Longitudinal MR Spectroscopy

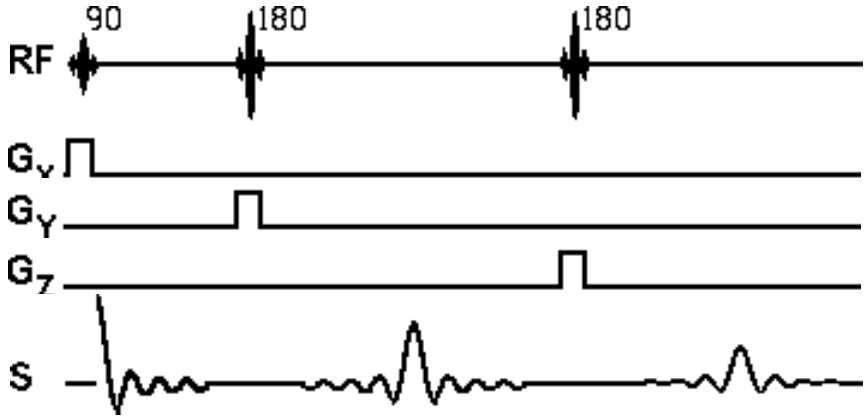
Dan Blezek
Ileana Hancu

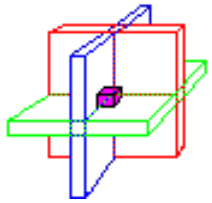
Contact: blezek@research.ge.com

imagination at work

Brief introduction to MRS

- Collecting signals from chemical compounds in the body.
- Each compound has one or more resonance frequencies
- Essentially the same as NMR.
- MRS: water suppression RF pulses, followed by 3 localization pulses, followed by detection
- Only signal coming from the intersection of the 3 planes contribute to the signal





"Magnetic resonance spectroscopy in medicine: clinical impact", Ian Smith, Laura Stewart, Progress in NMR Spectroscopy, 40 (2002), 1-34

Metabolites

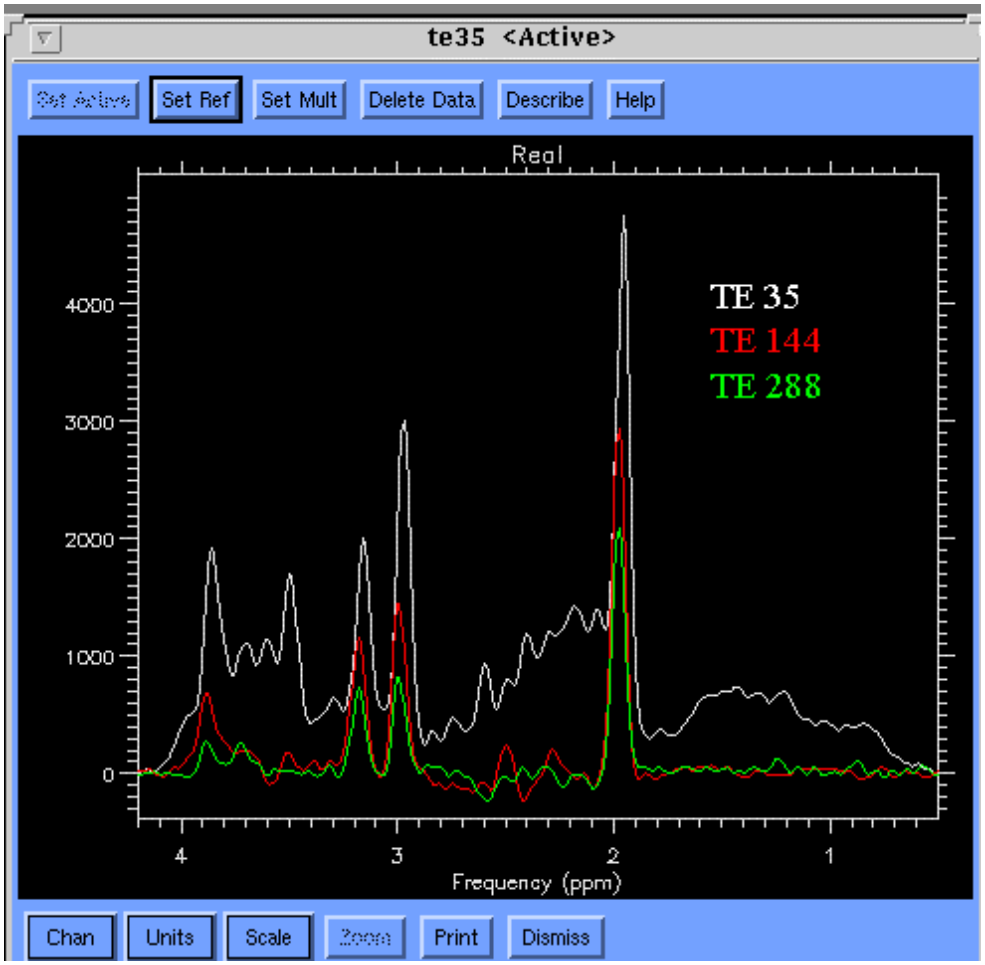
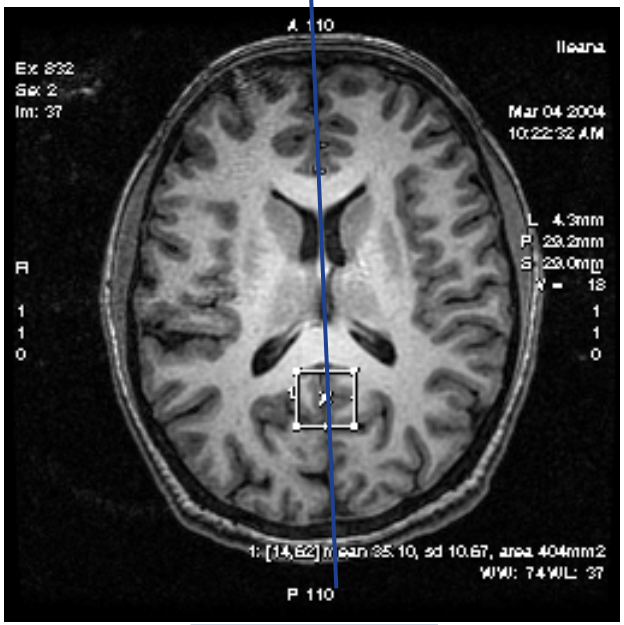


Table 2. Ranges of MR-observable metabolite concentrations reported for normal adult human brain and biopsy tissues obtained using a variety of analytical techniques including *in vivo* MRS. Values have been rounded to one decimal place

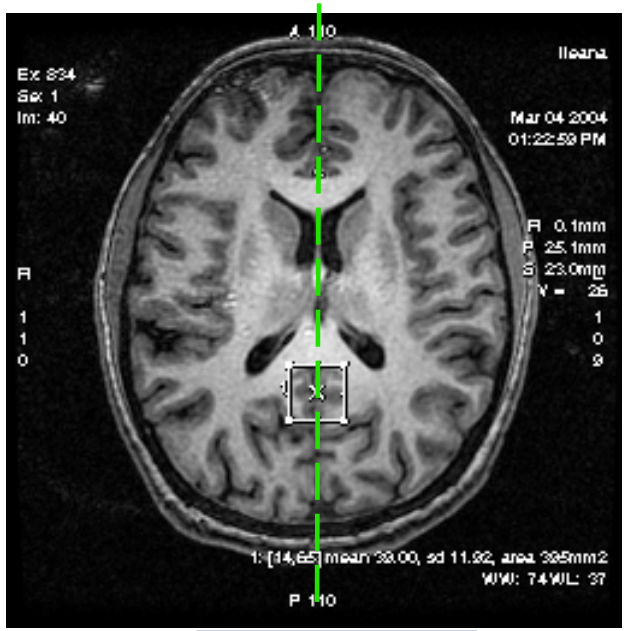
Metabolite	Concentration range (mmol/kg$_{ww}$)	References
Acetate	0.4–0.8	31
NAA	7.9 16.6 (average 10.3)	50,72
NAAG	0.6–2.7	59
ATP	3.0	63
Alanine	0.2–1.4	72,161,162
GABA	1.3–1.9	72,161
Aspartate	1.0–1.4	72,162
Choline (total)	0.9 2.5	50,161
Creatine	5.1–10.6	50,72,161
Ethanolamine	3.3[a]	16
Glucose	1.0	90
Glutamate	6.0–12.5	72,76,161,162
Glutamine	3.0–5.8	14,72,162
Glutathione	2.0	162
Glycerol	<0.1	
Glycerophosphorylcholine	1.0	74
Glycine	0.4–1.0	161,162
Histamine	<0.1[a]	118
Histidine	0.09	162
Homocarnosine	0.23	162
Myo-inositol	3.8 8.1	50,72,161
Scyllo-inositol	0.3–0.6	137
Lactate	0.4	161
Phenylalanine	<0.1	162
Phosphocreatine	3.2–5.5	63,77
Phosphorylcholine	0.6	74
Phosphorylethanolamine	1.1–1.5	74,77,162
Pyruvate	0.2	31
Serine	0.4	162
Succinate	0.4	31
Taurine	0.9–1.5	72,161,162
Threonine	0.3	162
Tryptophan	<0.1	163
Tyrosine	<0.1	162
Valine	0.1	162

