

## Comparison of two Cytological Grading Systems with Correlation of Histological Grading System of Breast Carcinoma in a Tertiary Care Centre in South India

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### How to cite this article:

Poornima V Kamatar, Col US Dinesh, Ravikala Rao. Comparison of two Cytological Grading Systems with Correlation of Histological Grading System of Breast Carcinoma in a Tertiary Care Centre in South India. Indian J Pathol Res Pract. 2019;8(3):275-281.

### Abstract

**Background:** Cytological grading is a useful tool in preoperative prognostication of Breast carcinoma and its management. **Aim:** To cytologically grade breast carcinoma using Robinson's and Mouriquand's grading systems, compare each other and determine which correlates well with Modified Scarff-Bloom Richardson (MSBR) histological grading system. **Materials and Methods:** 60 cases of Breast lumps were studied from January 2007 to January 2012 whose FNAC and biopsy were performed in our institute. Cytological grading was carried out using Robinson and Mouriquand grading systems and were compared with each other and then each of them were correlated with Modified Scarff-Bloom Richardson histological grading system. Concordance and discordance was accordingly noted amongst them. **Results:** A total of 60 cases were studied, ages ranging from 35-79 years. By Robinson's system 20%, 56.67% and 23.33% aspirates were graded as grade I, grade II and grade III respectively. Using Mouriquand's grading 16.67%, 55% and 28.33% aspirates were graded as grade I, grade II and grade III respectively. Agreement between each other was 82.5%. Agreement between Robinson and MSBR histological grading was 89.17% and between Mouriquand and MSBR histological grade was 80%. Diagnostic accuracy of Robinson's system was 86.67% and specificity was 70% while Mouriquand system showed an accuracy of 76.67% and specificity of 30%. **Conclusion:** Comprehensive cytological grading of breast carcinomas was possible using Robinson's and Mouriquand's cytological grading system and the concordance between them was 65%. Further, of the 2 cytological grading systems Robinson's was better because of more objective criteria and easy reproducibility.

**Keywords:** Breast carcinoma; Cytological grading; Fine needle aspiration; Histological grading.

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Received on 10.03.2019,

Accepted on 16.04.2019

## Introduction

Breast cancer is the second most prevalent cancer among Indian women, the first being cervical cancer [1]. Breast cancer can be diagnosed early, as early stages are effective to treatment while cancers in their most advanced stages are usually almost impossible to treat [2]. Fine needle aspiration cytology (FNAC) is an ideal method to diagnose cancer in a palpable breast mass as it has the advantage of being a simple outpatient procedure, rapid, relatively painless and cost effective [3].

Grading of breast carcinoma, while the tumor is still in vivo, would be most ideal and desirable, as it would be helpful in the selection of patients for appropriate therapy [4].

Cytological grading should be part of all FNA reports of breast carcinoma so that preoperative prognostication could be evaluated [5].

The present study used Robinson's and Mouriquand's cytological grading system of Breast carcinoma and compared the two grading systems. Followed by correlating the two cytological grading systems with the Modified Scarff-Bloom Richardson histological grading system and determined which of these two methods correlates well with histological grade more accurately.

## Materials and Methods

The present study includes 60 patients of breast cancer from January 2007 to January 2012. Patients with malignant breast lumps attending surgical OPD/admitted in inpatient wards to SDM Medical College Hospital Dharwad which is a tertiary care centre in South India, whose FNAC and surgery done were studied. Cytology, histopathology slides and clinical data were collected from archives and from the medical record section of all diagnosed cases of breast malignancies were included.

A total of 60 patients of breast carcinoma with preoperative cytologic diagnosis by Fine needle aspiration cytology using 23 gauge needle and staining with standard stains like Haematoxylin and Eosin, Leishman and Papanicolaou stain were studied. Cytological grading is evaluated according to Robinson's [6] and Mouriquand's [7] grading system by two independent Pathologists. In Robinson's cytological grading [6] system 6 different parameters namely cell dissociation, cell size, cell uniformity; nucleolus, nuclear margin and nuclear chromatin were used to grade tumours. A score of 1-3 was given to each parameter and

tumour graded by adding the scores. Tumours that were scored in the range of 6 to 11 were graded I, score of 12 to 14 were graded II, and grade III with score ranging from 15 to 18.

In the Mouriquand's method [7] a score of 0 to 3 was given to different cellular characters (clustering- 0/isolated cells-3), nuclear features (anisokaryosis- 2/large size- 3/budding- 2/ naked- 3/hyperchromasia-3), nucleolus (blue-2/red-3) and mitosis ( $\geq 3/\text{slide}=1, \geq 6/\text{slide}=3$ ). The tumors were graded I if the combined score  $< 5$ , graded II for a score ranging from 5 to 9, and III if the score was  $>10$ .

