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Investigation of laser polarized xenon magnetic resonance

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PRINCIPAL INVESTIGATOR

Dr. Ronald L. Walsworth

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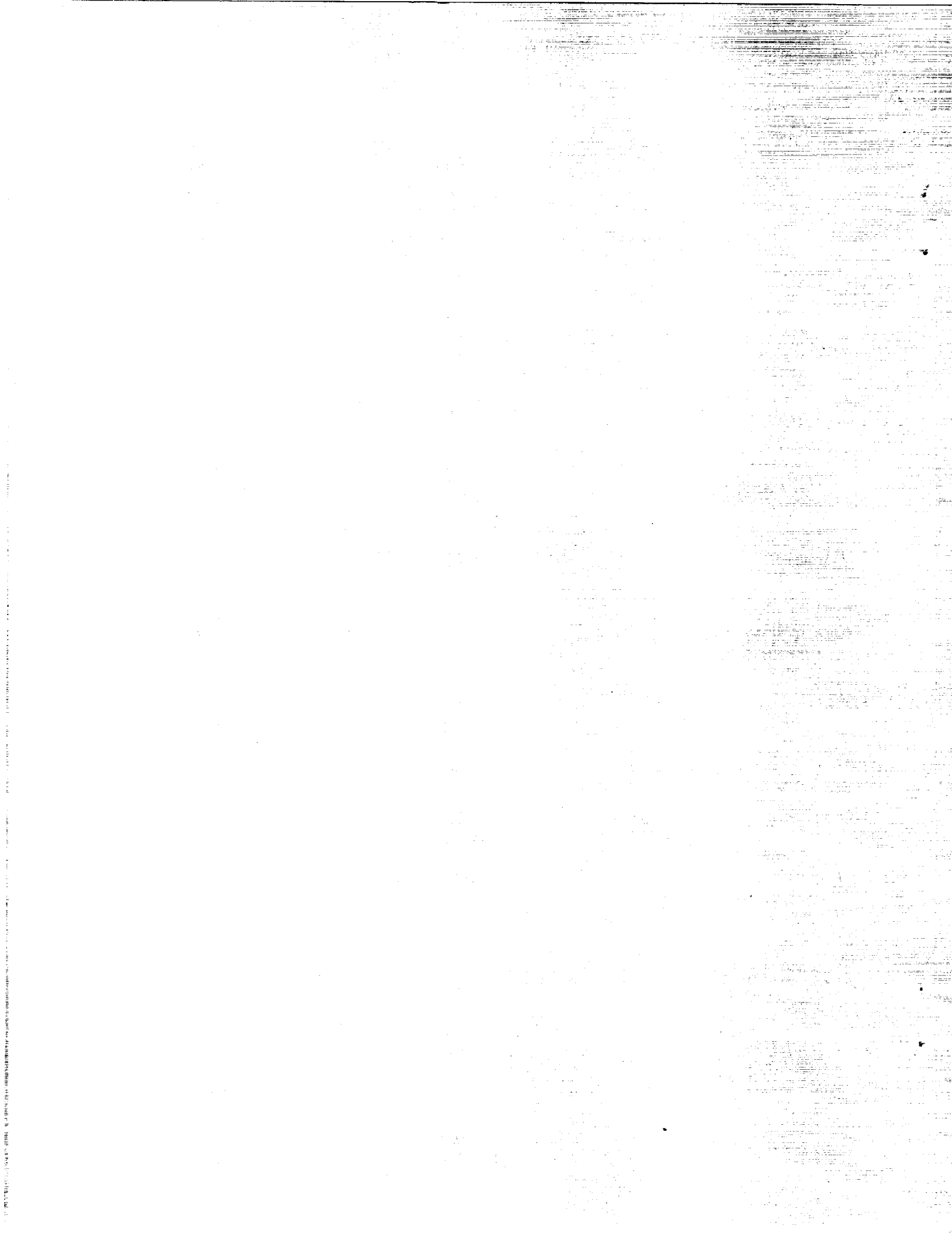
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Smithsonian Institution

Astrophysical Observatory

Cambridge, Massachusetts 02138

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Specific aims of research and accomplishments during grant period

