A dual birdcage coil for proton and fluorine 7 Tesla MRI

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Abstract

Object: Given the growing interest in fluorine, it is necessary to develop new multi-tuned RF coils. Therefore, our objective is to design a simple and versatile double-tuned RF coil that can be used as a transmitter and receiver double-tuned coil (^{1}H and ^{19}F) or as transmitter-only double-tuned coil.

Materials and Methods: A high-pass eight-element birdcage coil was built for ^{1}H and ^{19}F for a 7T scanner. PIN diodes and cable traps to block unwanted common mode currents in cables were introduced to confer more flexibility to the coil. S-parameters and quality factor were measured in workbench and signal to noise ratio as well as signal intensity profiles in imaging experiments.

Results: Bench measurements show S11 values less than -33 dB, S21 lower than -13 dB and quality factors ratio of the order of 1.8 that are in agreement with good performances of a RF coil, as well as values of -39 dB for ^{19}F and -30 dB for ^{1}H as good detuning values. Signal intensity profiles prove excellent homogeneity at ^{1}H and ^{19}F.

Discussion: We present a simple structure of a double tuned high-pass birdcage coil tuned to ^{1}H and ^{19}F that shows a great uniformity and sensitivity for ^{19}F.

Keywords: High-pass birdcage; Double-tuned; Fluorine; PIN diode

Introduction

Magnetic Resonance Imaging (MRI) is a widely used clinical diagnostic tool because it is non-invasive, has no tissue depth penetration limitations, no ionizing radiation issues, and provides the combination of structural and functional imaging in the same study at reasonably high spatial resolution. Most MRI studies use ^{1}H as the nucleus of choice for imaging, but other nuclei, such as sodium (^{23}Na) or fluorine (^{19}F) can be imaged even using simultaneous multinuclear acquisition methods. Imaging with these nuclei introduces the possibility of using MRI for molecular imaging with higher specificity than conventional proton MRI. ^{19}F MRI imaging allows direct visualization of molecules of interest containing ^{19}F nuclei. Since MRI signal from endogenous ^{19}F in tissues is negligible, and ^{19}F is a nucleus with similar sensitivity to proton, molecules containing ^{19}F with the concentration limits of milli- to micromolar typical for NMR, results in a hot-spot, with very high contrast and specificity characteristics.

Important applications of ^{19}F MRI are lung imaging using perfluorinated gases [1], cell tracking using perfluorocarbons [2, 3], inflammatory processes (such as atherosclerosis) [4]. Lung imaging using ^{19}F MRI, together with hyperpolarized gas MRI, has provided insights in lung structure and function. ^{19}F gas MRI offers very low signal compared to hyperpolarized gas MRI, due to the lack of hyperpolarization. However, imaging with fluorinated gases is much easier and cheaper, they can be mixed with oxygen and do not need hyperpolarization. ^{19}F gas imaging has used SF_6 [5, 6], C_2F_6 [7] and C_3F_8 [8] to measure diffusion, which is a proxy for airspace size [6, 7], ventilation/perfusion ratios [9] and 3D gas density maps [8].

Another important ^{19}F MRI application is imaging of liquid perfluorocarbons [10]. These have been used for cell tracking [2, 3, 11–16], visualization of pulmonary inflammation [4, 17], evaluation of response to antibiotic therapy [18], to assess the relationship between folate receptor expression and tumor proliferation [19] and to assess tumor oxygenation [20].

This renewed interest in non-proton MRI has brought the need to develop new designs of multi-tuned radiofrequency (RF) coil configurations. Multinuclear studies typically require more than one RF coil to acquire all required information. In the case of fluorine, whose resonance frequency is close to the proton one, a double-tuned RF coil allows co-registration of both information, i.e. ^{1}H MRI is used to localize anatomical structures and ^{19}F, depending on the application, for functional or molecular imaging. This double configuration is mandatory to reduce unpleasant situations to the subject of study, such as replacing or retuning RF coils, and to prevent subsequent co-registration issues with proton-based anatomical imaging.

