advances
in radiation oncology

Scientific Article

Magnetic Resonance Imaging for Breast Tumor Bed Delineation: Computed Tomography Comparison and Sequence Variation

Nicola Lowrey, MBBS,[a] Christine A. Koch, MD, PhD,[a,b] Thomas Purdie, PhD,[a,b] Anna Simeonov, MRT,[a] Leigh Conroy, PhD,[a,b] and Kathy Han, MD, MSc[a,b,]*

[a]Radiation Medicine Program, Princess Margaret Cancer Centre, University Health Network, Toronto, Ontario, Canada; [b]Department of Radiation Oncology, University of Toronto, Toronto, Canada

Abstract

Purpose: Our purpose was to investigate the interobserver variability in breast tumor bed delineation using magnetic resonance (MR) compared with computed tomography (CT) at baseline and to quantify the change in tumor bed volume between pretreatment and end-of-treatment MR for patients undergoing whole breast radiation therapy.

Methods and Materials: Forty-eight patients with breast cancer planned for whole breast radiation therapy underwent CT and MR (T1, T1 fat-suppression [T1fs], and T2) simulation in the supine treatment position before radiation therapy and MR (T1, T1fs, and T2) at the end of treatment in the same position. Two observers delineated 50 tumor beds on the CT and all MR sequences and assigned cavity visualization scores to the images. The primary endpoint was interobserver variability, measured using the conformity index (CI).

Results: The mean cavity visualization scores at baseline were 3.14 (CT), 3.26 (T1), 3.41 (T1fs), and 3.58 (T2). The mean CIs were 0.65, 0.65, 0.72, and 0.68, respectively. T1fs significantly improved interobserver variability compared with CT, T1, or T2 ($P < .001$, $P < .001$, and $P = .011$, respectively). The CI for T1fs was significantly higher than T1 and T2 at the end of treatment (mean 0.72, 0.64, and 0.66, respectively; $P < .001$). The mean tumor bed volume on the T1fs sequence decreased from 18 cm^3 at baseline to 13 cm^3 at the end of treatment ($P < .01$).

Conclusions: T1fs reduced interobserver variability on both pre- and end-of-treatment scans and measured a reduction in tumor bed volume during whole breast radiation therapy. This rapid sequence could be easily used for adaptive boost or partial breast irradiation, especially on MR linear accelerators.

Introduction

Multiple randomized controlled trials have established adjuvant radiation therapy after breast-conserving surgery as standard of care in the management of early-stage breast cancer to reduce the risk of local recurrence (LR).[1-3] An updated meta-analysis of randomized trials also reported a significant reduction in the risk of breast cancer death at 15 years.[4] LR risk is greatest within the region of the tumor bed.[5] Accurate delineation of the

lumpectomy tumor bed is therefore fundamental to the success of both breast boost and partial breast irradiation (PBI) in preventing LR.[6-8]

Although computed tomography (CT) is superior to clinical-based planning in defining the tumor bed volume,[9-11] studies have shown variable results in tumor bed delineation between observers, with conformity indices (CIs) between 0.31 and 0.76.[12-16] Features of the lumpectomy tumor bed on CT associated with lower interobserver agreement include small volume, low cavity visualization score (CVS), retroareolar location, dense breast parenchyma, and close proximity to the pectoralis muscle.[12-15,17,18] Surgical clips to delineate the tumor bed have been recommended,[19,20] but this has not been uniformly adopted in North America, including at our center.

To further improve tumor bed visualization and interobserver variability in tumor bed delineation, magnetic resonance imaging (MRI) has been compared with CT. Previous investigations comparing the 2 modalities have yielded wide ranging results, however, with some finding no benefit of MRI over CT[21-24] and others finding significant improvements in tumor bed visualization and CIs with the use of MRI.[25-27] Past investigations have used a variety of MRI sequences, but conclusions on the ideal sequence are inconsistent and uncertainty still exists.[28,29]

Several studies using serial CT scans have also found that the lumpectomy surgical bed significantly decreases in volume with time from surgery, which can lead to larger volumes of normal breast tissue being irradiated in boost and partial breast treatments.[30-34] Adaptive planning may be useful for some patients who have significant reductions in the tumor bed volume over time. To our knowledge, only a single study has used MRI to investigate patterns of tumor bed volume change in the setting of PBI.[35]

The aims of this study were to investigate the interobserver variability in tumor bed delineation using 3 MRI sequences compared with CT at baseline and to quantify the change in tumor bed volume between pre- and end-of-treatment MRI for patients undergoing whole breast radiation therapy.

