

Running a Hyperpolarised Exam

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Hyperpolarised MRI: Nuclei

Nucleus	T1	Frequency at 3T	Natural abundance	Polarisation method	Application
^1H	too short (<1s in vivo)	127.73	99.98%	DNP	Perfusion
^3He	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

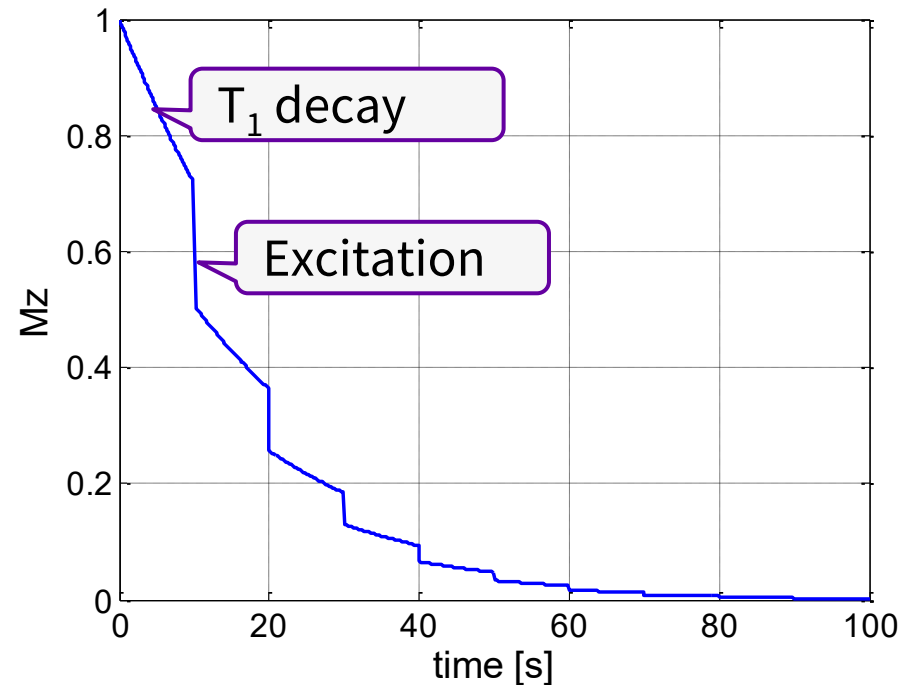
- $\gamma_{13\text{C}} = 1/4 \gamma_{1\text{H}}$ → 4·gradients for same spatial resolution
- $\gamma_{15\text{N}} = 1/10 \gamma_{1\text{H}}$ → 10·gradients for same spatial resolution
- $\gamma_{3\text{He}} = 3/4 \gamma_{1\text{H}}$ → 30% higher gradients for same spatial resolution
- $\gamma_{129\text{Xe}}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

However: 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

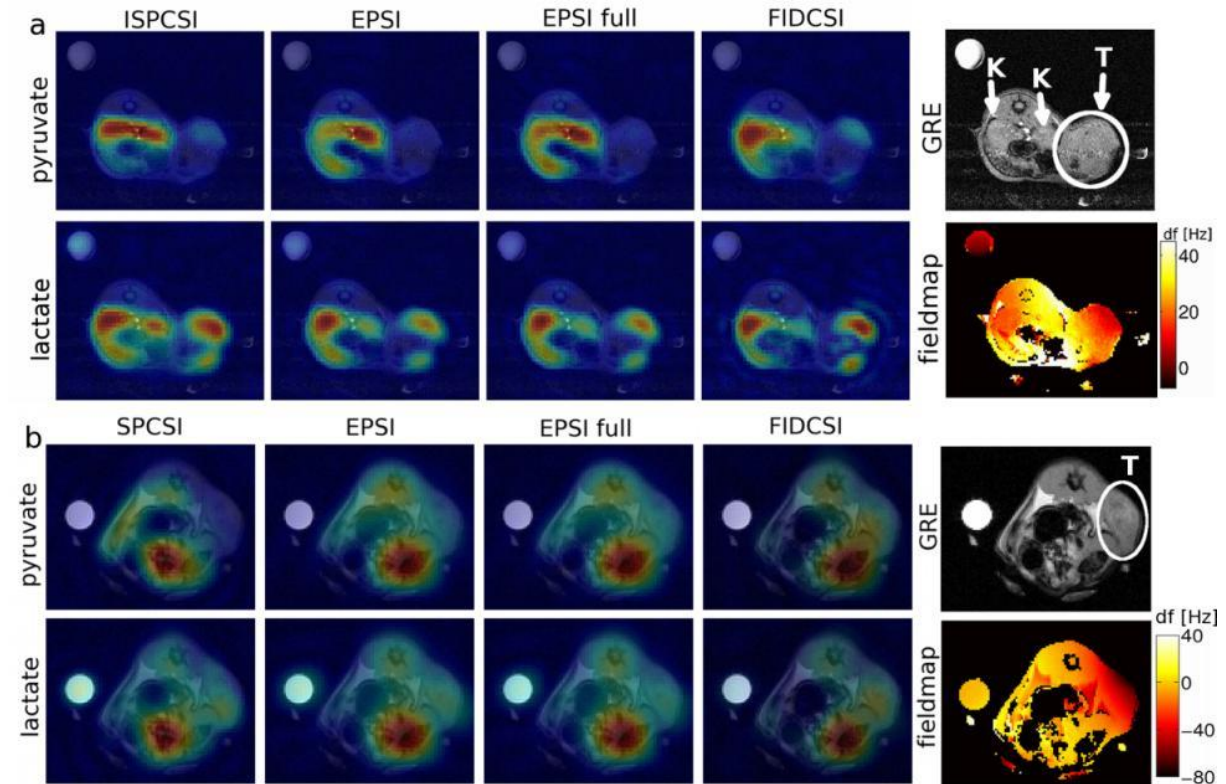
Basics

- 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.

^{13}C Metabolic Imaging

Challenge

- Encode large amount of information in a few seconds

Information

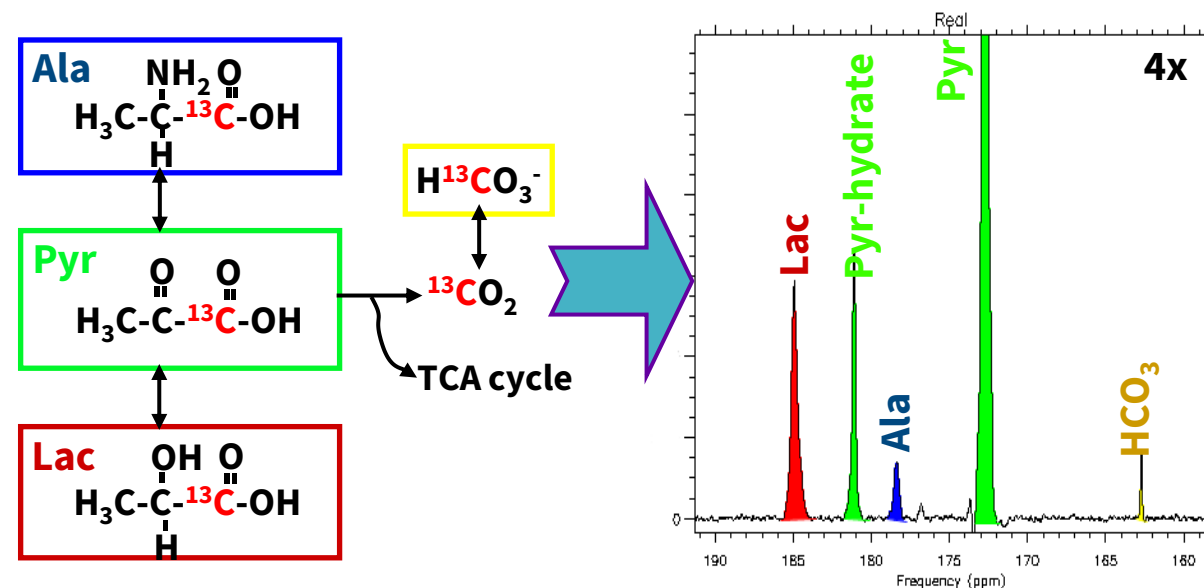
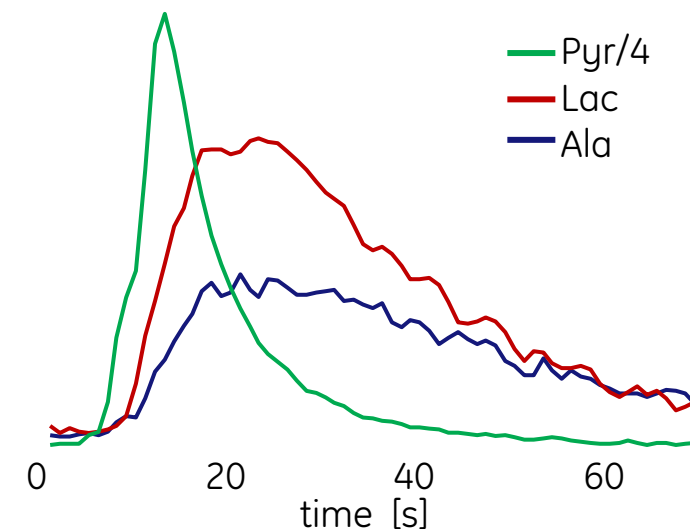
- 1D spectral, 3D spatial, 1D temporal = **5D**

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, ...



