

FastSurfer as an Alternative to FreeSurfer in HCP Minimal Preprocessing Pipeline

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ABSTRACT—Amidst the rising demands for artificial intelligence and brain disease research, neuroscience has received unparalleled attention. The Human Connectome Project (HCP), funded by the National Institutes of Health (NIH), aims to delineate the human brain's connectivity map using high-resolution structural Magnetic Resonance Imaging and Diffusion Tensor Imaging, enhancing the understanding of the interplay between brain function and structure. However, the computational intensity and time consumption of the FreeSurfer Pipeline, on which HCP's minimal preprocessing pipeline relies, limit its scalability for large-scale studies. This study investigates the implementation of the FastSurfer Pipeline as an efficient alternative to the FreeSurfer Pipeline for HCP structural data preprocessing, with a focus on ensuring seamless integration from PreFreeSurfer to FastSurfer and from FastSurfer to PostFreeSurfer. By adjusting the input and output, the atlas used, and the T2w to T1w transformation matrix, we successfully integrated the FastSurfer Pipeline into the HCP structural pipeline. Results indicate that the alternative pipeline maintains high consistency with the original in terms of gray and white matter surface reconstruction, volume, and cortical area segmentation, while significantly enhancing processing efficiency. However, local negative values in Myelin mapping were observed, likely due to FastSurfer's exclusion of T2-weighted information. The findings of this study hold significant implications for accelerating the structural preprocessing pipeline of HCP and for the selection and refinement of data processing methodologies in future neuroscience research.

INDEX TERMS—HCP minimal preprocessing pipeline, FreeSurfer, FastSurfer

INTRODUCTION

HUMAN CONNECTOME PROJECT (HCP)

The brain, being the most complex organ, is central to advancing artificial intelligence and combating brain diseases, drawing increased focus to neuroscience. Among its developments, the Human Connectome Project (HCP) [1], initiated in 2009 by the National Institutes of Health (NIH) and involving multiple institutions, aims to map human brain connectivity using structural Magnetic Resonance Imaging (sMRI) and Diffusion Tensor Imaging (DTI). This endeavor seeks to uncover the intricate connections and networks within the brain, facilitating a deeper understanding of its functions and their relation to cognition, emotion, and behavior.

Distinguished from standard MRI, HCP employs a specially designed connectome 3T scanner for higher resolution and distinct distortion data capture [2]. Although HCP has made extensive brain imaging data available, its unique nature necessitates complex preprocessing, particularly for correcting gradient non-

linearity distortions in obliquely sliced images. These challenges have been addressed in the HCP Minimal Preprocessing Pipeline.

HCP MINIMAL PREPROCESSING PIPELINE

The HCP Minimal Preprocessing Pipeline was developed collaboratively by the WU–Minn HCP and MGH/UCLA HCP consortia [2]. This pipeline encompasses the preprocessing of HCP structural imaging data, along with foundational preprocessing for functional and diffusion imaging (Figure 1). Utilizing the HCP minimal preprocessing pipeline allows researchers to bypass the design of repetitive preprocessing tasks, enabling spatial preprocessing to be conducted in a standardized manner. Additionally, the preprocessing results include files that integrate volume and surface with volumetric space, facilitating the comparison of HCP data with other datasets.

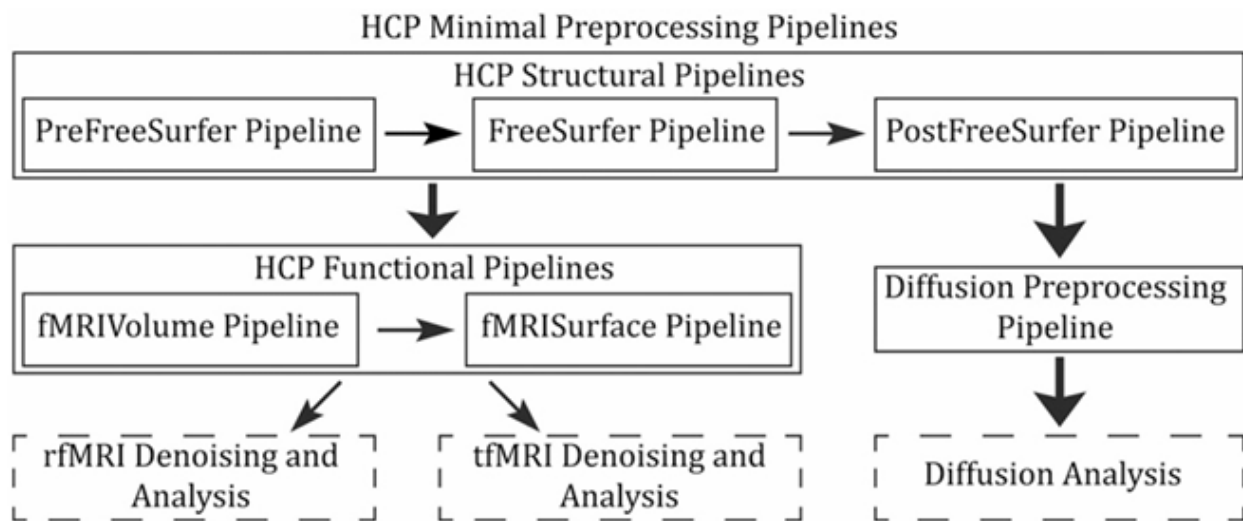


Figure 1 An overview of the HCP Minimal Preprocessing Pipelines. The HCP Structural Pipelines are run first, and then either the HCP Functional Pipelines or the Diffusion Preprocessing Pipeline can be run. Afterwards, resting state, task, and diffusion analysis can proceed.

