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The Growing Spectrum of Neuroimaging

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Commentary

The past four decades have seen significant advances in neuroimaging techniques, methodology and sophisticated insights into brain organization. Advanced approaches are now available for measuring blood flow of the brain, biochemistry, metabolism and brain receptors.

Positron Emission Tomography (PET) Scan

In the 1940s, Kety and Schmidt pioneered the utilization of nitrous oxide in quantifying cerebral blood flow [1]. This technique provided global cerebral flow data, however it did not address regional cerebral blood flow. This led to the utilization of radioactive tracers that were administered either by injection in the carotid artery, or by inhalation in combination with radiation detectors to measure the clearance from different brain regions [2].

The above techniques had several limitations, which led to the development of positron emission tomography (PET) that applies tracer compounds that allow quantitation of the regional radioactivity which can be imaged and measured by a mathematical model that describes *in vivo* behaviour of the applied radioactive material. The first PET scan was developed at Washington University in St. Louis by Ter-Pogossian and colleagues in the mid 1970's [3]. PET is being increasingly used in non-invasive quantification of cerebral blood flow, metabolism, and receptor binding.

Positron emission tomography (PET), while being second to functional MRI with regard to brain mapping, remains a highly promising neuroimaging technique due to its continuing advancement in the fields of molecular imaging, and neuroreceptor mapping. PET is superior to functional MRI (fMRI), and MR spectroscopy with regard to imaging specific tracers (or biomarkers) *in vivo.*

Judenhofer et al. outlined a technical advance of PET of a machine that performs simultaneous PET and MRI. The primary challenge that was overcome in creating this system was the fact that PET scanners incorporate photomultiplier tubes which are sensitive to magnetic fields [4]. One solution is the use of optical fibres that lead scintillation light outside the magnetic field. For this system, an alternative solution was used. A novel PET detector based on lutetium oxyorthosilicate scintillation crystals and avalanche photodiodes was used in the MRI bore. This was demonstrated to work just as well as conventional detectors. PET-MRI has more potential in biomarker tracing and anatomical imaging. It can synergistically combine fMRI, anatomical MRI, spectroscopy, and PET, opening up new avenues in research.

Diffusion-Weighted and Diffusion-Tensor Imaging

Diffusion-weighted MR imaging can detect an acute infarct (stroke) in the majority of patients in less than 30 minutes after the occurrence of the stroke. A more sophisticated extension of diffusion imaging is diffusion tensor imaging or DTI. DTI is a non-invasive method for mapping white matter fibre tract trajectories in the human brain and spinal cord. This can provide critical information to the neurosurgeon in cases of brain tumours by displaying the relation of a tumour to an adjacent white matter tract.

Diffusion tensor imaging (DTI) involves the characterization of white matter, and the directionality of white matter tracts. Functionally relevant anatomical information may be derived from white matter anisotropy as well as from tract-related connectivity measures. With regard to MRI tractography, the primary problem is the requirement for a sufficient resolution to separate crossing fibres from those that approach each other within a voxel and then go in parting directions [5]. One solution is to image at higher spatial resolution. Other solutions include application of diffusion gradients in more than just the three perpendicular directions, thus performing a more detailed directional encoding.

MR Spectroscopy (MRS)

MR Spectroscopy (MRS) is a non-invasive technique capable of measuring chemicals within the human brain. MR spectroscopy equipment can be adjusted to pick up signals from different chemical nuclei within the body. This information is displayed as peaks in graph concentrations of the different chemicals in diseased tissues. This helps to distinguish pathologies such as tumours from other lesions such as infections. An elevated choline in a mass suggests the diagnosis of an aggressive tumour, whereas a normal choline level may support the diagnosis of radiation necrosis over recurrence of a

tumour. In menigiomata, elevated alanine levels may be seen [6].

Functional MRI (fMRI)

Functional MRI refers to the demonstration of brain function with neuro-anatomic localization in a real-time imaging. fMRI has become the tool of choice for the cognitive neuroscience community. It is essential for studying the functional correlates of behaviour and disease. The implementation of functional has grown mainly because of its non-invasiveness, relative ease of implementation, high spatial and temporal resolution. The vast majority of f MRI studies are performed using 'Blood Oxygen Level Dependent' contrast or BOLD. The principle of the BOLD technique of F-MRI is that a pre-defined cognitive task leads to regionally increased neuronal activity and localized hemodynamic changes that produce a MR signal response.

Blood flow in the brain is highly locally controlled in response to oxygen and carbon dioxide tension of cortical tissue. When a specific region of the cortex increases its activity in response to a task, the extraction fraction of oxygen from the local capillaries leads to an initial drop in oxygenated haemoglobin (oxy-Hb) and an increase in local carbon dioxide (CO_2) and deoxygenated haemoglobin (deoxy-Hb). Following a lag of 2-6 seconds, cerebral blood flow (CBF) increases, delivering a surplus of oxygenated haemoglobin, washing away deoxy-haemoglobin. It is this large rebound in local tissue oxygenation that is imaged. fMRI is able to detect this change due to the difference in the paramagnetic properties of oxy-Hb and deoxy-Hb. Deoxygenated haemoglobin is paramagnetic whereas oxygenated haemoglobin is not [7].

Intraoperative MRI

Till recently, MR imaging determining intraoperative performance has been based on images obtained preoperatively. However, real-time imaging may be crucial, as the brain shift during the course of surgery cannot be predicted from preoperative imaging. The development of intra-operative MRI allows the surgeon to view the brain at all times during surgery and helps him (her) remove tumours without damaging adjacent brain structures. This technique applies a high strength MRI scanner integrated within the surgical suite with a neuro-navigation and digitized image transfer and projection system. Establishing an intraoperative MRI suite will require training on MRI safety, customizing the MRI strength, architectural planning, training, human vigilance and building MRI-safety policies [8].

The Surgiscope

One of the most elegant systems proposed for intraoperative assisted lesion resection was the SurgiScope (Elekta Inc, Norcross, GA). The device could robotically position a microscope to a preplanned trajectory, utilize laser localization to pinpoint the area of proposed access, and could be repositioned continuously to assist lesion resection. It can offer the benefits of magnification, illumination, precision, image guidance, and robotic navigation [9].

Magneto Encephalography (MEG)

Neuronal generation of MEG signals: Electric currents are accompanied by an electromagnetic field. The main generators of the MEG signals-and of EEG as well-are synchronous postsynaptic (intracellular) currents in the pyramidal neurons of the cerebral cortex. In the spherical volume conductor formed by the head, the orientation of the magnetic field pattern reflects the direction of the intracellular current. In cortical pyramidal neurons, the net neural current flows normally to the local cortical surface. MEG is most sensitive to cortical currents tangential to the skull, such as in the walls of cortical fissures, whereas EEG more readily picks up signals also from the depth of the brain and from the convexial cortex, because of their different sensitivities to source orientations and locations, MEG and EEG complement each other.

MEG provides millisecond time resolution and allows real-time tracking of brain activation sequences during sensory processing, motor planning and action, cognition, language perception and production, social interaction, and various brain activities. Future MEG breakthroughs are expected through advanced signal analysis and combined use of MEG with functional magnetic resonance imaging (fMRI) [10].

Conclusion

The field of brain imaging has become a dynamic, multidisciplinary activity. Remarkable advances in neuroimaging have been made in the past few decades which opened new horizons in the study of brain anatomy and physiology. Understanding the limitations and challenges of each modality is key to effective utilization of these new tools.

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