Methods and Materials

Patients

Research ethics board approval and patient consent were obtained for this study. Between August 2013 and October 2014, 48 female patients planned for whole breast radiation therapy after breast-conserving surgery for in situ or early stage invasive breast cancer (Tis, T1-2; N0-1, American Joint Committee on Cancer, 7th edition)[36] were enrolled in the study. Two patients had bilateral breast cancer. Therefore, a total of 50 lumpectomy tumor beds were included for analysis. All patients were prescribed 42.4 Gy/16 fractions to the breast, except for 3

50 Gy/25 fractions. Sequential cavity boost was prescribed to 27 patients for young age (≤50) and/or close margin <2 mm. As per institutional surgical practice, cavities were closed superficially and surgical clips were not routinely placed in the tumor bed, with clips placed in only 5 of the 50 tumor beds.

Imaging

Patients initially underwent planning CT at a median time from surgery of 46 days (range, 14-187) in the supine position on an MT-350 breast board (CIVCO Medical Solutions, Kalona, IA), with the ipsilateral arm raised and abducted. Two-millimeter slices were acquired from midneck to below the diaphragm on a Brilliance wide-bore CT Scanner (Philips Medical Systems, Bothell, WA), with in-plane resolution of 1 mm x 1 mm. The clinically palpable breast tissue and surgical lumpectomy scar were outlined with radio-opaque wires.

All patients underwent 2 sets of MRI in the same treatment position, the first before breast radiation therapy at a median time from planning CT of 1.9 days (range, 0-17), and the second in the final week of radiation therapy at a median time from the first MRI of 35 days (range, 18-67). Imaging was performed on an open bore 3.0-T Verio system (Siemens Medical Systems, Erlangen, Germany) incorporating an 8-channel Spine Matrix coil with an 8-channel torso coil placed on the chest, with a field-of-view of 400 mm, in-plane resolution of 1.3 × 1.3 mm, and slice and gap thicknesses of 3 mm and 0.5 mm. Three-dimensional (3D), noncontrast axial images were acquired on voluntary inhale breath hold and 3 sequences were performed at each timepoint: T1-weighted volumetric interpolated breath hold examination (VIBE), T1 fat-suppression (T1fs) spectrally adiabatic inversion recovery, and T2 half-Fourier acquisition single shot fast spin echo. The T1 and T1fs sequences were each performed in a single breath hold with a scan time of 19 seconds (s) and a spinal coil bandwidth of 490 Hertz per pixel (repetition time = 4.19 ms, echo time = 1.47 ms, flip angle = 9°). The T2 sequences were performed in a total scan time of 1 minute and 21 s (16s per breath hold), with a bandwidth of 781 Hertz per pixel (repetition time = 2000 ms, echo time = 98 ms, flip angle = 150°).

Lumpectomy tumor bed definition and analysis

Each tumor bed was assigned to 1 of 3 locations using CT: within fatty glandular breast tissue, within dense glandular breast tissue, or against the chest wall musculature. With surgical clips absent in 90% of the tumor beds in our study, identification of tumor bed (or "cavity") varied across cases. Two observers (a radiation oncologist [KH] and a clinical fellow [NL]) first assigned individual

CVSs to each image set as per the guidelines of Landis et al,[12] where: CVS-1 = cavity not visualized; CVS-2 = cavity visualized but margins indistinct; CVS-3 = cavity visualized with some distinct margins and heterogeneous appearance on CT; CVS-4 = cavity with mild heterogeneity on CT and majority of margins distinct; and CVS-5 = homogenous appearance of the cavity on CT and all margins clearly seen. Mean CVS ± standard deviation (SD) were calculated for CT and each MRI sequence from the average of the observers' CVS. Each observer then independently contoured the lumpectomy tumor bed on all CT and MRI, blinded to one another's contours. The interobserver variability between each paired observers' contours was assessed by measurement of the CI: the ratio of the common volume to the union volume. CI ranged from 0, in which there was no overlap in volume between the observers' contours, through 1, which indicated complete concordance.

Lumpectomy volumes and statistical analysis

The mean tumor bed volumes ± SD were first calculated for each observer's contours on CT and the pretreatment MRI sequences and compared. Then, relationships between tumor bed volume and CVS and mean tumor bed volume on the pre- and end-of-treatment MRI sequences were also evaluated using Pearson correlation coefficients and paired t test, respectively. CVS, CI, and volumes from the CT and MRIs were compared using the repeated-measures analysis of variance test. When the P value from the analysis of variance test was < .05, differences were determined using the Tukey posthoc test.

Results

Patient and tumor characteristics are listed in Table 1.

Lumpectomy tumor bed volumes

The mean ± SD tumor bed volumes at baseline were 18.67 ± 20.13 cm^3 for CT, 17.16 ± 17.32 cm^3 for T1, 18.13 ± 17.25 cm^3 for T1fs, and 17.08 ± 18.18 cm^3 for T2 (Table 2). There were no significant differences in mean overall volumes between the MRI sequences and CT, with MR:CT volume ratios of 0.92, 0.97, and 0.92 for T1, T1fs, and T2, respectively. At the end of whole breast radiation therapy, the mean surgical bed volumes had significantly reduced on each MRI sequence in comparison to the baseline MRIs ($P \leq .0001$), with a mean volume reduction of approximately 30% from 18.1 to 13.0 cm^3 for T1fs, and 90% of the surgical beds reducing in volume over time. As planning CT was not repeated at the end of treatment, comparisons with MRI were not performed at that timepoint.

Table 1   Patient and tumor characteristics

Characteristic	Value
Age (years)	
Mean	59
Range	39 − 83
Menopausal status	
Premenopausal	8
Postmenopausal	40
Laterality*	
Right	27
Left	23
Tumor Bed Location*	
Against chest wall musculature	15
Within dense breast tissue	14
Within fatty breast tissue	21
Pathological TNM stage (AJCC 7th Ed)*	
Tis	12
T1	35
T2	3
N0	48
N1	2
M0	50
Histology	
Ductal carcinoma in situ	12
Invasive ductal carcinoma	34
Invasive lobular carcinoma	2
Other	2
Grade	
1	9
2	27
3	14
Margin (mm)	
< 1	11
1 − 2	10
> 2	29
Time from surgery to initial planning (days)	
Median	46
Range	14 - 187
Time from baseline MRI to second MRI (days)	
Median	3518 - 67
Range	
Adjuvant chemotherapy	
Yes	7
No	41
Whole breast dose (Gy)	
42.4 Gy/16 fractions	47 (94%)
50 Gy/25 fractions	3 (6%)
Tumor Bed Boost	
Yes	27 (54%)
No	23 (46%)

  *   2 patients had bilateral breast cancer.

Cavity visualization score

The mean ± SD CVSs at baseline were 3.14 ± 1.08 for CT, 3.26 ± 0.99 for T1, 3.41 ± 0.97 for T1fs, and 3.58 ± 1.04 for T2. At the end of treatment, the mean ±

Table 2 Mean lumpectomy tumor bed volumes ± SD (cm³) overall and as a function of CVS

Imaging	Baseline			End of whole breast radiotherapy		
	Overall	CVS < 4	CVS ≥ 4	Overall	CVS < 4	CVS ≥ 4
CT	18.67 ± 20.13	10.45 ± 9.17 (n = 31)	32.07 ± 25.68 (n = 19)	–	–	–
T1	17.16 ± 17.32	10.04 ± 7.87 (n =30)	27.84 ± 21.80 (n = 20)	12.44 ± 13.78*	8.05 ± 6.86 (n = 36)	23.72 ± 19.98 (n = 14)
T1fs	18.13 ± 17.25	9.38 ± 7.48 (n = 27)	28.41 ± 19.83 (n = 23)	12.96 ± 13.25*	8.34 ± 6.63 (n = 31)	19.12 ± 17.57 (n = 19)
T2	17.08 ± 18.18	8.43 ± 8.20 (n = 23)	24.45 ± 21.09 (n = 27)	11.51 ± 12.98*	7.57 ± 6.72 (n = 27)	16.14 ± 16.83 (n = 23)

Abbreviations: CT = computed tomography; T1fs = T1 fat-suppression; CVS = cavity visualization score

* p ≤ 0.0001 compared to baseline.

SD CVSs were 3.15 ± 0.96 for T1, 3.29 ± 0.94 for T1fs, and 3.31 ± 1.03 for T2. There were no significant differences between the 2 observers' mean CVS. The CVS tended to be higher for larger tumor beds (Pearson's correlation coefficient, 0.53). Compared with CT, baseline T1fs and T2 MR sequences significantly improved the CVS ($P < .01$). There were no significant differences in CVS between T1fs and T2. At the end of treatment, there were no significant differences in mean CVS among T1, T1fs, and T2 sequences ($P = .20$).

