# Running a Hyperpolarised Exam

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# Overview

- **Specifics for hyperpolarised spins**
- Specifics for thermally-polarised spins
- MNS Prescan
- Localisation
- Sequences
- Discussion

# Specifics of Hyperpolarised MRI: Nuclei

| Nucleus | T1 | Frequency at 3T | Natural abundance | Polarisation method | Application |
|---|---|---|---|---|---|
| $^{1}H$ | too short (<1s in vivo) | 127.73 | 99.98% | DNP | Perfusion |
| $^{3}He$ | hours in cell; minutes in vivo | -97.30 | 0.00013% | SEOP | Lung ventilation |
| $^{13}C$ | up to ~1min | 32.12 | 1.08% | DNP, PHIP | Metabolism, perfusion |
| $^{15}N$ | up to ~5min | -12.95 | 0.37% | DNP | Perfusion |
| $^{129}Xe$ | hours in cell; minutes in vivo | -35.33 | 26.44% | SEOP | Lung ventilation, update |

# Specifics of Hyperpolarised MRI: Gradients

**Spatial encoding proportional to gyromagnetic ratio of nucleus**

- $\gamma_{13C}=\frac{1}{4}\gamma_{1H}$ → 4·gradients for same spatial resolution
- $\gamma_{15N}=\frac{1}{10}\gamma_{1H}$ → 10·gradients for same spatial resolution
- $\gamma_{3He}=\frac{3}{4}\gamma_{1H}$ → 30% higher gradients for same spatial resolution
- $\gamma_{129Xe}=\frac{1}{4}\gamma_{1H}$ → 4·gradients for same spatial resolution

<u>However</u>: often SNR is main limitation to resolution, not gradients

# Specifics of Hyperpolarised MRI: Magnetisation

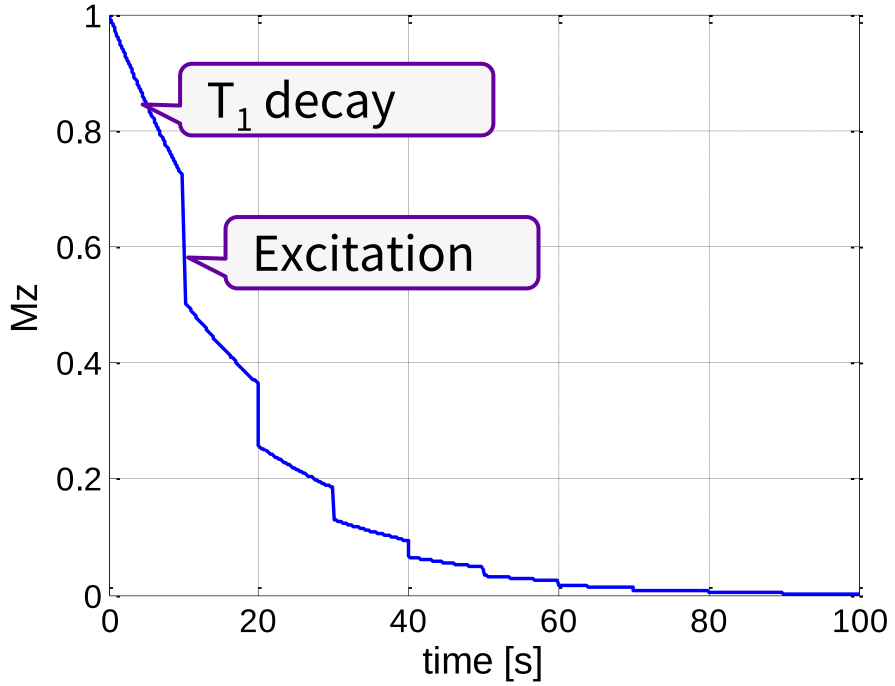
## Magnetisation (=polarisation) is very precious

- thermal polarisation typically negligible: no recovery
- disappearing with $T_1$ relaxation & excitation

→ requires efficient acquisitions:
optimally use polarisation, fast in comparison to $T_1$

→ observable processes (e.g., metabolism) fast in comparison to $T_1$

→ limits pre-scanning



# 13C

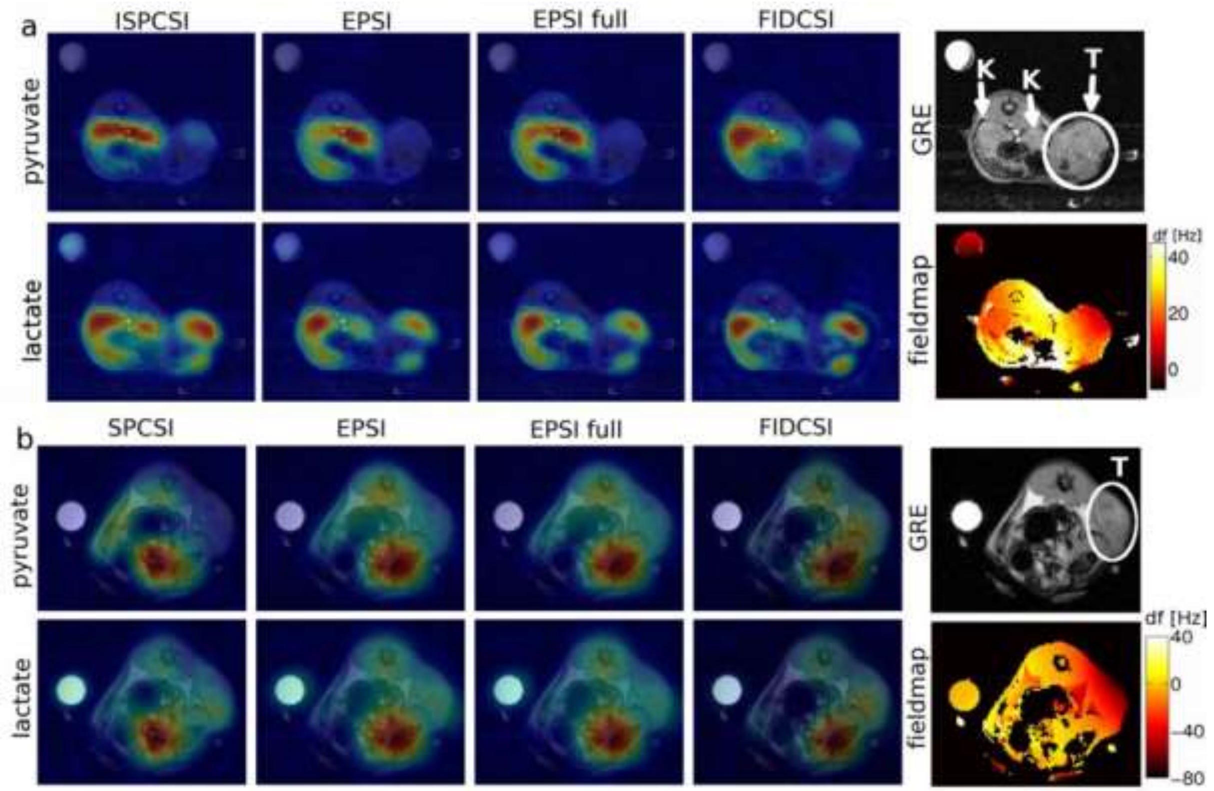
**Basics**

- 32.1MHz @3T, spin ½
- 1.1% natural abundance
- Injection of hyperpolarised 13C compounds (eg [1-13C]pyruvate)
- Metabolic conversion (eg Lac, Ala, BC)
- Thermal: non-localised

**Applications**

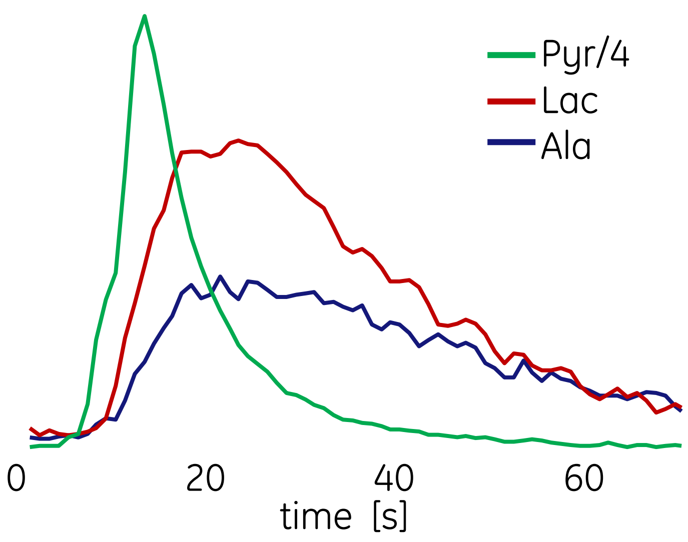
- Detect altered metabolism: tumours, cardio, neuro, …

13C Sequence Comparison in Rat Kidneys




Comparison of Acquisition Schemes for Hyperpolarised 13C Imaging. Durst M, Köllisch U, Frank A, Rancan G, Gringeri C, Karas V, Wiesinger F, Menzel MI, Schwaiger M, Haase A, Schulte RF. NMR Biomed. 2015;28(6):715-25.

# 13C Metabolic Imaging




## Challenge

- Encode large amount of information in a few seconds

## Information

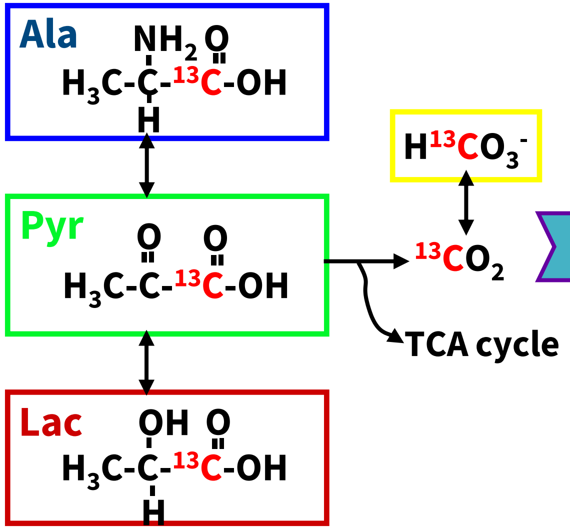
- 1D spectral, 3D spatial, 1D temporal = **5D**

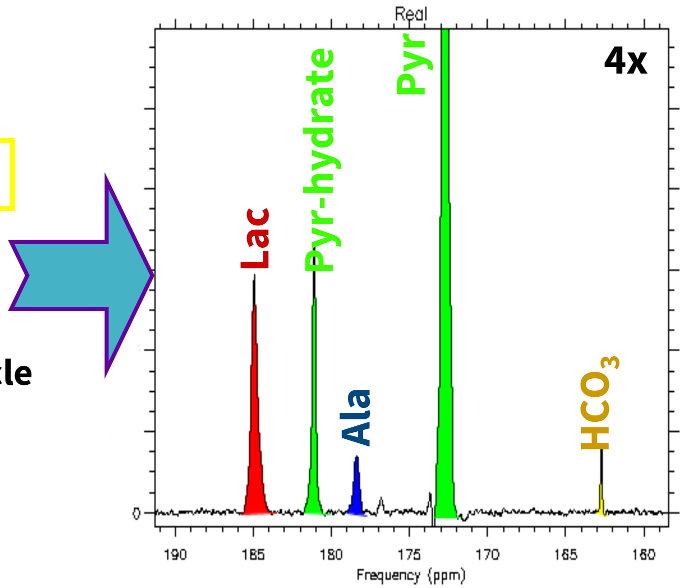
## Constraints

- Polarisation disappearing after 30-60 sec and 90° excitation
- In-vivo conditions inherently difficult

## Approaches

- FID, MRSI, EPSI, Spirals, IDEAL, spectral-spatial excitation, SSFP, spin-echo, …

