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Application of Artificial Neural Network to Live Predict Brain Lesions like Multiple Sclerosis, Glioma, Glioblastoma and Metastases and Superiority of Refractive Index Over other Parameters

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ABSTRACT

Artificial Neural Network an extremely authoritative method of Supervised Machine Learning was applied to detect the different pathological lesions in the brain, like multiple sclerosis MS, glioma of different grades and metastasis. Structural changes in the brain lesions may be noticed in MR images. MR spectroscopic graph may be informative to some extent but is not so easy to diagnose the disease accurately always. Use of ANN helps identifying the condition in doubtful cases. ANN train different data collected from various patients such as – Refractive Index, T2 relaxation values, Apparent Diffusion Coefficient (ADC), Creatine (CR), Choline (CHO), NAA (N-Acetyl Aspartate), ratio of CR/NAA, LIP/LAC (Lipid/lactate), MI (Myoinositol), CHO/CR and T2 value in the periphery of lesion. Prediction by ANN after training the data, shows high accuracy in diagnosis. RI was found to be unique and most accurate amongst these parameters.

Keywords: Artificial Neural Network (ANN); Magnetic Resonance Imaging (MRI); Metabolites of MR Spectroscopy; Refractive Index (RI); Independent Numeric and dependent Variable; Prediction.

1 Introduction

For proper treatment of different brain lesions correct diagnosis is needed. Tissue discrimination is not possible by noting the morbid changes in the MR images only without performing a brain biopsy (Figure1) [1,2]. Glioma in different stages, Glioblastoma, metastasis from primary cancer site and benign diseases like multiple sclerosis (relapsing remitting or tumefactive multiple sclerosis) sometimes create confusion [2]. Even MR Spectroscopy (MRS) fails to detect the exact character of the lesion from the graph generated by the peak of different metabolites along with the quantity [3,4].

1.1 Artificial Neural Network (ANN)

Live prediction of the lesions or characterization of the tissue is possible by data analyzing method of ANN [5]. From the prior research work of the authors [6-8] data like Refractive indices (RI) , T2 relaxation and Apparent Diffusion Coefficient (ADC) values determined from the MRI and different

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chemical metabolites available from the MRS like N Acetyl Aspertate (NAA), Choline (CHO),Creatine(CR), Lipid (Li), Lactate (La) Myoinisitol(MI) along with ratio of these metabolites have been tabulated [4]. These data were used as input for ANN to get output value or prediction of lesions [6-10].

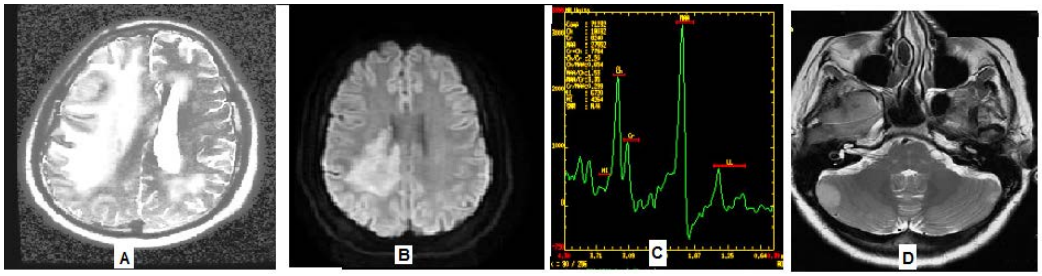


Figure 1. a-Glioblastoma b. Diffusion weighted image of Tumefactive MS mimicking Tumor c. MRS of MS. d. Lesion in the right cerebellar hemisphere-diagnosed as metastasis, biopsy shows benign lesion.

2 Background of ANN

ANN, one of the important strategies of Supervised Machine Learning was implemented as data analyzing method for live prediction of diseases [11]. In the Excel spread sheet the data collected were tabulated as inputs column (**Independent numeric variables**) and rows and **Dependent variable** to be predicted as disease or different tissues in the extreme left of the column. If the supporting data are available ANN can predict the diseases 95 to 98% correctly [12]. Program of Neural network includes artificial intelligence to analyze the data by applying algorithms that replicate basic brain neuronal (cortical cell) functions to study the structure of data and to discriminate data patterns [13] . This is regarded as training of the Data Set. New information then can be utilized by the program of ANN to predict the output of problems using "untrained data".

2.1 Prediction by ANN

PNN or Probabilistic Neural Network technique is a nonlinear method with training of a category dependent variables. A Probabilistic Neural Net will be trained. A "node" represents the element of the NET of the training case [10]. A prediction for a case with unknown dependent value is obtained by interpolation from training cases with neighbouring cases giving more weight after dividing the data set into training and testing subsets[11-14].

Optimal interpolation parameters were found during training [11]. It was implemented to assess the virtual pathological condition from the data obtained. ANN having amazing exceptionality in data analyzing and handling skill, nonlinearity and knowledge of simplification, was used to characterize or to classify the disease [8, 9]. Therefore multiple input nodes (ten) or independent numeric variables were used.

ANN represents one layer (hidden) having ten nodes [10]. It has output of 7 different nodes of brain tissue (such as gray and white matters, CSF) and diseases (or pathological abnormalities). These diseases were MS, low and high grade glioma and metastasis. By running the predict command specifies settings for predicting values were used with a trained neural net [11,12].

The data like T2 relaxation value, ADC values, metabolites generated directly from the MR Magnet and RI value determined by the Abbey Refractometer would be used as inputs. Output is the Dependent

numeric variables like diseases and tissues [6]. A schematic diagram is given in the Figure2 about the independent numeric variable and Dependent numeric variable [6, 9].

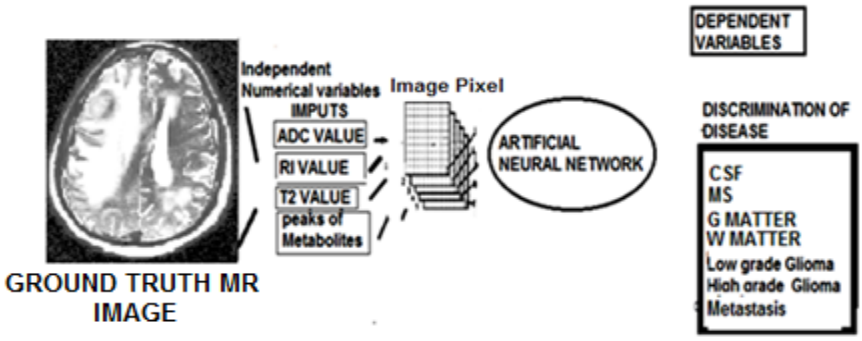


Figure 2. ANN for live prediction of diseases as Dependent variables using independent numerical variables as inputs [Ref 6].

2.2 To recapitulate the inputs and outputs [6]

2.2.1 Independent variables as inputs:

RI values ,T2 value ,ADC value ,Quantities of metabolites , (Choline,Creatine,MI ,NAA, Lipid/ lactate)

Ratio of Choline NAA ,Ratio of Creatine NAA,Ratio of Cho Cr

2.2.2 To live predict (Output or decision) :

Diseases like MS, Glioma, Glioblastoma (Grade III/IV Astrocytoma), metastasis and tissues like Gray /white matters, CSF are regarded as dependent variables [6,9].

