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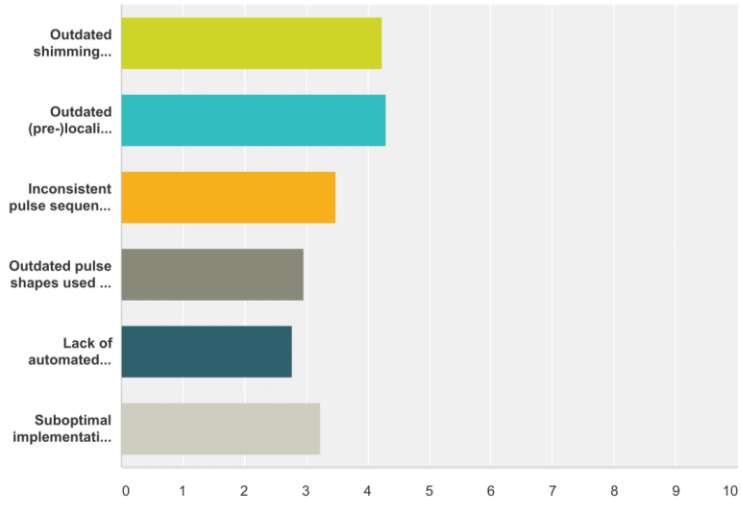
A Survey results

The following pages provide a summary of the survey responses. For ranked questions (e.g. Q1) the responders were asked to rank items in order of importance with 1 being the highest and 6 being the lowest. However, to create intuitively clear bar plots, an inverse score was calculated with highest importance reflected by the highest score. This score is listed in the rightmost table column and was calculated by multiplying the frequency of ranked responses by an inverse weight (i.e., rank of 1 has the maximum weighting of 6 and rank 6 has the minimum weight of 1). The score is finally divided by the number of responders. For example, the score in the first row of Q1 is calculated as follows: (7*6+12*5+8*4+1*3+ 4*2+3*1)/35=4.23. Answers provided in free text format (e.g. Q7) have not been listed.

Q1 What is the greatest pulse-sequence related barrier preventing MRS from becoming more widely used in the clinical environment? Please rank with 1=most important.

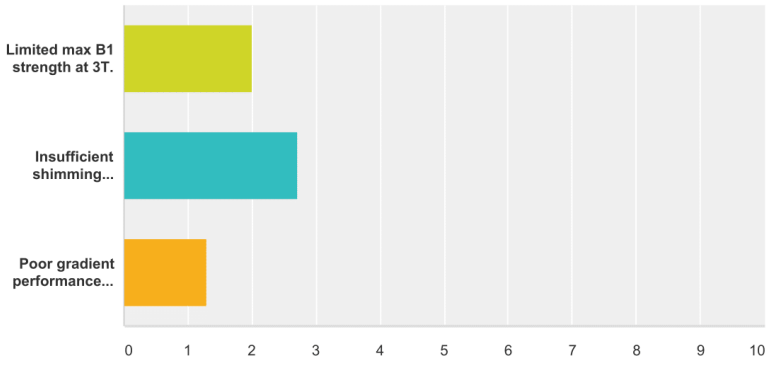
Answered: 35 Skipped: 0



	1	2	3	4	5	6	Total	Score
Outdated shimming algorithms.	20.00% 7	34.29% 12	22.86% 8	2.86% 1	11.43% 4	8.57% 3	35	4.23
Outdated (pre-)localisation methodology (STEAM, PRESS).	31.43% 11	17.14% 6	17.14% 6	22.86% 8	8.57% 3	2.86% 1	35	4.31
Inconsistent pulse sequence implementations between vendors.	17.14% 6	14.29% 5	22.86% 8	14.29% 5	8.57% 3	22.86% 8	35	3.49
Outdated pulse shapes used in MRS sequences.	8.57% 3	5.71% 2	11.43% 4	34.29% 12	28.57% 10	11.43% 4	35	2.97
Lack of automated motion/B0 drift correction.	8.57% 3	11.43% 4	11.43% 4	14.29% 5	25.71% 9	28.57% 10	35	2.77
Suboptimal implementation of (pre-)localisation methodology.	14.29% 5	17.14% 6	14.29% 5	11.43% 4	17.14% 6	25.71% 9	35	3.23

Q2 What is the greatest hardware related barrier preventing MRS from becoming more widely used in the clinical environment? Please rank with 1=most important.

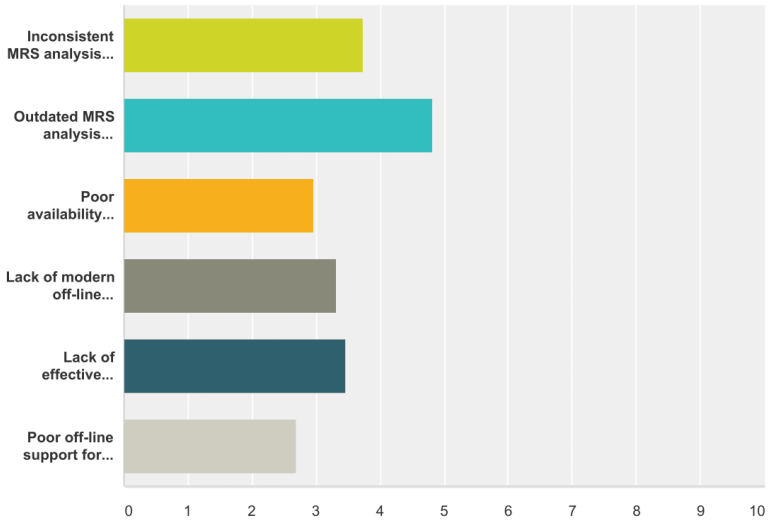
Answered: 35 Skipped: 0



	1	2	3	Total	Score
Limited max B1 strength at 3T.	**25.71%** 9	**48.57%** 17	**25.71%** 9	35	2.00
Insufficient shimming hardware to consistently generate adequate B0 homogeneity for some brain areas.	**74.29%** 26	**22.86%** 8	**2.86%** 1	35	2.71
Poor gradient performance resulting in eddy current distortions.	**0.00%** 0	**28.57%** 10	**71.43%** 25	35	1.29

Q3 What is the greatest analysis related barrier preventing MRS from becoming more widely used in the clinical environment? Please rank with 1=most important.

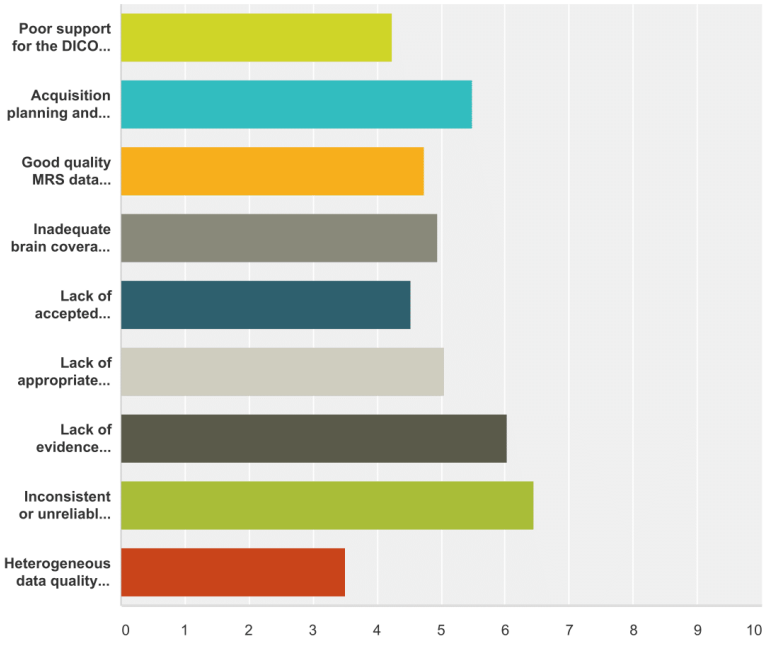
Answered: 35 Skipped: 0



	1	2	3	4	5	6	Total	Score
Inconsistent MRS analysis methodology between vendors.	5.71% 2	40.00% 14	11.43% 4	20.00% 7	11.43% 4	11.43% 4	35	3.74
Outdated MRS analysis methodology supplied by vendors.	48.57% 17	11.43% 4	20.00% 7	14.29% 5	5.71% 2	0.00% 0	35	4.83
Poor availability of modern off-line automated analysis methods.	8.57% 3	5.71% 2	22.86% 8	17.14% 6	28.57% 10	17.14% 6	35	2.97
Lack of modern off-line automated analysis methods with appropriate regulatory approval (FDA/CE marking).	20.00% 7	8.57% 3	14.29% 5	14.29% 5	25.71% 9	17.14% 6	35	3.31
Lack of effective automated methods to evaluate spectral quality.	17.14% 6	20.00% 7	11.43% 4	14.29% 5	17.14% 6	20.00% 7	35	3.46
Poor off-line support for combined visualisation of: 1) MRS localisation information (voxel position/grid placement...) 2); MRS metabolic information (spectra, metabolic maps...) 3); other MR data (anatomical or functional MR).	0.00% 0	14.29% 5	20.00% 7	20.00% 7	11.43% 4	34.29% 12	35	2.69

Q4 What is the greatest practical barrier preventing MRS from becoming more widely used in the clinical environment? Please rank with 1=most important.

Answered: 35 Skipped: 0

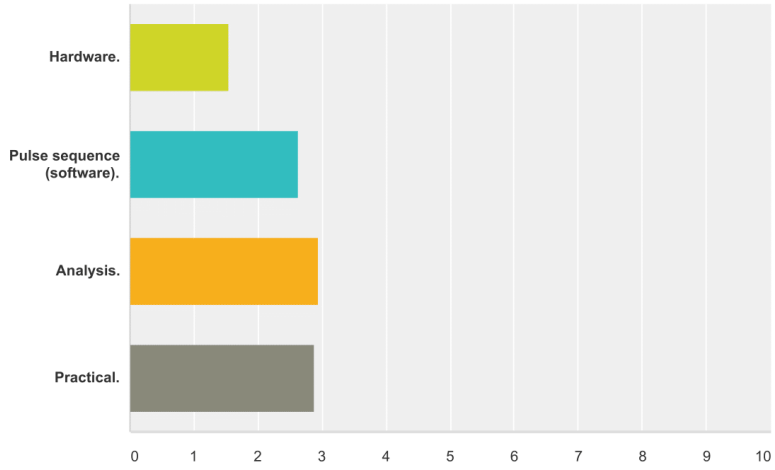


	1	2	3	4	5	6	7	8	9	Total	Score
Poor support for the DICOM MRS data format.	2.86% 1	8.57% 3	8.57% 3	20.00% 7	8.57% 3	8.57% 3	8.57% 3	11.43% 4	22.86% 8	35	4.23
Acquisition planning and positioning is too difficult/takes too long and needs to be automated.	17.14% 6	5.71% 2	14.29% 5	11.43% 4	11.43% 4	22.86% 8	5.71% 2	2.86% 1	8.57% 3	35	5.49
Good quality MRS data acquisition takes too long.	2.86% 1	2.86% 1	17.14% 6	14.29% 5	20.00% 7	8.57% 3	20.00% 7	11.43% 4	2.86% 1	35	4.74
Inadequate brain coverage within a reasonable time.	5.71% 2	8.57% 3	8.57% 3	25.71% 9	8.57% 3	8.57% 3	14.29% 5	20.00% 7	0.00% 0	35	4.94
Lack of accepted normative metabolite values or spectra.	8.57% 3	5.71% 2	11.43% 4	11.43% 4	11.43% 4	14.29% 5	8.57% 3	14.29% 5	14.29% 5	35	4.54
Lack of appropriate training for radiologists or technicians.	5.71% 2	20.00% 7	11.43% 4	2.86% 1	20.00% 7	14.29% 5	5.71% 2	2.86% 1	17.14% 6	35	5.06

