



University of
Sheffield



Polarised lung and respiratory imaging Sheffield
POLARised Imaging Systems

Methods for and applications of hyperpolarised ^{129}Xe gas MRI

Jim Wild
Aarhus 2026

Disclosures

Researcher led grants / collaborations :

GE Healthcare, Vertex and Astra Zeneca

Founder University of Sheffield spinout, Sheffield SpinTec Ltd



^{129}Xe polariser physics



^{129}Xe Image
acquisition



RF coil integration



Integrating with
clinical MRI

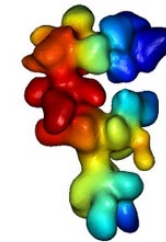
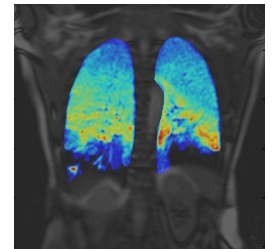


Image processing
and quantification

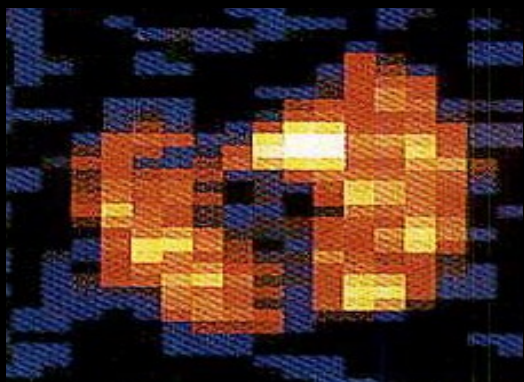


Clinical
evaluation

Methodology and applications of hyperpolarised gas and lung MRI

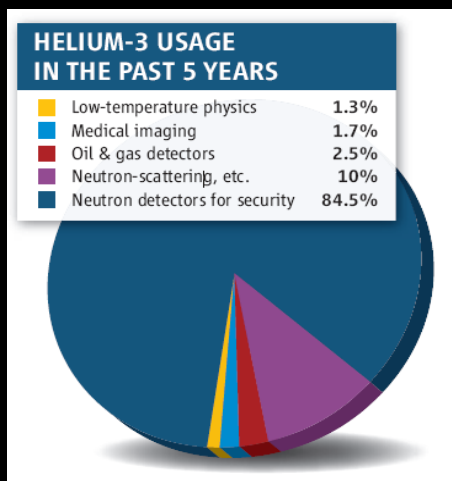
Overview

- ^{129}Xe MRI – background physics and engineering
- ^{129}Xe MRI acquisition and quantification methods
- Pathophysiological sensitivity – ventilation, microstructure, gas exchange - quantitative metrics
- Examples of clinical utility

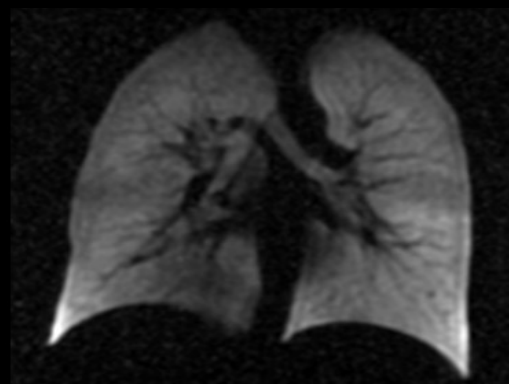


First ^{129}Xe gas MRI mouse lungs

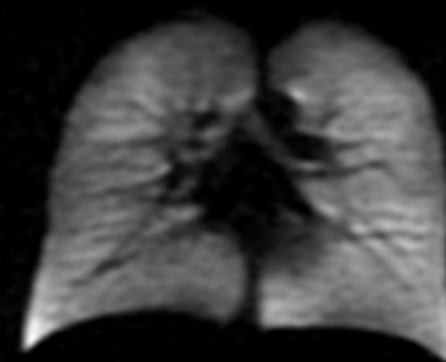
Albert et al Nature 1994



Science 2009 vol 326



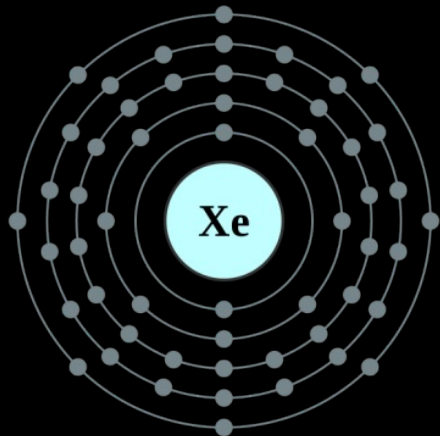
^3He



^{129}Xe

Hyperpolarised ^{129}Xe MRI

18
2 He
10 Ne
18 Ar
36 Kr
54 Xe
86 Rn
118 Uuo



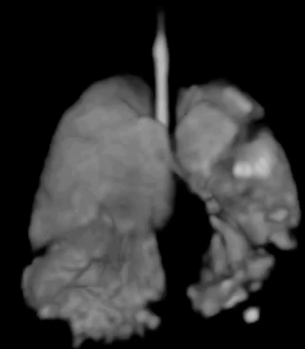
Xenon - derived from
Greek '*xenos*' - stranger



Laser
hyperpolariser

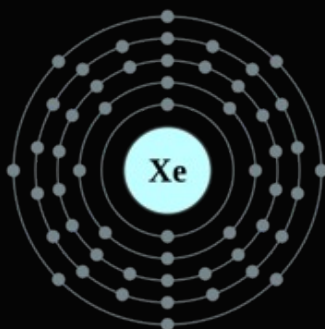


Inhaled ^{129}Xe lung
image



NMR properties

18
2 He
10 Ne
18 Ar
36 Kr
54 Xe
86 Rn
118 Uuo

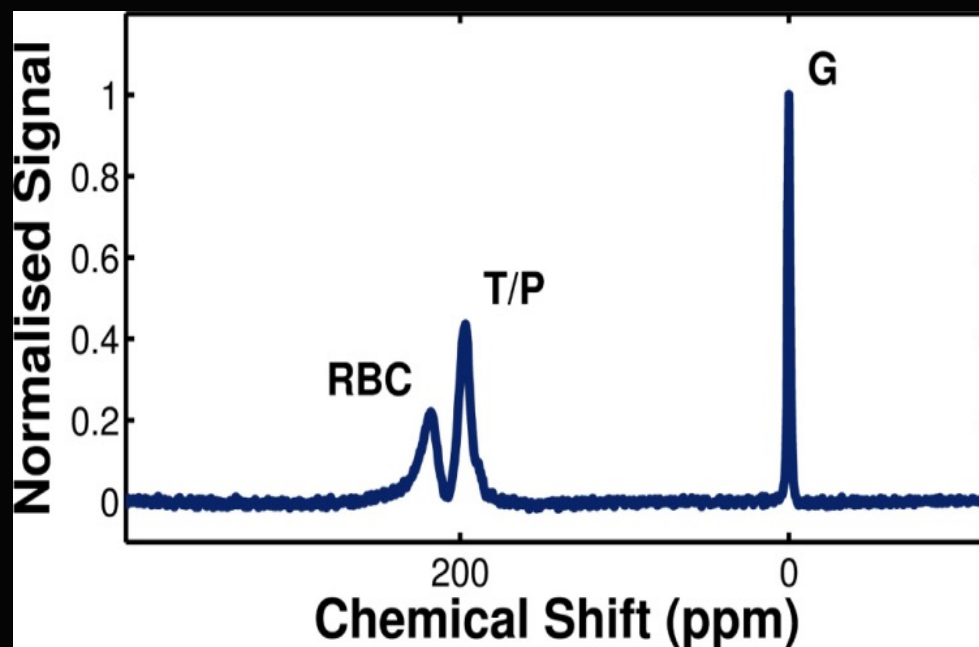
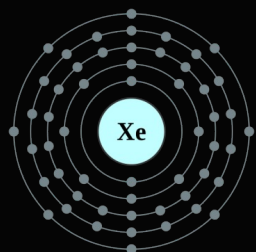


Xenon -
Greek '*xenos*'
stranger



Property	^1H	^3He	^{129}Xe	^{19}F
Nuclear spin, I	1/2	1/2	1/2	1/2
Gyromagnetic ratio, γ (MHz/T)	42.58	-32.44	-11.78	40.07
T2* in gas phase		14-28 ms	30-50 ms	~4 ms
T1 in gas phase	-	20 s	40 s	~12 ms
T1 dissolved in blood /tissue			2-10 s	
ADC in healthy lungs (cm^2s^{-1})	-	~ 0.2	~ 0.04	~0.015 (C_3F_8)
Cost (£/L)	-	~ 500?	~ 200 £/l ~80%)	
			~ 20 £/l (NA ~ 26%)	2 (>10L needed)

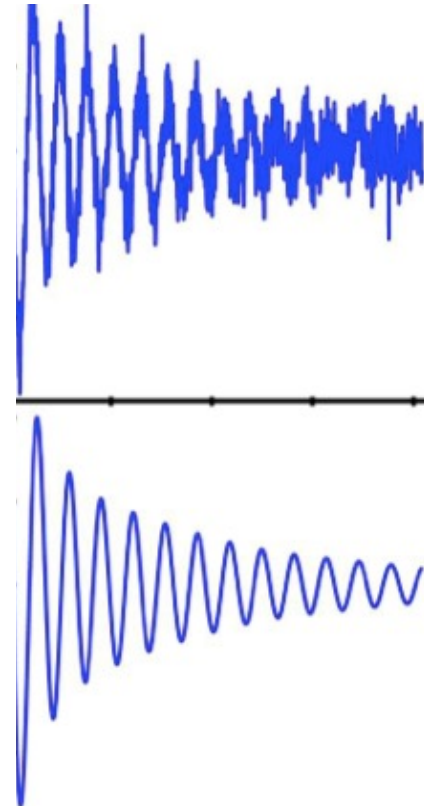
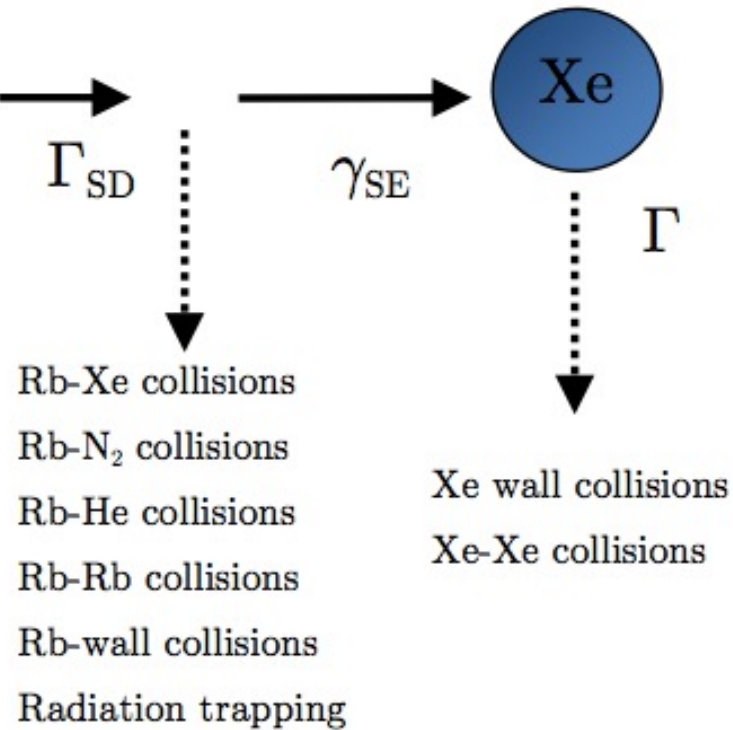
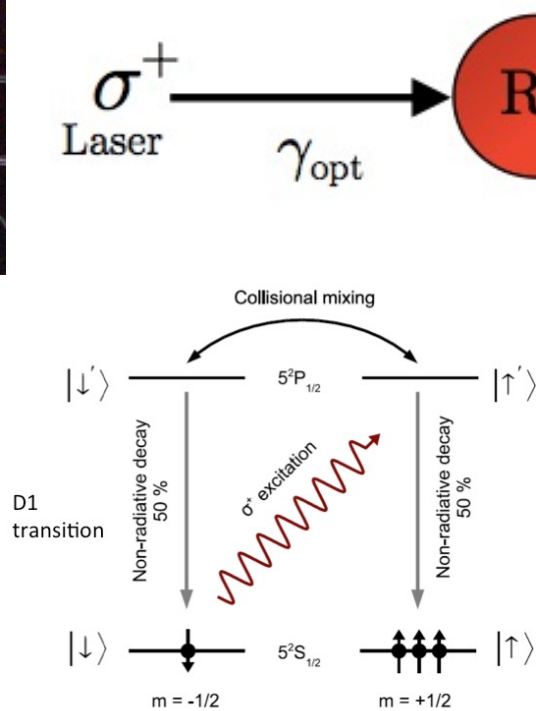
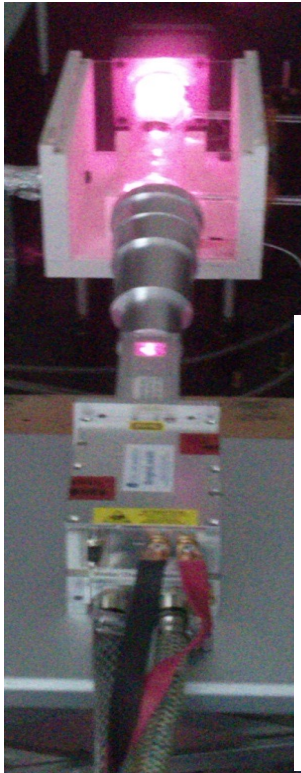
^{129}Xe solubility and chemical shift



^{129}Xe lung spectrum

Solvent	Ostwald Solubility Coefficient, λ	Chemical shift, δ (ppm)
Distilled H_2O	0.083	190
Saline	0.078 – 0.093	194 – 196
Olive oil	1.79 – 1.83	198
Adipose tissue	1.715	191
Plasma	0.091 – 0.103	192 – 197
RBCs	0.19 – 0.27	216 – 222

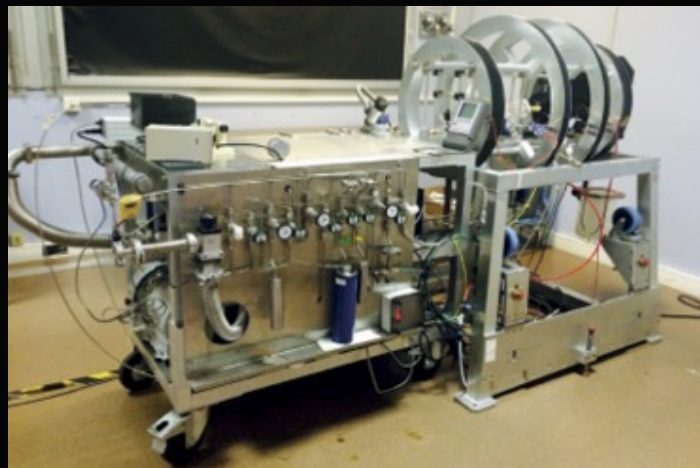
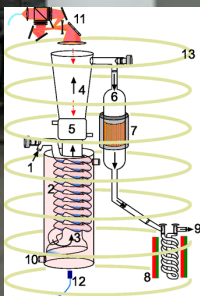
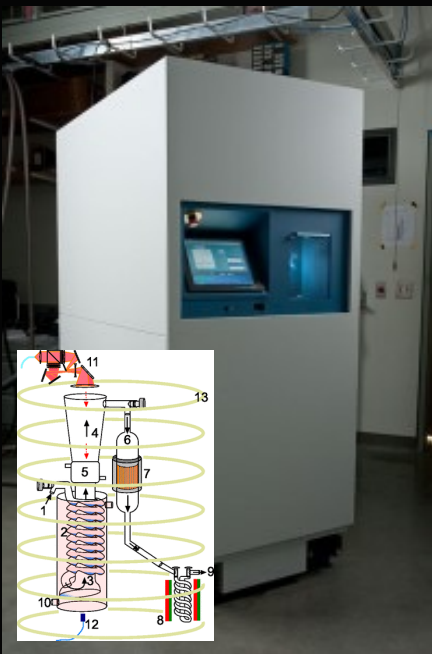
^{129}Xe hyperpolarisation with spin exchange optical pumping



Laser power - IN

Nuclear spin polarisation - OUT

^{129}Xe SEOP Polarisers



large-scale ^{129}Xe SFC

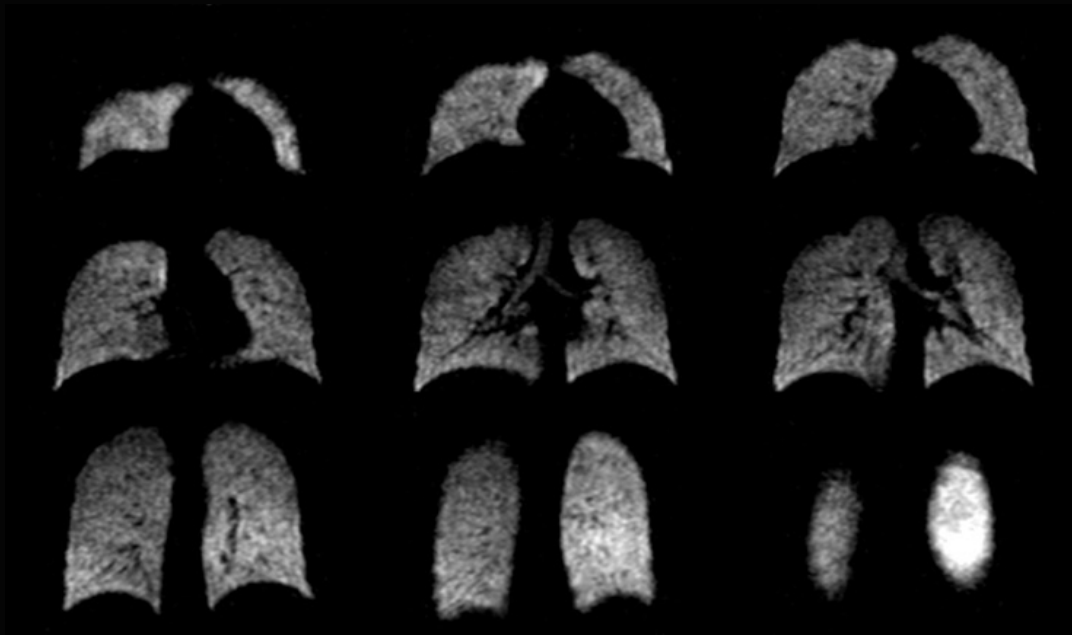


- Generation of 500 mL ^{129}Xe “o

Phys Rev Let 121, 153201 (2018)

