

## Review Article

## A Concise Review of High Dose Rate (HDR) Brachytherapy (BT) Boost as part of Breast Conserving Treatment (BCT) for Breast Cancer (BC)

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### ABSTRACT

Breast cancer (Ca) comprises commonest cancer in female population and is an important causative factor in deaths associated with cancer worldwide. Current multimodality treatment includes resection, radiotherapy, systemic treatment combinations. In the context of adjuvant RT, high level evidence suggests improved treatment results of local control (LC), overall survival (OS) with reduction in breast Ca related mortality in selected patient subgroups. Resection for management typically includes breast conserving surgery (BCS) or mastectomy. Many factors could affect on selection of surgical modality for breast Ca management including patient characteristics and preferences along with contemplated therapeutic results such as LC, OS, and associated toxicity profile. Nevertheless, an increase exists for using conservative surgical resection instead of removal of the whole breast with supporting high level evidence. When the selected surgical modality consists of BCS, adjuvant irradiation is strongly suggested primarily to achieve improved LC. Adjuvant irradiation of the breast after BCS may include boost radiotherapy (RT) focused on lumpectomy cavity. This boost therapy may be delivered using several techniques. RT is a critical component of BCT. Whole breast radiotherapy (WBRT) with an additional boost dose focused on lumpectomy cavity is a widely accepted treatment strategy. While benefit of adding boost RT to WBRT has been demonstrated with accumulating evidence from several centers around the globe, there may be concerns about adverse effects associated with irradiation such as induration, fibrosis, telangiectasia and overall cosmesis. In this context, normal tissue sparing techniques are being used in WBRT. BT may offer an excellent method of administering the additional boost dose after WBRT with its inherent advantages of improved conformality and reduced surrounding tissue exposure, which may potentially translate into decreased risk of late effects. This has been supported by several comparative studies and experiences from different centers. Clearly, future studies may provide high level evidence. Here in, we provide a concise review of high dose rate (HDR) brachytherapy (BT) boost as part of breast conserving treatment (BCT) for breast Ca.

### INTRODUCTION

Breast cancer (Ca) comprises commonest cancer in the female population and is an important causative factor in deaths associated with cancer worldwide [1]. Current multimodality treatment includes

resection, radiotherapy, systemic treatment combinations. In the context of adjuvant RT, high level evidence suggests improved treatment results of local control (LC), overall survival (OS) with

reduction in breast Ca related mortality in selected patient subgroups. [2].

Resection for management typically includes breast conserving surgery (BCS) or mastectomy. Many factors could effect on selection of surgical modality for breast Ca management including patient characteristics and preferences along with contemplated therapeutic results such as LC, OS, and associated toxicity profile. Nevertheless, an increase exists for using conservative surgical resection instead of removal of the whole breast with supporting high level evidence [3,4]. When the selected surgical modality consists of BCS, adjuvant irradiation is strongly suggested primarily to achieve improved LC [5,6]. Adjuvant irradiation of the breast after BCS may include boost RT focused on lumpectomy cavity. This boost therapy may be delivered using several techniques. Herein, we provide a concise review of high dose rate (HDR) brachytherapy (BT) boost as part of breast conserving treatment (BCT) for breast Ca.

## **LITERATURE REVIEW**

Several dose fractionation schemes have been utilized for radio therapeutic management of patients after BCS mostly including conventionally fractionated schemes, and incorporation of adaptive treatment strategies has been suggested to improve critical organ sparing. Whole breast RT (WBRT) is a widely accepted treatment strategy for adjuvant irradiation using daily fraction sizes of 1.8 to 2 Gy to deliver the cumulative therapy directed at affected breast within 5 to 6 weeks. However, irradiation of the whole breast using this dose-fractionation scheme may not be adequate for optimal LC with the need for supplementary dose of RT focused on lumpectomy cavity. Rationale of focusing on the tumor bed for boost irradiation is the consideration that local recurrences mostly occur in this region particularly in patients with unfavorable factors such as larger tumor size, younger age, higher grade or mitotic activity,

extensive intra ductal component with or without close or involved surgical margins [7-11].

