Toward a more accurate delimitation of the epileptic focus from a surgical perspective

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Topic 4: New targets for innovative diagnostics and treatment

Presurgical epilepsy evaluation

Candidates: Patients suffering from pharmacoresistant epilepsy
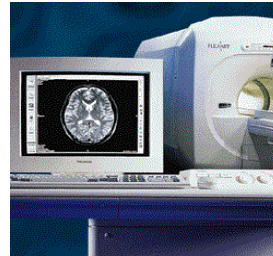Around 0.2% of the population

Principal question: Where is the focus localized and can it be resected?

Principal methods used: Phase 1: Non-invasive
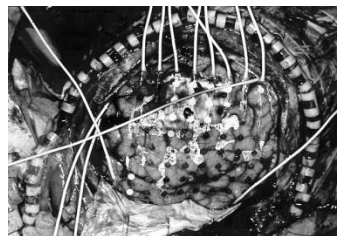
Video- EEG   MRI   PET / SPECT
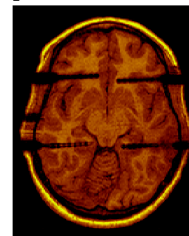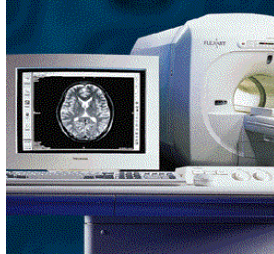

Phase 2: Invasive (in about 20%)

Subdural electrodes   Depth electrodes

About 10-15% of difficult-to-treat patients become surgical candidates

Presurgical epilepsy evaluation

Candidates: Patients suffering from pharmacoresistant epilepsy
Around 0.2% of the population

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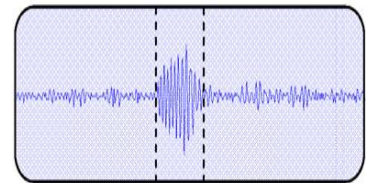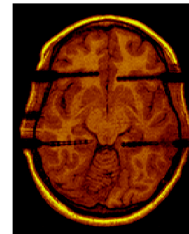**Video- EEG**   **MRI**   **PET / SPECT**   **EEG- fMRI**   **High density EEG***

* Or MEG in selected centers
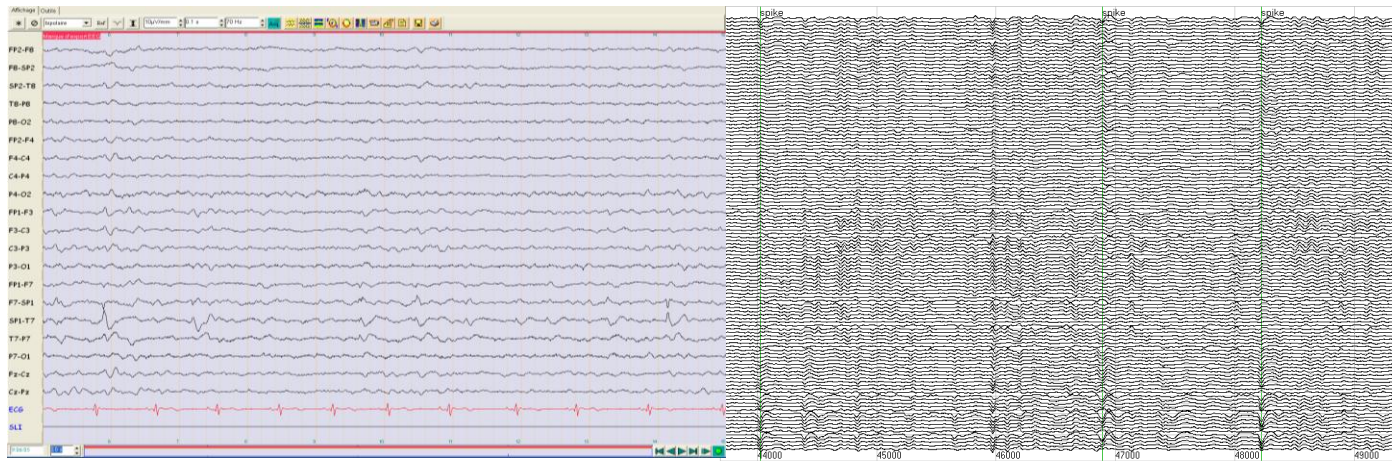
Phase 2: Invasive (in about 20%)
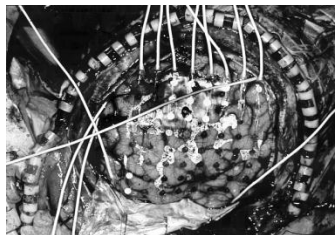
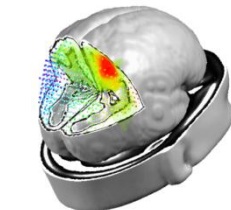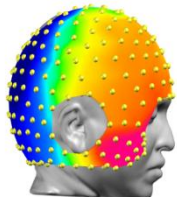**Subdural electrodes**   **Depth electrodes**

