Physics for Medicine PARIS

POSTDOC POSITION – 24 MONTHS

Feasibility of brain connectivity imaging using functional ultrasound imaging (fUS) in term and preterm neonates

PROJECT DESCRIPTION

The role of the post-doc is central in a **research project called CONEXUS involving a small clinical trial using a new fUS (functional ultrasound) neuroimaging device and starting at the beginning of year 2023**. The aim is to include around 50 neonates, and the idea is to explore this new type of neuroimaging data. fUS imaging is a brain imaging modality sensitive to local cerebral blood volume, with a very high spatial (200µm) and temporal (<1s) resolution, and promising for evaluating the cerebral connectivity. Very preliminary proofs of concept of fUS imaging in Neonates have been done in the lab [1], [2], and this work is the continuation of these.

The main objective of CONEXUS is to develop a first-of-its-kind neuroimager, capable of assessing and monitoring brain functional connectivity (fC) in neonates at bedside, for an early diagnosis of neonatal abnormal cerebral development. This unique tool will be based on functional ultrasound imaging (fUS), a technique pioneered by our lab. Our research hypothesis is that fUS-based fC imaging could give access to early biomarkers of perinatal cerebral diseases while being low cost, non-invasive and performed at the bedside. Furthermore, its very good temporal resolution and sensitivity could give access to unprecedented data for the dynamic study of the cerebral networks existing in the preterm and term neonate. From a fundamental perspective it could also enable the monitoring of the evolution and maturation of those networks in the first days of life after birth. This hypothesis is supported by our preliminary work on fUS for neonatal brain imaging. So far we published data on the possibility to perform fUS imaging in neonates through the fontanel, showing 1/ the feasibility of acquiring fUS data along with EEG/ECG at bedside on long periods of time without motion artifacts, and 2/ the correlation of the cerebral mapped fUS activity with underlying electrical cerebral activity (sleep state, epileptic seizures) [1]. We also obtained preliminary data on the feasibility of fC imaging (evaluation of how cerebral regions are working together) and observed differences between control neonates and a pathological case in the dynamic occurrence of cerebral states, emphasizing the importance of having a dynamic picture of the connectivity states rather than a static snapshot at a given instant. Based on this preliminary work, we expect to discriminate different stages of neonatal development from the assessment of connectivity states and networks, but also most likely the time occurrence of these connectivity states and the transitions between them. We also foresee differences between control and pathological cases which could lead to the definition of fC-based early biomarkers. Achievement of CONEXUS will result in the development of a fC imaging instrument which will be the first step towards a clinical product available to neonatal intensive care units. This project would therefore have a major impact for the management of at-risk newborns.

There is novelty on several aspects: fUS data will be acquired at several time points for the preterm neonates, in a more controlled way (precise developmental age), with a 2D brain-wide field of view (compared to a very small f-o-v with the previous system), with the possibility to scan the brain in 3D (the probe can move and scan the brain, but fUS is still performed only in 2D planes).

So there will be room for publication both on the technological aspects (new machine, 2.5D fUS connectivity imaging in the neonate, etc) and on the neuroscientific aspects (are we able to grasp the different degree of maturation of the connectivity in the preterm at different time points? do we identify something else than a modification of the thalamo-cortical connectivity thanks to our now brain-wide field of view? can we identify the precursors of the connectivity networks (somatosensory, auditory, salience, etc) at this level of development?) which are more unknown and exciting.

PROFILE

We are looking for a postdoc, for 24 months, someone who is in the field on neuroimaging preferentially, i.e. who has to offer an expertise in processing or advanced processing of neuroimaging data. We are indeed looking for someone that offers a complementary experience to our lab (physics and particularly ultrasound and bioimaging lab). This way the post doc will be able to obtain all the mentorship needed on the physics side of the project (ultrasound, wave propagation), on the clinical aspects (i.e. how to image the neonate patients, how to get this particular expertise, and this is done along with clinicians at Robert Debré Hospital in Paris close to the lab, one of the biggest neonatology center of France), and how to obtain the basic neuroimaging data from the raw signal we record on the neonates.

But we would be very interested in **someone that can propose innovative solutions on the processing of these neuroimaging data**: methods for dynamic connectivity imaging, for data-driven parcellation of the brain, for data driven connectivity network identification, etc. we have several ideas on this, but someone very versatile on those subjects to think out of the box would be very appreciated. Also, good programming skills are mandatory, we mostly use matlab in the lab, small experience in C or C++ is appreciated but not to worry too much about this. Given the duration of the project and the need for a quick set up of the candidate, it is best to be readily familiar with these tools.

TASKS

- **Acquire data by following an experimental procedure on the neonate patients at the hospital**: it involves setting the fUS system on the head of the neonate and using the fUS machine (looking for the imaging planes, starting the acquisitions, backuping the data, etc), then removing and cleaning the system when the exam is done. A clinician will help for that matter.
- Process the data offline at the lab. This involves several aspects: propose matlab routines for filtering, artefact removal, 2D imager registration, etc, then use MRI based atlases to register the 3D ultrasound volume and the 2D fUS in-plane acquisitions, derive connectivity analysis using ROI-based parcellation or data-based parcellations. **The candidate will rely for that on previous work we did to derive fUS dynamic connectivity, or fUS homotopic connectivity; but will also propose new relevant approaches.**
- The candidate will propose an easy-to-use toolbox implementing those processing methods for easier use on the 50-neonate cohort.

SKILLS

Matlab programming, neurosciences, neuroimaging data processing, signal and image processing, experimental research in Neuroscience, relational skills (interaction with the patient and sometimes with parents).

CONTACT

Please send your CV and publication list to charlie.demene@espci.fr

References

[1] C. Demene et al., "Functional ultrasound imaging of brain activity in human newborns," Science Translational Medicine, vol. 9, no. 411, p. eaah6756, Oct. 2017, doi: 10.1126/scitranslmed.aah6756.

[2] J. Baranger et al., "Bedside functional monitoring of the dynamic brain connectivity in human neonates," Nature Communications, vol. 12, no. 1, Art. no. 1, Feb. 2021, doi: 10.1038/s41467-021-21387-x.