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CLINICAL INVESTIGATION **Breast**

POSTOPERATIVE SEROMA FORMATION AFTER INTRAOPERATIVE RADIOTHERAPY USING LOW-KILOVOLTAGE X-RAYS GIVEN DURING BREAST-CONSERVING SURGERY

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Purpose: To determine the frequency and volume of seroma after breast-conserving surgery (BCS) with or without intraoperative radiotherapy (IORT).

Methods and Materials: Seventy-one patients with 73 breast cancers (IORT group) treated with IORT (20 Gy Intrabeam) as a boost during BCS were compared with 86 patients with 88 breast tumors (NO-IORT group) treated without IORT. Clinical examination and measurement of seroma volume on treatment-planning CT (CT-seroma) was done at median interval of 35 days after BCS.

Results: Seroma were found on palpation in 37 patients (23%) and on CT in 105 patients (65%; median volume, 26.3 mL). Interval between BCS and CT was significantly shorter in patients with palpable seroma (median, 33 days) or CT-seroma (33 days) compared with those with no palpable seroma (36.5 days; $p = 0.027$) or CT-seroma (52 days, $p < 0.001$). The rate of palpable seroma was not different (IORT $n = 17$, 23%; NO-IORT $n = 20$, 23%; $p = 0.933$), whereas fewer patients required puncture in the IORT group [3 (4%) vs. 10 (11%)]. In contrast, more patients showed CT-seroma after IORT (IORT $n = 59$, 81%; NO-IORT $n = 46$, 52%; $p < 0.001$). The interval between BCS and CT was significantly shorter in patients with IORT as compared with the NO-IORT patients (median, 33 days vs. 41.5 days; $p = 0.036$).

Conclusion: Intraoperative radiotherapy with low-kilovoltage X-rays during BCS is not associated with an increased rate of palpable seroma or seroma requiring treatment. The rate of seroma formation on CT was higher after IORT compared with the NO-IORT group, which might be because of the shorter interval between BCS and CT. © 2010 Elsevier Inc.

IORT, Breast cancer, Breast-conserving therapy, Seroma.

INTRODUCTION

Intraoperative radiotherapy (IORT) of the tumor bed in breast cancer patients treated with breast-conserving surgery (BCS) is increasingly used, using different devices (electrons, photons, or low-kilovoltage X-rays) and different concepts. There is some information regarding acute toxicity and cosmetic outcome of patients treated with low-kilovoltage X-rays (Intrabeam; Carl Zeiss, Oberkochen, Germany) as a boost (1, 2). Although our initial report (1) showed no significant increase of wound-healing problems in patients treated with IORT, we have reported on a qualitative basis that IORT patients more often show postoperative seroma in the treatment-planning CT compared with patients without IORT. The accumulation of breast seroma after BCS is estimated to occur in 9–15% of patients (3). Often a seroma is palpable and can be visualized during external-beam radiotherapy (EBRT) planning and might influence the shape and the volume of the breast, but is not clinically relevant. Only a small portion of patients show clinically significant seroma. The present retrospective analysis was performed to quantitatively evaluate the frequency and volume of both seroma formation (clinically nonrelevant and clinically relevant) after BCS with or without IORT and to identify influencing factors.

METHODS AND MATERIALS

Seventy-three breast cancers in 71 patients (IORT group) treated consecutively at the Department of Radiation Oncology, University Mannheim Medical Center (Mannheim, Germany) between 2005 and 2007 with BCS and IORT (20 Gy 50-kV X-rays prescribed at the applicator surface; Intrabeam) as previously

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reported (4, 5) for tumor bed boost irradiation were included in this analysis. Eighty-eight breast tumors in 86 patients treated in our institution during the same interval with BCS without IORT (NO-IORT group) were evaluated accordingly. For baseline patient characteristics, see Table 1.

All 157 patients (161 breasts) underwent a CT scan (Brilliance CT Big Bore; Philips, Cleveland, OH) for EBRT planning after a median interval of 35 days after BCS (minimum, 12 days; maximum, 237 days). The rate of a seroma formation (CT-seroma; Fig 1) was documented and seroma volume measured. Using the Oncentra Masterplan (Nucletron, Veenendaal, The Netherlands), the seroma volume was contoured manually on each slice and calculated with OTP. At the same time a clinical palpation of the breast was performed by an experienced radiation oncologist. A differentiation was made between no clinical finding, clinically palpable seroma, and clinically palpable seroma requiring puncture. Additionally, clinical and treatment-related factors were analyzed, including patient age, height, weight, body mass index (BMI), volume of the treated breast (contoured and computed using the planning system software), tumor size (as recorded in the final pathohistology report), and tumor localization. Systemic treatment (chemotherapy and/or antihormonal treatment with either tamoxifen or aromatase inhibitors) was documented for each patient.

