

## **Supplementary material**

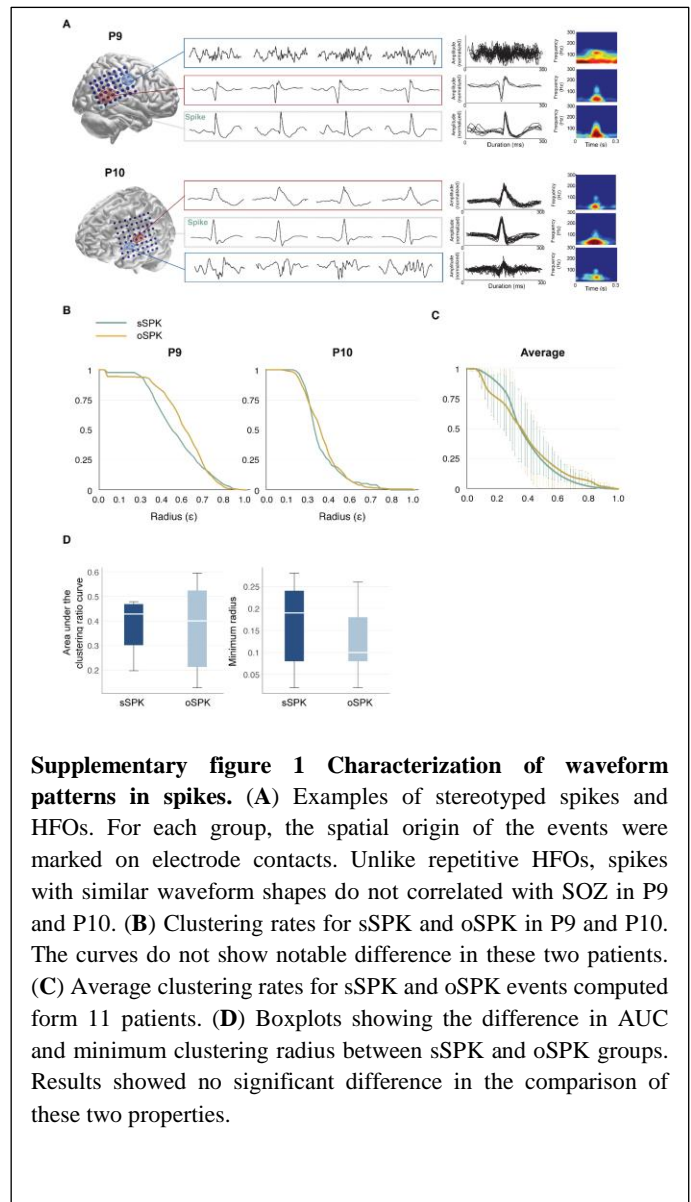
### **Functional Mapping of Cortex and Anaesthesia Procedures in Control Subjects**

In five control subjects, the contact points on the grids are stimulated in increments of 1 mA starting at 1 mA to elicit a response. These intraoperative recordings are carried out routinely as a baseline to confirm the presence of functioning cortex in and around the brain tumor. In our cases, each control subject was able to move instructed hand or finger or responded to the stimulus in the correct way in the OR and the detected functional areas through DCS were in accordance with anatomical landmarks and therefore these areas are accepted as normal functional regions. The HFO waveforms captured from the functional region of epilepsy patients and control subjects were similar and did not differ significantly.

Anesthesia technique and medications: In our surgeries, the asleep-awake-asleep anesthetic technique was adopted as described by Huncke et al. 1998. After MRI-compatible patient monitors (in vivo) are applied, the patients received 4 mg of ondansetron, 20 mg of famotidine, and 10 mg of metoclopramide, all given intravenously. In order to induce anesthesia, we intravenously administered 50 – 100 mg of propofol plus 0.1 – 0.2  $\mu\text{g}/\text{kg}/\text{min}$  of remifentanyl with or without 50 mg of rocuronium. After the craniotomy flap is opened, the dura mater is blocked with a 1:1 mixture of 1% lidocaine and 0.25% bupivacaine. Once the dura is opened, the patient is gradually awakened. At this point, all medications are stopped, usually with a 30-minute lead time requested. Hence during the awake portion in general the patient has no medications administered. This helps in better monitoring of the patient's motor and speech responses in a more reliable manner. If the patient becomes uncomfortable during the resection, remifentanyl (0.02  $\mu\text{g}/\text{kg}/\text{min}$ ) is restarted. Once the awake testing portion is complete along with resection of the tumor, the patients requiring reintubation with the laryngeal mask airway are re-sedated with the application of general anesthetic.