Lack of evidence clearly demonstrating how MRS can be used to alter clinical practice for the better.	**34.29%** 12	**8.57%** 3	**14.29%** 5	**2.86%** 1	**5.71%** 2	**2.86%** 1	**14.29%** 5	**8.57%** 3	**8.57%** 3	35	6.03
Inconsistent or unreliable data quality/reproducibility.	**22.86%** 8	**31.43%** 11	**5.71%** 2	**8.57%** 3	**5.71%** 2	**5.71%** 2	**5.71%** 2	**14.29%** 5	**0.00%** 0	35	6.46
Heterogeneous data quality within a given dataset (MRSI).	**0.00%** 0	**8.57%** 3	**8.57%** 3	**2.86%** 1	**8.57%** 3	**14.29%** 5	**17.14%** 6	**14.29%** 5	**25.71%** 9	35	3.51

Q5 Please rank the following barriers in order of importance (please rank with 1=most important):

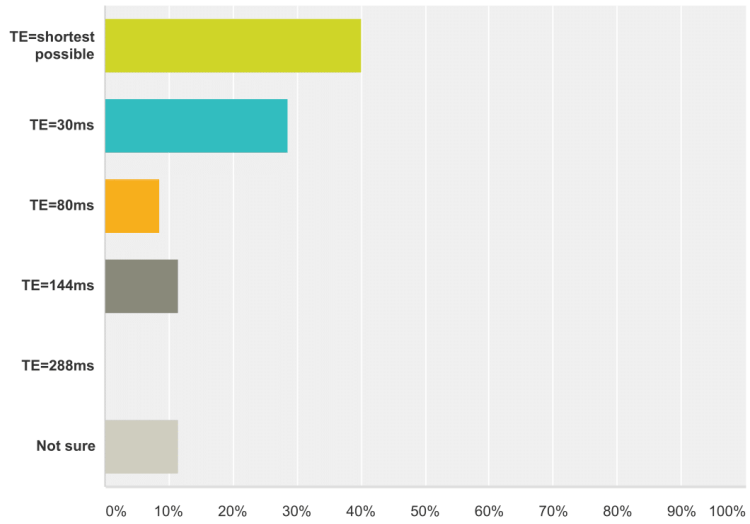
Answered: 35 Skipped: 0



	1	2	3	4	Total	Score
Hardware.	**5.71%** 2	**8.57%** 3	**20.00%** 7	**65.71%** 23	35	1.54
Pulse sequence (software).	**22.86%** 8	**25.71%** 9	**42.86%** 15	**8.57%** 3	35	2.63
Analysis.	**28.57%** 10	**42.86%** 15	**22.86%** 8	**5.71%** 2	35	2.94
Practical.	**42.86%** 15	**22.86%** 8	**14.29%** 5	**20.00%** 7	35	2.89

Q6 Which echo time would you recommend for routine clinical SVS and large multi-centre trials for brain regions where good quality SVS† can be reliably collected?† spectra with: metabolite linewidth < 0.07 PPM; symmetric lineshape; void of artefacts (residual water, out-of-volume lipids etc) that interfere with analysis in the spectral region between 0-4.0 PPM.

Answered: 35 Skipped: 0



Answer Choices	Responses	
TE=shortest possible	40.00%	14
TE=30ms	28.57%	10
TE=80ms	8.57%	3
TE=144ms	11.43%	4
TE=288ms	0.00%	0
Not sure	11.43%	4
Total		35

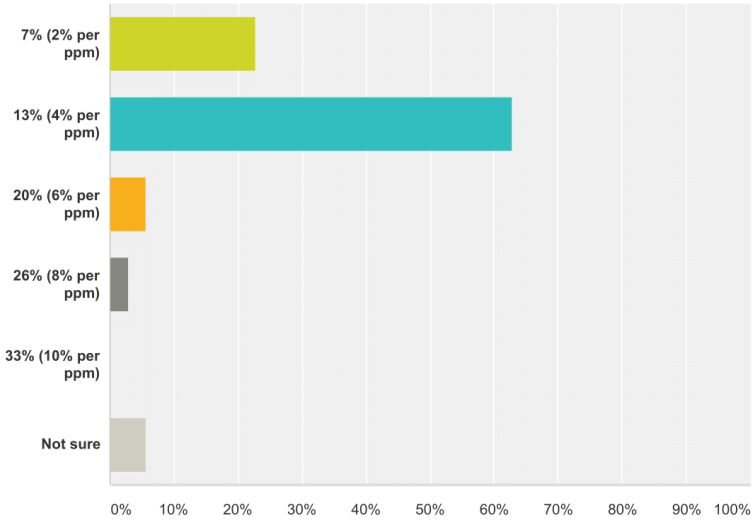
Q7 Please indicate cases where you would opt for a different SVS TE to the one given above and explain why. For example : TE=144ms for Lac/lipid discrimination in brain tumours. If you think one SVS TE is best suited for all cases then please leave this section blank.

Answered: 18 Skipped: 17

This question was a text based response and has therefore has not been summarized.

Q8 What is the maximum acceptable level of chemical shift displacement (CSD) for routine† clinical SVS across the typical spectral width (0.9ppm-4.2ppm)?† appropriate for 90% of examinations collected at your centre.n.b. at 1.5T the maximum CSD for short TE PRESS is generally < 5% per ppm. Values of 2% can be achieved for short TE full-intensity MRS at 3T using modern methods (sLASER) without hardware modifications.

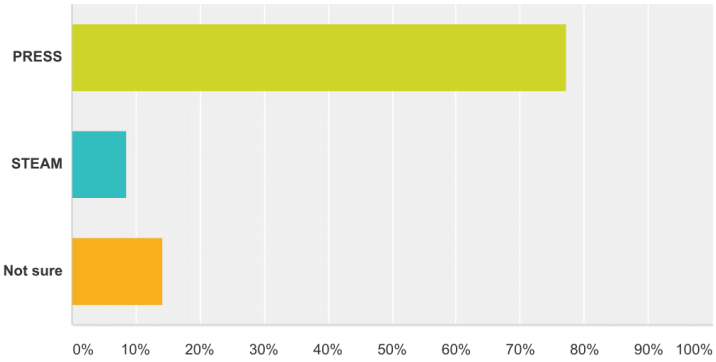
Answered: 35 Skipped: 0



Answer Choices	Responses	
7% (2% per ppm)	22.86%	8
13% (4% per ppm)	62.86%	22
20% (6% per ppm)	5.71%	2
26% (8% per ppm)	2.86%	1
33% (10% per ppm)	0.00%	0
Not sure	5.71%	2
Total		35

Q9 Which widely available localisation method would you recommend for routine clinical SVS and large multi-centre trials - assuming CSD is at an acceptable level?

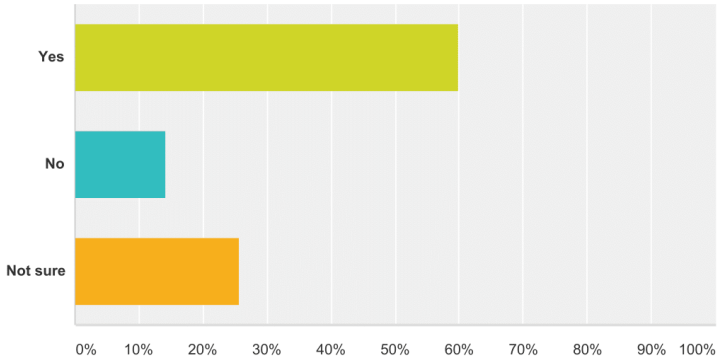
Answered: 35 Skipped: 0



Answer Choices	Responses	
PRESS	77.14%	27
STEAM	8.57%	3
Not sure	14.29%	5
Total		35

Q10 Would you recommend the use of STEAM over PRESS when PRESS CSD is beyond the acceptable level specified in Q8?

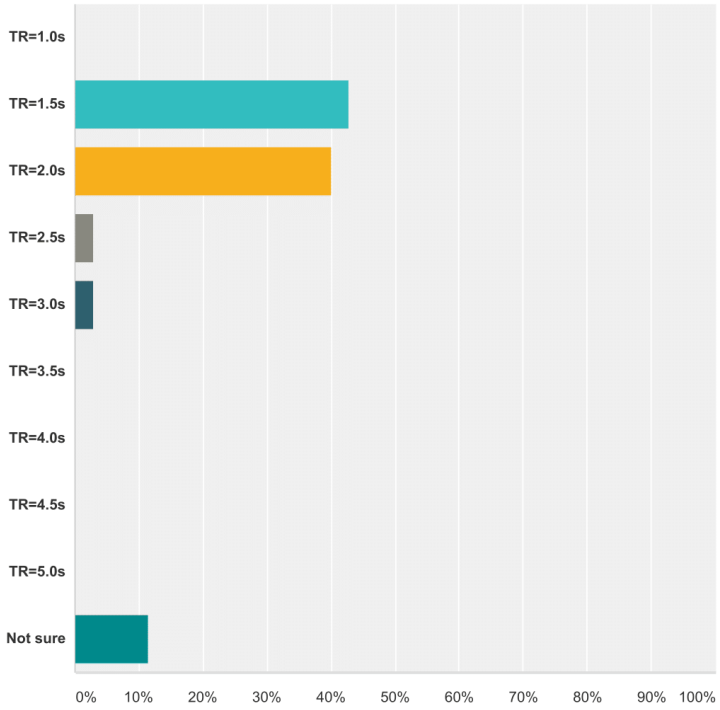
Answered: 35 Skipped: 0



Answer Choices	Responses	
Yes	60.00%	21
No	14.29%	5
Not sure	25.71%	9
Total		35

Q11 Which repetition time would you recommend for routine clinical SVS and large multi-centre trials at 1.5T? Note - a reduced TR reduces scan time at the cost of increasing T1 saturation.

Answered: 35 Skipped: 0

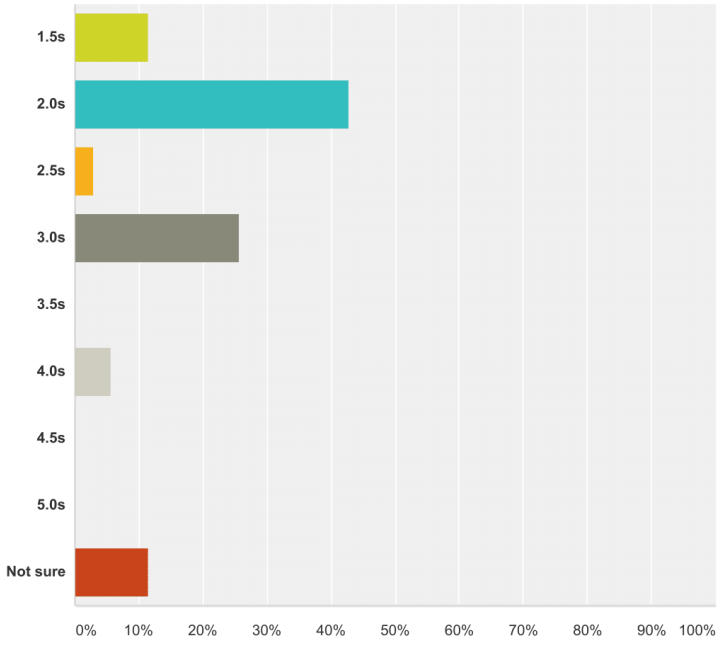


Answer Choices	Responses	
TR=1.0s	0.00%	0
TR=1.5s	42.86%	15
TR=2.0s	40.00%	14
TR=2.5s	2.86%	1
TR=3.0s	2.86%	1
TR=3.5s	0.00%	0
TR=4.0s	0.00%	0

TR=4.5s	**0.00%**	0
TR=5.0s	**0.00%**	0
Not sure	**11.43%**	4
Total		**35**

Q12 Which repetition time would you recommend for routine clinical SVS and large multi-centre trials at 3.0T? Note - a reduced TR reduces scan time at the cost of increasing T1 saturation.

