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The role of machine learning in detecting primary brain tumors in Saudi pediatric patients through MRI images

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A R T I C L E I N F O

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A B S T R A C T

Background and aim: Brain tumors are defined as the uncontrollable growth of cells. They are known as the leading cause of death among pediatric patients. Artificial Intelligence is considered as one of the techniques used to improve radiology departments. Magnetic Resonance Imaging (MRI) is a key tool in detecting brain tumors. Medical images can be challenging and time-consuming for radiologists, particularly in the case of pediatric patients where the tumors may be small and difficult to detect. This study aims to explore the role of AI and measure the accuracy of AI methods in detecting primary brain tumors in pediatric patients by using MRI images.
Methodology: A retrospective and analytical study was conducted, MRI images of pediatric patients with primary brain tumors were acquired from the Picture Archives and Communication System (PACS) of the radiology department at King Abdullah Specialist Children Hospital (KASCH). This study continues a total of (6435) MR images, this dataset was divided and expressed in different subsets, 70% of the images were trained (4493 in total) for model accuracy evaluation, and the rest which is 30% (1942) were tested images contains three types of primary brain tumors, glioma, Primitive Neuro-Ectodermal Tumors and pituitary tumors. Moreover, this dataset also contains normal images. Image classification and detection have been done by using Machine Learning algorithms which are coded in Python programming language.
Results: After applying Machine Learning algorithms on MRI images, Artificial Neural Network method resulted in an accurate detection of pediatric primary brain tumors and matched the radiologist's report.
Conclusion: New Artificial Intelligence techniques applied in the imaging department have increased the information obtained from images to improve the accuracy of diagnosis along with radiologist's reports which will aid in better management of the patient's condition.

1. Introduction

In 2020, an estimated 251,329 fatalities worldwide were caused by primary brain cancer and central nervous system malignancies (Almatroudi, 2022). In Saudi Arabia, pediatric patients had the highest number of reported brain tumors (Almatroudi, 2022). A 2018 Cancer Incidence Report in Saudi Arabia revealed that brain and Central Nervous System (CNS) cancers were the second-highest types of cancer among pediatric patients after leukemia (Shaari et al., 2021). The nervous system is divided into two parts: the peripheral nervous system and the Central Nervous System (Shaari et al., 2021). The CNS is composed of the cerebrum, cerebellum, and brain stem, where tumors can develop in any of these areas (Shaari et al., 2021).

A brain tumor is defined as an abnormal growth of cells originating

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from the brain tissue and referred to as either primary or secondary, depending on the spread of the tumor (NCI Dictionary of Cancer terms). The World Health Organization (WHO) has a grading system specifically made for brain and spinal cord tumors (grades 1–4) to determine if they are malignant or benign (non-malignant) based on their molecular characteristics and anatomical location (Shaari et al., 2021). The preponderance of brain tumors among pediatric patients, based on the American Association of Neurological Surgeons, are:

Glioma**:** a primary brain tumor that arises from glial cells such as Astrocytomas, Ependymomas, and Oligodendrogliomas. Depending on the type of glial cell the tumor originates from and the location, the characteristics and symptoms differ (Types of brain and spinal).

Pituitary adenoma: benign tumors mainly arising from the anterior fossa; despite being benign, they might be difficult to manage due to their difficult location (Types of brain and spinal).

Primitive Neuro-Ectodermal Tumors (PNET): Malignant primary brain tumors ranked as grade 4, mainly found in the brain with the possibility of spreading to other parts of the central nervous system. The cause remains unclear, yet some types are associated with genetic changes (Types of brain and spinal).

