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Microscopic Localization of Calcifications In and Around Breast Carcinoma

A Cautionary Note for Needle Core Biopsies

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Objective
To detail the microanatomic localization of microcalcifications (Ca^{++}) occurring in association with breast carcinoma and thereby to determine their reliability as a marker of breast carcinoma in small tissue core biopsies.

Summary Background Data
Identification of the pathology associated with Ca^{++} in mammograms has acquired increasing importance in the early detection of breast carcinoma. With recent advances enabling computer-guided stereoscopic needle biopsy of calcified foci, histopathologic diagnosis is rendered on increasingly small tissue samples, raising the risk of misdiagnosis. Knowledge of the microanatomic distribution of Ca^{++} in relation to diagnostic epithelial elements is essential for assessing their significance in small tissue biopsies.

Methods
All 32 carcinomas with Ca^{++} within 1 cm of carcinoma diagnosed by open biopsy at the New England Deaconess Hospital from January 1994 to January 1995 were studied. Ca^{++} were classified as being within ductal or lobular carcinoma *in situ*, invasive carcinoma, carcinoma-associated stroma, benign stroma >1 mm from carcinoma, or benign ducts or terminal duct–lobular units. If Ca^{++} were peritumoral, their distance from the tumor was measured.

Results
Ca^{++} were present only in malignant components in 31%, only in benign components in 34%, and in both in 34% of cases. The most common locations of Ca^{++} were benign peritumoral ducts (62%) and ductal carcinoma *in situ* (54%). The microanatomic distribution of benign peritumoral Ca^{++} in relation to the mass is detailed.

Conclusions
In carcinomas with Ca^{++} in the area of tumor, Ca^{++} may not be localized to malignant tissue. Caution should be used when interpreting the finding of Ca^{++} in benign components of small tissue samples of breast masses.

The potential utility of the stereoscopic computer-guided needle biopsy for diagnosing breast lesions is under investigation.[1–3] This technique has the capacity to target a lesion, with the potential to supplant the open biopsy.[4–6] It is particularly attractive for the evaluation of mammographically detected calcifications (Ca^{++}). Ca^{++} have long been known to develop within and around carcinoma, but their distribution and microanatomic localization have not been comprehensively detailed.[7] This study was undertaken to assess the distribution of Ca^{++} in both benign and malignant components in and about malignant breast masses. The question of whether Ca^{++} in small biopsies taken near breast cancers can be misleading with respect to the pathology present is addressed, and inferences with respect to the stereotactic breast biopsy are drawn.

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METHODS

All breast carcinomas diagnosed by open surgical biopsy from January 1994 to January 1995 were abstracted from the archives of New England Deaconess Hospital and reviewed for the histologic presence of Ca^{++}. Only cases in which a biopsy was obtained for the evaluation of mammo-

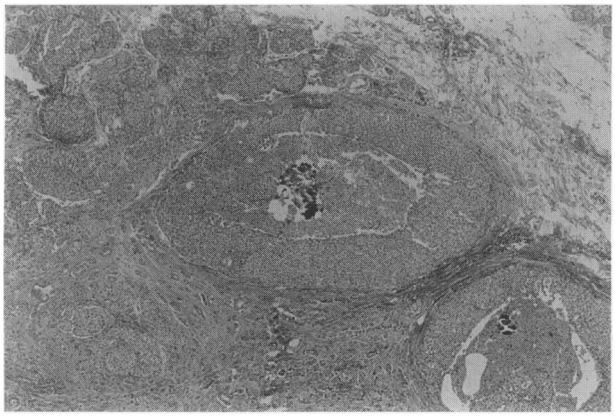

Figure 1. Ca^{++} within ductal carcinoma *in situ*.

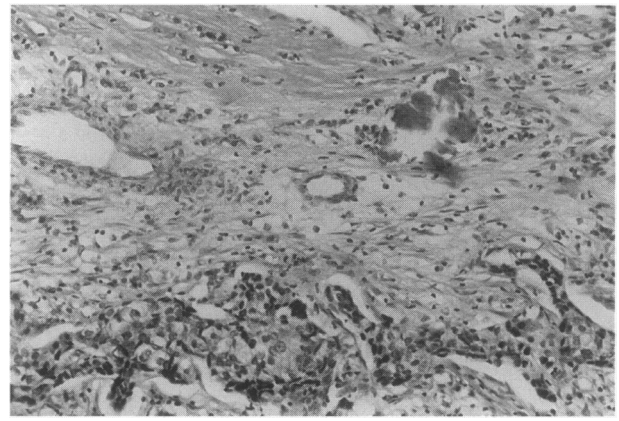

Figure 3. Ca^{++} within stroma associated with invasive carcinoma.

graphically evident Ca^{++} within 1 cm of a mass, or clustered so as to be suspicious for carcinoma without mass, were studied to create a model for calcified, mammographically detectable lesions that might be subjected to the stereotactic core needle biopsy for diagnosis.