Several designs for double-tuned RF coils have been reported. Each of these solutions present advantages and disadvantages mainly related to the compromise to minimize the effect of complicated manufacturing and annoying tuning processes. One of the first double-tuned configuration used variable length transmission line [21], but this solution is not optimal due to size constraints. The replacement of the transmission line with discrete elements, inductors and capacitors, results in the well-known RF coil with trap circuits (LC circuit) [22–26], although this solution requires a large frequency separation and is not suitable for dual proton and fluorine MRI applications. LC circuit has a high impedance at lower resonance frequencies, which is equivalent to an inductor, whereas at higher frequencies presents a low impedance and is then equivalent to a capacitor, i.e. allowing a double-tuned RF coil. This trap circuit has been widely used in combination with birdcage coils [27–29]. Different shield radius is another method to achieve a double-tuned RF coil [30] when frequencies are close, as in this case, or to tune RF coil moving RF shield along the coil [31]. The need to reassemble the coil with each frequency limits its use. Another approach to manufacture a double-tuned coil is through two coaxial structures [32–35]; however, signal to noise ratio (SNR) can decrease significantly due to the coupling effect. The use of varicaps is an alternative to switch both frequencies [36, 37] but due to its low quality factor it reduces the performances of the RF coil. Nowadays, active components (PIN diodes) have been used in many RF coil designs to reduce coupling or switching between RF coils[38]. PIN diodes are an alternative to replace trap circuits [39]. This solution plays an important role for active detuning and switching between transmit and receive coils [40, 41]. However, SNR could be decreased due to the resistance of the PIN diodes, especially when they are placed in series with the coil and they are forward-biased. Finally, recent research in microelectromechanical systems (MEMS) open new developments in double-tuned RF coils [42] but it is still in development. The switch technology in MEMS allows increased switching speed and reduced insertion loss. This solution is not only valid for double-tuned RF coils but in array coils to switch conductive elements and reconfigure coil field of view [43].

It is well known that the birdcage coil is one of the most versatile RF coils. It can perform double resonant or quadrature excitations, as well as generate highly homogenous radiofrequency magnetic fields [44–46]. Birdcage coils have the wires uniformly spaced in azimuthal angle. In transmission mode, a current is passed through providing an ideal cosine current distribution along the coil surface, which generates a homogeneous magnetic field. A birdcage coil has two orthogonal resonant modes [47]. Since ^{1}H and ^{19}F nuclei have close resonant frequencies (300 MHz and 282 MHz, respectively at 7T) one can take advantage of these two channels and tune each of them to a different frequency [48, 49]. Therefore, the coil assures almost identical B_1 profiles for the two nuclei.

In this work, we have designed and constructed a versatile design of a dedicated RF volume coil that can be used in many configurations, for instance, as a transmitter and receiver (TX/RX) double-tuned coil (^{1}H and ^{19}F) or as transmitter-only (TX) double-tuned coil to operate together with an array coil tuned in proton or fluorine. The configuration of our double-tuned volume RF coil is based on the advantage of the quadrature mode of the birdcage coil into two separate linear modes and tune it into each frequency to achieve double resonance. The configuration as transmitter coil uses active components, PIN diodes, to switch between the transmission and reception coils. The PIN diodes are located in parallel to each capacitor placed in the end-ring of the high-pass birdcage coil to reduce additional resistance when they are forward-biased and therefore do not degrade its performance. This versatile home-made RF coil is optimized for fluorine and can still acquire good quality proton MR images for anatomical information. Due to this versatility, the proposed design is suitable for use either as a double-tuned RF coil or in combination with an array coil for both the proton or fluorine frequencies.

Materials and Methods

A versatile home-made RF coil was built and optimized for rat imaging. A double resonant high-pass birdcage coil for ^1H and ^{19}F was designed for imaging at 7T, resonant frequency of 300 MHz and 282 MHz respectively. The length of the coil was 11.4 cm, the radius 3.6 cm and the RF shield radius was 5.6 cm. The coil dimensions were adjusted to fit the samples and enhance a good filling factor. Adhesive copper tape (3M Corporation, St Paul, MN, USA) of 5 mm width was used to construct a high-pass eight-element birdcage coil. An eight-element high-pass birdcage coil was chosen to achieve enough homogenous radiofrequency magnetic field without compromising its facile adjustment. This seems an optimal balance between adding more elements to yield a better B_1 homogeneity and the complexity of construction. Non-magnetic fixed capacitors (Series 100B, American Technical Ceramics, USA) were used in the eight elements and placed at each end-rings. High voltage variable (1-25 pF) capacitors (Voltronics, USA) were used to perform fine tuning and matching adjustment when high-pass birdcage coil is loaded by the samples for both ^1H and ^{19}F nuclei. The high-pass birdcage coil was optimized for fluorine experiments with the capacitor distribution shown in Figure 1. To achieve double (^1H, ^{19}F) resonance, as birdcage coils have a cosine current distribution, C_0 and C_4 capacitors, which correspond to the minimum current distributions, can be modified without changing B_1 profiles. Balanced capacitive matching circuits were used to match the coil’s impedances to the real values of 50 Ω in each channel (^1H and ^{19}F).