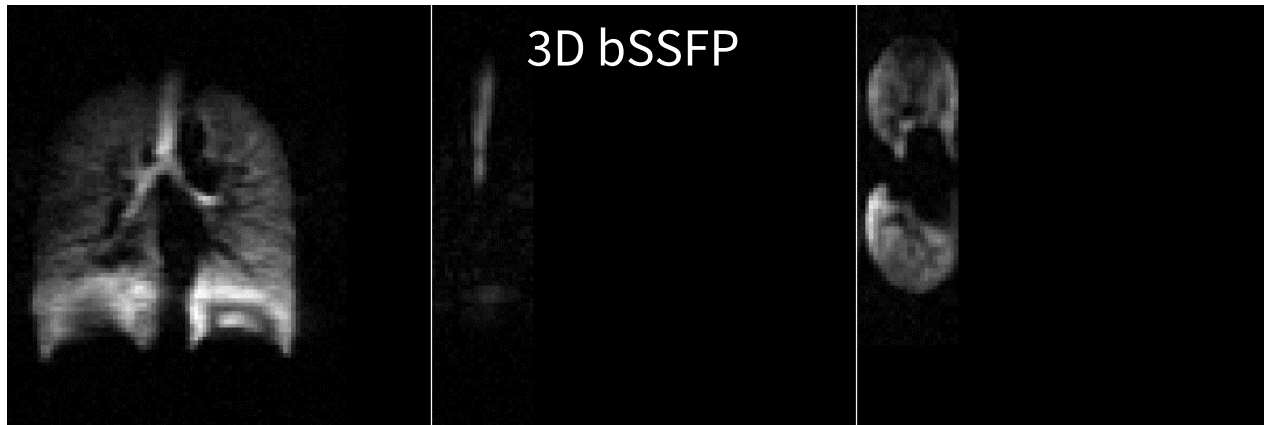
^{129}Xe

Basics

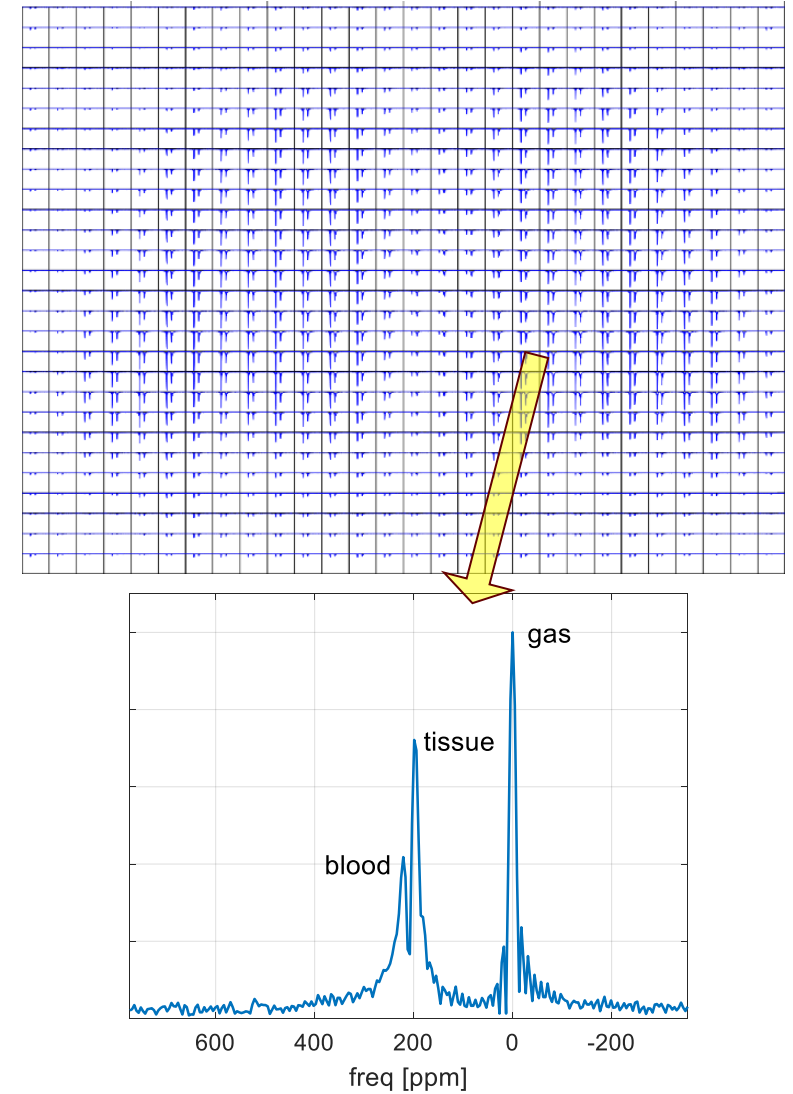
- -35.3MHz @3T, spin $\frac{1}{2}$
- 26.4% natural abundance
- Inhalation of hyperpolarised ^{129}Xe gas
- Gas uptake: direct measure of lung function

Applications

- Long Covid, asthma, chronic obstructive pulmonary disease, cystic fibrosis, interstitial lung disease, ...



3D density-weighted MRSI



129Xe Lung Ventilation Imaging

Information

- 3D spatial

Constraints

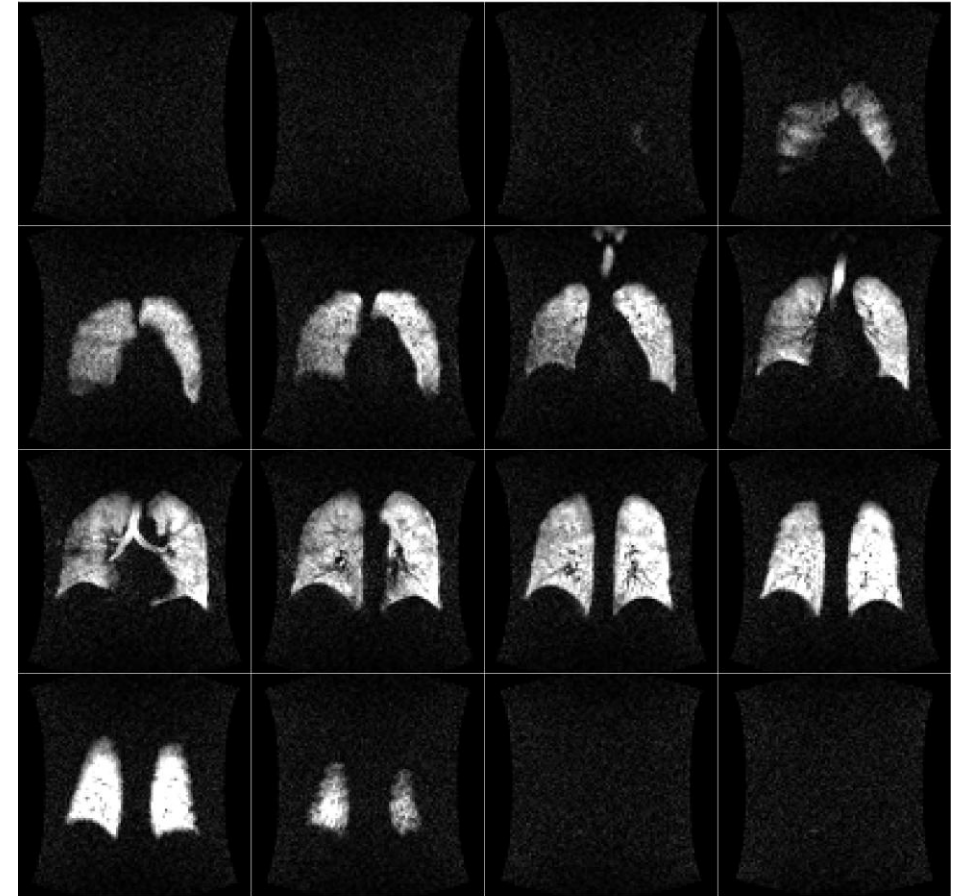
- Scan must fit into one breath-hold $\leq 10\text{-}15\text{sec}$

Approaches

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

Consensus group recommendation

- 2D Cartesian GRE: voxel size= $4\times 4\times 15\text{mm}^3$



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

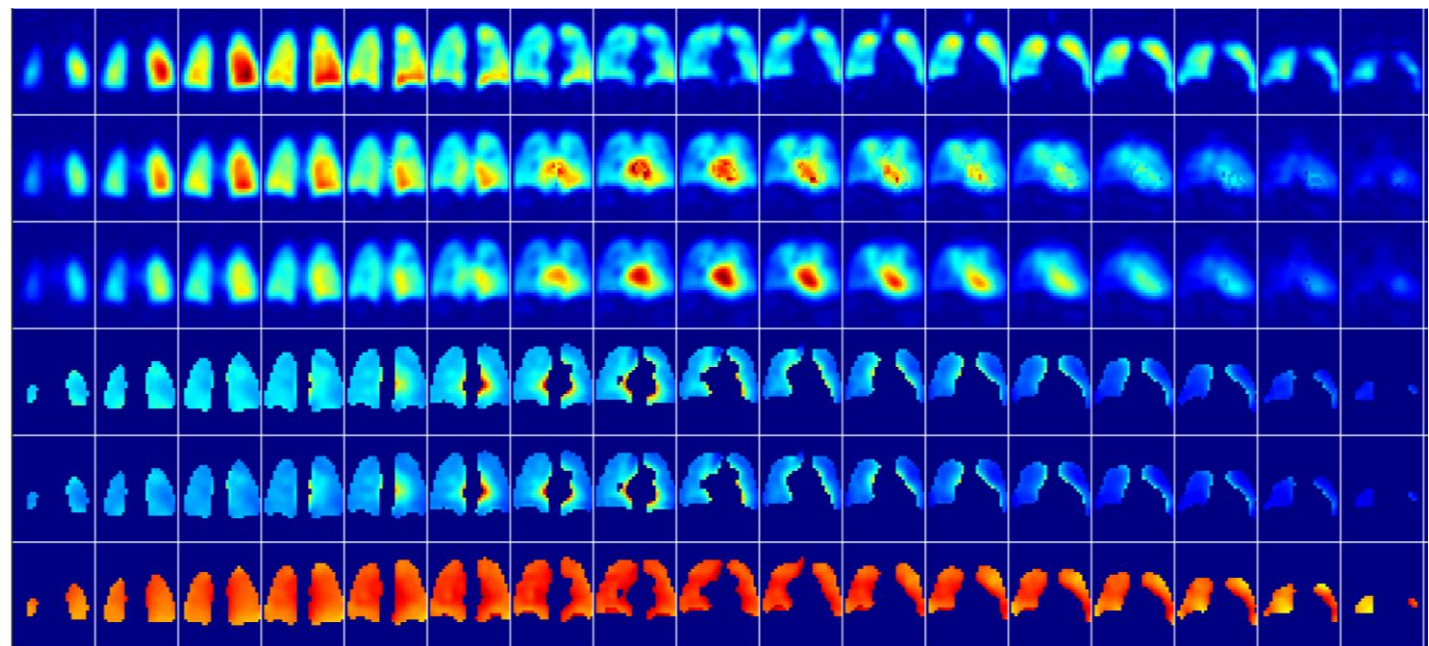
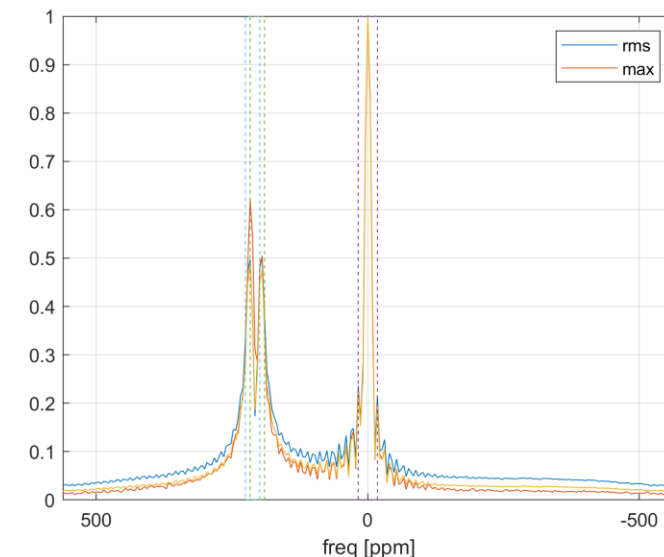
- 3D spatial, 1D spectral

