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## COMPARATIVE STUDY OF FINE NEEDLE ASPIRATION CYTOLOGY AND HISTOPATHOLOGY IN GRADING BREAST CARCINOMA

**DR.VIJAYALAXMI.S.PATIL\*<sup>1</sup>, DR.R.M.POTEKAR<sup>2</sup>,  
DR.B.R.YELIKAR<sup>3</sup> AND DR.M.H.KARIGOUDAR<sup>4</sup>**

*Department of Pathology, BLDE University's Shri B.M.Patil  
Medical College Hospital & Research Centre, Bijapur – 586103, Karnataka, India.*

### ABSTRACT

Grading of tumors in Fine Needle Aspiration Cytology (FNAC) is a useful tool for selecting therapy and prognosis in breast carcinoma patients. A total of 38 patients of Infiltrating ductal carcinoma of breast who underwent FNAC and mastectomy were cytologically and histologically graded (employing Taniguchi's cytological grading system and Scarff Bloom Richardson grading method respectively). Statistical analysis was done using 'Z' test and ' $\chi^2$ ' test. The lymph nodes were also studied for detection of metastasis. Total concordance between Cytological grade(CG) and Histological grade(HG) was seen in 78.95% of cases and Positive correlation between the two grading systems was also noted. Lymph node metastasis was seen in 52.63% of cases which was maximum in grade III cases. Cytological grading of breast carcinoma correlates well with histological grading and it may be useful in the prognostic evaluation of the cases without additional morbidity or expense to the patient.

**KEYWORDS:** Fine needle aspiration cytology, Invasive ductal carcinoma, Taniguchi grading, Scarff Bloom Richardson grading.



**DR.VIJAYALAXMI.S.PATIL**

Department of Pathology, BLDE University's Shri B.M.Patil  
Medical College Hospital & Research Centre, Bijapur – 586103, Karnataka, India.

## INTRODUCTION

Breast cancer is the second most common cancer among Indian females with a cumulative incidence of 1-2% until 64 years of age<sup>1</sup>. Carcinoma breast is a malignant disease with heterogenous prognosis. Many factors other than clinical stage like tumor type, histological grading, hormone receptor status, DNA ploidy, cell proliferation markers and expression of different oncogenes determine prognosis in a given patient<sup>2,3</sup>. Two of the most important microscopically derived morphologic prognostic factors for breast carcinoma patients are histologic type of tumor and nuclear grade<sup>4</sup>. Nottingham method described by Elston and Ellis for histological grading of breast carcinoma is a widely accepted tumor grading system and has been found to have good prognostic correlations<sup>2</sup>. Fine needle aspiration is a safe, reliable, time saving OPD procedure routinely used for diagnosing benign and malignant lesions of breast, but it can also provide additional information about intrinsic features of the tumour as well as prognostic factors<sup>5,6</sup>. As neoadjuvant therapy, including preoperative chemotherapy and tamoxifen is becoming increasingly common for early breast cancer, it is desirable to grade tumors before surgery so that the most appropriate medical regimen can be selected<sup>7</sup>. Cytological grading of breast carcinoma is easy to perform. It has been found that it correlates well with tissue nuclear grade. Hence nuclear grading should be included as a fundamental cytological parameter in the FNAC report whenever possible<sup>8,9</sup>. The National cancer Institute

Bethesda has recommended that tumor grading on FNA material should be incorporated in FNA reports for prognostification<sup>2</sup>. In this study, cytological grading was done on aspirates of breast carcinomas and histological grading of corresponding specimens was done using Scarff Bloom Richardson's grading and the lymph nodes were also studied for detection of metastasis.

## MATERIALS AND METHODS

A total of 38 female patients with breast carcinoma in the age range of 22 - 65 years, seen between August 2007 and July 2009, were included in this study. FNA was performed using a 10ml disposable syringe and 23-gauge needle. Papanicolaou (Pap) and hematoxylin and eosin (H and E) stained FNA smears and hematoxylin and eosin (H and E)-stained tissue sections (obtained from mastectomy specimens) were evaluated for cytological and histological grading respectively. The cases were graded cytologically using Taniguchi's grading method on Pap smears & H&E stained smears [Figures 1 - 4] and histological grading was performed using Scarff Bloom Richardson (SBR) grading. In the Taniguchi's grading system (TGS) for breast carcinoma, seven different cytological parameters were used to grade the tumors<sup>10</sup> [Table 1]. Each parameter was assigned a score and a total score was obtained by adding the scores of all the seven parameters.