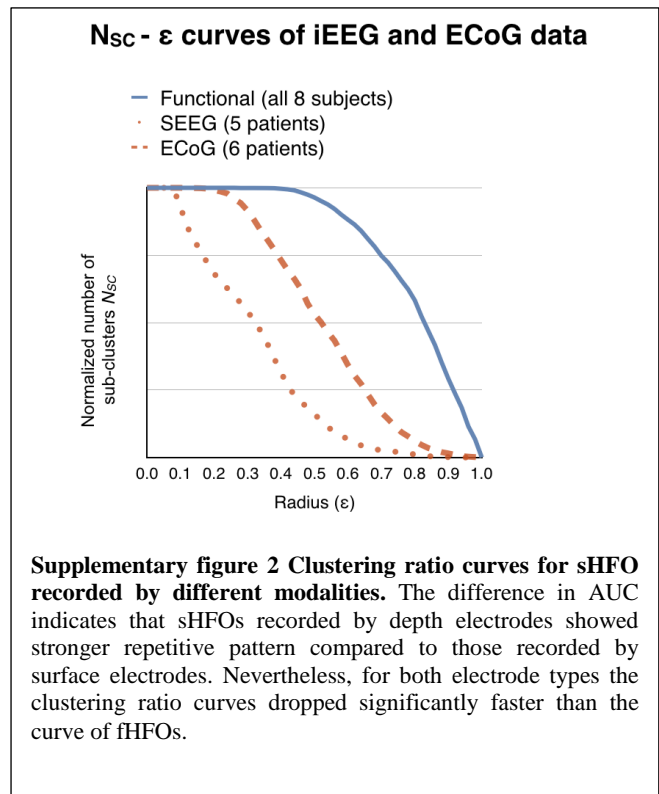
## Characterization of interictal spikes

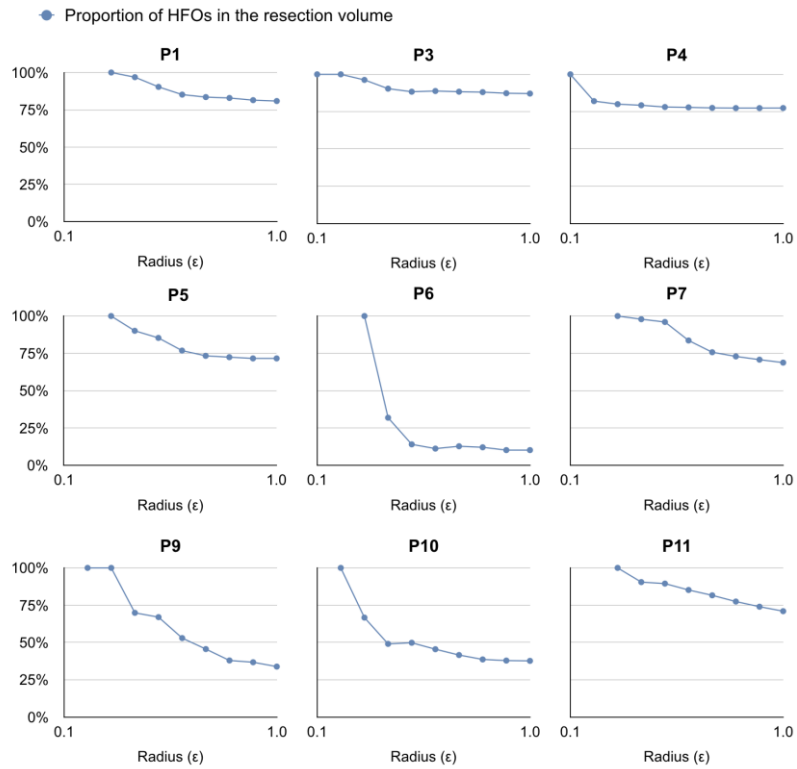
In order to answer whether epileptic spikes inside the SOZ tend to be more repetitive in shape compared to those recorded from outside the SOZ, we applied the same unsupervised method to explore the waveform patterns in spikes in P1 – P11. Overall, 11010 spikes were isolated by GMM clustering in 11 patients, which were then labeled as sSPK (if originated from the SOZ) or oSPK (if outside the SOZ). Supplementary Fig. 1 illustrate the difference in waveform patterns of spikes detected inside and outside the SOZ. As it is shown in supplementary Fig. 1A, repetitive spike cluster with highest signal similarity did not correlate with seizure onset channels. In supplementary Fig. 1B and 1C we prove the clustering ratio curves for sSPK and oSPK events in P9 and P10, as well as the average plot computed from all 11 patients. The small difference in clustering rates between two spike groups indicated that interictal spikes typically presented with repetitive waveforms regardless of their spatial origins. The AUC and minimum clustering radius of sSPK and oSPK presented no significant difference (supplementary Fig. 1D), suggesting the infeasibility of using stereotyped waveforms of spikes to identify the SOZ.



