Published in final edited form as:

Lab Chip. 2011 July 7; 11(13): 2197–2203. doi:10.1039/c1lc20056a.

A Magnetic Resonance (MR) Microscopy System using a Microfluidically Cryo-Cooled Planar Coil

Chiwan Koo^a, Richard F. Godley^b, Jaewon Park^b, Mary P. McDougall^{a,b}, Steven M. Wright^{a,b}, and Arum Han^{*,a,b}

^a Department of Biomedical Engineering, Texas A&M University, College Station, TX, 77843 USA

^b Department of Electrical & Computer Engineering, Texas A&M University, College Station, TX, 77843 USA

Abstract

We present the development of a microfluidically cryo-cooled planar coil for magnetic resonance (MR) microscopy. Cryogenically cooling radiofrequency (RF) coils for magnetic resonance imaging (MRI) can improve the signal to noise ratio (SNR) of the experiment. Conventional cryostats typically use a vacuum gap to keep samples to be imaged, especially biological samples, at or near room temperature during cryo-cooling. This limits how close a cryo-cooled coil can be placed to the sample. At the same time, a small coil-to-sample distance significantly improves the MR imaging capability due to the limited imaging depth of planar MR microcoils. These two conflicting requirements pose challenges to the use of cryo-cooling in MR microcoils. The use of a microfluidic based cryostat for localized cryo-cooling of MR microcoils is a step towards eliminating these constraints. The system presented here consists of planar receive-only coils with integrated cryo-cooling microfluidic channels underneath, and an imaging surface on top of the planar coils separated by a thin nitrogen gas gap. Polymer microfluidic channel structures fabricated through soft lithography processes were used to flow liquid nitrogen under the coils in order to cryo-cool the planar coils to liquid nitrogen temperature (-196°C). Two unique features of the cryo-cooling system minimize the distance between the coil and the sample: 1) The small dimension of the polymer microfluidic channel enables localized cooling of the planar coils, while minimizing thermal effects on the nearby imaging surface. 2) The imaging surface is separated from the cryo-cooled planar coil by a thin gap through which nitrogen gas flows to thermally insulate the imaging surface, keeping it above 0°C and preventing potential damage to biological samples. The localized cooling effect was validated by simulations, bench testing, and MR imaging experiments. Using this cryo-cooled planar coil system inside a 4.7 Tesla MR system resulted in an average image SNR enhancement of 1.47 ± 0.11 times relative to similar room-temperature coils.

Introduction

Magnetic resonance imaging (MRI) is generally considered to be a signal-to-noise ratio (SNR) limited technique, particularly in the case of MR microscopy.^{1,2} Because SNR is proportional to the number of spins in a given voxel, decreasing the voxel size by a factor of 10 in each dimension, for instance, results in a decreased SNR by a factor of 1000, if all other parameters remain constant. Recovering all of the loss through signal averaging is

impractical, as the SNR increases only as the square root of the number of averages; thus, one million averages would be required to maintain the same SNR as was obtained when the resolution was a factor of 10 poorer.

SNR can be enhanced by other means such as using higher magnetic field strengths, or in some cases through clever sequence design. In general, however, one must reduce the size of the coil to recover SNR. When using very small coils, (or alternatively larger coils with very small samples), it becomes apparent that the dominant noise source is the thermal noise generated by the resistance in the coil conductor. Therefore, to improve SNR, several efforts have been made to reduce the noise of MR coils using cryo-cooled copper or high-temperature superconducting (HTS) MR coils, with SNR improvements of 2–3 fold reported.^{1,3–6} However, due to the large size of conventional cryostats and the requirement to keep the sample at near-room temperature, the distance between receiver coils and samples often increases in cryo-cooled coils. It is generally accepted that the most useful region of sensitivity for a coil exists within approximately one coil width above it. Thus, this increased coil to sample distance has also limited the use of cryocooling to coils with larger dimensions,^{4,6}

