EUROPEAN SYNCHROTRON RADIATION FACILITY

INSTALLATION EUROPEENNE DE RAYONNEMENT SYNCHROTRON

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:** **Synchrotron-generated X-ray interlaced microbeam therapy of mesiotemporal lobe epilepsy**	**Experiment number**: MD571
Beamline: 17	**Date of experiment**: from: March 2nd, 2010 to: March 3rd, 2010	**Date of report**: 18/09/2012
Shifts: 6	**Local contact(s)**: Christian Nemoz and Elke Brauer	*Received at ESRF:*

Names and affiliations of applicants (* indicates experimentalists):

Jean Laissue – Institute of Pathology Bern
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Antoine Depaulis* - Grenoble Institut des Neurosciences, INSERM U836
Elke Brauer-Krisch* - ESRF
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Benoit Pouyatos* - Grenoble Institut des Neurosciences, INSERM U836
François Estève - Grenoble Institut des Neurosciences, INSERM U836

Report:

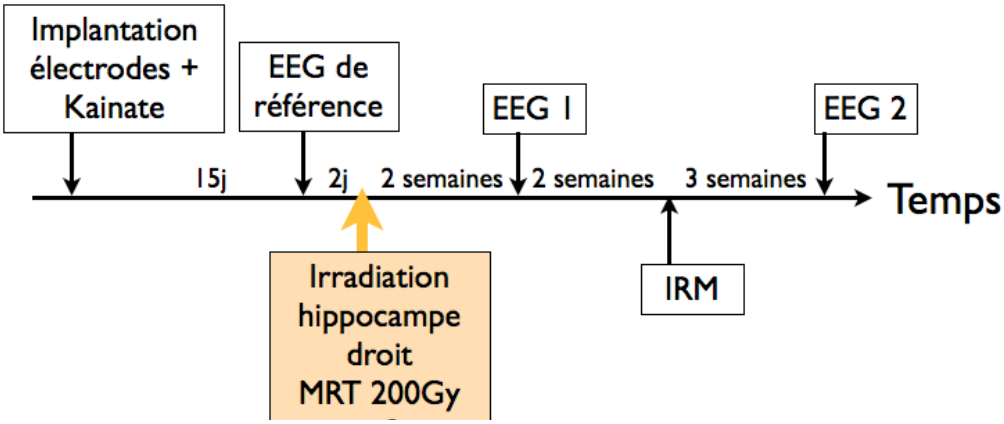
Rationale:

MD438 and MD531 beamtime allocations allowed us to investigate the effects of synchrotron-generated interlaced MRT coupled to pink-beam imaging on the GAERS rat. Since recent data had shown that absence seizures arise within the somatosensory cortex before they diffuse to the rest of the cortex and the thalamus, we irradiated this cortical region bilaterally using 4 interlaced ports of 50µm-wide microbeams resulting in a homogenous dose of 200Gy into the targeted areas. This procedure resulted in a 50% reduction of the seizure duration compared to sham animals that appeared as soon as 3 weeks after irradiation and was still significant after five months. Histological and electrophysiological data suggest that this effect is not mediated through simple tissue necrosis, but probably via a disruption of the local cellular network, which prevents the neurons from hypersynchronizing and generating epileptic discharges, without impairing their ability to perform their physiological tasks. This non-destructive effect of MRT becomes extremely suitable when seizures originate from a brain structure with a critical role like the hippocampus - the structure most commonly involved in pharmacoresistant MTLE. ***In order to address the applicability of MRT on MTLE, we propose to investigate its effects on a predictive and drug-resistant model of MTLE obtained after intrahippocampal injection of kainate in the mouse***. This mouse model was preferred to the one developed in the rat because of the stability and recurrence of

the seizures over a long time period, (ii) the resistance to several anti-epileptic drugs and because (iii) intracellular recordings were recently collected by our group in this model.