The present NASA grant (NAGW-5025) supports ground-based investigations of a new biomedical diagnostic technology: nuclear magnetic resonance of laser polarized noble gas. Large nuclear spin polarizations (> 10%) can be created in dense samples of the spin 1/2 noble gases (^3He and ^{129}Xe) using the technique of spin-exchange optical pumping. Such large polarizations greatly enhance the nuclear magnetic resonance (NMR) detection sensitivity of ^3He and ^{129}Xe , enabling fast, gas space magnetic resonance imaging (MRI), studies of gas diffusion in porous media, and investigations of fluids using the soluble ^{129}Xe species. Laser polarized ^3He and ^{129}Xe can be benignly inhaled by humans with minimal loss of spin-polarization ($T_1 \sim 5$ to 50 seconds, depending on the organ and tissue) and then detected with NMR. Potential biomedical applications include improved lung imaging (important for emphysema diagnosis); the imaging of lipid membranes in the brain (useful in the diagnosis of multiple sclerosis and in research on brain function); and better measurement of blood flow to tissue (important for stroke and ischemia diagnosis, and also useful in research on cardiopulmonary and brain function). In addition, noble gas laser polarization occurs external to the body and does not require a large magnetic field for high sensitivity NMR detection—unlike conventional NMR of ^1H in liquid water, et al. which typically employs magnetic fields of ~ 1 tesla to create thermally polarized nuclear spin polarizations of $\sim 10^{-5}$. Thus at low magnetic fields (< 0.01 tesla), water NMR signals are not observable without extensive signal averaging; whereas laser polarized noble gas NMR images can be obtained clearly and rapidly in a single measurement. Low-field noble gas NMR may be practical in a small, low-power device and enable both portable ground-based and practical space-based biomedical MRI systems. Our biomedical investigations with laser polarized noble gas are in collaboration with the Magnetic Resonance Division of the Brigham and Women's Hospital, headed by Dr. Ferenc Jolesz.

The specific research aims of the present grant fall into three general areas: (i) development of a large-scale noble gas laser polarization system; (ii) biomedical investigations using laser polarized noble gas in conventional (high magnetic field) NMR systems; and (iii) the development and application of a low magnetic field system for laser polarized noble gas NMR.

Below is a description for each specific aim of what has been accomplished during the tenure of NASA grant NAGW-5025 (4/1/96 to 9/30/97).

1. Development of a large-scale noble gas polarization system.

- *Optimization of polarization chamber geometry.*
Model calculations of the noble gas laser polarization process were performed. One of the variables analyzed was polarization chamber geometry. Also, development was begun on a low magnetic field noble gas NMR system (see specific aim 3 below). This low field system will be used to investigate polarization chamber geometry, with the results to be compared to the model calculations. The results of these studies will be used to improve the large-scale noble gas polarization system.
- *Optimization of polarization chamber gas pressures.*
The optimization of polarization chamber gas pressures was also studied via model calculations. Again, the results of these studies will be used to improve the large-scale noble gas polarization system.
- *Incorporation of large power diode laser arrays.*
The large-scale noble gas polarization system incorporates four 15 watt diode laser arrays. Each laser is fiber-coupled, and then the four fiber bundles are merged into a single meta-fiber bundle that provides up to 60 watts of optical pumping light onto the polarization chamber.
- *Optimization of laser optics (lenses, quarter wave plates, etc.).*
A compact optics package has been developed that allows $\sim 90\%$ of the power from the 60

watt diode laser array system to be circularly polarized and projected through the volume of a polarization chamber up to ~ 0.5 m in length.

- *Comparison of polarization system location in high or low magnetic field.*
The large-scale noble gas polarization system allows operation in either high or low magnetic field (resulting from the fringe field of an NMR magnet). Comparative tests of system configuration have not yet been performed.
- *Development of systems for cryogenic storage of polarized ^{129}Xe .*
The large-scale noble gas polarization system currently polarized ^{129}Xe in the solid phase at liquid nitrogen temperatures (~ 77 K). At these temperatures we measured the ^{129}Xe polarization lifetime (T_1) to be about 2.5 hours, in agreement with previous work.