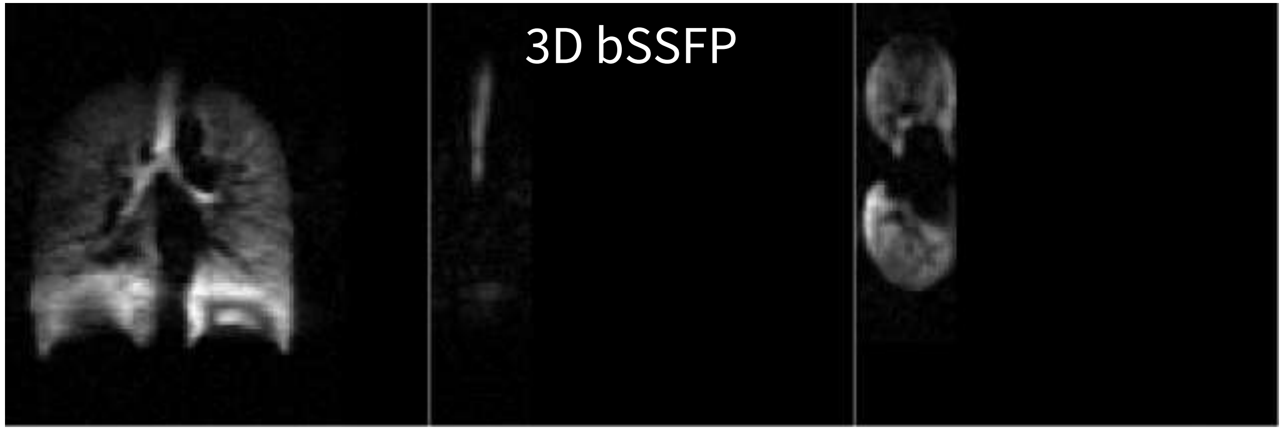


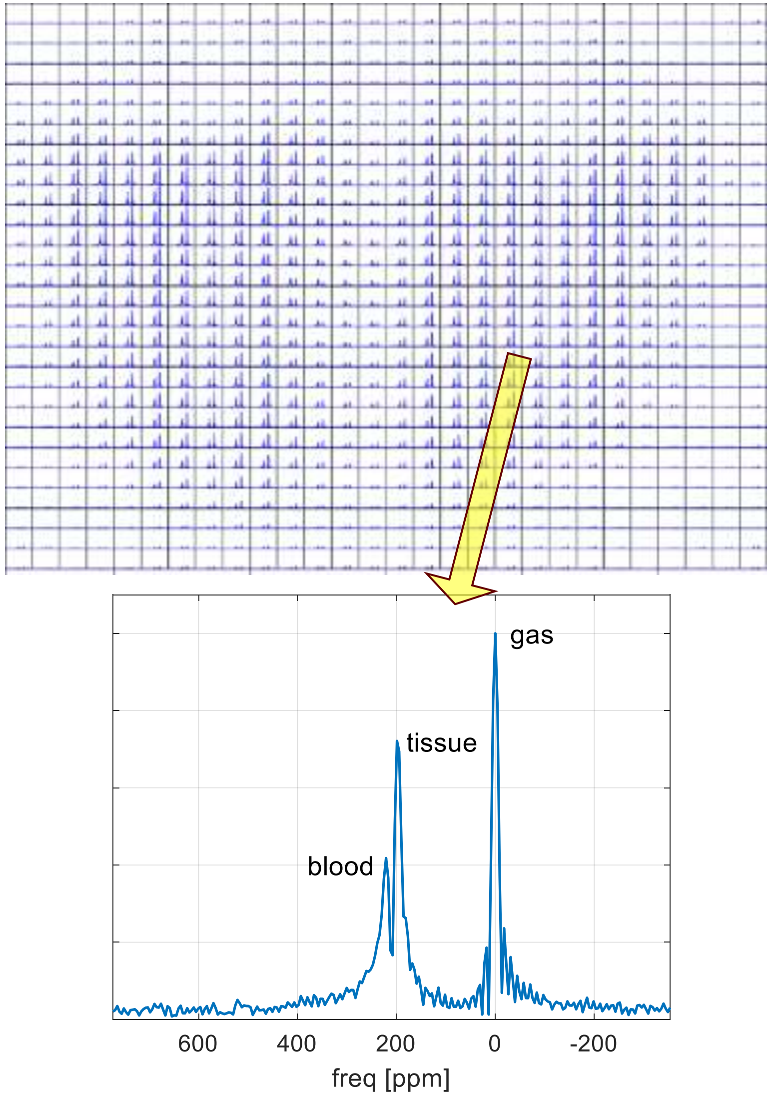
# 129Xe

## Basics
- -35.3MHz @3T, spin ½
- 26.4% natural abundance
- Inhalation of hyperpolarised 129Xe gas
- Gas uptake: direct measure of lung function

## Applications
- Long Covid, asthma, chronic obstructive pulmonary disease, cystic fibrosis, interstitial lung disease, …




3D density-weighted MRSI




MRM 2023; in collaboration with Guilhem Collier, Jim Wild

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The University Of Sheffield.

# $^{129}Xe$ Lung Ventilation Imaging

## Information

- 3D spatial

## Constraints

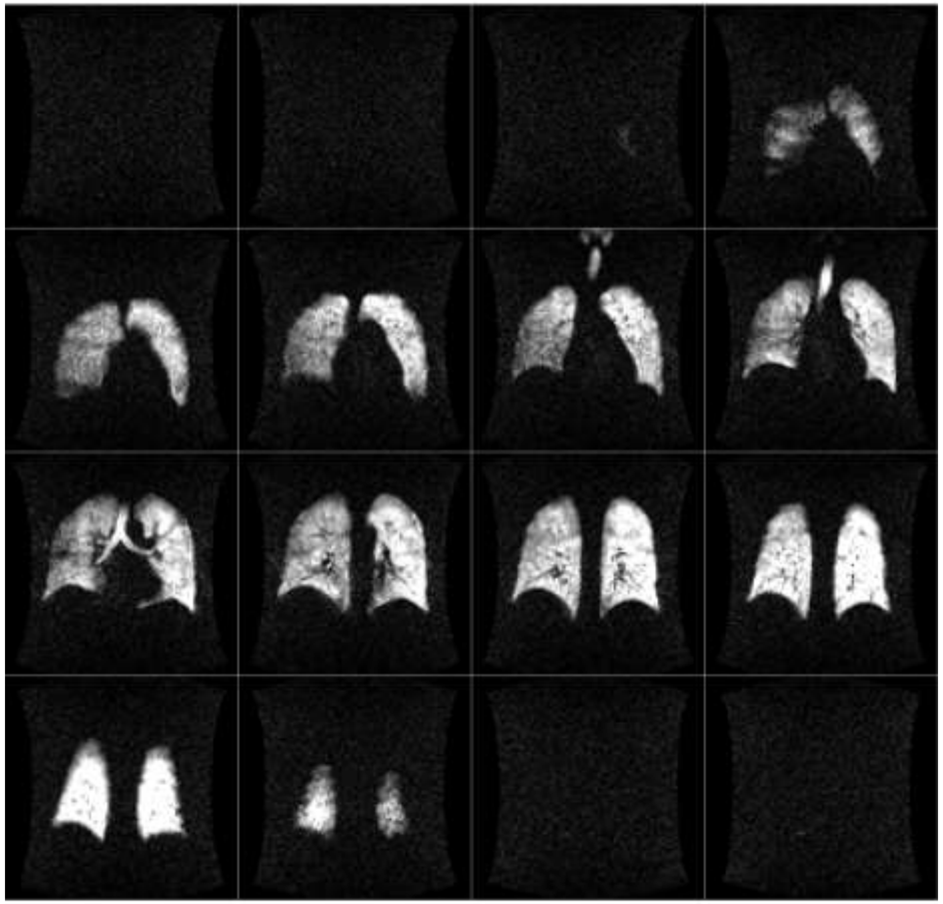
- Scan must fit into one breath-hold ≤ 10-15sec

## Approaches

- MRI: 2D/3D GRE/bSSFP, Cartesian or non-Cartesian

## Consensus group recommendation

- 2D Cartesian GRE: voxel size=4×4×15mm$^3$



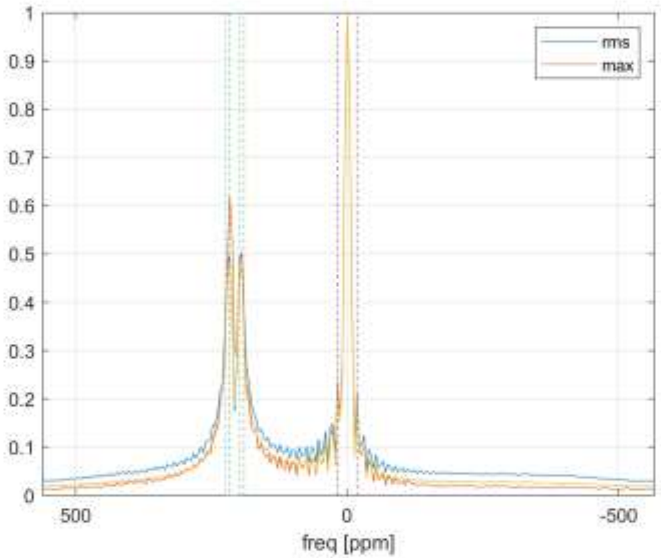
Protocols for multi-site trials using hyperpolarized 129 Xe MRI for imaging of ventilation, alveolar-airspace size, and gas exchange: A position paper from the 129 Xe MRI clinical trials consortium.
Niedbalski PJ, Hall CS, Castro M, Eddy RL, Rayment JH, Svenningsen S, Parraga G, Zanette B, Santyr GE, Thomen RP, Stewart NJ, Collier GJ, Chan HF, Wild JM, Fain SB, Miller GW, Mata JF, Mugler JP 3rd, Driehuys B, Willmering MM, Cleveland ZI, Woods JC.
Magn Reson Med. 2021 Dec;86(6):2966-2986. doi: 10.1002/mrm.28985.

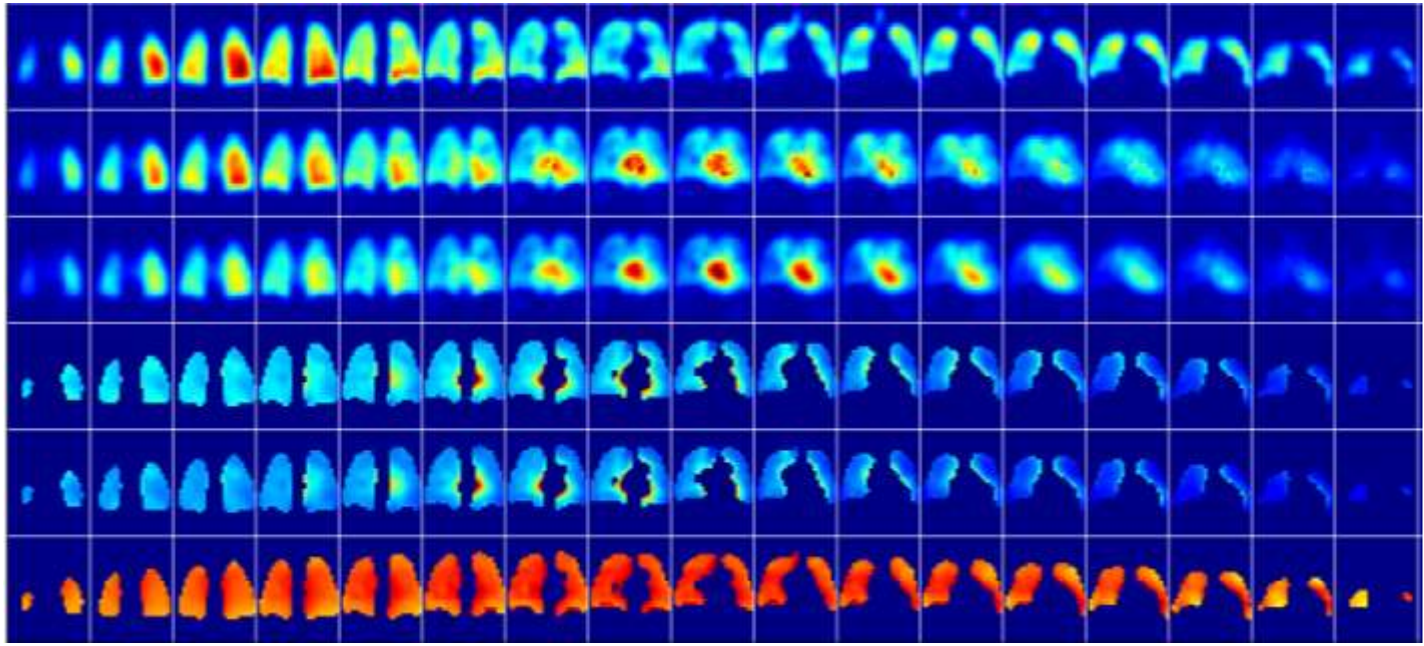
# 129Xe Lung Dissolved Phase Imaging

**Information**
- 3D spatial, 1D spectral

**Constraints**
- Scan must fit into one breath-hold ≤ 10-15sec
- Signal levels: gas >100 times dissolved

**Approaches**
- Frequency-selective/tailored excitation
- 3D MRSI, radial EPSI, Dixon



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# Overview

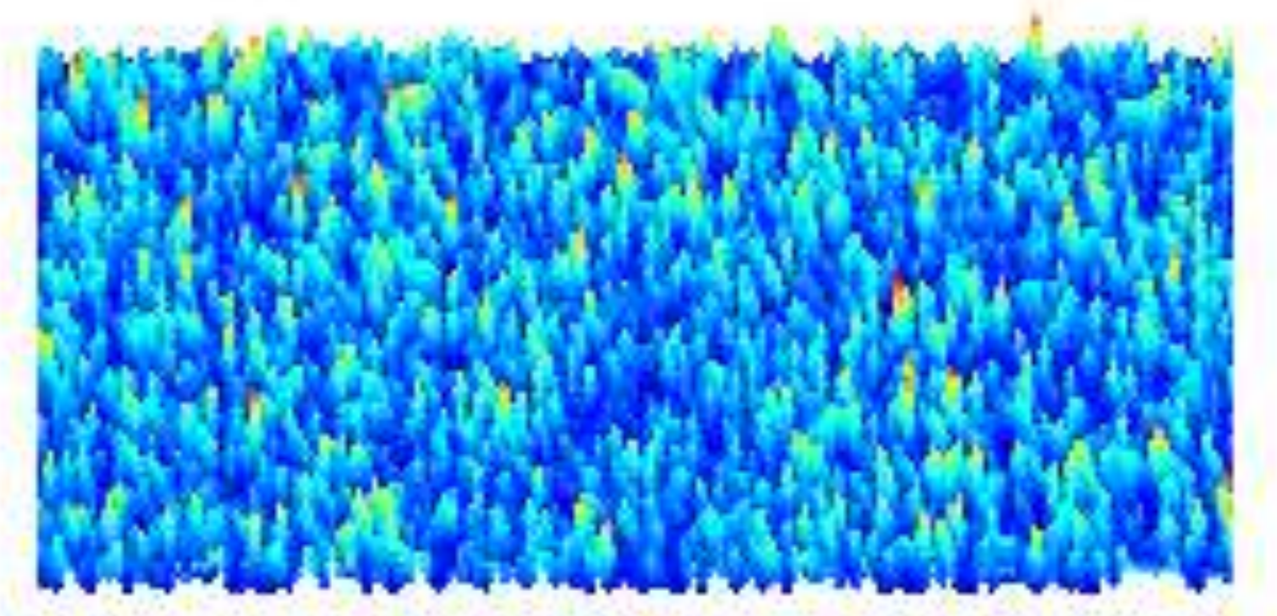
- Specifics for hyperpolarised spins
- **Specifics for thermally-polarised spins**
- MNS Prescan
- Localisation
- Sequences
- Discussion