Methods:

- *Timeline*



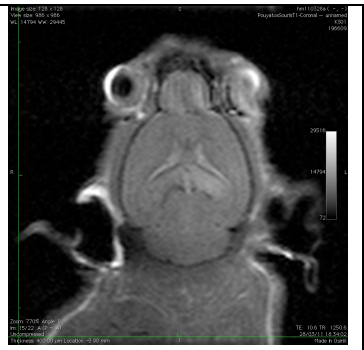
Note: the electrodes were custom-made MRI compatible carbon electrodes.

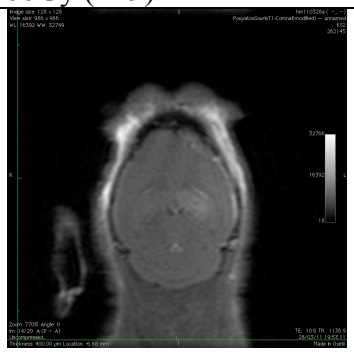
- *Experimental groups:*
  Irradiated mice 200Gy n=9
  Control mice (0Gy) n=4

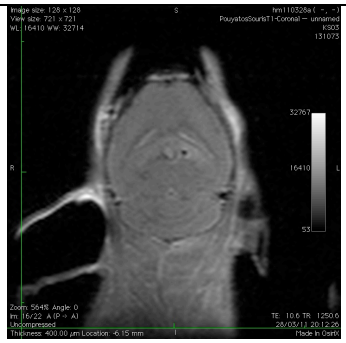
Results:

- *MRI*

Souris Irradiées MRT entrelacée 200Gy (n=9)


KS1 Gado IV


KS2 Gado IV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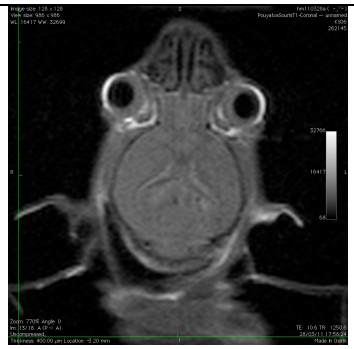
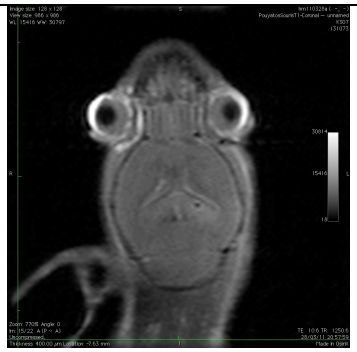
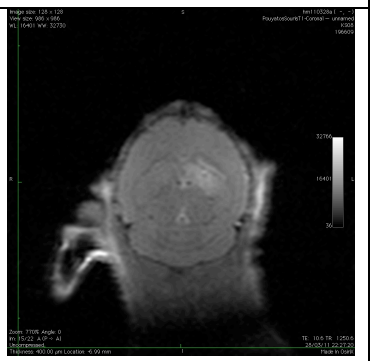
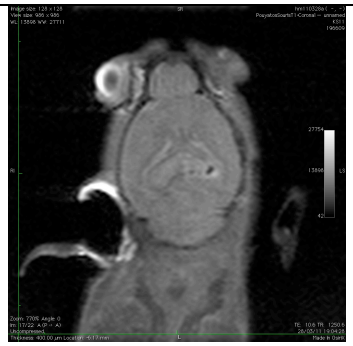
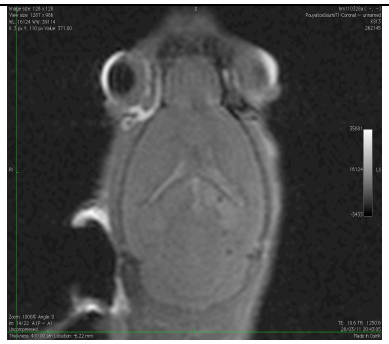

