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Classification of Brain Tumour using Adaptive Recursive Partitioning Analysis based on Morpho – Histological Features obtained by Optimal Two – Phase Feature Selection Algorithm

P. Usha[1*] and Dr. J. G. R. Sathiaseelan[2]

[1] Assistant Professor, Department of Computer Science, Bishop Heber College, Affiliated to Bharathidasan University, Tiruchirappalli-620 024, Tamilnadu, India.

[2] Associate Professor, Department of Computer Science, Bishop Heber College, Affiliated to Bharathidasan University, Tiruchirappalli-620 024, Tamilnadu, India.

*Corresponding author: email: usha.it@bhc.edu.in

Emails of coauthors:

[1] usha.it@bhc.edu.in, [2]jgrsathiaseelan@gmail.com

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ABSTRACT

Brain tumour is the second most common leading disease in the world. It reduce the survival rate of a patient. Many automated systems and classification algorithms are available to detect brain tumours using MR images. World Health Organization initiates a next step to classify the brain tumours based on molecular features which helps to identify the histological subgroups for better prediction system. In this paper, instead of considering MR images, risk factors are used to identify histological type of tumours. To identify the best risk factors two phase feature selection algorithm is used, which composed by enhanced filtrate feature selection algorithm in phase I to identify the dependency and iterative feature displacement algorithm in phase II to achieve high quality and dimensional optimal dataset. The selected risk factors are classified in two ways such as by morphology and histology using new algorithm called Adaptive Recursive Partition Analysis (ARPART) based on target feature. The selected risk factors are also analysed using random forest, support vector machine and linear regression model. The proposed ARPART algorithm enables classification of tumour patient into more homogeneous and prognostic groups for better diagnosis process. The main aim of ARPART is to produce a homogeneous terminal node. ARPART algorithm shows 99.93% of accuracy in Histological based and shows 98.19 % of accuracy in morphological based. The proposed algorithm outperforms than other classifier models.

Keywords: MR images, enhanced filtrate, iterative displacement, ARPART, classification.

1. INTRODUCTION

Brain tumour is one of the most dangerous and leading cause of death in India and Worldwide. In 2021, National Cancer Institute statistics [1] shows 1.3 % of brain tumour cases are registered among 24,530 cases and the death rate is registered as 3.1 % out of 18,600 cases. According to

Hospital Based Cancer Registry (HBCR) [2], 32.5 % of males and 36.5 % of females were affected by brain tumour during 2020-2021. In [3], World Health Organization (WHO) identifies brain tumours into 155 types based histology and molecular features. Two categories are there. Benign: Nor grown, not aggressive. Malignant: More aggressive and fast growing tumour cells.
There Morphological band and classification of tumours in Central Nerve System (CNS) depends on histological characteristics and area recognized as tumour. Immunohistochemical method is a method which is used to demonstrate the gene expression by antigen of a cell type to assist the classification process. Morphological features of each tumour is represented using International Classification of Disease for Oncology third edition (ICD – O - 3) code published by WHO, which is a standard to categorize tumours in brain.
Morphological terms are used in diagnosis to increase the survival rate. CNS tumours are characterised using ICD-O code [4]. For example C72.0 – 9 for Cranial Nerves, Spinal cord and other parts of CNS tumours; C70.0 – 9 for Meninges, C71.0 – 9 for brain etc. Morphological terms are used to identify histological subgroups and its behaviour is coded as. /0 for benign, /1 for low malignant, /2 for recurrent malignancy and /3 is aggressive and malignant. The common histological subgroups are astrocytoma, glioma, gliomamultiform, diffuse astrocytoma, oligodendroglioma, ependymoma, medullobalstoma etc.
RPART is developed by Radiation Therapy Ontology Group (RTOG). It is a greedy algorithm based on top down approach. It results a tree in which each branch is represented as a value based on splitting target feature and end node shows the prediction results. ARPART is used to improve the survival rates, to understand prognostic variables which is used in decision making process.
The main objective of this paper is to classify brain tumours based on risk factors. The contribution of this paper is as follows:

1. To identify the feature dependency of risk factors using Enhanced Filtrate Feature Selection Algorithm [5].
2. To refine EFFS risk factors to obtain optimal dataset using Iterative Feature Displacement algorithm [6].
3. To classify brain tumors based on morphological feature by optimal risk factor dataset using ARPART.
4. To classify brain tumor based on histological types identified by risk factors using RPART.
5. Analyze the performance of ARPART with comparison of random forest and support vector machine.

The pare is organized as, related review of literature in section 2, proposed methodology and block diagram in section 3, dataset in section 4, results and discussion in section 5 and concludes with conclusion and references.

2. LITERATURE REVIEW

In [7], Takanori Yamashita,Yoshifumi wakata et al. Propose a Diagnosis Procedure combination & clinical path way to classify the post-operative patient status. To avoid long term hospitalization this epath is used in which Machine Learning algorithms are used in classification. epath is used to standardize the structure of medical records. In [8], Jobeda Jamal Khanam & Simon Y. Foo, compare, Neural Network & Machine Learning algorithm to predict diabetes. In this work, seven machine learning algorithms arte used. Linear Regression & Support Vector Machine performs well and shows 76-78% of accuracy & NN model shows 88-57% of accuracy with two hidden layers

In [9], Nazin Ahmed, Rayhan Ahammed propose a web based application to predict diabetes based on Machine Learning algorithm using clinical data. In this work dataset is preprocessed by

label encoding and normalization to improve accuracy. Using feature selection algorithm important risk factors are identified. Compared to existing Machine Learning algorithm this smart web application increases accuracy from 2.71% to 13.13%. In [10], Md Mahmudul Hasan, Gary J. Young et al. Algorithm propose a Machine Learning framework to identify the risk factor of Opioid disorder from healthcare data. Clinical & Prescription histories are used as features. Chi-squared used as a Feature Selection algorithm. The selected features are scaled, encoded compare with RF, DT, LR & GB MC algorithm RF shows higher accuracy then other models.

