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An Initial Experience with Rapid Microwave Processing in the One-Stop Breast Clinic

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Abstract

Background Rapid microwave processing allows core biopsy results to be obtained within a 3- to 4-h time period. This study was designed to compare the accuracy and reporting time of microwave-processed breast biopsies with samples processed using traditional methods.

Methods Concordance of the preoperative biopsy report with postoperative histology for tumor type, grade, and detection of lymphovascular invasion was recorded for both techniques. Also reviewed were the time taken between day of biopsy and day of reporting, waiting time between biopsy and surgery, and number of preoperative outpatient appointments.

Results In the microwave-processed group (MG; $n = 43$), there was a 92% concordance rate between preoperative biopsy and postoperative histology for tumor type. In the traditional group (TG; $n = 43$), it was 80% ($P > 0.05$). For tumor grade, there was a concordance rate of 64% in MG and 93% in TG ($P > 0.05$). For detection of lymphovascular invasion, there was agreement in 88% of cases in MG and 67% in TG ($P > 0.05$). Twenty-five patients from MG were informed of their diagnosis on the day of biopsy. There was no difference in waiting time from biopsy to surgery or number of preoperative outpatient appointments between MG and TG ($P > 0.05$).

Conclusions Microwave processing allows safe and accurate immediate histological reporting. As a result, surgical management can be planned at the initial outpatient consultation.

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Introduction

One-stop breast clinics where patients receive results of clinical, radiological, and pathological investigations on the same day have become less prevalent in recent years. This is primarily because surgeons are preferring to assess patients with suspected cancer by performing core biopsy, which requires overnight processing, rather than fine needle aspiration cytology (FNAC) [1]. Core biopsy distinguishes invasive carcinoma from in situ disease and provides information on tumor type, grade, and evidence of lymphovascular invasion, which allows a more accurate preoperative diagnosis to be made and thus treatment can be planned with greater certainty.

Core biopsy, especially when combined with ultrasound and/or stereotactic guidance, has been shown to be a highly accurate diagnostic tool with a sensitivity of approximately 90% and false-negative rates of between 2 and 9%. Compared with FNAC, the inadequacy rate of core biopsy is lower and more patients receive unequivocal results [2–6]. Core biopsy is therefore felt to be superior to FNAC both for the preoperative assessment of malignant lesions and also for the definitive diagnosis of benign disease.

Traditionally the main limitation of core biopsy has been pathology turnaround time, with tissue samples requiring overnight processing before analysis by the histopathologist. This means that patients must return at a later date for their results [1, 7]. By contrast, provided that adequate cytology resources are available onsite, FNAC can be reported within the time constraints of a single one-stop clinic visit. As a result, FNAC is still widely practised [8, 9].

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Rapid microwave processing is an attractive alternative because it allows tissue to be made available for analysis much faster than when traditional methods of core biopsy processing are employed. Microwave irradiation accelerates the fixation process by enhancing the diffusion of liquids into and out of cells and there also is a reduction in the number of steps of tissue fixation used in reported microwave-assisted protocols, both of which lead to shorter processing times [10–13].

When microwave processing is employed, core biopsy results can be reported on the same day, allowing the diagnosis and subsequent implications of this to be discussed with the patient during their first visit to the breast clinic. If appropriate, surgery is planned at the initial consultation and the patient leaves with a clear management plan in place. When our institution changed from a rapid cytology-based service to one that utilized microwave processing, the goal was to maintain a rapid diagnostic process while being able to utilize the more detailed information and greater diagnostic accuracy of core biopsy.

We report our initial experience with rapid microwave processing for breast core biopsies. We aimed to determine the concordance of preoperative biopsy with postoperative histology for microwave and traditional techniques. Pathology reporting time also was reviewed to establish how many patients in the microwave group received their biopsy results on the same day and to see whether this made any difference to the timing of surgery.

Materials and methods

Patients in the microwave-processing group (MG) underwent needle core biopsy at the one-stop breast clinic at North Manchester General Hospital, UK, and all samples were subsequently processed in the rapid microwave processor (RHS Processor, Milestone®, Sorisole, Italy) (http://milestonemedsrl.com/histopathology/products/microwave_main.html). Comparison was made with patients who underwent core biopsy at the one-stop clinic at the same institution before acquisition of the microwave processor. This group of biopsies [TG] were processed using traditional methods of tissue processing. Information was collated retrospectively from a pathology department logbook of biopsy codes, histology reports, patient notes, and computerized clinic letters.