Recently improved technology used in medical imaging modalities allows non-invasive methods to acquire useful information about the tumor for better diagnosis and guidance in therapy (Badž et al., 2020). Computed Tomography (CT) is a non-invasive imaging procedure that produces images of the brain using X-ray measurements, providing more information than standard head X-rays about brain tissue and structures (Shaari et al., 2021). The clinical gold standard for diagnosing brain tumors in both adults and children is gadolinium-enhanced Magnetic Resonance Imaging (MRI) (Shaari et al., 2021). Due to sensitization to various contrast values in MRI techniques, both normal and abnormal brain physiology may be thoroughly examined (Shaari et al., 2021). The main benefits of MRI include being non-invasive and painless, in addition to providing high spatial resolution, direct multi-planar viewing, and superior soft tissue contrast (Shaari et al., 2021). MRI images are stored in two categories: scanner format and image processing format. Scanner format is the output of the computer used to extract MR pictures, while image processing format is developed by translating the original MRI scanner format (Shaari et al., 2021). The common MRI sequences are T1 and T2-weighted scans; T1-weighted images are created using short TE and TR intervals, while T2-weighted images are created using longer TE and TR durations (Jibon et al., 2022).

MRI is the most successful choice for brain tumor diagnosis; however, traditional MRI is difficult to use (Shaari et al., 2021). Advanced MR techniques such as magnetic resonance spectroscopy (MRS), diffusion-weighted imaging (DWI), susceptibility-weighted imaging (SWI), perfusion-weighted imaging (PWI), and diffusion tensor imaging (DTI) have gained importance in the evaluation of neoplastic histology (Shaari et al., 2021). However, the diagnosis of the tumor cannot be complete without proving its malignancy, so a biopsy is usually performed (Shaari et al., 2021). To obtain a precise diagnosis and avoid subjectivity, it is crucial to develop an effective diagnostic tool for tumor segmentation and classification from MRI images (Shaari et al., 2021).

Artificial Intelligence (AI) is a field in which computer science is programmed to imitate human cognitive ability (Vobugari et al., 2022). A branch of AI called Machine Learning (ML) uses specialized qualities to find patterns that can be utilized to assess a given situation (Almadhoun et al., 2022). The computer may then "learn" from this knowledge and use it to predict similar situations in the future (Almadhoun et al., 2022). Instead of using a static algorithm, this prediction tool can be used to individualize patient care in clinical decision-making (Almadhoun et al., 2022). Algorithms for ML are categorized into three types: supervised, unsupervised, and reinforcement learning. Supervised learning algorithms learn from datasets with labels, while unsupervised algorithms learn from datasets without labels (Vobugari et al., 2022). A reinforcement learning system trains an agent via rewards and penalties for desired and undesired behaviors (Vobugari et al., 2022). ML has developed into a field today referred to as Deep Learning (DL) (Vobugari et al., 2022). DL is a type of ML that uses supervised learning algorithms to acquire certain types of knowledge; it is a significant part of data science that includes statistics and predictive modeling (Vobugari et al., 2022). Moreover, DL consists of methods to build an Artificial Neural Network (ANN) that can later learn and make decisions independently, much like the human brain (Almadhoun et al., 2022). Another type of DL is Gradient boosting, which is used for classification and regression tasks (Madeh et al., 2021). It provides a prediction model in the form of an ensemble of decision tree-like weak prediction models (Madeh et al., 2021). Gradient-boosted trees, a resulting approach that typically outperforms Random Forest when a decision tree is a weak learner, are used in this situation (Madeh et al., 2021). Logistic regression is another generic form of statistical model for categorization, and predictive analytics plays an important role in DL (Saini, 2021). Based on a given dataset of independent variables, Logistic regression calculates the likelihood that an event will occur (Saini, 2021). Supervised machine learning algorithms such as Random Forest are frequently employed in classification and regression issues (R, 2023). It creates decision trees from various samples, using their average in the case of regression and the majority vote for classification, which means in tasks requiring classification and regression, it performs better (R, 2023).

