

## The comparison between cytological and histological grading of breast cancers in a Nigerian tertiary hospital

\*Odujoko O.O.<sup>1</sup>, Omoniyi-Esan G.O.<sup>1</sup>, Komolafe A.O.<sup>1</sup>, Sabageh D.<sup>2</sup>

### Abstract

**Background:** Breast cancer is one of the most common cancers in Nigeria. The tumour grade is an important prognostic factor and is also important in treatment of patients. Fine needle aspiration cytology can be used as an initial diagnostic tool for planning definitive management. Grading of tumours on cytology further guides therapeutic decisions. The aim of this study is to compare the correlation between the cytological and histological grading of malignant breast lumps using the Robinson's cytological grading system and Nottingham histological grading system respectively. The Objectives are, to determine the age distribution of breast cancer in our environment, to grade breast cancers cytologically using the Robinson's cytological grading system and to grade breast cancers histologically using the Nottingham histological grading system.

**Methods:** This was a one year prospective study that involved 30 patients who had malignant smears on fine needle aspiration cytology of their breast lump. These smears were graded using the Robinson's cytological grading system and compared with the Nottingham histological grading systems of same lumps obtained from either tissue biopsies or mastectomies.

**Results:** The mean age of the study participants was 50.23±10.11 years with a range of 35-70 years. Most (56.7%) malignant smears were of cytologic grade 3. The histological grade was 2 in 16(53.3%) and 3 in 14(46.7%) of the same breast tissue samples. The grade 2 tumours had the highest concordance rate of 83.3%. The absolute concordance rate between Robinson's cytological and Nottingham histological grading system of breast cancers was 73.3%.

**Conclusion:** The Robinson's cytological and Nottingham histological grading systems showed good correlation.

**Keywords:** Breast Cancer, fine needle aspiration cytology, cytological grading, histological grading.

### \*Correspondence author

Odujoko O.O.

<http://orcid.org/0000-0002-5759-7907>

Email: wol\_odujoko@yahoo.com

<sup>1</sup>Department of Morbid Anatomy and Forensic Medicine, Obafemi Awolowo University Teaching Hospital, Ile-Ife, Nigeria

<sup>2</sup>Department of Histopathology, Wexham Park Hospital, Slough, United Kingdom.

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## La comparaison entre le classement cytologique et histologique des cancers du sein dans un hôpital tertiaire Nigérian

\*Odujoko O.O.<sup>1</sup>, Omoniye-Esan G.O.<sup>1</sup>, Komolafe A.O.<sup>1</sup>, Sabageh D.<sup>2</sup>

### Resume

**Objectif:** Le cancer du sein est l'un des cancers les plus répandus au Nigéria. Le grade de la tumeur est un facteur pronostique important et est également important dans le traitement des patients. La cytologie par aspiration à l'aiguille fine peut être utilisée comme outil de diagnostic initial pour la planification d'une gestion définitive. La classification des tumeurs sur la cytologie guide davantage les décisions thérapeutiques. Le but de cette étude est de comparer la corrélation entre la classification cytologique et histologique des masses mammaires malignes en utilisant respectivement le système de classification cytologique de Robinson et le système de classification histologique de Nottingham. Les objectifs sont, pour déterminer la répartition par âge du cancer du sein dans notre environnement, de classer cytologiquement les cancers du sein en utilisant le système de classification cytologique de Robinson et de classer histologiquement les cancers du sein en utilisant le système de classification histologique de Nottingham.

**Méthodes:** Il s'agissait d'une étude prospective d'un an portant sur 30 patientes présentant un frottis malin lors de la cytologie par aspiration à l'aiguille fine de la masse de leur poitrine. Ces frottis ont été classés à l'aide du système de classification cytologique de Robinson et comparés aux systèmes de classification histologique de Nottingham des mêmes masses obtenues à partir de biopsies de tissus ou de mastectomies.

**Résultats:** L'âge moyen des participants à l'étude était de  $50,23 \pm 10,11$  ans, avec une fourchette de 35 à 70 ans. La plupart (56,7%) des frottis de malignat étaient de grade cytologique 3. Le grade histologique était de 2 sur 16 (53,3%) et 3 sur 14 (46,7%) des mêmes échantillons de tissu mammaire. Les tumeurs de grade 2 présentaient le taux de concordance le plus élevé, soit 83,3%. Le taux de concordance absolue entre le système de classification cytologique de Robinson et le système de classification histologique de Nottingham était de 73,3%.

