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Molecular Mutation Classification of Glioblastoma Multiforme Using Metric-Meta-Learning Approach Based on Siamese Neural Networks: A Retrospective Study

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Abstract

Background: Glioblastoma is the most common malignant primary brain tumor in adults. It has been classified into mutant and wild-type subtypes of isocitrate dehydrogenase (IDH). Patient therapeutic options in Glioblastoma vary across subtypes. Therefore, preoperative classification of IDH mutation status is important for therapeutic decision-making .This study aimed to develop and evaluate a metric-meta learning approach based on a Siamese Neural Network model for noninvasive classification of IDH mutation status in patients from magnetic resonance imaging (MRI) scans, based on their similarity.

Methods: MRI scans from 93 patients (2018-2024) with glioblastoma tumors were collected and subdivided into IDH-mutant and IDH-wildtype scans. After preprocessing MRI scans, a Siamese Convolutional Neural Network was combined with two pre-trained models, InceptionResNetV2 and ResNet152V2, as an embedding function to differentiate between classes using a small dataset. The network extracts relevant features to classify patients' IDH-mutation status. We propose a self-attention mechanism combined with a Siamese neural network to improve model accuracy.

Results: We evaluate a Siamese Neural Network on MRI scans of brain tumors. After adding an attention mechanism to the Siamese Neural network, we obtain classification accuracy (73.33% - 70%), precision (68.42% - 68%), recall (86%- 73.33%), and F1-score (76.20%-70.96%) on our dataset.

Conclusion: Our proposed model demonstrated promising results after combined with an attention mechanism to perform classification of IDH-mutation status using a limited number of brain tumor images and accuracy of this model has improved.

Keywords: Glioblastoma; IDH-mutation; magnetic resonance imaging; Image classification; Siamese Neural Network.

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Introduction

Glioblastoma (GBM) is the most common and most lethal grade IV malignant brain tumor in adults, with an annual incidence of about three cases per one hundred people.[1,2] The general treatment for GBM includes surgical tumor resection, accompanied by radiotherapy, blended with concurrent and adjuvant temozolomide chemotherapy. Despite those competitive treatment plans, the median overall survival stays very low, usually starting from 12 to 18 months afterdiagnosis.[3] The genetic profile of GBM without delay impacts analysis, treatment, and survival results (three). One of the key genetic biomarkers in GBM is isocitrate dehydrogenase (IDH).[4] The most common subtype, formerly known as primary glioblastoma and accounting for ninety percent of cases, is the bad-diagnosis IDH-wild-type glioblastoma. Within this group, the giant cellular glioblastoma variant shows a much longer survival (approximately 1313), whereas the currently identified epithelioid glioblastoma, which primarily affects adults, has a more aggressive clinical course. The 2nd main subtype, previously known as secondary glioblastoma and now diagnosed as IDH-mutant glioblastoma, accounts for for remainingining 10% of cases and usually occurs in younger patients, resulting in better outcomes.[5]

Tumors with IDH-mutation have a better prognosis than those with IDH-wildtype. IDH-mutated tumors also have distinct therapeutic responses compared to IDH-wildtype tumors. As a result, exclusive therapeutic tactics are important for IDH-mutated and IDH-wildtype glioblastoma. Therefore, the preoperative prediction of IDH status is important for

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appropriate treatment planning. Currently, the only way to conclusively detect an IDH-mutated glioblastoma is through immunohistochemistry or gene sequencing of a biopsy or surgical resection specimen.[6,7] The biopsy-based strategies might also face incomplete sampling due to the spatial heterogeneity of GBMs, characterised by multiple intra-tumoral habitats and variable genetic expression (eight). Thus, developing a noninvasive, stratified assessment of IDH mutation prevalence is a pressing requirement for personalized treatment and to improve patient survival.[8] Medical imaging, including magnetic resonance imaging (MRI), has been proposed as a possible candidate due to its noninvasive nature and its current role in recurring medical care.[9,10] However, MRI interpretations are not straightforward due to tumor heterogeneity, as evidenced by varying degreesancement, infiltrative.

In recent years, deep learning has emerged as a transformative technology across various fields, including medical image analysis. Deep learning, a branch of machine learning, involves training algorithms to learn from large amounts of medical images.[11] However, the lack of annotated medical images limits the performance of deep learning models, which typically require large-scale labeled datasets. Few-Shot Learning (FSL) is an actively studied area that aims to overcome this limitation.

Few-Shot Learning techniques require only a few labeled examples for training.[12] Meta Learning, or Learning to Learn, is the foundational technique used by most FSL algorithms. It is a subfield of machine learning that focuses on learning priors from previous experiences to enable efficient learning of new tasks. Meta Learning can be classified into three approaches: metric-based, optimization-based, and model-based.[13]

Metric learning, such as Siamese Neural Networks (SNNs), involves learning a distance function over data samples.[14] The Siamese Neural Network is one of the simplest metric-based learners and is widely used in one-shot learning problems. Its main architecture was proposed initially in 1993 for fingerprint similarity estimation. In this retrospective study, we had access to clinical information for a limited number of patients with Glioblastoma tumors, so we aim to evaluate the potential of Siamese Neural Networks as a noninvasive, novel method for classifying molecular mutations in Glioblastoma Multiforme using only small datasets of brain tumor images for personalized treatment.[10]

