



Hyperpolarization Shows Promise for Realizing the Early Health Model

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The early health model is based upon a broader, more efficient model of healthcare that enables clinicians to diagnose and treat disease at the earliest possible point in time. GE Healthcare understands this early health model: early diagnosis to find disease when it is more treatable; delivering information earlier in a form that makes a difference throughout patient treatment and subsequent monitoring; and earlier treatment for more precise therapy and follow up.

Changing the paradigm from 'late disease' to 'early health' means providing critical information whenever and wherever it is needed. This includes identifying patients at risk and enabling accurate diagnosis earlier to facilitate and track targeted treatments.

The need for earlier and better diagnosis is prevalent in many diseases. Take for example prostate cancer. Current screening methods – such as a digital exam and Prostate Specific Antigen (PSA) blood test lack specificity that may lead to false positive results, which could result in unnecessary biopsies. Metabolic changes occur during the evolution and progression of prostate cancer resulting in changes in the citric acid cycle, glycolysis and fatty acid synthesis. These actions provide a signature that defines the prostate cancer stage. Metabolic MRI can help measure this biochemical 'fingerprint' of tissue and drive the transformation to early health.





GE's patented approach: Metabolic MRI

GE Healthcare has patented an approach to Metabolic MRI using hyperpolarized agents. SPINlab™ harnesses hyperpolarized ^{13}C to view metabolic processes in real-time, using advanced GE MR technology for functional metabolic imaging. This approach increases the MR signal more than 20,000 times for studying real-time metabolism of disease, opening up new possibilities for MR imaging to move beyond morphology and functionality onto a new platform that may help clinicians visualize information about flow, perfusion, excretory function and organ and cell viability in living creatures.

Metabolic MRI with hyperpolarized agents shows promise by helping support the differentiation of benign and malignant lesions, separating aggressive from slow growth tumors and facilitating non-invasive treatments. The vision of Metabolic MRI with hyperpolarized ^{13}C is to measure the biochemical 'fingerprint' of tissue for earlier diagnosis, improve staging and influence treatment decisions. For example, elevated conversion of Pyruvate into Lactate compared to normal tissue is a strong indicator of prostate cancer.

Why ^{13}C ?

Carbon, the 6th element on the periodic table, is fundamental to biochemistry and abundant in all forms of life. It has two stable isotopes: ^{12}C (six protons and six neutrons) and ^{13}C (six protons and seven neutrons). More than 99 percent of naturally-occurring carbon is ^{12}C with no MR signal. ^{13}C represents approximately one percent of naturally-occurring carbon. As a stable isotope that is magnetically active, ^{13}C can be used in spectroscopy to probe molecular structure. Although changes in molecular structure correspond to metabolic changes, the ^{13}C signal in vivo is too small for use in a clinical setting until the advancement of a hyperpolarization.

Overcoming the challenge of MR imaging ^{13}C

Traditional MR imaging relies on the high concentration proton (^1H) signal associated with water or fat; metabolites occur at a thousand times lower concentration. Additionally, only about one percent of metabolites contain ^{13}C . Finally, ^{13}C generates four times less signal than protons, making in vivo

^{13}C nearly impossible to image. GE's solution is to hyperpolarize the ^{13}C metabolites using Dynamic Nuclear Polarization (DNP), which provides more than a 20,000-fold increase in signal making it possible to detect real-time changes to metabolism.

Hyperpolarization is achieved by placing the ^{13}C sample in a special device – a polarizer – that keeps the sample at a very low temperature (<4 K) in a high magnetic field (>3.0T) where the electrons are nearly 100 percent polarized. The sample is then irradiated with microwave energy at a frequency corresponding to the electron spin resonance transferring the polarization from the electrons to the ^{13}C . This phenomena is DNP.

MR systems must be optimized to image ^{13}C metabolic activity. Since polarization does not recover there is a demand for real-time metabolic imaging, which requires fast imaging sequences. In addition, ^{13}C processes at different frequencies than protons used in standard MR imaging, requiring dedicated RF coils and a broadband system. A low abundance and polarization of naturally-occurring ^{13}C requires a system calibration independent of ^{13}C .

Imaging of metabolism with hyperpolarized ^{13}C requires dedicated local transmit coils tuned to the ^{13}C resonant frequency for signal excitation. For signal reception, dedicated receive array coils tuned to the ^{13}C frequency and capable of acceleration through parallel imaging is also required. These coils must be designed to work in conjunction with existing proton transmit and receive arrays which are used concurrently for anatomical imaging. Dealing with multiple transmit and receive arrays simultaneously can be a challenge to patient set-up. To address this, GE is developing special purpose, dual-tuned coils that work at both proton and ^{13}C frequencies.

Conclusion

Hyperpolarization shows much promise for imaging metabolic synthesis to identify the early footprint of disease. To make this research a reality, GE has integrated its Biosciences and Engineering technology with advances in MR imaging. The Signa® MR750 3.0T MR system provides ultra-fast imaging and multi-channel, multi-nuclear capabilities required to visualize cell metabolism using ^{13}C . ■