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GENERIC METHOD FOR TRACKING THE PROGRESSIVENESS OF PARKINSON DISEASE (SPEECH SIGNAL): REGRESSION TECHNIQUE

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Abstract: Parkinson's disease (PD) is a neurodegenerative disorder with a long time course which increases significantly with age. With the progressive nature of PD, performance in voice gets degraded. Hence, dysphonia measures of voice signals are used for detecting and tracking of PD symptom progression. The purpose of this paper is to estimate the Unified Parkinson's Disease Rating Scale (UPDRS) score, elucidate monitoring the PD progression on a weekly basis, and tracking the UPDRS for a six-month period and propose a tree based method for predicting the progression of PD. Statistical regression techniques such as Iteratively Reweighted Least Squares (IRLS) – a linear approach defines a mapping between dysphonia measures and UPDRS score – and Classification And Regression Tree (CART) – a non-linear tree based approach constructs a regression tree for estimating UPDRS score – are used for tracking the progression of PD symptoms.

Key Words: ***Parkinson disease progression, IRLS, CART, tracking PD, Dysphonia measures, UPDRS score***

1. INTRODUCTION

Among neurological disorders, the next most common disease is PD after Alzheimer. The main reason behind PD is dopamine deficiency in neuron. Normally, there are brain cells (neurons) in the human brain that produce dopamine. These neurons concentrate in a particular area of the brain, called the substantianigra. Dopamine is a chemical that transfers messages between the substantianigra and other parts of the brain to control movements of the human body. Dopamine helps humans to have smooth coordinated muscle movement. Tremor is often the first symptom that people with PD notice. As the disease progresses, the tremor that appear in one side may spread to both sides of the body. Other symptoms may include depression and other motional changes: difficulty in swallowing, chewing, and speaking; urinary problems or constipation; skin problems; and sleep disruptions.

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PD is a progressive and physical test observations are mapped to a metric specifically designed to follow disease progression, typically UPDRS, which reflects the existence and severity of PD symptoms. Nowadays, remote monitoring of patients with various diseases is an increasing requirement. Specially, patients with various neurological disorders need regular monitoring. But, most of the times, patients fail to come for a regular check-up and it is not possible for the doctors or caregivers to monitor each patient by visiting them. Intel Corporation's At-Home Testing Device (AHTD) is a unique telemonitoring system facilitating remote, Internet-enabled measurement of a range of PD-related motor impairment symptoms. It records both manual deftness and speech tests; specifically vowel phonations. Various signals, including ECG, speech and gait, have been undertaken for diagnosis of PD. Since most of the people with PD suffer from speech disorders, it could be considered as the most reasonable way for detection of PD.

The paper is organized as follows. Section 2 and 3 deals with literature review and proposed system in the detection and tracking of PD. Section 4 discuss about the dataset used in this work. Section 5 explains the methods used. Section 6 explains the experimental results and section 7 provides the conclusion and the future work.

2. LITERATURE REVIEW

Little et al. considered both traditional and non-standard methods to detect dysphonia through which they could distinguish the PD patients from the healthy people and also introduced a new measure called Pitch Period Entropy (PPE). Their experiments on 31 people (23 with PD and 8 healthy) provided 91.4% correct classifications and were also suitable for telemonitoring applications to provide remote diagnosis of patients.

A combination of genetic programming and the expectation maximization algorithm is proposed to create learning feature function for separating healthy subjects from those with PD. Kenneth Revett et al. used rough set approach for feature selection in PD there by to differentiate healthy people from people with Parkinson (PWP). The rapid finger-tapping test (RFT) is an important method for clinical evaluation of movement disorders, including PD. A clinical expert system has been developed for detection of PD. This system extracts features from voice recordings and considers an advanced statistical approach for pattern recognition using Bayesian approach.

Detection of PD using fuzzy k-nearest neighbour approach is comprised of two stages. In the first stage, PCA is used to eliminate the redundant features and in the second stage optimal FKNN model is used to perform the classification tasks. Another system, a combination of features selection algorithm, relief-F which reduces no. of features and an automatic recognition system, Support Vector Machine (SVM) classifier which is built for speech signals is developed for distinguishing the healthy people from those with Parkinson's disease with 96.88% of accuracy. Dr. M. Pushparani and B. Kalaivani proposed a paper that discusses about identifying the movement disorders with particular reference to PD and Huntington's disease using gait analysis. Smita S Sikchi et al. proposed a generic FES implemented using visual basic and Matlab to diagnose cardiac diseases.

