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Enhanced Postoperative Brain MRI Segmentation with Automated Skull Removal and Resection Cavity Analysis

Sobha Xavier P., Sathish P. K. and Raju G.

Department of Computer Science, Christ (Deemed to be University), Bengaluru, Karnataka, India

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Corresponding Author:
Sobha Xavier P.
Department of Computer Science, Christ (Deemed to be University), Bengaluru, Karnataka, India
Email: sobha.xavier@res.christuniversity.in

Abstract: Brain tumors present a significant medical challenge, often necessitating surgical intervention for treatment. In the context of postoperative brain MRI, the primary focus is on the resection cavity, the void that remains in the brain following tumor removal surgery. Precise segmentation of this resection cavity is crucial for a comprehensive assessment of surgical efficacy, aiding healthcare professionals in evaluating the success of tumor removal. Automatically segmenting surgical cavities in post-operative brain MRI images is a complex task due to challenges such as image artifacts, tissue reorganization, and variations in appearance. Existing state-of-the-art techniques, mainly based on Convolutional Neural Networks (CNNs), particularly U-Net models, encounter difficulties when handling these complexities. The intricate nature of these images, coupled with limited annotated data, highlights the need for advanced automated segmentation models to accurately assess resection cavities and improve patient care. In this context, this study introduces a two-stage architecture for resection cavity segmentation, featuring two innovative models. The first is an automatic skull removal model that separates brain tissue from the skull image before input into the cavity segmentation model. The second is an automated postoperative resection cavity segmentation model customized for resected brain areas. The proposed resection cavity segmentation model is an enhanced U-Net model with a pre-trained VGG16 backbone. Trained on publicly available post-operative datasets, it undergoes preprocessing by the proposed skull removal model to enhance precision and accuracy. This segmentation model achieves a Dice coefficient value of 0.96, surpassing state-of-the-art techniques like ResUNet, Attention U-Net, U-Net++, and U-Net.

Keywords: Cavity Segmentation, Enhanced U-Net, Post-Operative Brain MRI, Skull Removal, VGG16 Backbone

Introduction

Magnetic Resonance Imaging (MRI) has emerged as an indispensable tool in the field of medical imaging, particularly in the realm of brain tumor segmentation (Rajasekaran and Gounder, 2018). However, one of the inherent challenges associated with MRI data, especially for brain tumor analysis, lies in its three-dimensional nature. While 3D MRI provides comprehensive spatial information (Madan, 2015), it also results in significantly larger datasets compared to traditional 2D imaging. These formidable data sizes can strain computational resources, hinder efficient storage, and impede timely analysis. When it comes to storing and analyzing brain MRI datas, two common formats are Digital Imaging and Communications in Medicine (DICOM) and Neuroimaging Informatics Technology Initiative (NIfTI) (Samuel *et al*., 2020). These formats contain not only the brain structures of interest but also the entire skull, adding an extraneous layer of complexity. To address these issues and streamline the preprocessing pipeline, there is an urgent need for an automatic skull removal model. This model plays a pivotal role in dimensionality reduction by effectively eliminating non-brain regions, thereby optimizing MRI data for subsequent segmentation tasks (Fatima *et al*., 2020). In essence, the development of an automated skull removal approach is instrumental in unlocking the full potential of MRI in brain tumor segmentation, providing more efficient and precise analyses.

