

Calcifications and the Therapeutically Irradiated Breast

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Mammograms of 81 patients who received radiation therapy to the breast were analyzed for patterns of pre- and postirradiation calcifications. Malignant calcifications may remain stable, diminish, or completely disappear following irradiation. The persistence of calcifications need not indicate residual cancer. Calcifications can develop following irradiation which are similar to either intraductal or secretory calcifications. Unusual calcifications may develop at the site of an irradiated cancer. It is important to recognize that benign calcifications can develop so that they will not be confused with recurrent malignancy.

Mammography should be an effective method of following patients who have received therapeutic irradiation for carcinoma of the breast. Few reports, however, are available on the appearance of the breast following radiation therapy. Little is known about the fate of malignant calcifications in the breast, nor is much information available regarding the possible development of benign calcifications after irradiation. This report describes changes in malignant calcifications and the development of benign calcifications following radiation therapy.

Materials and Methods

Clinical Material

Records of all patients at M. D. Anderson Hospital and Tumor Institute who received radiation therapy to the breast for carcinoma were reviewed. Those with mammograms both before and after radiation therapy and who had complete clinical follow-up data were included. Of the 81 who met these criteria, 35 received therapy following excision biopsy (tumorectomy) and 46 underwent therapy following either needle biopsy or incisional biopsy. The average age for the two groups was 51 and 55 years, respectively.

Malignant calcifications were seen in 12 patients in the needle/incision group. The appearance of the calcifications following irradiation was noted. Benign calcifications developed in four patients who underwent tumorectomy and in seven of the needle/incision biopsy group. Three patients with malignant calcifications subsequently developed benign calcifications elsewhere in the treated breast.

Method of Treatment

The radiation therapy regimens can be divided into three types.