Structural processing within this pipeline primarily employs the recon-all pipeline from the FreeSurfer suite [3], with several enhancements. This is a well-tested and robust process. However, due to its reliance on multiple traditional image transformation steps, some of which require fine-tuning of parameters and extensive numerical optimization, it is computationally intensive and time-consuming, significantly limiting scalability in large cohort studies or clinical workflows.

FASTSURFER PIPELINE VS FREESURFER PIPELINE

FastSurfer, proposed by the German Center for Neurodegenerative Diseases in 2020, emerges as an alternative to the FreeSurfer pipeline [4]. Leveraging the FastSurferCNN deep learning architecture, it achieves rapid and accurate segmentation of cortical and subcortical structures (Figure 2). The introduction of spectral spherical embedding and the direct mapping of cortical labels from images to surfaces facilitate swift cortical surface

reconstruction and thickness analysis. The FastSurfer Pipeline offers a comprehensive substitute for the FreeSurfer Pipeline, enabling volume analysis in under a minute and surface-based thickness analysis in approximately one hour.

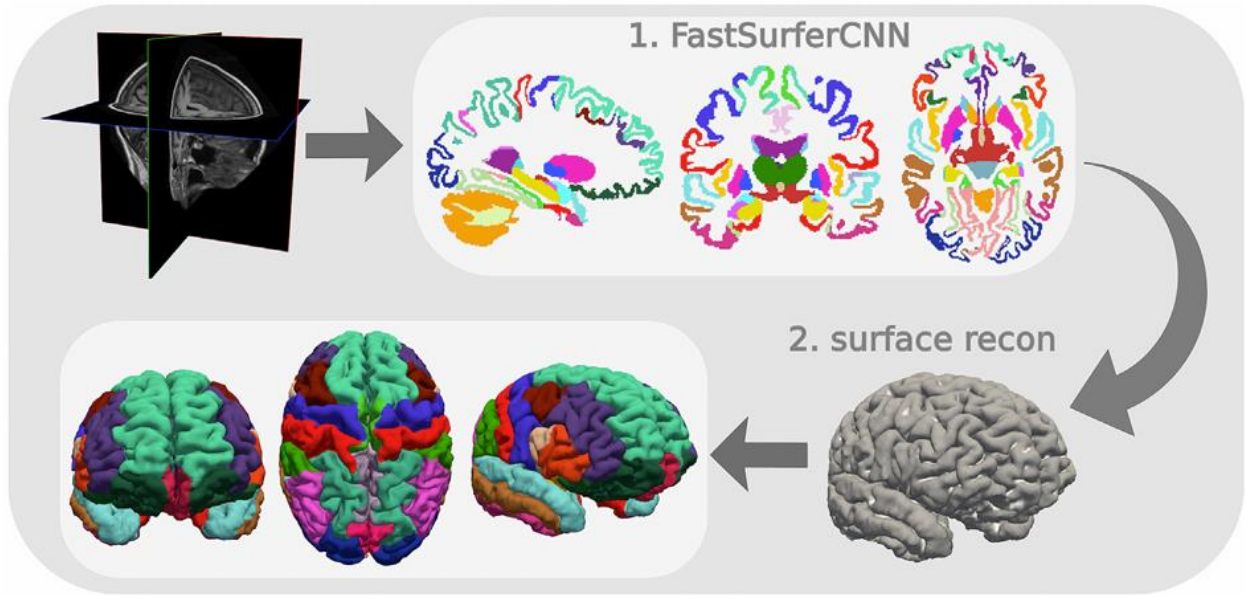


Figure 2 FastSurfer- A fast and accurate deep learning based neuroimaging pipeline.

Our research aims to implement the FastSurfer Pipeline as an alternative to the FreeSurfer Pipeline within the HCP Minimal Preprocessing Pipeline, to expedite the structural preprocessing of the HCP while maintaining data processing quality.

RELATED WORK

Our replacement work is grounded in the HCP Minimal Preprocessing Pipeline; therefore, we first describe the structural processing workflow within this pipeline and the inputs and outputs of each stage to facilitate understanding of the subsequent methods section. The structural processing in the HCP Minimal Preprocessing Pipeline is divided into three parts: PreFreeSurfer Pipeline, FreeSurfer Pipeline, and PostFreeSurfer Pipeline [2].

PREFREESURFER PIPELINE

The primary function of the PreFreeSurfer Pipeline stage is to generate a distortion-free native structural volume space for each subject and register the subject's native structural volume space to the MNI152 standard space (Figure 3). The process is as follows: distortion correction due to MR gradient nonlinearity is performed using the `gradient_nonlin_unwarp` package from a customized version of FreeSurfer, T1 and T2 images are pre-aligned to MNI and averaged to fsaverage space using FSL's FLIRT, and averaged T1 and T2 images are aligned to MNI ACPC using FSL's robustfov. Brain extraction is performed using FSL's FLIRT and FNIRT, with readout distortion corrected using FLIRT with 6DOF. Next, undistorted T2 images are cross-modally registered to

undistorted T1 images using FLIRT with the BBR cost function, followed by bias field correction using a method proposed by Glasser and Van Essen (2011) for correcting intensity non-uniformity in myelin imaging [5]. Finally, T1w images are registered to MNI space using FLIRT with 12DOF affine transformation and FNIRT non-linear registration, producing the final non-linear volume transformation from the subject's native volume space to MNI space.

The input for the PreFreeSurfer Pipeline consists of unprocessed HCP data, minimally requiring one scan sequence each for T1 and T2, as well as their corresponding BIAS and Fieldmap amplitude and phase images. The output is organized into a folder (default name: T1w) containing the original volume space images, and another folder (default name: MNINonLinear) containing images in MNI space, with a T2 folder containing some process files.

