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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

Reports supporting requests for additional beam time

Reports can be submitted independently of new proposals – it is necessary simply to indicate the number of the report(s) supporting a new proposal on the proposal form.

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.

Deadlines for submission of Experimental Reports

- 1st March for experiments carried out up until June of the previous year;
- 1st September for experiments carried out up until January of the same year.

Instructions for preparing your Report

- fill in a separate form for each project or series of measurements.
- type your report, in English.
- include the reference number of the proposal 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:** Monitoring inflammation in stroke using combined high resolution magnetic resonance imaging and synchrotron radiation-phase computed tomography (SR-PCT) of the mouse brain	**Experiment number**: LS2292
Beamline: ID19	**Date of experiment**: from: April 2014 to: June 2014	**Date of report**: June 15, 2015
Shifts: 15	**Local contact(s)**: Vincent Fernandez, Lukas Helfen	*Received at ESRF:*

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Report:

Study#1-Fast virtual histology of unstained mouse brains using in-line X-ray phase tomography

This work was accepted for an oral presentation at the European Molecular Imaging Meeting 2015 (1). Complementary analysis are in progress for publication.

Introduction:

Whole-brain imaging with cell resolution is one of the most important challenges in neuroscience. Conventional histology techniques are laborious and require tissue staining and sectioning. We have previously proposed an in-line phase contrast tomography set-up that identified mouse brain anatomy as clearly as histology in 44 min (2). The current work presents an optimized pipeline and demonstrates its potential for fast virtual histology in a mouse model of acute cerebral injury.

Methods:

Six mice (healthy: N=1, acute cerebral ischemia: N=5) were imaged in-vivo with MRI. Imaging of brains fixed with PFA4% was performed on beamline ID19 at ESRF at 19 keV selected from undulator radiation. An indirect detection-based detector with a LuAg scintillator, standard microscope optics and a 2048x2048 pixel CCD camera was positioned 1 m from the sample to have phase contrast. The pixel size was set to 7.5 µm. Acquisition time was 14 minutes per brain.

Results:

Figure 1 shows 3 different virtual histologic slices of the healthy brain (Fig 1A;E;G). Minimum intensity projection (MinIP) resulted in angiography with sufficient resolution to visualize pial vessels (Fig 1B-C). T2-weighted MRI revealed abnormal hyperintense signals (Fig 1D, arrow), corresponding to a choroid plexus (CP) cyst as clearly depicted on phase contrast images (Fig 1E). CP layers were well resolved (Fig 1F). In the cerebellum, there was an excellent contrast between grey and white matter (Fig 1G-H), with detection of individual Purkinje cells (arrow in Fig 1I).

