MAGNETOENCEPHALOGRAPHY IN DRUG RESISTANT EPILEPSY

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BRAIN SUMMIT 2020

UT SOUTHWESTERN MEDICAL CENTER

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COI

- NOTHING TO DISCLOSE

CONTENT OUTLINE

-What is DRE or Drug Resistant Epilepsy
-Principles: physiology and MEG basics
-What is MEG/MSI (Magnetic Source Imaging)
-EEG vs MEG and how they work together
-Indications for MEG
-MEG and epilepsy surgical outcomes

DRUG RESISTANT EPILEPSY

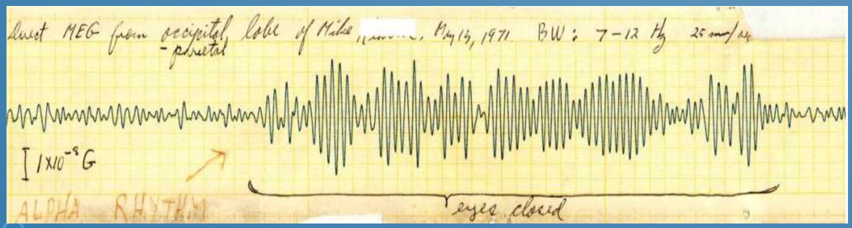
- -WHAT DEFINES DRE?
- -WHAT OPTIONS DO WE HAVE FOR THESE 1/3 OF PATIENTS?

MAGNETOENCEPHALOGRAPHY (MEG)

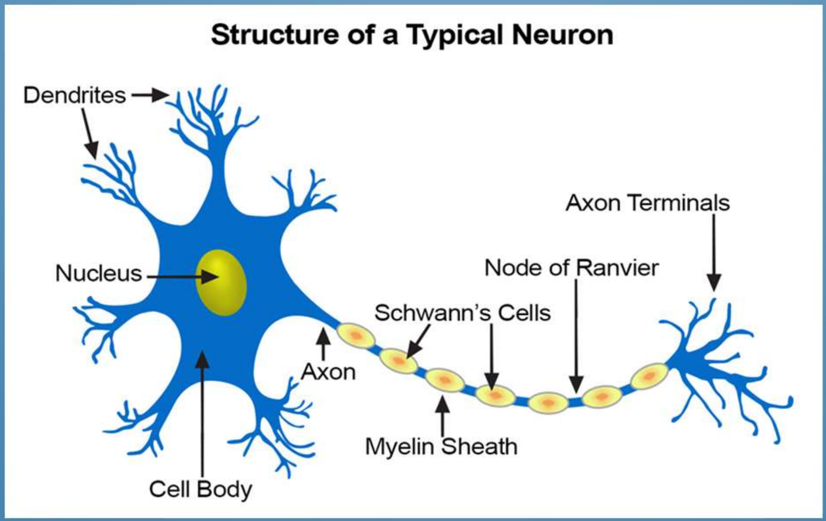
-1929: Hans Berger recorded the occipital alpha rhythm as proof of principle

-MEG: Non-invasive technique for measuring brain activity with a millisecond time scale

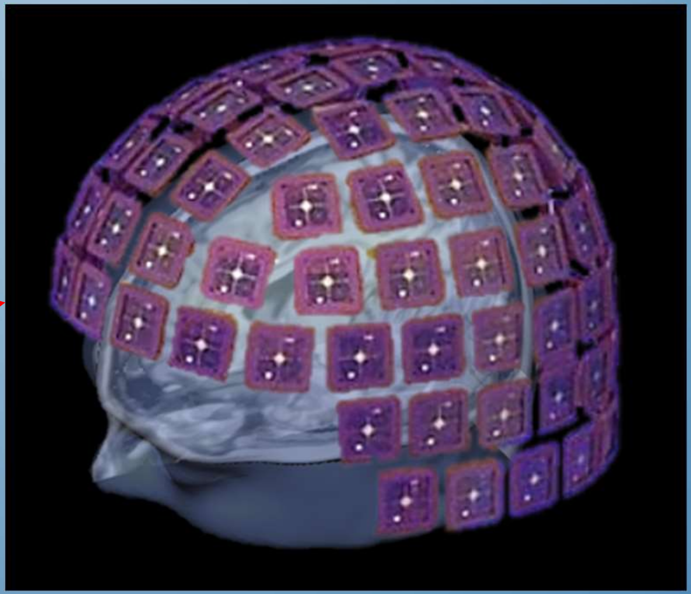
-1968: David Cohen records the first human MEG brain signal at MIT using one sensor; First measurement was taken in 1971



- Post-synaptic potentials create electrical currents known as intracellular currents



Today: High-density MEG



306 Superconducting Quantum Interference Devices (SQUIDs)

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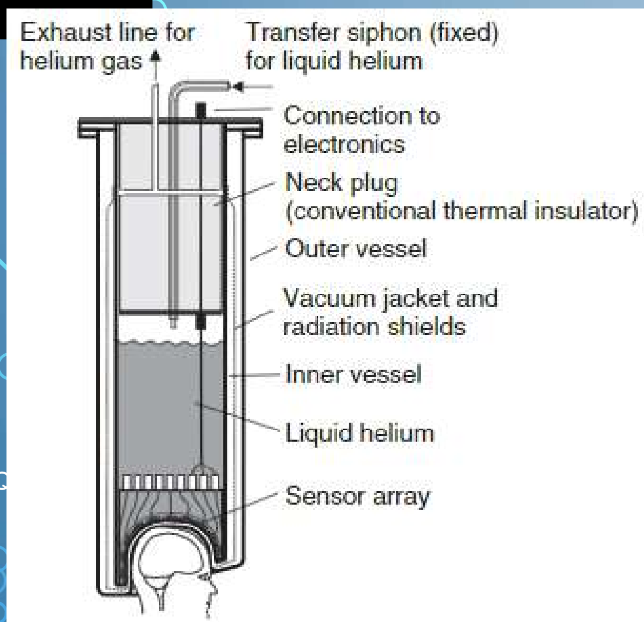
MEG System Components

