

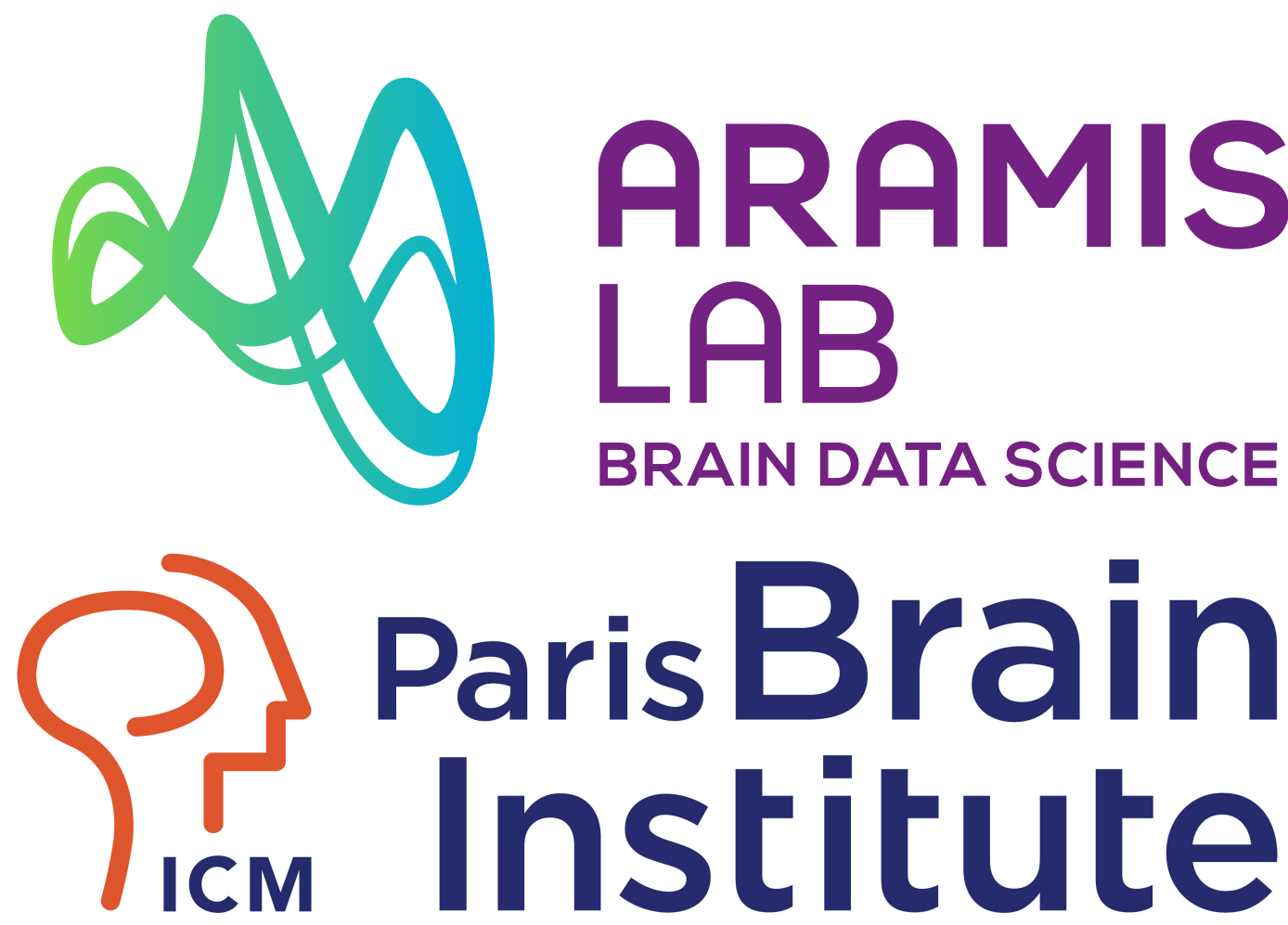
2-Step 3D U-Net for the Automatic Segmentation of the Choroid Plexuses

