# Fine needle aspiration of breast masses: an analysis of 1533 cases in private practice

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**The diagnostic efficacy of fine needle aspiration cytology of breast masses and the causes for unsatisfactory specimens in private practices were investigated in Hong Kong. All specimens that were submitted to the histopathology unit at the Canossa Hospital between 1 January 1996 and 30 April 1997 formed the basis of this report. A total of 1533 specimens were received from 1447 patients; 274 (17.8%) cases were unsatisfactory for assessment, 1080 (70.4%) were benign, 51 (3.3%) atypical, 19 (1.2%) suspicious, and 67 (4.4%) malignant. The specimens were submitted by 105 doctors, who each performed between 1 and 561 smears. The proportion of unsatisfactory samples was high for doctors who performed an occasional fine needle aspiration (48%; overall mean, 25%). Histological correlation was available in 165 cases. The overall sensitivity was 79%, specificity 98%, positive predictive value (including the 'suspicious' category) 92%, and negative predictive value 94%. Two false positive cases that were reported as suspicious were found to be fibroadenomata following subsequent excision biopsy. No adverse clinical outcomes were recorded for the false positive cases. There were six false negative cases (reported as a cyst in one case, benign in two cases, and atypical in three cases). The results compared favourably with published data and affirmed the effectiveness of the test in private practice.**

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## Introduction

Fine needle aspiration (FNA) cytology has been widely used for the diagnosis of palpable breast masses. The technique involves the insertion of a fine needle (between 21 and 25 gauge) into a lesion and the extraction of a small sample of cellular material which is smeared onto glass slides. The cells are stained and examined morphologically by cytopathologists. Fine needle aspiration is simple, fast, and can be performed as an office procedure, since it requires no special equipment, causes minimal morbidity, and has high patient acceptance.[1-3] Most reports about the accuracy of FNA techniques are from tertiary institutions and specialised breast clinics. We carried out an audit of our breast FNA data to determine the accuracy of the technique in private practice in Hong Kong and as an internal quality assurance exercise for our laboratory.

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## Materials and methods

All FNAs were performed by clinicians and radiologists in private practice and were submitted to our laboratory for interpretation. All cases of breast FNA that were submitted between 1 January 1996 and 30 April 1997 were reviewed. As the FNAs were performed by clinicians in different surgeries, the technique used in each individual case was not known. It is routine practice, however, to use 22 to 23 gauge needles that are attached to 10 mL syringes. The needle is placed within the lesion and a vacuum is applied by gently withdrawing the plunger of the syringe. The needle is moved back and forth within the lesion and the negative pressure is released prior to withdrawing the needle. Some clinicians prefer to perform the procedure without suction; instead, they rely on the capillary action of the needle to draw cellular material into the barrel of the needle. Samples are usually smeared onto glass slides; slides can be fixed immediately with cytology fixative (Surgipath Medical Industries, Richmond, Illinois, USA) or left to dry. The wet-fixed smears are stained with Papanicolaou stain while the air-dried smears are stained with 'Diff-Quik'

(Dade Diagnostic, Aguada, Puerto Rico). Some radiologists routinely rinse needles in buffered normal saline (0.9% sodium chloride; B Braun Pharmaceutical, Penang, Malaysia) after the smears have been made.

Cell blocks are made from the needle rinses if particulate material is present: such samples accounted for less than 1% of all cases in this study. Alternatively, cytospin slides are prepared from the needle rinses if no particulate matter is present. Most of the FNAs that were performed by radiologists in this study were from palpable lumps; occasionally, the FNAs are performed using ultrasound guidance.