In [11], Beibei shi, Hua ye et al. analyse covid-19 severity using Machine Learning algorithm with enhanced optimisation of brain storming (BSO). SVM used with BSO & provides 91.91% of accuracy. This BSO-SVM can be treated as a computer aided technique in covid-19 prediction using coagulation index. In [12, 18, 20, 21 predict the survival of spine metastasis who have undergone radiation therapy using recursive partitioning analysis based on prognostic index. RPA used to determine the risk groups associated with survival in United States who have undergone surgery or radiation therapy for spine metastasis.

In [13, 17], Darius Phiri et al. and M.M. Menebo produce an assessment of environmental and socioeconomic factors of the COVID-19 spreads in Zambia using classification tree approach. This study shows the district details of COVID-19 is associated with the socioeconomic factors such as population density, HIV rates, country borders and proximity to airports. In [14, 19], propose a systematic study to identify factors which are associated with the initiation of systematic treatment after radiation therapy. RPA is very helpful to predict the patients with brain metastases who have undergone radiation therapy.

In [15] Yubin Xie et al. construct a cancer staging model using RPA. They develop web server called autoRPA to construct prognostic stage and compare the performance of different staging model. autoRPA establish a decision making tree and provide further spontaneous method to clinicians. autoRPA serve as a gateway to build cancer stages and supports the decisions for therapeutic methods for several cancer. In [16, 22] propose a modified RPA for predicting overall survival rate in patients with lung cancer and CNS metastases in which curves are generated by the survival tree.

3. PROPOSED METHODOLOGY

ARPART is a simple and nonparametric technique used for classification and prediction process. It is used as a decision maker which displays a tree based on succession rules to derive a target or predictor feature. In ARPART trees and its rules are repeatedly drawn and allows cross validation to predict. The structure of ARPART is shown in Fig 1.

Notations in ARPART:

Root node: Represented as circle in the top of a tree from which the tree is grown. Internal node: Intermediate node between root and leaf cable for further splitting. Terminal node: Predictor node shows decision value which cannot be splited further. Left and Right Daughter node: Splited root node depends on predictor expression. Offspring node: Use same ancestor variable as a splitting variable Split: homogeneity between two daughter nodes.

Representation of ARPART:

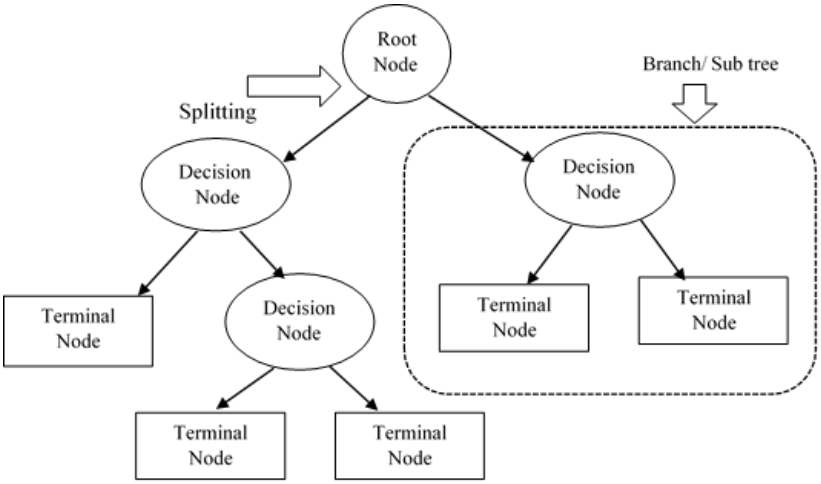

Fig 1: Structure of ARPART

Procedure:

1. Enhanced Filtrate Feature Selection (EFFS) algorithm select best features from Mutual Information Gain, Chi Squared, Correlation and Fisher score filter [5, 6] methods. Top ranked features are selected based on occurrences of each attribute. It is represented as,

$$Best(Select_{Best}) = Mutual\_Info(Select_{Feature}) \bigcup Chi\_square(Select_{Feature}) \bigcup Heat\_Map(Select_{Feature}) \bigcup F\_Scor \quad (1)$$

$$EFFS_{Feature} = Max\_Occurrence\big(Best(Select_{Best})\big) \quad (2)$$

2. Iterative Feature Displacement algorithm computes weight and rank for each feature obtained from EFFS and obtain optimal feature from IFD selected feature. It is denoted as,

$$IFD_{Feature} = Top\ (\ New_R[Feature]) \quad (3)$$

$$OTPFS_{Feature} = Top\ (\ IFD_{Feature}) \quad (4)$$

3. Identifies candidate split: To select a target variable, in case of categorical variable take as it is, in case of continuous variable use mean. It is called as separation condition and is denoted as,

