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Predicting Recurrence in Cervical Cancer Patients Using Clinical Feature Analysis

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Authors' contributions

This work was carried out in collaboration between all authors. Author RB responsible for the development of model for study and statistical analysis along with author CMS. Author SKS designed the draft of the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

The paper demonstrates an analytic approach for prediction of recurrence in the cervical cancer patients using a probabilistic model. The techniques used for classification and prediction are based on recognizing typical and diagnostically most important test features relating to cervical cancer. The main contributions of the research involve predicting the probability of recurrences in no recurrence (First time detection) cases. The conventional statistical and machine learning tools are applied for the analysis. The experimental study demonstrates the feasibility and promising the proposed approach for the said cause with real data.

Keywords: Cervical cancer; recurrence; no recurrence; probabilistic; classification; prediction; machine learning.

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1. INTRODUCTION

The cervical cancer is known as malignant a neoplasm of the uterine cervix. The main factor responsible is out of control growth of abnormal epithelial cells on the uterine cervix, which is the lower part of the uterus that opens into the vagina. The infection of cervical mucosa by human papillomavirus (HPV) with high oncogenic potential is considered a necessary cause, although not sufficient, for development of cervical cancer, being responsible for virtually all cases of the disease. Out of 100 known HPV genotypes, at least 15 of which can cause cancer of the cervix and other sites. The HPV 16 and 18, the two most common oncogenic types responsible for approximately 70% deaths throughout the world [1].

Cervical cancer is one of the leading causes of death in the world for women. In the past 30 years, however the number of deaths from cervical cancer has significantly decreased as many women getting regular Pap tests. According to the cancer research statistics (United States), in 2010 out of 11,818 women detected positive for cervical cancer, 3,939 died because of the disease. As per the statistics it is the 17th most common cause of casualty due to cancer.

2. BACKGROUND

According to K. Narayan, Fisher and D. Bernshaw, in advanced Cervical cancer patients, tumor volume and uterine body involved have independent diagnostic value. Potential prognostic factors considered were FIGO stages, volume of tumor, histology, age, cell diameter to detect the volume of tumor MRI was used and to check whether tumor invaded corpus uteri. The study involved the cases of 179 patients with the four clinical factors, FIGO stage, tumor diameter, corpus invasion and tumor volume were strongly positively correlated ($p<0.001$ in each case). It was concluded that in patients having advanced Cervical cancer, tumor volume and corpus invasion provided important prognostic information [2]. Narayan, Bern Shaw, Fisher also examined the case of 32 patients with stage and stage 2 Cervical cancer and compared MRI images with corresponding linear measurements. They also correlated clinical tumor diameter as a part of FIGO staging with MRI derived tumor volumes. Their aim of the study involved correlating the results obtained from MRI images recorded with the corresponding results to verify that the individual linear measurements, location and orientation of the tumor was the same with respect to both modalities [3]. In another study by T. Jobling, Narayan and R.J. Hicks aimed to assess whether positron emission tomography (PET) or Magnetic Resource Imaging (MRI) could obviate the need for surgical staging in patients with locally cervical carcinoma being planned for radiotherapy (RT). They concluded that positive predictive value of PET in the pelvis and para aortic region were sufficient to obviate lymph nodal sampling. Still requirement of sampling is needed to exclude small volume disease cranial to sites of abnormality on PET.MRI was not sufficient accurate for the staging of nodal. [4]. Sang-Young Ryu, Moon-Hong Kim and others worked on the detection of early recurrence with 18 F-FDG PET in patients with Cervical cases. They observed that 82 percent of recurrence was detected within 6-18 months after diagnosis, and 89 percent of recurrence occurred in FIGO stage IIB and Stage patients. It was concluded that 18-FDG PET was effective in detecting early recurrences in cervical cancer patients with no evidence of disease [5].In another study by James B Unger, Joseph, aimed to detect the recurrence of Cervical carcinoma in both symptomatic and asymptomatic women through FDG and PET scan test. 44 records of cervical patients were reviewed out of which 47 underwent post treatment whole body FDG scan in an attempt to detect recurrent disease. 26 scans were performed in asymptomatic women and 21 with symptoms of recurrence. As a result 30.8% of asymptomatic women had recurrent disease detected by PET compared with 66.7% of women in the symptomatic ones [6].