imagination at work

The Problem

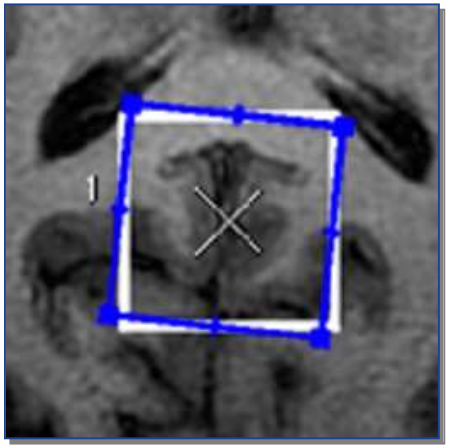


Baseline



Follow/Up

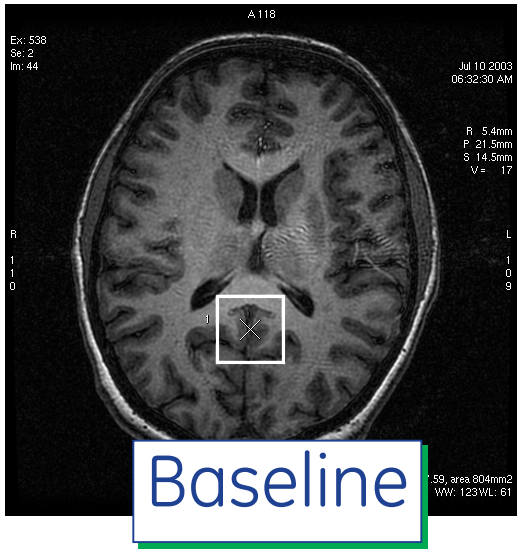
Manual Placement
Center Delta: 3.7 mm
Rotation: ~2^0
Overlap: ~75%



MR Spectroscopy Registration

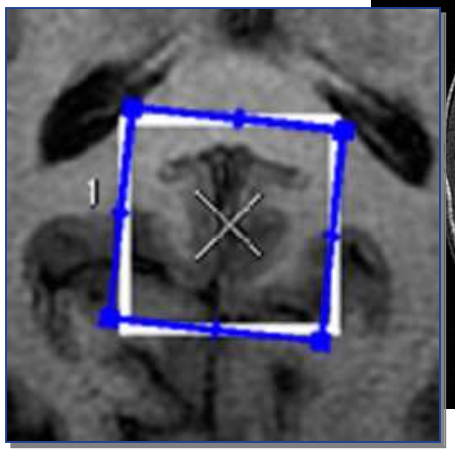
Manual voxel replacement

- 8*cc* voxel (20x20x20*mm*)
- Visually correct placement
- Mis-aligned by 4mm
- Occurs out of plane
- Rotated voxel reduces overlap



Voxel repositioning error:

#	Avg/Std(mm)	%	N
1	2.9 / 1.3	79.5	15
2	1.4 / 0.8	89.4	12
3	3.9 / 2.3	72.2	12
4	3.3 / 3.4	76.4	15



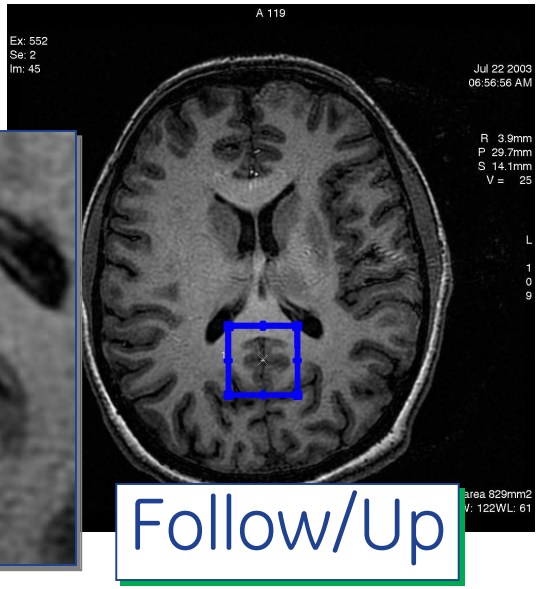


Image Registration

Mutual Information

Joint Entropy of two random variables, A & B:

$$H(A,B) = \int p_{AB}(a,b) \log p_{AB}(a,b)\, da\, db$$

If A & B are independent:

$$p_{AB}(a,b) = p_A(a)\, p_B(b)$$

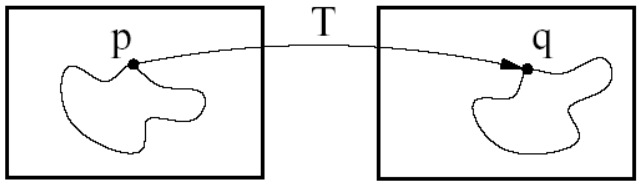
$$H(A,B) = H(A) + H(B)$$

If there is any dependency:

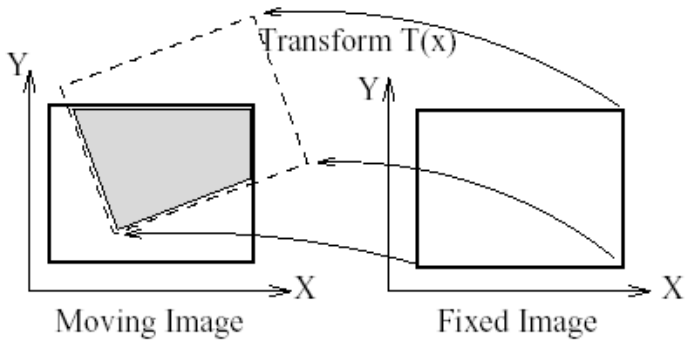
$$H(A,B) < H(A) + H(B)$$

Maximize the "Mutual Information" equation:

$$I(A,B) = H(A) + H(B) - H(A,B)$$

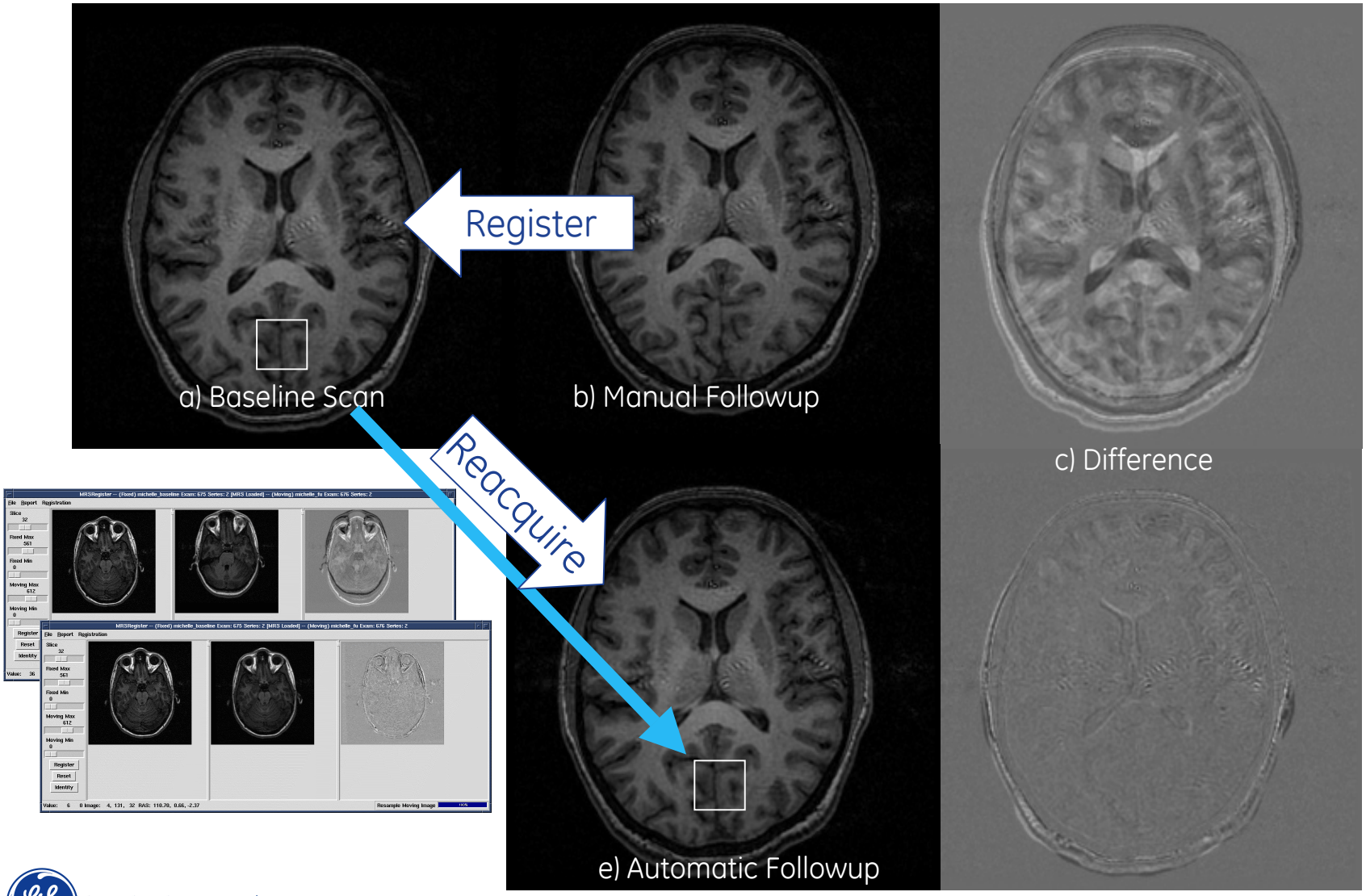


Finding a transform from one space to another.

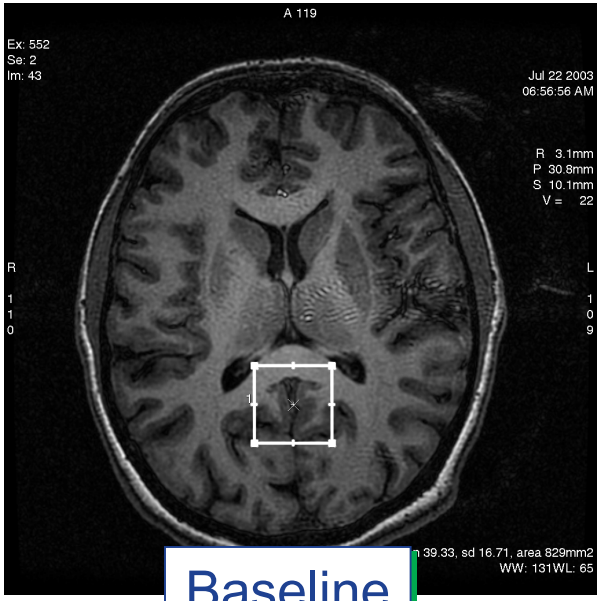


P. Viola and W. M. Wells III. *Mutual information: An approach for the registration of object models and images*. Inter. J. Comp. Vis., 1997.

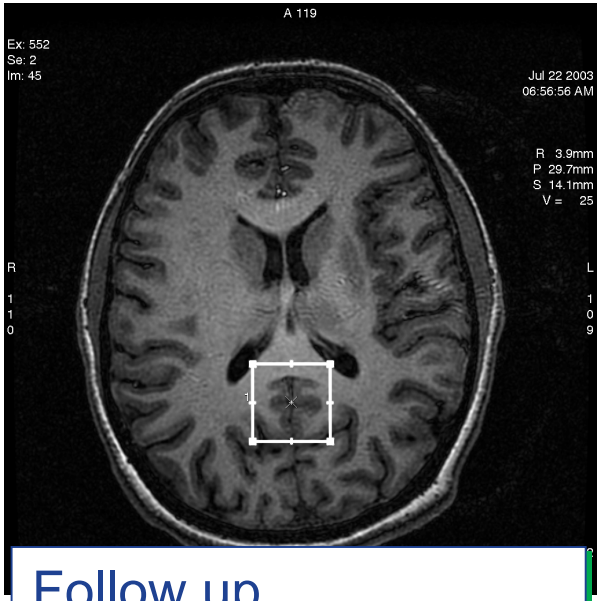
Application to MR Spectroscopy: 1.5T



Retrospective Evaluation

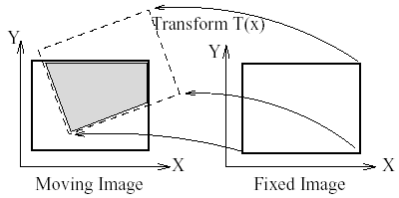


Baseline



Follow up
Actual placement
Slice: 45
Center: R4, P29, S14

Follow up
Predicted location
Slice: 44
Center: R3, P31, S10



Overlap Calculation

Results

Volunteer	1	2	3	4	Average	Avg. Displacement
Manual Overlap (%)	84	86	87	89	86%	1.85*mm*
Automatic Overlap (%)	94	94	94	94	94%	0.79*mm*

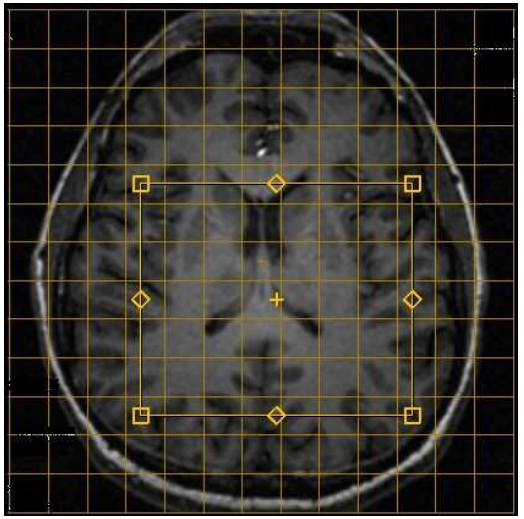
	Cr	Glu	Glu/Cr	mI	mI/Cr
Manual	3.84	7.40	6.96	6.18	5.7
Automatic	<u>2.76</u>	<u>6.23</u>	6.89	6.01	5.15

	Cho	Cho/Cr	NAA	NAA/Cr
Manual	4.53	5.33	4.32	3.65
Automatic	4.82	<u>4.73</u>	4.22	4.12

Table: Intra-session average coefficient of variation for manual and automatic MRS voxel placement. Underlined values indicate > 10% improvement for automatic placement.

Registration for CSI

- Continuation of MGH collaboration
- Automatic CSI grid placement
- Joint ISMRM abstract
  - Drs. Gonzalez and Ratai
  - Martinos Ctr. For Biomedical Imaging, MGH



	CSI grid	Center voxel
Visual repos. overlap	83	67
Automatic repos. overlap	95	89

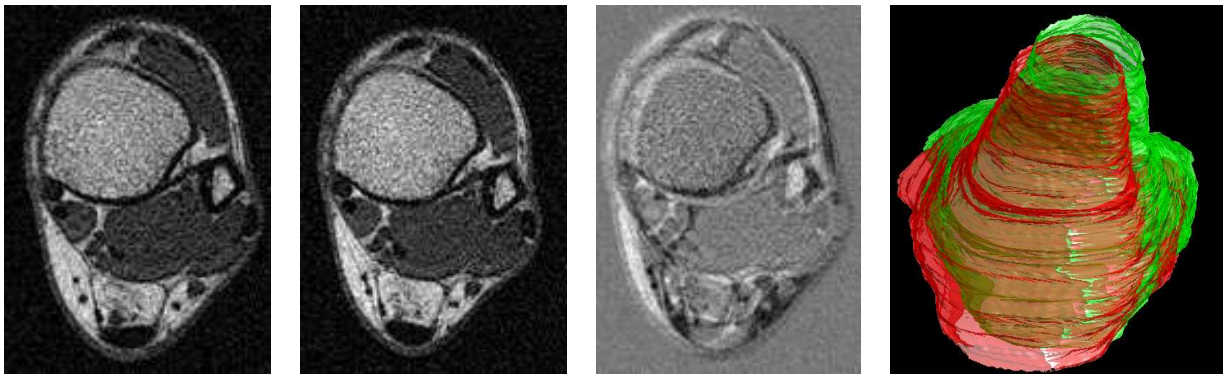
Table 2: % overlap between baseline and f/u CSI grids and individual, interior center voxel.