Data are presented as summary statistics (mean and median with standard deviation, as well as frequency tables). Group-wise comparisons (IORT vs NO-IORT) were performed using the χ^2 *test, t test, and Mann*-Whitney *U* test according to the nature of the variables. In general, a p value of <0.05 was considered significant. Univariate and multivariate logistic regression analyses were used to identify baseline characteristics related to seroma development. Variables showing p values of <0.1 by univariate analysis were considered for multivariate analysis (backward likelihood ratio method). All computations were performed using the SPSS program (version 16.0.2; SPSS, Chicago, IL).

RESULTS

Patient characteristics

Both patient groups were equally distributed with respect to patient age, height, weight, tumor size, and tumor localization (Table 2). There was a difference with regard to a larger breast volume for the IORT patients (median breast volume, 1263.9 mL for the IORT group vs. 1088.6 mL for the NO-IORT group; $p = 0.004$). The BMI was significantly higher in the IORT group compared with the NO-IORT group (median, 27.3 kg/m^2 vs. 24.9 kg/m^2, respectively; $p = 0.025$), and the time interval between BCS and treatment-planning CT was significantly shorter in the IORT group compared with the NO-IORT group (median, 33 days vs. 41.5 days, respectively; $p = 0.036$).

Regarding all breasts there were no clinically palpable seroma in 124 of 161 cases. Seroma were found on palpation in 37 breasts (23%; mean seroma volume, 60.5 ± 48.0 mL; median, 50.0 mL; minimum, 3.7 mL; maximum, 226.2 mL) and on CT in 105 breasts (65%; mean seroma volume, 39.2 ± 39.5 mL; median, 26.3 mL; minimum, 0.9 mL; maximum, 226.2 mL). Mean seroma volume on CT of the non-palpable seroma was 27.6 ± 28.3 mL (median, 17.6 mL; minimum, 0.9 mL; maximum, 130.3 mL). Thirteen breasts that had to be treated with puncture had a mean seroma volume of 99.1 ± 52.2 mL (median, 96.9 mL; minimum, 34 mL; maximum, 226.2 mL). Interval between BCS and CT was significantly shorter in cases with palpable seroma (median, 33 days) or CT-seroma (33 days) compared with those with no palpable seroma (36.5 days; $p = 0.027$) or CT-seroma (52 days; $p < 0.001$).

Table 1. Baseline patient characteristics

Characteristic	IORT	NO-IORT
n	71	86
BCS	73	88
Invasive cancer	73	75
Ductal carcinoma *in situ*	0	13

Abbreviations: IORT = intraoperative radiotherapy; BCS = breast-conserving surgery.

Risk of seroma in IORT vs. NO-IORT patients

Comparison of the IORT and NO-IORT groups showed that the rate of palpable seroma was not different, whereas fewer breasts required puncture in the IORT group. In contrast, significantly more breasts showed CT seroma after IORT. There were no palpable seroma in 56 IORT cases and palpable seroma in 17 IORT cases (22%), of which three seroma (4%) required puncture. Mean volume of the 17 cases with palpable seroma was 73.1 ± 50.1 mL, and mean volume of the three seroma to be punctured was 149.8 ± 66.2 mL. Regarding the NO-IORT group, there were 68 breasts with no palpable seroma and 20 breasts (23%) with palpable seroma, of which 10 had to be treated by puncture (11%). Mean volume of the 20 cases with palpable seroma was 49.9 ± 44.5 mL, and mean volume of the 10 seroma to be punctured was 83.9 ± 39.3 mL.

Seroma formation in CT was found significantly more often after IORT ($p < 0.001$). There was a CT-visible seroma in 59 breasts (81%) of the IORT patients and no visible seroma in 14 breasts, whereas only 46 (52%) of the NO-IORT cases had CT-seroma and 42 (48%) showed no findings on CT. No findings on clinical examination but seroma on CT was seen in 42 (58%) of the IORT cases and

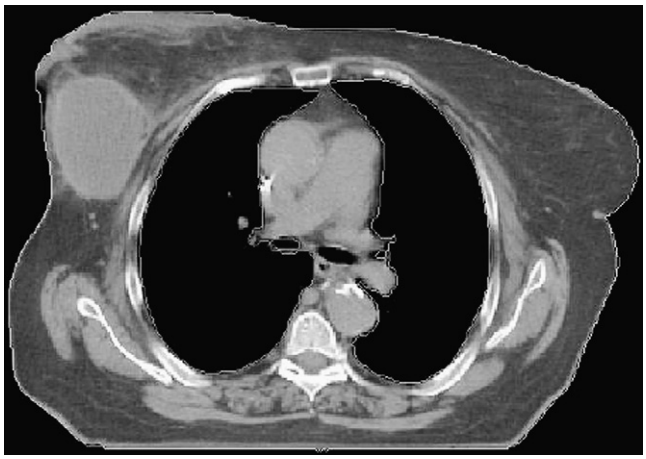

Fig. 1. Treatment-planning CT in the supine position (arms elevated), showing postoperative seroma in the right breast.