Double-tuned Radiofrequency Coil for $^{19}$F and $^1$H Imaging

Yosuke Otake*, Yoshihisa Soutome, Koji Hirata, Hisaaki Ochi, and Yoshitaka Bito

Central Research Laboratory, Hitachi, Ltd.
1–280 Higashi-koigakubo, Kokubunji-shi, Tokyo 185–8601, Japan

(Received September 30, 2013; Accepted December 11, 2013; published online July 2, 2014)

We developed a double-tuned radiofrequency (RF) coil using a novel circuit method to double tune for fluorine-19 ($^{19}$F) and $^1$H magnetic resonance imaging, whose frequencies are very close to each other. The RF coil consists of 3 parallel-connected series inductor capacitor circuits. A computer simulation for our double-tuned RF coil with a phantom demonstrated that the coil has tuned resonant frequency and high sensitivity for both $^{19}$F and $^1$H. Drug distribution was visualized at 7 tesla using this RF coil and a rat administered perfluoro 15-crown-5-ether emulsion. The double-tune RF coil we developed may be a powerful tool for $^{19}$F and $^1$H imaging.

Keywords: $^{19}$F imaging, drug distribution imaging, molecular imaging, multi-nuclei MRI, RF coil

Introduction

Fluorine-19 ($^{19}$F) and $^1$H double-nuclei magnetic resonance (MR) imaging has many advantages in imaging the distribution or metabolism of $^{19}$F-containing drugs because $^{19}$F has a relatively high MR signal compared to other nuclei and is acquired with no background signal. Most $^{19}$F imaging studies have been conducted using tunable single-tuned radiofrequency (RF) coils developed for $^{19}$F/$^1$H imaging because the gyromagnetic ratios of $^{19}$F nuclei (40.05 MHz/T) and $^1$H nuclei (42.58 MHz/T) are very close. However, retuning the RF coil during in vivo animal experiments is time consuming, and differing distributions of the RF fields between $^{19}$F and $^1$H are inconvenient for quantifying $^{19}$F distribution using the $^1$H sensitivity map. Many double nuclei studies have been using double-tuned RF coils with shunting method and multiple poles circuits, methods developed for 2 resonant frequencies that are well separated, such as combinations of $^1$H and $^{31}$P (17.24 MHz/T) and $^1$H and $^{13}$C (10.71 MHz/T). Therefore, these methods are not well suited for $^{19}$F/$^1$H imaging because they use impractical capacitors and inductors in the multiple pole circuit. A $^{19}$F/$^1$H double-tuned RF coil fabricated using a coupled resonator method was recently developed for small-animal imaging at 4.7T. However, this method cannot be applied to the much larger inductance of a sample coil at higher magnetic fields, such as over 200 nH in, for example, a solenoid coil for animals or a surface coil for humans, because the capacitors in the coupled resonator circuit become impractical (below one pF), and it is difficult to adjust the capacitance.

To overcome this problem, we developed a double-tuned RF coil for $^{19}$F/$^1$H imaging using a novel circuit method to double tune. The double-tuned RF coil consists of 3 parallel-connected series inductor capacitor (LC) circuits. We also demonstrated $^{19}$F-labeled drug distribution monitoring using a rat at 7 tesla.

Materials and Methods

Developed double-tuned RF-coil

Figure 1 shows the equivalent circuits of the double-tuned RF coil using a novel circuit method to double tune. Each equivalent circuit consists of 3 parallel-connected series LC circuits (with resonant frequencies $f_A$, $f_B$, and $f_C$) each having inductors ($L_A$, $L_B$, and $L_C$) and capacitors ($C_A$, $C_B$, and $C_C$). The $L_A$ and $C_A$ are the equivalent inductor and...
capacitor of a sample coil. These circuits were designed so that the 2 resonant frequencies (f_{LF} and f_{HF}) of the double-tuned coil are sandwiched between the 3 resonant frequencies of the series LC circuits:

\[ f_C < f_{LF} < f_A < f_{HF} < f_B. \]  

The impedance \( Z_S \) and resonant frequency \( f_S \) of a series LC circuit can be written as:

\[ Z_S = j(2\pi f L_S - \frac{1}{2\pi f C_S}) \]

and

\[ (2\pi f_S)^2 = \frac{1}{L_S C_S}, \]

where \( f \) is the input frequency and \( C_S \) and \( L_S \) are the capacitor and inductor of the series LC circuit. The series LC circuit behaves like a capacitor \( C' \) at a lower frequency than the \( f_S \) of the series LC circuit. Similarly, a series LC circuit behaves like an inductor \( L' \) at a higher \( f_S \) than the resonant frequency of the circuit. Its impedance \( Z_S' \) can be written as:

\[ Z_S' = -j\left(\frac{1}{2\pi f C'}\right) = j\left(\frac{1}{2\pi f C_S}\right)((f/f_S)^2 - 1), \quad (f < f_S) \]

and

\[ Z_S' = j2\pi f L' = j2\pi f L_S \left(\frac{(f/f_S)^2 - 1}{(f/f_S)^2}\right), \quad (f < f_S). \]

