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D. Kulkarni, T. Irvine, R.J. Reyes

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Authors: D. Kulkarni, T. Irvine, R.J. Reyes

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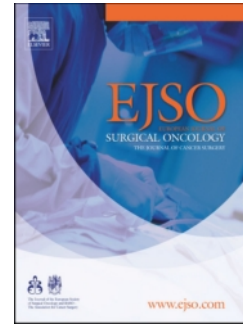
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The Use of Core Biopsy Imprint Cytology in the 'One-Stop' Breast Clinic.

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Authors:

Kulkarni D,

Irvine T,

Reyes R. J.

Acknowledgement:

Walters T. K

Khan M.

The Magill Breast Unit
Queen Mary's Hospital NHS Trust
Frognal Avenue, Sidcup
Kent DA14 6LT.

Abstract:***Aims:***

The aims of this study were to evaluate the sensitivity, specificity; accuracy, usefulness and role of core biopsy imprint cytology (CBIC) in the one-stop breast clinic in a District General Hospital.

Methods:

A retrospective study was made of symptomatic patients attending a district general hospital one-stop clinic over a five year period where a core biopsy had been performed and an imprint of the core had been made for cytological analysis. The performance of the technique was evaluated by comparing the results of CIBC with the definitive histological analysis of the core biopsy tissue.

Results:

Over a five year period, imprints were made from 819 core biopsies. Adequate cellularity for cytological analysis was found in 94.8% (778/819) of the imprints. Out of the 778 lesions analysed, 432 were malignant (55.5%). The sensitivity, specificity, positive predictive value, negative predictive value and concordance were 97.7%, 94.2%, 93.1%, 98.1% and 95.5% respectively.

Conclusion:

Core Biopsy Imprint Cytology is a rapid, reliable and accurate technique which enhances the known benefits of automated core biopsy. It allows core biopsies to be used successfully in the 'one-stop' clinic setting and obviates the need to use Fine Needle Aspiration Cytology (FNAC).

When CBIC is used, there is a reduction in diagnostic waiting time (over core biopsy on its own) and an increase in diagnostic performance (over FNAC).

This translates to an improvement in the management of patients with breast cancer through the earlier availability of the diagnosis and fewer out-patient appointments.

Introduction:

41,000 new breast cancers are diagnosed in the United Kingdom every year¹.

Attendance to a breast clinic usually generates anxiety for the patient. It is beneficial to the patient and therefore desirable, to reduce both the time that the patient has to wait for results and the number of out-patient appointments that they have to attend.

A reduction in waiting time for the diagnosis of malignancy means that a patient can start coming to terms with this distressing diagnosis at the earliest opportunity. This is as important as the prompt diagnosis of benign disease so that the patient can be discharged from the clinic.

Historically, 'one-stop' rapid diagnostic clinics used fine needle aspiration cytology (FNAC) as their main diagnostic method for breast lumps, as a cytological diagnosis was available within an hour or so. However there are several drawbacks to using FNAC. Often, a fine needle aspirate contains insufficient cells for diagnosis (C0/C1) with the consequence that the aspirate needs to be repeated or the patient is called back for a core biopsy. This core biopsy might have to be performed on another day.

Core biopsies however, take much longer to formally process and for this reason alone, cannot deliver results quickly enough for this assessment technique to be useful in the rapid diagnostic one-stop setting.

Nevertheless, the superior diagnostic performance of core biopsy has resulted in many breast units adopting this technique in preference to FNAC. However, the trade-off has been a reduction in speed of diagnosis.

Imprint cytology on/from core biopsy (CBIC) offers a potential solution to all these problems. It offers an equally as rapid result as FNAC as it is itself, a cytological method. There is also evidence that imprinting yields more cells than FNAC with a reduction in inadequate sampling rates. The advantage of a histologically based definitive diagnosis (from the core biopsy) for the patient speaks for itself.

The technique of CBIC has been successfully used in lung and mediastinal tumour assessment and in several small series in breast clinics.

The aim of this study therefore, was to assess the accuracy and usefulness of touch imprint cytology in a one-stop rapid diagnostic clinic in a district general hospital.

Patients and methods:

Data was collected from both symptomatic and screening patients attending the one-stop rapid-diagnosis and screening assessment clinics over a 5 year period at Queen Mary's Hospital, Sidcup, Kent, U.K.

All patients who underwent an automated core biopsy (ultrasound-guided or clinical) and who had a cytological imprint made from this core biopsy tissue were included in this prospective study. Data was retrieved from the patient notes and the patient database of the Department of Pathology.

In all cases a 14-gauge needle (2.5cm throw) in a core biopsy gun was used with the great majority of the biopsies being image guided.

Imprints were made from the core biopsy specimens by wiping/rolling the core of tissue on a glass slide immediately after the core was taken. An average of 4 slides were imprinted from each core biopsy.

Half of the slides were air dried and the other half were fixed in alcohol. The slides were stained with Haematoxylin and Eosin and the stained core specimens embedded in paraffin and processed in the usual manner. The slides were reviewed by a cytopathologist and were graded 'I' (for imprint) 1-5, in a manner identical to that used for cytology grading (Table 1).

Clinical:

Patients were informed that a 'quick test' was being performed on their core biopsy. They were also told that the result of this quick test was not the final result and any result given would be provisional and subject to final confirmation, when the full processing of the core biopsy specimen had taken place.

Ethical approval was not required for this study.

Table 1: Imprint cytology classification

Grade	Result	Summary
I1	Inadequate	Insufficient epithelial cells to allow diagnosis.
I2	Benign	A good yield of clearly benign epithelial cells.
I3	Probably benign	Cells exhibit some atypical features so that the imprint cannot definitely be called benign.
I4	Probably malignant	Cytological features suggestive of malignancy but insufficient to allow the definite diagnosis of cancer.
I5	Malignant	Unequivocal cytological evidence of malignancy.