Answered: 35 Skipped: 0

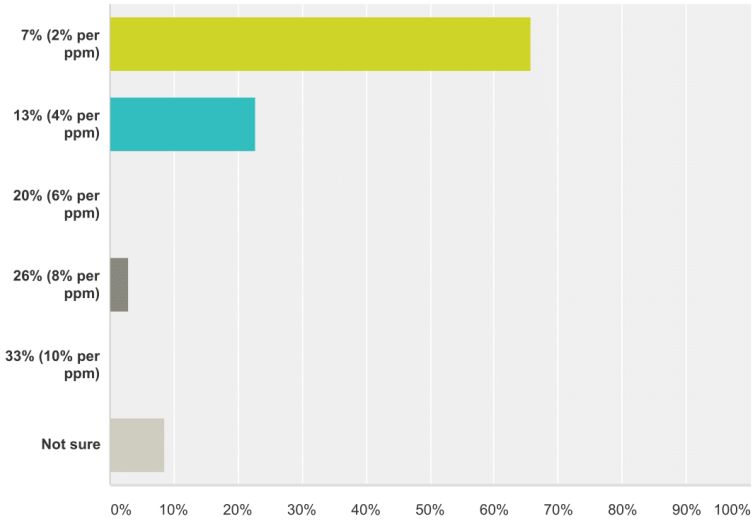


Answer Choices	Responses	
1.5s	11.43%	4
2.0s	42.86%	15
2.5s	2.86%	1
3.0s	25.71%	9
3.5s	0.00%	0
4.0s	5.71%	2
4.5s	0.00%	0
5.0s	0.00%	0
Not sure	11.43%	4

Total	**35**

Q13 What is the maximum acceptable level of chemical shift displacement (CSD) for routine† clinical MRSI across the typical spectral width (0.9ppm-4.2ppm)? Please assume that saturation bands cannot be used in combination with the gradient based localisation scheme.† appropriate for 90% of examinations collected at your centre.n.b. at 1.5T the maximum CSD for short TE PRESS is generally < 5% per ppm. Values of 2% can be achieved for short TE full-intensity MRS at 3T using modern methods (sLASER) without hardware modifications.

Answered: 35 Skipped: 0

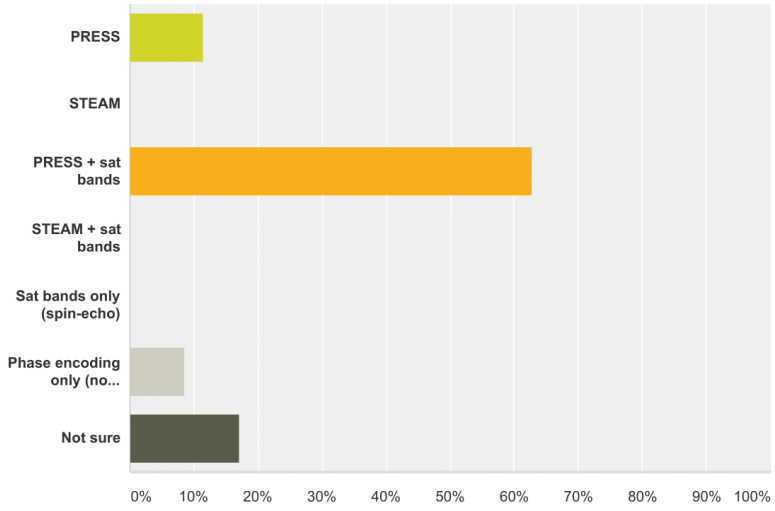


Answer Choices	Responses	
7% (2% per ppm)	65.71%	23
13% (4% per ppm)	22.86%	8
20% (6% per ppm)	0.00%	0
26% (8% per ppm)	2.86%	1
33% (10% per ppm)	0.00%	0

Not sure	8.57%	3
Total		**35**

Q14 Which widely available pre-localisation method would you recommend for clinical 2D MRSI - assuming CSD is at an acceptable level?

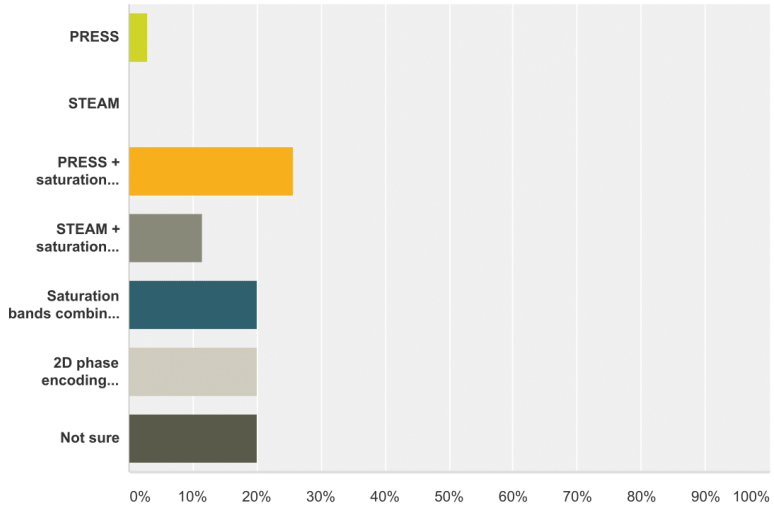
Answered: 35 Skipped: 0



Answer Choices	Responses	
PRESS	11.43%	4
STEAM	0.00%	0
PRESS + sat bands	62.86%	22
STEAM + sat bands	0.00%	0
Sat bands only (spin-echo)	0.00%	0
Phase encoding only (no pre-localisation)	8.57%	3
Not sure	17.14%	6
Total		**35**

Q15 Which of the below techniques would you recommend when PRESS CSD is beyond the acceptable level specified in Q13?

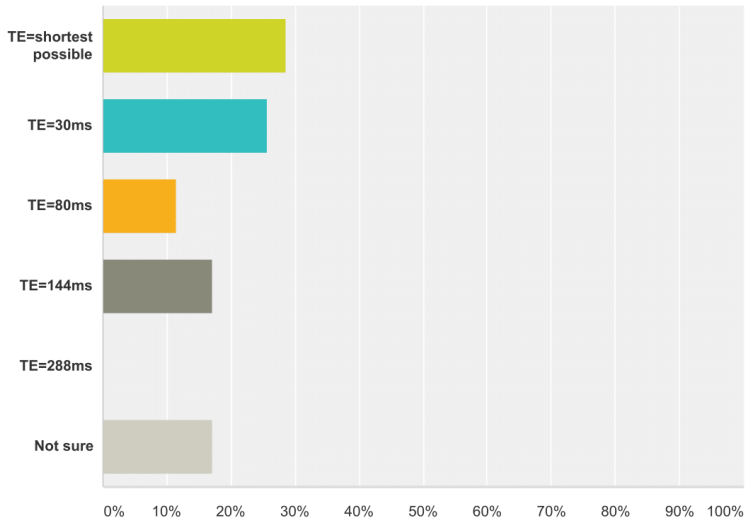
Answered: 35 Skipped: 0



Answer Choices	Responses	
PRESS	2.86%	1
STEAM	0.00%	0
PRESS + saturation bands	25.71%	9
STEAM + saturation bands	11.43%	4
Saturation bands combined with 1D slice selection (spin-echo)	20.00%	7
2D phase encoding combined with 1D slice selection (no pre-localisation)	20.00%	7
Not sure	20.00%	7
Total		**35**

Q16 Which echo time would you recommend for routine clinical 2D MRSI and large multi-centre trials for brain regions where good quality MRSI† can be reliably collected?† spectra with: a metabolite linewidth < 0.07 PPM; symmetric lineshape; void of artefacts (residual water, out-of-volume lipids etc) that interfere with analysis in the spectral region between 0-4.0 PPM.

Answered: 35 Skipped: 0



Answer Choices	Responses	
TE=shortest possible	28.57%	10
TE=30ms	25.71%	9
TE=80ms	11.43%	4
TE=144ms	17.14%	6
TE=288ms	0.00%	0
Not sure	17.14%	6
Total		35

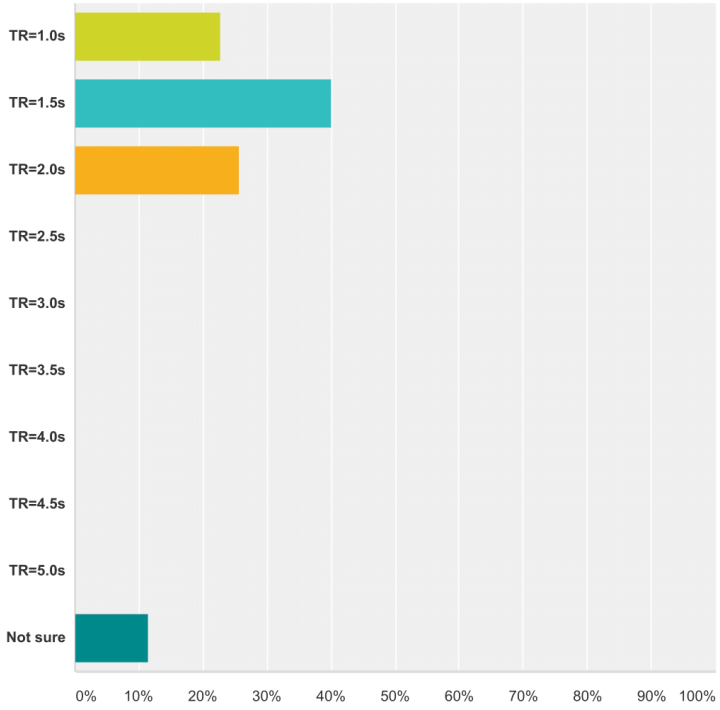
Q17 Please indicate cases where you would opt for a different MRSI TE to the one given above and explain why. For example : TE=144ms for Lac/lipid discrimination in brain tumours. If you think one MRSI TE is best suited for all cases then please leave this section blank.

Answered: 17 Skipped: 18

This question was a text based response and has therefore not been summarized.

Q18 Which repetition time would you recommend for routine clinical 2D MRSI and large multi-centre trials at 1.5T? Note - a reduced TR reduces scan time at the cost of increasing T1 saturation.

Answered: 35 Skipped: 0

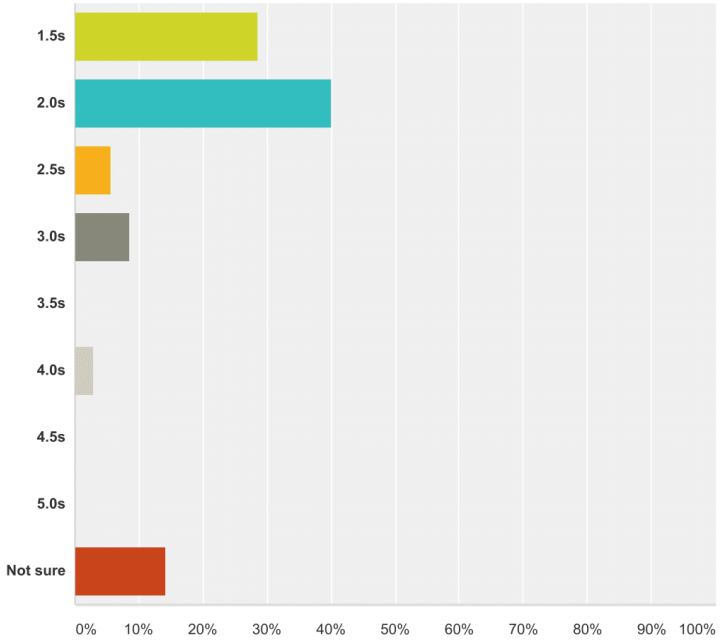


Answer Choices	Responses	
TR=1.0s	22.86%	8
TR=1.5s	40.00%	14
TR=2.0s	25.71%	9
TR=2.5s	0.00%	0
TR=3.0s	0.00%	0
TR=3.5s	0.00%	0
TR=4.0s	0.00%	0

TR=4.5s	**0.00%**	0
TR=5.0s	**0.00%**	0
Not sure	**11.43%**	4
Total		**35**

Q19 Which repetition time would you recommend for routine clinical 2D MRSI and large multi-centre trials at 3.0T? Note - a reduced TR reduces scan time at the cost of increasing T1 saturation.