Active decoupling was performed by using a MA4P7006F-1072T PIN diode (MACOM, Lowell, MA, USA) in series with an inductor L (~ 64 nH or 44 nH) that is introduced in parallel to the capacitor (4.7 pF or 6.8 pF, respectively) of each element of the high-pass birdcage resonator. Thus, it can be used together with an array coil tuned either in ^1H or ^{19}F. Each PIN diode was powered by a voltage source via 1.2 μH RF chokes (Coilcraft. IL, USA). During the operation of the high-pass birdcage coil, in transmission mode, all PIN diodes were reverse-biased by -36 V

(PIN diode OFF), forming an open circuit and the inductor L is disconnected, so it works as a conventional double-tuned high-pass birdcage coil (Figure 1B). In receive mode, the PIN diodes are forward-biased by 5 V (PIN diode ON), inductor L is connected to the capacitor and the parallel LC circuit is on resonance, forming a high impedance circuit that blocked current flowing in the coil and detuned the high-pass birdcage coil (Figure 1C). As the PIN diode are in parallel to the high-pass birdcage coil, no additional resistance is introduced and therefore SNR does not decrease. This LC circuit (PIN diode ON) is tuned to a middle frequency between proton and fluorine to be able to detune the high-pass birdcage coil at both frequencies. A series-parallel combination of the PIN diode is chosen to achieve better detuning of our high-pass birdcage coil. A total of 5 V and a required current of 400 mA is applied to switch on all PIN diodes.

A cable trap was placed in each of the two channels to minimize the coupling between cables by blocking unwanted common mode currents [50, 51]. It consists in a parallel resonant circuit and it was built with a capacitor and an inductor formed by a semi-rigid cable UT47C-TP-LL (Micro-Coax, PA, USA). The cable traps were tuned to ^{1}H and ^{19}F frequency.

Bench measurements were performed in an 8712ET Network Analyzer (Agilent Technologies, Palo Alto, USA). The reflection (S11) and transmission (S21) coefficient were measured for both nuclei. Quality factor (Q) measurements were used to characterize the performance of the coil. Q factors were measured without (Q_u) and with (Q_l) sample load (a home-made phantom, described below) at both frequencies.

A proton-^{19}F phantom was manufactured in house consisting of 5 lab tubes of 15 mm diameter filled with different solutions of 2,2,2-trifluorethanol (3 equivalent ^{19}F nuclei per molecule) dissolved in water: 79.5, 53, 26, 13 mM and 5 mM. All MRI experiments were performed on a 7 T MR scanner, Bruker Biospec 70/30 USR (Bruker BioSpin, Rheinstetten, Germany) for small animals located at CIC BiomaGUNE (San Sebastian, Spain). Axial images were acquired using a Multi Slice Multi Echo (MSME) sequence. Acquisition parameters for ^{1}H imaging were:

repetition time (TR) = 1151 ms, echo time (TE) = 11.77 ms, 1 average, field of view of 6 x 6 cm^2, and acquisition matrix of 256 x 256. Parameters for ^{19}F images were: repetition time (TR) = 1151 ms, echo time (TE) = 8.65 ms, 1 average, field of view of 6 x 6 cm^2, and acquisition matrix of 64 x 64 for a total acquisition time of 3 minutes and 12 seconds. Shimming and pulse calibration were performed using the standard adjustment tools of the scanner. Paravision PV 6.0.1 (Bruker BioSpin, Rheinstetten, Germany) and ImageJ 1.52 (National Institutes of Health, Bethesda, Maryland, United States) software were used to show the profiles and to calculate SNR.