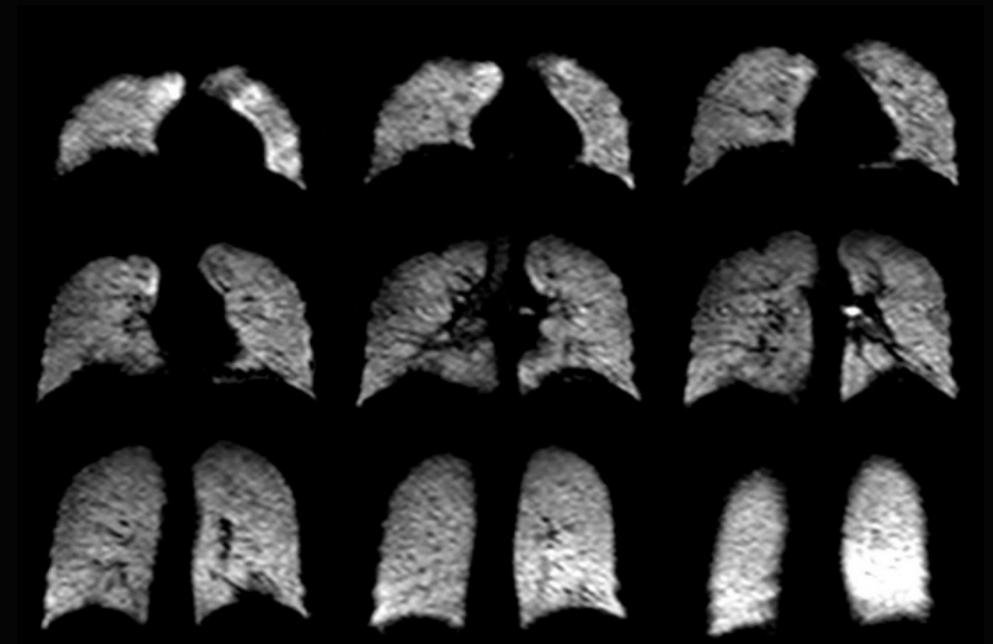


HP ^{129}Xe Gas MRI - field strength dependence



1.5 T

17.7 MHz
T2* 25-52 ms



3 T

35.4 MHz
T2* 18-24 ms

Cystic Fibrosis lung ventilation MRI @ 1.5T and 3T

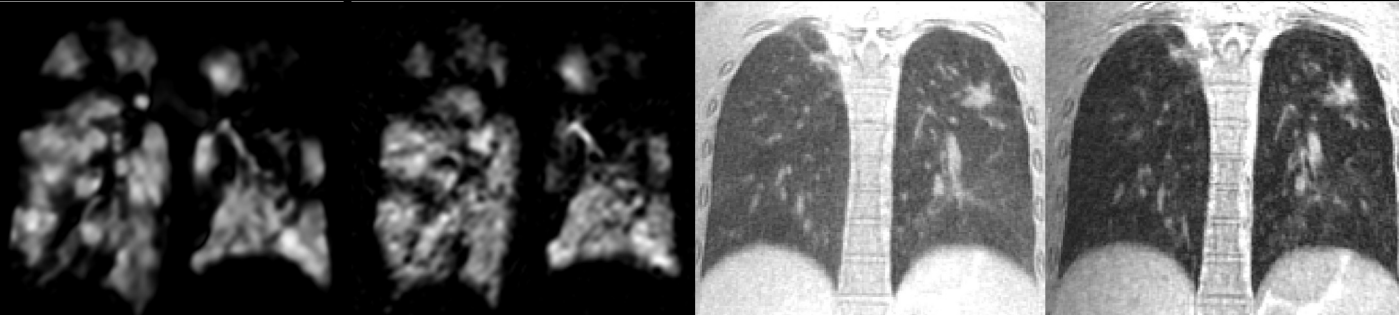
1.5T Xe

3T Xe

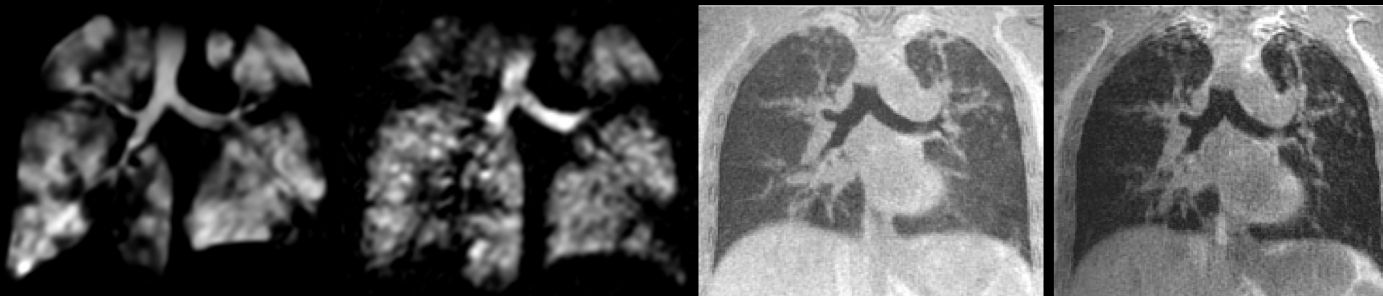
1.5T UTE

3T UTE

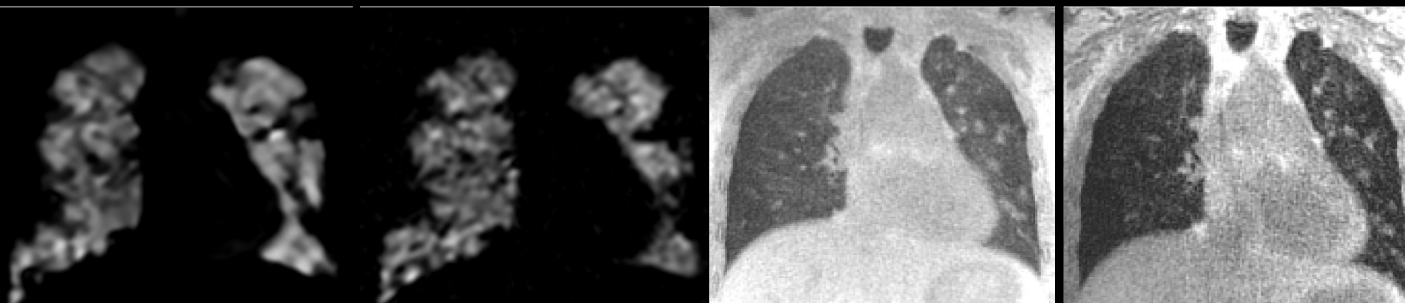
Posterior



Central



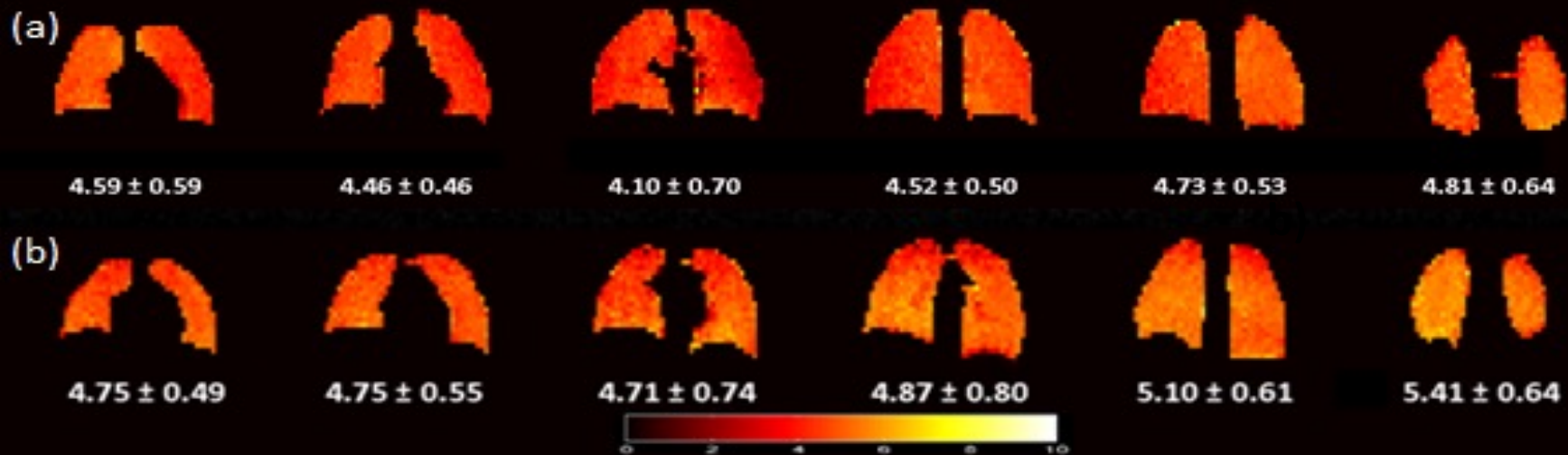
Anterior



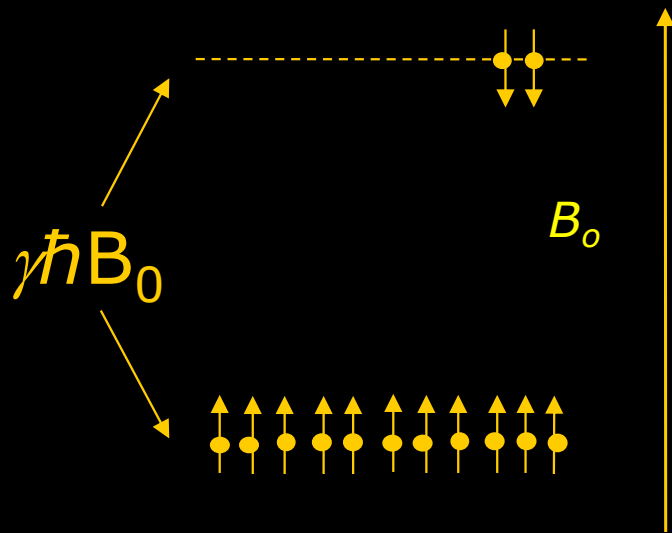
RF coils for ^{129}Xe – T/R



Vest



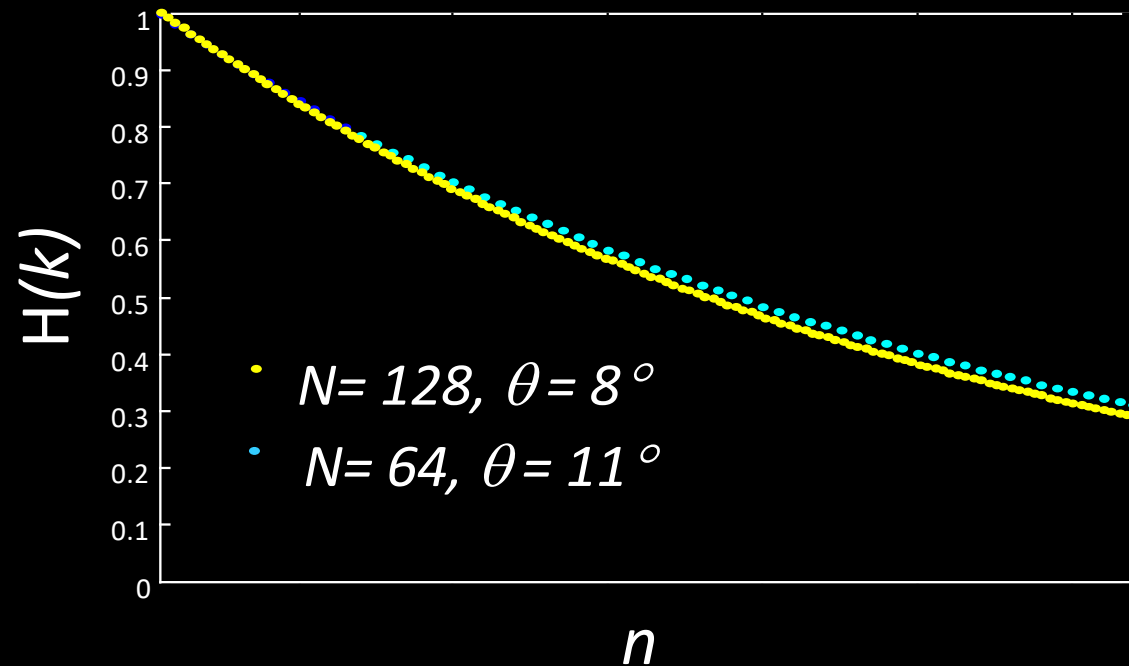
Best use of hyper- polarisation



small flip angles with spoiled sequences

$$S(n) = S_0 \sin \alpha (\cos(\alpha))^{n-1}$$

RF flip angle and k-space filter effect



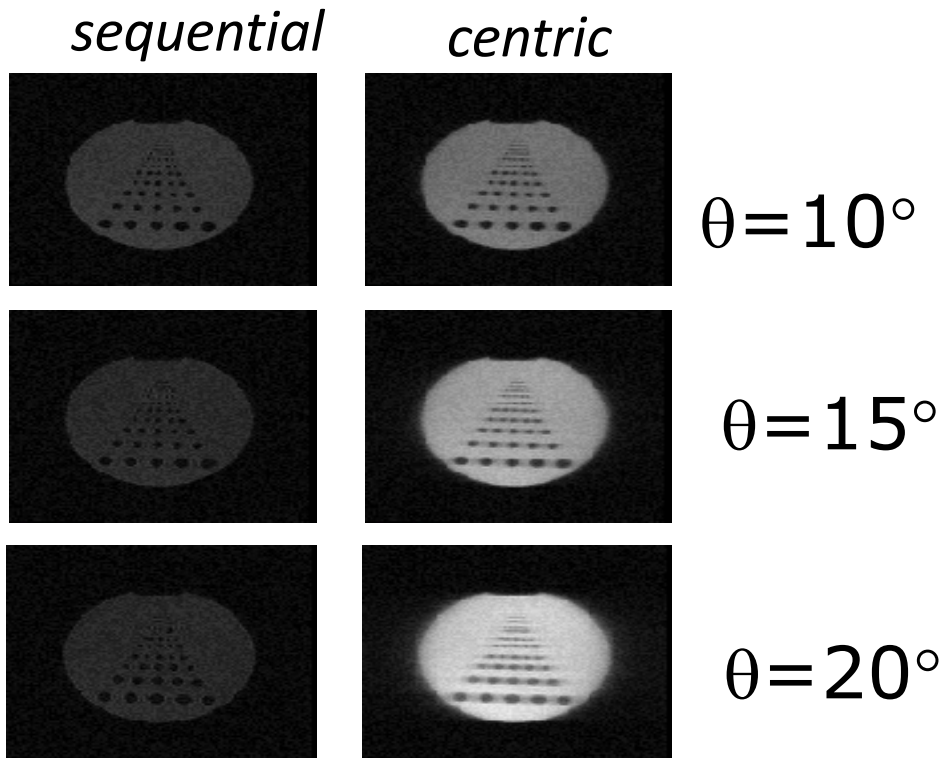
Undersampling – increase the FA when reducing N to overcome the SNR penalty ($\text{SNR} \propto \sqrt{N}$)

Polarisation constraint

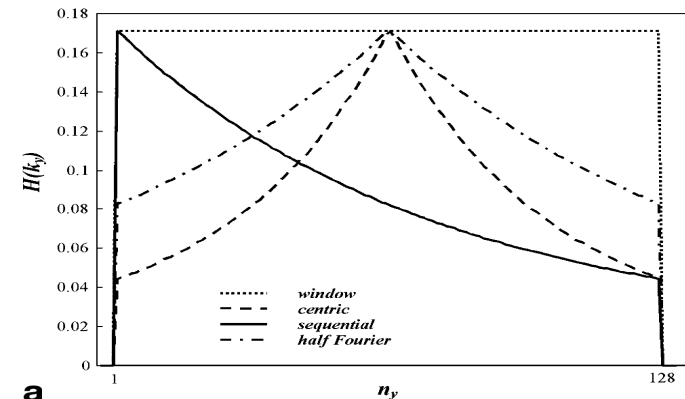
$$M_y(n) = M_0(\cos \theta)^{n-1} \sin \theta \exp(-NT_R/T1(p0_2))$$

RF k-space filter $H(k_y)$

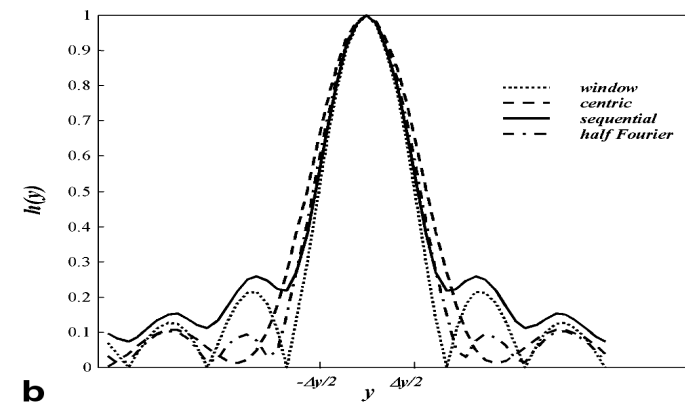
$$\tan(\alpha_{opt}) = \left(\sqrt{(N/2) - 1} \right)^{-1}$$



Magn Reson Med, 47, 687, 2002.



k_y -filter



PSF

Variable flip angle spoiled gradient echo

Use a progressively increasing F.A. to maintain constant transverse magnetisation M_{xy}

use ALL the Longitudinal magnetisation up – most efficient use of polarisation

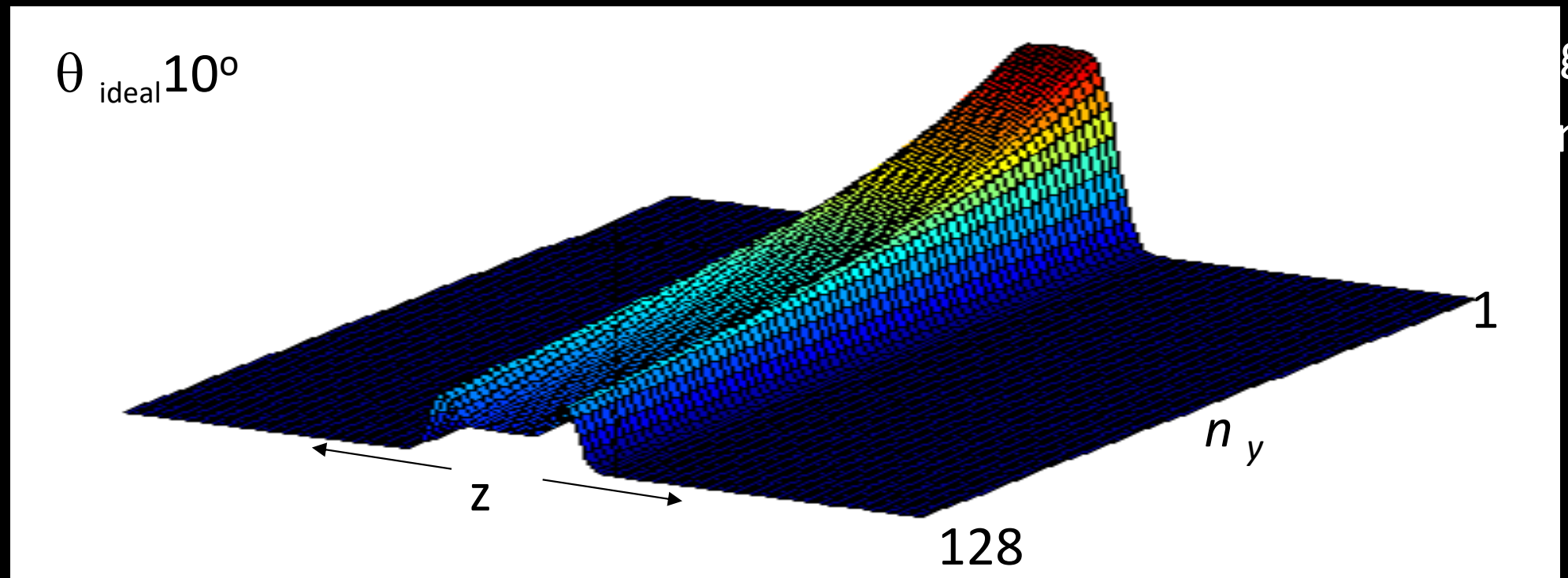
For a given N ; $SNR \propto \sin\theta_1$ $\theta(n) = \arctan\left(\frac{1}{\sqrt{N-n}}\right)$

VFA technique introduces no additional blurring :

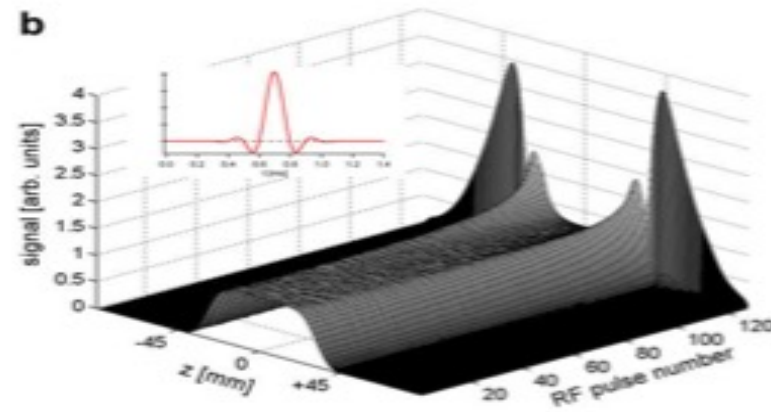
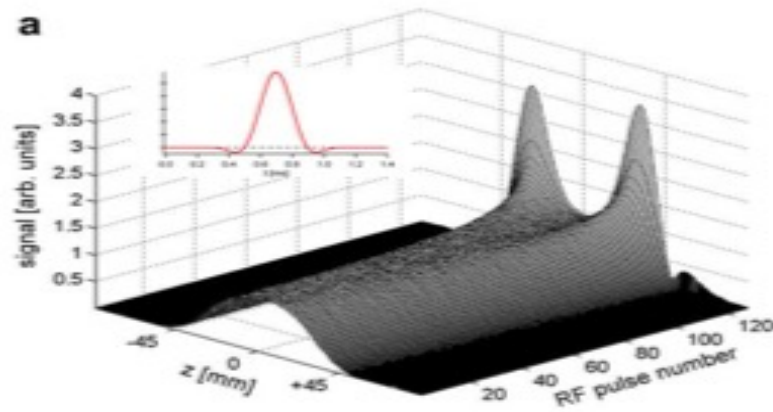
$H(k_y) = \text{constant}$

$$\tan(\alpha_{opt}) = \left(\sqrt{(N/2)-1}\right)^{-1}$$

2D or 3D?

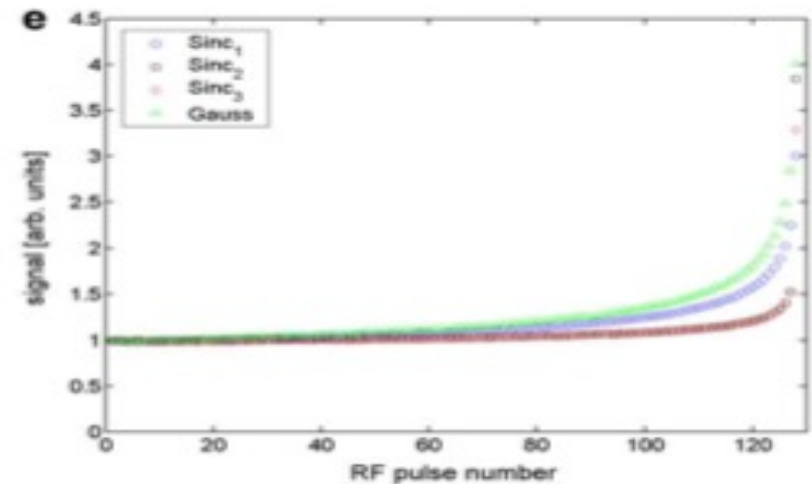


Slice profile effects with variable flip angle



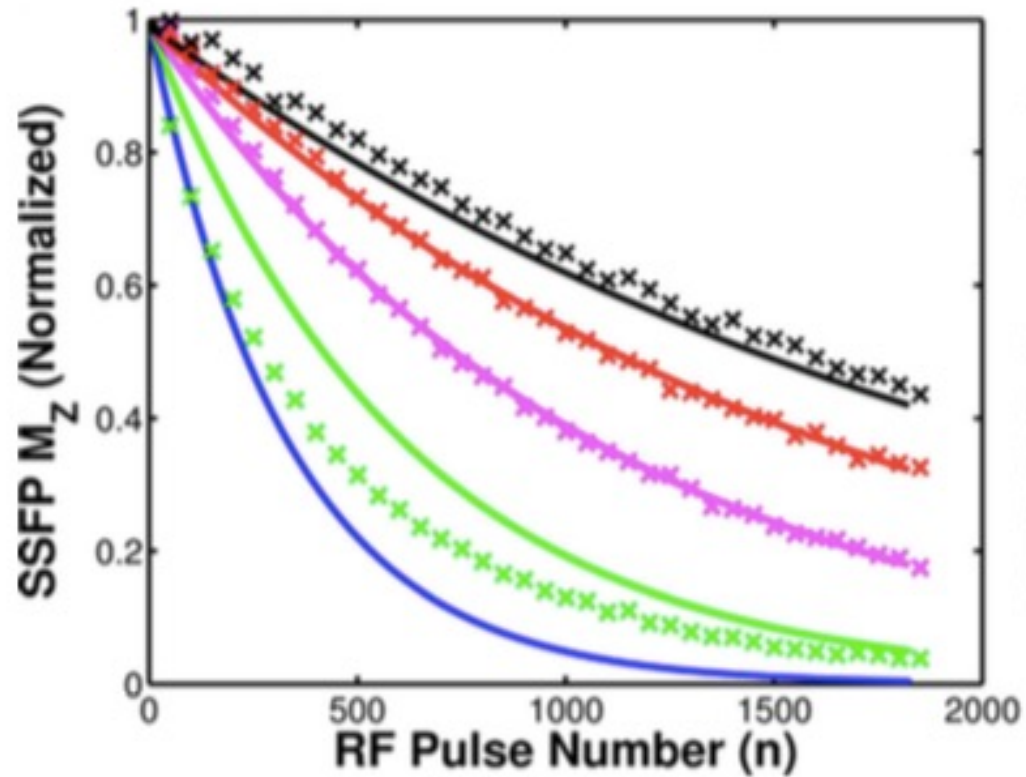
Compensate by :

- discarding data
- pulse –pulse slice profile modulation

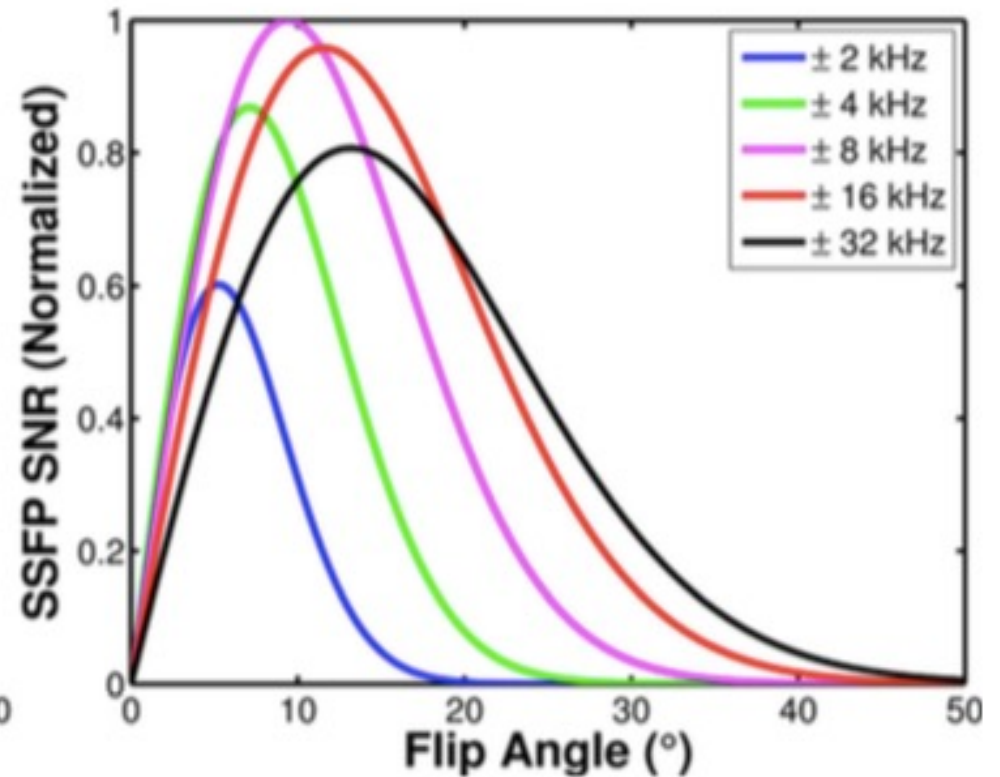


Journal of Magnetic Resonance 202 (2010) 180–189

Recycle magnetisation - SSFP

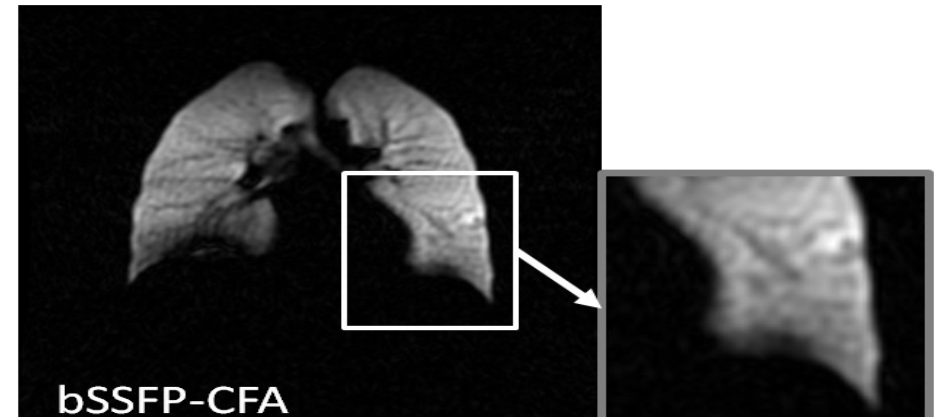
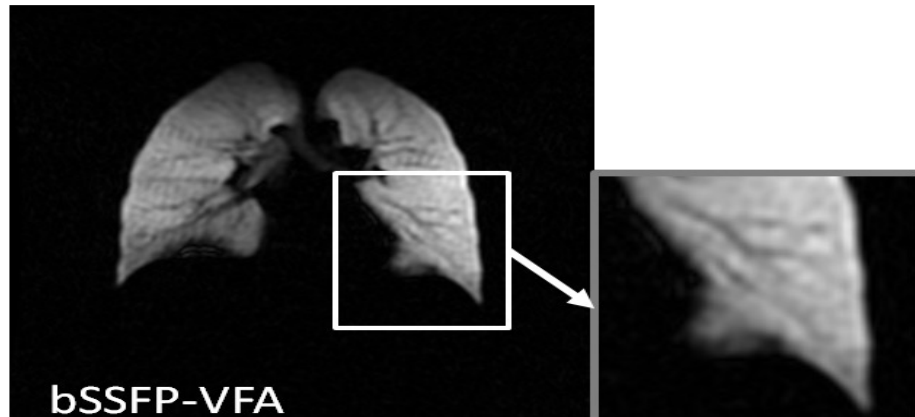


