"How did I spend the Siemens – NACP Grant 2008"

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First of all, I would like to express my compliments to all the parties who made my visit to Mainz possible. The visit was funded by the Siemens – NACP Grant established by Siemens Medical Solutions (Siemens AB) and Nordic Association for Clinical Physics (NACP). I am grateful to Professor Laura Schreiber and her research group for allowing me to observe closely their work in the Section of Medical Physics at the Mainz University hospital. I would like to thank Dr. Kerstin Münnemann and Dr. Zahir Salhi for introducing their research groups and projects. And finally, special thanks to Florian Meise for all the practical arrangements and the in-depth introduction of the local culture and the city of Mainz.

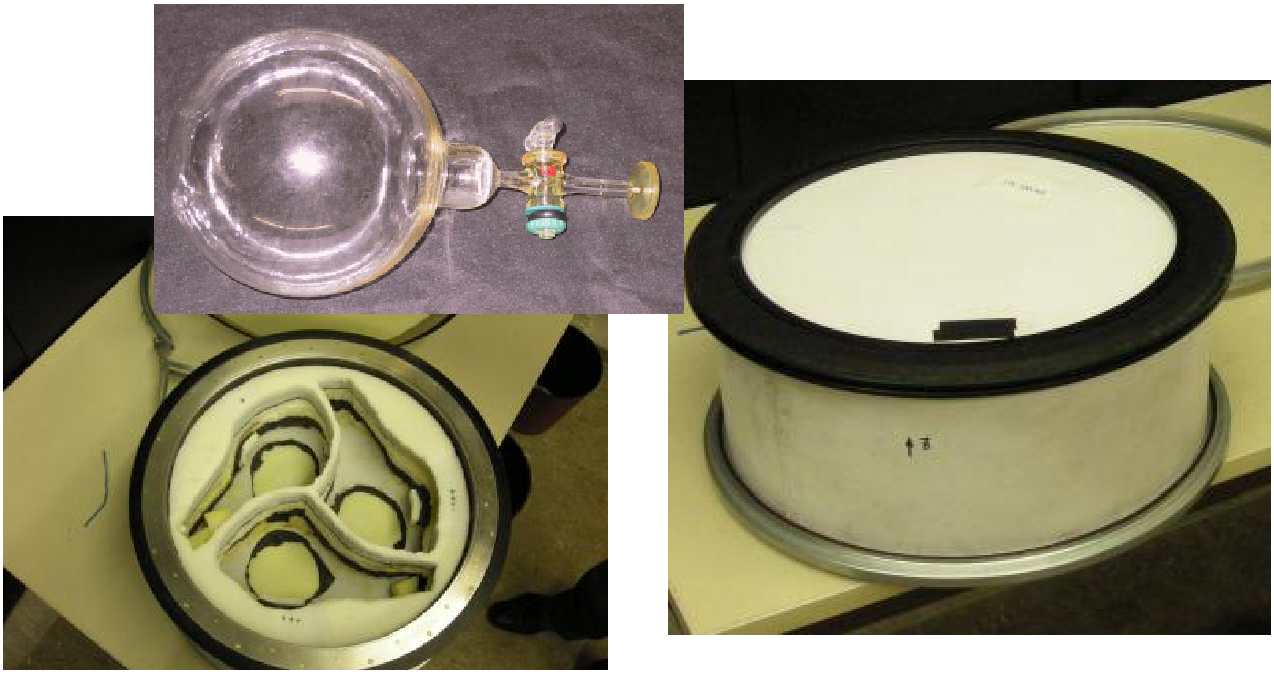
My interest to visit in Mainz arises from the years I spent as a PhD student in the NMR Research Group at the University of Oulu. Part of my work was planning and constructing a hyperpolarizer for xenon and at that time I got introduced to the hyperpolarized noble gases. Magnetic Resonance Imaging (MRI) became my speciality as I moved to the field of medical physics. The use of hyperpolarized gas for MRI of the lung unites my interests, so I have been following this field of research closely. The PHeLINet consortium (www.phelinet.eu), financed by the European Union, has arranged "open to all" training schools which have given possibility to familiarize me with the research within network and to meet researchers working in this field.