ESI possible with any electrode array
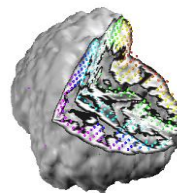
128 – 256 channel net

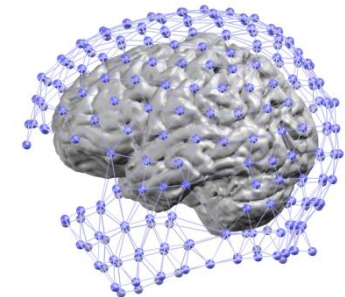mounting time: 10-20 minutes
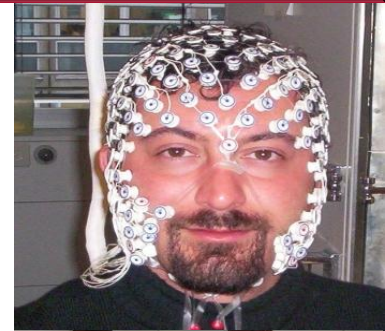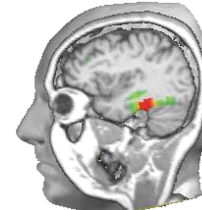
$$\Phi = G\,L\,J_v + n$$

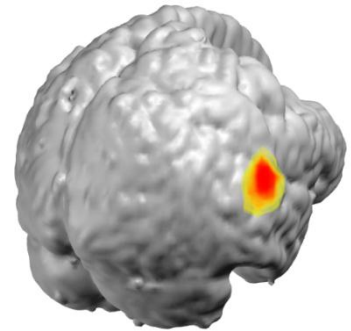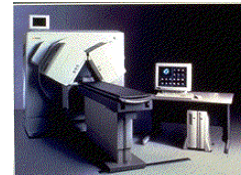**Inverse solution calculation**
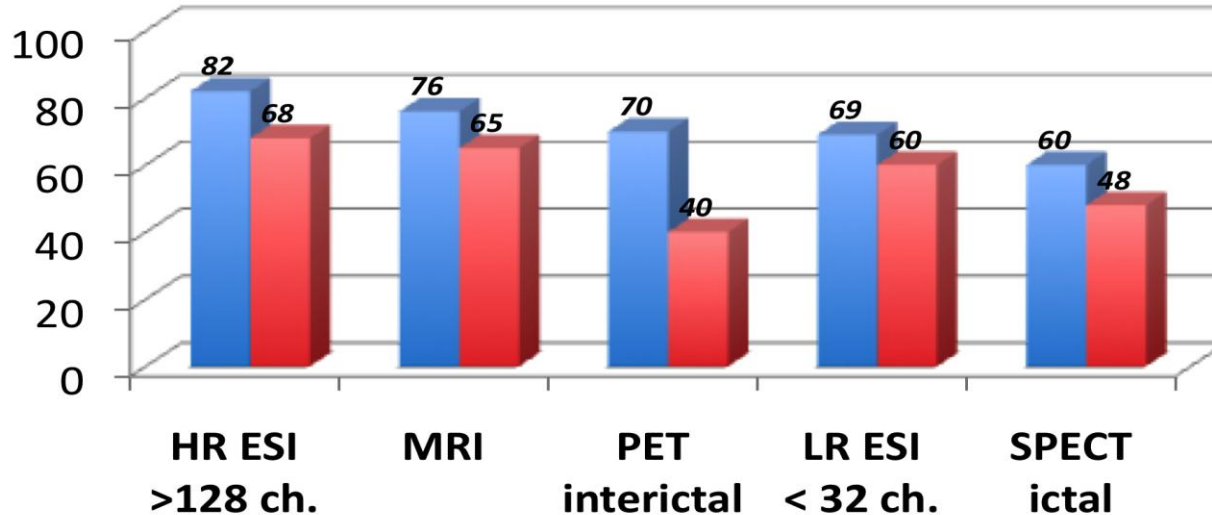
Source model   *Head model*

Clinical yield of ESI: localizing the interictal spikes

A prospective study of 152 operated epileptic patients with > 1 year follow-up

	Sensitivity in SOZ & seizure free	Specificity outside SOZ & not seizure free
HR ESI >128 ch.	82	68
MRI	76	65
PET interictal	70	40
LR ESI < 32 ch.	69	60
SPECT ictal	60	48

**Very good precision :   in children and adults
in temporal and extratemporal foci
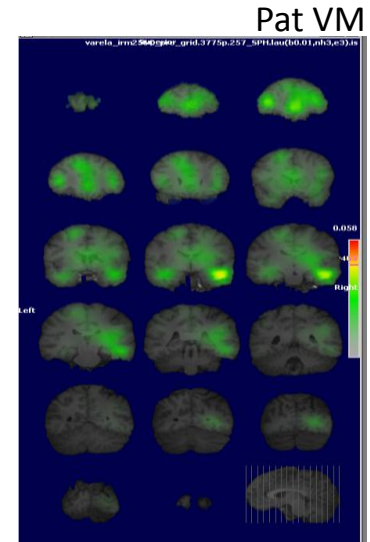in MRI-negative epilepsy**

