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ORIGINAL ARTICLE

Positive malignant margins in clinically diagnosed and excised benign breast lumps: a five year retrospective study at the Korle-Bu teaching hospital, Ghana

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This study was aimed at utilizing retrospective descriptive data to evaluate the percentage of clinically benign breast lumps that turned out to be histologically malignant and the prevalence of positive tumour margins among the malignant cases. A total of 2,917 registered cases of excised breast lump at the Department of Pathology spanning January 2005 to December 2009 were reviewed to evaluate the presence of malignancy and positive margins. Three hundred and twenty-two (11.0%) of the excised breast lumps were found to contain malignant tumours, out of which 142(44.1%) had positive tumour margins. Size of primary tumour (p=0.001) and histologic subtype (p=0.002) showed significant positive and negative associations in relation to positive tumour margins respectively. No significant association was observed between the positive tumour margins and histologic grade (p=0.363).The study showed that clinically benign breast lumps could be malignant and not completely excised, therefore increasing the risk of local recurrence. Thus, it is recommended that all women with breast lumps have the triad (diagnostic workup) of clinical and radiological assessment, followed with histological studies.
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Keywords*:* Breast cancer, Excision biopsy, recurrence, positive margins

INTRODUCTION

Simple excision biopsy is a standard surgical treatment procedure performed for clinically benign breast lumps, such as fibroadenoma, fibrocystic change and duct ectasia. Unfortunately, some of these lumps tend to be malignant, and not completely excised thus giving rise to the phenomenon of positive margins. There is no consensus as to what constitutes a positive or negative margin (Arriagada *et al.*, 2002; Blichert-Toft *et al.*, 1992). While there is debate about 1 or 2 mm margins, most will accept a margin of 3 mm as being negative (Kurtz, 1992). Published rates of positive margins in lumpectomies vary widely, ranging from 4% to 31% (Elkhuizen *et al.*, 1998; Kurtz *et al.*, 1989; Voogd *et al.*, 2001; Vrieling *et al.*, 2003).

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Positive margins are associated with certain clinico-pathologic factors; such as age at diagnosis, size of the primary tumour, histologic subtype and histologic grade (Barthelmes *et al.*, 2003; Blichert-Toft *et al.*, 1992; Malik *et al.*, 2000).

In Ghana, there is no published literature on the prevalence of positive tumour margins among surgically excised breast lumps. This retrospective study was conducted to evaluate the percentage of clinically benign breast lumps that are histologically malignant, and to determine the prevalence of positive tumour margins among these cancerous lumps and also offer recommendations for the managements of early breast cancers.

MATERIALS AND METHODS

Study site and design

All data were collected from the Department of Pathology, University of Ghana Medical School. The department receives surgical specimens from

Korle-Bu Teaching Hospital, Greater Accra Metropolis, and neighboring towns and Districts outside Accra, as well as other regions of the country. The study reviewed all cases of excised breast lumps that were clinically benign from January 2005 to December 2009.

Sampling technique, Sample size and Sample processing

A total of 2,917 (71.0%) out of 4,109 breast specimens diagnosed clinically as benign were reviewed between January 2005 and December 2009. For each registered case, patient age, clinical characteristics of the breast cancer, histologic findings and margin status were recorded. Investigations were done on paraffin-embedded breast tissue stained with haematoxylin and eosin (H&E).

Classification of breast tumours

Histologic sub-typing of tumours was based on the architecture and cytologic features of the tumour and grading was done according to the modified Bloom-Richardson grading (Bloom, 1950). Breast lumps diagnosed as clinically benign such as; fibroadenoma, fibrocystic change, duct ectasia, benign phyllodes tumour and duct papilloma in females were included. Positive margin was also defined as: tumour cells within 2 mm of one or more resection margins; tumour cells within one or more inked margins or tumour extendind to one or more resection margins as stated by the pathologist. Breast lumps diagnosed in females as clinically malignant but had simple excision or wide local excisions were excluded from the study.

Statistical analysis

Data was collected by the first author and cross checked by the third author. Categorical data were presented as proportion whilst continuous data were presented as mean±SD. Association was assessed using Pearson's product moment correlation. All data entry and cleaning were done using Microsoft Excel 2010 (Microsoft corporation) and statistical analyses performed using GraphPad Prism v6.0 (GraphPad software, San Diego California USA, www.graphpad.com). In all analyses, $p<0.05$ was considered as statistically significant.