$$X\ <= Mean\ (x_i\ , x_{i+1}) \quad (5)$$

4. Evaluate Split criteria: To obtain the split criteria, Gini cost function is used to find the impurity of a variables and is used to create different decision nodes. Gini index takes value from 0 to 1. Minimum Gini value is always preferred for splitting. It is calculated using the formula,

$$Gini\ = 1\ -\ \sum_{i=1}^{n}(p_i)\ \ ^2 \quad (6)$$

5. Partitioning: Repeat step 2 to obtain terminal node for decision making.
6. Pruning criteria: Step 2 and 3 repeated until decision node turns into terminal node. It use minimal cost complexity function to prune a tree. It is represented for T as,

$$Cost_a(T)\ = R(T)\ + aL(T) \quad (7)$$

Where R (T) is misclassified ratio of training data, L (T) denotes number of leaves in tree T and a is the complexity factor. Tree is pruned by any one of the following criteria is reached: 1. same target value 2. User defined tree size 3. Tree depth = pre-defined

maximum value 4. Lesser minimum cases 5. Meaningless split (split doesn't improve purity).

7. Select best tree with clarified terminal nodes as a final tree using cross validation or average of error rates.

Adaptive Recursive Partitioning Analysis (ARPART) Workflow Model

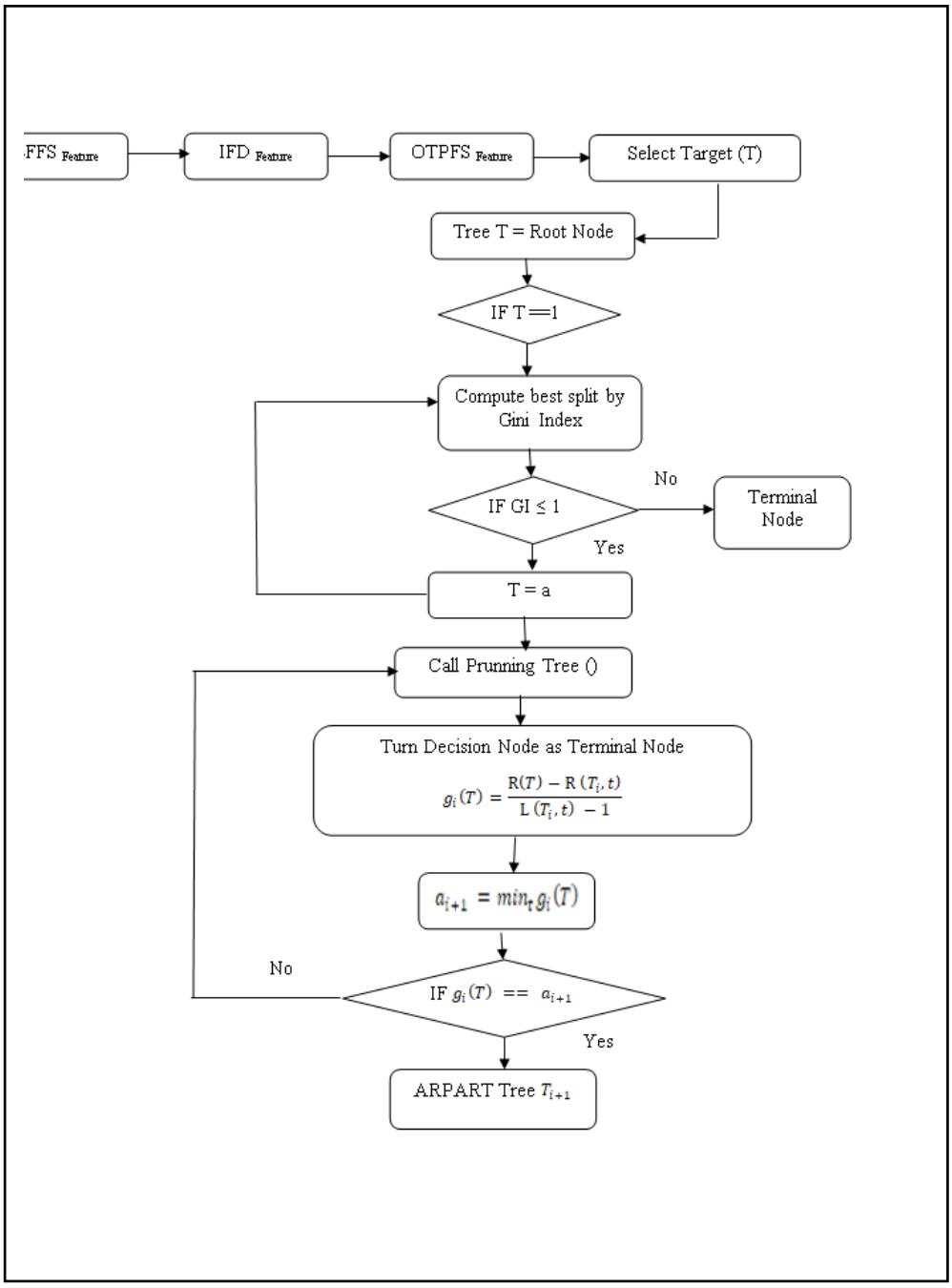

Fig 2. Adaptive Recursive Partitioning Analysis (ARPART) Workflow Model

Adaptive Recursive Partitioning Analysis (ARPART) Algorithm:

Input Training Dataset $OTPFS_{Feature}$, Attribute set A, Output variable y
Output ARPART Tree

Procedure ARPART_Tree ($OTPFS_{Feature}$, A, y)

{
Tree $T = Root\ Node$
IF ($Prunning\ criteria == 0) THEN$
$Return\ Root\ Node\ as\ ARPART\ Tree$
$ELSE$
{
Select a target variable in T
$X <= Mean\ (x_i , x_{i+1})$
$Find\ a \in A, Best\ Split\ by\ Gini\ Index$

$$Gini = 1 - \sum_{i=1}^{n} (p_i)^2$$

$Label\ T \leftarrow a$
$FOR\ each\ v\ in\ a$
$IF\ (v = a)\ THEN$
$X = subset(X)$
$A = Attribute\ se\ A - best\ split\ a$
$ARPART(OTPFS_{Feature}$, A, y)
$Connect\ v \leftarrow a$
}
$Reture\ PruningTree\ (OTPFS_{Feature}$, A, y)
}

$PruningTree\ (OTPFS_{Feature}$, A, y)
{
$T_1 = T(0), a_1 = 0\ and\ i = 1$
$WHILE\ T_i == 1$
$FOR\ ALL\ t \in T_i$
$g_i(T) = \frac{R(T) - R(T_i, t)}{L(T_i, t) - 1}$
$a_{i+1} = min_t g_i(T)$
$IF\ (g_i(T) == a_{i+1})\ THEN$
$Return\ T_{i+1}$
$i - i \perp 1$

4. DATA ANALYSIS

In this paper brain tumour dataset is downloaded from cancer imaging archive, cptac-data-portal and proteomic and cbioportal. Dataset is fine-tuned from EFFS and IFD algorithms and returns OTPFS dataset which contains 35 features out of 46 features. Dataset contains gender, age, morphology, grade, histology, tumour type, origin of tumour, treatment type, symptoms like vomiting, hearing problems, neurological sign, movement disorder, eye squint, walking changes, behaviour changes, visual effects, head growth, head tilt etc.

The implementation of this work is done in R programming (Rattle Package). It is a Graphical User Interface based package which is used to analyse and predict dataset and models. It provides a sophisticated environment for data science problem solving. It is an open source software, model can be implemented and updated easily.

5. RESULTS AND DISCUSSION

ARPART is most effective in the classification of both continuous and categorical variables. The obtained output is easily interpreted in the form of rules. Each path is connected from root to leaf and is represented as a form a rule.

Data Distribution: Dataset contain 35 most significant features are selected using optimal two phase feature selection algorithm. Fig 3 shows the distribution of data objects in a sample dataset. In Fig 3, (1) represents distribution of gender object with two values 0 and 1 for male and female. (2) shows the distribution of various tumours based on age, the people who have approximately age from 25 to 58 were affected (3) shows Morphology and is represented by ICD code which is used for future treatment suggestion (4) shows histological distribution like astrocytoma, anaplastic astrocytoma, glioma, oligodendroglioma. (5) shows the distribution of brain tumours based on location or origin of the tumour. (6) Brain tumours are graded from 1 to 4, grade 1 and 2 are benign they are not as much as aggressive, grade 3 and 4 are most aggressive and spread to other parts of the brain, the distribution of tumours based on grade are shown. (7) There are two varieties of brain tumours benign and malignant and distributions are shown and is represented as 0 and 1. (8) Brain tumour can be treated in four ways such as by surgery, chemotherapy, radio therapy and pharmaceutical therapy and distribution is shown.

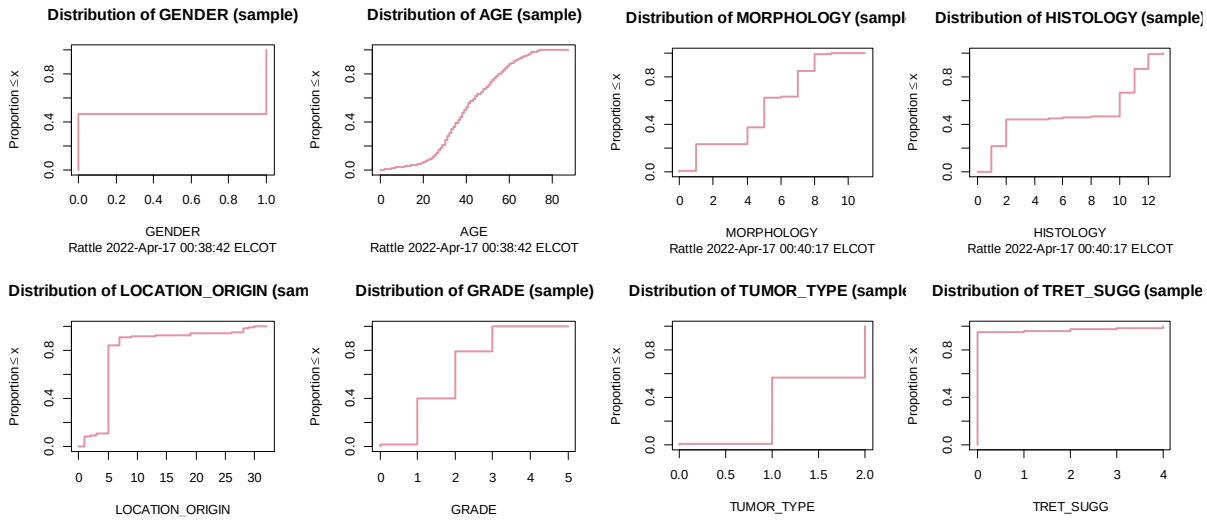

Fig 3. Distribution of Features (1) Gender (2) Age (3) Morphology (4) Histology (5) Location (6) Grade (7) Tumour Type (8) Treatment Suggestion