3 Methods

After taking proper institutional ethics, 137 patients of different age (from 7 to 81 years) and gender were examined in a 3 Tesla MR Magnet (SIGNA HDxt, GE,USA). Materials collected from the Stereotaxic and post surgery biopsies were sent for histo-pathological diagnosis. At the same time following sets data or parameters were collected:

3.1 Parameters

3.1.1 RI Values

RI of tissues collected from biopsies of brain materials were determined by Abbe Refractometer (Suprashes Model AAR-33, India)[6-8]. RI map of a T2 weighted image (Figure 3.f) can be generated from the T2 values from a linear relationship between them. RI =4.338 X1/T2 value + 1.3338 [6,8].

3.1.2 T2 Relaxation Values

In the said 3T MR, T2 mapping was done with the help of multi ECHO read out train (with different echo times 30,60,90,120,150,180ms respectively) keeping a TR of 4000ms.T2 relaxation value of various brain tissue and brain lesions were generated from the map by exploiting the formula:

$S=S_0\, e^{-TE/T2}$ [8]. T2 map was thus generated by the inbuilt program (tool) of the MR Scanner. By placing the cursor in the Region of Interest (ROI), T2 values of the gray/white matter, CSF and tumours were determined from the T2 map as well [6] (Figure 3a). T2 values within the tumour and in the perilesional edema was also noted [6].

3.1.3 ADC (APPARENT DIFFUSION COEFFICIENT)

By making ADC map in the MR magnet, ADC values of the tissues are measured applying Stejstal-Tanner Equation $S=S_0e^{(-b.ADC)}$, which measure rate of diffusion of water within the tissues in units of mm^2/sec (Figure3c) . The ***b-value*** is a factor that reflects the strength and timing of the gradients used to generate diffusion-weighted images. S is the signal intensity [6,9,10] (Figure3b).

3.1.4 Metabolites Quantification of MR Spectroscopy (MRS)

Quantification of metabolites like CHO,CR,NAA,MI, Lipid, Lactate, CHO NAA,CHO CR and CHO NAA ratio were determined by single or multi voxel Spectroscopy applying PRESS technique. TR- 9602 and TE-35 to 144ms were used [3,4,6,9] (Figure3d)

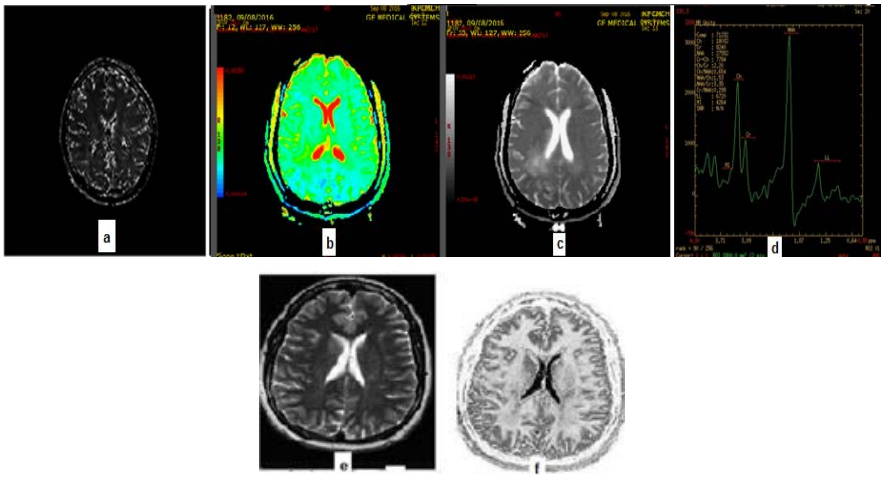


Figure 3a. T2 Mapping b. ADC Mapping c. DWI image d. MRS showing quantification of metabolites e. T2W and f. RI mapping of Brain

The values were then tabulated (Table1) in the Excel Spread Sheet for the application of **NEURAL TOOL 7.5** (Palisade Inc. UK). Column A to K represents independent variables and L depicts dependent variable or diseases.

3.1.5 Ground Truth MR Input Image

Therefore a **Ground Truth MR image** contains information like RI values (derived from RI mapping), T2 values (from T2 mapping) and ADC values (from ADC mapping) and metabolites from the MRS quantification (Table1) [6,7].

TABLE 1. Data of RI, T2, ADC Value,CHO, CR, CR/ NAA,CHO/NAA,CH/CR from Column A to K as Independent Variable and column L represent Dependent variable as Diseases . A column has influence on the L column or disease/tissues outcome

	A	B	C	D	E	F	G	H	I	J	K	L
1	RI	T2	CHO	ADC	CR	CR/NAA	LIP/LAC	MI	CH/CR	T2peri	CHO/NAA	DISEASE
2	1.3333	400	1010	300	1400	0.346	1400	910	1.13	400	0.402	CSF
3	1.3334	395	1680	320	1800	0.367	1760	1056	1.14	395	0.412	CSF
4	1.3335	390	1700	330	1967	0.389	1600	1076	1.15	390	0.432	CSF
5	1.3336	384	1890	340	1989	0.411	1675	1080	1.14	384	0.498	CSF
6	1.3421	340	11750	145	8320	0.557	4160	2912	1.40	240	0.779	MS
7	1.3439	328	8904	135	2800	0.433	4490	5576	3.15	241	1.39	MS
8	1.3498	316	7896	124	4560	0.225	3570	3536	1.73	243	0.389	MS
9	1.3497	304	5947	120	5400	0.7396	6766	4294	1.1	245	0.389	MS
10	1.3589	249	3448	75	3320	0.7112	5423	2322	1.02	230	0.821	MS
11	1.3641	245	1610	73	2212	0.941	1440	364	0.495	227	0.465	MS
12	1.3956	130	1601	76	2209	0.938	1441	363	0.491	166	0.461	g.matter
13	1.3956	125	1601	77	2208	0.937	1440	362	0.491	168	0..460	g.matter
14	1.3957	123	1589	78	2219	0.941	1467	345	0.491	167	0.459	g.matter
15	1.3952	121	1458	80	2320	0.878	1443	321	0.494	169	0.456	g.matter
16	1.4251	95	1180	70	2443	0.788	1345	312	0.488	148	0.453	w.matter
17	1.4256	89	1108	71	2435	0.771	1341	320	0.468	146	0.447	w.matter
18	1.4259	85	1098	77	2387	0.774	1211	321	0.467	150	0.445	w.matter
19	1.3741	160	1231	84	2216	0.776	1123	325	0.467	246	0.443	edema
20	1.3823	182	1331	180	2321	0.787	1011	321	0.456	243	0.442	edema
21	1.3821	182	1298	128	2314	0.781	1009	314	0.454	244	0.441	edema
22	1..3822	184	1444	131	2310	0.778	1001	313	0.445	245	0.441	edema
23	1.4331	90	1443	127	2243	0.766	989	310	0.423	175	0.431	GLIOMA
24	1.4446	99	1.365	177	2254	0.712	917	300	0.343	170	0.341	GLIOMA
25	1.4551	110	2655	156	2112	0.678	900	311	0.311	195	0.332	G.BLASTOMA
26	1.4512	116	2774	142	3280	1.06	2240	312	0.844	190	0.907	G.BLASTOMA
27	1.4562	118	2661	140	3189	1.02	2134	314	0.7881	185	0.89	G.BLASTOMA
28	1.4611	123	1281	139	2998	1.01	2098	316	0.7662	175	0.876	G.BLASTOMA
29	1.4768	135	1321	127	2532	0.654	1011	340	0.432	200	0.432	METS
30	1.4834	147	1388	139	2211	0.667	1021	341	0.445	219	0.411	METS
31	1.4911	151	1411	131	2019	0.713	119	356	0.449	223	0.423	METS

