Background and rationale. Hearing loss, vestibular defect or tinnitus affect individuals of every age, significantly decreasing their quality of life. Socially disabling, those defects can lead to speech acquisition impairment, education delay, unemployment and stigma with the respective impact for the patient, their relatives and society. While non-invasive hearing aids seem to be the obvious choice of treatment when possible, implantable neuroprosthesis have been proven very successful to treat severe sensory neural hearing loss. This is the case of cochlear implants (CI) which are implanted in nearly 600.000 patients worldwide. However, cochlear implants still suffer from limitations in the quality of auditory function that can be restored and cannot convey highly complex acoustic contents such as music. Moreover, physiological or anatomical reasons can sometimes prevent implantation of a cochlear implant. Other auditory neuroprostheses such as the auditory brainstem and midbrain implants (ABI & MBI) have been proposed and clinically tested but the difficulty of placement in the depth of the brain triggers the activation of nearby non-auditory structures. To avoid associated secondary effects, most of the electrodes are therefore inactivated leaving patients with a poor resolution device, poor hearing outcomes, and at the end unaddressed hearing loss.

Objectives. This project aims at developing and perform clinical testing of a general approach to restore hearing using a surface neuroprosthesis that targets the auditory cortex (AC). Based on promising preliminary data, the cortical prosthesis will be translated to patients after steps of optimization in rodents. The objective is to decode at the level of the cortex, complex natural acoustic environment that we will further match with electrical stimulation. If successful, we can hope to improve user's experience of patients already implanted with any type of auditory neuroprostheses.

Methods. To achieve this goal the research revolves around 5 main axes. 1) we will optimize cortical prosthesis in rodents by decoding responses to natural hearing environment using deep learning algorithm and recreate these responses with electrical stimulation. This methodical optimization will be then translated to patients. 2) we will compare cortical stimulation to other strategies such as optogenetic cochlear implant outcomes or sonogenetics. This will imply collaborations within the institute and beyond. 3) we will study brain plasticity using models of deafness: how the proof of concept obtained in well hearing models translate in a deaf animal? 4) We will perform in-depth study of the cortical-cortical auditory pathway as well as assessing cortical stimulation biosafety. 5) We will recruit human patients to assess the efficiency of cortical stimulation as a way to restore meaningful hearing percept and as a way to treat tinnitus.

Expected Results and Impact. The research line of my group would pave the way to the development of new generation of cortical prosthesis in human. The ongoing development of a novel therapeutic strategy to restore hearing in sub optimally-addressed deaf patients is of relevance in the perspective of the patient community, health care system and more generally the field of neurosciences. Not only this new cortical prosthesis can be used to restore hearing, they can also be tailored to be used for tinnitus patients (by direct stimulation of the AC or by AC recording to do neurofeedback). The use of the device will be entirely optimized through systematic way of linking responses to stimuli. This work could serve as a foundation for auditory neuro-prosthesis optimization in general. Ultimately, the goal is to improve the quality of hearing restoration in every implanted patient by offering unique, custom and adequate stimulation.