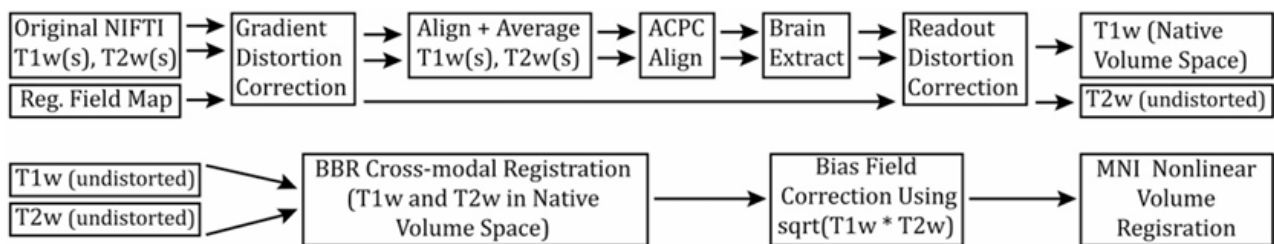


Figure 3 The steps of the PreFreeSurfer pipeline. The PreFreeSurfer pipeline produces the Native and MNI Volume Spaces, which will be used in later pipelines and analyses.

FREESURFER PIPELINE

The FreeSurfer pipeline is primarily utilized for segmenting brain volumes into predefined structures, reconstructing white and gray matter cortical surfaces, and registering them to a standard surface atlas (Figure 4). The process involves downsampling undistorted T1 images using Splines, initializing white matter surfaces with recon-all, fine-tuning the registration of T2w images with FSL's BBR, and continuing with recon-all to generate gray matter-pial surfaces. This is followed by high-resolution pial surface localization and normalization using gray matter density information, exclusion of dura and vascular artifacts using registered T2w images, and anatomical parcellation of surfaces and volumes. Additionally, morphometric measurements such as structural volumes, surface areas, and thicknesses are conducted.

The input for the FreeSurfer pipeline is the undistorted T1 and T2 images, with the output path defaulting to T1w/subjectID. The results are primarily located in the mri, surf, and label folders. The mri folder contains various MRI data formats, such as raw T1w and T2w images and segmentation results of the brain; the surf folder includes information on cortical surfaces, such as three-dimensional models and curvature data; the label folder contains various regional labels, including brain and cortical area labels.

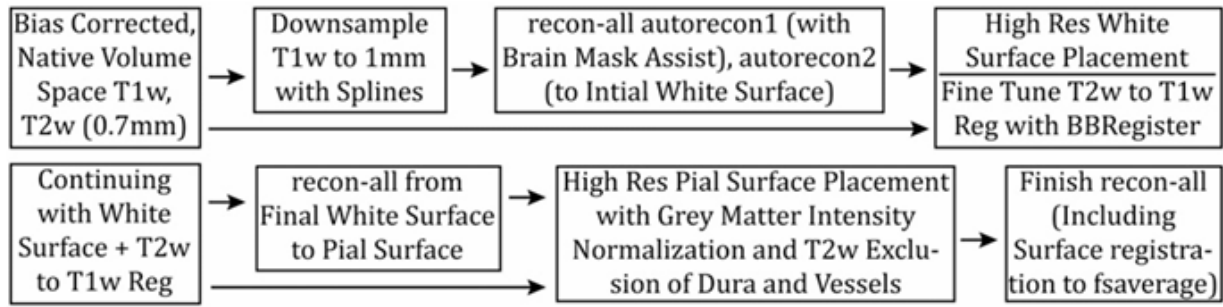


Figure 4 The steps of the FreeSurfer Pipeline. FreeSurfer's recon-all forms the basis of most of the pipeline, but it is interrupted at certain steps to improve the robustness of the brain extraction, to fine tune the T2wtoT1w registration, and to more accurately place the white and pial surfaces with high-resolution 0.7mm T1w and T2w data. These inputs are fed back into recon-all at each stage.

POSTFREESURFER PIPELINE

The PostFreeSurfer pipeline takes the output folder from the FreeSurfer pipeline as its input. Its main function is to generate NIFTI volumes and GIFTI surface files for viewing in the Connectome Workbench [6], register surfaces to the Conte69 surface template, perform parcellation based on the DKT atlas on the registered surfaces, and create myelin maps (Figure 5). The process also involves using intermediate files from the T2wtoT1w registration in the FreeSurfer Pipeline to improve the T2toT1 registration in this step, followed by the creation of mid-thickness and inflated surfaces by averaging white matter and pial surfaces. These files are organized into a "spec" file located in the subject's Native space, for individual analysis of myelin content maps and quality control of surface reconstruction, with data default stored in the T1w/Native folder.

Furthermore, the native volume is registered to MNI space and then mapped onto the surface. The generated spec files contain standard anatomical datasets, stored in the MNINonLinear/Native folder. Finally, previous group-averaged myelin maps on the Conte69 mesh are brought to each individual's Native mesh through the inverse transformation of surface registration performed in the PostFreeSurfer process.

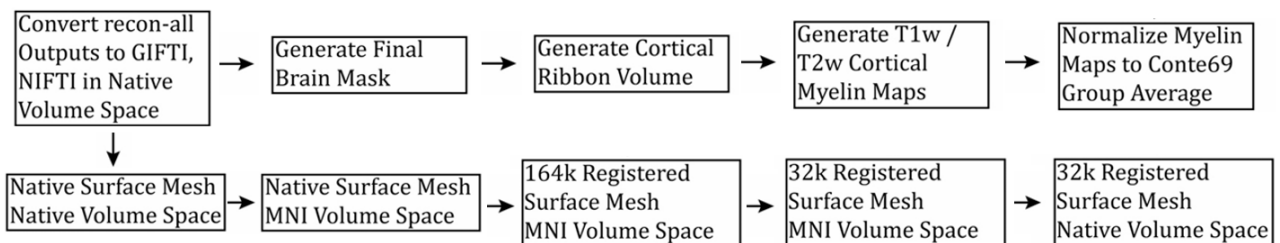


Figure 5 An overview of the PostFreeSurfer pipeline. In addition to generating a final brain mask and myelin maps, it converts data to NIFTI and GIFTI formats and creates Connectome Workbench spec files in the surface spaces.