**Conclusion:** les systèmes de classification cytologique de Robinson et histologique de Nottingham ont montré une bonne corrélation.

**Mots-clés:** cancer du sein, cytologie par aspiration à l'aiguille fine, classement cytologique, classement histologique.

### \*Correspondence author

Odujoko O.O.

<http://orcid.org/0000-0002-5759-7907>

Email: wol\_odujoko@yahoo.com

<sup>1</sup>Department of Morbid Anatomy and Forensic Medicine, Obafemi Awolowo University Teaching Hospital, Ile-Ife, Nigeria

<sup>2</sup>Department of Histopathology, Wexham Park Hospital, Slough, United Kingdom.

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## INTRODUCTION

Breast cancer is one of the commonest cancers in developing countries including Nigeria. The incidence of breast cancer is on the rise compared to figures obtained for this disease a few decades ago in lower income countries.(1) Even though, the incidence of breast cancer is lower in blacks compared to whites, it tends to present at a lower age group in the former and the mortality rate also tends to be higher in blacks than in the white population.(2) Various studies have tried to find out the reason for the increased mortality of this disease in Africans. Possible reasons would include factors such as late presentation, poor access to quality healthcare as well as an intrinsically more aggressive disease.

The level of aggressiveness of breast cancer can be measured by morphological behavior of the tumour cells as evidenced by the degree of pleomorphism, the amount of necrosis as well as the number of mitotic figures observed in the tumour cells. These morphologic criteria can be summed up in grading systems of breast cancer. Other predictive factors are tumour type, hormone receptor status, DNA ploidy, genetic factors such as *TP53* gene mutation and *BRCA* mutation amongst others (3).

The histological grade of breast cancer is very important in predicting the biologic behavior of the tumour, especially in lymph node negative tumours. Patients with high grade tumours tend to have a relative recurrence risk that is 4.4 times that of the reference group (4).

In a low resource setting, Fine needle aspiration cytology of palpable breast lumps have come to stay as an initial diagnostic tool in patients presenting in the clinic with breast lumps. It is rapid and the fast result helps the surgeon in planning for a definitive management of the patient. The level of aggression of the tumour can also be predicted by morphologic features of the cells which are incorporated into a cytological grading system that becomes helpful in treatment plans (5). Cytological nuclear grading was first introduced by Black and Spear (6). Afterwards many researchers made modifications of the nuclear grading of cytological smear before Robinson came up with a composite cytological grading system (7).

The Robinson's cytological grading system has been correlated with adverse prognostic factors in breast cancer such as lymph node metastasis by some authors (8). Regional lymph node metastasis can predict the outcome of breast cancer to a reliable extent, therefore the cytological grading of breast cancer can be a

useful tool in predicting the possible outcomes in patients with breast cancer. In areas where facilities for a tissue biopsy are not immediately available, a fine needle aspirate of a malignant breast mass can be done. In such cases, a cytological grading would be of significant value in guiding initial treatment strategy for such lesions.

Patients with breast cancer at some point have a histological diagnosis obtained from either a trucut biopsy or mastectomy specimen. This histological diagnosis can also be graded by different grading systems such as Nottingham grading system and Scarf-Bloom-Richardson (SBR) grading system.

Different researchers have tried to correlate the cytological grading of malignant breast smears to the histological grading of same tissues in order to view the level of reliability of the cytological grading systems. Pandey *et al* in 2014(9) did a correlation study between three cytological grading systems; Cytograding, Robinson's and Moringaud's grading systems and histological grading system using the SBR system. Overall concordance rates of 76.66%, 83.33% and 66.66% were obtained. The Robinson's cytological grading system was found to have the best outcome and had a very good correlation with histological grading system. Other studies have also found good correlation between cytological grading and histological grading of malignant breast smears (10,11).

Relatively few articles exist in the literatures that have compared cytological and histological grading systems of breast cancer. There is paucity of local data in the literature with this information.

This study aims to compare the level of correlation of cytological grading of breast cancers using the Robinson's cytological grading system as well as the Nottingham histological grading system of same lumps after excision or mastectomy.