Wild et al J MagnReson, 183 (2006) 13–24,

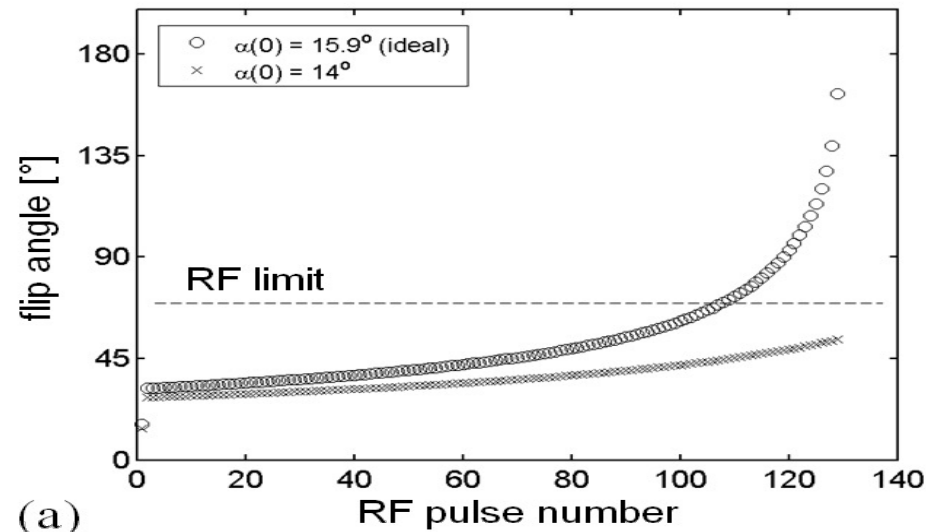


N. J. Stewart et al., Magn Reson Med, 74, 2 (2015).

VFA-SSFP



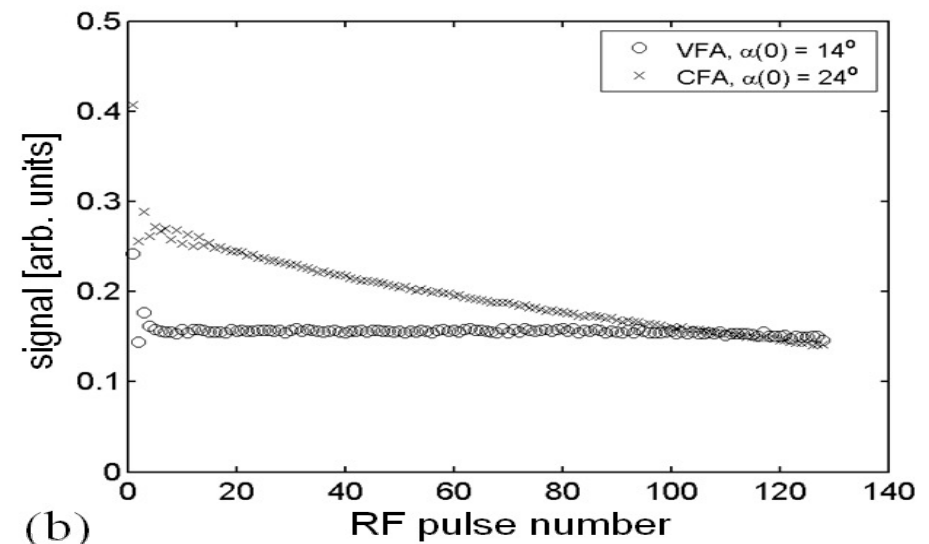
(a)



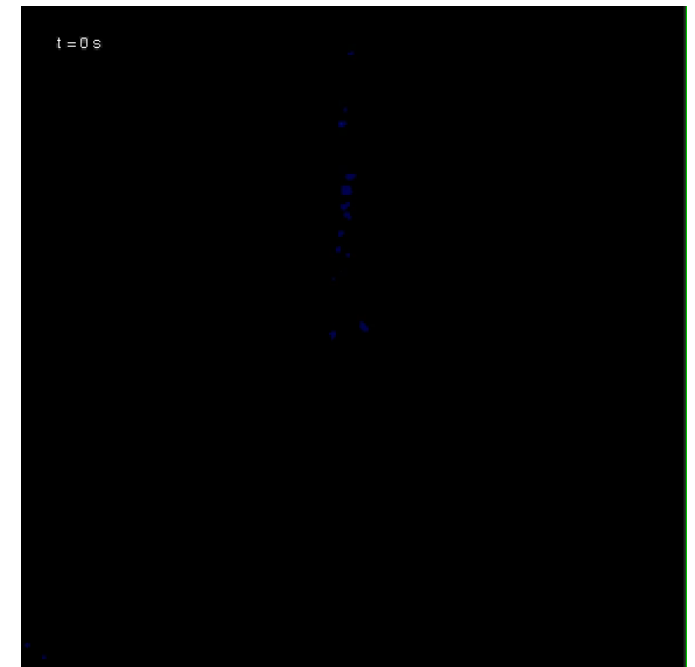
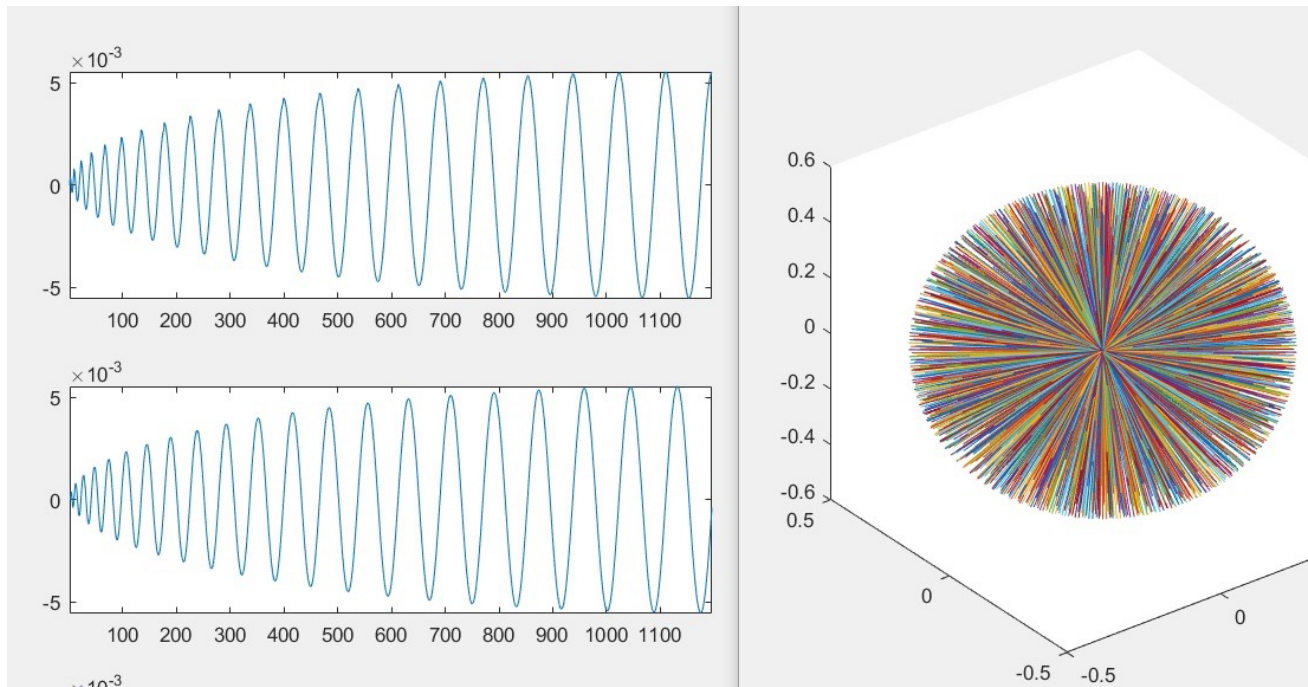
(c)

(a)

(b)

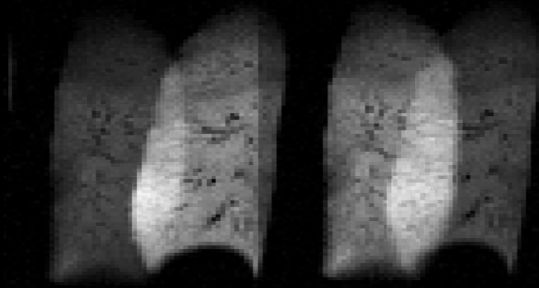


Non Cartesian sampling

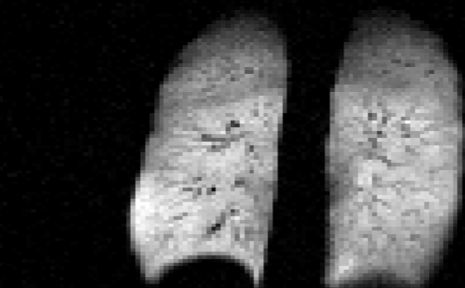


- short TE for dissolved ^{129}Xe
- undersampling and view sharing for dynamic imaging

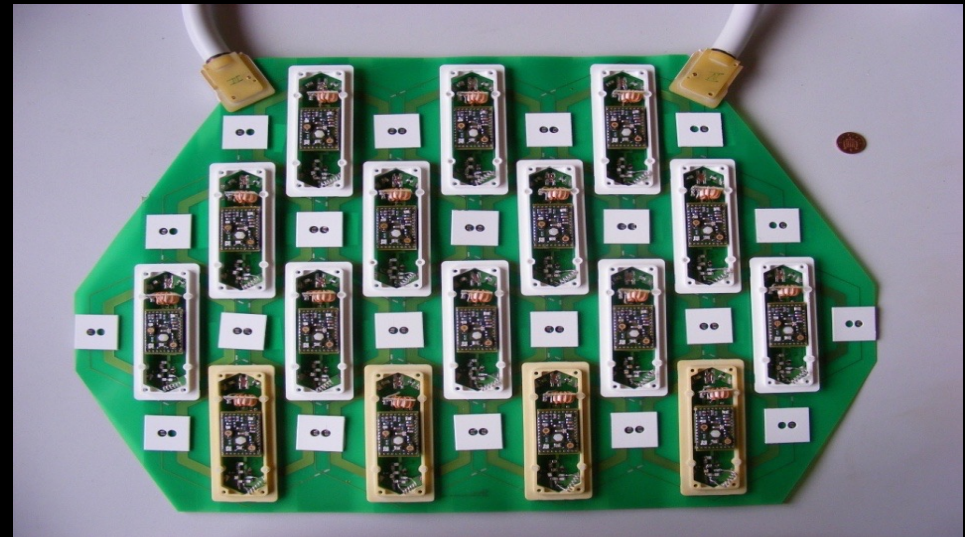
Parallel Imaging – efficient use of polarisation



$R=2$

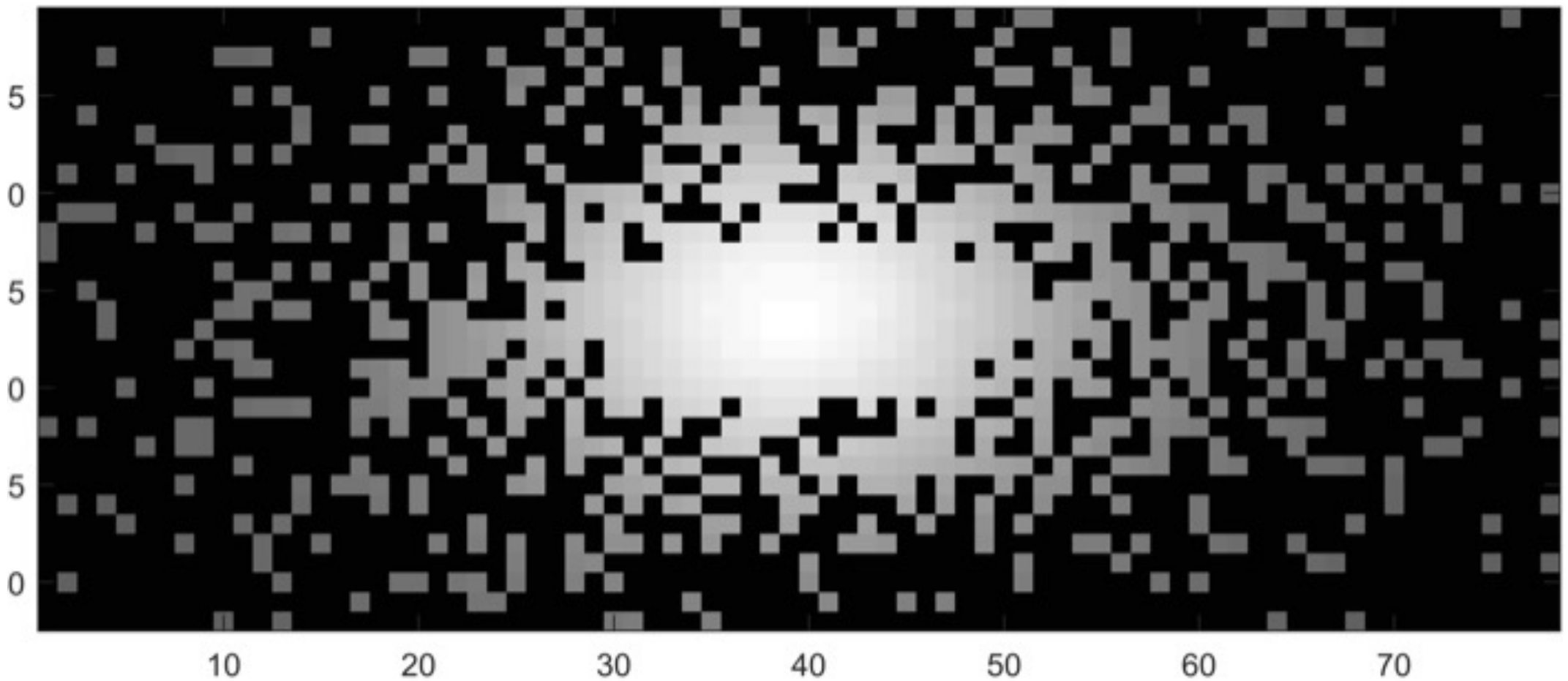


$R=4$



Deppe et al Magn Reson Med. 2011 Dec;66(6):1788-97.

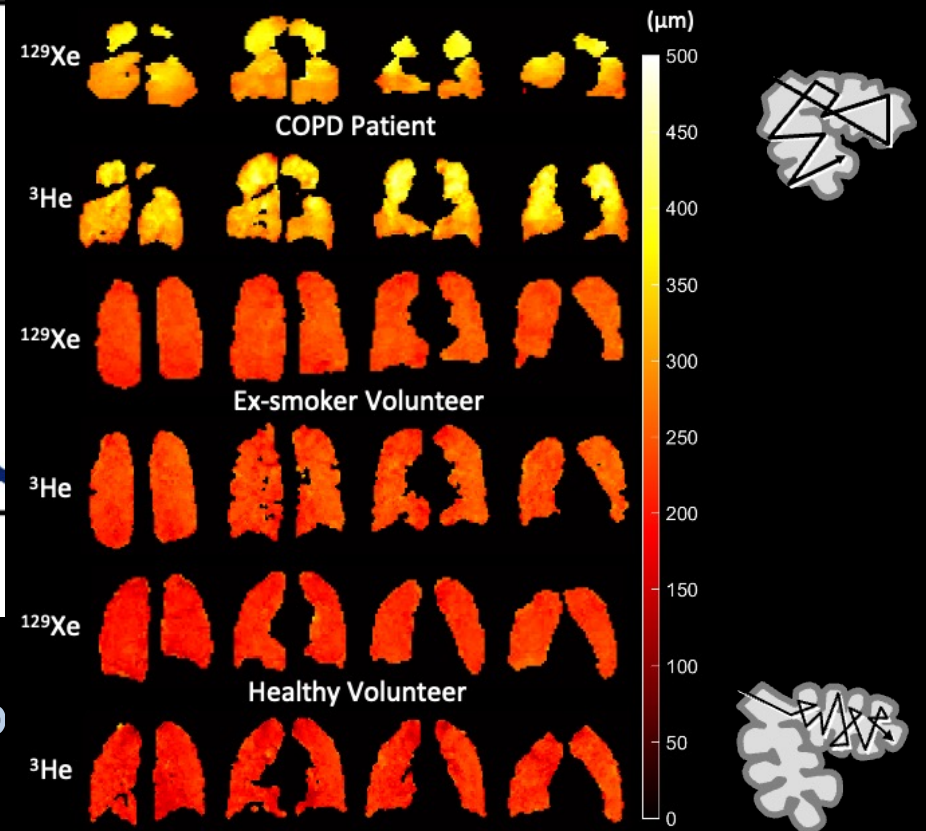
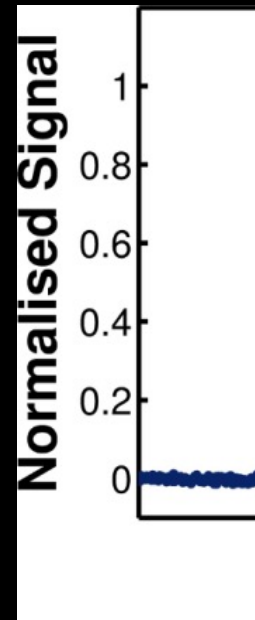
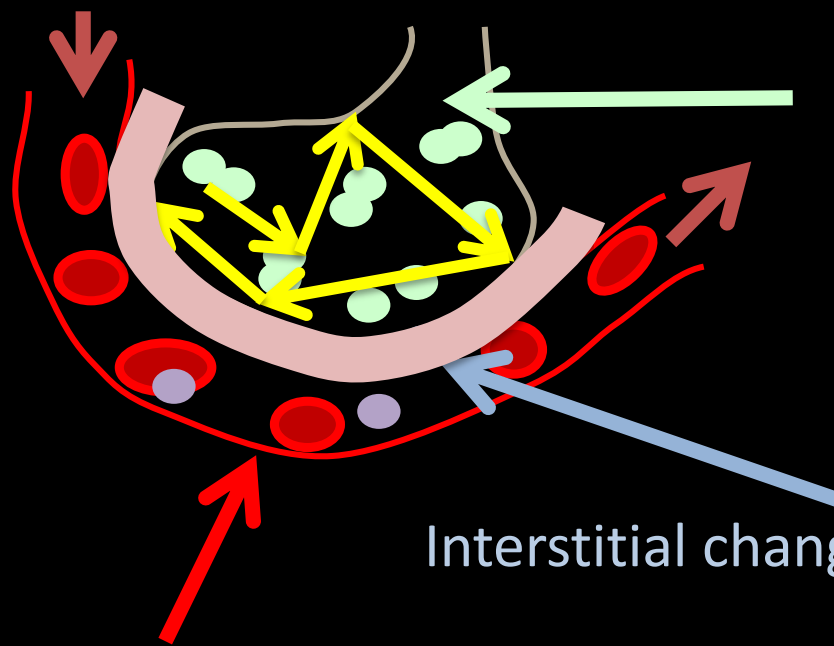
Image acceleration with 3D Compressed Sensing



Collier et al Magn Reson Med. 2019 Jul;82(1):342-347.

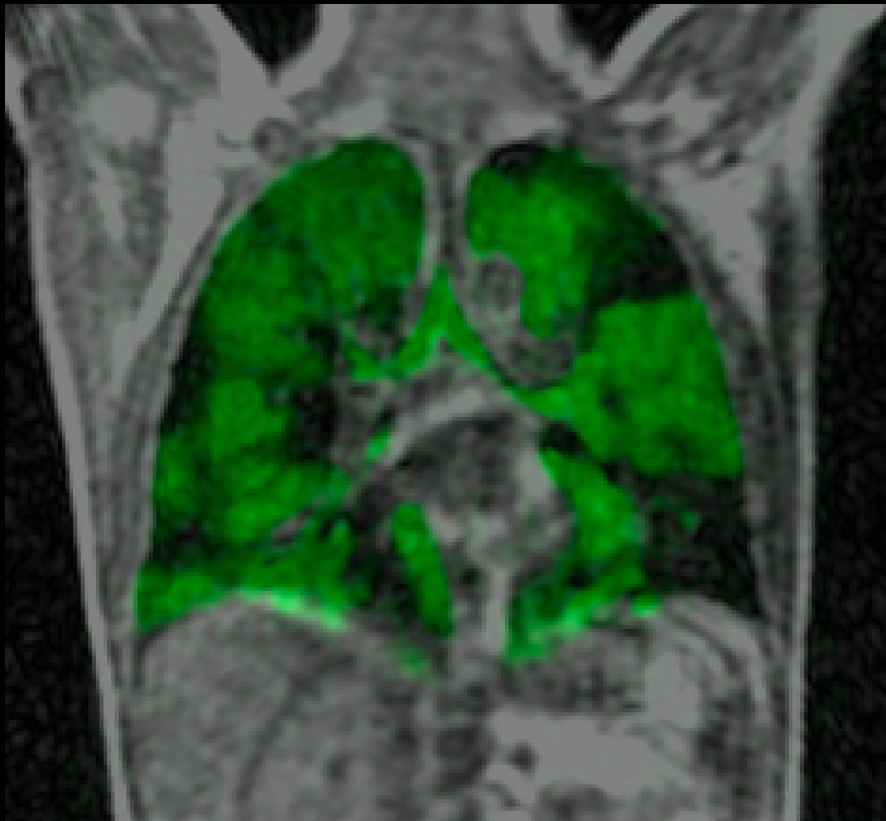
Ajraoui et al Magn Reson Med. 2010 Apr;63(4):1059-69

^{129}Xe MRI - assessment of structure and function



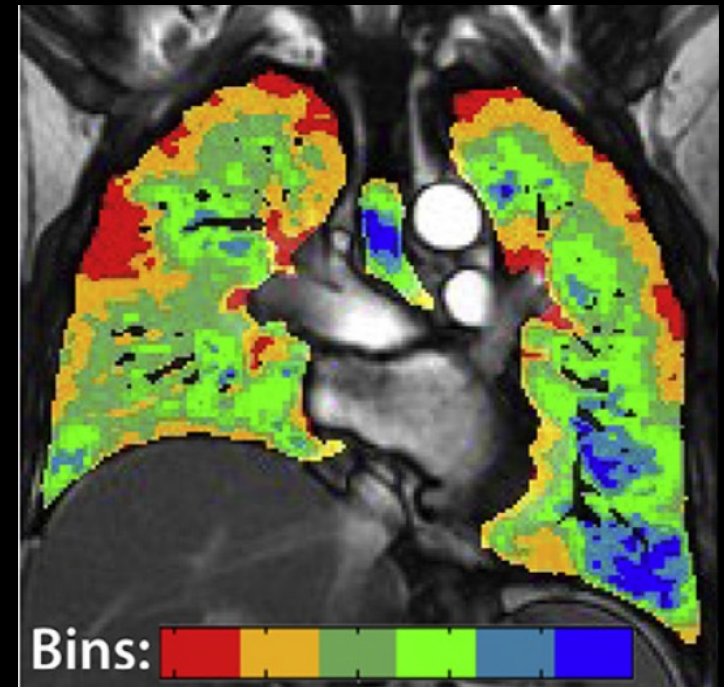
Acinar microstructure - Brownian diffusion weighted MRI (DW-MRI)
 Absorbed by RBCs - capillary perfusion

Ventilation defect percentage ($VDP = 1 - \text{VV}/\text{TLV}$)



Ventilation Image
 ^1H Proton MRI

Image
segmentation



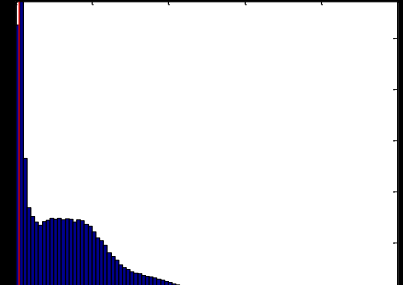
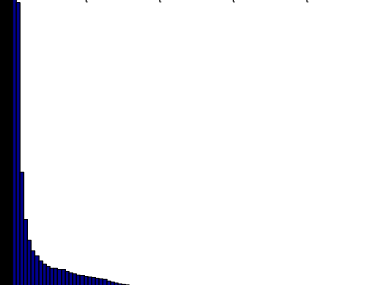
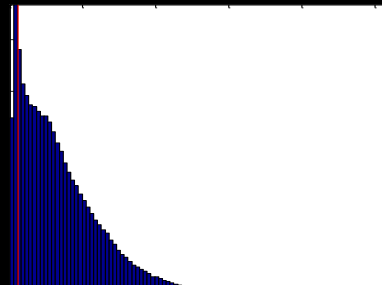
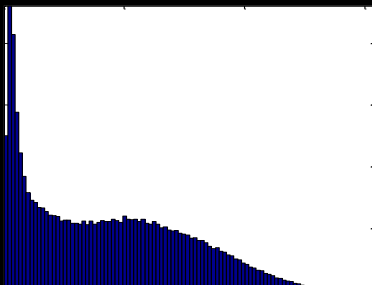
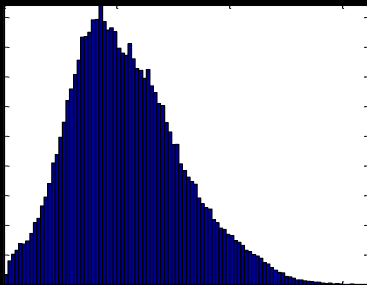
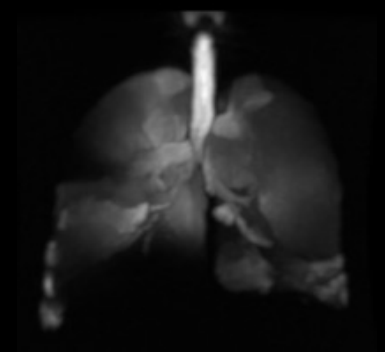
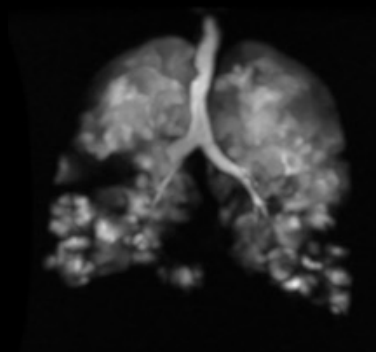
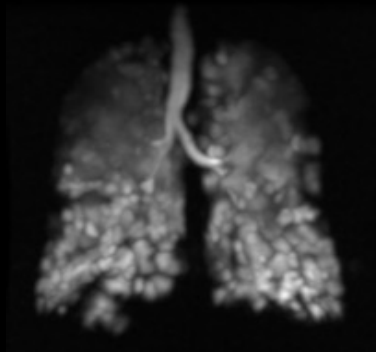
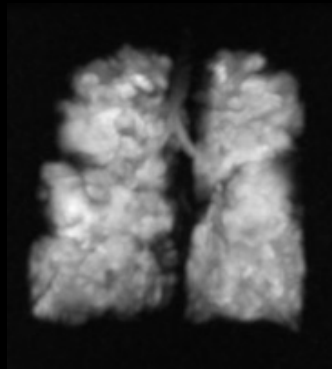
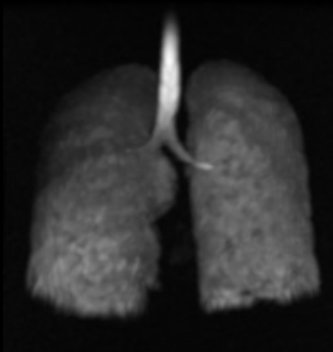
Ventilation Mask
 ^1H Proton Mask

