

## Applicability of Cytological Grading of Carcinoma Breast

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### ABSTRACT

**Background:** In India breast cancer incidence is on rise and large number of cases occur before 50 years of age. Early diagnosis and proper treatment are known to increase the survival of the patients. As fine needle aspiration cytology is widely used as a preliminary mode for the diagnosis of breast malignancies, adding a reliable grading system in reporting shall aid in planning the management options.

**Methods:** It's a prospective study done on 100 cases of breast malignancies from June 2018 to May 2020 in department of Pathology JLNMC, Ajmer. Cytology smears were stained with H&E and Geimsa and graded according to Robinson's cytological grading system while their corresponding histopathological sections were stained with H&E and graded as per Elston and Ellis modification of Scarff Bloom & Richardson grading system and the results were compared.

**Result:** Out of 100 cases of breast cancer evaluated in cytology 29% were grade I, 56% were grade II and 15% were grade III. On histopathological evaluation 25% were grade I, 54% were grade II while 21% were grade III. A highly significant association between the two grading systems was observed with coefficient of correlation 0.831, p value of <0.001 and concordance rate 80%.

**Conclusion:** There is high degree of concordance between the Robinson's and Elston and Ellis modification of Scarff Bloom & Richardson grading system. Robinson's method is an easy and quick and reliable method to grade carcinomas of breast, hence it should be included in cytology reporting of breast carcinomas.

**Keywords:** FNAC, H&E, MBR

### Introduction

Breast cancer is now vastly spread in both developed (794,000 cases) and developing regions (883,000 cases). It is the most common cancer among women, consisting of about 25% of all cancers (about 1.67 million newly diagnosed cases in 2012). It is the fifth most common cause of mortality from cancer, but mortality rate is much higher in developing regions. [1]

In 2012, about 144,937 new cases of breast cancers were diagnosed in India, which accounts for 27% of cancer cases along with mortality of 21.5% of all cancer cases. [2]

Breast cancer grade is a major determinant of prognosis. Fine-needle aspiration cytology (FNAC) which is widely used for the diagnosis of breast malignancies before planned surgery, is used only to differentiate benign from malignant and the morphology of tumour. [3]

The assessment of grading in cytology allows assessment of the tumor *in situ* which facilitates in deciding the most suitable treatment. Also, overtreatment of low-grade tumors can be avoided hence reduces the post treatment morbidity. [4]

Such grading would allow assessment of the tumor *in situ*, and the morbidity associated with over-treatment of low-grade tumors could be avoided. [4]

The grade predicts the outcome or prognosis. A lower grade usually means the cancer is slower-growing and less likely to spread. A higher grade means an aggressive tumour. [5]

Treatment is mainly determined by the Stage of tumour but as neoadjuvant therapy is now an integral part of primary treatment of breast cancer it makes grading of the neoplasm even more important than before by fine-needle aspiration cytology (FNAC). It is commonly done for early breast cancer, so knowledge about grade of the tumor before surgery is desirable. [6]

Cytological grading of breast cancer is not routinely done although grade of carcinoma is a widely evaluated entity in pathological specimens. [6]

Various cytological grading systems are: Robinson's, Mouriquand's, Hunt's, Simplified black's, Fisher's modification of black's nuclear grading, Khan's.

## Materials and Methods

This is a prospective study of two-year duration from June 2018 to May 2020 conducted in department of pathology JLN Medical College Ajmer (Rajasthan).

Study material comprised of 100 cases of mastectomy specimens received in the department and their corresponding cytology smears. Written informed consent was taken from all patients.

Sections were stained with Hematoxylin & Eosin and Smears were stained with Hematoxylin & Eosin and May Grunwald Giemsa; special stains were done wherever required.

On FNAC smears Robinson's cytological grading system [7-10] (Table 1) was used and on their corresponding histopathology sections Elston and Ellis modification of Scarff Bloom & Richardson grading system [11-14] (Table 2) was used and the results were correlated.

## Result

In the present study out of total 100 cases maximum cases (56%) belong to cytological grade II, followed by 29% cases in cytological grade I and least percentage of cases (15%) belonged to cytological grade III. While on histological examination 54% cases belong to Grade II, followed by 25% cases in histological grade I and least percentage of cases (21%) belonged to histological grade III.

