

Manual refinements of deformation fields improve the alignment between patient and template space

# Precision neuroimaging via manual refinement of deformation fields

Simón Oxenford<sup>1,\*</sup>, Ana Sofía Ríos<sup>1</sup>, Clemens Neudorfer<sup>1,2,3</sup>, Andreas Horn<sup>1,2,3</sup>

<sup>1</sup>Movement Disorders and Neuromodulation Unit, Department of Neurology, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt Universität zu Berlin, Department of Neurology, 10117 Berlin, Germany.

<sup>2</sup>Center for Brain Circuit Therapeutics Department of Neurology Brigham & Women's Hospital, Harvard Medical School, Boston MA 02115, USA.

<sup>3</sup>MGH Neurosurgery & Center for Neurotechnology and Neurorecovery (CNTR) at MGH Neurology Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114, USA. \*simon.oxenford@charite.de

## INTRODUCTION

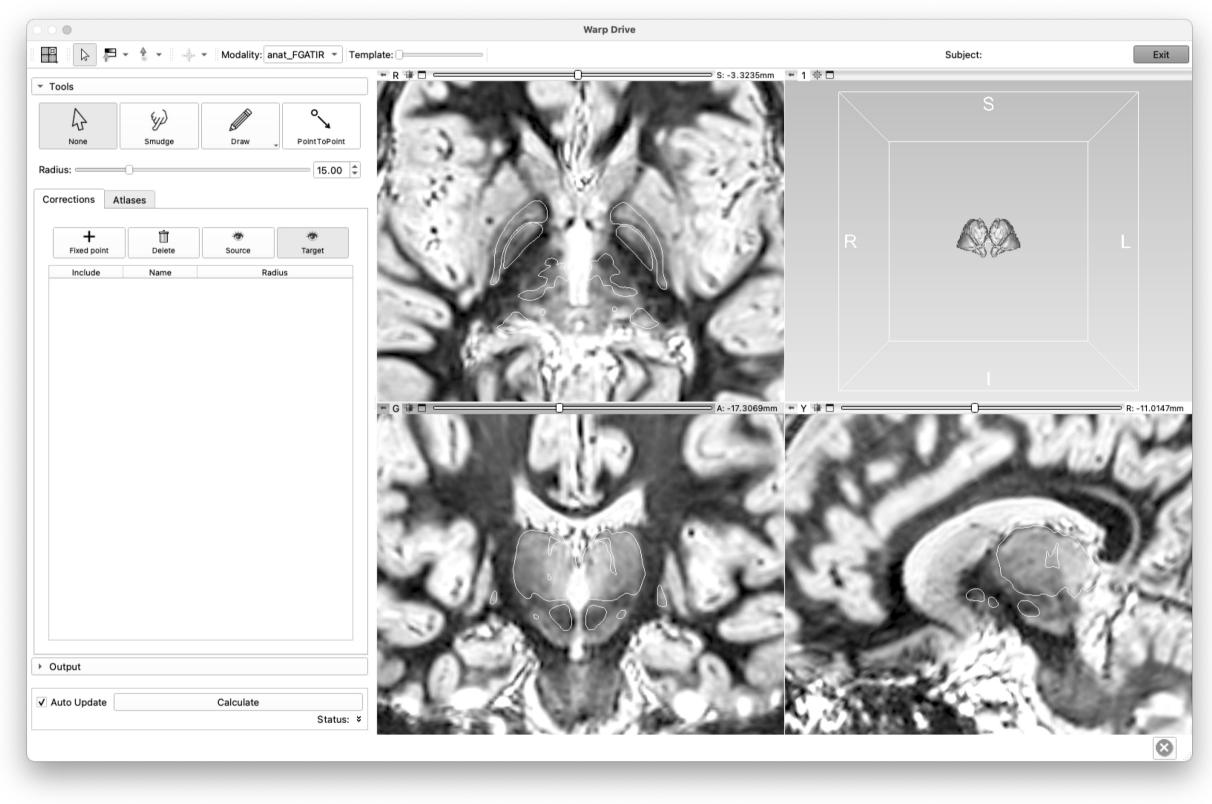
Determining the spatial relationship between clinical images, template spaces, and other imaging data is a key processing step when combining and analyzing different sources of neuroimaging information. The correspondence between spaces is typically represented by means of non-linear deformations using automatic registration algorithms. These are based on different image intensity metrics and usually converge to a local minimum that does not represent the expected match across the whole image.