	Cr	Cho	Cho/Cr	NAA	NAA/Cr
% SD visual repos.	19.0	19.3	19.6	13.7	16.8
% SD automatic repos.	13.5	14.7	11.8	13.4	12.5

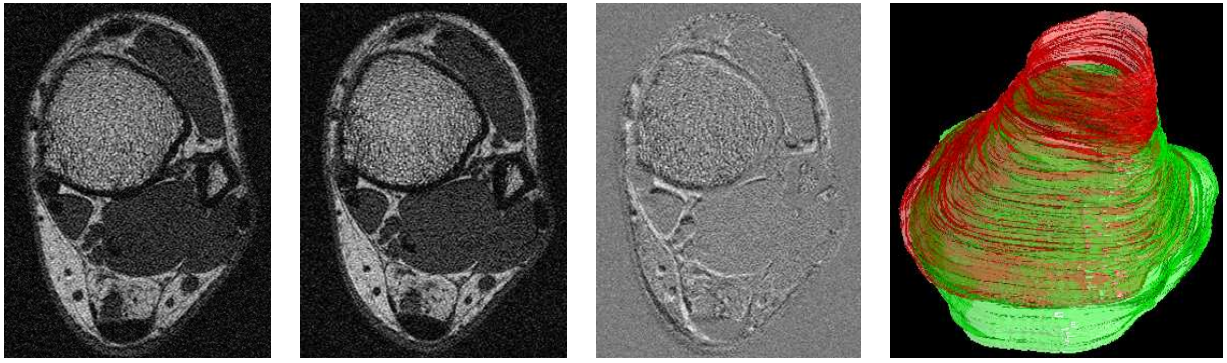
Table 1: Average % SD for all the voxels and volunteers included in the study.

Musculoskeletal Registration

- UCSF collaboration
- Musculoskeletal registration



Manual Prescription



Auto-prescription

Images courtesy of Janet H. Blumenfeld, Julio Carballido-Gamio, Radhika Srinivasan, Sharmila Majumdar Department of Radiology, University of California, San Francisco, San Francisco, California, USA

Status & Next Steps

Published

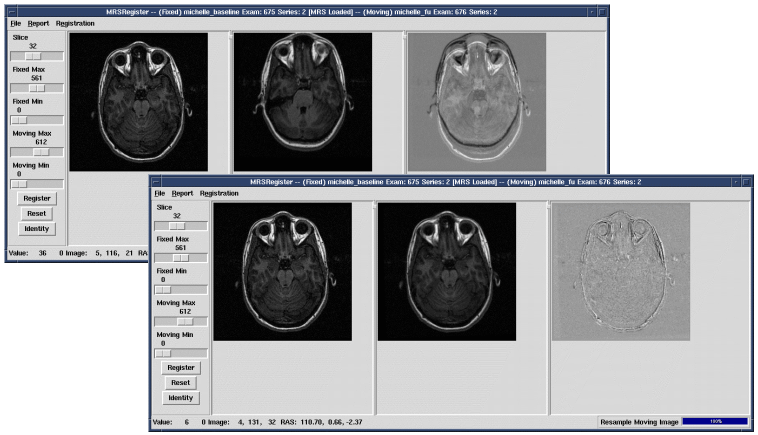
- NMR in Biomedicine

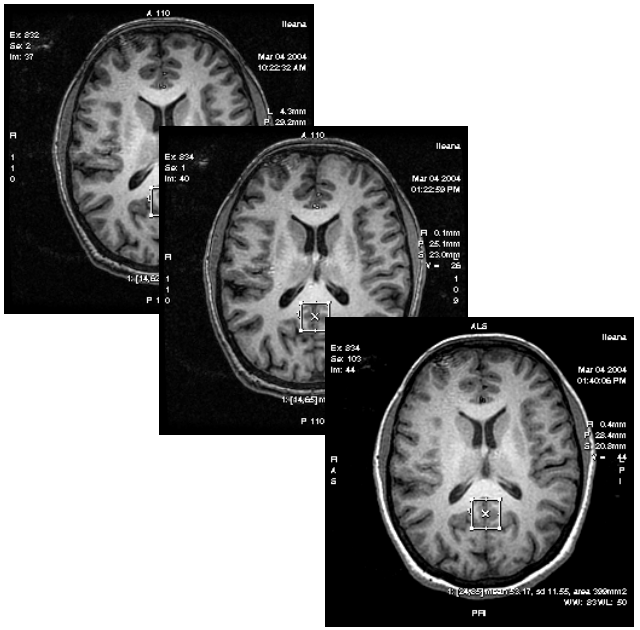
Software

- Host registration software
- Custom PSD to acquire triple oblique
- Improved workflow in 12M4

