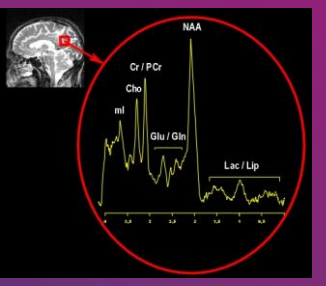
Spectroscopy and braintumours

jatta.berberat@ksa.ch

Introduction

- Background
- Metabolites
- Shimming
- Sequences
- Summary



Spectroscopy

- Nuclear magnetic resonance spectroscopy (MRS) is an analytical tool, based on nuclei that have a spin
  - nuclei with an odd number of neutrons and/or protons like 1H, 13C, 17O, 19F, 31P etc..
- The electron cloud around an atom that shields the nucleus from the magnetic field to a greater or lesser degree
  - This naturally results in slightly resonant frequencies, which in turn return a slightly different signal.
- spectroscopy requires radio frequency (RF coils) tuned to the Larmor frequency of chosen nuclei

Larmor equation

- In magnetic resonance, nuclei resonate at a frequency f given by the Larmor equation

$$f = \gamma B_0$$

B_0 is the strength of the external magnetic field

γ is the nucleus' gyromagnetic ratio

For protons γ = 42.58 MHz/Tesla.

- If all the proton nuclei in a mixture of molecules had the same Larmor frequency, magnetic resonance spectra would be limited to a single peak.

Larmor equation

- The magnetic field B_0 experienced by the nucleus is shielded by the covalent electron structure surrounding the nucleus.
- nuclei with different chemical neighbors will have slightly different resonance frequencies (f) given by

$$f = \gamma B_0(1-\sigma_{cs})$$

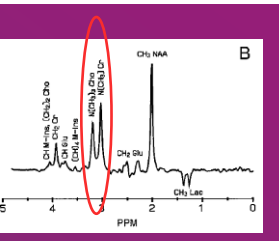
σ_{cs} is a screening constant ($\sigma_{cs} << 1$).

- This small change in the resonance frequency is the basis for magnetic resonance spectroscopy.
- Both, the overall molecular structure and the proton(s) position within the molecule, will determine s_{cs} or f.

Magnetic resonance signal

- In spectroscopy, the strength of the MR signal is proportional to the number of protons at that frequency.
- MRS data are displayed in the frequency domain.
- In the frequency domain, the area under a specific peak is proportional to the number of protons precessing at that frequency.
- The frequency axis itself is reversed from ‘‘normal’’ for historical precedent:
  - Before the introduction of the FFT in 1965, almost all spectrometers employed continuous-wave irradiation
  - The abscissa for spectra went from low field to high field
  - the protons precessing at the highest frequencies would be recorded first (left -> right)
- spectra is still displayed historically with the abscissa displaying decreasing frequency from left to right

J coupling



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- Another feature of spectra is peak splitting or multiplets
- Multiplets are caused by *J* coupling (spin–spin)
- With *J* coupling, the nuclear magnetic energy levels are split by quantum interactions, via
  - covalent bond electrons,
  - with other nuclei whose magnetic moments may be parallel or antiparallel to the main magnetic field.
- J coupling can be homonuclear (1H–1H) or heteronuclear (1H–13C)

J coupling

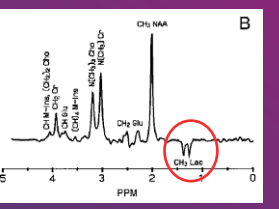
- Example: nucleus *A* is coupled to nucleus *X*

A = X

Nucleus *A* will be split into two equal peaks.

X has an equal probability of being in a parallel or an antiparallel spin state.

- The peak of nucleus *A* that is coupled to nucleus *X* parallel to the main field will have higher frequency; the peak of nucleus *A* that is coupled to nucleus *X* antiparallel to the main field will have lower frequency.
- For lactate, the CH3 nucleus at 1.31 ppm is coupled to the CH nucleus at 4.10 ppm, and the CH3 nucleus is split into two equal peaks doublet separated by 6.93 Hz.