Primary outcome measures assessed the accuracy of the rapid microwave processing technique compared with traditional overnight processing and were as follows:

- Correlation of tumor type on the preoperative core biopsy report with tumor type on the postoperative histology report
- Correlation of tumor grade on biopsy with tumor grade on the postoperative histology report
- Correlation of lymphovascular invasion detected on biopsy with the presence or absence of lymphovascular invasion on the postoperative histology report

Secondary outcome measures reviewed the one-stop diagnostic pathway for the two patient groups and were as follows:

- Number of patients diagnosed on the day the biopsy was taken (i.e., one-stop patients)
- Waiting time in days between the day of biopsy and the day the results were reported
- Waiting time in days between the day of biopsy and the day the patient underwent definitive surgery for malignancy
- Number of preoperative outpatient appointments

Each core biopsy was taken in the outpatient clinic using a standardized aseptic technique. The skin was cleaned with antiseptic solution (Videne®; Ecolab® St. Paul, MN) and then infiltrated with 10 ml of local anaesthetic (Xylocaine® 1% with epinephrine 1:200,000). A Tru-Core® II Biopsy Instrument (Angiotech® Medical Device Technologies, Inc., Gainesville, USA) was used to obtain samples.

The technique employed for MG is outlined in Fig. 1 [14]. If the pathology department was expecting a biopsy from the one-stop clinic and a specialized histopathologist was available, then the result could be reported and conveyed to the patient within 4 h.

TG biopsies underwent traditional overnight tissue processing. In this group, same-day reporting was not possible and further arrangements were made for the patient to return to the clinic at a later date to discuss results and further management.

Biopsy results were reported in accordance with the National Health Service Breast Screening Guidelines [15]. Because a new processing technique had been introduced, any patients from MG given a benign diagnosis were kept under short-term follow-up.

Statistical analysis was performed using SPSS (SPSS Inc, Chicago, IL). Spearman's rank correlation coefficient was used to compare rates of histologic concordance between MG and TG. Comparison between one-stop diagnostic outcomes for patients in the two groups was made using a Wilcoxon signed-rank test. $P < 0.05$ was taken as statistically significant.

Results

Core biopsy results for 86 one-stop breast clinic referrals were examined. Data from 43 consecutive patients who

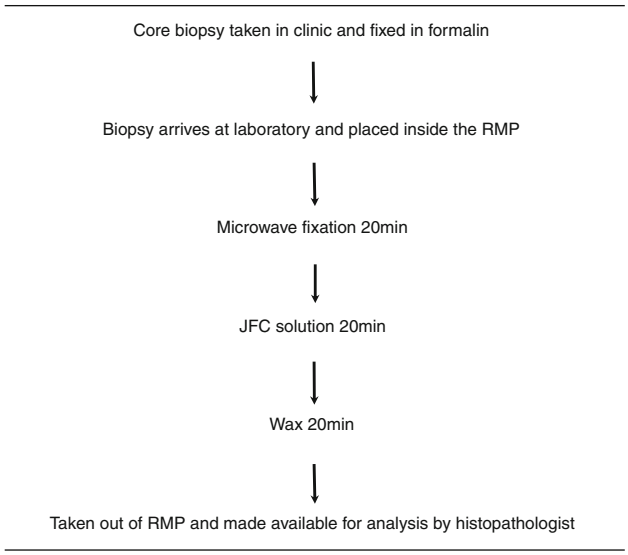

Fig. 1 Fixation process for microwave-processed samples. *RMP* rapid microwave processor (RHS Processor, Milestone®, Sorisole, Italy), *JFC* organic solvent mixture of ethanol, isopropanol and a long chain hydrocarbon (JFC solution, Milestone®)

underwent core biopsy that was subsequently processed using the microwave processor (MG) [median age, 54 (range 27–101) years] was compared with 43 consecutive patients who underwent core biopsy processed using traditional methods (TG) [median age, 64 (range 41–94) years]. Table 1 outlines patient demographics and the distribution of pathologies on postoperative histology reports for the two groups.

