Original paper

Comparing a volume based template approach and ultrasound guided freehand approach in multicatheter interstitial accelerated partial breast irradiation

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Abstract

Purpose: Currently, there are two described methods of catheter insertion for women undergoing multicatheter interstitial accelerated partial breast irradiation (APBI). These are a volume based template approach (template) and a non-template ultrasound guidance freehand approach (non-template). We aim to compare dosimetric endpoints between the template and non-template approach.

Material and methods: Twenty patients, who received adjuvant multicatheter interstitial APBI between August 2008 to March 2010 formed the study cohort. Dosimetric planning was based on the RTOG 04-13 protocol. For standardization, the planning target volume evaluation (PTV-Eval) and organs at risk were contoured with the assistance of the attending surgeon. Dosimetric endpoints include D_{90} of the PTV-Eval, Dose Homogeneity Index (DHI), V_{200}, maximum skin dose (MSD), and maximum chest wall dose (MCD). A median of 18 catheters was used per patient. The dose prescribed was 34 Gy in 10 fractions BID over 5 days.

Results: The average breast volume was 846 cm^3 (526-1384) for the entire cohort and there was no difference between the two groups ($p = 0.6$). Insertion time was significantly longer for the non-template approach (mean 150 minutes) compared to the template approach (mean: 90 minutes) ($p = 0.02$). The planning time was also significantly longer for the non-template approach (mean: 240 minutes) compared to the template approach (mean: 150 minutes) ($p < 0.01$). The template approach yielded a higher D_{90} (mean: 95%) compared to the non-template approach (mean: 92%) ($p < 0.01$). There were no differences in DHI ($p = 0.14$), V_{200} ($p = 0.21$), MSD ($p = 0.7$), and MCD ($p = 0.8$).

Conclusions: Compared to the non-template approach, the template approach offered significant shorter insertion and planning times with significantly improved dosimetric PTV-Eval coverage without significantly compromising organs at risk dosimetrically.

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Key words: APBI, brachytherapy, breast cancer, interstitial, multicatheter.

Purpose

Breast conservation surgery (BCS) followed by whole breast irradiation has become the standard of care for early breast carcinoma [1-4]. However, the duration of treatment remains between 5 to 6 and a half weeks. The need for whole breast irradiation has been questioned and several centres have evaluated the feasibility and efficacy of accelerated partial-breast irradiation (APBI) [5-7]. Accelerated partial-breast irradiation represents a technique that allows for the delivery of adjuvant therapy after BCS in 1 week or less with multiple techniques being available at this time. To date, at least seven phase III trials comparing different techniques of APBI to conventional WBI have been initiated [8-12]. Polgár *et al*. [13] demonstrated excellent long-term local tumour control, survival, and cosmetic results with a low-rate of long-term toxicity in a 12 year prospective study using multicatheter interstitial brachytherapy. Currently, the American Brachytherapy Society recommends proper patient selection for APBI and the current guidelines are for APBI in age (> 50 years old), tumor size (< 3 cm), histology (all invasive subtypes and ductal carcinoma *in situ*), surgical margins (negative), lymphovascular space invasion not present, and negative nodal status [14].

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Controlling local disease using radiation therapy relies on adequate target volume coverage. Retrospective studies show a strong positive correlation between local recurrence and inadequate coverage [15]. The ability to consistently and reproducibly localize and fully irradiate the tumor site is very important in radiation therapy. Brachytherapy relies on accurate catheter insertion, where immobilization and guidance are key factors [16]. Patient immobilization has many aspects, ranging from limiting movement of the patient's body to specific tissue immobilization devices. The Kuske breast applicator (Nucletron, an Elekta company, Elekta AB, Stockholm, Sweden) is currently widely used in multicatheter interstitial brachytherapy as an immobilization device. It is an adjustable template with integrated guiding plates that are used to compress the breast and guide placement of brachytherapy needles. Another technique that has been used in multicatheter interstitial brachytherapy is the ultrasound guided free hand method, in which ultrasound guided visualisation of the cavity is used to guide catheter insertion into the cavity with needle placement being marked on the skin prior to the insertion. While both techniques have their advantages and remain popular at different centres, there is no published data that compares the two techniques. In this study, we look at both techniques comparing the insertion time, planning time, and the dosimetric outcomes.

Material and methods

Between August 2008 and March 2010, 20 consecutive patients treated with APBI with multicatheter HDR interstitial brachytherapy were included in the study. All patients underwent lumpectomy and axillary nodal evaluation either by sentinel node biopsy or axillary clearance. Patients were selected as per the criteria of European Society of Radiotherapy and Oncology (ESTRO) APBI consensus guidelines [17], which included: 1) tumours of less than 3 cm in size; 2) no lymph node involvement; 3) negative surgical margins; 4) no multicentric disease or extensive intraductal component; 5) patients > 40 years of age with no prior history of cancer. Institutional ethics approval was obtained and informed consent was attained from each patient.

Implant technique

Within 8 weeks of lumpectomy and axillary nodal evaluation, patients underwent an interstitial implant using either an ultrasound guided free hand method (non-template) or a template method [18]. Both methods were performed in the supine position. In the non-template method, the target volume was first mapped out on the skin surface with ultrasound visualisation of the lumpectomy cavity (Fig. 1). Needle placement was marked on the skin with a 1.5 cm interval. Needles were placed using the Paris system parallel to each other, ensuring adequate coverage of the cavity with generous use of a local anaesthetic mixture. Initially, a deep plane of needles was placed on the pectoralis major fascia with real-time ultrasound guidance. This was followed by at least one superficial plane resulting in a multiplane implant for adequate geometric coverage of the target volume.

In the template method, once the cavity was localized, the ipsilateral breast area was surgically prepared under sterile conditions. To avoid injury to the underlying chest wall structures or causing a pneumothorax, the overlying breast was pinched and gently lifted off the chest wall before applying the template and securing it. 3-5 anchoring needles were then placed in an asymmetric pattern usually involving C-12. C-12 was the grid coordinates of the template that corresponded to the center of the template. The purpose of the asymmetric pattern is to aid easy orientation of the template in reference to the patient's anatomy, as well as to secure and prevent slipping of the template from the breast (Fig. 2). A CT scan was then obtained with the anchoring catheters in-situ. These images were then reconstructed on the Oncentra planning system (Nucletron, an Elekta company, Elekta AB, Stockholm, Sweden).

Planning technique

The planning target volume (PTV) was formed by expanding 20 mm from the clinical target volume (CTV), which was determined from the contrast enhanced tumor

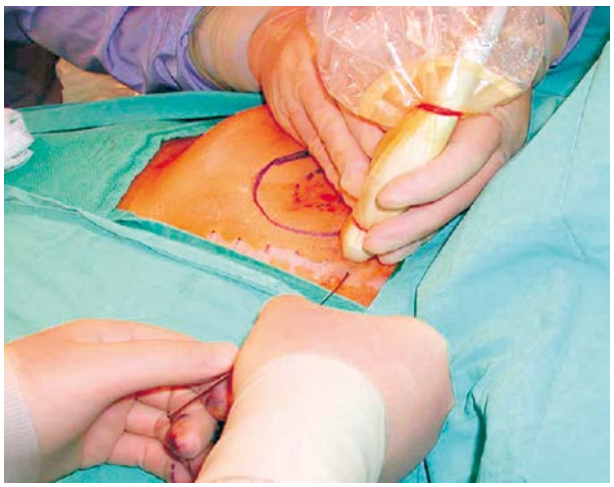

Fig. 1. Ultrasound localization of the target volume in the free hand technique

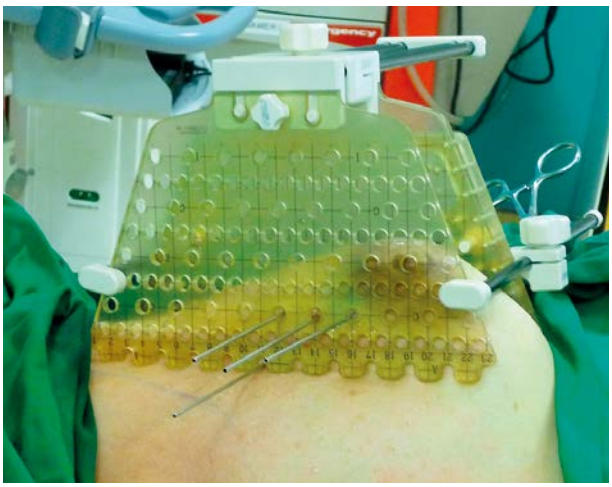

Fig. 2. Insertion of catheters with the use of a template

cavity and any surrounding surgical clips. The PTV-Eval was formed by excluding the 5 mm skin rind, as well as the underlying chest wall muscle layer. The skin was also contoured on the sagittal slice depicting the largest breast contour (usually the slice showing the nipple), and the most anterior chest wall surface was also contoured. The images were then reoriented in Oncentra to depict the "template view" to determine the location of the remaining catheters. Next, an overlying photocopy of the template on a transparency was placed on top of the screen and the "template view" template magnification was matched 1 : 1 to the overlaid template transparency (Fig. 3). The corresponding anchoring needle positions were then marked on the overlaid transparency and the chest wall, and PTV-Eval contour were outlined onto the transparency. Once done, the catheter placement for the remaining catheters was easily determined.

In both procedures, the final step required replacing the needles with polyethylene tubing with a hemispheric button at each end. Extra attention was given to make sure that the button on the connector side of the remote afterloader was flush to the skin. After each catheter was trimmed and numbered, an *en face* picture of the implant showing the catheter numbers with respect to the breast anatomy was obtained to aid in the reconstruction of the catheters. CT-based simulation of the patient was performed with the patient in supine position and the images were then transferred to the Oncentra (Nucletron, an Elekta company, Elekta AB, Stockholm, Sweden) treatment planning system.

Dosimetry

A total of 34 Gy in 10 fractions, two fractions per day, 3.4 Gy per fraction, separated by at least 6 hours, given on 5 treatment days was delivered via a ^{192}Ir remote afterloader in supine position. Target coverage was ≥ 90% of the prescribed dose covering ≥ 90% of the PTV-Eval (D_{90} ≥ 90%). Care was taken to ensure that the skin dose did not exceed the prescription dose [19]. In our study, the dose constraint for the skin was set as less than 100% of the prescribed dose. To assure appropriate dose homogeneity throughout the implant, two parameters were used: the volume of tissue receiving higher doses and a Dose Homogeneity Index (DHI). The actual volume of tissue receiving 150% (V_{150}) and 200% (V_{200}) of the prescribed dose was limited to ≤ 70 cc and ≤ 20 cc, respectively. The DHI, as represented by the volume ratio ($1 - V_{150}/V_{100}$), will be ≥ 0.75 (V_{150} represented the volume of tissue receiving 150% of the prescribed dose, and V_{100} represented the volume of tissue receiving the prescribed dose). The maximum skin dose (MSD) and maximum chest wall dose (MCD) were also recorded for each patient.

In addition, < 60% of the ipsilateral whole breast reference volume received ≥ 50% of the prescribed dose. The online Breast Atlas from the RTOG website was used to target the whole breast reference volume [20].

Insertion and planning time

Insertion time was defined as the time taken from start of patient's clean and drape sterile prep to the time when the CT simulation images were acquired. Planning time was defined from the start of contour voluming to the time of plan approval.

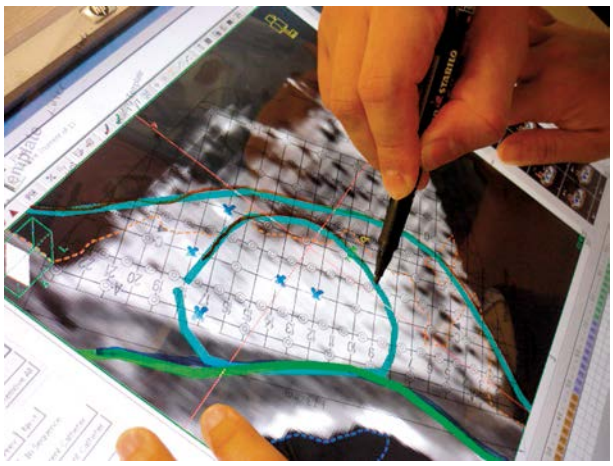

Fig. 3. Use of an overlaid transparency to mark the chest wall contour and the cavity

Statistical analysis

The results were analysed statistically using the Stata v11.0 (Statacorp USA). The two-sample Wilcoxon rank sum (Mann Whitney *U* test) was used in the analysis given the small sample size.

Results

Of the 20 patients in the study, 12 underwent the non-template method and 8 underwent insertion using the template method. A median of 18 catheters was used per patient (range 16-24) and median time to insertion was 2 weeks post surgery. Average breast volume was 846 cm^3 (range 526-1384) and the average PTV-Eval volume was 256 cm^3 (range 182-416).

Patient characteristics

There were 16 patients with T1-2 breast tumours and 4 patients with DCIS treated in our study group. The average age of the patients was 56. The average breast size of our patients was 816.5 cc (range 526.4-1384.7). The average number of catheters used was 17.2 (range 14-18).

Comparison between both techniques

We found that insertion time and planning time was significantly longer for the non-template method compared with the template method. The difference was 60 minutes longer on average for insertion and 90 minutes longer for planning.

When we compared dosimetry from the plans, we found that the D_{95} was 3.13 Gy (92% of the prescribed dose) on average with the non-template method, which was significantly lower compared to 3.3 Gy (97% of the prescribed dose on average) with the template method (p value < 0.01). Other dosimetric parameters such as the V_{200}, MSD and DHI were not significantly different between the two techniques. See Table 1.

Table 1. Comparison between the ultrasound guided freehand and template techniques

Factor	Freehand (non-template)		Template		
	Mean	Range	Mean	Range	
D_{90}	3.13 Gy (92%)	3.06-3.13	3.30 Gy (97%)	3.26-3.33	$p < 0.01$
DHI	74%	72-76	76%	75-77	$p = 0.14$
V_{200}	9.6 cm^3	6.9-12.1	8.0 cm^3	7.0-9.4	$p = 0.21$
MSD	100%	90-110	90%	80-100%	$p = 0.7$
MCD	80%	50-100	60%	40-80	$p = 0.8$
Insertion time	150 minutes	130-180	90 minutes	60-120	$p = 0.02$
Planning time	240 minutes	200-260	150 minutes	120-180	$p < 0.01$

Table 2. Comparison of our results with other institutions

Factor	Freehand (non-template)	University of Wisconsin (n = 50)	Template	Tufts University (n = 75)
D_{90}	3.13 Gy (92%)	96%	3.30 Gy (97%)	95%
DHI	74%	70%	76%	80% (mean excision volume for Tufts was 92 cm^3)
V_{200}	9.6 cm^3	*10 ccm^3	8.0 cm^3	12 cm^3
MSD	100%	100%	90%	100%
MCD	80%	80%	60%	80%

**Personal communication with Dr Patel*

Discussion

Our study shows that using the template had the advantages of saving both planning and insertion time, as well as a dosimetric benefit of superior dose coverage. Individually, our results compared well with centres that specialized in either technique. For departments wishing to start multicatheter interstitial breast brachytherapy, we believe that the template approach offers superior dosimetric outcomes and shorter treatment procedure times compared to the non-template approach even in novice hands.

Multicatheter interstitial brachytherapy has been gaining popularity as an adjuvant treatment in early breast cancer due to its short time of delivery, good outcomes, and excellent cosmesis [21,22]. There are many techniques currently in use at different centres. Despite this, there are no studies that compare the different techniques and look at the advantages of one technique over another. This study is the first to compare two popular methods of multicatheter interstitial brachytherapy. While preference of technique is dependent on a large number of factors including staff training, tumour location, and patient breast size, our comparison shows significant gains of the template method in saving time and improving dosimetry. In our centre, our radiation oncologists were trained in both techniques giving flexibility in technique selection for each patient. The current Radiation Therapy Oncology Group trial RTOG 04-13 technical guidelines for interstitial brachytherapy are a target coverage of (≥ 90% dose received by ≥ 90% target volume, $V_{150} < 70\ cm^3$, $V_{200} < 20\ cm^3$ and dose homogeneity index ≥ 0.75) and skin dose volume histogram parameters (maximum 100% of prescribed dose). Our results using both techniques compare favourably with these guidelines.

We compared the results of our non-template technique and our template technique with the results from the University of Wisconsin [18] and Tufts University [23], respectively. These two institutions are centres for APBI training in these techniques. Our results were comparable to these institutions (Table 2).

Limitations

As technique selection was not randomised in this study, there were some patients in whom the non-template technique was used because of small breast size or because the tumour cavity was located very medially or laterally. This could have been a source of bias in technique selection. APBI in these patients could be technically difficult reflecting the longer insertion time. APBI in the technically difficult patient is a field of further study and development that we are researching.

In this study, only 16 patients were recruited as this is a pilot study comparing two different techniques. Subsequent studies into APBI should compare various techniques of catheter insertion and dose delivery, as well as planning techniques to decrease planning and insertion time.

Current developments in other breast brachytherapy techniques include multilumen balloon catheters (Con-

tura, SenorX Corp, USA), which do not require a template and may be suitable in certain patients. The APBI program in our centre was introduced 5 years ago and since then we have treated over one hundred patients in the program using either technique, but predominately favouring the template approach. This has allowed us to build up adequate experience in both techniques. We have no local recurrences or Grade 3 toxicity in our patients and the cosmesis of this procedure at our centre remains excellent. Our experience shows that adequate training of staff, exposure, and use of various techniques in brachytherapy can allow diversity in a centre and allow comparisons between techniques.

Conclusions

Compared to the non-template approach, the template approach offered significantly shorter insertion and planning times with improved dosimetric PTVeval coverage without significantly compromising organs at risk. This template approach should form the starting point for any department wishing to commence multicatheter interstitial breast brachytherapy.

Disclosure

Authors report no conflict of interest.

References

1. Bartelink H, Horiot JC, Poortmans H et al. Impact of a higher radiation dose on local control and survival in breast-conserving therapy of early breast cancer: 10-year results of the randomized boost versus no boost EORTC 22881-10882 trial. *J Clin Oncol* 2007; 25: 3259-3265.
2. Fisher B, Anderson S, Bryant J et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med* 2002; 347: 1233-1241.
3. Veronesi U, Cascinelli N, Mariani L et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *N Engl J Med* 2002; 347: 1227-1232.
4. Morrow M. Rational local therapy for breast cancer. *N Engl J Med* 2002; 347: 1270-1271.
5. Antonucci JV, Wallace M, Goldstein NS et al. Differences in patterns of failure in patients treated with accelerated partial breast irradiation versus wholebreast irradiation: a matched-pair analysis with 10-year follow-up. *Int J Radiat Oncol Biol Phys* 2009; 74: 447-452.
6. Arthur DW, Winter K, Kuske RR et al. A phase II trial of brachytherapy alone after lumpectomy for select breast cancer: tumor control and survival outcomes of RTOG 95-17. *Int J Radiat Oncol Biol Phys* 2008; 72: 467-473.
7. Benitez PR, Keisch ME, Vicini F et al. Five-year results: the initial clinical trial of Mammosite balloon brachytherapy for partial breast irradiation in early stage breast cancer. *Am J Surg* 2007; 194: 456-462.
8. Polgár C, Strnad V, Major T. Brachytherapy for partial breast irradiation: the European experience. *Semin Radiat Oncol* 2005; 15: 116-122.
9. Vicini FA, Arthur DW. Breast brachytherapy: North American experience. *Semin Radiat Oncol* 2005; 15: 108-115.
10. Polgár C, Major T. Current status and perspectives of brachytherapy for breast cancer. *Int J Clin Oncol* 2009; 14: 7-24.
11. Gifford KA, Nelson CL, Kirsner SM et al. On the feasibility of treating to a 1.5 cm PTV with a commercial single-entry hybrid applicator in APBI breast brachytherapy. *J Contemp Brachytherapy* 2012; 4: 29-33.
12. Skowronek J, Wawrzyniak-Hojczyk M, Ambrochowicz K. Brachytherapy in accelerated partial breast irradiation (APBI) – review of treatment methods. *J Contemp Brachytherapy* 2012; 4: 152-164.
13. Polgár C, Major T, Fodor J et al. Accelerated partial-breast irradiation using high-dose-rate interstitial brachytherapy: 12-year update of a prospective clinical study. *Radiother Oncol* 2010; 94: 274-279.
14. Shah C, Vicini F, Wazer D et al. The American Brachytherapy Society consensus statement for accelerated partial breast irradiation. *Brachytherapy* 2013; 12: 267-277.
15. Verhey LJ. Immobilizing and positioning patients for radiotherapy. *Semin Radiat Oncol* 1995; 5: 100–114.
16. Wazer D, Arthur D, Vicini F. Accelerated Partial Breast Irradiation: Techniques and Clinical Implementation. 2nd ed. Springer-Verlag 2010.
17. Polgár C, Limbergen E, Pötter R et al. Patient selection for accelerated partial-breast irradiation (APBI) after breast-conserving surgery: Recommendations of the Groupe Européen de Curiethérapie-European Society for Therapeutic Radiology and Oncology (GEC-ESTRO) breast cancer working group based on clinical evidence (2009). *Radiother Oncol* 2010; 94: 264-273.
18. Das R, Patel R, Shah H et al. 3D CT-based high dose rate breast brachytherapy implants: treatment planning and quality assurances. *Int J Radiat Oncol Biol Phys* 2004; 59: 1224-1228.
19. NSABP B-39: A Randomized Phase III Study of Conventional Whole Breast Irradiation (WBI) versus Partial Breast Irradiation (PBI) for Women with Stage 0, I, or II Breast Cancer. http://www.rtog.org/ClinicalTrials/ProtocolTable/StudyDetails.aspx?study=0413. Last accessed on 10th Nov 2013.
20. http://www.rtog.org/CoreLab/ContouringAtlases/BreastCancerAtlas.aspx. Last accessed on 10th Nov 2013.
21. Tanaka E, Yamazaki H, Yoshida K et al. Objective and longitudinal assessment of dermatitis after postoperative accelerated partial breast irradiation using high-dose-rate interstitial brachytherapy in patients with breast cancer treated with breast conserving therapy: reduction of moisture deterioration by APBI. *Int J Radiat Oncol Biol Phys* 2011; 81: 1098-1104.
22. Garsa AA, Ferraro DJ, Dewees TA et al. A prospective longitudinal clinical trial evaluating quality of life after breast-conserving surgery and high-dose rate interstitial brachytherapy for early- stage breast cancer. *Int J Radiat Oncol Biol Phys* 2013; 87: 1043-1050.
23. Wazer D, Kaufman S, Cuttino L et al. Accelerated partial breast irradiation: an analysis of variables associated with late toxicity and long-term cosmetic outcome after high-dose-rate interstitial brachytherapy. *Int J Radiat Oncol Biol Phys* 2006; 64: 489-495.