Wide-volume Partial Breast Interstitial Brachytherapy Alone after Lumpectomy in Breast-conserving Treatment for Early Breast Cancer

RKY Wong, RKC Ngan, F Tang
Department of Clinical Oncology, Queen Elizabeth Hospital, Hong Kong

ABSTRACT
As most local recurrence after breast-conserving treatment occurs within 2 cm around the lumpectomy cavity, wide-volume partial breast rather than whole breast irradiation has been actively investigated with a view to decreasing radiation toxicities. Replacing external beam radiotherapy by wide-volume interstitial brachytherapy offers the advantages of more accurate treatment volume coverage and a shorter duration of radiation treatment. Incorporating high-dose-rate treatment in brachytherapy has the additional advantage of allowing dosimetric optimisation. This article reports our technique and experience of high-dose-rate wide-volume partial breast brachytherapy, also known as accelerated partial breast irradiation, in breast-conserving treatment.

Key Words: Brachytherapy, Breast neoplasms, Cancer treatment protocols

INTRODUCTION
Breast-conserving treatment (BCT) has evolved in the last two decades to become a well-established treatment approach for early breast cancer. External beam radiotherapy (EBRT) to the whole breast after lumpectomy has been proven an alternative to mastectomy. In the 1990s, it was observed that the majority of local recurrences after BCT, occur within 2 cm around the lumpectomy cavity. This led to a surge of interest in limiting the breast irradiation volume to the high-risk region around the lumpectomy cavity, later called partial breast irradiation.

In delivering partial breast irradiation, both the physical and dosimetric advantages of brachytherapy prompted investigators to use either low-dose-rate or high-dose-rate (HDR) wide-volume partial breast brachytherapy alone to replace EBRT after lumpectomy in selected patients. The additional logistic advantages of shortening the course of radiation treatment from 6 weeks of EBRT to 1 week through brachytherapy and hence avoiding patient inconvenience in daily transport over a protracted period also made brachytherapy more attractive.

Early results of phase II prospective studies utilising wide-volume breast brachytherapy alone in selected patients have shown local relapse rates (3-4% in 4-5 years), complication rates and cosmesis outcome to be similar to that of EBRT. The early results of the Radiation Therapy Oncology Group (RTOG) 9517, reported at the 2004 American Society of Clinical Oncology (ASCO) Annual Meeting, showed only a 3% local recurrence rate after HDR wide-volume partial breast brachytherapy, also known as accelerated partial breast irradiation (APBI), with a median follow-up of 3.7 years. A recent report presented by Vicini et al at the 2006 ASCO Annual Meeting using the MammoSite breast brachytherapy device (Cytys Corporation, Alpharetta, GA, USA) to deliver APBI also showed similar encouraging findings. Procedural feasibility was virtually 100%. Mild acute grade I/II toxicities (erythema, oedema, pain) and late grade I/II toxicities (fibrosis, telangiectasia) were reported to occur in approximately 20%; grade III toxicities (haematoma, abscess, fat necrosis) were reported in only 2-3%. More than 90% of patients scored 'good' to 'excellent' in...
cosmesis outcome. Further, early results of one prospective randomised trial comparing brachytherapy alone to whole breast EBRT demonstrated similar rates of tumour control and radiation side effects at a median follow-up of 30 months.\textsuperscript{16}

This paper reports the use of APBI in BCT for a small group of selected patients at Queen Elizabeth Hospital in Hong Kong.

**PATIENTS AND METHODS**

**Patient Eligibility**

Patients with invasive ductal carcinoma of the breast with a primary tumour size of 3 cm or less, together with all of the following criteria were selected for this treatment approach:

1. negative lumpectomy margins (by National Surgical Adjuvant Breast and Bowel Project definition: $\geq 2$ mm);\textsuperscript{1,3}
2. absence of extensive intraductal carcinoma (extensive intraductal carcinoma by Harvard definition = more than 25% of tumour is ductal carcinoma in situ);\textsuperscript{17}
3. no indication for radiotherapy to the axilla (surgically staged nodal status is mandatory); and
4. absence of distant metastases.

**Pre-implantation Virtual Imaging Simulation**

The patient was positioned on the computed tomography (CT) couch with the same degree of ipsilateral shoulder abduction as to be adopted in the operating theatre. A purpose-made perspex template device (Figure 1a), consisting of two movable templates along a bridge, was placed over the lumpectomy site and taped into position. The holes in the template were arranged in an equilateral triangle at multiple planes with 2 cm separation between holes. Imaging by CT was then performed. The target volume (2 cm around the lumpectomy cavity) was defined after clip identification. Surgical clip placement at the tumour bed cavity during lumpectomy was required. Then, CT guidance was used to adjust the position of the template device, such that the target volume was held well within the two templates of the template device. Reference points on the template device were then marked, and corresponding points tattooed on to the skin.