Materials and Methods

Study Dataset

The present research was approved by the ethics committee of the Faculty of Medical Sciences and Technologies, Islamic Azad University, Science and Research Branch (Ethics Codes: IR.IAU.SRB.REC.1403.310). The inclusion criteria for enrollment were: (a) histopathologically confirmed Glioblastoma Multiforme based on the WHO classification system, (b) known IDH mutation genotype determined by immunohistochemistry, and (c) available preoperative anatomical MR images acquired using an identical data acquisition protocol. These images were retrospectively collected from the Shohada Tajrish Hospital picture archiving system between March 2018 and May 2024. Based on these criteria, a cohort of 93 patients (mean age = 53.21 years; 62 males and 31 females) with newly diagnosed GBM was considered in this study. Of these, 68 patients (108 scans) had the IDH-mutant genotype, and 25 patients (71 scans) had the IDH-wild-type genotype. The acquired MR sequences included axial contrast-enhanced T1-weighted imaging. All MRI scans were performed on a 1.5 T scanner (Magnetom Sonata, Siemens, Erlangen, Germany) with participants in the supine position.

Immunohistochemistry was conducted after tumor surgery or biopsy. For evaluating IDH mutation, the IDH-1 R132H antibody was used. The test result was positive if diffuse immunopositivity was detected, and negative if no tumor cells showed immunopositivity.

Image preprocessing

The present study used image preprocessing to address image sharpening, resizing, and normalization.[16] Image sharpening is a crucial preprocessing step that enhances the contrast between bright and dark regions, thereby bringing out edge

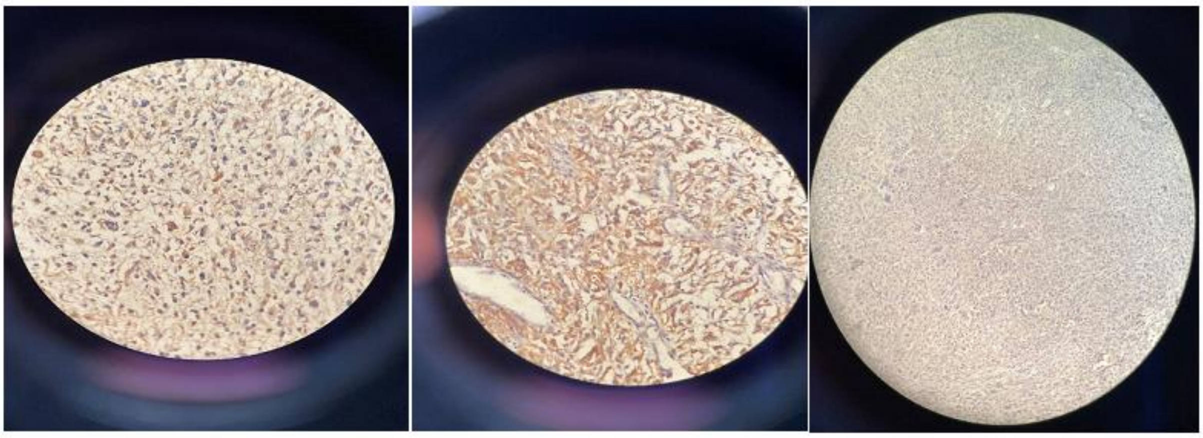

Figure 1. Microscopic (histologic) images. Pathology confirmed isocitrate dehydrogenase (IDH) mutations: mutant and wildtype.

features. It enhances the subtle elements already present and improves the edge steepness.[14] As each tumor was different in size, all images were resized to 128 X 128. All MRI images were normalized to the range [0,1].

Siamese Neural Network: Model Architecture

This paper focuses on metric learning using a Siamese Neural Network (SNN). A Siamese Neural Network (SNN) structure consists of neural networks that assign equal weights and are joined at one or more layers and used a couple of the same convolutional neural networks (CNNs) with shared weights as achieved in Siamese Networks for image verification.[13] SNNs use case pairs as input at both the training and test levels to expand item-to-object similarity knowledge. We define the bottom network as a convolutional network for feature extraction. We build convolutional layers with rectified linear unit (ReLU) activations and max pooling, followed by a flatten layer and a couple of fully connected layers, producing a function vector of size 100. The entire network uses ReLU activations, and the prediction layer uses smooth max activation. Cosine similarity calculates the similarity between two feature vectors. Figure 2 represents the principal tiers of our Siamese neural network.

To evaluate the performance of the Siamese community structure on this dataset, we conducted an empirical assessment using alternative baseline architectures as embedding layers: InceptionResNet-V2 and ResNet-152V2.

Inception-ResNet-v2 is a convolutional neural architecture that builds on the Inception family of architectures but contains residual connections (changing the filter concatenation stage of the Inception structure).[19] In the Inception-Resnet block, a couple of sized convolutional filters are combined by means of residual connections.

