 2 basic protocols, all in the sagittal direction: one 3D and one 2D. The basic 3D protocol (3D_1) was a T_1-w Fast Field Echo, TE = 1.5 ms, TR = 3.14 ms, % sampling 49.6%, Slice thickness = 3.5 mm, in plane resolution 1.25 mm, Flip angle = 12°, 6 slices, Dynamic scan time (TDyn) = 5.52 s, Phase oversampling. The basic 2D protocol (2D_1) was a T_1-w Fast Field Echo sequence slice thickness 4 mm, TE/TR = 2.6/5.4 ms, TD yn = 3.03 s, in-plane resolution 1.33 mm. Using these two basis protocols as baseline, respectively a 2D and 3D sequence (protocol 2D_1 and 3D_1), sequence parameters were varied as described below.

Table 1
Parameters varied and investigated range. An extended description of all the protocols is given in the supplemental material.

Parameter	Range
Acquisition type	2D/3D
Slice thickness	3.5–4.5 (mm)
Repetition time	3.2–4.6 (ms)
Echo time	1.5–2.6 (ms)
Number of averages	2–3
Percent sampling	50–100
Nr of slices	4–6
Flow compensation	Y/N
Partial Fourier frequency	Y/N
Partial Fourier phase	Y/N
SENSE	Y/N

A list of the investigated parameters is given in Table 1. Full details of all protocol parameters are given in Table 2 and the Supplemental material. In short, for the series of 3D protocols the scan was first accelerated by means of partial Fourier imaging (3D_2), then the effect of the breathing artefacts was assessed by moving to the lumbar region (3D_3). The slice thickness (spatial resolution in the 2nd phase direction) was then changed to 4.5 mm and the number of slices reduced to 5 (protocol 3D_4). The number of acquisitions (NEX) was subsequently changed to 3 to increase SNR at the cost of dynamic scan time (protocol 3D_5, TDyn = 7.36 s). This protocol was further modified to increase speed by means of SENSE (protocol 3D_6), effectively reducing TDyn to 4.18 s. We then investigated the effect of Flow compensation by modifying protocol 3D_4 (best protocol until then) by adding flow compensation and consequent increase in echo time (TE) and repetition time (TR) (protocol 3D_7). To reduce TE/TR, partial Fourier imaging was added (Protocol 3D_8) and in protocol 3D_9 the effect of a longer TE/TR was investigated without flow compensation. 11 subjects 1 were investigated with different MR Protocols. Two subjects received the same MRI protocol as two previously scanned patients.

2.3. DCE MR image analysis

The in-house developed *Dynamo* software was used for analysis of the dynamics scans. Details of the analysis software are given elsewhere [22].

2.3.1. Drawing of the ROIs

For each patient 3 regions of interest (ROI) were drawn on post-contrast T_1-w images by a radiologist with 10 years' experience. One ROI was placed in the in one unaffected vertebra, one in the spinal cord and one in the erector spinae muscle. In drawing the ROIs the radiologist was blinded for the DCE-MRI parametric images.

2.3.2. Semi-quantitative analysis

The DCE-MRI datasets were analysed to provide parametric maps of Maximum Enhancement (ME) and initial slope of increase.

2.3.3. TIC-shape analysis

All the individual TICs were classified (on a pixel by pixel basis) as to belong to any of 7 types according to [23], and colour coded parametric maps were generated. Briefly, these classes are the following: