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FULL PAPER

Randomized controlled trial of stereotactic 11-G vacuum-assisted core biopsy for the diagnosis and management of mammographic microcalcification

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Objective: To compare the accuracy of 11-G vacuum-assisted biopsy (VAB) with 14-G core needle biopsy (CNB) to diagnose mammographic microcalcification (MM) and effect on surgical outcomes.

Methods: Following ethical approval, VAB and CNB (control) were compared in a randomized prospective study for first-line diagnosis of MM and subsequent surgical outcomes in two breast-screening units. Participants gave written informed consent. Exclusions included comorbidity precluding surgery, prior ipsilateral breast cancer and lesions >40 mm requiring mastectomy as first surgical procedure. The final pathological diagnosis was compared with the initial biopsy result. Quality-of-life (QOL) questionnaires were administered at baseline, 2, 6 and 12 months. 110 participants were required to show a 25% improvement in diagnosis with VAB compared with CNB (90% power).

Results: Eligibility was assessed for 787 cases; 129 females recalled from the National Health Service breast screening programme were randomized. Diagnostic accuracy of VAB was 86% and that of CNB was 84%. Using VAB, 2/14 (14.3%) cases upgraded from ductal carcinoma *in situ* to invasion at surgery and 3/19 (15.8%) using CNB. Following VAB 7/16 (44%) cases required repeat surgery *vs* 7/24 (29%) after CNB. Both groups recorded significant worsening of functional QOL measures and increased breast pain at follow-up.

Conclusion: VAB and CNB were equally accurate at diagnosing MM, and no significant differences in surgical outcomes were observed.

Advances in knowledge: The first randomized controlled study of VAB for diagnosis of microcalcification using digital mammography showed no difference in diagnostic accuracy of VAB and CNB, or in the proportion of participants needing repeat non-operative biopsy or second therapeutic operation to treat malignancy.

INTRODUCTION

Accurate non-operative diagnosis of impalpable malignant breast lesions minimizes numbers of therapeutic surgical procedures.[1] The National Health Service Breast Screening Programme (NHSBSP) stipulates targets for non-operative diagnosis and benign surgery rates to reduce numbers of operations for females attending the programme.[2,3] Delineation of malignant mammographic microcalcification (MM) and accurate non-operative diagnosis is important because lesions upgraded or diagnosed at surgery may require repeat operations to stage the axilla and to achieve complete excision.

Stereotactic 14-G core needle biopsy (CNB) of MM is challenging. Multiple needle insertions retrieve samples <2 mm in diameter (30 mg). Non-contiguous samples may give inadequate quantitative information to permit differentiation of atypical lesions or ductal carcinoma *in situ* (DCIS). Limited information regarding lesion architecture and failed microcalcification retrieval may give false-negative results or fail to diagnose invasive cancer within DCIS (*underestimate*).[4] For CNB, this *clinically* important accuracy measure (underestimation/upgrade rate) is quoted in studies of predominantly calcified lesions between 17% and 32% in meta-analysis.[5–8]

Published evaluations of stereotactic vacuum-assisted biopsy (VAB) of the breast, introduced in 1995, suggest improved diagnostic accuracy using VAB, which produces larger contiguous specimens (100 mg for 11 G), usually with single device insertion, leading to lower underestimation rates.[5,9–11] Improved accuracy of non-operative diagnosis may relate to larger numbers of samples routinely obtained using VAB, but this is not a consistent finding.[5,9,11–14] The use of specimen radiography to confirm representative calcification retrieval following stereotactic biopsy improves diagnostic accuracy, and digital mammography may contribute to improved accuracy of diagnosis for MM.[15–21] The need for repeat biopsies of MM may reduce with VAB but inadequate (B1) sampling is not eliminated, even in large centres performing many procedures.[2,19,22–25] Complications associated with stereotactic breast biopsy include bleeding, haematoma formation, pain and scarring, and some evidence suggests that complications are more frequent using vacuum assistance.[19,24,26,27]

The few studies which have analysed VAB performance to diagnose MM lesions (without associated mammographic or ultrasound abnormality) show that underestimation of invasive disease persists following VAB (11–29%).[5,7,9,10,28–32] Meta-analysis of cohort studies which were predominantly retrospective evaluations suggested that VAB may have better diagnostic accuracy than CNB; however, prospective evaluation of the techniques has been recommended.[8,30]

VAB in the breast has been adopted for first-line diagnosis in North America and Europe; however, additional costs of VAB have inhibited widespread first-line diagnostic use in the UK, and 14-G CNB remains the standard technique in many centres. Greater diagnostic accuracy using VAB may prove cost effective if diagnosis with VAB leads to fewer repeat operations.[6,32–35] A prospective randomized study was performed to compare diagnostic accuracy of 11-G VAB and 14-G CNB for MM and to evaluate impact on the surgical management of these cases.

METHODS AND MATERIALS

Design

Prospective randomized trial to compare 11-G VAB (*intervention*) with 14-G CNB (*control*) for diagnosing microcalcification (*primary end point*) and subsequent surgical outcomes (*secondary end point*).

Participants

Ethical approval was obtained from the National Research Ethics Service and the local research and development committee at each site. Consecutive patients attending the symptomatic service, referred from family history or breast cancer surveillance, or from the NHSBSP who underwent MM evaluation (M3–5) without a palpable lesion were assessed for eligibility between 7 March 2011 and 4 July 2013.[36] Two breast-screening units participated; a teaching hospital and tertiary referral site and a district general hospital. Additional views and clinical assessment were performed.[37] Patients with mammographic microcalcification which was likely to result in recommendation for mastectomy as the first surgical procedure were excluded in order to permit capture of secondary surgical end points, *i.e.* prior history of ipsilateral breast cancer or suspicious microcalcification >40 mm in extent. Similarly, patients potentially requiring two-site biopsy were excluded. Patients with comorbid conditions or taking medications which may influence the accuracy of the test or surgical decision-making were also excluded. Patients with inadequate compressed breast thickness to accommodate safe deployment of VAB needle (<40 mm), which prevented use of VAB at one centre without lateral arm capability, were also excluded (Table 1). Eligible patients were approached and given information sheets. Written informed consent was obtained.

Randomization

The Department of Medical Statistics used a computer-generated block randomization programme to allocate patients (1 : 1) to two groups, stratifying by size (<20/≥20 mm). Staff not involved with the study prepared concealed randomization allocations in sequential randomization envelopes in the two strata.

Intervention

CNBs were performed by eight radiographer advanced practitioners using Siemens Mammomat 3000 (Siemens Medical Solutions, Inc., Malvern, PA) or GE Senographe DMR system (GE Medical Systems Ltd, Amersham, UK) with add-on devices for stereobiopsy. Microcalcification was localized within the biopsy window. Two mammographic projections at +15/−15° were selected for targeting. One to three specks of microcalcification were targeted, providing three co-ordinates in three-dimensions (x, y and z). CNB was brought to the skin entry point overlying the x and y co-ordinates above the z co-ordinate, permitting accurate local anaesthesia infiltration with 5 ml of 2% xylocaine with adrenaline. A small skin incision was made. The needle, set to acquire 22-mm samples, was advanced to the z co-ordinate depth ensuring targeted calcification lay centrally within the needle throw (14-G Bard®MaxCore® disposable core biopsy instrument; Bard® Biopsy Systems Inc., Tempe, AZ) or Achieve® 14-G disposable needle (Achieve® CareFusion, Waukegan, IL). Following needle deployment, offset images at +15/−15° confirmed correct needle positioning related to the target. Specimen X-ray demonstration of microcalcification in three cores after at least seven CNB samples confirmed adequate sampling. For very small clusters of microcalcification, adequate sampling was confirmed by removal of the entire cluster within one or two samples.[18,37]

Radiologists performed VAB (11-G) using a Mammotome® device (Devicor® Medical Systems Inc., Cincinnati, OH) with either Giotto Image SD full-field digital biopsy system and Giotto Mammobed prone table [Internazionale Medico Scientifica (IMS), Bologna, Italy] or GE DMR system and GE lateral arm (GE Medical Systems Ltd) in the upright position. The central fleck of clustered microcalcification was targeted prior to local anaesthetic infiltration with 10 ml of xylocaine 2% with adrenaline. The VAB needle was advanced to target and fired into the sampling position. Pre- and post-fire images, as indicated, were obtained at +15/−15° to check the target position relative to the sampling notch. 12 samples were routinely retrieved with the multidirectional biopsy aperture rotated in 30° increments. Sampling continued until representative microcalcifications were demonstrated on specimen

Table 1. Participant inclusion/exclusion criteria

Inclusion criteria	Exclusion criteria
Age 18–90 years	Refusal of informed consent for the procedure
Written informed consent	Previous history of ipsilateral breast carcinoma
Impalpable mammographic microcalcification	Contraindication to either biopsy technique *e.g.* significant musculoskeletal problems impacting on patient positioning and reducing accuracy
	Recurrent breast cancer
	Bleeding diathesis/anticoagulation on warfarin
	Significant comorbidity which would contraindicate surgery
	Suspicious microcalcification (M4/5) ≥40 mm requiring two site biopsy or multifocal microcalcification requiring two site biopsy
	Compressed breast thickness ≤40 mm

X-ray as above.[18,37] When either biopsy removed most of the lesion, a titanium marker was left *in situ*.

Quality of life (QOL) assessment was made using the validated European Organisation for Research and Treatment of Cancer QOL core questionnaire, QLQ-C30, and breast cancer module and supplementary questionnaire, QLQ-BR23, at baseline, 2, 6 and 12 months.[38,39] Non-responders were followed up once at 2 weeks.

A study *pro forma* issued at randomization recorded anonymized demographic details, lesion assessment information and background mammographic density using visual estimation by the radiologist and the length of the procedure (total length of time that the patient was in the biopsy room). Duration of procedure was measured this way to provide the most consistent assessment and includes information related to post-biopsy care of the patient which is important in consideration of resource use. Biopsy and surgical data were recorded and verified on hospital and breast-screening databases and entered onto Excel® (Microsoft®, Redmond, WA) including encoded QOL data.

Non-operative biopsy specimens were reported according to national guidelines by four consultant breast pathologists.[2] Core biopsy samples underwent rapid processing and serial slicing, whereas the larger volume of tissue obtained at VAB was submitted to more extensive processing including weighing the specimen and even distribution of biopsy material on the cassette. Both VAB material and core specimens were examined to the same level of detail. Biopsy results were discussed at multidisciplinary team (MDT) meetings consisting of at least one consultant surgeon, radiologist and pathologist.[40] Where repeat non-operative biopsy was recommended, the second result was discussed and outcomes were recorded. Participants were discharged with concordant benign result or referred for diagnostic or therapeutic surgery.[3] Post-operative MDT decisions and pathology were recorded.

Statistical analysis

55 patients are required in each arm to detect a statistical difference in accuracy between two biopsy methods with 90% power at the 5% significance level, assuming 95% were diagnosed at the first assessment with VAB compared with 70% (local audit data) with CNB.[41]

To detect a significant difference between the 2 groups in the percentage of patients needing >1 operation (15% *vs* 40%; a 25% difference) for 90% power, 74 patients needing an operation in each group were required. Audit data indicated 37% of patients required an operation.

The proportion of correct diagnoses at first biopsy in each group and the proportion of patients requiring more than one operation were compared using Fisher's exact test. Data on time to initial diagnosis, final diagnosis and completion of treatment were highly skewed and were log e transformed before carrying out *t*-tests for the comparison of the two groups. QOL data were analysed using longitudinal linear or binary logistic regression analysis with generalized estimating equations. Primary analyses were carried out by intention to treat and used the conventional two-sided 5% significance level. Per protocol and subset analyses were carried out as secondary analyses.

An analysis (blinded to the main investigators) was planned after randomizing 200 patients to assess whether the true difference in the secondary end point was likely to be around 25%.