Our group has investigated the use of coils that are small in one dimension (2 mm wide and up to 80 mm long) as array elements for parallel imaging.^{7,8} Using 64-channel arrays of these elements, we have demonstrated imaging in a plane parallel to the array in a single echo - a technique called “Single-Echo Acquisition” imaging, or SEA imaging.^{9,10} As with conventional small coils, the dominant noise source in the receiver coils (array elements) is the thermal noise of the copper. Even though the coils are long in one direction, they are very narrow (the imaging voxel width in the case of SEA imaging) in the second direction, and thus have a relatively shallow imaging region. The application of cryogenic cooling is obviously of interest to improve the available SNR, but the cryostat must eventually cover an entire array to work with SEA imaging. Because even a small increase in the distance between the coil and a target sample can significantly degrade the achievable SNR, a cryo-cooling system that significantly increases the distance between the SEA coils and the sample cannot be used. The work presented here describes the use of integrated microfluidic channels running along the long dimension of the receiver coil to achieve this objective.

The use of microfluidics has seen a huge surge in a variety of applications during the past decade. One important microfluidic application is in cooling, mainly for electrical circuits and components. Increased power consumption of more advanced and complex systems coupled with smaller system size causes serious thermal management issues, requiring advanced cooling schemes.¹¹ Many efforts have focused on developing miniaturized fluidic systems that can drive liquid-phase coolants through micrometer-scale fluidic channels.^{12–15} The high surface to volume ratio of microfluidic channels enhances heat dissipation through the coolant.

Although these miniaturized liquid cooling systems show significantly higher cooling efficiency over conventional systems, their main applications are for cooling heated electronic components or systems down to room temperature. This is different from cryogenic cooling systems which are mainly used to cool components down to liquid nitrogen temperature for improved sensitivity and low noise. There have been reports of developing micropumps for compact cryogenic cooling system for high-temperature superconducting systems or charged-coupled devices,^{16,17} but those systems are not applicable to cryo-cool small MR coils.

Here, we present a microfluidic cryo-cooling system designed for integration with the miniature MR coils described above. Two features in particular allow for close placement of

the cryo-cooled coil and the sample. First, the system consists of a microfluidic channel placed directly over the coil, through which liquid nitrogen is pumped, cryo-cooling the coil to liquid nitrogen temperature in a localized manner. When liquid nitrogen flows through a micrometer scale fluidic channel, the microliter volume of liquid nitrogen is minute compared to a fluidic channel used in conventional cryostats. Due to the small heat capacity associated with the small volume of the microchannel, only the area directly adjacent to the microchannel will be cooled down to liquid nitrogen temperature. Secondly, by separating the imaging surface from the cryo-cooled coil by a thin air gap and flowing nitrogen gas through the gap, convective heat transfer to the imaging surface is minimized, effectively preventing the sample from freezing.

Methods

Design

The design concept was threefold: 1) Locally cryo-cool the MR coil with microfluidic channels carrying liquid nitrogen while simultaneously minimizing the distance between the coil and the imaging surface for maximum SNR. 2) Maintain the temperature of the imaging surface above 0°C. 3) Minimize liquid nitrogen consumption.

The device consists of a cryo-cooling microfluidic channel through which liquid nitrogen can flow, integrated with a 2 mm wide by 57 mm long planar RF coil and an imaging surface on which target samples to be imaged can be placed (Fig. 1a & b.).

Poly(dimethylsiloxane) (PDMS, thermal conductivity = 0.18 W/mK) was used as the microchannel material. Since only a small amount of liquid nitrogen was carried through the micrometer-scale channel, only areas directly adjacent to this channel were cooled to liquid nitrogen temperature. The cryo-cooling microfluidic channel was 30 μ m deep and 2 mm wide to cover the planar coil width.

The coil was fabricated on a 0.5 mm thick poly(methyl methacrylate) (PMMA) substrate using microfabrication. Since the PMMA material has lower thermal conductivity (0.17 W/mK) than silicon (1.6 W/mK) or glass (1.1 W/mK), it reduces the heat flux between the liquid nitrogen channel and the nitrogen gap. The coil was a standard planar pair design,¹⁸ consisting of three copper traces, each 0.25 mm wide with 0.5 mm spacing between them (Fig. 1c). The overall length of the coil was 57 mm. This design was based on our previous design of a 64 element array of planar pair coils for highly accelerated SEA MR imaging.⁹ To bond the planar coil substrate and the cryo-cooling microfluidic channel layer, a 0.1 mm thick spin-coated PDMS adhesion layer was used.

