A Six-Fold Throughput Improvement For Preclinical Cancer Studies

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Introduction

To promote the use of MRI for preclinical evaluation of experimental cancer therapies, a high-throughput multi-animal imaging strategy can be used to reduce cost, improve logistics of coordinating scanner access with treatment schedules, and reduce experimental variance of longitudinal studies by scanning more animals over a shorter window of disease progression. Based on simulating multi-animal array configurations to optimize throughput, a five-mouse imaging strategy with a system of five shielded transmit-only volume coils and 15-receive only surface coils has been developed [1]. Such hardware permitted the use of both multi-animal and parallel imaging (PI) acceleration strategies for improving the throughput of preclinical dynamic contrast-enhanced (DCE-) MRI studies on a 7-T 30-cm Bruker Biospec system by more than six-fold compared to that which can be achieved with a standard commercially available single-animal imaging setup. Development of the accelerated multi-animal DCE-MRI protocol and imaging workflow are described along with a comparison of study throughput, image quality, and consistency of resulting pharmacokinetic (PK) parameters with respect to the single-animal setup.

Materials and Methods

A standard preclinical DCE-MRI protocol may typically consist of up to 8 acquisitions. Three anatomical acquisitions are used to setup animal positioning (scan 1) and provide reference images for subsequent slice prescription (scans 2 and 3). Prior to injection of contrast, axial T_2- and T_1-weighted spin echo images are acquired (scans 4 and 5), along with a saturation recovery T_1-mapping series (scan 6). A 10-minute T_1-weighted fast spoiled gradient echo image series (scan 7) is acquired before, during, and after high- and low-molecular weight contrast agents (Figure 1) are intravenous administered [2]. Finally, a post-injection anatomical reference of contrast agent distribution is acquired (scan 8).

For the multi-animal protocol, PI was used to reduce anatomical imaging scan times by R = 2 (including GRAPPA [3] autocalibrating lines: R_{eff} = 1.8). The 10-minute duration of scan 7 was fixed, however PI was used to partially compensate for the reduced image update rate resulting from a duty cycle reduction to avoid excessive heating in the B-GA20 gradient coil (ID = 20 cm, G_{max} = 200 mT/m): the repetition time was increased from 40 ms to 160 ms and PI was used to reduce the number of phase encoding lines required for an image update.

Two weeks prior to imaging, the right thyroid glands of 20 Nu/Nu mice were orthotopically injected with 2.5 × 10^5 papillary thyroid carcinoma (BCPAP) cells [4]. On the imaging day, mice were anesthetized and placed either on a single-animal imaging sled and scanned with a 35-mm ID linear mouse birdcage coil (1P 8102) or on a custom-built five-mouse animal sled and scanned with the 20-coil array system. Each of the two protocols was sequentially acquired and animal preparation and protocol execution times were recorded. Normalized blood volume fractions, extravascular extracellular volume fractions, and permeability maps were formed and statistically compared.

Results and Conclusion

The quality of PI-accelerated anatomical mouse images is consistent with phantom-based measurements that indicated superior SNR in the multi-animal array compared with the single-animal birdcage coil (> 1.25× in each volume center). The three-element circumferential arrays permitted PI with R_{eff} = 1.8 without detrimental artifacts (Figure 2). Normalized multi-animal PK maps were calculated (Figure 3) and no statistically significant difference ($p > 0.05$) between PK parameters calculated from mice scanned with the two configurations was detected. On average, a single-animal protocol required 29.6 minutes and the multi-animal protocol required 23.7 minutes. Animal preparation time required approximately 4 minutes per mouse, allowing the next set of mice to be prepared during the imaging protocol for an efficient workflow. In conclusion, a DCE-MRI study throughput of just over six times that which is possible with a standard single-animal setup can be achieved with a novel multi-animal array system.

References

[1] Ramirez MS, et al. 19th ISMRM meeting 2011:1820. [2] Radjenovic A, et al. Phy Med Biol 2006:51(9). [3] Griswold MA, et. al. Magn Reson Med 2002:47(6). [4] Fabien N, et al. Cancer 1994:73(8).

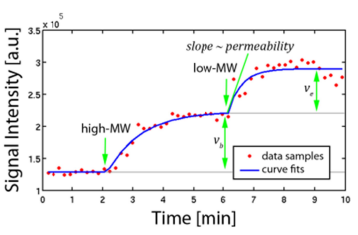

Fig 1. Example DCE-MRI pixel time course illustrating calculation of PK parameters based on imaging the circulation of high- and low-molecular weight contrast agents.

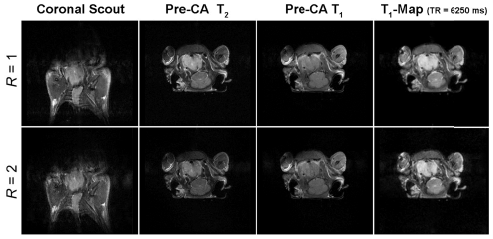

Fig 2. A comparison of unaccelerated (top) and PI-accelerated (bottom) anatomical images from the same mouse illustrates a readily accepted tradeoff in image quality for improving the acquisition speed of the DCE-MRI study.

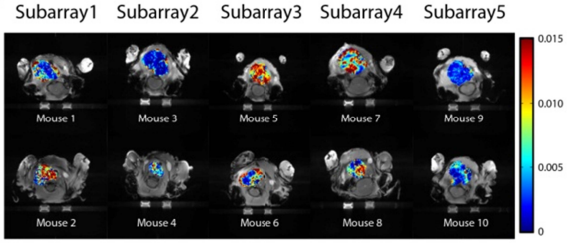

Fig 3. Normalized multi-animal permeability maps as calculated from the initial slope of the low-molecular weight contrast agent extravasating into the extravascular extracellular space.