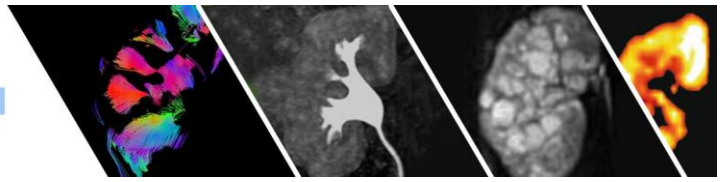

Assessment of Kidney Physiology using Dissolved Hyperpolarized 129-Xenon Magnetic Resonance Imaging

Action number CA16103
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Grantee name Jorge Chacón Caldera

PURPOSE OF THE STSM (max 500 words)

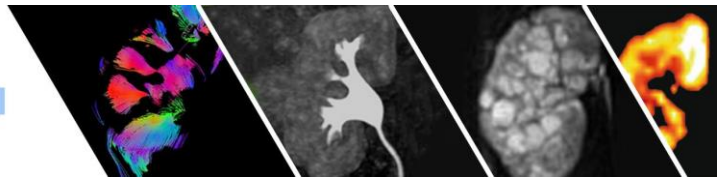
The early diagnosis of chronic kidney diseases is very challenging since a decrease in function in one kidney can be compensated by the other. It is not until the function of both kidneys has been severely affected that methods based on global filtration are able to detect abnormalities. MRI methods to assess renal physiology can analyse each kidney individually. However, they use gadolinium as contrast agent which is contraindicated in patients with kidney diseases. Novel contrast mechanisms e.g. those based on hyperpolarization could allow the assessment of single kidney function safely non-invasively. Here, dynamic spectroscopy and static imaging of dissolved hyperpolarized xenon-129 in the kidney have been recently demonstrated. This hints to a potential of xenon-129 to study renal function.

The purpose of the STSM was to establish and optimize methods (RF coils, sequences and protocols) to acquire hyperpolarized dissolved xenon-129 spectra and images in the human kidney at 3.0 T. In particular, the aim was to dynamically image the uptake of xenon-129 in the kidney and characterize the signal evolution in healthy volunteers. Based on this, an initial assessment of the standpoint and limitations of xenon-129 as a biomarker to analyse renal physiology could be performed.

Another purpose of the STSM was to begin a cooperative partnership between two renowned research groups with complementary expertise to investigate kidney function. In this sense, we intend to complement the know-how of hyperpolarized methods of the University of Sheffield and the expertise in proton (DCE and ASL) and 23Na methods of Heidelberg University. This can allow a more complete and accurate analysis of renal function.

DESCRIPTION OF WORK CARRIED OUT DURING THE STSM (max 500 words)

A crucial difference between traditional and hyperpolarized MR methods is that the polarization is finite and decreases with time (T1 relaxation mechanisms) and with deposited RF power. Thus, two important limitations are: 1) signal-to-noise ratio (SNR) and 2) RF pulses. Firstly, the SNR is an intrinsic limitation of the measurement technique since only a small fraction of the



inhaled xenon-129 gas is dissolved into the blood and transported to the kidneys. Moreover, the transit time from the lungs to the kidneys is in the order of seconds which entails some T1 relaxation. Secondly, the RF power i.e. the flip angle and pulse length as well as the number of pulses and the delay between them should be optimized. In our first approach, a purpose-built RF coil array was designed using a transmit-only-receive-only setup. Two receive coils were initially positioned posteriorly as near as possible to the kidneys to increase the sensitivity and consequently, the SNR. The coil count was later increased to six to further boost SNR. The transmit-only coils were likewise positioned targeting the kidney to decrease RF power deposition in the lungs and the aorta which would depolarize the xenon-129 in transit before reaching the kidneys. The purpose-built arrays were compared to a commercial volumetric quadrature transmit-receive coil.

Using global spectroscopy with a local transmit-receive coil, four peaks were recently shown in the kidneys using dissolved xenon-129 at 1.5 T (Miller GW, et al. 2017). In this STSM, we used global (dynamic) and localized (1D CSI, static) spectroscopy methods to investigate the peaks yielded by the xenon-129 in the kidneys at 3.0 T and compare to the previously found spectra. These experiments were also used to optimize the imaging protocols. More specifically, spectroscopy allowed us to select the centre frequency yielding the higher SNR which corresponded to the location (in frequency) of the peak with the greatest amplitude.

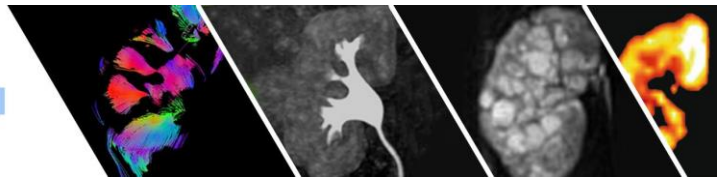
Two sequences, balanced and spoiled gradient echo (bSSFP and SPGR, respectively), were then tested using two different centre frequencies. The bSSFP sequence is known to be able to yield higher SNR images than SPGR when reaching steady-state. However, the minimum time between each dynamic acquisition is determined by the availability of signal in the kidneys. After the acquisition of one image, the RF pulses depolarize the xenon-129 in the kidneys. A delay allows the replenishment of polarized xenon-129 but prevents reaching the steady-state. In contrast, the SPGR is less sensitive to off-resonances and artefacts.

