This is a repository copy of *Assessment of brain perfusion using hyperpolarized 129Xe MRI in a subject with established stroke.*.

White Rose Research Online URL for this paper:
https://eprints.whiterose.ac.uk/142223/

Version: Accepted Version

Article:
Rao, M.R., Norquay, G., Stewart, N. et al. (3 more authors) (2019) Assessment of brain perfusion using hyperpolarized 129Xe MRI in a subject with established stroke. Journal of Magnetic Resonance Imaging, 50 (3). pp. 1002-1004. ISSN 1053-1807

https://doi.org/10.1002/jmri.26686

This is the peer reviewed version of the following article: Rao, M. R., Norquay, G. , Stewart, N. J., Hoggard, N. , Griffiths, P. D. and Wild, J. M. (2019), Assessment of brain perfusion using hyperpolarized 129Xe MRI in a subject with established stroke. J Magn Reson Imaging, which has been published in final form at https://doi.org/10.1002/jmri.26686. This article may be used for non-commercial purposes in accordance with Wiley Terms and Conditions for Use of Self-Archived Versions.

Reuse
Items deposited in White Rose Research Online are protected by copyright, with all rights reserved unless indicated otherwise. They may be downloaded and/or printed for private study, or other acts as permitted by national copyright laws. The publisher or other rights holders may allow further reproduction and re-use of the full text version. This is indicated by the licence information on the White Rose Research Online record for the item.

Takedown
If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.

eprints@whiterose.ac.uk
https://eprints.whiterose.ac.uk/

Keywords

Hyperpolarized xenon, stroke, perfusion magnetic resonance imaging, comparison study.

Introduction

Recently, the possibility of directly imaging the uptake of hyperpolarized (HP) ^{129}Xe gas in the brain tissue of healthy normal subjects was demonstrated at the concentration achieved following the inhalation of a moderate (1 L) gas dose in the lungs (1-3). Inhaled xenon crosses the alveolar-capillary interface and is transported to the brain following the same pathway as oxygen. In this report, we demonstrate the clinical feasibility of hyperpolarized (HP) ^{129}Xe as an inhaled contrast agent for imaging cerebral tissue perfusion and viability, in a subject with an established stroke.

Material and Methods

The 52 year old subject provided informed written consent. He had a stroke 2 years 3 months before the current study and the intracranial arterial occlusion with collateralization was originally diagnosed on catheter angiography that was performed for clinical purposes. The study was conducted with the approval of UK Ethics committee.

1 L of ^{129}Xe was hyperpolarized to ~35% polarization using a spin-exchange optical pumping polarizer in less than 20 minutes (4). In vivo imaging was performed on a 1.5 T GE HDx MRI scanner using an RF coil array and MRI methods as described in an earlier study (1). The imaging parameters were; spoiled gradient echo pulse sequence; center frequency = 17660800 Hz (198 ppm downfield from the ^{129}Xe gas resonance); echo time (TE) = 1.7 ms; repetition time (TR) = 34 ms; flip angle (FA) = 12.5°; bandwidth (BW) = 4 kHz; field of view (FOV) = 22 cm. One 50 mm slice was acquired in an axial plane with the matrix size of 32 x 32, reconstructed to 80 x 80. Three images were acquired during a single breath hold at 8, 16 and 24 seconds after the inhalation of the xenon gas dose and were averaged.

For comparison with HP ^{129}Xe images, routine ^{1}H imaging was performed on a Philips Ingenia 3.0 T MRI scanner using a 32 channel ^{1}H RF coil array from the same manufacturer. ^{1}H imaging sequences were; T_2 weighted imaging (Multi-shot spin echo, TE = 80 ms, TR = 3 s, BW/Pixel = 217 Hz, slice thickness = 4 mm), pseudo-continuous Arterial Spin Labeling (Echo planar imaging, matrix = 80 x 80, slice thickness = 7 mm, FA = 40°, TE = 15 ms, TR = 4 s, labeling duration = 1650 ms, post label delay = 1525 ms) and Time of Flight vascular MR angiography (Gradient Echo, TE = 3.5 ms, TR = 23 ms, FA = 18°, BW/Pixel = 108 Hz). A map of cerebral blood flow (CBF) was estimated using the recommended parameters (5,6). 7 contiguous ASL images from the same anatomical location as the ^{129}Xe brain image were summed to form an effective slice of thickness of 49 mm, approximately the same as the HP ^{129}Xe brain image.

Results

The subject tolerated the xenon dose well and showed no marked change in SpO_2 as measured by finger probe. The subject had had a stroke resulting from an occlusion of the left internal carotid artery extending onto the origins of the anterior and middle cerebral arteries as shown in Figure 1. The stroke involved the anterior watershed region of the left hemisphere as shown in Figure 2(a). Previous X-ray catheter angiographic studies showed substantial collateralization of blood supply to the normal appearing brain around the infarction. CBF maps (5,6) from pseudo-continuous ASL (Figure 2(b)) indicate an increase in blood perfusion in the cortex of the left frontal and parietal lobes and the adjacent white matter as shown in Figure 2(c). The MRI from ^{129}Xe dissolved in the brain tissue is shown in Figure 2(d), which shows a much larger area of signal hypo-intensity, when compared with the routine T_2 weighted imaging (Figure 2(a)), ASL (Figure 2(b)) and CBF (Figure 2(c)).

