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To cite this version:

HAL Id: inserm-01939451
https://www.hal.inserm.fr/inserm-01939451
Submitted on 5 Dec 2018
FLAWS imaging improves depiction of the thalamic subregions for DBS planning in epileptic patients

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Synopsis
Accurate localization of the thalamic subregions is of paramount importance for Deep Brain Stimulation (DBS) planning. Current MRI protocols use T2 and Gadolinium-enhanced T1 images, to visualize both the basal ganglia and the vessels, in order to define the electrode trajectory and target. This study shows the usefulness of Fluid and White Matter Suppression, i.e. FLAWS imaging, in eleven drug-resistant epileptic patients for preoperative Deep Brain Stimulation planning and anterior thalamic nucleus targeting.

Introduction
Accurate localization of the thalamic subregions is of paramount importance for Deep Brain Stimulation (DBS) preoperative planning in movement disorders treatment and recently in epilepsy surgery1. In particular, DBS of the anterior thalamic nucleus (ATN) was associated with a 69% reduction in seizure frequency in drug-resistant patients with epilepsy in the USA. The ATN is implicated in the limbic circuit and is poorly visible on T1 and T2 MR images. Current DBS MRI protocols use T2 and Gadolinium-enhanced T1 images, to visualize both the basal ganglia and the vessels, in order to define the electrode trajectory and target. In recent years, FLAWS (Fluid and White Matter Suppression)2 imaging - which is a variant of the MP2RAGE3 sequence - providing in a single sequence both FGATIR4 and MPRAGE images, has been proposed for improved visualization of brain structures and of basal ganglia in particular. As such, it could be of interest for applications such as DBS. The usefulness of FLAWS imaging was evaluated here for the first time in patients in the context of drug resistant epilepsy and preoperative DBS planning.

Material & Methods
After approval from the IRB, eleven drug-resistant epileptic patients referred for DBS surgery as part of a national study were scanned at 3T (MAGNETOM Verio, Siemens Healthcare, Erlangen, Germany) with the M2PRAGE prototype sequence adapted for 3D FLAWS imaging (TR/TE=5000/2.68ms, T1/T2=409/1300ms, alpha1/alpha2=5/5°, voxel size 1mm³, acquisition time 11min). 3D Gadolinium enhanced T1 imaging was also performed for vessel visualization (TR/TE/Ti=1900/2.26/900ms, voxel size 1mm³, acquisition time 4min30s). The division image of the two FLAWS images was also computed. Brain/tissue contrast and contrast-to-noise values were measured with FGATIR-like (FLAWS1) and MPRAGE-like (FLAWS2) images. Regions of interest were drawn using ImageJ (1.48b)5 in the corpus callosum (splenium) for WM, caudate nucleus (head) for GM, and ventricles for CSF. Contrast-to-noise was computed as described in 2. Before DBS surgery, the 3D datasets were fed into in the PyDBS pipeline6 allowing registration to an atlas of the basal ganglia, fusion and 3D visualization for preoperative planning of electrode trajectories.

Results
Example images for FLAWS1, FLAWS2 and division image are shown in Figure 1 and a zoomed excerpt is shown in Figure 2. Contrast-to-noise values obtained for FLAWS1 and FLAWS2 images in patients are reported in Figure 3. The values obtained in the original study in healthy subjects are also reported for comparison. The FLAWS images were used in the PyDBS pipeline and the basal ganglia atlas was registered with the FLAWS data as shown in Figure 4, here on the division image.

Discussion
Previous studies on DBS targeting have employed FGATIR, which is a modification of the MPRAGE sequence. The FGATIR sequence provides images where the WM signal is suppressed, just like FLAWS1. In the same acquisition time, FLAWS provides both FGATIR-like images and standard, anatomical MPRAGE-like images. Thus, no additional anatomical imaging, i.e. acquisition time is necessary. Quantitative Susceptibility Mapping is another promising surrogate as demonstrated for the subththalamic nuclei6 but still gives poor contrast in the thalamus.

Conclusion
The objective to use FLAWS data was to better visualize the thalamic nuclei, especially the ATN to treat epilepsy. Excellent depiction of the thalamic subregions and the ATN on FLAWS images was reported by the neurosurgeon. This qualitative assessment was confirmed by tissue contrast and contrast-to-noise values, which were in agreement with the values reported in the original study in healthy subjects. The FLAWS images could smoothly be used in the PyDBS pipeline for the neurosurgeon to visualize the basal ganglia delineation extraction from the atlas, superimposed on FLAWS data. The visualization of thalamus subregions allowed confident definition of target and electrode trajectory before surgery. Postoperative results on reduction of seizure frequency need to be evaluated at a few years distance and are not available yet.

Acknowledgements
MRI data acquisition was supported by the Neurinfo MRI research facility from the University of Rennes I. Neurinfo is granted by the the European Union (FEDER), the French State, the Brittany Council, Rennes Metropole, Inria, Inserm and the University Hospital of Rennes.

References

**Figures**

Example images for FLAWS1 (FGATIR-like), FLAWS2 (MPRAGE-like) and division contrasts

Zoom on the anterior thalamic nucleus on FLAWS1

<table>
<thead>
<tr>
<th>Patients</th>
<th>Patients</th>
<th>Tanner et al.</th>
<th>Tanner et al.</th>
</tr>
</thead>
<tbody>
<tr>
<td>FLAWS 1</td>
<td>FLAWS 2</td>
<td>FLAWS 1</td>
<td>FLAWS 2</td>
</tr>
<tr>
<td>WM/GM</td>
<td>0.55 [0.47-0.67]</td>
<td>0.5 [0.43-0.56]</td>
<td>0.55 [0.43-0.65]</td>
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<tr>
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<td>0.64 [0.57-0.72]</td>
<td>0.66 [0.57-0.72]</td>
</tr>
<tr>
<td>GM/CSF</td>
<td>0.17 [0.11-0.21]</td>
<td>0.28 [0.15-0.22]</td>
<td>0.16 [0.14-0.17]</td>
</tr>
</tbody>
</table>

Contrast-to-noise values obtained for FLAWS1 and FLAWS2 images in patients (present study). Values obtained in the original study (Tanner et al.) in healthy subjects are reported for comparison.

PyDBS atlas superimposed on FLAWS division images showing amygdala (pink); caudate nucleus (light blue); hippocampus (dark pink); lateral pallidum (green); lateral, third and fourth ventricles (dark blue); medial pallidum (dark orange); putamen (dark purple); red nucleus (red); subthalamic nucleus (light orange); substantia nigra (gray); thalamus (yellow). Red lines represent the bilateral electrode trajectory.