Klinikum rechts der Isar
Technische Universität München

Atrophy Assessment via Freesurfer SynthSR: A Clinical Validation

Severin Schramm[1], Melissa Thalhammer[2], Benita Schmitz-Koep[1], Kirsten Jung[1], Dennis Hedderich[1]

[1]Department of Diagnostic an Interventional Neuroradiology, Klinikum Rechts der Isar, TUM School of Medicine and Health, Munich, Germany
[2]TUM-Neuroimaging Center, Klinikum rechts der Isar, Technical University of Munich, Munich, Germany

S. Schramm, Abteilung für Diagnostische und Interventionelle Neuroradiologie, Klinikum rechts der Isar, TU München
Ismaningerstr. 22, 81675 München
severin.schramm@tum.de

Introduction

Structural magnetic resonance imaging (MRI) continues to inhabit an important position in research and clinical assessments of neurodegeneration, with one of its primary uses lying in the detection and monitoring of brain atrophy patterns [1, 2]. In clinical practice however, structural imaging protocols are often heterogeneous and subject to low spatial resolution, resulting in suboptimal image quality for brain volume assessments and limiting data quality for scientific analyses [3].

Adressing this issue, Freesurfer is a widely used open-source software package, employed among other use-cases in volumetric and surface-based analyses of neuroimaging [4]. Since the recent release of version 7.3, Freesurfer includes SynthSR, a convolutional neural network based approach able to generate 1 mm isotropic 3D T1-like synthetic imaging (T1s) from heterogeneous input sequences trained on data from 20 subjects [3]. In previous validation approaches, the developers report strong correlations between T1s and real 3D T1 imaging [3]. Reliable generation of T1s could improve clinical brain atrophy assessments and unlock much larger datasets of neurodegeneration-related imaging than currently available. In the present study, we attempt to further validate T1s against the gold standard of 1 mm isotropic 3D T1 imaging (GS) by investigating bilateral hippocampus volume (VHip), a notable imaging parameter in neurodegeneration assessment in patients and healthy controls (HC) [2].

Methods

We selected a dataset of 10 representative Alzheimer's Disease (AD) cases, as well as 10 HC scanned on a 3T Siemens Biograph scanner in our local clinic. We employed Freesurfer SynthSR [3] to generate T1s from three different scenarios of imaging input: 1 mm 3D isotropic T2 FLAIR (Sc1), 4 mm axial T2 FLAIR (Sc2) and 4 mm coronal T2 (Sc3). The resulting T1s and GS were further segmented via CAT12 according to the LONI Probabilistic Brain Atlas (LPBA40) [5, 6]. VHip were extracted from GS and the three sets of T1s for subsequent testing against one another via paired t-tests.

Results

After Bonferroni correction, we observed significantly higher VHip in T1s based on Sc3 compared to GS in AD (Figure 1; GS 5.867 ± 0.580 ml vs. Sc3 6.368 ± 0.604 ml, p = 0.01126). Notably, no significant differences were observed between GS and T1s of HC (GS 7.183 ± 0.644 ml; Sc1 6.979 ± 0.889 ml; Sc2 6.769 ± 0.742 ml; Sc3 7.061 ± 0.750 ml). T1s VHip overestimation was strong enough in some cases to be visually notable (Figure 2).

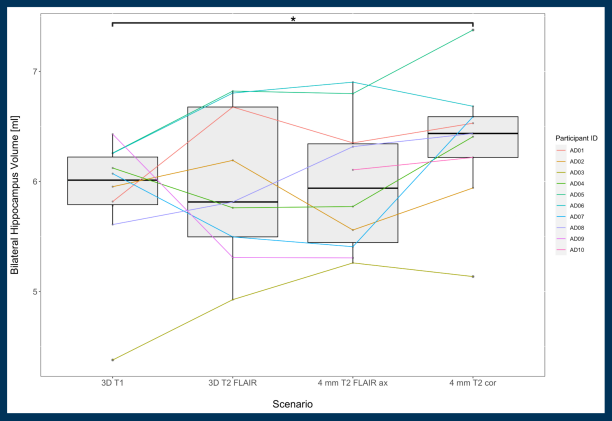

Figure 1: Distribution of bilateral hippocampus volume in ml for our cohort of Alzheimer's Disease (AD) patients split according to imaging scenario. Synthetic T1 (T1s) based on Scenario 3 (Sc3; input 4 mm coronal T2) resulted in significantly higher hippocampus volumina compared to gold standard (GS; 1 mm isovoxel 3D T1).

