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Deep Learning Approach to Detect Gliomas Brain Tumour through Classification at Earlier Stage

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Abstract: Brain tumors with glial cell origins are known as Gliomas. Treatment and Prognosis planning depends greatly on how these tumors are graded and categorized. World Health Organization (WHO) introduced the Central Nervous System (CNS) for Gliomas classification standards. Genomics and Histology combined to meet the categorization criteria for Gliomas. The molecular approaches to CNS Tumour Taxonomy Consortium were founded in 2017 and offer current guidelines for classifying CNS tumours. In this paper, proposed the novel technique in suggesting a new Gliomas analytical method which integrates digital analysis-derived cellularity features in the incorporation of molecular characteristics into images of brain histopathology. A novel over-segmentation approach proposed to identify Region of Interest (ROI) in large histopathology datasets, an enhanced tumour classification method based on the fusion of cellularity and molecular features is then developed using Fast Recurrent Convolutional Neural Networks (FRCNN). Using data from the Cancer Genome Atlas, evaluate the proposed method using 549 patient cases. For Higher and Lower-grade Gliomas which are HGG and LGG with the FRCNN achieved 93.81% cross-validation accuracy LGG II and LGG III both achieved 98.6%.

Keywords: *Fast Recurrent Convolutional Neural Networks, Gliomas, Brain Tumour, Classification; Deep Learning*

1. Introduction

Hepatopathological phenotypes and molecular genetics parameters are considered by the current WHO classification of CNS Tumors. Since Isocitrate Dehydrogenase (IDH) mutations have been linked to good results in Gliomas, clinical evaluation of Gliomas patients must consider these findings [1]. There have been some recent attempts to predict IDH1 genotypes before surgery using radiological images. There are more and more digitized versions of the results of radiological and pathological imaging [2]. Utilizing digital radiology's data to its full potential has become clear and it is possible to identify biomarkers from pathology images using Machine Learning (ML) that include details on the fundamental physiology and biology of different malignancies [3]. Molecular genetics markers are being used more often to diagnose tumors, but histology still plays a significant part in the diagnosis of frozen sections, serving as a diagnostic guide and a means of tracking the development of diseases. Recent advances in deep learning have enabled it to overcome earlier challenges by learning high-dimensional representations of imaging data [4]. New, fully automated post processing algorithms are coming for advanced and standard MRI shortly [5]. The fact that these analyses are entirely automated and offer objective assessments regardless of the operator, their background, or their experience makes them particularly appealing [6]. Standard and advanced Magnetic Resonance Imaging (MRI) have been fully automated post-processed with Deep Learning (DL) analyses, which have produced high accuracy results, even at 92.8% accuracy, 92.6% sensitivity, and 93.1% specificity [7]. Deep Convolutional Neural Network (DCNN) models are prone to error even though it can be very effective at predicting IDH for Gliomas most important aspect of a decision support system is interpretation, which is inherently difficult due to overfitting to their given training datasets [8-9].

The categorization of tumors is made following the new criterion using both genotypic and phenotypic data. Higher-grade Gliomas generally result in a shorter overall survival time for the patient [10]. Therefore, a reliable and accurate prediction of the Gliomas subtype offers a useful framework for managing treatment and diagnosis. In the past, pathologists have been responsible for identifying or grading brain tumors, which employ a light microscope to inspect tissue samples fixed to glass slides. However, manual grading and diagnosis are labour-intensive and prone to human error [11]. It is therefore highly desirable to classify brain tumour subtypes using computers.