**Table 1**  
**Taniguchi cytological grading method**

Parameter	Score			
	0	1	2	3
1.Necrosis	Absent	Present		
2.Cellular size		< 3 x RBC size	3-4 x RBC size	> 4 x RBC size
3.Nuclear/Cytoplasmic ratio		< 50%	50 – 80%	>80%
4.Nuclear pleomorphism		Uniform	Mildly pleomorphic	Markedly pleomorphic
5.Nucleoli		Indistinct	Noticeable	Prominent
6.Chromatin granularity		Fine	Moderately granular	Coarse
7.Density of chromatin		Not hyperchromatic	Moderately hyperchromatic	Markedly hyperchromatic

\*Grade I – Score 6-9, Grade II – Score 10-11, Grade III – Score 12-19

Histological grading was performed on formalin-fixed paraffin-embedded sections from mastectomy specimens using SBR grading<sup>11</sup> method which takes three parameters into consideration namely tubule formation, nuclear pleomorphism and number of mitoses [Table 2]. Each parameter was assigned a score and scores of all the parameters were added to obtain the total score. Lymph nodes were detected in the specimens and were studied for metastatic deposits.

**Table 2**  
**Scarff Bloom Richardson grading method**

Tumor Tubule Formation	Score
>75% of tumor cells arranged in tubules	1
>10% and <75%	2
<10%	3
Number of Mitoses (low power scanning (X100), find most mitotically tumor area, proceed to high power (x400))	
<10 mitoses in 10 high-power fields	1
>10 and <20 mitoses	2
>20 mitoses per 10 high power fields	3
Nuclear Pleomorphism (nuclear grade)	
Nuclei with minimal variation in size and shape	1
Nuclei with moderate variation in size and shape	2
Nuclei with marked variation in size and shape	3

\* Grade I – Score 3-5, Grade II – Score 6-7, Grade III – Score 8-9

The cytological grade was then compared with the histological grade and lymph node status. Data were analysed by using Spearman's correlation coefficient (r value) for correlation between two grading systems and Chi square test was done to determine the p value to find the association between the two grading systems.

## RESULTS

Of the 38 cases graded cytologically by Taniguchi's method, 2 (5.26%) cases were of grade I, 16 (42.11%) cases were of grade II and 20 (52.63%) cases were of grade III. On histological grading according to the Scarff Bloom Richardson method, 1(2.63%) case was grade I, 20 (52.63%) cases were grade II and 17 (44.74%) cases were grade III tumors. Out

of 2 cases on Taniguchi's cytological grade I, 1 case was of Grade I and the other case was upgraded as grade II on SBR histological grade. Out of 16 cases on cytological grade II, 14 cases were of grade II and 2 cases were upgraded as grade III on histological grade. Out of 20 cases on cytological grade III, 15 cases were graded as grade III and 5 cases were downgraded as grade II on histological grade[Table 2]. Total concordance between

cytological grade and histological grade was seen in 30 cases out of 38 cases accounting for 78.95% of total cases. Of the discordant 8 cases, 3 cases were underdiagnosed and 5 cases were overdiagnosed on cytology. The discrepancy in these 8 cases may be due to sampling error, technical error, presence of different degrees of atypia within the same tumor.

**Table 2**  
**Comparison of cytological grade with histological grade**

Cytological grade (TGS)	Number of cases (cytology)	Histological grade (SBR)		
		I (Score 3-5)	II (Score 6-7)	III (Score 8-9)
I (Score 6-9)	02	01	01	-
II (Score 10-11)	16	-	14	02
III (Score 12-19)	20	-	05	15
Total	38	01	20	17

a)TGS – Taniguchi grading system    b)SBR – Scarff Bloom Richardson grading system

In the study, lymph node metastasis was seen in 1 out of 2 cases of grade I ,7 out of 16 cases of grade II and 12 out of 20 cases of grade III carcinomas. Totally about 20 cases among the 38 cases studied showed lymph node metastasis which accounted for 52.63% of cases. The maximum number of grade III cases (60%) showed lymph node metastasis. In grade I and grade II carcinomas, metastasis was noted in 50% and 43.75% of cases

respectively. The Spearman's correlation coefficient was determined. The r value was 0.684 which indicates that there is a strong correlation between Taniguchi's cytological grading system and Scarff Bloom Richardson's histological grading system. The Chi – square test was performed and the p value was determined which was less than 0.05, thus indicating a strong association between the grading by these two methods.

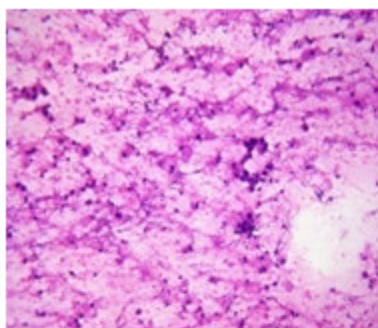


Fig 1: Grade III carcinoma breast:  
Background showing necrosis,  
Score – 13 (H&E smear, x40)

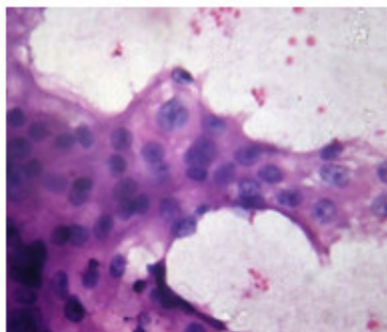


Fig 2: Grade II carcinoma breast:  
Malignant cells with prominent  
nucleoli, Score- 10(Pap smear, x400)