Postoperative brain MRI plays a pivotal role in assessing tumor resection extent and monitoring post-surgery changes. The postoperative resection cavity in the brain represents the space remaining after the surgical removal of a brain tumor or lesion. Precise segmentation and analysis of postoperative MRI images enable healthcare professionals to extract valuable information about resection extent (Arnold *et al*., 2022), residual tumor presence, and postoperative brain changes. Manual segmentation is labor-intensive and prone to errors. Computer-assisted techniques have gained attention for their potential to enhance efficiency, accuracy, and reproducibility. However, automating the segmentation of surgical cavities in these images presents challenges due to image artifacts, tissue reorganization, and diverse appearances. Therefore, the development of dedicated algorithms that consider postoperative features is crucial for effective segmentation. State-of-the-art techniques for brain MRI segmentation primarily utilize Convolutional Neural Network (CNN)-based models (Hesamian *et al*., 2019), particularly U-Net models. However, the efficacy of deep learning models, such as U-Net, heavily depends on having ample annotated datasets. Post-operative brain MRI, unfortunately, confronts a scarcity of annotated data due to ethical and practical considerations. These constraints underscore the urgency for innovation and advancement in this crucial domain. The shortage of adequate annotated data remains a significant obstacle, frequently curbing the adaptability and universality of deep learning models.

To address this challenge, our study introduces a two-stage architecture that initially preprocesses the input images, followed by the prediction of a brain tissue mask from the entire skull MRI. Subsequently, this predicted region of interest is cropped and input into the cavity segmentation network for the second stage. The proposed post-operative cavity segmentation model is an enhanced U-Net model, which incorporates an attention-enabled U-Net with a pre-trained VGG16 encoder and residual connections. This hybrid framework aims to enhance resection cavity segmentation precision. The model was trained on the publicly available post-operative dataset EPISURG (Pérez-García *et al*., 2021).

Additionally, this research presents a novel model for automatic skull removal: An enhanced U-Net with a pre-trained VGG16 backbone (Zhang *et al*., 2018). The objective of the skull removal model is to enhance post-operative brain MRI cavity segmentation. It begins with image preprocessing, including tasks like intensity normalization, bias field correction, and noise reduction. After that, morphological procedures are used to create a brain extraction mask, isolating the brain tissue and aligning it with anatomical edges using edge detection. The largest connected area of white pixels in the mask represents the brain tissue, effectively separating it from the background. This binary mask is applied to the original MRI image to produce a skull-stripped brain image. Optionally, post-processing steps like smoothing or artifact correction can be applied to refine the results. Automatic skull removal is crucial for accurate brain analysis in neuroimaging and medical image processing. These steps collectively form a typical pipeline for automatic skull removal in MRI image processing. This model is trained with the NFBS dataset (Pravitasari *et al*., 2020). Compared to existing skull removal models, the proposed model outperforms them with a Dice score of 0.98. To assess the impact of skull removal on the cavity segmentation model, we further evaluated the performance of the proposed cavity segmentation model on a dataset containing skull-stripped images compared to a dataset with skulls included, resulting in an improved Dice coefficient of 0.96 from the initial 0.92.

Two distinct areas are thoroughly examined in this section. The first examines current developments in automatic skull removal methods, highlighting research gaps and their contributions. A thorough analysis of the current post-operative segmentation models is the second.

Automated Skull Removal Methods

Deep learning models require large datasets for training, which poses a significant challenge, especially in the case of three-dimensional MRI data, where each volume can be several gigabytes in size. Loading such massive datasets demands terabytes of memory and considerable CPU resources, making it a daunting task. Typically, researchers resort to resizing the dataset to lower dimensions to make it manageable, but this inevitably impacts the model's accuracy. However, an alternative approach is to automatically extract the brain region from the entire skull, reducing the MRI image's size and potentially enhancing the training model's accuracy. Hence, there is a need for an automatic skull removal model. Automatic skull removal is a multi-step process used in MRI image analysis (Swiebocka-Wiek, 2016).

In their work, Pei *et al*. (2022) harness the capabilities of 3D convolutional neural networks to automate skull removal in multiparametric MRI scans, providing a versatile solution for diverse imaging scenarios. However, the reliance on large datasets and the inherent complexity of deep learning models may present challenges in resource-constrained environments and interpretability. Azam *et al*. (2023) introduced an innovative deep learning-based skull removal method using Mask-RCNN, showcasing superior performance compared to traditional approaches. While it offers enhanced accuracy and automation, its computational intensity and model complexity may pose challenges for resource-constrained environments.