The use of residual connections not only prevents the degradation problem caused by deep structures but also decreases the training time. The residual connections in Inception-Resnet-V2 help mitigate vanishing gradients, enabling the training of profound networks and better feature learning. Figure 3 shows the basic network architecture of Inception-Resnet-V2.[21] Residual networks (ResNets) were proposed as a family of deep neural networks with similar architectures but varying depths. A ResNet network is composed of multiple residual blocks with varying convolutional kernel sizes. ResNet introduces a structure called a residual learning unit to alleviate the degradation of deep neural networks. This unit's structure is a feedforward network with a shortcut connection, which adds new inputs into the network and generates new outputs. The foremost advantage of this unit is that it improves classification accuracy without increasing the model's complexity. ResNet-152V2, or Residual Network 152 Version 2, is a variant of ResNet with 152 layers. It preserves the bypass connections from the original ResNet architecture, facilitating efficient training of deep networks.[22] Figure four shows the simple network structure of ResNet-152V2.

To improve the accuracy of similarity measures in this study, we use a self-attention mechanism. We believe our proposed model will achieve promising results when combined with an attention mechanism for classifying glioblastoma multiforme molecular mutations using a limited number of MR images.

Model Training

The Siamese Neural Network includes two identical networks. The dataset (179 labeled scans) was split into 80% for training and 20% for testing, with Pair creation completed after

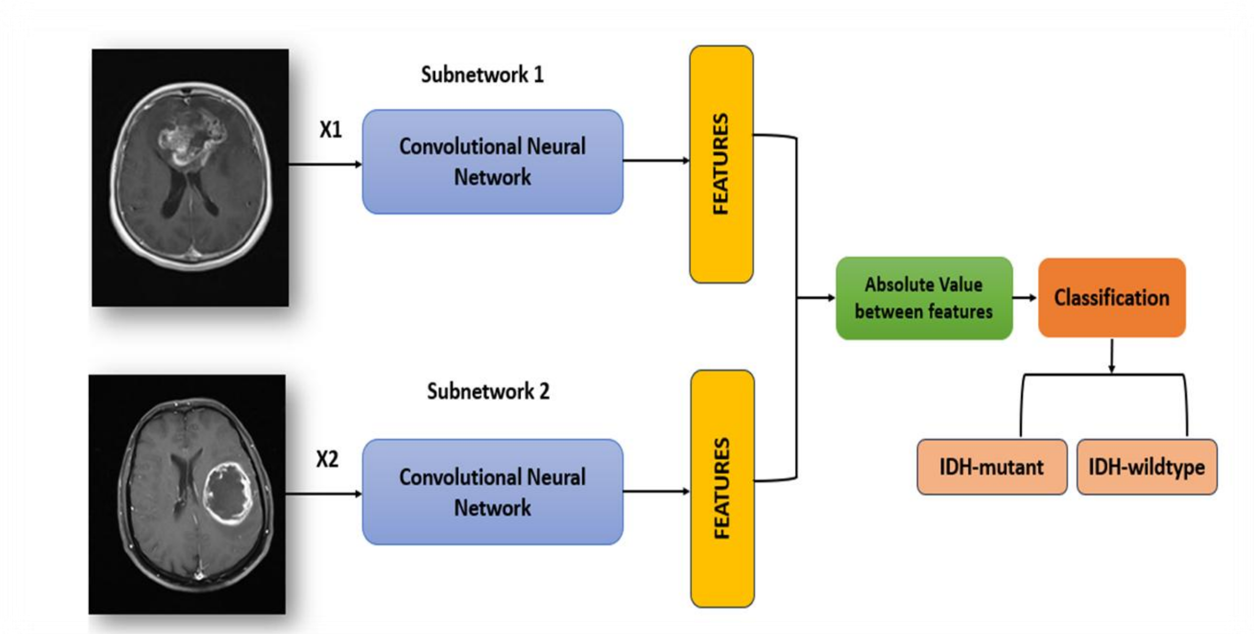

Figure 2. Important stages of the Siamese Neural Network.

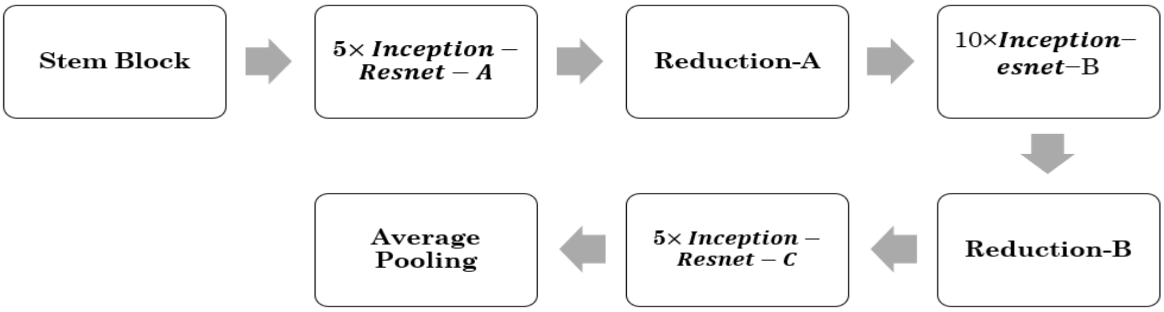

Figure 3. The basic architecture of Inception-ResNet-V2.

splitting. For every case in the dataset, two pairs were created: a genuine pair (with a random case from the same class) and an impostor pair (with a random case from a different class). This allows the network to develop a multi-dimensional space based on case features, where genuine pairs are pushed closer together, and impostor pairs are pulled further apart.

