Transcranial Doppler Ultrasound

Evans D H

Department of Medical Physics, Leicester Warwick Medical School.

Doppler ultrasound is generally an excellent technique for measuring blood flow and blood flow changes in large and medium sized blood vessels. It has the significant advantages over most other techniques of being non-invasive, so it can be used for monitoring purposes and repeated at will, and of having excellent temporal resolution, so that beat-to-beat blood flow changes can be observed. There are however three difficulties to be overcome when making Doppler measurements through the intact skull using the transcranial Doppler (TCD) technique. The first of these is the very significant attenuation of ultrasound by bone which means that in order to obtain adequate signal levels it is necessary to work at relatively low transmitted frequencies (usually about 2MHz), which in turn means the wavelength is relatively long and spatial resolution relatively poor, and that the scatter from blood is relatively weak. The second difficulty is also associated with the physical properties of the skull in that the high ultrasound velocities in the bone together with its non-planar shape leads to significant distortion of the ultrasound beam. The final difficulty is that, unlike most arteries in the body, it is not necessarily valid to assume that the mean diameters of cerebral vessels are relatively constant over short time periods. Despite these challenges TCD has proved to be of tremendous utility in several areas, but particularly in the study of cerebral vasoreactivity and autoregulation, and in the detection and characterisation of cerebral emboli. Furthermore transcranial colour-coded images are now improving to such an extent (particularly with the help of ultrasonic contrast agents) that useful diagnostic information may be obtained simply and rapidly. It is important that users of the TCD techniques understand the assumptions associated with the measurements they make, so that they do not over-interpret their results, but with this in mind the TCD technique is capable of providing tremendous insight into cerebral haemodynamics and the clinically important problem of cerebral embolisation.

Stereotactic Radiotherapy

Warrington J

The Royal Marsden Hospital, London and Surrey

The last twelve years has seen the growth of the technique of ‘stereotactic radiotherapy,’ or ‘SRT,’ which evolved from ‘radiosurgery’, a neurosurgical procedure invented by Lars Leksell[1] in 1951. SRT uses multiple fractions of customised, high energy x-ray beams to treat patients with small, semi-benign or malignant lesions in the brain. It has also provided a useful template for introducing the latest intensity modulation techniques in radiation oncology.

Stereotactic radiotherapy has been facilitated by the rapid evolution and increasing availability of CT scanners and magnetic resonance imaging (MRI). The continued development of radiotherapy treatment planning systems has kept pace with this computerised imaging revolution and specialised stereotactic planning modules provide the necessary software for image registration and external beam planning. However, the impetus for successful SRT was provided by the invention of a precisely re-locatable, stereotactic head frame by Steve Gill[2] in the late 1980’s. This device allowed accurately reproducible immobilisation of the patient’s head for both imaging procedures and at each ensuing treatment fraction, a fundamental requirement for high precision radiotherapy.

Precise SRT beams are most commonly delivered by the medical linear accelerator or 'linac', which continues to be developed as an extremely accurate and versatile treatment modality. Multileaf collimation systems, either integral or attached to the accelerator head, enable customised radiation beams to be delivered to the patient. Linac mounted electronic portal imaging devices (EPIDs) are increasingly used for geometric and more recently, dosimetric verification. The efficient networking and quality assurance of these computerised elements are a constant challenge for the radiotherapy team.

The stereotactic method, the treatment planning and delivery stages along with problems identified in introducing SRT into a busy radiation oncology department, will be described. The lecture will conclude with some recent developments plus a few interesting quirks.

References

[1] Leksell, L.T. 'The stereotactic method and radiosurgery of the brain,' Acta Chir. Scand. **102**, 316 (1951)

[2] Gill, S.S, Thomas, G.T., et al, 'Relocatable frame for stereotactic external beam radiotherapy,' Int. J. Radiat. Oncol. Biol. Phys. **20(3)**, 599-603 (1991).

Imaging Brain Structure and Function in Dementia

O'Brien J

Institute for Ageing and Health, Wolfson Research Centre, Newcastle General Hospital, Newcastle upon Tyne

Dementia is a common condition, affecting approximately 5% of the over 65's, with the current number of 750,000 cases in the UK set to double over the next 30 years. Accurate clinical diagnosis of the main sub-types of dementia in later life (Alzheimer's disease, dementia with Lewy bodies and Vascular dementia) is increasingly important to inform appropriate management and determine prognosis, especially now that specific anti-dementia drugs are clinically available. Neuroimaging has an important role both in the clinical assessment and diagnosis of patients presenting with dementia and in terms of furthering research aimed at improving differential diagnosis, understanding the neurobiological basis of symptoms, monitoring disease progression and investigating new therapeutic approaches.

Whilst the main use of structural neuroimaging (Computer Tomography (CT) and Magnetic Resonance Imaging (MRI)) to date has been to exclude a space occupying lesion as a cause for cognitive decline, it is increasingly playing a role in both differential diagnosis and early diagnosis. For example, hippocampal atrophy is associated with Alzheimer's disease whilst modern co-registration techniques can detect serial brain volumes change of less than one ml which may be useful for early diagnosis. Single Photon Emission Computer Tomography (SPECT) may also assist with differential diagnosis, for example blood flow SPECT using Tc-HMPAO can assist with the diagnosis of Alzheimer's disease whilst new ligands aimed at specific transmitter systems may help the identification of other disorders. The presentation will illustrate the different uses of neuroimaging using data from ongoing prospective research studies in dementia. The uses and limitations of different methods of analysis (visual rating, volumetric analysis, co-registration, statistical parametric mapping and voxel-based morphometry) will be demonstrated.