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J coupling

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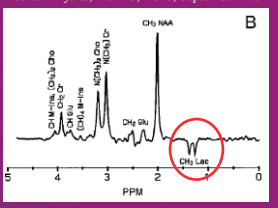


- **Peak splitting** from *J* coupling has the same absolute value in Hz, regardless of the main magnetic field strength.
- *J* coupling also causes phase evolutions that cause peak and baseline distortions that vary with echo time (TE) and field strength
- *J* coupling explains the well known observation that the lactate doublet has negative peaks ~180° out of phase at TE=135-140 ms for a PRESS sequence
- *J* coupling also causes **overlapping** multiplet peaks within individual metabolites and between metabolites to cancel each other due to dephasing at later echo times under typical *in vivo* field homogeneities.
- For this reason, metabolites such as glutamine (Gln), glutamate (Glu) and g-aminobutyric acid (GABA) cannot be measured using long echo times (TE>50 ms) with *in vivo* proton spectroscopy.

Metabolites

- Metabolites containing protons that can be measured in the brain at 1.5/3 T include
- **N-acetyl aspartate (NAA)**
  - Considered to be present only in neurons and dendrites =neuronal marker
- **N-acetylaspartylglutamate (NAAG)**
  - suggested to be involved in excitatory neurotransmission
- **Creatine phosphocreatine (Cr)**
  - a reservoir for high energy phosphate for generation of adenosine triphosphate (ATP)
- **Choline phosphocholine/glycerophosphorylcholine (Cho)**
  - Associated with glial cell membrane integrity (GABA)
- **glutamate (Glu) and glutamine (Gln)**
  - important in neurotransmission, but very difficult to quantify *in vivo* due to multiplets and *J* coupling effects
- **myo-inositol (M-Ins)**
  - important in cell growth and possibly a glial cell marker
- **Lactate (Lac)**
  - indicative of anaerobic metabolism. NAA is considered a neuronal marker, changes in NAA from
- brain proton MR spectra may also contain peaks due to water, lipids, and macromolecules

Metabolites

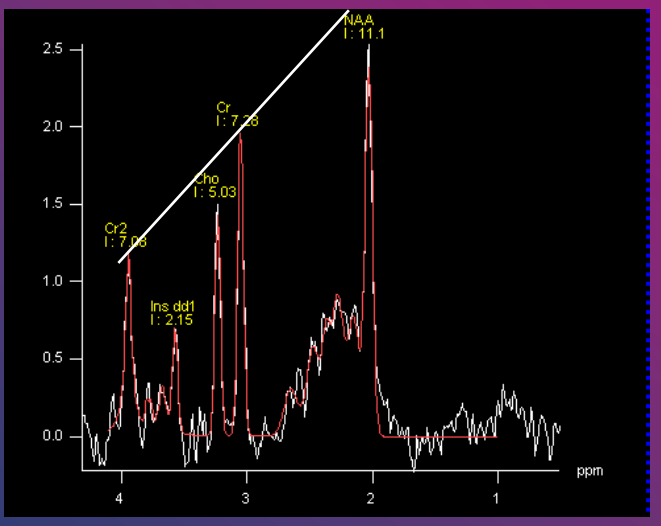
Tumor:

- NAA decrease
  - NAA decreases as tumor growth displaces or destroys neurons
- creatine decrease
  - Very malig-nant tumors have high metabolic activity and deplete the energy stores, resulting in reduced creatine.
- Choline increase
  - Very hypercellular tumors with rapid growth elevate the choline levels
- lactate increase
  - lactate appears when tumors outgrow their blood supply and start utilizing anaerobic glycolysis.
- lipids increase
  - Lipids are found in necrotic portions of tumors

