Ladder-design volume coil with good uniformity and signal to noise for hyperpolarised ^{13}C investigations of animals on a 3T clinical system

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Introduction: The chemical specificity and lack of background signal in ^{13}C NMR enables the study of metabolic pathways and may be used to detect early cancer treatment response [1]. Current advances in MR signal enhancement, in particular by Dynamic Nuclear Polarisation (DNP), make it possible to conduct real-time measurements of low concentration metabolites *in vivo* [2]. Implementation of preclinical work on clinical systems for DNP studies is attractive, but severely limited by surface coils when moving from subcutaneous to orthotopic and genetically modified models. **In this study**, we characterised and compared a custom-made ^{13}C volume coil (Hoult-Deslauriers modular radiofrequency resonator [3,4], or 'ladder coil'), together with a ^{13}C tuned loop surface coil. Coils were initially tested using a phantom, followed by hyperpolarised ^{13}C MRS in mice bearing a subcutaneous cancer xenograft. The ladder coil design is particularly relevant for groups who require volume coverage of small animals on a clinical system.

Methods: **A ^{13}C ladder coil** (Coil L) was designed (**Fig. 1**, Autodesk Inventor) and built to provide B_1 field coverage of an entire mouse for preclinical studies at 3T. The coil consists of five inductively coupled 45mm diameter elements and an inductively coupled drive loop. Each element was made from 4mm strips of copper tape (0.05mm thick) with an 8mm separation between elements. Capacitor values for the elements were chosen to allow tuning of the lowest eigenmode to the NMR frequency of ^{13}C at 3T (32MHz). A 20mm diameter **^{13}C surface coil** (Coil S, constructed from 1mm diameter copper wire, tuned to 32MHz) provided an optimal filling factor for subcutaneous tumour measurements enabling comparative assessment. Interaction between ^{1}H and ^{13}C mode frequencies, Q factors and stability were checked on a network analyser with and without load. ^{1}H imaging was performed using an adapted clinical endorectal coil (**Fig. 1**, coil E). **Phantoms**: A round-end cylinder phantom (31ml, 1M [1-^{13}C]acetic acid, 1.5mM Gd (Dotarem) in saline) was used to characterise both ^{13}C coils; a 1.5ml microtube containing the same solution was used for measurements at the centre of the surface coil. ^{13}C SNR ratios (determined using the NEMA subtraction method [5]) and B_1 maps (obtained using the double flip angle method [6]) were calculated for both coils (**Fig. 2 & Table 1**). Hyperpolarised ^{13}C: 26mg [1-^{13}C]pyruvic acid (99% isotopically enriched, Sigma Aldrich) was prepared and polarised in a HyperSense DNP polariser (Oxford Instruments) according to the *in vivo* protocol in [7] and injected into a flow phantom (1mm inner diameter capillaries immobilised in a 50ml tube filled with saline, **Fig. 3**). Imaging was performed using a gradient echo EPI sequence (EPI factor=3, FA=10, TA=1s, TR/TE=50/8ms, 1×1mm, BW=418Hz) immediately after the injection of DNP enhanced solution. Data were processed in Matlab (Mathworks). ***In vivo***: A dynamic series of ^{13}C spectra were acquired *in vivo* with both coils using a slice selective spectroscopy sequence (**Fig. 4**) (slice thickness: 10mm (surface coil) and 13mm (ladder coil), FA=20, TR=3s) following injection via lateral tail vein of 175µl 80mM hyperpolarised [1-^{13}C]pyruvate into a mouse bearing an HT29 (surface coil) or COLO320 cancer xenograft (ladder coil). [1-^{13}C]pyruvate and [1-^{13}C]lactate signals were quantified using the Amares fitting tool in jMRUI. These data were then fitted with the modified Bloch equations [1] to obtain kinetic rate constants of pyruvate-lactate exchange.

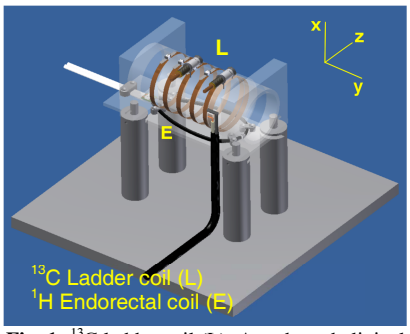

Fig. 1: ^{13}C ladder coil (L). An adapted clinical endorectal coil (E) is attached to the baseplate of the ^{13}C coil for ^{1}H reference imaging.