Information on tumor type after surgical excision was available for 27 patients in MG. There were 20 cases of invasive ductal carcinoma, 3 of invasive lobular carcinoma, 2 of ductal carcinoma in situ, 1 of apocrine carcinoma, and 1 of metaplastic carcinoma. Of the remaining 16 patients in MG, 2 patients declined treatment and 1 patient had advanced disease at presentation and did not undergo surgery. There also were 11 benign diagnoses; 3 patients underwent surgical excision and had the diagnosis confirmed at postoperative histology, 4 had a follow-up ultrasound scan, 2 had repeat FNAC, and 2 were followed-up in the outpatient department. Two histology records were incomplete for tumor type in MG.

All patients in TG were diagnosed with malignancy because FNAC was still employed as a first-line investigation when these patients were being assessed. There were 34 invasive ductal carcinomas, 4 invasive lobular carcinomas, 1 case of ductal carcinoma in situ, 1 of tubulo-lobular carcinoma, 1 of pleomorphic lobular carcinoma, and 1 of Paget's carcinoma. One histology record was incomplete for tumor type in TG.

Information on tumor grade after excision was available for 26 patients in MG. There were 5 tumors of grade 1, 10 of grade 2, and 11 of grade 3. Thirteen patients did not undergo surgery for malignancy and four records were incomplete.

In TG there was 1 tumor of grade 1, 20 of grade 2, and 15 of grade 3. Tumor grade was not reported for the one case of Paget's and one tubulo-lobular carcinoma. Five histology records were incomplete for tumor grade in TG.

Lymphovascular invasion was present in 12 specimens in MG and absent in 15. Thirteen patients did not undergo surgery and three records were incomplete. In TG it was present in 16 excised specimens and absent in 22. Five records were incomplete.

Table 2 compares rates of concordance of preoperative biopsy with postoperative histology for tumor type, grade, and detection of lymphovascular invasion for rapid microwave and traditional processing techniques. Ninety-two percent of tumor types reported on MG biopsy were in concordance with postoperative histology reports, whereas

Table 1 Patient demographics and pathologies

	MG ($n = 43$) median age 54 (range 27–101)	TG ($n = 43$) median age 64 (range 41–94)
Total excisions	27	43
Invasive ductal carcinoma	20	34
Invasive lobular carcinoma	3	4
Ductal carcinoma in situ	2	1
Apocrine carcinoma	1	0
Metaplastic carcinoma	1	0
Tubulo-lobular carcinoma	0	1
Pleomorphic lobular carcinoma	0	1
Paget's carcinoma	0	1
Benign diagnosis	11	0
Did not undergo surgery	2	0
Incomplete records	3	1
Grade 1	5	1
Grade 2	10	20
Grade 3	11	15
Incomplete records	4	5
Lymphovascular invasion present	12	16
Lymphovascular invasion absent	15	22
Incomplete records	3	5

Table 2 Rates of concordance for tumor type, grade and detection of lymphovascular invasion

	MG	TG	*P* value
Concordance rate for tumor type	0.92	0.80	0.564
Concordance rate for tumor grade	0.64	0.93	0.18
Concordance rate for lymphovascular invasion	0.88	0.67	0.317

Table 3 All infiltrating ductal carcinomas with grade on biopsy and final histology

	MG ($n = 20$)	TG ($n = 34$)
Concordance for grade	11/20	25/34
Nonconcordance for grade	7/20	7/34
	5 upgraded from 2 to 3	3 upgraded from 2 to 3
	1 upgraded from 1 to 2	1 upgraded from 1 to 2
	1 downgraded from 3 to 2	2 downgraded from 3 to 2
		1 downgraded from 2 to 1
Incomplete records	2/20	1/34
Initial benign biopsy report	0/20	1/34

there was an 80% concordance rate in TG ($P = 0.564$). There was a 64% concordance rate with tumor grade in MG compared to 93% in TG ($P = 0.18$). The accuracy in detecting the presence or absence of lymphovascular invasion on MG biopsies was 88% compared with 67% in TG ($P = 0.317$).