Answered: 35 Skipped: 0

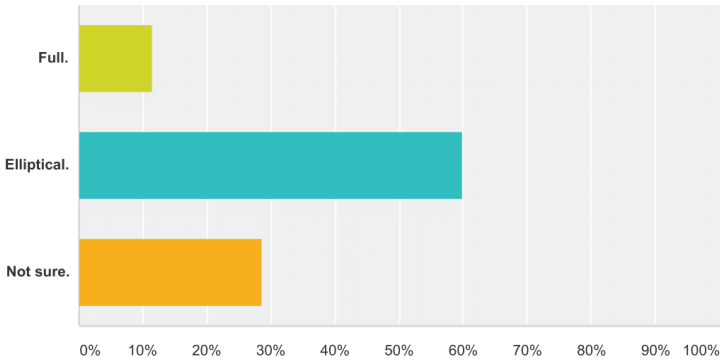


Answer Choices	Responses	
1.5s	28.57%	10
2.0s	40.00%	14
2.5s	5.71%	2
3.0s	8.57%	3
3.5s	0.00%	0
4.0s	2.86%	1
4.5s	0.00%	0
5.0s	0.00%	0
Not sure	14.29%	5

Total	35

Q20 Which 2D k-space sampling scheme would you recommend for clinical 2D MRSI and large multi-centre trials?

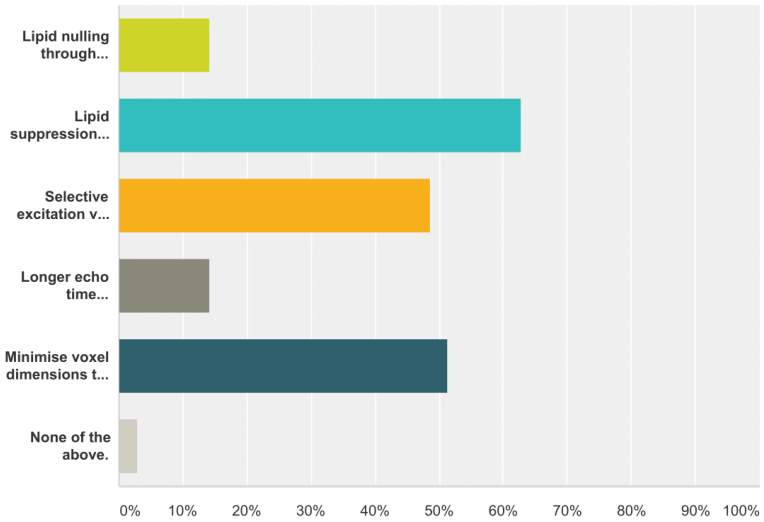
Answered: 35 Skipped: 0



Answer Choices	Responses	
Full.	11.43%	4
Elliptical.	60.00%	21
Not sure.	28.57%	10
Total		35

Q21 I recommend the following acquisition method(s) to reduce scalp lipid contamination:

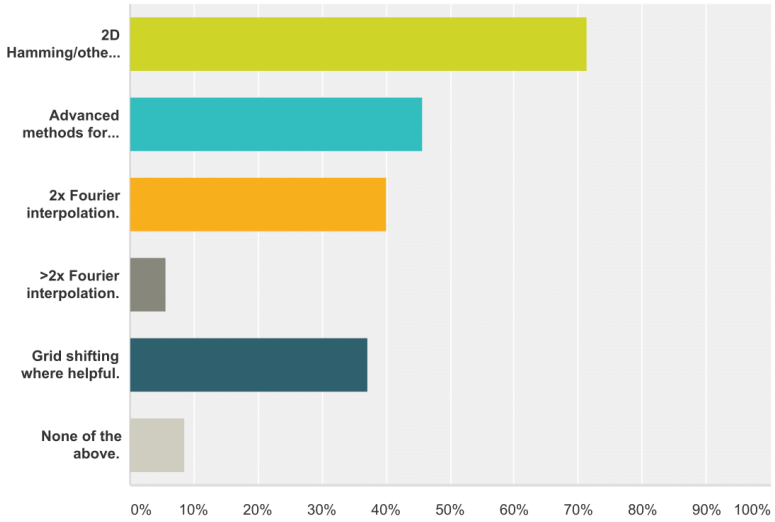
Answered: 35 Skipped: 0



Answer Choices	Responses	
Lipid nulling through inversion recovery.	14.29%	5
Lipid suppression through pre-saturation pulses.	62.86%	22
Selective excitation via PRESS or STEAM to avoid lipid areas.	48.57%	17
Longer echo time acquisition (>100ms) to reduce lipid resonance intensity.	14.29%	5
Minimise voxel dimensions to improve the PSF and therefore reduce signal bleed into adjacent voxels.	51.43%	18
None of the above.	2.86%	1
Total Respondents: 35		

Q22 Which post-processing steps would you recommend for clinical 2D MRSI?

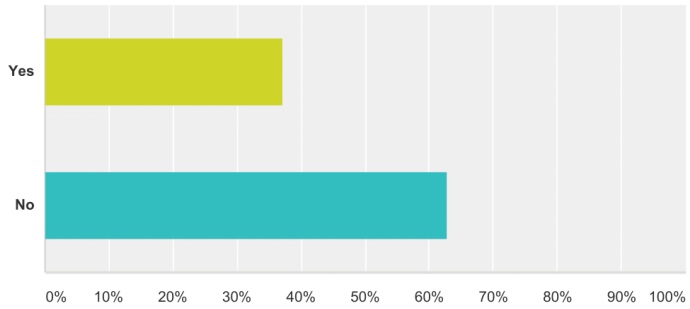
Answered: 35 Skipped: 0



Answer Choices	Responses	
2D Hamming/other k-space filter to reduce ringing.	71.43%	25
Advanced methods for reducing lipid contamination (reconstruction based).	45.71%	16
2x Fourier interpolation.	40.00%	14
>2x Fourier interpolation.	5.71%	2
Grid shifting where helpful.	37.14%	13
None of the above.	8.57%	3
Total Respondents: 35		

Q23 Do you think it is important for vendors/platforms to standardise on a single water suppression method?

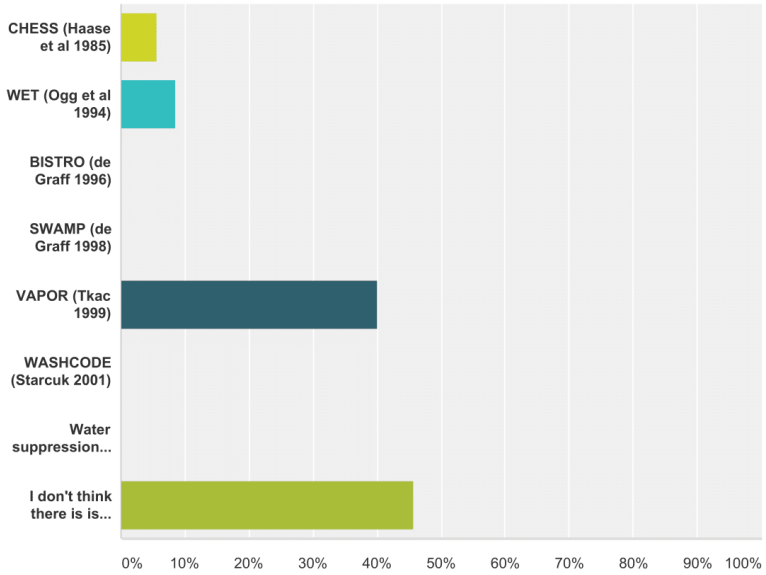
Answered: 35 Skipped: 0



Answer Choices	Responses	
Yes	37.14%	13
No	62.86%	22
Total		35

Q24 I recommend the following water suppression method:

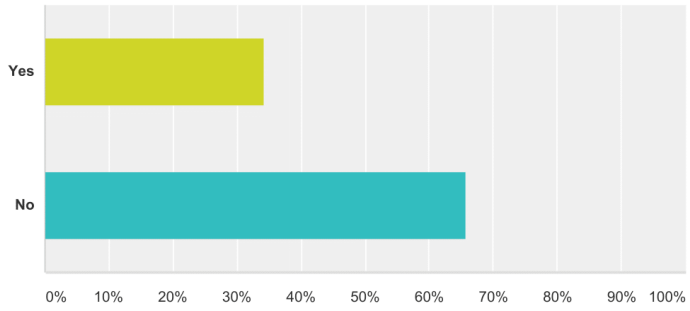
Answered: 35 Skipped: 0



Answer Choices	Responses	
CHESS (Haase et al 1985)	5.71%	2
WET (Ogg et al 1994)	8.57%	3
BISTRO (de Graff 1996)	0.00%	0
SWAMP (de Graff 1998)	0.00%	0
VAPOR (Tkac 1999)	40.00%	14
WASHCODE (Starcuk 2001)	0.00%	0
Water suppression cycling (Ernst 2011)	0.00%	0
I don't think there is is enough evidence to choose a particular method at this time.	45.71%	16
Total		**35**

Q25 Do you think it is important for vendors/platforms to standardise on a single shimming method?

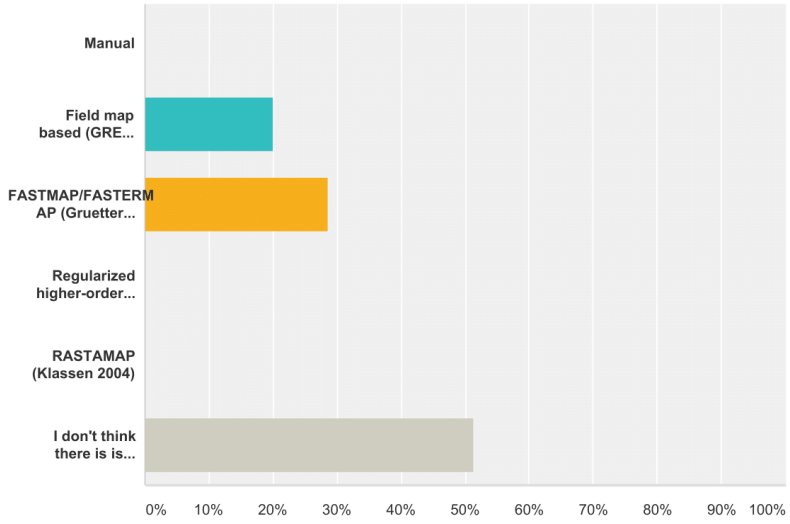
Answered: 35 Skipped: 0



Answer Choices	Responses	
Yes	34.29%	12
No	65.71%	23
Total		35

Q26 I recommend the following shimming method:

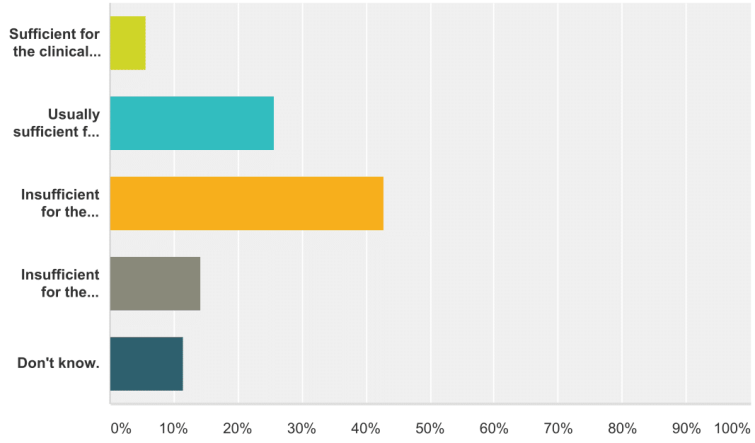
Answered: 35 Skipped: 0



Answer Choices	Responses	
Manual	0.00%	0
Field map based (GRE shim)	20.00%	7
FASTMAP/FASTERMAP (Gruetter 1993/Shen 2004)	28.57%	10
Regularized higher-order in vivo shimming (Kim 2002)	0.00%	0
RASTAMAP (Klassen 2004)	0.00%	0
I don't think there is is enough evidence to choose a particular method at this time.	51.43%	18
Total		**35**