How can we measure the concentration of substrates and metabolites in the human brain?

Hutchinson P J, O'Connell M T, Kirkpatrick P J and Pickard J D

Academic Department of Neurosurgery and Wolfson Brain Imaging Centre, Addenbrooke's Hospital, University of Cambridge, UK.

Changes in the cerebral concentration of substrates and metabolites are fundamental to several disease processes including ischaemia, seizures and neoplasia. The ability to measure the concentration of these substances is increasing our understanding of the pathophysiology of trauma, stroke, epilepsy and tumours. Advances in (1) probe and (2) imaging technologies have enabled the cerebral levels of substrates e.g. glucose and oxygen, metabolites e.g. pyruvate and lactate and neurotransmitters e.g. glutamate and γ-amino-butyric acid (GABA) to be determined.

(1) Probing the brain

There are two types of catheters used to determine the concentration of substances in the human brain:

- Microdialysis

This technique involves the insertion of fine catheters lined with dialysis membrane into the cerebral parenchyma. The catheters are perfused with a physiological solution e.g. Ringer's at ultra-low flow rates. Molecules diffuse from the extracellular space across the membrane into the solution, which is then collected for analysis

- In vivo sensors

Miniature electrodes and spectrophotometers have been incorporated into fine sterile probes and applied to measure tissue gas pressures and the pH of the brain.

Microdialysis and in vivo sensors have been applied to investigate the pathophysiology of patients with head injury, subarachnoid haemorrhage and epilepsy.

(2) Imaging the brain

There are two types of functional imaging which have been applied to measure human cerebral metabolism:

- Positron Emission Tomography

By imaging the tissue take-up of a labelled compound circulating in the blood, Positron Emission Tomography (PET) can determine the level of oxygen consumption, glucose utilisation, protein synthesis and radioligand binding/drug pharmacokinetics / dynamics in the human brain.

- Magnetic Resonance Spectroscopy

Magnetic resonance spectroscopy (MRS) involves the application of magnetic resonance imaging techniques to assess the metabolism of tissues. The application of proton MRS enables the tissue concentration of various substances including choline, creatine, N-acetyl-aspartate (a neuronal marker), lactate, glucose, glutamate and GABA to be determined.

PET and MRS have been applied to patients with head injury, subarachnoid haemorrhage, tumours and epilepsy.

The probe and imaging techniques differ in their approach. Probes enable the long-term (over several days) monitoring of metabolism but only a focal volume of brain within the region of the probe can be assessed. Imaging can determine metabolism of the brain both regionally and globally but only for the duration of the scan. These two approaches are therefore complementary. The applications of these techniques, including advantages and disadvantages will be addressed, together with the need to use functional imaging for the targeting of the probes.

Proton MR spectroscopy: basic principles and clinical application

Birchall D
Neuroradiology Department, Newcastle General Hospital, Newcastle upon Tyne

Proton MR spectroscopy is a relatively recently developed MR modality and is becoming more widely available as a clinical imaging method throughout the country. The technique allows the analysis of the metabolic content of imaged tissue, and is used to characterise pathology by demonstrating specific abnormalities within the metabolic profile. MR spectroscopy is predominantly applied to cranial imaging, and has a role in differentiating and characterising intracranial mass lesions and pathologies. As such, it may have a role as a form of noninvasive biopsy.

A summary of the principles of MR spectroscopy will be followed by illustrative examples of the use of spectroscopy in routine clinical neuroradiological practice.

Electromagnetic Investigation of the Brain

Barber C
Queen's Medical Centre, Nottingham, UK

Dating back to the work of Hans Berger and of Lord Adrian in the 1930s, this methodology has a long pedigree in functional investigation of the human brain. And right from the beginning, it encompassed cognitive as well as sensory and motor function. Despite the crudeness of their equipment, the degree of insight achieved by the early workers was impressive.

Initially, the work centred on the intrinsic rhythms of the brain but, with the introduction of averaging by Dawson, activity could be related to specific stimuli. The measurement of evoked potentials led to great advances in understanding of sensory function and to widespread clinical application. The introduction of magneto-cortical stimulation led to similar advances with regard to motor function. Event-related potentials brought new understanding of cognitive processing, though their complexity limited clinical application.

The technique always offered exquisite temporal resolution, but the impedance of the skull limited the spatial resolution attainable. Nonetheless, valuable work was carried out on dipole source modelling. The development of sensitive SQUID-based magnetometers opened the possibility for more advanced source localisation, due to the transparency of the skull to magnetic fields. Modern magneto-encephalography (MEG) systems with more than 200 channels provide very respectable spatial resolution in a patient-friendly way. It remains, unfortunately, rather expensive. The information produced can be reconciled with really high spatial resolution images produced by, for example, MRI and fMRI and leads to a fruitful complementary approach to functional brain imaging.

This lecture will briefly rehearse the development of these techniques and review areas of currently exciting progress, focussing particularly on clinical applications in hearing and vision.