## MATERIALS AND METHODS

This is a one-year prospective study comparing malignant breast smears obtained from fine needle aspiration (FNA) with same breast lesions that were diagnosed to be malignant histologically. The study was carried out at the department of Morbid Anatomy and Forensic Medicine, Obafemi Awolowo University Teaching Hospital, Ile-Ife between August 2012 to July 2013. One hundred and sixty-four (164) patients with FNA requests of breast lumps had the procedure done during the

study after obtaining informed consent. Of the 164 patients, 52 of them had malignant breast lumps diagnosed cytologically and 30 of the 52 patients with malignant lumps were available for either a tissue biopsy or mastectomy which confirmed the diagnosis histologically.

The mean age of the study participants was  $50.23 \pm 10.11$  years with a range of 35-70 years. The patients were told to lie supine and the breast lumps palpated. The skin overlying the area was cleaned with methylated spirit. The lump was aspirated with a 21-gauge needle fitted to 10mls syringe. About three or more passes were made on each lump depending on the yield of each pass.

The aspirates were smeared on six glass slides, three of which were air-dried and stained with Diff-Quik while the other three were fixed in 95% alcohol and stained with haematoxylin and eosin. The smears were reviewed and classified as recommended by the National Health Services Breast Screening Programme (NHSBSP) of Britain into five categories; Unsatisfactory, Benign, Atypical probably benign, Suspicious for malignancy and Malignant smears (12). This was done by the primary investigator.

All malignant smears were noted and graded using the Robinson's cytological grading system. The Robinson's cytological grading system assesses cell dissociation, nuclear size, cell uniformity, nucleolus, nuclear margin and chromatin pattern. Each of the parameters is given a score between 1 and 3 and the total is summed up. Lesions with a total score of 6-11 were graded as 1, 12-14 were graded as 2 and 15-18 were graded as 3(7). The slides were then compared with the histological slides of same lesions that were either biopsied or had mastectomies. The corresponding malignant histological slides were graded using the Nottingham grading system. The Nottingham grading system assesses the nuclear pleomorphism, mitotic count and tubule formation. Each parameter is scored 1-3 and the total scores summed up. A total score of 3-5 is graded as 1, 6-7 is graded as 2 and 8-9 is graded as 3 (13).

The cytological and histological grading systems were then compared using SPSS with level of significance put at 0.05. The absolute concordance rate between the two grading systems was also done. Ethical approval with protocol number ERC/2012/09/07 was obtained from the Ethics and Research committee of the Obafemi Awolowo University Teaching Hospital, Ile-Ife.

## RESULTS

A total of 164 breast lumps were aspirated during the study period. Fifty-two (31.7%) of the 164 breast lumps were diagnosed as malignant cytologically and subsequently graded with the Robinson's cytological grading system.

Out of the 52 patients that had malignant cytological smears, only thirty of them had either tissue biopsy or mastectomy specimens available for histological confirmation and comparison with their cytological smears.

Of the thirty patients that had both cytological and histological malignant lesions, four (13.3%) were between the ages of 30-40 years, thirteen (43.3%) of them were between the ages of 41-50 years, five (16.7%) were between 50-60 years of age and eight (26.6%) of them were between the ages of 61-70 years. The youngest patient was 35 years and the eldest was 70 years (Table 1).

The Robinson's cytological grading system revealed one case (3.3%) with grade of 1. Twelve cases (40%) were graded as 2 while 17 cases (56.7%) were graded as 3. (Table 2)

The same lesions were graded histologically using the Nottingham grading system. No case was graded 1 histologically. Sixteen cases (53.3%) were graded as 2 while 14 cases (46.7%) were graded as 3. (Table 3)

Comparison of the Robinson's cytological grading system and Nottingham histological grading system showed a chi square value of 8.679 with a p-value of 0.013 which implies that the relationship between the two grading systems is statistically significant. Likelihood ratio was also significant with a p-value of 0.009.

The concordance rate for grade 2 tumours was highest with a value of 83.3% while the concordance rate for grade 3 tumours was 70.6%, hence tumours that were graded as 3 had higher discordance when compared to histological grading system. The absolute concordance rate is 73.3%. (Table 4).

## DISCUSSION

The peak age of presentation of malignant breast lesions of 41 to 50 years in this study is similar to that obtained in the same centre by Omoniyi-Esan *et al.* (14). Similar studies in Maiduguri, Nigeria and Pakistan also found the same peak age of breast cancer to be in the fifth decade of life (15,16). However a similar study in Norway found the peak age of occurrence to be in the sixth and seventh decades of life (17). This

shows a different age pattern of presentation of breast cancer in Caucasian population studied by Weedon-Fekjaer *et al* and the studies in black population.