All patients diagnosed as breast carcinoma by FNAC are followed up by surgery constituting Lumpectomy, Mastectomy, Modified Radical Mastectomy, or Quadrantectomy with or without Axillary lymphnode dissection. The tissue received was then processed, stained with haematoxylin and eosin and examined. Histological grading according to Modified Scarff-Bloom Richardson grading system [8] is followed. Mitotic figures were scored using Olympus CH20i with field of view number 18 and high power field area of 0.152 mm<sup>2</sup>. Accordingly total number of mitotic figures per 10 high power fields was recorded. Upto 5 mitosis/10 hpf was given 1 point, 6-10 scored 2 points and more than 11 scored 3 points.

## Statistical Analysis

The data were analysed and the grading reported in terms of percentages. The agreement between the methods was assessed by the Kappa statistics. Correlation between the scores was evaluated using Spearman rank correlation and its significance evaluated using "t" test. Pearson's correlation test was used to examine the degree of correlation between cytological and histological grades.

## Results

Total number of Breast carcinoma patients studied were 60. All were females with age ranging from 35 to 79 years with mean age of 51.7 years. 39 cases were postmenopausal and 21 were premenopausal.

Out of 60 patients 9 (15%) were in the age group of 30-39 years, 17 (28.33%) between 40-49 years, 18 (30%) between 50-59 years, 14 (23.33%) between 60-69 years and 2 (3.33%) between 70-79 years.

Out of 60 cases majority were invasive ductal carcinoma NOS type constituting 52 (86.66%) cases, followed by medullary carcinoma 3 (5%)

cases, mucinous carcinoma 2 (3.33%) and 1 (1.66%) each of tubular carcinoma, mixed IDC with lobular carcinoma and mixed IDC with mucinous carcinoma.

The agreement between Robinson cytological system and Mouriquand cytological system was assessed using kappa statistics (Table 1) which showed 82.5% agreement which was found to be statistically significant ( $p < 0.05$ ).

Correlation of Robinson cytological grading system with MSBR histological grading system results were (Table 2): Robinson's cytological grading system shows an absolute concordance with the histological grade in 47 (78.33%) out of 60 patients. 7 were of grade I, 28 were grade II and 12 were grade III. Of the 13 cases showing discordance in grading, there was one grade difference in all the cases. Eight cases were cytologically under-graded and five cases were over-graded as compared to histological grade.

The agreement between Robinson cytological grading system and MSBR histological grading system was 89.17% which was found to be statistically significant ( $p < 0.05$ ).

Correlation of Mouriquand cytological grading system with MSBR histological grading system results as in the Table 3. Mouriquand's cytological grading system was compared with histological system, which showed an absolute concordance in 36 (60%) of the 60 patients. 3 were of grade I, 22 were grade II and 11 were grade III. Out of 24 cases discordant, there was one grade difference in all the cases. 11 cases were cytologically under-graded and 13 cases were over-graded as compared to histological grade.

The agreement between Mouriquand cytological grading system and histological grading system was 80% agreement which was found to be statistically significant ( $p < 0.05$ ).

Comparison of discordant cases of Robinson and Mouriquand with histological system showed that 8 cases were under-graded by Robinson method while 11 cases were under-graded using Mouriquand's method, 5 cases were over-graded by using Robinson's method and 13 cases by Mouriquand's method.

**Table 1:** Comparison of Cytological grading by Robinson's with Mouriquand's system

	Grade	Mouriquand cytological grading system			
		Grade I	Grade II	Grade III	Total
Robinson cytological grading system	Grade I	5	7	0	12
	Grade II	5	23	6	34
	Grade III	0	3	11	14
	Total	10	33	17	60
Agreement	Expected Agreement	Kappa value	Std. Err.	Z-value	p-value
82.5%	65.78%	0.4886	0.0947	5.1600	0.0000*

\* $p < 0.05$

**Table 2:** Correlation of Robinson cytological grading system with MSBR histological grading system

	Grade	MSBR histological grading system			
		Grade I	Grade II	Grade III	Total
Robinson cytological grading system	Grade I	7	5	0	12
	Grade II	3	28	3	34
	Grade III	0	2	12	14
	Total	10	35	15	60
Agreement	Expected Agreement	Kappa value	Std. Err.	Z-value	p-value
89.17%	66.67%	0.6750	0.0946	7.1400	0.0000*