NOTE: MS= Multiple sclerosis g. matter-Gray Matter w. matter=White matter

G BLASTOMA= Glioblastoma METS= Metastases

3.2.1. Neural Network [11,12,13,14]

Trial version of Neural Tool 7.5 (Palisade Inc) was applied to perform the prediction. The method of working of the Neural Tool is shown in the Figure.4.

1. In the Excel spread sheet the values derived from the ground truth MR images are tabulated (Table 1) in such a way that the Dependent Variables (disease or tissues) remain in the extreme left column (L column) and Independent Numeric variable (Usually RI, T2, ADC values, Choline : NAA ratio etc) in the right side of the column (A through K).The efficacy of the parameter in the A column clearly influences the accuracy of prediction rate.

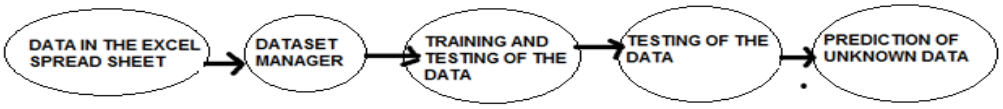


Figure 4. Steps of events occuring in Neural net work

3.2.2 A **data set manager** was created from the values tabulated in the excel spread sheet (Figure 5).

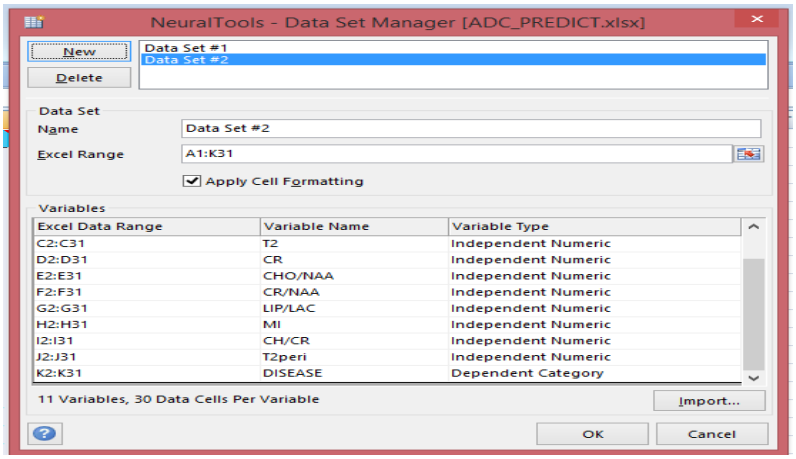
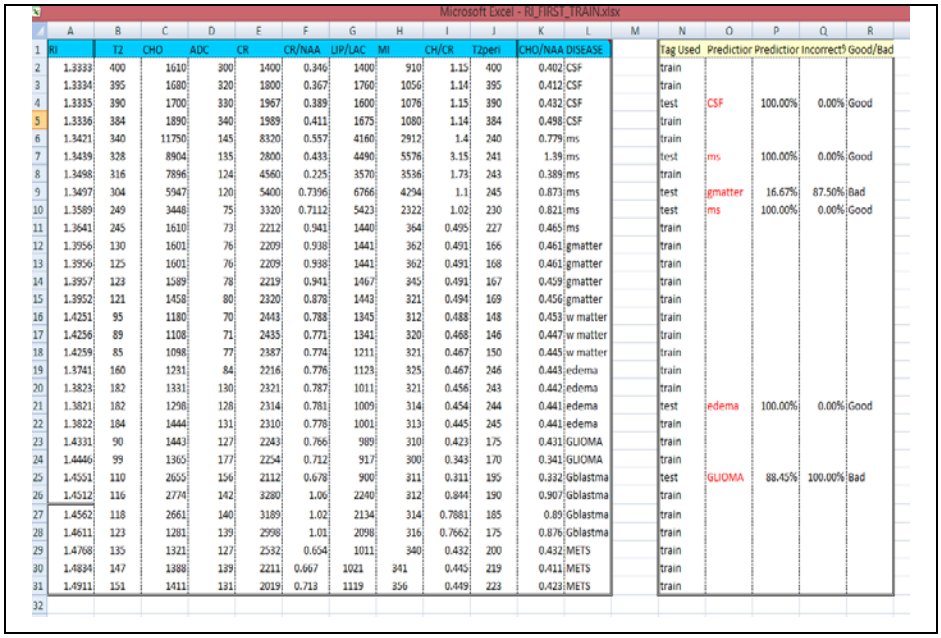


Figure 5. Data set manager [13].

3.2.3. Training and Testing

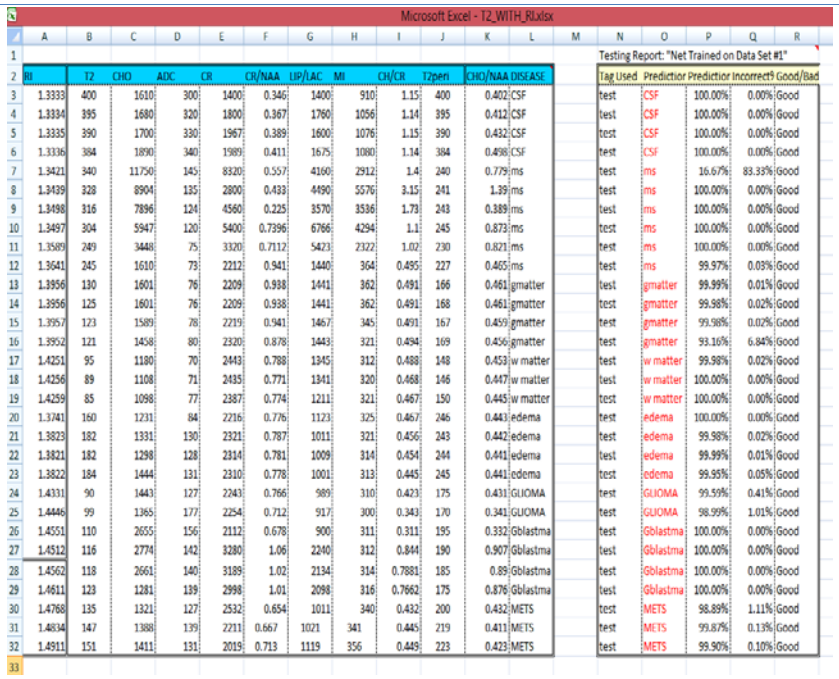
Training and testing of the data of the table were executed keeping RI, T2, ADC values, CHO, CHO /CR, CHO / NAA ratio one by one in the "**A"** column (Extreme right side of the table) and running the NET to assess the effectiveness of the parameters as efficacy of the parameters may vary (Figure 6 and 7). 12 independent variables (Table 2) of different parameters were kept away from the training.



