Nuclear spin imaging with hyperpolarized nuclei created by brute force method

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Abstract. We have been developing a polarized HD target for particle physics at the SPring-8 under the leadership of the RCNP, Osaka University for the past 5 years. Nuclear polarizaton is created by means of the brute force method which uses a high magnetic field (∼17 T) and a low temperature (∼ 10 mK). As one of the promising applications of the brute force method to life sciences we started a new project, "NSI" (Nuclear Spin Imaging), where hyperpolarized nuclei are used for the MRI (Magnetic Resonance Imaging). The candidate nuclei with spin $\frac{1}{2}\hbar$ are ^{3}He, ^{13}C, ^{15}N, ^{19}F, ^{29}Si, and ^{31}P, which are important elements for the composition of the biomolecules. Since the NMR signals from these isotopes are enhanced by orders of magnitudes, the spacial resolution in the imaging would be much more improved compared to the practical MRI used so far. Another advantage of hyperpolarized MRI is that the MRI is basically free from the radiation, while the problems of radiation exposure caused by the X-ray CT or PET (Positron Emission Tomography) cannot be neglected. In fact, the risk of cancer for Japanese due to the radiation exposure through these diagnoses is exceptionally high among the advanced countries. As the first step of the NSI project, we are developing a system to produce hyperpolarized ^{3}He gas for the diagnosis of serious lung diseases, for example, COPD (Chronic Obstructive Pulmonary Disease). The system employs the same ^{3}He/^{4}He dilution refrigerator and superconducting solenoidal coil as those used for the polarized HD target with some modification allowing the ^{3}He Pomeranchuk cooling and the following rapid melting of the polarized solid ^{3}He to avoid the depolarization. In this report, the present and future steps of our project will be outlined with some latest experimental results.

1. Introduction

For a long period, our RCNP group has been involved in spin physics in collaboration with many institutes including, for example, the SPring-8, DUBNA-Russia, Wisconsin-USA, IPN-France, and TRIUMF-Canada. Among the achievements obtained so far we have made remarkable progresses in the development of the polarized ^{3}He ion sources [1] and the polarized HD (Hydrogen Deuteride) target based on the brute force method for nuclear physics research [2, 3].

Based on the aforementioned rich experiences, we started carrying out a program of spin physics applied to other fields in addition to the fundamental spin physics encouraged by the recent success in the lung and brain MRI (Magnetic Resonance Imaging) using hyperpolarized rare gases, e.g., ^{3}He and ^{129}Xe in Europe and USA [4]. Though their projects are remarkably progressive, their practical use for the medical diagnosis is still restricted to test experiments because of difficulty in producing a large amount of highly polarized gases within a short time. This may be partly due to the fact that the methods that they use, i.e., the laser optical pumpings are insufficient in producing rare gases with a large volume in a short time.

Frossati [5] examined the possibility to nuclearly polarize ^{3}He gas with a large volume even up to 1000 ℓ/day by combination of the brute force method with the Pomeranchuk cooling [6]. His idea significantly owes to the success in producing a highly polarized liquid ^{3}He by Castaing *et al.* [7, 8, 9]. Encouraged by this success, Frossati and later the RCNP group started a project to produce highly polarized, i.e., hyperpolarized ^{3}He gas in collaboration with the group from the IPN in order to overcome difficulties associated with the laser optical pumping.

Encouraged by the success in the ^{13}C, and ^{15}N MRI, in which these nuclei were hyperpolarized by means of the DNP (Dynamic Nuclear Polarization) [10] or the PHIP (Parahydrogen Induced Polarization) [11, 12], we extended our project to a more general concept, i.e., the NSI (Nuclear Spin Imaging) since the brute force method which we employ can basically polarize any nucleus irrespectively of nuclear species. This is in striking contrast to other methods so far used, such as the laser optical pumpings, DNP, and PHIP because these methods are effective only for specific nuclei.

Then, our intial project on the hyperpolarized ^{3}He MRI has been modified so that it might include the MRI so that it might include MRI not only with hyperpolarized ^{3}He but also ^{13}C, ^{15}N, ^{19}F, ^{29}Si, and ^{31}P which are important in the biomedicine. Thus, our redefined project, NSI aims at the comprehensive research for the biomedicine involving the diagnoses not only of the COPD (Chronic Obstructive Pulmonary Disease) with ^{3}He but also of the cancer with a ^{13}C labeled glucose. In addition to general view of our project mentioned above, the more important reason to develop the NSI will be addressed in section 3.

2. Brute force method

The brute force method employed in the present NSI project is one of the general methods to polarize nuclei, though the method requires a sophisticated technology in low temperature and high magnetic field. In figure 1, the calculated polarizations for nuclei with a spin $\frac{1}{2}\hbar$ (most of them are important nuclei in biomedicine) attainable by the brute force method are plotted as a function of temperature for B = 17 T. Note that sizable amounts of the polarization could be obtained for nuclei studied here by this method, though there are some differences depending on the magnitude of the nuclear magnetic moment.

