Radiotherapy and Oncology 117 (2015) 477–482

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Breast radiotherapy

MRI-guided single fraction ablative radiotherapy for early-stage breast cancer: a brachytherapy versus volumetric modulated arc therapy dosimetry study

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ARTICLE INFO

Article history:
Received 19 January 2015
Received in revised form 1 September 2015
Accepted 20 September 2015
Available online 1 October 2015

Keywords:
MRI-guidance
Single fraction
Ablative
Breast cancer
VMAT
Interstitial multicatheter brachytherapy

ABSTRACT

Background and purpose: A radiosurgical treatment approach for early-stage breast cancer has the potential to minimize the patient's treatment burden. The dosimetric feasibility for single fraction ablative radiotherapy was evaluated by comparing volumetric modulated arc therapy (VMAT) with an interstitial multicatheter brachytherapy (IMB) approach.

Methods and materials: The tumors of 20 patients with early-stage breast cancer were delineated on a preoperative contrast-enhanced planning CT-scan, co-registered with a contrast-enhanced magnetic resonance imaging (MRI), both in radiotherapy supine position. A dose of 15 Gy was prescribed to the planned target volume of the clinical target volume (PTV_{CTV}), and 20 Gy integrated boost to the PTV of the gross tumor volume (PTV_{GTV}). Treatment plans for IMB and VMAT were optimized for adequate target volume coverage and minimal organs at risk (OAR) dose.

Results: The median $PTV_{GTV/CTV}$ receiving at least 95% of the prescribed dose was $\geqslant$ 99% with both techniques. The median PTV_{CTV} unintentionally receiving 95% of the prescribed PTV_{GTV} dose was 65.4% and 4.3% with IMB and VMAT, respectively. OAR doses were comparable with both techniques.

Conclusion: MRI-guided single fraction radiotherapy with an integrated ablative boost to the GTV is dosimetrically feasible with both techniques. We perceive IMB less suitable for clinical implementation due to PTV_{CTV} overdosage. Future studies have to confirm the clinical feasibility of the single fraction ablative approach.

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The current standard treatment in early-stage breast cancer is breast-conserving therapy (BCT), consisting of breast-conserving surgery (BCS) followed by whole breast irradiation (WBI) with or without a boost [1,2]. Despite its proven effectiveness [3], the protracted radiotherapy (RT) duration ranging from 3 to 7 weeks with a hypofractionated or conventional regimen, can provide a substantial treatment burden. Post-operative accelerated partial breast irradiation (APBI) to the tumor bed offers a promising alternative to WBI in low-risk breast cancer patients due to reduced treatment volume and RT duration. Furthermore, Palta et al. have shown that preoperative APBI for stage I breast cancer results in substantial treatment volume reduction when compared to a post-operative approach [4]. Preoperative ABPI could therefore enable treatment acceleration [5] to further decrease treatment burden. However, when aiming at alternatives to BCT with minimal treatment burden, the role of RT could be exchanged for a radiosurgical approach, as already employed in certain patients, e.g. with lung cancer or brain metastasis. For a radiosurgical approach, accurate tumor localization is critical. Since tumor size on magnetic resonance imaging (MRI) is highly correlated to microscopic tumor size, MRI-guidance is required in addition to planning CT-scan, in order to adequately identify tumor extent [6,7]. The MRI-linac, a hybrid system consisting of an 8 MV accelerator and an integrated 1.5 Tesla MRI scanner, and MRI-guided brachytherapy, is currently being investigated for several tumor sites [8,9]. For breast oncology, our department focuses on MRI-guided radiotherapy developments as a substitute for surgical treatment for early-stage breast cancer with low-risk characteristics according to European and American Society for Radiation Oncology APBI guidelines [10,11]. The purpose of this study was

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http://dx.doi.org/10.1016/j.radonc.2015.09.023
0167-8140/

to evaluate the dosimetric feasibility for MRI-guided single fraction ablative RT for early-stage breast cancer. We conducted a planning study by comparing a volumetric modulated arc therapy (VMAT) versus interstitial multicatheter brachytherapy (IMB) approach.

Materials and methods

Patient characteristics

This study included patients from the pre-existing NTR3198 study, approved by our institutional review board [7]. Patients with tumors up to 30 mm, scheduled for breast-conserving surgery and whole breast irradiation were included. Baseline characteristics of the 20 patients are shown in Table 1. Patients underwent a contrast-enhanced (CE) CT and CE-MRI in supine RT treatment position on a wedge board at 10° of inclination, with arms in abduction above the head. Details on patient positioning and preoperative imaging parameters were previously reported [7].

Target definition and organs at risk

All delineations were performed using software developed at our department, Volumetool® [12]. Gross tumor volumes (GTVs) and organs at risk (OARs) were delineated by an experienced breast radiation oncologist on CE-CT, co-registered with CE-MRI (Appendix 1A). The GTV was uniformly expanded by 2 cm to create a clinical target volume (CTV), excluding the skin and chest wall. For VMAT, both GTV and CTV were uniformly expanded by 3 mm to obtain the planning target volumes PTV_{GTV} and PTV_{CTV}, respectively, excluding the skin. For IMB, the PTV_{GTV} and PTV_{CTV} were equal to the GTV and CTV, respectively. The ipsilateral breast was contoured using a CT/MRI compatible demarcation wire around the palpable glandular breast tissue. The lungs were automatically contoured. The skin was defined as the area within the first 5 mm under the ipsilateral breast surface, extended with a uniform 3.5 cm margin from the breast borders. The chest wall was delineated as one structure, including the bony structures (i.e. ribs, sternum, scapula) and muscles (i.e. intercostal, pectoral and part of the rotator-cuff). The heart contour started below the pulmonary trunk bifurcation and included the pericardium [13].