Microsoft Excel - RI_FIRST_TRAIN.xlsx

RI	T2	CHO	ADC	CR	CR/NAA	LIP/LAC	MI	CH/CR	T2peri	CHO/NAA	DISEASE		Tag Used	Predictior	Predictior	Incorrect%	Good/Bad
1.3333	400	1610	300	1400	0.346	1400	910	1.15	400	0.402	CSF		train				
1.3334	395	1680	320	1800	0.367	1760	1056	1.14	395	0.412	CSF		train				
1.3335	390	1700	330	1967	0.389	1600	1076	1.15	390	0.432	CSF		test	CSF	100.00%	0.00%	Good
1.3336	384	1890	340	1989	0.411	1675	1080	1.14	384	0.498	CSF		train				
1.3421	340	11750	145	8320	0.557	4160	2912	1.4	240	0.779	ms		train				
1.3439	328	8904	135	2800	0.433	4490	5576	3.15	241	1.39	ms		test	ms	100.00%	0.00%	Good
1.3498	316	7896	124	4560	0.225	3570	3536	1.73	243	0.389	ms		train				
1.3497	304	5947	120	5400	0.7396	6766	4294	1.1	245	0.873	ms		test	gmatter	16.67%	87.50%	Bad
1.3589	249	3448	75	3320	0.7112	5423	2322	1.02	230	0.821	ms		test	ms	100.00%	0.00%	Good
1.3641	245	1610	73	2212	0.941	1440	364	0.495	227	0.465	ms		train				
1.3956	130	1601	76	2209	0.938	1441	362	0.491	166	0.461	gmatter		train				
1.3956	125	1601	76	2209	0.938	1441	362	0.491	168	0.461	gmatter		train				
1.3957	123	1589	78	2219	0.941	1467	345	0.491	167	0.459	gmatter		train				
1.3952	121	1458	80	2320	0.878	1443	321	0.494	169	0.456	gmatter		train				
1.4251	95	1180	70	2443	0.788	1345	312	0.488	148	0.453	w matter		train				
1.4256	89	1108	71	2435	0.771	1341	320	0.468	146	0.447	w matter		train				
1.4259	85	1098	77	2387	0.774	1211	321	0.467	150	0.445	w matter		train				
1.3741	160	1231	84	2216	0.776	1123	325	0.467	246	0.443	edema		train				
1.3823	182	1331	130	2321	0.787	1011	321	0.456	243	0.442	edema		train				
1.3821	182	1298	128	2314	0.781	1009	314	0.454	244	0.441	edema		test	edema	100.00%	0.00%	Good
1.3822	184	1444	131	2310	0.778	1001	313	0.445	245	0.441	edema		train				
1.4331	90	1443	127	2243	0.766	989	310	0.423	175	0.431	GLIOMA		train				
1.4446	99	1365	177	2254	0.712	917	300	0.343	170	0.341	GLIOMA		train				
1.4551	110	2655	156	2112	0.678	900	311	0.311	195	0.332	Gblastma		test	GLIOMA	88.45%	100.00%	Bad
1.4512	116	2774	142	3280	1.06	2240	312	0.844	190	0.907	Gblastma		train				
1.4562	118	2661	140	3189	1.02	2134	314	0.7881	185	0.89	Gblastma		train				
1.4611	123	1281	139	2998	1.01	2098	316	0.7662	175	0.876	Gblastma		train				
1.4768	135	1321	127	2532	0.654	1011	340	0.432	200	0.432	METS		train				
1.4834	147	1388	139	2211	0.667	1021	341	0.445	219	0.411	METS		train				
1.4911	151	1411	131	2019	0.713	1119	356	0.449	223	0.423	METS		train				

Figure 6. Screen shot image of Neural Tool data viewer showing training and testing of the data along with Training Report :Prediction accuracy with Good or Bad remark.



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1.3421	340	11750	145	8320	0.557	4160	2912	1.4	240	0.779	ms
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1.3589	249	3448	75	3320	0.7112	5423	2322	1.02	230	0.821	ms
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1.3956	130	1601	76	2209	0.938	1441	362	0.491	166	0.461	gmatter
1.3956	125	1601	76	2209	0.938	1441	362	0.491	168	0.461	gmatter
1.3957	123	1589	78	2219	0.941	1467	345	0.491	167	0.459	gmatter
1.3952	121	1458	80	2320	0.878	1443	321	0.494	169	0.456	gmatter
1.4251	95	1180	70	2443	0.788	1345	312	0.488	148	0.453	w matter
1.4256	89	1108	71	2435	0.771	1341	320	0.468	146	0.447	w matter
1.4259	85	1098	77	2387	0.774	1211	321	0.467	150	0.445	w matter
1.3741	160	1231	84	2216	0.776	1123	325	0.467	246	0.443	edema
1.3823	182	1331	130	2321	0.787	1011	321	0.456	243	0.442	edema
1.3821	182	1298	128	2314	0.781	1009	314	0.454	244	0.441	edema
1.3822	184	1444	131	2310	0.778	1001	313	0.445	245	0.441	edema
1.4331	90	1443	127	2243	0.766	989	310	0.423	175	0.431	GLIOMA
1.4446	99	1365	177	2254	0.712	917	300	0.343	170	0.341	GLIOMA
1.4551	110	2655	156	2112	0.678	900	311	0.311	195	0.332	Gblastma
1.4512	116	2774	142	3280	1.06	2240	312	0.844	190	0.907	Gblastma
1.4562	118	2661	140	3189	1.02	2134	314	0.7881	185	0.89	Gblastma
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1.4768	135	1321	127	2532	0.654	1011	340	0.432	200	0.432	METS
1.4834	147	1388	139	2211	0.667	1021	341	0.445	219	0.411	METS
1.4911	151	1411	131	2019	0.713	1119	356	0.449	223	0.423	METS

Tag Used	Prediction	Prediction	Incorrect%	Good/Bad
test	CSF	100.00%	0.00%	Good
test	CSF	100.00%	0.00%	Good
test	CSF	100.00%	0.00%	Good
test	CSF	100.00%	0.00%	Good
test	ms	16.67%	83.33%	Good
test	ms	100.00%	0.00%	Good
test	ms	100.00%	0.00%	Good
test	ms	100.00%	0.00%	Good
test	ms	100.00%	0.00%	Good
test	ms	99.97%	0.03%	Good
test	gmatter	99.99%	0.01%	Good
test	gmatter	99.98%	0.02%	Good
test	gmatter	99.98%	0.02%	Good
test	gmatter	93.16%	6.84%	Good
test	w matter	99.98%	0.02%	Good
test	w matter	100.00%	0.00%	Good
test	w matter	100.00%	0.00%	Good
test	edema	100.00%	0.00%	Good
test	edema	99.98%	0.02%	Good
test	edema	99.99%	0.01%	Good
test	edema	99.95%	0.05%	Good
test	GLIOMA	99.59%	0.41%	Good
test	GLIOMA	98.99%	1.01%	Good
test	Gblastma	100.00%	0.00%	Good
test	Gblastma	100.00%	0.00%	Good
test	Gblastma	100.00%	0.00%	Good
test	Gblastma	100.00%	0.00%	Good
test	METS	98.89%	1.11%	Good
test	METS	99.87%	0.13%	Good
test	METS	99.90%	0.10%	Good

Figure 7. Screen shot image of Neural Tool data viewer showing testing of the data along with Testing Report: Prediction accuracy as Good or Bad remark.