2. Related Works

Intra-tumoral heterogeneity is one of the essential causes for poor therapy response and quick recurring, where variations may exist structurally inside a tumor with significant micro that may contain a compound of molecularly diverse tumoral

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regions with no homogeneity [12]. It is consequently critical to have a better knowledge of intra-patient tumoral variations. Previous research has tried to describe intra-tumoral variance using cell biology and histopathology approaches, but have significant drawbacks [13]. These tests rely heavily on tumor tissues and are thus limited to a specific geographic region inside the mixed tumor. In situations where a portion of the tumor is left apart because of a broad wound or participation of the erudite cortex, along with in situations with varifocal tumors, the disease will be categorized based on the selected sample tissue, which may underperform to offer an extensive marker because the tumor left apart may be pathologically distinct [14-15]. Additionally, when the lesion is present in a prominent location, the danger of serious morbidity could be raised by an invasive resection used for instance for spatial context [16]. Finally, difficulties with multi-institutional clinical comparisons may arise due to the complexity of the assay's coverage. MR imaging scans that provide quantitative genotype information have been the subject of recent research because they can be used as tools to provide non-invasive preoperative prognoses, in addition to providing information on grade and mutation status will also facilitate early therapeutic intervention and allow patient-specific treatment plans[17].

Quantitative techniques and intensity features play a major role in the development of prognostic markers for Gliomas, especially those that use the textures of images, which are generally referred to as "radionics". This combination of features is typically used to create a distinctive probabilistic biomarker in a multivariate machine-learning framework because it is anticipated to facilitate complementary information [18]. Additionally, recent developments in Artificial Intelligence (AI), DL are crucial in Computer-Assisted Diagnostics (CAD) has been possible to predict the genomic characteristics of tumors using techniques and radiological images. Radio genomics is the term used to describe the use of data informatics and image features to predict tumour genotypes and has seen significant research in the past few years, making it a growing field of interest.

3. Methodology

A novel approach proposed that makes use of an over-segmentation method to efficiently choose ROIs from a Whole Side Imaging (WSI). Instead of tiling the WSI, choose the ROI shown in Figure 1 using an over-segmentation technique. We over-segment the thumb-nailed image after obtaining thumbnail images of the WSI to produce numerous super-pixels based on tissue similarity [19]. As the final object from the WSI, concerning the desired size crop the image. Figure 1 illustrates a suitable case of ROI selection from WSI using over-segmentation.

3.1 Proposed Method

The foundational model for tumor grading that employ is a FRCNN. As a stepwise binary classification issue, a multi-class classification issue is posed. Initially, standard FRCNN to distinguish between LGG and HGG. To differentiate between LGG III and IIA ResNet used for LGG. Figure 2 depicts the pipeline that has been proposed that our suggested method makes use of both molecular data and digital pathology images, two distinct DNN types are used in the outcome.

The literature's first demonstration is that cellularity data can improve subtype understanding and tumor type grading efficiency. The LGG/HGG DNN model is comparable to the LGG/grade II/III DNN model. However, the network has additional layers that could detect a minute distinction between two comparable tumor grades. ResNet is the network used in this instance with additional layers. Table 1 provides the comprehensive structure of these FRCNNs.

