http://journals.uct.ac.za/index.php/UR
DOI 10.15641/ur-at-uct.v1i1.25

Fine Needle Aspirate Cytology of Breast Lumps a Study of the GSH Breast Clinic

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ABSTRACT

The cytological results of 2899 fine needle aspirates from 2012 and 2013 from the Groote Schuur Hospital Breast Clinic were compared with the histological results of 1954 corresponding biopsies of the same lesions. On aspiration, a diagnosis of malignancy was made in 516 cases, 504 of which were confirmed histologically. There were 8 false positive cytological diagnoses and 49 false negative diagnoses made. 875 aspirates were categorized as inadequate, a rate of 30.18%. Possible reasons for such a high rate are discussed. Seventy three aspirates were taken from males during this two year period. The average age of patients at the clinic is 45.21 years. The results from this study are compared with previous data from the same clinic. The merits and drawbacks of fine needle aspiration of breast lesions are also discussed.

Keywords: Breast cancer, fine-needle aspiration cytology, core needle biopsy

Introduction

Breast cancer is the most common cancer among women in South Africa, and indeed in women worldwide (Herbst, 2014; International Agency for Research on Cancer, 2012). Therefore breast cancer places a significant monetary and human resource burden on the health system. Different parts of the world have different preferred methods of diagnosis, but the triple assessment method of diagnosis is most widely accepted. Triple assessment uses three separate tools to diagnose malignancy, namely clinical examination,

radiological imaging (mammography and/or ultrasound) and pathology (fine needle aspirate cytology (FNAC) or core needle biopsy (CNB)). When all three diagnostic tools are used, diagnostic accuracy is almost 100% (Berner *et al*., 2003:344). The preference of FNAC or CNB in initial diagnosis is the major difference in the triple assessment in different parts of the world. In many western countries (such as the USA, Canada and the UK) CNB is preferred, while other parts of Europe and many developing countries (including South Africa) still favour using FNAC (Challa, 2013:1).

The Breast Clinic was started at Groote Schuur Hospital in 1951 in order to streamline the treatment of patients with breast cancer (Department of Surgery, 1996). In 1982, cytology was introduced into the outpatient clinic, which allowed for rapid on site evaluation of FNAs (fine needle aspirate) (Learmonth *et al*., 1987:525). In 2014, fine needle aspiration is still the favoured methodology at The Breast Clinic as an essential part of the triple assessment. At The Breast Clinic, an aspirate is prepared in two ways: air-dried and stained using the Giemsa stain, and fixed and stained using the Papanicolaou stain. Each aspirate is checked by numerous people before a definitive diagnosis is made. First, by a senior cytotechnologist at the clinic; then by a pathology registrar, who subsequently checks the diagnosis with a consultant. The case may also be discussed at a meeting with a multidisciplinary team.

According to previous research, there are various reasons why FNAC should be used, and various other reasons that it is not reliable enough in diagnosing breast lesions. FNAC is extremely reliable in distinguishing benign lesions from those that are malignant, however it is not able to subcategorise those lesions (Learmonth *et al*., 1987:525). In order to further categorise a lesion, histology must to be used. Cytology also cannot be accurately used to assess the receptor status of a malignant tumour; histology is used for this purpose (Willems, van Deurzen & van Diest, 2012:287). Successful cytological diagnosis of FNAs depends largely on the skill and experience of the clinician performing the FNA. It is essential that clinical details of the patient are known to the clinician performing the aspirate and also to the cytotechnologist or pathologist evaluating the aspirate (Learmonth *et al*., 1987:525). The clinician should know

where the lesion is and whether it is palpable. These details can heavily influence the quality of the sample, and inadequate sample quality contributes to the varying success of cytology, leading to inadequate and false negative results (Dennison *et al*., 2003:491; Arisio *et al*., 1998:462). Various studies report that sensitivity and success rates of FNAC vary (Dennison *et al*., 2003:491; Sun *et al*., 2001:421). The pathologist should know clinical details, such as the patients age and relevant past medical history so that the pathologist does not miss a malignancy in a post menopausal patient, whose cells may look more benign, than a malignancy in a younger patient (Learmonth *et al*., 1987:525). Furthermore, cytology cannot accurately distinguish between in situ and invasive carcinoma. A biopsy must be performed to do this (Willems, van Deurzen & van Diest, 2012:287).