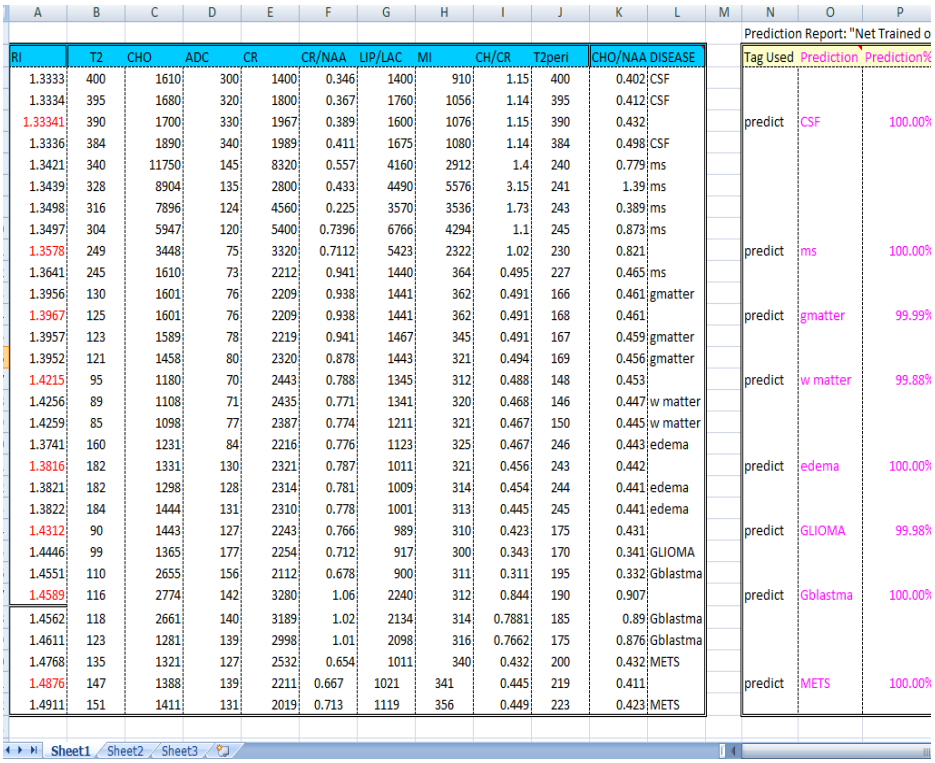
3.2.4. Prediction

After training and testing**,** untrained values (Table2) of RI,T2,ADC or metabolites of various diseases and tissues were put into the Column A one by one and net was run for prediction.

TABLE 2. Untrained Variables (in Red) to be used in the A column one after another to note the prediction accuracy.

T2	RI	CHO	ADC	CR	CR/NAA	LIP/LAC	MI	CH/CR	T2peri	CHO/NAA	DISEASE
387	1.33345	1704	333	1976	0.388	1589	1078	1.47	387	0.423	CSF
384	1.3338	1878	332	1987	0.414	1675	1084	1.42	378	0.489	CSF
331	1.3482	8878	134	2878	0.432	4491	5478	3.15	241	1.88	ms
311	1.3441	5975	122	5401	0.7389	6756	4289	1.11	244	0.874	ms
233	1.3611	1613	74	2211	0.913	1439	359	0.487	226	0.461	ms
119	1.387	1589	78	2219	0.941	1467	345	0.491	167	0.459	gmatter
87	1.4312	1154	74	2431	0.772	1342	319	0.479	144	0.441	wmatter
179	1.3823	1331	132	2315	0.777	1019	320	0.456	241	0.4429	edema
88	1.4321	1441	127	2231	0.775	978	311	0.421	177	0.432	glioma
100	1.4456	1323	167	2251	0.713	915	300	0.342	170	0.334	glioma
119	1.4566	2656	141	3178	1.03	2133	315	0.7868	182	0.887	gblastoma
141	1.4876	1320	129	2543	0.659	1011	332	0.435	210	0.431	mets

Prediction thus created by the Neural Tool was shown in the Figure 8a,b,c using different parameters like RI, T2 and ADC values and metabolites . To scrutinize the accuracy (percentage) of Prediction "untrained data set" of different variable in this Column **A** was tried one by one.

