**In vivo** imaging of encapsulated laser-polarized helium³

V. Callo1, J. Brochet2, E. Canet3, H. Humbert4, M. Viallon1, A. Brigitet1, H. Tournier2, Y. Creminilleux1.

1 Laboratoire de RMN, CNRS UPR ESA 5012, Université Claude Bernard Lyon-1-CPE, France. 2 Creatis, CNRS UMR 5515, Hôpital de la Croix-Rousse, Lyon, France. 3 Bracco Research, Geneva, Switzerland. 4 Institut Laîné-Langevin, Grenoble, France.

**INTRODUCTION**

The use of hyperpolarized (HP) gases as blood tracers has been reported recently by several teams [1, 2]. In the case of helium, one has to deal with lower solubility in liquids or tissues compared to xenon. In this work, we propose an approach based on helium encapsulation in lipid-based carrier agents of 2 micrometers average diameter. T1 and T2 relaxation times have been measured and are compatible with **in vivo** imaging experiments as demonstrated in animal studies.

**METHODS**

Polarized ³He was produced at the Laîné-Langevin Institut in Grenoble (France) via the metastable-exchange method [3], with a polarization up to 55% at the end of the optical pumping process.

Encapsulation substrates were provided by Bracco Research SA (Geneva, Switzerland). Microbubbles were formed after vigorous shaking, during several seconds, of a syringe containing substrates, saline and HP ³He. Measured microbubbles mean diameter was equal to 2 µm.

NMR studies were performed on a 2 Tesla 17 cm bore diameter magnet using a SMS console (Guildford, England). Experiments were achieved using a double tune (¹H/³He) 6 cm diameter Alderman-Grant coil.

For **in vivo** experiments, male Sprague-Dawley rats (280-350 g) were anesthetized using Valium and ketamine. Catheters were inserted either in the jugular vein or in a vein tail in order to realize the intravenous injection of microbubbles solution. Several dedicated HP ³He imaging sequences were developed and used, depending on the **in vivo** experiments. These sequences include Projection-Reconstruction, Spiral or Turbo-Spin-Echo acquisitions.

**RESULTS AND DISCUSSION**

Longitudinal and transverse relaxation times of encapsulated ³He were measured in vitro and found respectively equal to 25 s and 305 ms. Typical apparent relaxation times in **in vivo** were in the range of 3 s.

In order to follow the passage of the ³He microbubbles solution through the heart and the lungs vasculature, a series of 25 transverse slice-selective images positioned on the heart were acquired using a spiral sequence (12 interleaved spiral trajectories, 4 revolutions per spiral, 240 ms/image). Typically, intravenous injections in the jugular or tail vein of 3 to 4 ml of solution were completed in less than 10 s. Using the spiral technique, one can easily visualize highlighted right and left cardiac cavities. These images show that a large amount of ³He polarization survives the transit from the heart right cavities to the left cavities. One example of ³He image in the heart cavities averaged from a complete series of spiral acquisition is shown in figure 1. Signal to noise ratio (SNR) measured in the left and right heart cavities are respectively equal to 73 and 90.

The small losses of polarization after circulation through the lung vasculature are confirmed from coronal images acquired in the abdominal region of the animal. Images were obtained, using a Turbo-Spin-Echo sequence, following intravenous injection in the jugular vein (Figure 2). The abdominal aorta is clearly delineated while smaller arteries such as the hepatic one are also enhanced as confirmed from coregistration with proton images.

**CONCLUSION**

In this work, the feasibility of intravascular imaging using encapsulated ³He is demonstrated in animals. Heart cavities can be visualized and arteries have been imaged after microbubbles circulation through the heart and the lung vasculature. Furthermore, ³He images corresponding to microbubbles distribution in the lung vasculature have been obtained. These results may open up new applications for HP ³He regarding angiography or tissue perfusion studies.

**REFERENCES**