Out of 29 cases of cytological Grade I, 25 cases correlated with histological Grade I and remaining 4 cases were

upgraded as Grade II. Out of 56 cases of cytological Grade II, 45 cases correlated with histological Grade II and remaining 11 cases were upgraded as Grade III. Out of 15 cases of cytological Grade III, 10 cases correlated with histological Grade III and remaining 5 cases were downgrade as Grade II on histology.

The highest concordance rate between cytological and histological grade was found in Grade I tumors (86.2%) followed Grade II tumors (80.3%) and least in Grade III tumors (66.7%), Out of 100 cases 80 cases showed agreement between the respective cytological and histological grades. Absolute concordance rate was 80%.

A significant statistical association between the grades assigned to cytologic and histologic specimens was observed ( $r=0.831$ ,  $p<0.001$ ).

Sensitivity of Robinson's cytological grading system was maximum in cytological Grade I tumors (100%), followed by Cytological Grade II tumors (83.3%) and least in cytological Grade III tumors (47.6%).

Specificity of Robinson's cytological grading system was similar in cytological Grade I and Grade III tumors (94.6% and 93.7% respectively) and least in cytological Grade II tumors (76.09%).

Multiple regression analysis of cytological features with histological grade showed that all of the features included in Robinson's cytological grading system were statistically significant ( $p=0.000$ ) and all of them equally contributed in determining the histologic grade of the tumor.

**Table 1: Robinson's cytological grading system** 7-10

Criterion	Score 1	Score 2	Score 3
Cell dissociation	Mostly cluster	Single cells, cluster	Mostly single cells
Nuclear size	1-2 times size of RBC	3-4 times size of RBC	>/=5 times of RBC
Cell uniformity	Monomorphic	Mildly pleomorphic	Pleomorphic
Nucleoli	Indistinct /Small	Noticeable	Abnormal
Nuclear margin	Smooth	Slightly irregular/folds	Buds, clefts
Chromatin pattern	Vesicular	Granular	Clumping/clearing
Grade I : Score 6-11	Grade II : Score 12-14	Grade III :Score 15-18	

**Table 2: Elston and Ellis modification of Scarff Bloom Richardson grading system** 11-14

	Feature	Feature score
I	<b>Percent tubule formation (extent within tumour)</b>	
	>75%	1
	10-75%	2
	<10%	3
II	<b>Nuclear pleomorphism</b>	
	Small, regular, uniform cells	1
	Moderate variation in size and shape	2
	Marked variation in size and shape	3

	Feature	Feature score
<b>III</b>	<b>Mitotic count per 10 high-power fields(hpf)</b>	
	0-5 mitoses/10hpf	1
	6-11 mitoses/10hpf	2
	>=12 mitoses/10hpf	3
<b>Histologic grade</b>	<b>Histologic type</b>	<b>Total Score</b>
Grade-I	Well differentiated	3-5
Grade-II	Moderately differentiated	6-7
Grade-III	Poorly differentiated	8-9

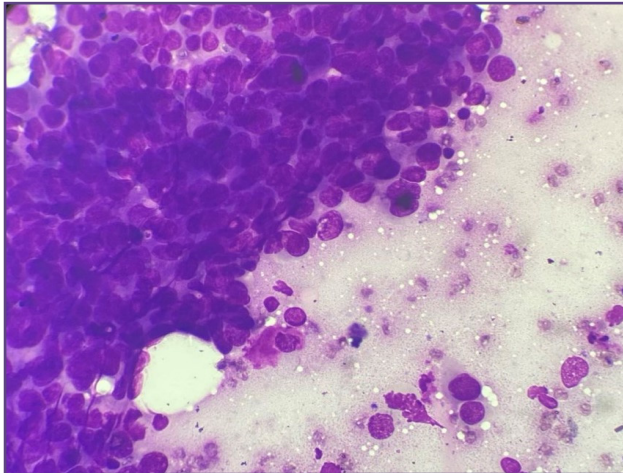


Fig. 1: FNAC Ductal carcinoma breast (Robinson's cytological grade I): Malignant epithelial cells arranged in clusters, mild pleomorphism, regular nuclear membrane, nuclear size 1-2 time of RBCs, vesicular chromatin and nucleoli indistinct noted. Cytological score 6. Giemsa stain 400x.