2. High-field biomedical investigations using polarized noble gas NMR.

- *Investigation of in vitro tissues.*
We measured the polarization lifetime (T_1) of laser polarized ^{129}Xe dissolved in fresh human blood in vitro. The T_1 of ^{129}Xe dissolved in the bloodstream is an important factor in determining the polarization delivered to target tissues for in vivo NMR using inhaled, laser polarized ^{129}Xe . A blood-foam preparation was used to enhance the NMR signal of ^{129}Xe dissolved in blood. We found that the dissolved ^{129}Xe T_1 is significantly shorter in oxygenated blood than in deoxygenated blood. To understand the oxygenation trend, T_1 measurements were also made on plasma and hemoglobin preparations. Extrapolating our blood foam results to in vivo oxygenation conditions, we estimate that the ^{129}Xe T_1 is 5-10 seconds in arterial blood and 15-25 seconds in venous blood. The measurement technique using a polarized ^{129}Xe gas-liquid exchange interface in a foam may also be generally useful in studying foam coarsening and other liquid physical properties. A paper reporting these results was published in the Journal of Magnetic Resonance.
- *Investigation of ventilated animals.*
We observed ^{129}Xe NMR spectra in the thorax of living rats breathing the laser polarized gas (see Fig. 1). We also obtained NMR images of laser polarized ^{129}Xe gas inside the rat lung (see Fig. 2). We observed three well-resolved ^{129}Xe tissue resonances, in addition to the gas resonance in the lung gas space. We identified these resonances as ^{129}Xe in solution in pulmonary tissue, red blood cells, and adipose tissue. Once xenon inhalation was stopped, the three ^{129}Xe tissue resonances were observed to decay with different time constants ranging from 11 to 50 seconds—i.e. longer than the blood circulation time in the animal. Thus it may be possible to perform dissolved-state ^{129}Xe MRI in animals and humans (and, in general, in complex fluid systems).

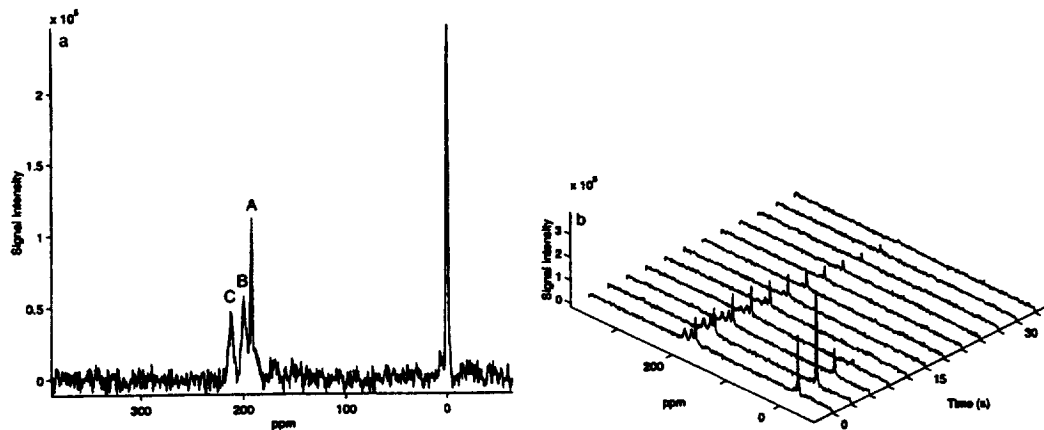


Figure 1. ^{129}Xe NMR spectra from a rat breathing the laser polarized gas. Spectral peaks A, B, and C are ^{129}Xe in solution in adipose tissue, pulmonary tissue, and red blood cells, respectively. Polarization decay after cessation of breathing is shown at right.