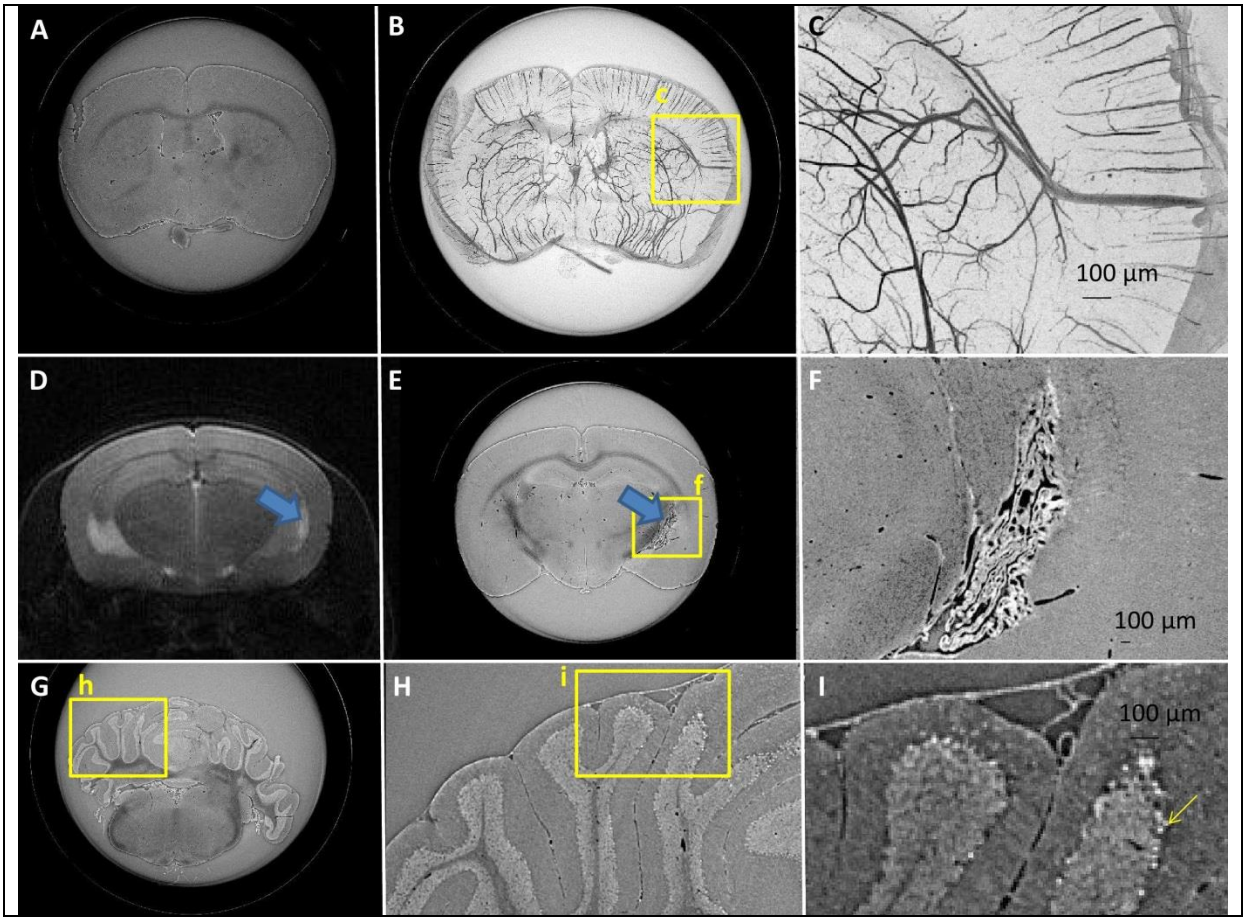

Fig 1- Virtual histology of healthy mouse brain using in-line phase contrast tomography

In mice with ischemic injury, MRI showed an extensive lesion across the frontoparietal cortex (Fig 2A, plain line) with a well-delineated core (dotted line) and vasogenic edema along the ipsilateral external capsule (arrow). Native phase contrast images also discriminated the core/periphery of the lesion (Fig 2B). MinIP allowed further characterizing the

lesion, with a disorganization of vessels in the core and avascularity in the periphery (Fig 1C). In addition, maximum intensity projection (Fig 2D) showed (i) enhanced cellularity on the ipsilateral side (Fig 2E, arrow), (ii) vessels rich in collagen such as carotids (Fig 2F) and (iii) upregulation of collagen in the ischemic cortex (Fig 2G-H) (3).

