A RETROSPECTIVE STUDY TO EVALUATE MULTIPLE BIOPSIES OF MICROCALCIFICATIONS IDENTIFIED ON SCREENING MAMMOGRAPHY

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3 LEARNING POINTS

1. 83% histopathologic pair histology concordance when evaluating extent of calcification, indicating that one biopsy may be sufficient when assessing disease extent
2. Increasing histopathological concordance with higher mammographic suspicion (M4/ M5)
3. 18% of biopsy results when assessing separate clusters of calcification were paired B2 indicating over treatment in this group.

Introduction

Distinguishing between benign and malignant calcification on imaging alone is difficult and if there is concern regarding malignancy, a biopsy should be performed [1]. Appropriate management is needed for clients with indeterminate breast calcifications and as service providers we must be sure to not over or underestimate disease whilst utilising resources efficiently. Although rare, breast biopsy is not without complications - including infection [2]. Additionally, client anxiety when undergoing breast biopsy and awaiting results can be significant [3]. Within the context of a screening population i.e. “well-women” intervention should not be undertaken lightly.

Clinical guidance states that careful consideration also needs to be given to cases with multiple foci of abnormality or extensive microcalcifications. It is important to ensure that adequate sampling is undertaken to guide both the multidisciplinary team meeting (MDT) and the patient in their decision regarding surgery. For example, evidence by way of tissue diagnosis is needed to justify a mastectomy recommendation [1]. However, this recommendation is vague and there is a paucity of literature surrounding the management of women with extensive or multiple and distinct clusters of microcalcification.

Performing a single biopsy reduces the trauma to a client as well as the potential emotional stress. Also, the cost of establishing a diagnosis is reduced as well as resources such as departmental time, however any reductions in interventions need to be managed in a safe manner [4].

Method

Ours was a single centre study. Data was taken from MDT notes between August 2021- August 2022 and further information was obtained from NBSS. Unilateral, multiple 14G x-ray guided biopsy procedures to investigate indeterminate microcalcification, scored M3 or higher was our inclusion criteria and 65 clients were recruited [5].

Clients either had multiple biopsies to assess extent of disease, or multiple foci of microcalcifications. Distinguishing between these classifications can be difficult as multiple clusters of microcalcifications can after workup and subsequent surgery, be classified as a single lesion. However, we have tried to separate our data out into two categories:

Biopsies for:

- Extent of disease, contiguous calcification >25mm
- Separate clusters of microcalcifications at least 10mm apart

Results

Extent of disease:

Of the 65 clients, 18 (28%) had more than one biopsy to assess disease extent.

Identical biopsy results:

Result (pair)	Number of clients 15/18
B2	3
B3	2
B5a	8
B5b	2

Of those 18 clients, 15 clients’ (83%) biopsy pair results had histopathologic concordance as they were identical and this correlates with contiguous disease.

Dissimilar biopsy results:

Result	Number of clients 3/18
B5a/B1*	1
B5a/B2	1
B5b/B5a*	1

Only 3 clients, 16% of results were dissimilar. These results may indicate that under sampling has occurred (particularly the results with a *) However, the B5a/ B2 result may have helped decide management and surgical outcomes as this client ended up having a wide local excision.

M4/M5 results breakdown:

10 of the 18 clients (55%) were coded either M4 or M5 indicating high clinical suspicion and there was high concordance for malignancy in this group.

M4 Results	Number of clients
B5a	4
B5b/B5a	1
B3	1

The B3 result indicates under sampling occurred. The biopsy was repeated as a 9G vacuum and upgraded to E5.

M5 Results	Number of clients
B5b	1
B5a	3

Separate clusters:

Of the 65 multiple biopsy clients, 47 (72%) had separate clusters biopsied. Of those 47 clients, 30 (64%) had the same result indicating identical processes.

Identical biopsy results:

Result (pair)	Number of clients 30/47
B2	12
B3	5
B5a	9
B5b	4

Unfortunately, many of the multiple results were paired B2 (12 clients, 26% of the identical results group but 18% of the total cohort) indicating overtreatment and that additional biopsies may not be required when assessing separate clusters.

However, 13 clients (28%) had 2 paired malignant results (B5a, B5b) which may have influenced surgical planning regarding a mastectomy recommendation.

