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(I) On oxygen-enhanced MRI in the tumor microenvironment

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Low oxygen tension in tumour tissue has long been recognized as an indicator of poor outcomes and, independently, as an obstacle to effective treatment with radiation and chemotherapy drugs. Consequently, the search for non-invasive imaging techniques has been ongoing to guide diagnosis and monitor treatments. Dynamic contrast-enhanced MRI has seen the most widespread use but only visualizes a related, not overly direct measurement of blood supply. More recently attempts to measure oxygen saturation in tissue using MRI have been deployed with varying success. One vexing issue in TOLD (T1) and BOLD (T2*) experiments has been the many confounding influences on contrast.

We present a method of imaging the presence of oxygen more directly in tissue of tumour models using a dynamic oxygen-enhanced MRI imaging technique in the presence of a repeated oxygen gas challenge. Since many factors influence the T1-weighted signal intensity over the course of minutes, we use independent component analysis to separate the response to increased oxygen in the tumour microenvironment.
We have now tested our technique in a range of tumour models and compared to a ground truth of hypoxia status using pimonidazole staining on histology slices.
A remaining question of interest is the underlying cause of oxygen-mediated T1 changes: To what degree are there oxygen-modulated perfusion changes or true variations in the amount of tissue-dissolved, available oxygen? To elucidate this we are now also embarking on a simultaneous, dynamic measurement of T2*.

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