3. PATIENT SELECTION

This papers reports on methodologies and outcome of a study aiming at developing robust model to classify and predict probability of recurrence for cervical cancer in the patients.

The study aims to establish relationship between various clinical test features present in the dataset. The data of 237 patients including 82 cases of recurrence and 155 cases of no recurrence was analyzed. Each case was having attributes histology, FIGO test stages, clinical diameter, MRI (Magnet resonance imaging) volume, uterine body, primary, pelvic, abdomen, supra cavalry and distance test.

4. METHODS

The two hundred thirty seven patients were categorized as recurrence and no recurrence. The k nearest neighbor technique was used to predict the probability for each case using the attributes as mentioned in Table 1. Probability to be in class is calculated based on 'k' instances in the model that vote for an object to be in a given class.

Table 1. Patient characteristics

S no.	Attributes	Levels	No. of patients	%
1.	**Histology**			
		Endometroid	26	10.97
		SCC	204	86.07
		Clear Cell	5	2.10
		Serous	2	0.84
2.	**FIGO**			
		1b	69	29.11
		2a	34	14.34
		2b	81	34.17
		3a	9	3.79
		3b	43	18.14
		4a	1	0.42
3.	**Node PET +**			
		Yes	107	45.14
		No	130	54.85
4.	**Clinical diameter (cm)**			
		≥ 0.5 , ≤ 8.0	237	100
		Average=4.620		
5.	**MRI Vol (cc)**			
		≥ 0.07 , ≤ 628.32	237	100
		Average=55.91		
6.	**Uterine body**			
		Involved	169	71.30
		Not involved	68	28.69
7.	**Status**			
		Recurrence	82	34.59
		No Recurrence	155	65.40
8.	**Rel primary**			
		Yes	33	13.92
		No	204	86.07
9.	**Rel pelvic**			
		Yes	41	17.29
		No	196	82.70
10.	**Rel abdo**			
		yes	49	20.67
		No	188	79.32
11.	**Rel supra clav**			
		Yes	15	6.329
		No	222	93.67
12.	**Rel distant**			
		Yes	47	19.83
		No	190	80.16

(Datasource:http://www.igcs.org/files/TreatmentResources/CervicalCaDB/CervicalCancer_Narayan_IGCS.txt)

5. RESULTS

The analysis was done in R-statistics and following results were obtained.

5.1 Clinical Diameter

The recurrence cases (82) were having clinical diameter range from ≥ 2.0 cm to ≤ 8.0 cm. The mean value for the same was observed to be 5.0 cm. The predicted mean for probability of recurrence was 38%.

It was observed that for clinical diameter ≥ 5 cm the probability of recurrence was high (38% to 57%) compared to clinical diameter < 5 cm (20% to 32%).

The no recurrence cases (155) were having clinical diameter range from ≥ 0.5 cm to ≤ 8.0 cm .The mean value for the same was observed to be 4.41 cm. The predicted mean probability for recurrence was 32%.

5.2 MRI Volume

The recurrence cases (82) were having MRI volume from ≥ 2.88 cc to ≤ 628.32 cc. The mean value for the same was observed to be 75.21cc. The predicted mean for probability of recurrence was 47%.

The no recurrence cases (155) were having MRI volume from ≥ 0.07 cc to ≤ 269.55 cc. The mean value for the same was observed to be 45.69cc. The predicted mean for probability of recurrence was 27%.

5.3 Relationship between Probability of Recurrence and Clinical Diameter

The relationship analysis shows band wise increase in the probability of recurrence with an increase in the clinical diameter in various bands as shown in the Fig. 1 Same was observed for patients with recurrence and no recurrence as in Fig. 3 For patients with clinical diameter of 8 cm the probability of recurrence was observed to be more than 50% as can be seen in the Fig. 2 and Fig. 4 Although the number of cases differ in each set.

5.4 Relationship between Probability of Recurrence and Clinical Diameter

The relationship analysis shows band wise increase in the probability of recurrence with an increase in the MRI volume in various bands. High probability cases were observed for high MRI Volumes as shown in the Fig. 5, Fig. 6 and Fig. 7.

