Brindle *BMC Proceedings* 2010, **4**(Suppl 2):O24
http://www.biomedcentral.com/1753-6561/4/S2/O24

BMC Proceedings

ORAL PRESENTATION Open Access

Detecting tumor responses to treatment using hyperpolarized 13C magnetic resonance spectroscopic imaging

Kevin M Brindle

From 16th International Charles Heidelberger Symposium on Cancer Research
Coimbra, Portugal. 26–28 September 2010

Patients with similar tumor types can have markedly different responses to the same therapy. The development of new treatments would benefit significantly, therefore, from the introduction of imaging methods that allow an early assessment of treatment response in individual patients, allowing rapid selection of the most effective treatment [1]. We have been developing methods for detecting the early responses of tumors to therapy. This has included a targeted MRI contrast agent for detecting tumour cell death [2] and MR imaging of tumor cell metabolism using hyperpolarized ^{13}C-labelled cellular metabolites. Nuclear spin hyperpolarization techniques can increase sensitivity in the MR experiment by >10,000x. This has allowed us to image the location of labeled cell substrates and, more importantly, their metabolic conversion into other metabolites. We showed that exchange of hyperpolarized ^{13}C label between lactate and pyruvate, in the reaction catalyzed by the enzyme lactate dehydrogenase, could be imaged in tumors and that this flux was decreased in treated tumors undergoing drug-induced cell death [3]. We compared this method for detecting treatment response with measurements of fluorodeoxyglucose uptake [4]. We have shown, more recently, that hyperpolarized [1,4-^{13}C]fumarate can be used to detect tumor cell necrosis post treatment [5]. We have also shown that tissue pH can be imaged from the ratio of the signal intensities of hyperpolarized $H^{13}CO_3$- and $^{13}CO_2$ following intravenous injection of hyperpolarized $H^{13}CO_3$-. The technique was demonstrated with a study on a mouse tumor model, which showed that the average tumor pH was significantly lower than the surrounding tissue. Since bicarbonate is already used intravenously in humans, we propose that this technique could be used clinically to image disease and response to treatment [6].

Published: 24 September 2010

References

1. Brindle K: **New approaches for imaging tumour responses to treatment.** *Nature Rev Cancer* 2008, **8**:1-14.
2. Krishnan AS, Neves AA, de Backer MM, Hu DE, Davletov B, Kettunen MI, Brindle KM: **Detection of cell death in tumors using MRI and a gadolinium-based targeted contrast agent.** *Radiology* 2008, **246**:854-862.
3. Day SE, Kettunen MI, Gallagher FA, Hu DE, Lerche M, Wolber J, Golman K, Ardenkjaer-Larsen JH, Brindle KM: **Detecting tumor response to treatment using hyperpolarized 13C magnetic resonance imaging and spectroscopy.** *Nat Med* 2007, **13**:1382-1387.
4. Witney TH, Kettunen MI, Day SE, Hu DE, Neves AA, Gallagher FA, Fulton SM, Brindle KM: **A comparison between radiolabeled fluorodeoxyglucose uptake and hyperpolarized C-13-labeled pyruvate utilization as methods for detecting tumor response to treatment.** *Neoplasia* 2009, **11**:574-582.
5. Gallagher FA, Kettunen MI, Hu DE, Jensen PR, Zandt RI, Karlsson M, Gisselsson A, Nelson SK, Witney TH, Bohndiek SE, Hansson G, Peitersen T, Lerche MH, Brindle KM: **Production of hyperpolarized [1,4-13C)]malate from [1,4-13C)]fumarate is a marker of cell necrosis and treatment response in tumors.** *Proc Natl Acad Sci U S A* 2009, **106**:19801-19806.
6. Gallagher FA, Kettunen MI, Day SE, Hu DE, Ardenkjær-Larsen JH, in 't Zandt R, Jensen PR, Karlsson M, Golman K, Lerche MH, Brindle KM: **Magnetic resonance imaging of pH in vivo using hyperpolarized 13C-labeled bicarbonate.** *Nature* 2008, **453**:940-943.

doi:10.1038/nrc2289
Cite this article as: Brindle: Detecting tumor responses to treatment using hyperpolarized 13C magnetic resonance spectroscopic imaging. *BMC Proceedings* 2010 **4**(Suppl 2):O24.

Correspondence: kmb1001@cam.ac.uk
Department of Biochemistry, University of Cambridge and Cancer Research UK Cambridge Research Institute, Cambridge, UK