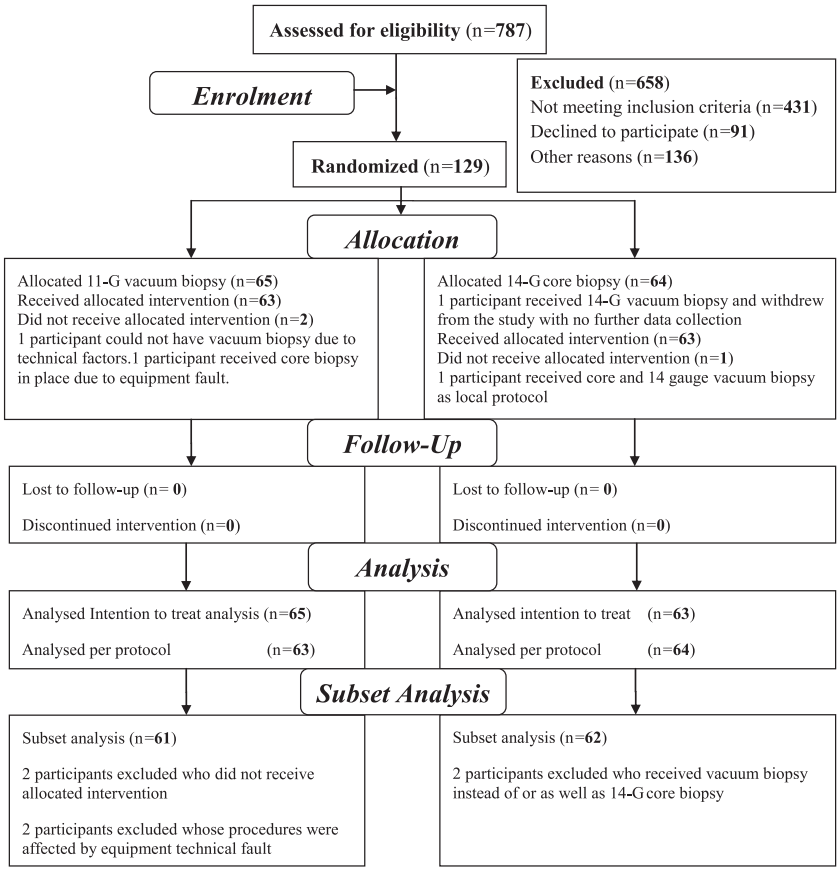
RESULTS

Recruitment

Between 7 March 2011 and 4 July 2013, 787 patients were screened for eligibility and 129 participants were recruited. One participant randomized to CNB withdrew from the study following biopsy, contributing no data (Figure 1). Following randomization of 129 participants, emerging data from both centres indicated a higher than expected accuracy of CNB for diagnosis of MM of approximately 90%. Thus, the size of the difference was reduced to approximately 5%, and a repeat power calculation based on this showed that 621 patients would be required in each group to detect a difference in accuracy between VAB and CNB (95% *vs* 90%) with 90% power.

Provisional analysis of secondary end points was performed to assess the futility of continuing the study, since failure to demonstrate superior diagnostic accuracy of vacuum biopsy suggested that no significant patient or health economic benefit would result from using vacuum biopsy. Secondary outcomes were found to be similar in both groups. The study was therefore

Figure 1. Consort diagram.



discontinued, following discussion with the sponsor and ethics committee.

Baseline data

Inclusion criteria stated that all females aged 18 to 90 years attending both centres would be eligible including high-risk females. In practice, all participants were referred following routine screening mammography in the NHSBSP. Patients from other categories of referral did not present for assessment during clinical sessions when patients could be randomized. Similar demographic and clinical characteristics were observed in each group (Table 2).

CNB procedures were performed by eight practitioners with 1–9 years' of experience performing CNB. VABs were performed by five radiologists and a breast physician with 4–13 years' of VAB experience.

Overall positive-predictive value of biopsy for MM was 30.5%. More samples were retrieved using VAB ($p < 0.001$) owing to routine acquisition of 12 samples prior to specimen radiography compared with 7 or 8 samples using CNB (Table 2). Mean duration of VAB was longer than that of CNB ($p < 0.001$). No significant difference in calcification retrieval was demonstrated ($p = 0.58$) (Table 2). Almost three-quarters of MM cases (73%) were smaller than 15 mm and 26% of cases were 5 mm or less.

Analysis

65 participants were randomized to VAB and 63 to CNB. Intention-to-treat analysis included 128 participants (Figure 1).

Technical issues with equipment led to two participants not receiving allocated VAB, and one participant underwent both core biopsy and 14-G vacuum at the same intervention (although randomized to CNB). To account for this protocol violation, a separate (*per protocol*) analysis was performed (Figure 1 and Table 3). *Subset* analysis excludes two participants whose biopsy procedures were impacted by technical problems with stereotactic equipment which affected outcomes (Table 3).

Following VAB, 2/14 (14.3%) cases "upgraded" from DCIS to invasive disease at surgery. Following VAB, 11/12 (91.7%) participants with DCIS as the final diagnosis had a correct non-operative diagnosis; 1 participant underwent repeat CNB to achieve this. One participant with a B3/4 lesion at VAB, following MDT discussion, proceeded to diagnostic excision through patient choice.

Inadequate sampling (B1, normal breast tissue lacking appropriate histological microcalcification) occurred using both biopsy techniques: with VAB, 5/63 (7.9%) were inadequate and 5/64 (7.8%) with CNB.[2]

After CNB, 3/19 (15.8%) cases upgraded from DCIS to invasive disease at surgery. Non-operative diagnosis of DCIS following

Table 2. Demographic and clinical features for each group

Demographic/clinical feature	Vacuum biopsy ($n = 65$)	Core biopsy ($n = 63$)
Age (years), median (range)	55.6 (47–73)	55.4 (48–75)
Lesion size (mm), median (range)	10 (2–35)	8 (2–39)
Positive predictive value of biopsy of MM	16/65 (24.6%)	23/63 (36.5%)
BIRADS density, number (%)		
1	5 (8%)	6 (10%)
2	31 (48%)	30 (48%)
3	28 (43%)	27 (43%)
4	1 (2%)	0 (0%)
Radiology score, number (%)		
M2	9 (14%)	9 (14%)
M3	49 (75%)	42 (68%)
M4	5 (8%)	10 (16%)
M5	2 (3%)	1 (2%)
Number of cores, median (range)	12 (2–36)	8 (1–18)
Duration of biopsy (min), mean (range)	54.6 (22–125)	37.0 (16–66)
Calcification in cores, number (%)	59 (91%)	55 (87%)

BIRADS, Breast Imaging-Reporting and Data System; MM, mammographic microcalcification.

CNB was 15/15 (100%); 3 participants had initial core biopsy and a subsequent biopsy (2 had VAB and 1 had CNB) to achieve this. One participant diagnosed with invasive disease following VAB (initial CNB was reported as B1) had DCIS only found at operation. Pathological review confirmed invasive disease was completely removed during VAB.

There were no differences between the groups in times to diagnosis and treatment completion (Table 4).

Following initial VAB, 16 participants underwent surgery (Table 5). Following MDT discussion, one participant with a diagnosis at VAB showing an incidental radial scar and a tiny

Table 3. Primary and secondary end point analyses

Primary/ secondary end point	Intention to treat analysis[a]			Per protocol analysis[b]			Subset analysis[c]		
	VAB ($n = 65$)	CORE ($n = 63$)	p-value	VAB ($n = 63$)	CORE ($n = 64$)	p-value	VAB ($n = 61$)	CORE ($n = 62$)	p-value
Accurate diagnosis[d]	54 (83)	55 (87)	0.62	54 (86)	54 (84)	1.00	54 (88)	54 (87)	1.0
Number of needle biopsy procedures									
1	57 (88)	58 (92)	0.56	57 (89)	57 (89)	1.00	57 (93)	57 (92)	1.0
2	8 (12)	5 (8)		6 (11)	7 (11)		4 (7)	5 (8)	
Number of surgical procedures									
1	9 (56)	17 (71)		9 (56)	17 (71)	0.50	9 (56)	17 (71)	
2	7 (44)	7 (29)	0.50	7 (44)	7 (29)		7 (44)	7 (29)	0.32