METHOD

DATASET

Dataset A total of 21 participants were randomly selected from the WU-Minn HCP Retest Data, a dataset publicly released by the Human Connectome Project (HCP). Their unprocessed data were downloaded and organized in accordance with the specifications outlined in the Minimal Preprocessing Pipeline. The acquisition of primary T1-weighted (T1w) and T2-weighted (T2w) structural images required 32 minutes for each. Additionally, auxiliary scans were conducted on a custom 3T Siemens Skyra scanner equipped with a 32-channel head coil, taking an extra 8 minutes. The T1w images were obtained using the 3DMPRAGE sequence, and the T2w images were captured using the Siemens SPACE sequence. Detailed parameters for the structural imaging acquisition within the HCP dataset are as TABLE I [2].

TABLE II Parameters for the Structural Imaging Acquisition within the HCP Dataset

Parameter/Sequence	T1w Images	T2w Images	Auxiliary Scans
Sequence	3D MPRAGE	Siemens SPACE	-
Resolution	0.7mm isotropic	0.7mm isotropic	2mm isotropic
Field of View (FOV)	224mm	224mm	-
Matrix Size	320	320	-
Number of Slices	256 sagittal slices	256 sagittal slices	-
TR	2400ms	3200ms	B1+:TR1/TR2=20/120ms
TE	2.14ms	565ms	B0: $\Delta TE=2.46ms$
TI	1000ms	-	-
Flip Angle (FA)	8°	-	AFI target flip angle is 50°
Bandwidth (BW)	210Hz/pixel	744Hz/pixel	-
Echo Spacing (ES)	7.6ms	-	-
Water Excitation Pulse	Binomial (1:1)	None	-
Phase Encoding			
Undersampling Factor (GRAPPA)	2	2	-
Readout Strategy	Asymmetric readout, 7.4 μs dwell time	2.1 μs dwell time	-
Total Echo Train Length	-	314	-
Echo Train Length	-	1105 echoes	-
B0 Field Map	-	-	Dual echo gradient echo sequence
B1- Receive Field	-	-	FLASH sequence (32-channel head coil and body coil)
B1+ Transmit Field	-	-	Actual Flip Angle Imaging (AFI)

ENVIRONMENT PREPARE

To ensure the reproducibility of our experiments and seamless integration of methodologies, we meticulously configured our computational environment following the prerequisites of the Human Connectome Project (HCP)

and FastSurfer pipelines. The configuration details are as follows:

Operating system: Windows Subsystem for Linux (WSL) with Ubuntu 20.04 LTS was employed for a Linux environment on Windows, facilitating the execution of Linux-specific software and scripts.

Neuroimaging software:

FMRIB Software Library (FSL): Version 6.0.7.7 for comprehensive FMRI, MRI, and DTI brain imaging data analysis.

FreeSurfer: Versions 6.0 (on Linux CentOS 6 x86_64, dated January 23, 2017) for PreFreeSurfer and PostFreeSurfer Pipeline and 7.4.1 (freesurfer_ubuntu22-7.4.1_amd64.deb under WSL2) for FastSurfer Pipeline.

Workbench (HCP): Command Line Utilities version 1.5.0 for Linux x64 were used for data visualization and manipulation.

MSM_HOCR: Version 3.0 of the Multimodal Surface Matching tool was integrated for high-resolution cortical registration, adhering to HCP recommendations.

HCP Pipelines: Version 4.7.0 provided tools for preprocessing and analysis of neuroimaging data according to HCP standards.

Environment and package management:

Conda: Version 23.7.4 was selected for creating isolated environments, ensuring compatibility and version control of dependencies. A custom Conda environment was created using a fastsurfer.yml file to encapsulate all libraries and packages required for FastSurfer execution.

OVERVIEW

In this study, our objective was to replace the FreeSurfer Pipeline within the Human Connectome Project (HCP) framework with the FastSurfer Pipeline (Figure 6). To this end, we focused on ensuring seamless integration between the output and input of the PreFreeSurfer Pipeline and the FastSurfer Pipeline, as well as between the FastSurfer Pipeline and the PostFreeSurfer Pipeline. Our goal was to achieve high consistency in the image processing results of these interconnected pipelines compared to the original HCP structural imaging pipeline.

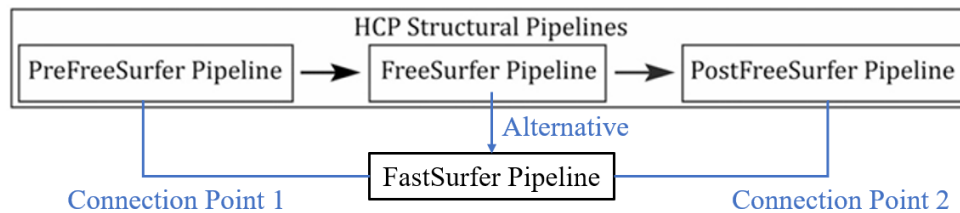


Figure 6 FastSurfer Pipeline as an Alternative to FreeSurfer Pipeline in HCP Structural Pipeline

FIRST CONNECTION POINT: PREFREESURFER PIPELINE - FASTSURFER PIPELINE

In the standalone execution of the FastSurfer Pipeline, it is possible to directly produce surface reconstruction results, related metrics, and volume and surface segmentation outcomes using only the individual subject's T1-weighted (T1w) images. To facilitate integration with the PreFreeSurfer processing steps, we employed a strategy of utilizing the subject's native space images generated by the PreFreeSurfer processing (specifically,

the brain-extracted, undistorted T1w images) as the input for the FastSurfer Pipeline. Specifically, by setting the environment variable in the FastSurfer Pipeline, which stores the input file path information, to point to the path of the T1w_acpc_dc_restore_brain.nii.gz file produced post-PreFreeSurfer Pipeline, we successfully configured the first connection point.

