

Subdural Pharmacotherapy Device for the Treatment of Intractable Focal Epilepsy

Medical Intractability affects approximately 30-40% of patients with epilepsy. It is estimated that of the total pool of surgical candidates, about 140,000 in the US are not candidates for surgery due 1) location of the epileptogenic focus (overlapping verbal, visual or motor areas), 2) widespread areas of epileptogenesis, 3) or bilateral foci. No approved therapies are available for these patients.

The Subdural Pharmacotherapy Device was originally designed by one of our scientist and named HNP (US Patent #6,497,69). The concept and basic architecture is of a fully implantable device to deliver small concentrations of potent anticonvulsant drugs or potentially simple peptides. The entire idea is based on the simple principle that one can achieve very high concentrations of a given drug avoiding systemic side effects. The 3 distinguishing feature of the SPD are the following: First, unlike all currently used neuroprostheses, it delivers a drug solution, instead of electrical stimulation, to achieve therapeutic effects. Therefore, as a “hybrid neuroprosthesis”, the SPD has the potential to pharmacologically correct the patient’s specific neurochemical abnormality in the epileptogenic zone, without disturbing the molecular systems not involved in seizure genesis. Second, the SPD delivers the drug solution into the neocortical epileptogenic zone(s) “transmeningeally, through the subdural/subarachnoid space. Thus, the device causes no damage to neural tissue with penetrating catheters or cannulas, yet able to deliver the therapeutic compound over the entire area of the epileptogenic zone(s). Third, the SPD is equipped with subdural EEG electrode contacts and RF communication capability. These features allow the transmission of electrophysiological data from the very site of drug delivery, for both post-implantation fine-tuning of the delivery parameters and periodic monitoring of the functional integrity of the device.

The SPD concept has been tested for the past 6 years in rodents and primates. A number of AED’s and other drugs have been tested in rodents. Muscimol was selected as the drug-of-choice for the subdural SPD because (a) it is water soluble, (b) stable in solution for months, (c) diffuses from the cranial subdural/subarachnoid space into the underlying cortical tissue as rapidly as about 30 seconds, (d) has marked antiepileptic effects upon transmeningeal delivery in as low concentrations as 0.04 - 0.8 mM (0.25 - 5.0 µg dose), without apparent side-effects, (e) it is more potent local antiepileptic drug in the neocortex than GABA, lidocaine, midazolam and pentobarbital, and (f) it is effective in preventing focal neocortical seizures in primates (Ludvig et al., 2009a,b; 2010). Recently, the entire SPD has been externally implanted on macaques for several months. The device monitors IEEG and flushes the catheters with artificial CSF to maintain patency.

The investigative team has filed two new patents since 2003. Grant funding is allowing further development of the SPD. A pre-IND meeting with FDA provided valuable feedback on the steps needed for submitting an IND/IDE in the future. Commercial approach began with the formation of an Ad-Hoc team of industry and legal expert advisors to secure IP and guide the investigator team to obtain the IND/IDE for human trials.