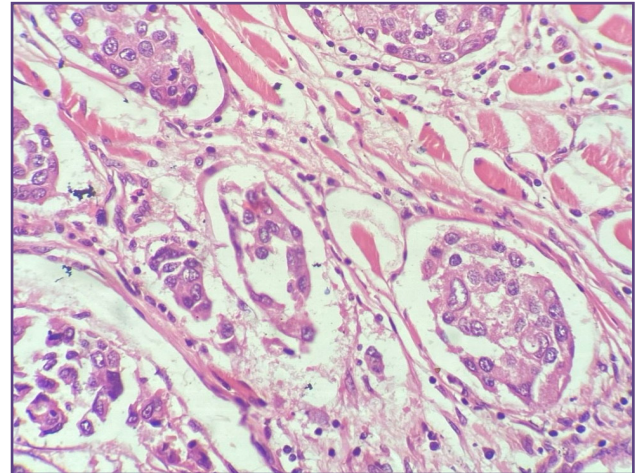


Fig. 2: Infiltrating ductal carcinoma breast (MBR grade I): Shows tubule formation in >75% tumor mass with moderate pleomorphism and mitosis 7/10hpf. MBR score 5. H&E 400x.

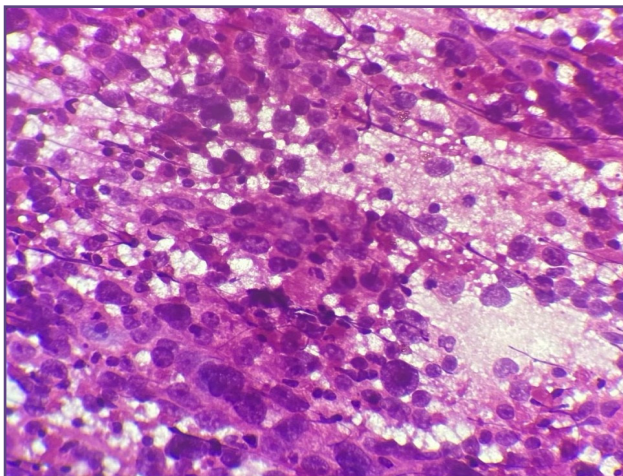


Fig. 3: FNAC Ductal carcinoma breast (Grade II): Malignant epithelial cells arranged singly with size 3-4 times size of RBC, moderate pleomorphism, noticeable nucleoli, irregular nuclear membrane and vesicular chromatin noted. Cytologic score 12. H&E 400x

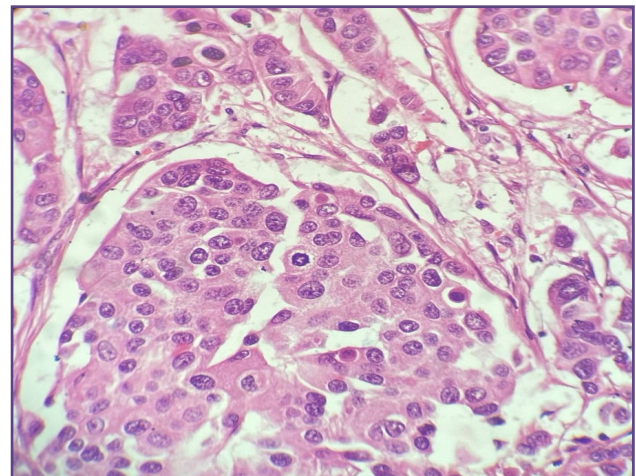
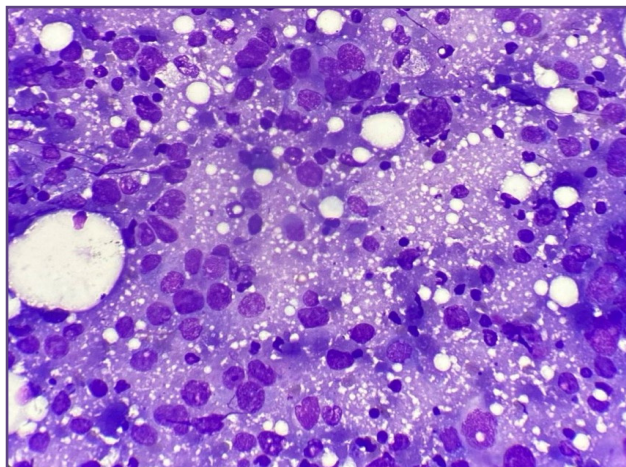