The microanatomic location of the Ca^{++} was determined and classified as within *in situ* carcinoma (Fig. 1), invasive carcinoma (Fig. 2), stroma associated with invasive carcinoma (Fig. 3), benign ducts or terminal duct–lobular units (Fig. 4), or benign stroma (Fig. 5). The distance of Ca^{++} in benign components to carcinoma was measured with an ocular reticule.

RESULTS

The study group comprised 32 women age 31 to 87 years (median 59 years). Eight had ductal carcinoma *in situ* without invasion, 3 had lobular carcinoma *in situ* without invasion, 17 had invasive ductal carcinoma associated with ductal carcinoma *in situ*, and 4 had invasive lobular carcinoma associated with lobular carcinoma *in situ*.

Ca^{++} were limited to malignant components in 10 (31%) and to benign components in 11 (34%); they were present in both in 11 (34%) of the 32 cases. Ca^{++} were present in 13 of 24 cases of ductal carcinoma *in situ* (54%), 3 of 7 cases of lobular carcinoma *in situ* (43%), and 6 of 21 cases of invasive carcinoma (28%). Stroma associated with invasive carcinoma contained Ca^{++} in 5 of 21 cases (24%). Twenty of the cases (62%) had Ca^{++} within benign ducts, five (16%) within benign lobules, and one (3%) within benign stroma (Table 1).

The microanatomic localization of peritumoral Ca^{++} was measured in cases grouped by on the presence or absence of

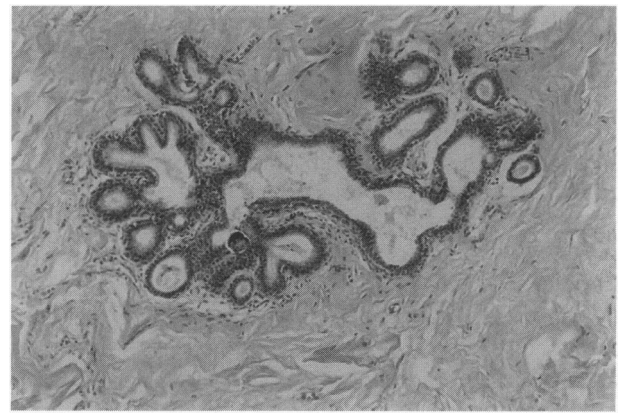

Figure 4. Ca^{++} within benign terminal duct–lobular unit.

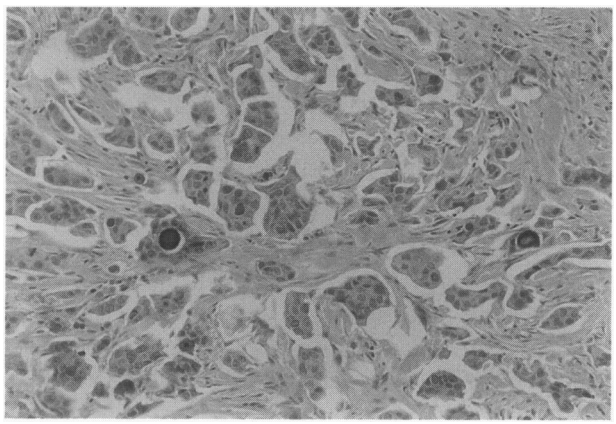

Figure 2. Ca^{++} within epithelial component of invasive ductal carcinoma.

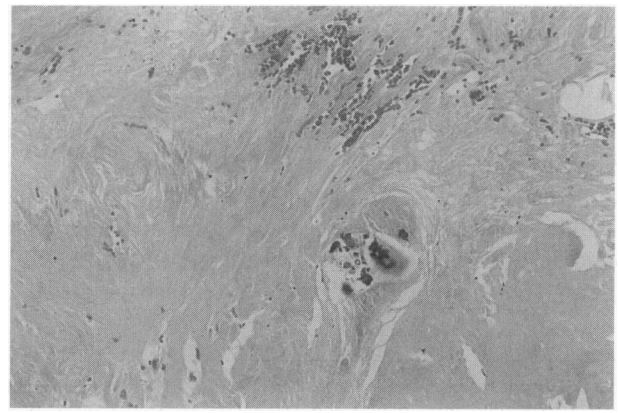

Figure 5. Ca^{++} within benign stroma.

Table 1. MICROANATOMIC LOCALIZATION* OF CA^{++}

DCIS (%)	LCIS (%)	Invasive Carcinoma (%)	Carcinomatous Stroma (%)	Benign Stroma (%)	Benign Ducts (%)	Benign Lobules (%)
13/24 (54)	3/7 (43)	6/21 (28)	5/21 (24)	1/32 (3)	20/32 (62)	5/32 (16)

* Number of cases with Ca^{++} in indicated component/total cases with that component.
DCIS = ductal carcinoma *in situ;* LCIS = lobular carcinoma *in situ.*

Ca^{++} within malignant components. Eleven patients had Ca^{++} within carcinoma *and* in benign peritumoral tissue the distribution that is shown in Figure 6; (the graphic includes four cases with benign peritumoral Ca^{++} in more than one location). In 11 cases with Ca^{++} were present only in benign peritumoral tissue (absent within the tumor), their distribution is shown in Figure 7 (these data include five patients with Ca^{++} in more than one location).