Quantitative analysis of ventilation

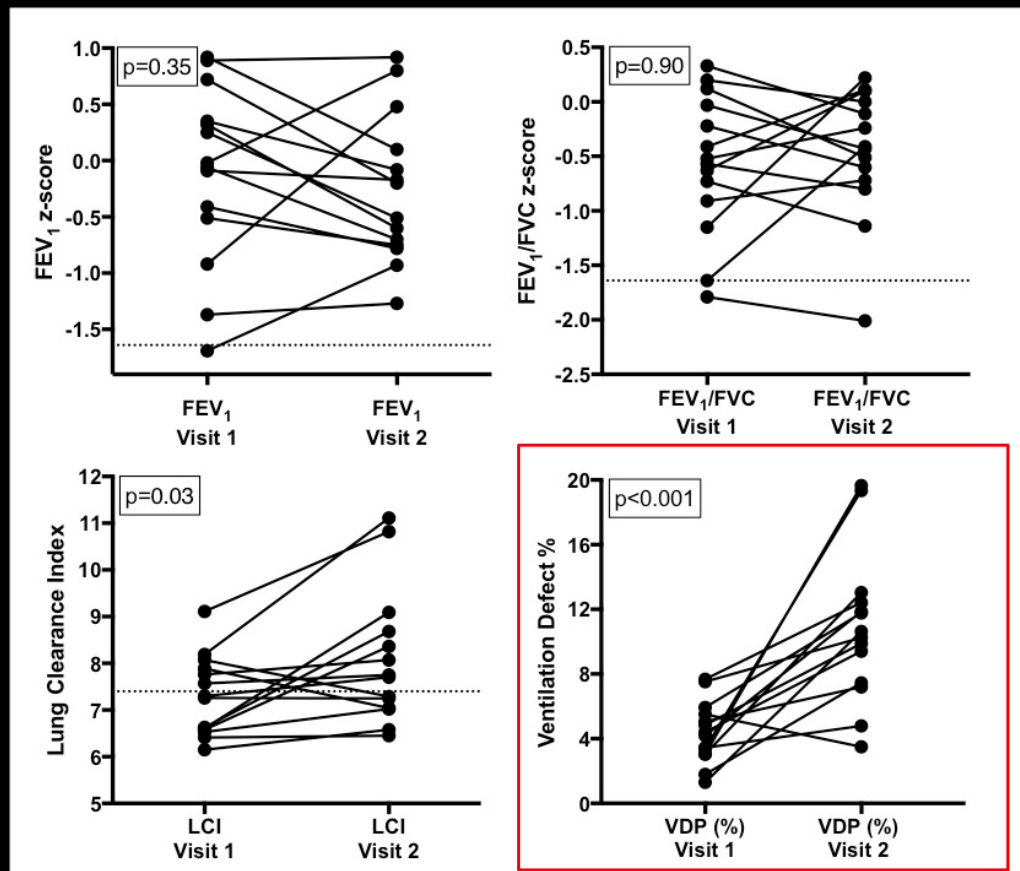
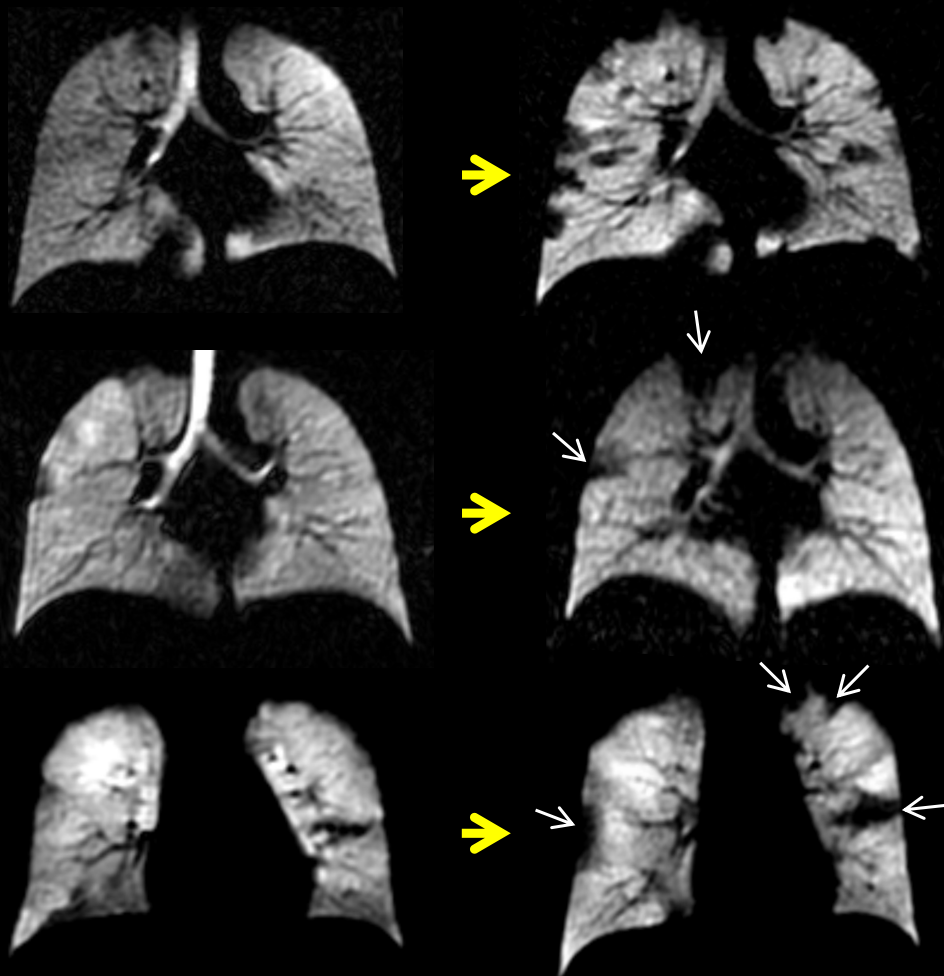
Healthy

Smoker

COPD



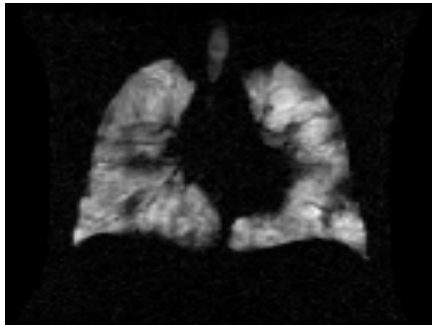
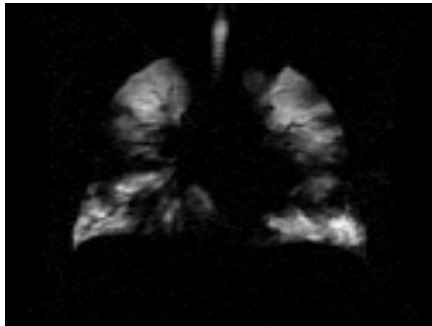
Longitudinal assessment of lungs in children with Cystic Fibrosis - 2 years



Smith et al, AJRCCM (2018)

Asthma - treatment response mapping

Mean baseline

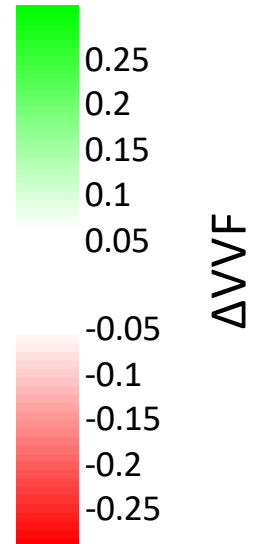


Post
Bronchodilator

Asthmatic pre and post bronchodilator



ΔVVF
(post - pre)



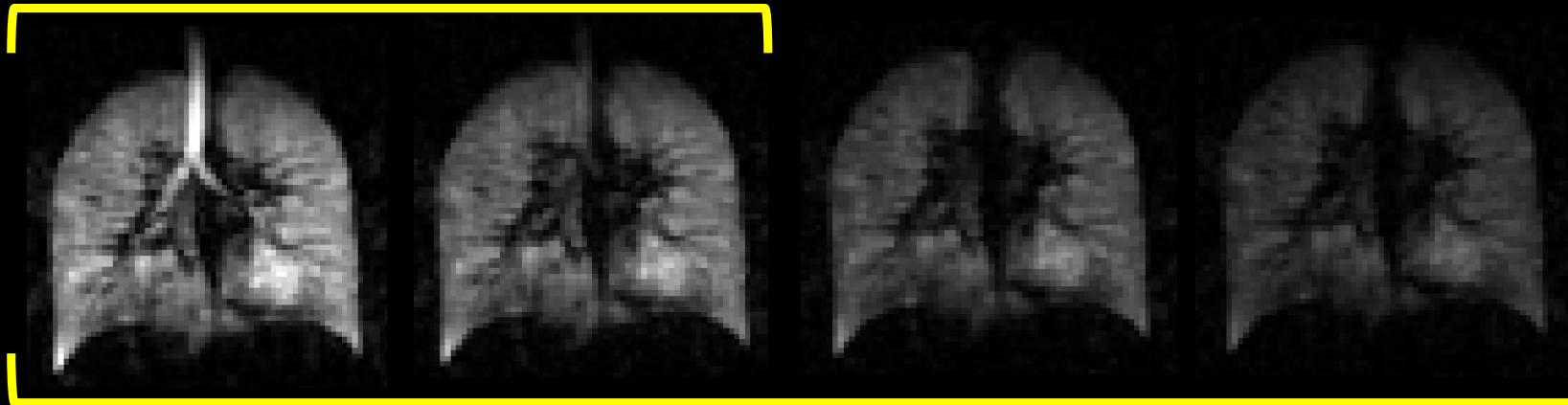
Horn et al Radiology 2017

Diffusion weighted ^{129}Xe MRI – interleaved acquisition

b-values
(diffusion)
gradients



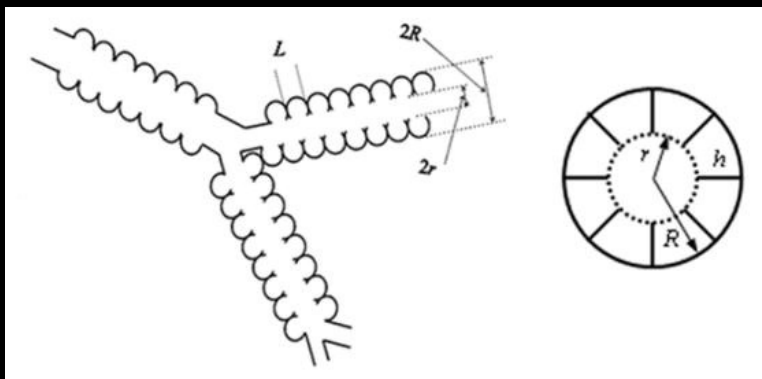
ADC = measurement of **diffusion**



Multiple b-values - sample non-mono exponential diffusion e.g. 0, 10, 20, 30 ...s/cm²

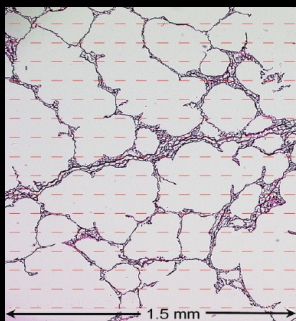
- In vivo theoretical gas diffusion models to extract **lung morphometry** parameters from the non-mono exponential signal decay

^3He and ^{129}Xe - 3D alveolar morphometry from diffusion MRI



Cylinder model

Sukstanski et al Magn Reson Med. 2012 Mar;67(3):856-66.

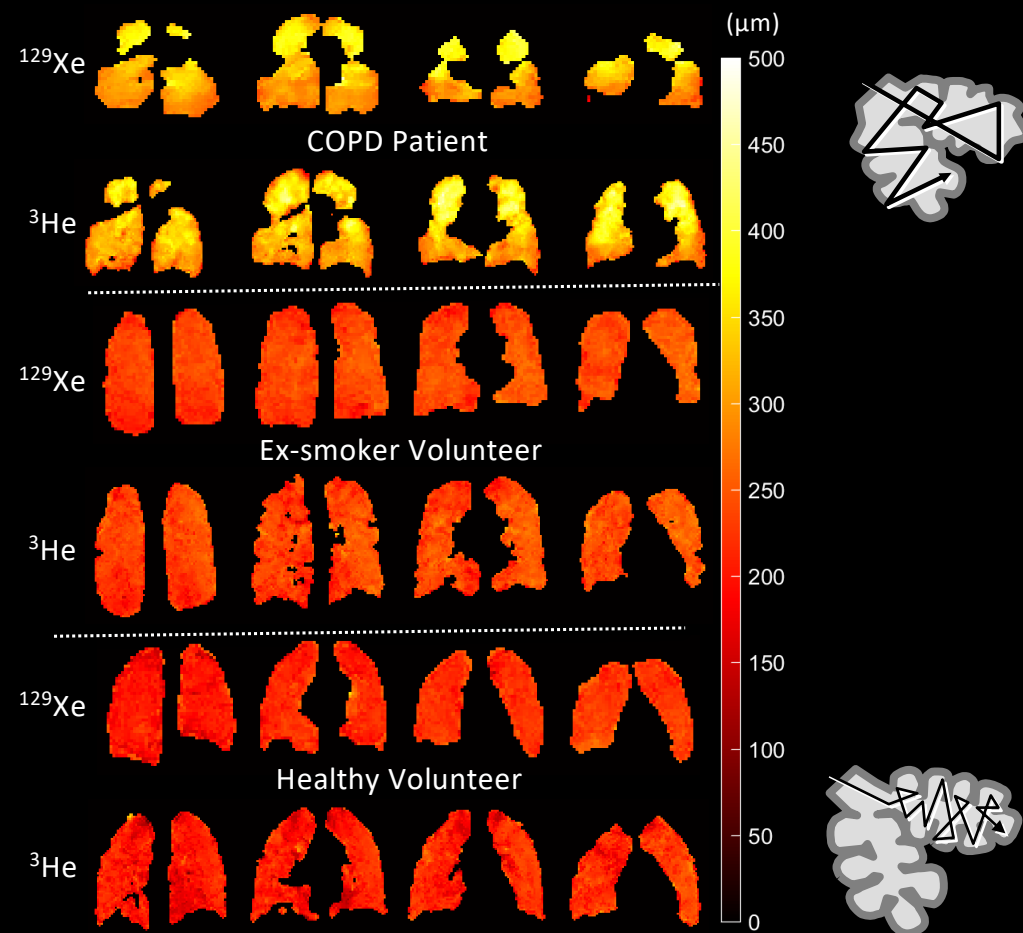


Stretch exponential model

Chan, et al. (2016). Magn Reson Med doi:10.1002/mrm.26279

$$\frac{S_b}{S_0} = \int_0^\infty p(D) e^{-bD} dD = e^{[-b \cdot DDC]^\alpha}$$

$$Lm_D = \int_0^\infty \sqrt{2\Delta D} p(D) dD$$

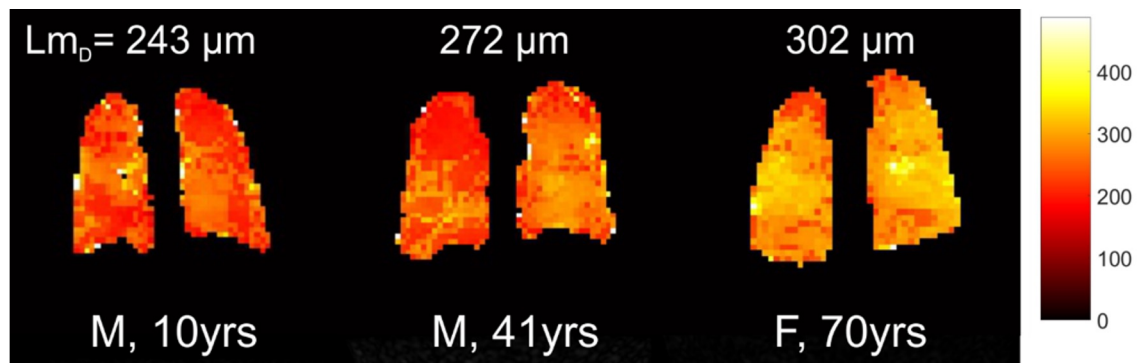
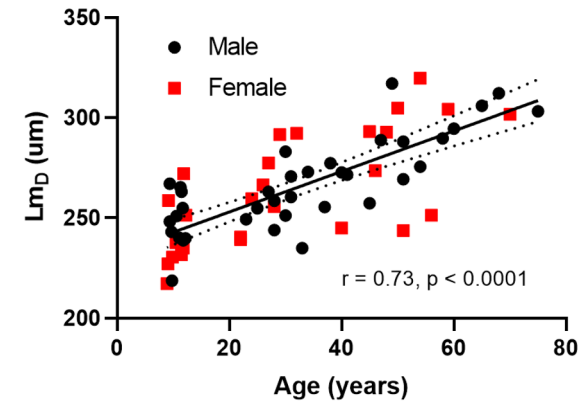
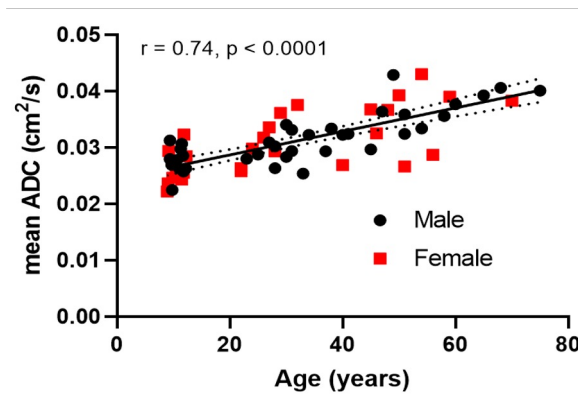
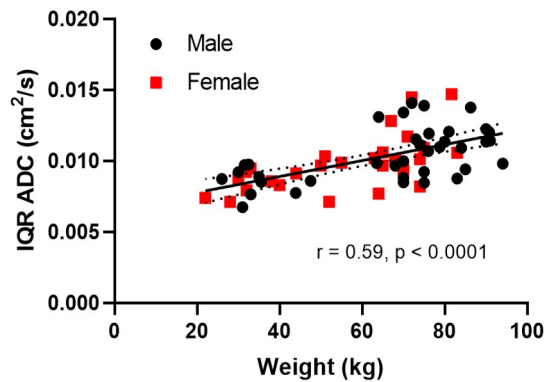
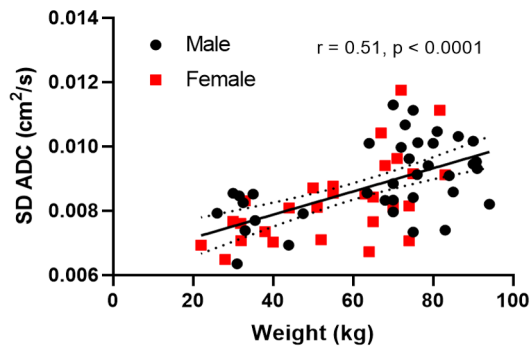


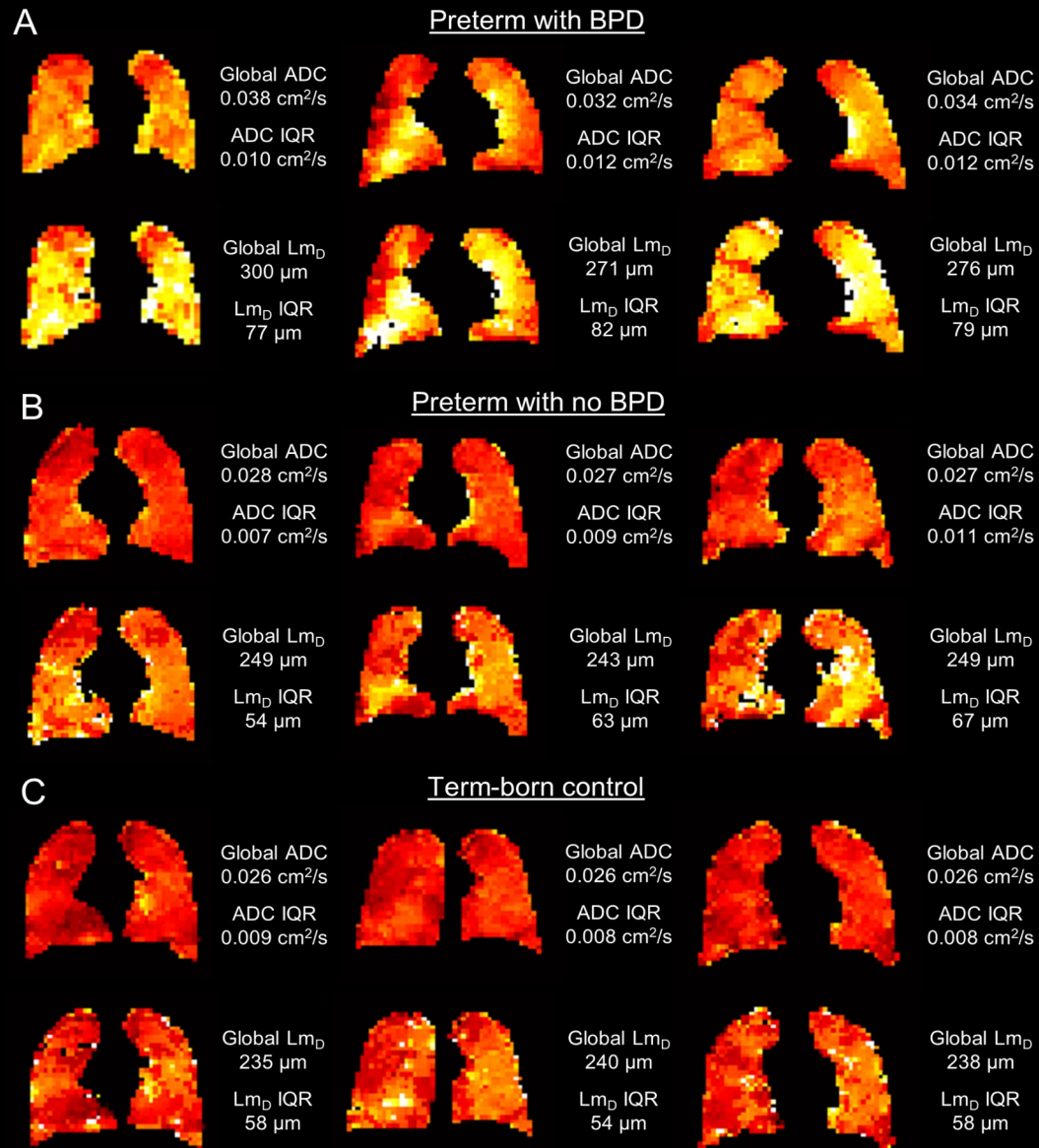
Age dependence of ^{129}Xe lung diffusion MRI

- Strong age dependence of ADC and Lm_D :

[?] $\text{Lm}_D = 1.01 \cdot \text{Age} + 233 \mu\text{m}$

[?] $\text{ADC} = 0.00021 \cdot \text{Age} + 0.0245 \text{ cm}^2/\text{s}$

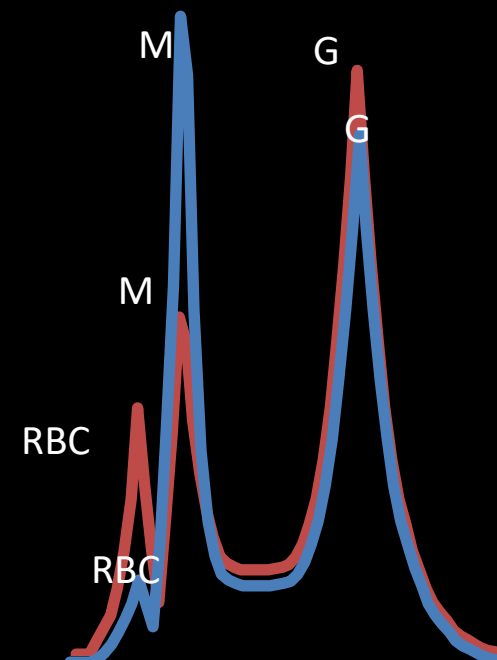
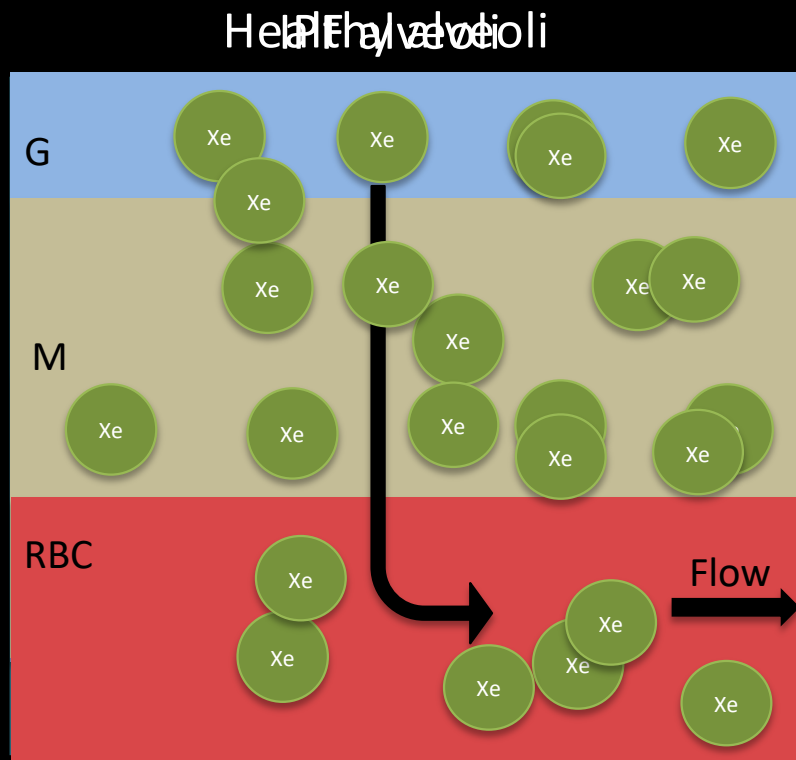