A database approach technique, providing computers with a way to learn how to diagnose patients, makes use of the deep learning or pattern recognition principle, which entails teaching a computer through repeated algorithms to recognize certain clusters of symptoms or specific clinical or radiological images (Amisha et al., 2019). Computer advancements in computational capabilities, hardware design, and data storage capacities have significantly benefited the field of diagnostic medical imaging, especially in the medical image analysis stage (Anwar et al.). Image analysis includes segmentation, classification, and disease detection using medical images from various modalities like CT and MRI (Anwar et al.). The usage of the outputs of these procedures in the medical field in order to help the physicians understand the imaging data is referred to as Computer-Aided Diagnosis (Abdalla & Esmail, 2018, pp. 1–71). CAD systems are a relatively new interdisciplinary technique that combines components of radiological image processing, digital image processing, and artificial intelligence (Abdalla & Esmail, 2018, pp. 1–71). CT and MRI imaging methods are commonly used in CAD, including applications such as MRS, MR perfusion, and functional MRI (Shaari et al., 2021)· CAD relies heavily on accurate medical image analysis, including segmentation and classification. This directly impacts clinical diagnosis and prognosis (Anwar et al.). Furthermore, CAD systems have been utilized widely in radiology for many years as an early type of AI (Wu et al., 2020).

In Saudi Arabia, pediatric patients were those with the most recorded cases of brain tumors (Almatroudi, 2022). The discipline of diagnostic medical imaging has greatly benefited from computers' advancements in computational power, hardware design, and data storage capacity, especially at the stage of medical picture interpretation (Abdalla & Esmail, 2018, pp. 1–71). This involves analyzing pictures from CT and MRI using processes such as segmentation, classification, and disease detection. CAD is the use of these methods' outputs to aid doctors in comprehending imaging data (Abdalla & Esmail, 2018, pp. 1–71). In this article, we focus on the role of AI in detecting primary brain tumors in pediatric patients through MRI images to improve the radiologist's expertise.

1.1. *Related work*

Previous studies have established the contribution of several ML methods to detecting primary brain tumors in pediatric patients (Topol, 2019). One study applied the DL methods to detecting and classifying posterior fossa tumors in pediatric patients, it had a sample size of 617 children, and the median age of the patients was seven years old (Quon et al., 2020). The sample for this study was collected from five different pediatric institutions with posterior fossa tumors: diffuse midline glioma of the pons (n = 122), medulloblastoma (n = 272), pilocytic astrocytoma (n = 135), ependymoma (n = 8), and the control sample (n = 199) (Quon et al., 2020). Furthermore, this study used a T2-weighted MRI image as an input to detect the presence of tumors and predict tumor classes. The performance of the deep learning model was compared with four radiologists' reports (Quon et al., 2020). The tumor histology served as ground truth except for the diffuse midline glioma of the pons tumor, which was primarily diagnosed by MR imaging (Quon et al., 2020). To conclude this study, model tumor detection accuracy exceeded the Area Under the Receiver Operating Characteristic Curve of 0.99 and was similar to the radiologists' reports (Quon et al., 2020).

In a different study, patients with Optic Pathway Glioma (OPG) progression underwent a retrospective case-control analysis (Pisapia et al., 2020). Progression is characterized by an increase of radiographic tumor or a decrease in eyesight (Pisapia et al., 2020). Optic nerves were manually highlighted, then diffusion tractography methods were used to segment optic radiations in order to create the model (Pisapia et al., 2020). The combination of variables most predictive of progression was identified by Support Vector Machine (SVM) which is a machine learning method (Pisapia et al., 2020). There were 83 MRI examinations and 532 characteristics that were retrieved (Pisapia et al., 2020). With 86% accuracy, 89% sensitivity, and 81% specificity, the prediction model performed well (Pisapia et al., 2020). According to their research, OPGs can benefit from the application of machine learning and image processing to create highly accurate MRI-based predictive models (Pisapia et al., 2020).