Tumor bed location

Mean overall CVS and CI as a function of tumor bed location are listed in Table 3. Cases in which the tumor bed was surrounded by fatty glandular breast tissue had the greatest mean overall CVS and CIs. Tumor beds located within dense glandular breast tissue had the lowest mean overall CVS and CIs for CT, T1fs, and T2.

Interobserver variability

At baseline, the mean ± SD CIs were 0.65 ± 0.15 for CT, 0.65 ± 0.14 for T1, 0.72 ± 0.15 for T1fs, and 0.68 ± 0.15 for T2. T1fs significantly improved interobserver variability compared with CT, T1, or T2 ($P < .001$, $P < .001$, and $P = .011$, respectively). A representative case of tumor bed delineation by the 2 observers is demonstrated in Figure 1. At the end of treatment, the mean ± SD CIs were 0.64 ± 0.12 for T1, 0.72 ± 0.12 for T1fs, and 0.66 ± 0.12 for T2. Interobserver variability was significantly improved with T1fs compared with T1 or T2 ($P < .001$ for both). For tumor beds with a mean CVS < 4 on CT, baseline T1fs alone significantly improved the mean CI compared with CT, from 0.58 to 0.67 ($P < .001$), T1, or T2 ($P = .001$ and $P = .038$, respectively). For tumor beds with a mean CVS ≥ 4 on CT, baseline T1fs alone significantly improved the mean CI compared with CT, from 0.76 to 0.80 ($P < .001$).

Discussion

This study investigated the interobserver variability in breast tumor bed delineation using 3 MRI sequences (T1, T1fs, T2) compared with CT at baseline and quantified the change in tumor bed volume between pre- and end-of-treatment MRI for patients undergoing whole breast radiation therapy. T1fs reduced interobserver variability on both pre- and end-of-treatment scans and measured a reduction in tumor bed volume during whole breast radiation therapy.

Appropriate treatment of the breast tumor bed for both boost and accelerated partial breast irradiation relies on accurate delineation of the tumor bed,

Table 3　Mean overall CVS and conformity index as a function of cavity location

Location (% of tumor beds)	CVS	Conformity index			
		CT	T1	T1fs	T2
Within fatty breast tissue (42)	3.92	0.73	0.71	0.78	0.72
Against chest wall musculature (30)	2.96	0.60	0.59	0.69	0.64
Within dense glandular breast tissue (28)	2.74	0.58	0.61	0.67	0.64

Abbreviations: CVS = cavity visualization score; T1fs = T1 fat-suppression
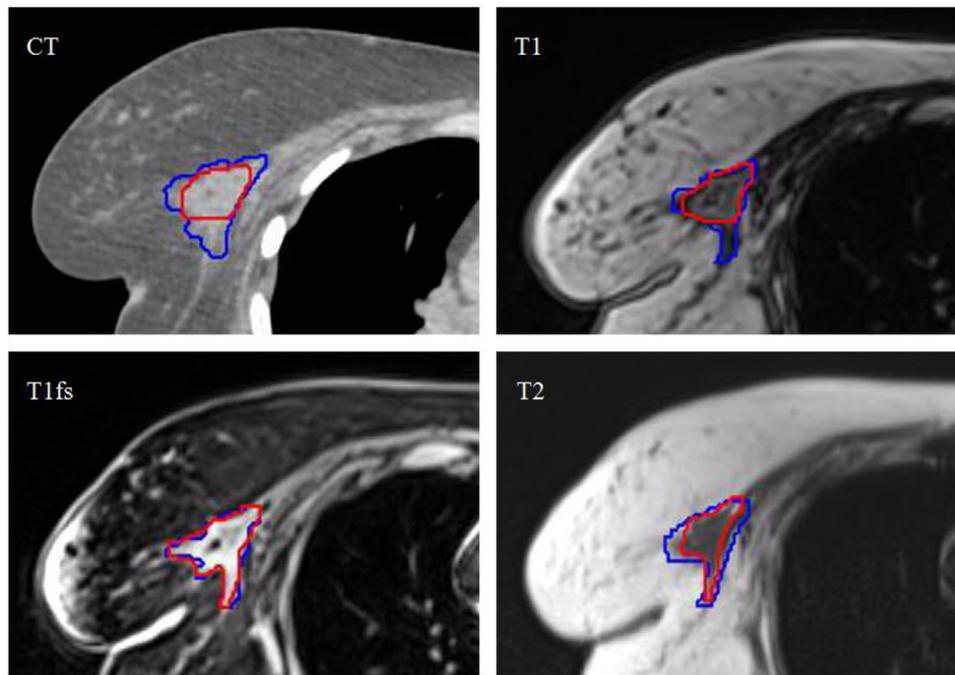

