Non-Invasive Demonstration of Instabilities in Tumor Oxygen Concentration using Dynamic 3D EPR Oxygen Imaging

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Summary

Structural and functional abnormality of blood vessels within malignant tumors influences delivery of oxygen, a key radio-sensitizer, resulting in two different types of hypoxia. Chronic hypoxia is attributed to large diffusion distances between tumor microvessels and longitudinal oxygen gradient, whereas acute hypoxia is though to be the result of transient vascular occlusion and fluctuation in red blood cell flux. Electron paramagnetic resonance (EPR) imaging is a sensitive method to non-invasively map tissue oxygenation distribution. To investigate the fluctuation of tumor oxygen concentration, dynamic 3D EPR oxygen imaging was applied to two different types of tumor bearing in mouse. Here, our current results showing tumor cell line dependent difference in the instabilities in tumor oxygenation will be presented.

Method

Murine Squamous Cell Carcinoma (SCC VII) or human colon cancer xenograft (HT29) bearing mouse legs were used as tumor models. Dynamic 3D oxygen images were obtained every 3 min for 30-60 min under continuous injection of oxygen sensitive probe TAM using a homebuilt 300 MHz time-domain EPR imager using single point imaging (SPI) sequence. Then, the mice were transferred to 7T MRI scanner to obtain T_2 weighted anatomic images and blood volume images by intravenous injection of USPIO. After imaging studies, tumors were excised for immunohistochemical analysis of microvascular density (CD31) and pericyte coverage (αSMA).

Results

EPR 3D oxygen images showed that there were both hypoxic and relatively well oxygenated regions in the both SCC and HT29 tumors. The oxygen concentration in the SCC tumor showed larger fluctuations over time than HT29 tumors. Immunohistochemical analysis indicated that microvasculatures in the HT29 were highly covered by perivascular cells compared with the SCC tumors. Collectively, dynamic 3D EPR oxygen imaging is a useful tool to non-invasively visualized the instabilities in oxygen level in solid tumors, which was well correlated with maturity of tumor microvessels.

Reference

Matsumoto S. et al. ***J. Clin. Invest.*** 2008, 118(5):1965-73

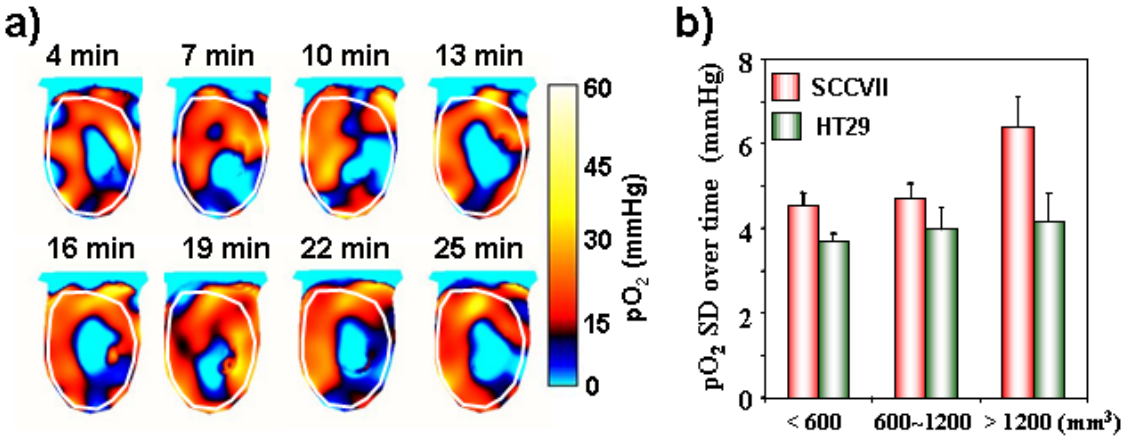

Fig.1 a) Dynamic 3D EPR oxygen imaging reveals instabilities of pO_2 in SCC tumors. b) Standard deviation of pO_2 over time in different size of tumors.