Frontiers in Biomedical Technologies Vol. 12, No. 3 (Summer 2025) 547-556

ORIGINAL ARTICLE

Combination of Graph and Convolutional Networks for Brain Tumor Segmentation from Multi-Modal MR Images In Clinical Applications

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Received: 18 July 2023 / Accepted: 10 December 2023

Abstract

Purpose: Brain tumors are very important for the overall health of humans, which happen due to the uncontrolled increase and duplication of abnormal cells. Therefore, brain tumor segmentation is a very important step in medical diagnosis and can help in early tumor detection, treatment planning, and tumor progression follow-ups. To solve the problems related to manual segmentation such as time-cost, inaccuracy and subjectivity, automatic segmentation with deep learning methods is presented. This study aimed to develop an automatic brain tumor segmentation based on the combination of convolutional and graph neural networks to overcome the shortcomings of each network when they are used individually.

Materials and Methods: The main goal of this study is to propose a novel architecture for brain tumor segmentation from multi-modal MR images and comparison of the results with related SOTA studies. The novel architecture uses a simple Convolutional Neural Network (CNN) and Graph Neural Network (GNN) sequentially. In the first stage, the volumetric 3D image with a combination of all modalities is fed to the simple convolutional network. After retrieving the feature representation of the CNN, a graph model is created and fed to the GNN. The CNN will help to capture local information of patches and GNN will retrieve the global information available in the data which together can provide promising results.

Results: The proposed model used for the segmentation of the BraTS2021 dataset showed the average Dice score of 0.86 and the average Hausdorff of 17.94. The results showed that the combination of CNN and GNN can the performance of the task at hand. Also, the heatmaps extracted can show the importance of adding the GNN into the CNN.

Conclusion: New and creative advancements in artificial intelligence and its applications for medical image segmentation are very promising. We proposed a hybrid network of CNN and GNN to capture local and global information and combine them in a way such that we can recreate an acceptable segmented result which is justified with Dice score and Hausdorff metrics quantitatively. The proposed methodology performed better in comparison with the other related methods. Also, the activation heatmaps confirm the reliability of the approach qualitatively.

Keywords: Brain Tumor; Segmentation; Convolutional Neural Network; Graph Neural Network; Magnetic Resonance Imaging.

DOI: https://doi.org/10.18502/fbt.v12i3.19178

Frontiers in BIOMEDICAL TECHNOLOGIES

1. Introduction

A brain tumor is caused by the uncontrolled growth of abnormal tissues that do not follow the natural cycle of cells. They may not be cancerous but if left untreated can put massive pressure on the cranium because of space. There are two types of brain tumors. First, the primary tumors begin in the brain boundaries, and, secondary tumors start in other parts of the body and metastasis to the brain and develop the brain tumors [1].

Early diagnosis of brain tumors plays an important role in increasing the chance of treatment and survival of patients. Tumor segmentation using neuro-imaging modalities such as MRIs is crucial for treatment procedure and planning [2], monitoring of tumor progression and response to treatment [3], and reducing healthcare costs by minimizing the need for extensive and late-stage interventions [4].

Clinicians usually check and detect tumors on MR images based on their experience and expert knowledge. MR images usually are made up of many slices and manual segmentation of them is time-consuming and with human errors, which should cause misdiagnosis [5]. Also, manual segmentation is time-consuming, inaccurate, and subjective due to the variation in size, morphological shape, and location of tumors. Hence, automatic brain tumor segmentation seeks to address the limitations of manual segmentation, reduces the subjectivity of manual tumor delineation, saves clinicians valuable time compared to manual methods, and improves workflow and patient care.

Machine Learning approaches used in brain tumor segmentation [6, 7] needed extensive feature engineering and the performance of the algorithms was not comparable with deep learning methods [8-10].