# Specifics of Thermally Polarised MNS: Nuclei

| Nucleus | T1 | T2 | Frequency at 3T [MHz] | Natural abundance | Concentrations | Application |
|---|---|---|---|---|---|---|
| $^{2}H$ | 50-350ms | 10-60ms | 19.61 | 0.015% | 1mM | Metabolism, perfusion |
| $^{7}Li$ | 2-10s | 10ms-10s | 49.64 | 92.4% | 0.2-1mM | Psychiatric drug |
| $^{17}O$ | 0.5-10ms | 0.5-10ms | 17.32 | 0.038% | 2-22mM | Oxygen metabolism |
| $^{19}F$ | 1-4s | 1-400ms | 120.23 | 100% | traces | Lung imaging, cell tracking |
| $^{23}Na$ | 20-60ms | 0.5-60ms | 33.79 | 100% | 10-350mM | Cell function |
| $^{31}P$ | 1-10s | 40-400ms | 51.71 | 100% | 0.01-40mM | Metabolism, pH |

# Main Limitation of MNS: SNR

- Generally (very) low sensitivity due to
  - low concentrations
  - low $\gamma$
- Huge voxels/ROIs
- Lots of averaging
- Fancy encoding highly limited



# 2H

## Basics

- 19.6MHz @3T, spin 1
- 0.015% natural abundance
- RF noise
- Ingestion/injection of 2H labelled compounds (e.g. [6,6'-$^2H_2$]glucose)
- Metabolic conversion (e.g. to Lac/Glx)
- Short T2* → small CS

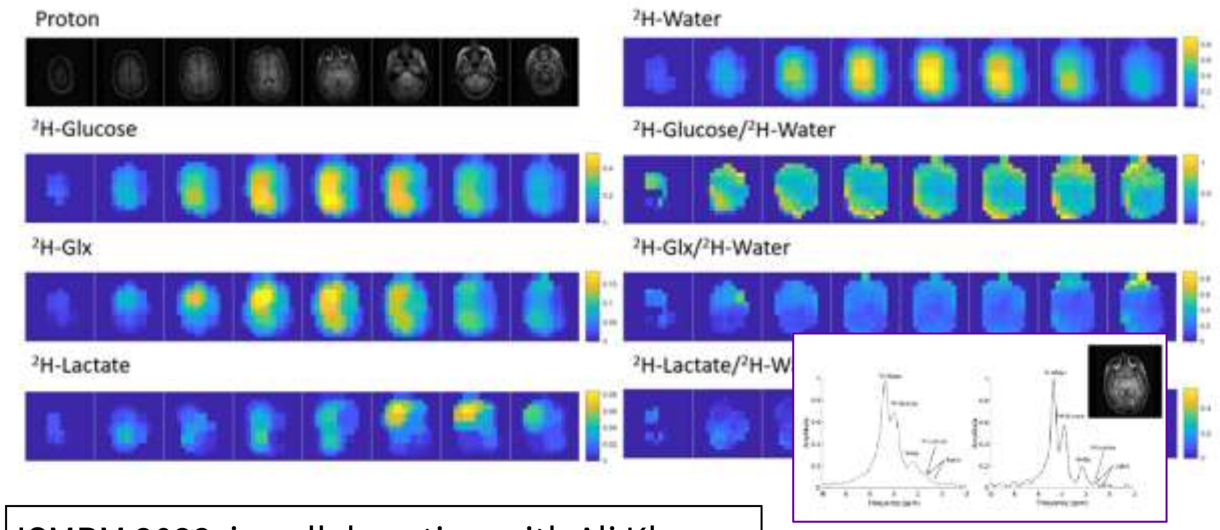
## Applications

- Metabolic disorders, tumours, …

## Sequences

- 3D MRSI

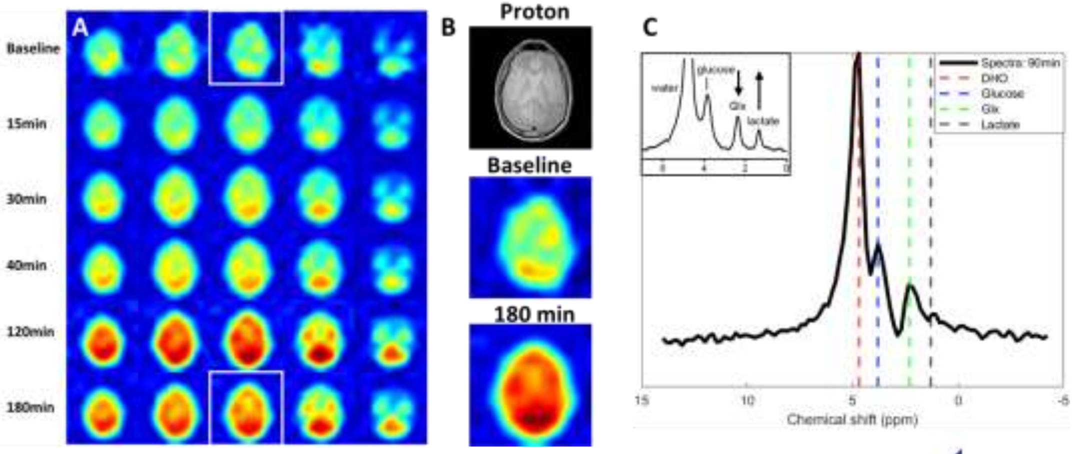
### Comparison 2H-Glc to 13C Pyr




ISMRM 2022; in collaboration with Ali Khan, Josh Kaggie, Mary McLean, Ferdia Gallagher

UNIVERSITY OF CAMBRIDGE

### Dynamic D2O after Glc ingestion




ISMRM 2022; in collaboration with Michael Vaeggemose, Christoffer Laustsen

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# 23Na

## Basics

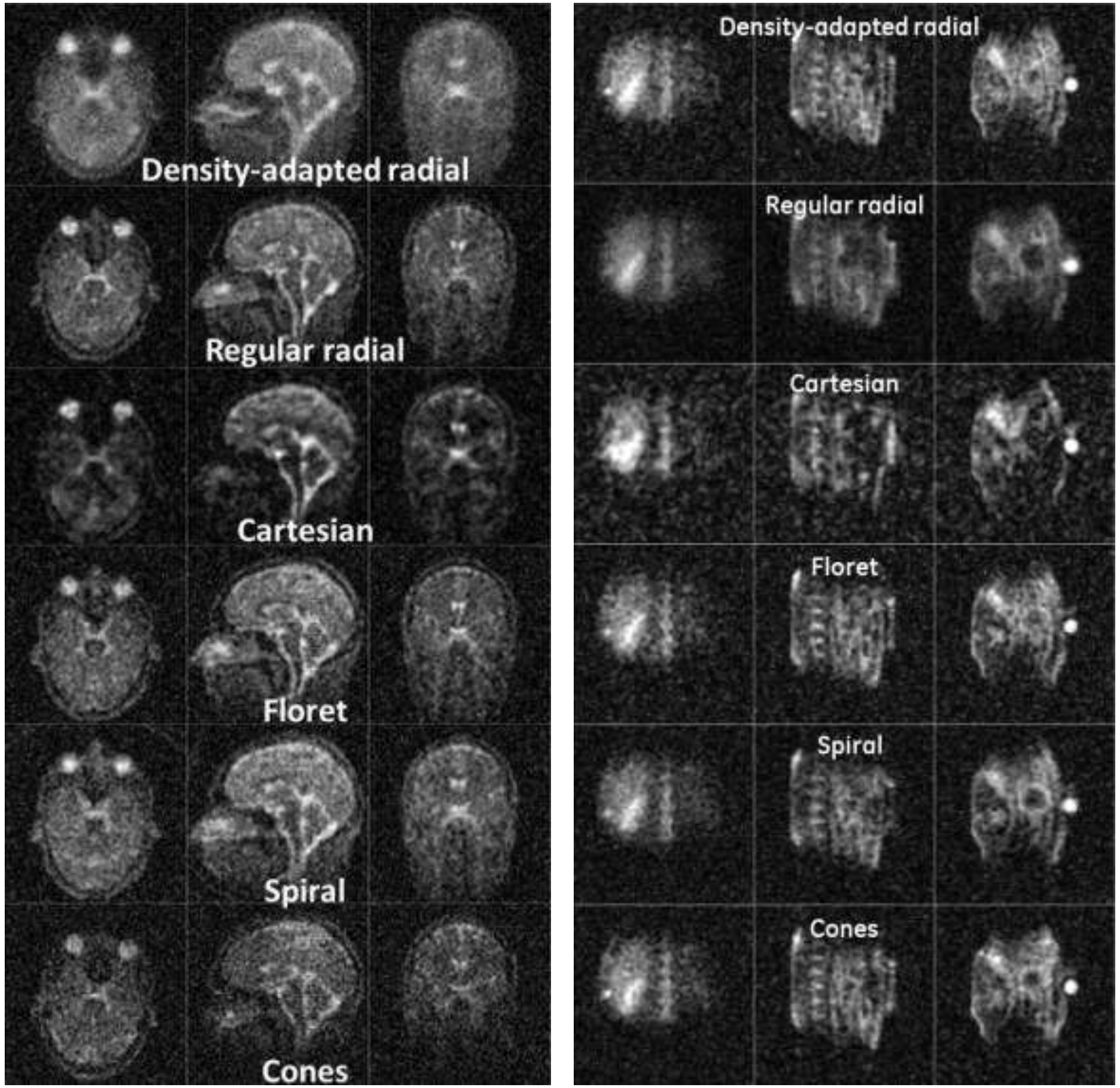
- 33.8MHz @3T, spin 3/2
- 100% natural abundance
- High endogenous signal

## Applications

- Stroke, tumours, cartilage, muscle, kidneys, …

## Sequences

- 3D GRE: radial, cones, …




In collaboration with Michael Vaeggemose, Esben Hansen, Christoffer Laustsen

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# 31P

## Dynamic muscle spectroscopy

### Basics

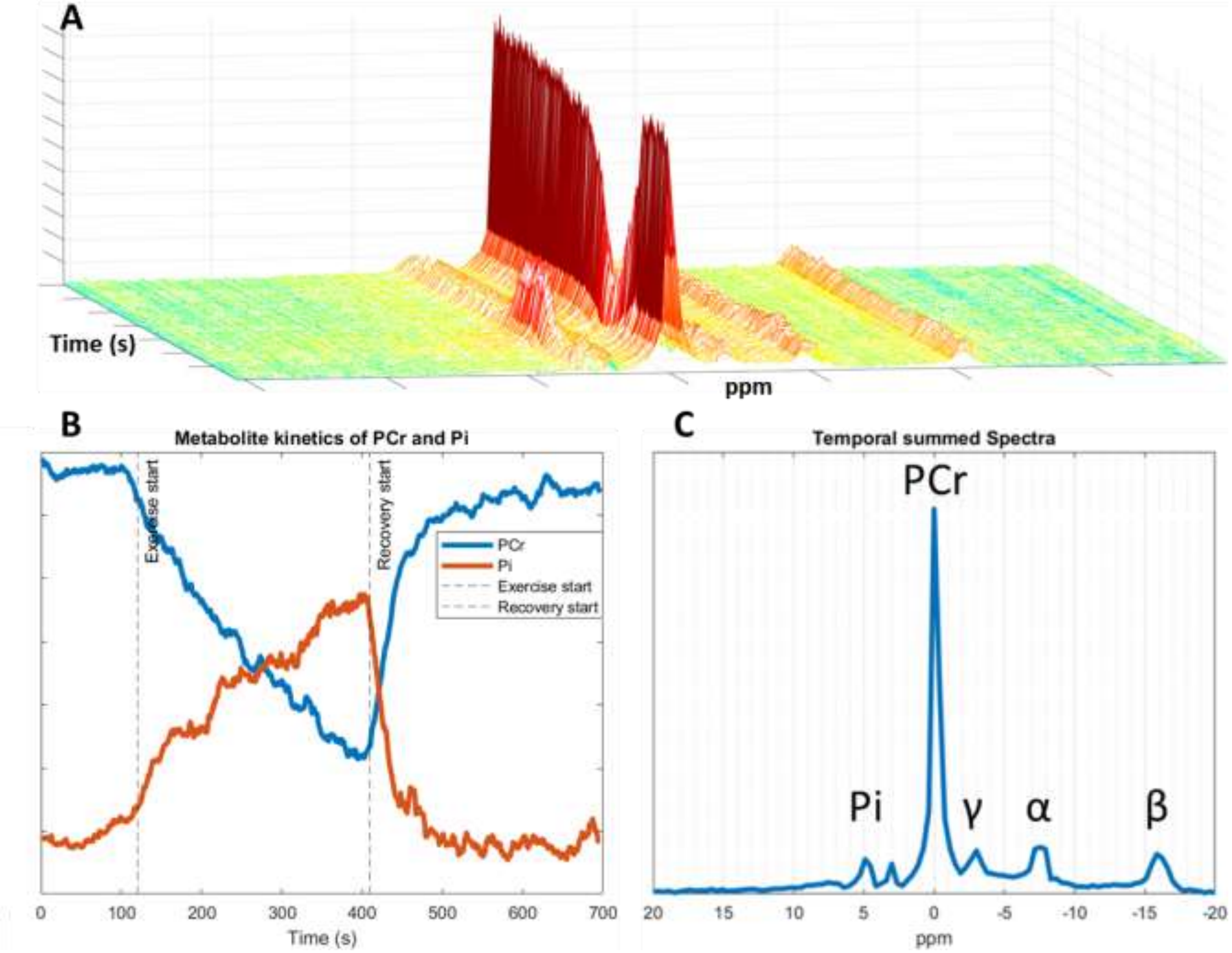
- 51.7MHz @3T, spin ½
- 100% natural abundance
- Endogenous signal