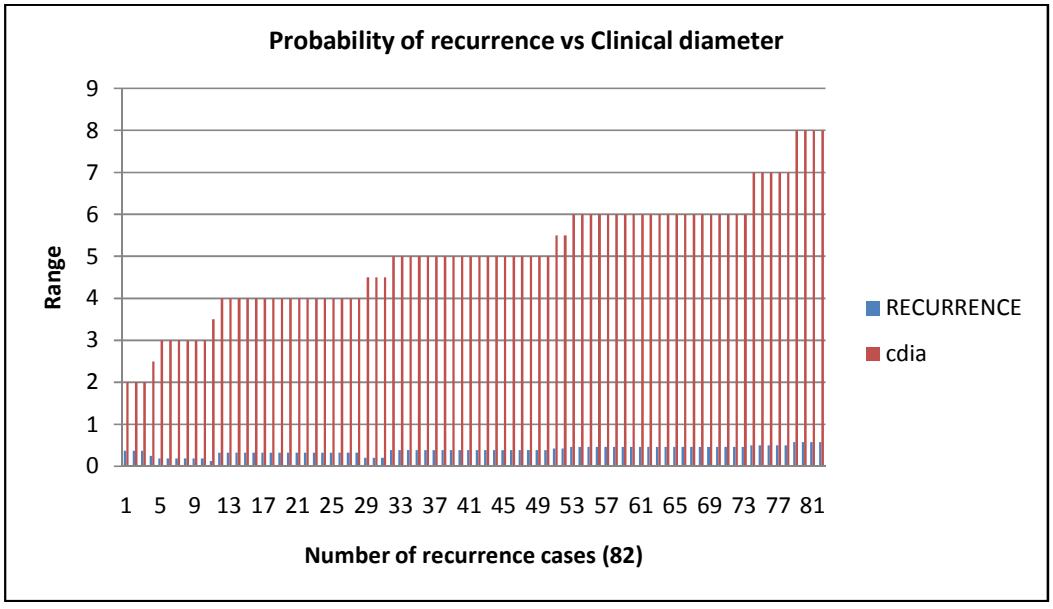

Fig. 1. Showing relationship between probability of recurrence and clinical diameter (sorted in ascending order)

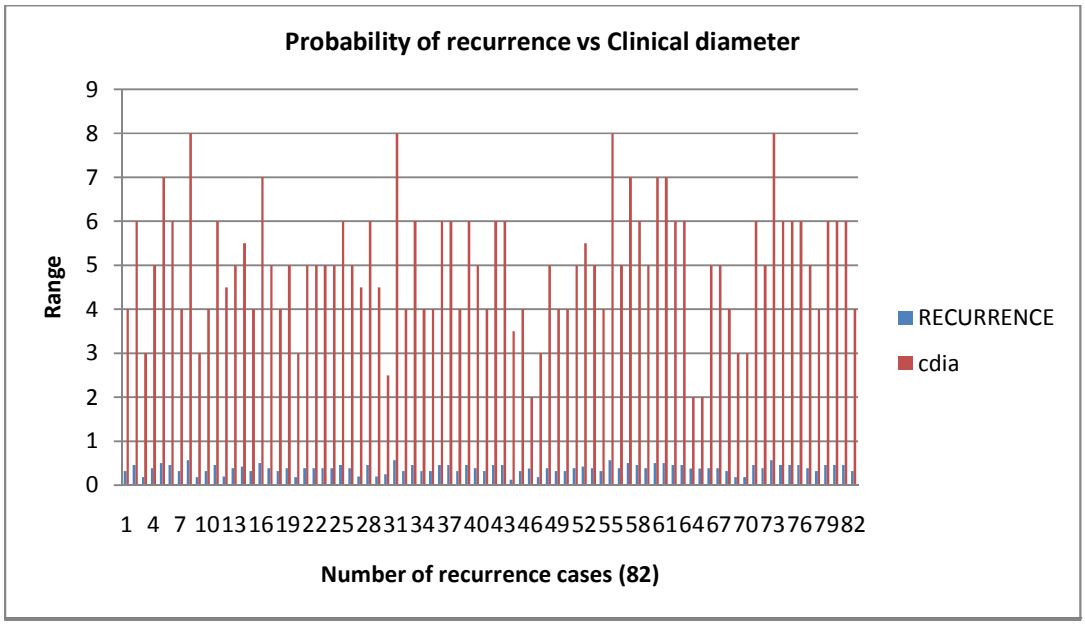

Fig. 2. Showing relationship between probability of recurrence and clinical diameter (unsorted).Four cases having clinical diameter of 8 cm were observed with probability of recurrence 57%