Fig. 1　A representative case of tumor bed delineation by observers 1 (blue) and 2 (red) on computed tomography (CT), T1-weighted, T1 fat-suppression (T1fs), and T2-weighted magnetic resonance imaging (MRI).

without which local control could be compromised or normal tissue unnecessarily exposed. Although it is established that CT is more accurate in defining tumor bed volumes than clinical mark-up alone, studies still show considerable variation exists between radiation oncologists when contouring tumor beds.[9-16] The use of MRI in breast radiation therapy has so far yielded variable results, but there is significant heterogeneity in the methods of the publications to date, with many studying small numbers of patients.

In our study, T1fs and T2 MRI were found to improve CVS compared with CT. Giezen et al[21] found no overall benefit of T1 MRI over CT in 15 patients with surgical clips, and moreover at low CVS found that CT achieved better CI than MRI, suggesting that surgical clips were important for better visualization of tumor beds on CT for low CVS. Although some studies have identified seroma extension beyond clips, and inconsistencies remain a problem at many centers with the number and location of clip placements (if placed at all), consistent placement of surgical clips can be helpful for accurate delineation of the tumor bed.[19,20,37,38] With surgical clips absent in 90% of the tumor beds in our study, both CVS and CI were improved by T1fs/T2 MRI over CT. Giezen et al[21] and Petersen et al[17] found that both CVS and CI decrease when tumor beds are located near the pectoral muscle or within dense glandular tissue, which our study confirms as well. Nonetheless, T1fs MRI sequence consistently achieved the least interobserver variability for all tumor bed locations compared with CT, T1, and T2 sequences. Our CI for tumor bed delineation on CT (0.65) was consistent with that reported previously in the literature: 0.31,[14] 0.516,[16] 0.52,[21, 22] 0.56,[15] and 0.76.[12] Tumor beds that were not well-defined on CT (mean CVS < 4) accounted for 82% of the tumor beds in our study, and for these patients, T1fs significantly improved interobserver variability. The T1fs sequence has the potential to be beneficial for defining smaller tumor beds and for tumor beds located within dense parenchyma or against the pectoral muscles.

CT-based studies have shown seroma volume can decrease in up to 86% of patients during whole breast radiation therapy.[30-34] Adaptive planning can reduce the volume of normal breast tissue irradiated, whether it be for sequential boosts, simultaneous integrated boosts, or PBI.[32,39,40] In our study, with a median time of 35 days from baseline MRI until the second MRI, there was a mean surgical bed volume reduction of 30% between the 2 MRI scans. Flannery et al[34] studied lumpectomy surgical bed volume changes after whole breast radiation therapy using CT. They concluded that surgical bed volume reductions may be dosimetrically significant for patients with an initial surgical bed volume ≥ 30 cm^3, as 92% of these patients had at least a 25% reduction in volume at second CT. In their study, approximately 57% of their patients had surgical beds ≥ 30 cm^3. In our cohort of patients, only 16% of surgical beds had a volume ≥ 30 cm^3, with half of these reducing in volume by $\geq 25\%$ over time. The remainder of patients in our study with surgical beds on T1fs of <30 cm^3 (excluding those 5 without a decrease in volume) had a mean surgical bed volume reduction of 29.2%, and altogether 43.2% of these surgical beds had a reduction in volume by $\geq 25\%$ over time. Jeon et al[35] published the first study, to our knowledge, of MRI monitoring of surgical bed volume changes over time in the setting of PBI. They found that 89% of patients had stable or decreasing seroma volumes during the 10 fractions and that the seroma reduction rate was inversely proportional to the time interval since surgery. Our patterns of volume reduction are consistent with Jeon et al and findings from past CT studies, and we conclude that adaptive planning with MRI may reduce normal tissue exposure while avoiding further ionising radiation exposure. This adaptive MRI planning strategy could be most beneficial for patients with larger tumor bed volume requiring boost and/or for PBI, especially with the use of MR LINAC. One institution recently reported their experience using MRI guidance for PBI, concluding they could routinely use a clinical target volume (CTV) to planning target volume (PTV) margin of 0 mm, resulting in a 52% decrease in PTV volume.[41,42] With adaptive planning, the treated volume could potentially be reduced further in those with decreasing tumor bed volumes. In our study, the T2 sequence measured the smallest overall mean surgical bed volumes of any modality or sequence, both at baseline and at the end of whole breast radiation therapy. Because T2 required multiple breath holds during acquisition though, some patients' data sets had motion artefact with loss of surgical bed information, which could have influenced the measured surgical bed size.