KS6 Gado IP


KS7 Gado IP

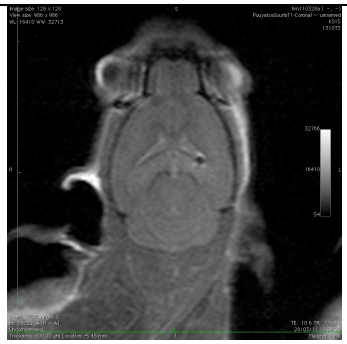

KS8 Gado IV



KS11 Gado IP



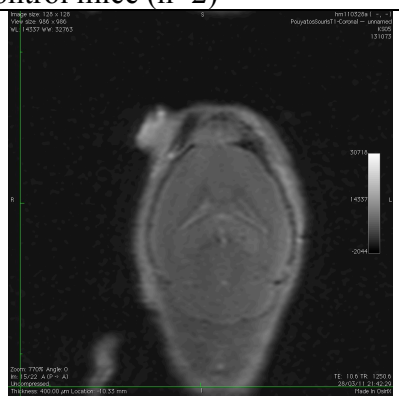
KS13 Gado IP



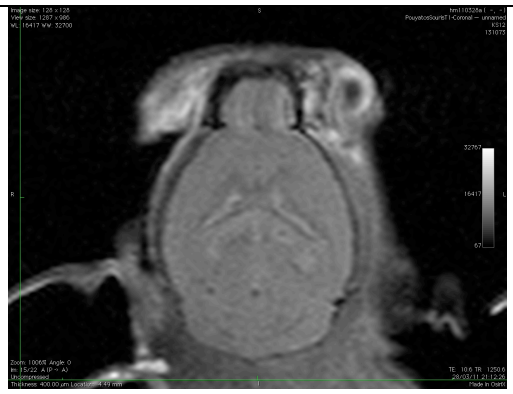
KS15 Gado IV

>>> Clear hypersignal within the right hippocampus. Except for KS6 which probably did not received kainate. Targeting seems OK.

Control mice (n=2)



KS5 Gado IV



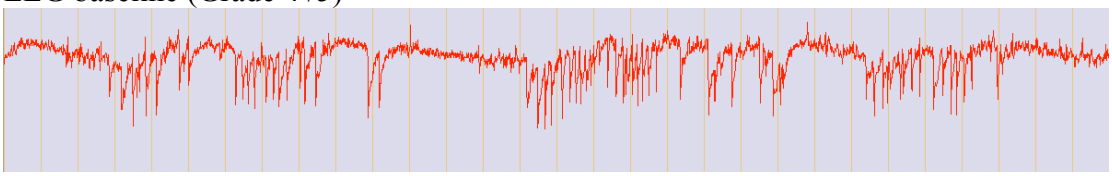
KS12 Gado IP

>>> Slight hypersignal within the right hippocampu due to kainate induced sclerosis.

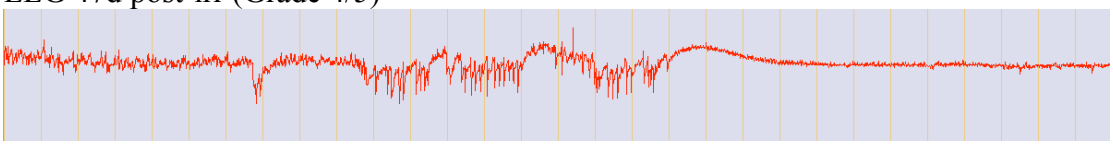
- *EEG*
- **Irradiated mice 200Gy (exemple of seizures)**

KS3

EEG baseline (Grade 4 /5)

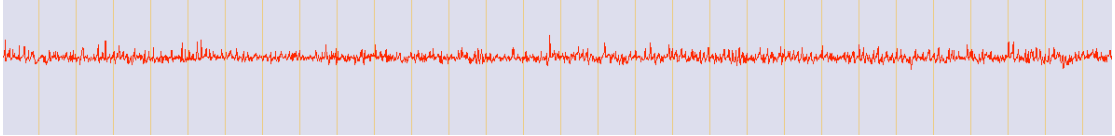


EEG 47d post-irr (Grade 4/5)