Addressing skull removal challenges for multi-contrast MR images, (Roy *et al*., 2018) introduced a deep learning framework that eliminates the need for deformable registration and extends its applicability to diverse species. This approach significantly enhances brain extraction accuracy in both healthy and pathological human and rodent images, emphasizing its potential for broader neuroimaging applications. Valvano *et al.* (2018) developed an advanced Convolutional Neural Network (CNN)-based skull removal method to automatically remove non-brain tissue from Magnetic Resonance (MR) brain scans. This innovative approach achieved a remarkable Dice metric score of 96.5% and a processing time of 4.5 sec per volume, demonstrating exceptional performance and efficiency on the NFBS public database. However, our aim is to further enhance this model's capabilities by creating an improved version capable of efficiently handling both pre-operative and post-operative brain MRI scans.

Deep learning-based skull removal methods, as exemplified by deep strip Zhou *et al*. (2020), deep skull Curnoe *et al*. (2016), Synth Strip Hoopes *et al*. (2022), and deep BrainSeg Tan *et al*. (2020), face challenges related to dataset availability, especially the need for comprehensive and well-annotated datasets spanning diverse MRI modalities and clinical contexts. Additionally, these models can be resource-intensive, limiting their accessibility for researchers with modest computational resources. Future research efforts could focus on developing more efficient deep-learning architectures tailored specifically for skull removal tasks. On a different note, models like ROBEX (Iglesias *et al*., 2011) and SPM Brain Extraction (Kazemi and Noorizadeh, 2014) have shown limitations regarding their sensitivity to data quality and noise, emphasizing the necessity for research that enhances the robustness of skull removal techniques, particularly when confronted with noisy and complex datasets. Classical image processing approaches (Lalande Lalande and Fournier, 2014; Tan *et al*., 2020; Roy *et al*., 2017; Kamnitsas *et al*., 2016), such as FSL BET, BET2 and AFNI 3dSkullStrip, are recognized for their susceptibility to artifacts. Prospective research directions should refine these methods to improve their accuracy when dealing with data containing artifacts.

Existing Models for Post-Operative Brain MRI Segmentation

The U-Net architecture, proposed by Ronneberger *et al.* (2015), has gained popularity in medical image segmentation tasks due to its ability to capture fine-grained details and contextual information. The U-Net model comprises an encoder-decoder architecture with skip connections that enable the incorporation of high-resolution features from the encoder into the decoder. These skip connections enhance spatial localization and mitigate the vanishing gradient problem during training. U-Net models have demonstrated success in various medical imaging applications, including organ segmentation, tumor detection, and lesion segmentation. The architecture's inherent flexibility allows adaptation to specific medical imaging tasks, including brain MRI cavity segmentation. Several studies have investigated U-Net-based approaches for cavity segmentation, achieving promising results in the context of preoperative brain MRI data.

In the domain of postoperative brain MRI segmentation, limited contributions have driven progress. It's essential to recognize the dedication of researchers to pushing the boundaries of this field. Bakas *et al*. (2016) introduced GLISTRboost, a semi-automatic method that employed a hybrid generative-discriminative model a milestone in postoperative brain MRI segmentation. Jungo *et al*. (2018) brought forth the Fully convolutional DenseNet, a specialized deep-learning model designed for segmentation tasks, utilizing dense connections and convolutional layers for precise results. Pérez-García *et al*. (2021) proposed a self-supervised learning approach for postoperative brain MRI segmentation. This method harnessed both labeled and unlabeled data to enhance the segmentation model's performance without extensive manual annotations. In the same year, the Brain Tumor Sequence Registration Challenge, as part of the MICCAI challenge, catalyzed the development of innovative brain tumor segmentation techniques. Additionally, Baheti *et al*. (2021) introduced a co-registration method, aligning preoperative and postoperative brain MRI scans to enhance segmentation accuracy. Arnold *et al*. (2022) presented a modified U-Net model, incorporating additional features and layers to enhance segmentation performance.