Fuzzy c-means (FCM) clustering and pattern recognition methods are used to classify PD dataset (voice dataset) between normal speaking persons and speakers with PD. The aim of the system is to automatically detect whether the speech/voice of a person is affected by PD. R Geetha Ramani proposed a system that predicts the motor and total UPDRS scores from the voice measures using Random Tree classification algorithm with the features filtered by the ReliefF algorithm and

also highlights the impact of six feature relevance algorithms and thirteen classification algorithms on the Parkinson Tele-monitoring dataset.

3. PROPOSED WORK

In this proposed work, linear method IRLS and a non-linear method CART are used for predicting the progression of PD. This paper deals with applying IRLS and CART methods to a voice dataset concerning PD with the aim of tracking the progression of PD symptoms. The statistical mapping between UPDRS and speech signals is discovered using IRLS and CART. The work is proposed to establish a statistical relationship between dysphonia measures of speech signal and UPDRS. This method is useful for UPDRS assessment, and demonstrates remote PD monitoring on a weekly basis, tracking UPDRS fluctuations for a six-month period to follow the progression of clinical PD symptoms on a regular basis.

3.1 Regression mapping between dysphonia measures and UPDRS score using IRLS

Initially the regression coefficient between all the 16 dysphonia measures and actual UPDRS score is evaluated using IRLS. Then the UPDRS score (motor and total) is predicted. The Mean Absolute Error (MAE) between actual UPDRS score and predicted UPDRS score is evaluated by applying the formulas. Similarly Mean Squared Error (MSE) is evaluated. Both MAE and MSE are evaluated for both training and testing dataset. However, the testing MAE and its standard deviation across the 1000-runs cross-validation was relatively low, suggesting that these indicative coefficients are sufficient for useful UPDRS prediction.

3.2 Regression mapping between dysphonia measures and UPDRS score using CART

A Regression tree is constructed to predict the motor-UPDRS and total-UPDRS for all the 16 dysphonia measures piecewise. Let x1 be the one of the dysphonia measures (ie MDVP:Jitter(%)). Start at the root node value. Repeat the below steps until leaf node is reached. Test the value of x1 using split criteria and Go to the left child if answer is yes otherwise go to right child. Note that the leaf node is the predicted UPDRS (motor and total) score. The MAE and MSE are evaluated for CART as in IRLS

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4. METHODS

4.1 Iteratively Reweighted Least Square(IRLS)

Iteratively Reweighted Least square (IRLS) is a linear regression technique used to solve certain optimization problems with objective functions by an iterative method in which each step involves solving a weighted least squares problem. It effectively reduces the influence of distant values from the bulk data (outliers) by predicting least square iteratively which reweight outlier at each step.

IRLS comes with two drawbacks. One is that, it works efficiently and produces accurate results for less number of input variables. Its performance degrades with more number of inputs. This problem of having larger inputs in IRLS method is referred as Curse of dimensionality. Another drawback is that the technique does not produce better accuracy when all the input measures do not combine linearly to predict output values. Here, all the dysphonia measures do not combine linearly to predict the UPDRS score. Hence a non-linear regression method is necessary when the prediction function y is non-linear combination of input values x. Thus CART, a non-linear method used to address both the drawbacks.

4.2 Classification and Regression Tree

Classification and regression tree (CART) is a non-linear statistical regression technique. It produces two types of trees: Classification tree and Regression tree. Classification trees are designed for categorical target variables with prediction error measured in terms of misclassification cost. Regression trees are designed for continuous target variables with prediction error measured by the squared difference between the observed and predicted values. It uses cross-validation to select the optimal tree.

CART handles missing values automatically and invariant to monotonic transformation of predictive variable. It provides a great way to explore and visualize the data and unlike linear regression technique, it is not sensitive to outliers in predictive variables.