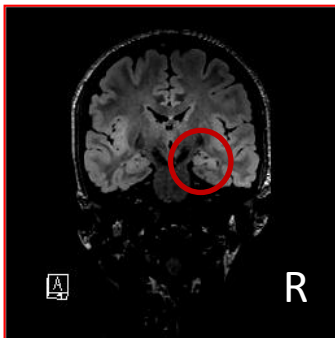Brodbeck et al , *Brain*, 2011

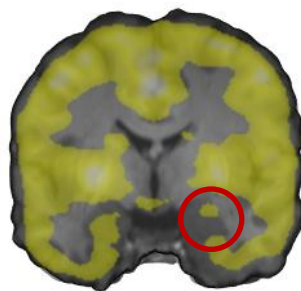# Bringing all information together …

Whole body PET-MRI

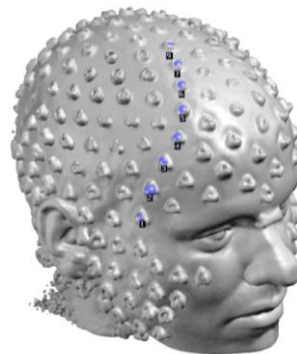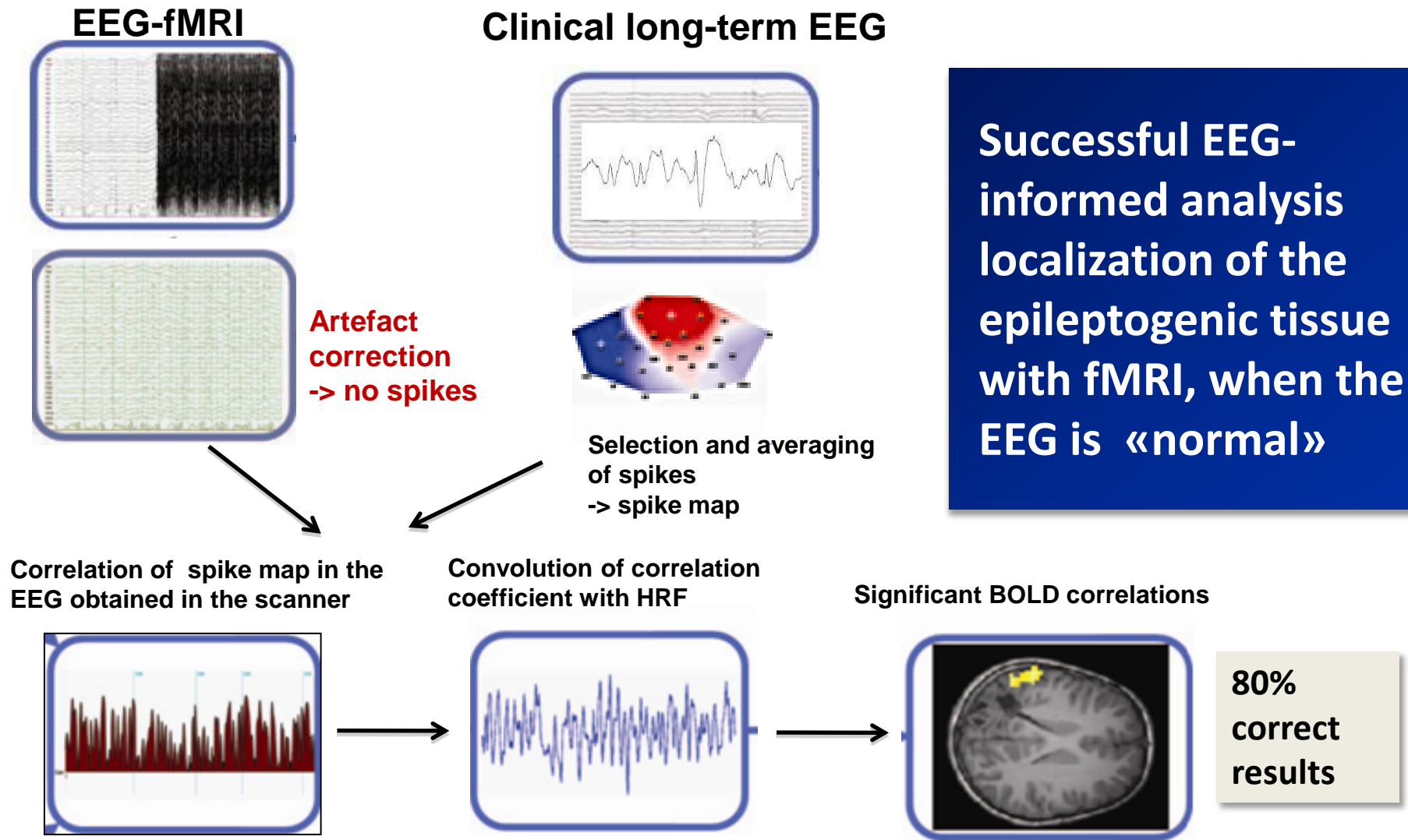fMRI with 256 MR-compatible EEG channels