Constraints

- Scan must fit into one breath-hold $\leq 10\text{-}15\text{sec}$
- Signal levels: gas >100 times dissolved

Approaches

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

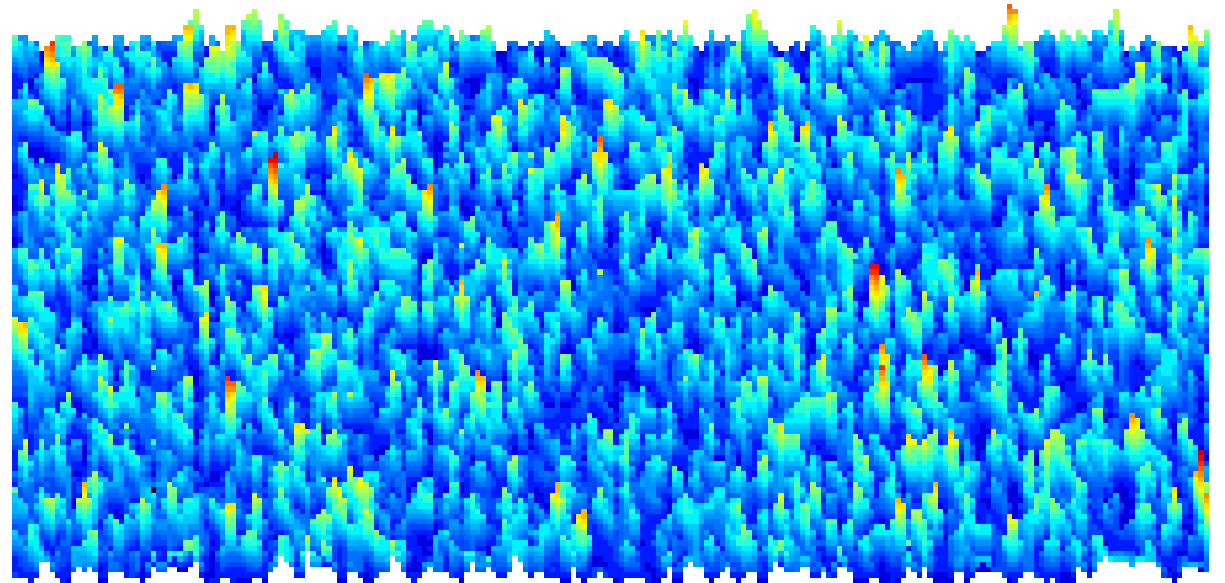


Specifics of Thermally Polarised MNS: Nuclei

Nucleus	T1	T2	Frequency at 3T [MHz]	Natural abundance	Concentrations	Application
^2H	50-350ms	10-60ms	19.61	0.015%	1mM	Metabolism, perfusion
^7Li	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

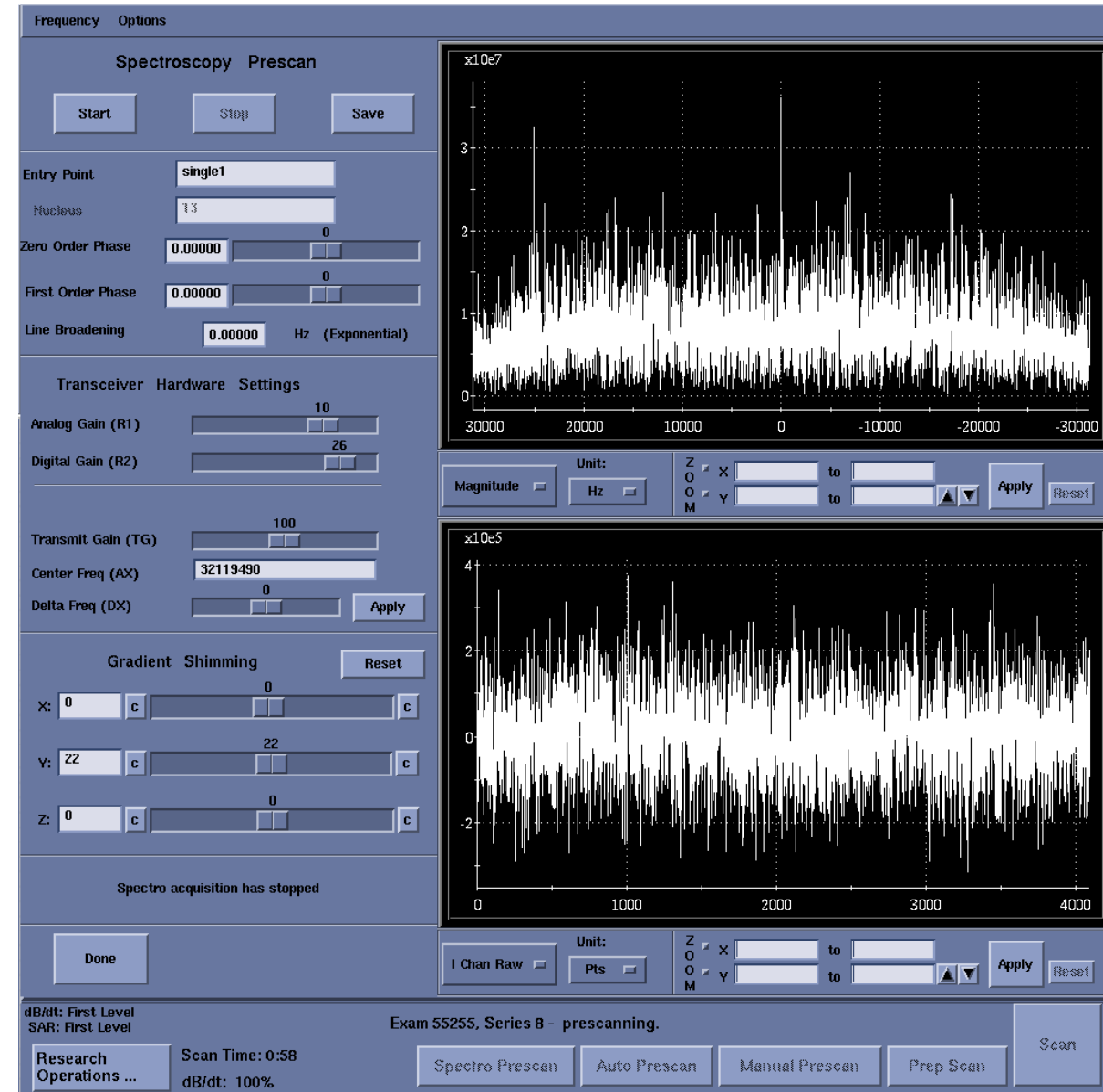
- Generally (very) low sensitivity due to
 - low concentrations
 - low γ
- Huge voxels/ROIs
- Lots of averaging
- Fancy encoding highly limited



MNS Prescan: Scanner Calibration

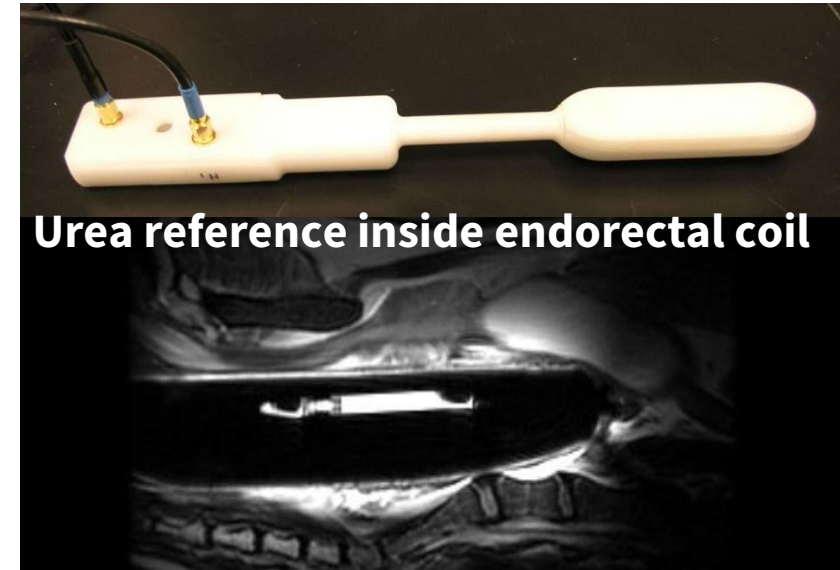
Parameters

- 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



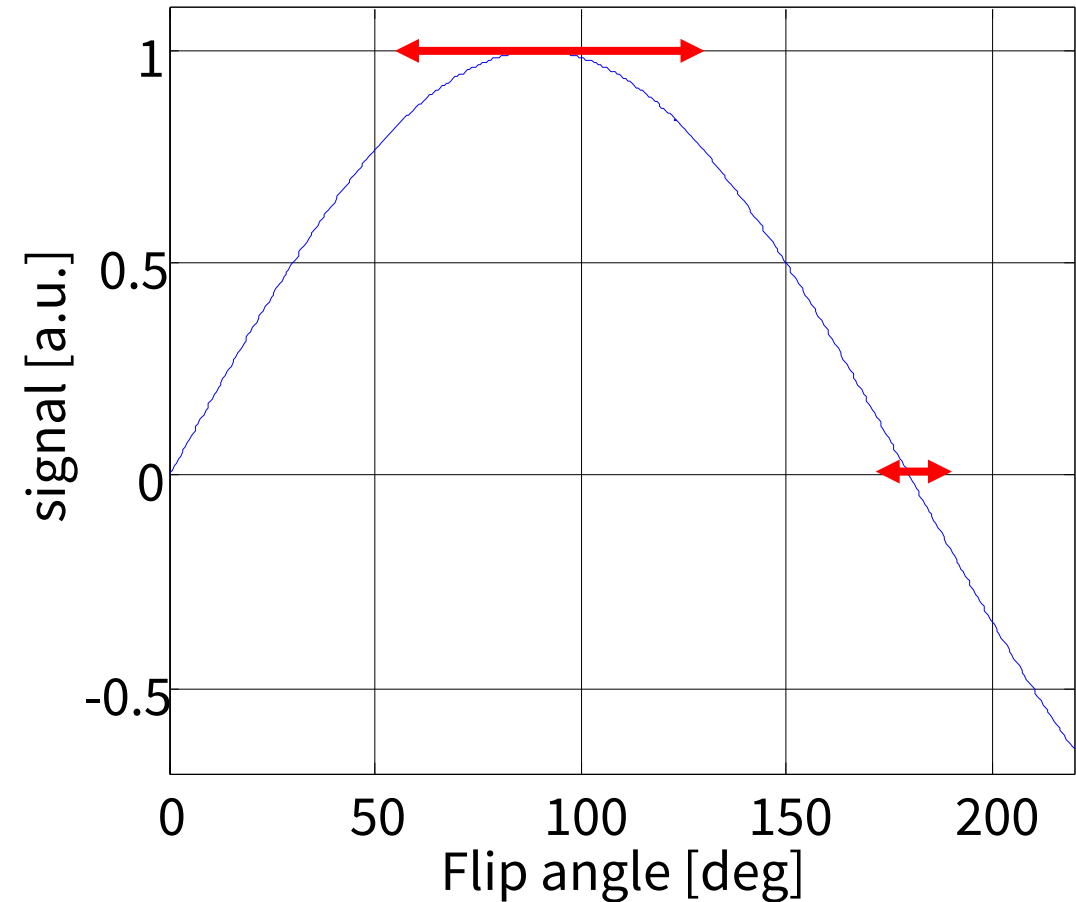
MNS Prescan

- Difficulty: natural signal too low; hyperpolarised signal too precious
- ^{13}C : external reference; e.g.,
[1- ^{13}C]lactic acid
[^{13}C]urea
 T_1 very long $\rightarrow$ 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
 $\rightarrow$ use stored values