Moreover, a study using the fuzzy C-Means clustering algorithm was developed as a technique to subtract brain tumors from 2D MR brain images, which was then followed by conventional classifiers and Convolutional Neural Networks (CNN) (Hossain et al., 2019). A real-time dataset with various tumor sizes, locations, forms, and image intensities was used for the experimental study (Hossain et al., 2019). They used six conventional classifiers, supported by sci-kit-learn, in the traditional classifier section: SVM, K-Nearest Neighbour (KNN), Multilayer Perceptron (MLP), Logistic regression, Naive Bayes, and Random Forest (Hossain et al., 2019). SVM gave them the highest accuracy (92.42%) among these traditional approaches; however, in an attempt to enhance the results, the study also employed CNN, which produced an accuracy of 97.87% (Hossain et al., 2019).

A similar paper presents an ANN for the classification of brain MRI images. It is trained with twenty brain MRI images and tested with 45 brain MRI images, with an accuracy of nearly 100% in identifying normal and abnormal tissues (El et al., 2020). Another previous study used a data set of 253 brain MR images consisting of normal brain images and confirmed the images with the presence of the following tumors: Pituitary, meningioma and glioma were represented in the study to assess the efficiency of the suggested model (Babayomi, Atinuke, Abdulrasheed, & Kadiri, 2023). To provide a broad and more representative sample, the data was pre-processed and enhanced (Babayomi et al., 2023). The C-XGBoost model was trained and validated using the dataset, and the results were compared to a non-hybrid CNN-based model (Babayomi et al., 2023). With an accuracy of 99.02 and an F1 score of 0.97, the hybrid C-XGBoost model that was suggested performed better than the CNN-based model (Babayomi et al., 2023). Better generalization to the test set was shown by the C-XGBoost model's decreased training and validation losses (Babayomi et al., 2023). According to these experimental findings, the C-XGBoost model successfully identified brain tumors from medical images with high degrees of accuracy, indicating that it is a useful method for the early diagnosis of brain tumors (Babayomi et al., 2023).

2. Methodology

In this study, pediatric brain MR images have been used for a retrospective analytical study conducted at King Abdullah Specialist Children Hospital (KASCH) in Riyadh, Kingdom of Saudi Arabia (KSA) to assess the role of different Machine Learning methods in detecting primary brain tumors. After receiving approval from the Institutional Review Board (IRB Log Number: **22–1004**) of Princess Nourah bint Abdulrahman University (PNU), during the period from Nov. 2022 to March. 2023, a manual dataset review was performed to determine the appropriate eligibility criteria for this study which include brain tumor MRI images for patients younger than 14 years old who were selected from PACS. Any patient in the same age group but shows another site of the tumor or, shows brain tumor but older than 14 years old will be excluded.

2.1. Data set

The dataset for this study was a total of (6435) MR images, containing three types of primary brain tumor, glioma, PNET and pituitary tumors. Moreover, this dataset also contains normal images (Fig. 1).

Image classification and detection have been done using ML algorithms which have been coded in Python programming language. Four different ML algorithms Gradient boosting, Logistic regression, Random Forest and ANN have been used in accordance with previous studies methods and their proposed results. This dataset contains 4493 images for training the models, and 1942 images for model accuracy evaluation.

3. Results

A total of (5416) pediatric patients' MR images showing brain tumors have been obtained from PACS.

4. Discussion

Artificial Intelligence has emerged as a powerful tool in the field of medical imaging, particularly in the detection and diagnosis of brain tumors. The aim of this study is to explore the role of AI in detecting primary brain tumors in pediatric patients using MRI images selected from the Picture Archiving and Communication System (PACS) in the radiology department at KASCH. Through applying AI methods, we can see the compatibility in image classification and detection with the radiologist's reports.

The inclusion criteria in our study were not biased regarding a specific gender but only selected a particular age group ranging from newborns to 14 years old and focused on primary brain tumors found in this age group. Using a dataset consisting of (6435) MR brain images diagnosed as normal or present with a tumor. Table 1 shows the primary brain tumors found in the images were three types: glioma, pituitary, and primitive neuro-ectodermal tumors. Our objective in this study is to improve the radiologist's expertise and the accuracy of AI in detecting primary brain tumors in pediatric patients.