Pat VM
ESI

MRI

PET
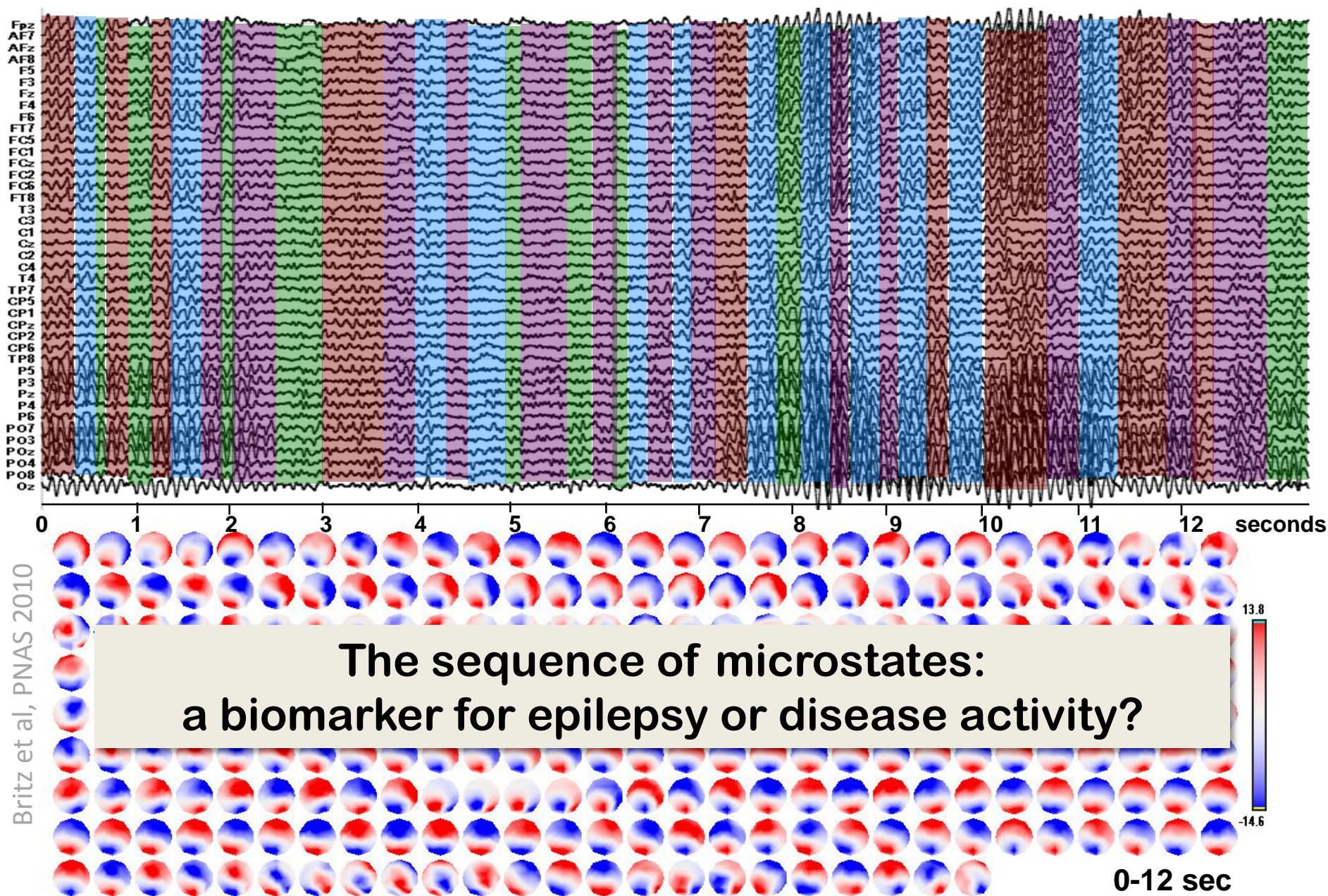

256 channel EEG

The likelihood to benefit from surgical treatment is markedly higher if more imaging modalities are concordant.

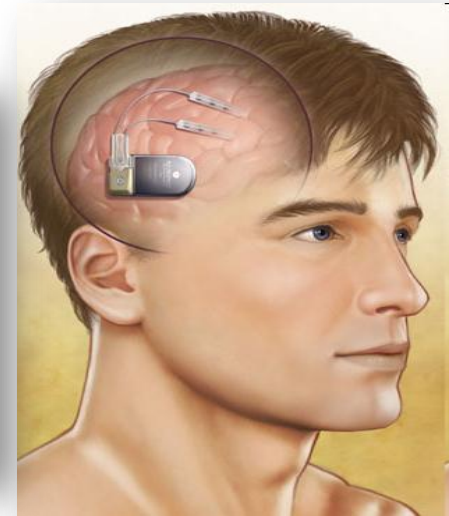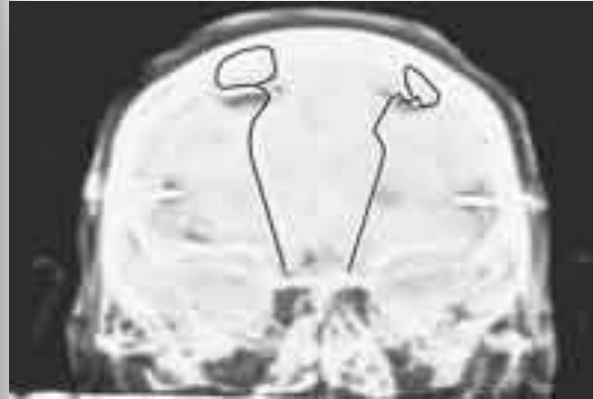Kurian et al, 2007; Knowlton et al, 2008; Huppertz et al, 2008