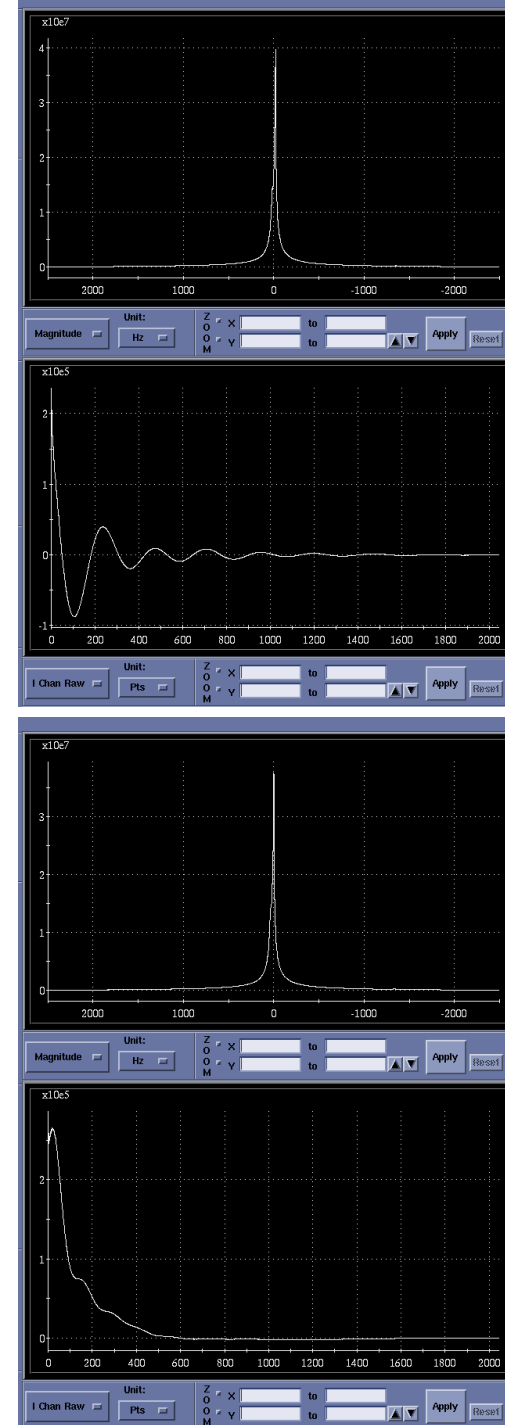
MNS Prescan: Manual TG Calibration

- 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:
 $\frac{1}{2}$ flip angle = $\frac{1}{4}$ 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 $\rightarrow$ BW $\approx$ 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

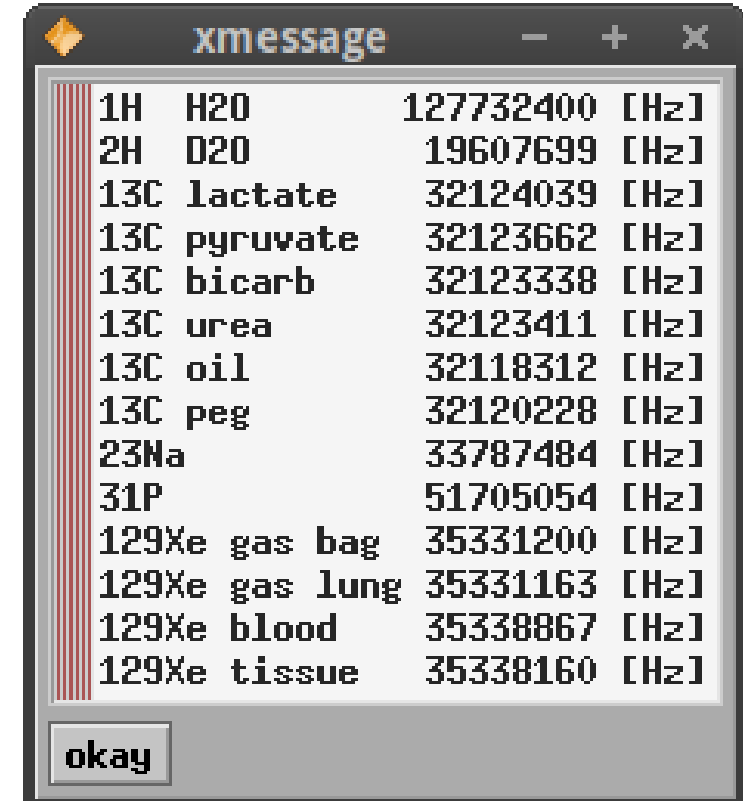


MNS Prescan: f_0 via $1H$ f_0

Use $1H$ centre frequency and conversion table to determine x-nuclear f_0

mnsfreq App: select suitable MRI scan, click button: reads $1H$ f_0 from dicom and displays xmessage window with different frequencies

IsotopicChemicalShifts.cfg: table with offset frequencies stored on MRI → set initial MNS f_0



A screenshot of an xmessage window titled 'xmessage'. It displays a table of nuclear frequencies for various isotopes and substances. The table has three columns: the isotope/substance, the frequency value, and the unit [Hz]. The data is as follows:

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]

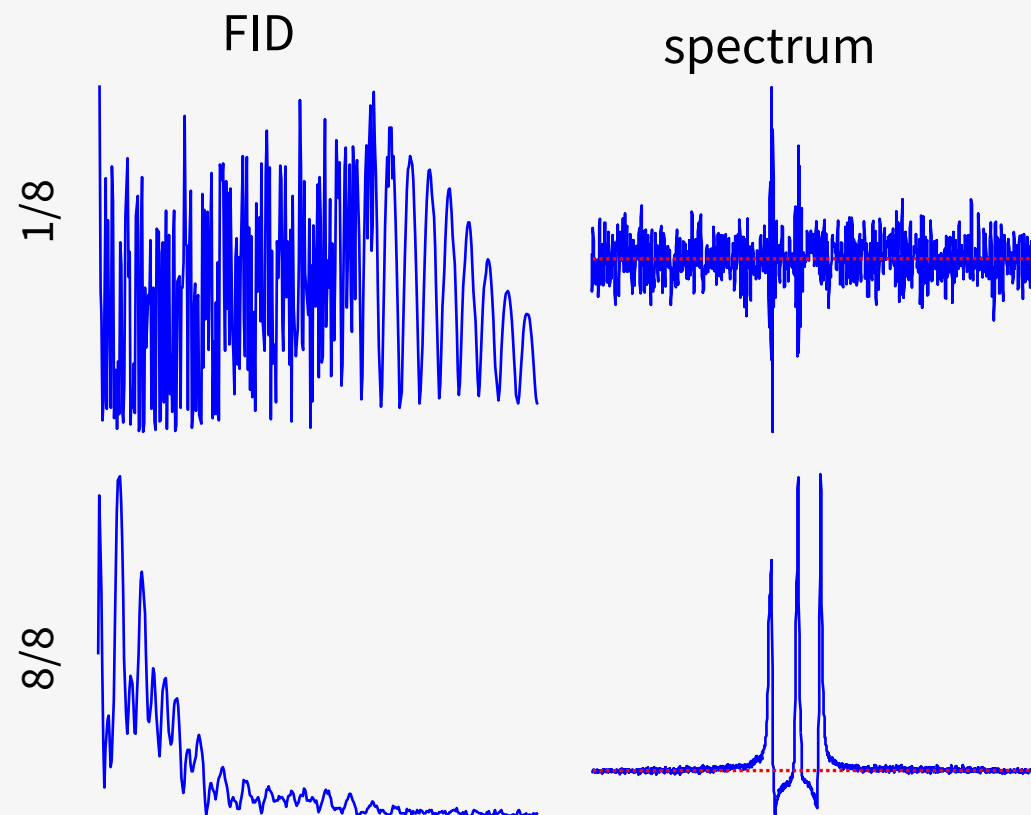
At the bottom of the window is an 'okay' button.

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 $R1+R2$)



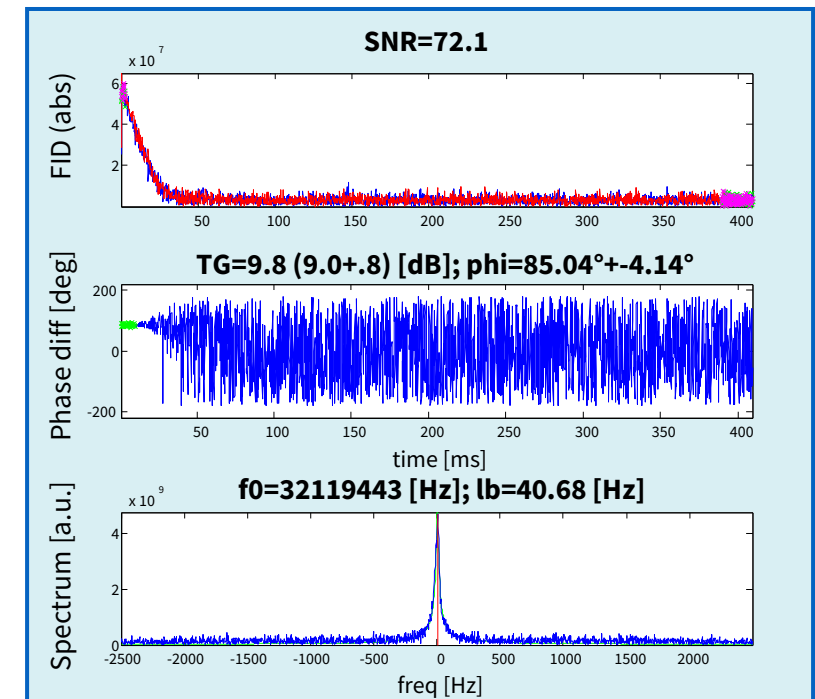
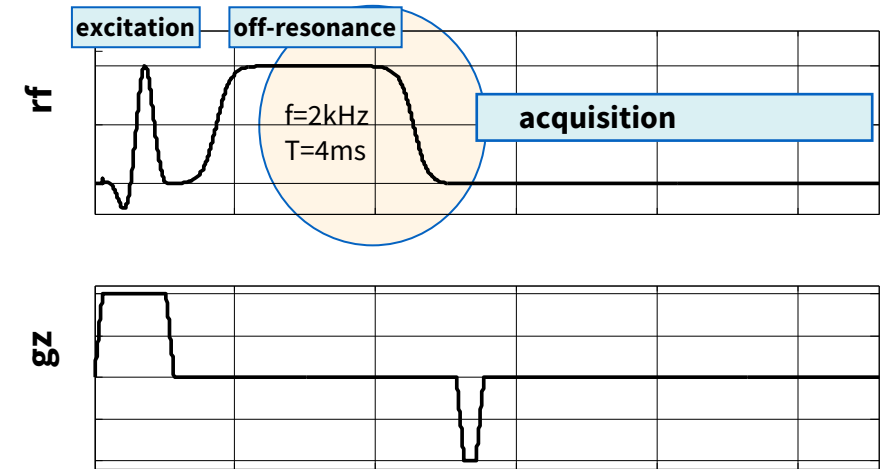
MNS Prescan: Bloch-Siegert