Algorithm for CART Method: There are two steps in the construction of tree a. Growing of tree. b. Pruning

a. Growing of tree

Find the best split of the input variables using sum of squared error, and partition the ranges of these variables into two sub-regions. This partitioning process is repeated on each of the resulting sub-regions, recursively partitioning the input variables into smaller and smaller sub-regions. The grown up tree gives a consecutively detailed mapping between the input data and the output variable (ie between dysphonia measures and UPDRS score).

b. Pruning

The constructed tree structure can easily over fit the data. That is, become highly sensitive to noisy fluctuations in the input data. To address this problem some splits are collapsed (a process known as pruning) and the amount of split reduction is determined by the pruning level.

5. EXPERIMENTAL EVALUATION

5.1 Source Data set

Voice measurement has shown a great progress in the advancement of PD detection. About 90% of people with PD present some kind of vocal deterioration. And hence in this paper, dataset on speech signals is chosen. It is composed of a range of biomedical voice measurements from 42 people who are affected with PD. There are totally 5,923 voice recordings from 42 subjects. The UPDRS score value was assessed at baseline (onset of trial) and after three months and 6 months.

Dysphonia is the medical term for disorder of voice. 5923 sustained phonation of the vowel “ahh...” were digitally processed using speech signal processing algorithm to produce 16 dysphonia measures. The descriptions of all the dysphonia measures are given in the Table I. KP-MDVP stands for Kay Pentax Multidimensional Voice Program.

TABLE I Descriptions of Dysphonia measures

Sl. No	Attribute	Description
1	MDVP:jitter%	KP-MDVP jitter
2	MDVP:jitter ABS	KP-MDVP absolute jitter
3	MDVP:Jitter:RAP	KP-MDVP Relative amplitute perturbation
4	MDVP:PPQ5	KP-MDVP five-point period perturbation quotient
5	Jitter:DDP	Avg absolute diff of diff between cycle divided by the average period
6	MDVP:Shimmer	KP-MDVP local shimmer
7	MDVP:Shimmer (dB)	KP-MDVP local shimmer in decibels
8	Shimmer:APQ3	Three point amplitute perturbation quotient
9	Shimmer:APQ5	Five point amplitute perturbation quotient
10	Shimmer:APQ11	KP-MDVP 11-point amplitute perturbation quotient
11	Shimmer:DDA	Average absolute differences between consecutive differences between the amplitudes of consecutive periods
12	NHR	Noise -to-Hormonics Ratio
13	HNR	Hormonics-to-Noise Ratio
14	RPDE	Recurrence period Density Entropy
15	DFA	Detrended Fluctuation Analysis
16	PPE	Pitch Period Entropy

6. EXPERIMENTAL ANALYSIS

Implementation is performed using statistical Analysis Toolbox in Matlab 2011b. IRLS and CART method are found in this toolbox.

The regression trees for predicting motor-UPDRS and total-UPDRS are constructed for all the 16 dysphonia measures piecewise using CART regression method. There are totally 32 regression trees, 16 regression trees with motor-UPDRS for all the dysphonia measures and 16 regression trees with total-UPDRS for all the dysphonia measures.

Figure 2 depicts regression tree for predicting total-UPDRS from one of the dysphonia measures, jitter(%). At each internal node, the value of x1 (jitter(%)) is tested and select either left or right path of the tree. The leaf node is the predicted value of total-UPDRS. For the x1 value (jitter(%)) less than 0.00276036, the predicted total-UPDRS score is 10.9651 (low) and for the x1 value between 0.00580624 and 0.00608684, the predicted total-UPDRS score is 47.7955 (high).