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Introduction

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Choroid plexuses (ChP) are **veil-like structures located in the brain ventricles** and composed of a single layer of epithelial cells. Their main role is the production of CSF which is **renewed several times a day**, allowing the maintenance of brain homeostasis through the regulation of fluid and electrolyte balance. They also contribute to the blood-cerebrospinal fluid barrier, as they integrate signals between the peripheral and the central nervous system, and serve as a neuro-immunological interface in physiological and pathological conditions. Finally, they endorse a secretory role, with **more than 200 proteins being**

secreted in the CSF, that may contribute to immunoregulation and neuroprotection [1]. These key functions have pushed research into their involvement in neurological diseases such as **Alzheimer’s, Parkinson’s disease, or multiple sclerosis** [2]. To date, the gold standard for ChP segmentation on MRI remains **manual annotation**, a time-consuming approach that is poorly applicable to large cohorts of subjects. In this study, we aim to develop a simple and highly reliable solution for ChP segmentation, that could be largely applied on MRI T1-weighted

sequences acquired in the clinical setting for the diagnosis or follow-up of neurological diseases, and that would require minimal preprocessing steps on images. For this purpose, we have designed a **2-step 3D U-Net** [3] for the automatic segmentation of the ChP. Training and validation were performed in **healthy controls and subjects with multiple sclerosis** and the last validation step was achieved on clinical data obtained in subjects with **Radiologically Isolated Syndrome (RIS)**, a preclinical form of MS.