Among deep learning approaches, Convolutional Neural Networks (CNN) play an important role in image segmentation [11-14]. For Brain tumor segmentation, three variants of CNN can be seen in studies: cascade CNNs [15-17], single and multi-path CNNs [18-20], and fully convolutional networks [21-23]. Iqbal *et al.* [13] proposed a deep CNN that made up several sequential layers for brain tumor segmentation. A CNN architecture with two pathways that emphasize both small and large contexts of MR images was proposed in [24]. Hussain *et al.* [25] developed a CNN-based algorithm for automated segmentation of brain tumors and to avoid over-fitting using max-out and drop-out is suggested. To improve the segmentation prediction results, a combination of CNN and full CRF is proposed in [26]. CNN-based approach do not need any feature engineering and different deep architectures have achieved good performances in brain tumor segmentation but there are some considerable problems. One of the main shortcomings of CNN-based algorithms which is mainly caused by the limited receptive field unless a very deep neural network is used, is the disability to capture long-range dependencies and global feature connections in related pixels and locations [27].

Transformers [28] using self-attention blocks are gaining so much respect in the field of image processing [29]. There are several studies on applications of Transformers or the variation of them [30] on brain tumor segmentation [31-33]. In order to use the advantage of both CNN and Transformer, a combination of them called TransBTS was developed by Wang *et al.* [31]. By inspiring TransBTS, Jia *et al.* [34] proposed an architecture that makes a feature representation of the skip connection. Zhang *et al.* [35] introduced a multimodal medical Transformer which can model local, global, and long-range correlations within each modality of MR images. The intra- and inter-modality correlation of MR images was explored by using a Nested Modality-aware Feature Aggregation module in [36]. The main problem of transformers in the field of medical image processing is the need for enormous datasets for training [37], and the high computational cost.

Graph Neural Networks (GNN) [38-41] are developed in such a way that can handle the issues mentioned above. By defining different hop levels, considering global features and long-range dependencies of an image are addressed. It is also so much easier to train a GNN and needs far less computational cost compared to Transformers. Several variations of GNNs have been developed for 3D brain tumor segmentation [42, 43]. Ma *et al.* [5] proposed spatial and channel reasoning modules in parallel for modeling long-range dependencies and contextual interdependencies of an image for brain tumor segmentation. This architecture works based on

Graph Convolutional Network (GCN) and Graph Attention Network (GAT). GAT is also used by Patel *et al.* [44] to identify the tumor type via a volumetric MRI.

Bagheri *et al.* [45] introduced a graph coloring approach for brain tumor segmentation that considered each pixel of the image as a graph's node and the brightness difference of a couple of pixels as an edge.

The main property of GNN is that it will perform on the basis of sampling neighbors in a node-wise manner and then aggregating the information retrieved from those neighbors.

Inspired by these observations, in this study with the combination of two widely used methods in deep learning for brain tumor segmentation, we have proposed a novel architecture by using CNN to find relevant representations to create a graph input for the GNN to exploit and aggregate features with the following specifications:

- A CNN for retrieving the local information available in near patches.
- In order to leverage the global information, after the CNN layer we have used GraphSage.
- By considering multiple hops for the sampling and aggregation of information of GNN it is possible to reach more nodes and hence more global information.
- Merging and combining the two networks can help to alleviate the drawbacks of standalone architectures, hence boosting the performance of the overall results.
- Deconvolution layers are used to recreate the main image size which is segmented.
- The proposed architecture will target important locations for brain tumor segmentation which is evident from the resulting heatmaps.

2. Materials and Methods

The proposed method is mainly composed of two architectures, connected together in Figure 1. The details of every part of the figure are available in the next sections. In order to achieve fine-grained local information from images, the data is fed into a CNN. The CNN will receive the 3D input image so the convolutional operations are all in 3D form. Extracted features from CNN will be used as nodes with proper embeddings in a 2D form and are available for GNN input. GNN will perform operations in a manner to capture global information. To recreate the information of the whole image size and as for the 3 main classes of the output result, deconvolution layers combined with 1×1 convolution layers are used.