Table 3 is a breakdown of all tumors classified as invasive ductal carcinoma and their corresponding grade as reported on biopsy and final histology. In MG, there was nonconcordance in 7 of 20 cases with 6 biopsies upgraded on final histology (5 samples from grade 2 to grade 3, 1 from grade 1 to grade 2) and only 1 downgraded (from grade 3 to grade 2). In TG there was nonconcordance in 7 of 34 cases with 4 biopsies upgraded (3 from grade 2 to grade 3, 1 from grade 1 to grade 2) and 3 downgraded (2 from grade 3 to grade 2, 1 from grade 2 to grade 1).

Table 4 displays results for pathology processing time and the effect of this on number of preoperative outpatient clinic appointments and the timing of surgery. Twenty-five MG patients were informed of the results of their core biopsy on the day it was taken. None of the patients from TG were given their diagnosis on the same day. Although a same-day diagnosis was not made in 18 MG patients, the median wait for this group was significantly less than in TG (MG, 0 days; TG, 5 days; $P < 0.001$). There was a trend toward fewer preoperative outpatient appointments in MG, but this difference was not statistically significant at the 5% level ($P = 0.059$). The waiting time between biopsy and surgery was no different: 24 days in both groups ($P = 0.811$).

Discussion

The continued use of one-stop breast clinics in the United Kingdom is supported by guidelines from the Department of Health, the National Institute of Clinical Excellence, and the Association of Breast Surgery at the British Association of Surgical Oncology [1, 7, 16]. The main driving force behind this is an attempt to reduce the time from referral to diagnosis. Intra-country variability in cancer survival rates across Europe has been attributed to differences in disease stage at diagnosis [17] with delays of 3–6 months being associated with lower survival rates in patients with breast cancer [18].

One-stop cytology-based clinics are becoming less prevalent due to an increasing number of surgeons performing core biopsy as one of the initial tools of triple assessment. In this system, patients return to the clinic on a separate occasion to discuss their biopsy results, which generates an additional outpatient consultation and could potentially delay the treatment process. Use of a rapid microwave processor places greater emphasis on effective same-day assessment without sacrificing diagnostic accuracy and as a result, some of the delays associated with traditional overnight processing techniques are avoided.

This technique may reduce patient anxieties because less time is spent waiting for definitive histology results. Patients with benign disease can be reassured at their initial consultation, and those diagnosed with malignancy can discuss possible treatment options. One-stop cytology-based clinics have been shown to reduce levels of anxiety associated with waiting for the results of diagnostic tests [19, 20]. By being able to offer a same-day diagnosis,

Table 4 Time from biopsy to reporting, time to surgery and number of preoperative outpatient appointments

	Biopsy					
	Reporting (days)		Surgery (days)		No. of preoperative outpatient appointments	
	MG	TG	MG	TG	MG	TG
Mean	1.3	4.53	26.25	29.53	2.07	2.60
SD	2.21	2.25	13.55	15.72	1.02	1.07
Median	0	5	24	24	2	2
P value	<0.001		0.811		0.059	

microwave processing may have a similar effect, although the psychological impact of a definitive one-stop histological diagnosis was not addressed in this study.

Rapid microwave processing also has the potential to reduce the length of the patient pathway. There was a trend toward fewer preoperative outpatient appointments in the MG group, and this difference may have reached statistical significance with a larger sample size. The same cannot be said for the time between diagnosis and surgery; however, this is dependent upon other external factors, such as the surgical case load at the time, which may have acted as a confounder.

Although the potential exists to turn around microwave-processed samples during a one-stop clinic visit, there are extensive logistical challenges that arise from using this method. In our study, biopsies that arrived at the laboratory after 12 o'clock could not be reported on the same day. This was the reason that 18 samples from MG not being reported at the initial consultation. At present, the pathology department cannot accept samples for rapid processing if they are taken in an afternoon clinic; therefore, the ability to provide a one-stop service such as this requires a tremendous amount of coordination between clinicians, clinic staff, and radiology and pathology services.