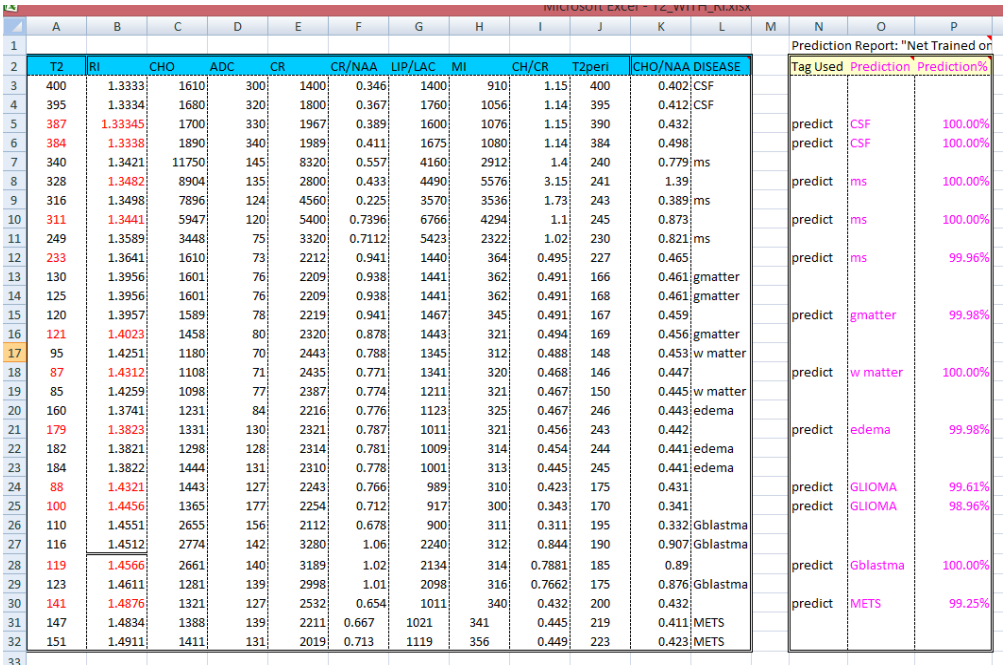


RI	T2	CHO	ADC	CR	CR/NAA	LIP/LAC	MI	CH/CR	T2peri	CHO/NAA	DISEASE
1.3333	400	1610	300	1400	0.346	1400	910	1.15	400	0.402	CSF
1.3334	395	1680	320	1800	0.367	1760	1056	1.14	395	0.412	CSF
1.33341	390	1700	330	1967	0.389	1600	1076	1.15	390	0.432	
1.3336	384	1890	340	1989	0.411	1675	1080	1.14	384	0.498	CSF
1.3421	340	11750	145	8320	0.557	4160	2912	1.4	240	0.779	ms
1.3439	328	8904	135	2800	0.433	4490	5576	3.15	241	1.39	ms
1.3498	316	7896	124	4560	0.225	3570	3536	1.73	243	0.389	ms
1.3497	304	5947	120	5400	0.7396	6766	4294	1.1	245	0.873	ms
1.3578	249	3448	75	3320	0.7112	5423	2322	1.02	230	0.821	
1.3641	245	1610	73	2212	0.941	1440	364	0.495	227	0.465	ms
1.3956	130	1601	76	2209	0.938	1441	362	0.491	166	0.461	gmatter
1.3967	125	1601	76	2209	0.938	1441	362	0.491	168	0.461	
1.3957	123	1589	78	2219	0.941	1467	345	0.491	167	0.459	gmatter
1.3952	121	1458	80	2320	0.878	1443	321	0.494	169	0.456	gmatter
1.4215	95	1180	70	2443	0.788	1345	312	0.488	148	0.453	
1.4256	89	1108	71	2435	0.771	1341	320	0.468	146	0.447	w matter
1.4259	85	1098	77	2387	0.774	1211	321	0.467	150	0.445	w matter
1.3741	160	1231	84	2216	0.776	1123	325	0.467	246	0.443	edema
1.3816	182	1331	130	2321	0.787	1011	321	0.456	243	0.442	
1.3821	182	1298	128	2314	0.781	1009	314	0.454	244	0.441	edema
1.3822	184	1444	131	2310	0.778	1001	313	0.445	245	0.441	edema
1.4312	90	1443	127	2243	0.766	989	310	0.423	175	0.431	
1.4446	99	1365	177	2254	0.712	917	300	0.343	170	0.341	GLIOMA
1.4551	110	2655	156	2112	0.678	900	311	0.311	195	0.332	Gblastma
1.4589	116	2774	142	3280	1.06	2240	312	0.844	190	0.907	
1.4562	118	2661	140	3189	1.02	2134	314	0.7881	185	0.89	Gblastma
1.4611	123	1281	139	2998	1.01	2098	316	0.7662	175	0.876	Gblastma
1.4768	135	1321	127	2532	0.654	1011	340	0.432	200	0.432	METS
1.4876	147	1388	139	2211	0.667	1021	341	0.445	219	0.411	
1.4911	151	1411	131	2019	0.713	1119	356	0.449	223	0.423	METS

Prediction Report: "Net Trained o

Tag Used	Prediction	Prediction%
predict	CSF	100.00%
predict	ms	100.00%
predict	gmatter	99.99%
predict	w matter	99.88%
predict	edema	100.00%
predict	GLIOMA	99.98%
predict	Gblastma	100.00%
predict	METS	100.00%

Figure8a. Screen shot image of Neural Tool data viewer showing Prediction using RI in the Column A.



T2	RI	CHO	ADC	CR	CR/NAA	LIP/LAC	MI	CH/CR	T2peri	CHO/NAA	DISEASE
400	1.3333	1610	300	1400	0.346	1400	910	1.15	400	0.402	CSF
395	1.3334	1680	320	1800	0.367	1760	1056	1.14	395	0.412	CSF
387	1.33345	1700	330	1967	0.389	1600	1076	1.15	390	0.432	
384	1.3338	1890	340	1989	0.411	1675	1080	1.14	384	0.498	
340	1.3421	11750	145	8320	0.557	4160	2912	1.4	240	0.779	ms
328	1.3482	8904	135	2800	0.433	4490	5576	3.15	241	1.39	
316	1.3498	7896	124	4560	0.225	3570	3536	1.73	243	0.389	ms
311	1.3441	5947	120	5400	0.7396	6766	4294	1.1	245	0.873	
249	1.3589	3448	75	3320	0.7112	5423	2322	1.02	230	0.821	ms
233	1.3641	1610	73	2212	0.941	1440	364	0.495	227	0.465	
130	1.3956	1601	76	2209	0.938	1441	362	0.491	166	0.461	gmatter
125	1.3956	1601	76	2209	0.938	1441	362	0.491	168	0.461	gmatter
120	1.3957	1589	78	2219	0.941	1467	345	0.491	167	0.459	
121	1.4023	1458	80	2320	0.878	1443	321	0.494	169	0.456	gmatter
95	1.4251	1180	70	2443	0.788	1345	312	0.488	148	0.453	w matter
87	1.4312	1108	71	2435	0.771	1341	320	0.468	146	0.447	
85	1.4259	1098	77	2387	0.774	1211	321	0.467	150	0.445	w matter
160	1.3741	1231	84	2216	0.776	1123	325	0.467	246	0.443	edema
179	1.3823	1331	130	2321	0.787	1011	321	0.456	243	0.442	
182	1.3821	1298	128	2314	0.781	1009	314	0.454	244	0.441	edema
184	1.3822	1444	131	2310	0.778	1001	313	0.445	245	0.441	edema
88	1.4321	1443	127	2243	0.766	989	310	0.423	175	0.431	
100	1.4456	1365	177	2254	0.712	917	300	0.343	170	0.341	
110	1.4551	2655	156	2112	0.678	900	311	0.311	195	0.332	Gblastma
116	1.4512	2774	142	3280	1.06	2240	312	0.844	190	0.907	Gblastma
119	1.4566	2661	140	3189	1.02	2134	314	0.7881	185	0.89	
123	1.4611	1281	139	2998	1.01	2098	316	0.7662	175	0.876	Gblastma
141	1.4876	1321	127	2532	0.654	1011	340	0.432	200	0.432	
147	1.4834	1388	139	2211	0.667	1021	341	0.445	219	0.411	METS
151	1.4911	1411	131	2019	0.713	1119	356	0.449	223	0.423	METS

Prediction Report: "Net Trained or

Tag Used	Prediction	Prediction%
predict	CSF	100.00%
predict	CSF	100.00%
predict	ms	100.00%
predict	ms	100.00%
predict	ms	99.96%
predict	gmatter	99.98%
predict	w matter	100.00%
predict	edema	99.98%
predict	GLIOMA	99.61%
predict	GLIOMA	98.96%
predict	Gblastma	100.00%
predict	METS	99.25%

Figure 8b. Screen shot image of Neural Tool data viewer showing Prediction using T2 in the Column A.

