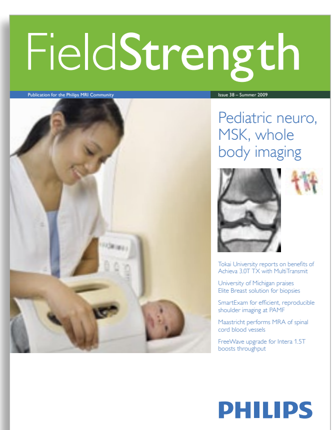
FieldStrength

Publication for the Philips MRI Community

Issue 38 – Summer 2009

Carbon-13 spectroscopy at 7.0T of calf muscle and brain

Researchers in Nottingham and Nashville are conducting in-vivo ^{13}C MR studies of glycogen metabolism



This article is part of
Field Strength issue 38,
Summer 2009

Carbon-13 spectroscopy at 7.0T of calf muscle and brain

Researchers in Nottingham and Nashville are conducting in-vivo ^{13}C MR studies of glycogen metabolism

Carbon-13 (^{13}C) spectroscopy allows researchers to study processes within the body beyond what conventional proton MR can do. When performed at 7.0T, ^{13}C spectroscopy is yielding a wealth of information on metabolism for Vanderbilt University Institute of Imaging Science, (VUIIS, Nashville, Tennessee, USA) and the Sir Peter Mansfield Magnetic Resonance Center (Nottingham, UK).

While conventional MR detects signal from nuclei of hydrogen atoms, mainly in water, multi-nuclear MR spectroscopy (MRS) enables detection of signal from other nuclei with magnetic signals at different frequencies, such as phosphorus-31, fluorine-19, sodium-23, xenon-129 and carbon-13 (1% natural abundance; the most abundant C isotope is carbon -12).

^{13}C spectroscopy produces spectra that can help monitor certain biochemical processes in the body. At 7.0T, the ^{13}C spectrum has a larger chemical shift dispersion than at lower field strengths, so is more spread out and peaks are sharper, to allow for easier observation of chemically distinct carbon atoms. The increased SNR also improves visibility of the low-abundance ^{13}C isotope.

Diabetes studies underway at Nottingham

Prof. Peter Morris

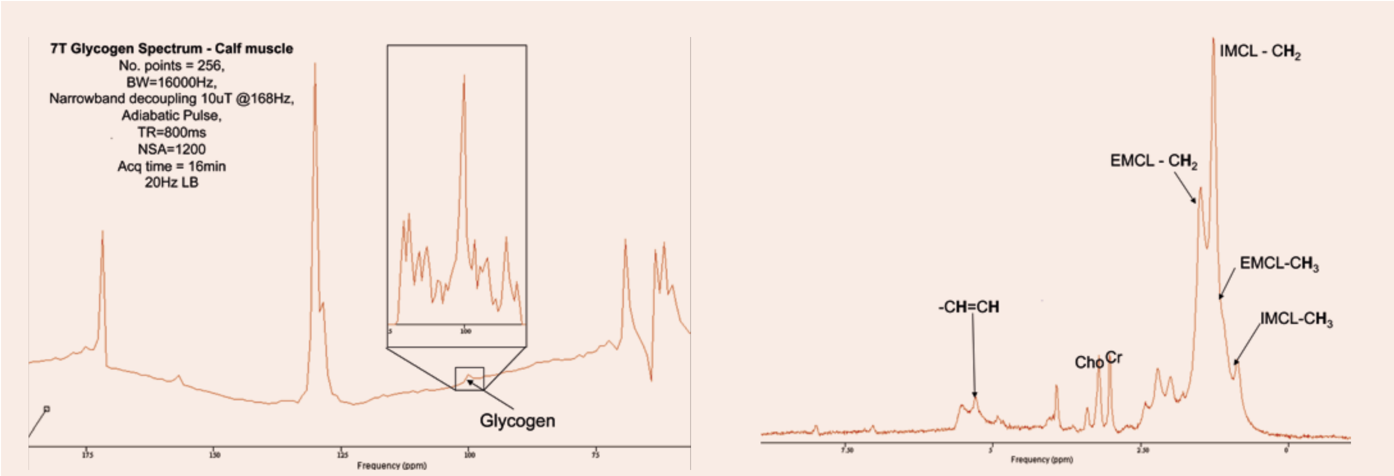
The Sir Peter Mansfield Magnetic Resonance Center has already undertaken ^{13}C MRS studies at lower field strengths, and expects to obtain better results at 7.0T. Prof. Peter Morris, PhD, says the center is looking at muscles and studying glycogen turnover. "This turnover is not only important in exercise physiology, but it's extremely significant in diabetes, which is often seen as a disease of glycogen storage. Simply being able to measure what's happening to these glycogen stores will help us determine how best to replete them. This study's goal is to find a way of actually probing diabetes and its reaction to new classes of drugs designed to increase glycogen stores, so ^{13}C is a very useful biomarker of whether those drugs are effective."