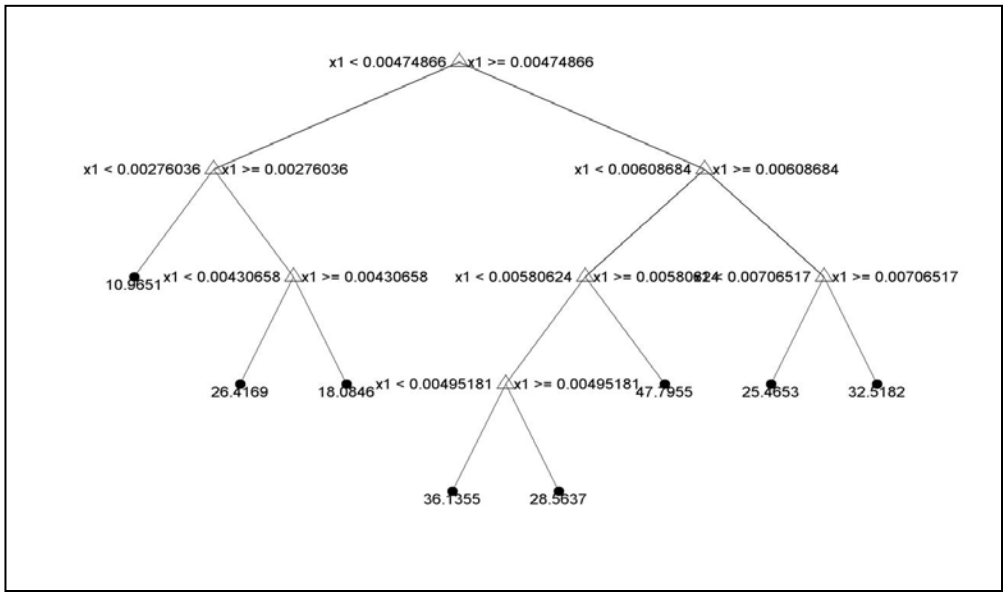

Figure 2 Total_updrs with jitter(%)

Figure 3 depicts regression tree for predicting motor-UPDRS from one of the dysphonia measures, shimmerDDA. At each internal node, the value of x1 (shimmerDDA) is tested and select either left or right path of the tree. The leaf node is the predicted value of motor-UPDRS. Here, for the x1 value (shimmerDDA) less than 0.0239271, the predicted total-UPDRS score is 40.71 (high) and for the x1 value between 0.0402209 and 0.0433308, the predicted total-UPDRS score is 8.307 (low)

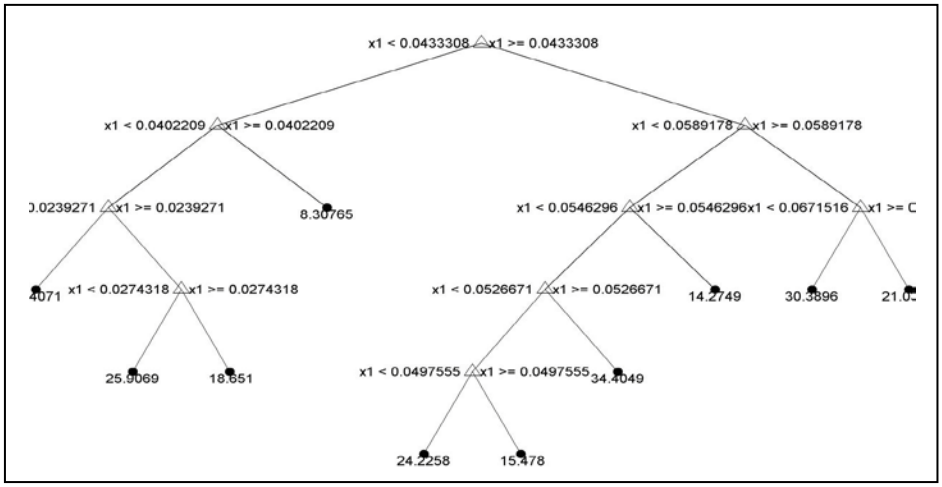

Figure 3 Motor UPDRS with shimmerDDA

Table II presents the MAE and MSE for both training dataset and test dataset with all dysphonia measures piece-wise against motor UPDRS using IRLS and CART.