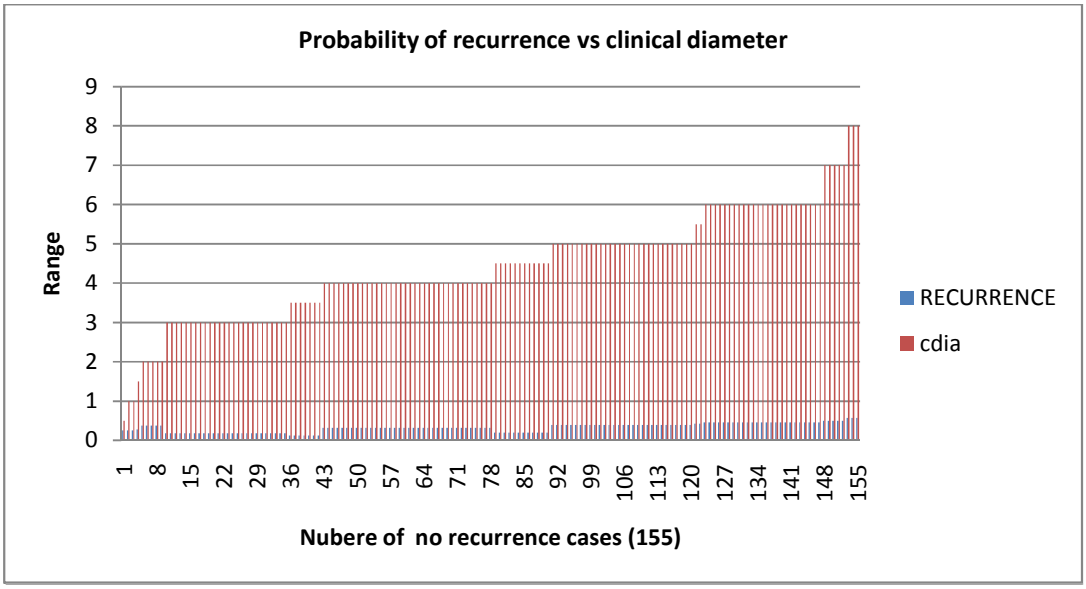

Fig. 3. Showing relationship between probability of recurrence and clinical diameter (sorted in ascending order)

5.5 Relationship between Clinical Diameter and MRI Volume

There was a close association between the Clinical diameter and MRI volume. High values for both contributed to high probability of recurrence in the observed cases as shown in Fig. 8, Fig. 9 and details in Table 2 confirms that cases with higher values for clinical diameter and MRI volume were having 57% average probability of recurrence.

