# Coregistration and Comparison of OMR and BOLD MR Images

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**Synopsis**

Tumor bearing mice were sequentially scanned with Overhauser enhanced MRI (OMRI) and BOLD MRI, two techniques which are sensitive to tissue oxygenation, in an attempt to coregister the two images. Markers containing image contrast agents were attached to each mouse in order to select comparable sections of tissue with each imaging technique and to improve the accuracy of image fusion. OMR and BOLD MR images of the tumors were coregistered using different fitting routines, and the correlation between the two images is presented.

**Introduction**

Solid tumors in humans and mice are known to contain hypoxic fractions, which may confer resistance to ionizing radiation and chemotherapy. Therefore, accurate and noninvasive techniques that identify and/or quantify hypoxia within tumor tissue offer the potential to improve understanding, better define targets, and systematically design and test therapies. OMRI relies on the transfer of the inherently greater polarization of the electron spin states of a suitable paramagnetic contrast agent to the tissue water protons, at a given magnetic field, enhancing the NMR signal intensity of the protons. The transfer of the polarization of the electron spin states is accomplished by irradiating the system with RF (radiofrequency) energy, corresponding to the frequency of the EPR (Electron Paramagnetic Resonance). Following this irradiation, the spin states of the protons become polarized to a greater extent than in the absence of the EPR irradiation. Based on the enhancement patterns of the MR images in the presence of the contrast agent, parametric images of oxygen concentration can be determined as a result of the free radical line width dependence on contrast agent spin-spin interactions with molecular oxygen. The purpose of this study is to compare two techniques for imaging tumor oxygenation by utilizing fitting routines to coregister the data matrices.

**Methods**

Mice bearing SCC tumors in the right hind leg with diameters of 1.3 ± 0.2 cm were imaged. To define comparable slice selections, three paired markers were fixed to the mouse, composed of OMRI (OX063) and MRI (Gd) contrast agents respectively. A 2 mmoles/kg bolus of OX063 was administered, followed by continuous infusion at 7 µl/min. For OMRI, a standard spin warp gradient echo sequence was used with each phase encode step preceded by an EPR saturation pulse (226 MHz), as well as field cycling between 8 and 14 mT for EPR and NMR respectively. The times for image collection with and without EPR irradiation were approximately 2.5 and 1.5 minutes respectively. OMR images were analyzed and $pO_2$ maps were generated using Matlab (Natick, MA) routines. For BOLD MRI, gradient echo images were acquired on a Bruker Biospin (4. 7 T) scanner and analyzed using MEDx (Sensor systems, Sterling, VA). Image coregistration was performed using different MIPAV fitting routines (McAuliffe MJ, et al. Medical Image Processing, Analysis & Visualization in Clinical Research. IEEE CBMS 2001, 381-386). The OMRI data matrices were first interpolated to obtain image resolutions equivalent to the BOLD MRI images.

**Results and discussion**

The figure below compares OMR and BOLD MR images. Image A displays the OMRI $pO_2$ map overlaying the raw, Overhauser enhanced image. Image B displays the BOLD signal enhancements overlaying the Gd contrast enhanced image. Image C is a fusion of the OMRI $pO_2$, BOLD enhancement, and contrast enhanced images. Images A-C interrogated tumor oxygenation in an attempt to identify and explain some of the similarities and differences between the two techniques. As can be seen, the regions in tumor where the OMRI technique reports relatively higher $pO_2$ values have minimal BOLD signals. This observation is consistent with the fact that, upon carbogen inhalation, strong BOLD signals are observed in tumor regions that are relatively hypoxic. The minimal overlap between BOLD MR images and OMR images from regions of higher $pO_2$ is consistent with the contrast mechanisms involved in each technique.