TABLE II MAE and MSE for Motor UPDRS using IRLS and CART

Sl. No	Parameters	Methods	Mean Absolute Error (MAE)		Mean Squared Error (MSE)	
			Training dataset	Test dataset	Training dataset	Test dataset
1	jitter%	IRLS	0.000025	0.003966	0.000025	1.633966
		CART	0.005490	0.006110	0.000102	0.000121
2	Jitter(ABS)	IRLS	0.000000	2.036780	21.9888	0.0000
		CART	0.000000	0.000022	0.0000	0.0000
3	Jitter:RAP	IRLS	0.0016	0.0016	0.0000	0.0000
		CART	0.0041	0.0044	0.0001	0.0001
4	Jitter:PPQ5	IRLS	0.0017	0.0017	0.0000	0.0000
		CART	0.0048	0.0051	0.0001	0.0001
5	Jitter:DDP	IRLS	0.0049	0.0049	0.0001	0.0001
		CART	0.0047	0.0050	0.0001	0.0001
6	Shimmer	IRLS	0.0170	0.0170	0.0008	0.0008
		CART	0.0094	0.0154	0.0003	0.0006
7	Shimmer(dB)	IRLS	0.1547	0.1548	0.0606	0.0605
		CART	0.3208	0.3371	0.1908	0.2010
8	Shimmer:APQ3	IRLS	0.0090	0.0090	0.0002	0.0002
		CART	0.3215	0.3367	0.1919	0.2005
9	Shimmer:APQ5	IRLS	0.0042	0.0105	0.0003	0.0003
		CART	0.0076	0.0107	0.0002	0.0003
10	Shimmer:APQ11	IRLS	0.0257	0.0134	0.0004	0.0004
		CART	0.0041	0.0041	0.0041	0.0041
11	Shimmer:DDA	IRLS	0.0236	0.0270	0.0018	0.0018
		CART	0.0122	0.0233	0.0007	0.0014
12	NHR	IRLS	0.0215	0.0231	0.0036	0.0035
		CART	0.0078	0.0211	0.0009	0.0024
13	HNR	IRLS	0.0219	7.7111	88.0999	88.2613
		CART	0.0124	0.0234	0.0007	0.0015
14	RPDE	IRLS	0.1731	0.1736	0.0425	0.0427
		CART	0.0048	0.0051	0.0001	0.0001
15	DFA	IRLS	0.0264	0.2079	0.0633	0.0633
		CART	0.0047	0.0050	0.0001	0.0001
16	PPE	IRLS	0.0284	0.0869	0.0123	0.0123
		CART	0.0094	0.0154	0.0003	0.0006

Table III presents the MAE and MSE for both training dataset and test dataset with all dysphonia measures piece-wise against total-UPDRS using IRLS and CART.

TABLE III MAE and MSE for total-UPDRS using IRLS and CART

SI.No	Parameters	Methods	Mean Absolute Error (MAE)		Mean Squared Error (MSE)	
			Training dataset	Test dataset	Training dataset	Test dataset
1	jitter%	IRLS	0.0031	0.0031	0.0000	0.0000
		CART	0.0056	0.0062	0.0001	0.0001
2	Jitter(ABS)	IRLS	0.0011	1.9704	1.9710	21.1221
		CART	0.0000	0.0000	0.0000	0.0000
3	Jitter:RAP	IRLS	0.0001	0.1515	0.1515	0.0371
		CART	0.0042	0.0045	0.0001	0.0001
4	Jitter:PPQ5	IRLS	0.0011	0.0972	0.0963	0.0238
		CART	0.0040	0.0043	0.0000	0.0000
5	Jitter:DDP	IRLS	0.0014	0.6867	0.6858	7.0447
		CART	0.0070	0.0083	0.0002	0.0002
6	Shimmer	IRLS	0.0014	0.7083	0.7075	7.0531
		CART	0.0098	0.0159	0.0005	0.0007
7	Shimmer(dB)	IRLS	0.0014	0.5555	0.5547	5.2958
		CART	0.2305	0.2418	0.1447	0.1705
8	Shimmer:APQ3	IRLS	0.0014	0.5818	0.5809	5.6456
		CART	0.0080	0.0106	0.0002	0.0003
9	Shimmer:APQ5	IRLS	0.0014	0.6029	0.6020	5.8801
		CART	0.0080	0.0110	0.0002	0.0003
10	Shimmer:APQ11	IRLS	0.0014	0.5961	0.5953	5.7967
		CART	0.0085	0.0128	0.0003	0.0004
11	Shimmer:DDA	IRLS	0.0014	0.5943	0.5935	5.7778
		CART	0.0125	0.0237	0.0009	0.0017
12	NHR	IRLS	0.0014	0.5953	0.5944	5.7891
		CART	0.0094	0.0225	0.0021	0.0034
13	HNR	IRLS	0.0014	0.5953	0.5945	5.7899
		CART	1.3046	2.6800	8.2598	14.7707
14	RPDE	IRLS	0.0012	0.6545	0.6539	6.3677
		CART	0.2305	0.2418	0.1447	0.1705
15	DFA	IRLS	0.0012	0.5170	0.5162	4.8344
		CART	0.0080	0.0106	0.0002	0.0003
16	PPE	IRLS	0.0014	0.5613	0.5605	5.4097
		CAR	0.0080	0.0110	0.0002	0.0003

