

PURPOSE: To measure the tumour oxygenation following VEGF ablation-induced changes in tumour models using dynamic oxygen-enhanced MRI (dOE-MRI) and independent component analysis.

METHODS: Mice implanted with SCCVII murine squamous cell carcinoma tumours were treated with 5mg/kg mouse anti-VEGF antibody (B20; bevacizumab equivalent) 48h prior to imaging and were compared to untreated controls. Imaging was performed using a 7T scanner and dOE-MRI scans were acquired using 2D FLASH sequence¹ 16 slices and a temporal resolution of 9.6s. Breathing gas was alternated between medical air and 100% oxygen every 2 minutes for a total of 3 air-oxygen-air cycles. The signal changes were detected using independent component analysis (ICA), a blind-source separation algorithm that separates multiple signal sources by maximizing statistical independence of individual components. Slice-matched histological sections were stained for blood vessels (CD31) and hypoxia (pimonidazole).

IMPACT: Anti-angiogenic treatment via VEGF-ablation therapy resulted in greater tumour oxygenation of SCCVII tumours compared to untreated controls, in an effect that was measurable using the described oxygen-enhanced MRI technique. These findings suggest the highly translatable dOE-MRI technique merits clinical investigation for utility in measuring patient tumour oxygenation, where it could inform targeted treatment studies and screen for patients with hypoxic tumours and those that may require more aggressive treatment.

REFERENCES:
 1. Fast and sensitive dynamic oxygen-enhanced MRI with a cycling gas challenge and independent component analysis. *Magn Reson Med*. 2019; 81: 2514– 2525. <https://doi.org/10.1002/mrm.27584>