KS6

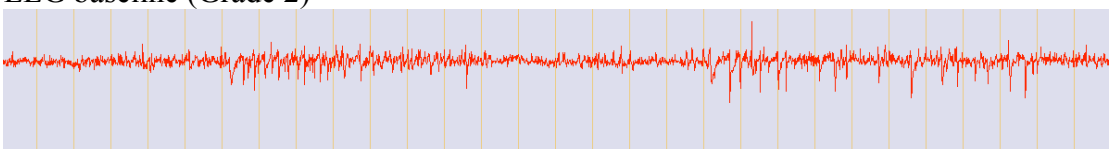
EEG baseline (Grade 0)



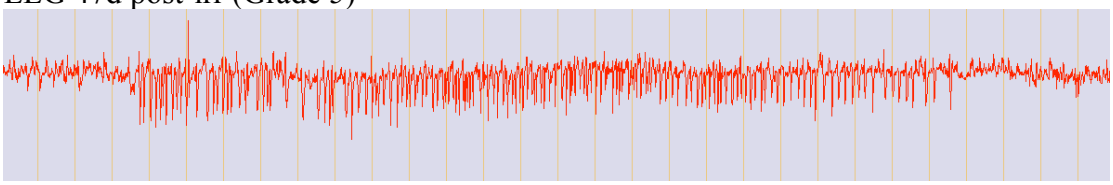
EEG 47d post-irr (Grade 0)

KS7

EEG baseline (Grade 2)

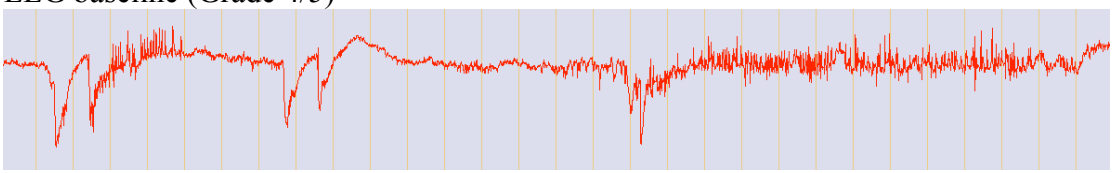


EEG 47d post-irr (Grade 5)



KS8

EEG baseline (Grade 4/5)



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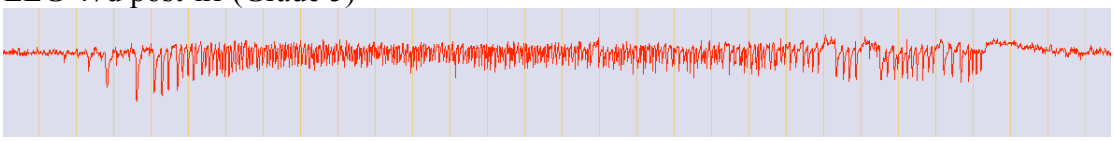
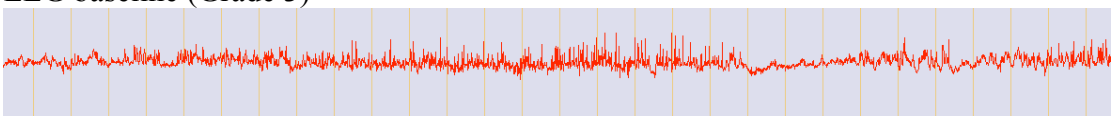
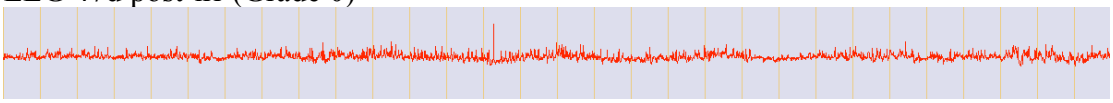


KS11

EEG baseline (Grade 3)