RESULTS

Characteristics of clinically benign breast lumps that are histologically malignant

From January 2005 to December 2009, 4,109 breast specimens were received in the Department of Pathology, of which 2,917(71.0%) were excised clinically benign breast lumps. Three hundred and twenty-two (11.0%) of the clinically benign breast lumps contained, malignant tumours. The ages of women with the malignant breast lumps ranged from 14 to 86 years, with a mean age of 49.1±14.0 years. Majority 97(31.1%) of these women were within the 40 -49 years age group (Table 1). The macroscopic size of the malignant tumours within the breast lumps at the time of histological diagnosis ranged from 0.4 to 15 cm in size, with a mean of 3.8±2.3 cm. About half 132(51.1%) of the malignant lesions were within 3-5 cm (Table 1). Of the 71(22.1%) women who had symptoms at presentation, many27 (38.0%) of them reported within 6-12 months of noticing the lump. Information on the laterality of the breast lumps were recorded for 294(91.3%) cases of which 163(55.4%) were on the left breast.

Table 1: Characteristics of clinically benign lumps that was found histologically to be malignant

Variable	Proportion
Age (yrs)	
<40	73(23.4%)
40-49	97(31.1%)
50-59	74(23.7%)
>60	68(21.8%)
Main symptoms	
Breast lump	388(98.7%)
Nipple discharge	5(1.3%)
Duration (months)	
1-2	15(21.2%)
3-5	17(23.9%)
6-12	27(38.0%)
>12	12(16.9%)
Tumour size (cm)	
≤2	65(25.3%)
3-5	132(51.4%)
>5	60(23.3%)

Histologic characteristics of excised breast lumps that are malignant

A total of 311(96.6%) breast tumours were epithelial cancers, with 11 mesenchymal cancers. Majority 300 (96.5%) of the epithelial cancers were invasive, with 11 non-invasive cancers (ductal carcinoma insitu; DCIS). More than two-thirds 257(85.7%) of the invasive cancers were invasive ductal carcinoma not otherwise specified (NOS). A total of 200(77.8%) of the NOS had combined Bloom-Richardson grading, of which many 89(44.5%) were grade 2 (Table 2). Fifty-seven of the NOS were not graded due to poor preservation and loss of cytologic features. We found that a total of 142(44.5%) of the clinically benign breast lumps that were histologically malignant had positive margins and thus, not completely excised) (Table 2).

Table 2: Histologic characteristics of invasive epithelial breast cancers

Variable	Proportion
Histologic type (n = 300)	
Invasive duct (NOS)	257(85.7%)
Lobular	11(3.7%)
Mucinous	6(2.0%)
Micropapillary	10(3.3%)
Medullary	4(1.3%)
Apocrine	2(0.7%)
Tubolo-lobular	2(0.7%)
Neuroendocrine	1(0.3%)
Others	7(2.3%)
Histologic grade (n=200)	
Grade I	58(29.0%)
Grade II	89(44.5%)
Grade III	53(26.5%)
Positive margins	142(44.5%)

Associations between positive malignant tumour margins and other tumour variables

Using Pearson's correlation, there was a significant positive association between positive tumour margins and the size of the primary tumour (r=0.14, p=0.002) and a negative association with the histologic type of tumour (r=-0.13, p=0.003) (Table 3).

Table 3: Association between positive tumour margins, tumour size, histologic type of tumour and tumour grade using Pearson correlation

Variables	Histologic type	Tumour grade	Positive margins
Tumour Size (cm)	0.14(0.001)	0.01(0.095)	0.14(0.002)
Histologic type		0.05(0.314)	-0.13(0.001)
Tumour grade			0.05(0.363)

KEY: r-value(p-value)

DISCUSSION

During the five year period of review (2005-2009), 11.0% of all the clinically benign breast lumps submitted to our institution contained malignant tumours. About 45% of the tumours were not completely excised and thus had positive tumour margins. This rate is high compared to published rates of positive margins in lumpectomies which is said to vary from 4% to 31% (Elkhuizen *et al.*, 1998; Kurtz *et al.*, 1989; Voogd *et al.*, 2001; Vrieling *et al.*, 2003). The observed difference could be due in-part to the difference in the definition of positive margins as well as the reason for the removal of the lump. Whereas in this study the lumps were removed for diagnostic purpose, in the available data, the lumps were removed for the treatment of histologically confirmed early breast cancer. Therefore, there was no initial diagnostic work-up (triad) (consisting of clinical, radiologic and pathological assessments) which could have enhance the suspicion of malignancy and thus a wide local excision with axillary lymph nodes dissection offered.