Past investigations have used a variety of MRI sequences, but conclusions on the ideal sequence are scarce. Ahn et al[28] investigated T1 3D spectral-spatial excitation magnetization transfer (SSMT) and T2 3D extended echo-train. They found that T2 extended echo-train achieved an acceptable signal-to-noise ratio, but if the seroma was difficult to visualise, then T1 SSMT was better, possibly because it enhances granulation tissue. Huang et al[26] used T1, short T1 inversion recovery, T2 fs, and dynamic contrast enhanced MRI sequences, concluding that short T1 inversion recovery achieved the best tumor bed visualization but had a slice thickness of 4 to 5 mm, which could lead to contouring errors. Jacobsen et al[29] used T1 VIBE and T2, concluding T2 achieved the best tumor bed visualization, but information on the methods used to reach this conclusion was lacking in this study to be able to reproduce the results. In our study, patients were scanned with inhale breath hold using T1 VIBE, T1fs, and T2 sequences, with good spatial resolution using 3-mm slice thickness. Compared with CT, both T1fs and T2 improved tumor bed visualization. T1fs also achieved the greatest improvement in interobserver variability for all tumor bed locations and was the only sequence to significantly improve CI for tumor beds with CVS < 4. In our cohort of 50 tumor beds studied, 60% of tumor beds had a mean tumor bed volume ≤ 15 cm^3 at baseline and 70% at the time of the second MRI. Also considering the finding of Ahn et al,[28] that T1 achieved better tumor bed visualization when seromas could not easily be seen, our findings support the use of T1fs sequence in patients with small or hard-to-define tumor beds. A further advantage of the T1fs sequence over T2 in our study is that it had a rapid acquisition time of 19 seconds, which could be achieved in a single breath hold. In contrast, T2 acquisition time was 1 minute and 21 seconds, requiring multiple breath holds, which introduced motion artefact and uncertainties in reproducibility.

Limitations of our study include the relatively modest number of patients and observers and the comparative nature of our study without possible evaluation against the "true" tumor bed. Surgical clips were not mandatory; thus a small subset had surgical clips, and comparisons including clips could not be performed. Given the goal to evaluate MRI delineation alone, registered CT/MRI delineation was not evaluated, as in most prior studies. Images were acquired on a 3T MRI scanner, not on MRI LINAC. Our study focused on interobserver variability in tumor bed delineation, not CTV or PTV, which could reduce variability because of the addition of fixed margins and CTV being bounded by anatomic borders (eg, breast/chest wall). Uncertainty as to the true dosimetric and clinical effect of MRI for breast tumor bed delineation also exists (ie, CTV/PTV will ultimately determine the clinical effect), and further prospective studies are required.

Conclusions

T1fs is the favored MRI sequence for tumor bed delineation in this study. It significantly improved CVS and interobserver variability compared with CT at baseline and also interobserver variability at the end of treatment compared with T1 and T2. T1fs also measured a reduction in

tumor bed volume during whole breast radiation therapy. Further studies on tumor bed delineation using the T1fs sequence are warranted, especially for its application in adaptive boost and/or partial breast radiation therapy.

