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13. ABSTRACT (Maximum 200 words) The research supported by this grant was focused on applications of laser-polarized ^3He and ^{129}Xe in magnetic resonance imaging and on the basic physics that makes this possible. During the past few years, magnetic resonance imaging of human lungs with laser-polarized ^3He and ^{129}Xe is being done with increasing frequency at a growing number of sites throughout the world. The resulting lung images are of unprecedented resolution and they clearly show pathologies that are more poorly diagnosed, if at all, by currently available modalities like x-rays or gamma-ray scintillography. A very important consideration in the use of laser-polarized ^3He and ^{129}Xe is that the nuclear spins of these gases do not relax at the surface of the container in which they are pumped or stored. This research has shown that in the case of ^{129}Xe in cells with polymer wall coatings, much of the relaxation is due to unusually long trapping of the ^{129}Xe atoms at sites surrounded by protons in the polymer.				
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FINAL TECHNICAL REPORT

For the Research Period
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THE PHYSICS OF SPIN POLARIZED ATOMIC VAPORS.

Submitted March 4, 1998

by

W. Happer, Co-Principal Investigator

1. Overview

The research supported by this grant was focused on applications of laser-polarized ^3He and ^{129}Xe in magnetic resonance imaging and on the basic physics that makes this possible. Formal clinical trials on human patients are about to begin at hospitals located at Duke University in Durham, NC and at the University of Virginia, in Charlottesville, VA. This exciting new diagnostic capability will have medical applications both in the Air Force, and also in the civilian sector. The new medical application could not have been developed without far-sighted support by AFOSR over many years.

Although the medical application of spin-polarized gases has received great publicity during the past few years, the work supported by this AFOSR grant has and will continue to have applications to other technologies of the United States Air Force. For example, the Rb clocks used in the GPS satellite system are based on optical pumped gas cells. The basic physical processes operating in these clocks is closely related to that of the cells used to polarize ^3He and ^{129}Xe gas for medical imaging. Surprising new developments continue to show up in the basic physics of these and other closely related systems.

Much of the work supported by this grant has already been published in peer-reviewed journals, as listed below, but we will give a brief summary of some of the more important accomplishments in the next section.

2. Major Accomplishments

Lung Imaging. During the past few years, magnetic resonance imaging of human lungs with laser-polarized ^3He and ^{129}Xe is being done with increasing frequency at a growing number of sites throughout the world. The resulting lung images are of unprecedented resolution and they clearly show pathologies that are more poorly diagnosed, if at all, by currently available modalities like x-rays or gamma-ray scintillography.

Surface relaxation. A very important consideration in the use of laser-polarized ^3He and ^{129}Xe is that the nuclear spins of these gases not relax at the surface of the container in which they are pumped or stored. In work led by Dr. Bastiaan Driehuys, we have shown that in the case of ^{129}Xe in cells with polymer wall coatings, much of the relaxation is due to unusually long trapping of the ^{129}Xe atoms at sites surrounded by protons in the polymer.

Relaxation of ^{129}Xe in Oxygen. For imaging studies of humans with laser polarized ^{129}Xe , some oxygen will be present in the inhaled xenon, either intentionally administered

for safety, or mixed with air left in the lungs from the previous breath. In work led by Dr. Brian Saam we have shown that an admixture of 20 % oxygen to xenon gas at atmospheric pressure shortens the nuclear spin relaxation time to about 10 seconds, not too short a time for excellent lung images to be acquired.

High-Volume Production of Laser-Polarized ^{129}Xe . In work led by Bastiaan Driehuys we have shown that large amounts (liters) of laser-polarized ^{129}Xe can be produced by continuous flow of a lean mixture of xenon in a helium-nitrogen carrier gas through a cell, pumped by a broad-band diode laser array. The nuclear spin polarized ^{129}Xe that results is accumulated by freezing it out of the gas stream in a cold trap at liquid nitrogen temperatures.