For the authors, the big question that readily comes to mind is; what is the fate of this ≈45% of women with positive margins? Studies have shown that positive margin is a major risk factor for local recurrence (Asgeirsson *et al.*, 2003; Borger *et al.*, 1994; Fourquet *et al.*, 1989; Jobsen *et al.*, 2003) and systemic disease (Clarke *et al.*, 1985). The likely options for these women are re-excision and mastectomy**.** Moreover, re-admissions for re-excision to obtain clear margins or for mastectomy will bring increase cost and emotional distress for patients, as well as the potential for more scaring and defor-

mation at the surgical site.

Women who with clinically benign breast lumps that were histologically malignant were young with mean age of 49.0 years (SD=14.0). The youngest age at diagnosis from this study with carcinosarcoma is 14 years old. This is in agreement with available reports among breast cancer patients in Ghana (Clegg-Lamptey *et al.*, 2009; Stark *et al.*, 2010).

From this study, about half of the malignant tumour size were between 3.0-5.0 cm. The size of the tumour was also directly associated with the positive tumour margins but inversely with the histologic type of tumour. Although this study was based on simple excised breast lumps, it is in agreement with some published literature on positive tumour margins in lumpectomies (Fourquet *et al.*, 1989; Voogd *et al.*, 2001; Vrieling *et al.*, 2003).

Majority (71.0%) of the NOS that had modified Bloom-Richardson grading were of high grade, similar to available data in Ghana (Edmund *et al.*, 2013). The lack of association between positive tumour margins and tumour grade from this study is contrary to studies that found tumour grade as a risk factor for positive (Barthelmes *et al.*, 2003; Malik *et al.*, 2000) but agrees with studies that found grade not to be risk factor for positive margins (Cao *et al.*, 2005; Dooley and Parker, 2005; Keskek *et al.*, 2004).

CONCLUSION

This study showed that 11.0% of clinically benign breast were histologically malignant. Of this number, about 45.0% had positive margins (not completely excised), and hence the risk of local recurrence. Since primary breast tumours in Ghanaian women are large and show association with positive tumour margins, it is recommended that all women with breast lumps have the triad (diagnostic workup) of clinical and radiological assessment follow with histological studies. This will enable surgeons offer the best management to reduce positive margins and local recurrence and if in doubt, patient should be offered wide excision.

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COMPETING INTERESTS

The authors declare that they have no competing interests.

REFERENCES

Arriagada, R, Le, MG, Contesso, G, Guinebretiere, JM, Rochard, F, Spielmann, M (2002) Predictive factors for local recurrence in 2006 patients with surgically resected small breast cancer. *Ann Oncol* 13(9): 1404-1413.

Asgeirsson, KS, McCulley, SJ, Pinder, SE, Macmillan, RD (2003) Size of invasive breast cancer and risk of local recurrence after breast-conservation therapy. *Eur J Cancer* 39(17): 2462-2469.

Barthelmes, L, Al Awa, A, Crawford, DJ (2003) Effect of cavity margin shavings to ensure completeness of excision on local recurrence rates following breast conserving surgery. *Eur J Surg Oncol* 29(8): 644-648.

Blichert-Toft, M, Rose, C, Andersen, JA, Overgaard, M, Axelsson, CK, Andersen, KW, Mouridsen, HT (1992) Danish randomized trial comparing breast conservation therapy with mastectomy: six years of life-table analysis. Danish Breast Cancer Cooperative Group. *J Natl Cancer Inst Monogr*(11): 19-25.

Bloom, HJ (1950) Further studies on prognosis of breast carcinoma. *Br J Cancer* 4(4): 347-367.

Borger, J, Kemperman, H, Hart, A, Peterse, H, van Dongen, J, Bartelink, H (1994) Risk factors in breast-conservation therapy. *J Clin Oncol* 12 (4): 653-660.