The imaging surface was thus 0.6 mm thick and was separated from the coil by a 1.0 mm thick nitrogen gas gap and supported by two vertical side support structures. This flowing nitrogen gap reduced direct thermal conduction between the cryo-cooled coil substrate and the imaging surface, preventing samples from freezing during MR image acquisition.

Thermal simulation

To predict the temperature of the coil and the imaging surface of the integrated cryo-cooling structure during operation, finite element method (FEM)-based models were implemented using a commercially available FEM software (Comsol MultiphysicsTM, COMSOL Inc., Los Angeles, CA). Thermal conductivity parameters of 400 W/mK, 0.18 W/mK, and 0.17 W/mK were selected for copper, PDMS, and PMMA, respectively. Room temperature (27°C) was used as the initial temperature of the structure. It was assumed that heat conduction and convection are negligible in the nitrogen gap area while nitrogen gas is flowing continuously; therefore the nitrogen area was left as a blank space. The imaging

surface temperature was also simulated for varying microchannel widths, from 0.76 mm (3 times the width of the coil trace) to 2.79 mm (11 times the width of the coil trace), and varying heights (0.03 mm to 1 mm). Finally, the effect of the nitrogen gap height (varying from 0.5 mm to 1.0 mm) on the imaging surface temperature was simulated.

Fabrication and Assembly

The overall fabrication steps are illustrated in Fig. 2. Chromium and copper films (25/300 nm) were deposited on 0.5 mm thick PMMA substrates. To define the planar coils, a 45 μm thick negative photoresist layer (NR2-20000P, Futurrex, Inc., Franklin, NJ) was patterned. The photoresist was developed in a water based developer (RD6, Futurrex, Inc., Franklin, NJ) without affecting the PMMA substrate.

Following photolithography, copper electroplating was carried out in a copper sulfate solution ($\text{CuSO}_4 : \text{H}_2\text{SO}_4 : \text{H}_2\text{O} = 250 \text{ g} : 25 \text{ ml} : 1 \text{ L}$) at a current density of 10 mA/cm^2 to obtain a 25 μm thick copper layer. Photoresist remover (RR4, Futurrex, Inc., Franklin, NJ) was used to remove the photoresist instead of commonly used acetone to prevent the PMMA substrate from being damaged by the solvent. The copper and chromium film was then etched. The coil fabricated substrate was rinsed with deionized water and dried with nitrogen gas. Finally, 100 μm thick PDMS (Sylgard 184, Dow Corning., Midland, MI) was spun and cured. This PDMS layer works as an adhesive layer to the PDMS cryo-cooling microfluidic channel and prevents the planar coil from lifting off of the PMMA substrate during the extreme temperature cycle between liquid nitrogen temperature and room temperature.

Next, the cryo-cooling microfluidic channel for liquid nitrogen delivery was fabricated in PDMS using soft lithography.¹⁹ The master mold was fabricated in SU-8TM (MicroChem, Newton, MA) on a silicon wafer, followed by PDMS replication. After releasing the polymerized PDMS replica from the master mold, this PDMS cryo-cooling microfluidic channel and the previously fabricated PDMS coated planar coils were bonded.

For fluidic interconnects, 3.18 mm outer diameter (OD) silicone tubings were inserted into an inlet and an outlet hole through PDMS channel. Following tubing insertion, uncured PDMS was applied on the top surface of the channel layer and cured to hold the inserted tubing tightly.

A separate PCB for coil matching and tuning was fabricated on standard FR-4 (Fig. 1c). It contained the matching capacitor, a tuning varactor diode (Microsemi, Irvine, CA) biased over the RF line to allow for the adjustment from outside the bore without moving the system, a chip resistor to prevent DC blocking to the tuning varactor diode, and a coaxial connection. The match/tune PCB was soldered directly to the end of the planar pair. In this initial design, the match/tune PCB could not be cryo-cooled by the cryo-cooling microfluidic channel due to its separate position.

The nitrogen gap and imaging surface were created in an acrylic block ($80 \times 210 \times 12 \text{ mm}$) using a rapid prototyping machine (MDX-40, Roland DGA Corp., Irvine, CA). On the inner surface of the nitrogen gap, a small pillar array (1 mm in width, 2 mm in length, and same height as the nitrogen gap) was fabricated to prevent the gap from being collapsed under an external clamping force after the final assembly.