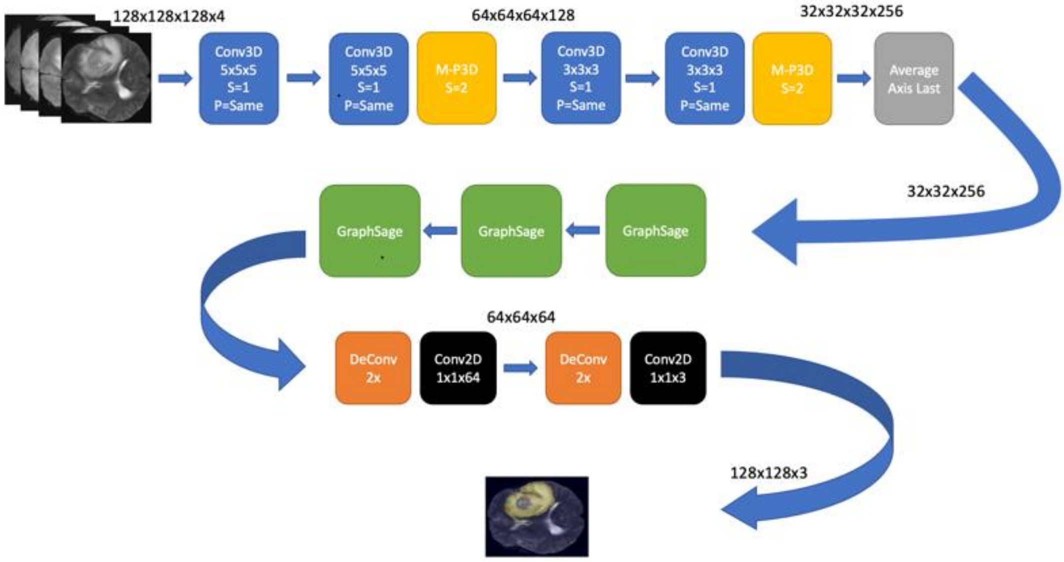

Figure 1. The main architecture of the proposed method

2.1. CNN Architecture

As explained in section 2.6, the data is in the shape of 128×128×128×4. The input contains information from the 4 modalities of the MRI datasets. So, the convolutional layers are all in 3D form. The CNN architecture is made up of 4 layers of convolutions. The Conv3D with a kernel size of 5 and 3, the stride of 1, proper padding, and N filters are connected to the 3D max-pool layer with a stride of 2. The process is repeated for other layers but with different numbers of filters. The output of CNN architecture is then averaged on the last dimension of data (not the feature size).

The simple architecture helps in 3 ways, first, it will utilize the information available in 3D form of data from the 4 modalities of MRI. Second, the 3D data will be transformed into a 2D shape with 256 embedding vectors for every data point which is later considered as nodes of GNN. Third, the local spatial information is preserved and explored before feeding into a GNN.

2.2. GNN Architecture

The proposed graph neural network architecture in this study contains GraphSage layers [41] (Figure 2). As illustrated in Figure 2, with only one hop every node uses its adjacent neighborhood, and combines it with the available information to update the information passed into the next step. The output of the previous section with the size of 32×32 is considered nodes with 256 embedding vectors. The information of every node is transformed by (Equation 1):

$$H_u^{l+1} = \sigma(W^l.(H_u^{(l)} concat\ mean(W_v \sigma(H_v^{(l)})\forall v \in V(u))) \qquad (1)$$

aggregation of the neighbor's information shown in Equation 1.

Where *Hu* at the beginning is the embeddings provided by CNN in the previous step and for other layers it is the feature matrix of node u at layer l, σ is an activation function to add non-linearity, W^l is a trainable weight matrix at layer l, W_v is another trainable weight matrix for neighbors, and *V(u)* is the subset of nodes which are directly connected to u via edges, also known as the neighborhood of u.

The output size of GNN does not change and it remains the same as the input, but the information aggregation and updates from different hops will be utilized to cover related global features from other nodes.

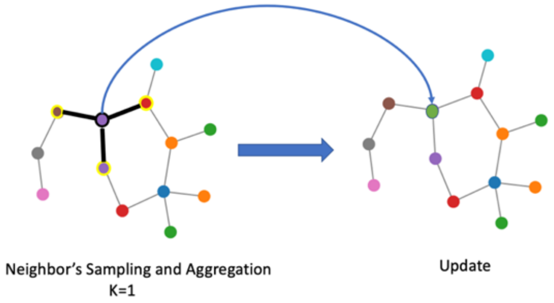

Figure 2. Detailed view of GraphSage layer

2.3. Deconvolution Model

In this section, the data is converted back into the original shape of the input so we can have the output segmented result. In order to achieve this, deconvolutions with a factor of 2 are used. 1×1 convolutions are leveraged to change the number of filters to the desired output channels.