Thus, its \( C' \) and \( L' \), as a function of frequency, are

\[ C'(f) = \frac{C_S}{1 - (f/f_S)^2} \quad [6] \]

and

\[ L'(f) = \frac{(f/f_S)^2 - 1}{(f/f_S)^2} L_S. \quad [7] \]

Therefore, the designed circuit tuned to Eq. [1] behaves as shown in Fig. 1b and c when fed by \( f_{LF} \) and \( f_{HF} \) RF signals, and the circuit is resonant at 2 resonance frequencies. Quantitatively, \( f_{LF} \) and \( f_{HF} \) are expressed as:

\[ f_{LF} = \frac{1}{2\pi \sqrt{L_B(C_A' + C_C')}} \]

and

\[ f_{HF} = \frac{1}{2\pi \sqrt{L_A'' + L_B''}} \]

where \( L_B', C_A' \), and \( C_C' \) are the inductor and capacitor when fed by the \( f_{LF} \) signal, and \( L_A'', L_B'', \) and \( C_C'' \) are the inductor and capacitor when fed by the \( f_{HF} \) signal given in Eqs. [6] and [7].

In this study, the circuit in Fig. 1 was implemented at 7T for \(^{19}\text{F} \) imaging at 282 MHz and \(^1\text{H} \) imaging at 300 MHz with an 8-turn solenoid coil. The solenoid coil, fabricated with 0.1-mm-thick Cu tape, was 65 mm in diameter and 125 mm long. The inductance of the coil \( L_A \) was about 1600 nH. The \( f_A \) was determined as 291 MHz, the \( f_B \) as 231 MHz, and the \( f_C \) as 351 MHz. The \( L_B, L_C, C_B, \) and \( C_C \) were calculated in accordance with Eqs. [6], [7], [8], and [9]. As a result, the \( L_B \) was 67 nH, and the \( L_C \) was 83 nH. The \( C_A \) was 0.19 pF, the \( C_B \), 3.0 pF, and the \( C_C \), 5.7 pF. The \( C_A \) was calculated to be below one pF, but this capacitance is practical in a sample coil. In general, the sample coil is designed to be larger to detect MR signals. On the other hand, the circuit to double tune must be designed to be smaller to suppress the coupling between its circuit and the sample coil. Therefore, compared with the circuit to double tune, the sample coil had enough space for the insertion of several capacitors (> one pF) in a series at regular intervals so that the effective capacitance became \( C_A \). Thus, this double-tuned RF coil was tuned to resonate at both resonant frequencies of \(^{19}\text{F} \) and \(^1\text{H} \) at 7T.

Impedance matching is performed by 2 methods. Figure 2 shows the matching circuits of this double-tuned RF coil, where \( R \) is coil resistance. To adjust each impedance matching, the frequency difference of \( f_A \) and \( f_B \) or \( f_A \) and \( f_C \) is changed. To adjust the entire impedance, reactance from the feed point is adjusted so as not to change the total reactance of the series LC circuit. When the input impedance \( Z_i \) to be matched is higher than 50\,\Omega, the \( L_C \) is split into \( L_{C1} \) and \( L_{C2} \), and a capacitor
C_D is added to minimize the change in the series resonant frequency (f_A, f_B, and f_C) (Fig. 2a). When the Zi to be matched is lower than 50 Ω, the C_C is split into C_C1 and C_C2, and C_D is added (Fig. 2b). In this case, we used Fig. 2a for impedance matching.

**Computer RF coil simulation**

We numerically simulated the characteristics of the RF coil using our own program, which is based on Richmond’s moment method. The simulation model took into account the electromagnetic effect of the sample with an arbitrary geometry and material properties by incorporating the impedance method into the moment method. We calculated the magnitude and phase of the input-impedance and sensitivity of RF coils with a sample (phantom). The sensitivity of a coil is defined by the circularly polarized B1 field strength generated by the coil when a signal of one W was applied to it. For simulation at 7T, we used the RF shield because it reduces radiative losses. Its inner diameter was 210 mm and its length, 200 mm. The sample diameter was 40 mm and the length, 78 mm. The conductivity of the phantom was 0.6 S/m and the relative permittivity, 75 S/m.