For the final assembly step, the planar coil substrate bonded with the cryo-cooling microfluidic channel was attached to the acrylic frame using Kapton[®] tape to form the closed nitrogen gap channel. A second acrylic frame was used to clamp this sandwich

structure using nylon screws. After the final assembly, the distance between the coil and the top of the imaging surface was 2.1 mm.

Liquid Nitrogen Supply Apparatus

To supply liquid nitrogen through the microfluidic channel, a 20 L dewar (Lab20 with withdrawal, Chart Industries, Inc., Garfield Heights, OH) was connected with a 6.35 mm OD polyethylene tubing (VWR, West Chester, PA), which was then connected with a 3.18 mm OD silicone tubing inserted into the cryo-cooling microchannel. The maximum pressure achievable with the dewar having the withdrawal apparatus is 34 KPa. To further increase the internal pressure of the dewar for faster liquid nitrogen pumping, nitrogen gas was pumped into the dewar through a 6.35 mm OD polyethylene tubing.

Characterization

The effect of the nitrogen gap on the imaging surface temperature was characterized using a digital thermometer (HH508, Omega Engineering, Inc., Stamford, CT). Nitrogen gap structures with gap depths of 0.5 and 1.0 mm were prepared. Nitrogen gas at 70 KPa of pressure was flowed through the nitrogen gap while the planar coil was cooled with liquid nitrogen. The surface temperature was then measured every 30 seconds for 20 minutes using the digital thermometer. The effect of the nitrogen gas pressure on the imaging surface temperature was also characterized. Three pressure setpoints (35, 70 and 97 KPa) were tested with the nitrogen gap structure having gap depth of 1.0 mm and the temperature on the imaging surface was measured every five minutes for one hour.

MR Coil Quality Factor (Q) Characterization

In general, the SNR of a microcoil (coil-loss dominated) is proportional to the square root of Q. Thus if the resistance of the microcoil is decreased with better components or conductors, without changing the coil configuration or distance to the sample, the SNR will be improved. However, when cryocooling, SNR is proportional to both the square root of temperature (in the cooled portion) and the square root of overall resistance. Theoretically, the SNR gain by cooling a copper coil can be predicted using the following equation:^{4,6}

$$\text{SNR}_{\text{improvement}} = \sqrt{\frac{R_{\text{unload,room}} T_{\text{room}} + R_{\text{sample}} T_{\text{sample}}}{R_{\text{unload,cooled}} T_{\text{cooled}} + R_{\text{sample}} T_{\text{sample}}}} \quad (1)$$

where R_{unload} is the resistance of the coil itself without sample loading and R_{sample} represents the resistance added by the sample. If the temperature of the coil decreases from room temperature ($T_{\text{room}} = 27^\circ\text{C}$ (300K)) to liquid nitrogen temperature ($T_{\text{cooled}} = -196^\circ\text{C}$ (77K)), the resistivity of the copper drops by a factor of eight.²⁰ However, because the skin depth is proportional to the square root of resistivity, the high frequency resistance of the coil at 27°C decreases by a factor of $\sqrt{8}$ ($=2.83$) at -196°C . Thus, from equation (1), the highest SNR improvement possible when cryocooling a copper-loss-dominated coil is 3.32, when $R_{\text{sample}} = 0$.

In order to characterize the SNR improvement of our device, the quality factor (Q) of the coil was first measured at room temperature and then at cryo-cooled temperature. From equation (1), the following Q related SNR improvement equation can be extracted since inductance and frequency were held constant and $Q = \omega_0 L/R$:

$$\text{SNR}_{\text{improvement}} = \sqrt{\frac{T_{\text{room}}/Q_{\text{unload,room}} + T_{\text{sample}}/Q_{\text{sample}}}{T_{\text{cooled}}/Q_{\text{unload,cooled}} + T_{\text{sample}}/Q_{\text{sample}}}} \quad (2)$$

The unloaded and loaded Q factors were measured with an S11 measurement using a network analyzer (HP4195A, Agilent Technologies, Santa Clara, CA). With the coil tuned to 200.1 MHz and matched to 50 ohm with 30dB return loss or better, the bandwidth (Δf) between the 7dB return loss points was measured. The Q values are calculated as $Q = f_0 / \Delta f$. This measurement is similar to the 3dB bandwidth used for standalone resonant circuits²¹, but 7dB is used due to the additional losses caused by matching the resonant circuit to the network analyzer.