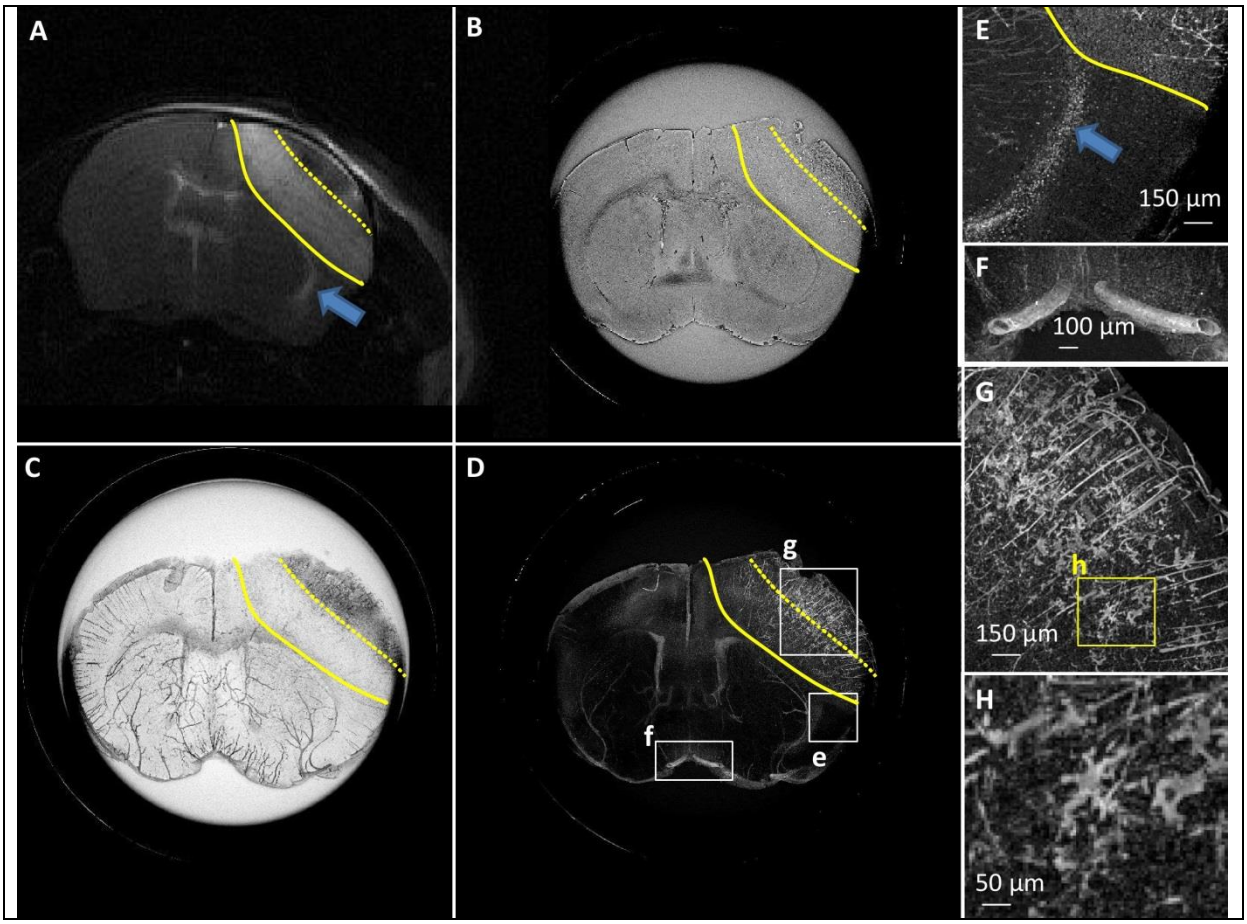

Fig 2- Virtual histology of ischemic mouse brain using in-line phase contrast tomography

Conclusion:

The proposed set-up of in-line phase contrast tomography allows fast virtual histology of the whole unstained brain, which is promising for phenotyping transgenic mouse and characterizing models of neurovascular diseases, with the potential to scan 30 brains in an 8-hours shift. Because it is non-destructive, this approach will be used for guiding further immunohistologic analysis of the brain.

Acknowledgments

This work was performed within the framework of the LABEX PRIMES (ANR-11-LABX-0063) of Université de Lyon and was supported by the European Synchrotron Research Facility (ESRF, project LS-2292) by allocation of beam time.

References

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3. Hawkes CA, Michalski D, Anders R, Nissel S, Grosche J, Bechmann I, . . . Hartig W. Stroke-induced opposite and age-dependent changes of vessel-associated markers in co-morbid transgenic mice with Alzheimer-like alterations. Exp Neurol 2013;250:270-281.