It is noteworthy that the PreFreeSurfer Pipeline scripts operate using FreeSurfer version 6, whereas the FastSurfer Pipeline employs operations based on FreeSurfer version 7. Therefore, prior to initiating the FastSurfer Pipeline, it is necessary to update the global variable indicating FreeSurfer's home directory in the script from the FreeSurfer version 6 path to the version 7 path. This step ensures that the FastSurfer Pipeline can seamlessly integrate into the HCP framework while maintaining compatibility with original FreeSurfer operations.

SECOND CONNECTION POINT: FASTSURFER PIPELINE - POSTFREESURFER PIPELINE

We observed that the output of the FastSurfer Pipeline maintains a high degree of organizational consistency with that of the FreeSurfer Pipeline, with primary results stored in the mri, surf, and label directories. Therefore, to facilitate a seamless integration between the FastSurfer and PostFreeSurfer Pipelines, we directly specified the environment variable used for storing output file paths in the FastSurfer Pipeline to the default path where the FreeSurfer Pipeline results are generated. This path, located under the T1w/subjectID directory, subsequently serves as the input path for the PostFreeSurfer Pipeline, thus configuring the second connection point.

It is important to note that the cortical parcellation in the FastSurfer Pipeline employs the Desikan-Killiany-Tourville (DKT) atlas [7], as opposed to FreeSurfer's default a2009s atlas. Consequently, in the FreeSurfer2CaretConvertAndRegisterNonlinear script of the PostFreeSurfer Pipeline processing steps, adjustments are made to convert and resample files based on the DKT atlas instead of the a2009s atlas.

Furthermore, the original PostFreeSurfer Pipeline utilizes the T2 to T1 transformation matrix (T2toT1.mat) obtained from the FreeSurfer Pipeline registration to fine-tune the registration of T2-weighted (T2w) to T1-weighted (T1w) images. This process allows for a more accurate analysis and depiction of myelin content distribution and characteristics, resulting in more precise myelin maps. After replacement, since the FastSurfer Pipeline does not include T2 to T1 registration, the T2toT1.mat transformation matrix is not generated. Therefore, when executing the convertwarp command in the subsequent PostFreeSurfer Pipeline, the application of the postmat parameter is omitted. A control experiment was conducted by re-running the PostFreeSurfer Pipeline with the T2toT1.mat generated by FreeSurfer in the modified workflow to compare the final output results and evaluate the impact of the absence of the T2toT1.mat transformation matrix on the ultimate post-processing outcomes.

Lastly, since the PostFreeSurfer Pipeline processing scripts operate using FreeSurfer version 6, it is necessary,

before initiation, to adjust the global variable indicating FreeSurfer's home directory in the script from the FreeSurfer version 7 path back to the version 6 path.

RESULT

COMPARISON OF OUTPUTS FOLLOWING THE FIRST CONNECTION POINT

In a comprehensive comparison of the outputs following the first connection point, we contrasted the intermediate processes before and after substitution, specifically comparing the predefined structured segmentation results of gray and white matter surfaces, as well as volumes generated by the FreeSurfer Pipeline and the FastSurfer Pipeline, respectively. The results indicate that both the FreeSurfer and FastSurfer Pipelines adequately fit the gray and white matter surfaces, with no significant differences observed in the segmentation outcomes (Figure 7). Detailed comparison screenshots for additional subjects are provided in the appendix.