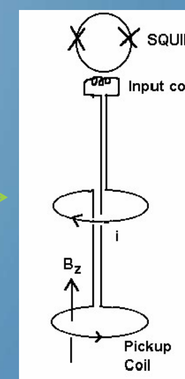
[redacted]

SQ



102 chips inside helmet

3 sensors per chip



sensor design

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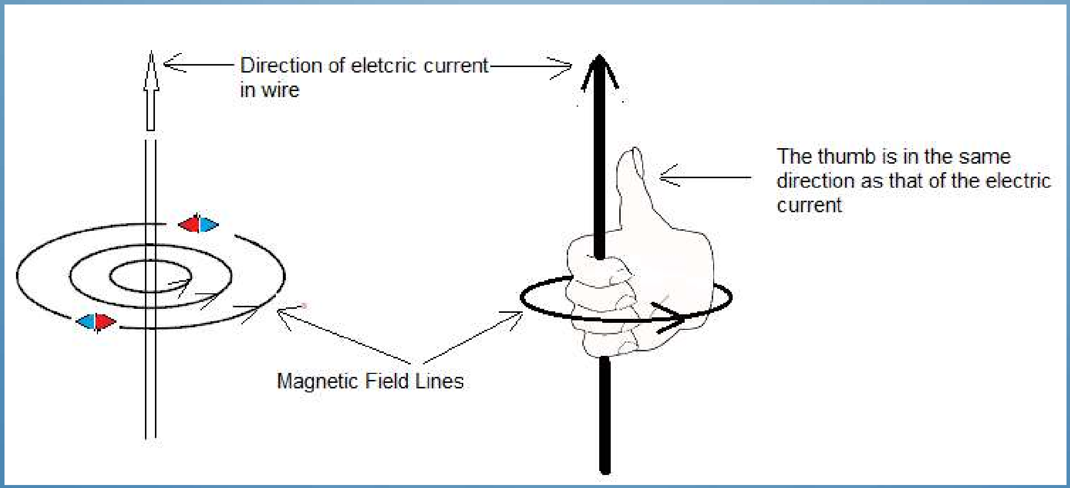
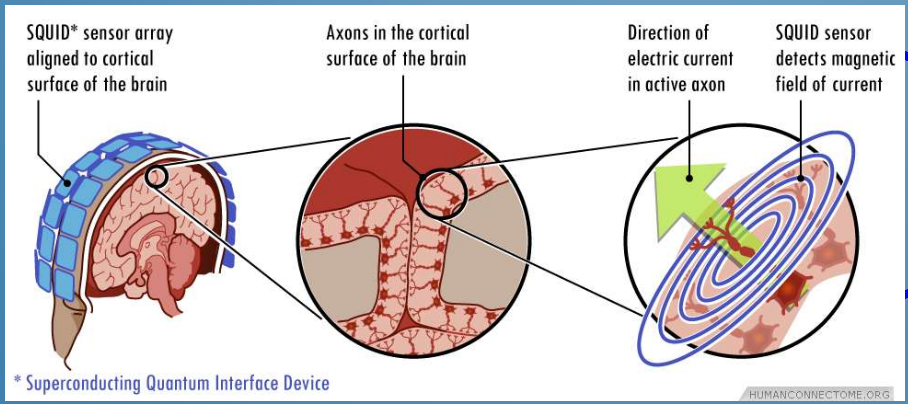
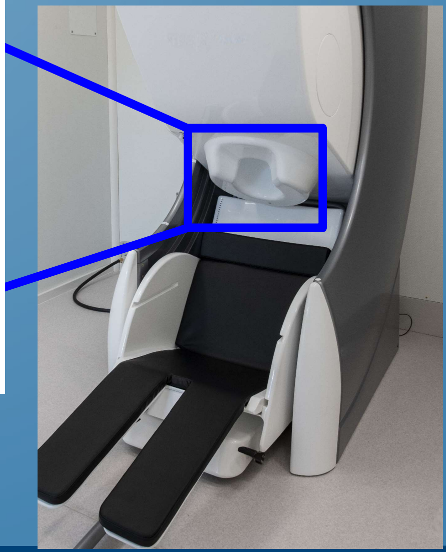
Right hand rule of magnetism (Maxwell's Equation)

- Electric currents produce magnetic fields
- Magnetic field lines make a ring around the direction of current flow