The study's insights uncover several crucial findings. Following surgery, CSF (cerebrospinal fluid) fills the resection cavities. Because of this, it is inherently difficult to distinguish RCs next to structures like sulci, ventricles, or edemas (Pérez-García *et al*., 2021). There is limited availability of annotated training data for post-operative resection cavity segmentation, posing a challenge for model generalization. Given the scarcity of annotated datasets, the utilization of pre-trained models can enhance segmentation results. Improving the efficiency of segmentation models can be accomplished by fine-tuning existing segmentation models with post-operative datasets.

Materials and Methods

Dataset Description

In this study, a publicly available dataset, the NFBS dataset (Pravitasari *et al*., 2020) (Neurofeedback skull removal dataset), is used as the foundation for training the automated skull removal model. The NFBS dataset is widely recognized in the neuroimaging research community and is specifically designed for skull removal tasks. The NFBS dataset features MRI data from 125 participants aged 21-45, encompassing various clinical and subclinical psychiatric conditions. It comprises structural T1-weighted anonymized (defaced) images, brain masks obtained through the Beast method with expert manual edits, and skull-stripped images, all at a 1 mm³ resolution in NiFTI format. This format is a standard for housing neuroimaging data. The NFBS dataset comprises two integral components: The unprocessed T1-weighted MRI raw image, which serves as our model's initial input; and the meticulously crafted brain mask, generated through a combination of the Beast method and manual expert adjustments, providing crucial guidance for defining the brain's boundaries.

The EPISURG dataset, or the Epilepsy Surgery Dataset, represents a valuable resource for postoperative cavity segmentation. It encompasses T1-weighted Magnetic Resonance Images (MRI) from a substantial cohort of 430 patients who have undergone resective brain surgery for epilepsy treatment. Within this dataset, there are both preoperative and postoperative MRI scans available. In this study, the trained skull removal model was applied to this dataset and removed non-brain structures from the MRI images.

Proposed Two-Stage Segmentation Framework

Using separate stages for skull removal and segmentation is a vital strategy for achieving accuracy. It enables the network to initially identify the anatomical position and then perform segmentation on the region of interest. This two-stage approach is more efficient, particularly when dealing with small regions of interest (Francis *et al*., 2022) or when they are surrounded by structures like surgical artifacts that could affect segmentation. It significantly enhances segmentation accuracy by reducing false positives, narrowing the search space, and improving overall robustness. The process begins with image preprocessing, which includes tasks like intensity normalization, bias field correction, and noise reduction. Morphological procedures follow, creating a brain extraction mask to isolate brain tissue and align it with anatomical edges using edge detection. The largest connected area of white pixels in the mask represents brain tissue, effectively separating it from the background. This binary mask is applied to the original MRI image to produce a skull-stripped brain image. The region of interest is then cropped and fed into the cavity segmentation network for the second stage. The framework of this proposed method is illustrated in Fig. 1. and comprises three main steps: ROI identification, Cropping, and cavity segmentation.

Automatic Skull Removal Model

Automatic brain extraction is essential due to its critical role in clinical applications and enabling accurate neuroimaging analyses. The automatic brain extraction method employed in this study is designed to extract the brain region from the entire skull from MRI scans.