In this study, we ensured an equal number of genuine and impostor pairs because generating truly random pairs led to an imbalance favoring genuine pairs. After pair creation, the model was trained for 100 epochs without using the Early Stopping callback in Keras, employing the RMSProp (Root Mean Square Propagation) optimizer with a learning rate of 0.001.

The output of the identical neural networks (o'' sub-networks') is a feature vector for each member of the input pair. The distance between these vectors is measured at the similarity layer todetermine whether they belong to the same class based on a threshold. There are three loss functions primarily used in the Siamese Mese neural network model to optimize the network, including Binary Cross Entropy, Contrastive Loss, and Triplet Loss. Binary cross-entropy is used when the classification problem is binary, i.e., when the classifier's output probability ranges from 0 to 1. The loss value is higher when the output and the actual output differ significantly. The loss for both the positive and negative images is calculated and concatenated.[18]

The loss function is described as: Loss= $-c\log p + (1-c)\log(1-p)$. Where c is the class and p is the prediction probability. In this study, after computing similarity using Cosine similarity as the distance metric, Binary cross-entropy loss is employed to maximize the similarity between similar samples in a pair and minimize it between dissimilar samples. We use transfer learning with Inception-Resnet-V2 and ResNet-152V2, both pre-trained on the ImageNet dataset.[24]

Since the Inception-Resnet-V2 uses a Global Average Pooling (GAP) layer after the Inception-Resnet-c module, the resulting output is a 1536-dimensional feature vector, which is used to calculate the absolute value of the difference. The feature vectors are subtracted, the absolute value of the difference is computed, and the images are classified into one of the two existing classes using a completely connected layer. This pre-trained model effectively mitigates overfitting by adding Dropout Layers and Batch Normalization, and is fine-tuned with frozen Layers.

The Residual Neural Network (ResNet152V2) is a

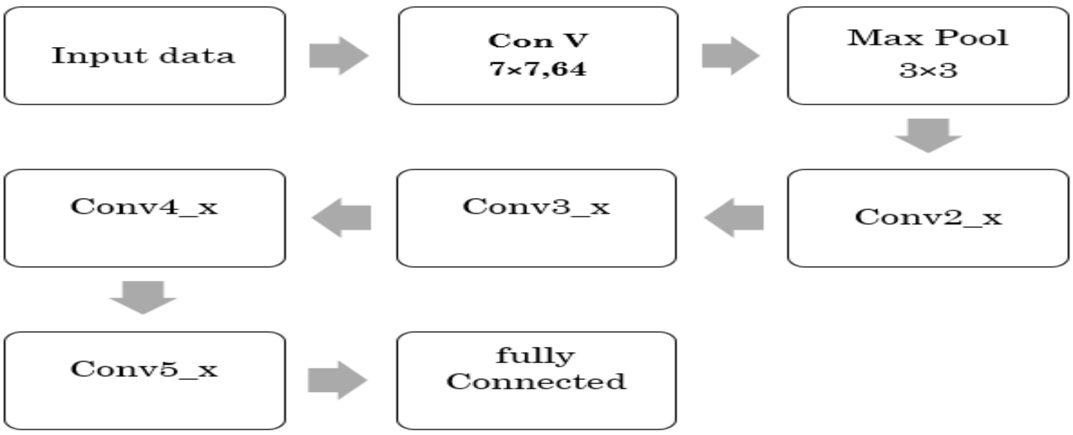

Figure 4. The basic architecture of ResNet152V2.

convolutional neural network with layers. The Adam optimizer is used to train and optimize this model's performance with an initial learning rate of 0.0001. This model's robustness and accuracy in handling complex image classification tasks make it a reliable choice for applications requiring high-level feature extraction.[23] Python version 3.10, which runs on Google Colab, is the programming language used in this study.

Model Evaluation for Two-Class Classification

This proposed model is trained based on the pair's similarity and dissimilarity and is tested on two classes. The model is tested on 20% of the whole dataset. The data is preprocessed and fed to the model for feature embeddings. Table 1 summarizes the classification performance of the proposed architecture, Siamese Net, compared with Inception-ResNet-V2 and ResNet-152V2 as our embedding layers.

The results reveal that the Siamese network clearly outperforms the other two models, with UAR and Precision values of 68.72% and 66.66%, respectively. The overall accuracy was not very high in absolute terms, but it is the best result known for this specific problem, IDH-mutation status classification from MR images.

The low accuracy achieved with ResNet-152V2 is most likely due to the numerous functions in MR images, which make model learning difficult. Finally, the Siamese network architecture achieves considerable performance improvement over the two baselines. However, the overall accuracy is still relatively low.

Self- Attention Mechanism Combined with Siamese Neural Network

Similarity measure methods typically use the measure function (or the enhanced measure function) or a hybrid similarity measure algorithm to calculate case similarity. Since the contribution of different features to the problem varies, directly using the above metric function to calculate similarity will reduce accuracy. In machine learning, the main concept of metric learning is to compute similarities between samples to decrease the distance between samples of the same class and increase the distance between samples of different classes. One effective method is to use a Siamese neural network for deep metric learning. However, it ignores the distribution of feature weights during computation, which can still affect the accuracy of the similarity measure. Hence, in the present study, we use the self-attention mechanism to capture global and key information, and combine it with a Siamese neural network to propose a weighted similarity depth measurement method based on the Self-attention Siamese neural network. The structure of the combination of Self-attention and a Siamese neural network is shown in Figure 5, which is divided into three sections: the Siamese neural network layer, the Self-attention layer, and the similarity measurement layer.

