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## Original Article

## Outcomes in Patients Treated with Post-mastectomy Chest Wall Radiotherapy without the Routine Use of Bolus

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## Abstract

**Aims:** The use of bolus in post-mastectomy radiotherapy (PMRT) varies significantly between institutions. We report on chest wall recurrence and acute toxicity rates for PMRT patients treated with selective use of bolus.

**Materials and methods:** We analysed PMRT patients who received adjuvant chest wall radiotherapy for invasive breast cancer between 2004 and 2009. Patient, tumour and cancer outcomes were collected from a prospective database, with additional radiotherapy and acute toxicity details supplemented retrospectively. Chest wall bolus was reserved for patients considered at high risk of local recurrence.

**Results:** There were 314 patients suitable for analysis: 52 received bolus, 262 did not. The mean age was 53.2 years. The median follow-up was 4.2 years. The most common T stage was T2 (37%), followed by T3/T4 (33%). There were 229 patients (73%) who had N+ disease; 213 (68%) patients had grade 3 cancer. Oestrogen receptor was positive in 176 (56%) cases, progesterone receptor was positive in 134 (43%) and HER2 receptor was positive in 24 (8%). Lymphovascular space invasion was present in 146 patients (46%), dermal invasion in 30 patients (10%) and positive margin in 14 patients (4%). The 4 year chest wall recurrence rate was 14% (95% confidence interval 5.4–26.8%) in the bolus group and only 3.5% (95% confidence interval 1.6–6.4%) in the non-bolus group. On univariate analysis, use of bolus was associated with a significant difference in chest wall recurrence (hazard ratio 3.09; 1.15–8.33;  $P = 0.025$ ). However, when taking into account margin status, this significance was lost (hazard ratio = 2.45; 95% confidence interval 0.80–7.50,  $P = 0.12$ ). There was a higher rate of acute grade 2 skin toxicity in patients receiving bolus compared with those without, 40% versus 21% ( $P = 0.01$ ).

**Conclusions:** The selective use of bolus resulted in a small risk of chest wall recurrence rates for low-risk patients. This suggests that the routine use of bolus in PMRT patients may be unnecessary.

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**Key words:** Bolus; breast cancer; outcomes; post-mastectomy radiotherapy; radiotherapy

## Introduction

In the setting of locally advanced breast cancer, post-mastectomy radiotherapy (PMRT) has been shown to lead to improved locoregional control as well as overall survival [1–3]. In these randomised trials, the anatomical region with the highest risk of locoregional recurrence (LRR) was the chest wall. Tissue equivalent bolus material is often

placed on the skin surface in the setting of skin-sparing megavoltage radiotherapy. The theoretical rationale behind the use of bolus in PMRT is to increase radiotherapy dose to the skin and dermal lymphatics, thereby reducing the risk of chest wall recurrences (CWR). However, bolus can lead to an increase in acute and late skin toxicities [4], and in some cases, significant moist desquamation, resulting in the early cessation of treatment and potentially inferior local control [5,6].

The routine use of bolus during PMRT remains a controversial issue, with limited clinical data to guide its optimal use. It is uncertain whether bolus is routinely required in all PMRT patients, or only those with a higher risk of CWR [7,8]. Patterns of practice, including routine

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use of bolus, thickness and frequency of application, vary significantly between institutions. This heterogeneity is highlighted in a survey carried out by Vu *et al.* [9], which showed a wide variation in practice with significant regional differences. Guidelines regarding the routine use of bolus reflect this uncertainty. The American Society of Clinical Oncology guidelines state ‘whether it is necessary to apply the bolus every day, less frequently, or at all is uncertain’ [10]. The American College of Radiology guidelines also acknowledge the uncertain need but recommend routine use with techniques using beam energies 6 MV or higher [11]. A recent American Society for Radiation Oncology survey again highlighted the variation in practice, with over half of radiation oncologists indicating they routinely use bolus, even in the post-reconstruction setting [12].