As seen in Tables 2–4, the total data set was divided and expressed in different sets, 70% of the images were trained (4493 in total) and the rest were 30% (1942) tested images. The trained dataset gave a number of true positive classifications starting with glioma scoring the highest due to the abundant amount of glioma MR images used to train the machine.

Four models were used to train the dataset to obtain the most accurate classification, which was: Gradient boosting, Logistic Regression, ANN and random forest represented in Table 5. According to Table 2, (2771) out of the (2797) images that were diagnosed with glioma and trained on an ANN model, only (26) were misclassified. Generally, medical images suffer from the possibility of image artifacts and degraded resolution which ultimately affect the performance of ML methods. Fig. 2 shows a sample of normal brain MRI images has been misclassified as abnormal MRI images, which can be due to all of the previously mentioned causes. Another model we used to train glioma images was logistic regression; out of the (2797) images, (2736) were classified correctly, as demonstrated in Table 2 This proves that the ANN

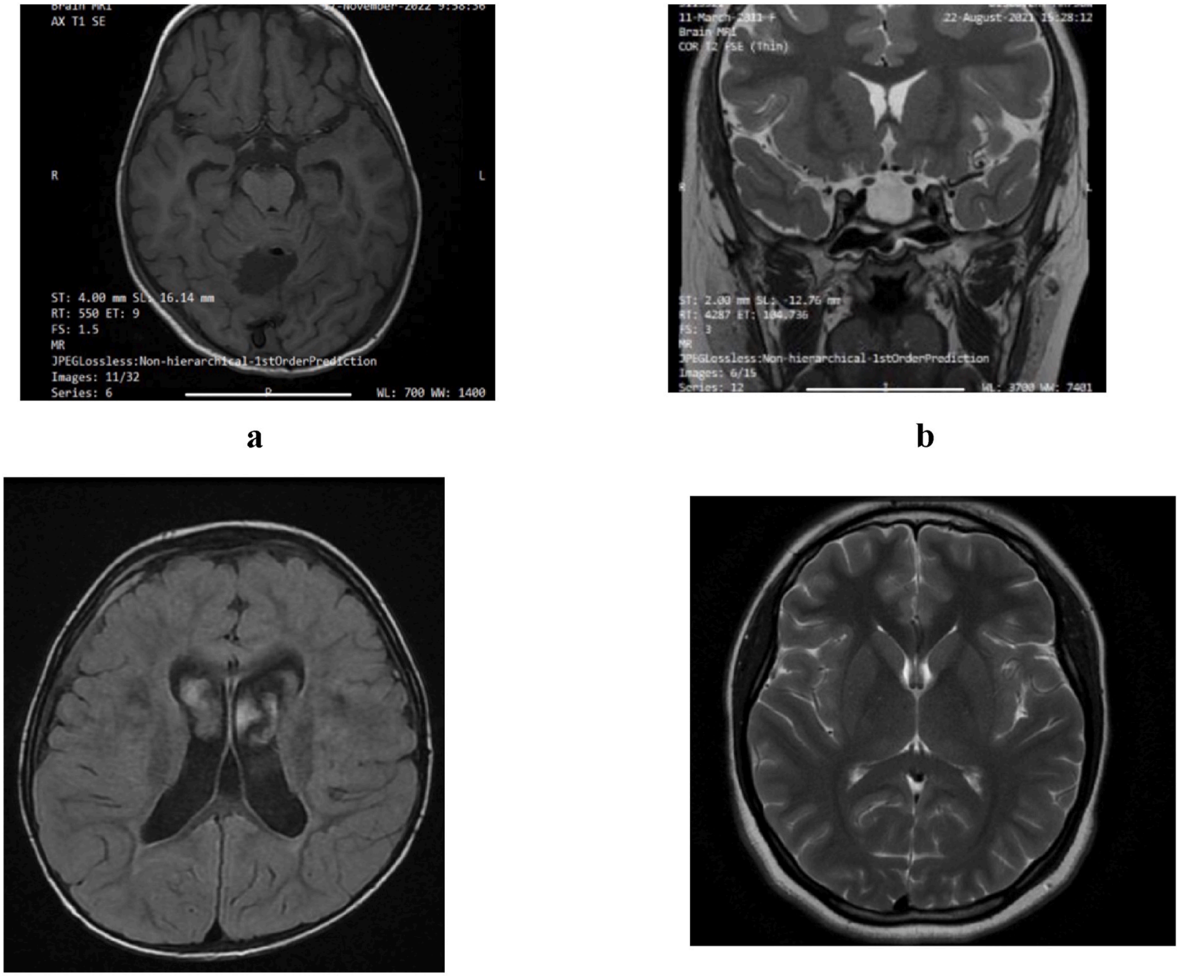

Fig. 1. Sample from the datasets. Axial T1W MRI shows glioma (a), Coronal T2W FS MRI shows pituitary tumor (b), Axial FLAIR MRI reveals PNET tumor (c), Axial T2W MRI shows normal brain.

Table 1
The number of images for each type of tumor.

Type of Tumor	Glioma	Pituitary	PNET
Number of Patients	7	2	1
Number of Images	3532	946	938

Confusion matrices are used to present the outcome of training and testing of different ML methods.

model has higher accuracy compared to the logistic regression model.

Other than gliomas, we also trained the AI machine learning models on other tumors, including primitive neuro-ectodermal tumors and pituitary tumors, as well as on normal images. In Table 3, the ANN model detected a PNET tumor in (656) images out of (706). It also only misclassified (Abdalla & Esmail, 2018, pp. 