Conclusion

Freesurfer SynthSR generally performed well compared to GS in generating T1s for VHip assessment in AD and HC. However, too low-resolution input imaging could lead to misestimations of brain volumina, which should be considered both in scientific setups as well as potential clinical use cases. More validation in preferably atypical atrophy patterns is required.

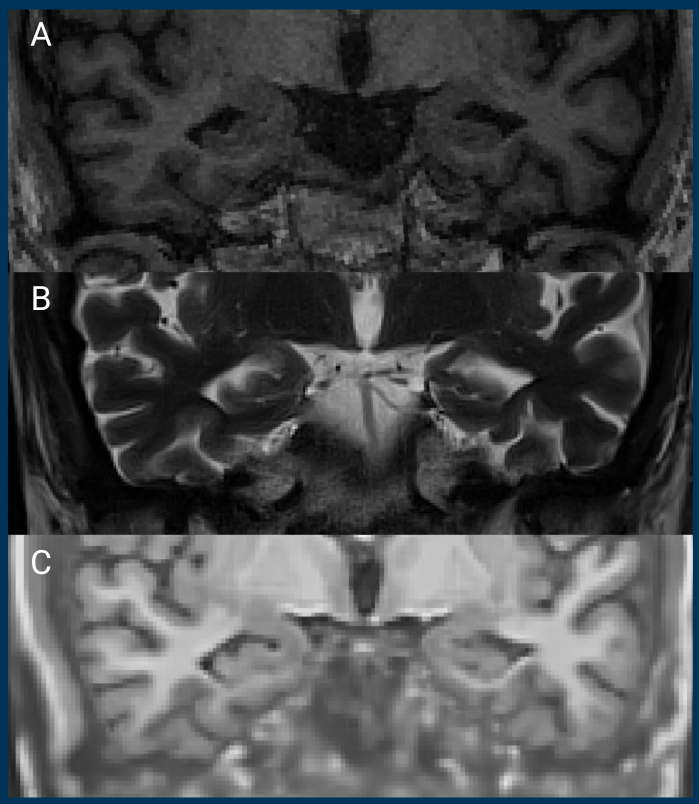

Figure 2: Three coronal slices in an exemplary Alzheimer's Disease (AD) patient in identical position. We observe a noticeable difference in hippocampal volume reconstruction, likely due to partial volume effects.

1. Young PN, Estarellas M, Coomans E, et al. Imaging biomarkers in neurodegeneration: current and future practices. Alzheimers Res Ther 2020;12:1-17.
2. Knopman DS, Jack CR, Wiste HJ, et al. Age and neurodegeneration imaging biomarkers in persons with Alzheimer disease dementia. Neurology 2016;87:691-698.
3. Iglesias JE, Billot B, Balbastre Y, et al. SynthSR: A public AI tool to turn heterogeneous clinical brain scans into high-resolution T1-weighted images for 3D morphometry. Science advances 2023;9:eadd3607.
4. Reuter M, Schmansky NJ, Rosas HD, Fischl B. Within-subject template estimation for unbiased longitudinal image analysis. Neuroimage 2012;61:1402-1418.
5. Gaser C, Dahnke R, Thompson PM, Kurth F, Luders E, Initiative AsDN. CAT--A computational anatomy toolbox for the analysis of structural MRI data. biorxiv 2022:2022.2006. 2011.495736.6.
6. Shattuck DW, Mirza M, Adisetiyo V, et al. Construction of a 3D probabilistic atlas of human cortical structures. Neuroimage 2008;39:1064-1080.