2.4. Loss Function

Cross-entropy loss is used to calculate the loss and backpropagate through the entire model (Equation 2). So, the whole architecture is trained jointly. SoftMax activation function for the last layer can help to classify different labels of the dataset.

$$L_{CE} = -\sum_{i=1}^{N} y_i log \widehat{y_i} \qquad (2)$$

2.5. Dataset

To evaluate the proposed method, the BraTS2021 dataset is utilized [46-48]. There are 1251 cases for training and 216 for validation in this dataset. Each sample included the four 3D MRI modalities: T1-weighted (T1), post-contrast T1-weighted (T1ce), T2-weighted (T2), and Fluid Attenuated Inversion Recovery (FLAIR). The input image size is 240 × 240 × 155. The labels are Label 1: Necrotic and non-enhancing tumor (NCR), Label 2: Peritumoral Edema

(ED) and Label 4: GD-Enhancing Tumor (ET). Label 3 is not available in BraTS 2020.

2.6. Pre-Processing

By observing each image of the dataset, it is obvious that every slice largely consists of a dark background without any useful information that can be ignored. In this matter, unnecessary columns and rows are removed in each slice and the image is resized to 128 × 128. Also, empty slices are dropped from the beginning and end of 155 slices, and 128 of them with more useful information are selected. As it is evident in Figure in the first column, the margins of the input image are black pixels, so in order to get rid of unimportant information we can remove them. The MRI device is recording images sequentially, so the first and last slices of the image are not useful, we can delete them so we have only 128 slices out of a total of 155 slices in every sample.

2.7. Implementation Details

The entire proposed architecture is trained simultaneously for 50 epochs with mini-batch sizes of 32 and a learning rate of 0.0003. Adam optimizer is used with default parameters. Python was used as the programming language. For the deep learning framework, we used the Pytorch 1.7 version with Pytorch Geometric. A Windows PC with an Intel i7-12700K, an RTX 3080 GPU and 32GB of RAM was the choice for training the model. The training and validation split is done by default on the provided dataset of BraTS. However, we utilized 80 percent of the training data as train data and 20 percent of that for validation and early stopping criteria.

2.8. Evaluation Metrics

Two widely used metrics, including the Dice Score (DSC) and the 95th percentile of the Hausdorff distance (HD95%), are used for quantitative evaluation. The Dice score considers the internal padding of the segmentation label, and the Hausdorff distance is used to measure the areas near the boundaries of segmented locations. In other words, the DSC is used to measure the similarity between the ground truth and the segmentation results (Equation 3) and the average HD is a widely used performance metric to calculate the distance between two point sets (Equation 4). In medical image segmentation, HD is used to compare ground truth images with segmentations allowing their ranking.

$$\mathrm{DSC}=\frac{2TP}{FN+FP+2TP} \tag{3}$$

$$HD\,(X,Y) = max\{\sup_{x\in X}\inf_{y\in Y} d(x,y), \sup_{y\in Y}\inf_{x\in X} d(x,y)\}, \tag{4}$$

Where *TP*, *FN*, *and FP* are the number of True Positive, False Negative, and False Positive voxels, respectively. And also *sup*, *inf*, and *d(,)* denote the supremum, infimum, and the function that computes the distance between two points, while x and y represent the points on surface X of the ground truth and surface Y of the predicted regions, respectively.

3. Results

The effectiveness of adding the two architectures together can be seen in an experiment done in Figure 3. Class Activation Maps (CAM) [49] can help to achieve a qualitative assessment of the proposed method. By using CAMs, the areas in which the proposed approach has looked for extracting the representations related to the segmentation task are shown. The CAMs are extracted in two steps, firstly from CNN alone without the use of a GNN sequentially, which shows that the approach couldn't look for relevant areas with rich information for the task at hand. After adding the GNN it is showing that adding the GNN can help the network to see into more related areas and extract features from tumor locations by ignoring unimportant background redundant information. The resulting segmentation after using a combination of networks is complete evidence of how the GNN can impact the performance of the CNN.