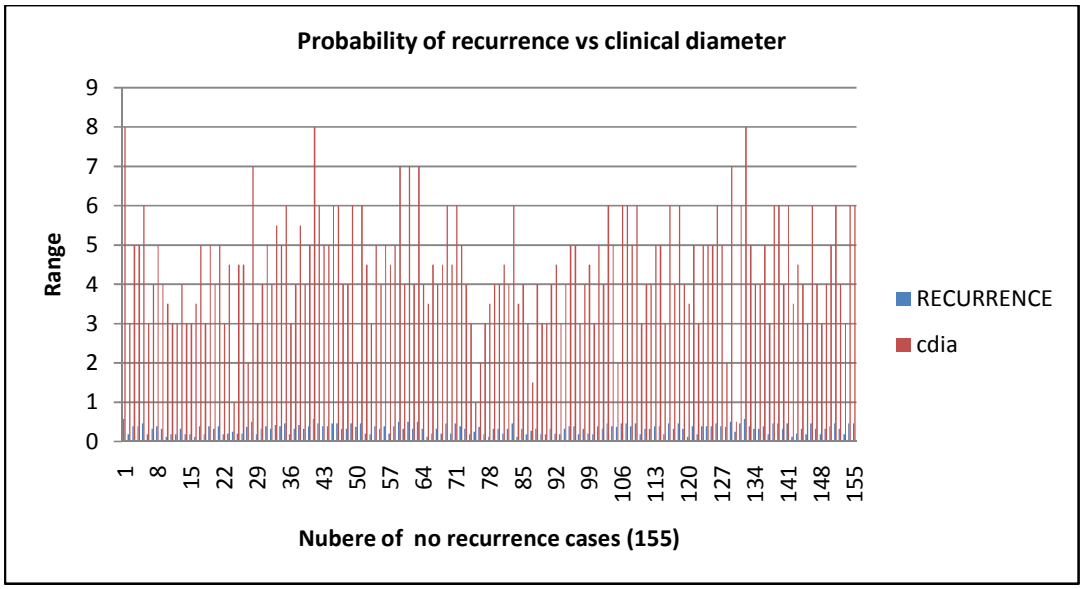

Fig. 4. Showing relationship between probability of recurrence and clinical diameter (unsorted).Three cases having clinical diameter of 8 cm were observed with probability of recurrence 57%

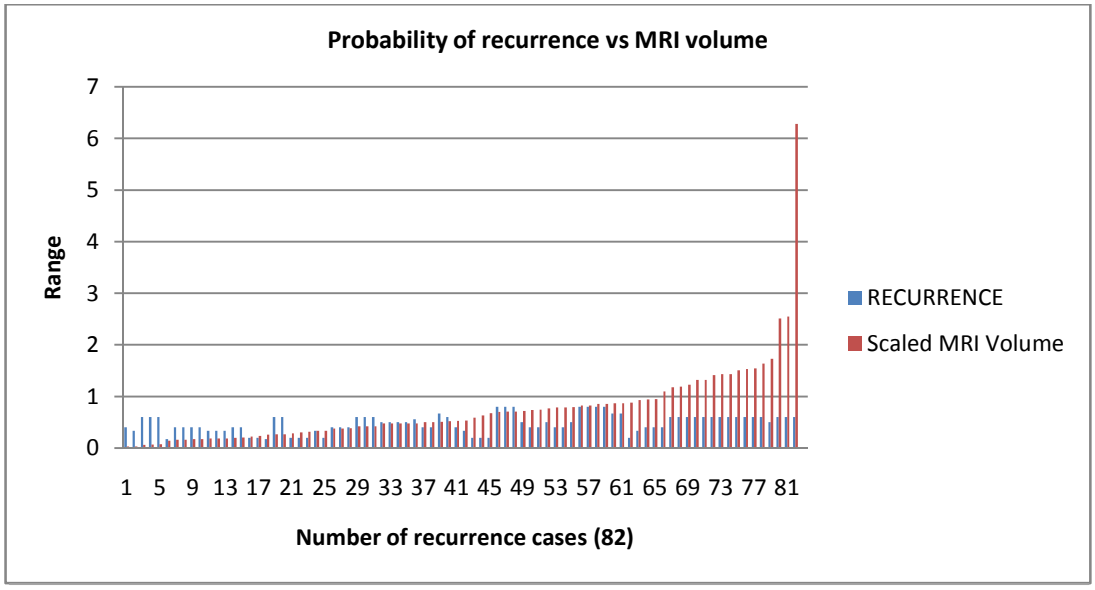

Fig. 5. Showing relationship between probability of recurrence and MRI volume (sorted in ascending order)

5.3 PET Node

From 155 cases of no recurrence, 53 were predicted against recurrence with a probability > 50% having PET node involved.

5.4 Primary Test

Recurrence predicted probability for 155 no-recurrence case was 0.24 compared to 49 cases of recurrence having negative value. Stressing that for positive primary test there is large probability towards recurrence.

5.5 Pelvic Test

Predicted probability for 41 recurrence cases for each was 0.21 with no pelvic section involvement and probability of 1 with the involvement.