1–71) images in the pituitary tumor, with an accurate detection of (648) images out of (661). Similarly, the logistic regression model also showed high accuracy in detecting other tumors. Table 3 shows the accuracy of the detection of PNET at (630) out of (706), as well as the detection of pituitary tumors at (648) images out of (661). Overall, the Logistic Regression was higher in detecting the PNET tumor, whereas in the pituitary tumor, both models had the same results, with only (Abdalla & Esmail, 2018, pp. 1–71) images misclassified. This proves that AI methods are accurate in detecting multiple tumors.

To further our claims, Table 5 compares the scores of the trained dataset models with regard to classification accuracy. Within the four models we used, it is shown that the least accurate model is the random forest with a score of 0.89, while gradient boosting has a higher accuracy of 0.93. Moreover, the logistic regression model has an accuracy of 0.95,

Table 2
The confusion matrix of the training dataset used to train the ANN method.

Predicted					
Actual	Glioma	Permeative neuroectodermal	Normal	Pituitary	Total
Glioma	2771	15	3	8	2797
Permeative neuroectodermal	44	656	1	5	706
Normal	18	4	306	1	329
Pituitary	12	1	0	648	661
Total	2845	676	310	662	4493

Table 3
The confusion matrix of the training dataset used to train the Logistic regression method.

Predicted					
Actual	Glioma	Permeative neuroectodermal	Normal	Pituitary	Total
Glioma	2736	34	5	22	2797
Permeative neuroectodermal	69	630	3	4	706
Normal	28	4	297	0	329
Pituitary	11	2	0	648	661
Total	2844	670	305	674	4493

Table 4
The confusion matrix of the test dataset used to test the ANN method.

Predicted					
Actual	Glioma	Permeative neuroectodermal	Normal	Pituitary	Total
Glioma	716	247	80	8	145
Permeative neuroectodermal	23	290	2	1	316
Normal	10	0	132	0	142
Pituitary	4	2	0	290	269
Total	753	539	214	436	1942

Table 5
The confusion matrix of the testing dataset used to evaluate the ANN method. The training data sets CA score, AUC, F1, Precision and Recall.