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

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

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

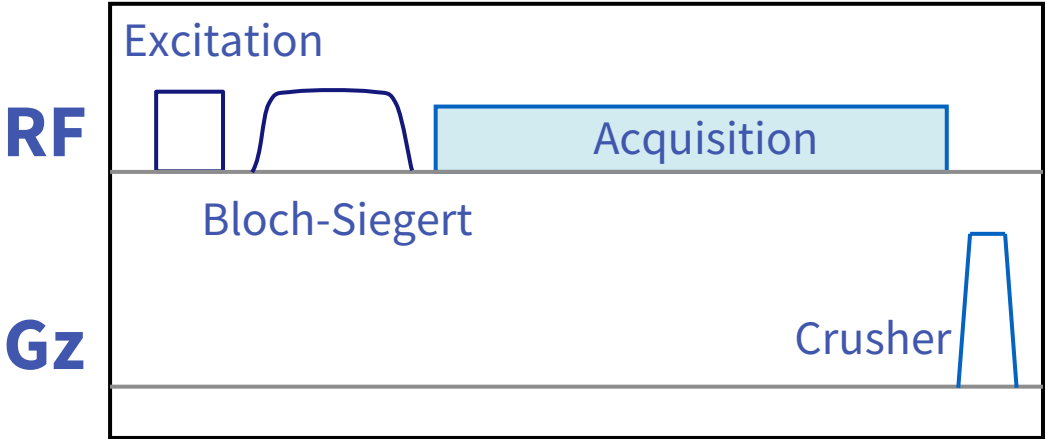
- Here: also SNR+f0+lb



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 γ + isotopic offset
TG	MNSXTG (Bloch-Siebert) – 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



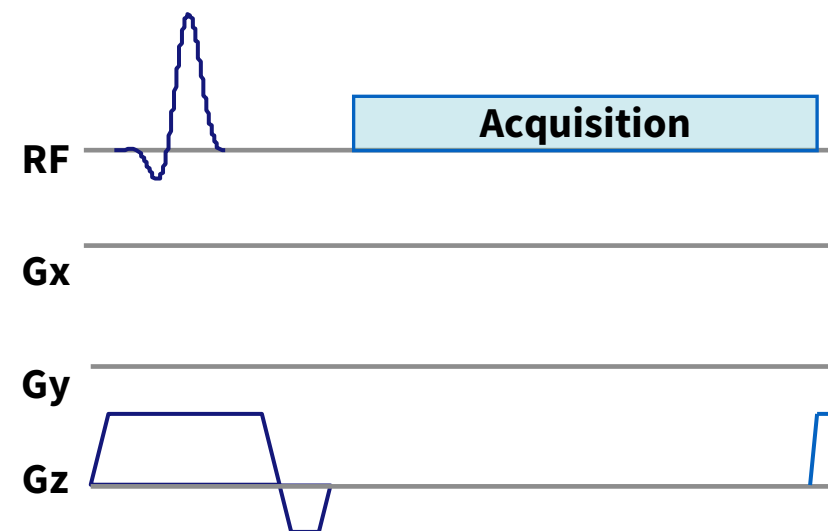
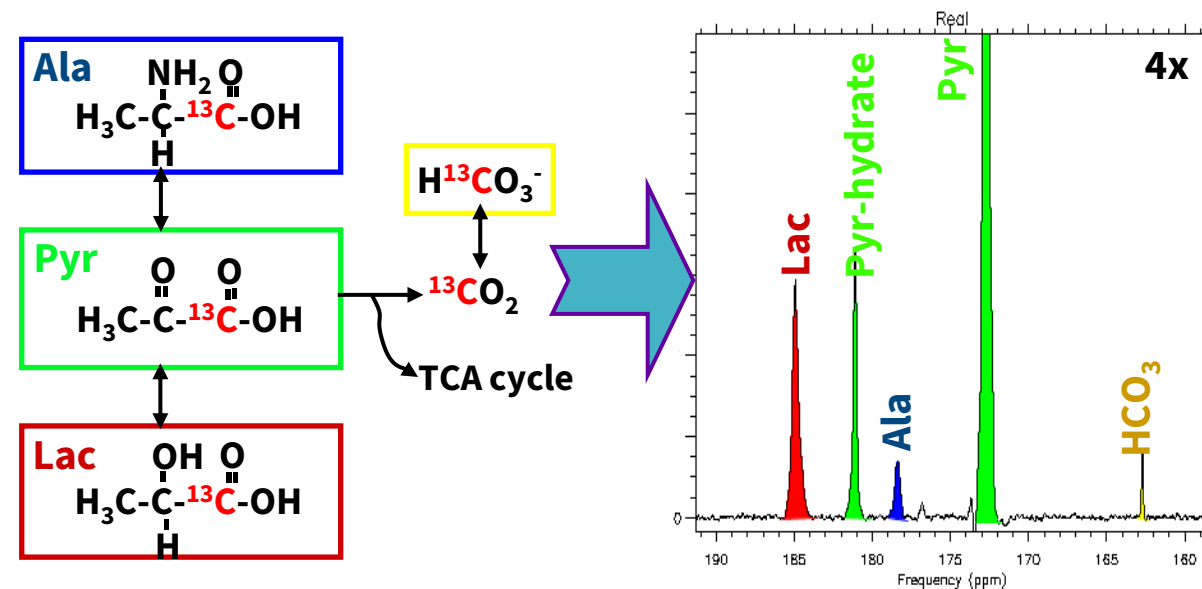
Localisation

- 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*

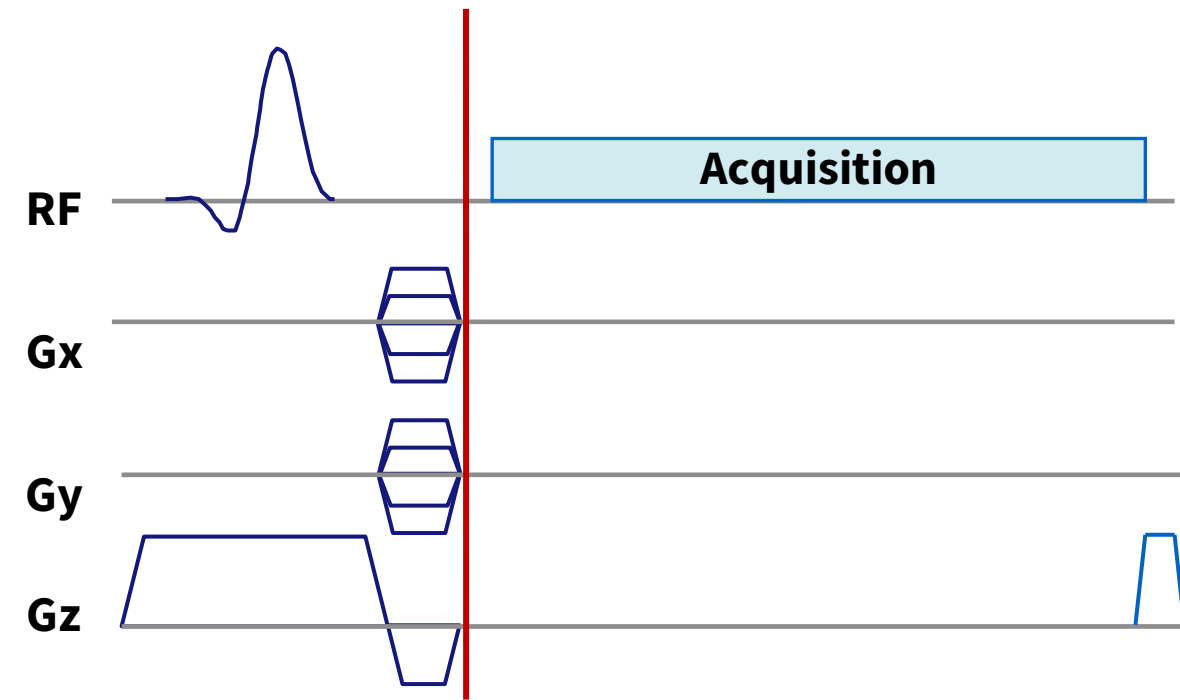
Sequences: MR Spectroscopy (MRS)