Most of the patients in this study had a Robinson's cytological grading of 2(40%) and only one patient had a cytological grading of 1. Pal *et al* (18) also found that of the 50 patients whose lesions were compared, most of them had a Robinson's cytological grading of 2, however, in his own study, more patients had a cytological grading of 1 and the lowest percentage of patients with malignant breast smears had Robinson's cytological grading of 3. Phukan *et al* (19) and Robinsons *et al* (7) also found that most of the patients studied had a cytological grading of 2, but more patients in their studies presented with malignant smears that were graded as 1 cytologically. Of the 50 cases studied by Phukan *et al* (19), 48% were graded as 2 while 28% were graded as 1. In the study by Robinson *et al*, of the 608 patients studied, 38.5% were graded as 2 and 38.3% were graded as 1 (7).

Late presentation by patients is a major problem in this part of the world. This may possibly explain why we only had one (3.3%) patient presenting with a lowest cytological grade tumour of 1 compared with that obtained by other studies. Tumours of longer duration may de-differentiate and thus have higher grades when compared to early tumours as seen in some low grade gliomas of the brain.(20) The fact that they had a larger sample size may also possibly explain this noted difference. Also, breast cancers in blacks are thought to be biologically more aggressive compared to other races (21). This may also partly explain why only one patient had a malignant smear graded cytologically as 1. There is paucity of data on cytological grading of breast cancer from West Africa and its surrounding regions, hence no local data to compare with the findings of the present study.

Robinson's cytological grade of 2 had the highest concordance rate of 83.3% with the Nottingham histological grading system. This is similar to the study by Phukan *et al* where the highest concordance was found in grade 1 and 2 tumours, however it is different from the findings by Sood *et al* (22) who found highest concordance in grade 1 tumours. The reason may be due to the fact that Sood *et al* (22) had more cases that were graded cytologically as 1 compared with this study. The absolute concordance rate of 73.3% in this study is very similar to that by Phukan *et al* (19) where they got an overall concordance rate of 72.2%. This

finding is less than that by Bukya *et al* (23) who got a concordance of 83.5% between the Robinson's cytological grading system and the Scarf-Bloom-Richardson grading system, however the finding in this study is higher than that by Sood *et al* (22) who had an overall concordance rate of 68.67%.

Einstein *et al* also did a similar study on 72 patients with breast cancer in Chennai, India. He found a concordance rate of 77.7% between the Robinson's cytological grading system and Nottingham histological grading system of breast cancers (24). This finding is also quite similar to the concordance rate obtained in this present study. The age range of patients he studied was between 34-79 years which also closely follows the age range of 35-70 years of patients seen in the present study. This may mean that the biographic data of patients in his study is very similar to that in this study, however, he had more tumours that were cytologically graded as 2 (55.5%) compared to the present study where most of the tumours were cytologically graded as 3(56.7%). This might still imply that patients in the present study presented with tumours of higher aggressive tendencies. Again, late presentation may still be a reason for this.

Other researchers including Bhargava *et al* (25) and Saha *et al* (26) and Walke *et al* (27) have also done similar studies with similar concordance rates of 77.78%, 76.3% and 76% respectively. Tumours that were graded as 3 cytologically had a higher discordance when compared to histological grading than tumours that were graded as 2 cytologically. This means that the likelihood of having a higher grade in cytology than on histology is significant. In this study, the FNAs were prepared with Diff-Quik and others with Haematoxylin and eosin. The Diff-Quik stain highlights the nuclear details making them more conspicuous than what is seen histologically, giving rise to a likelihood of having an overall higher grade compared to the histological grading because nuclear size is one of the components of the cytological grading system.

The concordance rate of 73.3% observed between the Robinson's cytological grading system and Nottingham histological grading system is acceptable enough to promote a good level of confidence on cytological grading of malignant breast lesions using the Robinson's cytological grading system. In our environment where late presentation is a common phenomenon, it may be helpful to start an initial therapy based on cytological reports in order to

save time of management of patients. A reliable cytological grading can also influence the choice of initial therapy that may be used in patients. The high level of concordance rate observed in this study shows that grading on FNA of malignant breast lesions can be an invaluable initial diagnostic tool for planning a definitive management plan for patients with breast carcinomas in our environment.