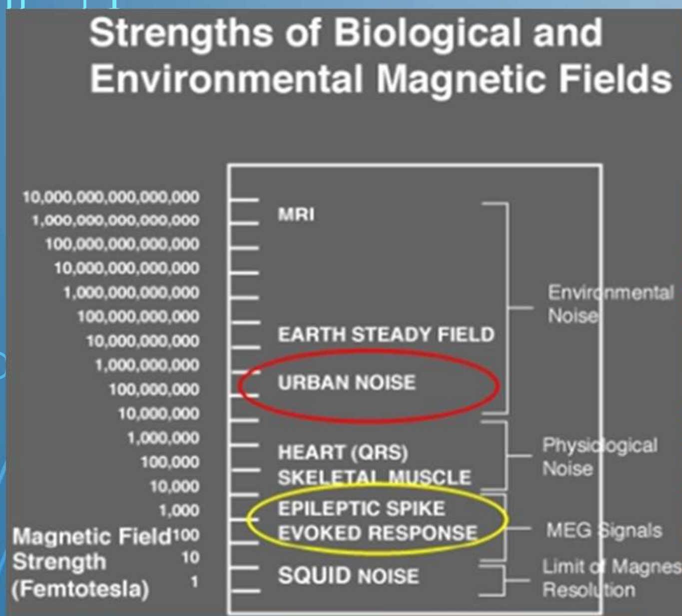
- PSP of tens of thousands of neurons can be detected by the MEG
  - About a 5x5mm patch of cortex

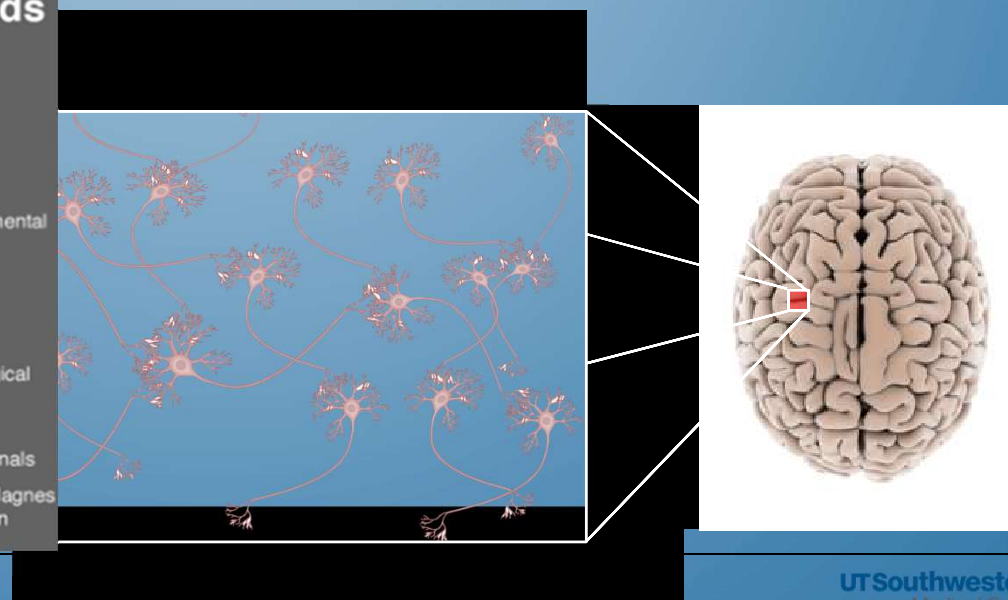




Magnetic Fields of Neurons

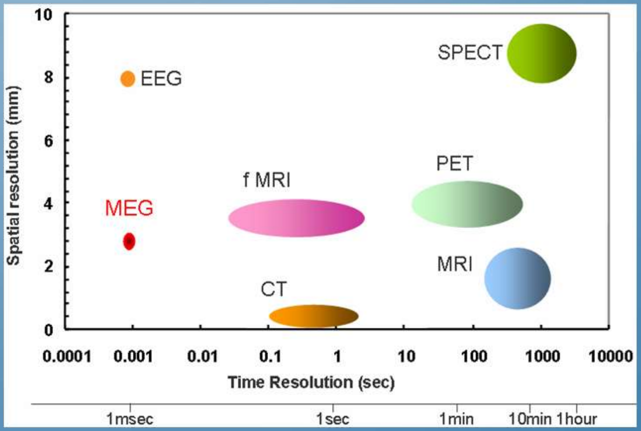
- Brain's magnetic fields are super weak (10^{-15})
- In reality, we are measuring the magnetic fields of populations of neurons (10,000+)





Why measure the neuromagnetic fields?

- Magnetic fields pass unperturbed through the skull and intervening tissues
- Electric currents are susceptible to smearing of signal
- By measuring the field (MEG) and not the charge (EEG), we enhance the spatial resolution by an order of magnitude
  - 2-3 cm with EEG vs. 2-3 mm with MEG