Before the short report of the actual visit, I would like to briefly introduce the concept of hyperpolarization, as this may be unfamiliar topic even for those regularly working with MRI. The basic requirement of MRI is the high homogenous magnetic field. MRI is based on the Nuclear Magnetic Resonance (NMR) and the nuclear spins must be polarized to attain observable signal. Nuclear spin polarization follows the Boltzmann distribution and is dependent on the gyromagnetic ratio of the nucleus, magnetic field and temperature. In the case of clinical MRI the only way to increase polarization is a stronger magnetic field. Unfortunately, even in the high magnetic fields modern MRI scanners (typically 1,5- 3 T), the spin polarization of ^{1}H nuclei is only in the order of 0,001 %. In case of other nuclei this is even less and due to their small amount in human body, the MRI scans with nuclei other than ^{1}H are rarely performed. Due to low spin density, imaging of gas is easily considered to be impossible. However, the nuclear spin polarizations of noble gas nuclei can be increased by Meta-stable (MEOP)- or Spin-Exchange Optical Pumping (SEOP) techniques. The main difference of these two techniques is that in SEOP alkali metal atoms (usually Rb) are optically pumped with circularly polarized laser light. The spin polarization is then transferred from alkali metal electrons to noble gas nuclei during collisions via hyperfine interaction. SEOP method is especially efficient for ^{129}Xe nuclei. In MEOP method, electrons of ^{3}He atoms are first excited to the meta-stable state and then optically pumped. Nuclear spin polarization is built up through the collisions of the meta-stable ^{3}He atoms in the low pressure optical pumping cell. Nuclear spin polarizations as high as 70-80 % can be attained with SEOP and MEOP techniques.

During my two weeks stay in Mainz I had an opportunity to visit in the Max Planck Institute for Polymer Research. Materials research is the main interest of the institute, but the Hyperpolarization Group lead by Dr. Kerstin Münnemann (joint employment 50% Max-Planck-Institute and 50% Section of Medical Physics) focuses on studying different polarization techniques: Dynamic Nuclear Polarization (DNP), Parahydrogen Induced Polarization (PHIP) and Spin Exchange Optical Pumping. The DNP technique is considered to be very interesting for MRI as well, because it makes the hyperpolarization of ^{13}C or ^{15}N nuclei possible. This is expected to enable a new kind of molecular imaging methods. The research group has a close collaboration with the Institute for Physics at the Johannes Gutenberg University of Mainz and the division of Medical Physics at the University hospital.

Visit to the Institute for Physics was very interesting for me as their ^{3}He-hyperpolarizer is probably the most advanced MEOP system in the world. Operation of the polarizer is controlled by a computer and can be fully automated. Its production rate is very impressive around 30 litres per day with the 75 % polarization rate and it is sufficient to serve several imaging facilities. In fact, hyperpolarized gas is delivered from Mainz to locations all over the world. The real problem now and in the future will be the availability of the ^{3}He gas. It is derived as a by product of the nuclear industry and due to minimal amounts of this isotope in stocks at the moment the price has risen up to several hundreds of euros per litre recently.

Snoopy visitor and the MEOP hyperpolarizer in the Physics Institute at the Johannes Gutenberg University of Mainz.

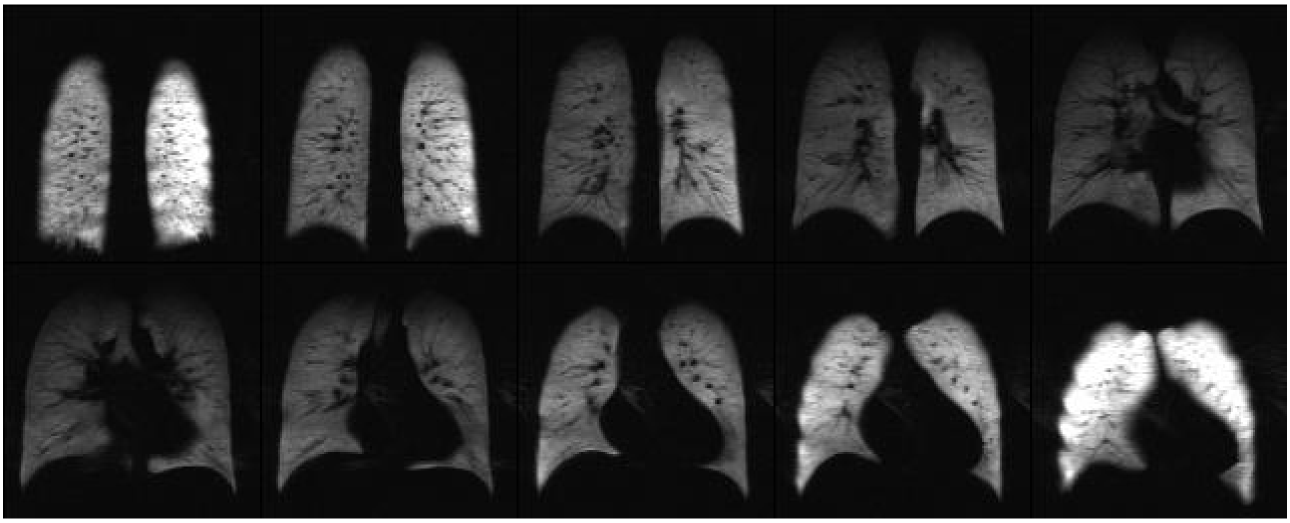


Special storage cells filled with polarized helium are packed in mu-metal shielded transport boxes. Inside the box a homogenous magnetic field is maintained, which leads to very long T_1 *relaxation time (tens of hours) of* ^3He *gas. This allows shipments all over the world.*

