

Introduction

Stroke is the third highest cause of death and the major cause of serious disability. Stroke is the result of a reduction in blood supply to the brain, that can lead to irreversible tissue damage and render patients permanently disabled. For a limited time window after the stroke there is a region of brain tissue surrounding the dead tissue, known as the penumbra, that still has a limited amount of blood supply. This tissue could potentially be salvaged if blood supply is restored, e.g. using thrombolytic or “clot busting” drugs.

Main Current Methods

Positron Emission Tomography (PET)

PET is the oldest imaging technique employed for penumbra detection in patients. PET provides spatially detailed, highly quantifiable data that is highly accurate. PET is currently considered the gold standard.

Disadvantages:

- (a) PET is expensive and has limited availability.
- (b) Radiation exposure.
- (c) Arterial catheterization constrains the use of PET as a tool for managing acute stroke patients and assessing investigational therapies.

Magnetic Resonance Imaging (MRI)

The current MRI standard for identifying ischemic penumbra is the perfusion/diffusion mismatch which is becoming clinically important in determining which patients will benefit from clot busting therapies. MRI diffusion/perfusion is increasingly available at major hospitals worldwide for the acute evaluation of stroke patients



Disadvantages:

In the case of MRI it is recognized that the diffusion/perfusion mismatch is an approximation of the ischemic penumbra because:

- (a) The perfusion techniques and data evaluation are not truly quantitative and vary among centres.
- (b) The thresholds used for defining perfusion abnormalities have not been validated against PET thresholds.
- (c) Abnormal diffusion regions do not represent accurately areas of irreversible damage tissue.

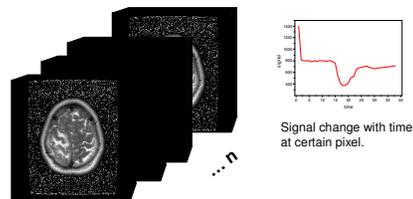


Figure 1. Example of Perfusion weighted imaging data.

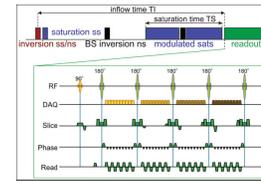


Figure 2. Example of a Perfusion weighted imaging MRI pulse sequence, ref 5.

Novel MRI techniques

Currently there is a collaboration between two groups at the University of Glasgow, the GEMRIC centre and our Neuroimaging group in the SGH. The objective is to develop and implement a novel MRI technique to define the ischemic penumbra.

This novel MRI technique detects metabolism indirectly through changes in oxyhemoglobin:deoxyhemoglobin rations and T_2^* MRI signal change during “Oxygen Challenge”. Both animal⁶ and human studies, have been carried out.

Multi-centre research

There is a Wyeth/TMRI PWI/DWI mismatch study, which is a collaboration between the Universities of Aberdeen, Edinburgh and Glasgow. The objective of this multi-centre investigation is to measure tissue viability thresholds for MRI (DWI/PWI) and CTP (Computer Tomography Perfusion imaging).

Future Work

- (a) To provide greater accuracy for penumbral identification, using more sophisticated data analyses.
- (b) Implementation and development of MRI techniques to measure perfusion. For example, arterial spin-labelling will enhance the ability of diffusion/perfusion MRI to define the ischemic penumbra more accurately.
- (c) To identify new biomarkers to determine the ischemic penumbra.

References

1. Baron JC. Cerebrovasc Dis. 1999, 9:193-201.
2. Baird AE, Benfield A, Schlaug G, et al. Annals of Neurology. 1997, 41(5):581-589.
3. Smith AM, Grandin CB, Duprez T, et al. J. of Magnetic Resonance Imaging. 2000, 12:400-410.
4. Wong EC, Buxton RB and Frank LR. 1997, 10:237-249.
5. Günther M, Oshio K and Feinberg DA. Magnetic Resonance in Medicine. 2005, 54:491-498.
6. Santosh C, Brennan D, McCabe C, et al. J. of Cerebral Blood Flow & Metabolism. 2008, 1-12.

Acknowledgements

Rosario Lopez is funded by SINAPSE.