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The testing error remains low and nearer to the training error. This indicates that the model has attained a reasonable estimate of the performance. Although IRLS performance is better, CART outpaces it, displaying the smallest deviation from the interpolated score.

The UPDRS tracking for a typical subject is demonstrated throughout the six month trial using IRLS and CART. CART attains smallest prediction error and tracks the linearly interpolated UPDRS more accurately. In the Table IV, the actual and predicted value of UPDRS (motor and total) score for a subject is calculated and presented using IRLS and CART. The difference between predicted and linearly interpolated UPDRS value is typically low.

TABLE IV Tracking of UPDRS (motor and total) using IRLS and CART

Sl. No	IRLS				CART			
	Motor-UPDRS		Total-UPDRS		Motor-UPDRS		Total-UPDRS	
	Actual	Predicted	Actual	Predicted	Actual	Predicted	Actual	predicted
1	19	18	25	25	20	21	25	35
2	20	19	28	28	21	16	26	30
3	21	18	28	28	22	16	27	35
4	22	19	29	29	23	15	28	29
5	23	17	30	28	24	20	30	35
6	24	19	31	29	25	20	31	25
7	25	18	32	29	26	11	32	26
8	26	19	33	28	27	20	33	26
9	27	15	34	29	28	24	34	25
10	28	14	35	27	29	30	35	35
11	29	19	36	27	30	25	35	25
12	30	22	37	28	31	26	36	26
13	31	19	39	30	30	27	36	31
14	30	17	37	25	29	15	35	35
15	29	16	36	30	28	20	34	25
16	28	14	30	25	27	20	33	30
17	27	13	32	25	26	19	32	25
18	26	13	31	25	25	20	31	35
19	25	14	30	24	24	10	30	30
20	24	20	29	24	23	19	29	30
21	23	19	28	30	22	20	28	29
22	22	25	27	25	21	21	27	28
23	21	17	26	35	20	20	26	27
24	20	15	25	24	19	25	25	35

Figure 4 depicts the motor-UPDRS tracking over 6-month trial for one of the subject using IRLS and CART and Figure 5 depicts the total-UPDRS tracking over 6-month trial for one of the

subject using IRLS and CART. The blue colour (rhombus dot) denotes the actual linearly interpolated UPDRS value and the red colour (square dot), predicted UPDRS. From the figure 4 and figure 5, it is clearly shown that the predicted UPDRS is more or less close to actual UPDRS for CART method than IRLS. CART attains the smallest prediction error and tracks the PD symptom progression more accurately than IRLS.