For ^{3}He, we plan to decrease the temperature down to a few mK by using the principle of the Pomeranchuk cooling, which is a behaviour specific only to ^{3}He, from which we expect the ^{3}He polarization exceeding 0.9.

3. Importance of NSI

In accordance with the development of medical diagnosis, cancer risk is increasing due to radiation exposures from these equipments such as the X-ray CT, PET, γ-ray scintigram, and so on. This risk is proportional to the number of the equipments and the chances of examination for each person. The number of the X-ray CT (Computer Tomography) and the PET (Positron Emission Tomography) per 1M population are listed in table 2. Here, those for MRI, though it is radiation free, are also listed as a reference for later discussion. Interestingly, Japan has

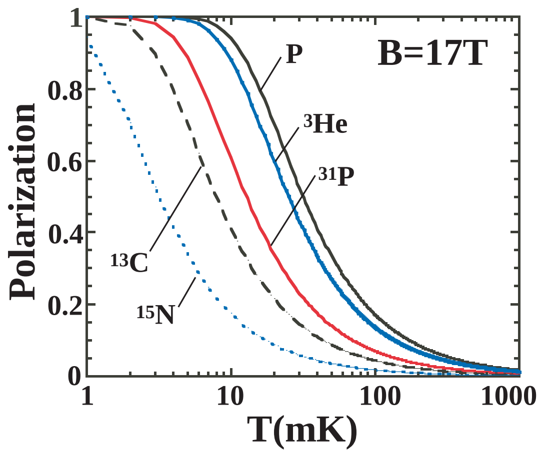

Figure 1. Temperature dependence of nuclear polarizations for some nuclei with a spin $\frac{1}{2}\hbar$ obtained by means of the brute force method. The strength of the magnetic field is kept at 17 T.

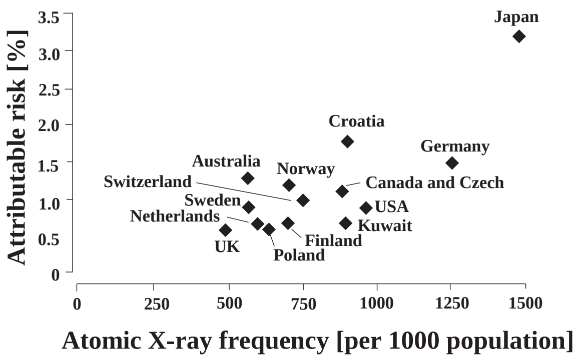

Figure 2. Attributable cancer risk per atomic X-ray frequency.

the largest number of equipment per 1M population nearly by an order of magnitude higher than those in the other developed countries. As a result, the attributable cancer risk due to the X-ray CT is strikingly high in Japan ($\geq$3.5 percent) as shown in figure 2, where an attributable cancer risk is plotted against atomic X-ray frequency per 1000 population. Here, figure 2 is modified from that appeared in the report of Berringt de Gonzàlez *et al.* [13]. Needless to say,

Table 1. The number of X-ray CT, PET, and MRI equipments per 1M population in Japan and in other countries.

Equipment	Radiation Exposure	Nr. equipments in Japan	Nr. in other countries
X-ray CT	Yes	92.6	13.3(World average)
PET	Yes	2.0	0.85(Australia), 0.1(China)
MRI	No	35.0	14.9(Canada), 8.0(OECD)

it is indispensable to quickly recover from the serious situation of the cancer risk in Japan and the other countries too. For this purpose, it is timely to start the NSI project based on the hyperpolarized nuclear MRI in view of the fact that the MRI principally is radiation free and the PET with the FDG (fluorodeoxy glucose labeled by ^{18}F) can possibly be replaced with the safer NSI, i.e., the MRI labeled by the hyperpolarized ^{13}C. If the validity of this method will be proven, the PET currently installed in the selected number of the large hospitals for the cancer diagnosis will hopefully be replaced with the NSI based on the MRI widely and conveniently used in the medium or small hospitals.

Another important advantage of the NSI is that strong magnetic fields ($\geq$ 1.5 T) required for the conventional MRI may be unnecessary. The NSI may work at a weak magnetic field, because the S/N ratio does not seriously depend on the magnetic field in case of the NSI. In fact, Bidinosti *et al.* succeeded in obtaining lung images by the hyperpolarized ^{3}He MRI operating at 3mT, though the spatial resolution should still be improved [15]. This success will substantially reduce the cost of both construction and operation in future.

