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Analysis of fat necrosis after adjuvant high-dose-rate interstitial brachytherapy for early stage breast cancer

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ABSTRACT

PURPOSE: To report the incidence and potential predictors of fat necrosis in women with early stage breast cancer treated with adjuvant high-dose-rate (HDR) multicatheter interstitial brachytherapy.

METHODS AND MATERIALS: Between 2003 and 2010, 238 treated breasts in 236 women were treated with accelerated partial breast irradiation using HDR interstitial brachytherapy. Selection criteria included patients with Tis–T2 tumors measuring ≤3 cm, without nodal involvement, who underwent breast-conserving surgery. Ninety-nine percent of treatments were to a total dose of 34 Gy. The presence and severity of fat necrosis were prospectively recorded during followup. Cosmesis was qualitatively scored in all patients. Cosmesis was quantitatively measured via the percentage breast retraction assessment in 151 cases.

RESULTS: Median followup was 56 months. The crude rate of fat necrosis was 17.6%. The rate of symptomatic fat necrosis was 10.1%. In univariate analysis, acute breast infection and anthracycline-based chemotherapy, number of catheters, volume encompassed by the prescription isodose, volume encompassed by the 150% isodose (V_{150}), volume encompassed by the 200% isodose, and integrated reference air kerma were significantly associated with fat necrosis. There was significant collinearity between the brachytherapy-related factors; of these, V_{150} was most predictive. In multivariate analysis, only V_{150} was significantly associated with fat necrosis. At 3 years, patients with fat necrosis were more likely to have a fair or poor cosmetic outcome and a larger percentage breast retraction assessment.

CONCLUSIONS: Mammary fat necrosis is a common adverse event after breast-conserving surgery and HDR interstitial brachytherapy. Fat necrosis is associated with worse qualitative and quantitative cosmetic outcomes. Minimizing exposure volumes, such as V_{150}, may decrease the incidence of fat necrosis and improve cosmesis.

Keywords: Breast cancer; Brachytherapy; Fat necrosis; Cosmesis; Partial breast

Introduction

For several decades breast-conserving therapy has been a standard treatment for early stage breast cancer. The use of whole-breast irradiation (WBI) after breast-conserving surgery (BCS) has been shown to reduce the risk of ipsilateral breast tumor recurrence (IBTR) over BCS alone (1). The observation that most local recurrences after BCS are at or near the lumpectomy site (2) has led to the investigation of accelerated partial breast irradiation (APBI) as an alternative to WBI. APBI can be completed within several days as

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compared with several weeks for conventional WBI. Various dose delivery methods have been used for APBI, including multicatheter interstitial brachytherapy, intracavitary brachytherapy, intraoperative radiation therapy, and external beam conformal radiation therapy. Early studies have reported low IBTR rates with these techniques (3).

Mammary fat necrosis is a benign sterile inflammatory process (4) that may be caused by trauma, biopsy, or breast surgery. Fat necrosis after adjuvant radiation therapy has been documented with external beam radiotherapy and interstitial or intracavitary brachytherapy (5–7). Fat necrosis may be an asymptomatic finding detected during breast cancer surveillance imaging. Mammographic findings may include a focal mass or an opacity, microcalcifications, or lipid cysts (8). During followup fat necrosis may present as some combination of a palpable mass, mastalgia, or overlying skin erythema. Mastalgia may require analgesic medication or surgical intervention for pain control.

In the setting of APBI, evaluation of patient, tumor, and treatment characteristics that may be associated with the development of fat necrosis and its clinical significance has been limited (5, 9, 10). In this study, a detailed analysis of fat necrosis has been performed on a large cohort of patients treated with APBI using high-dose-rate (HDR) multicatheter interstitial brachytherapy with a median followup of more than 4 years. We examine clinical- and treatment-related factors that could contribute to the risk of developing fat necrosis and its impact on cosmesis.