### Applications

- Energy metabolism: muscle, brain, liver; tumours

### Sequences

- Unlocalised FID
- 2D/3D MRSI
- ISIS: no advantage




Courtesy to Michael Vaeggemose, Christoffer Laustsen

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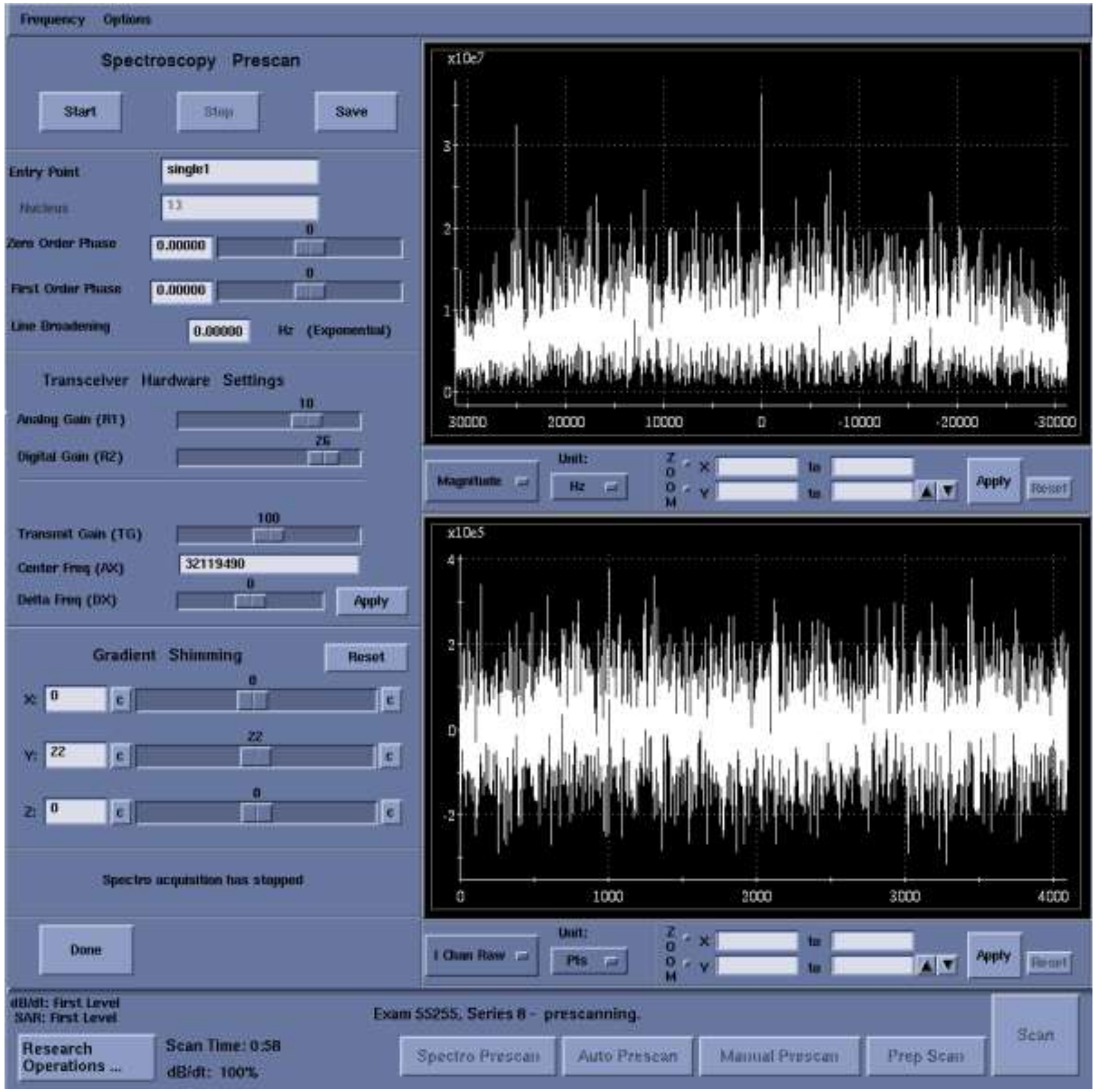
# MNS Prescan: Scanner Calibration

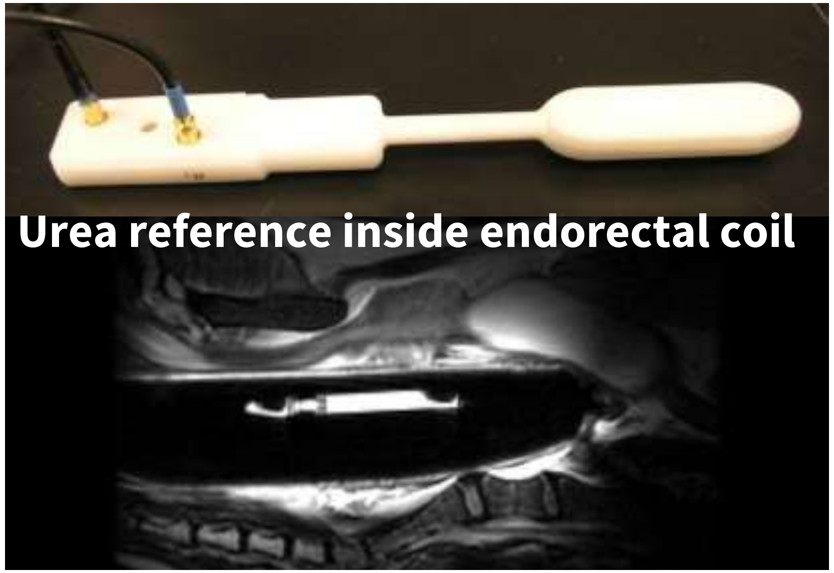
**Parameters**

- TG: transmit gain: aka flip angle calibration, transmit power calibration, …
  *GE: TG=0 → 20 dB attenuation; TG=200 → 0 dB attenuation*
- $f_0$: centre frequency [Hz]
  - Varies for different compounds
  - Scanners loose main magnetic field $B_0$ over time
  - $B_0$ varies after heavy use of scanner (e.g., gradient amp+coil heating)
- RG: Receiver gain: analog + digital
  *GE: R1 analog 1-13; R2=15 or 30 (EDR)*
- Shimming: can be done on 1H



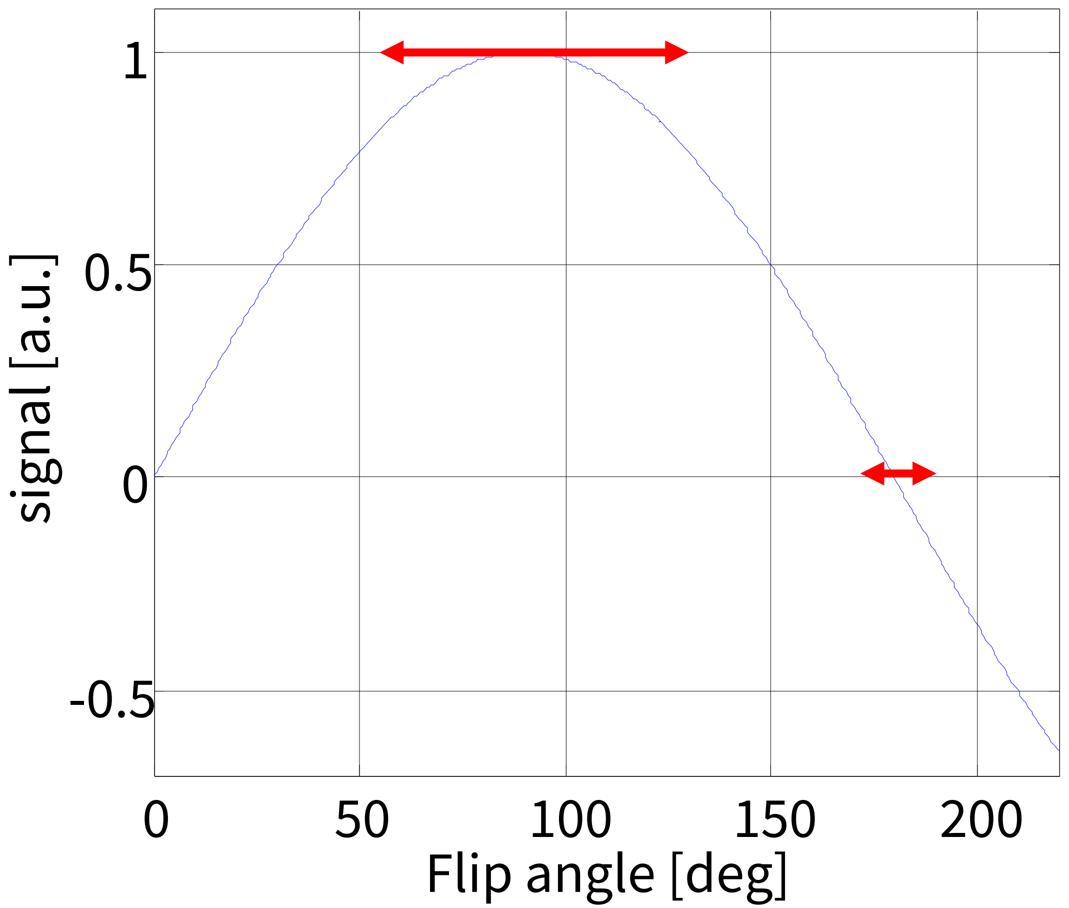
# MNS Prescan

- Difficulty: natural signal too low; hyperpolarised signal too precious
- $^{13}C$: external reference; e.g.,
  [1-13C]lactic acid
  [13C]urea
  $T_1$ very long → dope with ~2:100 chelated gadolinium contrast agent
- $^{129}Xe$: breath small gas dose for pre-scanning
  Low frequency: coils do not change much + loss of $B_0$ field small
  → use stored values



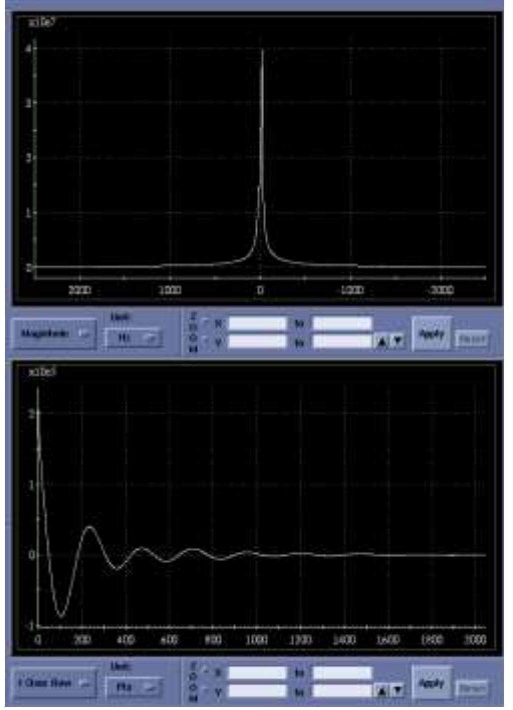

# MNS Prescan: Manual TG Calibration

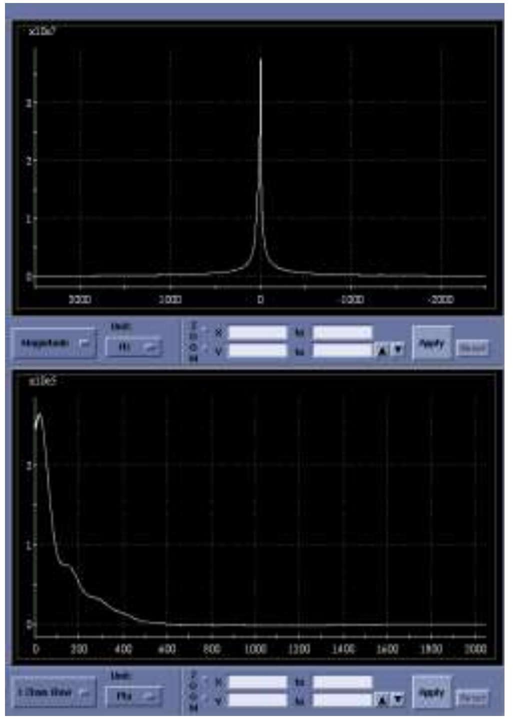
- Display Spectra
- Step through starting from sufficiently low TG values
- Look at the growth of signal
  → maximum = 90°
- Look for disappearance of signal
  → minimum = 180°
- Half the flip angle:
  ½ flip angle= ¼ of power= reduce by 6dB
  *(GE: reduce by TG=60)*
- Problems:
  - time-consuming
  - error-prone
  - difficult for small signal
  - signal not disappearing for surface coil with inhomogeneous $B_1^+$ field