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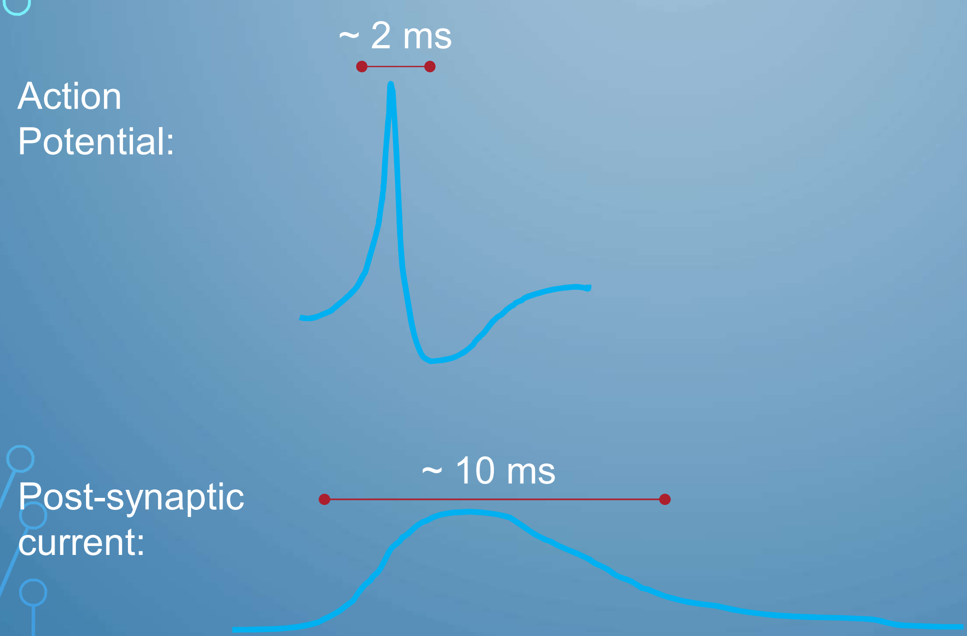
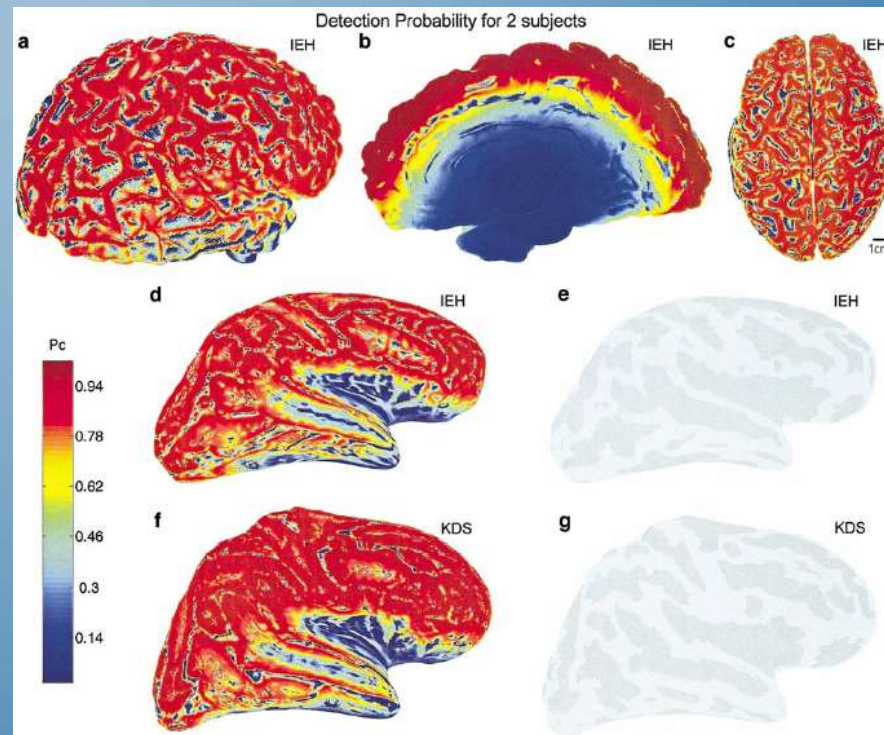
Postsynaptic Dendritic Currents

- Postsynaptic dendritic currents, NOT action potentials, generate the field



Sensitivity of Whole Head MEG

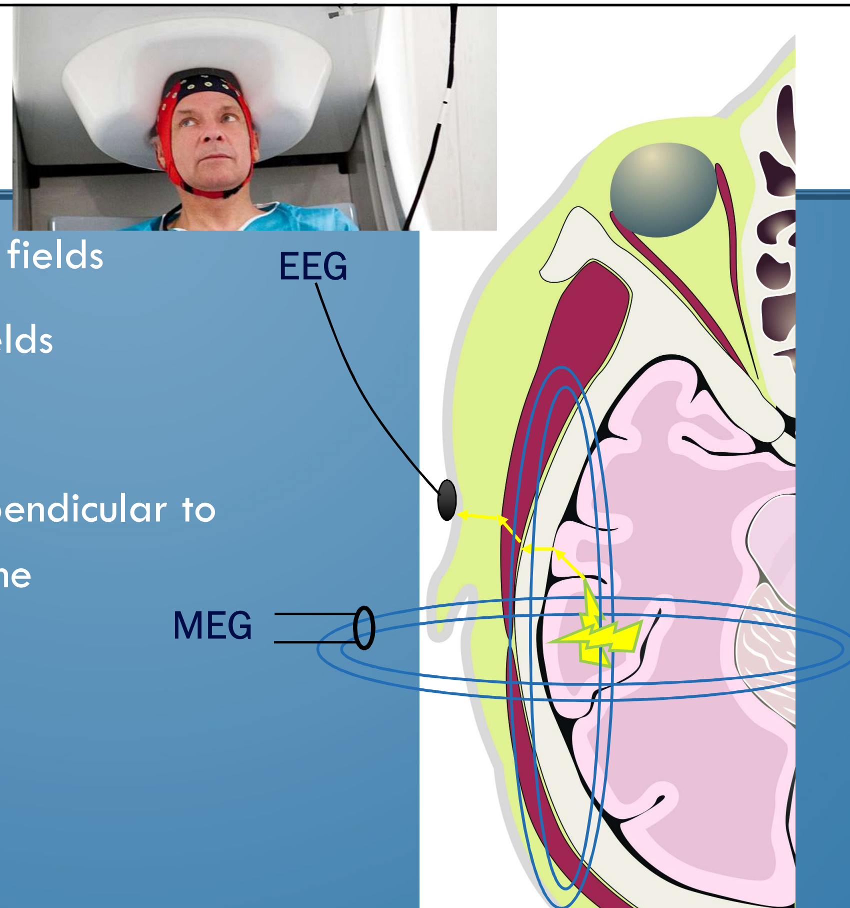
- The strength of a magnetic field falls off exponentially with distance from the source
- Neuromagnetic fields are very weak and the MEG sensors are ~2-3 cm away from the brain surface
- MEG has greatest sensitivity to the cortex