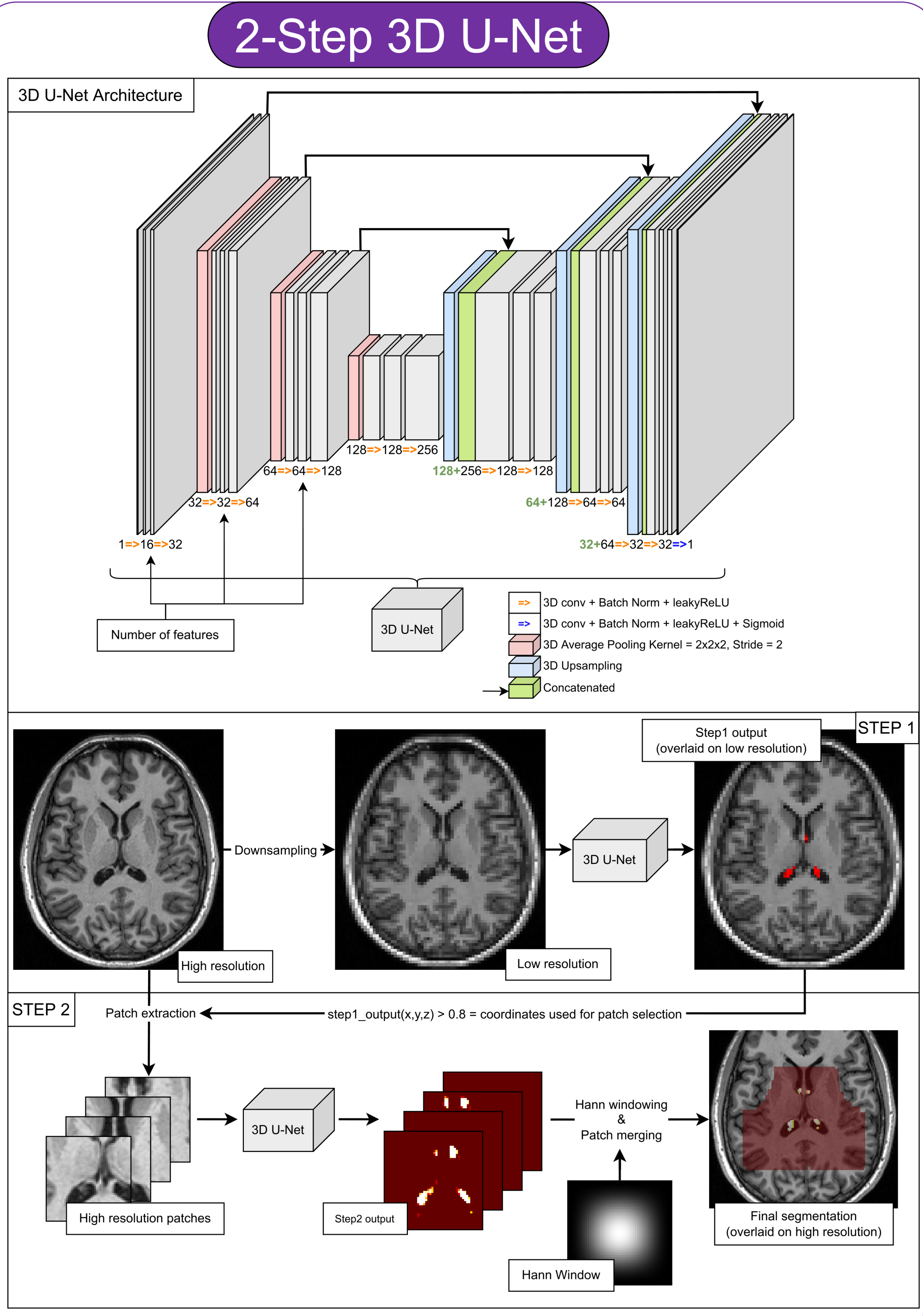
Materials & Methods

Datasets and Pre-processing

The first dataset is composed of **141 participants**: 44 healthy controls, 61 patients with relapsing-remitting multiple sclerosis (MS), and 36 patients with progressive MS. Images were acquired on two different Siemens 3T MRI scanners (Trio and Prisma) with a 32-channel head coil (92 on Trio and 49 on Prisma).

The second dataset is composed of **27 pre-symptomatic MS cases** fulfilling the 2009 criteria for Radiologically Isolated Syndrome (RIS) followed at the outpatient Neurology clinics of Pitié-Salpêtrière and Saint-Antoine Hospital in Paris, France.

Before manual segmentation, all images were corrected for MRI field inhomogeneities. On both datasets, the ChP in the two lateral ventricles was segmented by a trained neurologist and corrected by a senior neurologist with expertise in MRI processing (**annotator 1**). Segmentations were used as ground truth to train the proposed model and evaluate its performance. Finally, for the clinical dataset only, CPs were segmented a second time by a trained neurologist (**annotator 2**), independently from the previous annotator.



Training Procedure

The loss function used is the sum of the Sørensen–Dice loss and the binary cross entropy loss (BCE). Considering two probabilistic or binary segmentations X and Y, the Sørensen–Dice coefficient is defined as:

$$DL = 1 - \frac{2 \sum_i \min(x_i, y_i)}{\sum_i x_i + \sum_i y_i} \text{ with } x_i, y_i \in X, Y$$

Finally, the loss is equal to:

$$Loss = DL + BCE$$

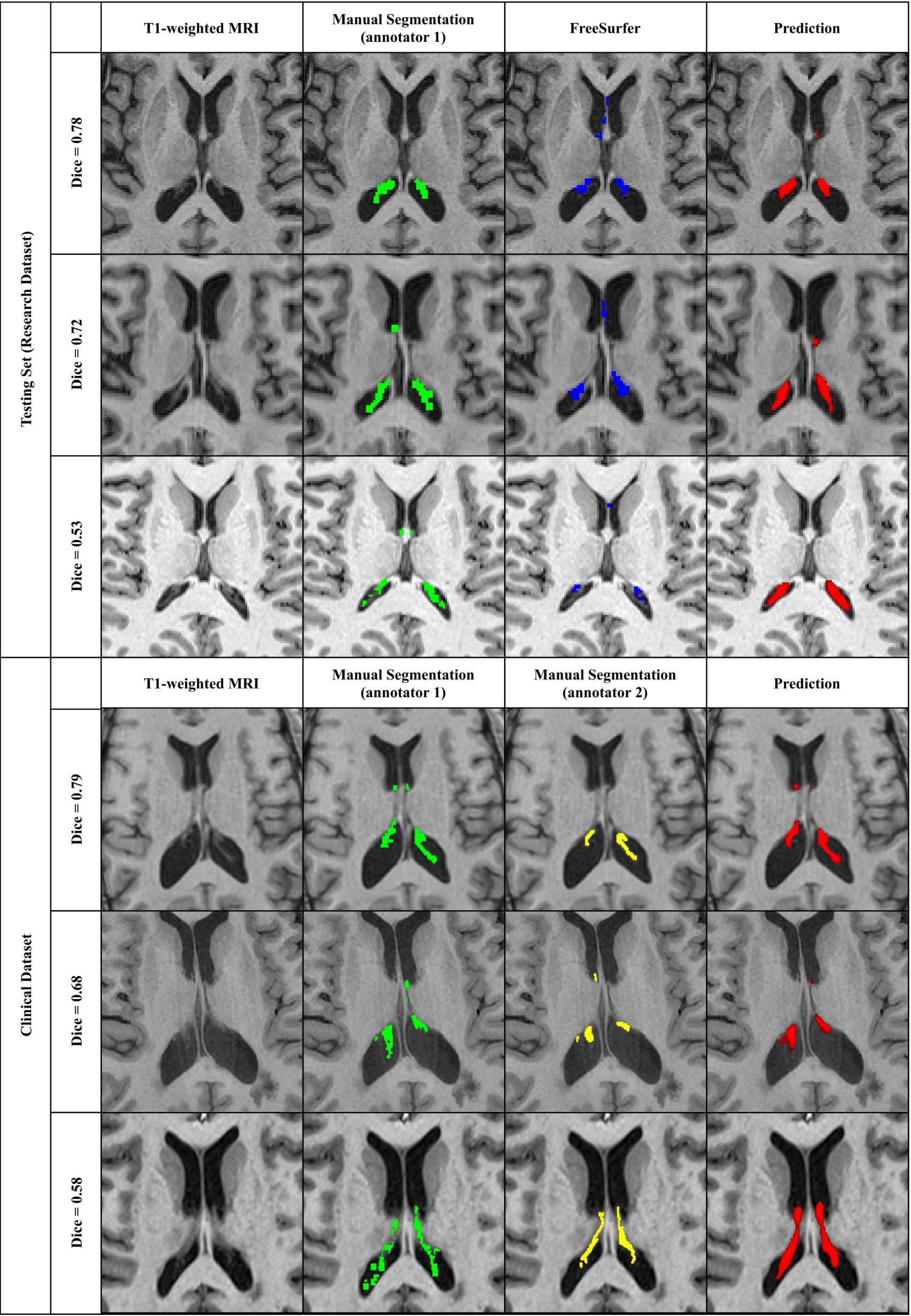
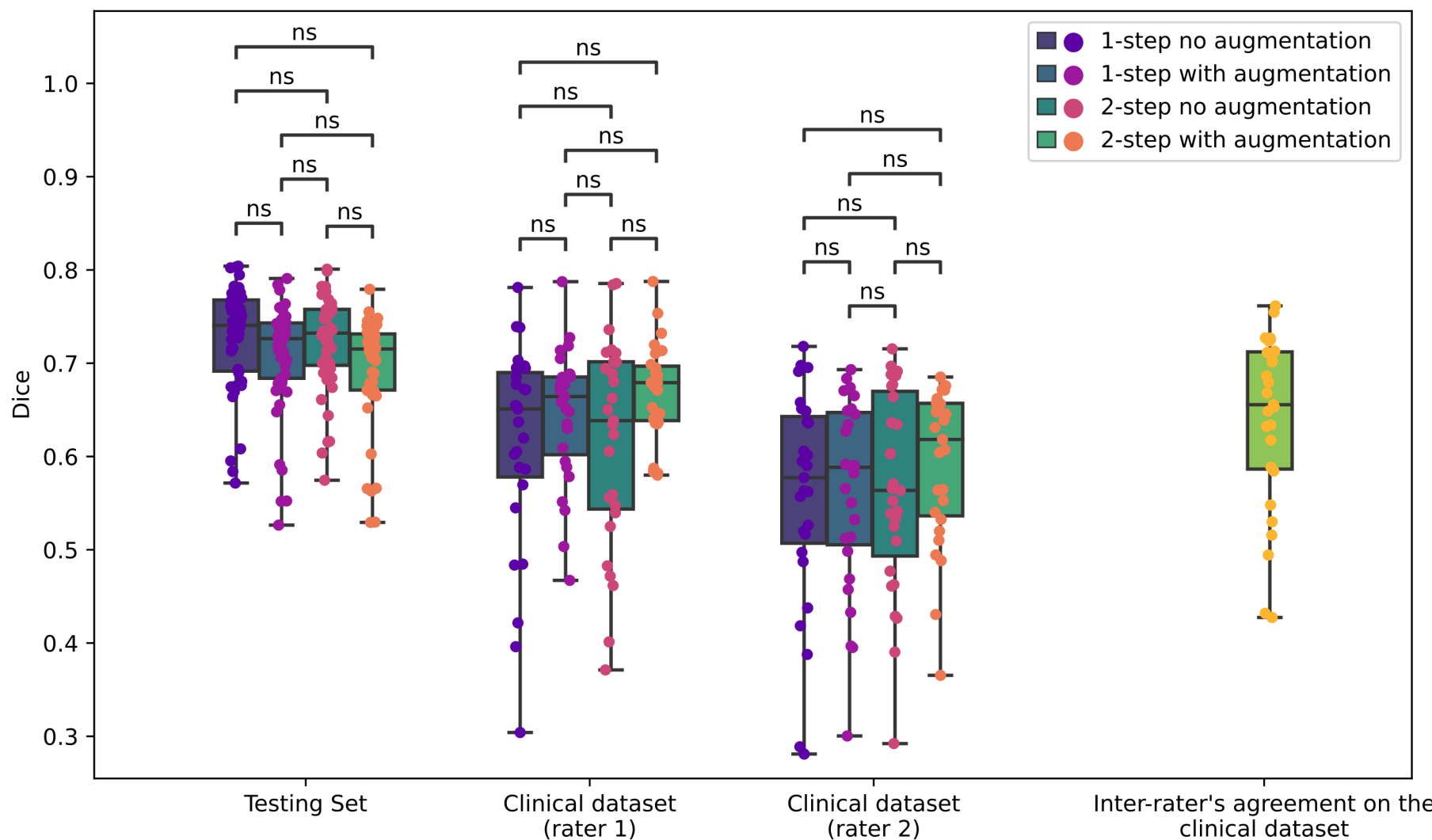
The loss of the 2-step approach is then defined as follows:

$$Loss_{2-step} = \begin{cases} Loss_{step1} & \text{if } N = 0 \\ Loss_{step1} + Loss_{step2} & \text{if } N > 0 \end{cases}$$

Data Augmentation	P	Characteristics
Left-Right flip	0.5	-
Affine transformations	0.3	max scaling = 0.3 ; max rotation = 15°
Image anisotropy	0.3	can be applied along all axes ; max down sampling factor = 2
MRI motion artifact	0.3	max rotation = 15°; max translation = 15mm; max number of movements = 2
MRI ghosting artifacts	0.3	number of ghosts = 2 ; can be along all axis
MRI spike artifacts	0.3	number of spikes = 1 ;
MRI bias field	0.3	maximum magnitude = 0.5 ; polynomial order = 3
Gaussian Noise	0.3	mean = 0 ; standard deviation = 1
Contrast modification	0.3	log(gamma) = 0.3

Results

- The 2-Step 3D U-Net allowed **multiplying the batch size by 4**.
- The proposed deep learning methods provided **considerably better performances compared to FreeSurfer and FastSurfer**, for all metrics.
- On the clinical dataset, performances were in general lower than those obtained on the research dataset (the range of average Dice on the clinical data set was 0.61-0.67 for annotator 1 and 0.56-0.59 for annotator 2 while it was 0.69-0.73 on the research dataset).
- The models also tended to provide higher segmentation metrics on the clinical dataset segmented by the **first annotator compared to the second annotator**.
- The automatic segmentation performance was of the **same order of magnitude as the inter-rater variability** (mean Dice=0.64±0.02 SEM).



Discussion

- The 2-Step 3D U-Net allowed **good segmentation performances with minimal preprocessing steps**.
- Reduced memory usage during training allowed to use larger batch sizes, beneficial to the learning process.
- The models had a tendency **to learn the first annotator’s “style”** as they had not been trained on images produced by annotator 2.
- The method seems ready for usage in large cohorts of subjects but might need to be further trained to segment ChP presenting cysts or calcifications which were not a common occurrence in the training dataset.

References

1. Lun, Melody P, “Development and Functions of the Choroid Plexus–Cerebrospinal Fluid System.” *Nature Reviews Neuroscience* 16 (8): 445–57.
2. Ricigliano, Vito, “Choroid Plexus Enlargement in Inflammatory Multiple Sclerosis: 3.0-T MRI and Translocator Protein PET Evaluation.” *Radiology* 301 (1): 166–77.
3. Çiçek, Özgün, “3D U-Net: Learning Dense Volumetric Segmentation from Sparse Annotation.” *ArXiv:1606.06650 [Cs]*, June.