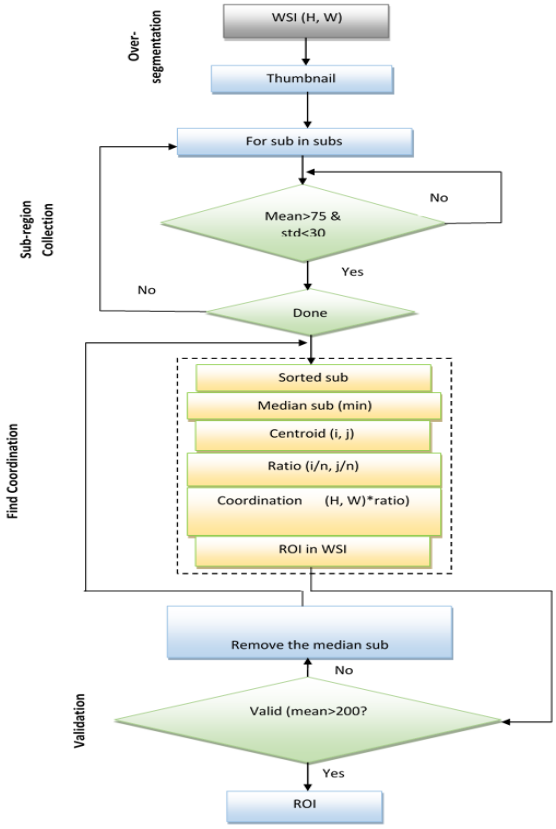

Fig. 1. The Proposed Method for ROI Selection from WSI

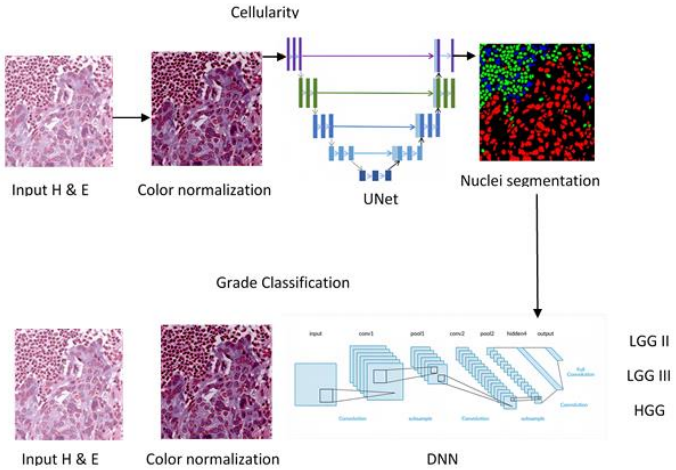

Fig. 2. Classification of Grade and cellular

Table 1: ResNet and FRCNN architectures

Layers	FRCNN output size	ResNet output size
Input	1000 × 1000 × 3	1000 × 1000 × 3
Block 1	500 × 500 × 8	500 × 500 × 64
Block 2	250 × 250 × 16	250 × 250 × 64
Block 3	125 × 125 × 32	125 × 125 × 128
Block 4	62 × 62 × 64	63 × 63 × 256
Block 5	31 × 31 × 128	32 × 32 × 512
Block 6	15 × 15 × 200	16 × 16 × 512
Block 7	7 × 7 × 256	8 × 8 × 512
Block 8	3 × 3 × 512	1 × 1 × 512
Block 9	1 × 1 × 1024	-
Layer 1 FC	512	512
Layer 2 FC	16	8
Layer 3 FC	2	2

3.2 Datasets

In the dataset in the Glioma Differentiated Cells (GDC) called the Cancer Genome Atlas use 549 WSI with molecular data for important alterations. There are 119 HGG grades IV, 229 LGG grades IV, and 201 LGG grades II in the 549 WSIs, respectively. Utilizing the ROI selection process outlined in the methods content, the final ROI with the measurements 1000x1000 is the top super-pixel from WSI [20]. Also use techniques for data augmentation to expand the pool of training samples shown in Table 2.

Table 1: Patient data molecular distribution

Gene	Type	LGG II	LGG	HGG	Total
IDH	MT	184	163	8	549
	WT	17	66	111	
ATRX	MT	85	71	9	549
	WT	116	158	110	
1p/19q	NC	125	162	119	549
		76	67	0	
MGMT	UM	28	45	67	549
	ML	173	184	52	

3.3 Preprocessing

Before training, T2 Weighted (T2W) images from The Cancer Imaging Archive (TCIA) dataset only underwent minimal standard pre-processing in Figure 3.Radiofrequency in homogeneity was removed from the images by applying the N4 bias correction algorithm using DCM2NII, the files were converted from DICOM to NifTI format to increase the computational effectiveness during training, the zero-mean intensity was normalized to lie between -1 and 1, and the image dimensions were resampled to 128x128. However, the design constraint for the Inception V4 model the original design called for an input image size of 299x299[21-22].