DISCUSSION

In this series of patients with carcinoma with Ca^{++}, 69% of the patients were found to have Ca^{++} in benign breast tissue. More importantly, in 34% of these carcinomas, Ca^{++} were present only in benign breast tissue near the tumors. These results suggest that small samples taken close to carcinoma have a substantial chance of containing Ca^{++} without showing carcinoma. Finding Ca^{++} in, specifically, needle core biopsies might lead to a false sense of security that the pathology of the mammographic anomaly had been identified.

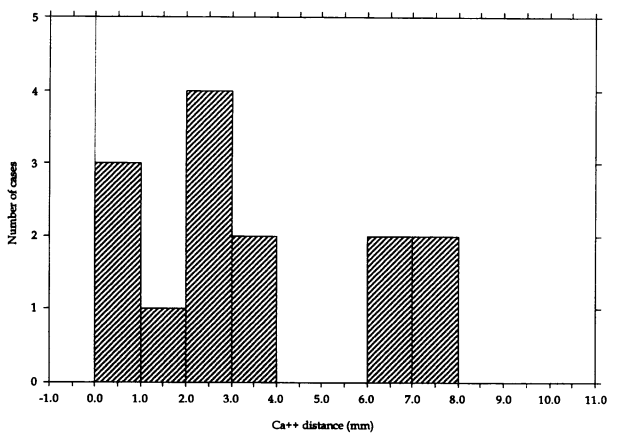

Figure 6. Distribution of benign peritumoral Ca^{++} in cases with Ca^{++} also in malignant elements.

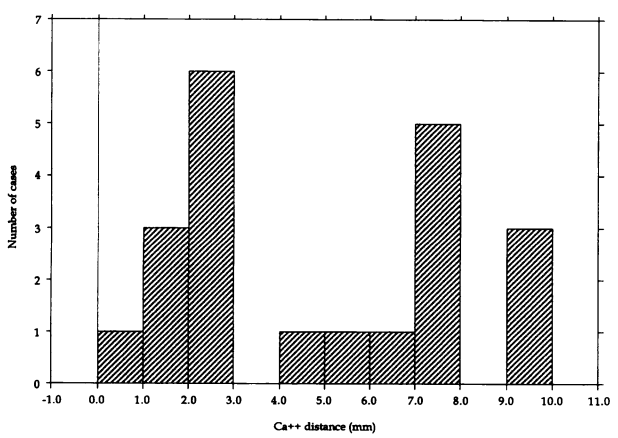

Figure 7. Distribution of benign peritumoral Ca^{++} in cases with no Ca^{++} in malignant elements.

The mammographic presence of Ca^{++} in breast lesions has been a topic of interest since the early 1950s. Previous studies have shown Ca^{++} to be present in 30% to 50% of cases of breast carcinoma and in 8% to 20% of cases of benign breast tissue.[8–10] The microanatomic location of Ca^{++} in relation to tumor has been explored in only a few cases. In 1966 Gerschon-Cohen et al.[11] observed a high incidence of Ca^{++} in benign sclerosing adenosis associated with carcinoma. Murphy and DeSchryver-Kecskemeti[12] found, in 11 cases of ductal carcinoma, 6 of them invasive, an 18.2% incidence of Ca^{++} only in benign components of the biopsy and 27% in benign as well as malignant components. In a similar study, Calbassani et al.,[13] in 15 ductal carcinomas, 6 of them invasive, observed that 20% of the malignant cases had Ca^{++} in adjacent fibrocystic disease, with an additional 20% of the cases having Ca^{++} in both malignant and benign tissue. These figures increased to 24% and 47%, respectively, in the study by Roses et al.,[14] which included lobular and tubular carcinomas with ductal carcinomas.

The potential advantages of stereotactically guided core biopsy as an alternative to needle-guided surgical biopsy include the avoidance of anesthesia, minimal breast distortion, a small scar, and reduced cost.[1,15,16] Studies to date suggest that the diagnostic accuracy of these biopsies depends on the target. When Ca^{++} are used to direct the biopsy, the accuracy is lower (62% accuracy using two core needle biopsies and 87% using five core biopsies) than for masses (91% and 98% accuracy, respectively).[17] In a multiinstitutional study, Brenner et al.[18] suggested sampling error and the distribution of Ca^{++} as possible explanations for this observed lower accuracy.

Our data represent the largest series to our knowledge where the microanatomic localization of Ca^{++} is analyzed in relation to carcinoma. The striking finding that Ca^{++} in many cases can be present only in peritumoral benign breast tissue and absent in carcinoma raises an important caution-

ary note when small representations of mammographic anomalies are being examined.

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