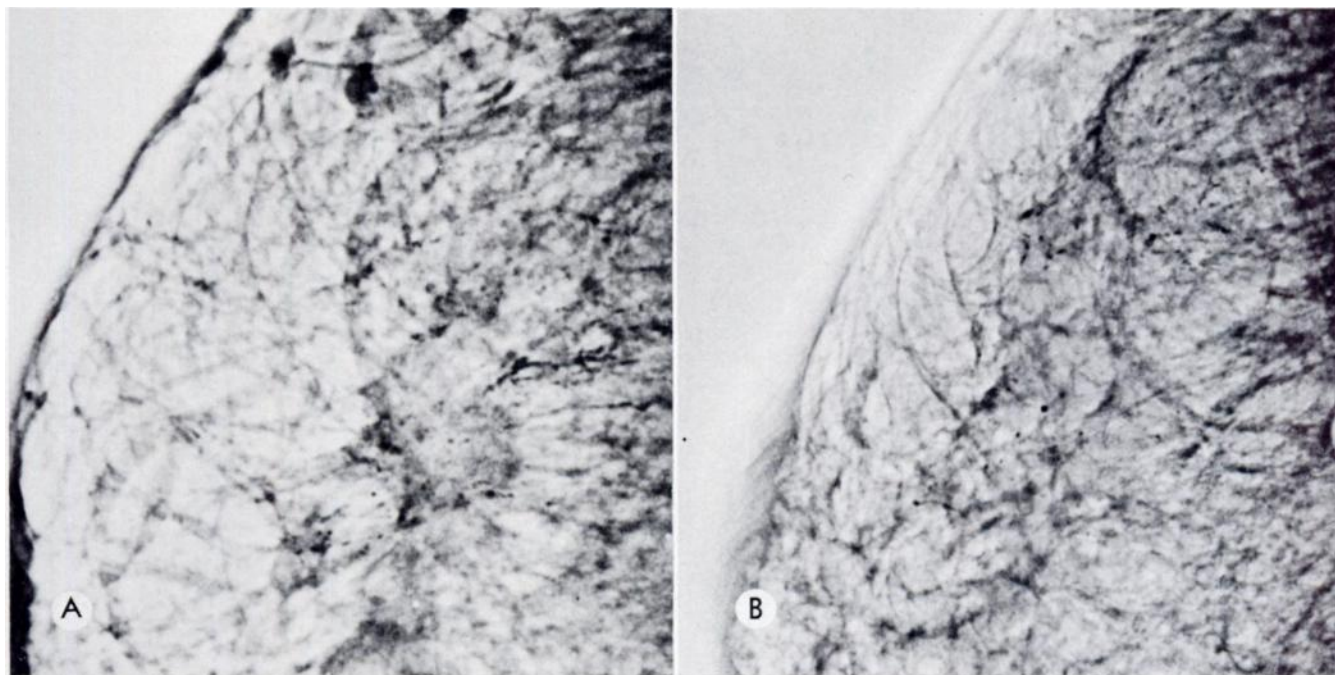


Fig. 1.—*A*, Enlarged craniocaudal view of breast showing cancer with associated malignant calcifications. *B*, Same breast 19 months after therapy (7,100 rad) showing disappearance of mass and decrease in malignant calcifications.

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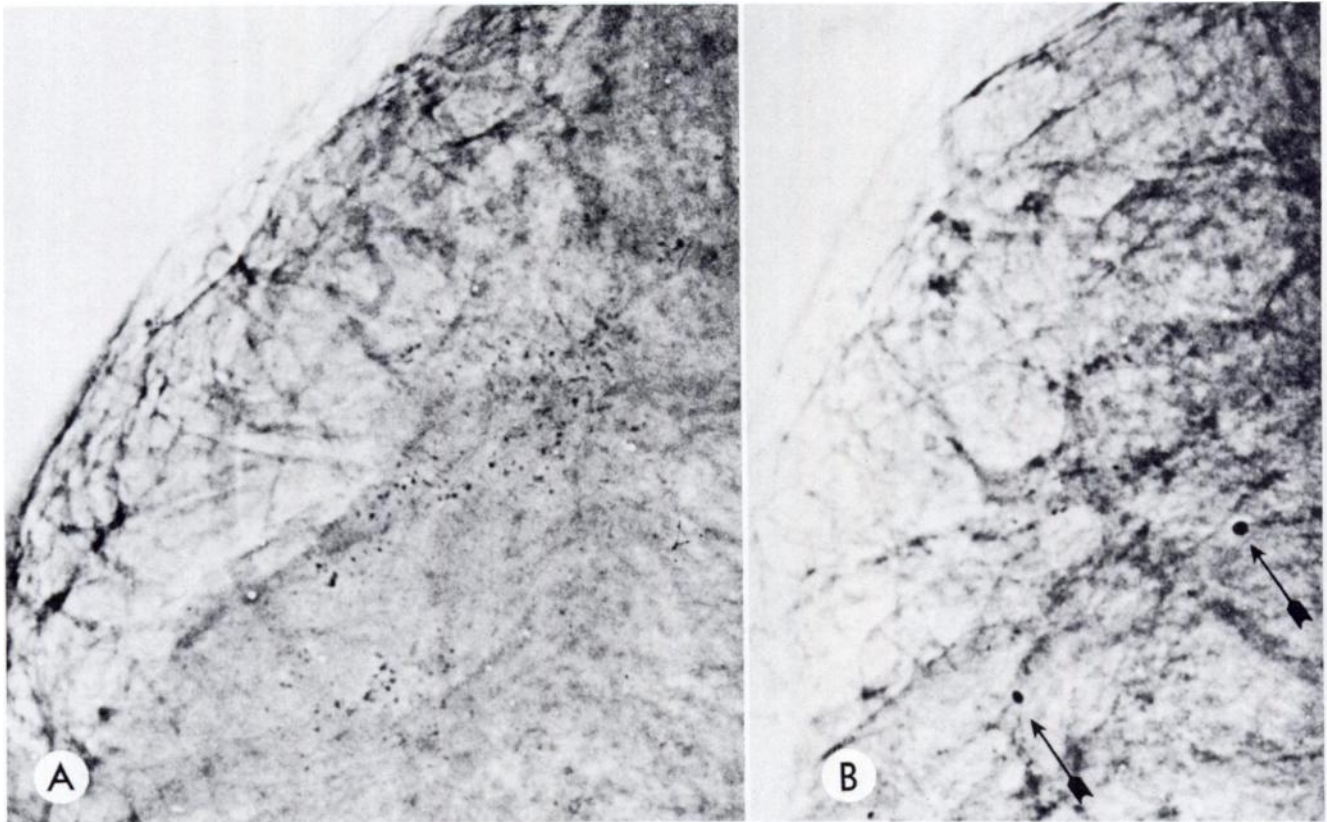
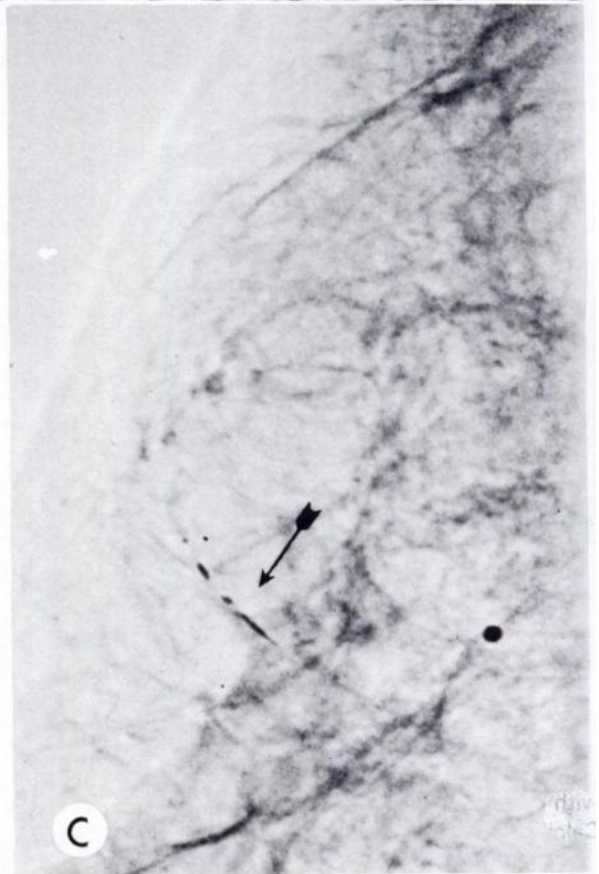


