In Vivo Imaging of Tumor Oxygen status using Overhauser enhanced MRI

Murali Krishna Cherukuri

Radiation Biology Branch, National Cancer Institute, NIH, Bethesda, MD 20892, USA

Abnormal values of pO2 are linked to many pathophysiological conditions. (e.g., ischemic diseases, reperfusion injury, and oxygen toxicity). Approximately one third of human tumors evaluated for oxygen status have shown significant oxygen deficiency, and oxygen deficiency increases the tumor's resistance toward cancer treatment modalities including radiation and chemotherapy. Additionally, hypoxic microenvironments in tumors are known to promote processes driving malignant progression, such as angiogenesis, elimination of p53 tumor suppressor activity, genetic instability, and metastasis. A priori determination of tumor hypoxia could lead to the development of diagnostic and prognostic markers for malignant progression, discovery of novel therapeutic targets, and the development of new constructs for gene therapy applications in human cancer.

An efficient non-invasive method for in vivo imaging of tumor oxygenation using a low-field magnetic resonance scanner and a paramagnetic contrast agent is described. The methodology is based on Overhauser enhanced Magnetic Resonance Imaging (OMRI), a novel functional imaging technique. OMRI experiments were performed on tumor bearing mice (SCC, squamous cell carcinoma) by intravenous administration of the contrast agent, Oxo63 (a highly derivatised tri-aryl-methyl (TAM) radical) at non-toxic doses in the range of 2?7 mmol/kg either as a bolus or as continuous infusion. Spatially resolved pO2 images from OMRI experiments of tumor-bearing mice exhibited heterogeneous oxygenation profiles and revealed regions of hypoxia in tumors (<10 mm Hg).

The pO2 measurements from OMRI were found to be in agreement with those obtained by independent polarographic measurements using a pO2 Eppendorf electrode. This work illustrates that anatomically co-registered pO2 maps of tumors can be readily obtained by combining the good morphological resolution of proton-based MRI, and the superior pO2 sensitivity of EPR. OMRI affords the opportunity to perform non-invasive and repeated pO2 measurements of the same animal with useful spatial (~1 mm) and temporal (2 min) resolution making this method a powerful imaging modality for small animal research to understand tumor physiology and potentially for human applications.