Treatment plan acquisition

The preoperative planning CT-images and delineations were exported from Volumetool® into the Oncentra Brachy 4.3® planning software (Elekta Ltd.) for the IMB plans and Monaco 3.2® (Elekta Ltd.) for the VMAT plans. Two radiotherapy dose levels were concomitantly prescribed in one single fraction: 15 Gy to the PTV_{CTV} and 20 Gy to the PTV_{GTV}. The 20 Gy single dose is equivalent to a 73.7 Gy dose in 2 Gy fractions (EQD2, α/β 4.7 Gy), resulting in a 100% 5 year tumor control probability for cT_1N_0 tumors [14]. The single 15 Gy dose corresponds to an EQD2 of 44.1 Gy (α/β 4.7 Gy), similar to the standard hypofractionated schedule of 16 fractions of 2.66 Gy at our institution.

OAR constraints were set to minimize the normal tissue volume receiving the prescription dose without compromising target volume coverage. Dose constraints for lungs and heart were converted from the QUANTEC 2 Gy fractions recommendations to a single dose equivalent using an α/β of 3 Gy [15]. The recommendation for both lungs, a mean lung dose < 7 Gy (physical dose) was converted to < 3.6 Gy in a single dose. In this study, a constraint of the mean ipsilateral lung dose < 3.6 Gy was maintained. A lower heart constraint than the QUANTEC recommendation (i.e. V_{25Gy} < 10%) was maintained, using V_{5Gy} < 10% (physical dose), in concordance to our clinical practice. This implied $V_{2.8Gy}$ < 10% of the heart in a single dose delivery. The chest wall objective was extrapolated from stereotactic lung RT studies. In order to avoid RT associated chest wall pain, a D_{20cc} < 16.3 Gy objective was formulated [16]. No reference data are available for acceptable skin dose in single dose irradiation. Since 15 Gy was prescribed to the CTV and no restrictions on tumor distance to skin were provided, a skin objective D_{1cc} < 16 Gy was perceived as minimum feasible.

Plans were optimized for adequate target volume coverage and a dose as low as possible to the OARs. Adequate target volume coverage was defined as 99% or more of the PTV receiving at least 95% of the prescribed dose, thus at least 19 Gy for the PTV_{GTV} and 14.3 Gy for the PTV_{CTV}.

For IMB planning, Oncentra Brachy 4.3® software was used. The implant configuration consisted of catheters centrally placed through the GTV and at the periphery of the CTV. IMB plans were generated using inverse planning simulated annealing (IPSA). For the plan optimization process, PTV and OAR weighting factors and dose objectives were set, depending on tumor location. The plans were also optimized with respect to the dose non-uniformity ratio (DNR) recommendation of the GEC-ESTRO APBI trial. This implied a ratio between 150% (22.5 Gy) and 100% (15 Gy) of the prescribed CTV dose of 0.35 or less. If adequate coverage or optimal DNR was not achieved, catheters were subsequently displaced or additional catheters in a triangular configuration were placed throughout the CTV. The spacing between the needles was less than 20 mm. The microselectron (Elekta Ltd.) HDR Iridium-192 was used as stepping source with 2.5 mm distance between dwell positions. With VMAT, plans were generated using Monaco 3.2® software, starting at a 180° angle, using two partial arcs (clockwise and counter clockwise) and a total angle of 210–240°. For the plan optimization process, PTV and OAR weighting factors and dose objectives were set, depending on tumor location.

Table 1
Baseline characteristics.

Baseline characteristics	Value	Range
Breast		
Left	11 (55%)	
Right	9 (45%)	
Tumor location in breast		
Lateral	13 (65%)	
Medial	4 (20%)	
Central	3 (15%)	
Median		
Clinical tumor size	13.5 mm	5.0–30.0 mm
Gross tumor volume	1.8 cc	0.2–12.7 cc
Distance to skin	10.0 mm	0.0–38.0 mm
Distance to chest wall	9.0 mm	0.5–46.0 mm
Ipsilateral breast volume	867.8 cc	479.1–3390.6 cc

Plan evaluation and data analysis

For each patient and planning modality, median values on target volume coverage, OAR dose and high dose volumes in the PTV_{CTV} and breast were assessed. High dose volumes to the PTV_{GTV} were not reported since our study design investigated the feasibility of an ablative dose to the tumor. The paired data were evaluated using the non-parametric Wilcoxon signed-rank test and IBM SPSS Statistics 20 (Chicago, IL, USA), with α significance level below 0.05.

Results

The tumor and ipsilateral breast characteristics are presented in Table 1. Tumors were mainly laterally located in the left breast. The