SNR Improvement Characterization through MR Imaging

For initial imaging experiments, two separate coils on the same substrate were prepared, one for room temperature (RT) characterization and the other for liquid nitrogen temperature (LT) characterization. The match and tune for each coil was accomplished using high-Q fixed capacitors and a high-Q varactor for fine tuning. This approach eliminated the issues associated with re-matching and tuning over the large range associated with cooled and uncooled copper and minimized losses associated with the (uncooled) matching network.

Following the separate coil experiments, a single coil was used for both RT and LT MR imaging using a matching network with two varactor diodes, one across the tuning capacitor and one across the matching capacitor as a more direct comparison.

Imaging was performed in a 4.7 Tesla MRI system (40 cm bore, Unity/Inova console, Varian, Palo Alto, CA). Fig. 3 shows the schematic of the MR imaging test setup. To load the integrated coil system to the center of the magnet and to support the liquid nitrogen tubing and nitrogen gas tubing, a 90 cm long acrylic board and cradle were prepared. To supply and vent liquid nitrogen from outside of the magnet to the cryo-cooled coil system, two 1.2 m long 6.35 mm (OD) segments of polyethylene tubing wrapped with insulating sponge foam tape (Frost King, Mahwah, NJ) were fixed under the long acrylic board and connected to the interface of the cryo-cooling channel using plastic tapered connectors.

The board was inserted into an actively detuneable birdcage volume coil that was used as the transmit coil and fixed to prevent any movement due to contractions when the cryogenics were applied. The entire assembly was positioned inside the magnet for imaging. A liquid nitrogen dewar and a nitrogen gas cylinder were connected with the coil system (Fig. 3c), with the liquid nitrogen dewar located within the RF screen room for proximity to the coil system.

RT MR images of a phantom (0.1% copper sulfate solution) were acquired in the axial plane (perpendicular to the imaging surface and the long axis of the coil) at the magnet isocenter. All images used a spin echo sequence with a matrix size of 256×256 , TR (repetition time) of 500 ms, TE (echo time) of 50 ms, 2 averages, slice thickness of 3 mm, and spectral width of 20 kHz. LT images were obtained after flowing liquid nitrogen to the planar coil for 30 – 40 min and verifying that liquid phase nitrogen was flowing from the outlet LN tubing. To prevent ice formation around the match/tune PCB from leading to unstabling tuning during MR image acquisition, an extra 3.18 mm OD tube was used to direct nitrogen gas at the RF components. Once cooled, the DC bias voltages to the varactors were adjusted to match and tune the cryo-cooled coil. Phantom images were obtained with the same parameters used for the RT imaging test.

MATLAB[®] was used to display images and to evaluate the SNR. First, 2D Fourier transform was used to reconstruct the magnitude image (256×256 matrix) without any correction filter. Then, the signal magnitude matrix was divided by the average of the noise value in a large noise region to obtain an SNR matrix. Two methods were used to calculate the SNR improvement. In the first method (method 1), the SNR peak was selected from the matrix at each temperature and the SNR improvement was calculated. In the second method (method 2), the SNR improvement was defined as the average ratio of the RT to LT SNR profiles over the first 10 pixels starting at the peak.

Results

Microfabricated Device and Liquid Nitrogen Flow

Figure 4 shows top and bottom views of the completely assembled cryocooled coil system.. An initial liquid nitrogen flow test with the $30\text{ }\mu\text{m}$ high microfluidic channel resulted in only gas phase flowing from the outlet of the microchannel due to the high fluidic resistance of the microchannel. Since our simulation results showed that the height of the microfluidic cryo-cooling channel mainly does not affect the localized cooling capability and the temperature at the imaging surface, the channel height was increased to 1 mm. Additionally, the internal pressure of the liquid nitrogen dewar was increased from the initial inner pressure of 34 KPa by injecting nitrogen gas into the dewar. A driving pressure of 45 KPa resulted in liquid-phase nitrogen flowing from the cooling channel outlet. Using this larger microchannel dimension and higher pressure, liquid nitrogen flowed through the system for more than 60 minutes without any difficulties.