No stereotactic biopsies were performed. The number of smears submitted varied from one smear to more than 10 smears per patient; the average number was about two smears per patient. The larger numbers of smears for some patients were usually submitted by surgeons and radiologists. All the smears were screened and interpreted by two pathologists. The FNA reports were classified into six groups: unsatisfactory, benign, atypical, suspicious, malignant, and 'others'. Poorly prepared smears that had smearing artefacts or air drying, or that were bloody or thick were considered unsatisfactory for cytological assessment. In addition, smears that were technically well prepared but that contained fewer than six clusters of at least 10 epithelial cells each were considered unsatisfactory. Smears were classified as benign if they contained cohesive clusters of epithelial cells, scattered myoepithelial cells, and a background of bare nuclei. Atypical smears usually contained scant atypical epithelial cells that had nuclear enlargement or hyperchromatism, against a background of benign epithelial material. Suspicious smears were usually highly cellular and contained atypical cells that were suggestive of but ambiguous for malignancy. Some smears showed features of more than one category, and scant bare nuclei were often noted in the background of these atypical smears, which were also classified as suspicious. Malignant smears were those containing abnormal cells—an unequivocal feature of malignancy. The malignant cases were usually highly cellular and showed loss of cellular cohesion, and abnormal dissociated individual cells with intact cytoplasm were scattered in the background. The number of cases in each diagnostic group was tabulated.

The surgical pathology of breast biopsies and mastectomies during the same period were also reviewed. Corresponding cases of FNA and histology were tabulated and slides of the cases of major discrepancy were reviewed.

## Results

A total of 1533 FNAs from 1447 patients were submitted during the study period. Six of the patients were male. No age was given in the case reports of 106 patients. The ages of the remainder varied from 14 to 91 years and the mean age was 38.6 years (standard deviation, 9.8 years). Eighty patients had two FNAs and three patients had three FNAs.

The smears were referred by 105 doctors. The identity of the referring doctors was not recorded in eight cases. The number of FNAs submitted and the number of doctors are tabulated in Table 1. The percentage of unsatisfactory aspirates (excluding cysts) was related to the experience of the aspirator. Doctors who performed the least number of smears submitted the highest proportion of unsatisfactory specimens. As doctors performed more aspirates, the percentage of unsatisfactory aspirates declined (Table 2). The overall proportion of samples that were unsatisfactory (25%) was higher than most reports in the literature and may be partly explained by the large number of doctors performing a small number of FNAs. Most of the reported series were from specialist FNA clinics

**Table 1. Number of referring doctors and the number of samples submitted**

| | No. of samples | No. of doctors |
|---|---|---|
| | 1 | 34* |
| | 2 | 18 |
| | 3 | 13 |
| | 4 | 7 |
| | 5 | 2 |
| | 6 | 1 |
| | 7 | 5 |
| | 8 | 3 |
| | 9 | 2 |
| | 10 | 1 |
| | 11 | 1 |
| | 12 | 1 |
| | 13 | 2 |
| | 14 | 3 |
| | 15 | 1 |
| | 17 | 1 |
| | 20 | 1 |
| | 23 | 1 |
| | 29 | 1 |
| | 30 | 1 |
| | 36 | 1 |
| | 42 | 1 |
| | 81 | 1 |
| | 132 | 1 |
| | 216 | 1 |
| | 561 | 1 |
| Total | 1533 | 105 |

* Doctors for eight samples that were submitted by different laboratories (and thus likely to be performed by eight different doctors) were unidentified

**Table 2. Proportion of samples submitted that were unsatisfactory**

| No. of samples | Proportion unsatisfactory (%) |
|---|---|
| <8 | 45 |
| <16 | 39 |
| <32 | 38 |
| <64 | 37 |
| <128 | 29 |
| >200 | 22 |
| Overall | 25 |

in tertiary institutions or were performed by pathologists with on-the-spot assessment of specimen quality.

Cysts were more commonly encountered by general practitioners and gynaecologists than surgeons who specialised in breast surgery (58% of all FNAs for those performing less than 15 smears, compared with 22% for those who performed more than 15 FNAs). Conversely, tumours such as fibroadenomata (8%) and carcinoma (5%) were more likely to be encountered in the smears provided by breast surgeons; corresponding figures were <1% and 2% for smears submitted by other clinicians. The diagnostic categories of all 1533 cases of FNA are shown in Table 3.