Collaborations

- Installed at: MGH, UCSF, Mayo, AMC
- In use for Pfizer trial at AMC





Longitudinal MR Spectroscopy

Dan Blezek
Ileana Hancu

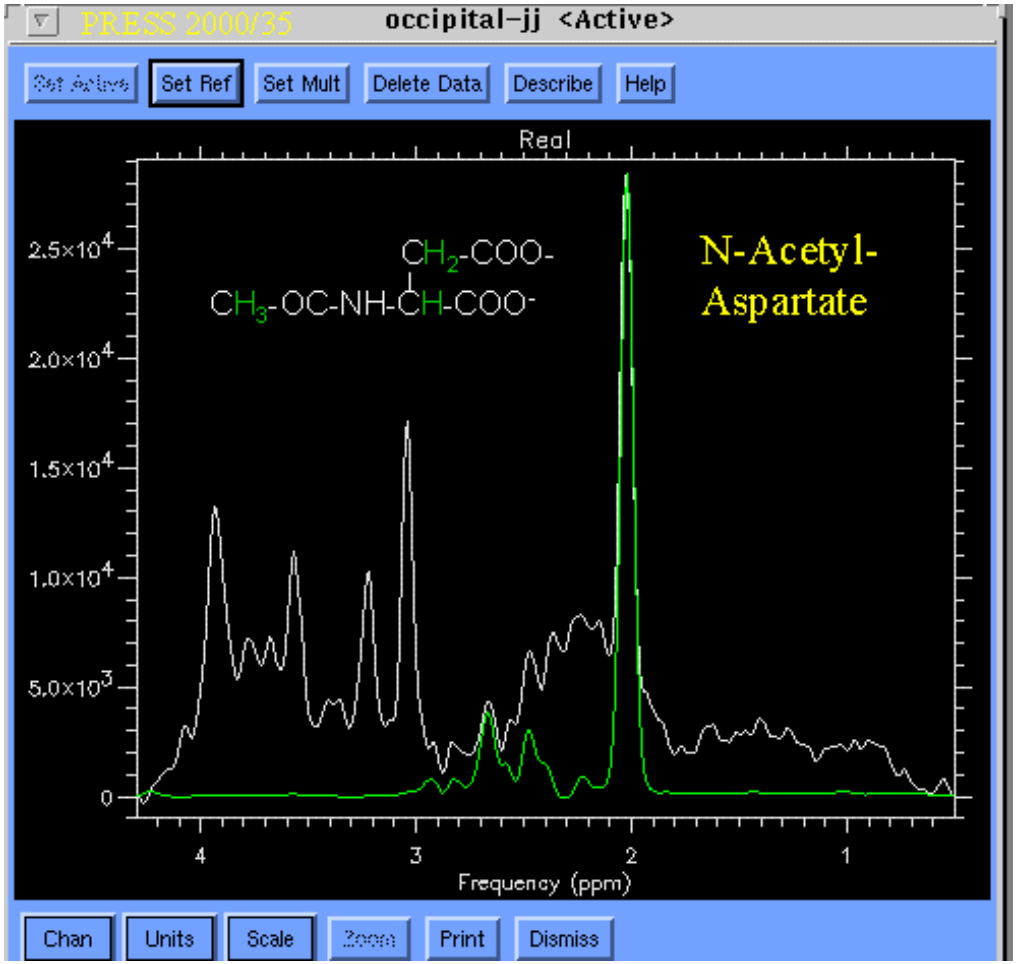
Contact: blezek@research.ge.com

imagination at work

Appendix

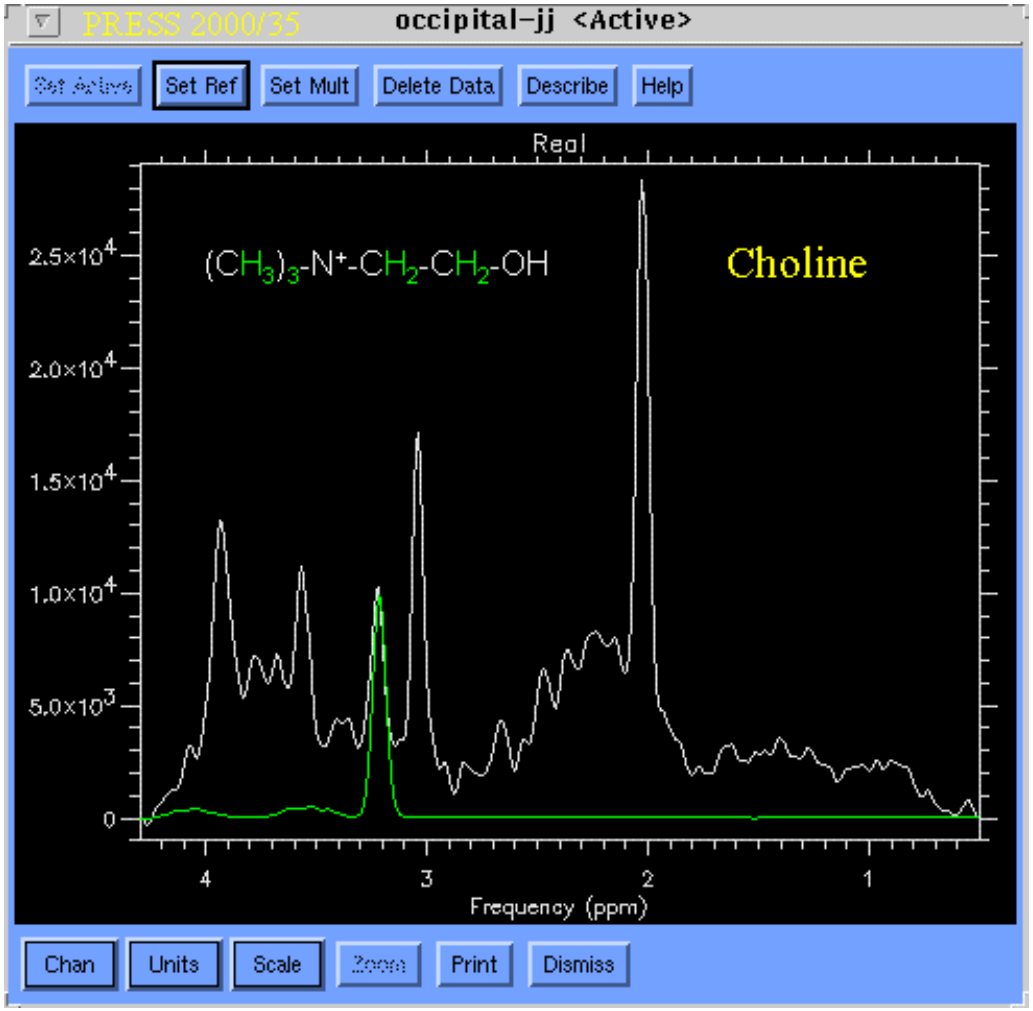
imagination at work

What each metabolite means: NAA



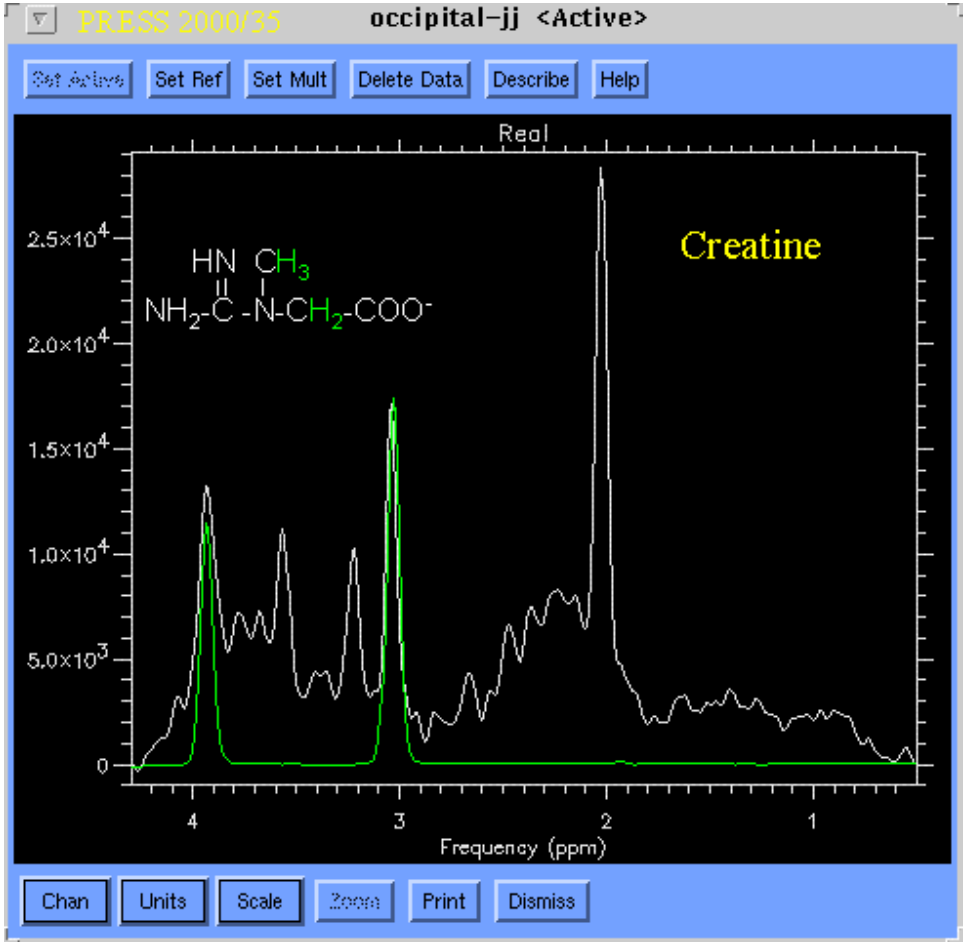
- ~10mM in a normal human brain
- NAA is predominantly intra-neuronal: marker of neuronal density
- also correlated to the rate of mitochondrial phosphorylation
- generally, regarded as a marker of neurometabolic fitness