**Alveolar abnormality
of preterm birth**

Teenagers

Gas Transfer MRI

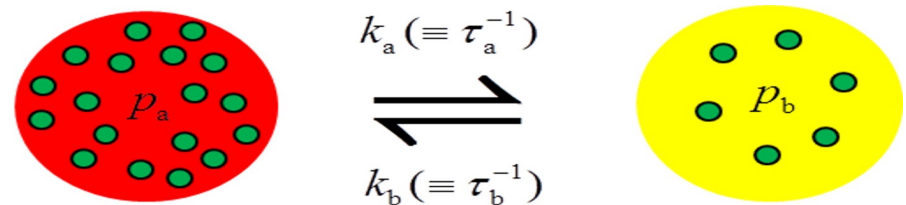
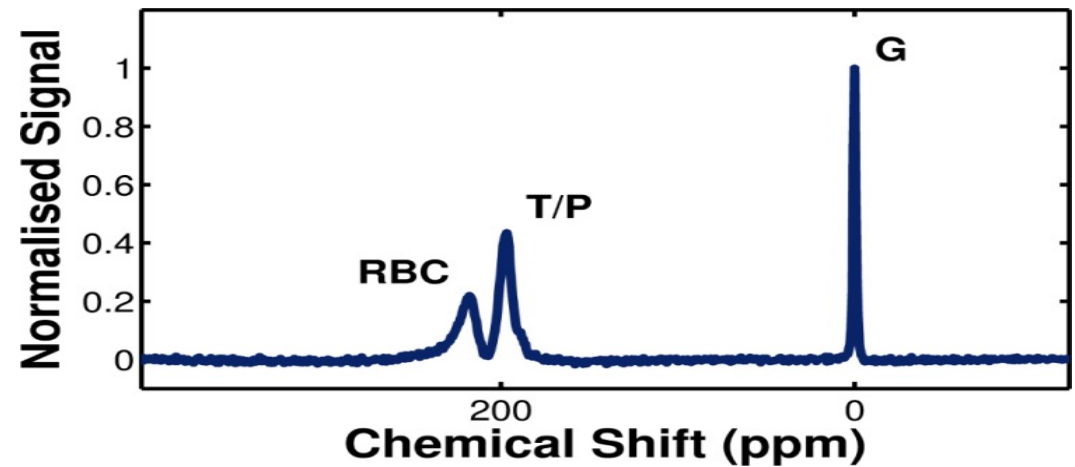
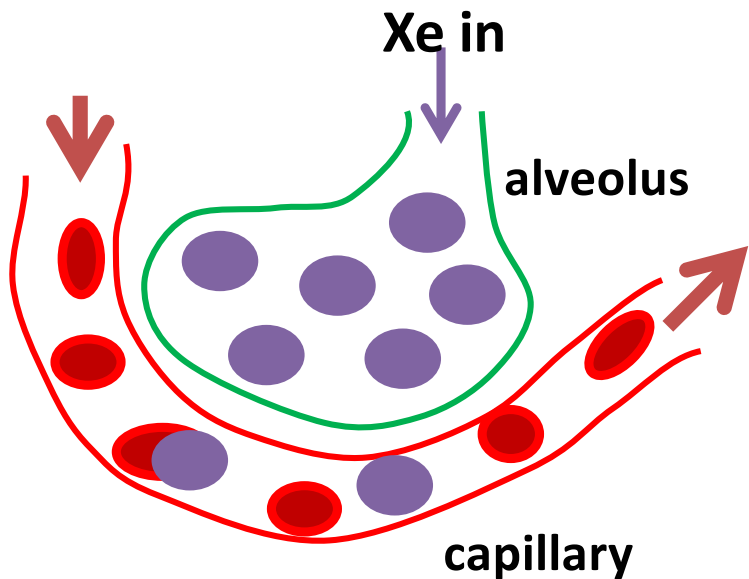


G = gas, M = membrane, RBC = red blood cells

Weatherley et al, Thorax 2019 74(5):500-502

Collier et al, Magn Reson Med 2021 85(5):2622-33

Dissolved-Phase ^{129}Xe

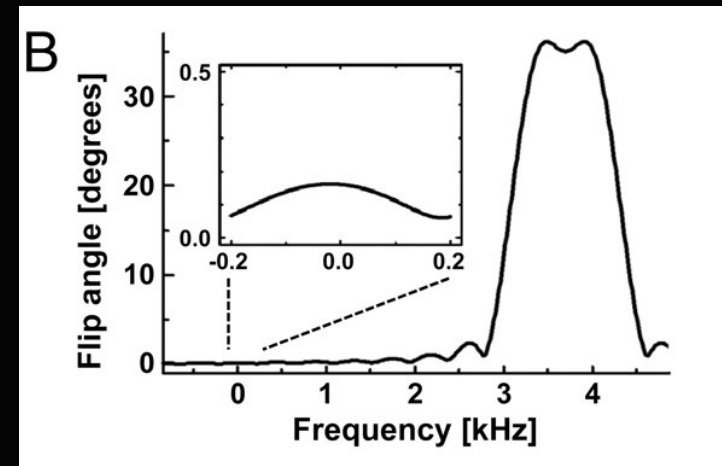
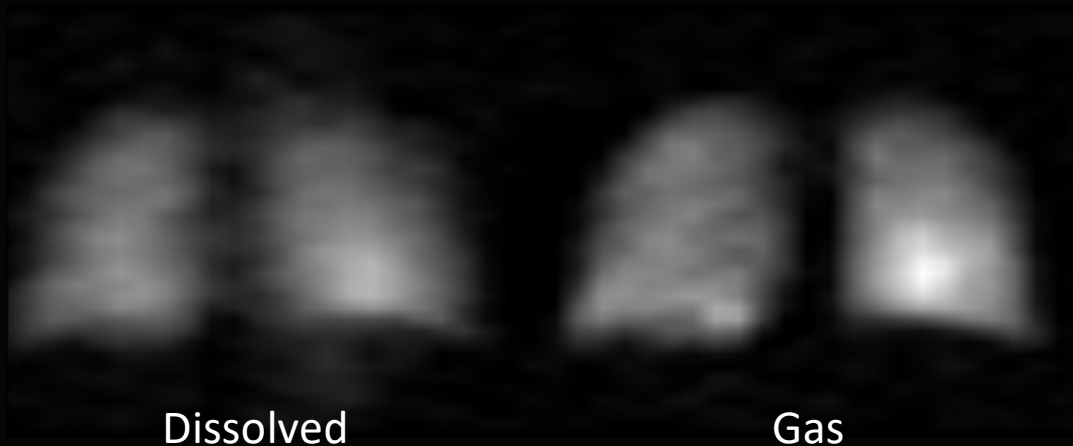


Considerations

- Small dissolved signal $\sim 2\%$ of gas
- Short T_2^* of dissolved $^{129}\text{Xe} \sim 1\text{-}2\text{ms}$ (chemical exchange) [1,2]

[1] J. P. Mugler III et al., *Proc ISMRM*, 1347 (2012). [2] X. Xu et al., *Proc ISMRM*, 4119 (2013).

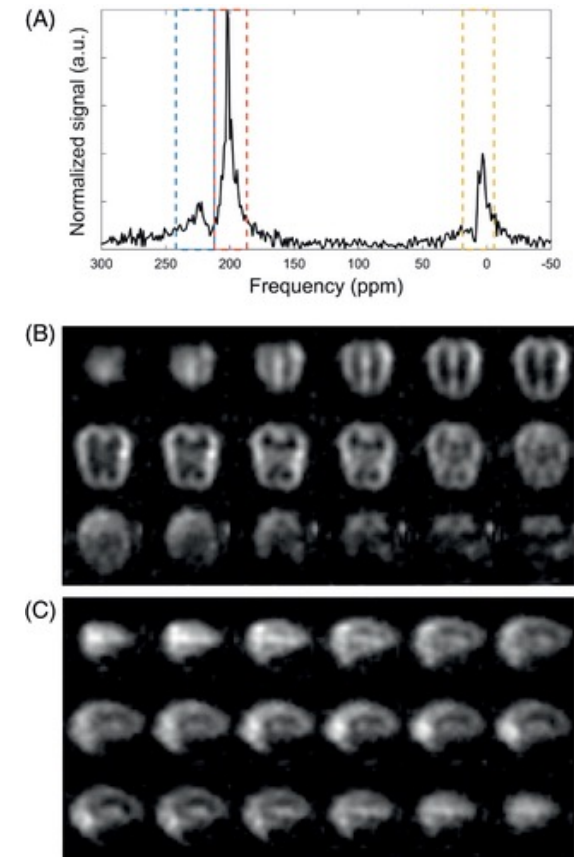
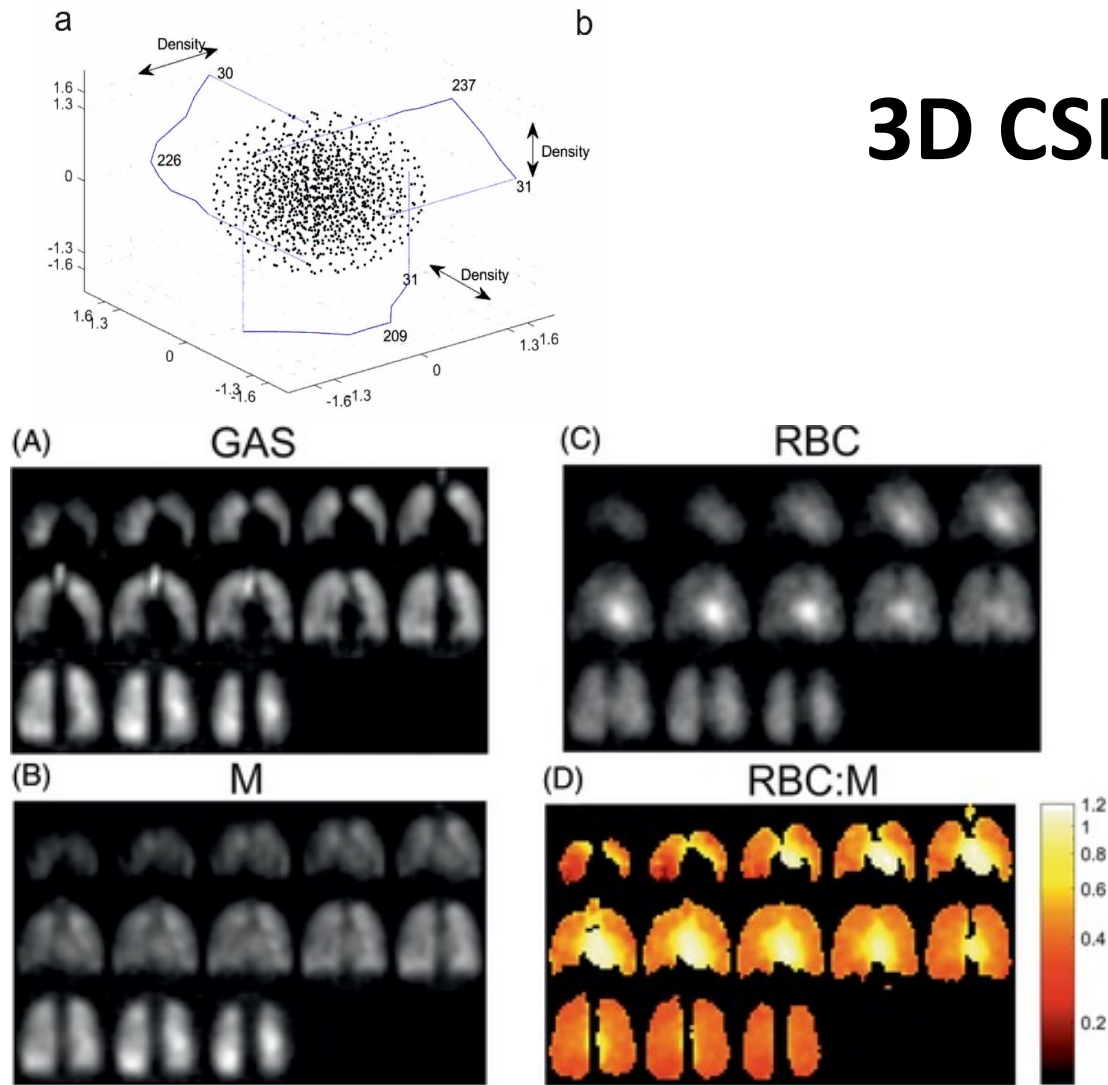
Dissolved-Phase ^{129}Xe imaging



- gas & dissolved ^{129}Xe separated in frequency direction [1]
- narrow band RF pulses for selective dissolved excitation [2]

[1] J. P. Mugler et al., PNAS, 107, 50 (2010). [2] Leung et al MRM

3D CSI for dissolved ^{129}Xe

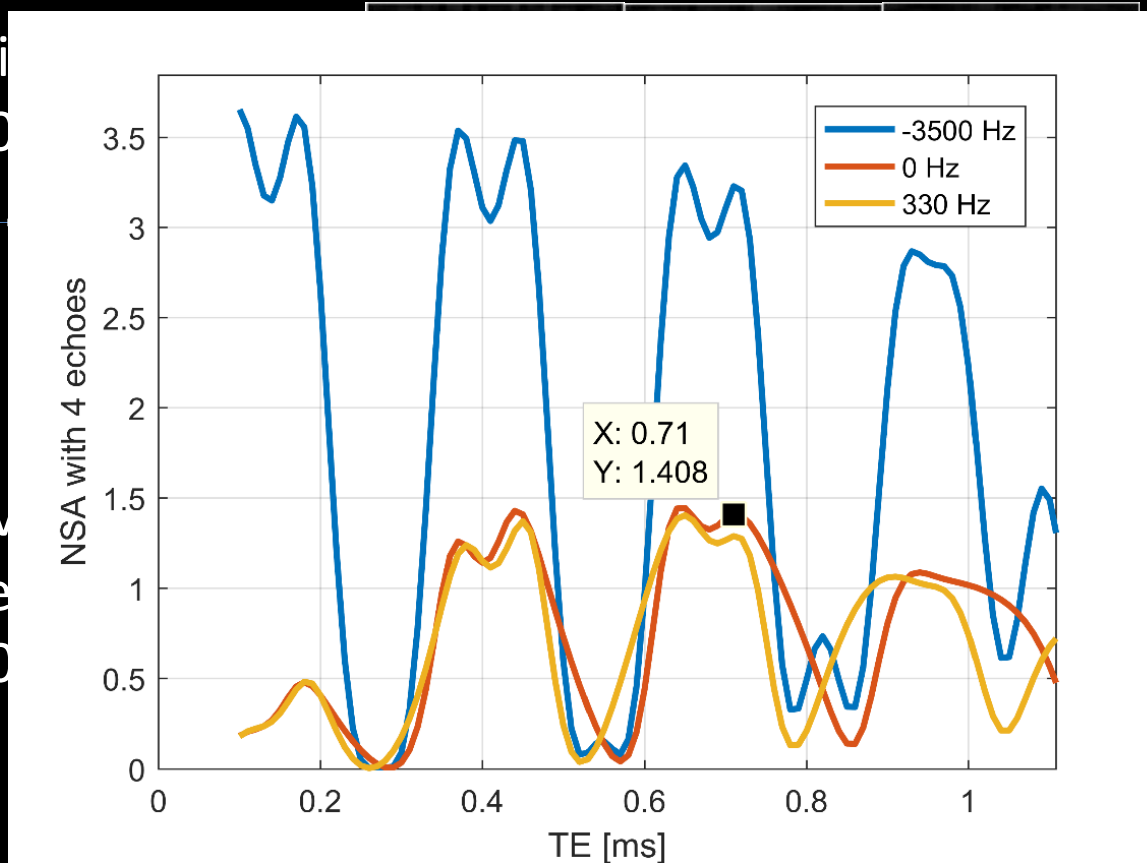


Collier et al Magn Reson Med. 2023 Jun;89(6):2217-2226. doi: 10.1002/mrm.29602.

4-echo IDEAL sequence for dissolved ^{129}Xe at 1.5T

GAS i
FA= 0

dissolv
Interle
FA= 40

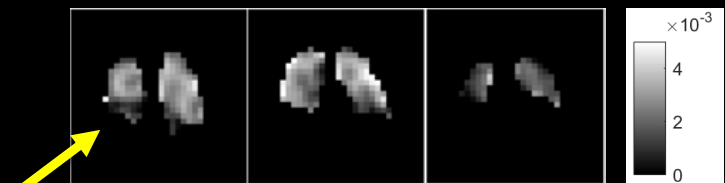


Ratio maps:

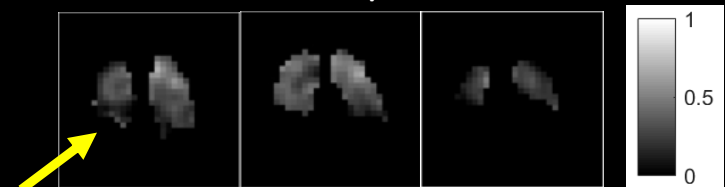
TP/GAS



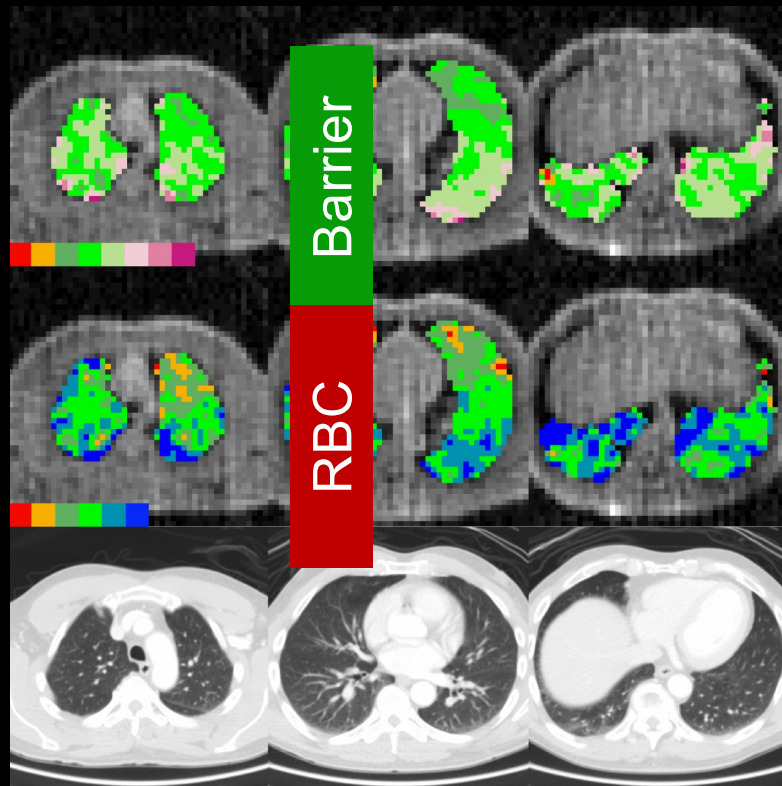
RBC/GAS



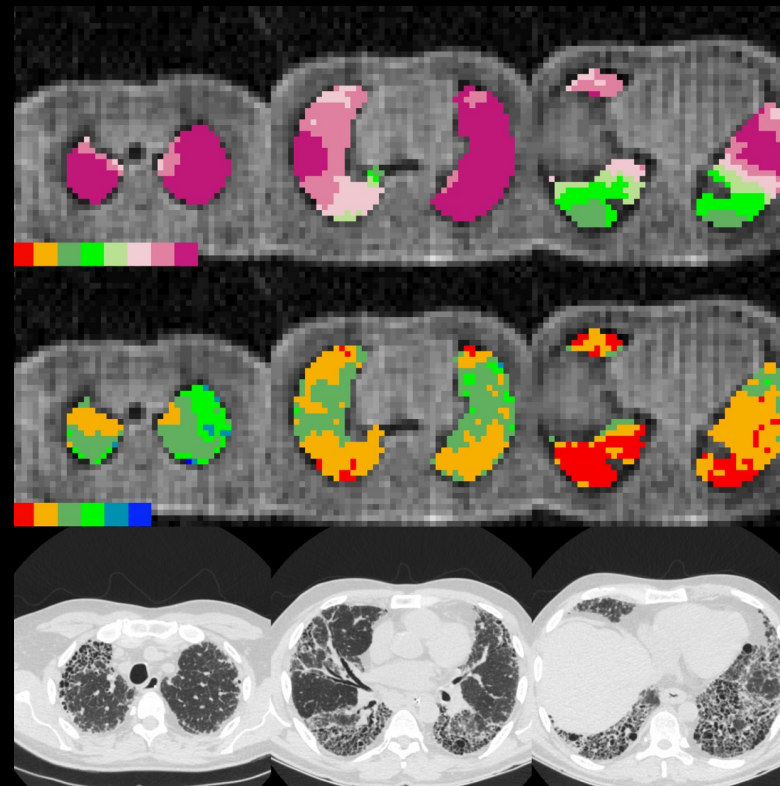
RBC/TP



Healthy



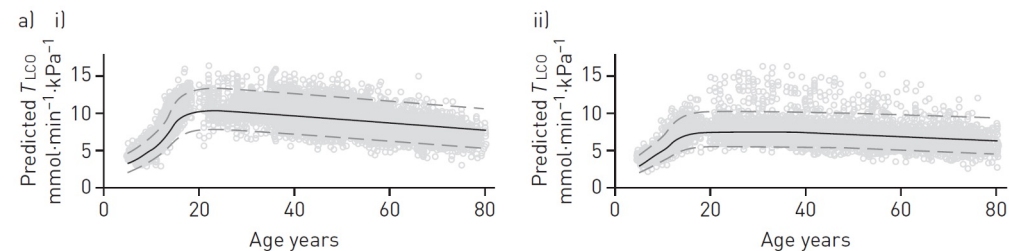
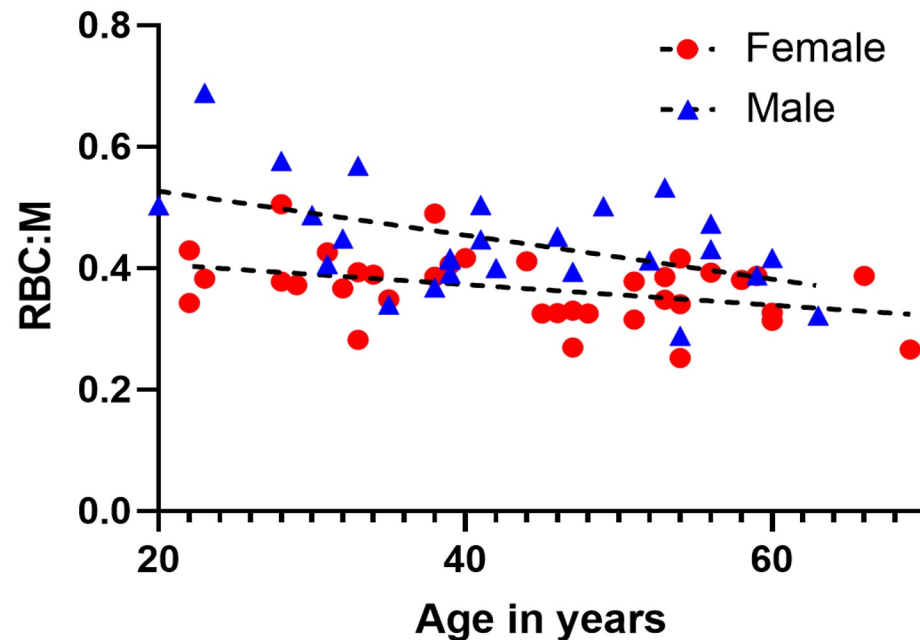
IPF Patient



Age, and sex dependence of ^{129}Xe MRI gas exchange metrics

- Healthy cohort of 62 volunteers: 26M/36F, 43 ± 12.4 years [20-69]
- Multiple linear regression analysis including Age, Sex, Weight, Height & BMI

