Hypoxia is recognized to influence solid tumor response to therapy and has been related to tumor aggressiveness, including growth, development, and metastatic potential [1]. In the context of this symposium, principles and methods based on nuclear magnetic resonance will be discussed, considering practicalities and limitations for applications ranging from the laboratory to the clinic [2].

^{19}F MRI oximetry based on perfluorocarbon reporter molecules not only indicates hypoxia *in vivo*, but significantly reveals spatial distribution of pO_2 quantitatively, with a precision relevant to radiation biology [3]. Successive measurements may be repeated non-invasively to reveal hypoxiation during tumor growth or as an acute response to interventions (*e.g.*, breathing hyperoxic gas or administering vascular disrupting agents). Analogous proton MRI methods are also feasible [4], but each requires an exogenous reporter molecule, currently limiting investigations to pre-clinical studies.

In patients, oxygen sensitive proton MRI of tissue water is particularly promising. BOLD (blood oxygen level dependant) contrast MRI is sensitive to the concentration of vascular deoxyhemoglobin, which is paramagnetic causing accelerated R_2* and signal loss in T_2*-weighted images. However, signal may additionally be perturbed by vascular volume, flow and hematocrit [5]. Meanwhile, TOLD (tissue oxygen level dependant) contrast MRI is directly responsive to pO_2, since the oxygen molecule in paramagnetic influencing the T_1 [6]. The TOLD response is typically smaller than BOLD, but we believe that together they validate interpretation of oxygen sensitivity. We believe that DOCENT (Dynamic Oxygen Challenge Evaluated by NMR T_1 and T_2*) offers a potential test to identify tumor hypoxia and responsiveness to interventions.

The ability to stratify patients according to the oxygen characteristics of a tumor becomes increasingly relevant with the development of high dose stereotactic body radiation therapy (SBRT). We believe we are at a historic juncture, where we not only have technologies for identifying hypoxia, but more importantly methods of tailoring therapy successfully to accommodate or exploit the killing of hypoxic cells.

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Learning Objectives:

1) Understand the principles of quantitative MRI oximetry.
2) Understand the possibilities of oxygen sensitive MRI (BOLD and TOLD).
3) Understand the criteria for clinical relevance