

## Quantitative Neuroimaging in Brain Tumor and Acute Ischemic Stroke

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### ABSTRACT

This thesis aims to develop clinically relevant, rapid, and reliable automated frameworks for quantitative analysis of brain tumors and acute ischemic stroke. Quantitative neuroimaging plays a significant role in improving diagnosis and guiding treatment decisions in neurological disorders. Conventional image assessment pipelines in clinical and research settings are fragmented and rely heavily on user input, which makes them time-consuming and subject to operator variability. Standard software tools available attempt to address these issues by providing an integrated framework, but these are general purpose tools that require manual input for region delineation and lack disease specific workflows for comprehensive assessment. To address these limitations, the work presented in the thesis involves development and optimization of methods to provide integrated artificial intelligence (AI) frameworks for automated analysis of multiparametric CT and MR data for brain tumors and acute ischemic stroke applications.

In this thesis, multiple deep learning (DL) frameworks were developed and evaluated across multiple datasets. A lightweight modality agnostic 2D U-Net (mU-Net) was developed for brain extraction, which was tested across five datasets comprising pre- and post-operative brain tumors, ischemic stroke, and healthy controls. A deep residual U-Net (DRU-Net)-based framework was developed for segmentation of healthy brain tissues (gray matter, white matter, and cerebrospinal fluid) and tumor regions using BraTS 2021 and local hospital datasets. For post-operative assessment of residual tumor in Glioblastoma Multiforme (GBM) patients, an integrated semi-automatic pipeline comprising the brain extraction and tissue segmentation, along with quantitative MRI, was developed. Quantitative perfusion parameters, including cerebral blood flow (CBF), cerebral blood volume (CBV),  $K_{trans}$ ,  $v_e$ , and  $v_p$ , are evaluated across different tumor regions. Patient data from three time points were analyzed to quantify tumor volumes and detect microvascular changes in tumor regions.

For stroke analysis on multiparametric CT scans, ten DL classifiers were evaluated across multiple combinations of CT and CT perfusion (CTP) maps (CBV, CBF, MTT, and  $T_{max}$ ) to detect ischemic stroke. Additionally, to accurately segment stroke lesions on CT and CTP maps, a novel DenseResU-NetCTPSS architecture was proposed. Explainable AI techniques, such as occlusion sensitivity maps and GradCAM, were used to make model predictions more interpretable to clinicians. A unified Inception-DenseResU-Net++ framework was developed for ischemic stroke and penumbra estimation on multiparametric MRI data. The framework was evaluated using ISLES 2022 and local hospital datasets. PWI–DWI mismatch scores derived from the proposed framework were correlated with those obtained from expert manual annotations. Additionally, the feasibility of EPI-based SWI as a non-contrast surrogate for perfusion imaging was investigated. Quantitative mismatch analysis and PHVS (Prominent Hypointense Vessel Sign) visibility were evaluated across different spatial resolutions.

The trained mU-Net achieved dice similarity coefficients (DSCs) of  $0.992 \pm 0.002$  and  $0.982 \pm 0.006$  for brain extraction on the pre-operative and post-operative brain tumor datasets, respectively. The DSCs for the acute ischemic stroke, IXI and QIN datasets was  $0.969 \pm 0.009$ ,  $0.964 \pm 0.017$ , and  $0.943 \pm 0.016$ ,

respectively. The proposed DRU-Net-based tissue segmentation pipeline achieved mean DSCs of  $0.83 \pm 0.07$  and  $0.77 \pm 0.05$  on BraTS 2021 and local hospital datasets respectively, for healthy tissue segmentation. For tumor segmentation, the DSCs for BraTS 2021 and local hospital datasets were  $0.86 \pm 0.10$  and  $0.82 \pm 0.10$ , respectively. In the postoperative residual tumor analysis for GBM patients, volumetric results showed that 80% of patients had reduced peritumoral vasogenic edema volumes at two-week follow-up. Similarly, 83% and 100% patients showed reduced non-enhancing and enhancing tumor core volumes at two-week follow-up. Perfusion values remained consistent in the peritumoral vasogenic edema across all three time points. 60% of patients showed elevated rCBF values in the non-enhancing region at two-week follow-up, suggesting tumor recurrence. In the tumor core region, the mean of individual perfusion parameter values decreased at two-week follow-up compared with preoperative imaging.

On ischemic stroke detection on multiparametric CT scans, the image combination of CBV, CBF, and  $T_{\max}$ , when evaluated on ResNet18, outperformed all other image combinations across all networks, achieving a classification accuracy of 94.79%. Conventional CT on NasNetMobile achieved a classification accuracy of 92.71%. Occlusion sensitivity maps revealed that the combination of CBV, CBF, and  $T_{\max}$  have high sensitivity for the stroke lesion, whereas CT images rely on bilateral symmetry to make the final classification decision. The proposed DenseResU-NetCTPSS architecture improved stroke segmentation accuracy on CT and CT maps by using CT, CBV, and  $T_{\max}$  as input images, achieving mean DSCs of  $0.65 \pm 0.19$  and  $0.45 \pm 0.32$  on the ISLES 2018 training and test datasets, respectively.

On MR images, the proposed Inception-DenseResU-Net++ for ischemic core segmentation, combining DWI and ADC maps, achieved a mean DSC of  $0.72 \pm 0.15$  on the ISLES 2022 dataset and  $0.78 \pm 0.13$  on the local hospital dataset. For complete hypoperfused region segmentation on the local hospital dataset using CBF maps, the framework achieved a mean DSC of  $0.75 \pm 0.08$ . The proposed framework also showed excellent correlation ( $\rho=0.97$ ,  $p\text{-value}<0.05$ ) between the deep learning-based PWI–DWI mismatch ratios and manual annotations. SWI-EPI showed good correlation with perfusion-based penumbra estimation at both 0.6 mm ( $r = 0.786$ ,  $p\text{-value} < 0.05$ ) and 1 mm ( $r = 0.731$ ,  $p\text{-value} < 0.05$ ) slice thicknesses. It also improved visualization of hypoperfused regions and reduced acquisition time compared to SWI-GRE.

These developed frameworks were integrated into dedicated software tools for brain tumor and ischemic stroke analysis. These tools enable visualization of tissue and lesion masks, quantitative perfusion analysis, volumetric assessment of tumor subregions and stroke lesions, and generation of structured reports. In addition, percentile-based analysis of perfusion parameters within tumor regions and interactive visualization for clinicians are provided, with minimal manual intervention, thereby facilitating streamlined workflows and improved interpretability in clinical settings.

This thesis presents a comprehensive analysis of AI-driven frameworks for automated analysis of brain tumors and acute ischemic stroke, along with their translation into clinically usable software tools. The proposed work addresses critical limitations of existing fragmented analysis pipelines by identifying optimal imaging sequences and modality combinations for key clinical tasks, and by translating methodological advances into software tools.