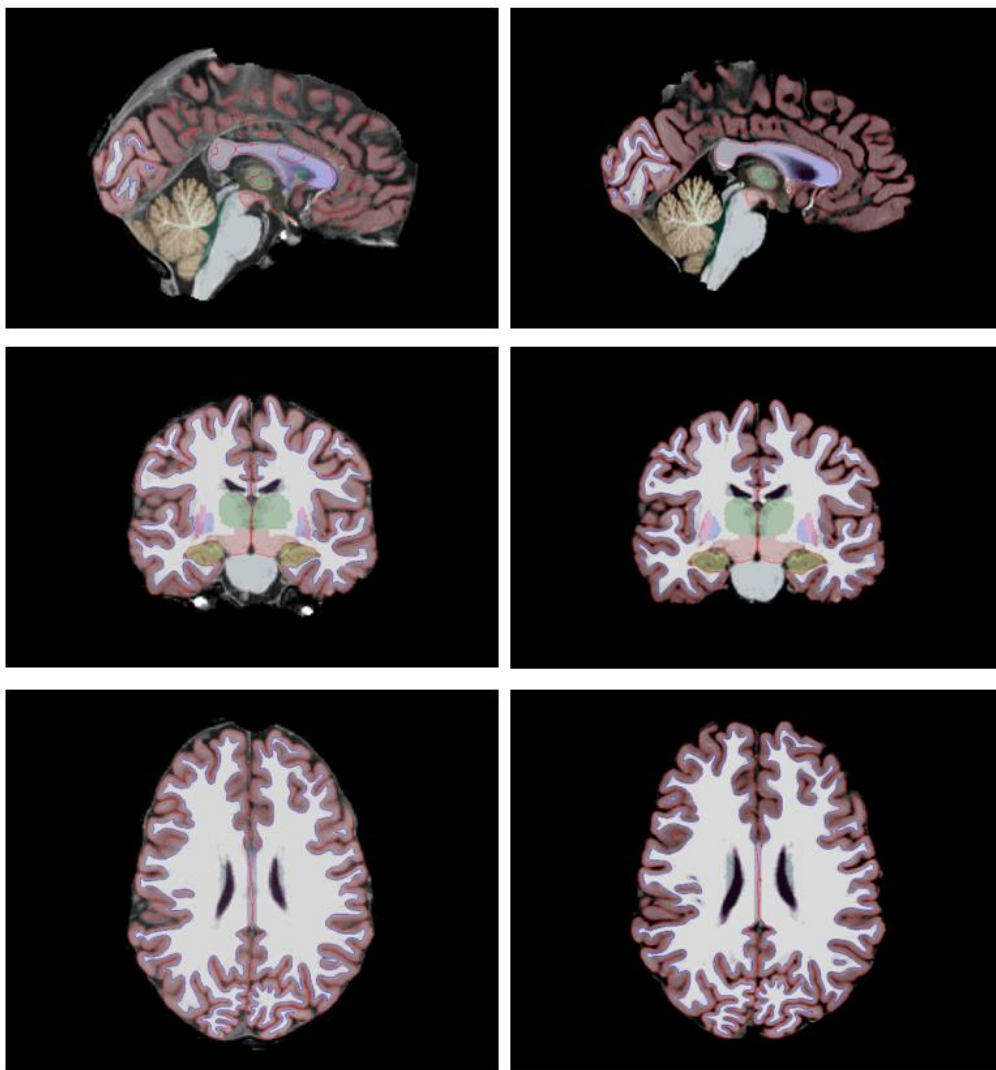


Figure 7 Processing results comparison between the FreeSurfer Pipeline (left) and the FastSurfer Pipeline (right), illustrating cortical reconstructions of the left and right gray and white matter, along with the outcomes of volumetric segmentation.

COMPARISON OF OUTPUTS FOLLOWING THE SECOND CONNECTION POINT

In comparing the outputs after the second connection point, we used the results from the FreeSurfer Pipeline and the FastSurfer Pipeline, before and after substitution, as inputs to run the PostFreeSurfer Pipeline. We compared the subjects' DKT atlas parcellation, myelin maps, and thickness maps (presented in both midthickness and inflated forms) at 164k resolution in MNI space (Figure 8) and 32k resolution in Native space (Figure 9). For a direct visual comparison, we intentionally set the colorbar range to the same fixed values in the Workbench visualization results.

In both MNI space and Native space, the analysis revealed that the parcellation results based on the DKT atlas were almost identical before and after substitution. However, some differences were observed in the myelin and thickness maps. Specifically, in the myelin maps, the distribution in the occipital region was smaller in the results processed with the FastSurfer Pipeline compared to before substitution, and in some subjects, the post-substitution results even showed localized negative values in this area. In the thickness maps, the relative distribution of median thickness was consistent before and after substitution, but the results processed with the FastSurfer Pipeline were generally 0.2-0.4 lower overall.

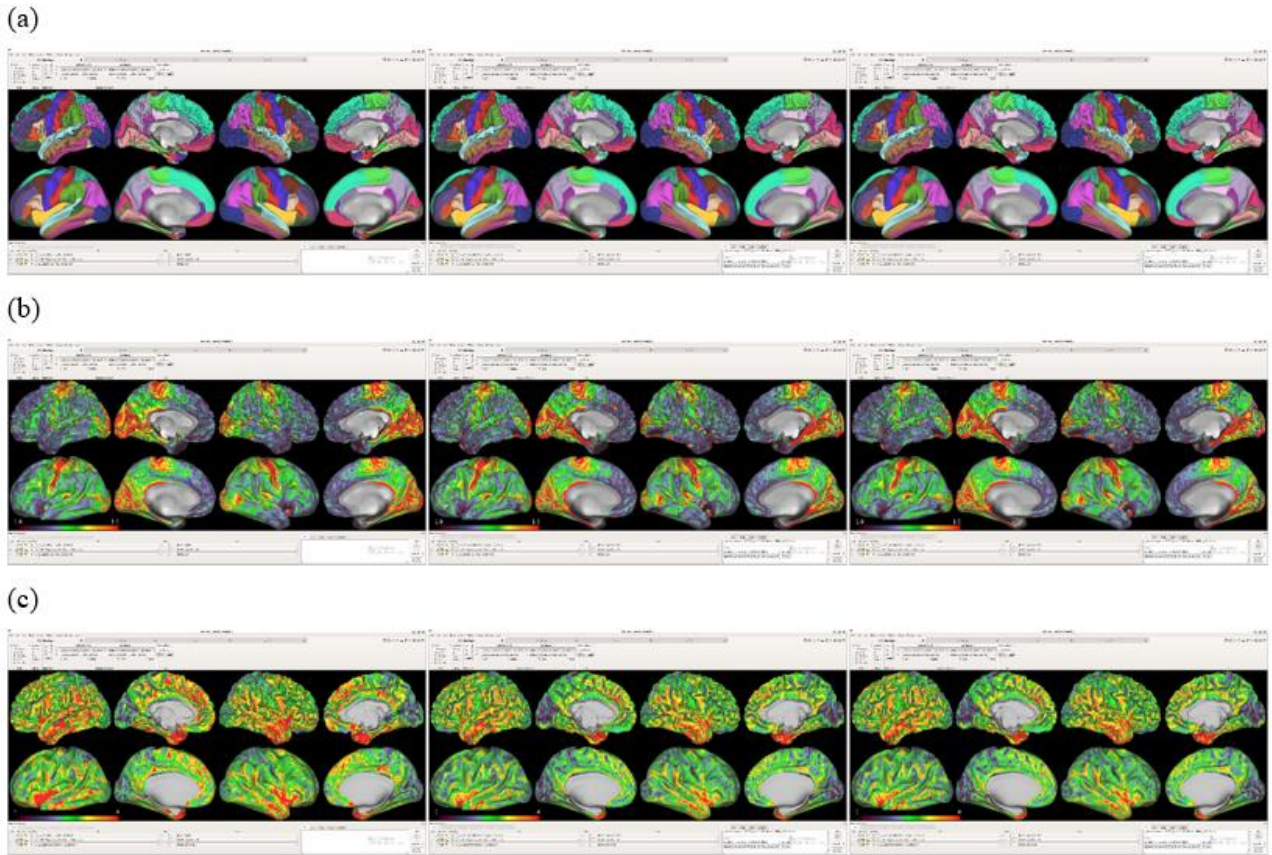
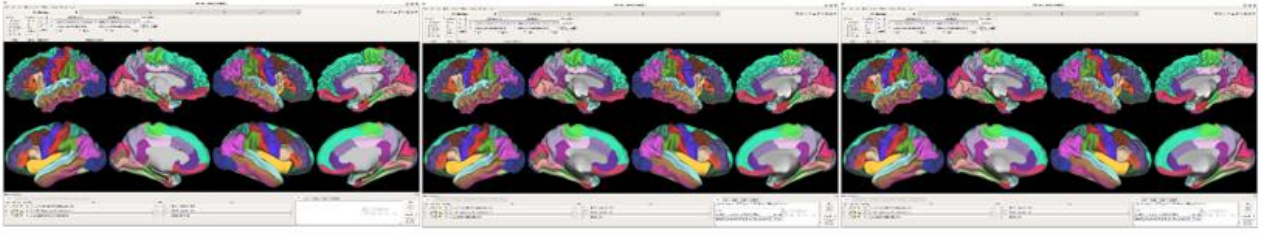
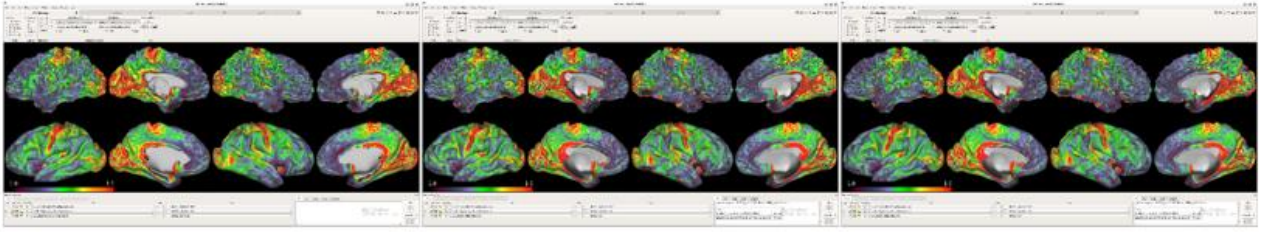