For SNR calculation, five regions of interest (ROIs) were drawn inside the tubes and one ROI in the background (Figure 2). In the tube's regions (SNR>0), pixel intensity follows a Rice distribution with two parameters, the noise σ and the SNR [52]. For this case, the first moment of the distribution is [53]:

$$\bar{M} = \sigma \cdot \sqrt{\pi/2} \cdot L_{1/2}\left(-SNR^2/2\right) \tag{1.1}$$

In the background, SNR = 0 and the pixel intensity follows a Rayleigh distribution with mean and standard deviation

$$\bar{M} = \sigma \cdot \sqrt{\pi/2} \qquad \sigma_M = \sigma \cdot \sqrt{(4-\pi)/2} \tag{1.2}$$

Here, $\bar{M}$ is the average of the magnitude signal, σ_M is the standard deviation of the magnitude signal and $L_{1/2}(x)$ is a Laguerre L polynomial.

The SNR calculation proceeds as follows. First, a quantile plot of pixel intensity in the background ROI using R (https://www.r-project.org) confirms that the background ROI is Rayleigh distributed. If this is not the case, another background ROI is drawn. Then, Equation 1.2 gives two different estimations of the noise σ, which are averaged. Then, a numerical solution of equation 1.1 using Mathematica (Wolfram Research, Champaign, Illinois, United States) provides the SNR in a straightforward way.

Results

A range of tests were performed on the RF coil both on the bench and imaging experiments to ensure good performances. These tests included quality factor measurements, checking B_1 homogeneity and active decoupling. We present here both measurements.

Bench measurements:

S-parameters were measured on the bench using a network analyser and confirmed that tuning and matching to 50 Ω was done at both frequencies considering the home-made phantom. S11 for both nuclei, ^{1}H and ^{19}F, was less than -33 dB, indicating a good impedance matching. Transmission coefficients S21 were lower than -13 dB for each channel.

For optimal RF coil operation at high frequencies, the resistive losses of the coil must be smaller than the sample losses. Table 1 shows quality factor measurements of the double-tuned high-pass birdcage coil with and without sample load. High ratio values of Q_u / Q_l imply high coil sensitivity and low coil losses, which result in higher SNR. As we can see in this table, Q values are slightly higher at ^{19}F since the high-pass birdcage coil has been optimized for fluorine.

When the PIN diode is forward-biased, the LC circuit is on resonance. The PIN diode and the series inductor L are in parallel to each capacitor located in the end-ring of the high-pass birdcage. No intrinsic resistance is added and thus Q values are not reduced. This parallel LC circuit was tuned to a frequency between proton and fluorine, around 290 MHz. A value of -24 dB was measured for the transmission coefficient S21 in both frequencies (^{1}H and ^{19}F), appropriate value for a good detuning in the receive mode. Once all LC circuits were adjusted, a series-parallel combination was implemented. A current intensity of 400 mA is applied to achieve the active decoupling of the double-tuned high-pass birdcage coil. S21 values were calculated as the difference between on-resonance and off-resonance states of the double-tuned high-pass birdcage. In this case, values of -39 dB for fluorine and -30 dB for proton were achieved. These values clearly display that the high-pass birdcage coil was sufficiently detuned with the PIN diodes during acquisition to avoid interference.

Imaging Experiments

Figure 2 shows axial images for both nuclei, ^{1}H and ^{19}F, obtained from the phantom using the double-tuned high-pass birdcage coil and its corresponding profiles. In these images, we can see the high homogeneity of B_1. Signal intensity profiles of this phantom are shown in Figure 2b for ^{1}H image and Figure 2d for ^{19}F image. Homogeneity within each tube, expressed using the Coefficient of Variation, are around 1.5% and 4.6% for ^{1}H and ^{19}F respectively. The selected configuration to tune each of the two orthogonal channels to proton and to fluorine in coexistence with the introduction of the PIN diodes to detune the coil when operated together with a receiver-only array coil yielded good results. B_1 homogeneity profiles are preserved in both nuclei. This design ensures high B_1 homogeneity within the RF coil.

In order to characterize the efficiency of the proposed coil, power consumption for a 90 degree pulse was measured for both nuclei and compared to a commercial coil. 3.8 W for ^{1}H and 3.6 W for ^{19}F were measured for our coil, whereas 3.1 W was obtained for ^{1}H in a linear commercial one (single tuned birdcage coil of similar dimensions).