Edge Enhancement. In work led by Dr. Brian Saam, we have shown that the hindered diffusion of spin-polarized gases at depolarizing walls leads to sharp peaks at the edges of the image. This image distortion is in good quantitative agreement with a theory of edge enhancement developed in our group. The natural functions for describing edge enhancement are Airy functions.

Imaging of Spin Polarization of Laser-Pumped Alkali-Metal Vapors. The nuclear spin polarization ^3He and ^{129}Xe , produced by spin exchange with optically pumped alkali-metal vapors, cannot exceed the volume averaged electronic spin polarization of the alkali-metal vapor. In work led by Dr. Stephan Appelt and Dr. Andrei Baranga, we have developed an effective imaging method, similar in spirit to magnetic resonance imaging of nuclear polarization, which has allowed us for the first time to determine the three-dimensional spin polarization of optically-pumped alkali-metal vapor.

Theory of Spin Rotation Interactions. One of the major spin loss mechanisms for optically pumped alkali-metal vapors is the spin-rotation interaction between the electron-spin of the alkali-metal atom and the rotational angular momentum of a collision partner or second atom in a van der Waals molecule. In work led by Dr. Happer, simple and effective theory of the spin rotation interaction for alkali-metal atoms in both high-Z buffer gases like xenon or low-Z buffer gases like helium has been developed. One prediction of the theory, that potassium should be a much better partner for spin-exchange polarization of ^3He than Rb or Cs has recently been confirmed by experiments of our group. The experimental findings will be published shortly in Physical Review Letters.

Hyperpolarized Liquid Xenon. In work led by Dr. Rich Fitzgerald and Ms. Karen Sauer, we have shown that laser polarized xenon, accumulated by freezing as described above, can be liquified with little loss in polarization. The nuclear spin relaxation time of ^{129}Xe in the liquid is 15 to 20 minutes, depending on the temperature. The relaxation rate is about the same in the earth's field as in fields of several tesla. So the polarized liquid xenon is very convenient for transporting about the laboratory, since no magnetic holding fields are needed. We have also shown that many polar substances dissolve readily in hyperpolarized liquid xenon, and polarizations of protons or ^{13}C nuclei in the dissolved molecules can be enhanced by factors of 10 to 100 compared to thermal equilibrium values.

3. Patents

A fundamental patent "Magnetic Resonance Imaging Using Hyperpolarized Gases," Patent Number 5,545,396 was issued to Princeton University and the State University of New York on August 13, 1996 for work supported in part by AFOSR. Three additional

Princeton patents on wall coatings for hyperpolarized gases, on the ^{129}Xe accumulator mentioned above, and on a system to polarize ^3He have been licensed to MITI. All of these patents were based on work supported by this AFOSR grant and its predecessor grants.

4. Technology Transfer

Much of the technology developed under this grant is being transferred to the startup company Magnetic Imaging Technologies, Inc. (MITI), located in the Research Triangle area of North Carolina through a licensing agreement with Princeton University. MITI has also benefitted from an STTR award from the United States Air Force to help develop gas imaging. Two of the key technical people at MITI, Dr. Bastiaan Driehuys, Director of Research and Dr. Paul Bogorad participated in AFOSR sponsored research while they were students and post doctoral research associates at Princeton. MITI aims to make magnetic resonance imaging with ^3He and ^{129}Xe a commonplace medical diagnostic procedure as soon as possible. In 1997, MITI was awarded a Tibbetts Award from the Technology Office of the U.S. Small Business Administration as an outstanding, high-technology startup company.

5. Publications

Activities receiving full or partial support from Grant AFOSR F49620-94-1-0466 have already resulted in the 15 refereed publication listed below, and several more are accepted and awaiting publication.

Hunter Middleton, Robert D. Black, Brian Saam, Gordon D. Cates, W. Happer, Gary P. Cofer, Robert Guenther, Lawrence W. Hedlund, G. Alan Johnson, Kim Juvan and John Swartz, "MR Imaging with Hyperpolarized ^3He Gas," *Magnetic Resonance in Medicine*, **33**, 271-275 (1995).

