Simultaneous vessel size and blood volume measurement in a human tumor outside the brain

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Introduction

The interest in MRI methods that are capable of non-invasively measuring the microvascular structure of tumors has grown steadily over the past years [1,2]. As shown in a previous work, we have developed an approach to joint blood volume and vessel size assessment via simultaneous R2 and R2* quantification pre and post injection of a super-paramagnetic blood pool agent [3]. Preclinical studies have validated the technique against histology and have demonstrated its sensitivity to subtle microvascular changes during anti-angiogenic / anti-vascular treatments [4]. This work reports from the experience in a patient with a pleomorphic sarcoma in the pubic bone and thus presents, to our knowledge, the first vessel size map outside the brain. It further proposes a protocol for fast and robust abdominal vascularization measurements, which accounts for the rapid washout of clinical contrast agents.

Methods

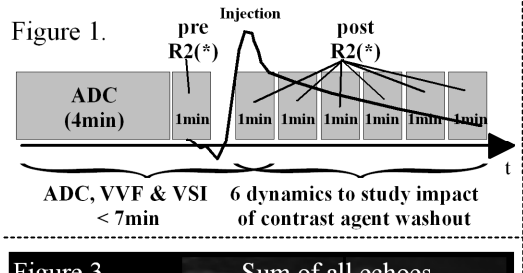
Informed consent was obtained from a 71 year old patient with a pleomorphic sarcoma in the left pubic bone. The experiment was carried out on a clinical 1.5T scanner, using a 5 element cardiac coil (Philips Achieva, The Netherlands). The tumor blood volume (vascular volume fraction, VVF [%]) and local mean vessel size (VSI [µm]) were obtained from the change of R2 and R2* (ΔR2, ΔR2*) induced by a super-paramagnetic SPIO contrast agent (1.4ml, Resovist, Bayer Schering Healthcare) and an ADC measurement (4 b-values between 0 and 1000smm^{-1}) using the equations given in [5-7], Fig. 1. ΔR2 and ΔR2* are quantified simultaneously from the ratio of multi-gradient-multi-spin-echo signals, acquired pre and post injection (7 FID echoes, 1 Spin echo at TE_{SE}=80ms, sampled by 17 gradient echoes. $dTE_{GE,FID}$=3.9ms, TR = 866ms) as described in [3]: A mono-exponential (Levenberg-Marquardt) fit can be employed, since the division of signals eliminates the impact of B0 and B1 inhomogeneities and slice imperfections. Prior to fitting, the ratio values are weighted with respect to the echo- and pixel-wise SNR to account for outliers when dividing by noisy data. Scan time was optimized by SENSE (factor 2, AP), half scan (factor 0.6) and FOV reduction (200x160mm) to permit volumetric ΔR2*/ΔR2 mapping (6 slices à 5mm, 1mm in-plane resolution) within 1min. Anatomic displacement after injection was corrected for by a rigid-body registration and correction algorithm [8]. To study the robustness of the physiologic analysis with respect to the timing of the post scan and the washout of the agent, all quantitative measures were tracked over 6 successive measurements after injection (Fig. 1).

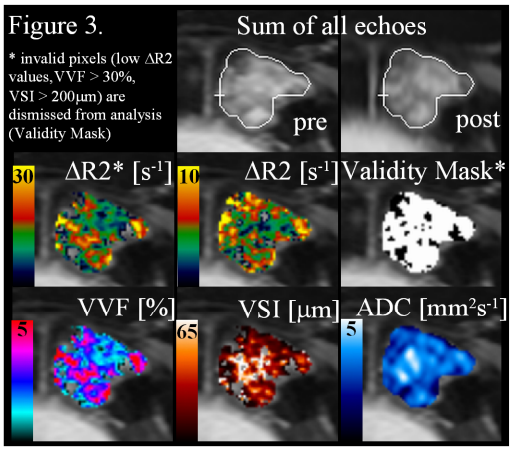
Results

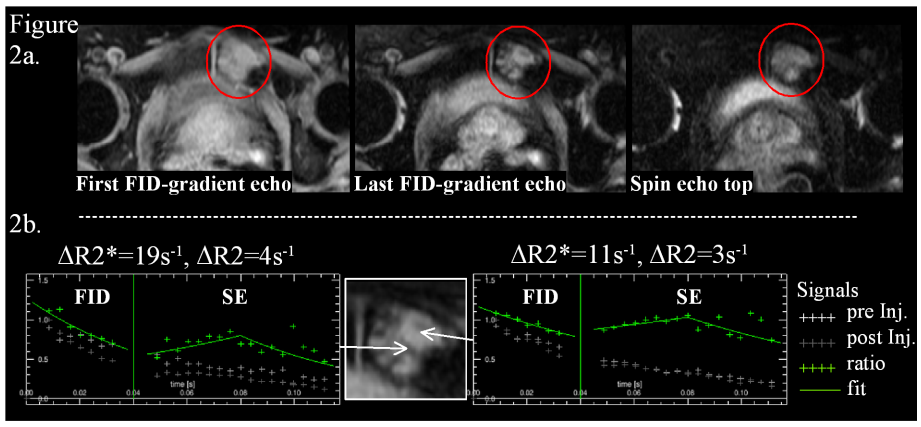
Fig. 1 outlines the MR protocol. Fig. 2 depicts example images of the first post ΔR2*/ΔR2 scan (a) and example signals from different regions of the tumor (b). Fig. 3 shows all relaxometry and physiologic maps, derived from the first post scan. Fig. 4 plots the mean tumoral ΔR2(*), VVF and VSI over all dynamic repetitions. Apart from a global anatomic displacement after injection (which was successfully corrected), the images were free of motion, flow, and SENSE artifacts (Fig. 2a). The echo timing allowed for appropriate coverage of the signal decays pre and post injection (Fig. 2b), ΔR2*/ΔR2 values of the tumor were sufficiently high to generate robust physiologic maps (Fig. 3), and the physiologic measures appeared to be independent from the contrast agent washout (Fig. 4).

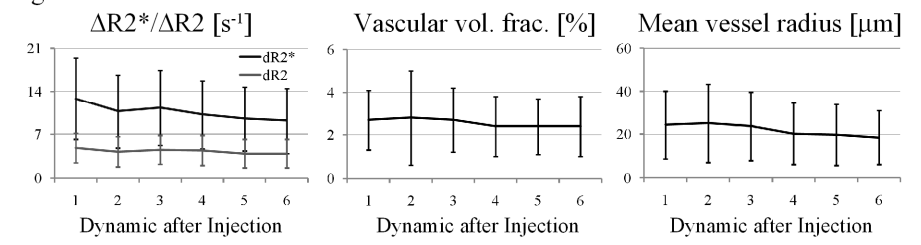
Discussion/Conclusion

Simultaneous blood volume and vessel size examinations with MRI have already shown very promising results in preclinical studies, in particular to monitor changes in response to anti-angiogenic treatments. This work proposes a solution for human applications that benefits from simultaneous ΔR2*/ΔR2 relaxometry and accelerated protocols to cope with the fast washout of the clinical available SPIOs. Simultaneous and efficient ΔR2*/ΔR2 quantification strategies for VSI, like the here presented method, are becoming even more important, considering the current downturn of availability of clinical SPIO agents. Future studies need to investigate, whether the approach is efficient and sensitive enough to compass the short perfusion period and lower R2(*) relaxivity of clinical gadolinium agents.









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