ESI: a powerful technique to identify invisible epileptogenic activity

EEG-fMRI

Artefact correction -> no spikes

Clinical long-term EEG

Selection and averaging of spikes -> spike map

Successful EEG-informed analysis localization of the epileptogenic tissue with fMRI, when the EEG is «normal»

Correlation of spike map in the EEG obtained in the scanner

Convolution of correlation coefficient with HRF

Significant BOLD correlations

80% correct results

Grouiller et al., *Brain* 2011

**The sequence of microstates:
a biomarker for epilepsy or disease activity?**

0-12 sec

# Intra- and extracranial neuromodulation in epilepsy

- Optimal patient profile unknown: up to know **palliative treatment: only 50% of patients benefit**
- Optimal stimulus parameters (pulse shape, frequency, intensity etc.) and best stimulated sites unknown
  - « One for all » or individually tailored?
- Need for powerful epilepsy biomarkers

# Intra- and extracranial neuromodulation in epilepsy
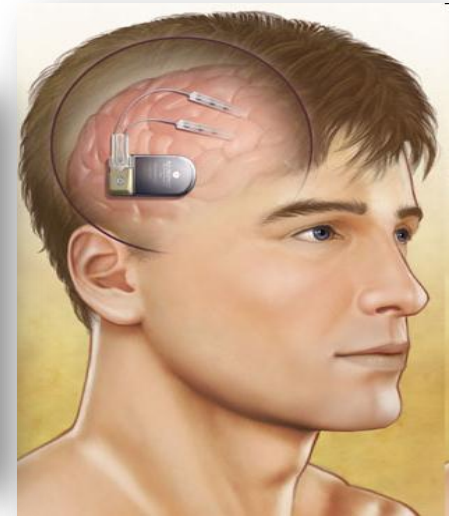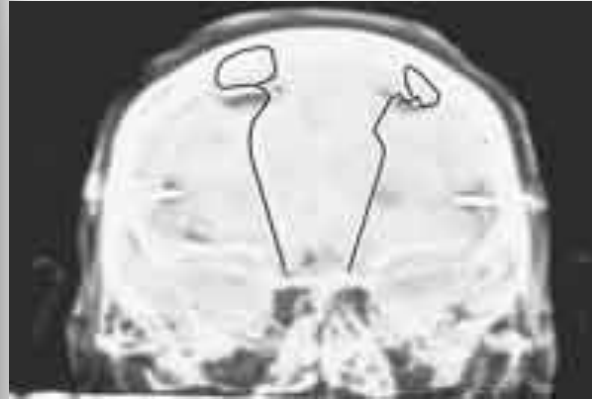
- Optimal patient profile unknown: up to know **palliative treatment**

- First successful feasibility study on a seizure prediction device

  - **Significant disprepancies between patient report and recorded seizures**
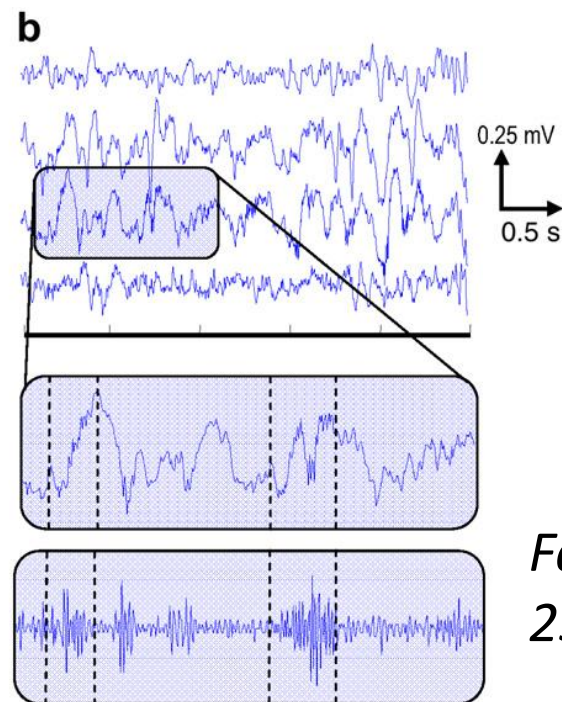
Cook et al, Lancet Neurology 2011
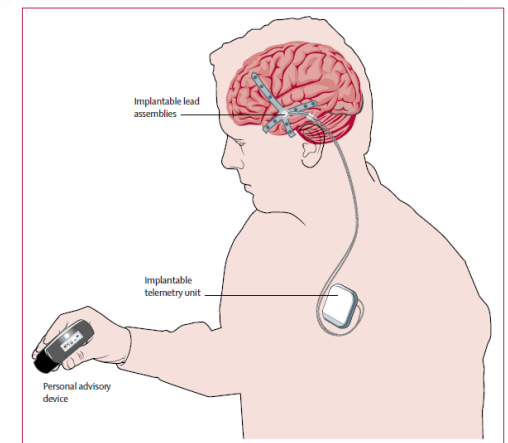
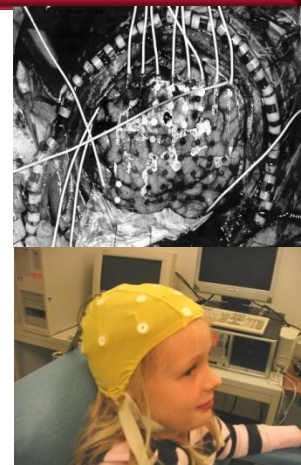**RECORDING NEURONAL ACTIVITY DIRECTLY IN THE HUMAN BRAIN**