dOE-MRI: A method to detect Tumour Oxygenation Changes after VEGF-Ablation

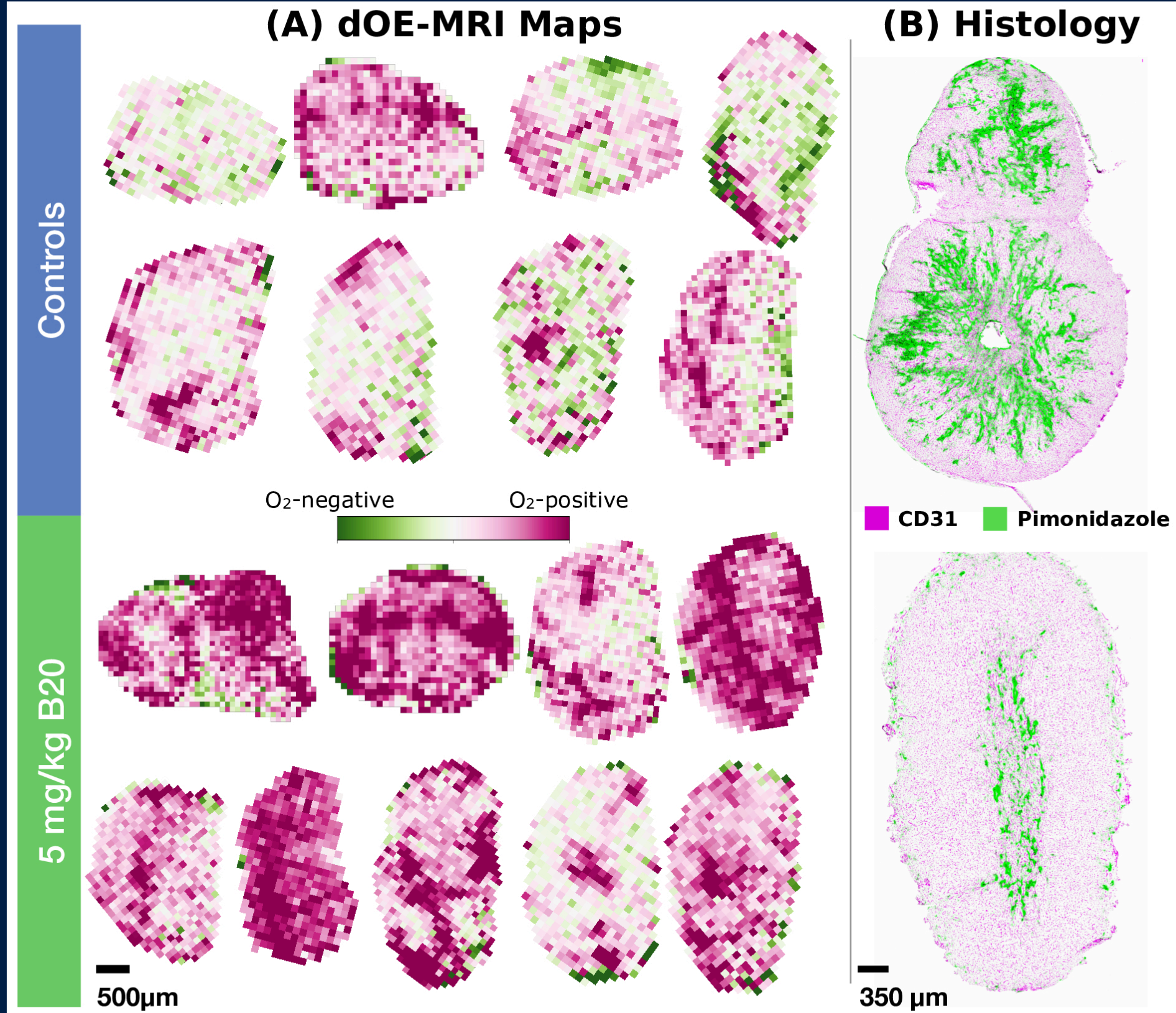


Figure 1. Representative slices of Control (A, top) tumours are shown relative to the more well-oxygenated, VEGF-ablation treated tumours (A, bottom) with greater amounts of O₂-positive signal. Slice-matched histology sections stained for hypoxia (pimonidazole; green) also show significant decreases in hypoxia in treated tumours (B, example slices show).

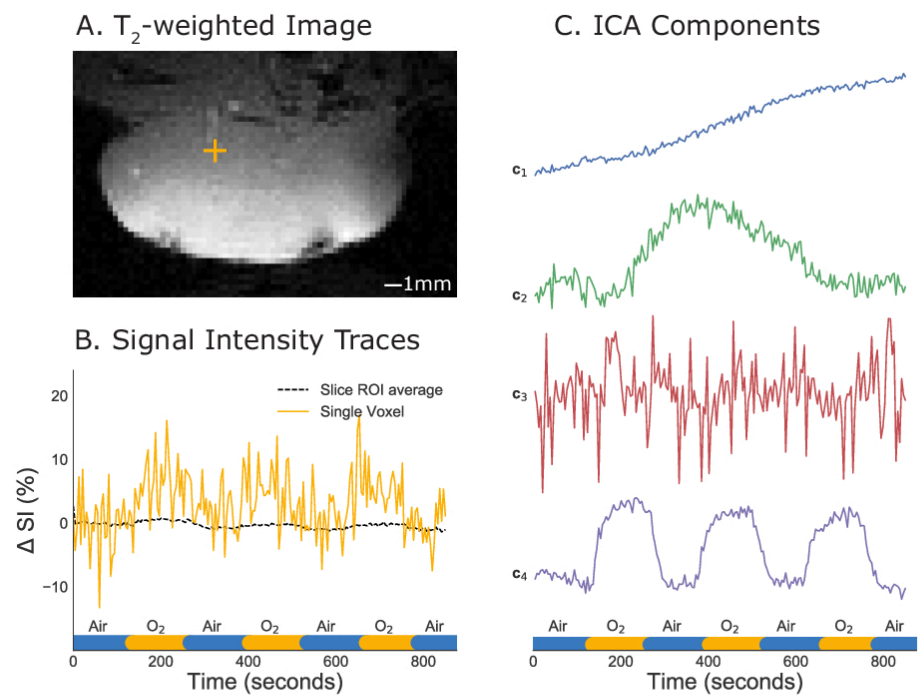


Figure 2. Description of the dynamic oxygen-enhanced MRI technique, including application of independent component analysis.

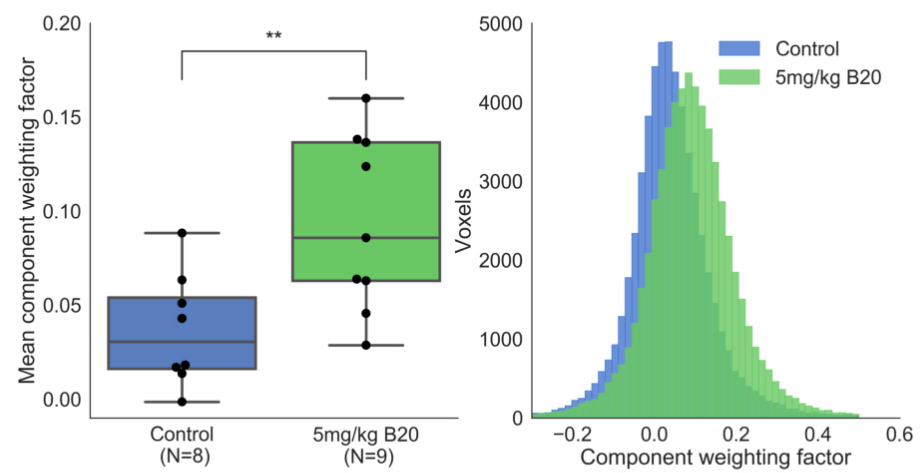


Figure 3. Group averages of the dOE-MRI signal for control and treated animals (mean NCWF values of 0.04 ± 0.01 and 0.09±0.04 respectively; 6-8 slices quantified for each animal), as well as the voxel distributions show a clear increase in oxygenation for the treated group (**p<0.01) and the effect size was large with Hedge's g=1.08.

CONCLUSION: We showed that dOE-MRI detects change in tumour oxygenation following VEGF ablation therapy in SCCVII tumours. These changes to the tumour microenvironment are quantitatively assessed by applying ICA to the data.