Model	AUC	CA	F1	Precision	Recall
Gradient Boosting	0.989	0.930	0.927	0.931	0.930
Logistic Regression	0.992	0.959	0.959	0.959	0.959
Artificial Neural Network	0.997	0.975	0.974	0.975	0.975
Random Forest	0.974	0.891	0.885	0.894	0.891

whereas the ANN model has the highest score of 0.97.

Our results contradict the claims of another study utilizing several models and comparing their accuracy with each other in regard to brain classification (Babayomi et al., 2023). The results of the study showed that the most accurate classifier, in terms of the number of problems with the best performance in the problems investigated, was gradient boosting. Opposingly, gradient boosting had a lower accuracy compared to other models in our study; the accuracy score was (0.93). Contrary to gradient boosting, two models had higher accuracy results: logistic regression (0.95) and ANN (0.97).

The objective of our study was to improve the expertise of radiologists and the accuracy of AI in detecting primary brain tumors in pediatric patients. AI is a new method in medical image analysis in recent years. Any investment in AI will help the radiologist in diagnosis accurately and easily, many ML methods including ANN and logistic regression methods as our study proposed, are expected to result in an accurate detection of primary brain tumors.

According to Table 5, the Area Under the Curve (AUC) which represents the classification performance of the presented models. As shown in Table 5, ANN and logistic regression have the highest AUC values compared with the gradient boosting and random forest. Whereas ANN has a higher AUC mean which was (0.997), compared with the logistic regression AUC which was (0.992). Additional image data and additional ML approaches resulted in a significant increase in the accuracy of detection. Our results support a previous study, which stated that Neural Network has the highest classification accuracy with a value of 0.978 compared with other ML methods such as logistic regression, which has a classification accuracy of 0.878 (Hossain et al., 2019).

Moreover, medical imaging suffers from the possibility of image artifacts and degraded resolution which ultimately affect the performance of ML methods.

Our study's overall findings are consistent with earlier studies stating that artificial intelligence is accurate in detecting brain tumors and that ANN is the superior model of ML. This study was particularly useful in using MRI images since they can be tailored to the patient's needs, allowing doctors to adjust the scan parameters to obtain the best possible results. Artificial intelligence is a precise, economical technique that can be used in several fields of medical imaging, particularly in the detection and diagnosis of brain tumors. This increases the radiologist's skill in diagnosing pediatric brain tumors, which could lead to faster

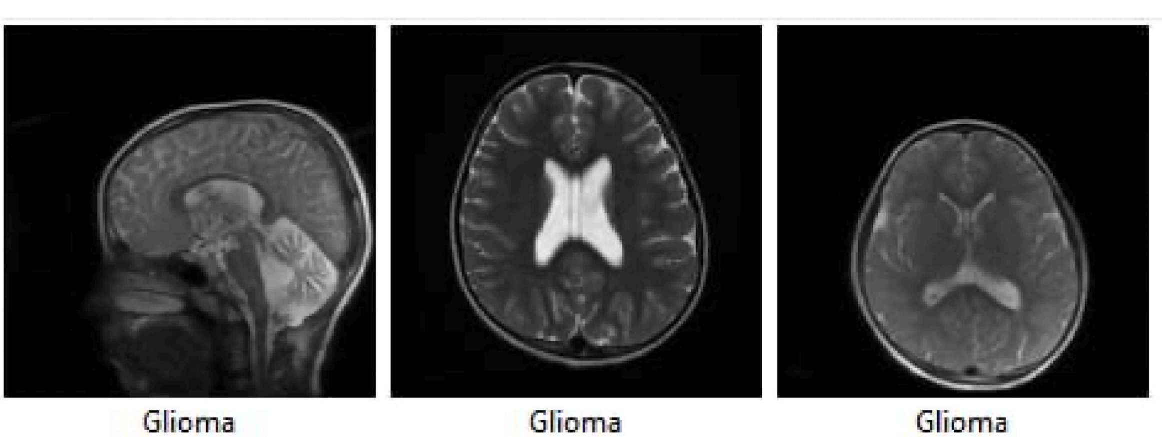

Fig. 2. Normal misclassified brain MR images by ANN model.

treatment.