Despite the various pitfalls to FNAC outlined above, there are many reasons why it is still in favour in many countries, including South Africa. Compared to CNB, FNAC is a simple procedure. It is easier for the clinician to perform and is a cheaper option for screening out those who do not need further investigation (Berner *et al*., 2003:344). Because initial assessment is made on-site at the clinic, additional material can be sampled on the same day if required (Sun *et al*., 2001:421). This saves the patient additional stress of possibly taking time off from work to come back to the hospital. It also shortens the time the patient needs to wait for a final diagnosis, allowing treatment to begin more quickly, and lessening the anxiety associated with not knowing what is wrong. Furthermore, CNB requires anaesthetic and can be perceived as a more serious procedure, further increasing anxiety for the patient. FNAC also carries less of a risk for complications such as excessive bleeding, haematoma and pneumothorax than CNB (Challa, 2013:1; Sun *et al*., 2001:421). Classification of FNAC results is very important, as a reliable benign result (without overwhelming clinical evidence to suggest otherwise) requires no further, more invasive investigations (Berner *et al*., 2003:344).

At The Breast Clinic, FNAC and CNB are both used, in order to complement each other. The combined sensitivity of FNAC and CNB is 100%,

and so when used carefully and accurately, can be effective in the diagnosis of breast cancer (Dennison *et al*., 2003:491).

The objective of this research is to examine the correlation between cytological diagnosis of FNA specimens of breast masses from the Breast Clinic at Groote Schuur Hospital (GSH) with the subsequent corresponding histological diagnosis on biopsy (TRUCUT, core, punch). Furthermore, the research aims to estimate the proportion of malignant and benign lesions that were found amongst patients attending the breast clinic in 2012 and 2013. Finally, the objective is to compare the results from 2012 and 2013 to previous studies at the same clinic.

Materials and methods

An Excel spreadsheet containing all consecutive FNA results from 2012 and 2013 at the Breast Clinic at GSH was used (2899 in total). The spreadsheet contained the SCY code, age, sex, and SNOMED codes for the result of each FNA. These results were sorted into four categories (benign, atypical or suspicious, malignant, inadequate) using the SNOMED codes. After this, the electronic DISA database was used to correlate the cytological results of the FNAs with the histological results of the TRUCUT, punch and core biopsies (and in some cases lumpectomies or mastectomies) of the same lesions. The histological results were also sorted into the same categories, namely benign, atypical or suspicious, malignant, or inadequate. If the FNA and biopsy were in the same category, they were said to correlate. An FNA was excluded from the data if there was no corresponding biopsy. Some cases were reviewed under the microscope with the supervisor in order to clarify results. To analyse the data, various Excel formulae were used. The results were transferred into various tables for further analysis.

This research was approved by the UCT Human Research Ethics Committee. Patient names were removed to retain anonymity.

Results

A total of 2899 fine needle aspirates were performed on breast lesions in 2012 and 2013. Of these, 1419 were performed in 2012 and 1480 were performed in 2013. Figure I details the break down of the results of all the FNAs from those two years.

