Development of a spin echo gradient echo sequence for simultaneous assessment of the biomarkers vessel size index, relative blood volume, and perfusion

S. Zwick[1], W. Reichardt[1], C. Weidensteiner[1], and D. von Elverfeldt[1]
[1]Dept. of Radiology, Medical Physics, University Medical Center, Freiburg, Germany

Introduction

The aim of this work, which is supported by the 2010 ISMRM Seed-Grant, was to implement and evaluate a sequence which enables simultaneous measurement of pharmacokinetic modeling parameters and the mean vessel size. Perfusion, permeability and relative blood volume usually assessed by dynamic contrast enhanced MRI (DCE-MRI), and the mean vessel size assessed by vessel size imaging (VSI) [1] are able to detect early anti-angiogenic therapy responses [2]. Anti-angiogenic drugs are of increasing importance in cancer therapy.
DCE-MRI is routinely performed with clinically approved Gd-based contrast agents (CAs) and is based on the change of R_1 during and after the injection of the CA. Up to now VSI is usually performed with iron-oxide particles which are not yet approved for clinical use. It is based on the change of R_2* and R_2 pre and post CA injection. Combination of both techniques using a single MR sequence and only one injection of a Gd-based CA results in reduced scan time and improved animal or patient comfort. Successful implementation of VSI with GD-DTPA has already been shown [3]. In our method DCE-MRI parameters will not be calculated by changes of R_1 but from the change in R_2 or R_2*.

Materials and Methods

All sequences were implemented on a 9.4 T animal scanner (BioSpec 94/20, Bruker, Ettlingen, Germany) using a mouse quadrature coil. The developed single shot gradient echo spin echo EPI sequence (GESE-EPI) consists of a 90 deg. excitation pulse and a 180 deg. refocusing pulse. Both, the FID (free induction decay) as well as the generated SE signal are acquired by an EPI readout. To analyze the accuracy of delta R2 and delta R2* quantification phantom measurements were performed on a custom-built phantom with the developed sequence and compared to standard relaxometry sequences. Sequence parameters were as followed: SEGE-EPI: single slice, TE_{GE}=80 ms, TE_{SE}=200 ms, acquisition time < 500 ms, FOV 30x30 mm², matrix 64x64, receiver bandwidth 300 MHz, readout time EPI module 15.2 ms. ΔR_2 and ΔR_2* were calculated from $1/TE*signal_1/signal_2$. Standard T_2 mapping was performed with a multi spin echo sequence (single slice, TR=2500 ms, 16 echoes with TE=11...176 ms in steps of 11 ms, acquisition time 8 min, FOV 30x30 mm², matrix 256x256) while T2* mapping was performed with a multi gradient echo sequence (FLASH, single slice, TR=350 ms, 6 echoes with TE=30...180 ms in steps of 30 ms, acquisition time 9 min, FOV 30x30 mm², matrix 256x256, flip angle 30 deg.). The phantom consists of several vials with different concentrations of Gd-DTPA. Gd-DTPA was diluted in saline (0.9% NaCl) yielding Gd concentrations of 2.8, 1.4, 0.7, 0.35, and 0.175 µM.

Fig. 1: SE image (left, TE=200 ms) and GE image (middle, TE=80 ms) acquired with the new GESE-EPI sequence and SE image from a standard multi SE dataset (right, TE=176 ms).

Results

GESE-EPI images of the phantom are shown in Fig. 1. The GE image shows typical susceptibility artifacts due to changes in susceptibility between fluid and air bubbles or fluid and vial wall while both GE and SE images show the EPI ghostings. ΔR_2 and ΔR_2* between the different vials were calculated (for all 3 sequences). GESE-EPI slightly overestimates ΔR_2 and underestimates ΔR_2* as compared to the standard sequences (Fig. 2). Note the dramatic differences in acquisition time between the GESE-EPI and relaxometry sequences. Furthermore, we found a linear dependency between CA concentration differences and ΔR_2 and ΔR_2*, respectively (R^2=0.999 and 0.98, data not shown).

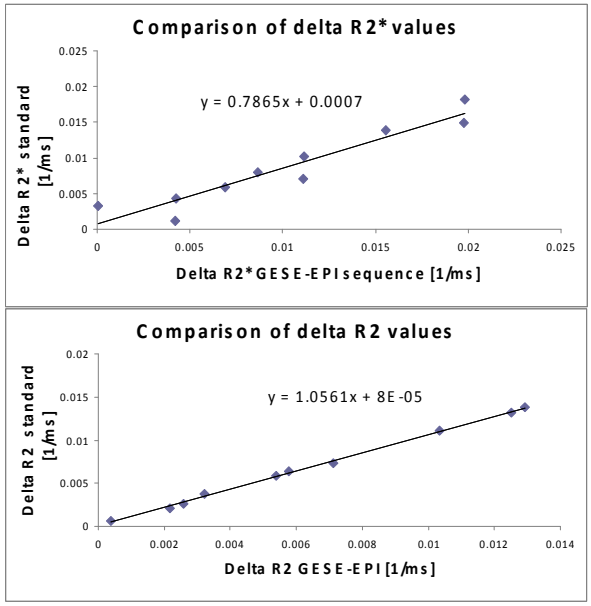

Fig. 2: Comparison between ΔR_2 (top)/ ΔR_2*(bottom) acquired with GESE-EPI (x-axis) and standard sequences (y-axis).

Discussion and Outlook

First phantom studies showed that the technique provides a reliable quantification of ΔR_2 and ΔR_2* in a very short acquisition time. A short acquisition time is important for a sufficient temporal resolution in dynamic MRI experiment during CA injection consisting of a series of GESE-EPI scans. The linear dependency between ΔR_2 and ΔR_2* and CA concentration difference should enable us to perform pharmacokinetic modelling based on a dynamic scan during CA injection.
The next step will be the evaluation of the GESE-EPI sequence in vivo in rats during i.v. injection of CA. Perfusion, blood volume, and vessel size measurement using the GESE-EPI sequence with Gd-DTPA will be compared to standard VSI with iron oxide particles and to standard DCE-MRI with Gd-DTPA.

References

1. Troprès I at al., *Magn Reson Med.* 2001;45(3):397-408. **2**. Zwick S et al., *J Magn Reson Imaging*. 2009;29(5):1125-33
3. Kiselev VG et al., *Magn Reson Med.* 2005 Mar;53(3):553-63.