As it is illustrated in Figure 4, the segmentation result can be very close to the ground truth. Each modality of the MR images provides some information. For example, if we want to segment the core tumor, the FLAIR can be used. If we combine the FLAIR with T1ce, the information about necrotic tissue can be added to segment NET regions. The CNN helps to get information about smoothed borders while the GNN will provide the information about approximations of the image. The combination of all

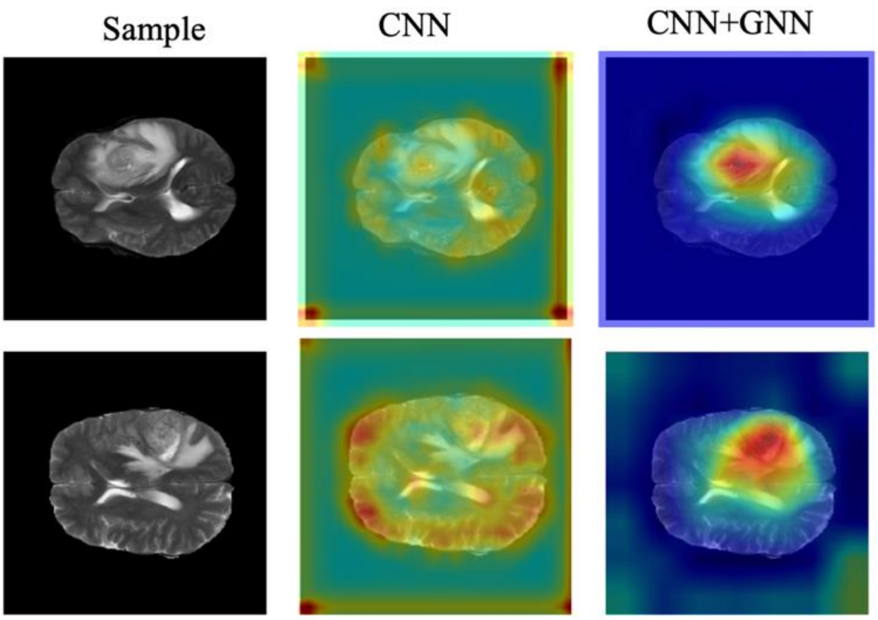

Figure 3. Extracted class activation maps of two samples of the BraTS2021 dataset. From left to right: T2 modality of MRI, class activation maps after applying CNN architecture alone and after applying the combination of CNN and GNN

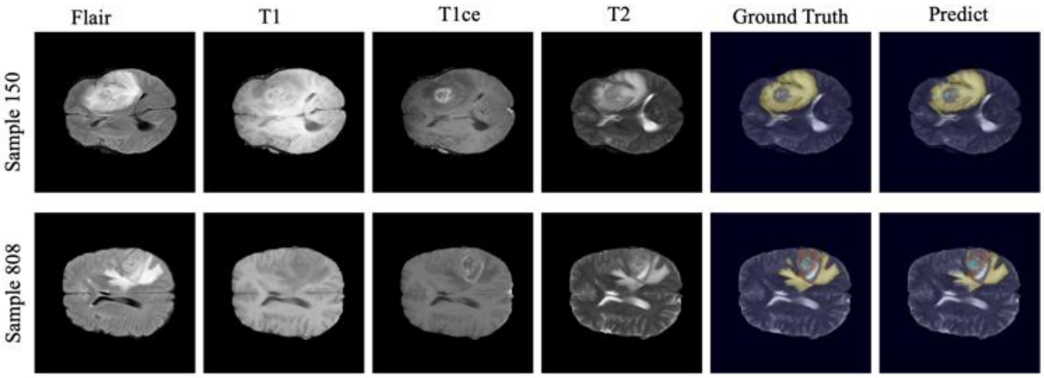

Figure 4. Sample results of the proposed method on BraTS2021 dataset. Columns 1-4 show four MRI modalities: Flair, T1, T1ce and T2. Columns 5 and 6 illustrate the ground truth and predicted tumor segmentation, respectively. Yellow=whole Tumor, Red=Enhancing Tumor, and Cyan= Tumor Core

the modalities can lead to a better performance which many studies ignore. We think that all the modalities can add a new level of information to the final segmentation results. The GNN clearly has taken advantage of the information provided by the CNN, in which the related areas are provided as node features.