What each metabolite means: Choline



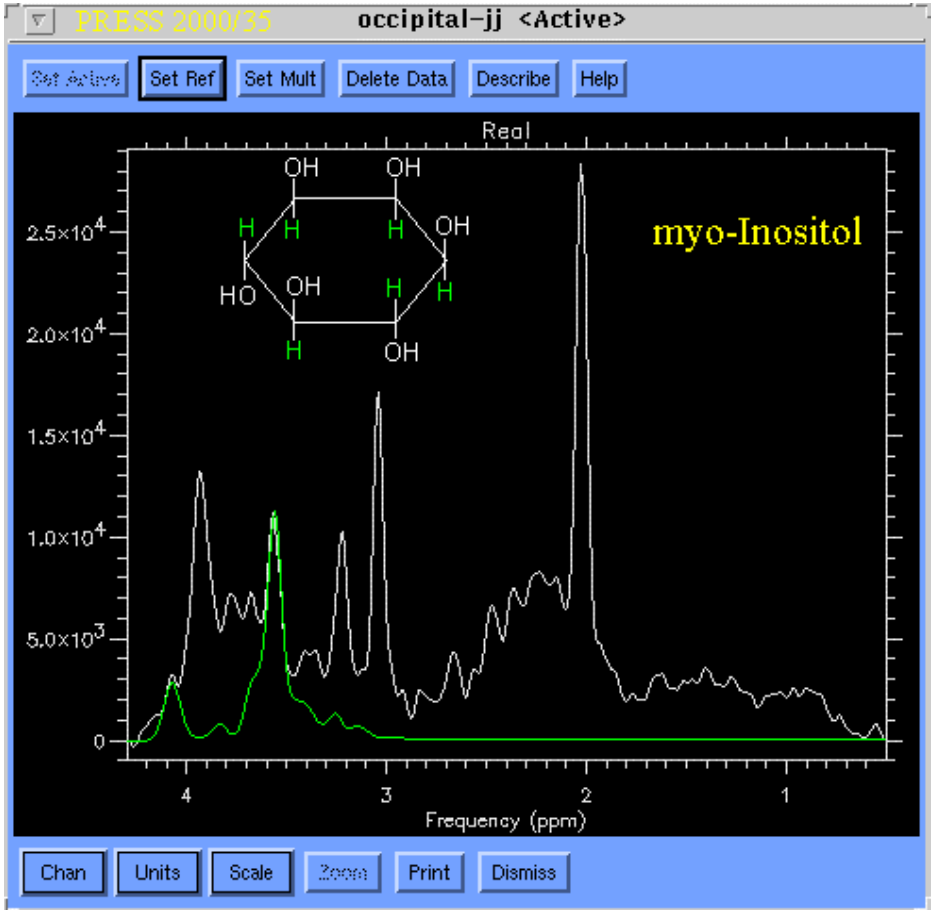
- ~2mM in a normal human brain
- Cho peak is a sum of free choline, acetylcholine, glycerophorycholine, phosphocholine
- rate limiting precursor to cell membrane phosphatidylcholine

What each metabolite means: Creatine



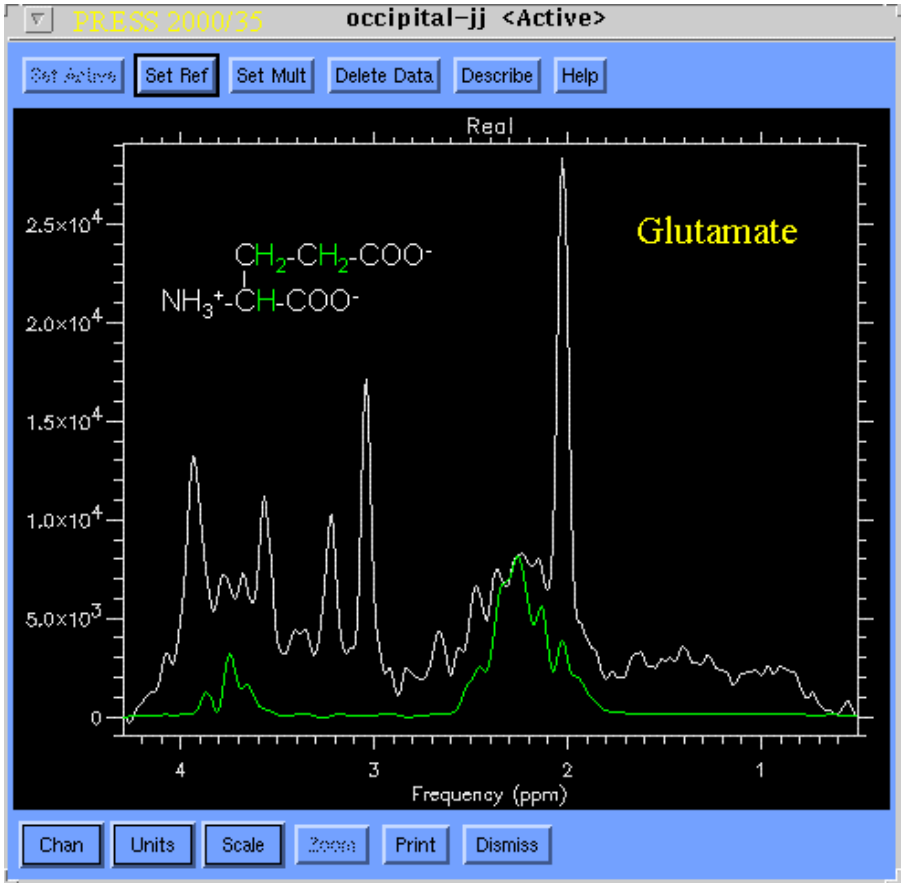
- ~7.5mM in a normal human brain
- Cr peak is a sum of Cr and PCr
- reserve for high energy phosphates, buffers cellular ATP/ADP ratios
- Cr signal generally reflects the health os systemic energy use and storage

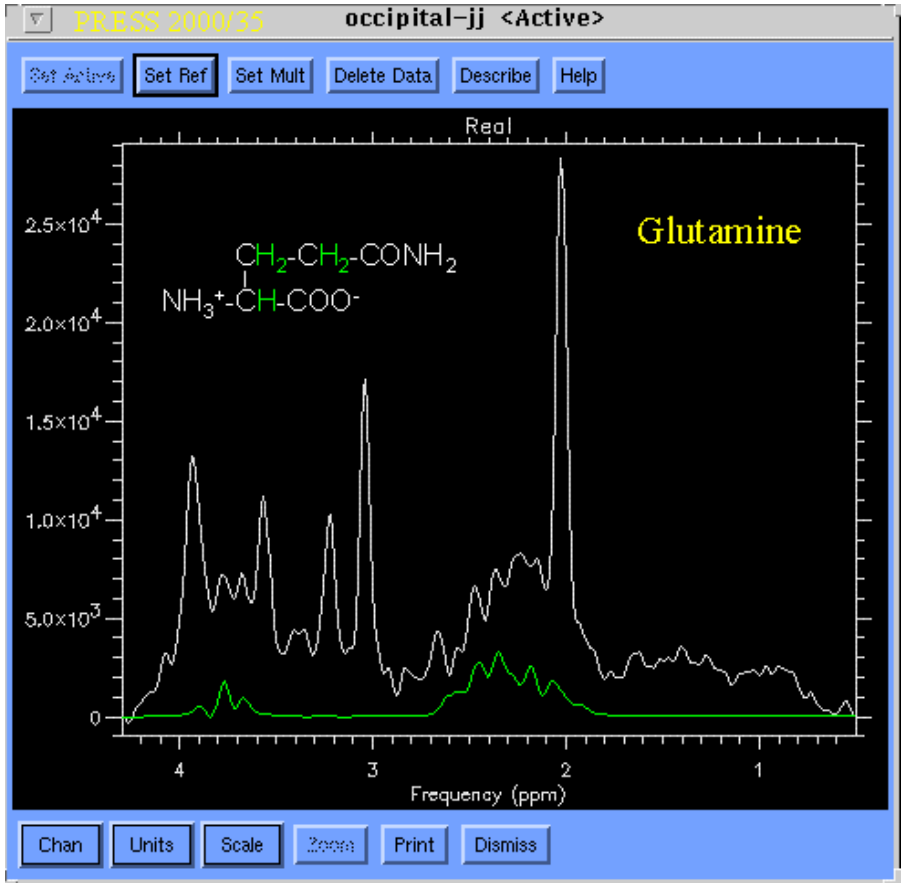
What each metabolite means: myo-Inositol



- ~7.5mM in a normal human brain
- mysterious sugar alcohol-structure similar to glucose
- MI acts as a marker of glial cell numbers, osmoregulator, intracellular messenger, detoxification agent in the brain and liver

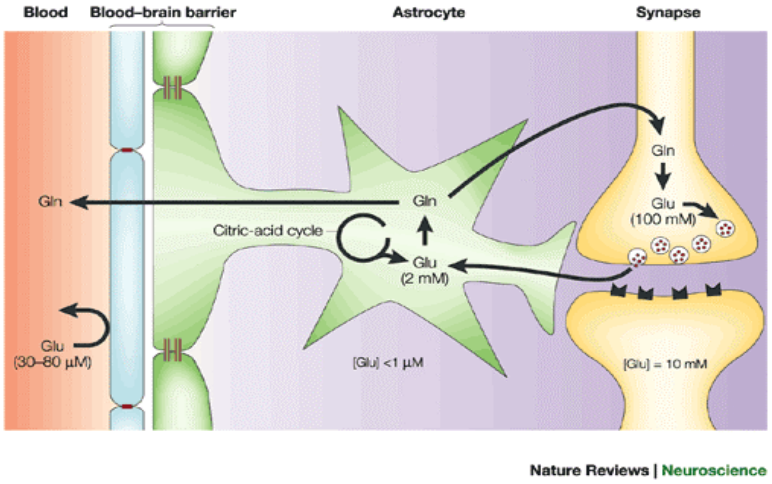
What each metabolite means: Glu and Gln





What each metabolite means: Glu & Gln

- Glu/Gln ~12.5/5mM in a normal human brain
- hard to distinguish in a spectrum- linked together through the TCA cycle