To assess the temperature gradient along the long axis of the coil, the coil substrate temperature (backside of the coil) was measured. This data is shown in Supplementary Materials. After 10 minutes of cryo-cooling, the inlet and outlet region temperatures were stable, and there was no temperature gradient along the coil axis.

Temperature Simulation

The temperature of the imaging surface was simulated and represented by the color gradient in Fig. 5. The cryo-cooling microchannel directly covers the planar coil through a $100\text{ }\mu\text{m}$ thick protective polymer layer (PDMS). As a result of this near-direct contact, the simulation result showed the coil temperature to be -194°C , almost identical to the liquid nitrogen temperature of -196°C . The temperature of the imaging surface during cryo-cooling was maintained at around 17°C . The temperature decreased to 2°C , however, when the nitrogen gap depth was reduced from 1.0 mm to 0.5 mm. A nitrogen gap depth of larger than 1.0 mm was not suitable since that would put the phantom outside the optimal imaging depth of the planar pair coil.

When increasing the cryo-cooling microchannel width from 2 mm to 3 mm, the imaging surface temperature dropped by 9°C . When varying the height from $30\text{ }\mu\text{m}$ to 1 mm while maintaining the width of the microchannel at 2 mm, the imaging surface temperature dropped only slightly by 7°C . Thus, it appears that the imaging surface temperature depended on the cryo-cooling channel width more than on the the height. Simulations showed that no special heat sink apparatus was required for our device because the cold temperature is very localized right around the liquid nitrogen flowing microfluidic channel due to the small heat capacity of the microchannel.

Temperature Characterization during Cryo-cooling

The imaging surface temperature was measured with the two different nitrogen gap dimensions used for simulations: 0.5 mm and 1.0 mm. The 1.0 mm nitrogen gap structure

was found to keep the imaging surface temperature at $6.5 \pm 1.5^{\circ}\text{C}$ whereas the 0.5 mm nitrogen gap structure caused the imaging surface temperature to fall to $-29 \pm 7^{\circ}\text{C}$ (Fig. 6a). These results show that the deeper nitrogen gap structure greatly reduced the cooling effect of the coil substrate on the imaging surface.

Next, the influence of nitrogen gas pressure on surface temperature was investigated. Fig. 6b shows that by applying a higher nitrogen gas pressure to the nitrogen gap, the temperature drop at the imaging surface could be reduced. This is due to the reduced heat convection from the coil to the imaging surface. A pressure of 70 KPa was determined to be sufficient to thermally insulate the imaging surface from the liquid nitrogen channel while minimizing nitrogen gas consumption. In this condition, the temperature of the imaging surface was kept at approximately 8.0°C . This measured result matched well with the FEM simulation result.

MR Image Acquisition

After imaging at RT and LT using the device, SNR improvement was calculated using SNR matrices obtained at both temperatures. Fig. 7 shows the SNR profile graphs as a function of y-position acquired from MR images at RT and LT (using method 2).

Table 1 shows five data sets of the SNR improvement ratios when using two separate coils - one matched at RT and the other one matched at LT. For each data set, the whole device was taken out of the magnet and placed into the magnet bore again before taking the images for five independent experiments. The two columns in Table 1 show an average SNR improvement of 1.50 ± 0.21 using the peak SNR comparison method (method 1) and an average SNR improvement of 1.39 ± 0.18 times when using the SNR profile method (method 2).

Table 2 shows three data sets of the Q and SNR measurements acquired (using method 2) with a single coil first matched and tuned at RT, then at LT. The Q of the coil inside the magnet bore was 28.2 ± 1.13 at room temperature and increased by a factor of 1.82 ± 0.08 after cryo-cooling to 51.4 ± 0.63 . The coinciding SNR improvement calculated from images was 1.47 ± 0.11 times. The RSD was 7.5%, which is much lower than the result when using two separate coils. This is likely due to the fact that when using two coils, they are 10 mm apart resulting in some unavoidable differences, such as minor tip angle variations due to inhomogeneity in the transmit field.