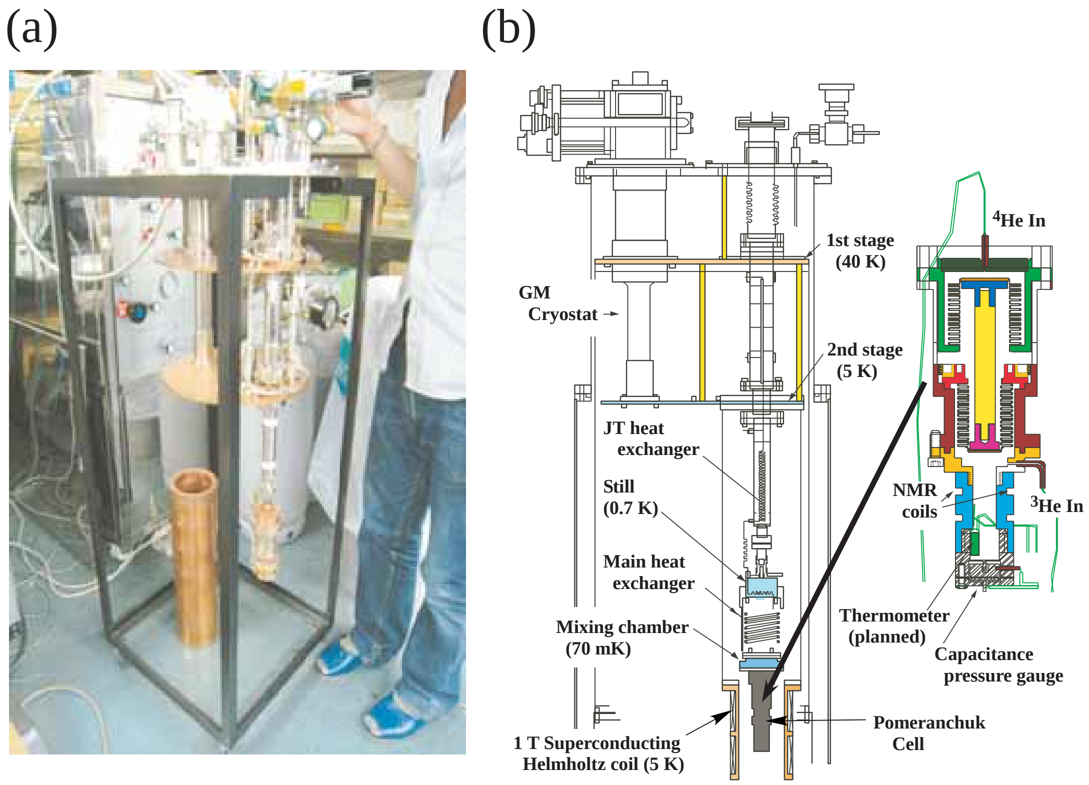

Figure 3. (a) Picture of the Cryofree ^{3}He/^{4}He dilution refrigerator, KOBE10μ. (b) Schematic drawing showing the KOBE10μ, Pomeranchuk cell and 1-T superconducting Helmholtz coil.

4. Present Status of development

As the first step of the NSI project, we are preparing to produce hyperpolarized ^{3}He gas by means of the brute force method followed by the rapid melting and gasification of the solid ^{3}He. This test will be done with the ^{3}He/^{4}He dilution refrigerator, DRS2500, which has a cooling power of 2500 μW at 120 mK. A superconducting solenoid coil can generate 17 T at the center of the Pomeranchuk cell. Since basics of our project was presented in Ref. [14], only the latest progress in the development is described in this report. Before making a test experiment with the DRS2500 system, we started preparing equipment allowing a pretest of Pomeranchuk cooling. For this purpose, we constructed a cryofree ^{3}He/^{4}He dilution refrigerator, KOBE10μ which has a refrigeration power of about 10μW at T=100 mK. In figure 3, a sketch of the whole equipment is depicted; a photo of the KOBE10μ dismounted, and a schematic view of the whole system including a Pomeranchuk cell and 1 T superconducting Helmholtz coil.

We are optimizing the whole system including the performance of the KOBE10μ itself so that the pretest of Pomeranchuk cooling at T=100$\sim$200 mK may be possible. Along with this effort, we are almost ready to measure the ^{3}He polarization by means of the NMR spectroscopy using either a conventional system manipulating analog signals or a modern software system employing a cutting-edge digital technique for a fast ADC and re-writable logic circuits with a high speed computer. Here, the NMR device has been developed for the HD target project [16]. For enabling the rapid melting of the hyperpolarized solid ^{3}He, we designed and constructed a thermal switch system to be attached to the DRS2500. A whole layout of the thermal switch system can be seen in figure 4. When the hyperpolarized solid ^{3}He is created by the brute force method, a thermal contact between the Pomeranchuk cell and the mixing chamber part of the

Figure 4. Picture of the thermal switch system ready to be attached to the DRS2500.

DRS2500 is released by a thermal switch manually operated. Then, the Pomeranchuk cell is lifted up to a higher tempature region, where rapid melting and gasification of the hyperpolarized solid ^{3}He are performed without a significant depolarization.

5. Future Prospects

After promising success in producing hyperpolarized ^{3}He gas, we will have a test experiment of the hyperpolarized ^{3}He MRI applied for lung imaging. Meanwhile, production of hyperpolarization for heavier nuclei, in particular ^{13}C will be developed. Then, with the hyperpolarized ^{13}C, we will start the basic study on the reaction mechanism of biomolecular compounds like glucose needed for the study of the metabolism by using an NMR spectrometer to be introduced if possible. This basic NMR study will hopefully facilitate the future hyperpolarized MRI.

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