Morpho- Histo Distribution by Age and Grade: Fig 4 (a) shows the histological distribution of data based on age factor. From the dataset, approximately people who have age from 25 to 45 affected by astrocytoma and 30 to 40's are affected by oligodendroglioma. (b) shows the histological distribution of brain tumours based on grade. Most of the oligodendrogliomas are comes under grade 2 and anaplastic astrocytoma grade 3 and 4 are occurred in the above specified age group peoples. (c) shows the morphological based distribution of brain tumours in which 9382/3 represents oligodendroglioma, 9400/3 astrocytoma, 9401/3 anaplastic astrocytoma, 9450/3 mixed glioma and 9451/3 represents anaplastic oligodendroglioma. According to the morphological feature the age from 5 to 45 are mostly affected by astrocytoma. (d) shows the distribution of morphological distribution based on grade, most peoples are affected by grade 2 oligodendroglioma and grade 3 anaplastic astrocytoma.

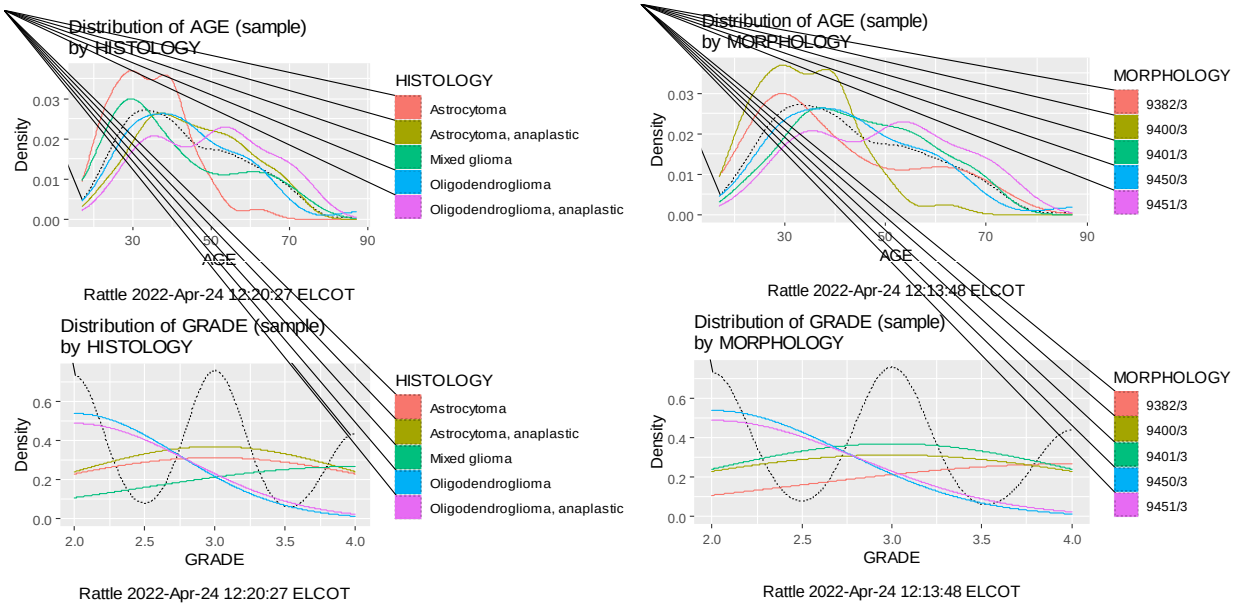

Fig 4. Distribution of Features based on (a) Age by Histology (b) Age by Morphology (c) Grade by Histology (d) Grade by Morphology

Morpho – Histo Classification of Brain Tumours: In 2016, WHO suggested and organize the brain tumours based on morphological features. There are 155+ histological types of brain tumours are found based on morphological ICD code. This will help to identify the histological type for further treatment process. In this paper, various risk factors and symptoms are used to identify the histological type thus it will increase the patients survival rate. Fig 5 shows the ARPART classification of brain tumour base on histology in which, there are two categories of anaplastic types such as anaplastic astrocytoma and anaplastic oligodendroglioma both are grade 3 or 4 types. It can be distinguished by first symptoms longest duration.

