UNIVERSITY OF BIRMINGHAM

NHS National Institute for Health Research

National Horizon Scanning Centre

Magnetic Source Imaging (MSI) for the characterisation and localisation of epileptic abnormalities and brain tumours.

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The National Horizon Scanning Centre Research Programme is part of the National Institute for Health Research

Magnetic Source Imaging (MSI) for the characterisation and localisation of epileptic abnormalities and brain tumours.

Target group

- Patients with refractory epilepsy being considered for surgery.
- Patients undergoing surgery for brain tumour, arteriovenous malformation, or epilepsy, if surgery may compromise critical motor, sensory, or cognitive functions.

Technology description

Magnetoencephalography (MEG) is a non-invasive diagnostic technology that measures extracranial magnetic fields spontaneously produced within the brain when electrical current flows along neurons. MEG is a passive recording device which shows an output as a set of waveforms, analogous to electroencephalography (EEG). The MEG output is simplified using mathematical modelling and superimposed onto a high-resolution magnetic resonance imaging (MRI) image, allowing the anatomical location of neurological activity to be displayed in real-time. The process of combining MEG data with an MRI image is known as magnetic source imaging (MSI) and is the most useful clinical application of MEG technology.

MEG requires about 37-70m^2 of space for installation, which may encompass a magnetically shielded room in which the MEG machine is situated, a MEG laboratory, and equipment storage room. MEG is not a novel technology and is currently operational at several institutions in the UK, mainly for research purposes.

Innovation and/or advantages

- MEG is non-invasive, and may complement or replace surface or invasive electroencephalography (EEG).
- MEG functionally maps the brain, and its output can be superimposed onto a magnetic resonance image in real time.

Developers

4-D Neuroimaging: manufacturer of Magnes 3600 WH - machines located at Liverpool University and York University.

Elekta AB: manufacturer of Neuromag – machines located at University of Oxford, and at the MRC Cognition and Brain Sciences Unit (MRC CBU) in Cambridge.

VSM MedTech Ltd[a]: machines located at Aston University, Cardiff University and University College London.

Place of use

☐ Home care e.g. home dialysis	☐ Community or residential care e.g. district nurses, physio	☐ Primary care e.g. used by GPs or practice nurses
☑ Secondary care e.g. general, non-specialist hospital	☑ Tertiary care e.g. highly specialist services or hospital	☐ Emergency care e.g. paramedic services, trauma care
☐ General public e.g. over the counter	☐ Other:	

[a] VSM MedTech no longer manufactures or markets magnetoencephalography machines.

Availability, launch or marketing dates, and licensing plans:

Limited availability for clinical use in the UK.

NHS or Government priority area:

This topic relates to the NHS Cancer Plan, the National Service Framework for Children, Young People and Maternity Services and the National Service Framework for Long-term Conditions.

Relevant guidance

NICE guidance:

- NICE guideline. Epilepsy in adults and children[1]. October 2004.
- Improving outcomes for people with brain and CNS tumours – the manual[2]. June 2006.
- NICE technology appraisal. Temozolomide for the treatment of recurrent malignant glioma (brain cancer)[3]. April 2001.

SIGN guidance:

- Diagnosis and management of epilepsies in children and young people[4]. 2005.
- Diagnosis and management of epilepsy in adults[5]. 2003.

NHS HTA programme

- A systematic review of the effectiveness and cost-effectiveness of neuroimaging assessments used to visualise the seizure focus in people with refractory epilepsy being considered for surgery[6]. 2006.

Clinical need and burden of disease

In the UK, epilepsy is the most common serious neurological condition[7]. Lhatoo *et al* report that 30,000 (estimated incidence, 50 per 100,000 population) people in the UK develop epilepsy annually, and around 6,000 (20%) may develop intractable epilepsy. Of these, an estimated ≤4,500 patients may require surgery, with 450 patients being added to this surgical pool annually[8].

In 2004 there were around 3,800 new cases of brain cancer registered in England and Wales[9,10], and around 3,000 deaths in 2005[11]. Although brain tumours account for only 1.5% of all primary cancers and 2% of cancer deaths, they result in 7% of life-years lost before the age of 70. About 55% of primary brain cancers occur in males. Approximately 29% of adult patients with brain cancer survive one year after diagnosis and 13% survive 5 years[12].

The total pool of patients with epilepsy or brain tumours who may benefit from MSI is 8,011, with 3,961 being added each year. A UK expert consulted considered that not all of these patients would benefit from, or even be appropriate for MSI evaluation, although it has the potential to improve the evaluation and outcome in a significant number of these cases.

Existing comparators and treatments

- Scalp EEG
- Invasive EEG
- MRI
- Functional MRI
- Positron emission tomography (PET).

Efficacy and safety

There are hundreds of studies concerning the potential accuracy and clinical utility of MEG in the literature, which are of varying quality. A sample of the larger studies reporting on the diagnostic accuracy and/or clinical utility are presented below.