Since the phantom has five different concentrations, the SNR of the five tubes was calculated to find out how sensitive our RF coil is. The calculated SNR values of the phantom are given in table 2. We point out that a concentration as small as tube 3 (26 mM) or even tube 4 (13 mM) results in a Contrast-to-noise ratio (CNR) superior to 4. Tube 5 (5 mM) is discernible even if SNR is low, CNR close to 2. Since our voxel size is 4.4 mm^3, a concentration of 22 nmol per voxel can be easily imaged in a short time (less than 4 minutes).

Discussion

In this study, we present an approach to a RF coil to be used in different configurations. We chose one of the most homogenous RF coils, a birdcage, and we took advantage of its performance in a quadrature configuration. Each of the two linear modes was tuned to ^{1}H and ^{19}F. PIN diodes were added to be able to use it as a transmitter-only RF coil together with an array coil.

Due to the high B_1 homogeneity of birdcage coils, it is one of the most suitable for transmission mode. Our results demonstrate that the double-tuned high-pass birdcage coil offers similar homogeneity at both nuclei.

This simple and versatile design shows a great sensitivity even to detect a ^{19}F concentration as low as 5 mM in a few minutes averaging time, which is comparable to a typical in-vivo concentration. Since our voxel size is 4.4 mm^3, this is equivalent to a concentration of 22 nmol per voxel. We decided to use this concentration to see the sensitivity of our measurements. Our results can be compared to those from van Heeswijk et al. [54], who used a gradient echo pulse sequence within a 10-minute measurement time limit for possible human applications. The final concentration of the perfluoro-15-crown-5 ether emulsion in their work ranged from 10 to 0.4 mM. Considering that this molecule has 20 chemically equivalent fluorine atoms whilst 2,2,2-trifluoroethanol has only three, the minimum concentration described as detection limit of this molecule for a typical gradient echo acquisition is about 0.4 mM, which is equivalent to 2.7 mM in our case. In our case, we only accumulated half the time as these authors did, TR was different in both cases and we did not use a quadrature coil.

Our design avoids the use of degrading trap circuits in series to the RF coil and therefore resulting in an improvement at both frequencies. The idea of tuning a trap circuit to a middle frequency provides good detuning values overall in ^{19}F as the high-pass birdcage coil is optimized for ^{19}F. The proposed design provides a simple and robust approach to a double-tuned RF coil design. Next studies will include the benefit of the TX mode with an array coil of four elements tuned to both frequencies.

Conclusion

For MRI with non-proton nuclei, it is necessary to develop some appropriate hardware such as multi-tuned RF coils. In this paper, we suggest the idea of building a multi-tuned RF coil based on one of the most homogenous RF coil design, the birdcage configuration, and take advantage of its performance. We present here a versatile and simple structure of a double-tuned high-pass birdcage coil tuned to ^{1}H and ^{19}F to be used in transmission and reception mode or as a transmitter-only RF coil with active component inside. High quality images for ^{1}H and ^{19}F nuclei were obtained using this RF coil.

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Author contributions

Villa-Valverde: project development, analysis and interpretation of data, drafting of manuscript. Rodriguez: analysis and interpretation of data, drafting of manuscript. Padró: acquisition of data. Benito: acquisition of data. Garrido-Salmon: critical revision. Ruiz-Cabello: acquisition of data, critical revision.

Compliance with ethical standards

Conflict of interest: The authors declare that they have no conflict of interest

Ethical approval: This article does not contain any studies with human participants or animals performed by any of the authors.

References

1. Kruger SJ, Nagle SK, Couch MJ, Ohno Y, Albert M, Fain SB (2016) Functional imaging of the lungs with gas agents. J Magn Reson Imaging 43:295–315.

2. Fox MS, Gaudet JM, Foster PJ (2015) Fluorine-19 MRI Contrast Agents for Cell Tracking and Lung Imaging. Magn Reson Insights 8:53–67.

3. Ahrens ET, Zhong J (2013) In vivo MRI cell tracking using perfluorocarbon probes and fluorine-19 detection. NMR Biomed 26:860–871.