Due to the exclusion of some patients from the sample, the results' generalizability is limited. The generalizability of the results would be greatly enhanced by including more patient groups, such as those with different pediatric tumor sites, different types of pediatric brain tumors, older age groups, and modalities of diagnosis other than MRI. Another limitation is our small sample size, which was mainly due to problems encountered when gathering the data and time limitations. A larger sample size would make our results more reliable and easier to interpret. Moreover, the manual sort of PACS images require a lot of time.

Other machine learning models can affect the results; a previous study compared the XGBoost model to the random forest and gradient boosting, and their results differed from ours (Babayomi et al., 2023). We only used four models due to time constraints; other models may increase the accuracy of the classifications and further support our objectives. Machine learning model applications are computationally demanding due to the need for additional hardware such as a Graphical Processing Unit (GPU) to support their operations. The memory and processing demands of machine learning models are substantial.

The future of AI in medicine is heavily dependent on ensuring the privacy and security of data. The prevalence of hacking and data breaches poses a significant challenge in the adoption of algorithms that may risk exposing sensitive patient medical history. Additionally, there is a concern regarding the intentional hacking of algorithms to cause harm on a large scale, such as administering excessive insulin to diabetics or triggering defibrillators in patients with heart disease. The advancement of technology has made it increasingly feasible to identify individuals through facial recognition or genomic sequencing from massive databases complicating the protection of privacy. Furthermore, the potential for generative adversarial networks to manipulate content without apparent limitations raises serious concerns for healthcare (Topol, 2019).

5. Conclusion

The research we conducted concluded that using images from MRI in a computationally challenging deep learning approach is necessary. The method effectively identified cases of primary brain tumors from those of normal brain tissue. We used an existing primary brain tumor dataset to train ANN for brain tumor classification in order to enhance the system's performance. The findings from the experiment showed that our algorithm outperformed the competitors in terms of accuracy. However, the classification accuracy can increase if more augmented data is added to the network and ANNs are used. It is still beneficial to learn about the process as a result.

6. Recommendations

Artificial intelligence methods have shown their effects on detecting brain tumors in pediatric patients. It has the potential to greatly enhance the capabilities of MRI and improve patient care. We recommend using AI algorithms since they can analyze large amounts of data from MRI scans with incredible accuracy and speed, which provides radiologists with a more comprehensive and precise understanding of a patient's condition. We also recommend applying AI methods as a diagnostic tool in medical imaging departments, as they can detect the smallest abnormalities that may be difficult for radiologists to identify. Moreover, in our insight ML methods will be in wider application in medical imaging departments.

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Data availability statement

All data generated or analyzed during this study are included in this article.

CRediT authorship contribution statement

Zuhal Y. Hamd: Writing – original draft, Investigation, Formal analysis, Conceptualization. **Eyas G. Osman:** Writing – original draft, Methodology, Investigation, Formal analysis. **Amal I. Alorainy:** Writing – original draft, Methodology, Investigation, Formal analysis. **Aljazi F. Alqahtani:** Writing – original draft, Validation, Software, Resources. **Noor R. Alshammari:** Writing – original draft, Software, Resources, Project administration, Methodology. **Omaymah Bajamal:** Writing – original draft, Validation, Software, Resources, Methodology. **Sawsan H. Alruwaili:** Writing – original draft, Visualization, Validation, Software, Resources, Data curation. **Shahad S. Almohsen:** Writing – original draft, Visualization, Resources, Methodology, Formal analysis. **Reema I. Almusallam:** Writing – original draft, Visualization, Validation, Supervision, Methodology. **Mayeen Uddin Khandaker:** Writing – review & editing, Visualization, Supervision.

Declaration of competing interest

The authors declared that they have no conflict of interest.

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