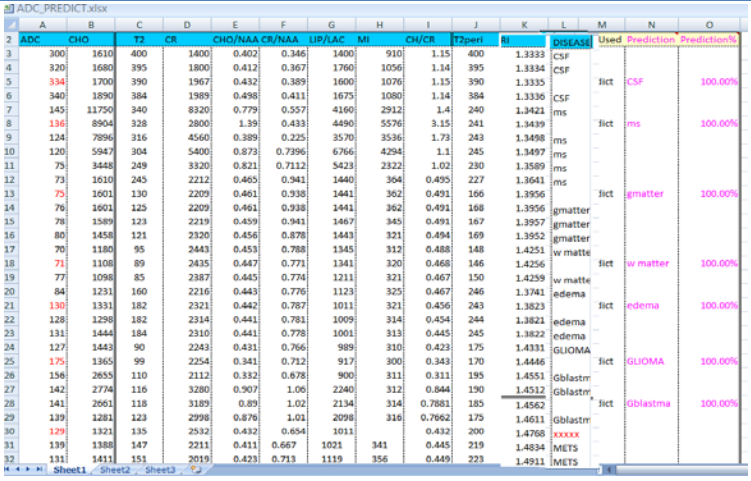


Figure 8c. Screen shot image of Neural Tool data viewer showing Prediction using ADC in the Column A.

4 Results and Discusion

4.1. It is evident that the 100 % prediction or characterization of tissue and pathological lesions when RI values are regarded as **independent numerical value** (in the column A) (Figure8 a). T2 also produces high accuracy. The prediction accuracy depends on the independent numeric variables or different physical or chemical parameters [6,13-16].

4.2. The NET depicts the statistical aspect of the prediction by RI in the Table 3. Minimum error was noted between 0.15 to 0.2 units. On the contrary, prediction is 20% to 60% in the context of ADC values (Figure8c) or Choline-Creatine ratio. Therefore the dataset had been trained in Neural Net and Auto tested in such a way that the wrong prediction reached the least amount and then the trained model data was run for testing (Table 3).

Table 3. Neural Tool : Net Training and auto testing

Location	This Workbook
Independent Category Variables	0
Independent Numeric Variables	**11 (RI, T2, CHO, ADC, CR, CR/NAA, LIP/LAC, MI, CH/CR, T2peri, CHO/NAA)**
Dependent Variable	Category Var. (DISEASE)
Training	
Number of Cases	24
Training Time	0:00:00
Number of Trials	108
Reason Stopped	Auto-Stopped
% Bad Predictions	0.0000%
Mean Incorrect Probability	0.0057%
Std. Deviation of Incorrect Prob.	0.0114%
Testing	
Number of Cases	6
% Bad Predictions	33.3333%
Mean Incorrect Probability	31.2500%
Std. Deviation of Incorrect Prob.	44.3412%
Data Set	
Name	Data Set #1
Number of Rows	30
Manual Case Tags	NO

4.3 Ten Fold Cross Validation

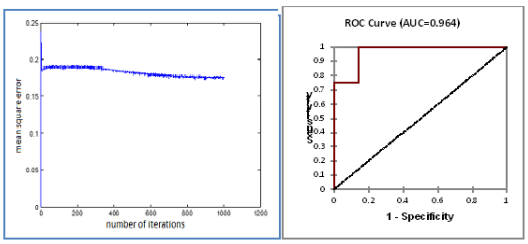
Cross-validation technique was adapted to evaluate predictive models by partitioning the original sample into a training set to train the model in relation to different samples of independent variable and a **test** set to evaluate it (Table4) [4,16,17].

10 fold cross validation method was used for wrong prediction, sensitivity and specificity and classification rate. The classification rate is quite high and very few blunders have been noticed in the prediction of test samples [11,12, 17]. Table 4 also discerns the consequent sensitivity and specificity. RI and T2 values produced the best results.

Table 4. Ten Fold Cross Validation [6]

Sample Number	In relation to different Independent Numeric variables	No. of incorrect Prediction (out of 24)	Classification Rate (in %)	Specificity (in%)	Sensitivity (in %)
1.	CR	4	83.33	86	78
2	CHO/NAA	3	87.5	91	76
3	T2 PERI	6	75.38	76.47	71.43
4	MI	4	83.33	87.5	75
5	RI	1	95.83	95	100
6	CHO/CR	3	87.52	85	100
7	ADC	3	87.55	88.89	83.33
8	T2	2	91.67	89.47	100
9	LIP/LAC	4	83.35	84.21	80
10	CHO	3	87.52	88.89	83.33

In most of the cases sensitivity is slightly lower than the specificity. However, in a few exceptional cases the sensitivity has reached 100% where all the diseased samples are identified. Hence, it can be concluded that the types of disease depend on RI and T2 values of the tissues, ADC values, metabolites like NAA, Choline, Creatine, Lipid and Lactate and their ratios [16,17]. From the Figure 9a it is noticed that the mean square error of the data during training decreases with iteration and finally becomes constant [6,17].



a b

Figure 9 a. Mean square error versus number of iteration b. Sensitivity versus specificity curve [6]

4.4 Pearson PHI(p Values)

Results derived from ANN was extracted statistically by **XLSTAT© (ADDINSOFT,** France**)** program to know "Correlation Tests" particularly of the continuous variables (for malignancies) and selected quantitative variables derived from the ground truth input images . **"p-values"** (Pearson Phi) [18] are shown in the Table 5a and b Figure 10.

Table5a. Correlations of the continuous variables (For malignancy) with the selected quantitative variables (Pearson's Phi) [6]:

Column2	Column3	Column4	Column5	Column6
Variable labels	Correlation coefficient	Test value	p-values	Variable labels
RI	0.687	4.261	0.000	RI
T2	-0.606	3.373	0.001	T2
MI	-0.249	0.750	0.230	MI
CH/CR	-0.247	0.741	0.233	CH/CR
LIP/LAC	-0.224	0.585	0.282	LIP/LAC
CR/NAA	0.210	0.495	0.313	CR/NAA
CHO	-0.116	-0.209	0.582	CHO
CR	-0.090	-0.443	0.669	CR
CHO/NAA	-0.064	-0.726	0.762	CHO/NAA
ADC	0.041	-1.043	0.846	ADC

Table 5.b p-values (Pearson)/ Group 1 Correlation test between the variables :

p-values (Pearson) / Group 1:

Variables	ADC	CHO	CR	CH/CR	CHO/NAA	CR/NAA	LIP/LAC	MI	RI	T2
ADC	**0**	0.861	0.733	0.599	0.600	0.603	0.687	0.221	0.557	0.508
CHO	0.861	**0**	0.469	0.485	0.447	0.509	0.401	0.292	0.176	0.240
CR	0.733	0.469	**0**	**0.010**	**0.011**	**0.010**	**0.005**	0.620	0.733	0.515
CH/CR	0.599	0.485	**0.010**	**0**	**0.001**	**0.000**	**0.009**	0.531	0.820	0.618
CHO/NAA	0.600	0.447	**0.011**	**0.001**	**0**	**0.003**	**0.006**	0.505	0.785	0.592
CR/NAA	0.603	0.509	**0.010**	**0.000**	**0.003**	**0**	**0.012**	0.551	0.841	0.632
LIP/LAC	0.687	0.401	**0.005**	**0.009**	**0.006**	**0.012**	**0**	0.538	0.693	0.500
MI	0.221	0.292	0.620	0.531	0.505	0.551	0.538	**0**	0.791	0.914
RI	0.557	0.176	0.733	0.820	0.785	0.841	0.693	0.791	**0**	0.052
T2	0.508	0.240	0.515	0.618	0.592	0.632	0.500	0.914	0.052	**0**
Values in bold are different from 0 with a significance level alpha=0.05										