Results:

819 patients had imprints made during the study period. Of these, 805 (98%) were female and 14 male (2%). On average, 4 imprint cytology slides were prepared per patient.

Inadequate cellularity was seen in 41 cases. Of these 29 were in cases where the final histology was benign and 6 where the final histology was malignant. In 6 cases, inadequate cellularity/tissue was reported but the ultimate diagnosis, benign or malignant, was not given.

These 41 cases were excluded from the study leaving 778 of the original population of 819 (95%) for inclusion in the analysis.

Of the 778 cases 415 (53%) were malignant and 363 (47%) benign (Table 2).

The 8 false positives were papilloma, fibrocystic change (x2), adenoma, high EZ (epithelial tumour marker) levels, fibroadenoma and fat necrosis.

Table 2: Summary of results – I1 excluded from subsequent analysis

	Core Benign	Core Malignant	Total
No diagnosis (excluded)			6
I1 (excluded)	29 CI	6 CI	35
I2	316	5	321
I3	22	20	42
I4	2	25	27
I5	6	382	388
Total (excl. inadequate)	346	432	778

In the analysis I3 results were included in the Imprint Benign group and I4 in the Imprint Malignant group (Table 3).

Table 3: Comparison of final histology and imprint results – used to calculate sensitivity and specificity

	Core benign	Core malignant	Total
Imprint Benign	338	25	363
Imprint Malignant	8	407	415
Total	346	432	778

This gives an overall sensitivity and specificity of 97.7% and 94.2% respectively with a concordance of 95.5%. The use of the imprint cytology to predict the final core result has a positive predictive value of 93.1% and negative predictive value of 98.1%.

Discussion:

There are many considerations when one is giving results to patients in the breast clinic. Obviously, one wants to give the patient an accurate result and giving results early can significantly reduce patient anxiety.

We have shown the sensitivity and specificity of CBIC in our usage.

The results of CBIC must be understood in context with the results of the other elements of the Triple Assessment (TA). If the other parts of the TA indicate that the lesion is likely to be malignant then this affects the way that the result of the CBIC can and should be interpreted and used.

If a lesion is thought on clinical and radiological grounds to be malignant, then a CBIC of I5 can be given with confidence but still with the caution that it will need to be finally confirmed by histological analysis of the core biopsy.

Given the sensitivity, specificity and PPV of an I5 score this is reasonable. The patient is told that all the elements of the TA are in agreement and that it is fairly certain that the lesion is malignant. This allows a frank discussion about the process and treatment that the patient might have to undergo (including surgery) and the patient can start coming to terms with the likely diagnosis.

The following week, after the results of the TA have been discussed at the Breast multi-disciplinary meeting (MDM), the diagnosis can be confirmed to the patient. The consensus view and treatment plan is also ready to be given to the patient. As a week has passed, the patient is usually ready for a full discussion about their treatment after which, in our experience, they are usually ready to sign their consent form.

If a lesion is thought on clinical and radiological grounds to be benign, then a CBIC of I2 can be given with confidence and the patient told that they will receive a letter confirming that the histological analysis of the core biopsy has confirmed only benign tissue. If there is a discrete lesion that has been sampled and the core biopsy histology shows only normal tissue and the absence of any discrete lesion, then the patient can be recalled for further biopsy.

The problem comes when the clinical and radiological elements of the TA are equivocal or suggest malignancy but the CBIC is I2 – benign. This is a problem because the suspicious lesion may have been missed by the core biopsy and normal tissue sampled. Normal tissue will return the score of I2 but clearly this may not be the correct result. In this situation therefore, a CBIC score of I2 cannot be relied upon.

In the situation where the TA is benign but the CBIC returns as I4 or I5, the final histology must be awaited and the patient warned of the irregularity in the ‘quick test’ and the need to wait for the final results.

CBIC has been found to be a sensitive and reliable method in the diagnosis of lung, bone marrow, gastrointestinal and lymph node lesions. **(1, 2, 3, 4)**

Several smaller series have also shown this technique to be safe and reliable in breast patients. **(5, 6, 7, 8, 9)**

The series we present appears to be the largest series of its kind and our results are comparable with those of other studies (Table 4).

Table4: Summary of studies including current paper

Centre	Author	Number	Sensitivity (%)	Specificity (%)
Sidcup	Kulkarni	819	97.7	94.2
Bristol	Jones	111	97	98
Athens	Veneti	351	97.1	99.4
Kiel	Anlauf	195	89	88
Marburg	Albert	173	96.5	90
Bury	Klevesath	128	96.2	100

Conclusion:

Core Biopsy Imprint Cytology is a rapid, reliable and accurate technique which enhances the known benefits of automated core biopsy. It allows core biopsies to be used successfully in the 'one-stop' clinic setting and obviates the need to use Fine Needle Aspiration Cytology (FNAC).

When CBIC is used, there is a reduction in diagnostic waiting time (over core biopsy on its own) and an increase in diagnostic performance (over FNAC).

This translates to an improvement in the management of patients with breast cancer through the earlier availability of the diagnosis and fewer out-patient appointments.

Conflict of interest

The authors state that they have no conflict of interest.

Legend

Table 1: Imprint cytology classification

Table 2: Summary of results – 11 excluded from subsequent analysis

Table 3: Comparison of core and imprint results – used to calculate sensitivity and specificity

Table 4: Summary of studies including current paper

ACCEPTED MANUSCRIPT

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