Q27 SVS vendor analysis software is:

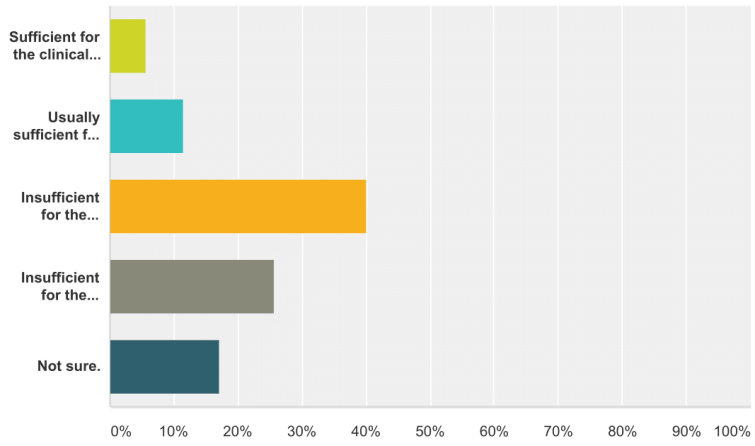
Answered: 35 Skipped: 0



Answer Choices	Responses
Sufficient for the clinical questions being asked at my centre.	5.71% 2
Usually sufficient for the clinical questions being asked, but non-vendor analysis software is sometimes required.	25.71% 9
Insufficient for the clinical questions being asked regularly, I process all MRS using non-vendor analysis software.	42.86% 15
Insufficient for the clinical questions being asked regularly, I would like to process all/some MRS using non-vendor analysis software - however difficulties with data transfer and file formats prevent this from happening routinely.	14.29% 5
Don't know.	11.43% 4
Total	**35**

Q28 MRSI vendor analysis software is:

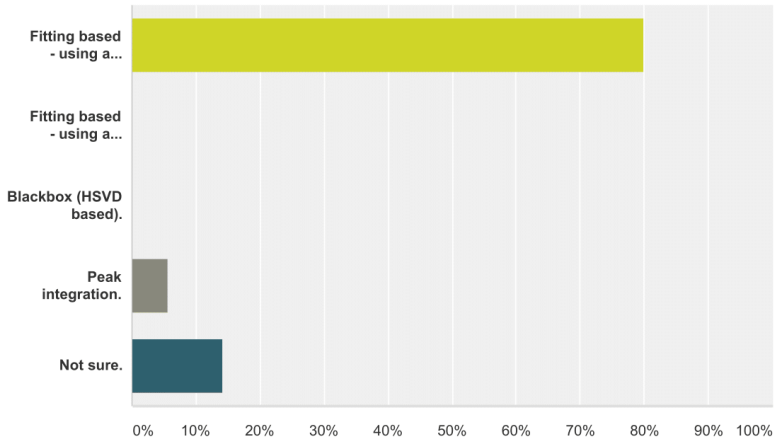
Answered: 35 Skipped: 0



Answer Choices	Responses
Sufficient for the clinical questions being asked at my centre.	5.71% 2
Usually sufficient for the clinical questions being asked, but non-vendor analysis software is sometimes required.	11.43% 4
Insufficient for the clinical questions being asked regularly, I process all MRS using non-vendor analysis software.	40.00% 14
Insufficient for the clinical questions being asked regularly, I would like to process all/some MRS using non-vendor analysis software - however difficulties with data transfer and file formats prevent this from happening routinely.	25.71% 9
Not sure.	17.14% 6
Total	**35**

Q29 The current best approach for 1H MRSI/SVS quantitation at short/medium echo (TE<100) is:

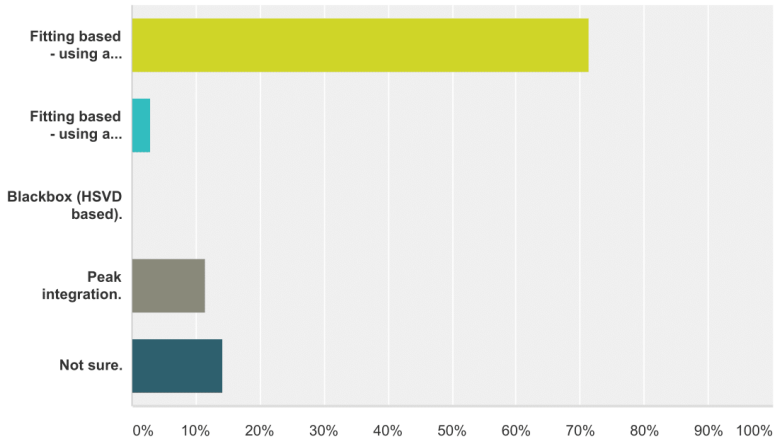
Answered: 35 Skipped: 0



Answer Choices	Responses	
Fitting based - using a metabolite basis set (LCModel, QUEST, TARQUIN...).	80.00%	28
Fitting based - using a dictionary of single peaks and constraints based on prior knowledge (AMARES, VARPRO).	0.00%	0
Blackbox (HSVD based).	0.00%	0
Peak integration.	5.71%	2
Not sure.	14.29%	5
Total		35

Q30 The current best approach for 1H MRSI/SVS quantitation at long echo (TE>100) is:

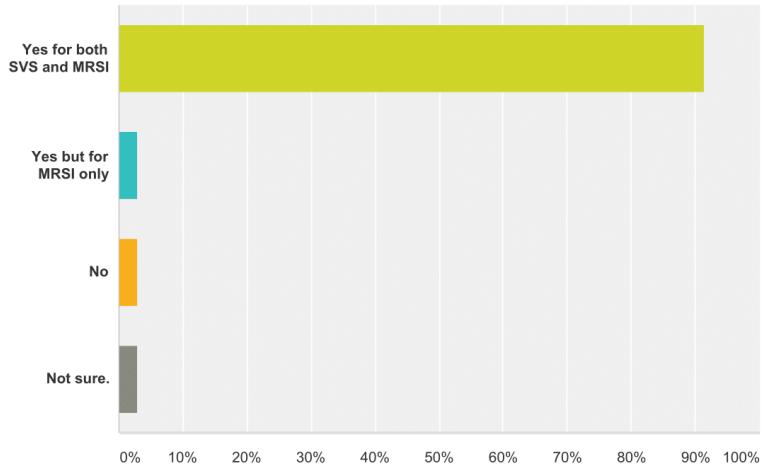
Answered: 35 Skipped: 0



Answer Choices	Responses	
Fitting based - using a metabolite basis set (LCModel, QUEST, TARQUIN...).	71.43%	25
Fitting based - using a dictionary of single peaks and constraints based on prior knowledge (AMARES, VARPRO).	2.86%	1
Blackbox (HSVD based).	0.00%	0
Peak integration.	11.43%	4
Not sure.	14.29%	5
Total		35

Q31 Is fully automated analysis an important requirement for clinical MRS/MRSI?

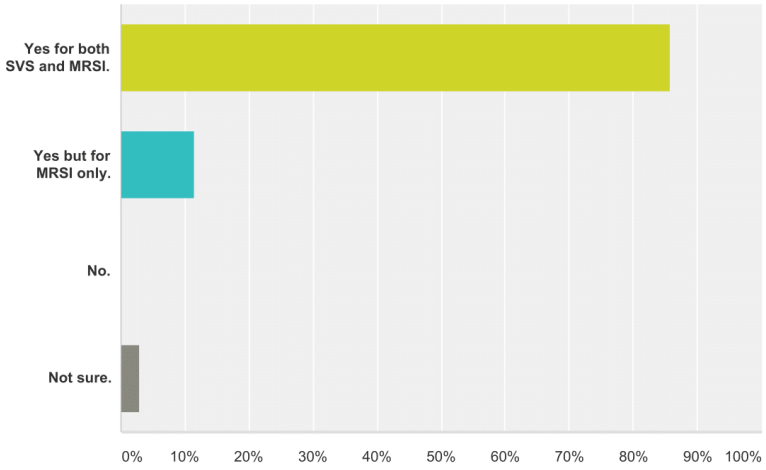
Answered: 35 Skipped: 0



Answer Choices	Responses	
Yes for both SVS and MRSI	**91.43%**	32
Yes but for MRSI only	**2.86%**	1
No	**2.86%**	1
Not sure.	**2.86%**	1
Total		**35**

Q32 Is fully automated QC† an important requirement for clinical MRS/MRSI?† a way to determine if a particular voxel is of sufficient spectral quality to be used in clinical decision making or part of a clinical trail.

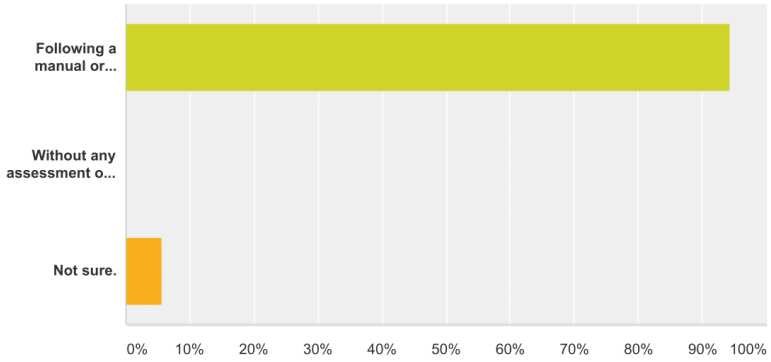
Answered: 35 Skipped: 0



Answer Choices	Responses	
Yes for both SVS and MRSI.	85.71%	30
Yes but for MRSI only.	11.43%	4
No.	0.00%	0
Not sure.	2.86%	1
Total		35

Q33 MRSI metabolite maps should be interpreted:

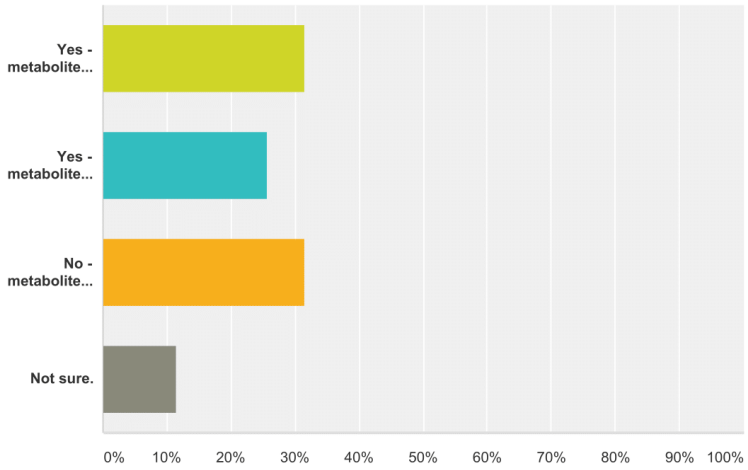
Answered: 35 Skipped: 0



Answer Choices	Responses	
Following a manual or automated assessment of spectral and analysis quality.	94.29%	33
Without any assessment of spectral or analysis quality.	0.00%	0
Not sure.	5.71%	2
Total		35

Q34 Do you think absolute metabolite measurements should be a part of routine clinical MRSMRSI?