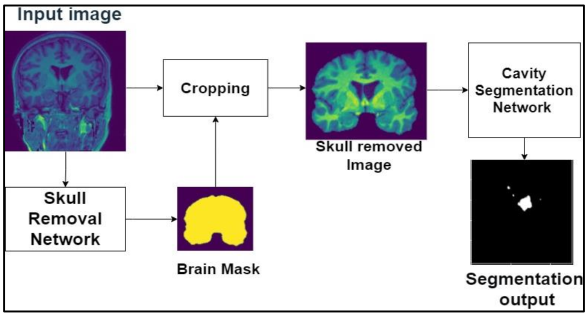

Fig. 1: Proposed two-stage segmentation architecture

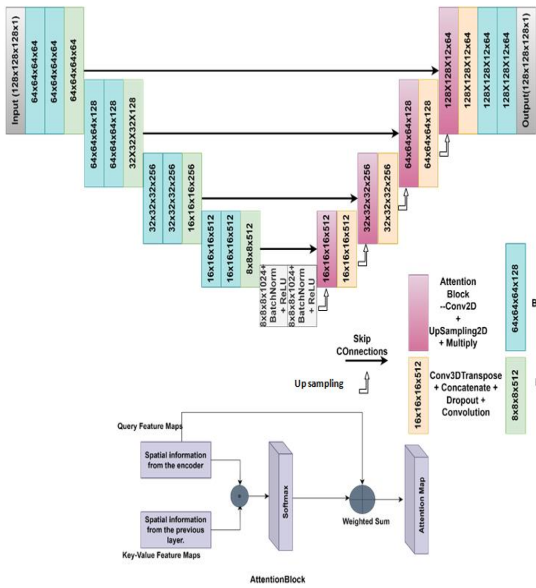

Fig. 2: Proposed automated skull removal model architecture

Figure 2 illustrates the architecture of the proposed skull removal using a VGG16 backbone and a U-Net architecture with attention gates. It is aimed at segmenting brain images and focuses on down-sampling (encoder) and up-sampling (decoder) components to facilitate the integration of features across large spatial regions. The input is a 3D image of dimensions (128, 128, 128, 1). It features an encoder-decoder structure, with the encoder consisting of ten convolutional blocks organized in pairs (Zhang *et al.*, 2018), followed by max-pooling and dropout layers for feature extraction and down-sampling. The decoder incorporates attention mechanisms and up-sampling layers, aiming to recover spatial information and facilitate feature integration. VGG16 is known for its ability to extract hierarchical features from images. Combining this feature extraction capability with the attention mechanisms of the U-Net architecture can improve the model's understanding of intricate details in brain MRI images. In summary, an attention U-Net with a pre-trained VGG16 backbone combines the advantages of attention mechanisms and transfer learning. The model output is a 3D image of dimensions (128, 128, 128, 1) with a sigmoid activation function applied. The model consists of a total of 11 convolutional layers, including 5 in the encoding path, 1 in the bottleneck, and 4 in the decoding path. Additionally, there are corresponding up-sampling layers and dropout layers in the decoding path to facilitate feature expansion and capture spatial details during the up-sampling process. The model uses the Adam optimizer with a batch size of four and employs Rectified Linear Unit (ReLU) activation functions to introduce non-linearity.

Automatic Cavity Segmentation Model

This is an improved version of the model discussed in our previous study, 'Post-Operative Brain MRI Resection Cavity Segmentation Model and Follow-Up Treatment Assistance' (Xavier *et al*., 2024). The proposed cavity segmentation model features an attention-enabled U-Net with residual connections and a VGG16 backbone. In this model, residual connections play a pivotal role in maintaining effective information flow during training. They mitigate the vanishing gradient problem, ensuring the model's ability to learn and extract features efficiently. The diagram illustrates the arrangement of convolutional layers, residual connections, and attention modules within the U-Net framework, underscoring their significance in achieving accurate segmentation. The VGG16 backbone consists of 13 convolutional layers grouped into five blocks, facilitating the capture of high-level image features. Integration of skip connections between encoder and decoder layers enhances the exchange of both low-level and high-level features for improved segmentation accuracy. Figure 3 illustrates the architecture of the proposed cavity segmentation model.