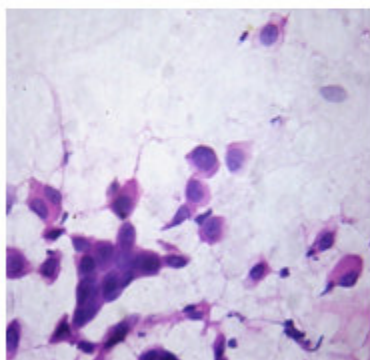


Fig 3: Grade III carcinoma breast:  
Malignant cells with high N/C  
ratio (more than 80%), Score- 12  
(Pap smear, x400)

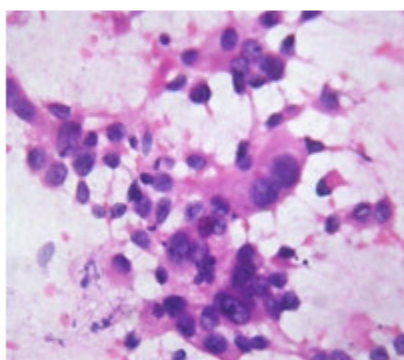


Fig 4: Grade III carcinoma breast:  
Malignant cells with marked nuclear  
pleomorphism, Score-14 (Pap smear,  
x400)

## DISCUSSION

The incidence of breast cancer in India is increasing nowadays and approaching to that in the western world<sup>12</sup>. The age standardized mortality rate for breast cancer in India is 11.1 per 100000 (12.5 per 100000 globally). As in other developing regions, the mortality rates for breast cancer in India are high in comparison to its incidence rates<sup>13</sup>. Although the incidence of early detection of breast cancer is increasing dramatically due to public awareness and widespread use of mammography, no significant decrease in mortality has been noted<sup>12</sup>. Fine Needle Aspiration is a safe, reliable and time saving out door procedure with little discomfort to the patient. The use of FNA is frequently limited to, establishing the benign or malignant character of a given

lesion, although it can provide additional information about intrinsic features of the tumor as well as its prognostic factors like nuclear grading, mitotic index, hormone receptor status and DNA contents<sup>5,6</sup>. As neoadjuvant therapy including preoperative chemotherapy and tamoxifen is becoming increasingly common for early breast cancer, it is desirable to grade tumors before surgery so that most appropriate medical regimen can be selected. Hence, much attraction is focused on grading tumors on FNAC. Such grading would allow assessment of the tumor in situ, and the morbidity associated with over treatment of low grade tumors could be avoided<sup>14</sup>. Large number of surgical pathology literature citations are there on the subject of invasive breast

carcinoma nuclear grade. But only a few citations on breast carcinoma nuclear grade are in the recent cytology literature<sup>15</sup>.

Nuclear grading on cytological aspirates of breast carcinoma is feasible, reproducible and correlates well with that of histological grading unlike other parameters like tubule formation and mitotic count<sup>16</sup>. A number of scoring systems with results similar to those obtained from histologic sections have been developed by fine needle aspiration studies, thus confirming the value of FNAC for predicting the histological grade of a certain tumor preoperatively and therefore its eventual biologic behaviour. The purpose of cytological grading is to identify fast growing (high grade) and slow growing (low grade) tumors. Fast growing tumors are more likely to respond to chemotherapy than the slow growing tumors which may be better suited to pretreatment with tamoxifen<sup>3</sup>. Assessment of biological aggressiveness by cytological grading without removing the tumor would, therefore, be of immense value<sup>7</sup>. In the present study histological grade correlated well with cytological grade. The high value of coefficient of correlation (0.684) showed a significant and marked association ( $p < 0.05$ ) between grades assigned to cytological and histological specimens, similar to Taniguchi et al,<sup>10</sup> Chabra et al<sup>17</sup>, Frias et al<sup>5</sup>, Moroz et al<sup>18</sup>, and Bhargava et al<sup>1</sup>. The overall concordance on cytological grading and histological grading

was 78.94 % which is comparable to those reported by Dash A et al<sup>14</sup>. The accuracy of grading systems by other authors varied from 53.89 to 83%. This variability may be due to several factors such as different systems used to assign cytologic grade, its evaluation in air dried materials, different staining techniques etc. In our study, we also studied lymph nodes for detection of metastasis which revealed deposits in about 20 cases among the 38 cases accounting to 52.63% of cases. Majority of the cases were of grade III, which is comparable to that reported by Frias et al<sup>5</sup>, and Dash et al<sup>15</sup>. This could be due to late presentation of the patients.

## CONCLUSION

Cytological grading is simple, takes little time, is reproducible and with rare exceptions, depending on sample limitations, correlates precisely with the histological grade. It allows prognostic evaluation of breast carcinoma along with diagnosis without additional morbidity or expense to the patient. Hence it is recommended that cytological nuclear grade should appear in FNAC reports of ductal breast carcinoma for proper management so that an appropriate decision regarding the preoperative neoadjuvant therapy can be taken and the over treatment of low grade cancers is avoided.

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