Regarding the accuracy and overall safety of the microwave technique, there was a difference in the rate of concordance between preoperative biopsy and postoperative histology for tumor type, grade, and detection of lymphovascular invasion for MG and TG, although none of these differences were statistically significant. For tumor type, it was 0.92 for MG and 0.80 for TG. Although a rate of 0.80 for TG may be below what would be expected, there was only one case where the biopsy was reported as invasive ductal carcinoma but the final histology was lobular carcinoma. Other cases classified as nonconcordance were for rarer histological subtypes and where the biopsy was reported as carcinoma in situ but there was invasive tumor in the excised specimen.

The microwave technique would appear to be less accurate for reporting tumor grade, as reflected by concordance values of 0.64 for MG and 0.92 for TG. There were five examples in MG where a biopsy was reported as a grade 2 invasive ductal carcinoma, but on final histology the tumor was found to be grade 3. It is possible that this difference did not reach statistical significance because the numbers are relatively small, which raises the possibility of underreporting grade 3 tumors using this technique. If this is the case, then that would have an impact on the treatment offered to such patients, but evidence from the literature is to the contrary [10–12]. Morales and colleagues reported no difference in histologic quality between rapid microwave-processed samples and conventional processing methods for a range of different tissues, and Leong et al. actually described enhancement and more consistent results for light microscopy when microwave processing is employed.

Concordance rates for evidence of lymphovascular invasion were similar; the microwave technique appeared to be slightly superior to the traditional method. One concern with rapid processing techniques is tissue shrinkage, but this tends to occur with larger samples and after prolonged fixation periods [21, 22]. Because the core biopsies require fixation for only 20 min with this method, the quality is comparable [23].

In terms of alternative rapid processing techniques, several studies have examined the use of imprint cytology of core biopsy specimens taken at a one-stop clinic breast clinic [24–26]. The main limitation of this technique is that patients still have to leave the clinic and come back for their definitive histology results at a later date. When microwave processing is used, immunohistochemistry apart, all other prognostic indicators, such as whether the disease is invasive or in situ, as well as tumor type, grade, and lymphovascular invasion, can potentially be reported within 4 h. There also is the opportunity to repeat biopsies immediately if they are thought to be nonrepresentative.

This study has several limitations that should be addressed. In MG there was a pathologist on standby for rapid reporting of biopsies, but in TG patients were given a rapid cytology result and came back at a later date to discuss their biopsy result, meaning that there was greater emphasis placed upon expedient reporting of biopsies in MG compared with TG. An absolute reduction in processing time was therefore not the only factor that reduced the amount of time between the biopsy being taken and the conveyance of results. Nevertheless, by being able to offer same-day reporting, other logistical factors that increase delay, such as the subsequent availability of a pathologist and the weekly outpatient clinic timetable, were avoided.

Second, because biopsies from the traditional group were taken at a time when FNAC was employed as a first-line investigation, all of these patients were diagnosed with malignancy, whereas there were some benign biopsies in the microwave group. This has lead to a difference in the distribution of pathologies and number of surgical excisions between the two groups.

Third, the method of core biopsy (ultrasound-guided, stereotactic, or free-hand clinical) was not controlled for and it is well documented that image-guidance has a higher rate of diagnostic accuracy than clinical core biopsy [3, 4].

Finally, an assumption is made that patients would prefer to obtain definitive results at their initial consultation, but patient satisfaction questionnaires were not given out at the time of their attendance at the clinic. It is felt that being able to reassure patients of a benign diagnosis at their initial consultation is beneficial [27], but it is currently

unclear as to whether the same can be said for patients who are given a cancer diagnosis at their first one-stop clinic visit and this issue is not addressed in this paper.

This study is the first to report on the clinical application of rapid microwave processing in a one-stop breast clinic. The technique did not affect the quality of tissue available for analysis by the histopathologist, and as a result would appear to be as accurate as traditional methods of core biopsy processing. From a purely diagnostic point of view, a one-stop service that aims to give definitive same-day histology results is superior to a clinic that combines FNAC and traditional overnight biopsy processing. Because results can be given on the same day, it has the potential to reduce the number of preoperative outpatient attendances and also the amount of time between referral and definitive surgical treatment. Being able to give patients core biopsy results at their initial consultation may represent the future of the one-stop breast clinic.

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