4. van Heeswijk RB, Pellegrin M, Flögel U, Gonzales C, Aubert J-F, Mazzolai L, Schwitter J, Stuber M (2015) Fluorine MR Imaging of Inflammation in Atherosclerotic Plaque in Vivo. Radiology 275:421–429.

5. Schreiber WG, Markstaller K, Weiler N, Eberle B, Laukemper-Ostendorf S, Scholz A, Bürger K, Thelen M, Kauczor H-U (2000) 19F-MRT der Lungenventilation in Atemanhaltetechnik mittels SF6-Gas. RöFo - Fortschritte auf dem Gebiet der Röntgenstrahlen und der bildgebenden Verfahren 172:500–503.

6. Ruiz-Cabello J, Pérez-Sánchez JM, Pérez de Alejo R, Rodríguez I, González-Mangado N, Peces-Barba G, Cortijo M (2005) Diffusion-weighted 19F-MRI of lung periphery: Influence of pressure and air–SF6 composition on apparent diffusion coefficients. Respiratory Physiology & Neurobiology 148:43–56.

7. Carrero-González L, Kaulisch T, Stiller D (2013) In vivo diffusion-weighted MRI using perfluorinated gases: ADC comparison between healthy and elastase-treated rat lungs. Magn Reson Med 70:1761–1764.

8. Couch MJ, Ball IK, Li T, Fox MS, Littlefield SL, Biman B, Albert MS (2013) Pulmonary ultrashort echo time 19F MR imaging with inhaled fluorinated gas mixtures in healthy volunteers: feasibility. Radiology 269:903–909.

9. Adolphi NL, Kuethe DO (2008) Quantitative mapping of ventilation-perfusion ratios in lungs by 19F MR imaging of T1 of inert fluorinated gases. Magn Reson Med 59:739–746.

10. Ruiz-Cabello J, Barnett BP, Bottomley PA, Bulte JWM (2011) Fluorine (19F) MRS and MRI in biomedicine. NMR Biomed 24:114–129.

11. Ruiz-Cabello J, Walczak P, Kedziorek DA, Chacko VP, Schmieder AH, Wickline SA, Lanza GM, Bulte JWM (2008) In vivo “hot spot” MR imaging of neural stem cells using fluorinated nanoparticles. Magn Reson Med 60:1506–1511.

12. Janjic JM, Ahrens ET (2009) Fluorine-containing nanoemulsions for MRI cell tracking. Wiley Interdiscip Rev Nanomed Nanobiotechnol 1:492–501.

13. Temme S, Bönner F, Schrader J, Flögel U (2012) 19F magnetic resonance imaging of endogenous macrophages in inflammation. Wiley Interdiscip Rev Nanomed Nanobiotechnol 4:329–343.

14. Ahrens ET, Bulte JWM (2013) Tracking immune cells in vivo using magnetic resonance imaging. Nat Rev Immunol 13:755–763.

15. Srinivas M, Tel J, Schreibelt G, Bonetto F, Cruz L-J, Amiri H, Heerschap A, Figdor CG, de Vries IJM (2015) PLGA-encapsulated perfluorocarbon nanoparticles for simultaneous visualization of distinct cell populations by 19F MRI. Nanomedicine (Lond) 10:2339–2348.

16. Gonzales C, Yoshihara HAI, Dilek N, Leignadier J, Irving M, Mieville P, Helm L, Michielin O, Schwitter J (2016) In-Vivo Detection and Tracking of T Cells in Various Organs in a Melanoma Tumor Model by 19F-Fluorine MRS/MRI. PLoS ONE 11:e0164557.

17. Stoll G, Basse-Lüsebrink T, Weise G, Jakob P (2012) Visualization of inflammation using (19) F-magnetic resonance imaging and perfluorocarbons. Wiley Interdiscip Rev Nanomed Nanobiotechnol 4:438–447.

18. Hertlein T, Sturm V, Jakob P, Ohlsen K (2013) 19F magnetic resonance imaging of perfluorocarbons for the evaluation of response to antibiotic therapy in a Staphylococcus aureus infection model. PLoS ONE 8:e64440.