Dissimilar biopsy results:

Result	Number of clients 17/47
B5a/B2	6
B5b/B5a	2
B5a/B3	3
B3/B2	3
B5a/B1*	1
B5a/B4*	1
B4/B3*	1
B1/B2	1

The results with a * indicate probable under sampling as a B5a result with a B1 is highly suspicious, as are all B4 results.

Differing biopsy results with a benign and malignant result (6 clients 13% had a B5a/ B2 result) may have impacted on surgical management regarding margin size. However, this result could also indicate that in the benign biopsy result, under sampling has occurred.

Discussion

There is a lack of definitive workup guidance when assessing suspicious breast microcalcifications. None of the literature found on the topic of multiple biopsies was from the UK indicating a need for more representative studies. Apart from Falkner et al., all other studies assessed symptomatic as well as screening clients. Falkner et al., advise multiple biopsies for targets which are >5cm apart [7]. Raj et al., advises multiple biopsies for calcification clusters in different quadrants of the breast [4]. Traditionally, clients with disease measuring >5cm would be advised to have a mastectomy, which would need to be supported by tissue diagnosis [4]. In recent years, studies have investigated the potential role of breast conserving surgery in these clients instead, but this is outside the scope of this study [6].

A couple of studies have looked at biopsy of contiguous calcification. Raj et al., found that one biopsy to assess contiguous disease was sufficient as they achieved 100% histopathologic concordance on biopsy pair results, indicating accurate disease representation [4]. In looking at disease extent, we achieved 83% pair concordance, Falkner et al., also had differing results to Raj et al., with 87% histopathologic pair concordance and they argue that a difference in 13% of cases merits additional biopsies. Our concordance rate is higher in the M4/M5 group at 90% demonstrating increasing histopathologic concordance with higher mammographic suspicion, which is a trend Falkner, et al., also reported. Notably, Raj et al., had much stricter inclusion criteria and only evaluated biopsies for calcifications >50mm scored M4 or M5; whereas Falkner et al., looked at calcifications >25mm scored M3 or higher, like our study. The difference in inclusion criteria helps to explain why our general concordance rate is closer to Falkner et al., (83% to their 87%). Additionally, Raj et al., only included 32 patients in their study which is not very representative whereas Falkner et al., had sample size of 171 [4,7].

Under sampling may have occurred in our dissimilar results which may also help explain our lower histopathologic concordance rate. Raj et al., used a 9G biopsy device whereas we used 14G. Vacuum Assisted Biopsy (VAB) enables larger volumes of tissue to be sampled and the RCP state that due to this, VAB has a lower equivocal sample rate and increased accuracy [2]. Our department has recently switched to first line VAB when assessing microcalcifications. Further audit is needed to assess if potential under sampling is resolved with the use of VAB. However, Falkner et al., did not find a statistical difference in histopathological agreement between VAB and 14G biopsies as their study included a mix of sampling techniques [7].

Looking at the management of women with two or more separate sites of microcalcification, Chang Sen et al., found that 20% of their patients had dissimilar pair histopathology results despite calcification of similar morphology when undergoing 14G. They are concerned that one result may not be sufficient for surgical management and that a benign result in one area does not rule out malignancy in another [8]. Their study cohort had a good sample size of 208 patients. Discounting our dissimilar results which are suspicious for under sampling (the figures with a *) the rate of dissimilar results in our separate cluster group is even higher than theirs at 30%.

Bode et al., found that 43% of the patients undergoing multiple biopsies had differing histopathologic pair results. Thus, they advocate for multiple biopsies when there are more than one cluster of indeterminate microcalcifications, even when morphologically similar. [9] This rate is much higher than our study or Chang Sen et al., and they used 9G VAB for sampling indicating as Falkner et al., found that histopathological agreement may not necessarily increase with the use of VAB.

Ultimately, the surgical plan will be decided by the client. If they opt to have a mastectomy rather than breast conserving surgery, further biopsies will not be required. This highlights the importance of the role of the MDT in managing further lesions on a case-by-case basis.

Limitations

Our study size was small with only 65 clients, so there may be issues regarding representativeness. As a tertiary centre that refers to many hospitals, full surgical information as well as hospital-based MDT notes are not available. We have used NBSS which holds limited information regarding surgical outcomes and discussions surrounding that topic. As Falkner et al., stated, it can be difficult to distinguish between widespread disease and separate microcalcification clusters and clusters that we have coded as separate may be all part of the same process [7].

Conclusions

In assessing the extent of disease, our study demonstrated 83% pair result histopathologic concordance indicating that a single biopsy may be enough to diagnose disease. When further differentiated to look at calcification scored M4 or M5, this rises to 90% concordance indicating increasing concordance with higher suspicion.

18% of our results were paired B2 when assessing separate clusters of microcalcification indicating overtreatment. This is something that needs to be reduced due to the morbidity to the women in the screening cohort and use of resources that could be more efficiently employed. However, reductions in interventions need to be managed safely and we found that 30% of our results were dissimilar, this rate of discordance is high and indicates that caution is needed when assessing separate clusters of microcalcification.

A change in practice to use first line 9/10G VAB may reduce under sampling issues, however further audit will need to assess this.

The surgical management of the client is always client centered and they may opt to have a mastectomy rather than breast conservation, negating the need for additional biopsies. Therefore, case-by-case review at MDT also impacts the management of further lesions.

There is a lack of literature surrounding the topic of multiple biopsies generally and more research would be beneficial in advising on best practice.

References

1. NHS Breast Screening Programme. Clinical guidance for breast cancer screening assessment Public Health England leads the NHS Screening Programme [Internet]. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/567600/Clinical_guidance_for_breast__cancer_screening__assessment_Nov_2016.pdf
2. Royal College of Pathologists (RCP). Guidelines for non-operative diagnostic procedures and reporting in breast cancer screening [Internet]. Available from: https://www.bing.com/ck/a?!&&p=783b39ccf9b7ba20JmltdHM9MTY4MjAzNTIwMCZpZ3VpZD0zZTIzNjFmYy0yYzhmLTZhMzctMmMzYi03MzY5MmQ3NDZiZGYmaW5zaWQ9NTE5MQ&ptn=3&hsh=3&fclid=3e2361fc-2c8f-6a37-2c3b-73692d746bdf&psq=Guidelines+for+non-operative+diagnostic+procedures+and+reporting+in+breast+cancer+screening&u=a1aHR0cHM6Ly93d3cucmNwYXRoLm9yZy9hc3NldC80Qjk2RjE5Qy1GN0JELTQ1NkMtQjlxMkY1NTdGODA0MEY2Ni8&ntb=1
3. Soo MS, Shelby RA, Johnson KS. Optimizing the Patient Experience during Breast Biopsy. Journal of Breast Imaging [Internet]. 2019 Apr 12;1(2):131–8. Available from: https://academic.oup.com/jbi/article/1/2/131/5446726
4. Raj SD, Sedgwick EL, Severs FJ, Hilsenbeck SG, Wang T, Sepulveda KA. Stereotactic Biopsy of Segmental Breast Calcifications: Is Sampling of Anterior and Posterior Components Necessary? Academic Radiology [Internet]. 2016 Jun 1 [cited 2023 May 4];23(6):682–6. Available from: https://www.sciencedirect.com/science/article/abs/pii/S1076633216000660#preview-section-recommended-articles
5. Dao KA, Rives AF, Quintana LM, Kritselis MA, Fishman MDC, Sarangi R, et al. BI-RADS 5: More than cancer. RadioGraphics. 2020; doi:10.1148/rg.2020200054.pres
6. Bleicher RJ, Ruth K, Sigurdson ER, Daly JM, Boraas M, Anderson PR, et al. Breast conservation versus mastectomy for patients with T3 primary tumors (>5 cm): A review of 5685 medicare patients. Cancer. 2015 Oct 19;122(1):42–9.
7. Falkner NM, Hince D, Porter G, Dessauvagie B, Jeganathan S, Bulsara M, et al. Added value of second biopsy target in screen-detected widespread suspicious breast calcifications. Journal of Medical Imaging and Radiation Oncology. 2018 Feb 22;62(3):299–306.
8. Chang Sen LQ, Huang ML, Leung JWT, Wei W, Adrada BE. Malignancy rates of stereotactic biopsies of two or more distinct sites of suspicious calcifications in women without known breast cancer. Clin Imaging. 2019 Nov-Dec;58:156-160. doi: 10.1016/j.clinimag.2019.07.007. Epub 2019 Jul 23. PMID: 31376706.
9. Bode M, Charlotte Huck L, Raaff V, Hitpass L, Braunschweig T, Nebelung S, et al. Digital breast tomosynthesis-guided vacuum-assisted biopsy of suspicious calcifications at different sites within one breast: Is biopsy of more than one location needed? European Journal of Radiology. 2022 Sep;154:110456.

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