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Improvement of brain atrophy evaluation using optimized brain masking

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CONTEXT & AIM OF THIS STUDY

In clinical studies, **SIENA** [1] is the reference tool to estimate **brain atrophy**, a key MRI-based feature strongly related to neurological and physical disabilities in small vessel disease as CADASIL [2]. The 1st step consists in **extracting brain** from skull using BET, pipeline highly sensitive to input parameters regards to MR acquisition and to severity of brain changes [3]. Its use for longitudinal studies in patients at various stage of a disease could be unlikely. We here proposed an **alternative pipeline** from ANTs suite [4] and compared both approaches.

MATERIALS & METHODS

❖ Acquisition

Database: CADASIL patients with NOTCH3 mutations included in a French prospective cohort (www.cervco.fr)
Imaging follow-up: every 18-24 months, MRI including 3DT1 and FLAIR acquired on $\left\{ \begin{array}{l} \text{a 1.5T SIGNA GE Medical Syst. (2003-2014),} \\ \text{a 3T SIEMENS Skyra Syst. (since 2014).} \end{array} \right.$

To overcome methodological issues [5]: brain atrophy estimated only between time-points with **scans from the same MRI protocol**

❖ MRI processing

Correction of image bias using N4 algorithm [6]
Correction of intensity inhomogeneities due to white matter hyperintensities using BIANCA algorithm from FSL toolbox [7,8]
Linear registration between each pair of data to work in the same field of view
Rescaling of intensity spans of T1w-MRI to match between them
Brain extraction using 1) BET with parameters adapted to most of data
2) **ANTs with default parameters**

Estimation of percentage of brain volume change (PBVC) using SIENA

❖ Data analysis

Results comparisons using the Wilcoxon test (significance at 0.05) and agreements illustrated using Bland-Altman plots

RESULTS

❖ Studied group

Among the 331 followed patients, 239 had at least 2 consecutive acquisitions with the same MRI protocol: 229 on GE (axial acquisition, TR/TE/TI 8.6/1.9/0ms, resolution: 1x1x0.8mm³) and only 10 on SIEMENS, including 8 with the same setting (sagittal acquisition, TR/TE/TI 2000/3.2/900ms, resolution: 0.4x0.4x0.4mm³). To work with identical samples sizes, 8 patients imaged on GE were randomly chosen. One couple of data was selected per patient. Nine over the 16 patients were women. At baseline, the mean age was 60.8 y (± 8.3).

❖ Brain extraction

Best BET parameters were '-B -f 0.1'. With such studied-adapted setting, extracerebral tissues remained in masks whereas **ANTs pipeline** set with default parameters provided visually **better outputs for all data** (Fig.1)

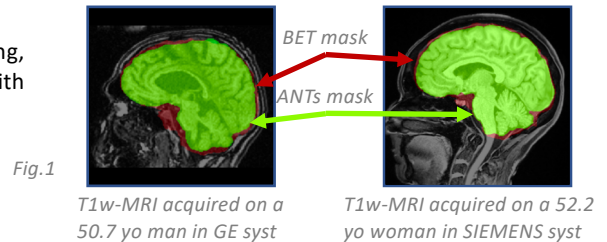


Fig.1

T1w-MRI acquired on a 50.7 yo man in GE syst

T1w-MRI acquired on a 52.2 yo woman in SIEMENS syst

❖ Results comparisons and agreements

Annual PBVC spanned in [-3.8;1.2] and [-3.4;1.3] for BET and ANTs pipelines respectively. PBVC estimated from the **ANTs-based masks** were **statistically greater than those estimated from the BET-based masks** ($p < 0.01$).

Bland-Altman plots showed agreements between annual PBVC estimated by both approaches depended on the MRI protocol and the estimated PBVC (Fig.2).

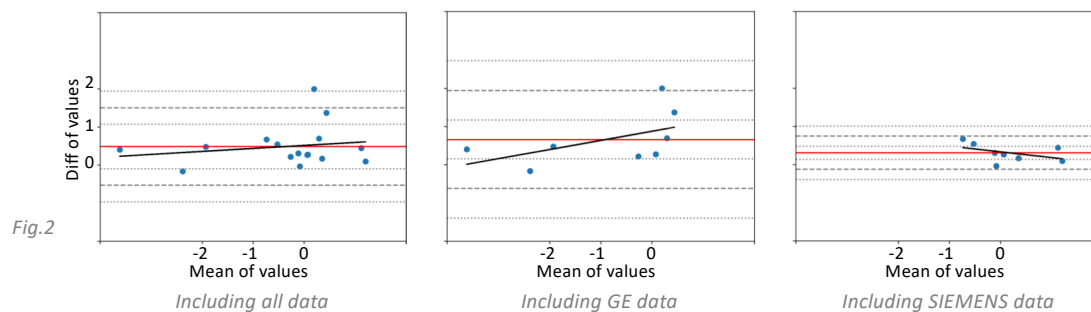


Fig.2

Including all data

Including GE data

Including SIEMENS data

DISCUSSION & CONCLUSION

This work confirms that the choice of BET pipeline is not a suitable first step to estimate brain atrophy in CADASIL patients. Whereas parameters were chosen to best fit with data, visual observations indicated **better brain extractions with ANTs pipeline set with default parameters**. In addition, as agreements between both approaches depended on the MRI protocol and the PBVC, we assumed erratic consequences on the brain atrophy estimates. **The ANTs-based approach** seems thus **more trustworthy for a longitudinal study in CADASIL**.

[1] Smith *et al.*, NeuroImage, 2002 [2] Jouvent *et al.*, Neurology, 2016 [3] Nakamura *et al.*, PLOS One, 2019 [4] Avants *et al.*, Neuroinformatics, 2011 [5] Opfer *et al.*, J. Neurology, 2018 [6] Tustison *et al.*, TMI, 2010 [7] Griffanti *et al.*, NeuroImage, 2016 [8] Ling *et al.*, Neuroinformatics, 2018

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