During the study period, 1248 breast biopsies were reported. There were 165 matching cases. The cytohistological correlation of the 165 cases is shown in Table 4. For the purpose of statistical analysis, FNAs that were reported as benign or atypical were considered 'negative' and smears that were reported

**Table 3. Diagnostic categories of all fine needle aspiration samples**

| Diagnostic category | No. of samples (%) |
|---|---|
| Unsatisfactory | 274 (17.87) |
| Benign | |
| benign | 531 (34.64) |
| cyst | 459 (29.94) |
| fibroadenoma | 90 (5.87) |
| Atypical | 51 (3.32) |
| Suspicious | 19 (1.24) |
| Malignant | 67 (4.37) |
| Others | |
| cystosarcoma | 1 (0.07) |
| inflammatory | 35 (2.28) |
| mucocele | 3 (0.20) |
| lymph node | 2 (0.13) |
| lipoma | 1 (0.07) |
| Total | 1533 |

suspicious or malignant were considered 'positive'. Using these criteria, there were two false positive cases in the suspicious category; these were actually fibroadenomata, one case of which had atypical ductal hyperplasia. There were six false negative cases (one cyst, two benign smears, and three atypical FNA reports). Unsatisfactory specimens and six cases in the 'others' category (Table 4) were excluded from the calculation. The aggregated results are shown in Table 5. The sensitivity, specificity, positive predictive value, and negative predictive values were calculated from this information. The positive predictive value for cases diagnosed as malignant were 100%, 66.6% for suspicious cases, and 16.6% for atypical cases.

**Table 4. Cytohistological correlation of fine needle aspirations of the breast**

| FNA* | Histology | | | | | | |
|---|---|---|---|---|---|---|---|
| | FCC† | Hyperplasia, papilloma | FA‡ | ADH§ | Carcinoma | Other | Total |
| Unsatisfactory | 12 | 4 | 7 | - | 6 | Siliconoma (1) | 30 |
| Benign | | | | | | | |
| benign | 17 | 6 | 27 | 2 | 2 | - | 54 |
| cyst | 12 | 3 | - | 2 | 1 | Inflammatory (1) | 19 |
| FA | 1 | - | 13 | - | - | - | 14 |
| Atypical | 3 | 4 | 6 | 1 | 3 | Haematoma(1) | 18 |
| Suspicious | - | - | 1 | 1 | 4 | - | 6 |
| Malignant | - | - | - | - | 19 | - | 19 |
| Others | | | | | | | |
| CP‖ | - | - | - | - | - | CP (1) | 1 |
| inflammatory | - | - | - | - | - | Inflammatory (2) | 2 |
| mucocele | - | - | - | 1 | - | Mucocele (1) | 2 |
| Total | 45 | 17 | 54 | 7 | 35 | 7 | 165 |

* FNA fine needle aspiration
† FCC fibrocystic change
‡ FA fibroadenoma
§ ADH atypical ductal hyperplasia
‖ CP cystosarcoma phyllodes

**Table 5. Summary of statistical analyses**

| FNA* | Histology | |
|---|---|---|
| | Benign | Carcinoma |
| Benign/atypia | 97 (TN†) | 6 (FN‡) |
| Suspicious/malignant | 2 (FP§) | 23 (TP‖) |

* FNA fine needle aspiration
† TN true negative
‡ FN false negative
§ FP false positive
‖ TP true positive

Sensitivity = (TPx100) / (TP+FN) = 79%
Specificity = (TNx100) / (TN+FP) = 98%
Positive predictive value = (TPx100) / (TP+FP) = 92%
Negative predictive value = (TNx100) / (TN+FN) = 94%

## Discussion

### *Unsatisfactory specimens*

As expected, the proportion of FNAs that were unsatisfactory was higher for doctors who performed an occasional FNA (45%) than it was for surgeons with a special interest in breast surgery (22%). The overall proportion of FNAs that were unsatisfactory in this report was 25%, which is within the range reported in the literature (0%-42%).[3] The importance of the aspirator's experience, and the influence of unsatisfactory aspirates on patients' clinical management have been previously documented.[4,5] The percentage of unsatisfactory samples is lower in specialist breast clinics and where cytologists perform FNA than when samples are mailed to a laboratory for interpretation by external physicians.[6] A non-diagnostic aspirate, however, is not without value when it is taken from a clinically benign breast 'thickening' and when the surgeons want to exclude occult malignancy. Many of these smears are poorly cellular or acellular, although we have encountered a case of unsuspected lobular carcinoma where the clinical impression was 'thickening'. Unsatisfactory specimens should be evaluated in conjunction with clinical and imaging appearances. To highlight the importance of triple diagnosis, six of the unsatisfactory samples in our series were in fact carcinomas, as shown by subsequent biopsy.