\* $p < 0.05$

**Table 3:** Correlation of Mouriquand cytological grading system with MSBR histological grading system

	Grade	MSBR Histological grading system			
		Grade I	Grade II	Grade III	Total
Mouriquand cytological grading system	Grade I	3	7	0	10
	Grade II	7	22	4	33
	Grade III	0	6	11	17
	Total	10	35	15	60
Agreement	Expected Agreement	Kappa value	Std. Err.	Z-value	p-value
80.00%	66.53%	0.4025	0.0955	4.2100	0.0000*

\* $p < 0.05$

Correlation between Robinson cytological grading, Mouriquand cytological grading and MSBR histological grading system by Spearman's rank correlation coefficient (Table 4) and Karl Pearson's correlation coefficient (Table 5) were as follows: Both showed significant and positive relationship between Robinson cytological & MSBR histological grading system scores ( $p < 0.05$ ), between Mouriquand cytological & MSBR histological grading system scores ( $p < 0.05$ ) and between Robinson & Mouriquand cytological grading system scores ( $p < 0.05$ ) at 5% level of significance. The agreement of all was found to be statistically significant.

In order to statistically evaluate which of the two cytological grading methods more closely corresponded to the histological grading, the grade I cases were considered as 'low grade' and both grades II and III cases were clubbed together as 'high grade' in both cytological as well as the histological grading methods. These two categories in cytological grading were then separately compared with the corresponding histological grading. Sensitivity, Specificity, Positive predictive value and Negative predictive value were calculated accordingly (Table 6 & 7).

**Table 4:** Correlation between Robinson cytological grading, Mouriquand cytological grading and MSBR histological grading system by Spearman's rank correlation coefficient.

Grading systems	N	Spearman's R	t-value	p-level
Robinson grading & Mouriquand grading system	60	0.6141	5.9256	0.00001*
Mouriquand grading & histological grading system	60	0.5461	4.9645	0.00001*
Robinson grading & histological grading system	60	0.7512	8.6682	0.00001*

\* $p < 0.05$

**Table 5:** Correlation between Robinson cytological grading, Mouriquand cytological grading and MSBR histological grading system by Karl Pearson's correlation coefficient

Grading systems	N	r-value	t-value	p-level
Robinson grading & Mouriquand grading system	60	0.7818	9.5493	0.00001*
Mouriquand grading & histological grading system	60	0.6022	5.7444	0.00001*
Robinson grading & histological grading system	60	0.7093	7.6629	0.00001*

\* $p < 0.05$

**Table 6:** Comparison of statistical parameters of Robinson cytological grading with MSBR Histological grading systems

Robinson Cytological Grading System	MSBR Histological Grading System		
	High Grade	Low Grade	Total
High Grade	45	3	48
Low Grade	5	7	12
Total	50	10	60

Sensitivity- 90.00% Positive predictive value- 93.75%

Specificity- 70.00% Negative predictive value- 58.33%

Diagnostic accuracy- 86.67%

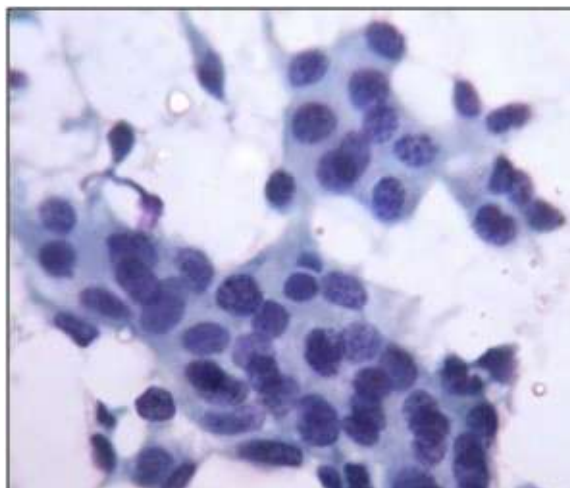
**Table 7:** Comparison of statistical parameters of Mouriquand cytological grading with MSBR Histological grading systems

Mouriquand Cytological Grading System	MSBR Histological Grading System		
	High Grade	Low Grade	Total
High Grade	43	7	50
Low Grade	7	3	10
Total	50	10	60