High frequency oscillations: a marker for the seizure onset zone (SOZ)?
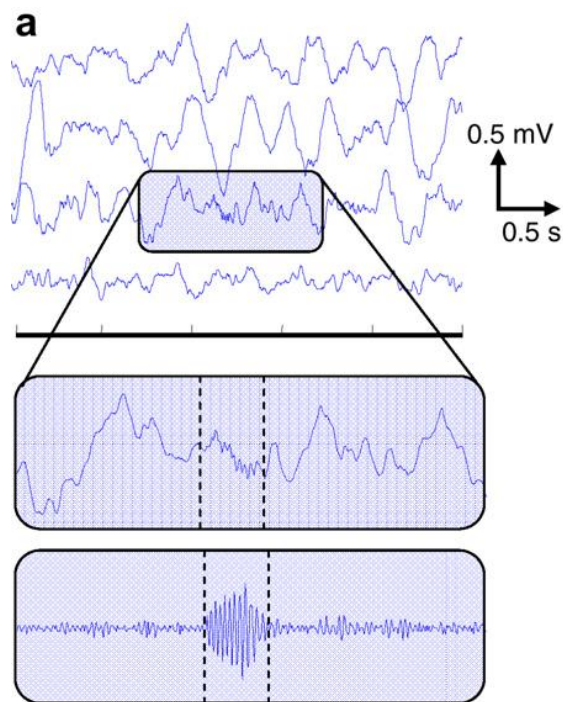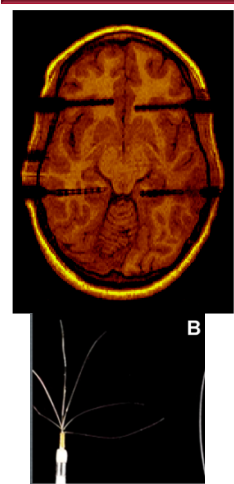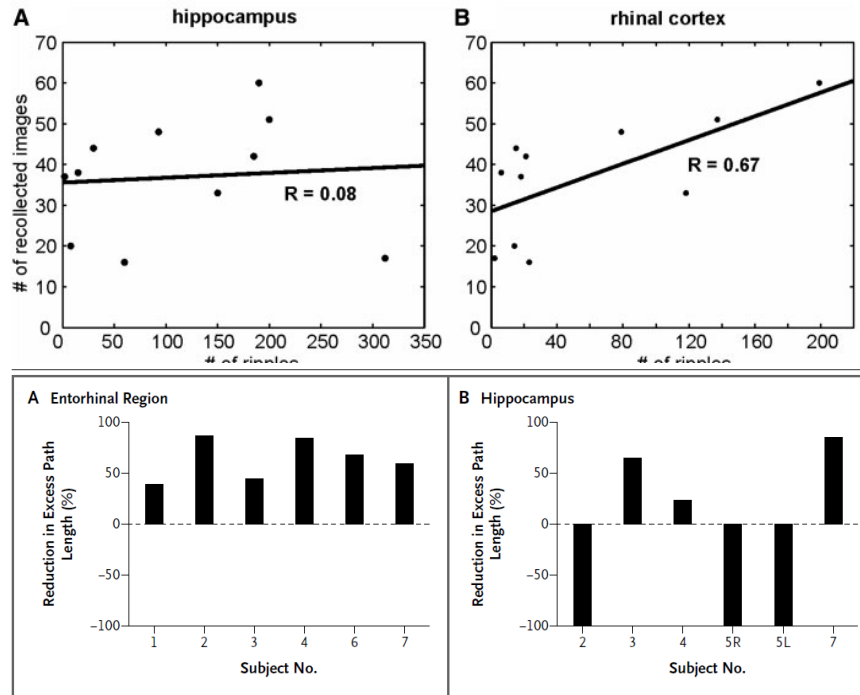

*Ripples
80-250 Hz*

*Fast Ripples
250 – 600Hz*

- HFO rates were more often linked to the SOZ than to the lesion and remote cortex
- *But: HFO are also found in non-epileptogenic cortex and during memory processes*