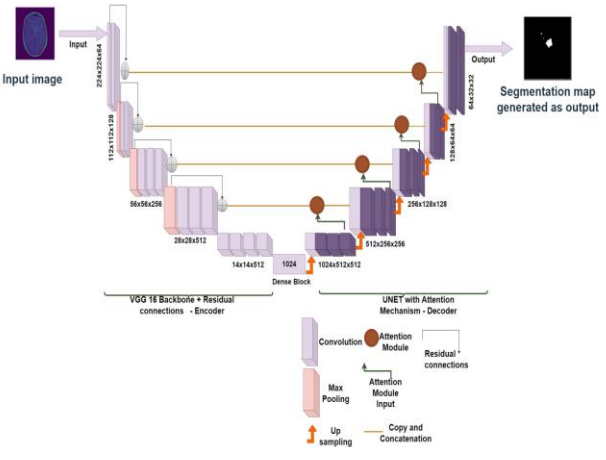

Fig. 3: Proposed automated cavity segmentation model architecture

Two additional modules are incorporated into the proposed design to enhance model performance. To mitigate the vanishing gradient issue inherent in deep neural networks with numerous layers, the residual block includes a skip connection that enables training to bypass certain layers. The attention gate, as illustrated in Fig. 2, is placed in the skip connection between the encoder and decoder of the U-Net structure. This gate highlights only relevant activations during training, minimizing computational resource waste on irrelevant activations.

Results

The skull removal model was trained on the NFBS dataset, which consists of data from 125 participants. To enhance the model's adaptability, the data augmentation technique of rotation was incorporated during training. The dataset was split into 360 samples for training and 20 samples for testing. For the cavity segmentation model, the EPISURG dataset was used. The skull removal model was employed as a preprocessing step, followed by splitting the skull-removed data into 240 samples for training and 20 for testing. Both models were implemented using the TensorFlow framework and trained on CoLab Pro with a batch size of 1. To reduce memory space requirements during training of the skull removal network, the input images and masks were downsized to a quarter of their original size. The Region of Interest (ROI) for each organ was identified from the ground truth mask and individual organ bounding boxes were created. The skull removal model underwent 30 epochs of training using these bounding boxes as labels to predict brain boundaries. Subsequently, the 3D ROI coordinates for all organs were calculated from the predicted outputs of the skull removal model, and the cropped images were prepared for segmentation. The models were trained separately and the model weights were saved. To enhance convergence, the model weights were updated during the training process using the Adam optimizer (Kingma and Ba, 2014).

The training of the proposed skull removal model on the NFBS dataset yielded impressive results, highlighting its effectiveness in accurately segmenting brain tumor regions. Figure 4 provides a summary of the training outcomes, showcasing the model's capability to delineate and segment the brain accurately in MRI scans with the skull.

For training the cavity segmentation model, the EPISURG dataset, consisting of postoperative brain MRI scans with annotated ground truth for cavity segmentation, was utilized. Initially, the model underwent training using the entire skull-inclusive dataset, and its segmentation accuracy was assessed. Subsequently, the same model was applied to the dataset after skull removal, and the results were evaluated. A comparison of the two result sets revealed a significant improvement in the Dice coefficient value, increasing from an initial 0.92-0.96 after skull removal. Figure 5 provides a visual summary of the training outcomes for the proposed cavity segmentation model.

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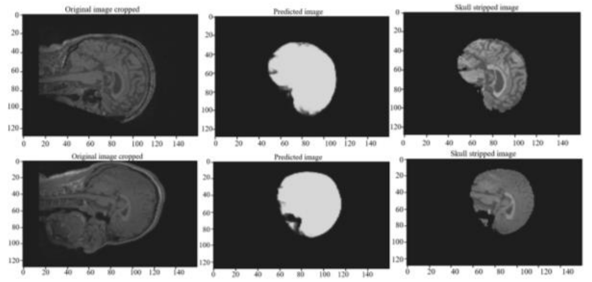

Fig. 4: Training outcomes of the proposed skull removal model on the NFBS dataset