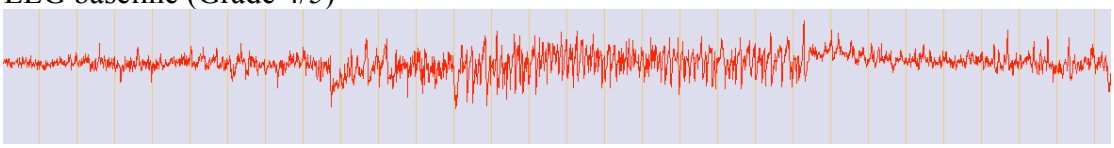


EEG 47d post-irr (Grade 0)

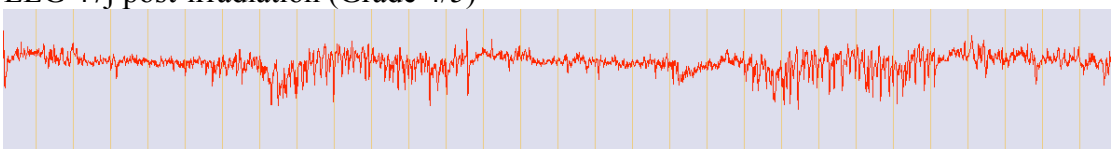


KS12

EEG baseline (Grade 4/5)

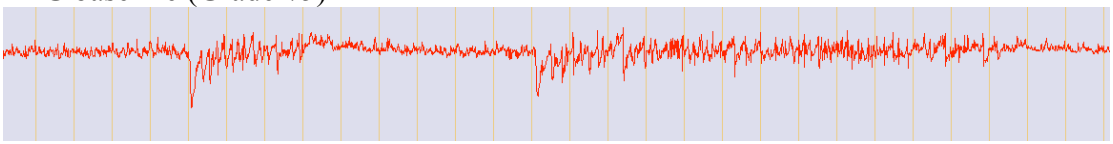


EEG 47j post-irradiation (Grade 4/5)

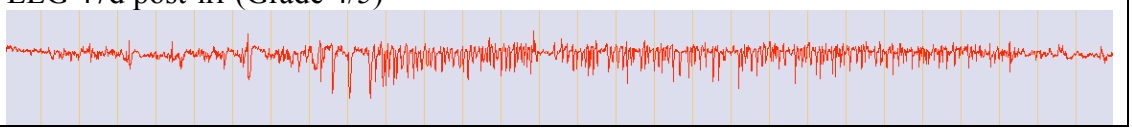


KS13

EEG baseline (Grade4/5)

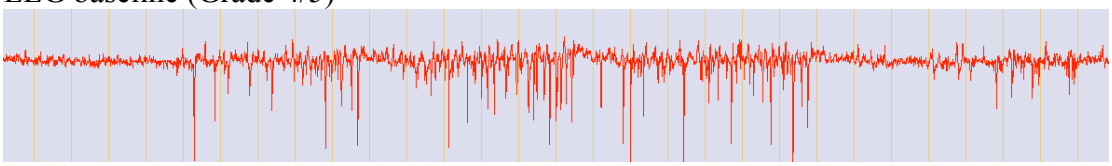


EEG 47d post-irr (Grade 4/5)

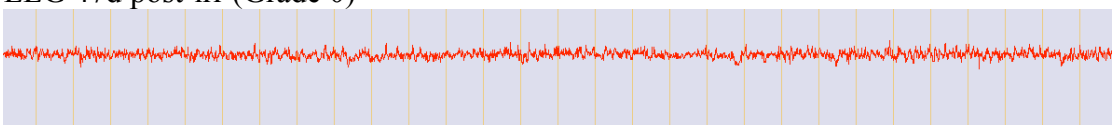


KS15

EEG baseline (Grade 4/5)



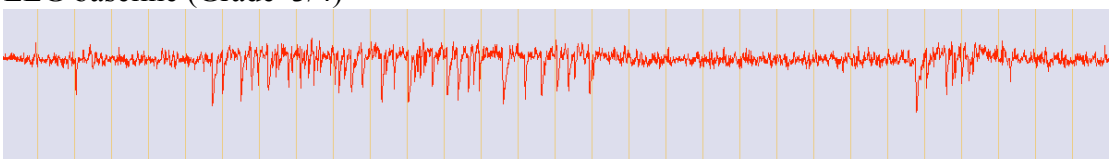
EEG 47d post-irr (Grade 0)