- Glu: principal excitatory neurotransmitter in the brain
- neurotransmission=>temporary increases in Glu_o, taken in by glial cells and converted to Gln, transferred back to neurons
- increase in Glu_o=>cell death (increase in Ca_i, free radical an NO production)

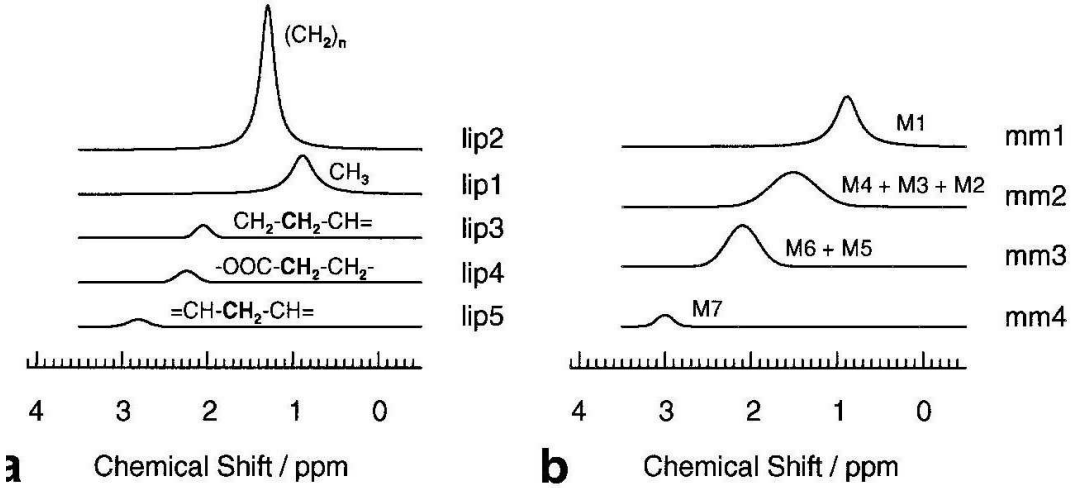
Brain ^{1}H MRS: uses

- STROKE
  - increased Lac/Cr, decreased NAA/Cr. Recovery from stroke accompanied by normalization of metabolite levels.
  - identify patients who respond to drug treatment

- BRAIN TUMORS
  - avoid morbidity associated with biopsies
  - attempt diagnosis (tumor management resection/chemo/rad therapy based on the particular type of tumor)
    - benign vs. malignant
    - different cancer types
    - invasiveness- rapidly proliferating or slowly growing

Brain ^{1}H MRS: uses: brain tumors

- lipid, macromolecule and lactate levels play an important role in assessing grade of tumor
- increased lipids, mm and lac are correlated to tumor grade (a measure of the invasiveness of the tumor), consistent with progression from hypoxia to necrosis



- ↓mI, ↓Cr meningiomas
- ↑mI grade 2 astrocytomas
- ↑Cho increases with grade for astrocytomas, but highly variable for GBM

Brain ^{1}H MRS: uses: brain tumors

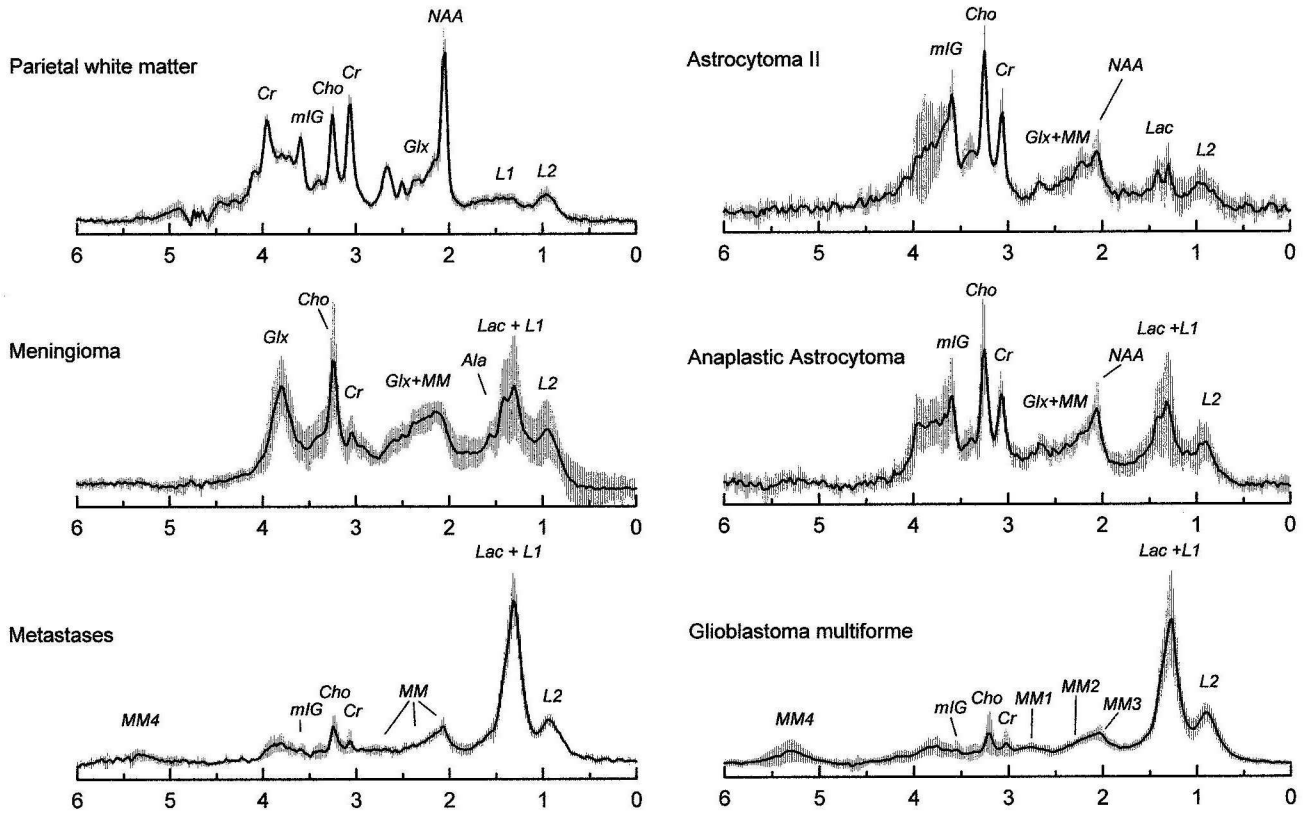


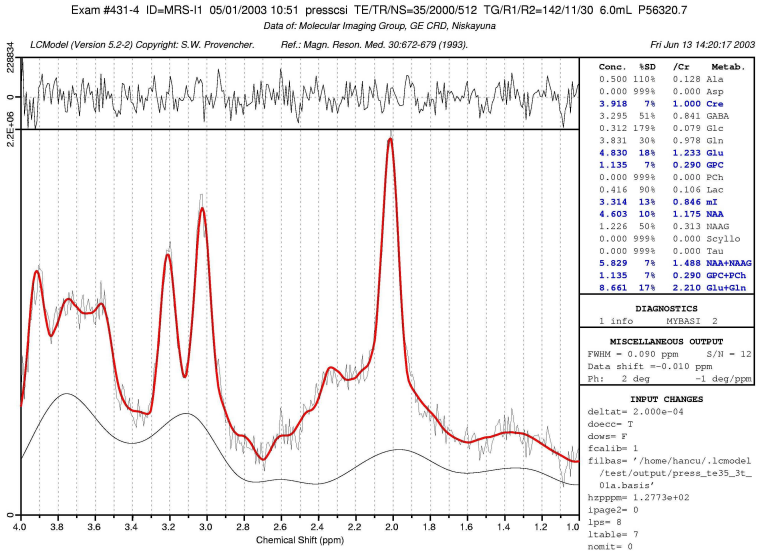
FIG. 1. Mean and SD (vertical lines) of normalized STEAM (TE = 30 ms) spectra: NWM (N = 6); meningioma (N = 8); metastases (N = 6); astrocytoma grade II (N = 5); anaplastic astrocytoma (N = 7); glioblastoma (N = 13).

