EUROPEAN SYNCHROTRON RADIATION FACILITY

INSTALLATION EUROPEENNE DE RAYONNEMENT SYNCHROTRON

ESRF

Experiment Report Form

The double page inside this form is to be filled in by all users or groups of users who have had access to beam time for measurements at the ESRF.

Once completed, the report should be submitted electronically to the User Office via the User Portal:
https://wwws.esrf.fr/misapps/SMISWebClient/protected/welcome.do

Deadlines for submission of Experimental Reports

Experimental reports must be submitted within the period of 3 months after the end of the experiment.

Experiment Report supporting a new proposal ("relevant report")

If you are submitting a proposal for a new project, or to continue a project for which you have previously been allocated beam time, you must submit a report on each of your previous measurement(s):

- even on those carried out close to the proposal submission deadline (it can be a *"preliminary report"),*
- even for experiments whose scientific area is different form the scientific area of the new proposal,
- carried out on CRG beamlines.

You must then register the report(s) as "relevant report(s)" in the new application form for beam time.

Deadlines for submitting a report supporting a new proposal

- 1st March Proposal Round - **5th March**
- 10th September Proposal Round - **13th September**

The Review Committees reserve the right to reject new proposals from groups who have not reported on the use of beam time allocated previously.

Reports on experiments relating to long term projects

Proposers awarded beam time for a long term project are required to submit an interim report at the end of each year, irrespective of the number of shifts of beam time they have used.

Published papers

All users must give proper credit to ESRF staff members and proper mention to ESRF facilities which were essential for the results described in any ensuing publication. Further, they are obliged to send to the Joint ESRF/ ILL library the complete reference and the abstract of all papers appearing in print, and resulting from the use of the ESRF.

Should you wish to make more general comments on the experiment, please note them on the User Evaluation Form, and send both the Report and the Evaluation Form to the User Office.

Instructions for preparing your Report

- fill in a separate form for each project or series of measurements.
- type your report in English.
- include the experiment number to which the report refers.
- make sure that the text, tables and figures fit into the space available.
- if your work is published or is in press, you may prefer to paste in the abstract, and add full reference details. If the abstract is in a language other than English, please include an English translation.

ESRF	**Experiment title:** **Insight into the 3D neuronal morphology in human subthalamic nucleus and substantia nigra affected by Parkinson**	**Experiment number**: MD1244
Beamline: Id16a	**Date of experiment**: from: 11/03/2021 to: 14/03/2021	**Date of report**: 15 16/02/2022 *Received at ESRF:*
Shifts: 9	**Local contact(s)**: JOITA PACUREANU Alexandra; KARPOV Dimitri	

Names and affiliations of applicants (* indicates experimentalists):

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5. ID16a , European Synchrotron Radiation Facility, Grenoble, France

Report:

The experiment was a success, despite the particular circumstances related to COVID at the time of the experience, and the reduced period of shifts. We were able to visualize for the first time in 3D Lewy bodies and to quantify and correlate the density of neuromelanin grains with the duration of Parkinson's disease for the first time in 3D. This project is the subject of a new beamtime application in order to increase the scope of our results by showing the presence of Lewy bodies in the organs responsible for the pre-motor symptoms of Parkinson's disease.
The data from this experiment will be presented in an oral communication at the European Academy of Neurology Congress in 2022 (see below) and will be the subject of a publication which is currently still in writing process.

Abstract to be presented at the 2022 European Academy of Neurology Congress in Vienna

Background :

Parkinson disease (PD) is the second most frequent neurodegenerative disease. It is histologically characterized by alpha-synuclein aggregates forming the Lewy Bodies (LB), mostly found in the substantia nigra (SN). Conventional imaging techniques such as MRI or TDM lack of spatial resolution. Histology and electronic microscopy do not allow 3D analysis, require staining and are limited in the size of sample (µm). Synchrotron Phase contrast X-ray imaging (S-PCI) is an emerging modality that exploits the differing refractive indices of materials to create additional contrast, especially in soft tissues. The aim of this study was to assess the ability of multiscale S-PCI to visualize the morphologic abnormalities present in human SN affected by PD.

Methods

Five samples of SN from four deceased-donors affected by PD and one age-matched control were imaged at the European Synchrotron Radiation Facility (ESRF, Grenoble, France). The whole SN was acquired at a resolution of 3 and 0.6 microns. Then, targeted regions were imaged at a resolution of 50 nanometers. No contrast agent was used in this study. All samples came from deceased donors. The bodies were treated with respect and respecting the French funerary legislation.