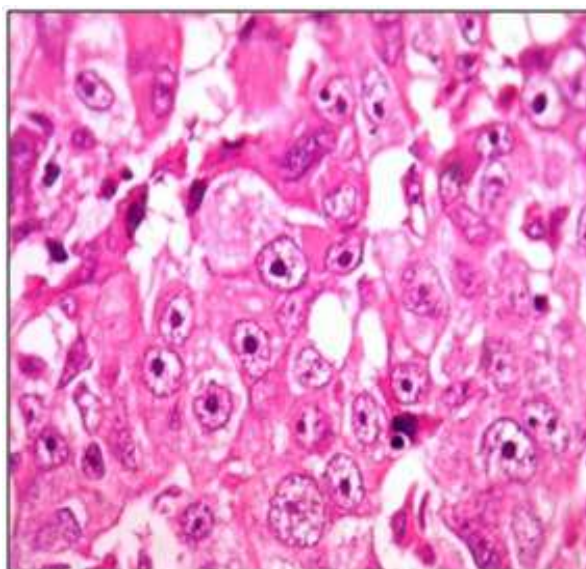
Sensitivity- 86.00% Positive predictive value- 86.00%

Specificity- 30.00% negative predictive value- 30.00%

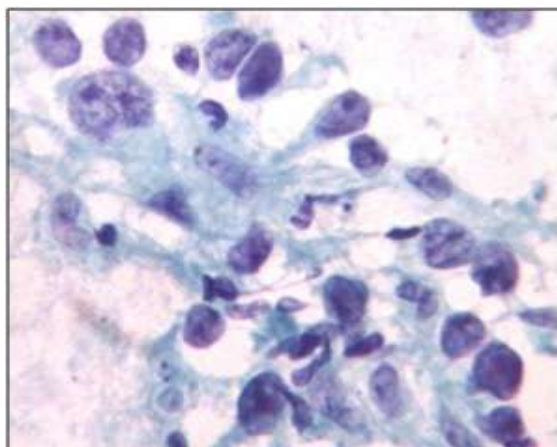
Diagnostic accuracy- 76.67%



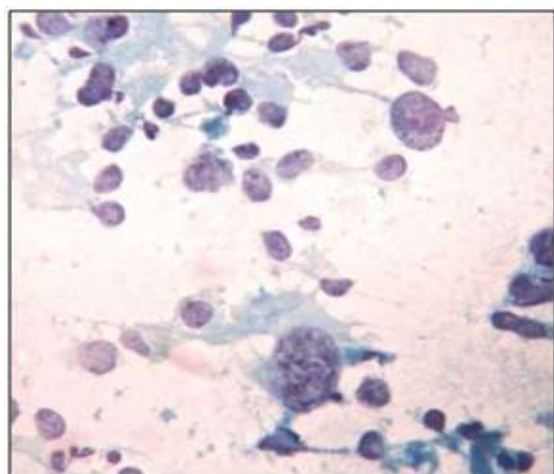
**Fig. 1:** Robinson Grade II showing tumour cells in clusters and singles with mild cellular pleomorphism and nuclei with granular chromatin. (Pap, x400)



**Fig. 4:** (40x)- MSBR Histological Grade III, showing 50% of tumour cells in tubules with marked nuclear pleomorphism with mitotic count > 11/ hpf. (H and E, x400)



**Fig. 2:** (40x)- Robinson Grade III showing tumour cells in singles with marked pleomorphism, nuclei displaying coarse clumped chromatin with prominent large nucleoli. (Pap, x400).



**Fig. 3:** (40x)- Mouriquand's Grade III, showing isolated tumour cells with large naked nuclei and prominent blue nucleoli. (Pap, x400)

### Discussion

The incidence of breast cancer in India is increasing and soon will be approaching that of the western world. The utility of Fine needle aspiration cytology in diagnosing Breast cancer is well known since long, though its use in its grading has been underestimated and hence being undertaken [9]. The evaluation of malignant breast aspirates, as pointed out in an editorial by Katz should provide not only the diagnosis of malignancy and type of tumor, but also information on the cytological grade of breast carcinoma [10]. The National cancer Institute (NCI), Bethesda, sponsored conference had also recommended that tumour grading on FNA material to be incorporated in FNA reports for prognostication [11].

Tumour grading does not require special procedures and therefore incurs no additional cost and effort. It is one of the most important prognostic factors in predicting outcome in breast cancer patients [12]. The purpose of cytoprognostic grading in Breast carcinoma is to identify fast growing tumours especially grade III tumours which are most amenable to chemotherapy than the low grade slow growing tumours which are best suited for pre treatment with tamoxifen [2].