Fig. 2.—*A*, Enlarged craniocaudad view of left breast showing extensive cancer with malignant calcifications. *B*, Same breast 17 months after therapy (8,400 rad) showing decrease in malignant calcifications and size of mass. Two rounded benign calcifications have developed (*arrows*). *C*, Same breast 44 months after therapy showing complete disappearance of malignant calcifications. Note development of linear benign calcification (*arrow*).

Seven patients were treated for locally advanced primary and/or axillary nodal tumor, all clinically inoperable. The treatment consisted of radical and protracted ^{60}Co irradiation with a range of tumor doses from 5,400 to 6,000 rad delivered to the entire breast in 8 weeks, followed by (in four patients) reduced boost irradiation ranging from 1,000 to 3,000 rad. One patient received photon irradiation under hyperbaric oxygen conditions, and another patient was treated with neutrons to the breast.

Eight patients were treated for classical inflammatory carcinoma, established on clinical observation of erythema, peau d'orange changes, and ridging. Four of these patients had either 5-fluorouracil or vincristine in combination with adriamycin, Cytosar, and either BCG or MER, given prior to radiation therapy, generally in three or four courses. Radiation then consisted of two fractions per day separated by at least 6 hr, all with ^{60}Co , for a total of 5,100 rad tumor dose plus a boost of 2,000 rad through reduced fields in seven patients; one patient received 5,400 rad tumor dose plus a boost of 3,000 rads to reduced fields.

Five patients had clinically operable tumors (i.e., primary tumors less than 5 cm and without grave signs). In these patients, primary tumors were excised and followed by radiation therapy, conserving the breast. Irradiation was conducted with ^{60}Co , delivering 5,000 rad in 5 weeks with fractions once a day, followed by reduced fields in the quadrant of the primary tumor for an additional 1,000–1,250 rad tumor dose in 4 to 5 days.