Methods and materials

Between February 2003 and January 2010, 238 treated breasts in 236 patients with at least 6 months of followup were treated with APBI using HDR interstitial brachytherapy at Barnes-Jewish Hospital and Washington University School of Medicine. WBI was not given. Selection criteria included patients with unifocal American Joint Cancer Center Commission (sixth edition) Tis–T2N0M0 breast cancers $\leq$3 cm treated with BCS. One hundred eighty-one of 187 patients with invasive disease had pathologic N0 disease assessed mainly by sentinel lymph node biopsy. Nine patients had prior radiation therapy with fields that were adjacent to or included the ipsilateral breast. Three of these patients had prior WBI and received adjuvant APBI for an IBTR after a second partial mastectomy. Three of these patients were treated for Hodgkin lymphoma, two were treated for soft tissue sarcoma of the upper extremity, and one was treated for non-Hodgkin lymphoma. The Washington University School of Medicine Human Research Protection Office Institutional Review Board approved this retrospective review for human subjects.

All patients were treated with HDR interstitial brachytherapy using a high-activity iridium-192 source. The interstitial implants were placed using a free-hand technique with the goal of encompassing the surgical cavity with a 2-cm margin of breast tissue in all directions. It was common for the surgical cavity to be less than 2 cm of breast tissue in the anterior and/or the posterior directions because of the presence of the skin anteriorly or muscle or chest wall posteriorly. In general, an intraplane catheter spacing of 1.2 cm and an interplane spacing of 1.5–2.0 cm were used. All implants were multiplanar, and the use of more than two planes was common. Interstitial implants were placed intraoperatively with an opened surgical cavity in the first 45 patients with the breast surgeon reincising the partial mastectomy incision and dissecting down to the surgical cavity. Thereafter, predominantly real-time ultrasound guidance was used without reopening the surgical cavity. The partial mastectomy surgical cavities were never surgically obliterated. Real-time ultrasound-guided implantation was performed using a strict sterile technique and under a combination of narcotic and anxiolytic sedation with local anesthesia. The direction of catheter planes was determined after considering how best to encompass the targeted breast tissue with the least catheters traversing a minimum amount of nontargeted breast tissue. The deepest plane of catheters, which was often at the level of but not into the pectoralis major muscle, was typically placed first. In some cases, the deepest plane was in breast tissue 2 cm posterior to the surgical cavity. The most superficial plane of catheters was created next, which was often 5 mm deep to the skin surface, but in some cases, it was 2 cm anterior to the surgical cavity. Intracatheter spacing of 1.2 cm was used. If the distance between the deepest and the most superficial planes of catheters was greater than 1.5–2.0 cm, then additional planes were created in the interior of the clinical target volume (CTV) using a 1.5–2.0-cm intraplane spacing. Catheters in different planes were placed such that a plane passing through the center of the implant, orthogonal to the planes of the catheter applicators, showed a triangular shape of the catheter cross sections.

The initial 8 patients had surgical clips placed at the time of implantation and underwent two-dimensional (2D) brachytherapy treatment planning using multiple sets of orthogonal plain films. In these patients coded, radiopaque dummies were placed in each catheter, which was in turn numbered. Several sets of 2D radiographs of the implant were then taken in a conventional simulator at various gantry angles. Each catheter and surgical clip were identified on each 2D image and then digitized into the Plato treatment planning system. This created a virtual three-dimensional (3D) space, which contained the 3D implant structure and the surgical clips without any patient anatomy. The surgical clips were used as guides to determine the active lengths of each catheter. Treatment planning proceeded and exposure volumes, such as volume encompassed by the 150% isodose (V_{150}) and volume encompassed by the 200% isodose (V_{200}), could be calculated and optimized in this virtual space, but no explicit CTV could be created. All subsequent patients underwent CT simulation (Brilliance CT Big Bore; Philips, Cleveland, OH) and 3D treatment planning. The Plato Brachytherapy planning system (Nucletron BV, Veenendaal, The Netherlands) was used through November 2006, after