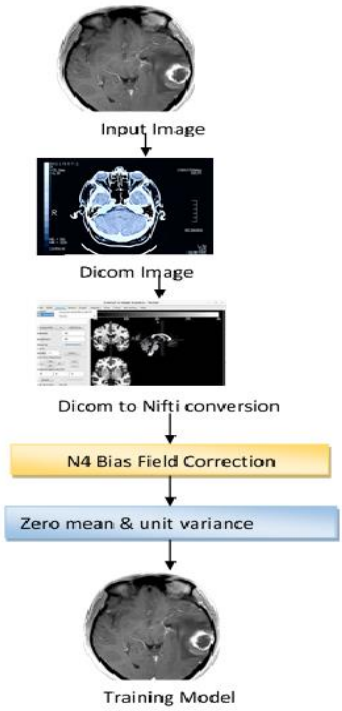

Fig.3. FRCNN model's training process

4. Results And Discussions

Create a set of paired data with and without genomic data to check the effect of molecular information on categorization efficiency. Figure 4 demonstrates performance comparison under the same experimental conditions, ResNet performs better than FRCNN. It is consistently more accurate to classify cases when pathology and molecular data are combined. The best efficiency results from including all information.

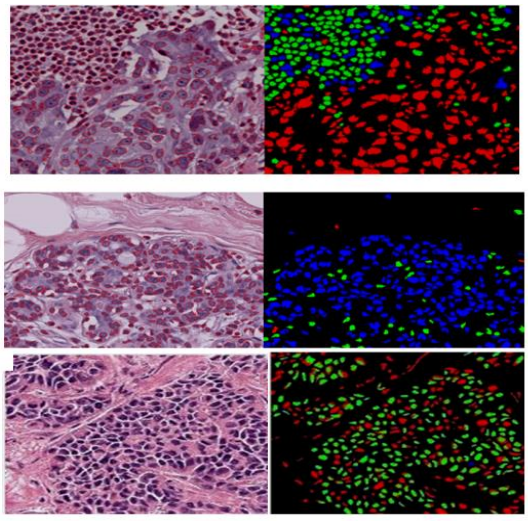

Fig.4. Demonstration of Performance Comparison

Comparatively, ResNet's capacity to identify subtle variations across all subtypes of gliomahas improved, which may greatly boost the accuracyof the categorization for differentiating LGG II from III. In Table 3, the confusion matrix FRCNN proposed method with cellularity explained.

Table 2: Confusion Matrix

Type		Actual		
		LGG II	LGG III	HGG
Predict	LGG II	149	47	7
	LGG III	45	169	14
	HGG	7	13	98

Figure 5 explains the Models, 1-6 use standard CNN, while models 7–12 use ResNet.Data from models 7 and 1, models 8 and 2, models 9 and 3, models 10 and 4, model 11 and 5, and models 12 and 6 contain pathology, pathology with molecular, pathology with cellularity and molecular, pathology with molecular and cellularity, pathology with molecular and cellularity, and pathology with molecular and cellularity.

In this study, 5-fold cross-validation is used to test the effects of various patient data combinations on tumour type categorization [23]. Table 4 displays the outcome that the highest classification accuracy values are, respectively, 93.81% and 1.98% for HGG vs. LGG and 73.95% and 3.73% for LGG II vs. LGG III. A robust model efficiency with little overfitting is indicated by the small standard deviation.