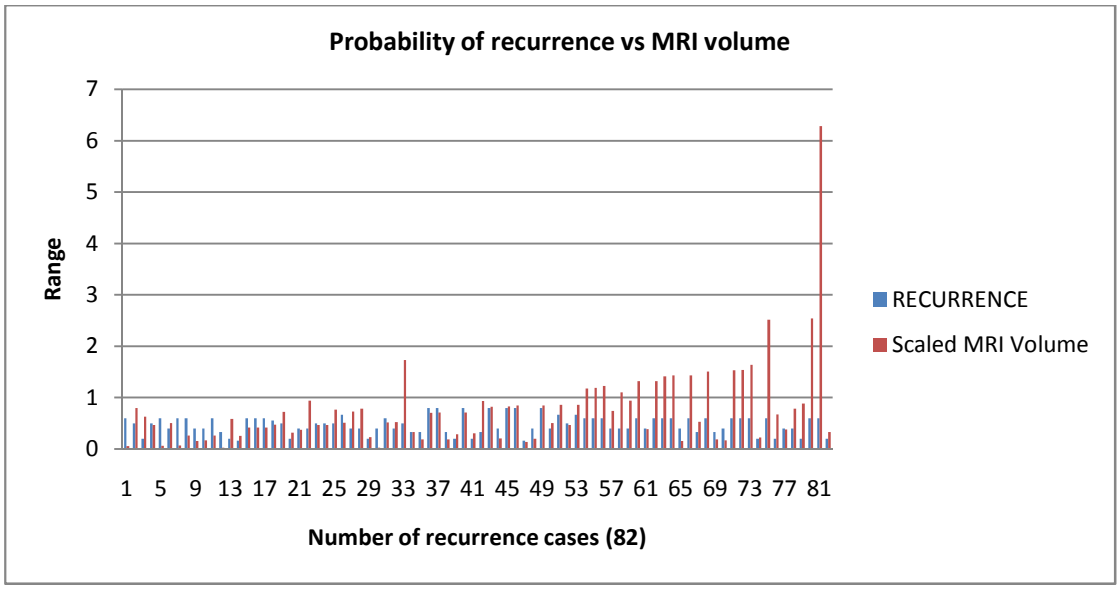

Fig. 6. Showing relationship between probability of recurrence and MRI volume (unsorted order)

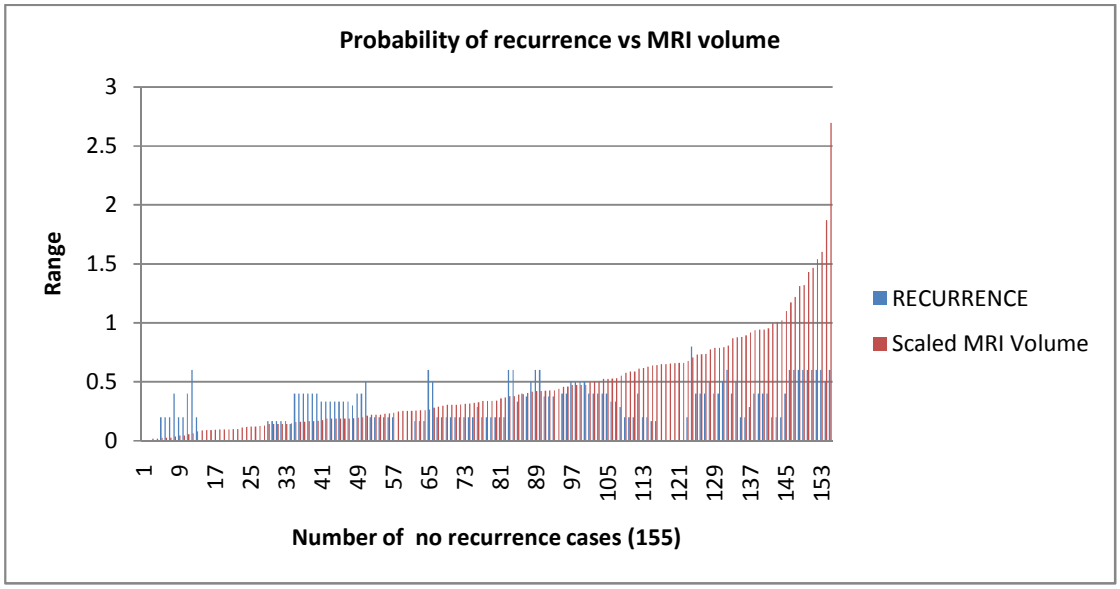

Fig. 7. Showing relationship between probability of recurrence and MRI volume (sorted in ascending order)

5.6 Abdomen Test

Predicted probability 0.175 was observed for 33 recurrence cases with abdomen test negative. Stressing that for a positive abdomen test there is large possibility of recurrence.