**Phantom and in vivo animal study**

We used a 7T animal MR imaging system (Varian MRI System 7.0T/310/AS, Agilent Technologies Inc, Palo Alto, CA, USA), which was equipped with transmit/receive (TX/RX) 1H and 19F imaging channels, a one-kW RF amplifier, and a gradient coil (SGRAD 305/210/H/D/S, Magnex Scientific Ltd., Abingdon, UK) with an inner diameter of 210 mm with maximum gradient strength of 200 mT/m and a linear region (±6%) of 12.0 cm.

We prepared a homemade nanoparticle contrast agent, pouring 1.5 g of surfactant (Pluronic F-68, Sigma, Poole, UK) and 16 mL of phosphate-buffered saline (PBS) into a glass tube and mixing them with an ultrasonic homogenizer (Branson Digital SONIFIER II, Branson Ultrasonic Co., Wilmington, NC, USA: amplitude 44%, one second on/one second off, 5 min), then adding 2 mL of perfluoro 15-crown-5-ether (PFCE: Wako Pure Chemicals, Osaka, Japan) to the glass tube and mixing with the homogenizer (amplitude 44%, one second on/one second off, 5 min) to prepare the emulsion. The above process was done on ice. We measured the size distribution of the obtained PFCE nanoparticles using a laser diffraction particle size analyzer (Beckman Coulter, Inc., Fullerton, CA, USA) and determined the average diameter of the particles was about 100 nm.

For the phantom study, PFCE nanoparticles were added to enclosed 1.8-mL tubes (10 w/v%–0.01 w/v%) and placed in a water (10 mM NiSO_4/0.675% NaCl) bottle phantom. We obtained 1H images using fast spin echo (FSE) with field of view (FOV), 200 × 200 mm², matrix size, 256 × 256, 2-mm slicing, repetition time (TR)/echo time (TE)/echo train length (ETL), 2000 ms/49 ms/16, and scan time, one minute. We obtained 19F images using fast spin echo with FOV, 200 × 200 mm², matrix size, 128 × 128 without slicing, TR/TE/ETL, 2000 ms/49 ms/16, and scan time, 10 min.

For the animal study, we employed a female Wistar rat (180 g) bearing Walker 256 tumors. The rat was anesthetized with 1.5 to 3.0% isoflurane administered in combination with 50% O_2 through a face mask. Initially, we obtained multislice 1H fast spin echo images using FSE with FOV, 200 × 200 mm², matrix size, 256 × 256, 2-mm slicing, TR/TE/ETL, 2000 ms/49 ms/16, and scan time, 10 min. We then adjusted the center frequency to the 19F signal of the contrast agent. Thereafter, we intravenously administered a bolus injection of 200 mg/kg of PFCE and cyclically measured 19F to obtain the time course. The total measurement period was about one hour. The 19F images were obtained using FSE with FOV, 200 × 200 mm², matrix size, 128 × 128 without slicing, TR/TE/ETL, 2000 ms/49 ms/16, and scan time, 10 min.

All animal studies were conducted in accordance with guidelines for the care and use of laboratory animals of Hitachi Central Research Laboratory.
Results

Simulation and experimental results of double-tuned solenoid coil

Figure 3a shows a simulation model of the double-tuned 8-turn solenoid coil using a novel circuit method. The $L_B$ was 29 nH, the $L_{C_1}$, 43 nH, and the $L_{C_2}$, 30 nH. The $C_A$ was 0.14 pF, the $C_B$, 2.9 pF, the $C_C$, 7.6 pF, and the $C_D$, 16 pF. The $C_A$ is effective capacitance constructed by a series connecting the 28 capacitors.

Figure 3b shows the simulated frequency characteristics of the double-tuned solenoid coil with the phantom. Two resonance points were observed at the resonant frequencies of $^{19}$F (282 MHz) and $^1$H (300 MHz), and the coil achieved impedance matching (50 $\Omega$) at both $^1$H and $^{19}$F frequencies. The measured loaded/unloaded quality factors of $^{19}$F and $^1$H were 141/354 and 78/320.

Figure 3c shows a line profile of the simulated sensitivity of the double-tuned solenoid coil and a conventional single-tuned solenoid coil. The sensitivity of the $^{19}$F and $^1$H frequencies at the center of the double-tuned coil were 6.3 and 6.7 A·m$^{-1}$ W$^{-1/2}$. In comparison, the sensitivity of the $^{19}$F and $^1$H frequencies at the center of the single-tuned coil were 7.1 and 6.8 A·m$^{-1}$ W$^{-1/2}$. The developed double-tuned circuit cased 13% and 2.1% loss of sensitivity for $^{19}$F and $^1$H.