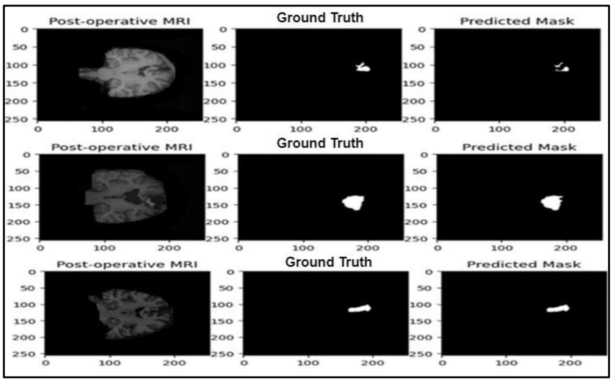

Fig. 5: Training outcomes of the proposed cavity segmentation Model on the EPISURG dataset

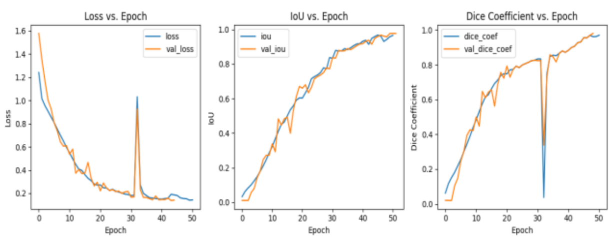

Fig. 6: Performance metrics of the proposed cavity segmentation model

The key evaluation metrics used to assess cavity segmentation quality in this study are Loss function, Intersection over Union (IoU), and Dice Coefficient (Jadon, 2020; Valvano *et al*., 2018). Loss (training and validation) serves as the foundation for model training and optimization, employing suitable loss functions like Mean Squared Error (MSE) or Binary Cross-Entropy to quantify dissimilarity between predicted segmentation and ground truth masks, aiming to minimize this loss during training for improved boundary accuracy. IoU measures spatial overlap between predicted cavity regions and ground truth masks, calculated as the intersection divided by the union. Similarly, the Dice Coefficient quantifies the similarity between predicted and actual cavity masks, computed as twice the intersection divided by the sum of their areas. Both IoU and Dice Coefficient provide valuable insights into segmentation accuracy, with higher scores indicating better alignment and robust performance, particularly beneficial when the cavity region is relatively small compared to the brain. Figure 6 summarizes the training outcomes of the proposed cavity segmentation model, showcasing a decline in both training and validation losses, improved Intersection over Union values (from 0.0323-0.9659 for training and 0.0105-0.9767 for validation), and an increasing Dice coefficient (from 0.0621-0.9593 for training and 0.0208-0.9622 for validation). These metrics collectively emphasize the model's precision and robust performance in segmenting both datasets.

Discussion

Using the skull removal method before segmentation proves beneficial in the postoperative context, allowing the network to identify the region of interest and extract minute features, ultimately improving segmentation accuracy. This research proposes an enhanced resection cavity segmentation framework with automatic skull removal, consisting of two parts. The first part automates skull removal in brain MRI scans, utilizing a U-Net model with a VGG16 backbone and attention gates for efficient feature extraction. This approach outperforms existing models, as demonstrated in Table 1 using the NFBS dataset.

The second part focuses on post-operative resection cavity segmentation in brain MRI, addressing challenges posed by surgical interventions and varying brain tissue structure. Accurate segmentation is crucial and our method, evaluated against top-performing models (U-Net, U-Net++, Attention U-Net, and ResuNet) on the post-operative EPISURG dataset, significantly enhances segmentation performance. This comparative analysis highlights the efficacy of our proposed cavity segmentation model. The performance metrics resulting from a comprehensive analysis of well-known brain MRI segmentation models U-Net, U-Net++, Attention U-Net, and ResUNet in post-operative cavity segmentation using the EPISURG dataset are presented in Table 2 and Fig. 7. The analysis demonstrates that the suggested cavity segmentation model surpasses previous models by incorporating automatic skull removal and an improved U-Net design. There is limited work on automated postoperative resection cavity segmentation. Pérez-García *et al*. (2021) utilized a self-supervised 3D CNN for Resection Cavity (RC) segmentation. Arnold *et al*. (2022) proposed a modified U-Net model for cavity delineation. Billardello *et al*. (2022) proposed a semi-automated region-growing algorithm for cavity segmentation. Table 3 summarizes the performance metrics reported in various studies on post-operative cavity segmentation models. These results indicate that existing segmentation models perform well in standard scenarios, such as preoperative scans, but encounter significant challenges with postoperative brain MRI data.