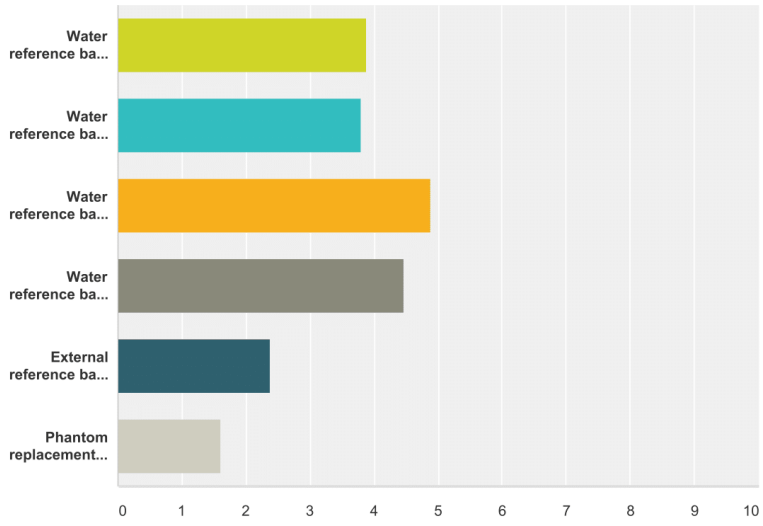
Answered: 35 Skipped: 0



Answer Choices	Responses
Yes - metabolite measurements should be a part of routine clinical MRS and MRSI.	31.43% 11
Yes - metabolite measurements should be a part of routine clinical MRS, however may not be appropriate for MRSI due to time constraints.	25.71% 9
No - metabolite ratio measurements are sufficient for the vast majority of clinical MRS examinations.	31.43% 11
Not sure.	11.43% 4
Total	**35**

Q35 Please rank the following absolute quantitation methods in order of how appropriate they are for routine clinical MRS. (Rank with 1=most appropriate).

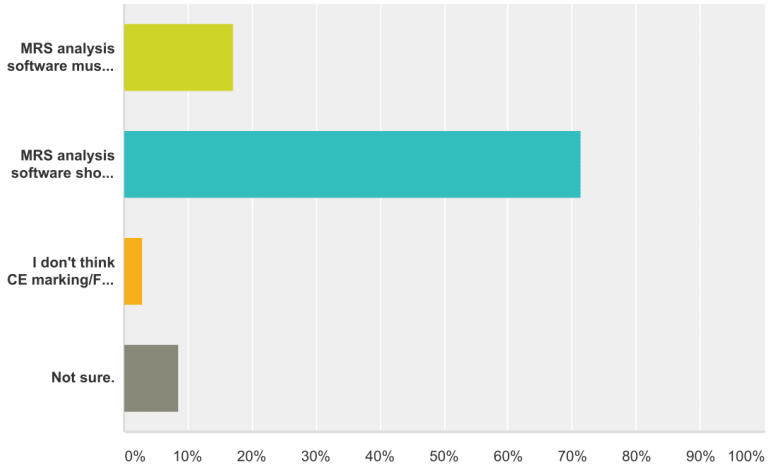
Answered: 35 Skipped: 0



	1	2	3	4	5	6	Total	Score
Water reference based measurements with assumed water T2 relaxation and assumed single compartment water concentration.	20.00% 7	20.00% 7	8.57% 3	40.00% 14	2.86% 1	8.57% 3	35	3.89
Water reference based measurements with measured water T2 relaxation (multi-TE) and assumed single compartment water concentration.	5.71% 2	22.86% 8	40.00% 14	11.43% 4	17.14% 6	2.86% 1	35	3.80
Water reference based measurements with assumed water T2 relaxation and measured WM/GM/CSF contributions.	37.14% 13	28.57% 10	20.00% 7	14.29% 5	0.00% 0	0.00% 0	35	4.89
Water reference based measurements with measured water T2 relaxation (multi-TE) and measured WM/GM/CSF contributions.	28.57% 10	25.71% 9	14.29% 5	25.71% 9	5.71% 2	0.00% 0	35	4.46
External reference based calibrations methods.	5.71% 2	2.86% 1	8.57% 3	0.00% 0	71.43% 25	11.43% 4	35	2.37
Phantom replacement based calibration methods.	2.86% 1	0.00% 0	8.57% 3	8.57% 3	2.86% 1	77.14% 27	35	1.60

Q36 How important is CE marking/FDA approval for MRS analysis software?

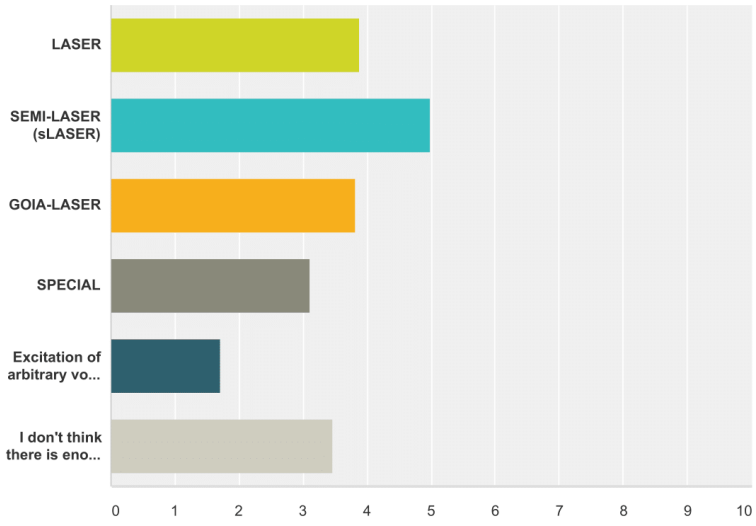
Answered: 35 Skipped: 0



Answer Choices	Responses
MRS analysis software must be CE marked/FDA approved before I can use it for clinical purposes.	17.14% 6
MRS analysis software should be CE marked/FDA approved, however I used non approved software for clinical purposes because it is produces better results and is vendor neutral.	71.43% 25
I don't think CE marking/FDA approval is particularly important for MRS analysis software used for clinical purposes.	2.86% 1
Not sure.	8.57% 3
Total	**35**

Q37 Which MRS localisation technique (SVS and MRSI) has the greatest potential to improve clinical MRS? Please rank with 1=most important.

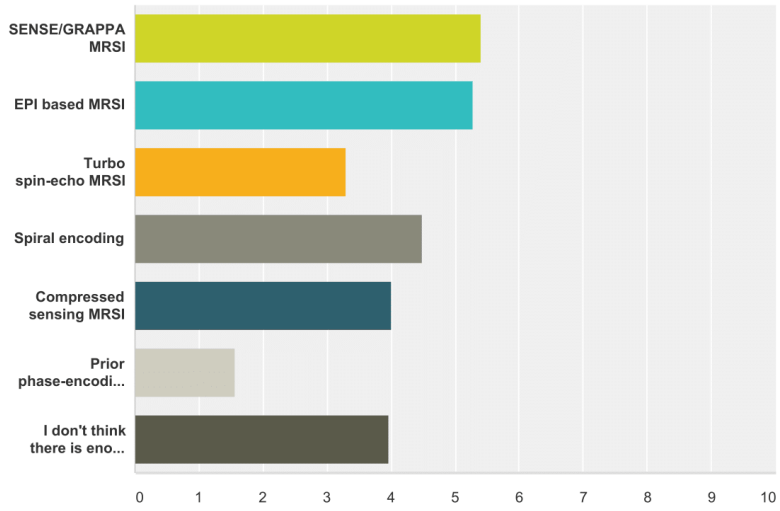
Answered: 35 Skipped: 0



	1	2	3	4	5	6	Total	Score
LASER	8.57% 3	31.43% 11	17.14% 6	28.57% 10	11.43% 4	2.86% 1	35	3.89
SEMI-LASER (sLASER)	34.29% 12	34.29% 12	28.57% 10	2.86% 1	0.00% 0	0.00% 0	35	5.00
GOIA-LASER	5.71% 2	22.86% 8	31.43% 11	31.43% 11	5.71% 2	2.86% 1	35	3.83
SPECIAL	2.86% 1	8.57% 3	20.00% 7	34.29% 12	34.29% 12	0.00% 0	35	3.11
Excitation of arbitrary voxel shapes	0.00% 0	2.86% 1	2.86% 1	2.86% 1	45.71% 16	45.71% 16	35	1.71
I don't think there is enough evidence to pick a single technique at this time	48.57% 17	0.00% 0	0.00% 0	0.00% 0	2.86% 1	48.57% 17	35	3.46

Q38 Which MRSI encoding technique has the greatest potential to improve clinical MRS? Please rank with 1=most important.

Answered: 35 Skipped: 0



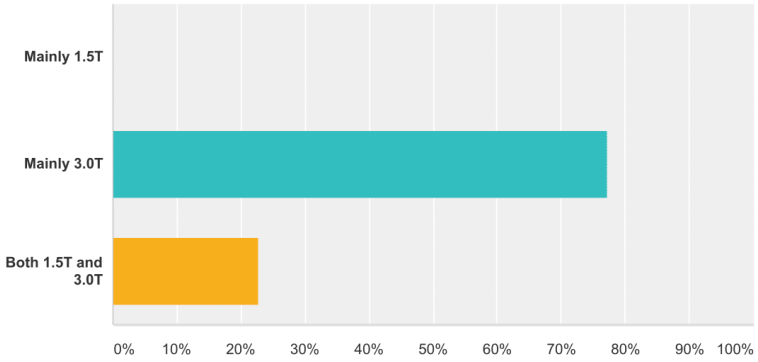
	1	2	3	4	5	6	7	Total	Score
SENSE/GRAPPA MRSI	22.86% 8	28.57% 10	25.71% 9	14.29% 5	5.71% 2	2.86% 1	0.00% 0	35	5.40
EPI based MRSI	11.43% 4	34.29% 12	31.43% 11	17.14% 6	5.71% 2	0.00% 0	0.00% 0	35	5.29
Turbo spin-echo MRSI	0.00% 0	0.00% 0	14.29% 5	28.57% 10	31.43% 11	22.86% 8	2.86% 1	35	3.29
Spiral encoding	20.00% 7	17.14% 6	2.86% 1	22.86% 8	25.71% 9	11.43% 4	0.00% 0	35	4.49
Compressed sensing MRSI	2.86% 1	17.14% 6	20.00% 7	14.29% 5	28.57% 10	17.14% 6	0.00% 0	35	4.00
Prior phase-encoding gradient based MRSI localization methods (SLIM/SLAM/SLOOP)	0.00% 0	0.00% 0	0.00% 0	2.86% 1	2.86% 1	42.86% 15	51.43% 18	35	1.57
I don't think there is enough evidence to pick a single technique at this time	42.86% 15	2.86% 1	5.71% 2	0.00% 0	0.00% 0	2.86% 1	45.71% 16	35	3.97

Q39 Please describe any additional barriers or solutions, for the use of clinical MRS, that have not been mentioned in this survey that you believe to be important:

Answered: 13 Skipped: 22

Q40 What field strength(s) are you typically using for clinical MRS/MRSI?

Answered: 35 Skipped: 0



Answer Choices	Responses	
Mainly 1.5T	**0.00%**	0
Mainly 3.0T	**77.14%**	27
Both 1.5T and 3.0T	**22.86%**	8
Total		**35**

Q41 Do you have any other comments, questions, or concerns?

Answered: 10 Skipped: 25

B Quality control and MRS artefacts

A visual assessment of MRS data quality is recommended to identify any data quality features that may cause bias or instability in the fitting phase of analysis. One of the most common issues with MRS data quality is B_0 inhomogeneity (poor shimming). For a given acquisition protocol, a reduction in B_0 homogeneity will impair the data in three ways:

1. The distinction between the metabolite signals and the inherent noise level will be reduced, resulting in reduced metabolite estimate accuracy.
2. The distinction between metabolite resonances will be reduced, due to greater overlap and therefore interference between broadened resonances.
3. Water suppression quality will be reduced, potentially resulting in baseline distortions and water sidebands interfering with metabolite signals (Figure S1 c,f).