These uncertainties prompted us to question whether the routine use of bolus in PMRT was required. Our primary aim was to: report the chest wall recurrence rates (CWRR) and survival in PMRT patients treated at an institution that used bolus for patients felt to be at high risk of CWR, based on clinical and pathological features, and compare the outcomes between the patients who were treated with and without bolus. Our secondary aim was to report the acute toxicity rates in these two groups.

## Materials and Methods

### Database Collection

After institutional research ethics board approval was obtained, the records of patients who had treatment with mastectomy and adjuvant chest wall radiotherapy  $\pm$  nodal irradiation for invasive breast cancer between 2004 and 2009 at the Princess Margaret Cancer Centre were retrieved. From an established prospective database, patient demographics, tumour and treatment characteristics, and outcomes data were collected. Specific radiotherapy technical details and radiation-associated acute toxicity details were supplemented retrospectively using the radiotherapy electronic medical record.

Patients were typically staged with bilateral mammogram and ultrasound, computed tomography scan of chest abdomen and pelvis, and a bone scan. Patients were excluded if they were treated with radiotherapy following CWR/LRR or with a diagnosis of bilateral breast cancer. Palliative patients were also excluded.

### Indications for Post-mastectomy Radiotherapy

Our treatment policy during this period specified PMRT for patients with either stage pT3/pT4 or pN2/pN3. Patients with clinical T3/T4 disease  $\pm$  biopsy-proven nodal disease before neoadjuvant chemotherapy were also treated with PMRT. In patients with N1 disease or high-risk pT2N0 disease, radiotherapy was discussed with the patient, with the final decision resting on a number of patient, tumour and treatment characteristics.

### Treatment Technique

Patients were treated with a planned dose of 50 Gy in 25 fractions daily to the chest wall  $\pm$  supraclavicular fossa and/or axilla and/or internal mammary chain. All patients were planned with computed tomography simulation. Patients were treated with a two-field tangential technique if only the chest wall was treated. This was either using a three-dimensional conformal technique (3D CRT) or an automated inverse-planned intensity-modulated radiotherapy (IMRT) technique to improve dose homogeneity, as previously described [13]. For patients who were having chest wall and regional nodes treated, the technique was using a three-field or four-field half-beam blocked technique with tangents for the chest wall and an anterior or anterior–posterior pair for the regional nodes. IMRT was not used for regional nodal radiotherapy; apart from the automated technique for the tangents as described above.

Additional chest wall boost was delivered to patients deemed by their treating radiation oncologist to be at significantly higher risk of local recurrence, e.g. positive margin. The technique used electrons, or photons if the high-risk clinical target volume was deeper than could be adequately covered.

The departmental protocol did not entail the routine use of chest wall bolus. Instead, the use of bolus was reserved for patients who were considered at high risk of local recurrence, including those with dermal lymphatic invasion and margin positivity. The bolus technique used was either daily or alternate daily to the whole chest wall via a 0.5 cm tissue-equivalent material, such as Superflab (frequency at the discretion of the treating radiation oncologist). Patients were reviewed weekly during treatment to assess toxicity.

### Statistical Analysis

The primary outcome was the CWRR. In the presence of competing risks, the cumulative incidence curve was used to estimate the probability of failure. In the absence of competing risks (i.e. overall survival), the Kaplan–Meier estimate was used. Secondary outcomes included Radiation Therapy Oncology Group acute radiation common toxicity criteria for skin toxicity, LRR, distant metastatic relapse rate and overall survival. LRR was defined as recurrence in the chest wall and/or locoregional lymph nodes. All time to event measures were taken from the first date of radiotherapy.

Baseline characteristics were analysed using Fisher’s exact test for categorical variables and Student’s *t*-test or the Wilcoxon test, as appropriate, for continuous variables. Groups were compared using Gray’s test [14], whereas cause-specific hazard ratios were calculated using the Fine and Gray competing risk regression model [15].

## Results

### Patient and Tumour Characteristics

There were 334 patients treated with PMRT between 1 January 2004 and 31 December 2009. Twenty patients were

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