Acknowledgments

References

1. Liljegren G, Holmberg L, Bergh J, et al. 10-Year results after sector resection with or without postoperative radiotherapy for stage I breast cancer: A randomized trial. *J Clin Oncol*. 1999;17:2326–2333.
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. Collaborative Early Breast Cancer Trialists', S Darby, McGale P, et al. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: Meta-analysis of individual patient data for 10,801 women in 17 randomised trials. *Lancet*. 2011;378:1707–1716.
5. Veronesi U, Marubini E, Mariani L, et al. Radiotherapy after breast-conserving surgery in small breast carcinoma: Long-term results of a randomized trial. *Ann Oncol*. 2001;12:997–1003.
6. Clarke DH, Le MG, Sarrazin D, et al. Analysis of local-regional relapses in patients with early breast cancers treated by excision and radiotherapy: Experience of the Institut Gustave-Roussy. *Int J Radiat Oncol Biol Phys*. 1985;11:137–145.
7. van Limbergen E, van den Bogaert W, van der Schueren E, Rijnders A. Tumor excision and radiotherapy as primary treatment of breast cancer. Analysis of patient and treatment parameters and local control. *Radiother Oncol*. 1987;8:1–9.
8. Salvadori B, Marubini E, Miceli R, et al. Reoperation for locally recurrent breast cancer in patients previously treated with conservative surgery. *Br J Surg*. 1999;86:84–87.
9. Bates AT, Swift CL, Kwa W, Moravan V, Aquino-Parsons C. A computed tomography-based protocol vs conventional clinical mark-up for breast electron boost. *Clin Oncol (R Coll Radiol)*. 2007;19:349–355.
10. Hepel JT, Evans SB, Hiatt JR, et al. Planning the breast boost: Comparison of three techniques and evolution of tumor bed during treatment. *Int J Radiat Oncol Biol Phys*. 2009;74:458–463.
11. Benda RK, Yasuda G, Sethi A, Gabram SG, Hinerman RW, Mendenhall NP. Breast boost: Are we missing the target? *Cancer*. 2003;97:905–909.
12. Landis DM, Luo W, Song J, et al. Variability among breast radiation oncologists in delineation of the postsurgical lumpectomy cavity. *Int J Radiat Oncol Biol Phys*. 2007;67:1299–1308.
13. Li XA, Tai A, Arthur DW, et al. Variability of target and normal structure delineation for breast cancer radiotherapy: An RTOG multi-institutional and multiobserver study. *Int J Radiat Oncol Biol Phys*. 2009;73:944–951.
14. Hurkmans C, Admiraal M, van der Sangen M, Dijkmans I. Significance of breast boost volume changes during radiotherapy in relation to current clinical interobserver variations. *Radiother Oncol*. 2009;90:60–65.
15. Struikmans H, Warlam-Rodenhuis C, Stam T, et al. Interobserver variability of clinical target volume delineation of glandular breast tissue and of boost volume in tangential breast irradiation. *Radiother Oncol*. 2005;76:293–299.
16. Kosztyla R, Olson R, Carolan H, Balkwill S, Moiseenko V, Kwan W. Evaluation of dosimetric consequences of seroma contour variability in accelerated partial breast irradiation using a constructed representative seroma contour. *Int J Radiat Oncol Biol Phys*. 2012;84:527–532.
17. Petersen RP, Truong PT, Kader HA, et al. Target volume delineation for partial breast radiotherapy planning: Clinical characteristics associated with low interobserver concordance. *Int J Radiat Oncol Biol Phys*. 2007;69:41–48.
18. Smitt MC, Birdwell RL, Goffinet DR. Breast electron boost planning: Comparison of CT and US. *Radiology*. 2001;219:203–206.
19. Coles C, Yarnold J. Localising the tumour bed in breast radiotherapy. *Clin Oncol (R Coll Radiol)*. 2010;22:36–38.
20. Coles CE, Wilson CB, Cumming J, et al. Titanium clip placement to allow accurate tumour bed localisation following breast conserving surgery: Audit on behalf of the IMPORT Trial Management Group. *Eur J Surg Oncol*. 2009;35:578–582.
21. Giezen M, Kouwenhoven E, Scholten AN, et al. MRI- versus CT-based volume delineation of lumpectomy cavity in supine position in breast-conserving therapy: An exploratory study. *Int J Radiat Oncol Biol Phys*. 2012;82:1332–1340.
22. Mast M, Coerkamp E, Heijenbrok M, et al. Target volume delineation in breast conserving radiotherapy: Are co-registered CT and MR images of added value? *Radiat Oncol*. 2014;9:65.
23. Kirby AM, Yarnold JR, Evans PM, et al. Tumor bed delineation for partial breast and breast boost radiotherapy planned in the prone position: What does MRI add to X-ray CT localization of titanium clips placed in the excision cavity wall? *Int J Radiat Oncol Biol Phys*. 2009;74:1276–1282.
24. Pogson EM, Delaney GP, Ahern V, et al. Comparison of magnetic resonance imaging and computed tomography for breast target volume delineation in prone and supine positions. *Int J Radiat Oncol Biol Phys*. 2016;96:905–912.
25. Jolicoeur M, Racine ML, Trop I, et al. Localization of the surgical bed using supine magnetic resonance and computed tomography scan fusion for planification of breast interstitial brachytherapy. *Radiother Oncol*. 2011;100:480–484.
26. Huang W, Currey A, Chen X, et al. A comparison of lumpectomy cavity delineations between use of magnetic resonance imaging and computed tomography acquired with patient in prone position for radiation therapy planning of breast cancer. *Int J Radiat Oncol Biol Phys*. 2016;94:832–840.
27. Al-Hammadi N, Caparrotti P, Divakar S, et al. MRI reduces variation of contouring for boost clinical target volume in breast cancer patients without surgical clips in the tumour bed. *Radiol Oncol*. 2017;51:160–168.
28. Ahn KH, Hargreaves BA, Alley MT, et al. MRI guidance for accelerated partial breast irradiation in prone position: Imaging protocol design and evaluation. *Int J Radiat Oncol Biol Phys*. 2009;75:285–293.
29. Jacobson G, Zamba G, Betts V, Muruganandham M, Buechler-Price J. Image-based treatment planning of the post-lumpectomy breast utilizing CT and 3TMRI. *Int J Breast Cancer*. 2011;2011: 246265.
30. Yang TJ, Elkhuizen PH, Minkema D, et al. Clinical factors associated with seroma volume reduction in breast-conserving therapy for early-stage breast cancer: A multi-institutional analysis. *Int J Radiat Oncol Biol Phys*. 2010;76:1325–1332.