"We can separate out the different metabolites in a way that's not possible at lower fields."

Neuro ^{13}C studies to begin soon

In another study, ^{13}C spectroscopy will be used to look at brain metabolism. After administering ^{13}C-labeled glucose, ^{13}C spectroscopy can be applied to measure the rates at which the ^{13}C label is transferred from glucose to glutamate. "This is actually a way to measure the rate of energy consumption in that part of the brain," Prof. Morris explains. "So in my view this is an indication of brain activity. We may not know exactly what the brain is doing, but we can measure how much energy it's consuming." This work goes hand-in-hand with functional MRI, he adds.

Prof. Morris plans to begin this study with healthy young volunteers. "But, of course there's good evidence that there are differences in the rates of neurotransmitter turnover in neurodegenerative diseases, as well as effects of aging that we can look at. So we hope to begin with healthy young volunteers, and then to look at different ages and a range of neurodegenerative diseases."



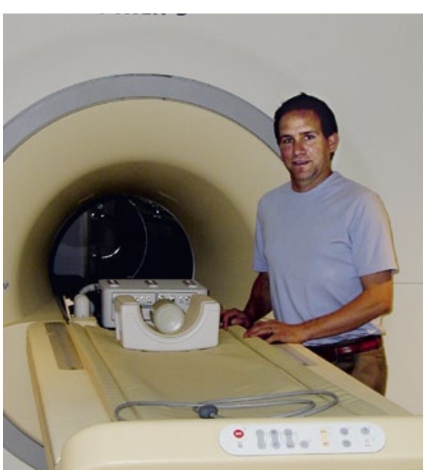
7.0T glycogen spectrum from calf muscle

Natural abundance ^{13}C (left) and ^{1}H (right) spectra recorded at 7.0T from human calf muscle. The ^{13}C C1 glycogen peak is clearly visible (inset).

"^{13}C spectroscopy can be applied to measure the rates at which the ^{13}C label is transferred from glucose to glutamate."

Prof. Morris says using the Achieva 7.0T system for multi-nuclear MR spectroscopy has lived up to his expectations. "We do see the improvement in sensitivity and the ability to get relatively better homogeneity at higher fields than in some of the lower field systems. We realize the advantage of the additional chemical shift dispersion, and can separate out the different metabolites in a way that's not possible at lower fields. At 7.0T, they are pulled apart and become much clearer."