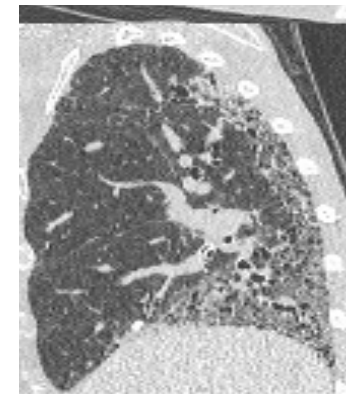
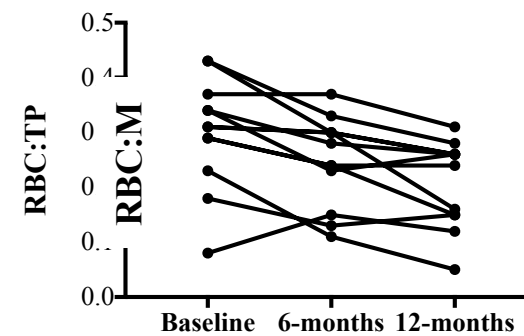
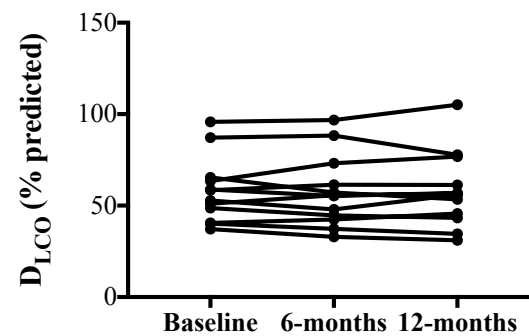
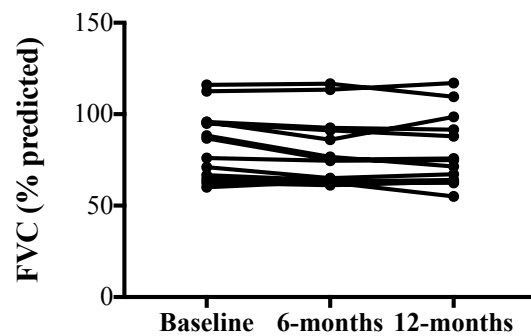
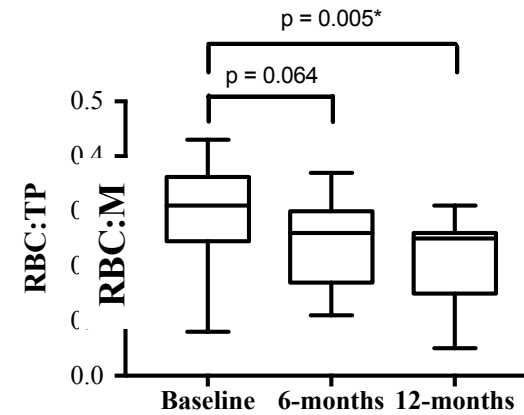
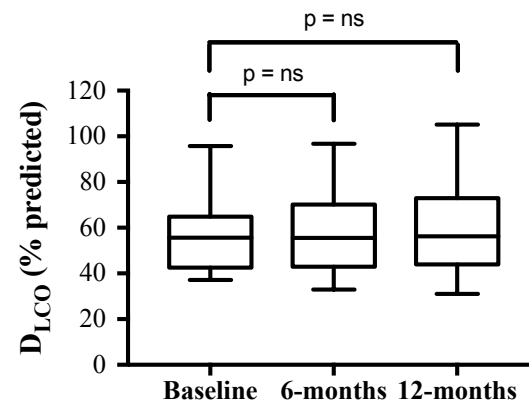
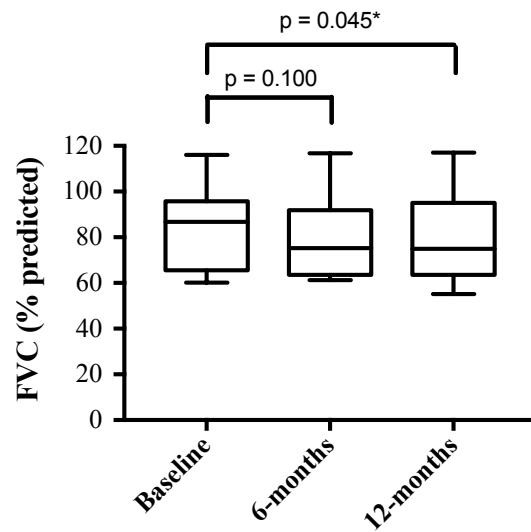
RBC:M
Age ($p=0.0006$) and Sex ($p<0.0001$) are significant predictors



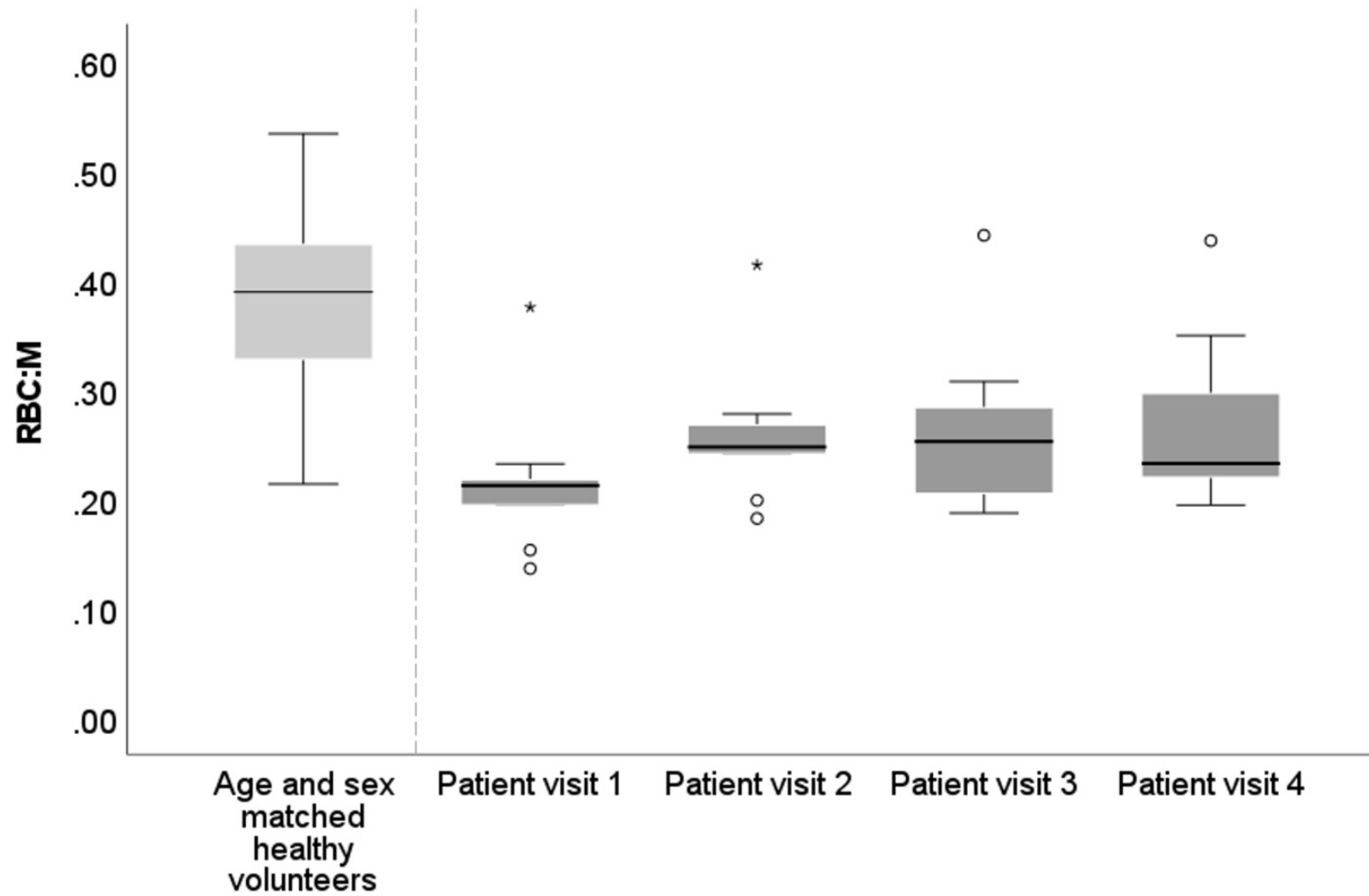
In agreement with GLI Predicted T_{LCO} equations
Stanojevic et al 2017 DOI: 10.1183/13993003.00010-2017

Using z-score to predict “abnormality”
(z-score values normally distributed)

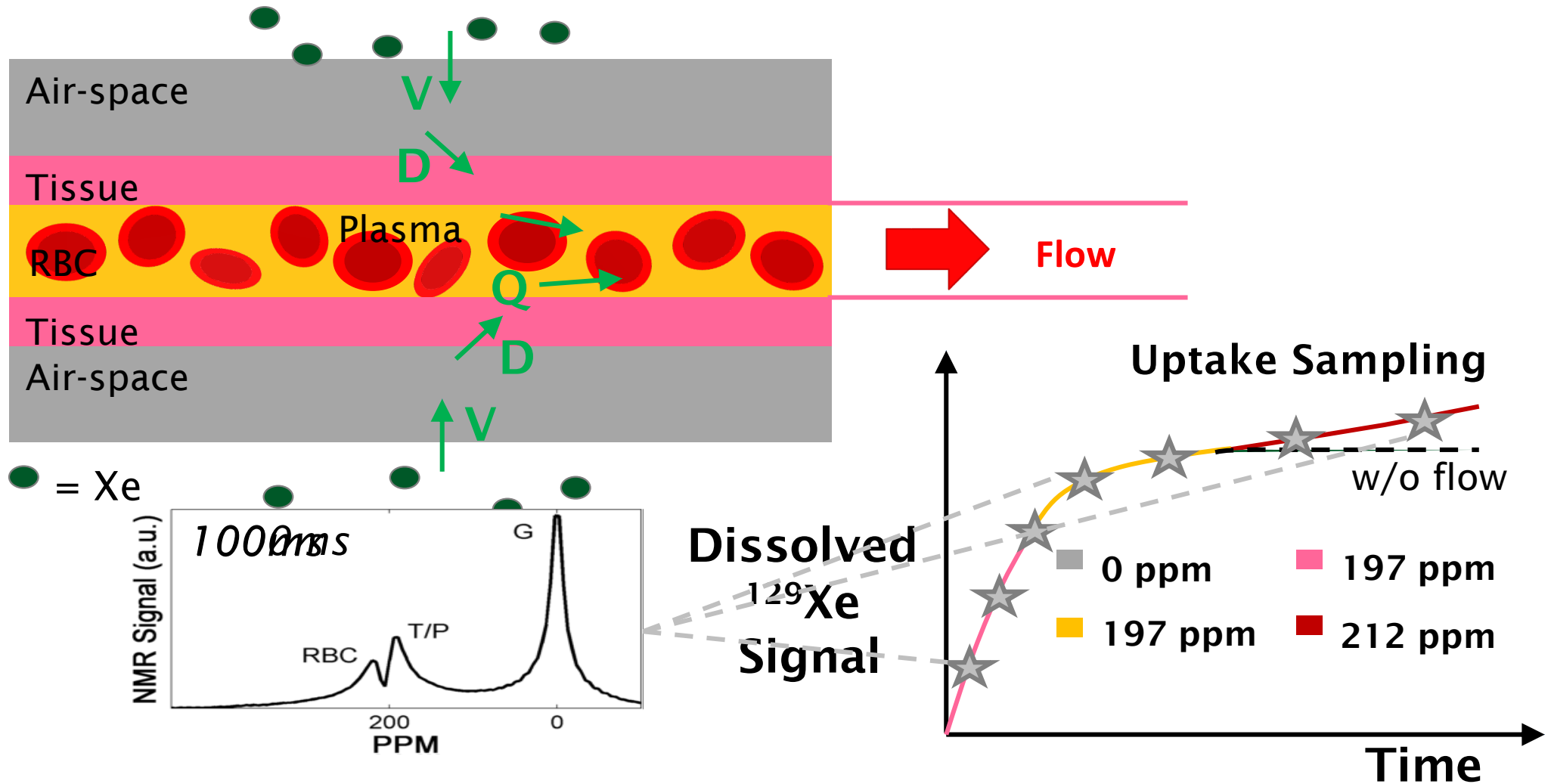
^{129}Xe MR longitudinal sensitivity in pulmonary fibrosis



¹²⁹Xe MRI in COVID-19 recovery

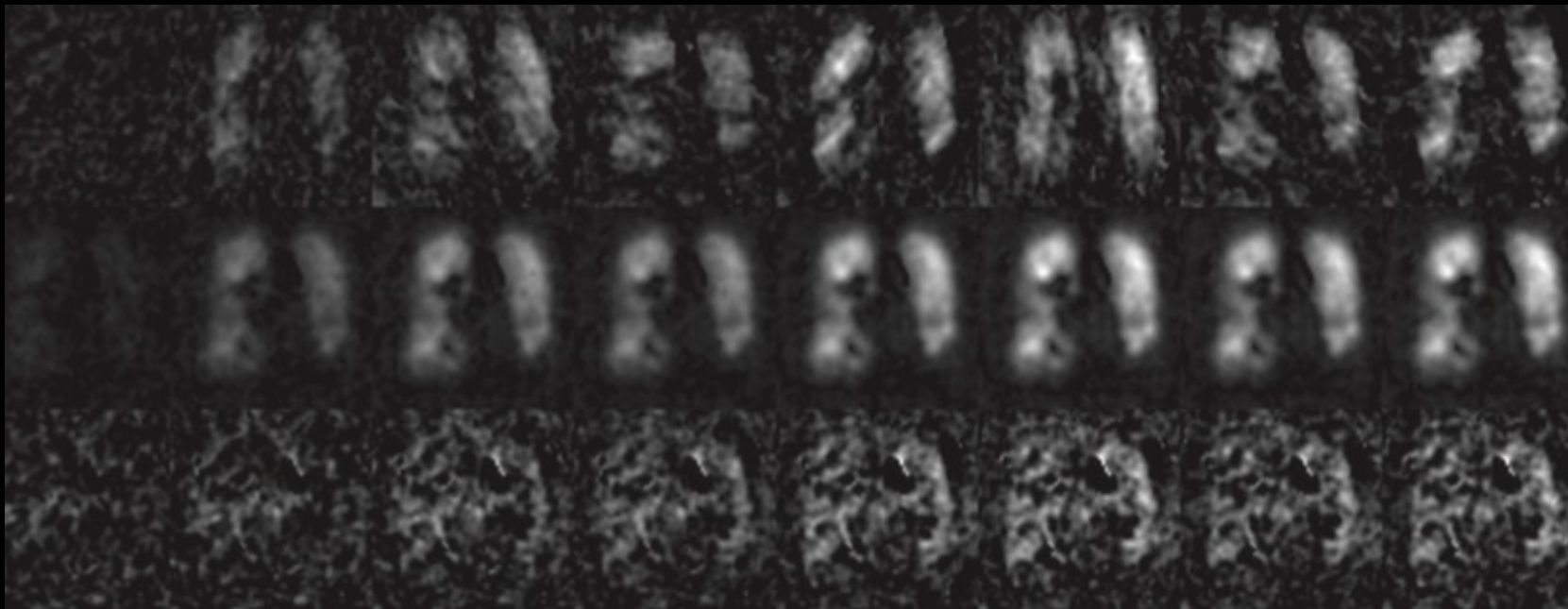


Gas-exchange MR with dissolved ^{129}Xe



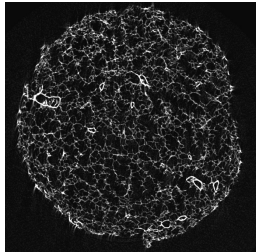
[1] N. J. Stewart et al., Magn Reson Med, 74, 1 (2015). [2] S. Patz et al., New J Phys, 13, 015009 (2011).

Dynamic spectroscopic imaging of xenon uptake



Kern et al Magn Reson Med. 2019 Apr;81(4):2360-2373.

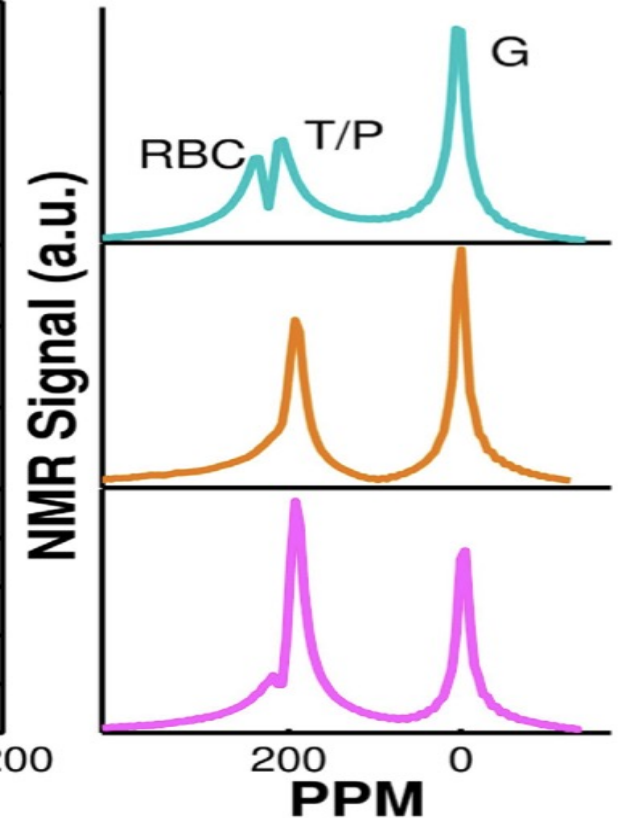
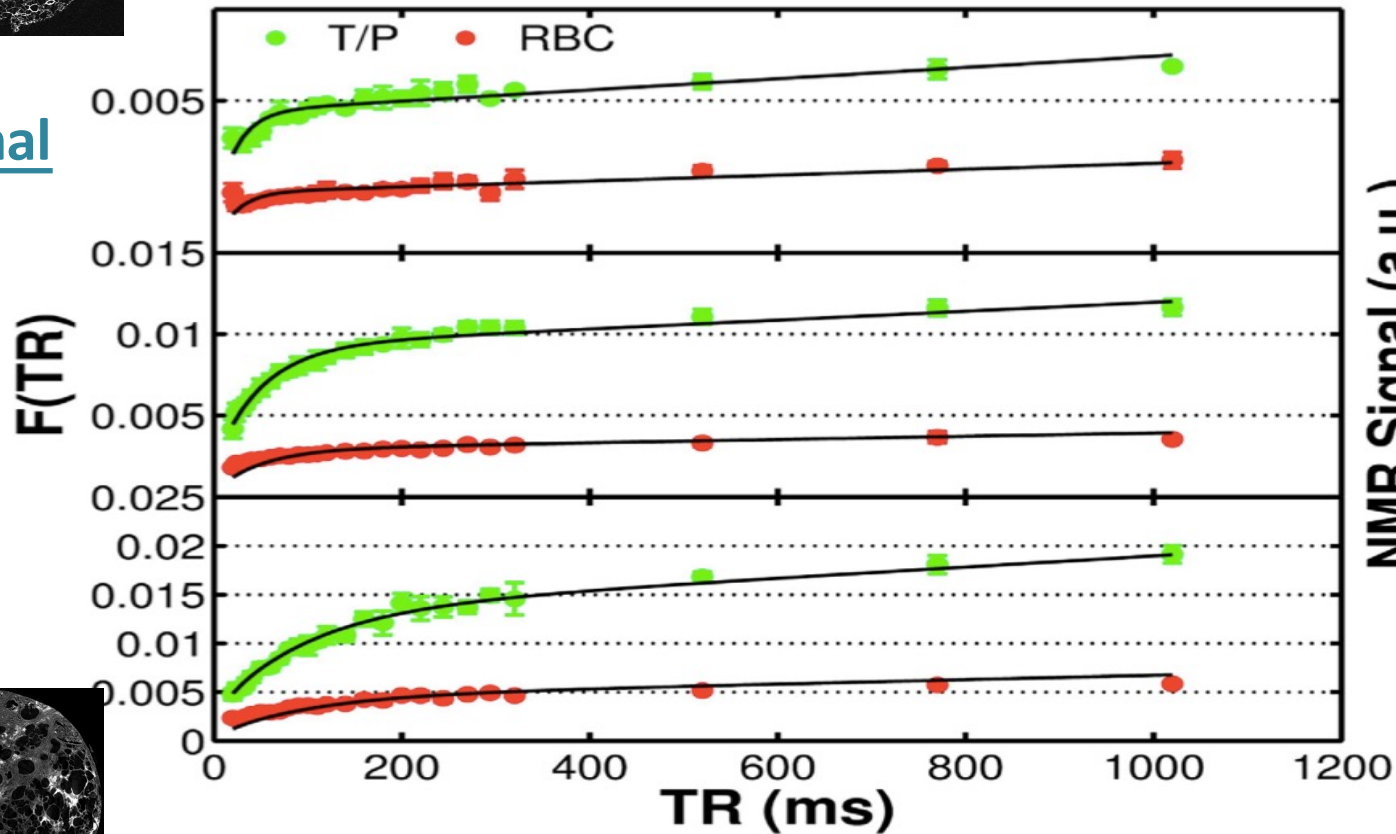
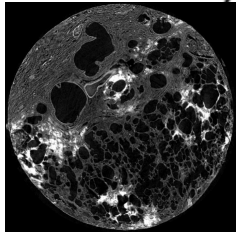
^{129}Xe MR alveolar-capillary gas exchange with CSSR in pulmonary fibrosis



Normal

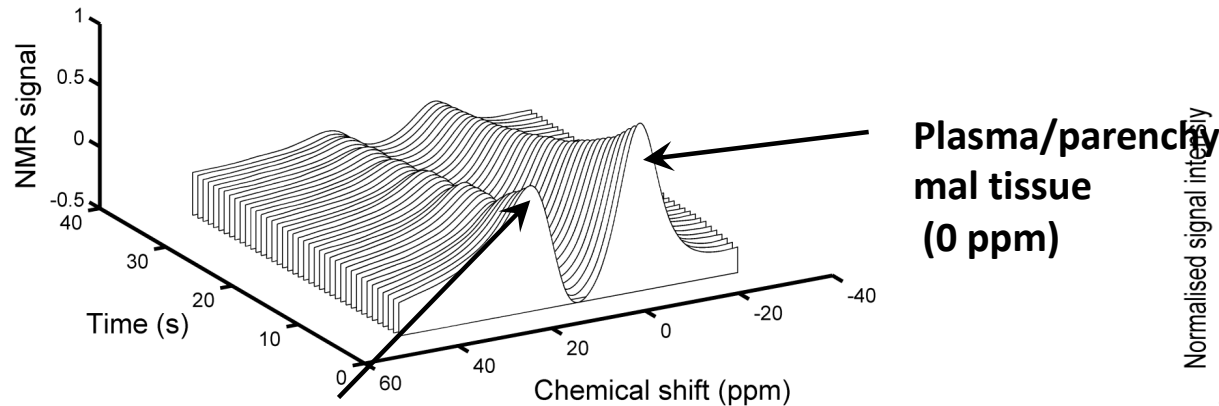
SSc

IPF

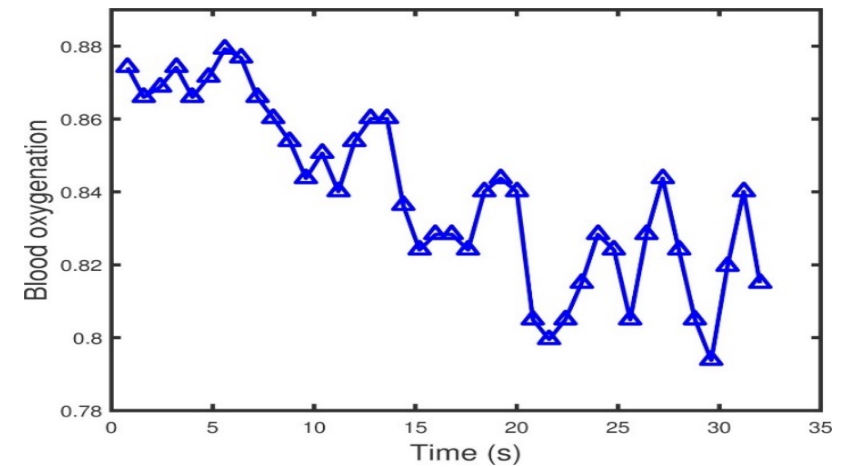
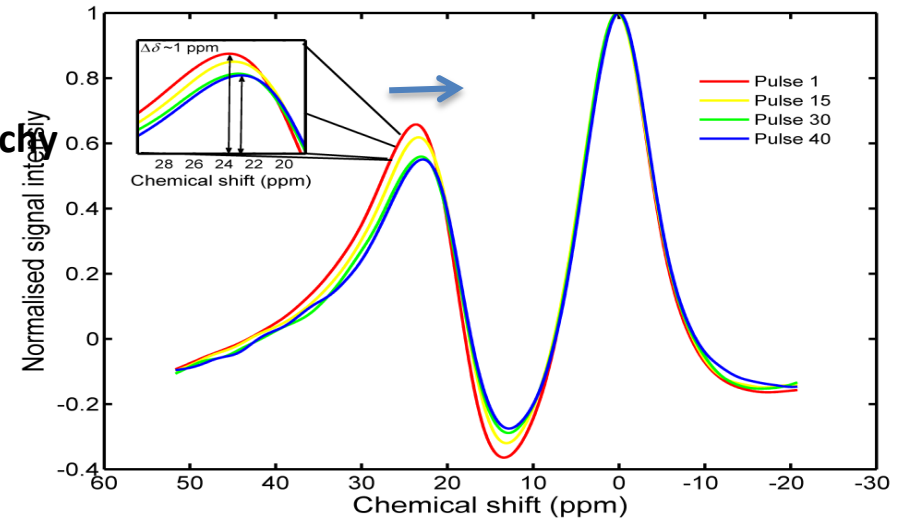
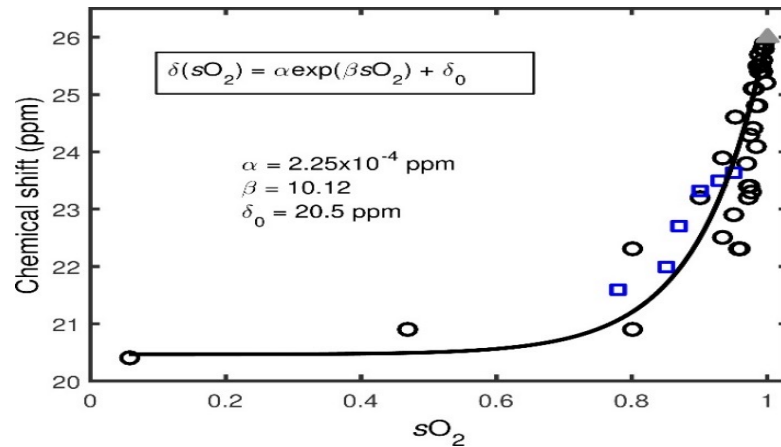


[1] N. J. Stewart et al., Magn Reson Med, 74, 1 (2015). [2] S. Patz et al., New J Phys, 13, 015009 (2011).