# MNS Prescan: Manual $f_0$ Determination

- Shift spectral peak into centre of frequency span
- Fine tuning: reduce FID beating pattern: smooth real part
- Problems with $f_0$ far off:
  1) frequency selectivity of RF pulses
     e.g., 0.5ms hardpulse → BW ≈ 2 kHz
     e.g., slice-selective pulses: slice easily outside due to chemical-shift displacement artefact
  2) receiver bandwidth (e.g., 5 kHz)
     signal filtered out





# MNS Prescan: $f_0$ via 1H f0

Use 1H centre frequency and conversion table to determine x-nuclear f0

**mnsfreq App:** select suitable MRI scan, click button: reads 1H f0 from dicom and displays xmessage window with different frequencies

**IsotopicChemicalShifts.cfg:** table with offset frequencies stored on MRI → set initial MNS f0

xmessage

| | | | |
|---|---|---|---|
| 1H | H2O | 127732400 | [Hz] |
| 2H | D2O | 19607699 | [Hz] |
| 13C | lactate | 32124039 | [Hz] |
| 13C | pyruvate | 32123662 | [Hz] |
| 13C | bicarb | 32123338 | [Hz] |
| 13C | urea | 32123411 | [Hz] |
| 13C | oil | 32118312 | [Hz] |
| 13C | peg | 32120228 | [Hz] |
| 23Na | | 33787484 | [Hz] |
| 31P | | 51705054 | [Hz] |
| 129Xe | gas bag | 35331200 | [Hz] |
| 129Xe | gas lung | 35331163 | [Hz] |
| 129Xe | blood | 35338867 | [Hz] |
| 129Xe | tissue | 35338160 | [Hz] |

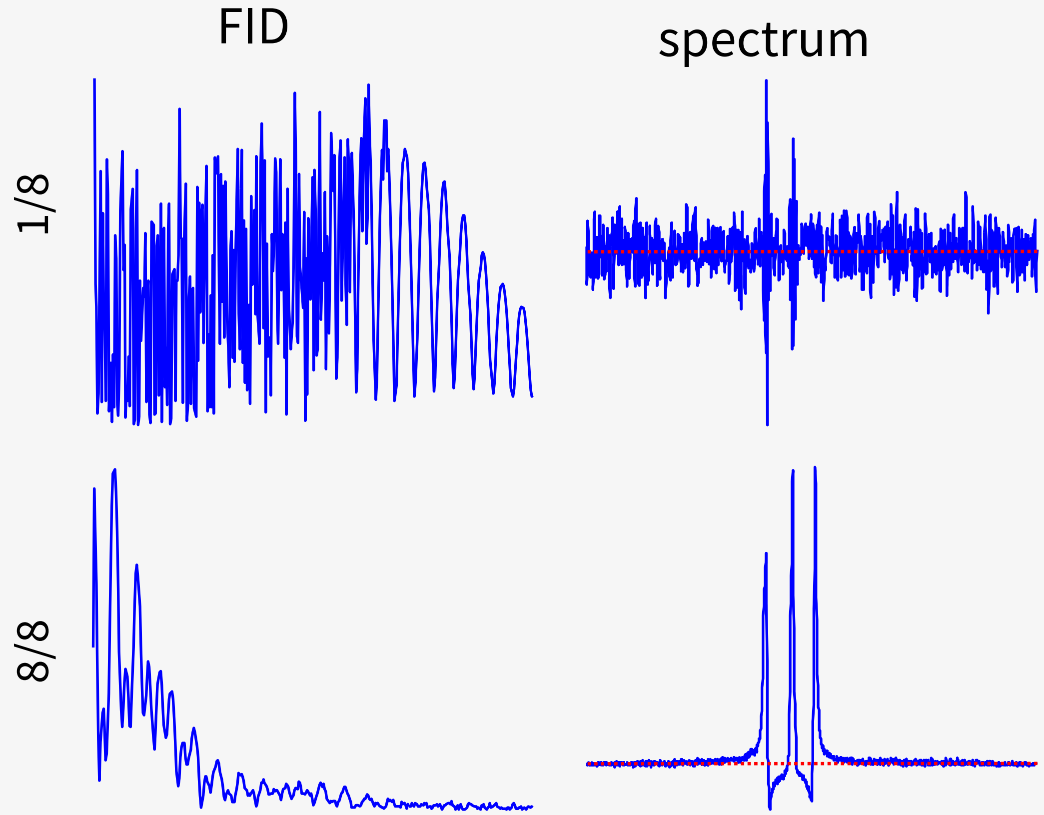
okay

# MNS Prescan: Manual RG Determination

- Receiver chain amplification
  *(GE: R1=analog; R2=digital)*
- Problem with too high RG:
  saturation of amplifiers
- Receiver chain good: even much lower RG still does not increase noise significantly
- Set to typical, known values
- Observe errors in log file

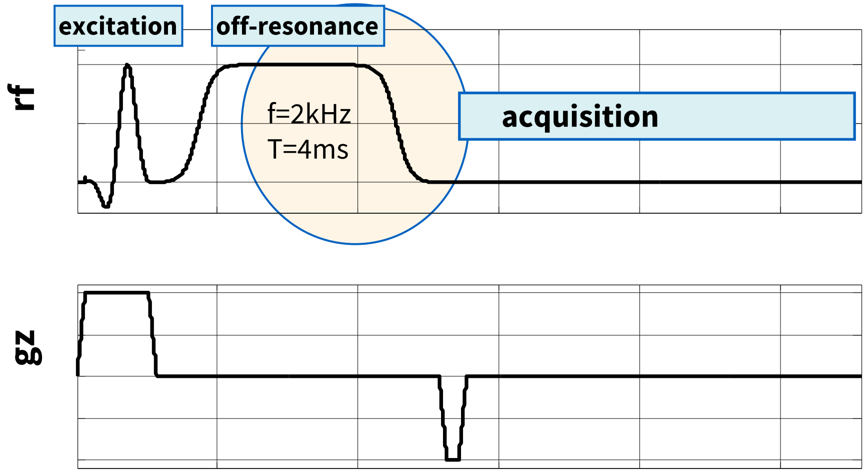
$$scale_{RG} = 2^{\left(\frac{R_1}{2}+R_2\right)}$$

**Measurement of hyperpolarised [1-13C]pyruvate syringe (too high R1+R2)**



# MNS Prescan: Bloch-Siegert

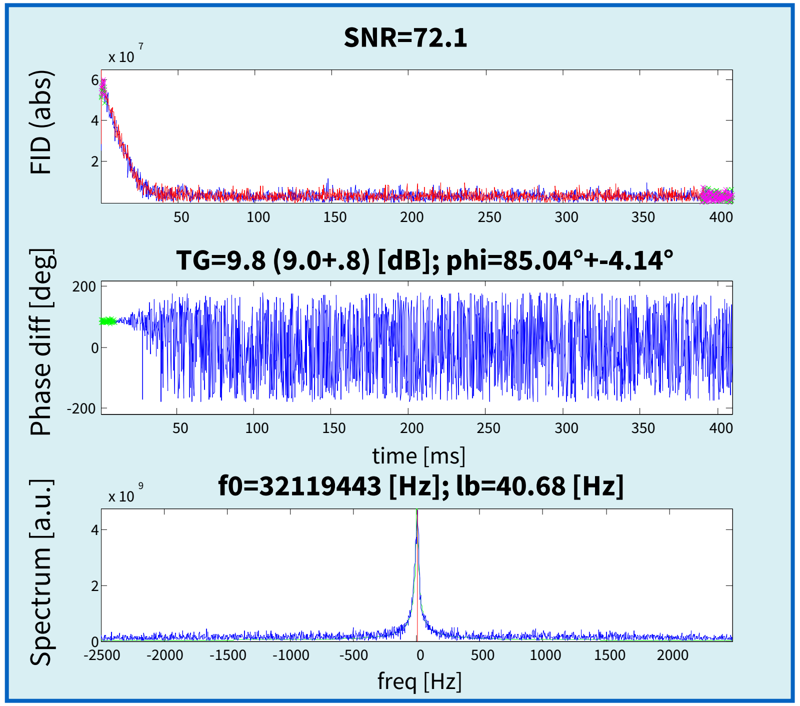
- Bloch-Siegert off-resonance pulse
  - Induce a transmit RF dependent phase shift
  - Measure +/- off-resonance frequency $\omega_{RF}$
  - Subtract out background phase




$$\phi_{BS} \approx \int_0^T \frac{\left(\gamma B_1^+(t)\right)^2}{2\omega_{RF}} dt$$

$$B_{1,peak} = \sqrt{\phi_{BS}/K_{BS}}$$

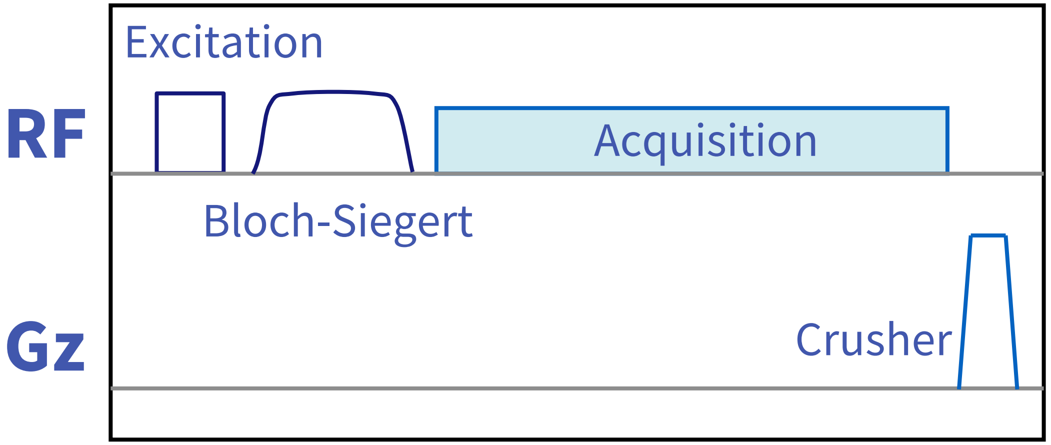
- Here: also SNR+f0+lb




Transmit Gain Calibration for Non-Proton MR using the Bloch-Siegert Shift
RF Schulte, L Sacolick, MH Deppe, M Janich, M Schwaiger, JM Wild, F Wiesinger.
*NMR in Biomedicine 2011*;24:1068.

# Automatic MNS Prescan (MR30.1)

| Step | With x-nuclei signal | No x-nuclei signal |
|---|---|---|
| CF | Peak maximum + center-of-gravity | Calculate from 1H using $\gamma$ + isotopic offset |
| TG | MNSXTG (Bloch-Siegert) – whole volume | Default from config file |
| AS (shim) | Turned off – recycle shim values from most recent 1H scan | |
| RG (R1/R2) | BB current protocol for nuclei with endogenous signal or good phantom signal | System default |



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# Localisation

- No localisation: hardpulse + homogeneous coil
- Localisation by coil sensitivities (surface coil)
- Slice-selection
- Voxel-selection: PRESS, Laser, STEAM, ISIS, …
- Above combined with spatial encoding
- T2 decay for echoes → only spins with sufficient T2
- T2* decay for FID → use short pulses for spins with short T2*

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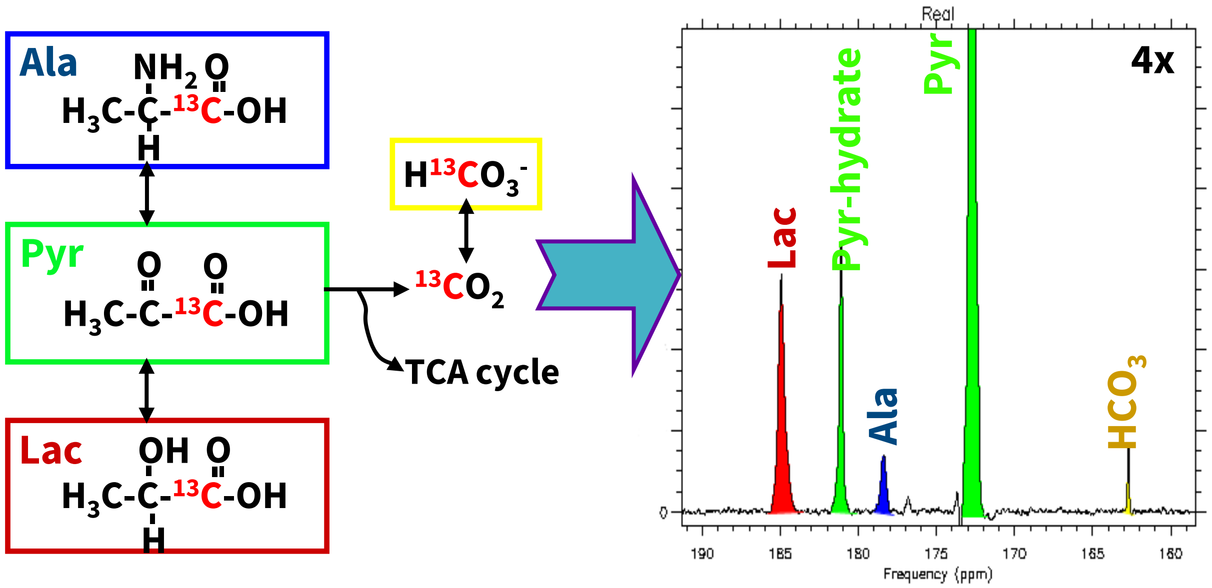
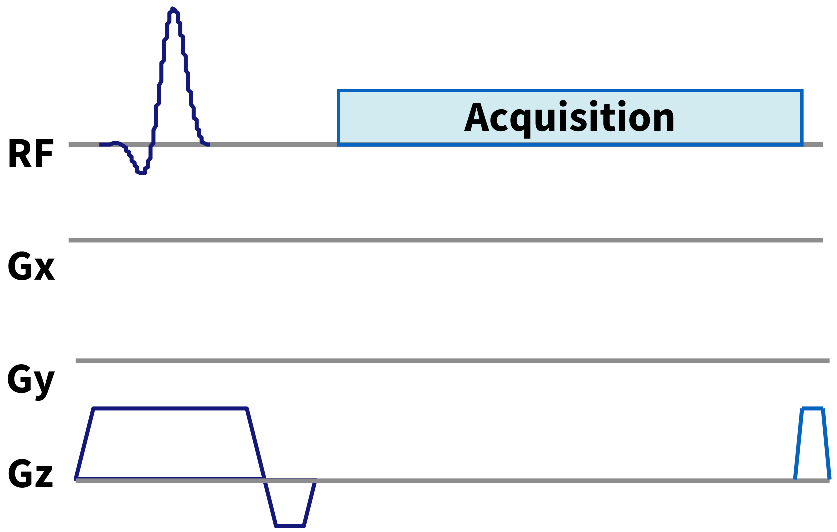
# Sequences: MR Spectroscopy (MRS)

