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Outline

• Introduction to MRI/MRS.

• Quantitive MRS and decision support systems.

• Future challenges for translating MRS into a clinical tool.
Nuclear Magnetic Resonance (NMR)

- MRI and MRS are both based on the principle of nuclear magnetic resonance.

- NMR allows the detection of signals from nuclei with non-zero spin (intrinsic magnetic moment).

- Due to their high sensitivity and natural abundance in tissue - $^1$H and $^{31}$P are the most commonly observed nuclei in-vivo.
Nuclear Magnetic Resonance Experimental Setup

- $B_1$ - weak oscillating field (RF)
- $B_0$ - strong static field

Felix Bloch
Edward Purcell
1946

RF generator and receiver

Computer
NMR Experiment

Net magnetisation generated

RF irradiation ($B_1$)

NMR signal
NMR signals

- Signal amplitude is proportional to number of nuclei.
- Oscillate at a frequency dependant on the static field strength ($B_0$), nucleus type ($^1H$, $^{31}P$...)) and its chemical environment.
- Decay rates depend on microscopic environment.
MRI

• MRI is based on the same principle as NMR.

• Magnets have to be much larger to fit patients, and as strong as possible (superconducting).

• Strong gradients are used to localise the NMR signal to generate an image.

• MRI is based on the detection of $^1\text{H}$ nuclei present in tissue water.
Clinical MR systems

Magnet generates a strong, uniform magnetic field ($B_0$)

Sample contains NMR sensitive nuclei

Head coil emits rapidly oscillating field and records the induced NMR signal ($B_1$)
Magnetic Resonance Imaging

T1 weighted MRI
1mm isotropic resolution
MRI v CT
MRI

- **Advantages:**
  - Excellent soft tissue contrast - ideal for brain imaging.
  - Non-ionising radiation (radio waves).
  - Can also provide functional information (metabolism (MRS), diffusion (DWI), activation (fMRI), tissue perfusion (DCE/DSC/ASL)).

- **Disadvantages:**
  - Time consuming, scans are typically 1h - not so good for emergencies - trauma, stroke…
  - Expensive, need special rooms to prevent interference.
  - Complex safety protocols (no metal implants, quenching procedure…)
Single voxel spectroscopy

Voxel is placed over the tumour

A spectrum is obtained
Manual spectral interpretation
Average spectra

PA

Epp.

MB

Normal brain

Davies 2008
TARQUIN analysis method

- Used to obtain metabolite concentrations from MRS data.
- Reads Siemens, GE, Philips MRS data formats.
- Fully automated, open source.
- Generates metabolite basis-set to match the acquisition parameters (based on quantum dynamic simulations).

Wilson and Reynolds et al. MRM 2006, 2011
Decision support system

Database of previous cases

Radiologist evaluation

Predicted diagnosis: Pilocytic astrocytoma
DSS example

- Frequency (PPM)
  - Av MB
  - New

- Frequency (PPM)
  - Av PA
  - New

- Frequency (PPM)
  - Av Epp
  - New

Predicted diagnosis: Medulloblastoma
MRS and field strength

1.5 Tesla

3.0 Tesla
1.5T + 3T MRS DSS

- Previous work has shown that MRS based DSS can be used to aid paediatric tumour diagnosis for 1.5T cases*.

- Hospitals increasingly have a mix of 1.5T and 3T MR systems.

- Can we use the large database of cases collected at 1.5T to predict the diagnosis of cases collected at 3T?

*Davies 2008, Vicente 2013
3T DSS performance

• Training set of 77 BCH cases collected at 1.5T.

• Tested prospectively on 22 cases from 3 centres (BCH, QMC, RLCH) collected at 3T.

• TARQUIN was used to obtain metabolite concentrations for classification.

• 86% accuracy was achieved - in agreement with other studies at 1.5T.
Key points

• MRS data can be interpreted qualitatively by visual comparison with average spectra or by using decision support systems (DSS).

• DSS based on automated MRS analysis software (TARQUIN) have the following advantages:
  
  • Methods can be reproduced at other centres without requiring MRS data processing or interpretation expertise. Important for multi-centre studies.
  
  • Can remove vendor and hardware dependance (eg field strength) by converting spectral information into metabolite concentrations.
MR Spectroscopic Imaging (MRSI)

- The most common clinical MRS exam for paediatric brain tumours is single voxel spectroscopy (SVS).
- MRSI exploits acquisition methods used in MRI to obtain MRS information with spatial encoding.
- This allows “metabolite maps” to be generated which may be particularly useful for investigating heterogenous lesions.
Example MRSI

- T1 weighted MRI
- TNAA map
Example MRSI

T1 weighted MRI

TChol map
Example MRSI

TCho map

m-Ins map
Example MRSI

TCho map

Normal

Tumour

CSF
MRSI challenges

- High quality automated analysis is not available on scanner software. - TARQUIN

- Large amounts of information make interpretation difficult for a non-expert. - DSS?

- 3T offers potential advantages for MRSI, however poor field uniformity and accurate localisation (CSD) are areas that require further R+D.
Translation from clinical research to clinical practice

• Currently, TARQUIN and the DSS can be used for research studies.

• However, since this software can be classified as a “medical device” it requires regulatory approval (directive 93/68/EEC) before it can be used for clinical purposes in Europe.

• This requires:

  • A company with ISO 13485 compliance.
  
  • CE marking procedure.

• Currently exploring CE marking procedure with an industrial collaborator with the aim to produce an MRS analysis product for clinical use.
Conclusion

• MRS is a useful and widely available technique for the non-invasive measurement of tissue metabolism.

• Automated quantitation and pattern recognition methods aid:
  • 1) Clinical interpretation.
  • 2) Disease biomarker development.

• The translation of these methods into clinical practice requires regulatory approval (CE marking) and therefore industrial collaboration.