Observable Proton Metabolites

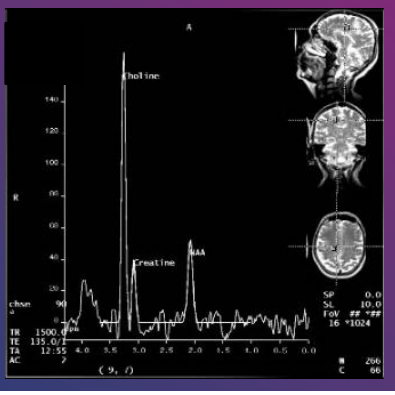
ppm	Metabolite	Properties
0.9-1.4	Lipids	Products of brain destruction
1.3	Lactate	Product of anaerobic glycolysis
2.0	NAA	Neuronal marker
2.2-2.4	Glutamine/GABA	Neurotransmitters
3.0	Creatine	Energy metabolism
3.2	Choline	Cell membrane marker
3.5	*myo*-inositol	Glial cell marker, osmolyte hormone receptor mechanisms
1.2	Ethanol	Triplet
1.48	Alanine	Present in meningiomas
3.4&3.8	Glucose	Increased in diabetes
3.8	Mannitol	Rx for increased ICP

Hunter's angle



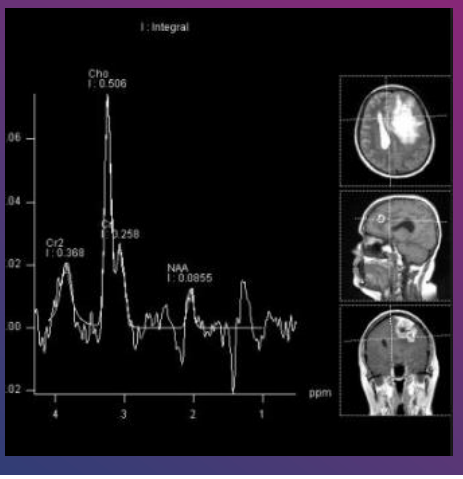
Spectra in specific conditions

- **Glioma**
  - MRS can help increase our ability to predict grade. As the grade increases, NAA and creatine decrease and choline, lipids and lactate increase.
  - In the setting of gliomas, choline will be elevated beyond the margins contrast enhancement in keeping with cellular infiltration.



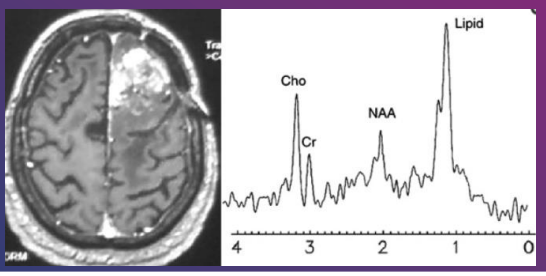
Spectra in specific conditions

- **Non-glial tumours: meningioma**
  - May be difficult but in general non-glial tumours will have little, if any, NAA peak.



Spectra in specific conditions

- **Radiation effects**
  - Distinguishing radiation change and tumour recurrence can be problematic. In recurrent tumour choline will be elevated, whereas in radiation change, NAA, choline and creatine will all be low, with lactate findings.



54-year-old woman after surgical resection and radiation for left frontal glioblastoma.(case 22) (a) Axial T1-weighted image after contrast administration shows a new area of contrast enhancement in left frontal lobe. (b) Spectra showed prominent lipid peak, with slightly decreased choline (Cho)/N-acetyl aspartate ratio (1.5) and decreased Cho/lipid ratio (0.6), indicating radiation necrosis, which was confirmed at histopathology

Magnetic field homogeneity

- Spectral resolution is determined primarily by three factors:

1. The transverse relaxation time (*T*2) of the metabolite is inversely proportional to the ideal peak width.

2. The *B*0 separation between peaks (in Hz) increases linearly with magnetic field strength.

3. The local magnetic field inhomogeneities widen and distort the spectral lines from their ideal Lorentzian forms.
   - Maximum homogeneity is accomplished by adjusting DC currents in the gradient coils and room temperature shim coils.