CORE, 14-G core biopsy; VAB, 11-G vacuum-assisted biopsy.
Values within parentheses are percentages; Fisher's exact test was used for all comparisons.
[a]Intention to treat analysis (Figure 1) 128 participants.
[b]Per protocol analysis, 127 participants. Two participants did not receive allocated VAB but underwent core biopsy. One participant underwent both biopsy types and was excluded.
[c]Subset analysis excluded participants where technical issues with biopsy or stereotactic equipment may have impacted on results.
[d]Accurate diagnosis—diagnosis obtained at first needle biopsy corresponds to final surgical pathology or benign concordant result determined at multidisciplinary review.

Table 4. Analysis of clinical end points

Clinical end point	Intention to treat analysis			Per protocol analysis			Subset analysis		
	VAB ($n = 65$)	CORE ($n = 63$)	p-value	VAB ($n = 63$)	CORE ($n = 64$)	p-value	VAB ($n = 61$)	CORE ($n = 62$)	p-value
Time to initial diagnosis (days)[a]	6.4	6.3	0.77	6.3	6.4	0.82	6.3	6.3	0.98
Time to final diagnosis (days)[a]	8.0	7.4	0.48	7.8	7.6	0.75	7.7	7.4	0.68
Time to completion of treatment (days)[a]	34.4	38.3	0.75	34.4	38.2	0.72	34.4	38.3	0.72

CORE, 14-G core biopsy; VAB, 11-G vacuum-assisted biopsy.
t-test used for all analyses.
[a]Geometric mean.

papilloma without atypia did not have surgery. One participant who underwent VAB for DCIS whose mammographic abnormality was removed and clip deployment failed underwent mammographic follow-up, following MDT discussion, which was normal at 24 months.

Following CNB, two participants with B3 diagnoses did not have surgery. One participant chose early recall following diagnosis of papilloma without atypia, and one participant underwent further VAB which showed no atypia. One participant elected to have diagnostic surgical excision following a B1 diagnosis after initial sampling using CNB.

Following VAB, 7/16 (44%) participants required repeat surgery, and following CNB, 7/24 (29%) required a second procedure ($p = 0.55$).

Quality-of-life data analysis

No differences were observed between VAB and CNB groups for most functional scoring measures (Supplementary Table A). Reductions in global health ($p = 0.001$); physical function ($p = 0.001$); role function ($p < 0.001$) and social function ($p = 0.003$) were observed at 12 months in both groups. A significant difference between the two groups in emotional function scores (group × time interaction; $p = 0.017$) was observed. Scores were reduced (poorer emotional function) at 12 months in the CNB group but increased at 12 months in the VAB group. No significant changes in cognitive function over time were demonstrated.

Differences in scores were observed between the groups for some physical symptoms. A difference in fatigue scores over time was seen between the two groups (group × time interaction; $p = 0.033$). Scores generally increased after baseline but a larger increase was seen at 2 months after CNB. The CNB group had increased arm symptom scores at 2 months (group × time interaction; $p = 0.22$) which then decreased, whereas scores following VAB were static until 12 months when symptoms increased. A borderline significant difference in insomnia scores was observed between the groups (group × time interaction; $p = 0.06$) with increased scores in the CNB group at 12 months.

Table 5. Surgical outcomes following biopsy for microcalcification

Surgical outcomes	VAB, $n = 16$	CORE, $n = 24$
Single operation, clear margins	7	14
No residual disease at surgical excision following B5a non-operative biopsy	1	2
Second operation to clear margins	5	4
Second operation to clear margins and sentinel node biopsy	2	1
Second operation for sentinel node procedure only	0	2
Single operation, benign findings	1	1

CORE, 14-G core biopsy; VAB, 11-G vacuum-assisted biopsy.

No differences were observed between the two groups for breast symptoms, pain and body image. Increases in breast symptoms at follow-up were seen in both groups ($p = 0.002$). Pain scores were higher at 2 months ($p < 0.001$) for both groups.