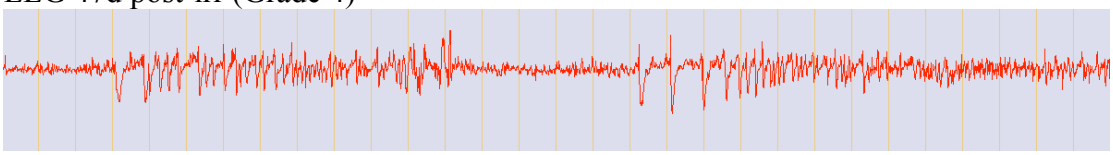
- **Souris Kainate Contrôles (0Gy)**

KS5

EEG baseline (Grade 3/4)

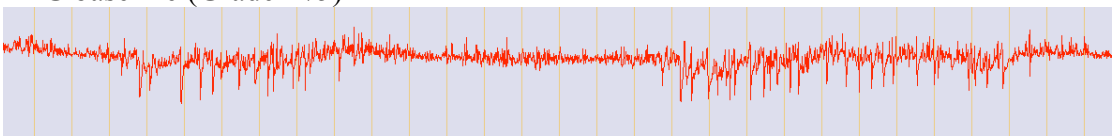


EEG 47d post-irr (Grade 4)

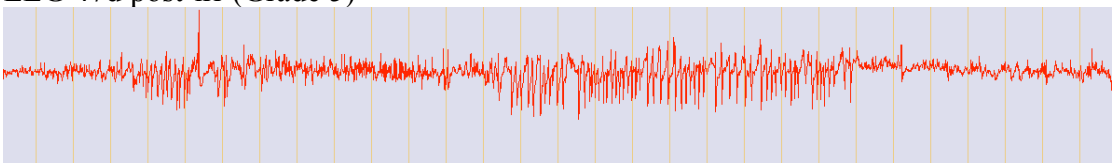


KS10

EEG baseline (Grade 4/5)

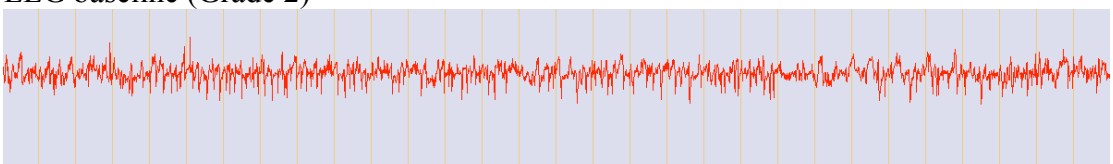


EEG 47d post-irr (Grade 5)

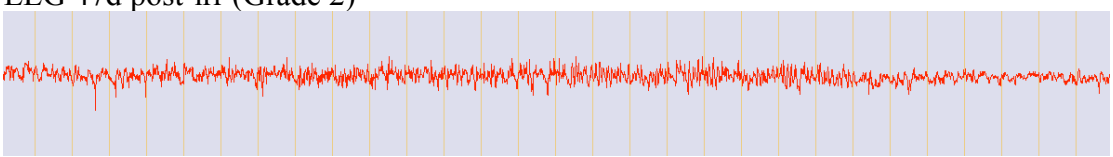


KS9

EEG baseline (Grade 2)



EEG 47d post-irr (Grade 2)



Conclusions:

Most of the mice (8 out of 9) were successfully rendered epileptic with kainate injection in the right hippocampus. However, most of the animals still had seizures 1,5 months after

200Gy irradiation. In only 2 out of 8 epileptic mice we obseved a disappearence of hippocampal seizures.
We suggest that the conformation of the irradiation must be improved. For the next round we propose to use variable microbeam sizes for the different port, in order to better match the complex shape of the hippocampus.
As of September 2012, histology on harvested brains is being performed.