Results

The experiment went well, without troubles during the data acquisition. Targeting of neuromelanin neurons was not difficult, and few artefacts were observed. Neuromelanin neurons, were individualizable in the SN (Fig1). Some Parkinsonian neuromelanin neurons contained dense spheric structures repelling the neuromelanin granulations, recognized as LB (Fig2 and Fig3). Pale bodies which are described as precursors of LB were identified too. We were able to visualize different densities of neuromelanin grains within the neuromelanin neurons, correlated to the duration of the disease, and quantify this difference in 3D (Fig 4).

Conclusion

In this study we proved non-inferiority of multiscale S-PCI for visualizing LB in PD compared with conventional histological technique, and the capacity to study them in 3D for the first time, as well as the amount of neuromelanin grains in the neurons affected by PD. A deeper understanding of LB 3D structure and their localization in pre-motor organs with the S-PCI technology could allow new therapeutic targets.

Figure 1. Components of SN

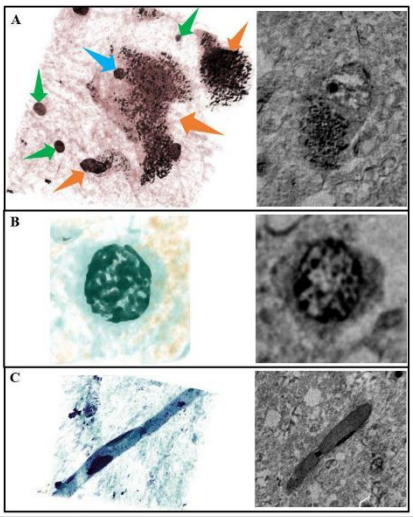
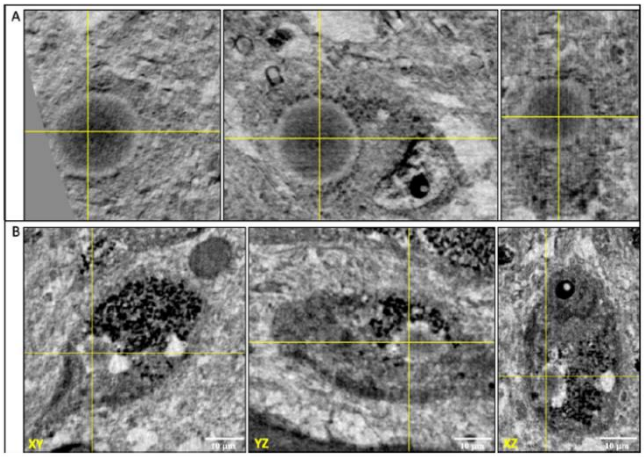


Figure 2. Lewy Bodies in neuromelanin neurons



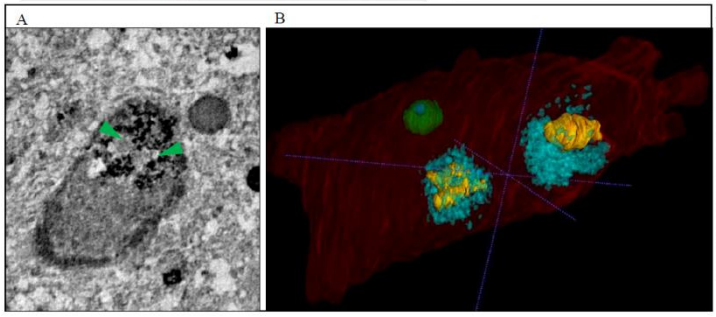


Figure 3. Lewy Bodies in 3D

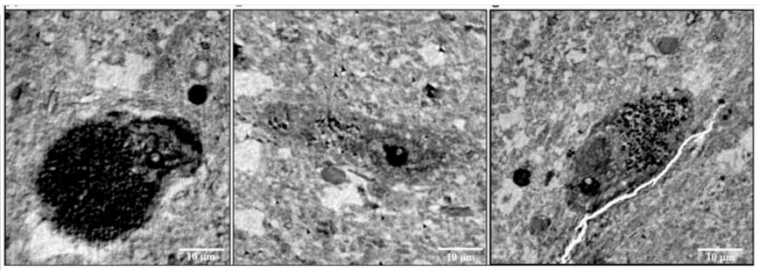


Figure 4. Difference of neurmelanin grains density in neuromelanin neurons from patients with different duration of Parkinson Disease