Category	Number	Percentage (%)
Benign	1212	41.81
Atypical or suspicious	296	10.21
Malignant	516	17.80
Inadequate	875	30.18
Total	2899	100

Figure I: Total FNAs in 2012 and 2013

Category	Number	Percentage (%)
Benign	593	41.79
Atypical or suspicious	126	8.88
Malignant	280	19.73
Inadequate	420	29.60
Total	1419	100

Figure II: Total FNAs in 2012

Category	Number	Percentage (%)
Benign	619	41.82
Atypical or suspicious	170	11.49
Malignant	236	15.95
Inadequate	455	30.74
Total	1480	100

Figure III: Total FNAs in 2013

Figures II and III show the breakdown of results from each year, 2012 and 2013. In 2012 and 2013, 1212 lesions were cytologically diagnosed as benign. During this period, a total of 296 lesions were diagnosed as having atypical cells or being suspicious for malignancy. From 2012 to 2013, the percentage of malignant diagnoses increased by over 2.5%. A total of 516 lesions were diagnosed as malignant, and from 2012 to 2013, the percentage of malignancies went down by almost 4%. The percentage of inadequacy remained relatively stable over the two years, with an increase of just over 1%.

Figure IV shows that 2823 females underwent fine needle aspiration, compared with 73 males.

Gender	Number	Percentage (%)
Female	2823	97.38
Male	73	2.52
Gender not stated	3	0.10
Total	2899	100

Figure IV: Gender distribution

Category	Number	Percentage (%)
Benign	919	47.03
Atypical/suspicious	19	0.97
Malignant	856	43.81
Inadequate	160	8.19
Total	1954	100

Figure V: Total biopsies in 2012 and 2013

Figure V shows that a total of 1954 fine needle aspirates were followed up for biopsy. There was a significantly lower number of atypical diagnoses for biopsies, than for fine needle aspirations. The percentage of malignant diagnoses for histology was 26.01% higher than the percentage of cytological malignant diagnoses. There were a total of 160 inadequate diagnoses histologically.

	2012	2013	All
Cytology	593	619	1212
No biopsy	257	299	556
Total biopsied	336	320	656
BIOPSY RESULT			
Benign	276	266	542
Atypical/suspicious	7	2	9
Malignant (false negative)	25	24	49
Inadequate	28	28	56

Figure VI: Histology results of benign cytology

	2012	2013	All
Cytology	126	170	296
No biopsy	6	13	19
Total biopsied	120	157	277
BIOPSY RESULT			
Benign	34	49	83
Atypical/suspicious	4	3	7
Malignant	82	101	183
Inadequate	0	4	4

Figure VII: Histology results of atypical cytology

	2012	2013	All
Cytology	280	236	516
No biopsy	3	0	3
Total biopsied	277	236	513
BIOPSY RESULT			
Benign (false positive)	5	3	8
Atypical/suspicious	0	0	0
Malignant	272	232	504
Inadequate	0	1	1

Figure VIII: Histology results of malignant cytology

	2012	2013	All
Cytology	420	455	875
No biopsy	190	177	367
Total biopsied	230	278	508
BIOPSY RESULT			
Benign	124	162	286
Atypical/suspicious	2	1	3
Malignant	61	59	120
Inadequate	43	56	99

Figure IX: Histology results of inadequate cytology

Figures VI-IX show the corresponding histological results of each category of cytological results (benign, atypical/suspicious, malignant or inadequate). Over half of lesions that had a benign cytological diagnosis underwent subsequent biopsy. Of these 656 benign FNAs which had corresponding biopsies, 49 were malignant on biopsy (false negative). Of the cytologically atypical or suspicious