**Insertion of Brachytherapy Needles and Catheters**

The patient’s position during CT virtual simulation was reproduced under general anaesthesia. The template device was positioned over the lumpectomy site according to the tattooed reference points, and secured by Tagaderm\textsuperscript{TM} (3M Deutschland, Germany). Free-hand insertion of the HDR rigid needles (Figure 1b; Nucletron BV, Veenendaal, Netherlands) into the breast through the template device holes (2 cm hole-to-hole separation) was performed under fluoroscopic guidance. This was followed by loading of the HDR brachytherapy catheters (Figure 1c; Nucletron BV) into the rigid needle tracks. The number of catheters and treatment planes needed were determined at the time of needle insertion, sufficient to cover the breast volume held within the templates of the device. The resulting implanted volume was in multiple planes of catheters, with about 2 cm separation between each catheter. Haemostasis was meticulously checked before anaesthesia reversal. The template device remained on the patient with the catheters during the entire course of radiotherapy. This was necessary for maintenance of catheter parallelism, and to avoid possible pressure necrosis of the skin at the exit points of catheters caused by the stopping buttons.

The patient, with the template device and catheters in situ (Figure 2), was positioned on the CT couch for CT imaging. Orthogonal X-ray simulation films were also taken for dosimetry. HDR fractionated treatment was used rather than low-dose-rate for the benefits of dosimetric optimisation, radiation protection and cost-effectiveness. The Paris system of dosimetry\textsuperscript{18} was followed, with dose optimisation to compensate for the occasional unsatisfactory catheter geometry. The Nucletron HDR-PLATO brachytherapy planning system (Nucletron BV), was used to optimise the dwell positions and the dwell time of the radioactive source.
radioactive source position was kept at a distance of at least 10 mm under the skin surface, to avoid radiation-induced skin necrosis. The calculated dosimetry was then finally superimposed on the CT images for dosimetric adjustment (Figure 3). A lumpectomy scar bolus was not routinely used.

**Brachytherapy Treatment**

The dose fractionation followed the RTOG 9517 protocol, delivering 34 Gy in 10 fractions over 5 days (2 fractions a day, at least 6 hours apart) at the isodose line, covering the target volume of 2 cm around the lumpectomy cavity. Radiation was delivered by connecting the HDR catheters to the MicroSelectron HDR machine (Figure 4; Nucletron BV). The biological equivalent dose of Gy-10 was 45.46 Gy, and of Gy-3 was 72.5 Gy, assuming the repair of normal tissue was completed within the 6-hour interval.

**RESULTS**

This technique was first introduced in our department in November 2002. Given the stringent patient selection criteria, patient concerns about surgery and general anaesthesia, together with the outbreak of sudden acute respiratory syndrome in 2003, only three patients (Table 1) were treated by this technique during the period of interest.

All three patients were admitted to hospital for the course of treatment, during which meticulous wound care was provided after the implantation procedure. The radiation treatment started on a Monday and was completed by Friday. Catheter positions were checked before every radiation treatment. The entire treatment course was well tolerated by all three patients, with only mild oral analgesics needed. All catheters were removed at the bedside after the last radiation fraction. The patients were discharged home after overnight wound observation.

There were no procedural difficulties. After brachytherapy, patients were seen in an outpatient clinic every 6 to 8 weeks. All three patients reported immediate pain and breast distension discomfort requiring mild analgesics in the first 4 weeks after treatment. At the first follow-up assessment, the majority of puncture wounds had already healed. The local protocol of baseline mammography at 6 months after brachytherapy and then annually was followed. The follow-up period for the three patients was 42 months, 42 months and 26 months. All were free from clinical and mammographic tumour-relapse at last follow-up. Cosmesis was scored excellent at 10 months after treatment, at which time the puncture sites were almost invisible (Figure 5). Breast firmness, though mildly increased, was considered acceptable.

**DISCUSSION**

The use of partial breast irradiation in BCT in selected patients with early breast cancer aims at reducing radiation toxicities and achieving good cosmesis, without jeopardising tumour control. The partial breast target volume for irradiation can be treated by interstitial
brachytherapy, the MammoSite brachytherapy device, three-dimensional conformal EBRT or external beam intensity-modulated radiation therapy. Brachytherapy offers the advantage of a shorter duration of treatment compared with EBRT. Results of phase II studies of partial breast irradiation by brachytherapy alone have showed promising outcomes with good local tumour control and excellent cosmesis.6-13 Our early experience with three selected patients echoes these promising treatment outcomes.

There were no procedural difficulties in applying this new technique to patients in our locality. However, meticulous multidisciplinary collaboration between clinical oncologist, anaesthetist, nurse, physicist and radiographer is essential to make this procedure a success. In our department, breast brachytherapy alone after lumpectomy was noted to have the additional advantages of sparing busy linear accelerator machine time and allowing early commencement of radiation treatment.

CONCLUSION
Results of phase II trials suggested that sole tumour bed irradiation might be an appropriate therapeutic alternative for selected breast cancer patients. This approach, using APBI, has been used successfully in a small number of selected patients at Queen Elizabeth Hospital in Hong Kong. More experience and data from phase III trials are necessary to define the ultimate role of brachytherapy in partial breast irradiation. At this time, total breast irradiation after lumpectomy remains the standard irradiation modality in the treatment of early stage breast cancer.

REFERENCES
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