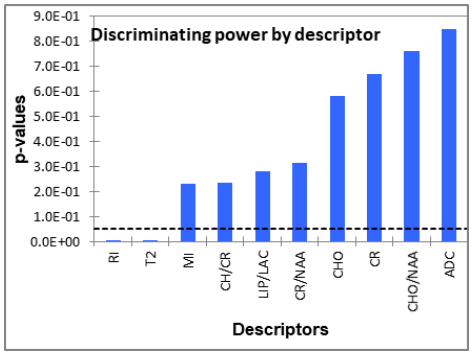
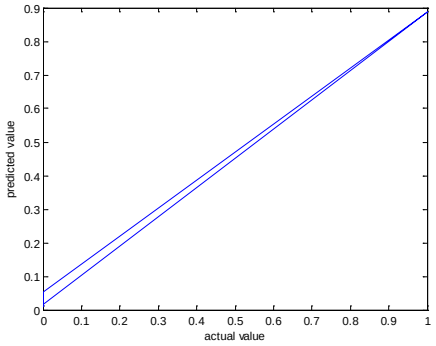


Figure10. p- values and discriminating power by descriptors[6]

4.5 Sensitivity and Specificity in ANN

From the results it has been found that Sensitivity is 87 to 89% whereas specificity is around 93 to 95%.From the various input data a presumptive diagnosis could be made which could be of immense help for the management of the patients [6] (Figure9b).



b

Figure 11. Actual versus predicted value in relation to RI [6]

4.6 Relationship of Predicted versus Actual Values

In this data set there are 240 samples. In this figure only one of them (RI—variable) has been plotted. The plot shows the number of prediction of disease (diagnosis) versus number of actual histopathological diagnosis from biopsy in the curve. Similar curves can be obtained for other samples as well. From the graph (Figure 11) it is observed that the actual and predicted values generate a straight slope.

5 Conclusion

ANN, an important data analytical process of Supervised Machine Learning method helps differentiating different disease process and brain tumors. To discriminate different issues in this regard, RI was regarded as superior to all other parameters like T2 values, ADC values and important metabolites and their ratio. Thus a presumptive diagnosis can be made from the Data derived from the ground tooth images before the biopsy. ANN can reduce the frequency of Stereotaxic Biopsy and its potential hazards to patients [19].

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REFERENCES

[1] Taghpour Zahir SH, Rezaei sadrabadi Dehghani F, *Evaluation of Diagnostic Value of CT Scan and MRI in Brain Tumors and Comparison with Biopsy*, Iranian Journal of Pediatric Hematology Oncology 2011 ;1.(4):121-125

[2] Hagen T, Nieder C, Moringlane JR. Feiden W,Konig J, *Correlation of preoperative neuroradiologic with postoperative histological diagnosis in pathological intracranial process*. Der Radiologe, Nov 1995; 35(11):808-15

[3] Horská Alena and Barker Peter B., *Imaging of Brain Tumors: MR Spectroscopy and Metabolic Imaging*, Neuroimaging Clin N Am. 2010 ; 20(3): 293–310.

[4] Jansen JF, Backes WH, Nicolay K, Kooi ME. *1H MR spectroscopy of the brain: absolute quantification of metabolites*.Radiology2006; 240 (2): 318–32.

[5] Stuart J. Russell, Peter Norvig (2010) *Artificial Intelligence: A Modern Approach, Third Edition*, Prentice Hall ISBN 9780136042594.

[6] T K Biswas, R Bandopadhyay, A Dutta*, Validating The Discriminating Efficacy Of MR T2 Relaxation Value Of Different Brain Lesions And Comparison With Other Differentiating Factors: Use Of Artificial Neural Network And Principal Component Analysis*. The Internet Journal of Radiology. 2017 Volume 20 Number 1. ISPUB DOI**:** 10.5580/IJRA.52614

[7] Biswas TK, Gupta A. *Retrieval of true color of the internal organ of CT images and attempt to tissue characterization by refractive index : Initial experience. Indian Journal of Radiology and Imaging* 2002;12:169-178

[8] Biswas TK, Luu T *In vivo MR Measurement of Refractive Index, Relative Water Content and T2 Relaxation time of Various Brain lesions With Clinical Application to Discriminate Brain Lesions.* The Internet Journal of Radiology 2009;13(1).

[9] T K Biswas, S R Choudhury, A Ganguly, R Bandopadhyay, A Dutta, *Refractive Index As Surrogate Biological Marker Of Tumefactive And Other Form Of Multiple Sclerosis And Its Superiority Over Other Methods,* Internet Journal of Radiology, https://print.ispub.com/api/0/ispub-article/46167.

[10] Kono K*,* Inoue Y*,* Nakayama K*, et al. The role of diffusion-weighted imaging in patients with brain tumors.* AJNR Am J Neuroradiol 2001*;* 22*:* 1081–1088*.*

[11] G. James *Variance and Bias for General Loss Functions, Machine Learning* 2003; 51, 115135. (http://www-bcf.usc.edu/~gareth/research/bv.pdf

[12] Haykin S., *Neural Networks: A Comprehensive Foundation*, 2nd edition, Pearson Educ. Asia, Hong Kong, 2001.

[13] *Neural Network*,http://www.palisade.com/neuraltools/neural_networks.asp.

[14] Bishop C.M., *Neural Networks for Pattern Recognition*, Clarendon Press, Oxford, 1995.

[15] Jain Sparsh, Biswas Tapan K, Bandyopadhyay Rajib; *Diagnosis of Brain Lesions, Glioma, Multiple-Sclerosis and Metastases from MRI: An efficient classifier-aided method using Refractive Index as a surrogate Biological Marker*. Journal of Biomedical Engineering and Medical Imaging, 2018;5 (3) :19-26

[16] Samuel, Arthur*, Some Studies in Machine Learning Using the Game of Checkers*. IBM Journal of Research and Development,1959;Vol **3**(3): 210–229

[17] Stone, Mervyn, *Asymptotics for and against cross-validation*. *Biometrika* 1977;**64** (1): 29–35.

[18] Ronald L Wasserstein, Nicole Lazar. A *The ASA's Statement on p-Values: Context, Process, and Purpose* 2016; 70(2): *129-133.*

[19] Wells, S Lillian, *Stereotaxic Brain Biopsy*, https://neurosurgery.ufl.edu/residency/about-us/clinical-specialties/stereotactic-brain-biopsy/