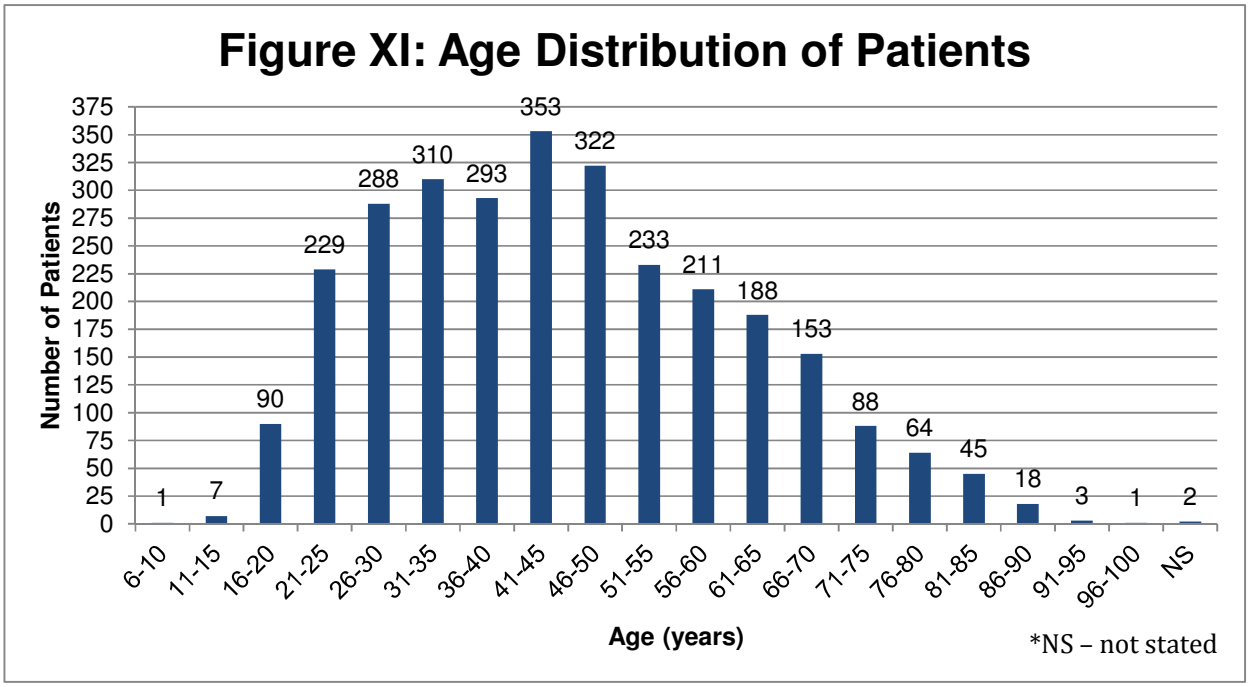
lesions that underwent biopsy, 66.06% were malignant on histology. There were 8 false positives; that is 8 lesions were malignant on cytology, but benign on histology.

FNA total	73
Benign	38
Atypical/suspicious	8
Malignant	5
Inadequate	22
No biopsy	30
Total biopsies	43
Benign	30
Atypical/suspicious	0
Malignant	4
Inadequate	9

Figure X: Cytology and histology results for males in 2012 and 2013

Figure X shows the results for males in 2012 and 2013. There were 5 malignancies on cytology, and four on histology. There was 1 false positive for males, which, on histology, was found to be gynaecomastia.

The minimum age of the patients was 8 years and the maximum was 98.



Therefore there was a range of 90 years, with the mean being 45.21 years. The median and mode age were both 44 years. Figure XI shows the distribution of age of the patients that underwent FNAC in 2012 and 2013.

Discussion

As mentioned in the results section, 2899 FNAs were performed in 2012 and 2013. This procedure is well established, and is performed on anyone suspected of having breast cancer. In 2012, 29.60% of FNAs were categorized as inadequate, while in 2013, 30.74% of FNAs were inadequate. Previous figures from The Breast Clinic presented at the International Academy of Pathology Congress in 2012 show a steady increase in the percentage of inadequate FNAs since 1982 (Fenwick & Learmonth, 2012). From 1982 to 1985, 19% of FNAs were inadequate. From 2008 to 2009, 25% of FNAs were inadequate. From 2010 to 2011, 24% of FNAs were inadequate. There are various reasons this increasing inadequacy rate may occur. It may be because the clinicians performing the aspirate have not had adequate training or experience in the procedure and so miss the lesion or use the incorrect technique. It may also be that women are better educated, and so come to the clinic earlier, with smaller lesions, which may lead to geographical misses of the lesion. The inadequacies may also be due to the incorrect interpretation of a well differentiated neoplasm. In order to remain a feasible means of diagnosis, the number of inadequate samples needs to decrease. To do this, better training for the clinician should be given, and the emerging technique of doing ultrasound guided FNA, which is becoming more popular in other parts of the world, could be implemented, increasing the accuracy of each aspirate, more likely leading to an accurate diagnosis. Also of note, is that of the inadequate aspirates, 20% of the corresponding biopsies were also inadequate, further pointing to inadequate technique in biopsying the lesion, and so a suboptimal sample is received by the pathologist. Furthermore, when looking at the individual FNA results in chronological order, it was clear that there periods of time when there would be many inadequate aspirates, and other times when there would be very few inadequate aspirates. This further points to the skill of the individual clinician heavily impacting on the overall result, as the doctors rotate in and out of the clinic every few months. This means that a new doctor must gain experience and skill in the procedure every few months, often at