31. Sharma R, Spierer M, Mutyala S, et al. Change in seroma volume during whole-breast radiation therapy. *Int J Radiat Oncol Biol Phys*. 2009;75:89–93.

32. Chen X, Qiao Q, DeVries A, et al. Adaptive replanning to account for lumpectomy cavity change in sequential boost after whole-breast irradiation. *Int J Radiat Oncol Biol Phys*. 2014;90:1208–1215.

33. Mohiuddin MM, Nichols EM, Marter KJ, Flannery TW. Decrease of the lumpectomy cavity volume after whole-breast irradiation affects small field boost planning. *Med Dosim*. 2012;37:339–343.

34. Flannery TW, Nichols EM, Cheston SB, et al. Repeat computed tomography simulation to assess lumpectomy cavity volume during whole-breast irradiation. *Int J Radiat Oncol Biol Phys*. 2009;75:751–756.

35. Jeon SH, Shin KH, Park SY, et al. Seroma change during magnetic resonance imaging-guided partial breast irradiation and its clinical implications. *Radiat Oncol*. 2017;12:103.

36. Edge SB, Compton CC. The American Joint Committee on Cancer: The 7th edition of the AJCC Cancer Staging Manual and the future of TNM. *Ann Surg Oncol*. 2010;17:1471–1474.

37. Yang Z, Chen J, Hu W, et al. Planning the breast boost: How accurately do surgical clips represent the CT seroma? *Radiother Oncol*. 2010;97:530–534.

38. Goldberg H, Prosnitz RG, Olson JA, Marks LB. Definition of post-lumpectomy tumor bed for radiotherapy boost field planning: CT versus surgical clips. *Int J Radiat Oncol Biol Phys*. 2005;63:209–213.

39. Alderliesten T, den Hollander S, Yang TJ, et al. Dosimetric impact of post-operative seroma reduction during radiotherapy after breast-conserving surgery. *Radiother Oncol*. 2011;100:265–270.

40. Hurkmans CW, Dijckmans I, Reijnen M, van der Leer J, van Vliet-Vroegindeweij C, van der Sangen M. Adaptive radiation therapy for breast IMRT-simultaneously integrated boost: Three-year clinical experience. *Radiother Oncol*. 2012;103:183–187.

41. Acharya S, Fischer-Valuck BW, Mazur TR, et al. Magnetic resonance image guided radiation therapy for external beam accelerated partial-breast irradiation: Evaluation of delivered dose and intrafractional cavity motion. *Int J Radiat Oncol Biol Phys*. 2016;96:785–792.

42. Henke LE, Contreras JA, Green OL, et al. Magnetic resonance image-guided radiotherapy (MRIgRT): A 4.5-year clinical experience. *Clin Oncol (R Coll Radiol)*. 2018;30:720–727.