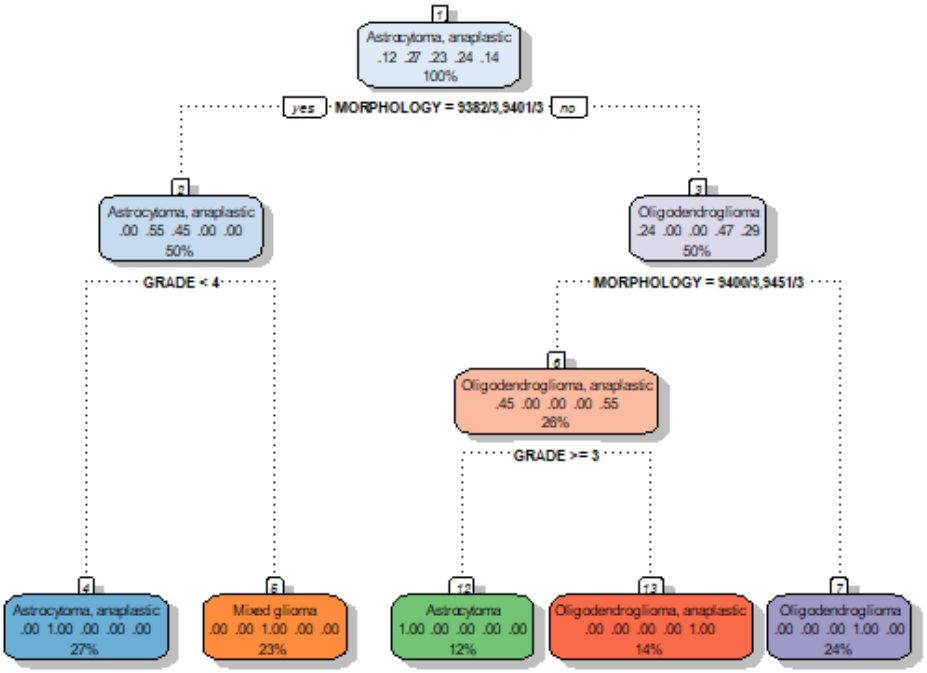

Fig 5. ARPART based on Histology

In the case of anaplastic astrocytoma, the longest symptom is seizures and in anaplastic oligodendroglioma headache it will be differ from normal headache. If the morphological ICD code is 9382/3 or 9401/3, it can be an astrocytoma types otherwise it will comes under oligodendroglioma types. Based on tumour type again it will be splitted as anaplastic

astrocytoma if it grade 4 and mixed glioma as grade 3. Further it cannot be extended so the pruning condition is reached and unique histological types are identified. Likewise in right side of ARPART, if ICD code is 9400/3 or 9451/3 is true, it may come under anaplastic oligodendroglioma grade 3 or anaplastic astrocytoma grade 3 otherwise it will be specified as oligodendroglioma grade 2. Fig 6 shows the ARPART classification based morphological ICD codes. If the ICD code is 9401/3 is true means it can have categories such as combination of astrocytoma, oligodendroglioma and mixed glioma as left child. If 9401/3 have grade 4 characteristics then it will be represented as anaplastic oligodendroglioma with ICD code 9382/3 otherwise it will be mixed glioma 9401/3. In the right side of the tree, if the grade of 9450/3 is greater than 3 it will be specified either astrocytoma (9400/3) or anaplastic oligodendroglioma (9451/3). If grade is less than 3 then it will represented as oligodendroglioma (94500/3). Finally the tree is pruned and unique morphology is identified.

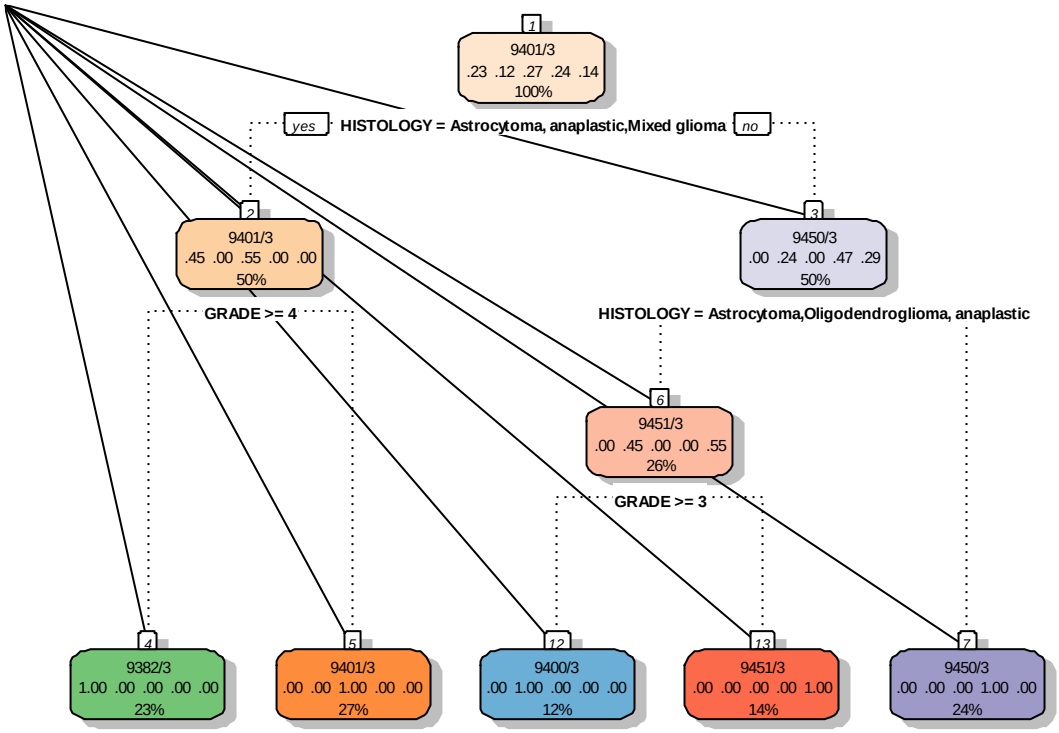

Fig 6. ARPART based on Morphology

Performance Measurements: The dataset is given as input to the classifier models. Performance of the proposed ARPART algorithm is evaluated using performance metrics from confusion matrix obtained. The confusion matrix is one of the evaluation feature that contains true positive, negative and false positive and negative values as rows and columns. All models are evaluated in terms of performance metric. The metrics are calculated as mentioned in Table 1.