The following provides a detailed explanation:

1- Siamese Neural Network Layer: Both Subnetworks include convolutional layers and a pooling layer, completely connected layers alternating with dropout layers. The ReLU activation function is used in each layer of the network. The dropout layer is used to prevent overfitting during network training and enhance the network'seralizability. The core function of the Siamese Neural Network layer is to realize the feature extraction and processing of the original data after the above multilayer network processing and convert the two inputs , x_i and x_j , into feature vectors, h_i and h_j.

2- Self-attention layer: The Self-attention layer projects the output feature vectors h_i and h_j received from the Siamese Neural Network layer into three subspaces: the query vector quantum space Q, the key vector quantum space K, and the value vector quantum space V. Then, the

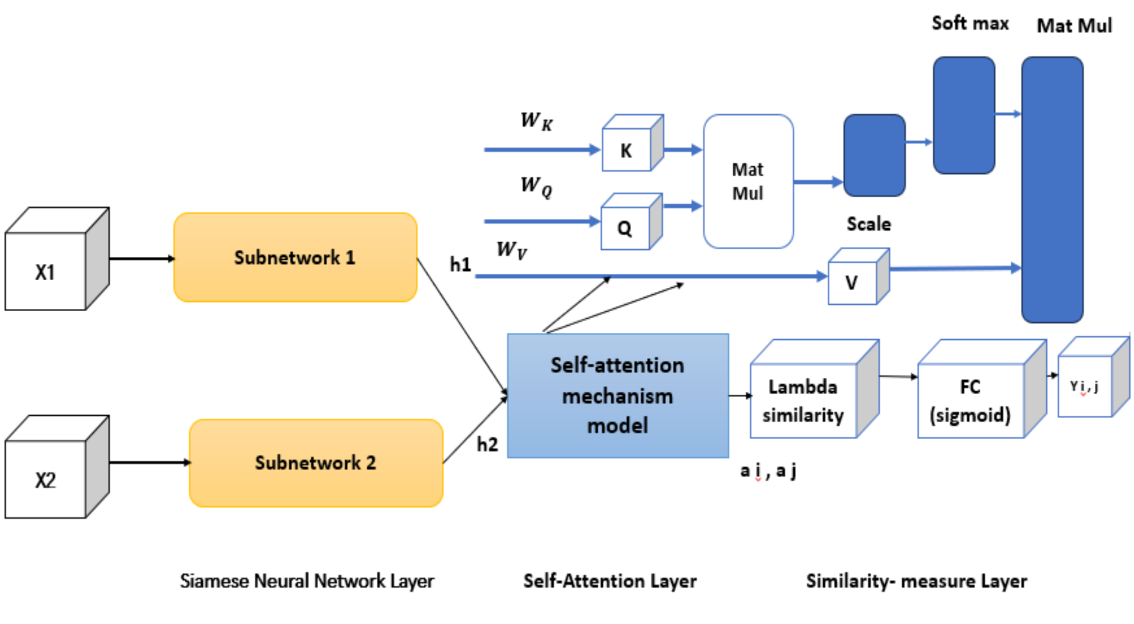

Figure 5. Self-Attention Siamese Neural Network Model.

Table 1. Model classification performance.

Model	Test Accuracy	Test Loss	Precision	Recall	F1-Score
Siamese Net	68.75%	0.6523	66.66%	75%	67.72%
SimeseNet+Inception-ResNet-V2	62.50%	0.9798	54.54%	75%	63.15%
Siamese Net +ResNet-152V2	56.25%	0.6789	53%	100%	69.56%

weight of each feature is calculated using the scoring function, and the weighted feature vectors a_i and a_j are output. The MatMul module performs the dot product operation. The Scale module scales the final attention distribution to smooth it. It can address the problem of the Softmax function's small gradient when the input vector's dimension is high.

Similarity measure layer: The similarity measure is computed over the weighted feature vectors a_i and a_j. The Cosine similarity metric is integrated into the lambda layer to construct the similarity-measure layer, where the similarity is computed. The sigmoid function compresses the numerical range of the calculation result to (0,1) and finally generates the similarity y_{ij} between x_i and x_j.

During learning, the optimizer minimizes the error for each training sample, updates the network parameters, and identifies the optimal model.[25]

Self-attention Layer combined with Inception-ResNetV2, ResNet 152V2

Certain limitations emerge while working with CNN-based pre-trained models. These models process the entire image without paying attention to its informative parts. The convolutional filters are used immediately on the whole image, extracting hierarchical features from lower-level edges and textures to higher-level patterns and object representations. Accordingly, the attention mechanism is introduced with the pre-trained models to extract features.

The attention mechanism in transformers enables the model to focus on essential image features that traditional CNNs can easily ignore while de-emphasizing less important ones. It enhances the feature extraction process and improves classifier accuracy. The updated architecture of the proposed model is depicted in Figure 6. Different attention layers are applied for each model to ensure that they are specifically optimized to complement the unique feature representations and architectural characteristics of each pre-trained model.[26] We have evaluated the performance of the proposed attention layer on two pre-trained deep networks, Inception-ResNet-V2 and ResNet152V2. The attention layer effectively identifies the most relevant information.

