# Prediction of Treatment Response in Pancreatic Cancer Using EPR Oxygen Imaging

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**Target audience:**
Clinicians and researchers of oncology

**Purpose:**
Pancreatic cancer is a malignant neoplasm with an extremely poor prognosis. The 5-year overall survival rate is below 10%. A new drug TH-302 in combination with gemcitabine was approved for Phase 3 clinical trial in locally advanced or metastatic pancreatic adenocarcinoma in December 2012. The TH-302 is a kind of drugs known as hypoxia-activated prodrug (HAP), which activated under hypoxia (low concentration of oxygen) and exhibits anti-tumor effect. A question derived is how clinicians select patients who receive most benefit from treatment with this hypoxia targeting new drug, instead of classical radiation therapy or gemcitabine monotherapy. Electron paramagnetic resonance imaging (EPRI) can non-invasively provide 3D absolute oxygen images. Here, we investigated if the EPR oxygen imaging can predict treatment benefit of oxygen dependent or independent therapies in three different pancreatic cancer xenografts.

**Methods:**
Three human pancreatic cancer cells Hs766t, MiaPaca2, and Su8686 were subcutaneously inoculated in hind leg of athymic nude mice. The tumor bearing mice were treated with TH-302 (80mg/kg, ip, 5 days), X-radiation (3Gy, 5 days), or gemcitabine (150mg/kg, ip, twice a week). Tumor oxygen imaging was conducted by a homemade 300 MHz pulsed EPRI scanner using an oxygen sensitive triarylmethyl probe OX063 (1), followed by anatomic MRI scan.

**Results:**
Three pancreatic cancer cell lines showed large difference in tumor oxygenation. Tumor median pO2 values are 9.1±0.7 mmHg for Hs766t, 11.1±1.0 mmHg for MiaPaca2, and 17.6±1.1 mmHg for Su8686. TH-302 treatment provided survival benefic of 28.6 days in hypoxic Hs766t tumors but only 1.0 days in the most oxygenated Su8686 tumors. In contrast, tumor growth delay by radiotherapy was 10.3 days in Hs766t, 18.6 days in MiaPaca2, and 19.3 days in Su8686 tumors. Gemcitabine treatment was effective in both hypoxic and oxygenated tumors but there seemed to be most effective against the hypoxic Hs766t tumors.

**Conclusion:**
Quantitative oxygen images by EPRI can predict difference in the benefit from oxygen-dependent anti-tumor treatments in individual pancreatic tumor cell lines that may help properly choose the best treatment in patients with pancreatic cancer if EPRI is available in clinic.

**Reference:**
Matsumoto S et al. Low-field paramagnetic resonance imaging of tumor oxygenation and glycolytic activity in mice. J Clin Invest. 2008;118:1965-73.