## OBJECTIVES

The aim of our work is to develop a method that allows to correct the mismatches between spaces after image registration. We demonstrate its utility by employing it in a group level deep brain stimulation (DBS) imaging analysis and comparing results to conventional registration routines.

#### **MATERIALS & METHODS**

Here we introduce WarpDrive, a toolbox which facilitates the interaction and refinement of non-linear deformations (warp fields) after image registration. The tool is implemented as a 3D Slicer module and translates user inputs into source and target fiducials used to refine the normalization. It is also integrated into Lead-DBS (https://www.lead-dbs.org/) as an additional step after image normalization.



We analyzed a cohort of 10 patients (5 female, mean age: 63.7, range: 39-74 years) that underwent DBS of the ventral intermediate (VIM) thalamic nucleus at our center. First, DBS electrode localization and volume of activated tissue calculation were carried out using the default Lead-DBS pipeline. Then, we repeated the processing but this time refined the automatic normalization output using WarpDrive.

Neudorfer et al. recently described an imaging marker in form of an oval shaped hypointensity which is readily appreciable on fast gray matter acquisition T1 inversion recovery (FGATIR) sequences. In their study, modulating this hypointensity correlated with clinical tremor improvements.

Here, we analyzed the relationship between clinical tremor improvement and overlaps between the volume of activated tissue and an atlas of the hypointensity defined by Neudorfer et al. 2022. We repeat this analysis twice, first on patients that were normalized in automated fashion and second with the same cohort after manual refinement of normalization using WarpDrive.

#### RESULTS

We developed a method to refine deformation fields based on manual user interactions (Figure 1).

The application of the tool improved the alignment of segmented patient specific hypointensities to a normative one (Figure 2).

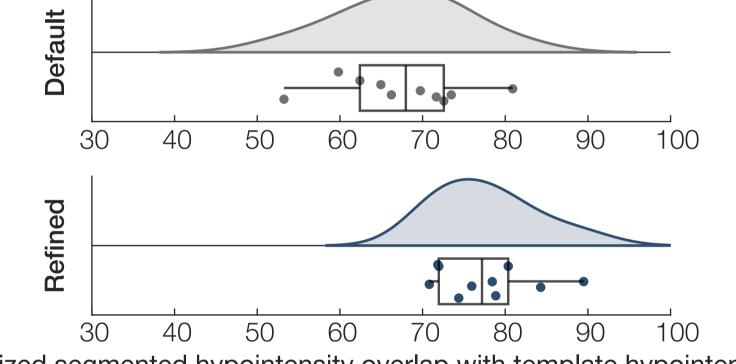
This translated into a group analysis in template space which matches expected results based on recent patient specific analysis (Figure 3).

## CONCLUSIONS

WarpDrive is a tool focused on precision that allows to accurately register specific areas of interest in one image space to their representations in another. This tool may be explicitly useful in DBS, where millimeters matter, key areas of interest are small and at times anatomically complex. The tool is made open-source (https://github.com/netstim/SlicerNetstim) and built upon established imaging processing platforms.