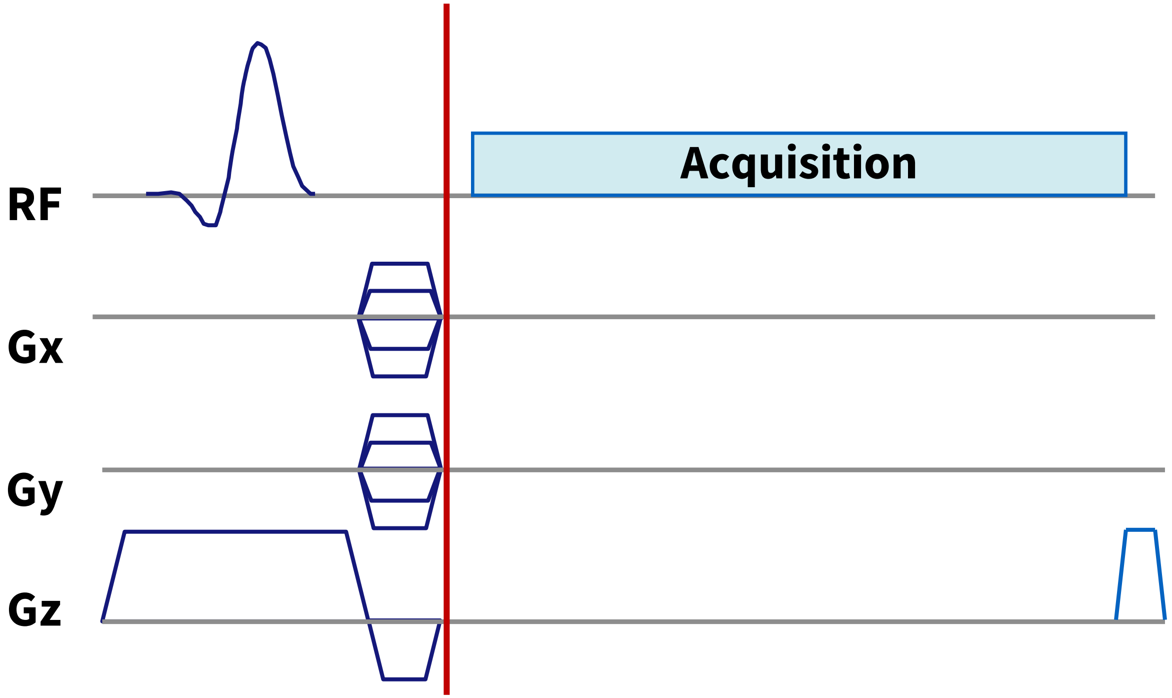
Metabolites have different chemical environments

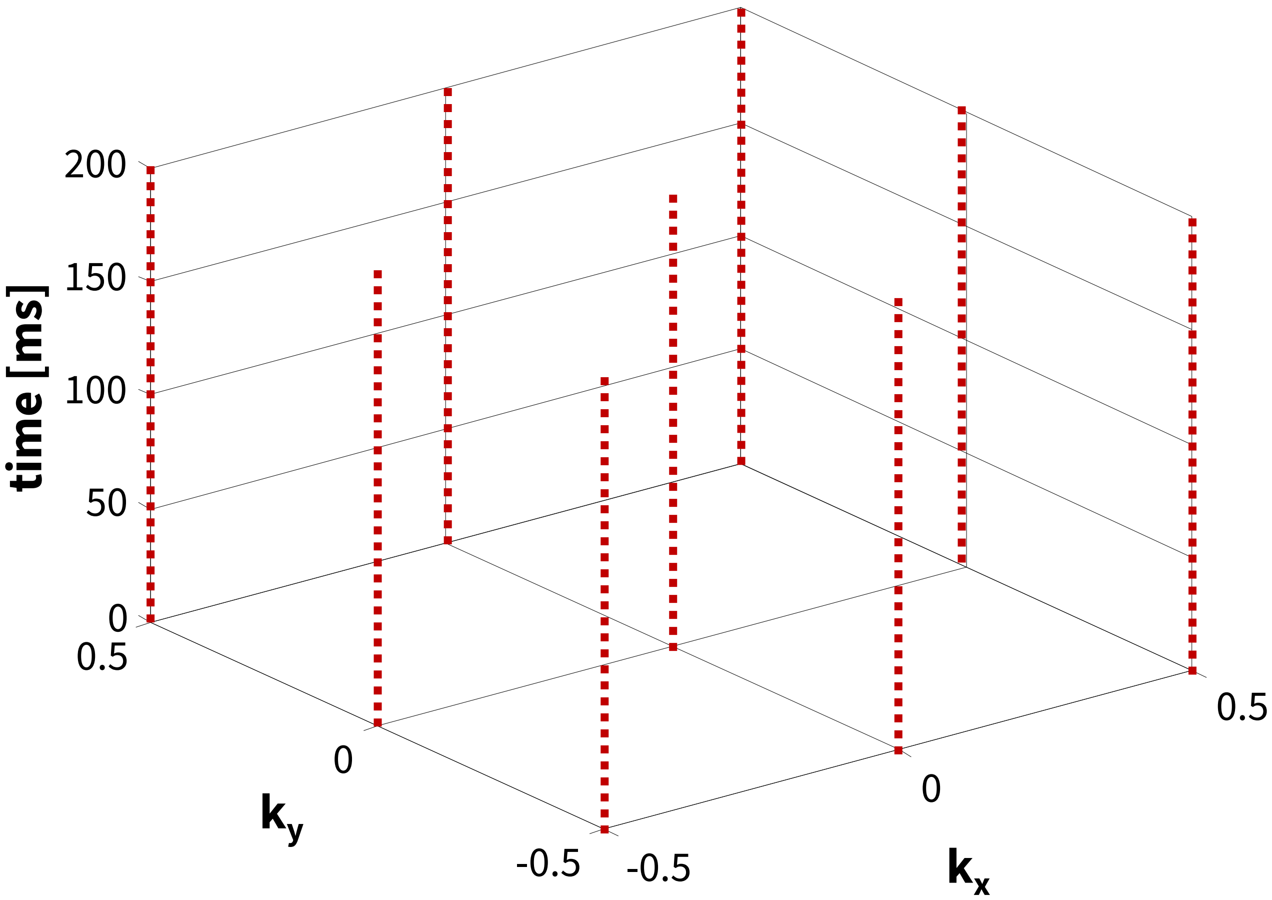
- (slightly) different magnetic shielding
- different resonance frequencies
- detect separately via MR spectroscopy
- skip MRI readout encoding gradient
- Fourier transformation along spectral dimension



# MR Spectroscopic Imaging (MRSI)

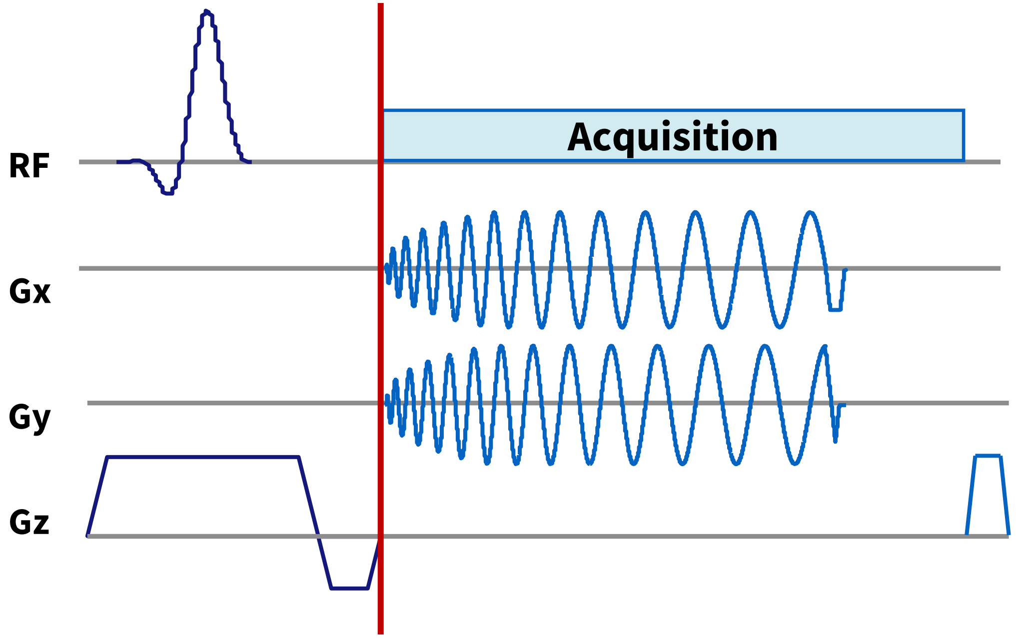


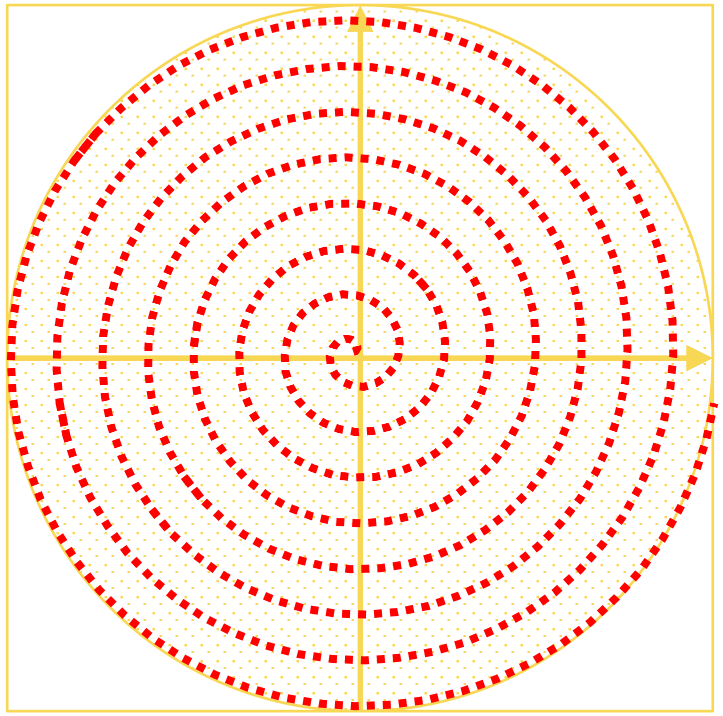




- Sequential phase encoding
- Acquisition of full spectra
- Aka Chemical-Shift Imaging (CSI)
- Fourier transformation along spectral and spatial dimensions

# MR Imaging (MRI)

- Single resonance frequency (like 1H H2O) → omit spectral encoding
- Add readout encoding gradients
- Many flavours to sample k-space existing, eg non-Cartesian spiral trajectories