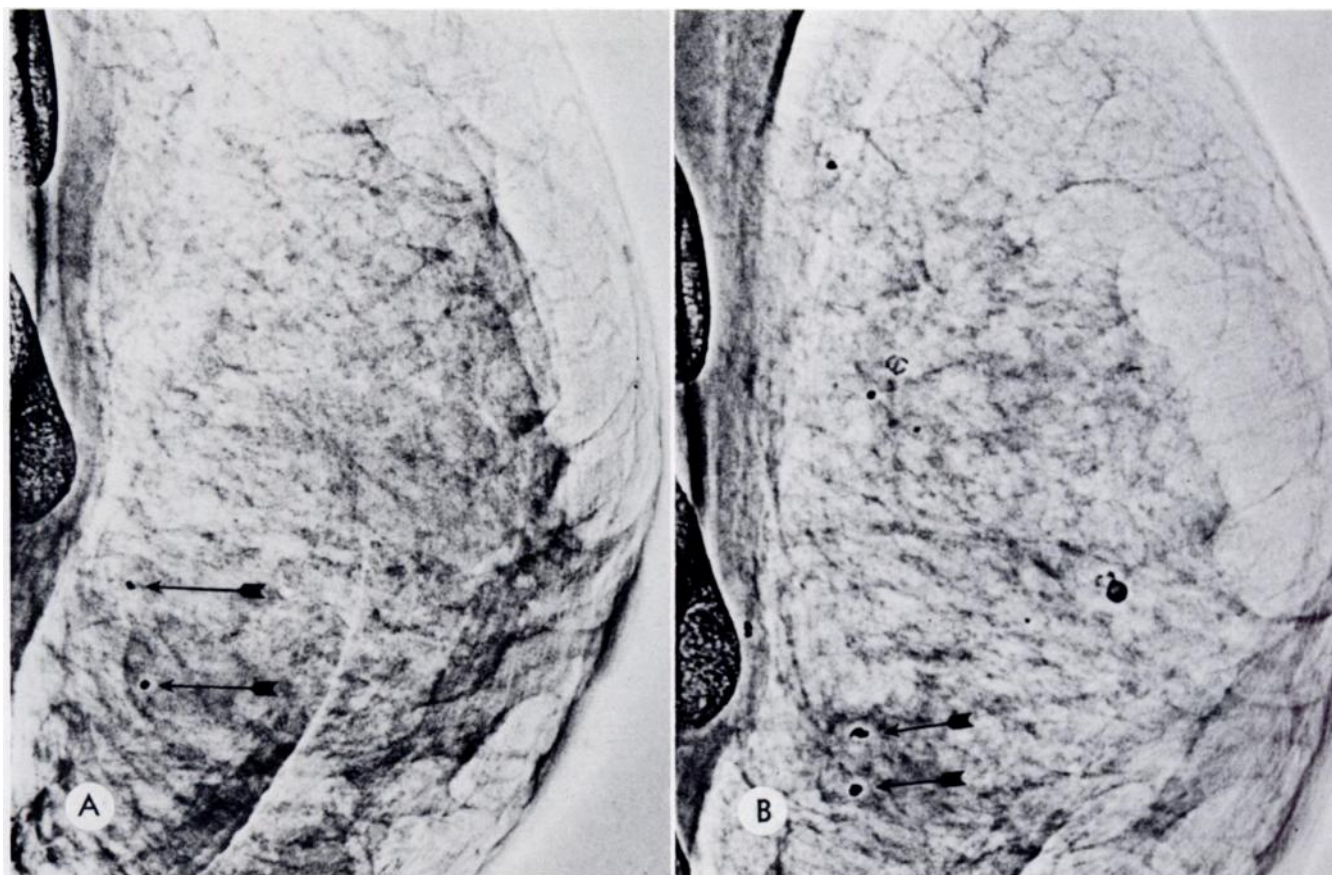


Fig. 3.—*A*, Mediolateral view of breast after tumorectomy but before radiation therapy. Note two benign calcifications (*arrows*). *B*, Same breast 16 months after therapy (9,500 rad) showing enlargement of benign calcifications in inferior portion of breast (*arrows*) and development of rounded calcifications similar to those in secretory disease.

Radiographic Findings

Radiographic findings are recorded separately for patients who had malignant calcifications prior to radiation therapy and those who developed calcifications following radiation therapy.