Most of the existing literature on comparison between Robinson's cytological grading and Nottingham histological grading system of breast cancers are from Asia and Europe. There is no local data to the best of my knowledge on this topic. This study however intends to add local data to the existing literature.

**Limitations:** This is a one-year prospective study and only patients that fell within the study period were recruited. Many patients with an initial cytological diagnosis of malignant breast lesions within the study period defaulted from the clinic resulting in fewer histological diagnoses to compare with cytological reports thereby affecting the overall study sample size.

## CONCLUSION

Breast cancer was seen in patients aged 35 to 70 years. Most breast cancers were graded as 3 using the Robinson's cytological grading system while the Nottingham histological grading system classified most breast cancers into grade 2. There is a high correlation between the Robinson's cytological grading system and the Nottingham histological grading system in this study. This means that Fine needle aspiration cytology can be used reliably as an initial diagnostic tool for planning a management modality for patients with breast cancer in this environment.

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**Table 1: Frequency of age groups of patients with malignant breast lumps**

Age	Frequency	Percentage (%)
31-40	4	13.3
41-50	13	43.3
51-60	5	16.7
61-70	8	26.7
Total	30	100

**Table 2: Frequency of Robinson's cytological grades of breast cancer**

Cytological grade	Frequency	Percentage (%)
Grade 1	1	3.3
Grade 2	12	40
Grade 3	17	56.7
Total	30	100

**Table 3: Frequency of Nottingham's histological grades of breast cancer**

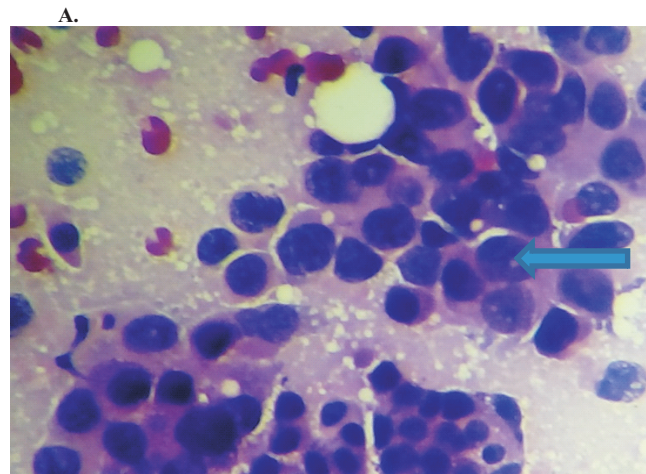
Histological grade	Frequency	Percentage (%)
Grade 1	0	0
Grade 2	16	53.3
Grade 3	14	46.7
Total	30	100

**Table 4: Comparison between Robinson's cytological grading and Nottingham histological grading of breast carcinomas.**

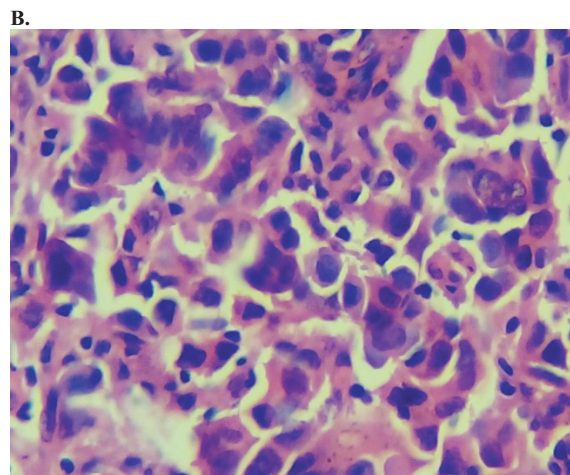
Cyto grading	Histology grading			Total	Concordance
	Grade 1	Grade 2	Grade 3		
Grade 1	0	1	0	1	0%
Grade 2	0	10	2	12	83.3%
Grade 3	0	5	12	17	70.6%
Total	0	16	14	30	

Chi square 8.679, P value= 0.013





**Figure 1a:** Photomicrograph of a malignant breast lump on cytology showing singly occurring malignant cells with marked nuclear hyperchromasia graded as 3. An enlarged hyperchromatic nucleus is depicted with blue arrow. (H and E x400).



**Figure 1b:** Photomicrograph of histology of the same breast lump shown above. The section shows pleomorphic malignant epithelial cells with large hyperchromatic nuclei and minimal attempt at gland formation. It was also graded as 3 histologically. (H and E x400)