Towards Monitoring the Function of Implantable Pancreatic Constructs with NMR: A preliminary *in vivo* result

N. Volland (U. Florida, Biomedical Engineering), N.E. Simpson (U. Florida, Medicine)

Introduction

A therapeutic approach toward curing diabetes is to implant insulin-secreting cells in a tissue engineered pancreatic construct. NMR imaging and spectroscopic techniques can non-invasively monitor an implanted construct and assess changes in construct function to identify early markers of construct failure in advance of end-point diabetic effects (e.g., hyperglycemia). An NMR-based method to non-invasively assess the viability of a bioartificial pancreatic construct was established by Stabler et al. [1,2]. This method, correlating the ^{1}H choline signal with cellular viability, was demonstrated both *in vitro* and *in vivo* using a 4.7 T magnet and a surface coil as the antenna for ^{1}H detection. However, signal-to-noise issues inherent in observing a bioartificial construct with external surface coils limit the utility of this approach. To address this, we have been implementing an inductively-coupled coil system [3] at 11 T to monitor a bioartificial construct *in vitro*, and now *in vivo*.

Experimental

Implantable loop-gap coils were manufactured and coated with polydimethylsiloxane elastomer (Factor II, Inc., Lakeside, AZ). Biocompatible (polyetheretherketone) mesh was added to the top and bottom of the ring to form a cavity. Blank alginate beads (containing no cells) were inserted (Fig. 1) and the entire construct was implanted into the peritoneal cavity of recipient mice in accordance with IACUC guidelines. NMR measurements were performed on an 11.1T horizontal bore magnet equipped with a Bruker Biospec console using a spin-echo pulse sequence (TR=3000 ms, TE=10 ms, 1-mm slice, 1 average) with a 4-cm-by-4-cm field of view (Fig. 2).

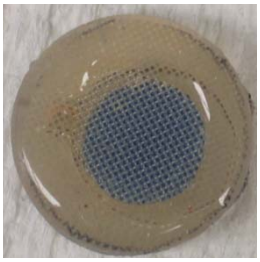

Fig.1. Implantable coil construct containing blank alginate beads (in blue).

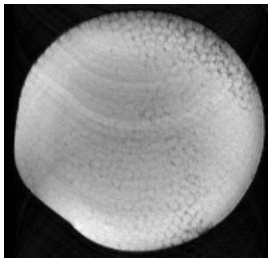

Fig.2. An *in vivo* spin-echo image of blank beads contained within the coil construct obtained through inductive coupling techniques.

Results and Discussion

Coil constructs can be manufactured and implanted into recipient animals. Additionally, these constructs could be kept in animals for extended periods (weeks) without immune response, allowing for future temporal studies. Images were easily obtained from an implanted coil construct through inductive coupling techniques, demonstrating the capability of this system. Moreover, the signal-to-noise from the inductively-coupled system was more than 2.5 times that obtained from a surface coil.

Conclusions

The data show that our implantable inductively coupled coil system was successful *in vivo*, and obtained large gains in signal-to-noise over that with a surface coil, opening the way for quantitative analysis of implanted functional bioartificial organs. Work now focuses on: 1) perfecting NMR acquisition parameters (e.g., eliminating artifacts); 2) studying a 'cellularized' construct *in vivo* through NMR imaging and spectroscopy (^{1}H choline observation); and 3) developing a miniaturized multi-frequency wirelessly tunable coil system that includes important nuclei in addition to ^{1}H (e.g., ^{31}P, ^{19}F).

Acknowledgements

This work was supported by NIH RO1 DK47858.

References

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[3] Schnall M.D., *et al*. J Magn Reson, **68**, 161-167 (1986).