Figure 8 Processing outcomes in MNI space for the original HCP structural processing (left), HCP structural processing with FastSurfer substitution (center), and HCP structural processing with FastSurfer substitution incorporating the T2wtoT1w.mat transformation matrix (right). Panel (a) displays the DKT atlas parcellation results, panel (b) presents the myelin maps, and panel (c) illustrates the midthickness thickness distribution maps.

(a)



(b)



(c)

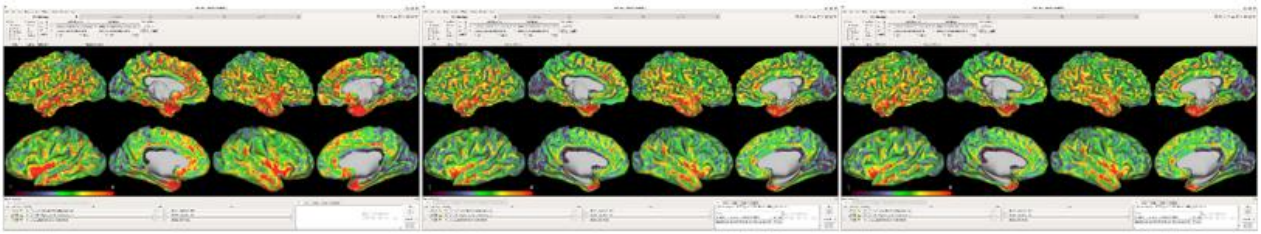


Figure 9 Processing outcomes in Native space for the original HCP structural processing (left), HCP structural processing with FastSurfer substitution (center), and HCP structural processing with FastSurfer substitution incorporating the T2wtoT1w.mat transformation matrix (right). Panel (a) displays the DKT atlas parcellation results, panel (b) presents the myelin maps, and panel (c) illustrates the midthickness thickness distribution maps.

It is noteworthy that when the outputs from the FastSurfer Pipeline were entered into the PostFreeSurfer Pipeline along with the T2toT1.mat transformation matrix generated during the FreeSurfer Pipeline process, the results were almost identical to those obtained by inputting only the FastSurfer Pipeline results. This indicates that the inconsistencies in the PostFreeSurfer Pipeline before and after substitution primarily stem from the differences in the processing results of the FreeSurfer Pipeline and the FastSurfer Pipeline. Detailed comparisons of more subjects' results can be found in the appendix.

COMPARISON OF PROCESSING TIME BEFORE AND AFTER ALTERNATIVE

In evaluating the impact of substituting the FreeSurfer Pipeline with the FastSurfer Pipeline within the HCP Structural Pipeline, we recorded and compared the processing time for each participant across various stages. Results in TABLE III indicated that in the original HCP Structural Pipeline, the intermediate steps processed by FreeSurfer represented the most time-consuming portion, requiring 3-4 hours. However, after implementing the FastSurfer Pipeline, the processing time for these steps was significantly reduced to approximately 0.7 hours, thus becoming the shortest duration within the entire workflow and reducing the total preprocessing time for structural components by about half.