Discussion

The MR signal of ^{129}Xe from the brain is weighted towards the most prominent spectroscopic peak, which is ^{129}Xe dissolved in the gray matter (1,2). Thus, imaging offers a method of imaging cerebral gas-uptake from capillaries to tissue rather than microvascular perfusion alone (1). The regions of signal hypo-intensity in the HP ^{129}Xe image (Figure 1(c)) indicate poor regional uptake of xenon, possibly due to delayed hyper-perfusion, impaired capillary gas exchange and tissue damage in the watershed region.

In contrast to xenon CT performed under steady-state breathing, where the concentration of xenon in the brain tissue is at equilibrium and is proportional to regional CBF (7), in this study (Figure 2(c,d)) we observe a signal hypo-intensity in the ^{129}Xe brain image that corresponds to a region of higher CBF (calculated from ASL). The mechanism of ^{129}Xe image contrast is a combination of capillary perfusion, gas-exchange, and T_1 relaxation and RF depolarization history of the dissolved signal on route to the brain tissue which does not directly equate to the mechanism of ASL.

The weaker regional ^{129}Xe signal may be due to a combination of factors, firstly a shorter regional mean transit time due to higher CBF may limit the diffusive transfer of xenon from the vasculature to the tissue reducing the initial concentration observed within a 24 s breath-hold, secondly this delayed blood supply to the infarcted region increases the residency time of HP ^{129}Xe in the blood before being delivered to tissue, which reduces the magnetization due to T_1 decay (8 s in blood (8); 15 s in grey matter (9)). Additionally, regional oxygenation may also contribute to contrast by changing the T_1 of ^{129}Xe (8). Considering these factors, the lack of differentiation between hypo-perfusion and hyper-perfusion can only currently be hypothesized, for example, acute stroke where hypo-perfusion due to thrombus is followed by hyper-perfusion after recanalization/collateralization. Nevertheless, the exact nature of these dynamic factors requires further investigations, which is the scope of future work.

In conclusion, we have demonstrated the feasibility of performing HP ^{129}Xe brain MRI in a clinical subject with an established cerebral pathology, thus introducing a technique which provides a distinct contrast to established imaging methods for regional cerebral tissue perfusion and diffusive gas uptake.

Acknowledgements: We would like to thank Julia Bigley for help and support in conducting some of the experiments.

References

1. Rao MR, Stewart NJ, Griffiths PD, Norquay G, Wild JM. Imaging Human Brain Perfusion with Inhaled Hyperpolarized (129)Xe MR Imaging. Radiology 2018;286(2):659-665.
2. Rao M, Stewart NJ, Norquay G, Griffiths PD, Wild JM. High resolution spectroscopy and chemical shift imaging of hyperpolarized (129) Xe dissolved in the human brain in vivo at 1.5 tesla. Magn Reson Med 2016;75(6):2227-2234.
3. Hane FT, Li T, Plata J-A, Hassan A, Granberg K, Albert MS. Inhaled Xenon Washout as a Biomarker of Alzheimer's Disease. Diagnostics 2018;8(2):41.
4. Norquay G, Collier GJ, Rao M, Stewart NJ, Wild JM. 129Xe-Rb Spin-Exchange Optical Pumping with High Photon Efficiency. Physical Review Letters 2018;121(15):153201.
5. Alsop DC, Detre JA, Golay X, et al. Recommended implementation of arterial spin-labeled perfusion MRI for clinical applications: A consensus of the ISMRM perfusion study group and the European consortium for ASL in dementia. Magnetic Resonance in Medicine 2015;73(1):102-116.
6. Buxton RB, Frank LR, Wong EC, Siewert B, Warach S, Edelman RR. A general kinetic model for quantitative perfusion imaging with arterial spin labeling. Magn Reson Med 1998;40(3):383-396.
7. Wintermark M, Thiran J-P, Maeder P, Schnyder P, Meuli R. Simultaneous Measurement of Regional Cerebral Blood Flow by Perfusion CT and Stable Xenon CT: A Validation Study. American Journal of Neuroradiology 2001;22(5):905-914.
8. Norquay G, Leung G, Stewart NJ, Tozer GM, Wolber J, Wild JM. Relaxation and exchange dynamics of hyperpolarized (129) Xe in human blood. Magn Reson Med 2015;74(2):303-311.

9. Kilian W, Seifert F, Rinneberg H. Dynamic NMR Spectroscopy of Hyperpolarized 129Xe in Human Brain Analyzed by an Uptake Model. Magnetic Resonance in Medicine 2004;51(4):843-847.

Figure Legends:

Figure 1: Brain angiogram images. A frontal projection of (a) X-ray CT angiogram performed for clinical purposes during the occurrence of stroke, 2 years 3 months before this study and (b) Time of Flight MR angiogram performed on the same day as this study for reference. The arrow on both images shows occlusion of the left internal carotid artery close to its bifurcation. Subject: Male Aged 52 years with established stroke.

Figure 2: Brain MR images acquired in the same session from the subject: Male Aged 52 years with established stroke. (a) Axial T_2 weighted image showing infarct in the centrum semiovale of the left cerebral hemisphere (arrow). (b) An axial image from pseudo-continuous arterial spin labelling (ASL) shows hyper-intensity in the cerebral cortex adjacent to infarction. (c) Map of cerebral blood flow (CBF) estimated from ASL in (b) shows increased perfusion. A peak CBF value of 110 ml / min / 100 g of tissue was observed as compared to the average value of 40 ml / min / 100 g of tissue in the healthy region. (d) Hyperpolarized ^{129}Xe brain image shows reduced uptake in the brain tissue supplied by the left internal carotid artery. The ^{129}Xe signal in the region of hypo-intensity in Figure 2(d) was 60 % lower when compared to the average signal in the healthy region.