Jacobs et al., Brain 2009; Staba et al., Epilepsia 2007; Ziljmans et al, Ann Neurol 2012, Urrestarazi et al, Brain 2007, Blanco et al, Brain 2011 n

# Epilepsy research: discoveries beyond epilepsy

Presence of HFO (ripples 80-140 Hz) in the rhinal cortex was positively correlated with recognition memory

Stimulation of the human rhinal cortex through intracranial electrodes leads to better spatial memory
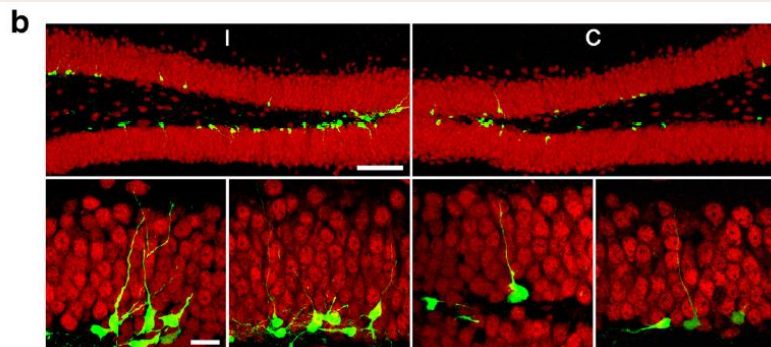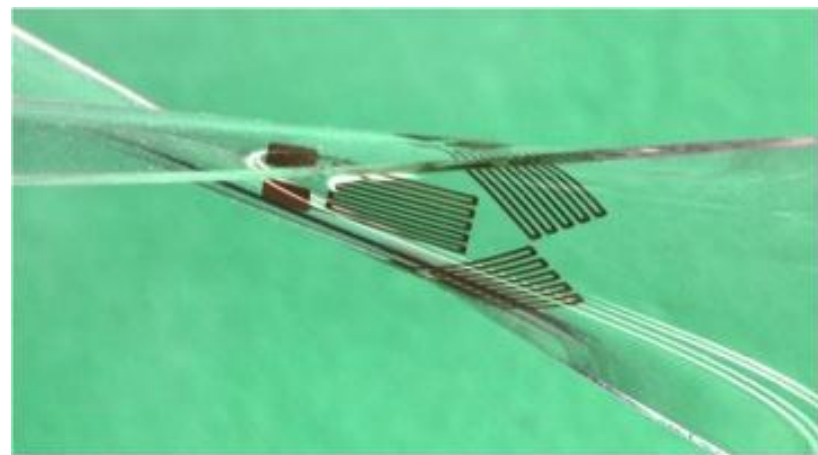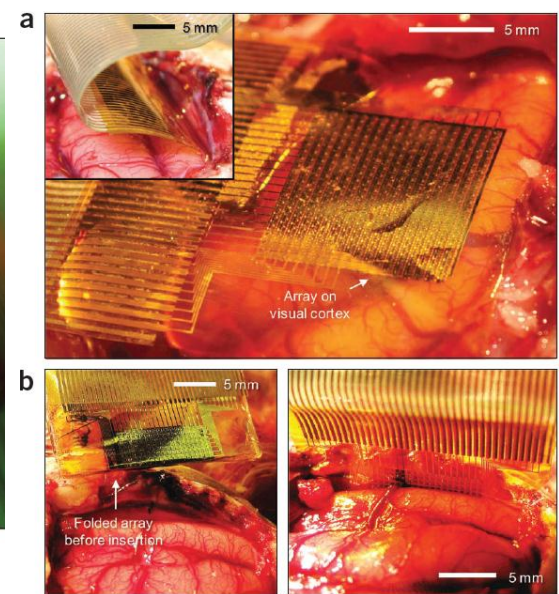
Stimulation of the entorhinal cortex leads to proliferation of new neurons, surviving several weeks
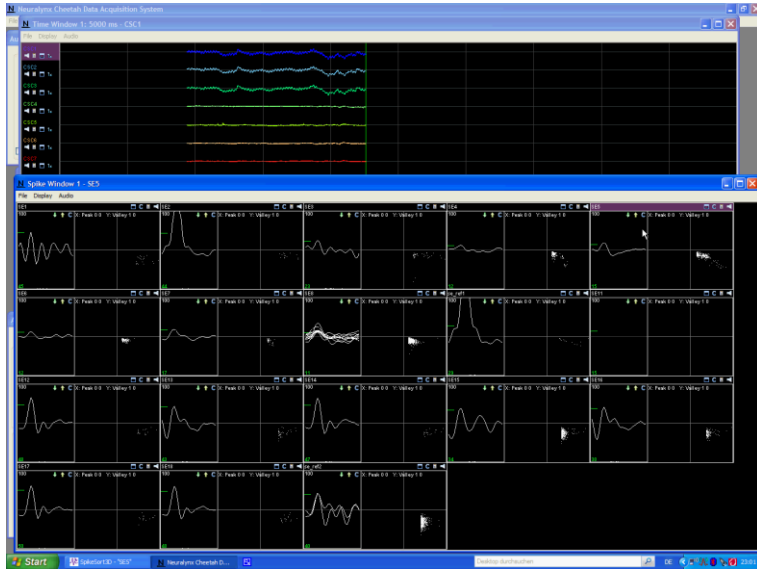
Axmacher et al, Brain 2008; Stone et al, J Neurosci 2011; Suthana et al, NEJM 2012
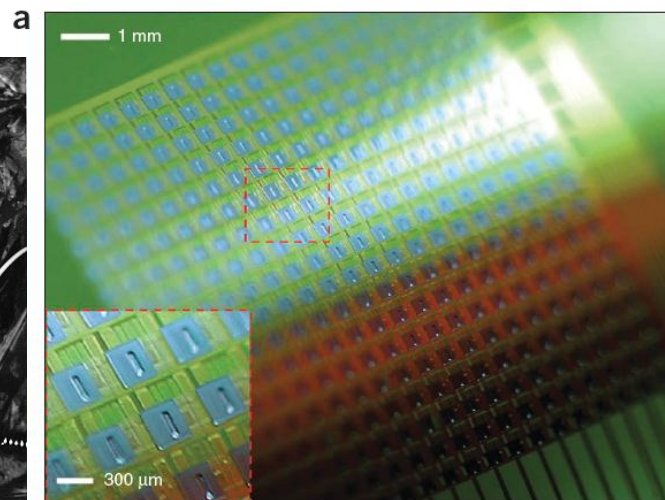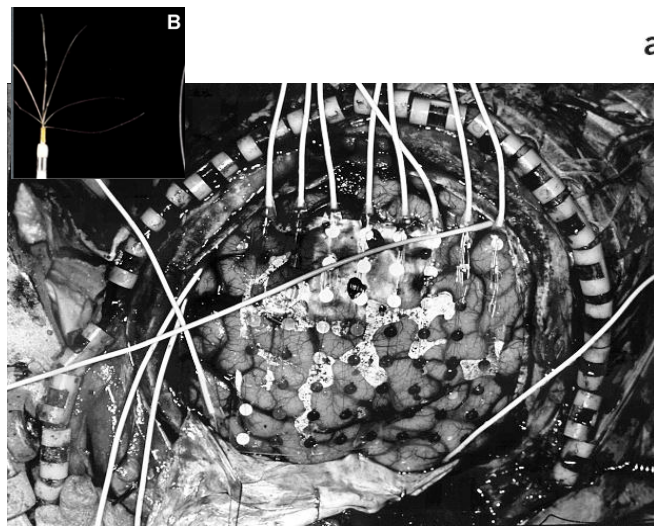
360 channel intracranial EEG

