Technical Memorandum

Ambature TM # 2016 - 02

To: Ron Kelly, CEO, Ambature Inc.

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From: Davis H. Hartman

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Re: **Opportunity for IP Growth in "Low-Field" Point-of-Care MRI**

Opportunity for IP Growth in "Low-Field" Point-of-Care MRI

Systems-Driven Technology Development (SDTD) is a method for exploring and exploiting new technology developments while enhancing their relevance to the changing marketplace. At Ambature, we use SDTD to enhance and grow our IP portfolio. Doing so allows us to efficiently utilize our limited resources by directing our technology threads toward relevant system level requirements without getting lost in the many details that define new technology.

By example, we are currently exploring the use of our a-axis growth technology in MRI markets. This market is currently evolving from the large B-field (> 0.5 Tesla) multi-million dollar units to smaller, more portable "point-of-care" units that must be priced much lower and would strongly benefit from portability. These market requirements (along with size, weight and power restrictions for portability) tend to imply the use of very low polarizing B field, or perhaps even the absence of a large electro-magnet altogether. As the attached Figure 1 shows, with the use of SQUID loop detectors in place of conventional Faraday detectors in the low B-field regime, significant Signal-to-Noise Ratio (SNR) improvement can accrue. We note in passing that in the high field regime, there is no advantage to using SQUID detectors, since the sample noise dominates in this regime.

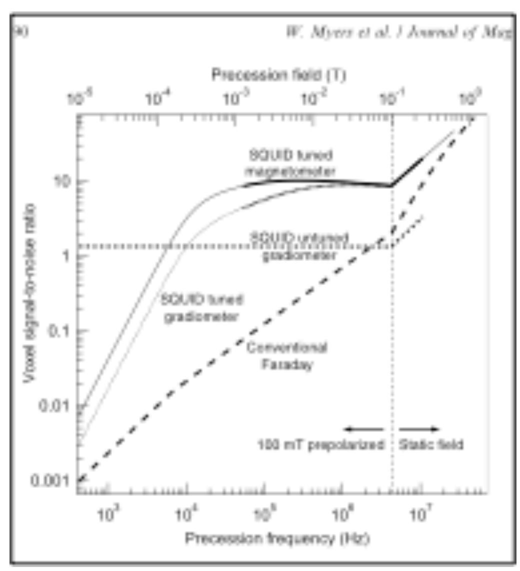

Figure 1: Low field MRI is possible when pre-polarization techniques are used.

Therefore we conclude that, from a systems perspective, the use of high temperature superconducting detectors in low B-Field MRI applications is advantageous, even though the operation at 77K is less sensitive than 4K LTS operation. We further conclude that with the use of HTS rather than low temperature superconducting solutions, the 4K cryo-environment can be altogether eliminated (further reducing size, weight and power), since low B-fields can be produced with ferro-magnets rather than superconducting magnets.

These advantages allow us to focus our technology development toward a set of specifications for HTS Josephson Junction devices that are consistent with the systems picture. This is what we mean by the term "System-Driven Technology Development".

There is still has remained a problem (and an opportunity) for point of care MRI architectures. The imaging signal strength derives from nuclear magnetic resonance in the sample and is produced by a strong applied magnetic field. A closer look at Figure 1 reveals that in the low field regime, some form of "pre-polarization" is called for to compensate for this loss of signal. In "pre-polarization", a strong magnetic field is pulsed on for a short time prior to polling the sample at the detector. While the approach produces a sufficient RF signal, it comes at the expense of the size, weight and power consumption that accompanies the electro-magnet; it is sort of like taking a shower in a raincoat. Nevertheless, the industry has pursued this path.

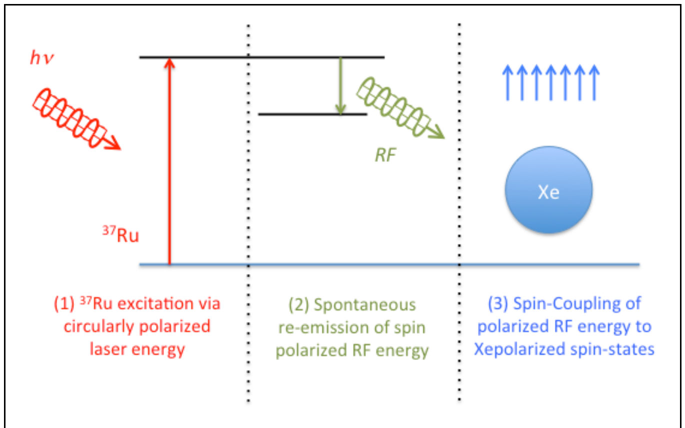

Figure 2: An example of Hyper-polarization technique of enhancing the MRI signal.

However, there has been progress in the past few years. Breakthroughs have occurred in finding alternative ways to pre-polarize samples without the need for a strong magnetic field. In fact, methods have been devised to pre-polarize samples without any externally applied magnetic field at all. This family of techniques is referred to as "Hyper-polarization".

With Hyper-polarization, nuclear spin-states are excited via laser or RF energy to invoke "spin coupling" interaction that produces spin polarization in samples that can far exceed the equilibrium states produced by strong applied magnetic fields.

In one example of Hyper-polarization, a three-step process occurs (see Figure 2). First, a sample of Rubidium (^{37}Ru) is illuminated by circularly polarized light from a high power laser (l=0.795

microns). The ^{37}Ru atoms absorb the laser energy and are elevated to a metastable excited state with aligned spins. The laser illumination is strong enough that more ^{37}Ru atoms are excited than would be the case in thermal equilibrium. This step is called optical pumping. In step-two, the atoms spontaneously fall into lower energy states by emitting spin-aligned energy at RF frequencies. In step-three, the spin-aligned RF energy then illuminates the xenon molecules. This interaction is referred to as spin-coupling. This illumination, if intense enough, results in spin-state population saturation.

In hyper-polarization, the spin-state configuration is not steady state, as it is with the application of a strong static magnetic field. Instead, the optical pump overpopulates the sample. The result is an NMR signal that is many times stronger than with conventional MRI architectures. The sample can be hyperpolarized by infusing it (through inhalation, ingestion or intravenous injection, for example) and then by imaging.

From the perspective of point-of-care MRI architectures, it is easy to see that the adoption of hyperpolarized MRI constitutes a major shift in the technology. Application of high temperature superconducting SQUID detection with this new sampling modality appears, from a systems perspective, to be an opportunity for lower cost a-axis grown HTS solutions.

The systems advantages described here allow us to focus our technology development toward a set of specifications for HTS Josephson Junction devices that are consistent with the systems picture. This is what we mean by the term "System-Driven Technology Development".

Regards,

Davis H. Hartman