CONSTRUCTION OF MRI 3D HIGH RESOLUTION SHEEP BRAIN TEMPLATES AND THE USE OF OPTIMIZED PRIOR PROBABILITY MAPS TO EXTRACT STRUCTURES IN THE CENTRAL NERVOUS SYSTEM

Arsene Longin Ella[1] and Matthieu Keller[1]

[1]*Department of Reproductive Physiology and Behavior, INRA - Centre Val de Loire UMR 7247 - CNRS - University of Tours – IFCE, Nouzilly, Tours, France*

INTRODUCTION

Sheep is a developing animal model used in the field of neurosciences for the study of many behavioral, physiological or pathophysiological mechanisms, including for example, the central control of social attachment[1], of reproduction[2] or the development of spongiform encephalopathies[3]. However, sheep remains an orphan species in the field of MRI. Therefore, a mean image (template), result of registrations of multiple subject images, and an atlas of brain structures are needed and currently do not exist. In this study, we: **i)** computed multimodal high resolution 3D in-vivo sheep brain templates of T1 weighted (T1W) and T2W images, **ii)** computed gray matter (GM), white matter (WM) and cerebrospinal fluid (CSF) prior probability maps using linear and optimized non-linear registrations **iii)** used non-linear GM prior probability maps to extract deep brain structures in the CNS.

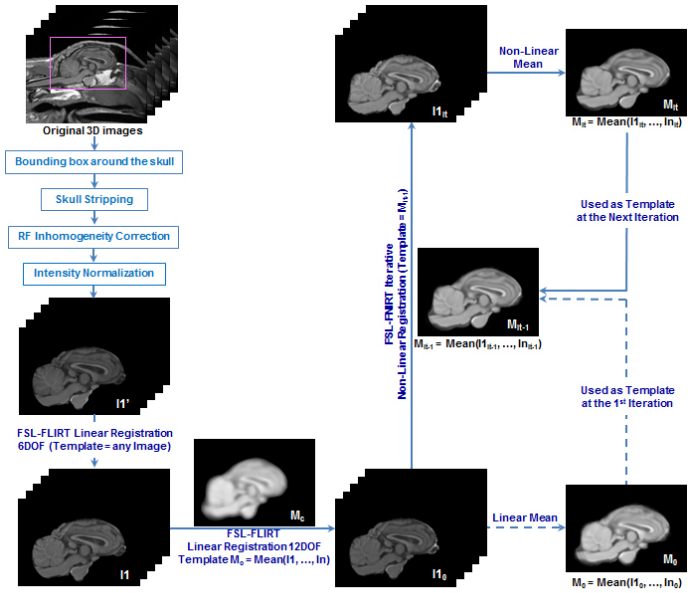

Figure 1: steps used in the construction of templates and prior probability maps

MATERIALS AND METHODS

MRI scans were acquired on anesthetized 18 female sheep of 4 years old (with 20 mg/kg of ketamine, intubated and maintained on 3% isoflurane vaporized in oxygen) with a 3T VERIO Siemens device at the CIRE platform of INRA Nouzilly France. Parameters were for the Magnetization Prepared Rapid Gradient Echo (MPRAGE) T1W: TR 2500 ms; TE 3.6 ms; TI 900; FA 12°; NEX 4; matrix 384×384; FOV192 mm; 288 sagittal slices with a thickness of 0.5 mm; and for the SPACE T2W: TR 4000 ms; TE 43 ms; FA 120°; NEX 5; matrix 512×512; FOV180 mm; 208 sagittal slices with a thickness of 0.35 mm, resampled to a voxel size of 0.5x0.5x0.5 mm^3. Then, images entered into the optimized multi-resolution registration process described in **figure 1** and scripted using FLIRT and FNIRT of FSL (FMRIB Analysis Group, Oxford, UK). First, each T1W image **Ij'** (j=1,…,18) was linearly registered (6DOF) to all the others resulting into **Ij**, and then averaged to build the 1st linear template $\mathbf{M_c}$. Then, another linear registration (12DOF) was applied to each **Ij'** image, using $\mathbf{M_c}$ as a target, to images $\mathbf{Ij_0}$ and averaged to build the 2nd linear template $\mathbf{M_0}$. Here, all deskulled T1W brain images $\mathbf{Ij_0}$ were segmented in 3 tissues (GM, WM and CSF) using FSL-FAST and averaged to build corresponding linear prior maps as described in [4]. This was followed by an iterative optimized non-linear registration giving at each iteration images $\mathbf{I_{it}}$, averaged into a template $\mathbf{M_{it}}$ which was re-used as a target $\mathbf{M_{it-1}}$ at the next iteration. A RMS (root mean square) difference between successive templates or prior maps was computed at each iteration until it converges to a minimum. T1W head images obtained after the bounding box operation was used to lead the non-linear registration, all brain templates and non-linear prior maps were computed from deformation fields generated during the non-linear registration.

