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What a difference a clip makes! Analysis of boost volume definition in radiation therapy for conservative breast surgery

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ABSTRACT

Purpose/objective(s): To evaluate the role of surgical clips placement in the definition of boost treatment volume.

Materials/methods: Clinical Target Volumes (CTV) were defined as: CTV Breast, CTV Quadrant (based on physical exam and pre-surgical images), CTV Boost, defined by clip plus margin (1 cm for 2 or more clips and 2 cm for 1 clip only) plus radiological changes, CTV NT (normal tissue), defined by CTV Quadrant minus CTV Boost and CTV MISS (CTV that would be outside the treatment volume), defined by CTV Boost minus CTV Quadrant.

Results: A total of 247 patients were included. Upper lateral quadrant was the most common clinical location (47.3%). The median number of clips used was three. The mean volumes were: CTV Breast:982.52 cc, CTV Boost:36.59 cc, CTV Quadrant:285.07 cc, CTV NT:210.1 cc and CTV MISS:13.57 cc. Only 50.6% (125) of the patients presented the CTV Boost completely inside the CTV Quadrant and in 47.3% (117), partially inside. Among patients with any CTV MISS, 80.3% (98) had 10% or more of CTV Boost outside the treatment volume. Regarding CTV MISS, there were no statistically significant differences between the groups with 1 clip versus 2 or more clips, nor between patients with or without reconstructive surgery. In average, the CTV Boost was 87% smaller than the CTV Quadrant. The whole quadrant irradiation would lead to unnecessary irradiation of 26% of normal breast tissue.

Conclusion: Surgical bed clipping is up most important in the definition of the boost volume irradiation to ensure precision minimizing geographical miss and optimizing surrounding normal tissue sparing.

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Introduction

Breast cancer is the most frequent malignancy in women, disregarding non-melanoma skin cancer, corresponding to about 25% of newly diagnosed cancer cases annually worldwide [1].

The impact of breast conserving surgery in early breast cancer started to be studied in the 70's. Since then, the oncological safety of the association of breast conserving surgery followed by whole breast irradiation has been proved, with similar results in terms of overall survival compared to radical mastectomy. This approach became a consensus during the 90's in the medical community [2]. At that time, several studies evaluated the radiation dose enhancement (boost) in the tumor bed, since most relapses occurred in that area. Romestaing et al. randomized 1024 patients, with early breast cancer (less than 3 cm) who had undergone breast conserving surgery and whole breast irradiation (50 Gy), to receive 10 Gy electron boost dose in tumor bed versus observation. After 5 years, less local recurrences were observed among patients in the boost group (4.5% versus 3.6%; $p = 0.044$) [3].

Similarly, the EORTC group confirmed the local control benefit. They randomized 5318 patients in two groups after whole breast irradiation: additional 16 Gy boost dose versus observation [4]. After 10 years of follow-up, the boost group presented lower local recurrence when compared to the observation arm (6.2% versus 10.2%; $p < 0.0001$). In a subgroup analysis, local control was higher in patients with 40 years or less [5].

In general, the boost volume delineation is based on pre-surgical (clinical examination, mammography, ultrasonography and magnetic resonance) and post-surgical (seroma/hematoma palpation, scars, surgical clips and tumor bed changes in images) information. The most common challenge is surgical bed definition especially in patients underwent to oncoplastic surgery.

Landis et al. showed that in situations where the surgical bed definition was not clear, there was agreement in only 57% of the planning target volume (PTV) boost volumes delineated by different physicians, regarding the same planning tomography (CT) [6]. Other authors showed the importance of the surgical clips in the boost volume delineation [7,8], improvement of tumor bed coverage and reduction of normal tissue irradiation [9,10].

However, the surgical bed clipping in breast conserving surgery is not a worldwide systematic practice, leading to a major difficulty in the definition of the boost volume. In practice, when the surgical bed is not marked, to compensate for uncertainties, the boost dose is given to the whole quadrant (tumor pre-surgical clinical location) [8].

In the last years, after a continuous and persistent discussion about the importance of marking the tumor bed with the breast and plastic surgeons at our hospital, patients submitted to conservative surgery due to breast cancer have their surgical bed marked with clips. This strategy raised a few questions regarding the period where clips were not routinely used for this purpose and that may reflect a situation, still present nowadays in many departments, where no markers are placed: are we missing the boost target? If so, how much? Is irradiation of the whole quadrant adequate when surgical clips are absent? How much normal tissue are we unnecessary irradiating? Breast reconstruction can impact in the surgical bed coverage? Thus, the purpose of this study was to try to answer these questions.

Materials and methods

This was a retrospective study of all patients with breast cancer treated between 2015 and 2016 at our institution, who underwent breast conserving surgery with clipping of the tumor bed. Radiation therapy simulation CT images of each patient were reviewed and the boost volumes were contoured by two radiation oncologists (TF

and KL). Five clinical target volumes (CTV) were defined, using two contouring softwares available in our institution (*Eclipse™ Treatment Planning System – Varian Medical Systems and Monaco® Treatment Planning System – Elekta Medical Systems*).

- 1) **CTV breast:** following RTOG consensus [11]:
 - cranial border: clinical reference plus second rib insertion
 - caudal: clinical reference plus loss of CT apparent breast
 - lateral: clinical reference plus mid axillary line typically
 - medial: sternal-rib junction
- 2) **CTV quadrant:** defined by clinical tumor location (physical exam/palpation, mammography/ultrasonography image data). The nipple was used as a central reference point to delineate the quadrants, as seen in Fig. 1. In the absence of the nipple, the central reference point was the intersection of the craniocaudal and transversal diameters in the center of CTV Breast. Each radius was divided in two equal segments by a perpendicular line, so each quadrant was divided in four numbered areas. This allowed the definition of CTV Quadrant when the tumor was located at the border of the quadrants (i.e.: junction of upper quadrants represented in Fig. 1 by numbers 2, 3, 6 and 7).
- 3) **CTV boost:** the clips were contoured and 1 cm (in patients with 2 or more clips) or 2 cm (in patients with only one clip) symmetrical margins were added to define the CTV Boost volume. Seromas, hematomas, or other imaging related alterations were included in the volume.
- 4) **CTV normal tissue (CTV NT):** defined as the result of the subtraction of CTV Boost from CTV Quadrant (CTV Quadrant – CTV Boost). This volume measured the normal tissue that would be unnecessary irradiated, if the whole quadrant was included in the boost volume.
- 5) **CTV MISS:** this volume represented the potential geographical miss of the surgical bed when only the affected quadrant was delineated. It was calculated by the subtraction of the intersection volume between CTV Boost and CTV Quadrant from CTV Boost as described by the formula:

$$\text{CTV MISS} = \text{CTV Boost} - (\text{CTV Boost} \cap \text{CTV quadrant})$$

All contours were cropped from the skin surface, muscles and chest wall.

Examples of contouring CTV Boost and CTV Quadrant are presented in Fig. 2.

To avoid the possible differences in the positioning of the clips in the tumor bed between different surgeons all surgeons followed the same protocol to placement of surgical clips: the clips were allocated into the surgical cavity after tumor resection and were subsequently sutured to the mammary parenchyma to avoid clips migration.

The potential geographical miss according to the number of surgical clips and the performance or not of a reconstruction surgery was evaluated by comparing CTV MISS volumes between patient groups: 1 clip versus 2 or more clips, and with or without oncoplastic surgery. The Mann-Whitney Rank-Test was used to compare the groups volumes and respective means. Statistical analysis was performed with the software SigmaPlot v.11.0® with the significance level set as 5% (p value < 0.05).

Results

In the studied period, 247 patients were selected. The median age was 58 years (range 32–87), 81.0% presented invasive carcinoma (not otherwise specified), 81.8% positive estrogen receptor, 76.1% positive progesterone receptor, 89.9% HER-2 negative, 88.2% Tis, T1 or T2, 92.9% N0-N1. Only 12.1% underwent oncoplastic

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