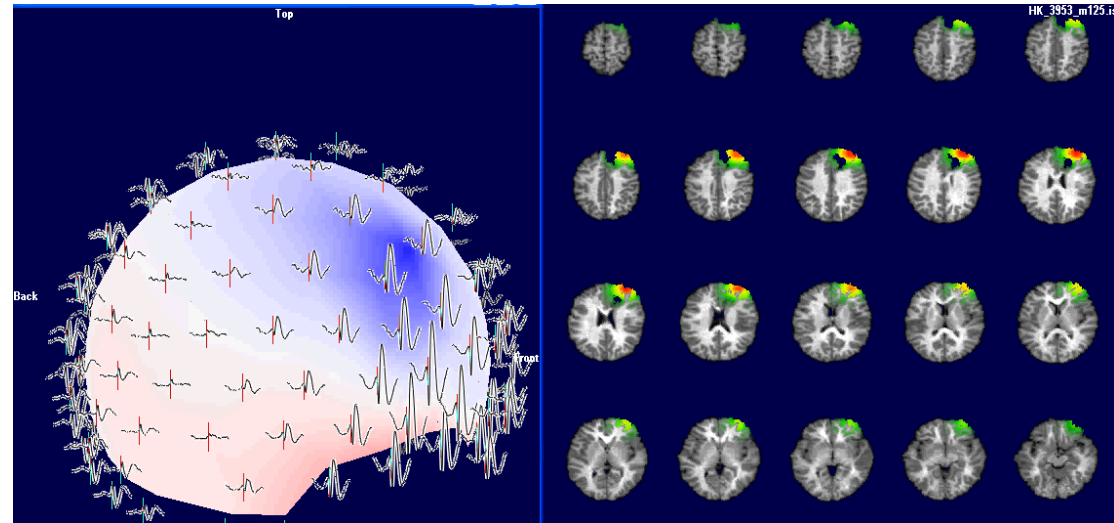Viventi et al, Nature Neurosci 2001; Courtesy of Prof Lacour, EPFL

Viewing the human brain at work

Microelectrodes
Diameter 17-50 µm
Distance < 150 µm

Scalp electrodes
Diameter 0.5 cm
Distance 1-4 cm

Pat MM

To obtain a more precise delimitation of the epileptogenic focus:

- Combine structural, metabolic and neurophysiological information
- Develop strategies to characterize large- and microscale networks
- Develop more powerful electrode types