Medical Dosimetry ∎ (2014) ∎∎∎–∎∎∎

Medical Dosimetry

journal homepage: www.meddos.org

Combined photon-electron beams in the treatment of the supraclavicular lymph nodes in breast cancer: A novel technique that achieves adequate coverage while reducing lung dose

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A R T I C L E I N F O

Article history:
Received 26 May 2014
Received in revised form
5 November 2014
Accepted 3 December 2014

Keywords:
Breast cancer
Supraclavicular
Electron
Photon
Lung dose

A B S T R A C T

Radiation pneumonitis is a well-documented side effect of radiation therapy for breast cancer. The purpose of this study was to compare combined photon-electron, photon-only, and electron-only plans in the radiation treatment of the supraclavicular lymph nodes. In total, 13 patients requiring chest wall and supraclavicular nodal irradiation were planned retrospectively using combined photon-electron, photon-only, and electron-only supraclavicular beams. A dose of 50 Gy over 25 fractions was prescribed. Chest wall irradiation parameters were fixed for all plans. The goal of this planning effort was to cover 95% of the supraclavicular clinical target volume (CTV) with 95% of the prescribed dose and to minimize the volume receiving $\geq$ 105% of the dose. Comparative end points were supraclavicular CTV coverage (volume covered by the 95% isodose line), hotspot volume, maximum radiation dose, contralateral breast dose, mean total lung dose, total lung volume percentage receiving at least 20 Gy ($V_{20\ Gy}$), heart volume percentage receiving at least 25 Gy ($V_{25\ Gy}$). Electron and photon energies ranged from 8 to 18 MeV and 4 to 6 MV, respectively. The ratio of photon-to-electron fractions in combined beams ranged from 5:20 to 15:10. Supraclavicular nodal coverage was highest in photon-only (mean = 96.2 ± 3.5%) followed closely by combined photon-electron (mean = 94.2 ± 2.5%) and lowest in electron-only plans (mean = 81.7 ± 14.8%, $p < 0.001$). The volume of tissue receiving $\geq$ 105% of the prescription dose was higher in the electron-only (mean = 69.7 ± 56.1 cm^3) as opposed to combined photon-electron (mean = 50.8 ± 40.9 cm^3) and photon-only beams (mean = 32.2 ± 28.1 cm^3, $p = 0.114$). Heart $V_{25\ Gy}$ was not statistically different among the plans ($p = 0.999$). Total lung $V_{20\ Gy}$ was lowest in electron-only (mean = 10.9 ± 2.3%) followed by combined photon-electron (mean = 13.8 ± 2.3%) and highest in photon-only plans (mean = 16.2 ± 3%, $p < 0.001$). As expected, photon-only plans demonstrated the highest target coverage and total lung $V_{20\ Gy}$. The superiority of electron-only beams, in terms of decreasing lung dose, is set back by the dosimetric hotspots associated with such plans. Combined photon-electron treatment is a feasible technique for supraclavicular nodal irradiation and results in adequate target coverage, acceptable dosimetric hotspot volume, and slightly reduced lung dose.

Introduction

Radiation therapy is an integral component in the management of breast cancer.[1] The benefits of using radiation therapy in patients with breast cancer have been confirmed by several randomized trials and include improvements in overall survival and decreased incidence of locoregional recurrence and distant metastases.[2-16] Unfortunately, the beneficial additions of radiation

This study was presented as a poster during 54th annual meeting of the American Society for Radiation Oncology; October 28 to 31, 2012.

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http://dx.doi.org/10.1016/j.meddos.2014.12.001
0958-3947/

therapy come with undeniable long-term adverse events. Numerous studies have addressed the increased incidence of ischemic heart and second primary malignancy following radiation therapy for breast cancer.[17-23] Similarly, radiation-induced pneumonitis is a well-described consequence in a proportion of patients following radiation therapy for this disease.

The occurrence of radiation pneumonitis is dependent upon several factors including baseline lung function, concurrent use of chemotherapeutic medications, total radiation dose, dose per fraction, and the proportion of lungs inside the radiation field.[24] As such, tireless efforts are used to decrease the mean lung dose in an attempt to limit this undesired adversity.

Inverse planned intensity-modulation radiation therapy (IMRT) has been introduced in breast cancer with the aim of decreasing both heart and lung dose, while achieving acceptable target coverage.[25,26] However, the use of IMRT in breast cancer comes with a number of disadvantages. First, it is technically complex to deliver and as such, is only available in a proportion of radiation oncology centers worldwide. Second, IMRT requires stringent quality assurance programs that are associated with excessive costs and are heavily labor intensive and time demanding. In addition, although IMRT is generally associated with highly conformal high-/medium-dose coverage and as such steep dose fall-off and subsequently improved lung and heart dose sparing,[25] low-dose deposition of radiation inside the lungs is probably higher than that seen with 2- or 3-dimensional conformal radiation therapy. This led some investigators to speculate that the risk of second malignancy might be higher following IMRT.[27,28]

Other researchers have proposed partial-breast irradiation as a novel and safe radiation technique, which could significantly limit radiation dose to both the heart and the lungs.[29] Nonetheless, partial-breast irradiation is only possible in a small fraction of patients; those presenting with early-stage disease and is not advised for patients with locoregionally advanced breast cancer.[30]

As such, alternative methods aimed at decreasing heart and lung dose are immensely required in patients with breast cancer undergoing radiation therapy for locoregionally advanced disease. In an attempt to decrease lung dose, we performed the following study with the aim of comparing combined photon-electron, photon-only, and electron-only plans in the radiation treatment of the supraclavicular lymph nodes in patients with breast cancer.