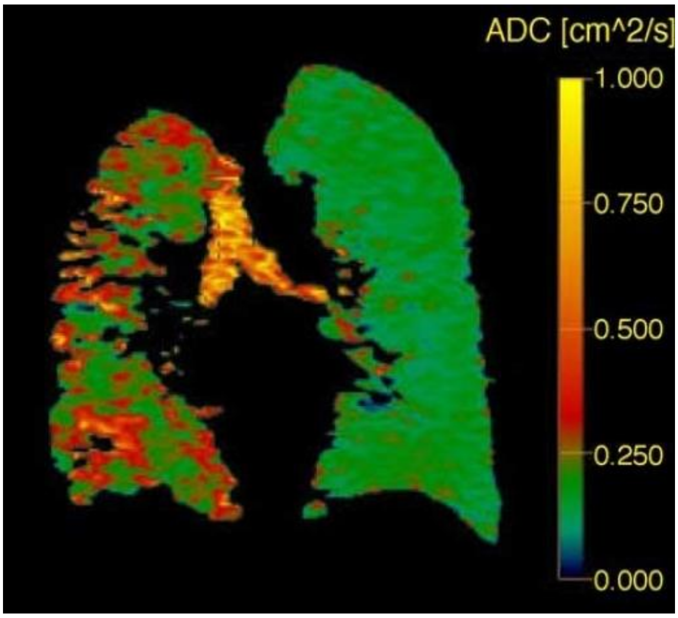
The Section of Medical Physics in the Department of Radiology at the Mainz University hospital is investigating and developing new measurement techniques, most of all in the field of magnetic resonance imaging (MRI). I had opportunity to learn more about cardiac perfusion studies and the theory beyond parallel acquisition techniques, but the reason I really wanted to visit in Mainz was their MRI studies of human lungs. Close collaboration with the Institute for Physics has made possible very advanced MRI studies with hyperpolarized ^3He. Research is focused on dedicated instrumental and methodological MRI developments for the extension of new research and routine medical applications using ^3He. One of the latest achievements is 32-channel coil for lung studies which allows efficient use of parallel acquisition techniques leading to faster and more accurate imaging.

Lungs have been kind of a “black hole” in MRI. Low spin density, susceptibility related issues and respiratory motion are among the reasons why MRI of the lung is a very challenging task. Hyperpolarized noble gases give rise to new possibilities since they act as contrast agents that diffuse rapidly to fill the airspaces of the lungs and allow visualization and measurement of the ventilated airways and alveolar spaces. However, it is important to understand the limitations of hyperpolarization method. Gas is pre-polarized and the polarization is non-recoverable. After 90 degree excitation nuclear spins return to thermal equilibrium, so it is very important to pay attention to the imaging sequences that are used. FLASH and other small flip angle methods are those most commonly used. Lot of work has been done to study more sophisticated sequences, but in clinical use simple sequences like FLASH are still considered to be useful. Diffusion weighted MRI can be used to measure the apparent diffusion coefficient (ADC) of the ^3He within the lung airspaces. In regions such as the trachea, the gas is largely unrestricted, but in the lung parenchyma, the gas is highly restricted by the walls of the alveoli and terminal bronchioles. As alveolar tissue degenerates in emphysema, for example, the gas is less restricted and can diffuse over greater lengths resulting in greater signal loss.

As a summary, hyperpolarized noble gases make possible ventilation, diffusion and dynamic imaging of the gas inside the lung. This may be a valuable tool when studying patients with asthma, COPD, cystic fibrosis or other pulmonary diseases. Chance to act as a volunteer patient in a lung study with hyperpolarized helium was very useful in order to understand demands the patient encounters. The patient has to be able to follow instructions strictly in order to complete the study successfully, but it has been reported that even young children aged four have been studied with this method, so with proper instructions it is applicable for anyone. Actual patients with lung disorders may find the long (15-30 seconds) breath-hold difficult, but use of modern coil and parallel acquisition techniques will allow even 3D imaging with very short scan times.



Acting as a volunteer patient proved that non-smoking way of life pays off. Image series of healthy lungs is shown in the picture. Normalization filters were not used, so signal intensity close to coil seems to be too high.



Actual patient with left lung transplantation. Low ADC values are seen in the transplanted lung and intermediate ADC values in the fibrotic lung.
Schreiber et al. / Respiratory Physiology & Neurobiology 148 (2005) 23–42

Members of the Medical Physics research group have several presentations in ISMRM 2009 meeting. I recommend anyone participating in the meeting to take a closer look in their work.

For more information:

Max-Planck Institute for Polymer Research, Hyperpolarization Group
http://www.mpip-mainz.mpg.de/groups/spiess/Research

Johannes Gutenberg – Universität Mainz, Insitut für Physik – Arbeitsgruppe Helium-3
http://www.physik.uni-mainz.de/exakt/helium3/

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