B. Driehuys, G. D. Cates and W. Happer, "Surface Relaxation Mechanisms of Laser-Polarized ^{129}Xe ," *Phys. Rev. Letters* **74**, 4943 (1995).

B. Saam, and H. Middleton and W. Happer, "Nuclear Relaxation of ^3He in the presence of O_2 ," *Phys. Rev. A* **52**, 862 (1995).

R. D. Black, H. L. Middleton, G. D. Cates, W. Happer, G. P. Cofer, B. Driehuys, L. W. Hedlund, G. A. Johnson, M. D. Shattuck and J. C. Schwartz, "In Vivo ^3He MR Images of Guinea Pig Lungs," *Radiology* **199**, 867 (1996).

James R. MacFall, H. Cecil Charles, Robert D. Black, Hunter Middleton, John Swartz, Brian Saam, Bastiaan Driehuys, Christopher Erikson, Gordon D. Cates, W. Happer, G. Allan Johnson, and Carl Ravin, "Technical Note: Potential for MR Imaging of Human Lung Air Spaces with Hyperpolarized ^3He ," *Radiology* **200**, 553-558 (1996).

B. Driehuys, G. D. Cates, E. Miron, D. K. Walter and W. Happer, "High-Volume Production of Laser-Polarized ^{129}Xe ," *Applied Physics Letters*, **69**, 1668 (1996).

B. Saam, N. Drukker and W. Happer, "Edge Enhancement Observed with Hyperpolarized ^3He ," *Chemical Physics Letters* **263**, 481 (1996).

T. G. Walker and W. Happer, "Spin Exchange Optical Pumping of Noble-Gas Nuclei," *Reviews of Modern Physics*, **69**, 629 (1997).

John P. Mugler et al. "MR Imaging and Spectroscopy Using Hyperpolarized ^{129}Xe Gas: Preliminary Human Results," *Magnetic Resonance in Medicine*, **37**, 809 (1997).

A. R. Young, S. Appelt, A. Ben-Amar Baranga, C. Erickson, and W. Happer "Three Dimensional Imaging of Spin Polarization of Alkali-Metal Vapor in Optical Pumping Cells," *Applied Physics Letters*, **70**, 3081 (1997).

T. G. Walker, J. Thywissen and W. Happer, "Spin-Rotation Interaction of Alkali-Metal-He Atom Pairs," *Phys. Rev. A* **56**, 2090 (1997).

W. Happer, "Medical NMR Imaging with Laser Polarized ^3He and ^{129}Xe ," *Atomic Physics Methods in Modern Research*, Springer Verlag, Eds. K. Jungmann, J. Kowalski, I. Reinhard, F. Träger, Vol. 499, p. 121 (1997).

G. Allan Johnson et al., "Dynamics of Magnetization in Hyperpolarized Gas MRI of the Lung," *Magnetic Resonance in Medicine*, **38**, 66 (1997).

K. L. Sauer, R. J. Fitzgerald and W. Happer, "Laser-polarized Liquid Xenon," *Chemical Physics Letters*, **277**, 153 (1997).

W. Happer, "Medical Imaging," *McGraw-Hill Yearbook of Science and Technology*, New York, p. 243 (1998).

6. Personnel

The following personnel received full or partial support from Grant AFOSR F49620-94-1-0466:

- Dr. William Happer, Co-Principal Investigator
- Dr. Gordon Cates, Co-Principal Investigator
- Dr. Eli Miron, Visiting Research Scientist
- Dr. Andrei Baranga, Visiting Research Scientist
- Dr. Bastiaan Driehuys, Research Associate
- Dr. Brian Saam, Research Associate
- Dr. Hunter Middleton, Research Associate
- Dr. Paul Bogorad, Research Associate
- Dr. Stephan Appelt, Research Associate
- Dr. Richard Fitzgerald, Research Associate
- Ms. Karen Sauer, Graduate Student, PhD candidate
- Mr. Christopher Erickson, Graduate Student, PhD candidate
- Mr. Dan Walter, Graduate Student, PhD candidate
- Mr. Benjamin Lev, Undergraduate Work/Study Student