Fate of Malignant Calcifications

Of the 46 patients who had either needle or incisional biopsy of the carcinoma, 12 showed malignant calcifications. This group was evaluated for changes in the appearance of the calcifications after radiation therapy. Notation was also made of the radiation dose, time after completion of therapy, and whether there was recurrence in the treated breast.

No change was noted in the appearance of tumor calcifications in three patients who were followed mammographically at 9, 11, and 78 months after completion of therapy, respectively. Decrease in the extent of the calcifications was noted in four patients who were followed at 0 (completion of therapy), 4, 5, and 9 months, respectively. No further change was noted at 19 months in the patient with diminution of the calcifications at 9 months (fig. 1). Calcifications completely disappeared in five patients (fig. 2) at 9, 10, 19, 24, and 28 months after therapy. In two

patients with interval mammograms, the disappearance of calcifications was gradual with diminution seen at 3 and 17 months and final disappearance at 19 and 28 months, respectively.

Evidence of recurrent malignancy in the breast was palpated in two patients. One of these patients had no change in calcifications and one had complete regression of calcifications. No new malignant calcifications developed after radiation therapy nor was there other mammographic evidence of recurrence in these two patients.

Development of Calcifications

Calcifications with benign radiographic characteristics developed after radiation therapy in four of 35 patients who had undergone tumorectomy and in seven of 46 patients who had either needle or incisional biopsy. Two patients developed calcifications at the site of the cancer, noted at 9 and 39 months following therapy.

The benign-appearing calcifications developed from 2 to 44 months after irradiation (fig. 3). These calcifications are presumed to be causally related to the radiation since the untreated breast was unaffected. Spontaneous benign calcifications in the breast that are intraductal or related to secretory disease are usually bilateral and relatively symmetrical.

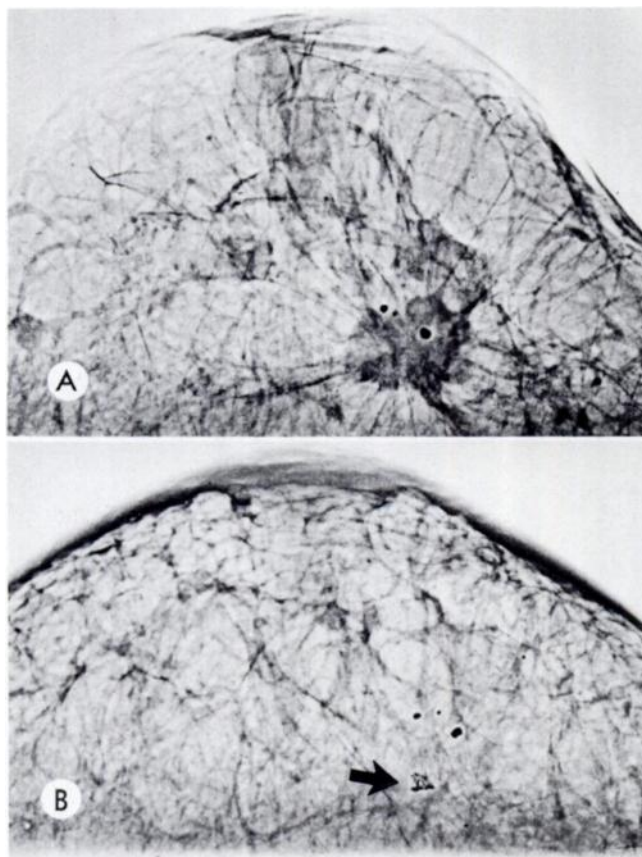


Fig. 4. — *A*, Craniocaudad view of breast showing cancer with benign calcifications superimposed. *B*, Same breast 9 months after therapy (9,000 rad) showing area of calcification (arrow) that developed at site of cancer. Benign calcifications remain unchanged.

The calcifications at the site of the cancers were unusual in appearance and not of the type generally associated with benign or malignant conditions of the breast (figs. 4 and 5).