Metabolites have different chemical environments

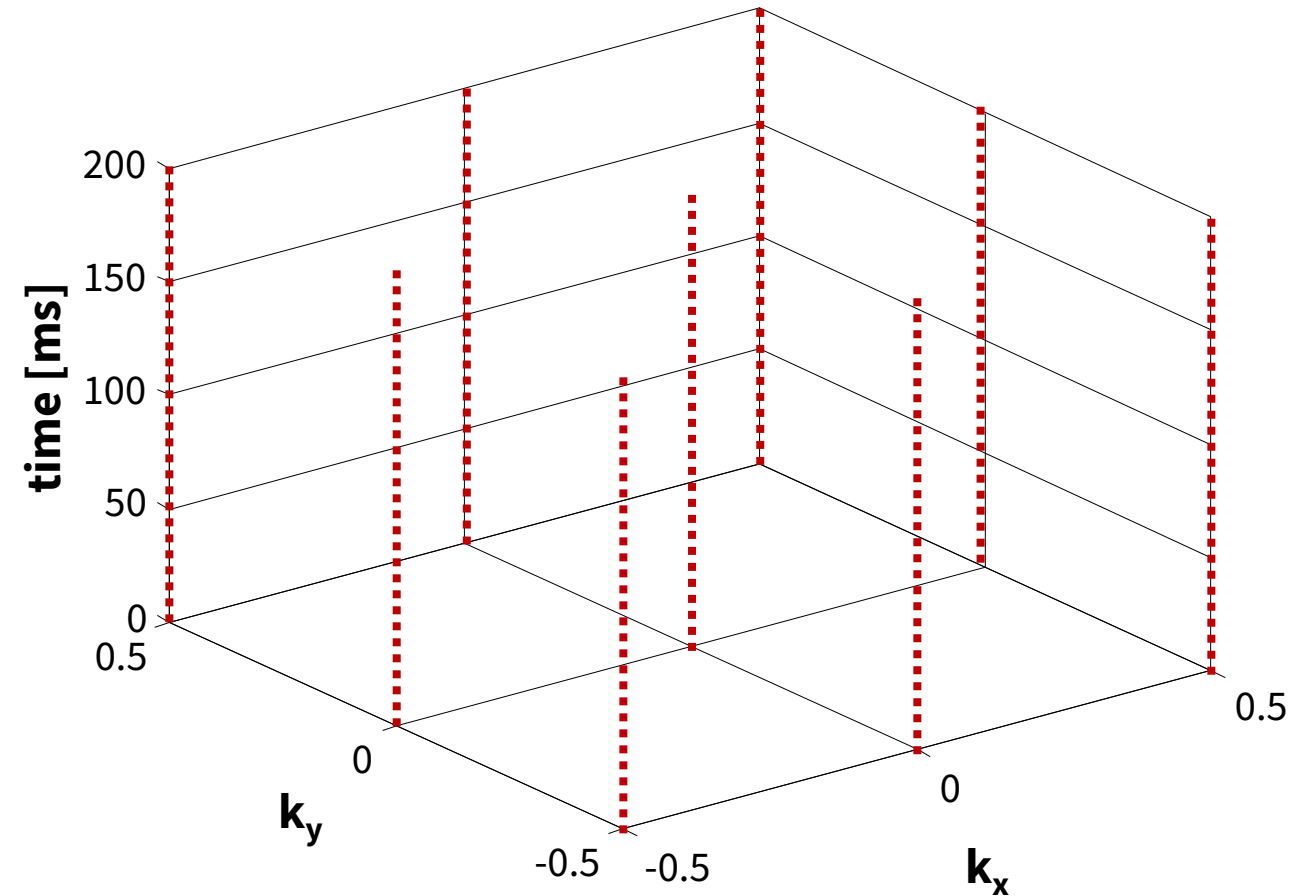
- (slightly) different magnetic shielding
- different resonance frequencies
- detect separately via MR spectroscopy
- skip MRI readout encoding gradient
- Fourier transformation along spectral dimension



MR Spectroscopic Imaging (MRSI)

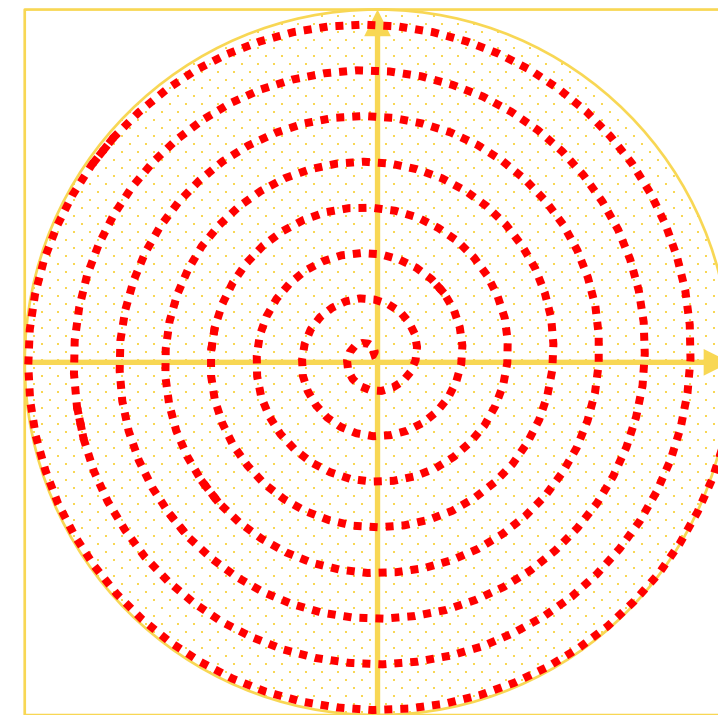
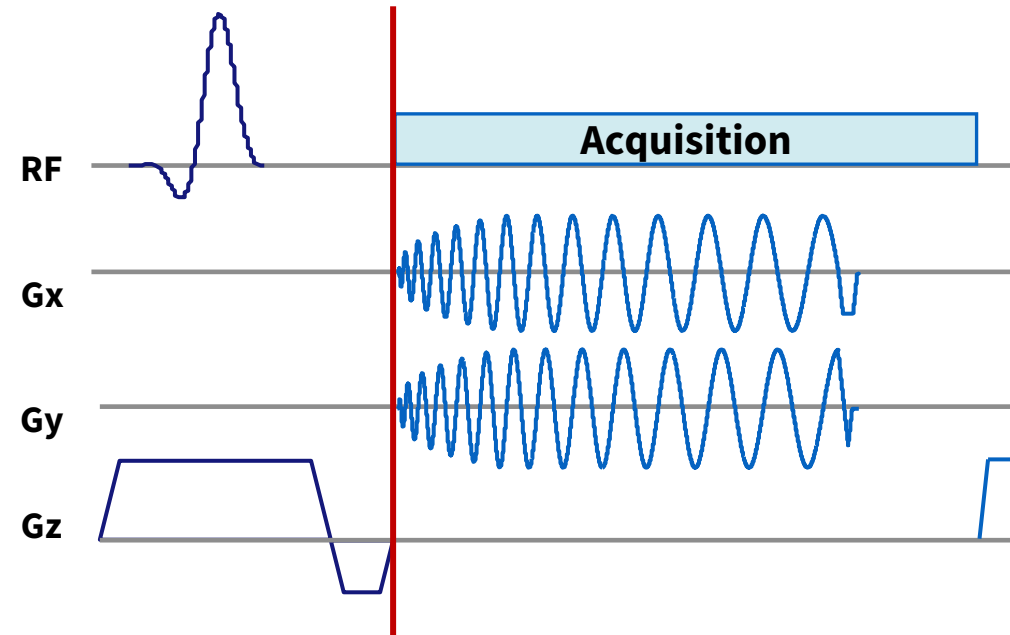


- Sequential phase encoding
- Acquisition of full spectra
- Aka Chemical-Shift Imaging (CSI)
- Fourier transformation along spectral and spatial dimensions



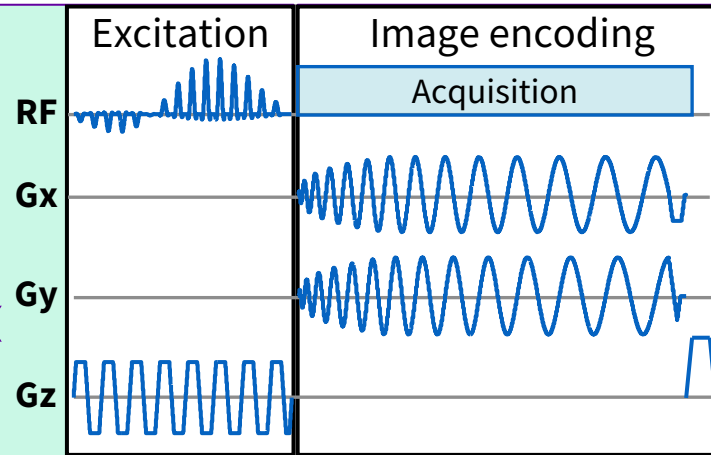
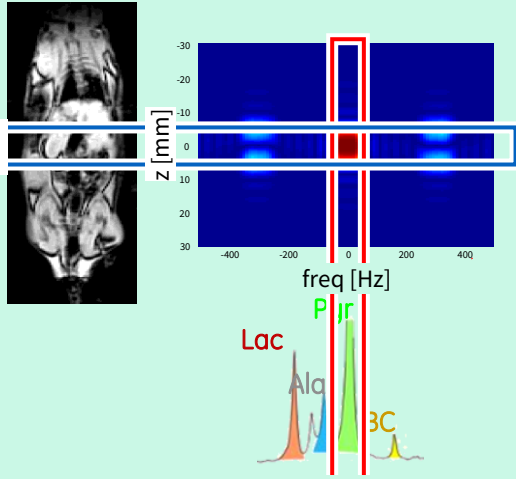
MR Imaging (MRI)

- Single resonance frequency (like ^1H H_2O)
→ omit spectral encoding
- Add readout encoding gradients
- Many flavours to sample k-space existing, eg non-Cartesian spiral trajectories

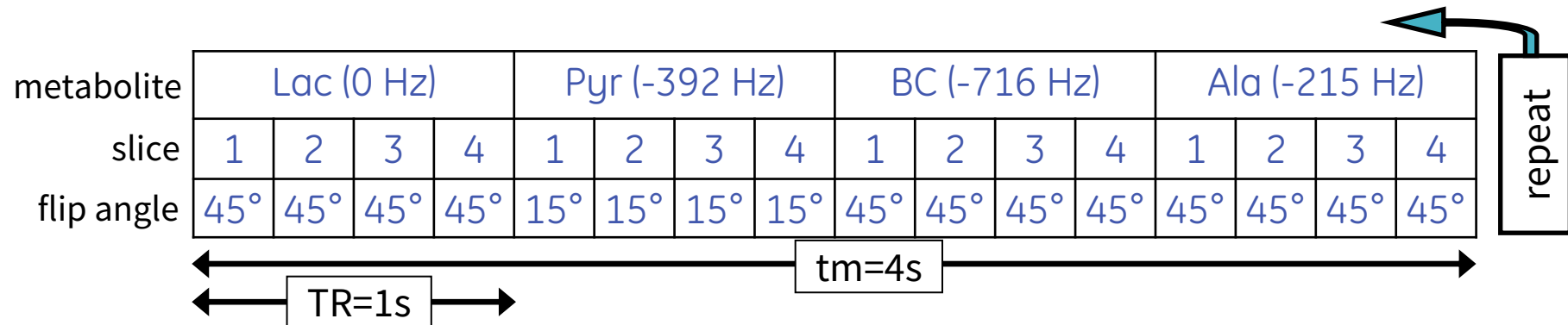
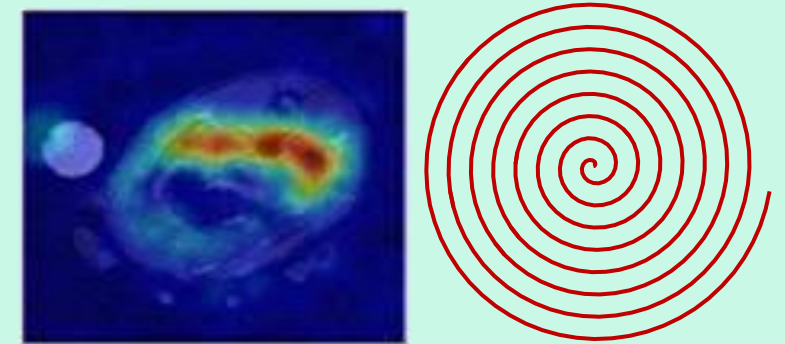