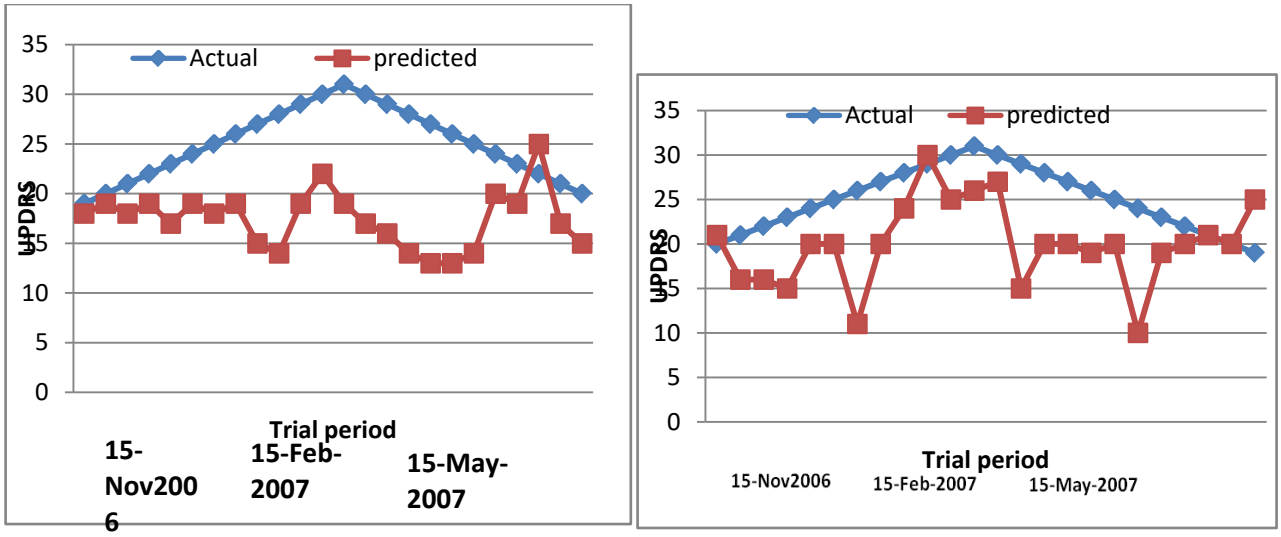

Fig 4. Motor-UPDRS Tracking for IRLS and CART

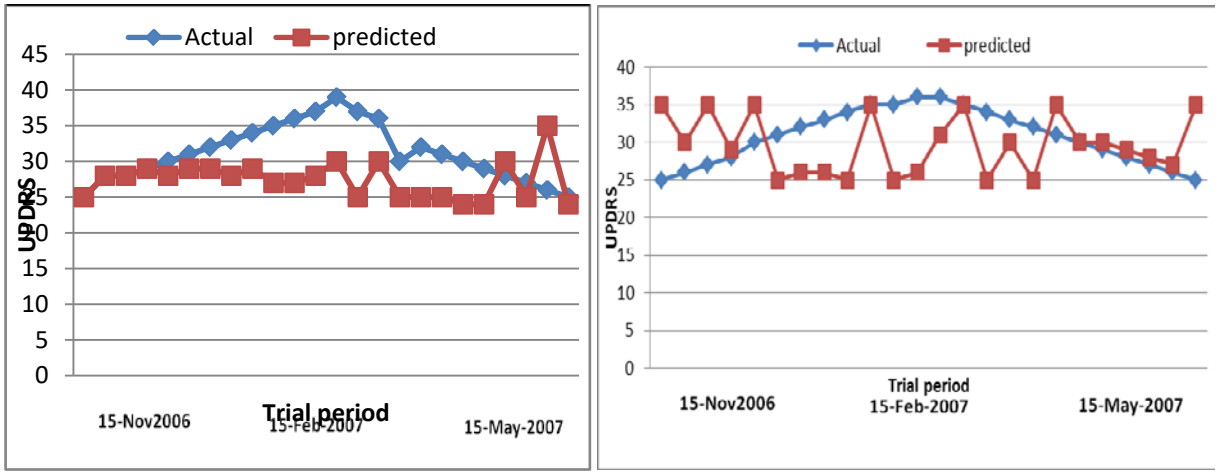

Fig 5: Total-UPDRS Tracking for IRLS and CART

7. CONCLUSION

PD targets the elderly population who show very slow response to treatment at advanced stages of the disease. Dysphonia measure of voice signal, an earliest indicator for PD is used for predicting and tracking the progression of PD Symptoms (UPDRS). Both statistical regression methods, IRLS and CART are used to evaluate motor and total UPDRS scores for the prediction of PD. The performance of IRLS and CART are studied for PD monitoring and UPDRS tracking for six months. The testing error remains low and nearer to the training error. This indicates that the model has achieved a reasonable estimate of the performance. Although IRLS performance is better, CART outpaces it, displaying the smallest deviation from the interpolated score.

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