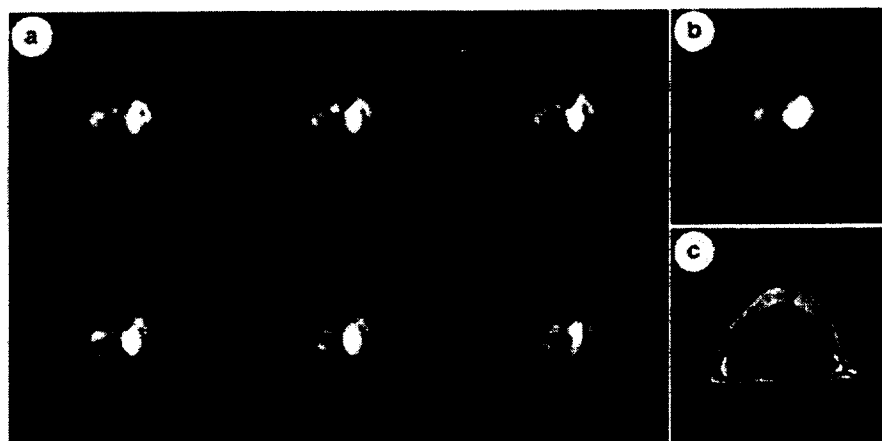


Figure 2. Axial slice NMR lung images of a living rat. (a) Temporal sequence of laser polarized ^{129}Xe NMR images from the lung gas space. (b) The summed image from the six images shown in (a). (c) Conventional proton NMR image of a corresponding slice. Note the complimentary nature of the noble gas and proton images.

- *Development of laser polarized ^{129}Xe MRI techniques.*
We investigated gradient echo imaging strategies for laser polarized ^{129}Xe MRI. We performed experiments on the use of different gradient echo pulse sequences and found that a variable flip angle approach can improve the ^{129}Xe signal to noise ratio and eliminate some typical image artifacts. We also demonstrated that although a constant signal intensity can be obtained with such an approach, the maximum spatial resolution achievable is constrained by the ^{129}Xe polarization lifetime, T_1 . A paper reporting these results was published in the Journal of Magnetic Resonance, Series B.
 - *Xenon uptake model calculations.*
We developed the first model calculation of the build-up of inhaled, polarized ^{129}Xe in human tissues. This model assumes the steady inhalation of laser polarized ^{129}Xe gas mixed with air, and accounts for ^{129}Xe depolarization in the lung, blood, and tissue of interest. With the caveat that important parameters such as the ^{129}Xe T_1 times in blood and tissues are not well known in vivo, we calculated that at 1.5 tesla the ^{129}Xe NMR signal-to-noise ratio in human brain tissues is ~ 1 -10% of that from proton NMR in typical water-rich tissue. At low field (< 0.01 tesla) the relative magnitudes of the ^{129}Xe and water proton NMR signal-to-noise ratios are expected to reverse.
3. Development and application of a low magnetic field MRI system.
- *Development of a low-field solenoid and pulsed gradient coils.*
A solenoid was constructed to provide a stable, homogeneous magnetic field < 0.01 tesla, with first through fourth order static-gradient correction coils. Pulsed gradient coils for 2D spectroscopy and imaging were also developed, providing up to $\sim 10^{-5}$ tesla/cm.
 - *Development of a low-RF system for magnetic resonance detection and excitation.*
Sensitive low-RF (~ 100 kHz) pulse and detection coils were developed to allow adiabatic fast passage (AFP), free induction decay (FID), and spin echo detection of laser polarized noble gas samples. Also, signal averaging techniques were developed to observe water proton NMR at low magnetic fields.
 - *Development of techniques for low-field imaging.*
A gradient echo signal was induced and detected from a cell containing laser polarized ^{129}Xe gas at ~ 30 gauss, using the prototype low-field MRI system. Such gradient echoes are important tools for low field imaging of laser polarized noble gas (with its finite magnetization).

Relevant papers published during grant period

- NMR of laser polarized ^{129}Xe in blood foam.*
C.H. Tseng, S. Peled, L. Nascimben, E. Oteiza, R.L. Walsworth, and F.A. Jolesz, J. Magn. Reson. **126**, 79 (1997).
- Gradient echo imaging considerations for hyperpolarized ^{129}Xe MR.*
L. Zhao, R. Mulkern, C.H. Tseng, D. Williamson, S. Patz, R. Kraft, R.L. Walsworth, F.A. Jolesz, and M.S. Albert, J. Magn. Reson., Series B **113**, 179 (1996).
- Demonstration of a two species noble gas maser.*
R.E. Stoner, M.A. Rosenberry, J.T. Wright, T.E. Chupp, E.R. Oteiza, and R.L. Walsworth, Phys. Rev. Lett. **77**, 3971 (1996).
- Determinants of tissue delivery for ^{129}Xe magnetic resonance in humans.*
S. Peled, F.A. Jolesz, C.H. Tseng, L. Nascimben, M.S. Albert, and R.L. Walsworth, Magn. Reson. Med. **36**, 340 (1996).
- Temporal dynamics of hyperpolarized ^{129}Xe resonances in living rats.*
K. Sakai, A.M. Bilek, E. Oteiza, R.L. Walsworth, D. Balamore, F.A. Jolesz, and M.S. Albert, J. Magn. Reson., Series B **111**, 300 (1996).