Trial author	Knowlton *et al*[13]	Alberstone *et al*[14]	Hund *et al*[15]	Smith *et al*[16]	Stefan *et al*[17]	Knake *et al*[18]	Wheless *et al*[19]
Location	US; Canada	US	US; Germany	US	Germany	US; Germany; Norway	US
Design	Diagnostic accuracy; clinical utility; independent and blind comparison	Diagnostic accuracy; clinical utility	Diagnostic accuracy; clinical utility	Diagnostic accuracy; clinical utility	Clinical utility	Diagnostic accuracy	Diagnostic accuracy
Participants, trial schedule	n=49; intractable partial epilepsy. MSI/MEG, EEG, and PET or single-photon emission computed tomography (SPECT).	n=26; both sexes; ages 11-75 years; intracranial mass lesions. MSI	n=40; both sexes; cortical lesions (12 arteriovenous malformations and 28 tumours). MSI	n=50; epilepsy; MRI; scalpsphenoidal EEG; depth/epidural electrodes. MSI	n=455; both sexes; ages 7-79 years; pharmacoresistant epilepsy. MSI	n=70; refractory epilepsy surgical candidates or considered for invasive EEG. MSI.	n=58; both sexes; ages 7-55 years; refractory partial epilepsy. MSI; EEG; video EEG (V-EEG).
Outcomes	Sensitivity; change in intracranial EEG (ICEEG) coverage with additional information from MSI/MEG.	Role of MSI for presurgical planning and intraoperative neurosurgical technique.	Usefulness of MEG mapping for presurgical planning and stereotactic operative procedures.	Extent to which MEG assisted in defining interictal epileptic zone in ablative epilepsy surgery candidates.	Contribution of MEG to presurgical epilepsy evaluation.	Sensitivity of MEG/EEG to detect interictal epileptiform (IED) activity.	Efficacy of each diagnostic method to identify the resected epileptogenic zone, when referenced to surgical outcome.
Key results	Positive predictive value for seizure location MSI/MEG=82-90%. Kappa score between MSI/MEG and ICEEG 0.2744 ($p<0.01$).	Based on MSI examination: 2 patients were not offered surgery, 4 patients underwent stereotactic biopsy, 10 patients had subtotal surgical resection; 7 patients were treated with complete surgical resection.	Based on MSI data – a non-operative approach was used for twelve patients, and an operative approach was used 28 patients with no postoperative neurological deficits.	MSI and EEG agreed in 28 cases, and agreed partially in six cases. In five cases, MSI and EEG disagreed; in eight cases there were no MSI dipoles; in three cases there was insufficient data. In five surgical cases, MEG data led to more extensive surgery than would have been planned with EEG alone.	Average sensitivity of MEG for specific epileptic activity was 70%. MSI supplied additional information in 35% of patients, and information crucial to final decision making in 10%.	In 67 patients, overall sensitivity to detect IED was 72% for MEG and 61% for EEG. In 13%, MEG only IED were recorded, whereas in 3% EEG-only IED were recorded. Combined sensitivity was 75%.	MEG (52%) was second to ictal intracranial video EEG (70%) in predicting the epileptogenic zone for patients who had an excellent surgical outcome. With extratemporal resection, ictal and intraictal EEG were superior to MEG in predicting the surgery site in patients with excellent outcome. For all patients who had a good surgical outcome, MEG was better than ictal or interictal scalp EEG in predicting surgical site.

Estimated cost and cost impact

MEG hardware costs and running costs	
MEG cost (including magnetically shielded room)	Approx £1,300,000 - £1,500,000
Liquid helium replacement	Between £17,000 - £25,000 per annum
Service contract agreement	Approx £40,000 - £65,000 per annum
Other costs	Personnel; customised peripheral equipment, such as neurological stimulators, 3rd party software etc.

Reimbursement costs per treatment of MEG within the US		
Technology	Description	Cost
MEG	MEG recording and analysis of spontaneous brain activity (e.g. epileptic cerebral cortex mapping).	$3,290 (£1,631)
MEG	MEG recording and analysis of 1st evoked magnetic field (e.g. visual cortex, motor, sensory, or other).	$691 (£342)
MEG	MEG recording and analysis of each additional evoked magnetic field (e.g. visual cortex, motor, sensory, or other).	$691 (£342)

Reference costs for related diagnostic tests[20]		
Technology	Description	Cost
EEG	EEG recording	£99 (Interquartile range [IQR]: 64 - 172)
MRI	MRI (not including merging of MEG and MRI data)	£244 (IQR: 197-403)

Potential or intended impact – speculative

Patients

- ☑ Reduced morbidity
- ☐ Reduced mortality or increased survival
- ☐ Improved quality of life for patients and/or carers
- ☑ Quicker or more accurate diagnosis and localisation of disease
- ☐ Earlier identification of disease
- ☑ Other: Increasing appropriateness and approach to surgery

Services

- ☐ Increased use e.g. length of stay, out-patient visits
- ☐ Service reorganisation required
- ☑ Staff or training required
- ☐ Decreased use e.g. shorter length of stay, reduced referrals
- ☐ Other:

Costs

- ☑ Increased unit cost compared to alternative
- ☐ Increased costs: more patients coming for treatment
- ☑ Increased costs: capital investment needed
- ☐ New costs:
- ☐ Savings:
- ☐ Other:

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