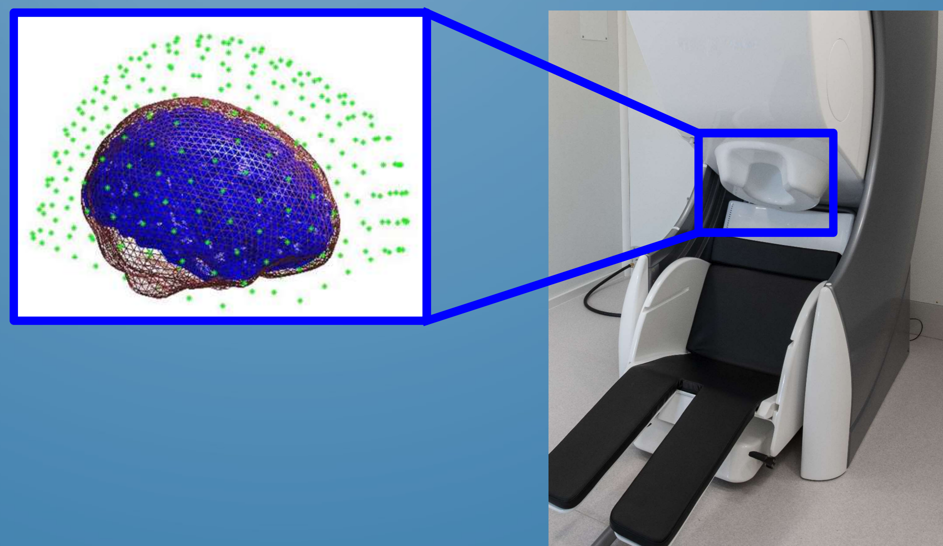
Hillebrand & Barnes (2002)

- MEG measures magnetic fields
- EEG measures electric fields

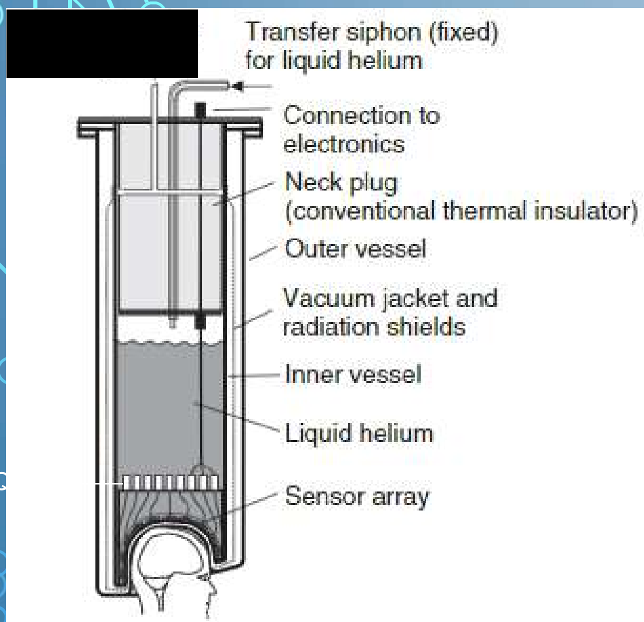
- Magnetic fields are perpendicular to the electric current, per the right-hand rule



- PSP of neurons can be detected by the MEG using
  - Superconducting quantum interference device (SQUID) sensors

