# Mapping of viable of tumor regions using Gd-DTPA DCE-MRI

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## Introduction:

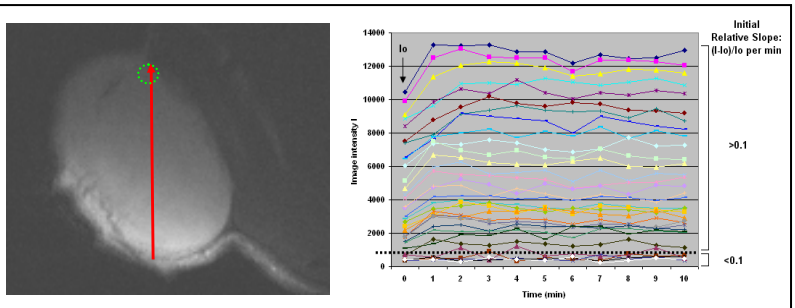
We hypothesize that inclusion of necrotic regions, common in tumor xenografts in rodents, may confound the correlation between interstitial $pO_2$ readings and PET-derived FMISO concentrations. Further, if we could identify and exclude such regions from data analysis, improved correlation between intra-tumoral $pO_2$ readings and FMISO image intensities could be achieved. In this study, we identified and excluded necrotic regions on the basis of slower Gd enhancement and then correlated $pO_2$ readings and FMISO intensities.

## Materials and methods:

Nude rats with Dunning R3327-AT prostate adenocarcinoma xenografts (~1 cm in diameter), anesthetized with 1.5% isoflurane/compressed air, were positioned in a custom-fabricated, animal-specific foam mold. Animals were sequentially imaged by (1) dynamic (1-min frame x 30 frames) MRI (Bruker BioSpin MRI Inc., Billerica, MA) following tail vein injection of gadopentetate dimeglumine (Magnevist; Berlex Laboratories, Wayne, NJ) (0.1 mmol/kg body mass); (2) microPET (Focus 120 microPET, Siemens Pre-clinical Solutions, Knoxville, TN) 1 to 2 hr post-tail vein injection of $^{18}$F-FMISO (~1.5 mCi); and (3) CT (X-SPECT, Gamma Medica, Alameda, CA). $pO_2$ was then measured at 0.5-mm increments along different tracks within the tumor using an OxyLite™ 4000 Oxygen probe (Oxford Optronix, Oxford, UK). The measurement tip of the $pO_2$ was advanced by a robot (Engineering Research Center for Computer Integrated Surgical Systems and Technology of Johns Hopkins University). CT-, PET- and MRI-visible fiducial markers were used to register the respective image and robot coordinate systems using a registration probe[1], thereby providing point-to-point correspondence between each $pO_2$ measurement and each image voxel. CT imaging was performed specifically to assist the registration between MR and microPET images, as animals were allowed to awaken and were returned to their cages between the MR and PET scans but were kept anesthetized in the position in a body-mold for multimodality imaging and $pO_2$ measurements. The reconstructed MRI, PET, and CT images were imported into the Slicer visualization program for registration and analysis.

## Results:

Measurements of 6 tracks (182 points) were performed. Registration accuracy was better than 0.2 mm between the robot and the PET image and better than 0.4 mm between the CT and MRI. Figure 1A shows an axial view of the T2-weighted MR image of the tumor, with the red arrow indicating a $pO_2$ measurement track. Figure 1B illustrates the time-dependent DCE-MRI image intensity curves. These separate into two populations - enhancing and non-enhancing curves (above and below the dotted horizontal line, respectively) - with the latter presumably corresponding to non-perfused and therefore necrotic tissue. Voxels with an initial relative slope, (I-Io)/Io per minute, of less than 0.1, were considered non-enhancing and necrotic[2] and were excluded from the correlation analysis (Io is the pre-contrast MR image intensity). As expected, voxel intensities of $^{18}$F-FMISO PET images were found to be negatively correlated with the intra-tumoral $pO_2$. Due to the fact that measurement points in the necrotic tumor regions had *both* low $pO_2$ readings *and* low FMISO PET image intensities, the negative correlation (r±SD) improved significantly (p = 0.037) - from -0.32 ± 0.37 to -0.61 ± 0.40 - if only points within viable tumor regions were considered. These preliminary results illustrate the utility of DCE MRI for identifying tumor necrosis and for improving validation studies of hypoxia imaging agents.




(A) (B)

Figure 1. (A) T2-axil MRI image. Red arrow shows the steps of the $pO_2$ needle going from sub-skin into the tumor. (B) Time intensity curve of the DCE-MRI images.

**References:** 1. Kazanzides et al. P. LNCS-I: 50-57,2006. 2. Dyke JP et al. Radiology 228:271–278, 2003.