## Electrode effect

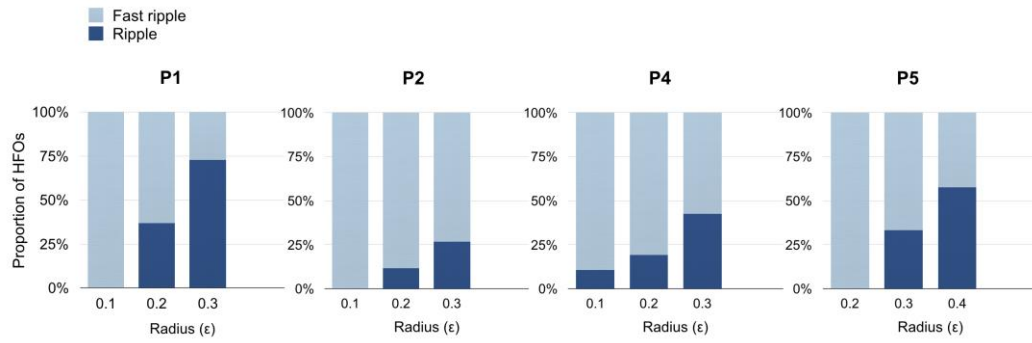
In this study, five patients with epilepsy had their seizure onset regions sampled by depth electrodes and 6 were recorded by surface grids. We compared the clustering ratio curves of sHFO recorded by these two different modalities, and noted a significant difference in the AUC between depth electrodes and surface electrodes ( $P < 0.05$ ). Nevertheless, HFOs recorded from the seizure onset zone (sHFOs) by both modalities showed stronger repetitive pattern compared to fHFOs ( $P < 0.01$ ). The group difference between sHFOs captured in surface and depth recording is provided in Supplementary figure 2.





**Supplementary figure 3 Proportion of HFOs clustered at different radius ( $\epsilon = 0.1 - 1$ ) inside the volume of resection.**

In nine patients, the HFO analysis was performed in relation to the resection volume based on clinical reports. The percentage of HFOs clustered by minimum radius (the most “repetitive” HFOs) achieved 100% in all patients. By contrast, 60% of the entire HFO population (10% – 87% per patient) were located outside the volume of resection.



**Supplementary figure 4 Proportion of stereotyped FR versus ripple clustered by different radius.** FRs were recorded in four patients, and consistently present a higher degree of signal similarity compared to ripples, as a small radius always identifies FRs at the first place. On the contrary, the proportion of ripples gradually increases as the level of intra-cluster similarity decreases.