Coil	Orient-ation	ROI centre (mm)	ROI (mm)	SNR
L	Sag.	x = 10	20x20	17.79
	Tra.	x = 10	45x20	12.97
	Cor.	x = 10	45x20	11.98
S	Sag.	x = 5	10x10	5.37
	Tra.	x = 5	10x10	6.17
	Cor.	x = 5	10x10	4.76
	Cor.	x = 0	8x8	17.92

Table 1. SNR ratios for ladder (L) and surface (S) coils. Cylindrical 83×23mm test object was used except x=0, Coil S where a 1.5ml microtube was used (same content).

Results & Discussion: The B_1 characteristics measured for both coils are shown in **Fig. 2** Sagittal plane B_1 uniformity of >90% was achieved over 6mm using the surface coil, and covered the entire test object region (23mm) using the ladder coil. For the ladder coil, transversal and coronal orientations achieved >90% B_1 uniformity over 41mm and 38mm regions, respectively. The results of SNR calculations are presented in **Table 1**. The ladder coil matched the maximum SNR of the surface coil and had significantly better SNR across a wider FOV than the surface coil. **Fig. 3** demonstrates the good SNR and imaging capabilities of the ladder coil, where a ^{13}C image of 80mM hyperpolarised [1-^{13}C]pyruvate was acquired from a 1mm diameter capillary. **Fig. 4** shows ^{1}H axial (A) and transverse (B) images of a mouse bearing a COLO320 subcutaneous tumour, and (C) shows *in vivo* pyruvate and lactate signals (dots, acquired with a ^{13}C ladder coil) with Matlab kinetic model fitting (lines).

Conclusions: We have demonstrated that a ladder coil for ^{13}C hyperpolarised MRS and MRI measurements generates a homogeneous B_1 field over a large field of view and provides excellent SNR with preclinically relevant volume coverage.

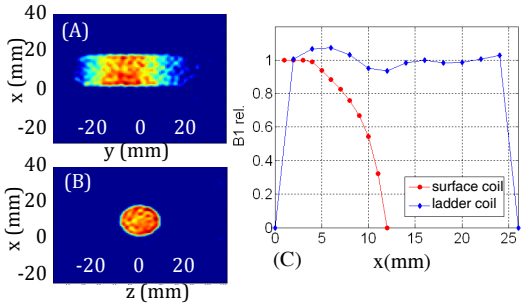

Fig. 2: (A, B) SNR maps of coil L in transverse and sagittal orientations. (C) B_1 profiles of coil L (blue) and coil S (red) in the sagittal plane (y=0).

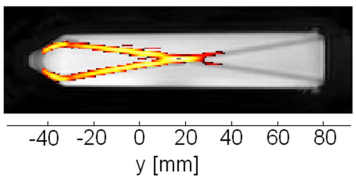

Fig. 3: Colour coded ^{13}C coronal image of hyperpolarised [1-^{13}C]pyruvate using coil L.

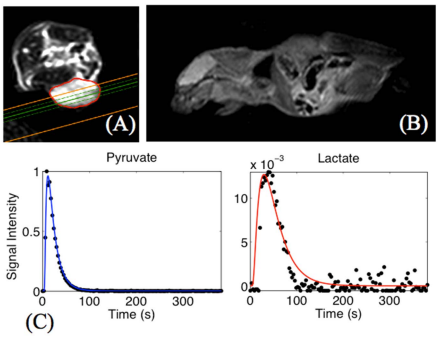

Fig. 4: (A) axial and (B) transverse ^{1}H images of a mouse bearing a COLO320 subcutaneous tumour acquired at 3T. Orange lines in (A) indicate spectroscopy acquisition slice. (C): dynamic ^{13}C spectral intensities (dots) of [1-^{13}C]pyruvate and [1-^{13}C]lactate acquired using coil L, with Matlab kinetic model fits (lines).

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