Table 1. Mathematical Formula for Performance Metrics

Metrics	**Formula**
Accuracy	$Accuracy = \frac{TP + TN}{TP + TN + Fp + FN}$
Sensitivity	$Sensitivity = \frac{TP}{TP + FN}$
Specificity	$Specificity = \frac{TN}{TN + FP}$

Precision	$Precision = \frac{TP}{TP + FP}$
F_score	$F\_score = \frac{2 * Precision * Sensitivity}{Precision + Sensitivity}$

In table 1, TP → True Positive, TN→True Negative, FP→ False Positive and FN→ False Negative . The performance is evaluated and compared with other existing model such as random forest, support vector machine and linear regression model. The values are shown in Table 2.

Table 2. Performance Evaluation based on Morphology as Target Value

Metrics/ Algorithm	Accuracy	Sensitivity	Specificity	Precision	F Score
RF	96.94	97.01	95.92	99.69	98.33
SVM	97.22	97.86	92.77	99.52	98.68
LR	97.01	94.41	83.87	98.87	96.59
ARPART	**98.19**	**98.49**	**94.64**	**99.95**	**99.21**

In Table 2 the classification accuracy of ARPART algorithm shows 98.19 % and is compared with existing model such as support vector machine, linear regression and random forest. 35 selected OTPFS are used as input to the model and morphology is fixed as target variable. RF shows 96.94 %, SVM shows 97.22 % and LR model shows 97.01 Other performance factors of ARPART model also shows greater value than existiong classifiers. The variations of performance metrics are reprsentes as a grapfh and is shown in Fig 7.

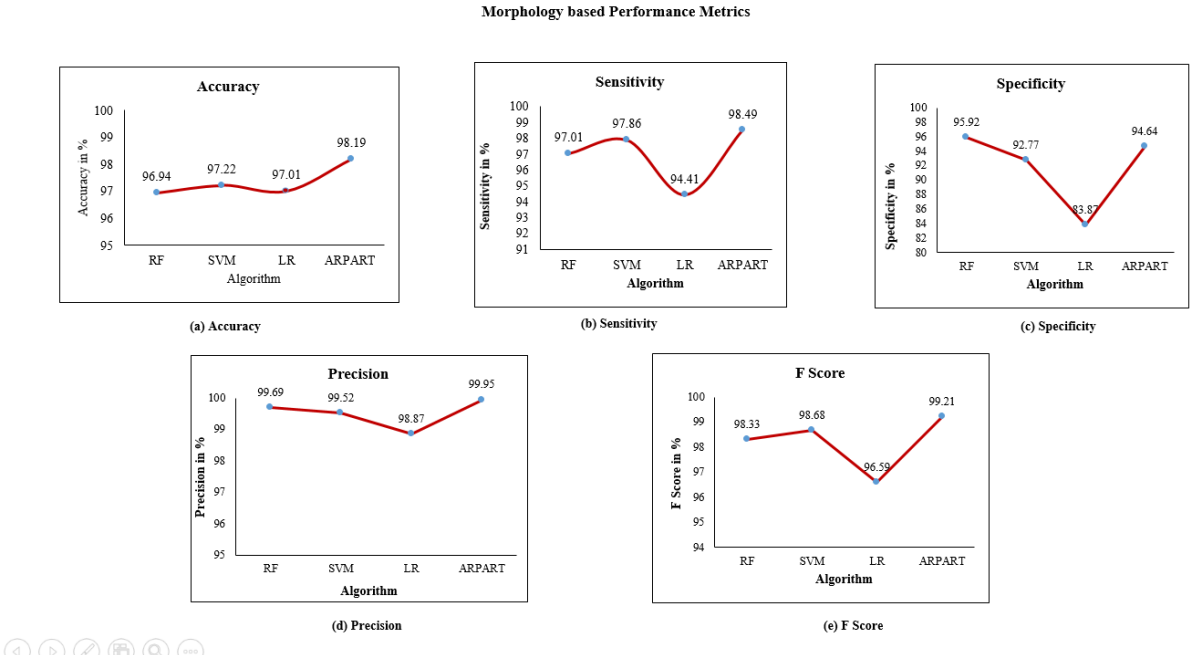

Fig 7. Performance Metrics based on Morphology
(a) Accuracy (b) Sensitivity (c) Specificity (d) Precision (e) F Score

In Table 3 the classification accuracy of ARPART algorithm shows 99.93 % and is compared with existing model such as support vector machine, linear regression and random forest. 35 selected OTPFS are used as input to the model and histology is fixed as target variable. RF

shows 98.81 %, SVM shows 98.12 % and LR model shows 98.54%. Other performance factors of ARPART model also shows greater value than existiong classifiers. The variations of performance metrics are reprsentes as a grapfh and is shown in Fig 8.