13C: Spectral-Spatial Excitation + Spiral Imaging

Spectral-spatial excitation:
1 slice + 1 metabolite per exc

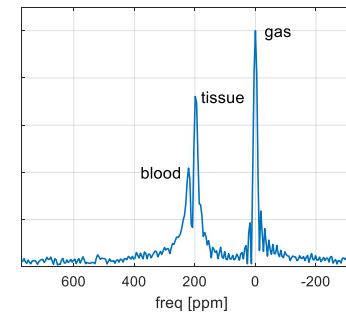
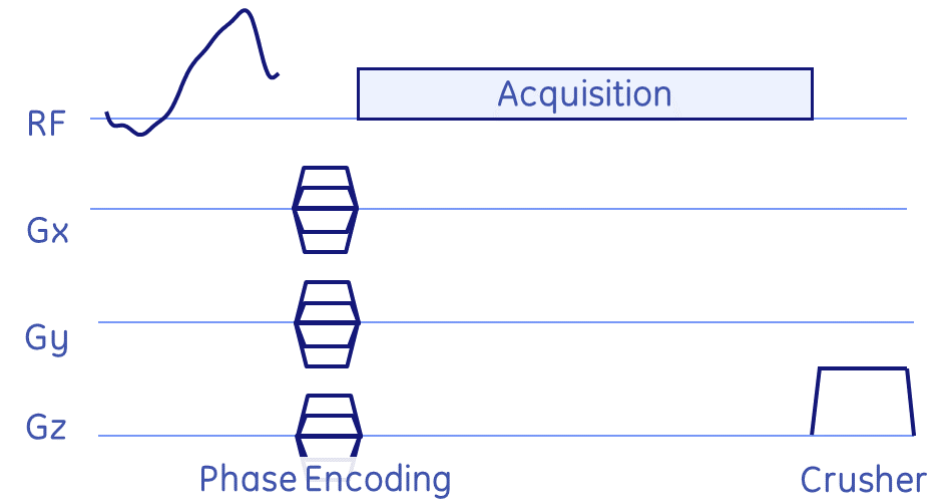


Single-shot readout (eg spiral)

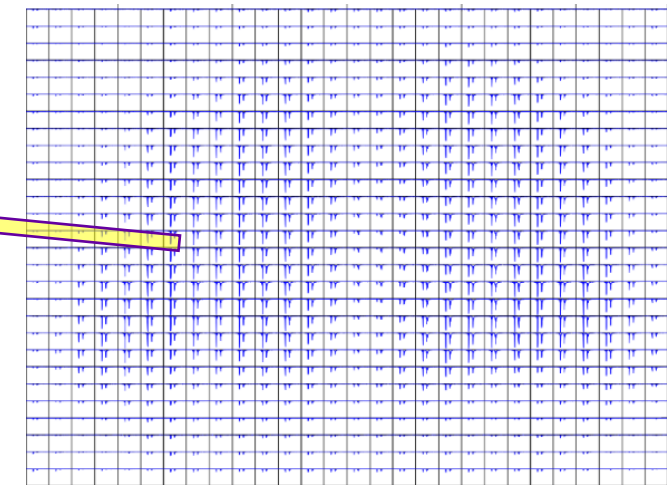
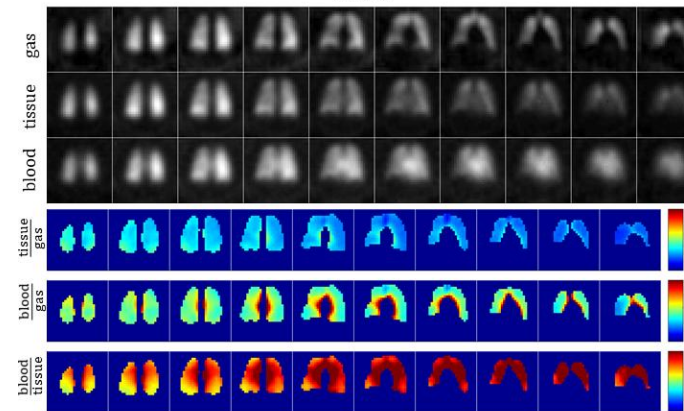


129Xe Dissolved-Phase MRSI

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



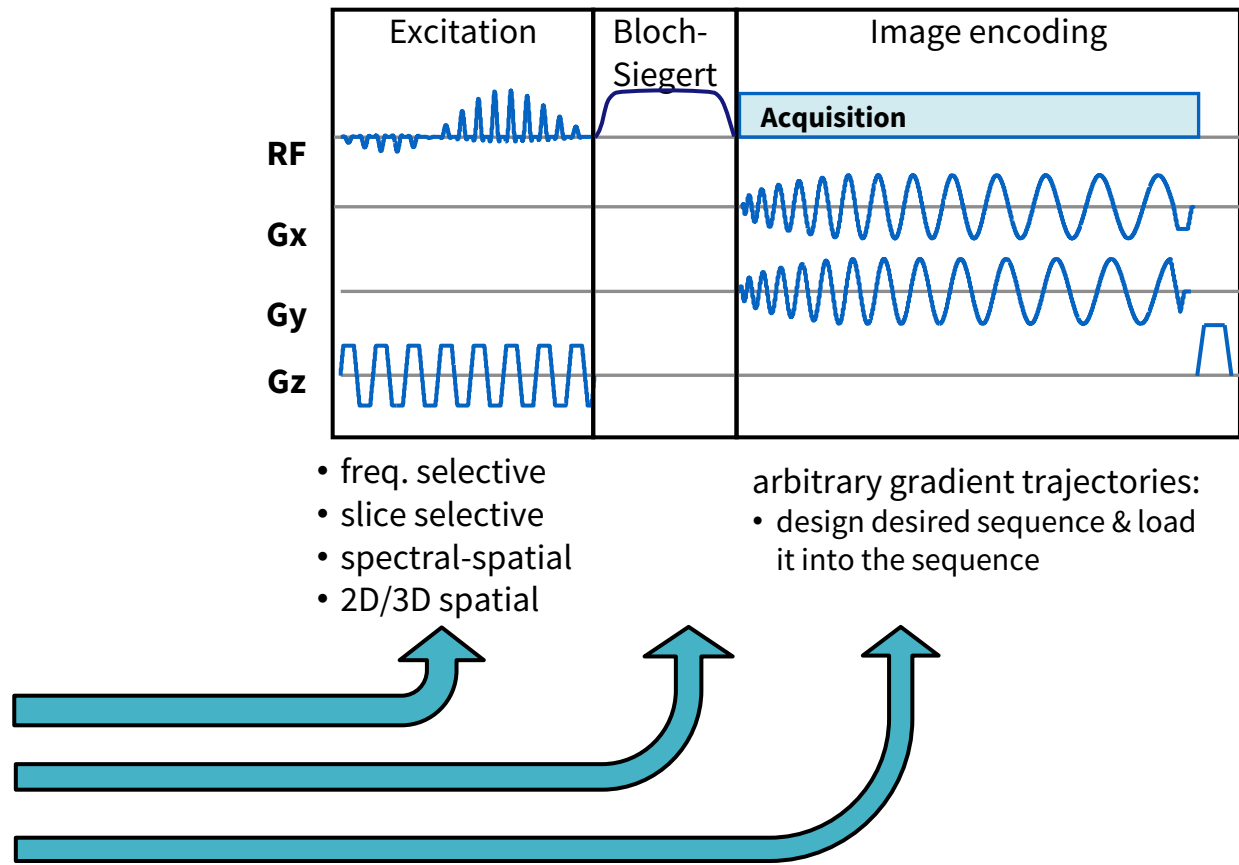
MRSI



In collaboration
with Guilhem
Collier, Jim Wild

MNS Research Pack

- MNS product basic: pulse-and-acquire sequence (*FIDCSI*); no MNS pre-scan; no advanced acquisitions
 - Idea: provide complete flexibility for advanced 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 IT: 1H, 2H, 23Na, 31P
- 2) Århus DK: 1H, 2H, 13C, 23Na, 31P, 129Xe
- 3) Sheffield UK: 31P, 129Xe
- 4) Oxford UK: 13C, 31P, 129Xe
- 5) Cambridge UK: 2H, 13C, 23Na
- 6) Nottingham UK: 13C, 31P, 129Xe
- 7) Bergen NO: 2H, 23Na, 31P
- 8) DTU DK: 1H, 2H, 13C, 15N
- 9) Aalborg DK: 2H, 23Na, 31P
- 10) Rostock DE: 23Na, 31P
- 11) London UK: 1H
- 12) Burdenko RU: 2H, 31P
- 13) Porto Santo Antonio PL: 23Na
- 14) LMU Munich DE: 1H MRI
- 15) San Raffaele IT: 1H MRI
- 16) Erasmus Rotterdam: 1H MRI
- 17) Brussels: 23Na, 31P

North America

- 18) Iowa US: 1H, 23Na, 31P, 129Xe
- 19) UCSF US: 1H, 2H, 13C
- 20) Cincinnati US: 1H, 129Xe
- 21) McMaster CA: 23Na, 31P, 129Xe
- 22) Stanford US: 2H, 23Na
- 23) Columbia US: 1H, 129Xe
- 24) MD Anderson US: 13C, 19F
- 25) Chicago US: 23Na, 129Xe
- 26) MCW US: 31P
- 27) Buffalo US: 2H
- 28) UCSD US: 19F, 23Na
- 29) UBCH CA: 129Xe
- 30) MSKCC US: 13C
- 31) Mayo US: 31P
- 32) UTSW US: 13C
- 33) City of Hope US: 1H
- 34) MGH US: 1H

Asia

- 35) Chengdu CN: 13C, 23Na, 31P
- 36) Haikou CN: 2H, 13C
- 37) Taipei CGMH TW: 1H, 13C
- 38) Hong Kong University CN: 1H
- 39) Hadassah IL: 2H, 13C
- 40) Hefei CN: 31P
- 41) BMRI Sydney AU: 31P
- 42) Fukushima JP: 2H, 13C, 23Na
- 43) Tokushima JP: 23Na
- 44) Gifu JP: 2H, 13C, 23Na
- 45) Lanzhou: 23Na, 31P
- 46) Yunnan: 23Na, 31P