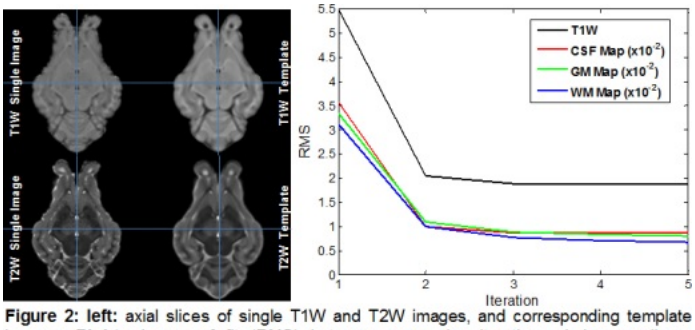

Figure 2: left: axial slices of single T1W and T2W images, and corresponding template images. **Right:** degree of fit (RMS) between successive iterations during non-linear registrations of the leading T1W image and prior probability maps of CSF, GM and WM.

RESULTS

Results showed that each RMS curve indeed converges to a minimum for the leading T1W and prior maps (**fig.2**, **right**) and that, templates were in accordance with single images (**fig.2**, **left**). Prior probability maps of GM, WM and CSF showed to correspond to areas representing associated brain tissues (**fig.3**); and extracted deep GM structures (**fig.4**) were already visible on the GM prior map.

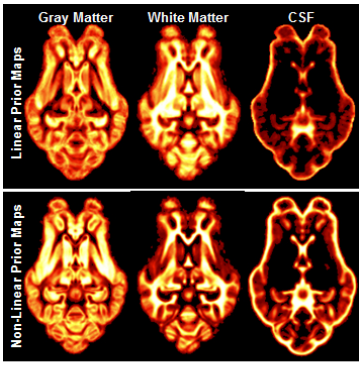

Figure 3: axial slices of GM, WM and CSF prior probability maps computed during linear and non-linear registrations.

DISCUSSION & CONCLUSION

Each image was checked after the non-linear registration and no misregistration was observed. This argues in favor of a successful registration process and supports results shown in **figure 2**. Prior maps are normally computed by averaging segmented and smoothed brain tissue images obtained after the 2nd 12DOF linear registration. But, the eigen variability of individual image shape screws the resolution of brain structures on linear prior maps (**fig.3**, **upper row**). That is the reason why we computed non-linear prior probability maps in order to improve the resolution of brain structures in each tissue, the ultimate goal being to use them in the construction of the whole sheep brain atlas as we already initiated it in **figure 4**.

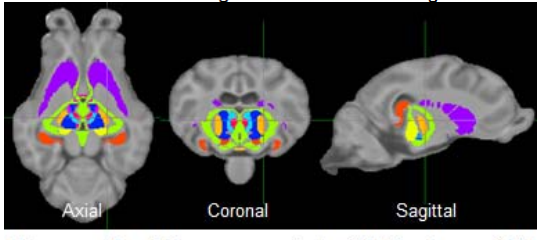

Figure 4: 3D segmented CNS deep GM structures overlapped axial, coronal and sagittal slices of the T1W template.

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