The attention block is integrated into the architecture following the Inception-ResNetV2 and ResNet152V2 architectures, as shown in Figure 6. This block consists of a

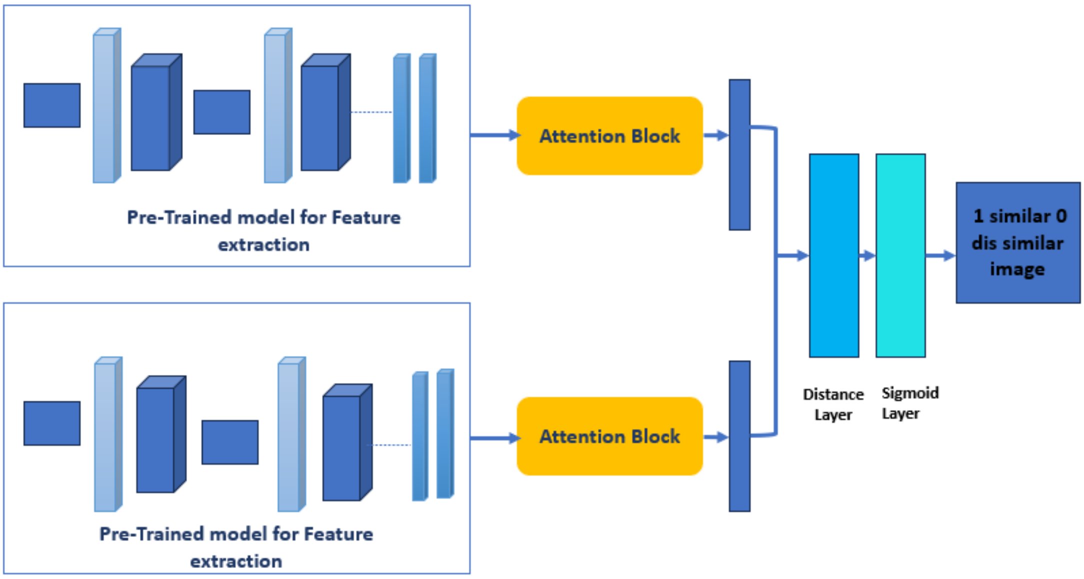

Figure 6. Our updated model architecture.

series of layers intended to direct the modmodel'scus towards the most informative parts of the input image, and a feature vector is extracted after the attention block.

Statistical Analysis

To investigate the performance of the proposed models, several metrics, including accuracy, sensitivity, precision, and F1 score, were utilized as follows:

True Positives (TP): Cases correctly recognized as positive by the model. False Positives

False Positive (FP): Cases incorrectly recognized as positive by the model. True Negatives

True Negative (TN): Cases correctly recognized as negative by the model. False Negatives

False Negative (FN): Cases incorrectly recognized as negative by the model.

According to these definitions, the performance metrics were calculated as follows:

These metrics were defined as follows: Accuracy:

The proportion of correctly classified cases (TP and true TN) out of the total number of cases, calculated as:

Accuracy $=\frac{TP+TN}{TP+TN+FN+FP}$

Sensitivity (Recall): The proportion of TP cases correctly recognized by the model, calculated as:

Sensitivity$=\frac{TP}{TP+FN}$

Precision: The proportion of TP cases among all cases predicted as positive by the model, calculated as:

Precision$=\frac{TP}{TP+FP}$

F1 Score: A balanced measure of precision and recall, calculated as the harmonic mean of precision and recall:

F1 score$=2\times\frac{Precision\times Recall}{Precision+Recall}$

Results

In our experiments, the models that were trained optimally were evaluated on the test set. The overall accuracy varied from 63.33% to 73.33%. The Siamese Net combined with a self-attention layer without pre-trained models achieved the highest accuracy (73.33%), with better F1-score (76.20%), recall (86%), and precision (68.42%) than the other methods.

Table 2 in this study presents the classification results of the Siamese Net using two pre-trained models for the embedding function, combined with a self-attention layer. With Self-attention Layers, this model can completely measure the significance of input features. By integrating a self-attention layer into Inception-ResNet-V2 and ResNet152V2, the models can enhance feature extraction. This approach is practical for medical image classification and identifying accurate features. In this mechanism the key parameters are Query (Q) representing the data being analyzed, Key (K) which means another part of the data that the query is compared against and Value (V) which signifies the data weighted according to similarity scores between Q and K. Attention scores are computed using similarity measures between Q and K, which are then normalized using the softmax function.[27] A self-attention Layer is added to two models to better focus on extracting features related to IDH mutation status during training, thereby effectively improving accuracy. It enhances the feature extraction process. Inception-ResNetV2 combines the Inception architecture with residual connections to achieve both efficiency and depth. This model comprises a 35 × 35 grid Inception Res Net-A module, a 35 × 35 to 17 × 17 Reduction-A module, a 17 × 17 grid Inception Res Net-B module, 17 × 17 to 8 × 8 Reduction-B module, and the last 8 × 8 grid Inception Res Net-C module.[20] In this model, Batch Normalization and Dropout are used to regularize, speed up convergence, and prevent overfitting. Through its hybrid architecture, it conducts robust feature extraction by capturing spatial hierarchies and fine-grained details across various scales.[28]

The Inception-ResNetV2 model's distinctive design and effective use of filters have achieved strong results in medical image classification tasks.[29]

The other well-known pre-trained deep learning model is modified ResNet152v2. ResNet152v2 is a deep neural network with 152 layers. This depth enables it to capture complicated patterns and features in images, making it suitable for complex image classification tasks.[30]

Figure 7 shows the accuracy graph of the Siamese neural network model, illustrating the relationship between the number of epochs and the model's accuracy. The results indicate that as the number of epochs increases, accuracy improves and loss decreases. In this study, 100 epochs were used.