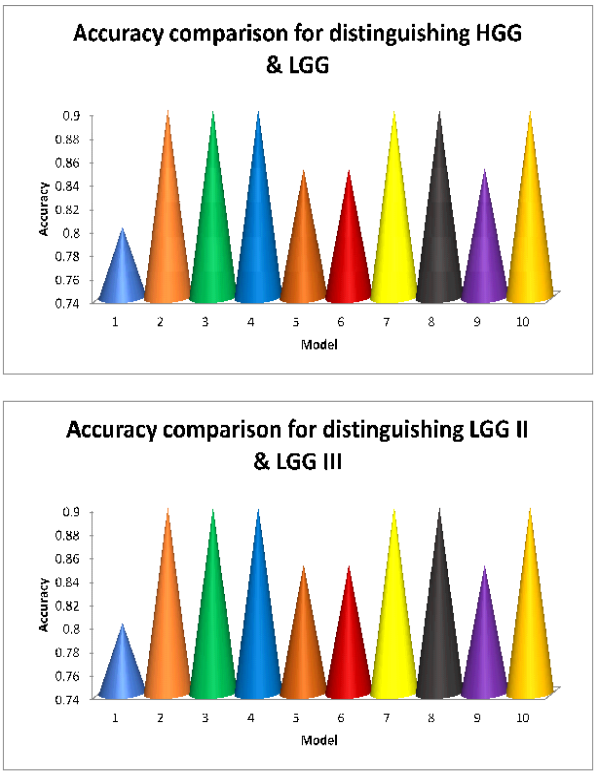

Fig. 5: Performance comparison using five-fold cross-validation

Table 3: Comparison of performance measures on various type of Tumour

Tumor Type	Data	Network type	Accuracy
HGG-LGG	Path.	ResNet	90.16% ± 3.20%
	Path. + gene	ResNet	92.72% ± 2.62%
	Path.+ gene+cell.	ResNet	93.81% ± 1.98%
LGG II-LGG III	Path.	ResNet	70.69% ± 1.72%
	Path. + gene	ResNet	72.56% ± 3.13%
	Path.+ gene+cell.	ResNet	73.95% ± 3.73%

The findings, which are displayed in Table 5, suggest a possible relationship between IDH and cellularity types [24]. It displays the standard deviation and average cellularity of Gliomas of various grades. Higher levels of cellularity are present in higher-grade Gliomas.

Table 5: IDH Type Average Cellularity

Tumour Grade	Mutant type IDH	Wild-type IDH
LGG II	0.1066±0.0628	0.0841±0.046
LGG III	0.1276±0.0603	0.1374±0.0641
HGG	0.2104±0.1242	0.2053±0.095

FRCNN provides a more accurate classification for differentiating tumor grade. The efficiency cannot be improved by cellularity inclusion during dilation, though. It is difficult to select the right dilation size. For instance, in our experiment, the 10 and 15-fold dilation performances are inferior to those of the control condition. Our research and experiment indicate that, if necessary, a dilation size of 11 or 12 should be used.

Recent advancements in healthcare technology, as evidenced by studies on diabetes prediction and abnormality detection in CT liver images, highlight the potential for enhancing early diagnosis and treatment outcomes for brain tumors [25-28]. Integrating advanced imaging techniques, such as MRI and PET scans, with artificial intelligence algorithms can significantly improve accuracy and efficiency in identifying and monitoring brain tumor progression [29-33]. Additionally, the utilization of drone-based imaging and image processing techniques for predicting plant leaf diseases indicates the feasibility of innovative approaches that could be adapted to enhance brain tumor imaging and analysis, ultimately leading to better patient care [34-37]. Furthermore, research on ultra-low latency communication technology for augmented reality applications and soldier health monitoring optimization models using biosensors demonstrates the ongoing efforts to integrate cutting-edge technologies into healthcare systems. By leveraging these developments, healthcare providers can implement more personalized and effective strategies for managing brain tumors, thereby improving patient outcomes and quality of life [38-40].

4.1 Comparative approach

In Table 6, we contrast the findings of this study with earlier literary works. As the methods, patient data, and patient count are all different for these works, to be clear, there is no quantitative comparison; rather, there is a qualitative comparison. Our proposed technique, with the inclusion of molecular data, provides the greatest accuracy for LGG grade II vs. LGG grade III categorization. In this research, we have many patient instances, which is much greater than the other research mentioned in this analysis.