Fig. 4: Infiltrating ductal carcinoma breast (MBR grade II): Shows tubule formation in 10-75% tumor mass with moderate pleomorphism and mitosis 13/10hpf. MBR score 7. H&E 400x



**Fig. 5: FNAC Ductal carcinoma breast (Robinson's cytologic grade III):** Malignant epithelial cells lying singly with marked pleomorphism, size > 5 times the size of RBC, noticeable nucleoli, irregular nuclear margin and granular chromatin noted. Cytologic score 15. Giemsa 400x.

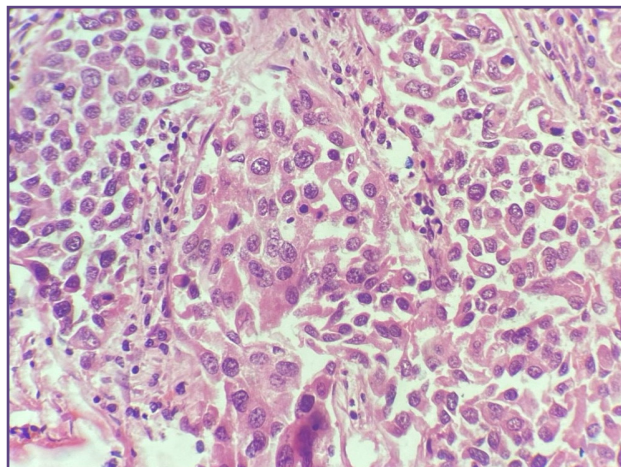
### Discussion

Fine-needle aspiration cytology is a routine investigation done globally for diagnosis of carcinoma breast from many decades. But even now its use is limited only for providing diagnosis and morphologic type of carcinoma. Grade of breast carcinoma has prognostic implications and knowledge of the grade of tumor before planning for line of treatment can be a boon to the patient. Many systems for grading systems have been suggested over the years, but none of them have been successfully implemented in routine cytology reporting.

In this study the concordance rate between the cytological grade using Robinson's system and histological grade was 80%, which is comparable to that reported by previous studies done by Das AK et al<sup>[15]</sup> (71.2%), Rekha TS et al<sup>[16]</sup> (82%), Pandya AN et al<sup>[17]</sup> (74.5%), Teronpi et al<sup>[18]</sup> (93.3%).

A statistically significant correlation between the cytological and histological grade with a Spearman correlation coefficient  $r = 0.831$  and  $P$  value of  $<0.001$ . Similar to studies done by Sinha A et al<sup>[3]</sup> ( $r = 0.97$ ,  $p < 0.01$ ) and Pal S et al<sup>[19]</sup> ( $r = 0.804$ ,  $p = 0.000$ ).

Concordance rates of individual cytological grades were 86.2%, 80.3% and 66.6% for Grade I, II and III respectively. So, Grade I showed highest concordance rate with histological grade, while Grade III showed lowest concordance in our study. Similar observations were made by Sood N et al<sup>[20]</sup> with concordance rate of 75.0%, 70.6% and 60.0% for cytological Grade I, II and III tumors.



**Fig. 6: Infiltrating ductal carcinoma breast (MBR grade III):** Shows tubule formation in <10% tumor mass, marked pleomorphism and mitosis 14/10hpf. MBR score 9. H&E 400x.

In the present study, we found sensitivities for cytological grade I, II, and III tumors as 100%, 83.3%, and 47.6% respectively. Pal S et al<sup>[19]</sup> reported a similar finding of lowest sensitivity of cytological grade III tumors (45.45%) as compared to 100% for cytological grade I and 82.14% for cytological grade II tumors.

### Conclusion

There is a high degree of concordance between Robinson's and Elston and Ellis modification of Scarff Bloom & Richardson grading system. So, Robinson's grading system should be included in routine reporting of breast carcinoma to aid in deciding proper line of treatment, as well as to avoid over-treatment and its associated morbidity in low grade carcinomas. This system is easy, takes little amount of time and is reproducible.

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### Competing Interests

None Declared

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