TABLE IV Processing Time for Each Stage in HCP Structural Pipeline Before and After Alternative

	PreFreeSurfer Pipeline	FreeSurfer/FastSurfer Pipeline	PostFreeSurfer Pipeline	entire Structural Pipeline
Average time before alternative (h)	1.78	3.49	0.93	6.20
Average time after alternative (h)		0.71	0.89	3.37

Moreover, Figure 10 depicting the processing time for each stage for all participants revealed that the duration for intermediate steps using the traditional FreeSurfer was long and variable, whereas the FastSurfer Pipeline not only shortened the processing time but also stabilized it. This substitution did not significantly affect the processing time of subsequent PostFreeSurfer Pipeline stages. These findings demonstrate that the adoption of the FastSurfer Pipeline significantly decreases processing time and enhances time stability, positively impacting the entire structural processing workflow. These results are of significant importance for improving processing efficiency and optimizing structural processing flows.

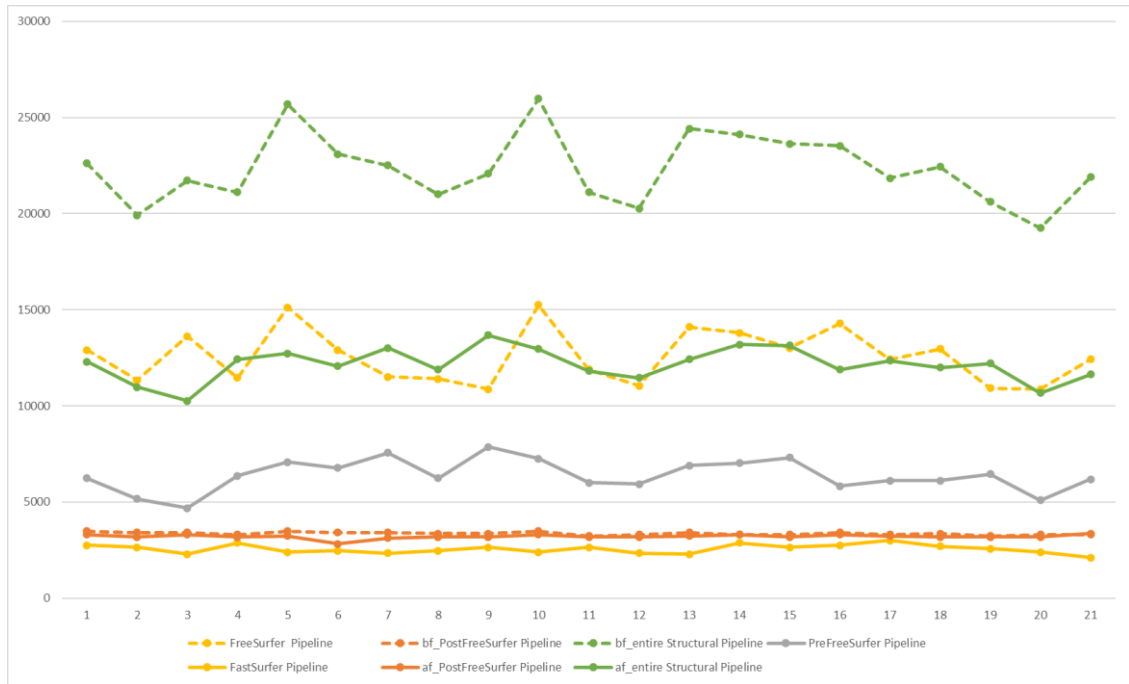


Figure 10 processing time for each stage for 21 subjects in HCP Structural Pipeline Before and After Alternative

DISCUSSION

This study examines the implications of substituting the FreeSurfer Pipeline with the FastSurfer Pipeline in the HCP Structural pipeline for neuroimaging data processing, particularly focusing on gray and white matter surface fitting, structural segmentation, and potential effects on myelin and thickness map analyses, as well as

comparing the processing time across the entire structural processing workflow before and after the substitution. Our findings reveal a high degree of consistency in gray and white matter surface reconstructions, volumetric and cortical region segmentations processed by the HCP Structural pipeline before and after the substitution, underscoring the efficacy of the FastSurfer Pipeline in enhancing processing efficiency. However, the use of FastSurfer for myelin map processing resulted in localized negative values in the occipital region, likely due to the absence of T2-weighted information in FastSurfer's surface processing.

Given that myelin map generation typically relies on T1 and T2-weighted MRI data, we hypothesize that retraining FastSurfer's convolutional neural network with T1 and T2 as dual-modal inputs and integrating the retrained model into the HCP pipeline could mitigate this issue. Future research should verify this hypothesis and compare post-substitution processing results to ensure the efficacy of the improvements.

Moreover, the results of this study are primarily based on qualitative analysis, lacking in quantitative evaluation, which limits the authoritative nature of our conclusions. Therefore, future studies should employ statistical methods for validation, such as calculating the spatial distance differences between white and gray matter surfaces in FastSurfer and FreeSurfer results, or assessing the differences in mean values and distributions of brain region heat maps in post-processing results, to provide stronger evidence support for the findings.

Lastly, considering the specific processing requirements of different studies, future work could develop an integrated Pipeline, allowing researchers to choose between FreeSurfer or FastSurfer for intermediate step processing as needed. Additionally, providing both FreeSurfer and FastSurfer-based processing results and their differential analysis could offer researchers greater flexibility and choice.

In conclusion, our study provides significant reference information for neuroimaging data processing, highlights the limitations of current methods, and suggests directions for future improvements. Through further research and enhancements, we aim to improve the accuracy and efficiency of neuroimaging analysis, offering deeper insights into brain structure and function.

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