Table 6: Performance measures

Authors	Image type	# of patients	Method	Accuracy of HGG vs LGG	Cross-validation	Accuracy of LGG II vs LGG III
14	MRIs	231	SVM	78.26%	-	-
15	WSI	7	CNN	96%	-	71%
16	WSI	302	Elastic Net classifier	93.1%	5	-
18	MRI+WSI	20	CNN	-	-	90%
19	MRI+Molecular	66	SVM	86%	10	-
21	WSI+Ki-67	146	SVM	92.46%	30	96.42%
proposed method	WSI+Molecular	549	FRCNN	93.81%	5	98.6%

Cross-fold and cross-class average metrics were calculated. The slice-wise IDH classification using the DenseNet-161 model's classification precision, accuracy, specificity, recall/sensitivity, AUC, and F1 score. The rank sum test is used for the subject- and slice-wise classification in both cases, Inception-v4 was significantly underwhelmed by the DenseNet-161 model. The DenseNet-161 and ResNet-50 models performed equally well on both slice-wise performance and subject-wise performance, with no statistically significant differences between them. However, for subject-wise classification, the DenseNet-161 model outperformed the ResNet-50 model in terms of mean cross-validation reliability and separation between folds of the cross-validation method.

Table 7: Accuracy Comparisons

5 fold cross-validation			
Model	Accuracy Training (%)	Accuracy Validation (%)	Accuracy Testing (%)
Inception-V4	64.9±7.5	72.3±7.0	1917/2523
FRCNN	98.1±0.6	96.5±0.7	(74.8±3.8)
DenseNet-161	97.1±0.5	96.5±0.7	2267/2523
			(89.8±1.3)
			2283/2523
			(90.6±1.1)

Table 8: Comparison of Accuracy, Precision, Recall

Methods	F1 score(%)	Precision(%)	Specificity(%)	Accuracy(%)	AUC	Recall(%)
Inception-v4	59.1±2.1	59.6±2.8	84.6±3.2	76.2±3.8	0.87±0.0	59.3±2.7
FRCNN	80.4±3.2	79.4±3.4	94.2±0.9	89.8±1.2	0.96±0.0	81.8±3.3
DenseNet-161	81.4±3.3	79.8±3.5	94.9±0.6	90.6±1.1	0.96±0.0	83.2±3.3

The inception-v4 model was outperformed by the FRCNN model, according to the results from Tables 7 and 8. In the residual block of the residual connections, FRCNN architecture maintains data from the preceding layer. In comparison to the other two models, the best performance was achieved by the DenseNet-161 model. This facilitated the transfer of knowledge from earlier layers to later ones.DenseNet-161, Slice-wise classification AUC scores of 0.95, 0.95, and 0.86 were obtained by FRCNN, Inception-v4, and similar systems. Performance between the Inception-v4 and DenseNet-161 models was significantly higher. The performance of the FRCNN and DenseNet-161 models did not differ in a statistically significant way, but for categorization based on subjects, less variability, Greater mean cross-fold validation, and accuracy between folds were all features of the DenseNet-161 model.

5. Conclusion

This work proposes a DNN-based approach for identifying and grading brain tumors. The cellularity feature derived from the morphology of brain tumor images is integrated to increase efficiency. We also suggest a new over-segmentation technique-based ROI selection strategy for histopathology WSIs. According to the tests, it may not be necessary to use a specific type of DNN to distinguish between LGG and HGG Gliomas. Differentiating LGG grade II from LGG grade III tumors may be significantly influenced by deep learning. Furthermore, it has long been believed that glioma cellularity increases with grade according to the pathology literature, although this has never been confirmed. Although FRCNN-based approaches outperform classic functionality approaches, feature interpretability is a prevalent challenge. The results may be more helpful if the underlying interpretability is also provided to medical professionals.

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Author contributions

All authors have equal contribution to this research paper.

Conflicts of interest

The authors declare no conflicts of interest.

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