19. Xu X, Yan Y, Liu F, Wu L, Shao M, Wang K, Sun X, Li Y, Beinpuo ESW, Shen B (2018) Folate receptor-targeted 19 F MR molecular imaging and proliferation evaluation of lung cancer. J Magn Reson Imaging. doi: 10.1002/jmri.26177

20. Zhong J, Sakaki M, Okada H, Ahrens ET (2013) In vivo intracellular oxygen dynamics in murine brain glioma and immunotherapeutic response of cytotoxic T cells observed by fluorine-19 magnetic resonance imaging. PLoS ONE 8:e59479.

21. Cross VR, Hester RK, Waugh JS (1976) Single coil probe with transmission-line tuning for nuclear magnetic double resonance. Review of Scientific Instruments 47:1486–1488.

22. Schnall M., Harihara Subramanian V, Leigh J., Chance B (1985) A new double-tuned probed for concurrent 1H and 31P NMR. Journal of Magnetic Resonance (1969) 65:122–129.

23. Doty FD, Inners RR, Ellis PD (1981) A multinuclear double-tuned probe for applications with solids or liquids utilizing lumped tuning elements. Journal of Magnetic Resonance (1969) 43:399–416.

24. Sunder Rajan S, Wehrle JP, Glickson JD (1987) A novel double-tuned circuit for in Vivo NMR. Journal of Magnetic Resonance (1969) 74:147–154.

25. Meyerspeer M, Serés Roig E, Gruetter R, Magill AW (2014) An improved trap design for decoupling multinuclear RF coils. Magn Reson Med 72:584–590.

26. Shen GX, Boada FE, Thulborn KR (1997) Dual-frequency, dual-quadrature, birdcage RF coil design with identical B1 pattern for sodium and proton imaging of the human brain at 1.5 T. Magn Reson Med 38:717–725.

27. Rath AR (1990) Design and performance of a double-tuned bird-cage coil. Journal of Magnetic Resonance (1969) 86:488–495.

28. Isaac G, Schnall MD, Lenkinski RE, Vogele K (1990) A design for a double-tuned birdcage coil for use in an integrated MRI/MRS examination. Journal of Magnetic Resonance (1969) 89:41–50.

29. Pascone R, Vullo T, Farrelly J, Mancuso R, Cahill PT (1993) Use of transmission line analysis for multi-tuning of birdcage resonators. Magn Reson Imaging 11:705–715.

30. Lu DF, Joseph PM (1991) A technique of double-resonant operation of 19F and 1H quadrature birdcage coils. Magn Reson Med 19:180–185.

31. Dardzinski BJ, Li S, Collins CM, Williams GD, Smith MB (1998) A birdcage coil tuned by RF shielding for application at 9.4 T. J Magn Reson 131:32–38.

32. Fitzsimmons JR, Brooker HR, Beck B (1987) A transformer-coupled double-resonant probe for NMR imaging and spectroscopy. Magn Reson Med 5:471–477.

33. Fitzsimmons JR, Beck BL, Brooker HR (1993) Double resonant quadrature birdcage. Magn Reson Med 30:107–114.

34. Murphy-Boesch J, Srinivasan R, Carvajal L, Brown TR (1994) Two configurations of the four-ring birdcage coil for 1H imaging and 1H-decoupled 31P spectroscopy of the human head. J Magn Reson B 103:103–114.

35. Hu L, Hockett FD, Chen J, Zhang L, Caruthers SD, Lanza GM, Wickline SA (2011) A generalized strategy for designing (19)F/(1)H dual-frequency MRI coil for small animal imaging at 4.7 Tesla. J Magn Reson Imaging 34:245–252.

36. Muftuler LT, Gulsen G, Sezen KD, Nalcioglu O (2002) Automatic tuned MRI RF coil for multinuclear imaging of small animals at 3T. J Magn Reson 155:39–44.

37. de Alejo RP, Garrido C, Villa P, Rodriguez I, Vaquero JJ, Ruiz-Cabello J, Cortijo M (2004) Automatic tuning and matching of a small multifrequency saddle coil at 4.7 T. Magn Reson Med 51:869–873.

38. Lee S-P, Choi I-Y, Kim S-Y (2000) Rapidly Switchable RF coil for 19F/1H NMR Studies. ISMRM. p 1416

39. Ha S, Hamamura MJ, Nalcioglu O, Muftuler LT (2010) A PIN diode controlled dual-tuned MRI RF coil and phased array for multi nuclear imaging. Phys Med Biol 55:2589–2600.