Figure 4a shows a fabricated double-tuned 8-turn solenoid coil. We used 10-mm-wide Cu sheets, 0.5-mm-diameter polyurethane-coated Cu wires, nonmagnetic chip capacitors (11 Series, Voltronics Corp., Denville, NJ, USA), and nonmagnetic variable capacitors (NMAP40HV, Voltronics Corp.; 1.5 to 40 pF). The $L_A$ was fabricated with 10-mm-wide Cu sheets of 65-mm diameter and 125-mm length,
and the number of turns was 8. The $L_{B}$, $L_{C1}$, and $L_{C2}$ were fabricated with a 0.5-mm-diameter polyurethane-coated Cu wire with a diameter of 5 mm, and the number of turns was 3 ($L_{B}$), 4 ($L_{C1}$), and 5 ($L_{C2}$). The $C_{A}$ was a series combination of eight 3.0-pF chip capacitors, 19 series-connected 3.9-pF chip capacitors, and one variable capacitor. The $C_{B}$, $C_{C}$, and $C_{D}$ were variable. To suppress the coupling between $L_{A}$ and $L_{B}$, $L_{C1}$, and $L_{C2}$, the circuits, except $L_{A}$, were designed to be smaller. Additionally, if the distance of each inductor was close, we placed inductors tilted at 90 degrees. Figure 4b shows the measured frequency characteristics of the coil with the phantom. As in the simulation, we observed 2 resonance points at the resonant frequencies of 19F and 1H, and the coil achieved impedance matching at both 1H and 19F frequencies in the experiment. The measured loaded/unloaded quality factors of 19F and 1H were 118/219 and 57/120. Note that the experimental results show the same tendency as the simulation, but the unload quality factor of the experimental results is clearly lower than that of the simulation results. In the unload experiment at high frequency, the quality factor was easily affected by each electromagnetic coupling between $L_{A}$ and other inductors ($L_{B}$, $L_{C1}$, and $L_{C}$). Additionally, the frequency characteristic of the RF coil was affected by the coaxial cable. Therefore, matching the results of the simulation and experiment is difficult when unloaded.

**19F/1H imaging**

Figure 5a shows 1H and 19F images of the phantom acquired using a fabricated double-tuned coil that we verified could receive 1H and 19F signals. Figure 5b shows the relationship between the nanoparticle concentration and measured signal-to-noise ratio (SNR) of these coils. The SNR of these coils decreased linearly as PFCE concentration decreased, suggesting that the developed coil can be used to evaluate the accumulation of PFCE in a body.

Figure 5c shows a 1H image and 19F time-course images of the rat acquired using a fabricated double-tuned coil. These images clearly show that the coil enables imaging anatomical information by 1H-MR imaging and drug distribution of PFCE emulsions by 19F-MR imaging. The 19F time-course images show that the 19F signal intensity increased for the liver and tumor tissues. We believe the increased signal intensity shows accumulations of PFCE nanoemulsion. These results suggest that this coil will be a powerful tool for measuring 19F distribution.

**Discussion**

We demonstrated that the double-tuned RF coil we developed can double-tune in the 19F and 1H frequencies without below the one pF capacitor except the $C_{A}$. The simulation results showed the relatively close sensitivity of our double-tuned coil
to that of a single-tuned coil. With the conventional method, the double-tuned circuit is connected in a series to the sample coil, so the resistance component of the double-tuned circuit causes direct signal loss, and the sensitivity of the RF coil using the conventional-double tuned design method is reduced.\(^9\) On the other hand, with this method, the double-tuned circuit \((L_B, L_C, C_B, \text{ and } C_C)\) is connected in parallel to the sample coil and feeding point, so the resistance component of the double-tuned circuit is reduced. Thus, the sensitivity of our double-tuned coil is relatively close to that of a single-tuned coil.