METI: Metabolic Imaging ATSM

Two PSDs

1. **fidcsi2.e**: MRI + FID + CSI

- Cartesian 2D GRE for ^{129}Xe lung ventilation imaging
(based on ^{129}Xe clinical trial consensus group <https://www.129xectc.org/>)
- MRSI for ^{129}Xe functional lung imaging

2. **fidspiral.e**: MRI

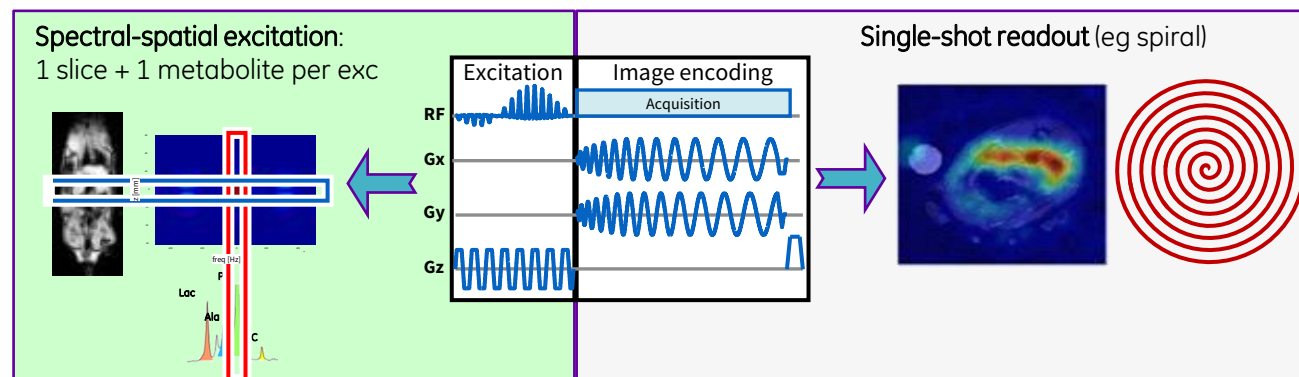
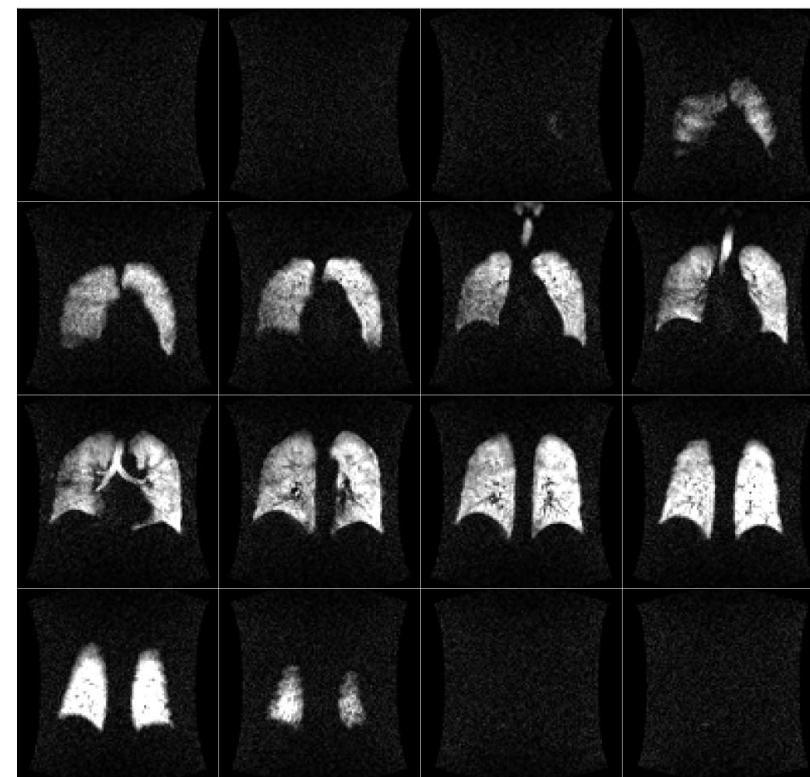
spectral-spatial excitation + spiral MRI for ^{13}C metabolic imaging

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

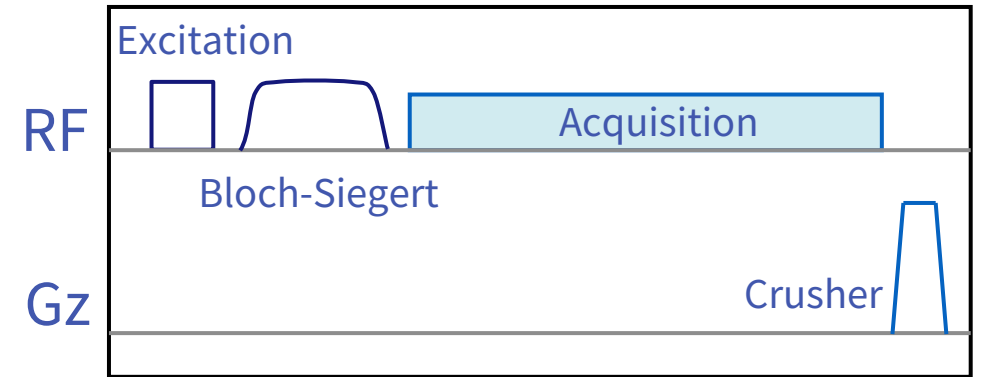
Goal

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



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 θ
 - repetition time TR
 - # excitations n

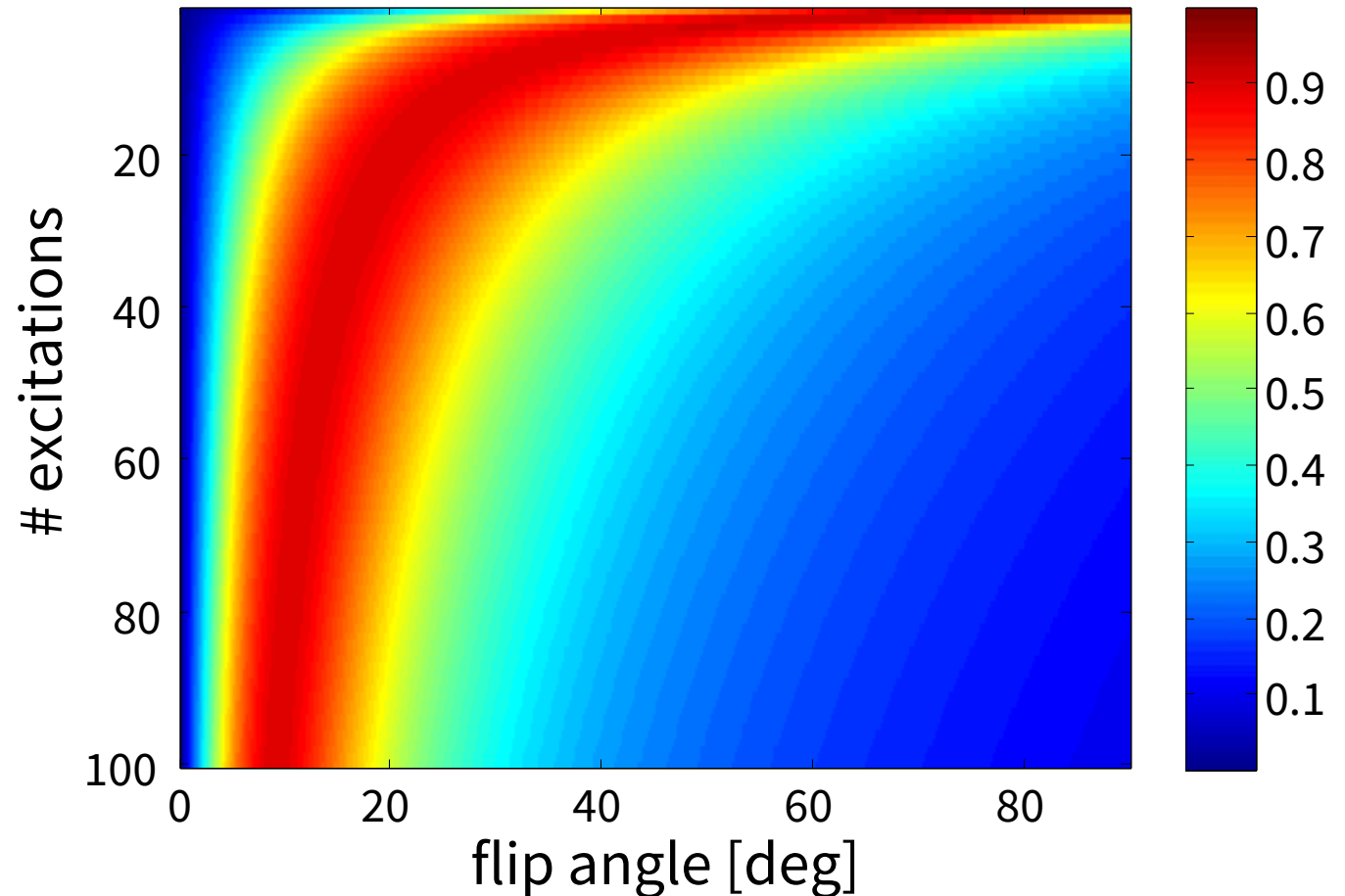
$$SNR = \sin \theta \frac{1-x^n}{(1-x)\sqrt{n}}$$
$$x = \cos \theta \exp\left(-TR/T_1\right)$$

- Neglecting TR + T1:
approximately same SNR for

$$\downarrow \theta + \uparrow n \approx \uparrow \theta + \downarrow n$$

- 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 ΔTE
 - Coils have better SNR
 - Better 1H MRI
 - Higher ADCs (3He 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 ☺)

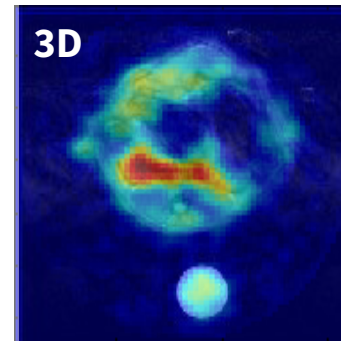
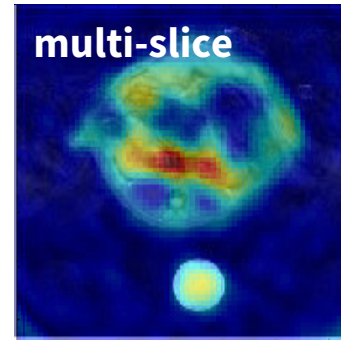
Thermally-polarised spins

- 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