B_0 inhomogeneity may be quickly assessed by looking at the overlap between the total-creatine and total-choline resonances at approximately 3 and 3.2 ppm, respectively. If the data point equidistant between the peaks (minimum overlap point) has a similar intensity to the baseline level (judged from a flat spectral region) then the B_0 inhomogeneity would be considered to be good (Figure S1a). An elevation of this point above the baseline level indicates poorer B_0 inhomogeneity, and unreliable spectra may be identified by comparing the ratio between the maximum intensity of the total-creatine resonance and the minimum overlap point. An extreme example of spectral overlap is show in Figure S1 f) where the total-choline and total-creatine peaks are indistinguishable. Whilst this assessment approach is convenient to use, it relies on the total-creatine and total-choline peaks having a similar intensity, which may not be the case in pathology or normal brain. A preferred method for assessing B_0 homogeneity is a measurement of the full-width half maximum (FWHM) of a singlet metabolite or unsuppressed water resonance. Figure S1 parts a) - c) show spectra with total-NAA FWHM values of 0.038, 0.076 and 0.138 ppm, respectively - demonstrating the reduced signal to noise ratio and increased metabolite overlap and baseline distortions commonly associated with increased B_0 inhomogeneity. FWHM values were measured using the TARQUIN analysis software (1) by automatically determining the largest singlet resonance (tNAA, tCr or tCho) following baseline subtraction, and measuring the FWHM of the fit to the singlet.

One approach to improve B_0 inhomogeneity is to reduce the voxel size, since it is easier to obtain an acceptable shim across a smaller volume. However, this results in reduced SNR and therefore a greater number of averages may need to be acquired to compensate. In addition, SVS voxel dimensions of less than 15 mm in any direction may not produce sufficient signal for some shimming methods to work effectively. Problems with shimming

small volumes may be mitigated by prescribing a separate, but larger, shim volume co-localized with the acquisition volume.

Strong lipid signals also interfere with metabolite estimation and may produce strong baseline artefacts. These signals may be identified from having a significantly broader FWHM than metabolites and always having a strong resonance at 1.3 ppm and a smaller one at 0.9 ppm. Whilst lipid signals may be present in pathology, they may also be an artefact originating from nearby scalp tissue - which has a high concentration of lipids. Distinguishing between genuine and out-of-volume lipids may be challenging, however out-of-volume lipids often have the following features:

1. They are often out of phase with the metabolite resonances (Figure S2b).
2. They are often much broader than genuine lipid signals due to B_0 inhomogeneity at the scalp.
3. The strongest lipid resonance is shifted in frequency away from 1.3 ppm, also due to B_0 inhomogeneity (Figure S1d).

For SVS, the most effective strategy for reducing out-of-volume lipid signals is to move the voxel away from the source. However, in certain cases this may not be practical and other approaches involve placing a saturation band over the lipid containing region, or exploiting the T_2 relaxation difference between metabolite and lipids by increasing the sequence TE. In sequences with significant CSD, it may also be beneficial to plan the voxel with the lipid excitation region alongside a metabolite region. Figure S2 shows how reversing the gradient polarity in the left-right direction can move the lipid excitation region away from the scalp – resulting in improved spectral quality. However, it should be noted that the use of high bandwidth pulse sequences, such as semi-LASER, is preferred over manually adjusting the gradient direction.

Figure S1 e) shows the typical appearance of “ghost” artefacts in the spectral region downfield of 3.3 ppm. Whilst they most commonly occur close to the water resonance, they may appear anywhere in the spectrum, overlapping with metabolite signals and therefore invalidating fitting assumptions. The origin of these signals is from regions of B_0 inhomogeneity outside the voxel boundary where signals have been insufficiently suppressed by crusher gradients. A practical method for reducing these artefacts is to rotate the voxel such that the last slice gradient is applied in the direction perpendicular to the region of B_0 inhomogeneity. For example, the last slice gradient should be in the axial direction when imaging frontal brain regions (2).

In conclusion, it is often possible to improve MRS data quality by recognizing artefacts and taking appropriate counter measures. This section is designed only to be a quick guide to identify and remedy the most common data quality issues with MRS data. For further information the reader should refer to the following references: (3–5).

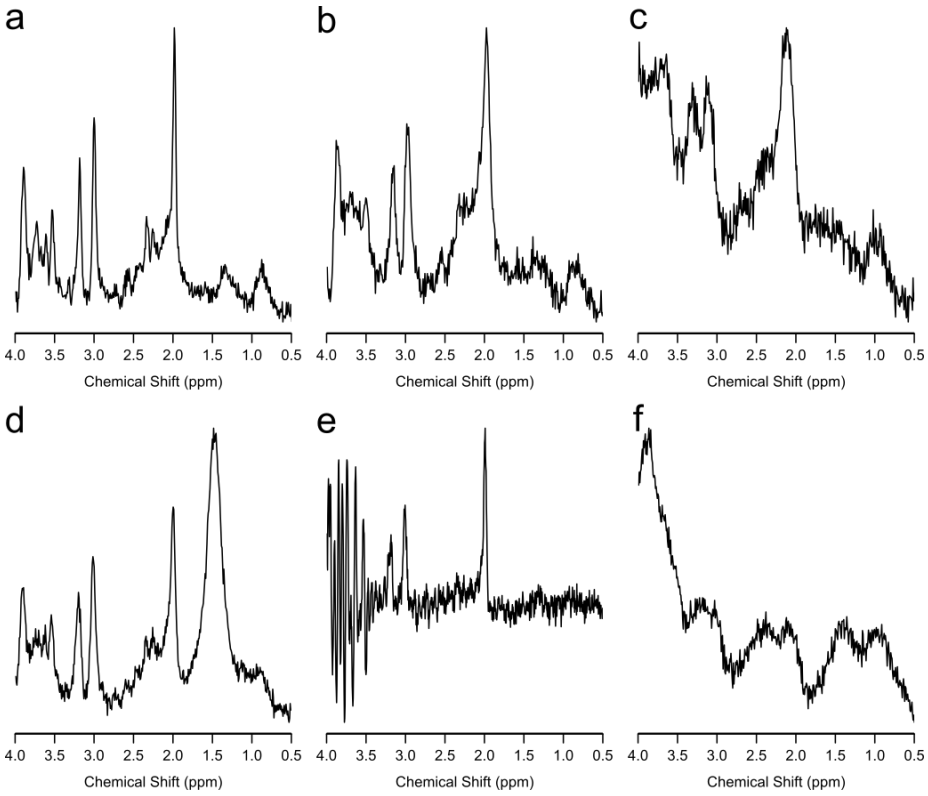


Figure S1. A selection of example spectra demonstrating the following features: a) good shimming; b) acceptable shimming; c) poor shimming and water suppression; d) out of volume lipid contamination; e) “ghost” artefact; and f) very poor shimming and water suppression. Further examples of poor spectra may be found in (3,6).

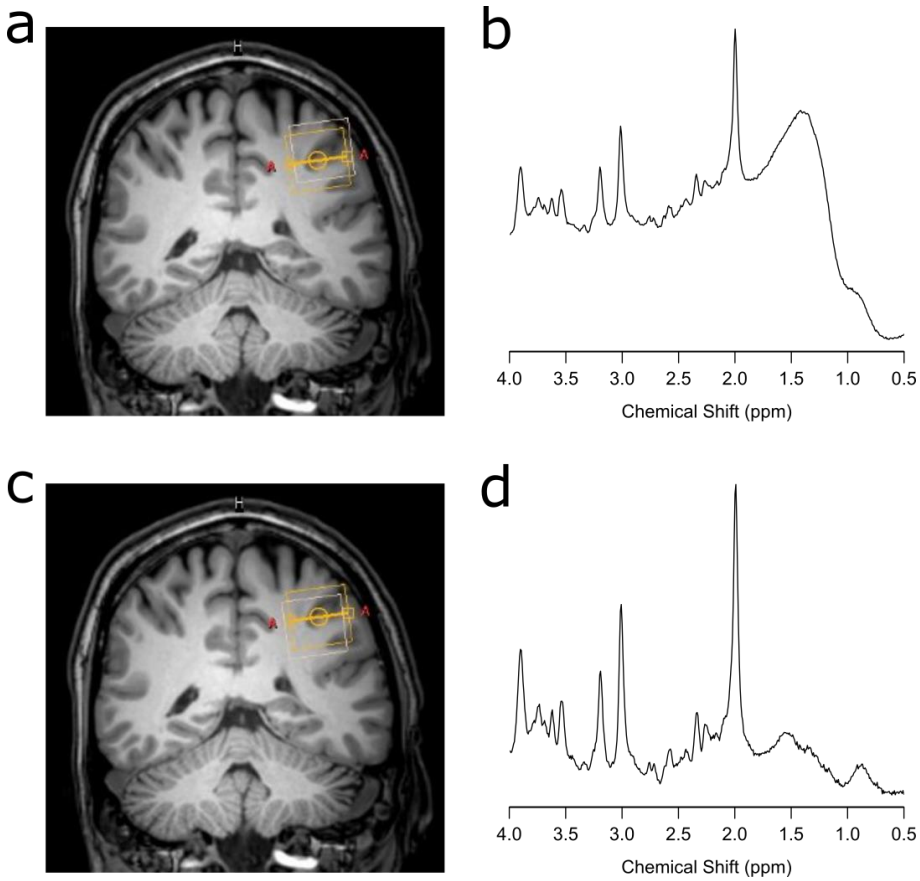


Figure S2. SVS planning with moderate chemical shift displacement. Incorrect (a) and improved (c) voxel planning by reversal of the gradient polarity in the left-right direction; corresponding spectra are shown in (b) and (d). Lipid and metabolite excitation regions are shown in cream and orange respectively.

C Assessment of relaxation time effects on metabolite quantitation and SNR

Maximum accuracy for metabolite quantification using tissue water as a reference requires T1 and T2 relaxation time effects to be minimized for both the metabolites and the tissue water. For routine clinical MRS, technical issues limit the minimum TE achievable, and there is a practical limit to the acquisition time that restricts the maximum TR, as well as the consideration of optimizing the SNR per unit time of the metabolite signal. Here we briefly discuss relaxation effects on metabolite quantification for normal and pathological brain tissue in relation to the consensus acquisition protocols.

The T1 relaxation times associated with the three main metabolite resonances (tCho, tCr and tNAA) observed in long and short TE spectra typically range from 1100 to 1300 ms at 1.5 T in normal adult brain, with only small variation between different white and grey matter regions. On average, these metabolite resonances show a 14% increase at 3 T compared to 1.5 T (see legend of Figure S3 for typical T1 of individual metabolites) (7). The SNR per unit time for these metabolites is plotted as a function of TR and field strength in Figure S3, and

shows maxima in the range 1000 – 2000 ms that is around 40% higher than that at TR 6000 ms. This equates to a factor of two in terms of number of averages to get similar overall SNR at this long TR compared to the shorter, hence it is not surprising that the shorter TR values are currently used in many clinical MRS studies. In pathological tissue such as tumors and oedema these particular metabolites have T1s still within the range found in normal brain (8–10). Metabolites with more extreme T1 values are mI, with a T1 of ≈1000 ms at 1.5 T with indications that it is reduced in some brain regions at 3 T (7), and lactate that has T1 ≈2000ms in gliomas at 3 T. The metabolite T1 relaxation times reported in (7) provide direct regional comparisons at 1.5 T and 3 T, and are also consistent with averages in other published work (data not shown). However, the difficulty of accurately measuring metabolite relaxation times leads to greater variability in these measures compared to tissue water relaxation time estimates. One study at 1.5 T, which stands apart from other evaluations in terms of defining the macromolecular baseline at the same time as the T1's and in terms of separating the singlet resonance from the other parts of the spectrum of the same molecule, has reported exceptionally high T1 relaxation times for the CH3 singlet peaks of NAA (1880ms) and Cr (1630ms) (11). With these values, T1 saturation effects for these singlets would be larger than shown in Figure S3 and some of the SNR of these singlets would be sacrificed for the sake of the rest of the spectrum. There is still a need to establish accurate normative ranges of metabolite T1 and T2 relaxation times in healthy and pathological tissue, and better understand how data acquisition and processing methodology affects their determination. For the purposes of this short review and recommendations we are using typical relaxation times that are currently reported. Our recommendations for TR 1500 ms at 1.5 T and 2000 ms at 3 T are based on where the maximum occurs in SNR per unit time curves averaged across several metabolites (Figure S3) and pragmatically is consistent with previous research to allow further comparative studies. There is little change in terms of metabolite SNR per unit time for 20% variability in actual metaboliteT1.