the expense of sample quality. Other studies have stated that the range of inadequate cytology is from 11% to 20% (Dennison *et al*., 2003:491). The significantly higher percentage in this study should be addressed, and a percentage of inadequacies between 11% and 20% should be the goal for the clinic.

Although the atypical or suspicious category is of little use clinically, it is an important group cytologically. The diagnosis of atypical is often made due to the sample quality, for example there may be low cellularity in the sample, or the cells may be only mildly atypical. The atypical category is also subjective, and may depend on the pathologist that is evaluating the aspirate. However, this category helps to reduce the number of false negatives, and so allows for more cautious care of patients. Of the 296 atypical FNAs, 277 were biopsied. Of those biopsied, 183 were found to be malignant (66.06%). This shows the value of the category, allowing for better care of the patients. If diagnosed cytologically as atypical or suspicious, a more invasive biopsy is recommended to definitively diagnose a benign or malignant lesion.

When looking at the 1954 biopsies performed, 43.81% of the lesions biopsied were malignant. This compares with less than 17.80% of aspirates having a malignant result. The proportion of malignant biopsies is higher than that of malignant FNAs, showing that cytology is successful as a minimally invasive procedure in screening out those who do not require further investigation.

In the dataset, there were 49 false negative and 8 false positive cytological results. The overall false negative rate was 2.51% and the false positive rate was 0.41%. The false negative rate may be due to geographical misses when sampling the lesion. The false negative rate may be due to incorrect evaluation of the aspirate. Because of the false positives and false negatives that may be encountered, it is essential that histological confirmation of the cytological result be obtained before starting treatment in order to prevent over treatment of patients (Learmonth *et al*., 1987:525).

The average age of patients that had FNA was 45.21 years old. The median and mode were both 44. This shows that younger women are coming into the clinic. It may be that women are getting cancer at younger ages. The possible changing age profile of breast cancer patients could be analysed in future research. Programmes may need to be tailored to younger women if women are getting breast cancer at earlier ages.

Conclusion

In conclusion, it is hoped that this research can be used for better planning of the GSH Breast Clinic. Furthermore, it is clear that The Breast Clinic plays an important role in screening for and the treatment of breast cancer in Cape Town. This research could also be used for the planning of future walk-in breast clinics in other areas of Cape Town and South Africa, as the GSH Breast Clinic is efficient and effective in accomplishing its mission. In order to make it even more effective, the inadequacy rate of FNAs need to be addressed, through regular training of clinicians and pathologists, and the implementation of ultrasound guided FNAC. It is also important to recognise the strengths and limitations of FNAC. FNAC is very effective at distinguishing between malignant and benign lesions, but it is less effective at further classifying the lesions. It is important for clinicians and pathologists to use their discretion when deciding whether to perform more invasive procedures after receiving the results of the FNA, and to use CNB in a way that compliments FNAC.

Acknowledgements

I would like to thank Dr Genevieve Learmonth for her guidance, and assistance throughout the research. She so generously gave of her time to teach me cytology. I would also like to acknowledge all the assistance Sharon Fenwick gave. Thank you for compiling the data and always being available to assist.

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