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## Molecular oxygen delivery to hypoxic tumors by ultrasound triggering

Hypoxiain tumors inhibit sensitivity to radiation therapy. We studied the delivery of oxygen to tumors using an ultrasound-sensitive microbubble platformdeveloped at Drexel consisting of a mixed surfactant shell surrounding either oxygen (SE61O2) or nitrogen (SE61N2). Oxygen release kinetics was measured using an Oxy Lite 2000 bare fiber pO2 probe. *In vitro* ultrasound used a Sonix RP scanner with a PA4-2 probe in power Doppler mode. Samples in 100 ml degassed saline were triggered over 20 minutes (readings obtained every 30s). *In vivo* proof of concept (two mice with MDA-MB-231 breast tumor xenografts) introduced the probe into the tumor via 21G catheter. Flash-replenishment imaging at the fiber tip was performed using a Vevo 2100 scanner in nonlinear imaging mode at 18 MHz during IV injection of 0.05 ml of agent. Partial oxygen pressures were recorded every 5s until returned to baseline. Release profiles were compared to untriggered SE61O2, and triggered SE61N2. Two ml of SE61O2 triggered with ultrasound elevated oxygen partial pressures of 100 ml of degassed saline 13.8 mmHg more than untriggered bubbles and 20.6 mmHg more than triggered nitrogen-filled bubbles. *In vivo* controls produced no discernible increase in oxygen partial pressure except for a brief (25s) 5.6 mmHg increases in one animal. Ultrasound triggered SE61O2 resulted in a 30.4 mmHg increase in one tumor, with elevated tumor oxygen levels lasting over 4 minutes, and an increase of 27.4 mmHg, with elevated tumor oxygen levels lasting 1.7 minutes in the second. We conclude that *in vivo* elevation of tumor oxygenation levels using SE61O2 appears feasible but highly tumor dependent.

### Biography

Margaret A Wheatley after a degree in Chemistry from Oxford University, UK, completed her PhD in Chemical Engineering at the University of Toronto and Postdoctoral studies at MIT, Cambridge MA, USA. She holds the John M. Reid chair of Biomedical Engineering at Drexel University in the School of Biomedical Engineering, Science and Health Systems. She has published more than 100 papers in areas of imaging, drug delivery and spinal cord repair.

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