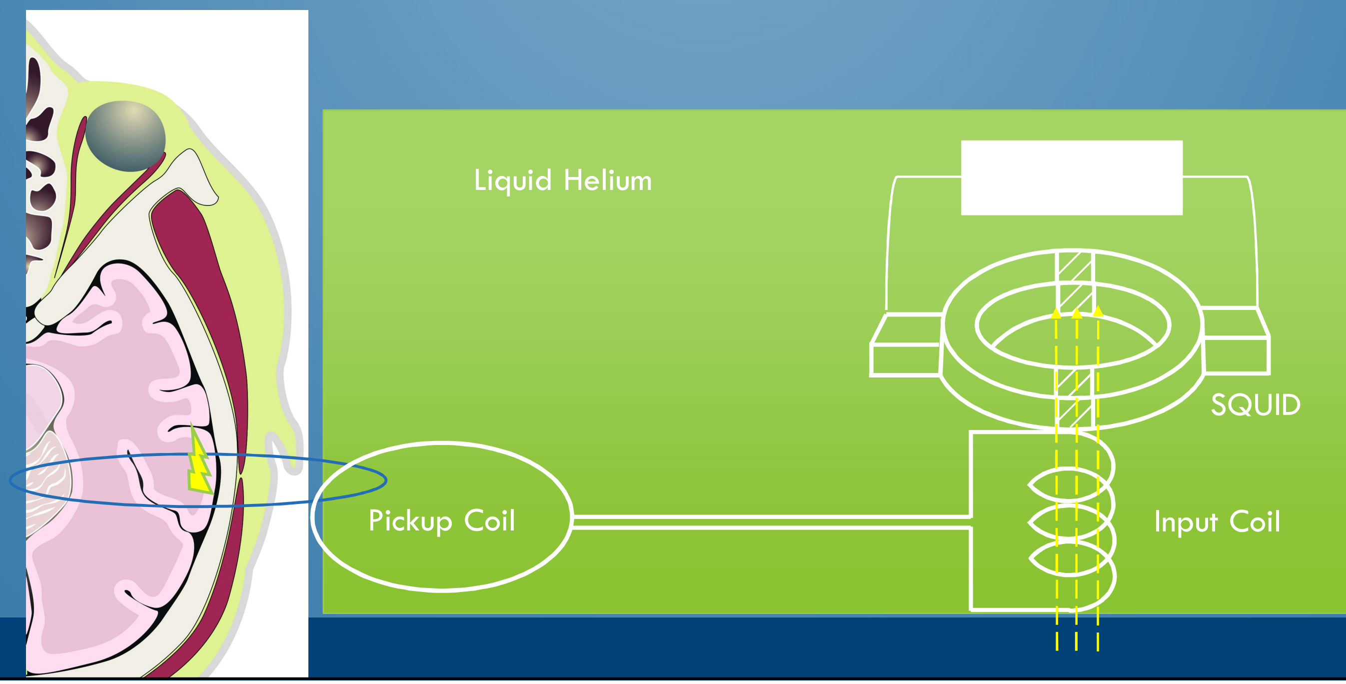


MEG System



- 306 sensors submerged in liquid helium
- Liquid helium = -452° F

- Liquid helium takes resistance of super conducting metals to near absolute zero.



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- There are three types of sensors:
  - Magnetometers
  - Gradiometers
    - Planar
    - Axial

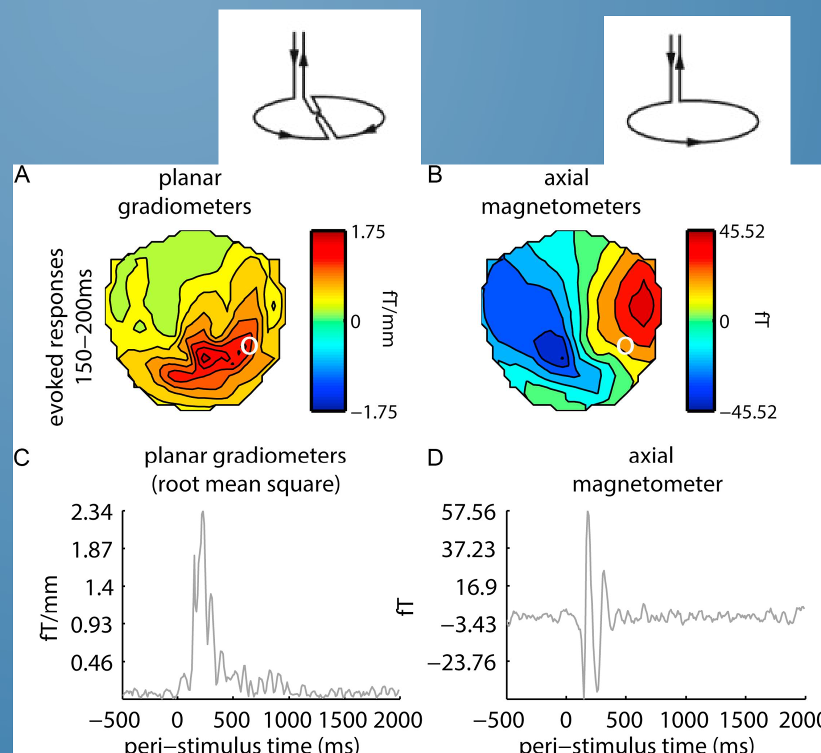
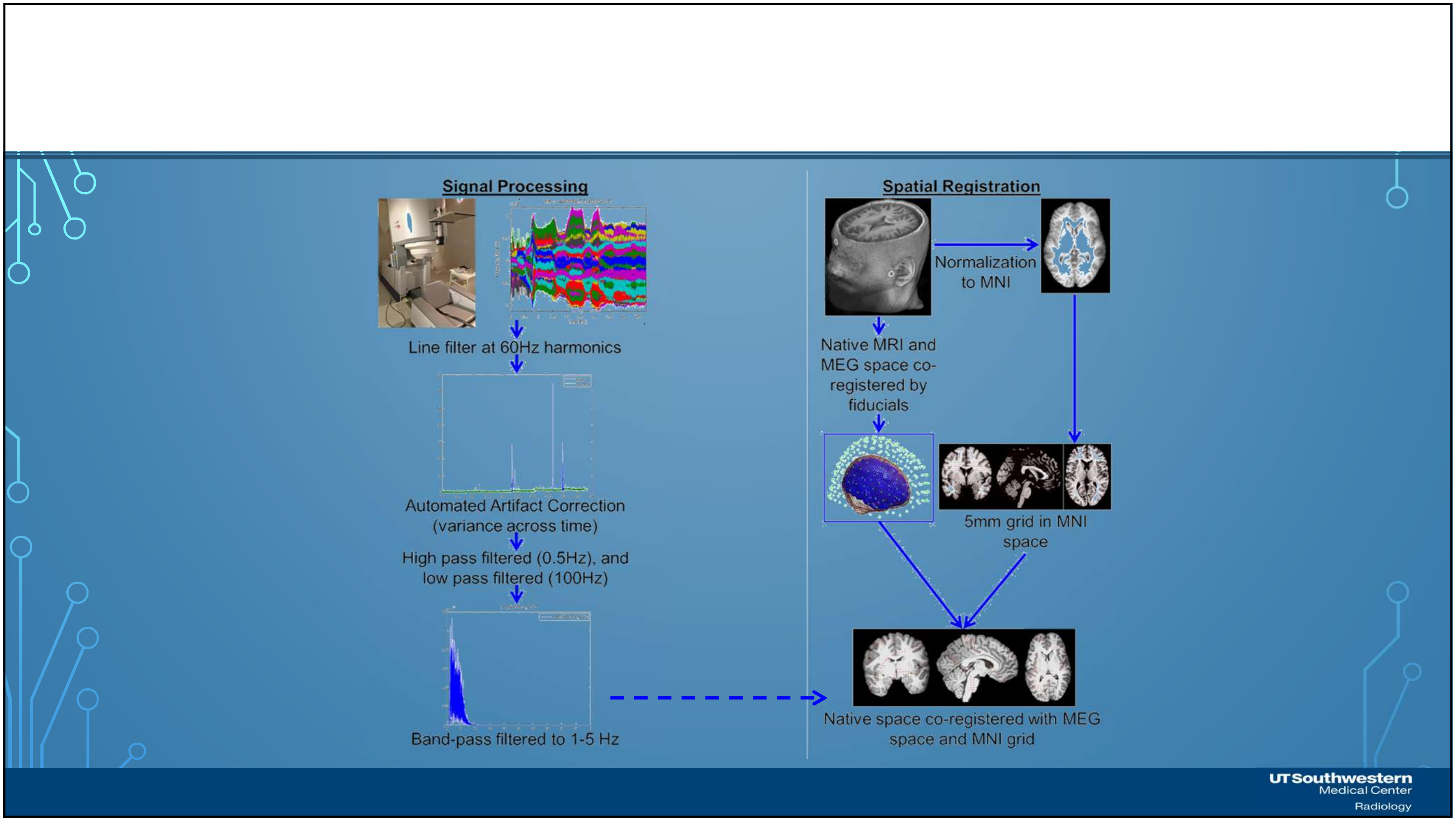