In the present study, 60 patients with carcinoma breast were cytologically graded by 2 systems and compared with histological grade. Robinson et al. [6] Das et al. [5] and Chhabra et al. [13] reported grade II tumours with 44%, 46% and 51%

respectively comprising the largest group followed by grade I and grade III. In the study by Wani FA [2] et al. which also showed predominance of grade II (42%) tumours but followed by grade III (33%) and grade I (25%). In our study, the distribution of cases according to Robinson grading system were 56.67% grade II followed by grade III with 23.33% and grade I with 20% which is comparable to the above studies.

In the study done by Das et al. [5] and Wani et al. [2] Mouriquand grading system showed grade I tumours constituting 9.61% and 25.45% respectively, grade II tumours 69.2% and 38.1% respectively and grade III tumours 21.1% and 36.36% respectively. Both the studies showed predominance of cases in grade II. However, Saha et al. [14] study showed majority of cases 70.17% as grade III tumours followed by grade II 26.31% and then grade I 3.5%. Distribution of cases in our study showed 16.6% of grade I tumours, 55% of grade II and 28.33% grade III. Majority of the cases are of grade II which was comparable to Das AK [5] and Wani FA et al. [2] study.

MSBR Histological grading done by Robinson I A et al. [6] and Meena S P et al. [9] showed 32.74% and 32.39% of cases as grade I respectively, 42.7% and 50.7% respectively as grade II and 24.55% and 16.9% respectively as grade III tumours. Majority of cases are of grade II followed by grade I and then grade III. Das A K et al. [5] also showed predominance of cases in grade II accounting for 55.76%, followed by grade III 26.92% and then grade I 17.30%. Our study showed 16.66% of grade I cases, 58.33% of grade II cases and 25% of grade III cases with majority being grade II which is comparable to Das et al. [5] study.

In the study by Robinson et al. [6] both Robinson cytological grading and MSBR histological grading showed predominance of cases in grade II with concordance of 56.93%.

In the study by Chhabra et al. [13] and Meena et al. [9] concordance between Robinson cytological grading and MSBR histological grading was 66.66% and 85.91% respectively and discordance was 33.34% and 14.09% respectively. Chhabra et al. [13] has shown that lack of correlation (discordance) may be due to tumour heterogeneity and observer subjectivity while assigning a cytological grade. In the present study concordance between Robinson cytological grading and MSBR histological grading was 78.33% and discordance was 21.67% which is comparable to Meena et al. [9] study.

In the study by Das A K et al. [5] concordance between Mouriquand cytological grading and MSBR histological grading was 71.15%. In the

present study concordance between Mouriquand cytological grading and MSBR histological grading is 60% which is comparable to above study. All the discordant cases had one grade difference with histological grading similar to above study. In the studies by Das et al. [5] and Meena et al. [9] statistical evaluation showed that sensitivity of Robinson cytological system was 81.39% and 90.77% respectively, specificity was 77.77% and 84.42% respectively, Positive predictive value was 94.59% and 83.1% respectively and negative predictive value was 46.66% and 91.55% respectively. Diagnostic accuracy was 80.76% and 87.32% respectively. In the present study sensitivity was 90%, specificity was 70%, positive predictive value was 93.75%, negative predictive value was 58.33% and diagnostic accuracy was 86.67%. All the percentages are comparable to Das et al. [5] study.

In the study by Das A K et al. [5] sensitivity of Mouriquand cytological grading was 95.3%, specificity was 33.33%, positive predictive value was 87.20%, negative predictive value was 60% and diagnostic accuracy was 84.6%. In the present study sensitivity was 86%, specificity was 30%, positive predictive value was 86%, negative predictive value was 30% and diagnostic accuracy was 76.67% which is comparable to above study.

In the present study the diagnostic accuracy (86.67% and 76.67%) and sensitivity (90% and 86%) of both Robinson's and Mouriquand's methods was similar. However, the specificity by Mouriquand's method was very low.

The criteria for grading tumour by the Robinson's method was easier and simpler to reproduce as compared to the Mouriquand's method.

## Conclusion

A comprehensive cytological grading of breast carcinoma was possible using both Robinson's and Mouriquand's cytological grading systems and the concordance between them was 65%. Further of the 2 cytological grading systems Robinson's was better because of more objective criteria and easy reproducibility.

Correlation of Robinson and Mouriquand cytological system with Modified Scarff- Bloom Richards on Histological grading showed agreement of 89% and 80% respectively proving that Robinson had a better correlation with histological grade.

All out effort should be made to incorporate cytological grading in all FNAC reports of breast

carcinoma, so that it will reflect the histological grading and thus the prognosis of the disease may be suggested.

*Conflicting Interest (If present, give more details): Nil*

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