Vanderbilt investigating glycogen synthesis

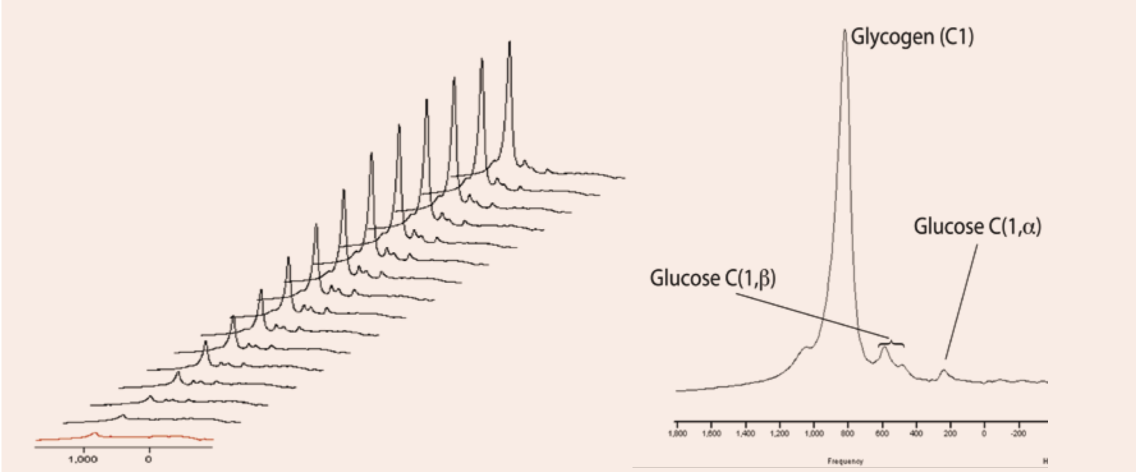


James Joers, PhD

James Joers, PhD, Assistant Professor of Radiology and Radiological Sciences at Vanderbilt University Institute of Imaging Science (VUIIS) is investigating glycogen synthesis from infused ^{13}C and metabolic changes in the calf muscles of healthy volunteers.

Dr. Joers hopes to begin similar research in other groups: people who are obese, people who have had bariatric surgery and people who have complications from obesity. "We expect to see significantly less glycogen synthesis in someone with insulin resistance. With bariatric surgery patients, we are less sure what to expect. Changes in intracellular hepatic and muscular lipid levels that are thought to regulate insulin sensitivity most likely change after surgery, thereby having an effect on glucose clearance. However, the metabolic changes due to contributions from surgery and those from the low-calorie diets that occur in conjunction with the surgery are largely unknown. We hope to find out what those metabolic contributions are, and how they manifest themselves in that particular realm of glucose consumption and usage."

He and his team are also in the process of developing and refining methodologies for studying localized ^{13}C in the brain at 7.0T. They hope to use both the muscle and brain spectroscopy to examine the metabolic differences between healthy and diseased populations.



Spectral time course after ingestions of ^{13}C

The spectrum shown in red is the pre-ingestion natural abundance spectrum. The other spectra are measured after ingestion of ^{13}C labelled glucose. The ^{13}C spectrum on the right shows the glucose/glycogen region 2.5 hours post-ingestion.

First experiments a success

"I was pleasantly surprised at how well our first experiences at 7.0T went," says Dr. Joers. "We received our Philips multinuclear spectroscopy (MNS) upgrade in October of 2008, and within two weeks we were getting natural abundance glycogen signal in a 10-minute scan from a human calf muscle. In the first in-vivo glycogen spectrum we took, the peaks just jumped out. And since the ^{13}C-infused glucose is still a little pricey, we had used natural abundance levels. Being able to observe the spectrum at such low levels was quite pleasing."

> "In the first in-vivo glycogen spectrum we took from a human calf muscle, the peaks just jumped out."

Philips has active role in 7.0T research

To enable multinuclear spectroscopy, the Achieva 7.0T systems at both sites are equipped with an additional receiver operating at ^{13}C frequency, and an RF amplifier operating at ^{13}C frequency. In addition, they are using special coils, and have developed some specific pulse sequences and higher bandwidth RF waveforms.

Prof. Morris appreciates Philips' participation in this type of research. "Philips has put a lot of effort into producing the multinuclear spectrometer. They've also built and refined the ^{13}C coil, and it has pretty much worked right out of the box. We are very pleased with the way it has all come together."

Dr. Joers adds, "Philips plays its role in the 7.0T research, and the Philips 7.0T user meetings are a valuable platform for feedback and information exchange. The future of 7.0T usability is wide open. The prospects are extremely promising, both for research in spectroscopy and in imaging."

References:

1. Shulman G.I. Rothman D.L. et al.
Quantitation of muscle glycogen-synthesis in normal subject and subjects with non-insulin-dependent diabetes by C-13 Nuclear Magnetic Resonance Spectroscopy."
NEJM 1990 322(4):223-228
2. Petersen K.F. and Shulman G.I.
Etiology of insulin resistance.
AJM 2006 119, (Suppl.) 5A:10S-16S.