iDQC anisotropy map imaging for tumor tissue characterization in vivo

R. T. Branca¹, G. Galiana², E. R. Jenista¹, C. Leuschner³, C. S. Kumar⁴, and W. S. Warren¹

¹Chemistry, Duke University, Durham, North Carolina, United States, ²Chemistry, Princeton University, Princeton, New Jersey, United States, ³Pennington Biomedical Research Center, Louisiana State University, Baton Rouge, Louisiana, United States, ⁴Center for Advanced Microstructures and Devices, Louisiana State University, Baton Rouge, Louisiana, United States

Introduction

Intermolecular multiple quantum coherence (iMQC) imaging is a new advanced technique that provides information not available from conventional MR imaging¹⁻³: this technique can enhance regions of anisotropy in structured samples⁴⁻⁸ and visualize local dipole fields created by super paramagnetic iron oxide nanoparticles (SPION)⁹. Though iMQC images generally have a very poor signal to noise ratio (SNR), our *in vivo* results demonstrate that we can get very clean images that highlight only regions of high anisotropy, most likely related to the regions of maximum loading of the nanoparticles.

Method

In this study nude mice were inoculated with human breast cancer cells. After the tumor vascularization the mice received an injection of a new kind of contrast agent, LHRH-SPION (luteinising hormone-releasing hormone-conjugated superparamagnetic nanoparticles)^{10,11}. In the LHRH-SPION contrast agent the cellular uptake of the SPIONs is improved by coating the magnetic core with luteinizing hormone releasing hormone (LHRH), which has receptor sites in breast cancer cells.

Standard spin echo and a series of three intermolecular double quantum images (iDQC) were acquired *in vivo* and *post mortem*. The combination of three different iDQC images (with the correlation gradient pointing in three orthogonal directions) gave us the anisotropy map.

Results

Figure 1 shows in vivo standard spin echo and the iDQC anisotropy map images. The iDQC anisotropy image (|z|-|x|-|y|), where x, y, and z represent the direction of the correlation gradient) shows an interesting new feature: tumor region highlighting. Theoretical results show that regions of high intensity signal correspond to regions of high anisotropy. Experiments suggest that anisotropy is more visible in tumors than surrounding tissue masses.



Figure 1:

a) in vivo axial spin echo image of the mice breast tumor;

b) in vivo iDQC image;

c) in vivo iDQC anisotropy map image;

d) post mortem iDQC anisotropy map image

References

[1] Richter W, Sanghyuk L, Warren WS, Qiuhong He. "Imaging with intermolecular Multiple-Quantum Coherences in Solution Nuclear Magnetic Resonance". Science 1995;267:654-657.

[2] Warren WS, Ahn S, Mescher M, Garwood M, Ugurbil K, Richter W, Rizi RR, Hopkins J, Leigh JS. "MR imaging contrast enhancement based on intermolecular zero quantum coherences". Science **1998**;281:247-252.

[3] Rizi RR, Ahn S, Alsop DC, Garret Roe S, Schnall MC, Leigh JS, Warren WS. "Intermolecular zero-quantum coherence imaging of the human brain". Magn Reson Med **2000**;43:627-632.

[4] Bowtell R and Robyr P. "Structural investigations with the dipolar demagnetizing field in solution NMR", Phys. Rev. Lett. **1996**;76:4971–4974.

[5] Bowtell R, Gutteridge S and Ramanathan C. "Imaging the long-range dipolar field in structured liquid state samples". J. Magn. Reson. 2001;150:147155.

[6] Bouchard LS, Rizi RR and Warren WS. "Magnetization structure contrast based on intermolecular multiple-quantum coherences". Magn. Reson. Med. 2002;48:973–979.

[7] Bouchard LS, Wehrli FW, Chin CL and Warren WS. "Structural anisotropy and internal magnetic fields in trabecular bone: coupling solution and solid dipolar interactions". J. Magn. Reson. **2005**;176:27–36.

[8] Ramanathan C, Bowtell R. "NMR imaging and structure measurements using the long-range dipolar field in liquids". Phys. Rev. E 2002;66: 1-10.

[9] Faber C, Heila C, Zahneisena B, Ballaa DZ and Bowtell R. "Sensitivity to local dipole fields in the CRAZED experiment: An approach to bright spot MRI". J Magn. Reson. 2006;315-324.

[10] Leuschner C, Kumar C, Hansel W, Soboyejo W, Zhou J, Hormes JF."LHRH-conjugated Magnetic Iron Oxide Nanoparticles for detection of breast cancer metastases". Breast Cancer Res Treat **2006**; 99(2):163-176.

[11] Zhou J, Leuschner C, Kumar C, Hormes JF, Soboyejo WO."Sub-cellular accumulation of magnetite nanoparticles in breast tumor metastases". Biomaterials 2006; 27(9):2001-2008.