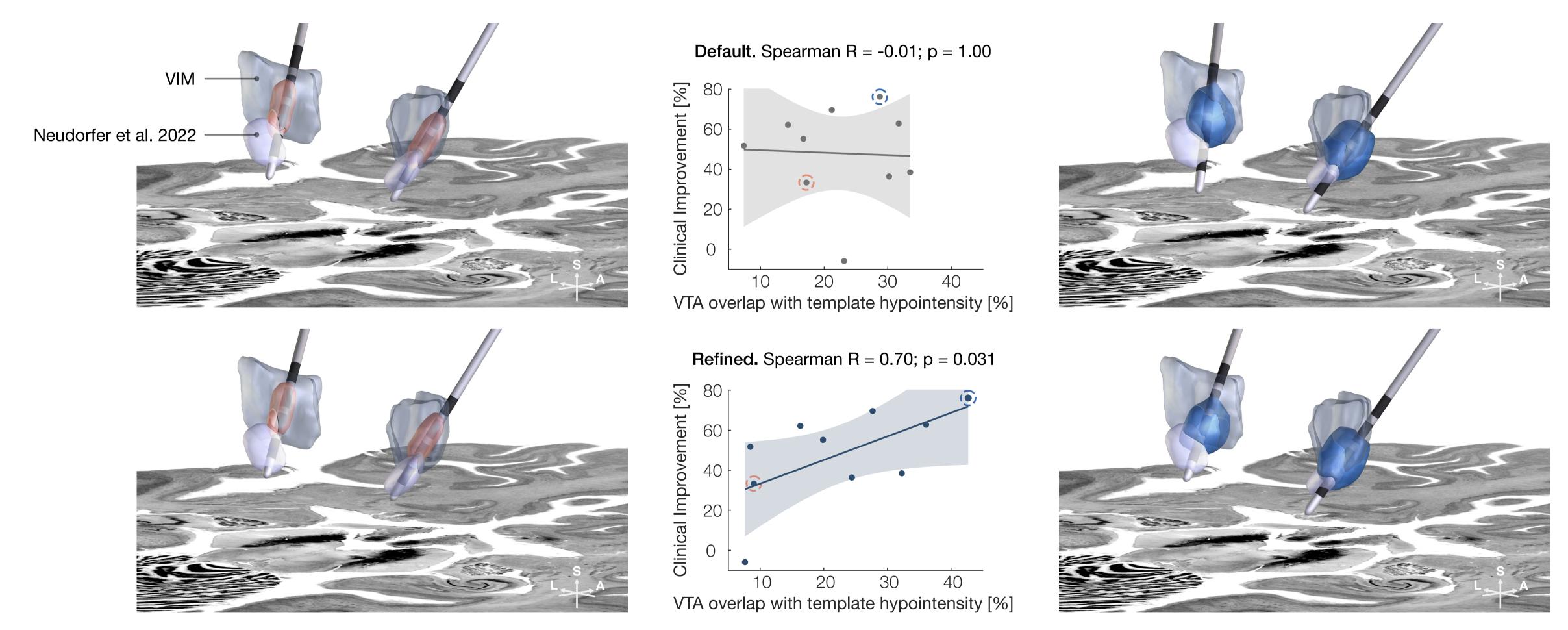
T = -3.24; p = 0.005

*Figure 1:* WarpDrive user interface. Different tools are made available to the user to interact with the output from automatic normalization. These interactions are translated into source and target fiducials with variable radius that are used to compute the refinements.



Normalized segmented hypointensity overlap with template hypointensity [%]

*Figure 2:* The group with normalizations refined using WarpDrive present a higher overlap between the manually segmented hypointensity and the template hypointensity introduced by Neudorfer et al 2022.



*Figure 3:* Group analysis in template space (MNI ICBM 2009b nonlinear asymmetric) comparing the relationship between clinical improvement and overlap of volume of tissue activated (VTA) with template hypointensity. For this analysis, we used the hypointensity described by Neudorfer et al. 2022. The top panel shows the analysis carried out using the default normalization strategy implemented in Lead-DBS and the bottom one was further refined using WarpDrive, the tool introduced here. This association was described by Neudorfer et al 2022., performing the analysis in patient specific space. Here, we replicate their findings in template space after refining the normalizations. Two example patients are shown pre- and post-refinement featuring electrode localization, VTA, the ventral intermediate (VIM) thalamic nucleus and the hypointensity introduced by Neudorfer et al. 2022.

## REFERENCES

Neudorfer, C., Kroneberg, D., Al-Fatly, B., Goede, L., Kübler, D., Faust, K., van Rienen, U., Tietze, A., Picht, T., Herrington, T. M., Middlebrooks, E. H., Kühn, A., Schneider, G.-H., & Horn, A. Personalizing deep brain stimulation using advanced imaging sequences. Annals of Neurology, 2022. https://doi.org/10.1002/ana.26326.





WarpDrive Video