Using the optimized coils, centre frequencies and sequences, additional parameters were optimized such as spatial resolution, temporal resolution and flip angle. The optimization allowed us to obtain high resolution images which display the distribution of dissolved hyperpolarized xenon-129 in the body with great detail.

DESCRIPTION OF THE MAIN RESULTS OBTAINED (max 500 words)

An increase of SNR in the kidneys was observed using the purpose-built arrays in comparison to the commercial coil. As expected, the RF power deposited and sensitivity over the lungs and aorta were reduced. However, despite a lower SNR for the same acquisition parameters, the more homogeneous commercial coil with larger coverage showed the transit of the xenon from the lungs to the kidney. This information could also be useful when implementing kinetic models for the analysis of the signal.

The global dynamic spectroscopy showed the 4 peaks (red blood cells, kidney tissue, an unassigned peak and fat) found at 1.5 T and their evolution in time. We expect this information to be also useful in studying renal physiology. However, these spectra arise from the



combination of both kidneys which compromises a potential diagnostic utility of the tool given the aforementioned compensatory mechanisms between kidneys. Localized spectroscopy using 1D CSI allowed us to utilize a slice gradient which we used to avoid the excitation of signal in the lungs. Moreover, each kidney was separately analysed and the signal of the aorta was used as a reference with the limitation that the acquisition was static in time.
Dynamic imaging was obtained using bSSFP and SPGR. Both sequences showed similar peak SNRs since the steady-state was not reached. As expected, bSSFP showed higher sensitivity to the choice of centre frequency which demonstrated a higher reproducibility when using SPGR.
The protocol optimization allowed us to obtain dynamic imaging for more than 40 seconds using a spatial resolution of 15x16 mm^2. The spatial resolution was increased to 8.75x8.75 mm^2 for a single-shot image using the dynamic acquisitions as signal averages. The temporal resolution was also increased from 4 to 1 second. However, the RF pulses depolarized the xenon-129 in the kidneys and the delay was not enough for polarized xenon-129 to arrive from the lungs. This reflects the transit time which is in itself a physiological parameter.
Formally, the results will be presented in the form of a journal paper that is currently under preparation.

FUTURE COLLABORATIONS (if applicable, max 500 words)

The work developed so far is setting the foundations for a future collaboration partnership between the groups in Germany and the UK. This collaboration will have the purpose to collect further data and develop kinetic models that can describe the signal evolution in time observed with the dissolved hyperpolarized xenon-129. Additional work will be required to translate the kinetic models into physiological parameters to study renal function.
Some of the physiological parameters will then be validated using common proton methods. For instance, perfusion can be validated using arterial spin labelling. Furthermore, these parameters can be correlated an complemented using other x-nuclei approaches such as imaging using sodium-23 which provides a direct measurement of tissue sodium concentration and is expected to have an inverse correlation with perfusion.
Ultimately, we expect to forge a productive partnership in which the studies can be run in parallel using proton, hyperpolarized and x-nuclei methods. This could provide thorough evaluations of renal function and find relevant biomarkers for the early diagnosis of kidney diseases.

STSM PUBLICATION (if applicable, max 500 words)

Title of publication

Dissolved hyperpolarized xenon-129 MRI in human kidneys.

Authors

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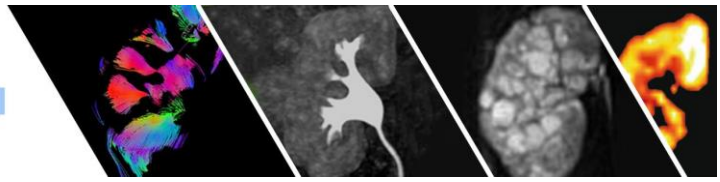


Abstract

Purpose

To assess the feasibility of using dissolved hyperpolarized xenon-129 (^{129}Xe) MRI to study renal physiology in humans at 3 T.

Methods

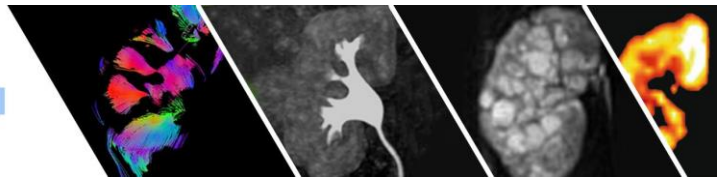
Using a flexible transceiver RF coil, dynamic and spatially resolved ^{129}Xe spectroscopy was performed in the abdomen after inhalation of hyperpolarized ^{129}Xe gas with 3 healthy male volunteers. A transmit-only receive-only RF coil array was purpose-built to focus RF excitation and enhance sensitivity for dynamic imaging of ^{129}Xe uptake in the kidneys using spoiled gradient echo and balanced steady-state sequences.

Results

Using spatially resolved spectroscopy, different magnitudes of signal from ^{129}Xe dissolved in red blood cells and tissue/plasma could be identified in the kidneys and the aorta. The spectra from both kidneys showed peaks with similar amplitudes and chemical shift values. Imaging with the purpose-built coil array was shown to provide more than a 3-fold higher SNR in the kidneys when compared with surrounding tissues, while further physiological information from the dissolved ^{129}Xe in the lungs and in transit to the kidneys was provided with the transceiver coil. The signal of dissolved hyperpolarized ^{129}Xe could be imaged with both tested sequences for about 40 seconds after inhalation.

Conclusion

The uptake of ^{129}Xe dissolved in the human kidneys was measured with spectroscopic and imaging experiments, demonstrating the potential of hyperpolarized ^{129}Xe MR as a novel, noninvasive technique to image human kidney tissue perfusion.



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