Figure: Furl, N. et al., Neuroimage 2017


Signal Processing
Line filter at 60Hz harmonics
Automated Artifact Correction
(variance across time)
High pass filtered (0.5Hz), and
low pass filtered (100Hz)
Band-pass filtered to 1-5 Hz
Spatial Registration
Normalization
to MNI
Native MRI and
MEG space co-
registered by
fiducials
5mm grid in MNI
space
Native space co-registered with MEG
space and MNI grid
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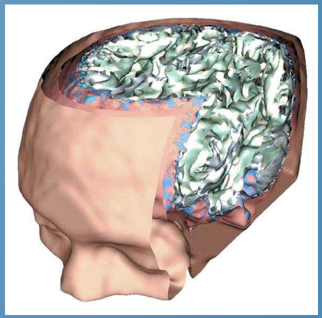
MEG

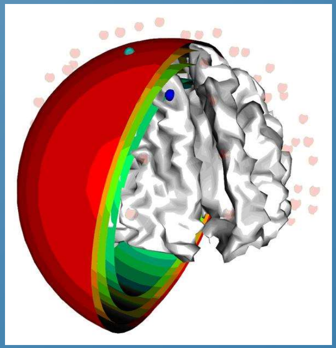
- Temporal resolution <1ms
- Channels >= 300
- Not mobile
- More sensitive to neocortical spike sources
- Better agreement with invasive EEG recordings
- Only detects tangential sources
- Standard spherical head shape model
- MEG dipole analysis is approved for clinical use

EEG

- Temporal resolution <1ms
- Channels ~100
- Long term video recordings
- Good agreement with invasive EEG recordings
- Detects both radial and tangential activity
- Complicated/computationally expensive head model
- Advanced surface EEG analytic techniques not typically approved for clinic

- MEG and EEG are theoretically equal when:
  - Advanced head models are used
  - Same number of channels are used (~300)
- However
  - Advanced head models are not always approved for clinical use/reporting.
  - An EEG with 300 leads is time consuming





(Vatta, Meneghini et al. 2010)

Magnetically Shielded Room

- MEG is performed in a highly shielded room to help block out other magnetic fields in the environment

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TABLE 66-1 Ten Common Evidence-Based Magnetoencephalography (MEG) Indications in Presurgical Evaluation of Patients with Drug-Resistant Epilepsy

