Study of real time 13C metabolic fluxes using Dynamic Nuclear Polarization and Magnetic Resonance Spectroscopy

Commonly used acronym: *DNP*
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SCOPE OF THE METHOD

Alternative method relates to	Animal health
Alternative method is situated in	Basic Research, Translational - Applied Research
Type of alternative method	Other: In vitro and in vivo method
This method makes use of	Animal derived cells / tissues / organs

DESCRIPTION

Method keywords

hyperpolarization

13C metabolic fluxes

13C-MRS

in vitro and in vivo tool

Scientific area keywords

tumor metabolism

cardiac function

metabolic disorders

13C metabolism

Method description

Hyper Polarized (HP) MR allows to considerably increase the sensitivity (>10.000) of MR spectroscopy and spectroscopic imaging. The hyperpolarized molecule can be injected at room temperature to a cell system or an *in vivo* model and its metabolism can be followed over a few minutes.The technique has been used *in vivo* or *in vitro* to assess changes in metabolic fluxes through glycolysis, citric acid cycle, and fatty acid synthesis. HP MR studies using 13C pyruvate showed an increase in signal to noise ratio of more than 50.000 of the substrate and its metabolites (lactate and alanine), allowing for unique dynamic mapping of metabolism using spectroscopic imaging.

Lab equipment

The oxford instruments HyperSense DNP system is combined with our 11.7T preclinical Magnetic Resonance system (Bruker Biospin) for *in vivo* application or with our Bruker Ascend 600MHz NMR system for *in vitro* application. The Hypersense allows hyperpolarization of 13C-enriched substrates, direct dissolution and cooling down of the substrates and allows consecutive injection in the vascular system of the animal under study or in cell media for intro application.

Method status

Published in peer reviewed journal

PROS, CONS & FUTURE POTENTIAL

Advantages

The method allows the assessment of real-time metabolic conversion (i.e. of 13C-pyruvate into 13C-lactate) with high sensitivity and non-invasively (while used *in vivo*). It constitutes a key tool to address fundamental questions in the scope of metabolism in several fields, including oncology, cardiology, metabolic disorders, etc...

Challenges

A major limitation of DNP is a requirement of a long relaxation time T1 for the 13C enriched substrate. The useful monitoring time is limited to 5X T1, which includes dissolution, injection, and imaging. Hence, for pyruvate, there is a maximum of 3 min of useful measuring time. Nevertheless, the technique has already shown numerous

applications for detecting treatment response in animals.

Modifications

No modifications are planned in the near future.

Future & Other applications

Metabolic disorders,
Cardiac function metabolism,
Cancer metabolism.

REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

References

Magnetic resonance imaging of cancer metabolism with hyperpolarized 13C-labeled cell metabolites. Hesketh RL, Brindle KM. Curr Opin Chem Biol. 2018 Aug;45:187-194. doi: 10.1016/j.cbpa.2018.03.004. Epub 2018 Jul 13.
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Associated documents

PARTNERS AND COLLABORATIONS

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