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### ► To cite this version:

Dorian Vogel, Jerome Coste, Jean-Jacques Lemaire, Simone Hemm. How Many is Enough? The Influence of patient count on structural normative template quality.. 9th European Medical and Biological Engineering Conference, EMBEC society, Jun 2024, Portoroz, Slovenia. pp.3545. hal-04569475

**HAL Id: hal-04569475**

**<https://hal.science/hal-04569475>**

Submitted on 6 May 2024

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## How Many is Enough?

### The Influence of patient count on structural normative template quality.

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Structural brain templates are the foundational element for group analysis in neuroscience, providing an anatomical reference when analyzing data from different patients. When creating such templates, the topic of the appropriate number of brains to obtain a stable anatomy must be addressed. The goal of this study was to estimate the number of patients required to reach convergence in the creation of a cohort-specific anatomical template through exemplary calculations for data (Ptolemee Electrophysiology project: IRB 5921, CE-CIC-GREN-18-03) from Clermont-Ferrand university hospital (France). Preoperative imaging data from a group of 47 patients (Parkinson's: 30, essential tremor: 17) who received deep brain stimulation was used in an iterative, non-linear, mixed-modality, unbiased anatomical normalization pipeline published previously. It consists of iterative non-linear normalization of all original images to an anatomical template updated after each iteration and implemented to use both T1 and WAIR (white matter attenuated inversion recovery, a modality specially designed to enhance grey matter contrast). During the pre-operative planning, up to 35 deep brain structures were manually labeled by a single expert. The normalization process was repeated, increasing the number of included patients, resulting in 5 different templates. The performance of the normalization was quantified using the pairwise overlap between anatomical structures across patients. A logistic function was then fitted on the median values of that score for each template to estimate the number of patients necessary to obtain a variation lower than 5%. In this study we estimated the number of patient images required to obtain a stable group-specific anatomical template. Manual segmentation of deep brain structures was used to benchmark templates with increasing number of patients included. Results might differ depending on the specific MR sequences used.

Acknowledgements: This work was supported financially by the Swiss National Science Foundation (205320\_207491).

Keywords: brain; normalization; non-linear; template; DBS.

Session(s):

Neuroscience and neuroengineering [main track]

Biomedical imaging and image processing [main track]

Abstract 3545