Evidence-Based MEG Indication	Evidence-Based Justification	Remarks
1. Lacking or imprecise hypothesis regarding a seizure onset	Additional nonredundant localizing information is provided by MEG in about one third of cases undergoing presurgical evaluation.[100,249] MEG-exclusive spikes are seen in 47% of patients without EEG spikes.[250-252] Retrospective MSI-guided review of MRI may disclose previously concealed lesions in up to 50% of patients.[8,88,250] Areas of interictal MEG spiking are associated with PET abnormalities in MRI-negative TLE.[253] ECD properties correlate with cortical thinning in left mesiotemporal epilepsy.[254]	Without MEG, these patients are frequently excluded from a complete presurgical evaluation or may be exposed to extensive invasive investigations that may not be entirely appropriate.
2. Negative MRI with a mesial temporal onset suspected	MSI-guided re-review of MRI may lead to a positive finding in up to 50% of seemingly negative MRIs.[8] MEG can detect mesial temporal spikes in about 85% of patients with mesial TLE.[255] MEG spike orientation may help in distinguishing mesial TLE from lateral TLE.[5,256-260] Spike orientation may predict epileptogenic side across cerebral sulci.[261] Vertical or horizontal MEG spikes in the anterior temporal pole indicate a higher chance of mesial TLE.[255]	MEG findings may help in identifying more surgical candidates, obviate a need for ICM in some cases, or at times lead to a direct resection.
3. Multiple lesions on MRI	An example of this is a patient with TS, where MEG was shown to be more accurate than an ictal scalp EEG[85] in identifying the epileptogenic zone, as well as recognizing the most active lesion (rarely identifiable with a scalp EEG),[85,86,112] and overall very useful in identifying suitable candidates for surgery[5,85,86,262] with a good long-term outcome.[263]	In the not too distant past, these patients would not have been considered for resective surgery. MEG contributed considerably to the change in clinical practice leading to identifying more surgical candidates in TS and similar populations, at times completely avoiding or better planning ICM, and performing more complete resections leading to more favorable surgical outcomes.
4. Large lesion on MRI	Large lesions introduce diagnostic complexity by changing the anatomy and making a scalp EEG unreliable.[5] MEG can identify an (the most) active part of a lesion or perilesional tissue.[5] MEG is more accurate than an ictal scalp EEG in patients with large lesions and altered anatomy.[5] MSI can guide a choice of an optimal access trajectory[264] and helps delineate the extent of resection of the epileptogenic zone.[109]	Because large lesions may not be amenable to complete resections, it is critical to know what part of perilesional areas are (most) active and thus tailor the degree of resection according to the highest likelihood of seizure improvement or full control in spite of incomplete resection.
5. Diagnostic or therapeutic reoperation	Operative or traumatic skull defects distort electric fields,[265] making spike identification difficult[266] and EEG susceptible to erroneous localization.[267] MEG is more accurate than an ictal scalp EEG in patients with altered anatomy because magnetic fields are relatively unaffected by the structure of the skull and MEG sensitivity and localization accuracy remain unaltered.[5]	MEG is not only overall superior to EEG in this setting, but may identify and localize incompletely resected parts of the original target area or a separate previously unsuspected epileptogenic focus (see Figs. 66-3E and 66-5).[100]
6. Ambiguous EEG findings suggestive of "bilateral" or "generalized" pattern	Propagation of interictal epileptiform EEG activity can lead to erroneous source localizations.[268] MEG helps distinguish between the primary focus and propagated activity,[25,269,270] and MEG spikes propagation may have prognostic implications for epilepsy surgery.[270]	These may be among the most complex patients considered for epilepsy surgery. In these settings, a working hypothesis may not be supported sufficiently to accept the risks of ICM, and having a clarification of localizing ambiguity may be a decisive factor in making an optimal decision.
7. Intrasylvian onset suspected	In spite of their overall complex anatomy, the major horizontal intrasylvian cortices (e.g., Heschl's gyrus and planum temporale) facilitate MEG sensitivity to the respective sources.[5] MEG can identify intrasylvian spikes in EEG-negative cases[228,271-273] or a single intrasylvian epileptogenic focus in patients with ambiguous EEG, such as in LKS, where MEG sensitivity is high (68%-100%)[228,274] and MSI-aided surgery may lead to a significant clinical improvement.[228,273]	Without MEG, these patients are frequently excluded from a complete presurgical evaluation or may be exposed to extensive invasive investigations that may not be entirely necessary.
8. Interhemispheric onset suspected	MEG can detect spikes from the interhemispheric area,[223,275,276] is more sensitive to frontal[277] and occipital[278] sources than EEG, and can lateralize medial frontal[276] and occipital[278] spikes even when the EEG is nonlateralizing. Almost 90% of ECoG spikes were associated with MEG spikes.[223]	Because frontal lobe epilepsy has the worst surgical outcome, and various EEG ambiguities may occur, the acquisition of additional noninvasive localizing information is essential.

TABLE 66-1 Ten Common Evidence-Based Magnetoencephalography (MEG) Indications in Presurgical Evaluation of Patients with Drug-Resistant Epilepsy—cont'd

Evidence-Based MEG Indication	Evidence-Based Justification	Remarks
9. Insular onset suspected	Because it is suspected that insular epilepsy may be accountable for failures of a significant number of TLE surgeries,[5,279] and MEG spikes can be captured in over 64% of patients with insular epilepsy,[271,280-282] MEG findings can improve diagnostic accuracy, substantiate ICM, and justify its risks.[5,271]	As a result of the low sensitivity of scalp EEGs to insular spikes, and the suspected frequent misdiagnosis of insular epilepsy as temporal, leading to a failure of anterior temporal lobectomy, the value of MEG is very high and may be decisive in justifying the risks of ICM and avoiding a surgical failure.
10. Negative (i.e., spikeless) EEG	MEG identifies interictal spikes in 47% of patients without EEG spikes.[250-252]	It is very important to avoid a misconception that patients with no spikes on EEG are unlikely to benefit from MEG and that MEG should be ordered only for "frequent spikers."

ECD, equivalent current dipole; ECoG, electrocorticography; EEG, electroencephalography; ICM, intracranial monitoring; LKS, Landau-Kleffner syndrome; MRI, magnetic resonance imaging; MSI, magnetic source imaging; PET, positron emission tomography; TLE, temporal lobe epilepsy; TS, tuberous sclerosis.