Obstacles to Diagnostic PASADENA Hyperpolarization in Humans

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Introduction

Magnetic resonance spectroscopy using hyperpolarized reagents provides the unique ability to assess the biochemical millieu of living cells, *in situ*. This technology has potential applications in early detection of cancer, coronary and carotid plaque and treatment, as well as neuropsychiatric and metabolic disorders. A versatile method of achieving hyperpolarization is called PASADENA (**p**arahydrogen **a**nd **s**ynthesis **a**llow **d**ramatically **e**nhanced **n**uclear **a**lignment), whereby hyperpolarized magnetic spin orders are transferred from parahydrogen to an array of heteronuclei. This method has been validated on a clinical MR scanner (GE 1.5T) equipped with 13CMRI/MRS [1-3]. Since patient safety is always the first concern in any new biomedical equipment, the sterility and sanitation of the PASADENA polarizer is paramount to the clinical success of PASADENA.

Purpose

Design and build a system to reliably deliver clean and sterile intravenous PASADENA reagents to patients.

Methods

Since all material going into and out of the polarizer must be free of organisms and contaminants, we have elected to make all fluid handling containers and tubing of the disposable type. Commercially available non-magnetic infusion pumps (Medrad) can be used to supply pressurized reactants to the polarizer, as well as pump hyperpolarized products from the polarizer to the patient. Within the magnetic reaction chamber of the polarizer itself, a sterile, disposable plastic container can be inserted. Two input ports and one output port must be attached to this container, much like an intravenous fluid bag with access ports. Leur locks can provide connections to sterile intravenous tubing. All of this tubing/container apparatus must be replaced before each PASADENA reaction. On the supply side, the necessary parahydrogen gas that is produced in-house can be sterilized by UV irradiation. Nitrogen gas is commercially available in a sterile form. An apparatus was built by our lab for preparing the chemical reactants (reagent precursors and reaction catalyst). All the tubing and chambers of this apparatus can be flushed clean with bleach.

Results

Fig. 1 shows the PASADENA apparatus. Within the silver upper housing is the solenoid coil magnet (Fig. 2) and reaction chamber (Fig. 3). Fig. 4 shows a disposable sterilized chamber insert. The three access ports will have leur locks. Fig. 5 shows the final configuration of sterile plastic insert within the reaction chamber, which in turn is within the magnet. Two infusion pumps would be needed (Fig. 6), one to deliver reactants to the polarizer, and one to deliver hyperpolarized product to the patient. Disposible sterile intravenous tubing would be used for all lines. The tubing of the reactant preparation apparatus (Fig. 7) can be flushed with bleach prior to use.

Discussion

A number of methods, ranging from UV/gamma irradiation to final product filtration to sterilizing gas, were considered for making the PASADENA polarizer sterile and clean. Given the short amount of time to work with the hyperpolarized product, time-consuming filtration and gas methods were eliminated. Moreover, given the limitless types of chemical reactions that may be devised for PASADENA, chemical and radiation sterilizing methods seemed counter-productive. Hence, we based our design on completely replaceable tubing and containers. Preparatory chemicals can be sterilized at leisure. Once the new apparatus is built, formal sterility testing will ensue.

References: 1. Bhattacharya P. et al. (2005). Magn. Reson. Mater. Phys. 18(5); 245-256. 2. Hövener J.B., et al. (2009). Magn. Reson. Mater. Phys. in press. 3. Hövener J.B., et al. (2009). Magn. Reson. Mater. Phys. in press.

Figure 1: The PASADENA polarizer, with reaction chamber in silver case, electronics in yellow case, and attendant parahydrogen and nitrogen gas cylinders.

Figure 2: Solenoid coil around reaction chamber.

Figure 3: Reaction chamber with two input and one output ports.

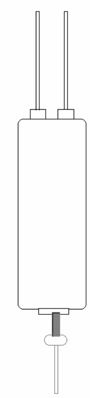

Figure 4: Proposed disposable sterile reaction chamber insert with leur lock ports.

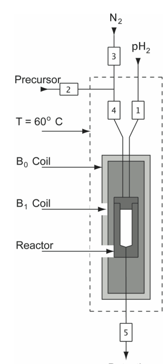

Figure 5: Final configuration with sterile insert within magnet and reaction chamber. N_2 = nitrogen input. pH_2 = parahydrogen input.

Figure 6: Medrad infusion pump

Figure 7: Sterilized reactant preparation