^{129}Xe chemical shift as a probe of oxygenation



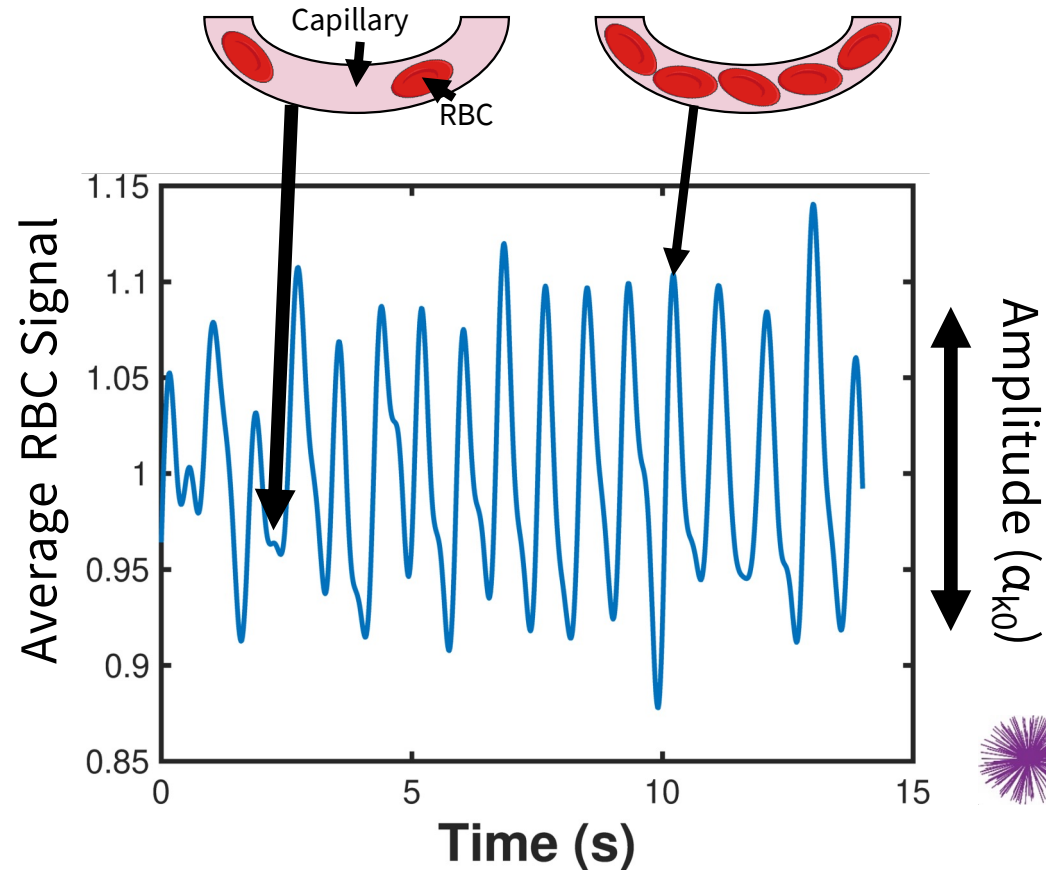
Red blood cells



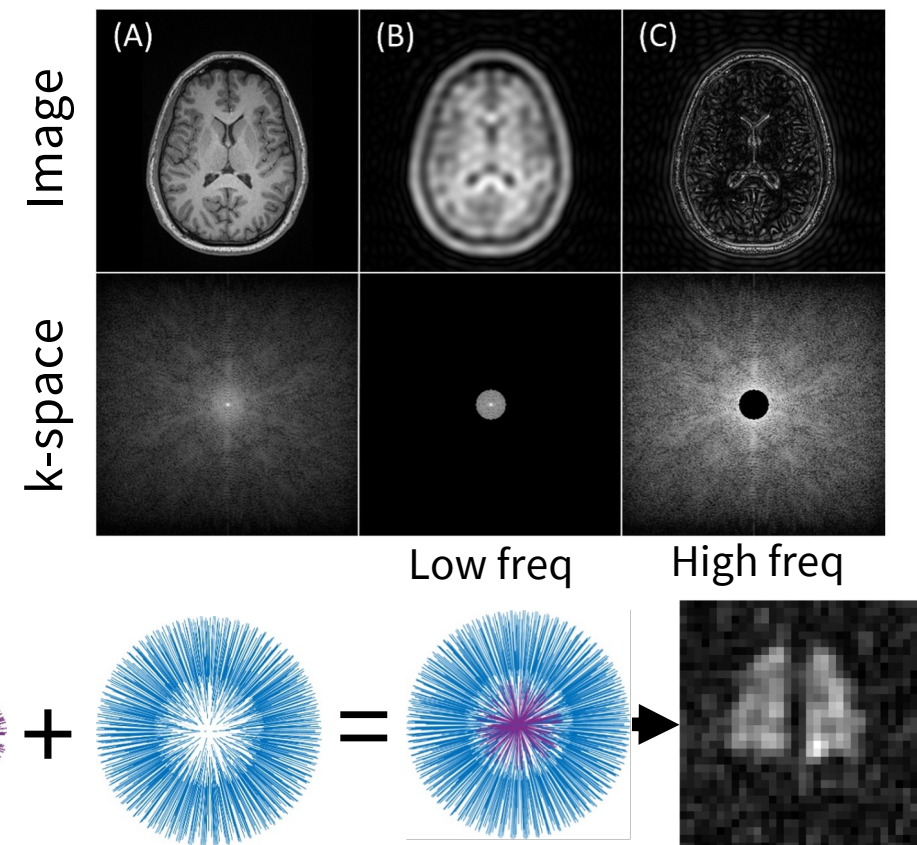
Wolber J, et al., NMR Biomed,13 (2000) 234-237

G. Norquay et al., Magn Reson Med. 2016 Apr 8

^{129}Xe RBC Oscillation Mapping



Reconstruct multiple images from the same MRI data

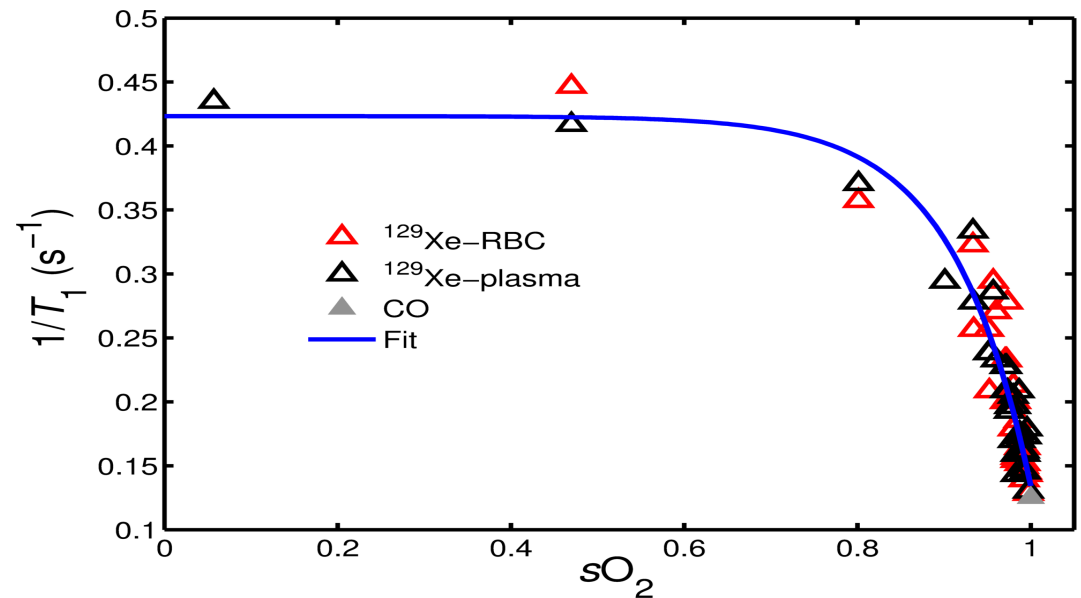
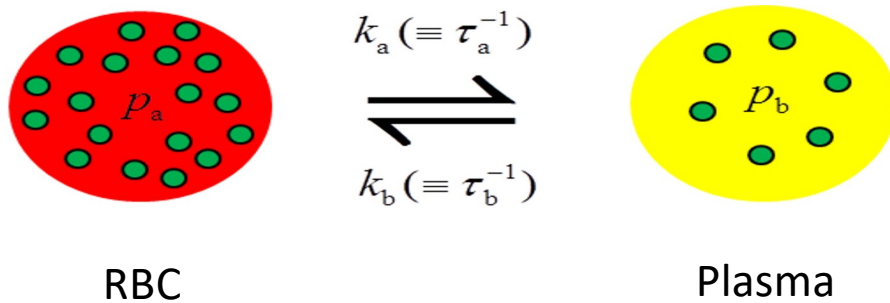


Wang et al, *Eur Respir J*, 2019. Mummy et al, *Radiology*, 2021. Collier et al, *Mag Res Med*, 2021. Bier et al, *NMR Biomed*, 2019. Bier et al, *ERJ Open Res*, 2022. Niedbalski et al, *J Appl Physiol*, 2020. Lu et al, *Mag Res Med*, 2024. Pilgrim-Morris et al, *Mag Res Med*, 2025.

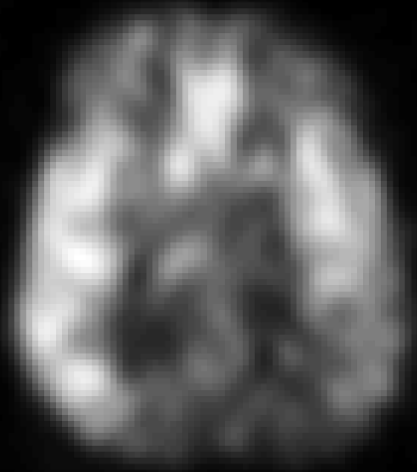
Dissolved ^{129}Xe - T1 in blood

T_1 of ^{129}Xe in oxygenated blood is sufficiently long for transport to distal organs

oxyHb ^{129}Xe -blood T_1	7.7 s
deoxyHb ^{129}Xe -blood T_1	2.4 s



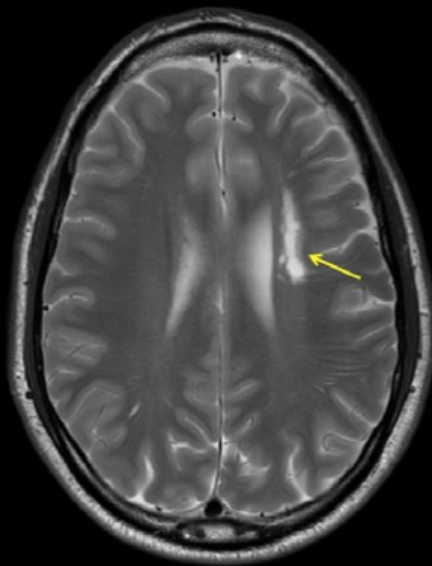
Xenon MRI beyond the lungs?



^{129}Xe brain - Stroke (3 months post)



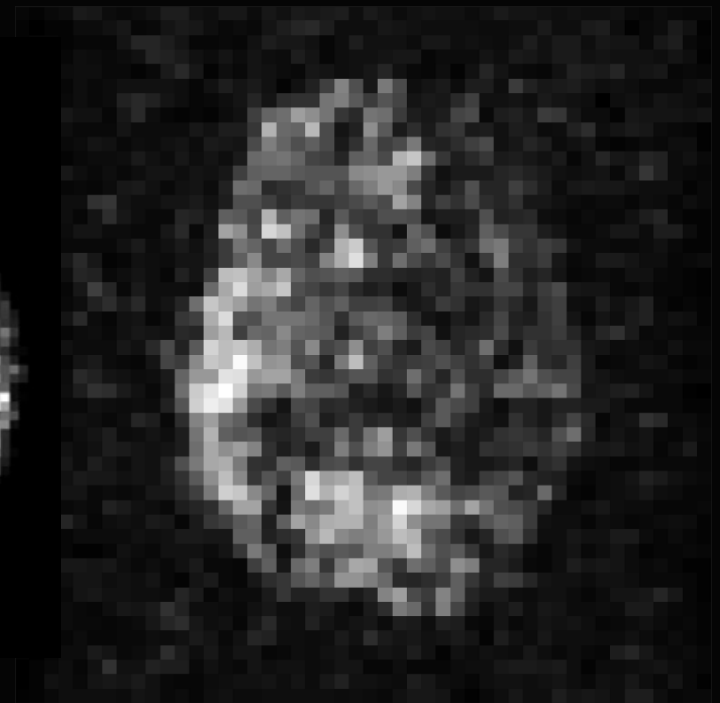
TOF



T2

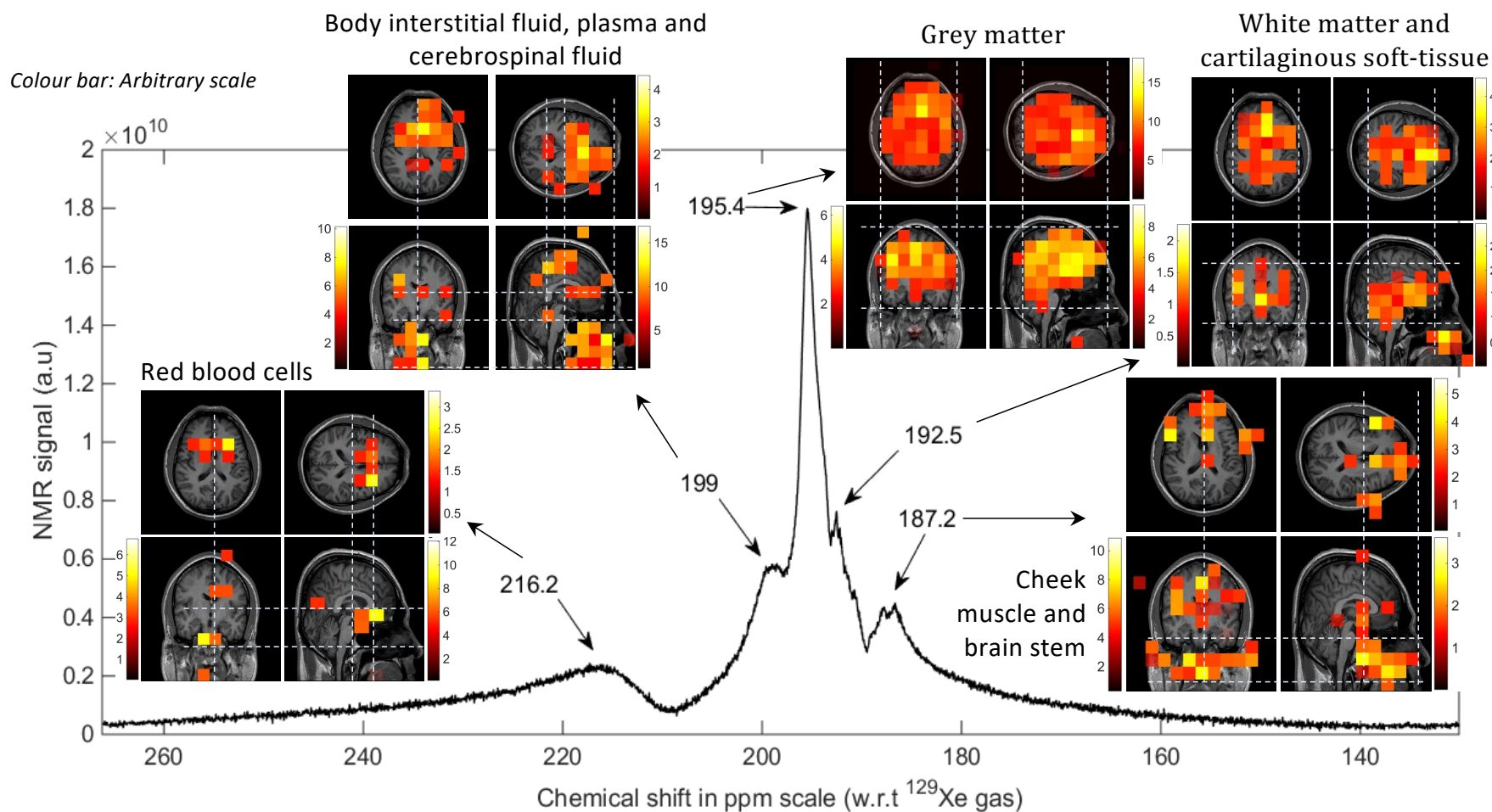


ASL



^{129}Xe

^{129}Xe brain chemical shift imaging



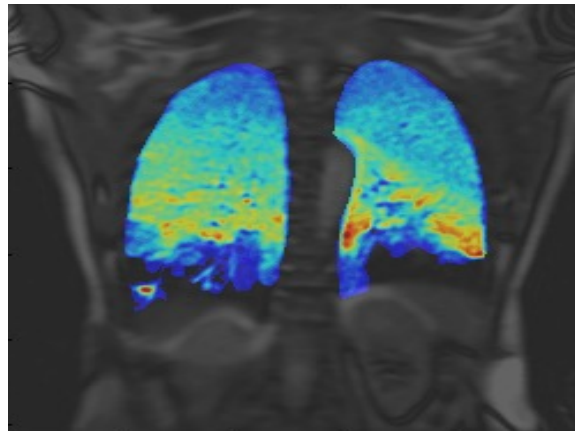
Xenon 1 L with ~30% polarisation

Rao et al. Mag Res Med (2016) 10.1002/mrm.26241

Imaging tools for pulmonary disease

Better understanding of lung
physiology and disease mechanisms

Early detection,
diagnosis



Better,
personalised and
regionally targeted
treatments

Sensitive *regional markers* of
therapy and progression

Clinical referral

1L natural-abundance NA Xe (~ £20 per scan)

MS NUMBER: MS 18739 Version: 1

MHRA
Regulating Medicines and Medical Devices

MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY
On behalf of the Licensing Authority under:
The Human Medicines Regulations 2012 (SI 2012/1916)

Manufacturer's "Specials" Licence

SECTION 1A

1. Licence Number
MS Number: MS 18739

2. Name of Licence Holder
UNIVERSITY OF SHEFFIELD

3. Address(es) of manufacturing/importing site(s)
(All authorised sites should be listed if not covered by separate licences)

MHRA SITE NUMBER	SITE NAME	ADDRESS
114966	UNIVERSITY OF SHEFFIELD	ACADEMIC UNIT OF RADIOLOGY, C FLOOR, DIVISION OF CLINICAL SCIENCES, ROYAL HALLAMSHIRE HOSPITAL, GLOSSOP ROAD, SHEFFIELD, S10 2JF, UNITED KINGDOM

4. Legally registered address of Licence Holder
ACADEMIC UNIT OF RADIOLOGY, C FLOOR, DIVISION OF CLINICAL SCIENCES, ROYAL HALLAMSHIRE HOSPITAL, GLOSSOP ROAD, SHEFFIELD, S10 2JF, UNITED KINGDOM

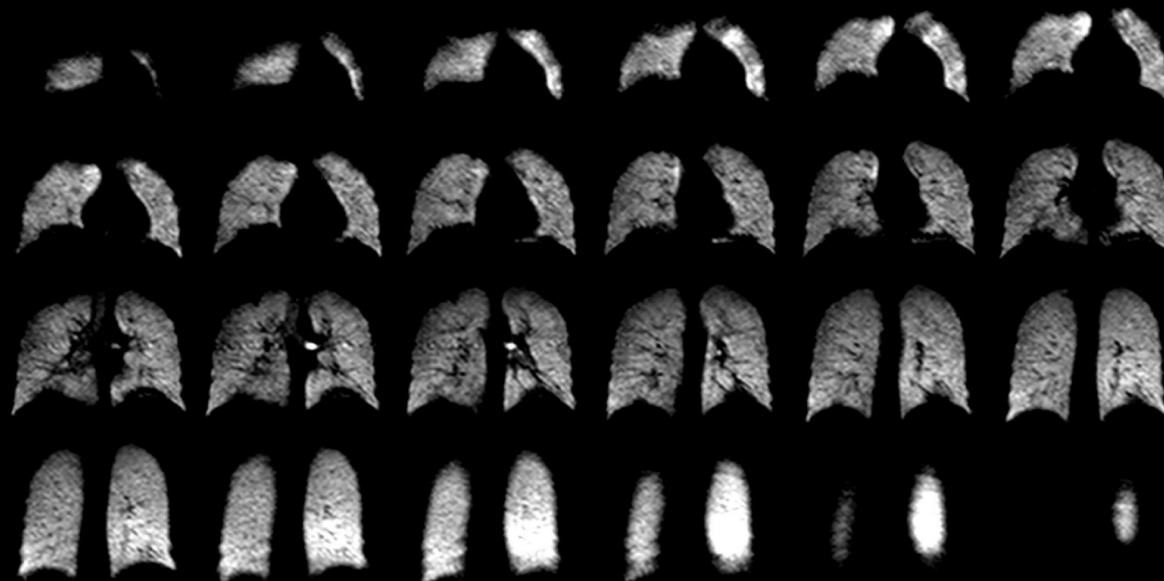
5. Scope of authorisation and dosage form
See ANNEX 1

6. Legal basis of licence
See Section 1B of licence.

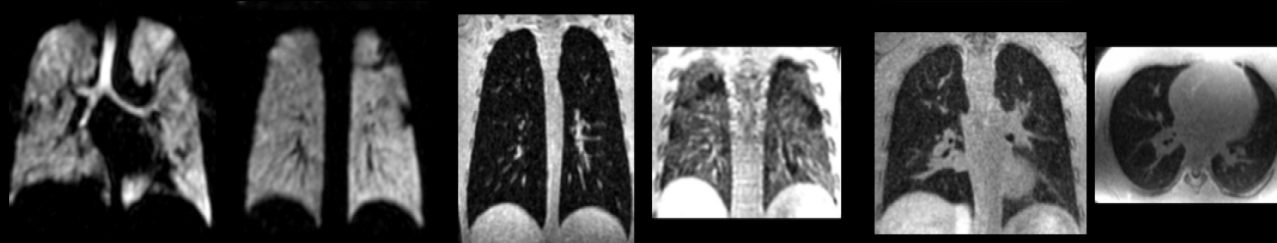
7. Name of responsible officer of the competent authority for manufacturing authorisation
Sean Kaiser

Medicines and Healthcare Products Regulatory Agency

Page 1



>7000 doses dispensed since 2016

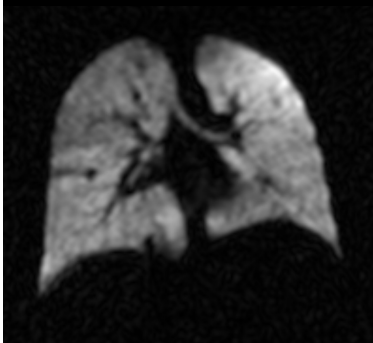


25 minute lung structure-function scanning

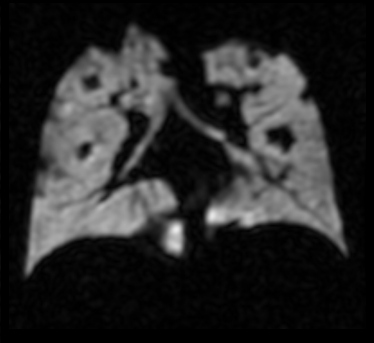
Cystic Fibrosis- annual review

3He – top row

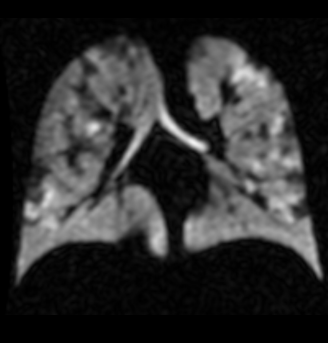
13/1/14



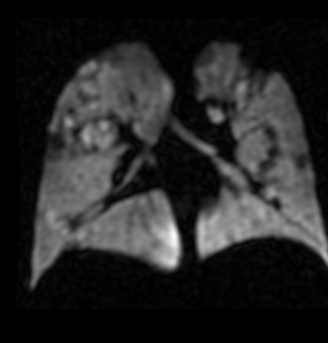
2/11/15



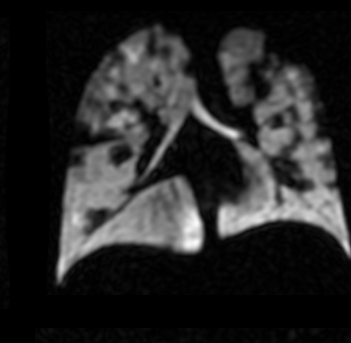
9/3/17



8/9/17



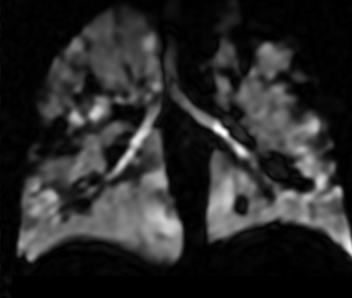
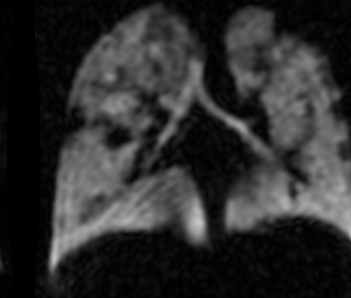
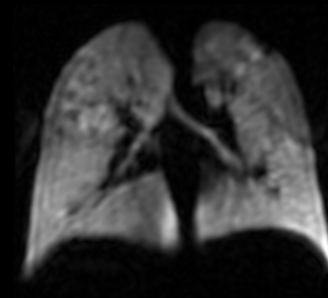
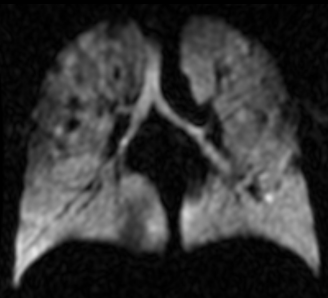
25/05/18



01/03/24



129Xe – bottom row



FEV1z = -
0.29
LCI = 6.95

FEV1z = 0.26
LCI = 7.24

FEV1z = -
0.85
LCI = 7.29

FEV1z = -
0.94
LCI = 10.03

Clinical Referral – Recent diagnosis of ABPA & CT showed right upper lobe collapse. Bronchoscopy performed and mucus removed. FEV₁ always ~100% and did not want to repeat CT. Therefore referred for initial ¹²⁹Xe and ¹H MRI

¹²⁹Xe MRI
FRC + bag vol.