According to Table 1 we have compared the results of our proposed method to other related studies in a quantitative manner. It can be inferred that the combination of CNN with GNN can improve the results for the segmentation of brain tumors. The dice score for TC of [44] is slightly better, and the Hausdorff for ET of [50] is shown to be better. For all the other tasks our proposed method outperformed other models. The overall results indicate that combining the local patch filters with global features can improve the performance of the network. The DSC for WT, TC, and ET of our proposed method is 0.93, 0.84, and 0.83 respectively. The HD95 of WT, TC, and ET is 6.99, 17.01, and 29.84 respectively. The simplicity of the CNN architecture is helping in reducing the computational costs and the GraphSage architecture for GNN also can help in that direction.

Table 1. Performance of various models on BraTS2021 validation dataset

Model	**Dice Score (%)**			**HD95**		
	WT	**TC**	**ET**	**WT**	**TC**	**ET**
GNN [51]	0.87	0.78	0.74	6.92	16.67	20.40
3D U-Net [50]	0.87	0.76	0.73	6.29	14.70	**30.50**
3D ResU-Net [52]	0.90	0.85	0.82	4.3	9.89	17.89
GAT [44]	0.91	**0.86**	0.79	5.91	6.08	9.52
Proposed Method	**0.93**	0.84	**0.83**	**6.99**	**17.01**	29.84

4. Discussion

We proposed an architecture composed of two main blocks. First, convolution layers and second, GraphSage layers. CNNs can alone produce acceptable results but due to the disability of capturing long-range dependencies, they require very deep architectures [53-55]. One of the main disadvantages of deep CNNs is the time required to train and the need for large datasets. As for the GraphSage the disability to handle exactly the same multi-sets with different structures is sometimes problematic.

The advantage of using this architecture is to alleviate the mentioned drawbacks. The simple CNN will provide a unique structure for the GraphSage. The simple architecture of CNN helps in 3 ways:

- First, it will utilize the information available in 3D form of data from the 4 modalities of MRI.
- Second, the 3D data will be transformed into a 2D shape with 256 embedding vectors for every data point which is later considered as nodes of GNN.
- Third, the local spatial information is preserved and explored before feeding into the GraphSage.

Also, using the deconvolution layers will provide proper information as there are learnable parameters. This combination also can produce smooth outputs, as it is a very important feature for segmenting brain tumors.

The CNN with 4 layers of convolution will result in a 2D graph which is fed into the GNN. The deconvolutional layers with learnable parameters in convolutional layers can result in a segmented image as output. In summary, the 3D combination of all modalities is fed into a CNN with 4 layers and the final feature representation is used as a node features information for GNN. We used 3 layers of GraphSage to exploit more relative information regarding the segmentation task.

The methodology was performed with an average DSC of 0.86 and an average HD of 17.94 for the BraTS2021 dataset. The results show that the proposed method could provide reliable performance, which is confirmed by qualitative and quantitative comparisons. For the qualitative comparison we have used CAMs and in the quantitative comparisons we have provided two metrics that are mostly reported in related studies.

5. Conclusion

New and creative advancements in artificial intelligence and its applications for medical image segmentation are very promising. In this work, we proposed a hybrid network consisting of CNN and GNN parts to capture local and global information and combine them in a way such that we can recreate a segmented result with acceptable performance. The 3D input of the model is made from a combination of all modalities of MRI. The input is fed into a simple CNN with 4 layers and the resulting feature representation is used as a graph for input to GNN. In GNN we have used 3 layers of GraphSage to exploit more relative information regarding the segmentation task.

To show the advantage of the proposed method we utilized the CAMs. CAMs illustrated that CNN alone could not provide the perfect results due to their limited receptive field, while GraphSage could explore neighbor pixels and accumulate information on tumor areas which are evident in CAM results. It showed that the method can learn and look for the potential information related to the task of brain tumor segmentation in multi-modal MR images. Also, the model achieved an average DSC of 0.86 and an average HD of 17.94 for the BraTS2021 dataset.

It is a good practice to use the Transformers [56] later, but it is important to keep in mind the importance of the computational cost of Transformers. So optimized versions of Transformers [57] combined with GNNs are proposed.

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