STEP : towards an innovative therapeutic approach of refractory epilepsies

The project called STEP (Synchrotron Therapy for EPilepsy), coordinated by Antoine Depaulis (Inserm Research Director at Grenoble Institute of Neuroscience) and funded by the National Research Agency, was launched on April 1st for a period of 4 years. This project, which brings together Grenoble teams from INSERM and CHU, the European Synchrotron Radiation Facility (ESRF), the IRMaGe imaging platform and the NuMeCan INRAE team in Rennes, aims to develop an innovative therapy for refractory epilepsies, using the unique properties of the synchrotron.

The need for new treatments for epilepsies

Epilepsy is a neurological disease that affects nearly 1% of the world's population (nearly 60 million patients), characterized by recurrent seizures and is often associated with cognitive and / or emotional impairments. Despite the discovery of several effective drugs, about a third of people with epilepsy cannot be treated effectively. For these people, the removal of the epileptic area of the brain by neurosurgery is currently the therapeutic option of reference. This technique is effective in 50 to 80% of cases and the Grenoble University Hospital has more than 30 years of experience in this therapeutic approach and the clinical examinations it requires. However, this very invasive technique is risky and can be accompanied by side effects. The development of innovative, non-invasive and less risky therapeutic approaches is one of the first priorities in epilepsy research.

X-ray microbeam irradiation

Over the past twenty years, the extremely high flux of photons generated by 3rd generation synchrotrons has enabled the development of new irradiation strategies which are very promising for innovative radiotherapy. In particular, the possibility of dividing the X-rays generated by the synchrotron, weakly divergent, into arrays of 50-microns microbeams, separated by 200-800 microns, has enabled the emergence of “Microbeam Radiation Therapy” or MRT. Several preclinical studies carried out by STEP partners and other groups have shown that MRT is a particularly safe procedure for treating specific regions of the brain, without the tissular, vascular or behavioral side effects sometimes induced by conventional radiotherapy. The collaboration between engineers, researchers and clinicians from the biomedical beamline (ID17) of the European Synchrotron Radiation Facility (ESRF) in Grenoble, teams from the University of Grenoble-Alpes, Inserm and CHU Grenoble- Alpes has shown the efficacy of MRT in animals to suppress epileptic seizures for several months, without deleterious effects. Thus, MRT has the potential to become a disruptive technology for the treatment of diseases where the target is surrounded by tissues whose function must be preserved, as is the case in focal epilepsies and in several other neurological diseases.

The main objective of STEP is to collect all the necessary preclinical data on the efficacy and safety of microbeams generated by synchrotron, in order to allow the very first clinical trial in patients with refractory focal epilepsy in 2025-2026. STEP represents the transition between 20 years of fundamental research on MRT and the clinical development of an innovative approach to brain disease radiosurgery that will fully benefit from the unique performance of the 4th generation ESRF synchrotron.

STEP brings together 4 research teams whose preclinical expertise and / or experience in irradiation by MRT, as well as close collaboration with the CHU Grenoble-Alpes, should allow the implementation

of the first clinical trial of the MRT. To achieve this ambitious goal, STEP will determine the optimal MRT protocol for effective suppression of seizures below toxicity thresholds. These data will make it possible to prepare the documentation required by the French regulatory and safety organizations to design a suitable protocol for the first clinical trial in epilepsy patients.

STEP: practical information
4 partners: Grenoble Institut des Neurosciences (Univ. Grenoble Alpes-Inserm), STROBE (Univ. Grenoble Alpes-Inserm), NuMeCan (Inrae, Inserm, Université de Rennes 1), Centre d'Investigation Clinique – Innovation Technologique de Grenoble (CHUGA)
2 facilities : ESRF, IRMaGe
Budget: 570,000 €
Duration: 4 years

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