Romestaing et al. [7] assessed supplementary irradiation for conservative management in a study of 1024 patients. The additional supplementary irradiation delivered sequentially after WBRT resulted in a significant decrease in risk of early local recurrences [8]. While the rates of telangiectasia were higher in patients receiving the boost treatment, self-assessment scores for cosmetic results were comparable [9].

Role of tumor bed boost was assessed by a randomized phase III study conducted between 1989 and 1996 with randomization of 5569 patients [10]. Long term results demonstrated significant reduction in lateral disease recurrence by use of a 16 Gy supplementary irradiation with largest benefit in younger patients [11,12]. Long term OS was not affected, and the boost group had a higher risk of adverse effects [13]. The authors suggested that avoidance of supplementary irradiation could be considered for elderly individuals [14].

Jones et al. [15] assessed the extra boost dose of 16 Gy for early stage breast Ca patients receiving BCT by analyzing a subgroup of patients from the EORTC boost vs no boost trial with central pathology review. Young age, high grade invasive ductal Ca were reported as the prominent risk factor for local relapse whereas margin status did not have significant influence [16]. Supplementary irradiation decreased the negative effects of both young age and high grade invasive Ca significantly [17].

Kindts et al. [17] in a Cochrane review evaluated 8325 patients in total. Adding supplementary irradiation yielded increased LC rates [18]. Cosmesis assessment by a panel revealed worse Cosmesis for supplementary irradiation group, however, no

difference has been reported in physician scored Cosmesis or breast retraction percentage <sup>[19]</sup>.

Use of low dose rate (LDR), pulsed dose rate (PDR), and HDR BT for supplementary irradiation has also been addressed by several authors <sup>[20-21]</sup>. BT, a unique form of irradiation utilized for cancer management for more than a decade, includes placement of sealed, radioactive sources into or in close vicinity of a tumor directly or via catheters <sup>[22]</sup>. This sophisticated technique may serve as an excellent therapeutic modality particularly with its capability for improved normal tissue sparing given that the sources exert their activity within the target volume and surrounding critical structures may be protected from excessive radiation exposure.

Considering that adverse effects including induration, fibrosis, telangiectasia and overall Cosmesis may have an association with the irradiated breast volume, BT may confer an advantage thanks to its limited surrounding normal tissue exposure <sup>[23]</sup>.

This has been supported by a recent study by Terheyden et al.. Results of diametric comparison revealed that HDR BT boost achieved improved normal tissue sparing compared to external beam boost which could translate into a relative reduction in long term adverse effects <sup>[24]</sup>. In the study by Polgár et al. <sup>[24]</sup> evaluating the role of HDR BT boost with multi catheter implants as part of BCT, excellent long term LC with acceptable cosmetic outcomes accompanied by few grade 3 late RT adverse effects have been reported at a median follow up duration of 94 months<sup>[25]</sup>. Electron beam boost techniques may include the subcutaneous vessels and the skin, however, BT with interstitial implants may offer improved conformity with potentially decreased risk of telangiectasia or fibrosis <sup>[26]</sup>.

## CONCLUSIONS AND FUTURE PERSPECTIVES

BCT is being more frequently used for management of breast cancers. RT is a critical component of BCT. WBRT with an additional boost dose focused on lumpectomy cavity is a widely accepted treatment strategy. While the benefit of adding boost RT to WBRT has been demonstrated with accumulating evidence from several centers around the globe, there may be concerns about adverse effects such as induration, fibrosis, telangiectasia and overall Cosmesis. In this context, normal tissue sparing techniques are being more commonly used in WBRT. BT may offer an excellent method for administering the additional boost dose after WBRT with its inherent advantages of improved conformity and reduced surrounding tissue exposure, which may potentially translate into decreased risk of late effects. This has been supported by several comparative studies and experiences from different centers. Clearly, future studies may provide high level evidence regarding the optimal treatment of patients after BCS.

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