Discussion

Little has been reported on either the development of calcifications in the breast after radiation therapy or the fate of malignant calcifications. In a study of similar material at another institution by one of us (H. I. Libshitz), development of calcifications was not observed [1]. Bloomer et al. [2] reported "no significant increase in the number of calcifications," and Nisce et al. [3] did not note benign-appearing calcifications after treatment.

Nisce and coworkers [3] reported that "tumor calcifications never completely regressed and were always associated with persistent disease." They suggested that disappearance of calcifications might not be expected even when the cancer was ablated, and they questioned the significance of persistent calcifications. No patients had malignant calcifications at the time of irradiation in the other two series [1, 2].

Two of our 12 patients with malignant calcifications developed recurrent disease in the treated breast. The

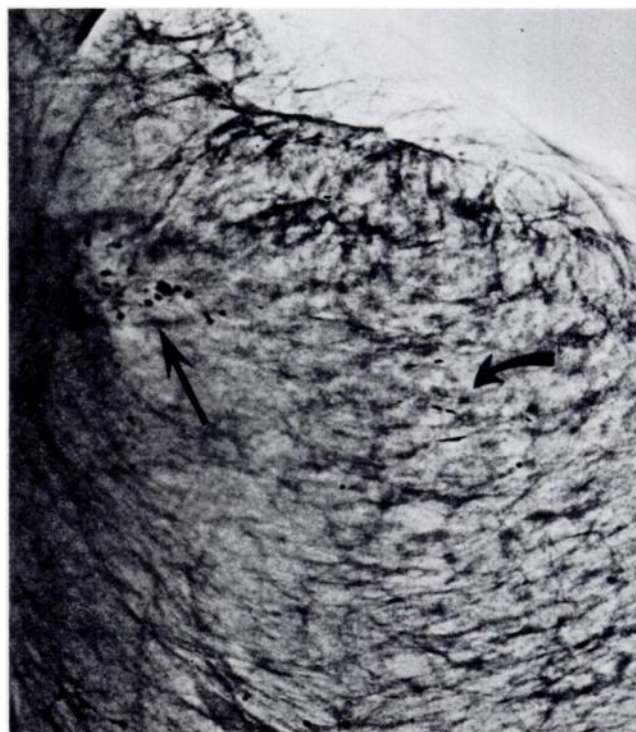


Fig. 5. — Mediolateral view of breast 39 months after therapy (9,000 rad) showing development of unusual collection of rounded calcifications (arrow) at site of irradiated cancer. Note linear, intraductal-like calcifications (curved arrow). Similar changes did not occur in opposite breast.

calcifications disappeared completely in one patient and did not change in 9 months in the other. In neither case were malignant calcifications noted. While Nisce et al. [3] reported that recurrence of tumor either at a new location or at the previous site was identifiable because of the appearance of mass or tumor calcifications, this was not the case in either of these patients.

Unfortunately, this series is too small to reach definite conclusions regarding the prognostic significance of alterations in calcifications. However, it is apparent that the persistence of malignant calcifications does not always indicate failure to control local disease. Two of three patients with no change in the calcifications are without evidence of local recurrence, and all four in whom decrease was noted are without evidence of local disease. Because disappearance of the calcifications is gradual, continued follow-up may reveal further change. Four of five patients in whom calcifications disappeared have no evidence of local recurrence. While it was hoped that disappearance of the calcifications might have favorable prognostic significance, such a conclusion is premature.

The development of benign-appearing calcifications in the breast, while not previously noted, is not surprising. Necrotic tissue, sloughed cells, and other cellular debris are present following radiation therapy. These calcifications are generally similar to intraductal calcifications or those associated with secretory disease. While their development cannot definitely be ascribed to radiation, the absence of similar calcifications in the untreated breast

points to this conclusion. Spontaneous benign calcifications are generally bilateral and relatively symmetrical.

While only 11 of 81 (14%) patients developed benign calcifications, it is important to recognize that benign calcifications can develop in an irradiated breast and do not indicate recurrent malignancy.

The finding of calcifications of a bizarre nature at the site of an irradiated tumor is important to note so that they will not be confused with recurrent tumor. Both patients in whom this was seen are well and without evidence of disease. These calcifications are assumed to be an incidental event secondary to tissue necrosis in the cancer.

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