Table 1: Comparison of deep learning-based automatic skull removal models Using NFBS Dataset

Architecture	Dice score
Multi-view U-Net (Fatima *et al*., 2022)	0.918
Enhanced U-Net (Valvano *et al*., 2018)	0.965
Proposed model	0.980

Table 2: Comparison of various segmentation models on a post-operative dataset

Model	Dice-coefficient
U-Net	0.6150
Attention U-Net	0.8234
U-Net++	0.7302
ResUNet	0.7145
Proposed model	0.9600

Table 3: Comparison of performance metrics in various post-operative cavity segmentation models

Model Used	Dataset Used	Dice coefficient
Self-supervised 3D CNN (Arnold *et al*., 2022)	EPISURG dataset	85.2
Modified U-Net model (Pérez-García *et al*., 2021)	Clinical dataset (62 images of epilepsy patients)	0.84±0.08
Semi-automated region growing (Fatima *et al*., 2022)	Clinical dataset (35 MRI of glioma patients)	0.83 (0.72 -0.85)
Proposed model	EPISURG dataset	0.96

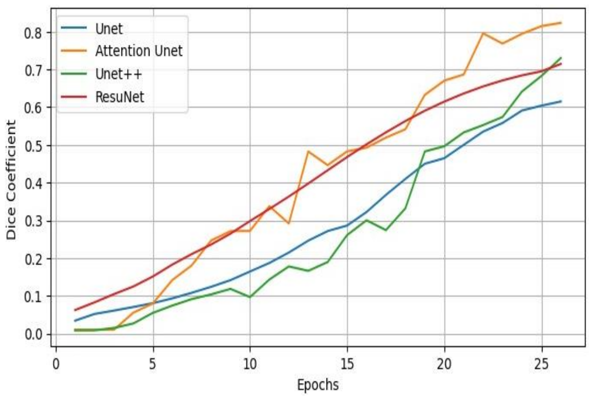

Fig. 7: Various segmentation models performance on EPISURG dataset

Conclusion

In conclusion, this research introduces a groundbreaking approach to postoperative brain MRI segmentation with an innovative two-stage architecture that incorporates an enhanced cavity segmentation model featuring automatic skull removal. The proposed model outperforms existing segmentation models, demonstrating superior accuracy on the EPISURG dataset. By utilizing a novel automatic skull removal model and a postoperative cavity segmentation model, this approach addresses memory space constraints and reduces false positive predictions, ultimately improving segmentation accuracy. The integration of attention gates and residual blocks enhances the feature extraction capability of the segmentation model, mitigating the vanishing gradient problem. This study not only contributes a robust framework for post-operative cavity segmentation but also sheds light on the broader challenges posed by limited annotated data in this domain. The proposed two-stage architecture, coupled with the enhanced U-Net model, presents promising results and opens avenues for more accurate and efficient neuroimaging analyses. The findings of this research hold significant implications for advancing medical diagnoses and treatments in the field of neuroimaging.

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Author's Contributions

Sobha Xavier P.: Handle the conception, design, implementation, and writing of the study.

Sathish P. K. and Raju G.: Responsible for the design, material preparation, and implementation analysis.

Ethics

We utilized the publicly available datasets for this study. We have duly confirmed that ethical approval is not required for this study.

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