The confusion matrices for the Siamese neural network with two pre-trained models provide insight into their performance in distinguishing between "similar" and "different" images. In the Siamese Neural Network's first confusion matrix, the model achieves 73.33% accuracy. The model's great efficacy

Table 2. Model classification performance with the self-attention layer.

Model	Test Accuracy	Test Loss	Precision	Recall	F1-Score
Siamese Net	73.33%	0.6758	68.42%	86%	76.20%
SiameseNet+Inception-ResNet-V2	70%	0.7857	68 %	73.33%	70.96%
SiameseNet+ResNet-152V2	63.33%	0.6375	61.11%	73.33%	66.66%

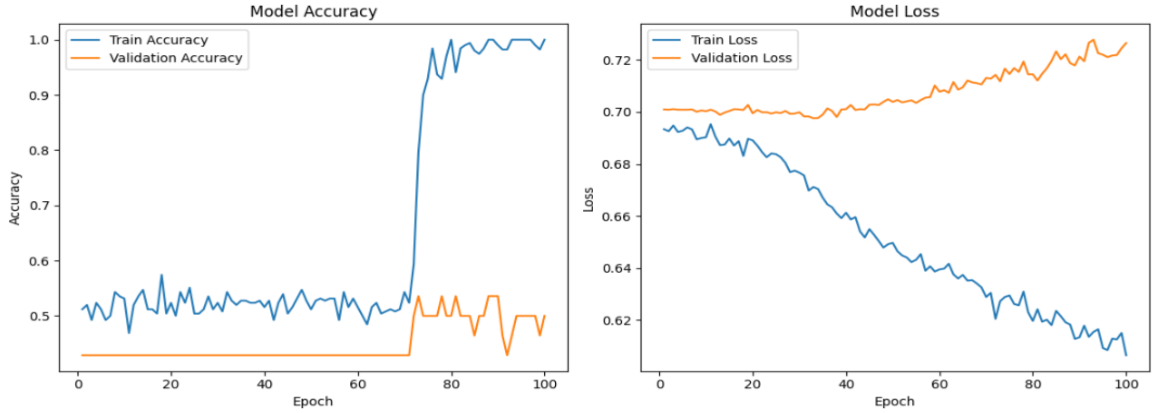

Figure 7. Accuracy and loss graphs of the Siamese neural network with a self-attention layer.

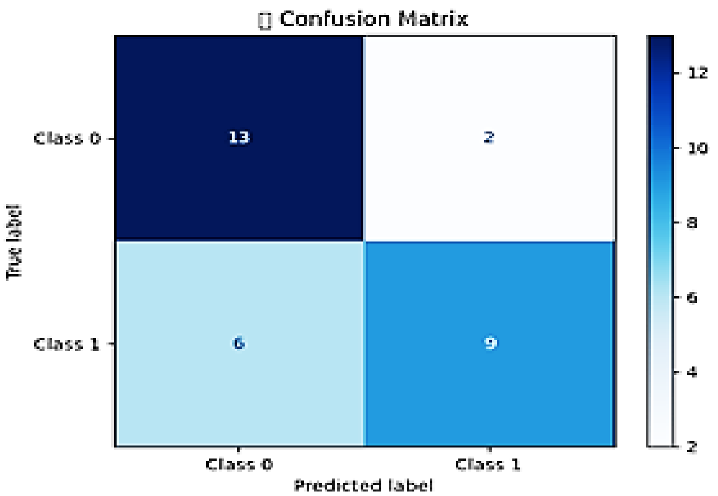

Figure 8. Confusion matrix of the Siamese neural network with a self-attention layer.

in precisely detecting both similar and dissimilar image pairs is demonstrated by the True Similar and True Different rates of 43.33% and 30%, respectively. The misclassification rates are minimal: only 6.66% of similar

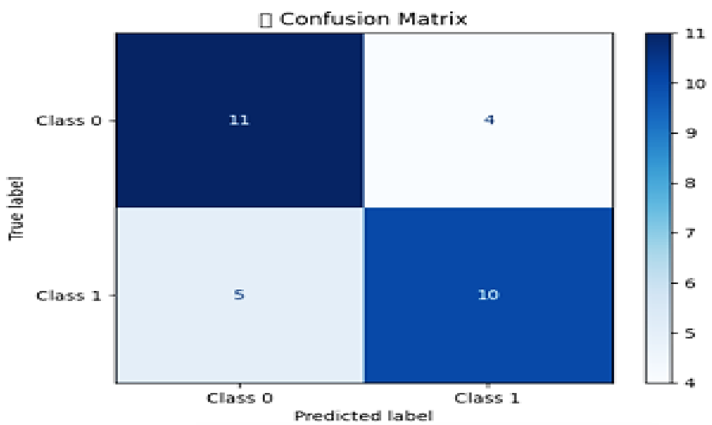

Figure 9. Confusion matrix of the Siamese neural network with Inception ResNet v2 and a self-attention layer.