Methods and Materials

Between January and February 2012, 13 patients with consecutive breast cancer treated in the radiation oncology department at King Hussein Cancer Center (Amman, Jordan) were selected for inclusion in this study. All patients had previously undergone modified radical mastectomy and were found to harbor locoregionally advanced breast cancer.

The corresponding computed tomography simulation images were electronically retrieved and used for this planning study following acquisition of institutional review board approval. In total, 3 radiation plans (combined photon-electron, photon-only, and electron-only supraclavicular nodal beams) were generated for all patients using Pinnacle3 version 9.2 (Philips Healthcare, The Netherlands).

Target volume and risk organ definition

The supraclavicular nodal clinical target volume (CTV) was contoured according to the Radiation Therapy Oncology Group (RTOG) atlas.[31] A 0.5-cm contraction from the external body contour was applied to the supraclavicular nodal CTV (Fig. 1). The depth of the supraclavicular CTV, determined by measuring the distance from the skin and the deepest CTV point, was recorded in all the cases.

The total (bilateral) lung volume was automatically generated, in the lung-window, using the autocontouring tool of the treatment planning system. Heart volume was defined from the heart apex till the caudal level of the pulmonary trunk and included all visible myocardium and pericardium. The contralateral breast contour encompassed any visible glandular breast tissue from the midline till the anterior edge of the latissimus dorsi muscle and from the second intercostal space to the lowest extension of glandular breast tissue after applying 0.5-cm contraction from the external body contour.

Field arrangement

A monoisocentric technique was used in all patients to eliminate the uncertainty associated with field matching. The isocenter was placed at the caudal aspect of the head of the clavicle at the ribpleural interface.

Chest wall field

Two tangential chest wall fields, using field-in-field technique (forward IMRT), were utilized in all patients. The fields were half-beam blocked in the medial and the cranial aspect to eliminate divergence into the lungs and the supraclavicular field, respectively. Attempts were made to minimize the amount of lung and heart (for left-sided tumors) inside the tangential field to approximately 2 cm (Supplementary Figs. S1 and S2, respectively).

Supraclavicular field

A single direct anteroposterior supraclavicular beam was allowed with the field borders fixed in the 3 radiation techniques (Supplementary Figs. S3 and S4). The use of motorized wedge was allowed, if necessary. The field was half-beam blocked in the caudal aspect to eliminate divergence into the chest wall field.

Radiation therapy plan

A dose of 50 Gy in 2 Gy fractions (25 fractions) was prescribed to the chest wall and supraclavicular nodal CTV.

Chest wall irradiation parameters were fixed for all treatment plans. The goal of this planning study was to cover 95% of the supraclavicular CTV with 95% of the prescribed dose and to minimize the volume receiving $\geq$ 105% of the dose. Achieving adequate target coverage was balanced with avoiding unnecessary dosimetric hotspots.

A single experienced dosimetrist planned all 13 cases in the following order; photon-only, electron-only followed by combined photon-electron beams with the aim of subjectively achieving a trade-off between target coverage and organ-at-risk/hotspot dose. The choice of the most appropriate electron/photon energy as well as the ratio of photon-to-electron fractions (the number of days a patient would receive either photon-only or electron-only beams) in combined beams was left to the judgment of the dosimetrist.

Plan evaluation

All plans were evaluated by inspecting the dose-volume histograms and documenting the following variables, which were used as comparative end points in this study.

(1) *Supraclavicular CTV coverage*: volume covered by the 95% isodose line
(2) *Hotspot volume*: volume receiving $\geq$ 105% of the prescription dose
(3) Maximum radiation dose
(4) *Mean total lung dose*: mean radiation dose received by the bilateral lung volume
(5) *Total lung* $V_{20\ Gy}$: lung volume percentage receiving at least 20 Gy

Contralateral breast dose (mean dose received by the contralateral breast) and heart volume percentage receiving at least 25 Gy ($V_{25\ Gy}$), which are unlikely to be affected by our studied beams, were reported for the sake of completion.

Statistical analysis

Descriptive statistics were used to summarize continuous data. To compare dosimetric results among the 3 radiation plans, one-way analysis of variance was applied. A $p < 0.05$ was considered statistically significant. Bonferroni correction technique for pairwise comparisons was used to perform multiple comparisons between the generated dosimetric results in the 3 radiation plans. An adjusted $p < 0.05$ was considered statistically significant. All statistical tests were performed using Minitab 16 statistical software (Minitab Inc., State College, PA).

Results

Radiation parameters of supraclavicular beam portals

Table 1 shows the details of the radiation parameters used in the 3 radiation plans. The beam energy in electron beams ranged from 8 to 18 MeV (mean = 12.5 MeV). The beam energy in photon beams ranged from 4 to 6 MV (mean = 5.8 MV). The most widely used photon-to-electron ratio in the combined photon-electron plans was 13:12 in 9 plans (69.2%). In 4 plans (30.8%), no wedge was used, whereas in 9 plans (69.2%), motorized wedge was