Relevant conference abstracts during grant period

- NMR of laser polarized ^{129}Xe in blood foam.*
C.H. Tseng, S. Peled, L. Nascimben, G. Wong, R.L. Walsworth, and F.A. Jolesz, presented at the 1997 April American Physical Society Meeting, Washington, D.C., 18-21 April 1997.
- Large scale polarization of noble gas for use in medical imaging.*
D. Hoffmann, G. Wong, C.H. Tseng, and R.L. Walsworth, presented at the 1997 April American Physical Society Meeting, Washington, D.C., 18-21 April 1997.
- Multiple echo techniques for hyperpolarized noble gas MRI.*
L. Zhao, R. Mulkern, C.H. Tseng, D. Williamson, K. Oshio, H. Gubbjartsson, R.L. Walsworth, F.A. Jolesz, and M.S. Albert, presented at the Sixth Annual Meeting of the International Society of Magnetic Resonance in Medicine (ISMRM), 12-18 April 1997.
- Optimization of RF pulses for hyperpolarized noble gas MRI: the variable flip angle approach.*
L. Zhao, R. Mulkern, C.H. Tseng, D. Williamson, S. Patz, R. Kraft, R.L. Walsworth, F.A. Jolesz, and M.S. Albert, presented at the Sixth Annual Meeting of the International Society of Magnetic Resonance in Medicine (ISMRM), 12-18 April 1997.
- Projection-reconstruction imaging with hyperpolarized ^{129}Xe .*
D.F. Kacher, K. Shimizu, R.L. Walsworth, F.A. Jolesz, and M.S. Albert, presented at the Sixth Annual Meeting of the International Society of Magnetic Resonance in Medicine (ISMRM), 12-18 April 1997.
- NMR of laser polarized ^{129}Xe in blood foam.*
C.H. Tseng, S. Peled, L. Nascimben, G. Wong, R.L. Walsworth, and F.A. Jolesz, presented at the 1997 Experimental NMR Conference (ENC), Orlando, FL, 24-28 March 1997.
- Optimal pulse sequences for hyperpolarized ^{129}Xe MR.*
L. Zhao, R. Mulkern, C.H. Tseng, D. Williamson, S. Patz, R. Kraft, R.L. Walsworth, F.A. Jolesz, and M.S. Albert, presented at Centre de Physique des Houches International Workshop on Perspectives of MR Imaging Using Polarized Gases, Les Houches, France, 9-11 October 1996.

Temporal dynamics of hyperpolarized ^{129}Xe resonances in living rats.

K. Sakai, A.M. Bilek, E. Oteiza, R.L. Walsworth, D. Balamore, F.A. Jolesz, and M.S. Albert, presented at Centre de Physique des Houches International Workshop on Perspectives of MR Imaging Using Polarized Gases, Les Houches, France, 9-11 October 1996.

Laser polarized ^{129}Xe spectra and lifetimes in in vitro blood and blood derivatives.

C.H. Tseng, S. Peled, L. Nascimben, G. Wong, R.L. Walsworth, and F.A. Jolesz, presented at Centre de Physique des Houches International Workshop on Perspectives of MR Imaging Using Polarized Gases, Les Houches, France, 9-11 October 1996.

Biological studies with laser-polarized ^{129}Xe .

C.H. Tseng, E.R. Oteiza, R.L. Walsworth, M.S. Albert, L. Nascimben, S. Peled, K. Sakai, and F.A. Jolesz, presented at DAMOP Meeting of the American Physical Society, Ann Arbor, MI, 15-18 May 1996.

Large-scale production of laser-polarized ^{129}Xe : comparison of laser-diode-array and Ti-sapphire optical pumping.

R.L. Walsworth, R.E. Stoner, C.H. Tseng, G.A. Wong, and E.R. Oteiza, presented at DAMOP Meeting of the American Physical Society, Ann Arbor, MI, 15-18 May 1996.