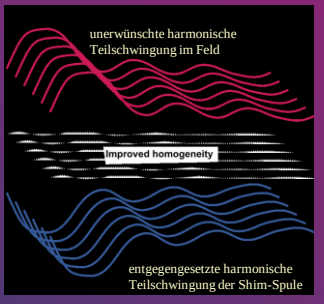
- The name of this process is ‘‘shimming’’

Magnetfeldhomogenität

- Die Auflösung des Spektrums wird hauptsächlich durch drei Faktoren bestimmt:
  1. Die transversale Relaxationszeit (*T*2) des Metaboliten ist umgekehrt proportional zur idealen Peak-Breite.
  2. Die *B*0-Auflösung zwischen den Peaks (in Hz) nimmt linear mit der Magnetfeldstärke zu.
  3. Die lokalen Magnetfeld-Inhomogenitäten verbreitern und verzerren die Spektrallinien gegenüber ihrem idealen Lorentz-Profil.

- Zur Erzielung einer maximalen Homogenität wird der Gleichstrom in den Gradientenspulen und den auf Raumtemperatur laufenden Shim-Spulen angepasst.

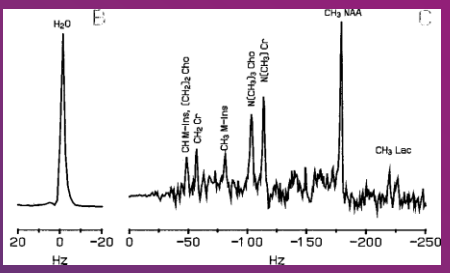
  Das bezeichnet man als „Shimmen“.



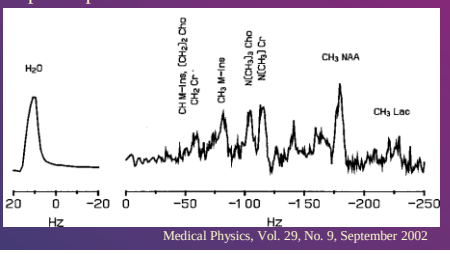
Shimming

- Improves magnetic field homogeneity
- increases *S/N*
- Narrows peak widths.
- improves
  - sensitivity and
  - spectral resolution.

Good shim: absorption spectrum from the water with a FWHM of 1.9Hz



Bad shim: absorption spectrum from the water with a FWHM of 5.6Hz



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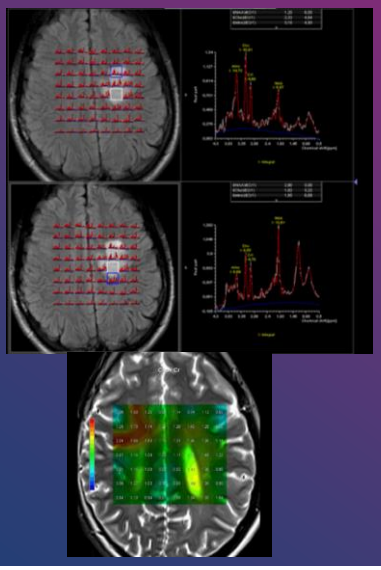
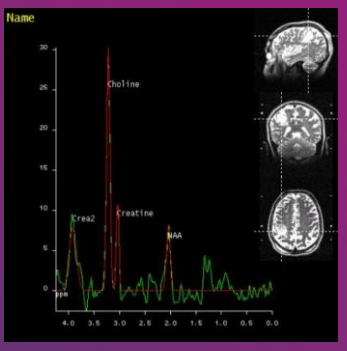
CSI vs Single Voxel





Spectroscopic Sequences

- If raw signal was processed then the spectra would be dominated by water, which would make all other spectra invisible.
- Water suppression is therefore part of any MRS sequence, either via inversion recovery (IR) or chemical shift selective (CHESS).
- If water suppression is not successful then a general slope to the base line can be demonstrated, changing the relative heights of peaks.

Summary

- In summary, consistent, high quality, short TE spectra *in vivo* are best acquired with the SVA technique. One should acquire a spectrum form the lesion and a control spectra from contralateral side.
- CSI is best when more VOIs are required.
- A long echo time (TE~130 ms) can be used to simplify the spectra and reduce the lipid and macromolecule signal, which will make metabolite quantification reasonably consistent. However, the long TE time reduces the number of quantified metabolites to NAA,Cho, Cr, and lactate.