### *Statistical analyses*

Although there are many reports of the statistical analyses of breast FNAs, it is often difficult to make direct comparison because the methods of analyses vary considerably. Some reports include cysts and unsatisfactory specimens in their calculations.[2] The management of atypical and suspicious cases also varies, which reflects the arbitrary categorization of a biological continuum. In practice, such reports are neither positive nor negative but indicate to clinicians the requirement for formal surgical excision of the breast mass. The various categories are useful, because they convey an increasing probability of malignancy, as illustrated in our series by the increasing positive predictive values of 16.6%, 66.6%, and 100% for atypical, suspicious, and malignant cases, respectively. We have elected to include suspicious cases with the malignant cases, and atypical cases with the benign cases in our analyses. Our statistical parameters are similar to those reported in the literature (sensitivity, 0.48-0.94; specificity, 0.35-0.98; positive predictive value, 0.995-1.00; negative predictive value, 0.51-0.97).[1,3]

### *False negative diagnoses*

False negative diagnosis may be due to technical failure, misdiagnosis, or the presence of mixed benign and malignant cytological features.[7] Examples of technical failure include acellular or insufficient cellular material, heavily bloodstained smears, partial air-drying, and smearing artefact resulting in cell disruption. It has been shown that some unsatisfactory aspirates are due to the histological stage and type of carcinoma.[8-10] The false negative cases in our series were as follows: six cases that were reported as unsatisfactory due to insufficient cellular material, one heavily bloodstained smear that had mixed cytological features, which was reported as a cyst, two misdiagnoses due to well-differentiated tumours in the benign category, and three cases that were reported as atypical (Table 4).

Review of the false-negative cystic lesion revealed one small cluster of degenerated atypical cells against a background of lysed blood, macrophages, and cellular debris. The abnormal cells had a high nuclear to cytoplasm ratio and hyperchromatic nuclei. Histological examination showed a well-differentiated, partly intracystic carcinoma that had focal areas of invasion. The tumour cells were bland and well differentiated. The three cases that were reported as atypical were poorly cellular and would have been classified as unsatisfactory, were it not for the presence of a few cytologically abnormal cells.

The two false negative misdiagnoses were reported as benign—one was an invasive lobular carcinoma and the other was a well-differentiated carcinoma in situ that was composed of small well-differentiated ductal cells; focal invasion was visible in the latter case. Review of the smears from the lobular carcinoma showed scant abnormal, dissociated cells that had intact cytoplasm and nuclear atypia, against a background of benign clusters of epithelial and myoepithelial

cells, and scattered bare nuclei of bland morphology. An 'Indian-file' strip of abnormal cells was visible occasionally. The smears that were predominantly carcinoma in situ were moderately cellular and had a background of blood. The epithelial cells were small and very cohesive. Nuclear morphology was difficult to assess because the nuclei overlapped. Dissociated cells were present occasionally and these were cytologically well differentiated. Careful attention to nuclear detail and a pattern of monomorphism should allow recognition of these false negative cases in the future.

***False positive diagnoses***

The two false positive diagnoses in our series involved smears that were classified as suspicious; no false positive diagnoses were made in the malignant category (Table 4). In concordance with a published report,[11] the most common cause of false positive diagnosis was fibroadenoma, and the next most common was ductal hyperplasia. In both false positive cases that were reported as suspicious, lumpectomies showed fibroadenomata; no adverse clinical outcomes were recorded.

***Utility of fine needle aspiration in Hong Kong***

More FNAs of breast lesions are being done in Hong Kong, as reflected in the increasing number of smears received by our laboratories. However, some clinicians are reluctant to use this modality of diagnosis due to inexperience with aspiration and smear preparation, the lack of knowledge about FNA, and the lack of confidence in the test. It is evident from this report that the test has a high degree of sensitivity, specificity, and positive and negative predictive values, especially when used in conjunction with clinical and imaging assessments. Fine needle aspiration of the breast has been shown to decrease the number of open biopsies[12] and is highly cost-effective.[13,14] The technique is simple and rapid diagnosis may be obtained in a considerable number of cases. In addition, FNA can be used to obtain preoperative diagnosis of carcinoma, thus allowing earlier counselling and preparation for clinical management for the patient.

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