Cao, D, Lin, C, Woo, SH, Vang, R, Tsangaris, TN, Argani, P (2005) Separate cavity margin sampling at the time of initial breast lumpectomy significantly reduces the need for reexcisions. *Am J Surg Pathol* 29(12): 1625-1632.

Clarke, DH, Le, MG, Sarrazin, D, Lacombe, MJ, Fontaine, F, Travagli, JP, May-Levin, F, Contesso, G, Arriagada, R (1985) Analysis of local-regional relapses in patients with early breast cancers treated by excision and radio-

therapy: experience of the Institut Gustave-Roussy. *Int J Radiat Oncol Biol Phys* 11(1): 137-145.

Clegg-Lamptey, JN, Aduful, HK, Yarney, J, Adu-Aryee, NA, Vanderpuye, V, Kyereh, M, Nkansah, A, Edwin, A (2009) Profile of breast diseases at a self-referral clinic in Ghana. *West Afr J Med* 28 (2): 114-117.

Dooley, WC, Parker, J (2005) Understanding the mechanisms creating false positive lumpectomy margins. *Am J Surg* 190(4): 606-608.

Edmund, DM, Naaeder, SB, Tettey, Y, Gyasi, RK (2013) Breast cancer in Ghanaian women: what has changed? *Am J Clin Pathol* 140(1): 97-102.

Elkhuizen, PH, van de Vijver, MJ, Hermans, J, Zonderland, HM, van de Velde, CJ, Leer, JW (1998) Local recurrence after breast-conserving therapy for invasive breast cancer: high incidence in young patients and association with poor survival. *Int J Radiat Oncol Biol Phys* 40(4): 859-867.

Fourquet, A, Campana, F, Zafrani, B, Mosseri, V, Vielh, P, Durand, JC, Vilcoq, JR (1989) Prognostic factors of breast recurrence in the conservative management of early breast cancer: a 25-year follow-up. *Int J Radiat Oncol Biol Phys* 17(4): 719-725.

Jobsen, JJ, van der Palen, J, Ong, F, Meerwaldt, JH (2003) The value of a positive margin for invasive carcinoma in breast-conservative treatment in relation to local recurrence is limited to young women only. *Int J Radiat Oncol Biol Phys* 57(3): 724-731.

Keskek, M, Kothari, M, Ardehali, B, Betambeau, N, Nasiri, N, Gui, GP (2004) Factors predisposing to cavity margin positivity following conservation surgery for breast cancer. *Eur J Surg Oncol* 30(10): 1058-1064.

Kurtz, JM (1992) Factors influencing the risk of local recurrence in the breast. *Eur J Cancer* 28(2-3): 660-666.

Kurtz, JM, Jacquemier, J, Torhorst, J, Spitalier, JM, Amalric, R, Hunig, R, Walther, E, Harder, F, Almendral, A, Brandone, H, et al. (1989) Conservation therapy for breast cancers other than infiltrating ductal carcinoma. *Cancer* 63 (8): 1630-1635.

Malik, HZ, Wilkinson, L, George, WD, Purushotham, AD (2000) Preoperative mammographic features predict clinicopathological risk factors for the development of local recurrence in breast cancer. *Breast* 9(6): 329-333.

Stark, A, Kleer, CG, Martin, I, Awuah, B, Nsiah-Asare, A, Takyi, V, Braman, M, Quayson, SE, Zarbo, R, Wicha, M, Newman, L (2010) African ancestry and higher prevalence of triple-negative breast cancer: findings from an international study. *Cancer* 116(21): 4926-4932.

Voogd, AC, Nielsen, M, Peterse, JL, Blichert-Toft, M, Bartelink, H, Overgaard, M, van Tienhoven, G, Andersen, KW, Sylvester, RJ, van Dongen, JA (2001) Differences in risk factors for local and distant recurrence after breast-conserving therapy or mastectomy for stage I and II breast cancer: pooled results of two large European randomized trials. *J Clin Oncol* 19(6): 1688-1697.

Vrieling, C, Collette, L, Fourquet, A, Hoogenraad, WJ, Horiot, JC, Jager, JJ, Bing Oei, S, Peterse, HL, Pierart, M, Poortmans, PM, Struikmans, H, Van den Bogaert, W, Bartelink, H (2003) Can patient-, treatment- and pathology-related characteristics explain the high local recurrence rate following breast-conserving therapy in young patients? *Eur J Cancer* 39(7): 932-944.

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