**Changes in high spectral and spatial resolution images of murine mammary tumors due to the introduction of carbogen**

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**Introduction**: In order to improve radiation-based treatment methods for cancer, it is necessary to increase the oxygen concentration in the tumor blood supply. This is often done with the introduction of carbogen (95% $O_2$ / 5% $CO_2$) to the air supply. However, because of the abnormalities associated with tumor vasculature, including tortuous architecture, endothelial fenestrae, and improper smooth muscle function (1), the effects of carbogen on tumor blood oxygen concentration is complicated and difficult to predict. MR signal variations due to the elevation in tumor blood oxygen concentration can be both positive, due to a disproportionate effect associated with decreased levels of deoxyhemoglobin (2), and negative, due to a “steal effect” associated with the redistribution of blood flow and blood oxygenation associated with the abnormal vascular architecture (3). This work used high spectral and spatial resolution (HiSS) imaging to investigate the variation in signal intensity in transgenic mouse mammary tumors due to the introduction of carbogen.

**Methods**: HiSS datasets of SV40 TAg mice (n=3) bearing mammary tumors were imaged at 9.4 T with echo-planar spectroscopic imaging (EPSI). Five baseline scans, with 98 µm in plane resolution, 0.5 mm slice thickness, and 6.6 Hz spectral resolution (TR=1200 ms, receiver bandwidth = 53.7 kHz), were performed with the rodent breathing medical air. Next, medical air was replaced with carbogen, and 10 scans were performed for ~50 minutes. Water peak-height images were constructed for each HiSS dataset, where the signal intensity was proportional to the peak of the water resonance for each tiny voxel imaged. An average baseline PH image was produced and subtracted from all pre- and during-carbogen breathing PH images. The tumor was manually segmented, from which tumor rim and tumor center ROIs were defined, and statistics were calculated.

**Results**: A typical during-carbogen minus pre-carbogen image is shown in Figure 1. Mean positive and negative percent changes in signal intensity pooled over all time points were calculated for during-carbogen for both ROIs; these were 25.8±2.5%, -18.7±2.8% and 25.4±2.6%, -18.6±4.0% for the tumor rim and center, respectively. Average time series data for percent positive and negative changes are shown in Figure 2. Both positive and negative responses to carbogen were extremely similar between the two ROIs ($R$ = 0.97 and 0.99 for positive and negative changes, respectively).

**Discussion**: Results indicate that the response to carbogen in the tumor does not differ between the rim and the center. Both demonstrate statistically significant positive and negative responses which are similar to one another. Further, strong correlations between time series data for both ROIs indicate that a characteristic response to carbogen is not localized to any specific region of the tumor. In fact, these results may indicate that this particular mammary tumor model is highly vascularized in the center as well as the rim. These findings could aid in therapy treatment planning by identifying regions of tumor vasculature and allowing for the characterization of architecture based on response.

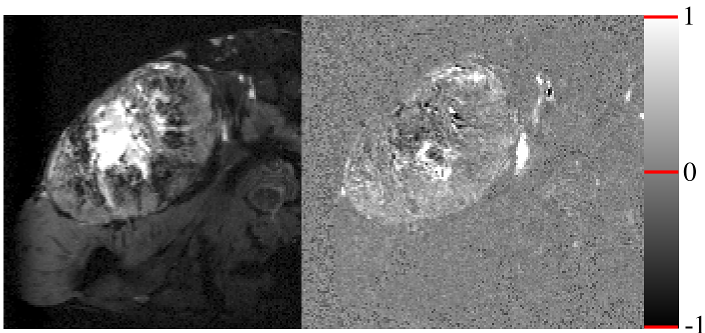


Figure 1. (a) Typical water PH image of mammary tumor in abdominal region of mouse. (b) Difference at 20 minutes after introducing carbogen to the air supply.

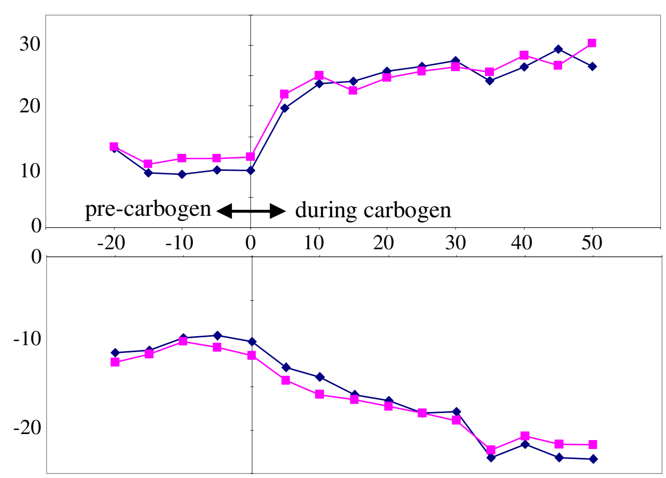


Figure 2. Mean pooled time series curves for positive (top) and negative (bottom) response. Blue - tumor center, pink - tumor rim. X-axis is in minutes. Y-axis is in units of percent. Note the strong correlation between ROIs.

**References**:
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