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## Surfing the Hippocampus Wave

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## Summary

The aim of this thesis, to optimize methods for hippocampus segmentation and atrophy measurements in the field of neuroradiology and radiotherapy, was addressed as follows:

The first topic presented in this thesis was the quantification of reproducibility and differences between manual and automatic segmentations (chapter 2). The most important finding of this study was that manual segmentations had poorer reproducibility for within-session rescans than one of the automatic segmentation methods (FSL-FIRST). Also, systematic regional differences between methods were detected. These findings reflected the different underlying definitions of the hippocampal structure used by the different methods, thus emphasizing the need for a harmonized hippocampal outlining protocol [1–3]. Furthermore, FSL-FIRST's higher outline reproducibility indicated that automatic methods can have reduced segmentation variabilities. However, the benefits of outline reproducibility should be treated with care, because good reproducibility in itself does not necessarily imply that the hippocampus is outlined accurately or that the method is sensitive to disease-related change.

In chapter 3 hippocampus segmentation agreement was determined between multiple observers using a radiotherapy delineation protocol (RTOG), for the purpose of planning hippocampus sparing radiotherapy. The ICCs of 0.56 and 0.69 for the left and right hippocampus respectively, were relatively low compared to segmentations performed in neuroradiology, which usually exhibit inter-rater ICCs higher than 0.85 [4]. Also, the average overlap index of all observers (0.62) was much lower than the average overlap index of the study from chapter 2 (0.79). Segmentations from the study of chapter 2 were performed by a single radiology technician with multiple years of hippocampal delineation experience. In chapter 3, the participating observers had different specialisms (radiotherapy technician, oncologist, neuroradiologist), and used a hippocampus delineation protocol which was relatively new to them. This might explain the difference between the overlap indices of these studies and it also leads to the conclusion of chapter 3 that conformity of delineations could for instance be improved by using a better delineation protocol and providing more training. Nevertheless, this variability had limited effect on the ability to reach the clinical goal of reducing the average radiation dose to the hippocampus because in almost all cases, all dose constraints were met.

In chapter 4, a novel semi-automatic delineation tool, FASTSURF, was presented. In this proof of concept study, sparse delineations were simulated and FASTSURF's performance was evaluated in comparison with manual and automatic segmentations. It was shown that FASTSURF segmentations have higher agreement with manual hippocampus segmentation than both tested automatic segmentation methods, even when only six to seven contours were used as input. Possible bias in favour of FASTSURF was limited by comparing the semi-automatic reconstruction to the manual delineation of a different back-to-back scan. The same conclusion, that five to eight input contours suffice, was reached for different outlining protocols and datasets where no back-to-back scans were available. It was also found that with only five input contours, FASTSURF was already better reproducible than the automatic methods FreeSurfer and FSL-FIRST.

The work described in chapter 5 evaluated whether FASTSURF can be used to segment subcortical structures such as the putamen, caudate nucleus and thalamus as a key ingredient of

a novel protocol to make a standard segmentation reference set in an optimized labour-saving manner. Similar to chapter 4, FASTSURF segmentations had excellent overlap with complete manual segmentations, concluding that FASTSURF is indeed a time-saving alternative to fully manual segmentations.

Hippocampal atrophy rates as measured on structural MRI are an important biomarker in clinical drug trials. Chapter 6 compared eight different methods to determine one-year hippocampal atrophy rates on structural MRI in presence of AD and MCI and evaluated plausibility, reproducibility and sensitivity of those methods. Results showed that registration-based methods outperformed manual segmentations regarding all three aspects. The registration methods with best performance, in descending order, were ANTs, Elastix and NiftyReg. This study specifically addressed the feasibility of using these methods to detect radiation-induced hippocampal volume loss. By consulting recent radiotherapy literature to obtain a rough estimate of the expected effect size, this chapter predicts that radiation-induced hippocampal volume loss should be detectable even with a fairly small sample size ( $N \approx 20$  per group) when one of these automated methods is used. Remarkably, with fully manual delineation with the outlining protocol used in [5] such detection would require much larger sample sizes ( $N \approx 90$ ).

## References

- [1] Boccardi M, Bocchetta M, Apostolova LG, Barnes J, Bartzokis G, Corbetta G, et al. Delphi definition of the EADC-ADNI Harmonized Protocol for hippocampal segmentation on magnetic resonance. *Alzheimer's Dement* 2015;11:126–38.
- [2] Frisoni GB, Jack CR, Bocchetta M, Bauer C, Frederiksen KS, Liu Y, et al. The EADC-ADNI Harmonized Protocol for manual hippocampal segmentation on magnetic resonance: evidence of validity. *Alzheimer's Dement* 2015;11:111–25.
- [3] Apostolova LG, Zarow C, Biado K, Hurtz S, Boccardi M, Somme J, et al. Relationship between hippocampal atrophy and neuropathology markers: a 7T MRI validation study of the EADC-ADNI Harmonized Hippocampal Segmentation Protocol. *Alzheimer's Dement* 2015;11:139–50.
- [4] Boccardi M, Ganzola R, Bocchetta M, Pievani M, Redolfi A, Bartzokis G, et al. Survey of protocols for the manual segmentation of the hippocampus: Preparatory steps towards a joint EADC-ADNI harmonized protocol. *Adv Alzheimer's Dis* 2011;2:111–25.
- [5] Jack CR. MRI-Based Hippocampal Volume Measurements in Epilepsy. *Epilepsia* 1994;35:S21–9.