Study on the Single Cell Detectability as the Concentration of Contrast Agent

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Introduction

Cellular and molecular imaging has attracted attention owing to its ability to monitor biological processes in living organisms at the cellular and molecular level [1-2]. Because of the intrinsic sensitivity to changes in magnetization and susceptibility structures, iMQC imaging signals provide a fundamentally different contrast mechanism from conventional MRI contrast [3-4]. Recently, the feasibility of intermolecular multiple quantum coherence (iMQC) MR imaging combining with contrast agents for single cell detection has been demonstrated [5]. Especially, comparing with the conventional SE and/or GE MR images, intermolecular double quantum coherence (iDQC) MR images exhibited some degree of detectability and contrast even at low spatial resolution and thick slice thickness conditions. In this study, to numerically evaluate how to change the detectability and image-contrast depending upon the concentration of contrast agents, we systematically compared the fractional signal losses of iDQC, EPI, and GE images of single cells labeled with different iron concentrations.

Materials and Methods

Cell labeling was accomplished by adding a Feridex IV solution with an iron concentration of 10, 20, 50, 100 and 200 μg Fe/mL to 10^6 cells in the culture medium for 4 hours. For MRI studies, the labeled cells were suspended in 1% agarose at cellular concentrations of 5000 cells/mL and placed in 5-mm NMR tubes. All experiments were performed on a 14.1 T NMR micro-imaging system (Bruker, Germany) and a 5 mm-saddle-type RF coil were used. The fractional signal loss ($\Delta S/S$) was used to assess the amount of contrast for a given signal void generated by an iron-labeled cell in the MR images and calculated by the equation in Fig 1 [6].

Results

We obtained the iDQC, EPI and GE MR images (Fig 1) and systematically compared the fractional signal losses of the iron labeled cell samples with different iron concentration (Fig 2). The results show the iDQC image has the better cell detectability at the same experimental conditions than EPI and GE images for all the 5 different cell samples. Especially at the high spatial resolution (78 × 78 μm^2 plane resolution and 0.5 mm slice thickness), the iDQC image contrast of the labeled cell in 10 μg Fe/mL contrast media is better than the EPI and GE images contrast of the labeled cell in the 50 μg Fe/mL contrast media. And at the low spatial resolution (150 × 150 μm^2 plane resolution and 2.0 mm slice thickness), the iDQC image contrast of the labeled cell in 50 μg Fe/mL contrast media is similar to the EPI and GE images contrast of the labeled cell in the 200 μg Fe/mL contrast media.

$$\Delta S / S = \frac{S(avg) - S_{cell}(min)}{S(avg)}$$

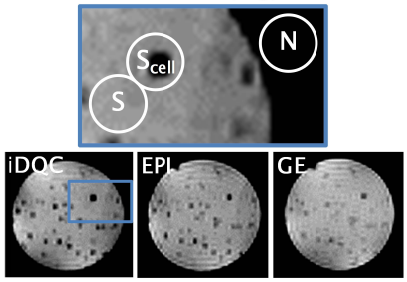

Fig 1. Equation (top) and the more magnified image (middle) for the fractional signal loss ($\Delta S/S$) calculation and iDQC, EPI and GE images (bottom) for the labeled cell sample in the 50 μg Fe/mL contrast media at 100 × 100 μm^2 plane resolution and 1 mm slice thickness.

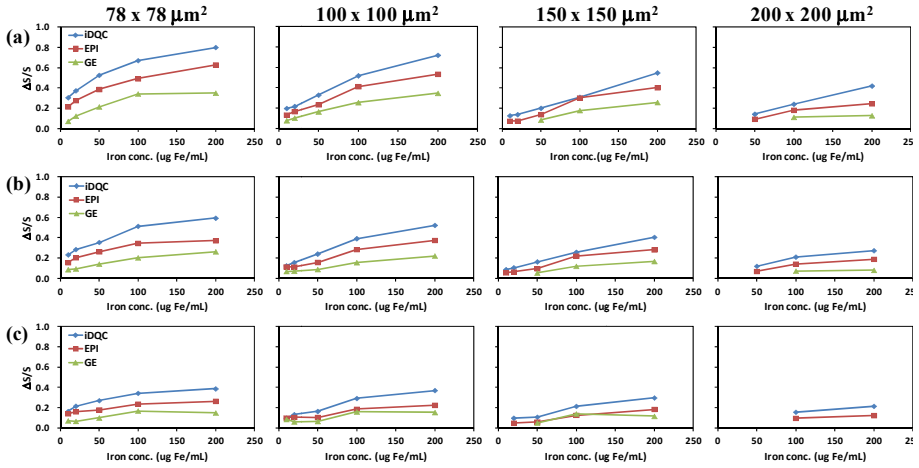

Fig 2. Comparison of the fractional signal loss of iDQC, EPI and GE images of single cells labeled with different iron concentrations. Slice thickness of each row is (a) 0.5, (b) 1.0 and (c) 2.0 mm.

Conclusion

The iDQC images visualized labeled cells more effectively and with a higher contrast-to-noise ratio than conventional EPI and GE images, especially at low resolutions and low iron concentration in cell. This implies that iDQC imaging with contrast agents could be a better alternative to conventional MR imaging for detecting labeled single cells or cell tracking under favorable conditions.

References [1] J.C. Wu et al., Circulation 108 (2003) 1302-1305. [2] M. Lewin et al., Circulation Nat. Biotechnol. 18 (2000) 410-414. [3] J.H. Cho et al., submitted to J. Magn. Reson. (2011). [4] Y. Lin et al., Magn. Reson. Med. 63 (2010) 303-311. [5] J.H. Cho et al., Magn. Reson. Imaging 25 (2007) 626-633. [6] C. Heyn et al., Magn. Reson. Med. 55 (2006) 23-29.