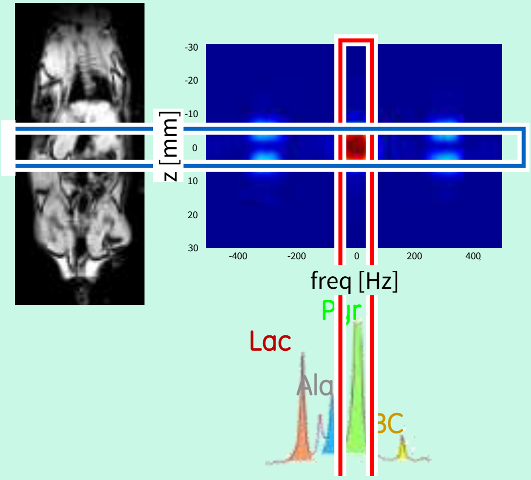


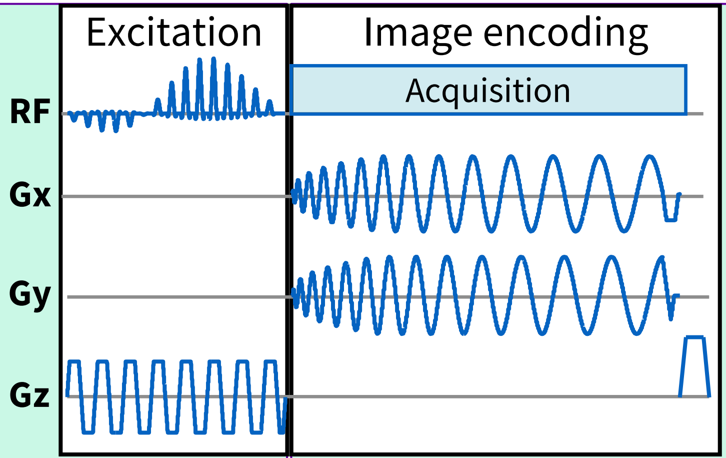



# 13C: Spectral-Spatial Excitation + Spiral Imaging

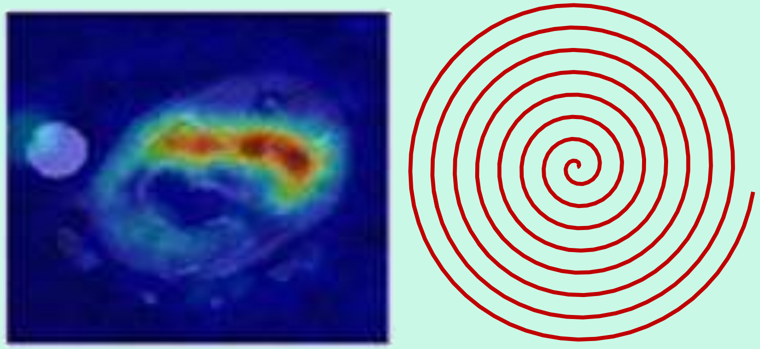
## Spectral-spatial excitation:

1 slice + 1 metabolite per exc




## Single-shot readout (eg spiral)



| metabolite | Lac (0 Hz) | | | | Pyr (-392 Hz) | | | | BC (-716 Hz) | | | | Ala (-215 Hz) | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| slice | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| flip angle | 45° | 45° | 45° | 45° | 15° | 15° | 15° | 15° | 45° | 45° | 45° | 45° | 45° | 45° | 45° | 45° |

repeat

tm=4s

TR=1s

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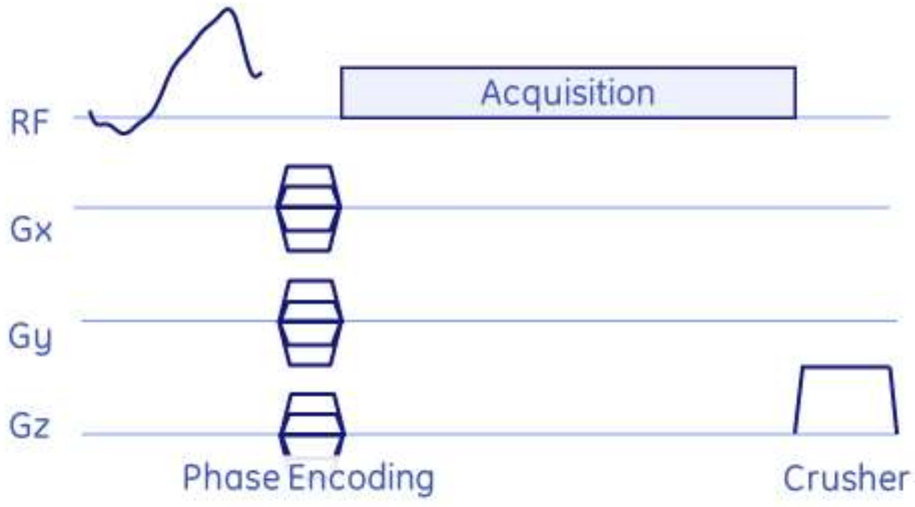
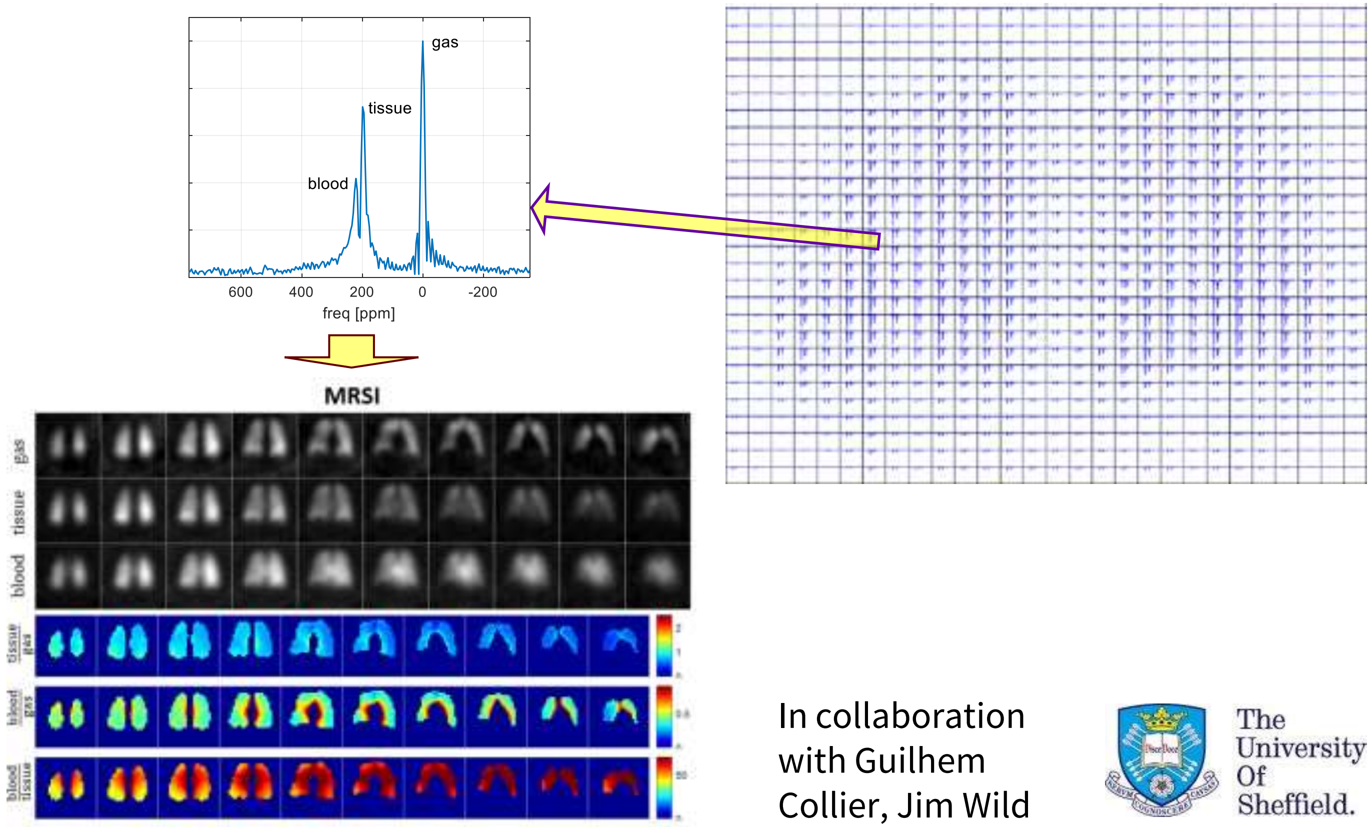
# 129Xe Dissolved-Phase MRSI

- Frequency-tailored RF pulse: excite gas with 1% flip angle of dissolved phase
- Phase encoding: 3D spatial
- Short readout: T2*≈1-2ms
- Fast TR: 8-10ms
- Typical voxel size: ~(2cm)$^3$




In collaboration with Guilhem Collier, Jim Wild

The University Of Sheffield.

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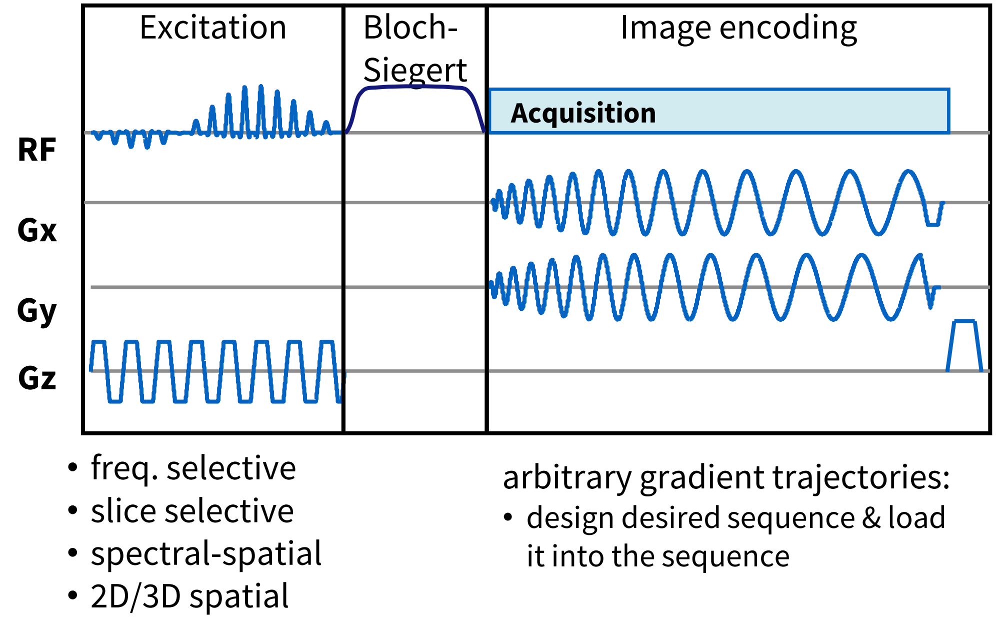
# MNS Research Pack




- MNS product basic: pulse-and-acquire sequence (*FIDCSI*); no MNS pre-scan; no advanced acquisitions
- Idea: provide complete flexibility for <u>advanced</u> users by
  - Reading in arbitrary RF
  - Bloch-Siegert off-resonance pulse
  - Reading in arbitrary gradients
  - Reading in lists with flip angles, TRs, TEs, RF phases, rotations, …
  - Changes for gating, SSFP, etc
- Plugins=waveforms+reconstruction: MNS Prescan, IDEAL Spiral CSI, SPSP Spiral Imaging, EPSI, MR Parameter Mapping, 3D radial UTE, Acquisition-Weighted MRSI

➔ *outsource EPIC to Matlab* ☺

- fidall PSD part of product from MR30.0 on (but no waveforms, recon, etc.)

# MNS Research Pack: Installations

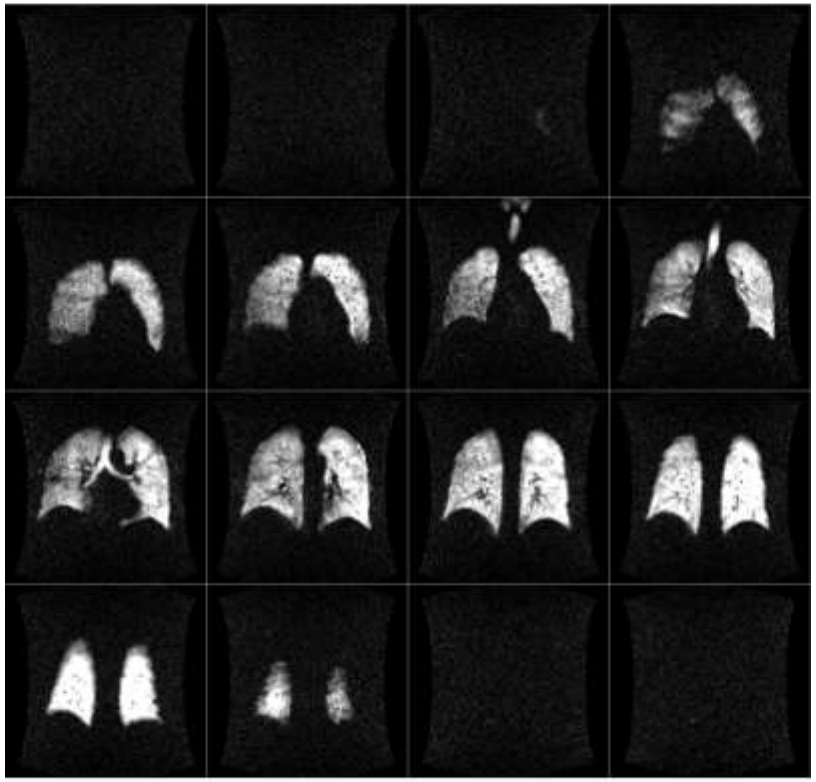
**Europe**
1) Imago7 Pisa: MRP, 23Na, 31P, 2H
2) Århus: 13C, 23Na, 2H, 31P, 129Xe, MRP
3) Sheffield: 129Xe
4) Oxford: 13C, 129Xe, 31P
5) Cambridge: 13C, 23Na, 2H, MRP
6) Nottingham: 13C
7) Rotterdam EMC: MRP
8) Bergen: 23Na, 31P
9) Paris: MRP
10) DTU: 13C, 15N, 2H, 1H
11) Aalborg: MRP
12) Rostock: 23Na, 31P
13) London: 1H
14) San Rafaele: MRP