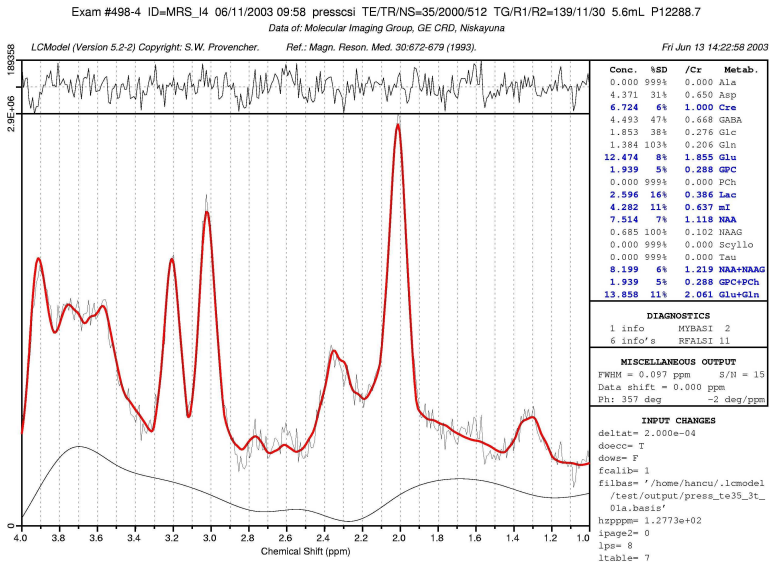
- obvious differences between certain types of tumors, less obvious between other types. MRS will not replace biopsy in all cases, but maybe in some
- clinical validation for using MRS as a decision maker for certain type of tumors in progress

MRM, 49 (2), 223-232, 2003

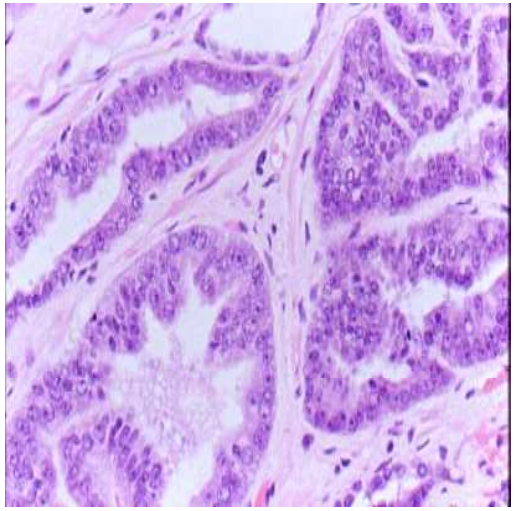
Brain ^{1}H MRS: uses

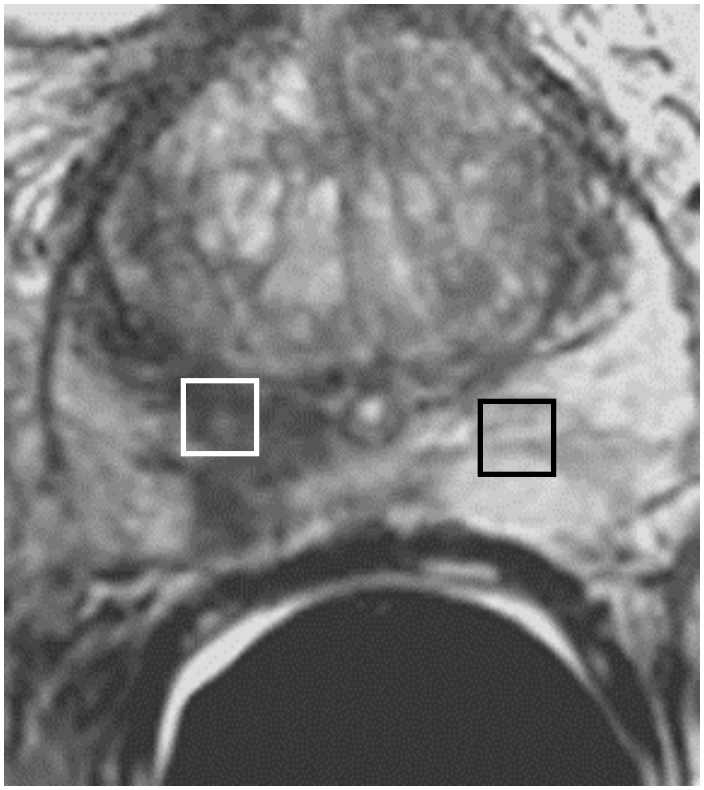
- EPILEPSY
  - maps of focal seizure regions prior to surgery
  - ↓ of GABA (major inhibitory neurotransmitter in the brain), ↓ NAA
- DEMENTIA
  - AD, reduced NAA, increased myoinositol, decreased Glu

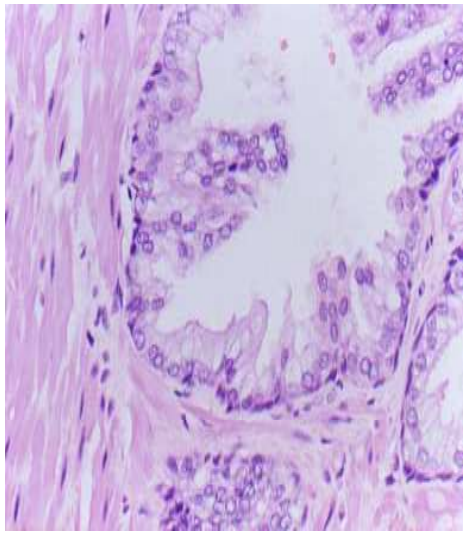


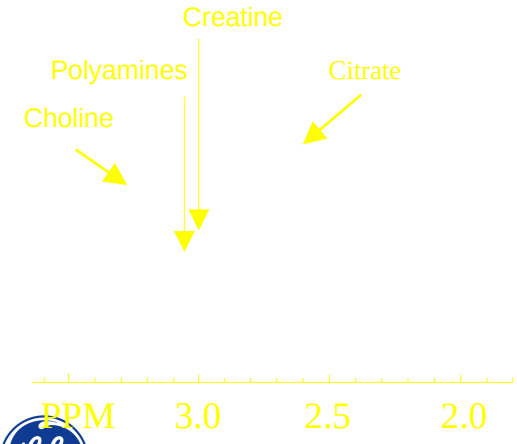


Prostate imaging and 1H MRS









low citrate, high choline

high citrate, low choline

Breast imaging and ^{1}H MRS

- High levels of Cho containing compounds for malignant breast tissue (high Cho/Cr ratios)
- alternative approach: wash-in-wash-out of paramagnetic contrast agent (GdDTPA)

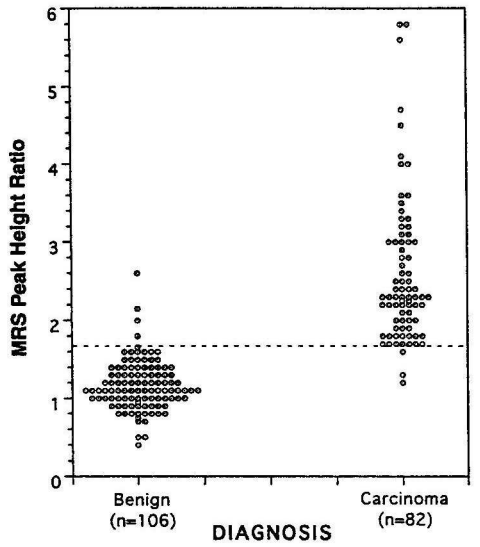


Fig. 11. ^{1}H MR at 360 MHz of findings of breast fine-needle biopsies from unequivocally benign versus infiltrating carcinoma. Data are grouped on the basis of the final histopathologic findings in tissue specimens. From: Ref. [102].