Harms and unintended effects

Three participants (4.7%) allocated to vacuum biopsy experienced brisk haemorrhage leading to procedure abandonment. All three participants subsequently underwent satisfactory stereotactic core needle biopsy. Following a vacuum biopsy procedure, a marker clip failed to deploy in one participant, with no residual microcalcification seen at follow-up views. Mammographic follow-up for the participant was normal at 1 year. Radio-opaque artefacts present on specimen radiograph led to termination of one procedure owing to presumed satisfactory sampling. Pathology revealed no histological calcification and a repeat stereotactic biopsy was performed.

DISCUSSION

Findings

This study was the first randomized comparison of CNB and VAB for diagnosis of MM using full-field digital mammography (FFDM). No difference in diagnostic accuracy was found using CNB or VAB for non-operative diagnosis of MM following randomization of 129 participants. The improved CNB accuracy achieved in the study, compared with initial estimates used in power calculation from audit from the two centres, may reflect use of modified sampling protocols, increased operator experience and the impact of full-field digital equipment used to do biopsies.[21] Both study sites converted to use of FFDM after the time frame in which initial audits were performed and used to estimate accuracy. A separate evaluation at one recruiting centre of the impact of FFDM on diagnosis and management of MM showed accuracy of core biopsy at the first attempt increased significantly following introduction of FFDM.[21] Improved diagnostic accuracy using CNB in the two centres in the study, which was similar to accuracy using VAB, may not be reproduced in other centres.

In addition, there was no difference demonstrated in this study between the groups in the proportion of participants undergoing repeat non-operative biopsy or second therapeutic operation to treat their breast malignancy. Most second surgical interventions were to clear surgical margins, a problem not overcome by more accurate pre-operative diagnosis of invasive status. Owing to the large difference in cost between VAB (£250) and CNB (£25) and the longer overall procedure time for VAB in this study, with the associated personnel resource implications, it is unlikely to prove cost effective to use VAB for diagnosis if no cost savings can be made from fewer repeat biopsies or repeat operations.

Generalizability

The results of this study are generalizable to a subset of females with single calcified breast lesions under 40 mm where stereotactic biopsy procedures were performed in either upright or prone position and CNB by radiographer advanced practitioners. Of 787 patients initially assessed for eligibility, over half did not meet inclusion/exclusion criteria and a further 11% declined to participate. The precise inclusion/exclusion criteria were designed to permit careful and valid comparison of accuracy and secondary end points such as numbers of surgical procedures. Strict inclusion/exclusion criteria considerably reduced the pool of eligible participants but did not favour either VAB or CNB. The remaining exclusions were due to unpredictable equipment and staffing issues which prevented randomization to one or other biopsy type.

A large proportion of small MM lesions up to 5 mm (26% ≤5 mm) were included in this study compared with other publications which have examined diagnostic accuracy using stereotactic biopsy.[5,23,28,31]

Limitations

Diagnostic accuracy for participants undergoing surgery was compared with the gold-standard pathological diagnosis. Benign results were not verified against pathology from excisional biopsy in line with NHSBSP guidelines and targets aimed at minimizing benign surgical operations for attendees.[3] Some participants await subsequent NHSBSP screening examinations, and potential inaccuracies are not verified. Technical issues with equipment led to participants receiving non-allocated biopsy procedures and multiple statistical analyses.

Neither participants nor investigators were blinded to allocated interventions as the biopsy procedures have unique distinguishing features. Similarly, pathologists could not be blinded owing to differing specimen sizes from the two techniques. Individuals from different professional groups performed VAB and CNB, and results must be interpreted in this context. Targeting and sampling protocol differences between techniques mean results relate both to needle performance and protocols used.