5.7 Supra Cavalry Test

Predicted probability for 15 recurrence cases was strongly supporting recurrence with supra cavalry test to be positive and for rest 67 cases in the absence of positive test the predicted probability was 0.30.

5.8 Distance Test

High predicted probability was noticed for 10 recurrence cases indicating high possibility of recurrence in those cases.

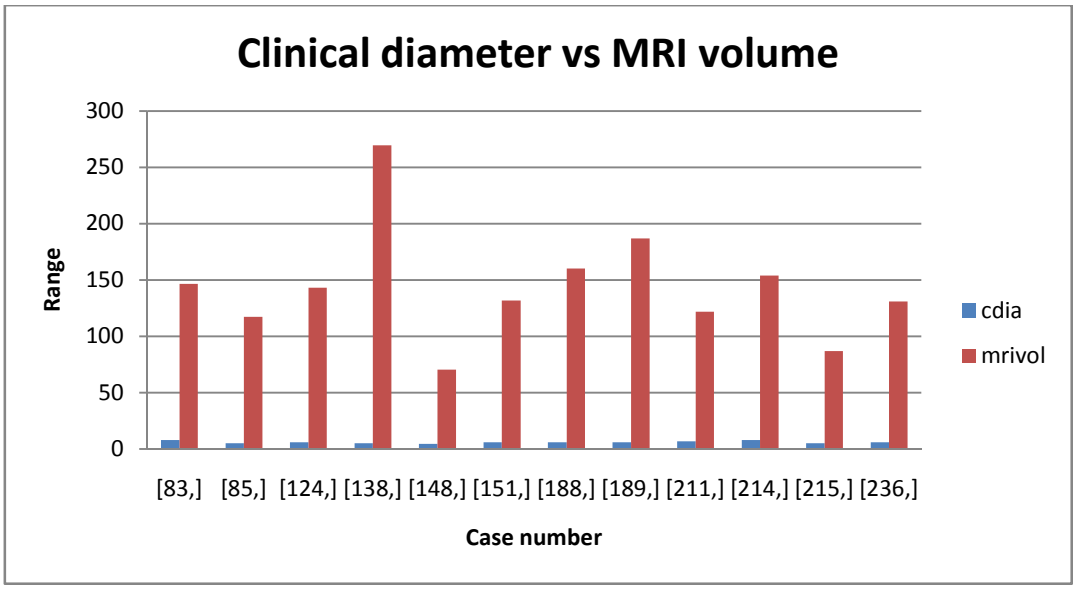

Fig. 8. Clinical diameter vs MRI volume for cases of no recurrence having recurrence probability >50%