Discussion

If all losses were due to thermal noise in the copper, cryo-cooling should yield a Q improvement of 2.83 and a corresponding SNR improvement of 3.29. Our lower Q improvement of 1.82 clearly shows the effects of the residual resistance in the matching network that was not cooled. We estimate that 70% of the resistance at RT was due to the coil, and the rest due to resistance in the matching network. Unfortunately, that 30% becomes the dominant noise source after cryo-cooling. This emphasizes the importance of low-resistance interconnects and high-Q RF components in the matching network. Further SNR improvement could be achieved by cryo-cooling the RF components. We are currently developing a revised device where the cryo-cooling microfluidic channel can also cool the tuning and matching network by directly incorporating these components on the same polymer substrate.

Conclusions

An integrated microfluidically cryo-cooled planar coil system for MR microscopy has been developed and SNR improved images were obtained using a 4.7T MRI system. The

microfluidic channel effectively cooled the MR planar coil without any liquid nitrogen leakage or damage to the coil, and made it possible to reduce the distance between the planar coil and imaging surface without freezing the imaging surface. The effect of the liquid nitrogen microchannel on the imaging surface temperature was simulated and evaluated with the fabricated device. In addition, we selected a proper nitrogen gap thickness and nitrogen gas pressure to balance between the imaging depth and the surface temperature. The SNR improved by a factor of 1.47 ± 0.11 , enabling a reduction in imaging time by a factor of two while maintaining comparable SNR to an uncooled coil. The integrated microfluidic cryo-cooling method will make it possible to obtain improved SNR from microcoils while maintaining temperatures compatible with living tissue. Importantly, the microfluidic approach can be extended to large coil arrays, potentially very important for performing wide-field-of-view MR microscopy.⁹

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This work was supported by the National Institutes of Health/National Institute of Biomedical Imaging and Bioengineering (NIH/NIBIB) under grant 1R21EB07297.

References

1. Heteren, JGv; James, TW.; Bourne, LC. Magnetic Resonance in Medicine. 1994; 32:396–400. [PubMed: 7984072]
2. Harel E. Lab on a Chip. 2009; 9:17–23. [PubMed: 19209329]
3. Black RD, Roemer PB, Mueller OM. IEEE Transactions on Biomedical Engineering. 1994; 41:195–197. [PubMed: 8026853]
4. Wright AC, Song HK, Wehrli FW. Magnetic Resonance in Medicine. 2000; 43:163–169. [PubMed: 10680678]
5. Ginefri JC, Darrasse L, Crozat P. Magnetic Resonance in Medicine. 2001; 45:376–382. [PubMed: 11241693]
6. Ratering D, Baltes C, Nordmeyer-Massner J, Marek D, Rudin M. Magnetic Resonance in Medicine. 2008; 59:1440–1447. [PubMed: 18421696]
7. Pruessmann KP, Weiger M, Scheidegger MB, Boesiger P. Magnetic Resonance in Medicine. 1999; 42:952–962. [PubMed: 10542355]
8. Bankson JA, Griswold MA, Wright SM, Sodickson DK. Magnetic Resonance Materials in Physics, Biology and Medicine. 2000; 10:93–104.
9. McDougall MP, Wright SM. Magnetic Resonance in Medicine. 2005; 54:386–392. [PubMed: 16032696]
10. Wright SM, McDougall MP. NMR in Biomedicine. 2009; 22:982–993. [PubMed: 19441080]
11. Tummala, RR., editor. Fundamentals of Microsystems Packaging. McGraw-Hill; New York: 2001.
12. Tuckerman DB, Pease FW. IEEE Electron Device Letters. 1981; 2:126–129.
13. Darabi J, Ohadi MM, DeVoe D. Journal of Microelectromechanical Systems. 2001; 10:98–106.
14. Yokoyama Y, Takeda M, Umemoto T, Ogushi T. Sensors and Actuators A. 2004; 111:123–128.
15. Wang EN, Koo LZLJMM, Maveety JG, Sanchez EA, Goodson KE, Kenny TW. Journal of Microelectromechanical Systems. 2004; 13:833–842.
16. Darabi J, Wang H. Journal of Microelectromechanical Systems. 2005; 14:747–755.
17. Grohmann S, Herzog R, Niinikoski TO, Perea-Solano B, Quack H, Vögele G, Wobst E. Cryogenics. 2005; 45:432–438.
18. Hyde JS, Froncisz W, Jesmanowicz A, Kneeland JB. Medical Physics. 1986; 13:1–7. [PubMed: 3951399]

