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Noninvasive Imaging of Oxygenation in a Transplanted Tumor.

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Electron paramagnetic resonance (EPR) spectroscopy, utilizing particulate oximetry probes, was used to perform repeated measurement and imaging of pO_2 in a transplanted tumor model. The probes were permanently embedded in the tumor for injection into mice by pre-internalization or co-implantation of RIF-1 (radiation-induced fibrosarcoma) cancer cells. This procedure enabled repeated measurements of the oxygen concentration in the tumor for more than 2 weeks during its growth phase. The particulates were stable and nontoxic to the tumor cells. An *in vitro* cellular membrane integrity assay showed no apparent effect on membrane permeability after 24-hour co-incubation of RIF-1 cells with the oxygen probe. However, *in vivo* tumor growth showed a decrease in tumor growth rate. The measurements indicated that the pO_2 of the tumor decreased rapidly with tumor growth in the model of co-implanted oxygen probe. However, the oxygen level was very low from the beginning of tumor development in the internalized model. EPR imaging revealed a non-uniform distribution of the embedded particulates in the tumor. Oxygen mapping of the tumor, obtained by spectroscopic EPR imaging, showed a significant variation of pO_2 within the tumor. In summary, EPR spectroscopy and imaging, using an embedded oximetry probe, enabled accurate and repeated measurements of pO_2 in growing tumors under non-perturbing conditions.