Table 3. Performance Evaluation based on Histology as Target Value

Metrics/ Algorithm	Accuracy	Sensitivity	Specificity	Precision	F Score
RF	98.81	98.87	57	99.36	99.11
SVM	98.12	98.93	54.54	99.29	99.11
LR	98.54	98.95	44	99.36	99.15
ARPART	**99.93**	**99.93**	**89.95**	**99.52**	**99.96**

All the performance metrics of proposed ARPART algorithm is compared with both morphology and histology. Compared to morphological features histological features are shows higher performances. Histological types are plays a vital role in the prediction and suggestion of brain tumour detection to increase the patients survival rate.

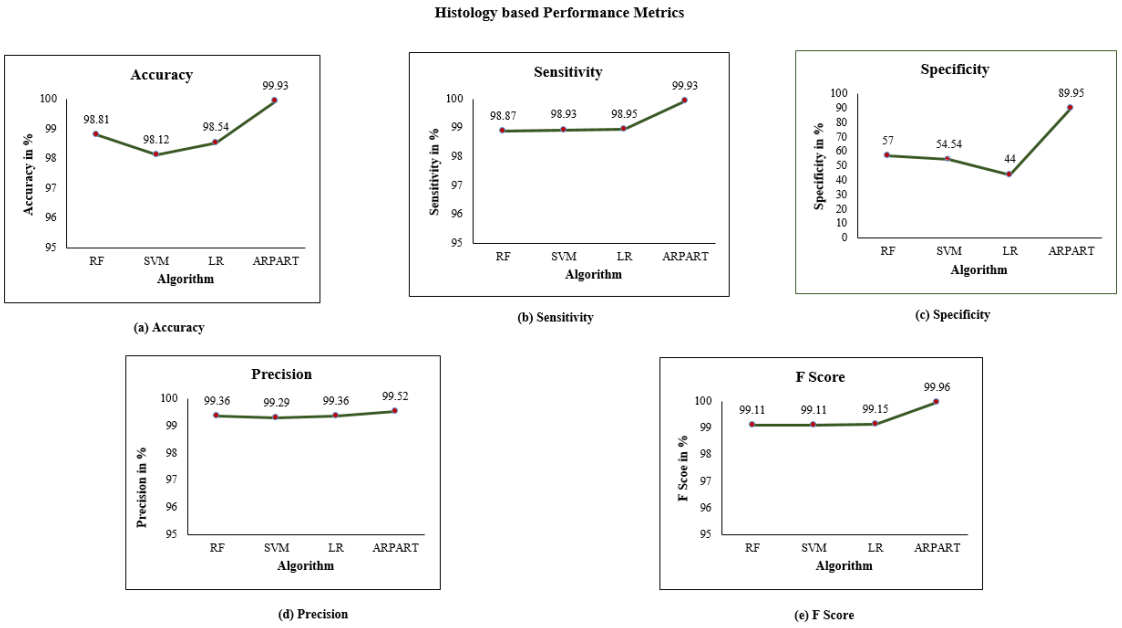

Fig 8. Performance Metrics based on Histology
(a) Accuracy (b) Sensitivity (c) Specificity (d) Precision (e) F Score

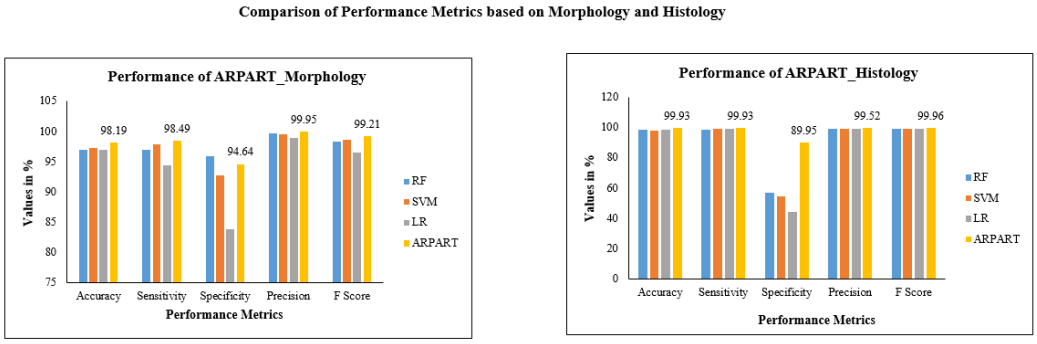

Fig 9. Comparison of Performance Metrics based on Morphology and Histology

CONCLUSION

In medical field decision trees are used by researcher to predict medicinal suggestion and treatment option. Recursive partition analysis is mostly used as a diagnosis tool in disease decision making process. In this analysis, symptoms and risk factor such as age, gender, location etc. are considered as input. Based on this the proposed algorithm classify the brain tumours by histology and morphology. According to the proposed analysis astrocytoma, grade 3 tumours are mostly occurred in the age group of 29-35 and in children under 5 years. Instead of using gene expression analysis, the risk and symptom based morpho- histo classification by ARPART algorithm give quick suggestion for further treatment option and it will increase the survival rate of a patient. The proposed ARPART algorithm shows 99.93% of accuracy than other famous models in Histological based and shows 98.19 % of accuracy in morphological based. This work focus only few types of brain tumours occurred in child and adolescents. In future this risk and symptom based morpho- histo classification predictive model is validated by physician in real-time application with more number of histological types.

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