We have demonstrated the double-tuned RF solenoid coil we developed for animal imaging at 7T. In fact, its design could be generally applied for humans as well. To prove the general application of our circuit, we implemented a typical coil for human imaging. Human body imaging employs a torso coil, which is based on a multi-surface coil. For example, the size of each surface coil is about \(10\, \text{cm} \times 10\, \text{cm}\) and its inductance, \(270\, \text{nH}\). The resonant frequencies of \(^{19}\text{F}\) and \(^1\text{H}\) are \(120\) and \(128\, \text{MHz}\) at 3T. Figure 6a shows a simulation model of a double-tuned surface coil with a torso phantom \((x = 352\, \text{mm}, y = 232\, \text{mm}, z = 304\, \text{mm}, \text{conductivity} = 0.6\, \text{S/m}, \text{relative permittivity} = 75)\). We simulated the double-tuned surface coil using computer RF coil simulation. We observed 2 resonance points at the resonant frequencies of \(^{19}\text{F}\) (120 MHz) and \(^1\text{H}\) (128 MHz) using \(L_B = 40\, \text{nH}, L_C = 41\, \text{nH}, C_A = 6.3\, \text{pF}, C_B = 25\, \text{pF}, C_{C_1} = 60\, \text{pF}, C_{C_2} = 70\, \text{pF}, \text{and } C_D = 77\, \text{pF}\) (Fig. 6b). Figure 6c shows the measured frequency characteristics of a fabricated double-tuned surface coil with the phantom. The experimental results show the same tendency as with the simulation and indicate the applicability of the double-tuned coil in human cases.

This study suggests that our developed double-tuned RF coil can substantially improve the design of double-tuned coils for close frequencies. However, this design method has a limitation. For well separated frequencies, e.g., \(^{31}\text{P}/^{1}\text{H}\), the frequency of the LC series resonance circuit \(f_B\) will be lower and that of \(f_C\), which is higher than the present construction. It follows that the inductance of these circuits will be very large (over one \(\mu\text{H}\)) and their capacitor will be very low (below one \(\text{pF}\)). However, it is difficult, or even impossible, to obtain a large value and a low-loss inductor and to adjust capacitance. Therefore, the developed double-tuned coil is suitable for close resonant frequencies, e.g., \(^{19}\text{F}/^{1}\text{H}\).

**Conclusion**

We developed a double-tuned coil for \(^{19}\text{F}\) and \(^1\text{H}\) imaging and demonstrated through computer simulation its sensitivity at \(^{19}\text{F}/^{1}\text{H}\) resonant frequencies and its relatively close sensitivity to that of a single-tuned coil. In rats administered a PFCE emulation, we demonstrated that the coil can monitor distributions of \(^{19}\text{F}\)-labeled drugs. Finally, we demonstrated that our double-tuned coil design can be applied to human imaging through simulation. The results indicate that the developed double-tuned coil may be a powerful tool for \(^{19}\text{F}\) and \(^1\text{H}\) imaging.
References

1. Terreno E, Castelli DD, Viale A, Aime S. Challenges for molecular magnetic resonance imaging. Chem Rev 2010; 110:3019–3042.
2. Ruiz-Cabello J, Barnett BP, Bottomley PA, Bulte JW. Fluorine (19F) MRS and MRI in biomedicine. NMR Biomed 2011; 24:114–129.
3. Kuribayashi H, Doi Y, Kanazawa Y. Application of 19F chemical shift imaging in studies of mice with orally administered 5-fluorouracil. Magn Reson Med 2001; 46:864–869.
4. Morikawa S, Inubushi T, Morita M, et al. Fluorine-19 fast recovery fast spin echo imaging for mapping 5-fluorouracil. Magn Reson Med Sci 2007; 6:235–240.
5. Cron GO, Beghein N, Ansiaux R, Martinive P, Feron O, Gallez B. 19F NMR in vivo spectroscopy reflects the effectiveness of perfusion-enhancing vascular modifiers for improving gemcitabine chemotherapy. Magn Reson Med 2008; 59:19–27.
6. Doty FD, Inners RR, Ellis PD. A multinuclear double-tuned probe for applications with solids or liquids utilizing lumped tuning elements. J Magn Reson 1981; 43:399–416.
7. Schnall MD, Subramanian VH, Leigh JS, Chance B. A new double-tuned probe for concurrent 1H and 31P NMR. J Magn Reson 1985; 65:122–129.
8. Kan S, Jehenson P, Leroy-Willig A. Single-input double-tuned Foster-type probe circuit. Magn Reson Med 1992; 26:7–15.
9. Mispelter J, Lupu M, Briguet A. NMR probeheads for biophysical and biomedical experiments: theoretical principles and practical guidelines. London: Imperial College Press, 2006.
10. Hu L, Hockett FD, Chen J, et al. A generalized strategy for designing 19F/1H dual-frequency MRI coil for small animal imaging at 4.7 Tesla. J Magn Reson Imaging 2011; 34:245–252.
11. Richmond JH, Geary NH. Mutual impedance of non-planar-skew sinusoidal dipoles. IEEE Transactions on Antennas and Propagation 1975; AP-23:412–414.
12. Ochi H, Yamamoto E, Sawaya K, Adachi S. Calculation of electromagnetic field of an MRI antenna loaded by a body. Proceedings of the 11th Annual Meeting of SMRM, Berlin; 1992; 4021.