Interpretation

Comparison with prior publications is problematic as similar methodological studies are not available. Most reports, systematic reviews and meta-analyses include multiple lesion types.[27,30] Despite inclusion of a larger proportion of small lesions (26% ≤5 mm) in this study, which increased the technical challenge of the procedures compared with prior publications, the clinically relevant accuracy measure of "DCIS underestimation rate" for VAB in this study (14.3%) is similar to previous cohort studies (12.3–29%) which reported on patient cohorts with >80% MM lesions.[5,9,10,23,24,28,31]

The accuracy of CNB in this study was higher than in previous studies reporting biopsy of MM with less underestimation of invasive disease within DCIS (15.8%).[5–7] Darling et al[7] showed that when a mean number of seven samples were obtained using 14-G CNB underestimation of DCIS was 18%. Whereas, reported outcomes of the Core Biopsy after Radiological Localisation (COBRA) study group which required a minimum of five samples using 14-G CNB demonstrated DCIS underestimation was 24%.[5,6] Jackman et al[5] published DCIS underestimation rates using CNB of 20.8%, compared with 12.2% using VAB but showed that where >10 samples were retrieved at biopsy, smaller differences were seen; DCIS underestimation was 13.6% with CNB and 9.9% with VAB. This study showed that more samples obtained at VAB (median 12 samples *vs* 8 for CNB) did

not increase accuracy. Accuracy of diagnosis at stereotactic biopsy is not simply related to numbers of specimens obtained as evidenced by conflicting findings in existing literature.[9,11–14,22,42]

A retrospective cohort study presented by Jackman et al[5] was one of the first publications to find improved pre-operative diagnostic accuracy using VAB compared with CNB. However, interpretation of their study is difficult as time frames for data collection for each biopsy technique were unclear and no acknowledgement was made regarding the impact of emerging knowledge and factors other than biopsy device which might affect accuracy. Published CNB outcomes and accuracy evaluations largely pre-dated subsequent reports of results using VAB. Many published results using CNB were achieved in the era prior to widespread implementation of FFDM when stereotactic techniques were also being refined. Contrastingly, outcomes of VAB evaluations reflected use of improving mammographic equipment and experiential learning which led to generic improvements in stereotactic biopsy technique over time.

Improved accuracy of CNB in this study may relate to several factors: as previously described, a multitargeting sampling protocol in this study (compared with single central target for VAB) may contribute to increased accuracy.[9] Dedicated practitioners have increased the accuracy of the stereotactic biopsy procedure by implementing contemporary CNB sampling protocols which emphasize the importance of demonstrating microcalcification on specimen radiography.[15–17,21] Skills of the operator also improve over time leading to increased sensitivity of breast biopsy, and use of FFDM has improved accuracy of diagnosis of MM.[21,25] Radiographer advanced practitioners performed all CNBs, and those participating in the study routinely performed 8–15 stereotactic procedures per week. In comparison, the medical personnel who performed VABs routinely performed fewer stereotactic biopsies per week, usually between two to four procedures. The difference in "current experience" between the professional groups as opposed to "years of experience" may have contributed to the accuracy achieved with CNB.

Inadequate biopsy (B1) pathology results are variably defined and reported in the literature. Technically difficult cases which are abandoned or fail to retrieve microcalcification are often excluded from analysis in published reports. One large published series of 11-G VAB procedures indicated that 63 of 769 (8.2%) cases were inadequate which is comparable to this study which included all attempted procedures in analyses.[23]

Significant intraprocedural bleeding complicated three VAB procedures in this study which required repeat biopsy procedures. Sampling of a large proportion of small lesions in this study led to complete excision of the mammographic abnormality using both biopsy techniques, and these cases required clip placement. The risk of these previously reported complications must be acknowledged and considered prior to needle selection for individual lesions.[19,24,26,30]

Previous investigators have suggested that no single needle type is suitable in every case, as performance varies between institutions and for different lesion types.[5,23] The choice of stereotactic needle must take into account local biopsy performance data, risk of complications and resource considerations (cost of disposables and operator time). Second-line use of VAB has greatly improved non-operative management of high-risk breast lesions and reduced surgical breast interventions. However, the high levels of diagnostic accuracy achieved in this study with CNB using FFDM suggest that the indications for VAB as a first-line diagnostic technique for MM may not be universally cost effective. Moreover, because repeat surgery to achieve clear surgical margins for MM lesions is frequent despite high diagnostic accuracy of non-operative biopsy, more work is needed to establish optimal pre-operative mapping of lesions and other techniques aimed at effective margin clearance.

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