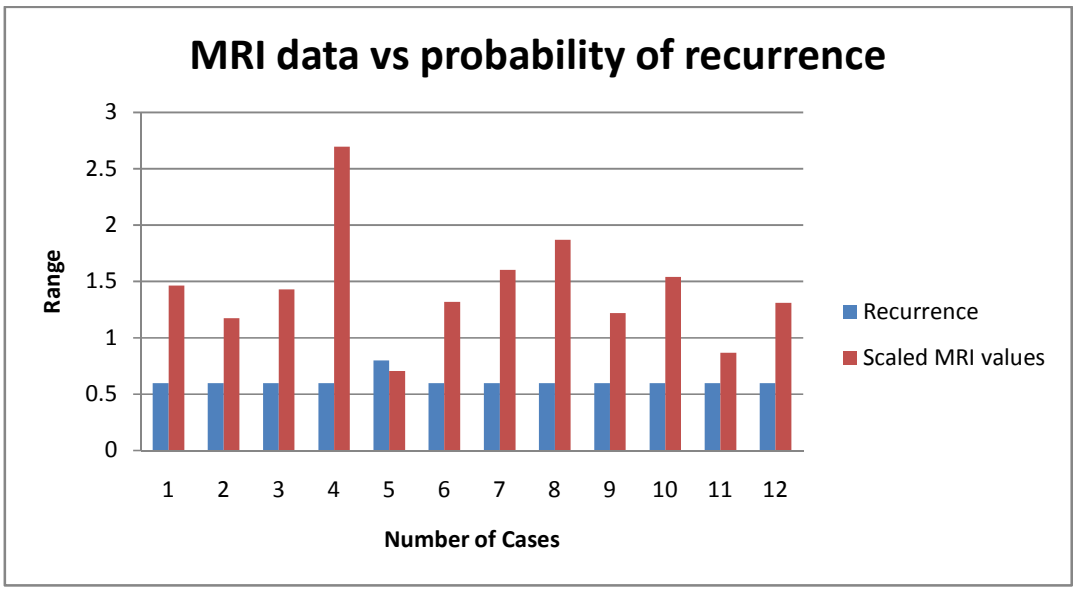

Fig. 9. Clinical diameter vs Scaled MRI volume for cases of no recurrence having recurrence probability >50%

Table 2. Showing relationship between clinical diameter and MRI volume with respect to probability of recurrence

S no.	Category	Number of case	Minimum clinical diameter	Maximum clinical diameter	Average clinical diameter	Average MRI volume	Average probability of recurrence
1.	Recurrence	82	2cm	8cm	5cm	75.21cc	38%
2.	No recurrence	155	0.5cm	8cm	4.41cm	45.69cc	32%
3.	No recurrence	3	8cm	8cm	8cm	129.50cc	57%
4.	No recurrence	152	0.5cm	7cm	4.34cm	44.04cc	32%

Table 3. Recurrence in twelve first time detection (no recurrence) cases with predicted probability >50%

S no.	Status	cdia	Prob. of recurrence	mrivol	figo	Histology	Node	ub	rpri	rpel	rabd	rsup	rdist
1.	No recurrence	8	0.6	146.61	1b	Clear cell	No	Involved	No	No	No	No	No
2.	No recurrence	5	0.6	117.29	2b	SCC	No	Involved	No	No	No	No	No
3.	No recurrence	6	0.6	142.94	3b	SCC	No	Involved	No	No	No	No	No
4.	No recurrence	5	0.6	269.55	1b	SCC	No	Involved	No	No	No	No	No
5.	No recurrence	4.5	0.6	70.69	2b	SCC	No	Involved	No	No	No	No	No
6.	No recurrence	6	0.6	131.95	3b	SCC	No	Involved	No	No	No	No	No
7.	No recurrence	6	0.6	160.22	3b	SCC	No	Involved	No	No	No	No	No
8.	No recurrence	6	0.6	186.98	2b	SCC	No	Involved	No	No	No	No	No
9.	No recurrence	7	0.6	121.8	2b	SCC	No	Not involved	No	No	No	No	No
10.	No recurrence	8	0.6	153.94	2b	SCC	No	Involved	No	No	No	No	No
11.	No recurrence	5	0.6	86.85	3a	SCC	Yes	Involved	No	No	No	No	No
12.	No recurrence	6	0.6	130.9	1b	Endometroid	No	Involved	No	No	No	No	No

6. CONCLUSION

1. Twelve no recurrence (first time detection) cases were predicted with probability > 50% for recurrence, mostly (10 cases) from histology category of SCC with no PET node involvement in (11) cases having uterine body involved in most cases (11). Remaining invasion attributes were negative for all the predicted cases as shown in Table 3.
2. The clinical diameter, MRI volume, PET node and uterine body are the most critical attributes for prediction of recurrence in cervical cancer. In other words higher the probability against these means more will be the probability for recurrence.
3. The probability of recurrence was predicted to be high (>50%) with clinical diameters >7cms.The average MRI volume for the same was observed to be 129.50cc.

CONSENT

Not applicable as the analysis of anonymised data in this context is done.

ETHICAL APPROVAL

Not applicable as the analysis of anonymised data in this context is done.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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