19. Kane RS, Takayama S, Ostuni E, Ingber DE, Whitesides GM. *Biomaterials*. 1999; 20:2363–2376. [PubMed: 10614942]
20. Lide, DR., editor. *CRC Handbook of Chemistry and Physics*. CRC Press/Taylor and Francis; Boca Raton, FL: 2010.
21. Collin, RE. *Foundations for Microwave Engineering*. Wiley-IEEE Press; New York: 2001.
22. Koo, C.; Feng, K.; Park, J.; McDougall, MP.; Wright, SM.; Han, A. *Proc. 23rd IEEE conference on MEMS*; 2010; Hong Kong, China. 2010. p. 1011-1014.

Fig. 1. Schematic diagrams of the microfluidically cryo-cooled MR planar coil device. (a) Illustration of each layer of the device. (b) Cross sectional view (A-A') of the device. (c) Design of the planar pair coil and a typical tuning/matching network (C_m : matching capacitor, C_v : tuning varactor, and C_b : DC blocking capacitor), with current paths indicated.

Fig. 2. Fabrication steps for the MR planar coil layer (a–c), the cryo-cooling microfluidic channel layer (d–f), and the final assembly and tubing insertion (g). (a) Negative photoresist patterning on a thin PMMA substrate with Cr/Cu as seed layers. (b) Cu electroplating and removal of the photoresist and Cr/Cu seed layers. (c) Thin PDMS coating. (d) SU-8 mold fabrication on a Si substrate. (e) PDMS casting on the master mold for liquid nitrogen channel layer fabrication. (f) PDMS channel layer releasing and hole punching for tubing insertion. (g) Bonding between the MR planar coil layer and the PDMS liquid nitrogen channel, and inlet/outlet tubing insertion.

Fig. 3. Schematics of the MR image acquisition experiment setup using the microfluidic cryo-cooled planar coil system. (a) The integrated cryo-cooled planar coil system on an acrylic board. (b) The coil system inserted into the volume coil and ready to be loaded into an MR magnet. (c) Nitrogen gas was used to drive liquid nitrogen out from the dewar as well as for flowing through the nitrogen gap of the surface coil system for temperature insulation.

Fig. 4. The fully assembled microfluidically cryo-cooled MR coil device. (a) Top and (b) bottom view of the assembled device.

Fig. 5.

FEM simulation result of the device temperature profile when liquid nitrogen flows through the microfluidic channel. Temperature at the coil was almost identical as the liquid nitrogen temperature (-196°C), and the temperature of the imaging surface was maintained above the water freezing temperature of 0°C when the nitrogen gap was 1.0 mm.

Fig. 6. Imaging surface temperatures at two different nitrogen gap heights and at three different N_2 gas pressure. (a) 0.5 mm and 1.0 mm high gap at 70 KPa of N_2 gas pressure ($n=3$), and (b) 35, 70, and 97 KPa N_2 gas pressure with a 1.0 mm high gap. (This result was presented at the 2010 IEEE MEMS conference²²).

Fig. 7. SNR profiles from MR images (inset) at room and cryo-cooled temperature are displayed as a function of y-position.

Table 1

SNRs before and after cryo-cooling, which were calculated by using the peak comparison method and the profile ratio method, with two separate coils – one is matched at room temperature and the other one is matched at cryo-cooled temperature.

Data Set	SNR improvement - Peak comparison - (times)	SNR Improvement - Profile ratio - (times)
1	1.81	1.50
2	1.39	1.42
3	1.62	1.63
4	1.35	1.21
5	1.34	1.21
Avg.	1.50 ± 0.21	1.39 ± 0.18

Table 2

SNR before and after cryo-cooling with a single coil matched and tuned by two varactor diodes at each temperature.

Data Set	Q factor (Room Temp.)	Q factor (Cryo-cooled Temp.)	Q Improvement (times)	Expected SNR Improvement (times)	Measured SNR Improvement (times)
1	29.5	51	1.73	1.56	1.46
2	27.5	52.1	1.89	1.72	1.58
3	27.6	51	1.85	1.68	1.36
Avg.	28.2 ± 1.13	51.4 ± 0.63	1.82 ± 0.08	1.65 ± 0.08	1.47 ± 0.11