

# Intermolecular Multiple-Quantum Coherence Imaging of Murine Tumors Depends on Choice of Dipolar Correlation Distance

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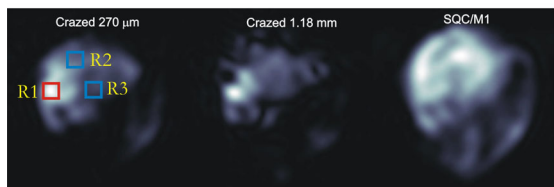
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**Synopsis.** Image contrast based on intermolecular multiple-quantum coherences (iMQCs) is predicted to be useful for enhanced tumor detection. We compare images of mouse RIF-1 tumors acquired with iMQC and conventional T2-weighted sequences and conclude that the tumor to normal tissue contrast is larger for iMQC in some regions of the tumor. We also observe a strong dependence of tumor to normal tissue contrast with the choice of correlation distance.

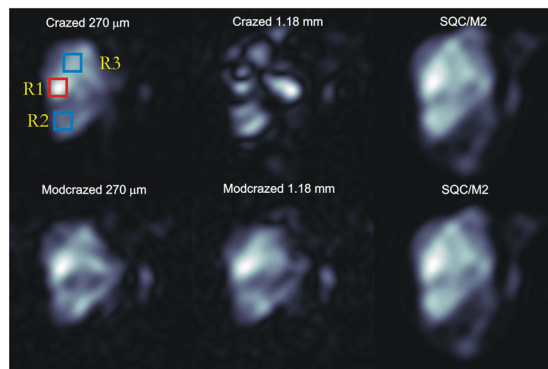
**Introduction.** Magnetic resonance imaging based on long-range dipolar field effects is known to be sensitive to resonance frequency differences [1] and local magnetization structure over the dipolar correlation distance [2]. Applications to fMRI and tumor detection have drawn considerable interest recently [3,4] as a new approach to provide distance selectivity and increased contrast. The correlation distance parameter ( $D_c = \pi/\gamma GT$ ) has been proposed as a means to probe material heterogeneities over a user-defined distance scale [2]. Tumors are a good example of structural heterogeneity which contains differences in local oxygenation and blood flow. We demonstrate the resulting iMQC image contrast strongly depends on the choice of correlation distance.

**Technique.** MR images were acquired at 4T on a GE Signa 5.8 imager equipped with a home-built probe with a 3.4 cm-diameter solenoidal rf coil. We used the iDQC ( $M=+2$ ) CRAZED [1] sequence:  $\Theta=120^\circ$ ,  $TR=4s$ ,  $TE=100ms$ ,  $\tau=15ms$ , Slice thickness=12mm, 4cm FOV, 32x32 matrix, correlation gradient GT along the slice thickness perpendicular to  $B_0$ , with BIR-4 plane rotation and slice-selective hyperbolic secant refocusing pulses to ensure uniform excitation and accurate flip angles (excitation of higher order harmonics depends on powers of  $\sin \alpha$ ). Four steps phase cycling of the first ( $\alpha$ ) rf pulse (x,-x,y,-y) was used. The correlation distance was varied according to: 77, 107, 270, 592, 1180  $\mu m$ . C3H mice ( $n=3$ ) with subcutaneously implanted RIF-1 tumors in the leg were anesthetized using ketamine/acepromazine at 50/5 mg/kg.

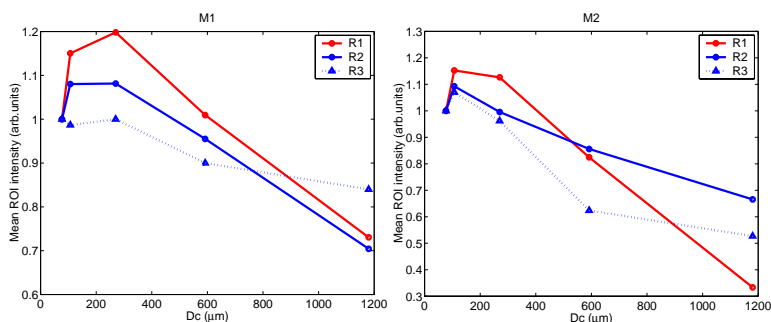
**Results.** Fig.1 shows iDQC CRAZED images for mouse 1 (M1) at two values of  $D_c$  (270 $\mu m$ , 1.18mm) and the corresponding conventional single-quantum coherence (SQC) T2-weighted image (32x32,  $TE=100ms$ ,  $TR=4s$ ). Fig.2 compares CRAZED and MODCRAZED [1] images for mouse (M2). The refocusing  $\pi$ -pulse in the evolution period of the MODCRAZED sequence reduces contributions from field inhomogeneities over the correlation distance [1]. To compare tumor contrast, three different ROIs were drawn for M1 (Fig.1) and M2 (Fig. 2): R1 is over a bright region of the tumor, R2 and R3 are regions with moderate intensity. All ROIs were picked over regions having SNR of at least 100:1. Plots of the mean ROI intensity for M1 and M2 are shown in Fig.3 with correlation distance.



**Fig.1** (left) iDQC images of tumor at two correlation distances. **Fig.2** (right) Comparison of iDQC CRAZED and MODCRAZED images at two correlation distances reveals presence of susceptibility gradients.



**Discussion.** It is clear that the anatomic iDQC CRAZED image contrast is different from the conventional SQC T2-weighted image, and that this contrast depends highly on the choice of correlation distance. In particular, the  $D_c=1.18mm$  images show important signal losses in various regions over the tumor. MODCRAZED images over the same regions recover most of the signal lost, suggesting that this phenomenon is likely due to the presence of important susceptibility gradients over the correlation distance. In general, iDQC CRAZED images show significant heterogeneity over the tumor region, especially at  $D_c=1.18mm$ , and all 3 tumors had hot spots which appeared much brighter than the normal tissue of the second leg (all images were normalized to their maximum intensity to allow contrast to be compared). High blood volume and oxygen contents such as those found in the peripheral regions of tumors are expected to increase signal, but high blood flow or low blood volume would decrease it. In Fig. 3, the ROI of high intensity (R1) peaks around 200-300 $\mu m$  but R2 and R3 behave differently. The differences are likely related to physiologic differences within the tumor. Separate experiments in which sealed test tubes filled with venous and arterial pig blood imaged ( $\tau=15ms$ ,  $D_c=100\mu m$ ,  $TE=100ms$ ,  $TR=4s$ ) within 3 minutes of extraction revealed a significantly larger signal for arterial blood.



**Fig.3** Comparison of ROI mean intensity over the tumor regions of M1, M2.

**Conclusion.** The iDQC CRAZED and MODCRAZED imaging experiments are promising new methods to be used for tumor detection which can potentially help elucidate the heterogeneous structure of tumors by mapping regions of significant susceptibility gradients present over a user-adjustable distance scale. This study suggests a series of experiments to be carried out to correlate the observed changes: mapping of tumor blood flow, oxygenation, blood volume and permeability.

**References** [1] S. Garrett-Roe, JMR 146, 1-13 (2000) [2] L-S. Bouchard, MRM 48:6, (2002) [3] W. Richter, MRI 18,489-494 (2000) [4]. W.S. Warren, Science 281, 247-50 (1998)