Compared to metabolites, the T1 relaxation time of tissue water has a stronger field dependence (≈30% increase at 3 T compared to 1.5 T) and a much greater range of values in normal brain ranging from 640 ms for WM at 1.5T to 1600 ms for GM at 3 T (12). In pathological tissue, where there is structural breakdown and increased water content, the T1 could potentially increase to >3000 ms for water in cystic regions and CSF. Hence although at a specific TR differences in metabolite T1 saturation may be small between normal and pathological tissue, there can be large differences in tissue water saturation (e.g. from 0.9 for WM to 0.6 for tumor tissue with T1 2000 ms as shown in Figure S4). Hence we recommend acquiring a water reference scan as a single average with a pre-delay of 9 s, for which there will be less than 5% saturation for T1 3000 ms. If this is not possible due to limitations

inherent in the scanner pre-scan and acquisition processes, then we recommend the same TR is used for the water reference as for the water suppressed metabolite scans, with dummy scans to ensure a steady state T1 saturation is achieved. In this situation it should be noted that without correcting for T1 effects there could be a range of +25% to -25% error in estimating the metabolite concentration depending on the relative T1s of the metabolites and tissue water (Figure S4).

Metabolite T2 relaxation times vary with brain region and pathology, and on average are ≈20% lower at 3T compared to 1.5 T (8,13–15). The T2 for metabolite singlet peaks ranges from ≈150ms for tCr at 3 T to 400 ms for tNAA at 1.5T, with pathological T2s also in this range. Hence at TE 32 ms the range of T2 signal loss is from 19% to 8%, leading to a systematic underestimation if T2 corrections are not made. However, when comparing individual metabolite estimates at different field strengths, in different brain regions or in the presence of pathological changes there is a more limited range of signal changes , on average ≈5% for a 50% increase in T2, and ≈ -10% for a 50% decrease in T2. For long echo acquisitions T2 relaxation effects can considerably alter the metabolic profile of the singlet peaks (15), hence the recommendation to use the minimum TE achievable.

The T2 of normal brain tissue water decreases slightly with field strength and is ≈80ms at 3 T (16), hence TE <10 ms is required to obtain less than 10% signal loss. At a minimum TE 32ms typical for clinical pulse sequences the signal loss is ≈33% for normal tissue, decreasing to 19% for T2 ≈150 ms found in gliomas (16) and < 2% for T2 >2000 ms for fluid. We make no specific recommendation for assessing pathological tissue water T2, but water acquisitions using the same MRS method at different TEs or multi-TE MRI data could contribute to reducing metabolite quantitation errors due to tissue water T2 relaxation time variability.

In conclusion, the largest errors in metabolite quantitation using water as a reference are due to variability in T1 and T2 relaxation times of tissue water with pathology and field strength (as well as due to changes in water proton density) if these are not taken into account. The effects of metabolite T1 and T2 and relaxation will lead to systematic errors in terms of absolute quantitation, but lower errors when comparing between brain regions and pathologies.

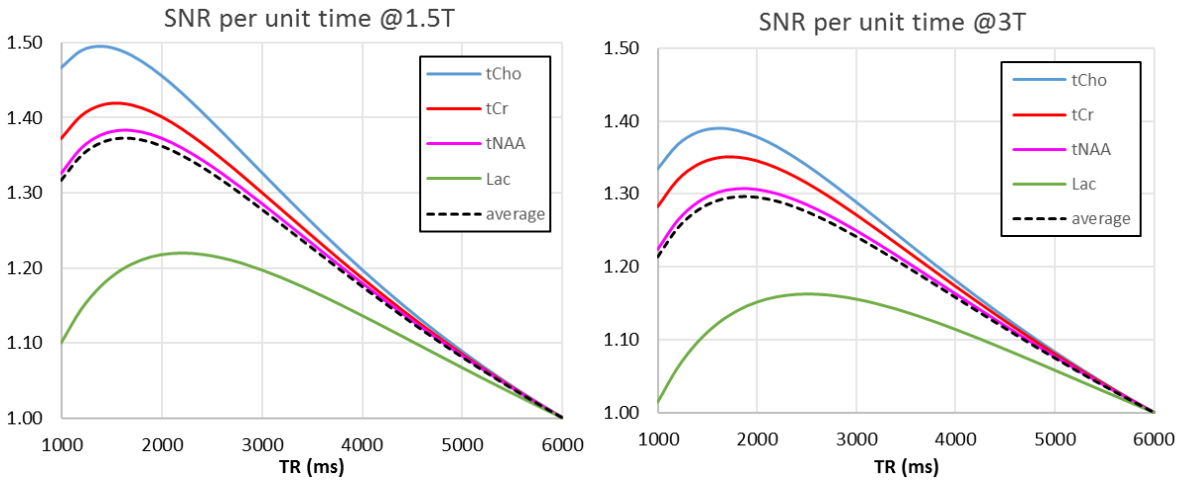


Figure S3. The effect of TR on the signal to noise (SNR) per unit time due to T1 saturation relative to that at TR 6000 ms. On average, across the four metabolite curves shown, the maximum SNR per unit time is close to 1500 ms at 1.5 T and 2000 ms at 3 T. Metabolite T1 values used are average values from different normal brain regions acquired with exactly the same acquisition and processing protocol at both 1.5 T and 3 T: tCho 1103/1290 ms; tCr 1232/1375 ms; tNAA 1303/1482 ms (7). A lactate T1 of 2000 ms at 3 T for high-grade gliomas was used (9) and this value scaled to 1754 ms for 1.5 T using a factor of 1.14, the average ratio of the normal tissue metabolite T1 values at the two field strengths.

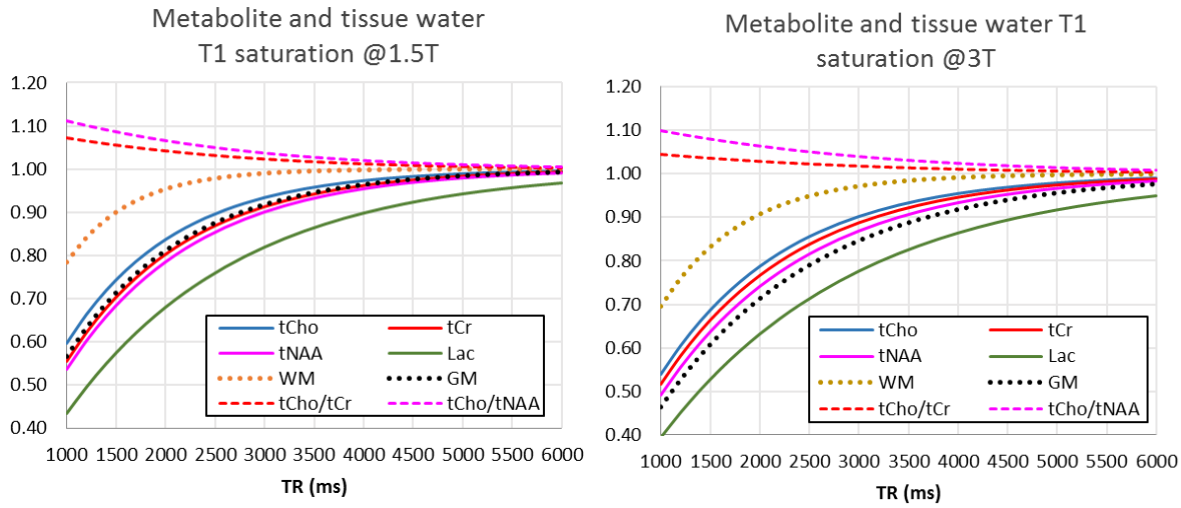


Figure S4. The effect of T1 saturation on tissue water signals and main metabolite signals and clinically relevant metabolite ratios. A TR of 6000 ms is required to maintain the signals shown within 95% of their unsaturated values. At 1.5T the T1s of three key metabolites and GM are similar, and although they are more dispersed at 3 T, have less variability than that for tissue water T1. Apart from lactate, the saturation curves for signal from pathological tissues are not shown, but pathological tissue with increased water content could have a

water saturation curve similar to that of lactate. See text for discussion on metabolite T1s in pathological tissue. Tissue water T1 relaxation times used for 1.5 T / 3 T calculations were: white matter (WM) – 650 / 840 ms; grey (GM) matter – 1200 / 1600 ms (12). Metabolite T1 values were those used in Figure S3.

D Reporting

The following Level 1 parameters are considered the minimum for proper and correct reporting of MRS studies:

Experimental design: definition of the clinical and any control group, inclusion and exclusion criteria, number of subjects, age and gender.

MRI system: field strength, manufacturer (including platform version and software release); gradient type; coil configuration (e.g., 8/32-channel).

Pulse sequence volume selection: type of sequence (e.g., PRESS) and commercial name of sequence if applicable (e.g., PROBE); TE (including TE1 and TE2 for non-standard PRESS); TR; TM if using STEAM; number of averages for metabolite signal data and for any unsuppressed water signal; number of complex points in the FID; filter bandwidth (Hz or kHz); water suppression method used (e.g., CHESS, VAPOR); localization volume dimensions; outer volume suppression if applied (e.g., whether standard and contiguous to the localization volume or VSS with OVERPRESS); the offset frequency for the metabolite spectrum (e.g., it is typically set to the NAA resonance at 2 ppm).

Pulse sequence MRSI: 2D (and number of slices and slice-gap if appropriate) or 3D; number of phase encodes and field of view in each direction; whether full or elliptical k-space; k-space filter (e.g., Hanning); SENSE or GRAPPA factor.

Localization criteria: details of anatomical localization or whether encompassing a lesion or within area of specific MRI characteristics; an example shown as a figure (ideally in three planes if anatomically located) and including any saturation bands.

Pre-processing for display: line broadening type and bandwidth (e.g,. Lorentzian 3 Hz); residual water removal method, if any; baseline correction method; include an exemplary figure over the range 0 – 4 ppm.

Quantitation (simple, suitable for long TE data): details above with analysis software package details and type of peak fit (Lorentzian, Gaussian, mixed), number and position of peaks and any constraints (e.g., maximum fitted linewidths, peak shift ranges).

Quantitation (complex): software package name and release number; metabolites and lipid signals used in the fit (and whether from simulated or acquired from metabolite solutions); method of baseline correction and removal of residual water signal; reference signal and assumptions used in the calculation of any molal or molar concentrations (e.g., tissue water molarity, T_1 or T_2 corrections applied)

Quality control: scanner reported linewidth of the water signal from the localization voxel; number of spectra rejected (and reasons such as artefacts, poor SNR) from the analysis; assessment of overall data quality as: SNR, water or metabolite linewidth, or CRLB as output from the analysis software. An example spectrum from each subject group should be shown that shows the fit and residual from the analysis package used.

Adherence to these minimum requirements and recommended guidelines would ensure that all MR spectroscopy papers provide the necessary information to reproduce studies as well as provide a basis for comparison for the evaluation of the studies across clinical domains. These details should be published either in the main text of the article, or as an online supplement.

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