**North America**
16) McMaster: 23Na, 31P, 129Xe
17) UBCH: 129Xe
18) MD Anderson: 13C, 19F
19) MSKCC: 13C
20) Mayo: 31P
21) Stanford: 2H, 23Na
22) Iowa: 129Xe, 23Na, 31P, MRP, 2H
23) UCSF: MRS, 13C
24) UTSW: 13C
25) Columbia: 129Xe, 1H
26) UCSD: 19F, 23Na
27) City of Hope: MRP
28) Chicago: 129Xe, 23Na
29) MCW: 31P
30) Buffalo: 2H
31) MGH: 1H MRSI

**Asia**
33) Taipeh CGMH: MRP, 13C
34) Hefei: 31P
35) Juntendo Tokyo: MRP
36) BMRI Sydney: 31P
37) Hadassah: 13C, 2H
38) Hong Kong: MRP
39) West China Hospital: 13C, 23Na, 31P

GE HealthCare

# METI: Metabolic Imaging ATSM



## Two PSDs

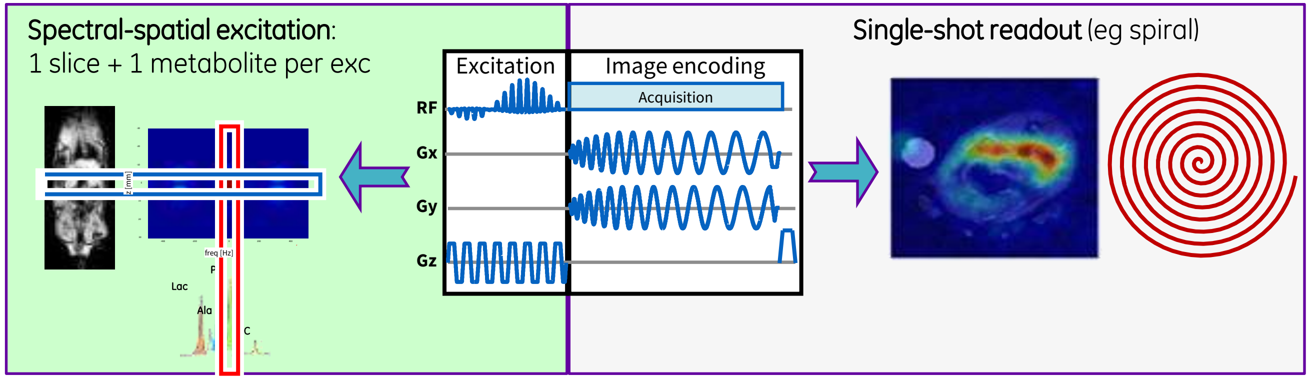
1. **fidcsi2.e**: MRI + FID + CSI
   - Cartesian 2D GRE for 129Xe lung ventilation imaging
     *(based on 129Xe clinical trial consensus group https://www.129xectc.org/)*
   - MRSI for 129Xe functional lung imaging
2. **fidspiral.e**: MRI
   spectral-spatial excitation + spiral MRI for 13C metabolic imaging

## Reconstruction

- GRE + spiral imaging: standard product Orchestra recon ( + son-of-host Matlab recon for debugging)
- CSI: son-of-host Matlab recon, to be replaced by Orchestra in medium term

## Goal

- Clinical solutions for 129Xe and 13C
- Greatly improved product for all other nuclei
- Customer feedback and validation
- Move to product asap

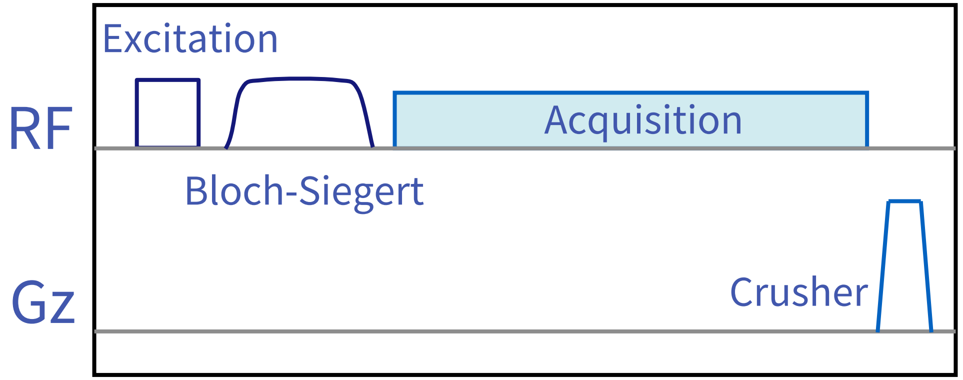


# Overview

- Specifics for hyperpolarised spins
- Specifics for thermally-polarised spins
- MNS Prescan
- Localisation
- Sequences
- **Discussion**

# MNS: New in Product on GEHC MRI

- MR30.0: fidall sequence
- MR30.1: automatic MNS Prescan
- Premier: more nuclei:
  1H, 2H, 3He, 7Li, 11B, 13C, 15N, 17O, 19F, 23Na, 29Si, 31P, 55Mn, 129Xe
- Premier: 32-channel receive
- Eddy current compensation:
  f0 modulation with correct γ



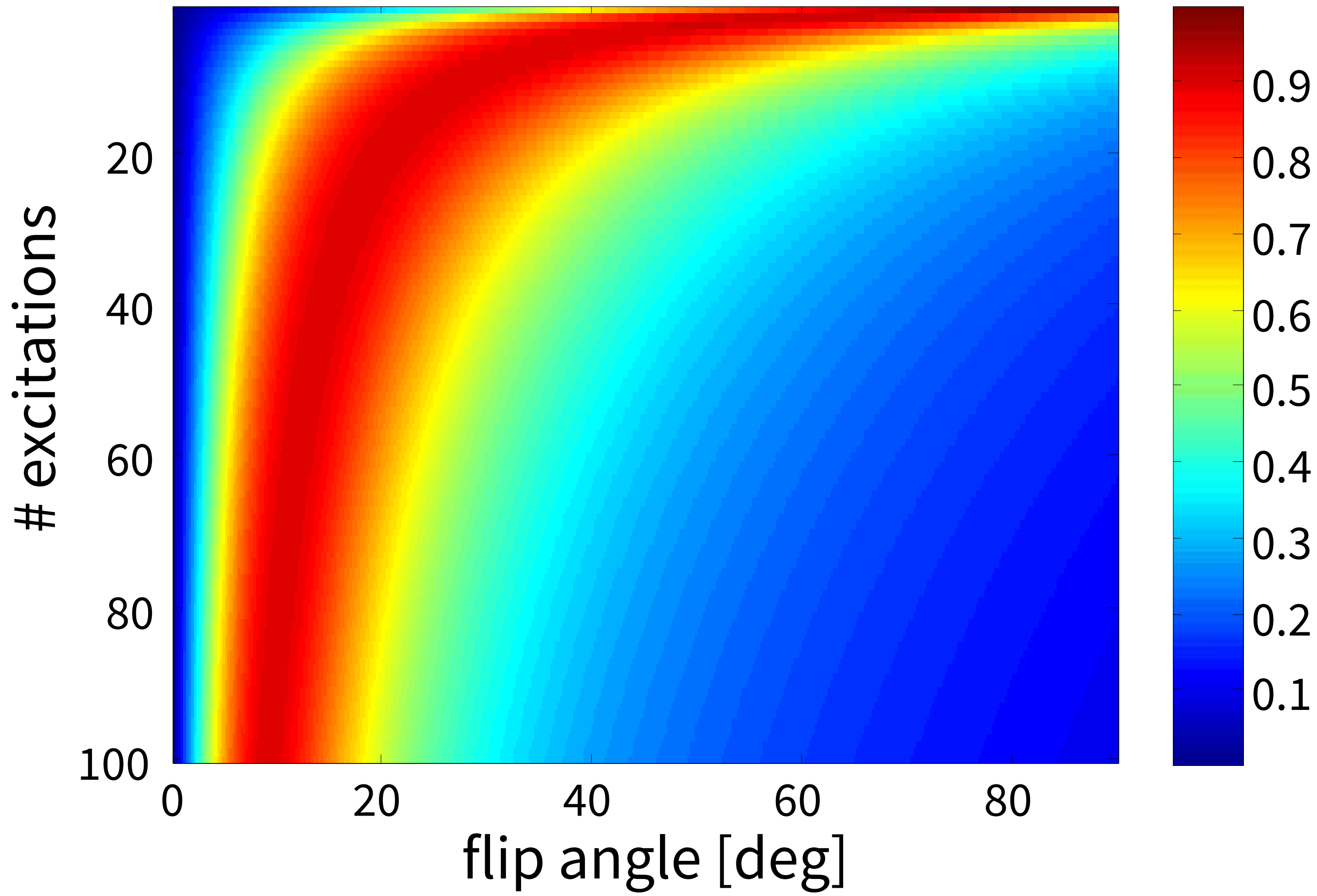
# Discussion: Parameter Selection for Hyperpolarised Spins

- Magnetisation disappearing non-recoverably
- Need for optimised
  - flip angle $\theta$
  - repetition time TR
  - # excitations $n$
- $SNR = \sin\theta \frac{1-x^n}{(1-x)\sqrt{n}}$

  $$x = \cos\theta \exp\left(-TR/T_1\right)$$
- Neglecting TR + T1: approximately same SNR for

  **↓$\boldsymbol{\theta}$ + ↑$\boldsymbol{n}$ ≈ ↑$\boldsymbol{\theta}$ + ↓$\boldsymbol{n}$**
- Simulations incorporating metabolic conversion → similar conclusion

**SNR Pot** (neglecting TR+T1)



# Discussion: Optimal $B_0$

**Hyperpolarised spins**

- *“Optimal field strength is the one you have”* (J.M. Wild)
- Spin polarisation not influenced by $B_0$
  → theoretically SNR will be similar
- **Advantages** of higher $B_0$ (e.g. 3T)
  - Higher chemical shift separation
    → shorter SPSP pulses, shorter IDEAL $\Delta$TE
  - Coils have better SNR
  - Better $^1$H MRI
  - Higher ADCs ($^3$He in lung)
- **Advantages** of lower $B_0$ (e.g. 1.5T)
  - Less $B_0$ inhomogeneity → $T_2^*$ longer
  - MR scanners cheaper (only advantageous for sites ☺ )

**Thermally-polarised spins**

- The higher the better: SNR increase w/o (yet) 1H high-field problems

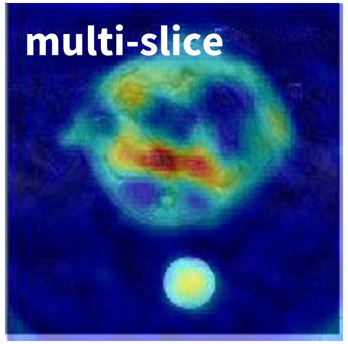
# Discussion: Multi-Slice or 3D?

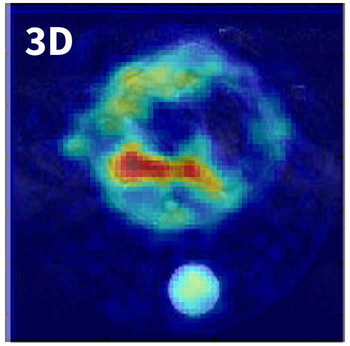
**Hyperpolarised spins**

- If TR + flip angle optimised: approximately same SNR
- 3D: poor point-spread function (along z), but better selectivity of exc pulse
- Main differences will be artefact behaviour:
  - Multi-slice: shorter encoding per slice
    → more data consistency (particularly with single-shot acq)
  - 3D: more averaging
    → average out motion and flow artefacts
- Experimental observations: no big difference, multi-slice simpler to implement

**Thermally-polarised spins**

- More SNR with 3D




3D Whole-Heart Cardiac Metabolic Imaging with [1-13C]pyruvate using IDEAL Spiral CSI . U. Köllisch, R.F. Schulte. M. Durst, J.H. Ardenkjaer-Larsen, F. Frijia, L. Menichetti, M. Lombardi, A. Haase, F. Wiesinger. ISMRM 2013; #3923.

# Conclusion

- Optimum  acquisition:
  highly depends on nucleus and applications
- Often similar results (after optimisation)
- Main limitation: SNR, not encoding

# Hands-on Course for Advanced Research on GE MR

**Target Attendees:** MR Physicist, Researcher, Scientist.

**Learning objectives:** The aim of the course is to allow research partners to get familiar to the GE MR scanners and how to effectively perform research on it. That includes an introduction to system architecture (hard- and software), how to interface to the system, pulse sequence programming, reconstruction, obtaining raw data, troubleshooting and more. Hands-on sessions on the MRI will provide direct learning experience.

**Requisites:** valid research key, Linux, C/C++, MATLAB, Python, knowledge of MR theory, operation of GEHC MR scanner

**Course Teachers:** Applied Science Laboratory Europe Team

**Location:** GE HealthCare, Oskar-Schlemmer-Str. 11, 80807 Munich

**Date:** January 20-23, 2025

**Registration Fee; Deadline:** 650€; Dec. 1, 2024

**Costs:** Registration fee includes VAT, lunch, dinner and refreshments. Participants are expected to cover their own travel expenses (flight, hotel, etc).

**Organizers:**

José de Arcos: jose.dearcos@gehealthcare.com
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Timo Schirmer: timo.schirmer@gehealthcare.com

**Info:** https://weconnect.gehealthcare.com/

**Registration:** https://axtravel.eventsair.com/ge-1st-hands-oncourse-for-advanced-research-on-ge-mr-2025/gehc/Site/Register