40. Barberi EA, Gati JS, Rutt BK, Menon RS (2000) A transmit-only/receive-only (TORO) RF system for high-field MRI/MRS applications. Magn Reson Med 43:284–289.

41. Garbow JR, McIntosh C, Conradi MS (2008) Actively Decoupled Transmit-Receive Coil-Pair for Mouse Brain MRI. Concepts Magn Reson Part B Magn Reson Eng 33B:252–259.

42. Maunder A, Rao M, Robb F, Wild JM (2018) Comparison of MEMS switches and PIN diodes for switched dual tuned RF coils. Magn Reson Med. doi: 10.1002/mrm.27156

43. Bulumulla SB, Park KJ, Fiveland E, Iannotti J, Robb F (2017) MEMS switch integrated radio frequency coils and arrays for magnetic resonance imaging. Rev Sci Instrum 88:025003.

44. Hayes CE, Edelstein WA, Schenck JF, Mueller OM, Eash M (1985) An efficient, highly homogeneous radiofrequency coil for whole-body NMR imaging at 1.5 T. Journal of Magnetic Resonance (1969) 63:622–628.

45. Tropp J (1989) The theory of the bird-cage resonator. Journal of Magnetic Resonance (1969) 82:51–62.

46. Pascone RJ, Garcia BJ, Fitzgerald TM, Vullo T, Zipagan R, Cahill PT (1991) Generalized electrical analysis of low-pass and high-pass birdcage resonators. Magn Reson Imaging 9:395–408.

47. Leifer MC (1997) Resonant Modes of the Birdcage Coil. Journal of Magnetic Resonance 124:51–60.

48. Joseph PM, Lu D (1989) A technique for double resonant operation of birdcage imaging coils. IEEE Trans Med Imaging 8:286–294.

49. Gajawada G, Li T, Couch MJ, Fox MS, Albert M A 19F - 1H Linear Dual Tuned RF Birdcage Coil for Rat Lung Imaging at 3T. ISMRM. p 1461

50. Mispelter J, Lupu M, Briguet A (2006) NMR probeheads for biophysical and biomedical experiments: theoretical principles & practical guidelines. Imperial College Press ; Distributed by World Scientific, London : Hackensack, NJ

51. Peterson DM, Beck BL, Duensing GR, Fitzsimmons JR (2003) Common mode signal rejection methods for MRI: Reduction of cable shield currents for high static magnetic field systems. Concepts in Magnetic Resonance 19B:1–8.

52. Gudbjartsson H, Patz S (1995) The Rician distribution of noisy MRI data. Magn Reson Med 34:910–914.

53. Rice SO (1944) Mathematical Analysis of Random Noise. Bell System Technical Journal 23:282–332.

54. van Heeswijk RB, Pilloud Y, Flögel U, Schwitter J, Stuber M (2012) Fluorine-19 magnetic resonance angiography of the mouse. PLoS ONE 7:e42236.

Fig 1. A) Schematic of double-tuned eight-element high-pass birdcage coil. B) Schematic in the transmitter and receiver mode. C) Schematic in the receiver mode, when the PIN diodes are switched on. CM is a variable capacitor for matching and CT is a variable capacitor for tuning.

Fig 2. MSME images of the five tubes containing different concentrations of 2,2,2-Trifluorethanol: a) ^{1}H image and c) ^{19}F image; b) and d) Profiles of ^{1}H and ^{19}F, respectively.

	$\mathbf{^{1}H}$	$\mathbf{^{19}F}$
$\mathbf{Q_{unloaded}}$	166	192
$\mathbf{Q_{loaded}}$	97	104
$\mathbf{Q_{ratio}}$	1.71	1.84

Table 1. Quality factors of the double-tuned high-pass birdcage coil for both nuclei.

Nucleus	**ROI 1**	**ROI 2**	**ROI 3**	**ROI 4**	**ROI 5**
^{1}H	180.45	181.22	173.70	172.94	166.85
^{19}F	29.26	19.68	10.23	4.82	1.41

Table 2. Calculated signal to noise ratio for both nuclei, ^{1}H and ^{19}F. SNR is calculated from each of the five tubes.