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Impact of adjuvant systemic chemotherapy on wound healing and cosmetic outcome in 224 women treated with accelerated partial breast irradiation using interstitial brachytherapy

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ABSTRACT

PURPOSE: To evaluate the impact of timing of adjuvant chemotherapy on wound healing and cosmetic outcome in women treated with accelerated partial breast irradiation (APBI).

METHODS AND MATERIALS: Between August 2000 to December 2011, 224 women were treated with APBI using multicatheter interstitial high-dose-rate brachytherapy. Patients were treated to a dose of 34 Gy/10#/5−7 days with bid regimen. Systemic chemotherapy was administered as per the standard guidelines.

RESULTS: Multicatheter interstitial brachytherapy technique was open cavity in 136 (60%) and closed cavity in 88 (40%). Adjuvant chemotherapy was given in 117 (52%). Wound complications (WCs) were observed in 24 patients (11%), which included wound infections (WIs) in 20 and wound dehiscence in 14. The median gap between chemotherapy and APBI was 13 days in women who developed WCs, 20 days for prechemo, and 32 days for postchemo APBI in its absence. On multivariate analysis, gap between APBI and chemotherapy of ≤3 weeks was the only significant factor ($p = 0.03$) affecting WCs. Acute WI ($p = 0.01$) and two-dimensional planning ($p = 0.04$) had significant impact on cosmesis resulting in fair to poor cosmetic outcome.

CONCLUSIONS: Gap of ≤3 weeks between APBI and chemotherapy resulted in increased WCs. WI and two-dimensional planning resulted in poorer cosmetic outcome. We recommend gap of at least 3 weeks for optimal outcome.

Keywords: Accelerated partial breast irradiation; Chemotherapy; Wound complications

Introduction

Accelerated partial breast irradiation (APBI) is increasingly being explored as an alternative to whole breast radiation therapy (WBRT) in well-selected patients after breast conserving surgery (1−7). The National Medicare population study of 30,000 early breast cancer (EBC) patients showed increase in APBI from 10% in 2006 to 15.8% in 2008−2009 (8). With the increasing use of APBI outside the clinical trials, Groupe Européen de Curiethérapie-European Society for Therapeutic Radiotherapy and Oncology (GEC-ESTRO) and the American Society for Radiation Oncology (ASTRO) published their consensus statements to aid in proper patient selection (9, 10). Guidelines for patient selection for APBI have also been given by American Brachytherapy Society (11, 12). ASTRO has recently updated their recommendations for APBI (13). A study done on surveillance epidemiology and end results database showed increase in the patients with suitable criteria and decrease in the patients with unsuitable

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criteria among patients treated with APBI before and after the ASTRO consensus statement (14). Recently, a GEC-ESTRO randomized Phase III trial has proven noninferiority of APBI using multicatheter interstitial brachytherapy (MIB) over WBRT in carefully selected patients (15). This trial will possibly have further impact on increase in the APBI outside the clinical trials.

Despite the increased use of APBI, there is a paucity of data regarding sequencing and the appropriate interval between chemotherapy and APBI. Few series have shown increased toxicity with addition of chemotherapy with APBI and have raised concerns regarding use of both modalities together (16–18). Data of APBI in intermediate risk or cautionary population as per GEC-ESTRO/ASTRO consensus have shown equivalent control rates (19–21). With such emerging data, more patients will be offered APBI outside the clinical trials routinely and will merit chemotherapy also. Hence, there is need for mature data regarding timing and sequencing of chemotherapy with respect to APBI. We present our data reporting the effect of timing and sequencing of chemotherapy on clinical outcome, cosmesis, and toxicity in EBC patients prospectively treated with APBI.

Methods and materials

Between August 2000 to December 2011, 249 women diagnosed with EBC were considered for APBI using high-dose-rate (HDR) MIB using iridium-192 afterloading system. Women with age >40 years, tumors ≤3 cm, and clinically negative axillary lymph nodes were considered suitable. Of these, 224 women completed the planned treatment of APBI as well as adjuvant therapy and are subject of current analysis. Twenty-five patients were not evaluable either due to removal of implant due to poor prognostic factors (13), patients opting for mastectomy (2), or unavailability of data (10). The data were retrieved from the prospectively maintained database as well as case records.

Breast conserving surgery which included wide excision of the tumor and axillary lymph node dissection was done in all patients. The procedure for intraoperative/postoperative brachytherapy has been described earlier (22–24). In short, consenting women were considered for either intraoperative or postoperative implant based on the time of the referral. In patients undergoing intraoperative placement (open cavity technique), histopathology was reviewed after the wide excision and axillary clearance with the help of frozen section facility wherein tumor size, cut margin, and axillary lymph node status was confirmed. Tumor bed was marked with radio-opaque clips, and cavity with 1–2 cm margin was defined as the target volume. Implant consisted of 2–4 planes with needles placed at a distance of 1.5 cm with interplanar separation of 1.5 cm depending on the volume of breast and excision. For postoperative brachytherapy (closed cavity technique), the implant placement was based on preimplant CT scan, preoperative mammogram, and scar location. The placement of needles, implant procedure, and dosimetry were similar to that of open cavity technique.

Orthogonal X-ray based planning was done till August 2005 after which we moved to three-dimensional computerized tomography (3DCT)-based planning. The procedure of orthogonal X-ray and 3DCT-based planning has been described earlier (22, 25). Orthogonal X-ray films were taken on simulator (Ximatron; Varian Associates, Palo Alto, CA), whereas CT scans were taken on Somatom Emotion (Siemens Medical Systems, Erlangen, Germany). A margin of 1–2 cm was then geometrically grown over the cavity volume to obtain a planning target volume (PTV). Radiotherapy planning was done on Plato Sunrise (Nucletron, Veenendaal, the Netherlands) planning system. The basal dose points were defined in the central axis according to the Paris system, and the reference dose prescription of 85% was chosen. For 3DCT-based planning, evaluation of the plan was done by slice by slice visualization of the cavity and PTV coverage. Plan evaluation also included the use of cumulative dose–volume histograms and indices such as cavity coverage index (CI cavity), PTV coverage index (CI PTV), and dose homogeneity index (DHI). CI was defined as the fraction of volume receiving a dose equal to or greater than the prescription isodose. DHI was defined as a fraction of PTV receiving dose between 100% and 150% of the prescription isodose. While finalizing the plan, the aim was to achieve the CI of cavity >90% and CI of PTV of 90%. Attempt was made to achieve DHI of >0.75 with optimization; however, a DHI of >0.70 was considered acceptable. We aimed to keep $V_{150} \leq 70$ cc and $V_{200} \leq 20$ cc. The loading of catheters near the skin was removed, and an attempt was made to restrict the doses to the skin below the prescription isodose. A dose of 34 Gy/10#/5–7 days with bid regimen was delivered.

Chemotherapy

Adjuvant systemic chemotherapy was considered as and when indicated. For the purpose of present analysis when APBI was followed by chemotherapy, the procedure was termed as prechemo APBI. These patients were mostly treated with open cavity technique. Brachytherapy was defined postchemo when it was done after completion of chemotherapy. These patients were treated with closed cavity technique. Majority of patients received their first dose of chemotherapy >2 weeks after completion of APBI.

Wound complications

After completion of the treatment, patients were initially evaluated weekly till the implant marks were healed. The events registered as wound complication (WC) included wound infection (WI), cellulitis, sinus tract development, wound dehiscence (WD), and ulcer.

Followup

Patients were followed up every 6 months for 5 years and yearly thereafter. At each followup, clinical assessment was