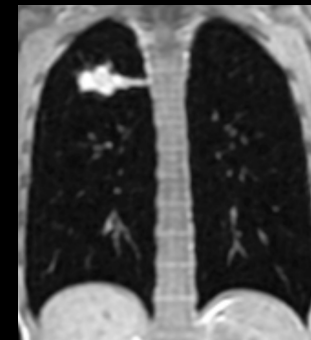
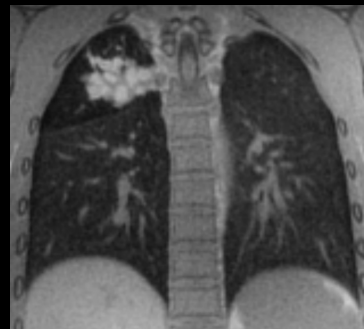
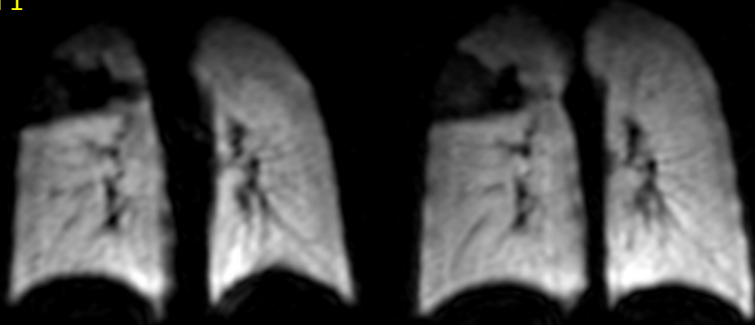
¹²⁹Xe MRI
Total lung capacity

¹H UTE MRI
Free-breathing
FRC

¹H SPGR MRI
Breath-hold
Total lung capacity

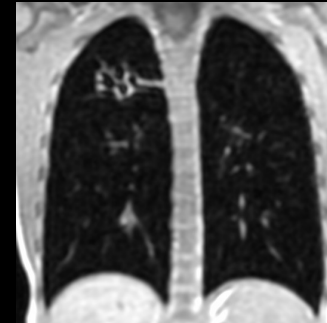
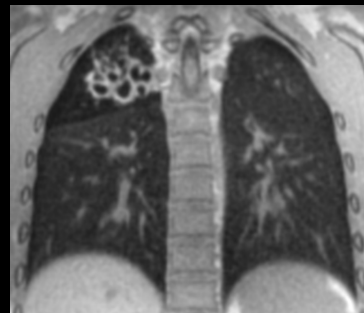
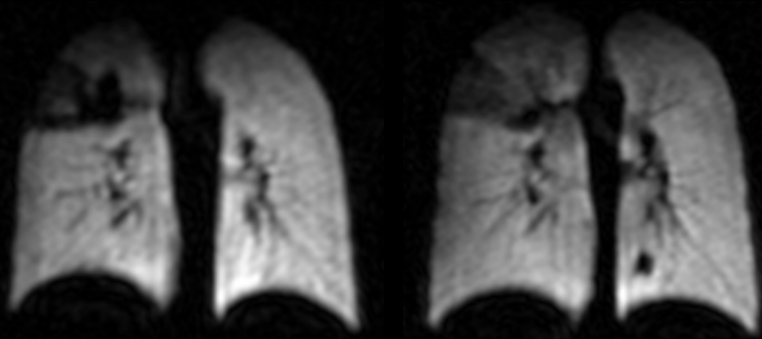
¹H SPGR MRI
Breath-hold
~ Residual volume

Scan 1



After reviewing the MR images, the patient had a further bronchoscopy with more mucus removed. A repeat MRI was performed approximately 2 weeks later

Scan 2



Case 2 – 8Y F, Engagement with Treatment

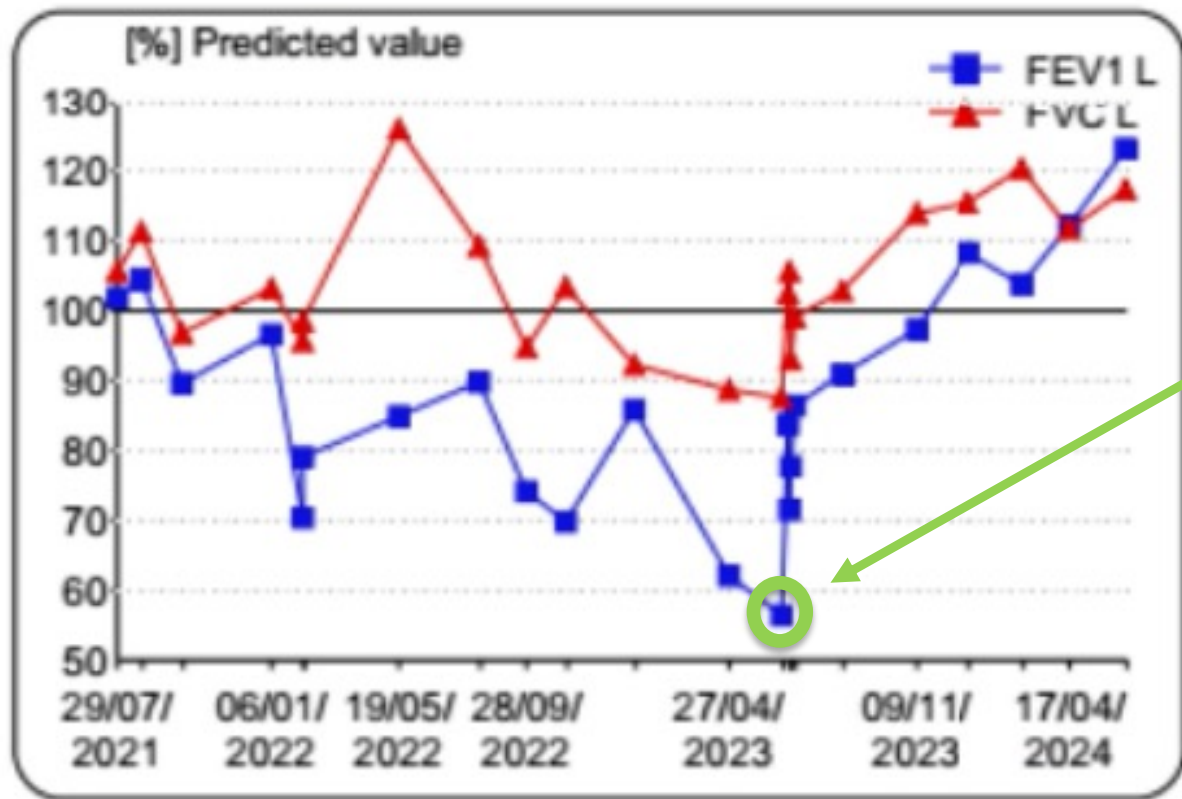
June
VDP 15.15%

July
VDP 1.47%

IV antibiotics,
&
chest
physiotherapy

After seeing this image, family agreed to intensive treatment
Family on-board with treatment decisions since, stated the images were key

Case 2 – 8Y F, Engagement with Treatment



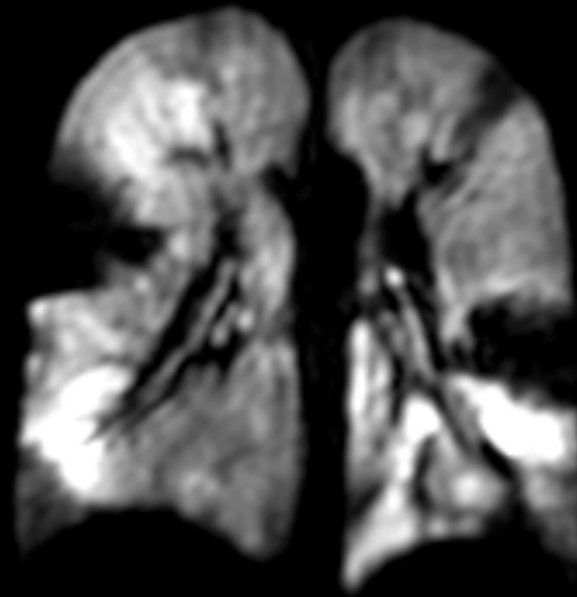
MRI
Performed
here!

Paediatric non CF bronchiectasis - IV antibiotics

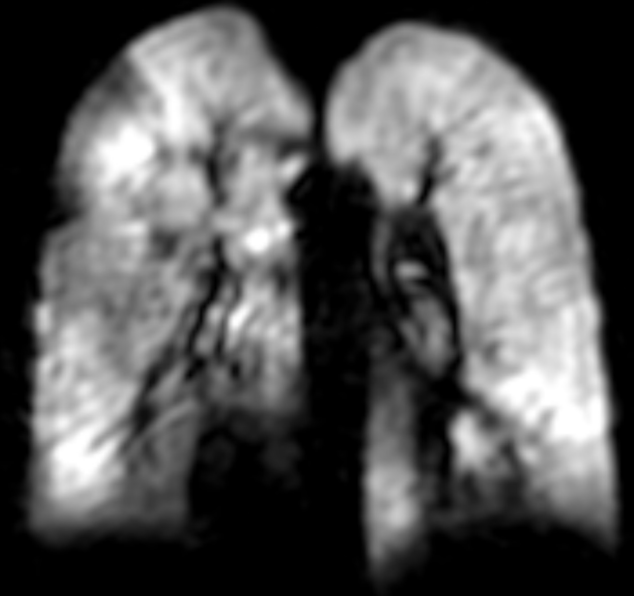
13 year old cross
country runner

↓ race times

FEV1 normal



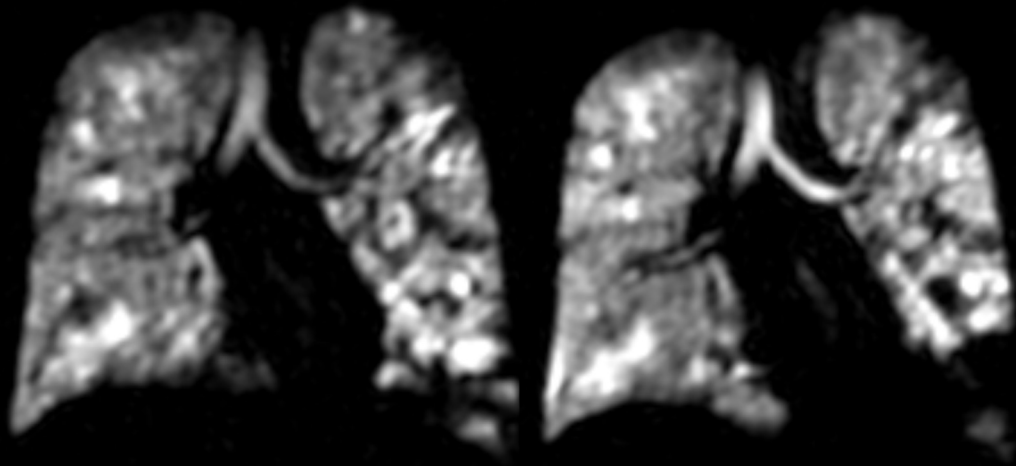
Baseline



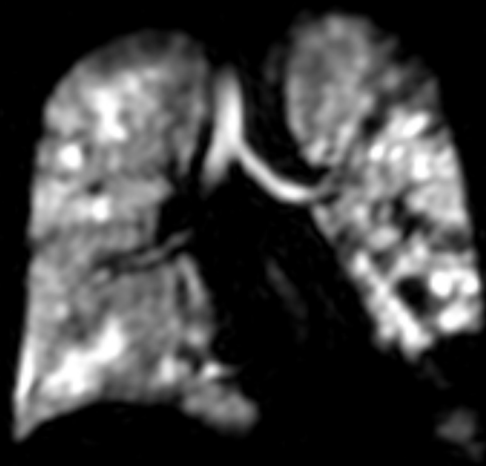
Post 2 weeks of IV
therapy

Case 6. Congenital diaphragmatic hernia (12y)

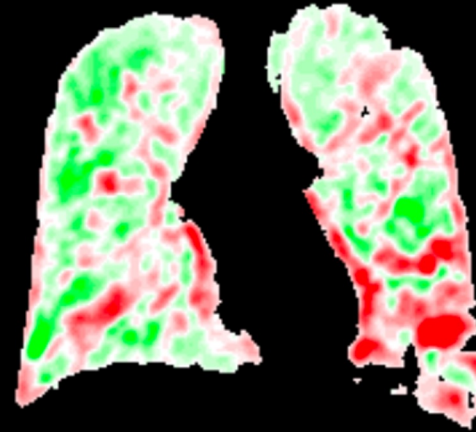
- Clinical question – increasing SOB ?asthma



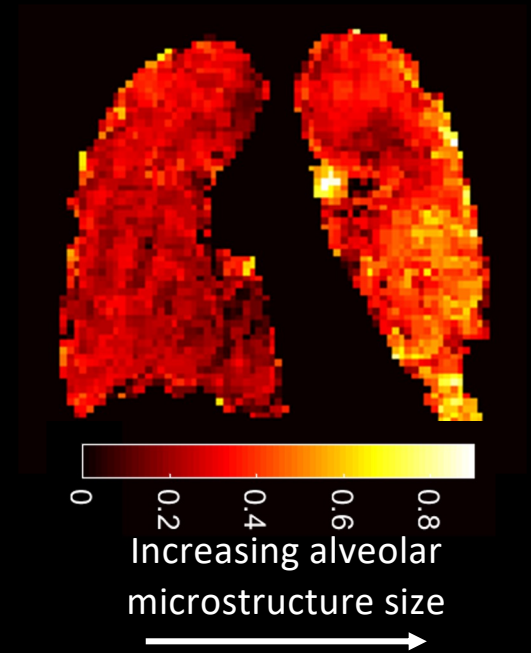
Baseline



Post salbutamol

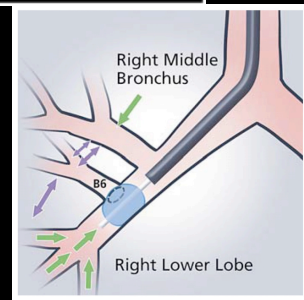
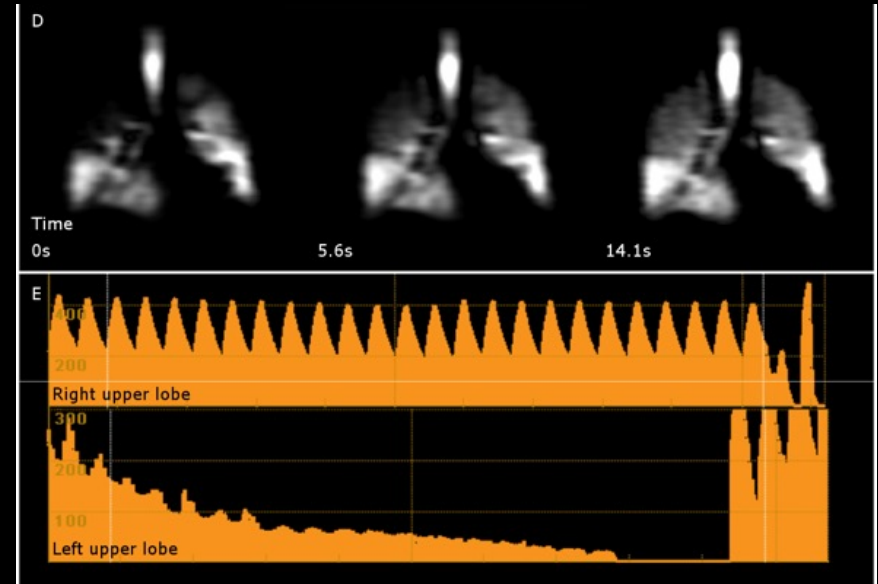
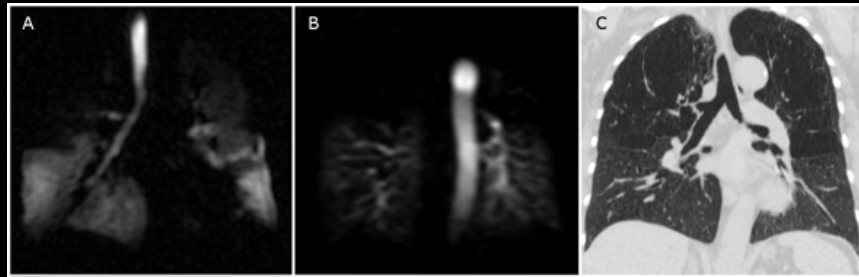


Treatment –
response map



- Clinical impression – left lung hypoplasia (probably from birth)
- right lung reversibility

Assessment for lung volume reduction in severe COPD



Johns et al, Proc Am Thorac Soc 2018; Marshall et al, Thorax 2012 67:613-17

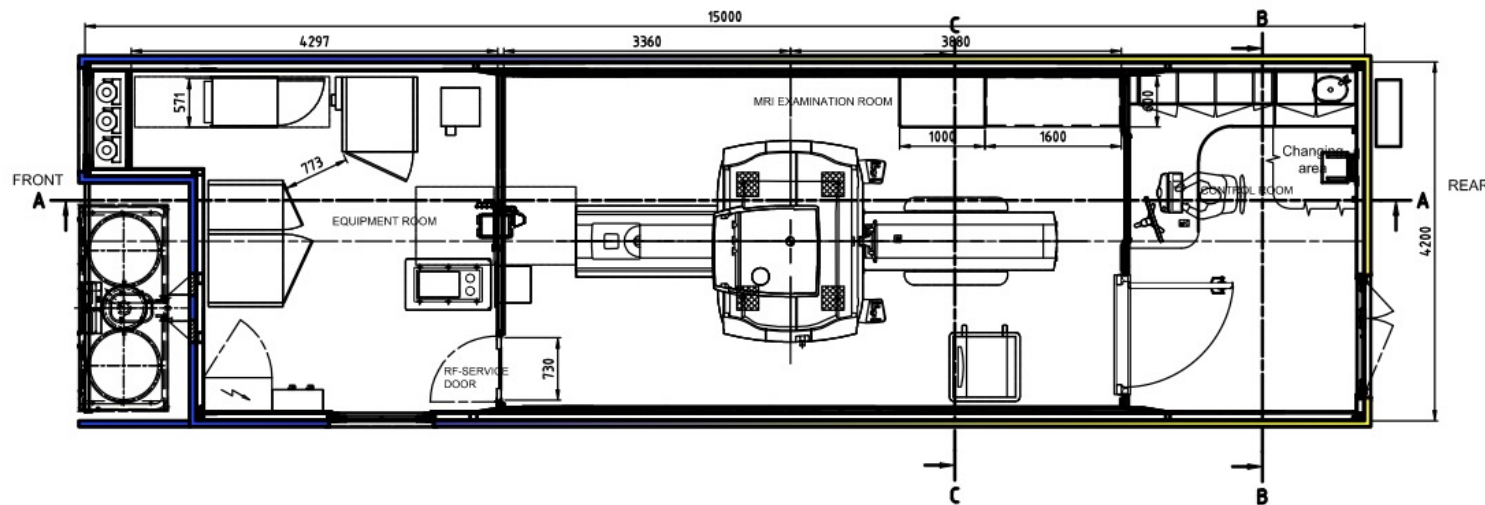
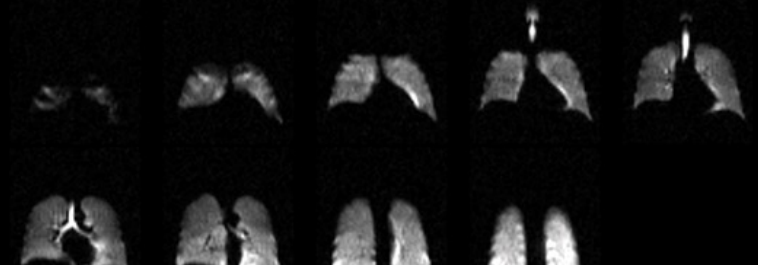
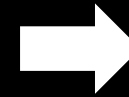
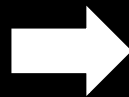
NHS healthcare economics

Exam	NHS Tariff rates
1H MRI with patient repositioning and/or more than one contrast agent	£308
CT two areas with contrast	£116
Nuclear Medicine - category 4	£357
Spirometry (FEV1, FVC)	£53
Transfer factor (TLCO)	£111

Local reimbursement - Xenon + 1H MRI structure function exam ~ £450

Accessibility and portability of technology

- ^{129}Xe lung imaging at novice clinical imaging centre
- no specialist equipment is needed for polarizer installation





☒ 1.5T ☐ 3T ☒ DCE ☒ ^{129}Xe
[Download protocols](#)
 Search for sequence..

All sequences

All sequences		
SSFSE (HASTE) cor	Images	Details
Dynamic SPGR Imaging (for FD MRI)	Images	Details
PROPELLER w/ navigator	Images	Details
PROPELLER w/o navigator	Images	Details
T1-mapping (Look-Locker)	Images	Details
UTE	Images	Details

High resolution proton density weighted imaging with retrospective gating.

Acquire images during free-breathing, using the respiratory bellows where possible (otherwise use k0 / DC signal) for retrospective gating.

Reference: Johnson, KM
et al.



Healthy

[illegible]

Xe 3D Ventilation

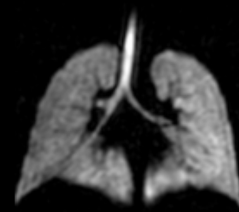
Images

Details

Xe 3D SSFP Ventilation
(Research sequence)

High resolution 3D
FIESTA sequence to
generate maps of lung
ventilation.

Localized ventilation defects can be visualized, characteristic of obstructive lung diseases.

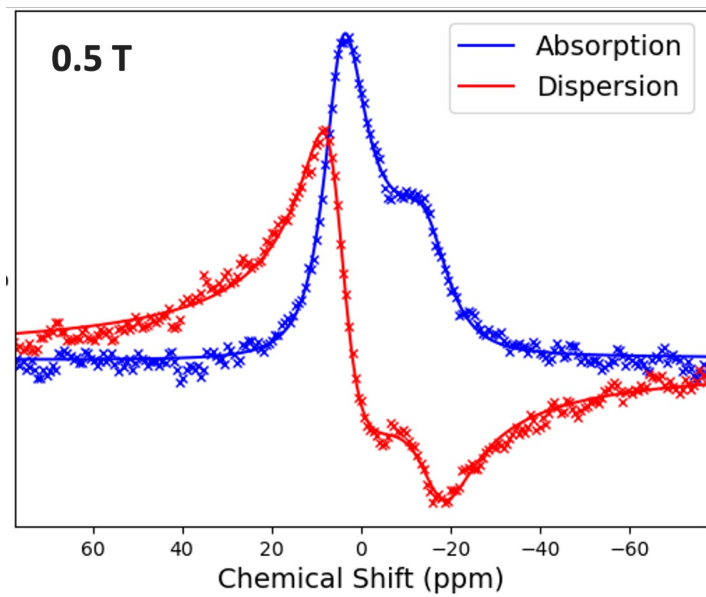


Healthy

Marshall, H et al.
Detection of early
subclinical lung disease
in children with cystic

[illegible]

^{129}Xe MR at 0.5T



Logistical considerations for ^{129}Xe MRI

Cost

- RF coils & broad band RF amplifier ~ £200 k
- Gas polariser ~ £400-600 k
- Gas ~ £20-200/L

Technical support

- MR physicist and MR radiographer

Clinical interest

- Respiratory medicine / pharma
- Regulatory licencing



MS NUMBER: MS 18739 Version: 1

MHRA
Medicines and Healthcare Products Regulatory Agency

On behalf of the Licensing Authority under:
The Human Medicines Regulations 2012 (SI 2012/1916)

Manufacturer's "Specials" Licence

SECTION 1A

1. Licence Number
MS Number: MS 18739

2. Name of Licence Holder
UNIVERSITY OF SHEFFIELD

3. Address(es) of manufacturing/importing site(s)
(All authorised sites should be listed if not covered by separate licences)

MHRA SITE NUMBER	SITE NAME	ADDRESS
114988	UNIVERSITY OF SHEFFIELD	ACADEMIC UNIT OF RADIOLOGY, C FLOOR, DIVISION OF CLINICAL SCIENCES, ROYAL HALLAMSHIRE HOSPITAL, GLOSSOP ROAD, SHEFFIELD, S10 2JF, UNITED KINGDOM

4. Legally registered address of Licence Holder
ACADEMIC UNIT OF RADIOLOGY, C FLOOR, DIVISION OF CLINICAL SCIENCES, ROYAL HALLAMSHIRE HOSPITAL, GLOSSOP ROAD, SHEFFIELD, S10 2JF, UNITED KINGDOM

5. Scope of authorisation and dosage form
See ANNEX 1

6. Legal basis of licence
See Section 1B of licence.

7. Name of responsible officer of the competent authority of the member state granting the manufacturing authorisation
Sean Kaiser

Medicines and Healthcare Products Regulatory Agency

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International Workshop for Pulmonary Functional Imaging 2028

Sheffield 2028