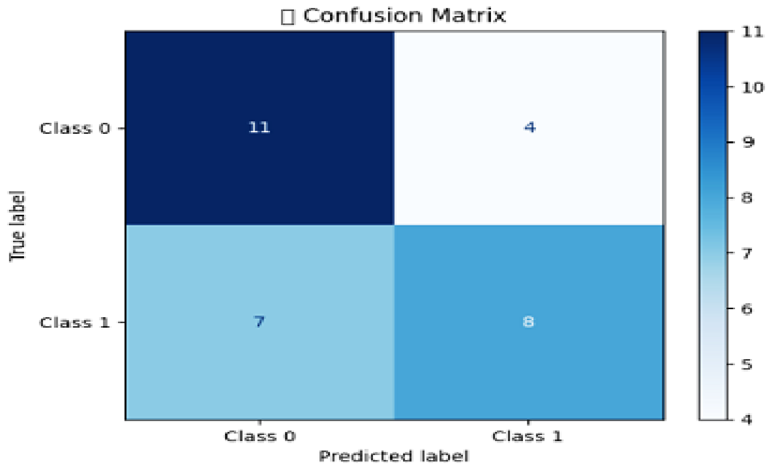

Figure 10. Confusion matrix of the Siamese neural network with ResNet152v2 and a self-attention layer.

images are misclassified as dissimilar, and 20% of dissimilar images are misclassified as similar.

These low error rates reflect the Siamese Neural Network's strong capability to recognize similarities and differences with very little confusion, as illustrated in Figure 8.

The second confusion matrix for the Siamese neural network using InceptionResNetV2 shows an accuracy of 70%. The True Similar rate is 36.66%, and the True Different rate is 33.33%, with 13.33% misclassifying similar pairs and 16.66% misclassifying different pairs. misclassification of dissimilar pairs. These results demonstrate the model's near-perfect ability to distinguish between image pairs, as seen in Figure 9.

The third confusion matrix for the Siamese neural network with ResNet152V2 shows an accuracy of 63.33%. While the True Similar rate is 33.66%, the True Different rate is 26.66%. 23.33% of dissimilar pairs were misclassified as similar (false-different), and the false-similar rate is 13.33%. These results demonstrate that the Siamese Neural Network with ResNet152V2 struggled to achieve the appropriate features to differentiate dissimilar images, leading to high misclassification rates and poor overall performance, as illustrated in Figure 10.

Discussion

Using the advanced search in the web search engine (Google Scholar), no articles or theses were found on classifying molecular mutations in glioblastoma Multiforme using various few-shot Learning methods. To the best of our knowledge, this is the first study to classify the molecular mutations of Glioblastoma Multiforme using a few-shot learning approach with a small dataset.

In one study, researchers, after collecting MR images of 57 Patients, examined them to differentiate IDH-mutant grade 4 astrocytomas from IDH-wild-type glioblastomas. A deep learning-based data augmentation method (CTGAN) was implemented to synthesize 200 datasets from the training sets and to develop a prediction model for distinguishing IDH-mutant grade 4 astrocytomas from IDH-wild-type GBMs.[31] According to studies, Gaussian naïve Bayes performs poorly on raw images and does not generalize well to unseen data.

In this study, we propose a Siamese Neural Network architecture for the classification of Molecular Mutations in GBM, based on the premise that an accurate preoperative prognosis for GBM patients can provide crucial information for personalized treatment.

To evaluate this, several Siamese neural networks were trained using the cross-entropy loss function, and their performance in classifying GBM molecular mutations was investigated. To hinder potential bias resulting from class imbalance, equal numbers of images were maintained in each class. Data augmentation was not applied in this study because we believe that creating image pairs provides an effective form of indirect augmentation. Two pre-trained models, Inception-ResNetV2 and ResNet152V2, were used as embedding functions and trained and tested on axial views of our MR image dataset. They are further enhanced by incorporating self-attention layers, which improve feature extraction by guiding the model's attention to the most informative parts of the input image. This attention mechanism effectively boosts prediction accuracy.

The improvement in these models' performance after adding the Self-attention layer was minimal. This could be due to various factors, with the primary reason likely being the insufficient number of samples available to train the models effectively. Transformer's self-attention often underperforms on small datasets due to weak local feature interactions and its lack of sensitivity to positional information.[32] In this study, the training and evaluation datasets were relatively small because it was a single-center retrospective study. Specifically, MR images from only 93 patients were included. To improve the model's performance, a helpful strategy would be to collect and access additional data from other teaching hospitals while selecting an equal number of scans from each patient.

Conclusion

The few-shot learning approach based on a Siamese Neural Network has the potential to serve as a basis for future studies. For future research, it is recommended to collect MR images from multiple teaching hospitals in Tehran and to explore the application of additional vision-transformer mechanisms to improve classification accuracy further.

Acknowledgments

None.

Ethical consideration

All participants were informed about the procedure, and their satisfaction was obtained. The present research was approved by the ethics committee of the Faculty of Medical Sciences and Technologies, Islamic Azad University, Science and Research Branch (License Number: IR.IAU.SRB.REC.1403.310).

Competing Interests

The authors declare no conflict of interest.

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