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Original paper

The evaluation of the feasibility of carotid sparing intensity modulated radiation therapy technique for comprehensive breast irradiation

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ABSTRACT

Purpose: To investigate the feasibility of carotid sparing intensity modulated radiation therapy (CS-IMRT) to minimize the radiation dose to carotid arteries for comprehensive irradiation of breast cancer patients who have risk factors for atherosclerosis. The dose distribution of CS-IMRT technique and the conventional irradiation technique were also compared.

Patients and methods: Ten patients who were previously treated with comprehensive three-dimensional conformal radiation therapy (3DCRT) were selected. DICOM data were used to contour the carotid artery and to create the virtual CS-IMRT plans for each patient. 3DCRT and CS-IMRT plans were compared in terms of conformity index, homogeneity index, and the doses to organ at risk and carotid arteries.

Results: The homogeneity and conformity indices were better with CS-IMRT plans compared to 3DCRT plan. The homogeneity index was 1.13 vs 1.11 ($p = 0.007$) for 3DCRT and CS-IMRT and the conformity index was 0.96 vs 0.97 ($p = 0.006$) for 3DCRT and CS-IMRT. The radiation dose to the carotid arteries were reduced by applying CS-IMRT without compromising the target volume coverage. When the carotid artery was considered as organ at risk for CS-IMRT planning, the median of V50 was decreased to 0% from 12.5% compared to 3DCRT plans ($p = 0.017$). The median of the maximum dose to the carotid artery was decreased under 50 Gy with CS-IMRT.

Conclusions: CS-IMRT can significantly reduce the unnecessary radiation dose to the carotid arteries compared with conventional 3DCRT technique while maintaining target volume coverage. CS-IMRT technique can be considered for breast cancer patient with high risk of atherosclerosis.

1. Introduction

Radiation therapy (RT) is the mainstay of comprehensive treatments for breast cancer. The prognosis of these patients has been improved over the past decades as a result of early diagnosis with the use of new treatment modalities. Although this population is growing and the incidence of hypertension, valvular disease and cardiomyopathy has been increasing comparing to general population, the cardiovascular effect of cancer therapy has become one of the serious problems for the general health of cancer survivors [1,2].

Long-term follow-up in some trials has shown that RT can associate with the increased risk of cardiovascular morbidity in breast cancer patients due to increased coronary artery disease [3,4]. However, few studies have examined the other potential reasons of vascular morbidity and mortality such as carotid artery stenosis [5–7].Vascular damage due to the radiation is usually thought to be the secondary damage of microvasculature that results in endothelial dysfunction, inflammation, oxidative stress, occlusion of the vasa vasorum and accelerated atherosclerosis [8]. However, the recognition of large vascular toxicity, which is a major sequel of irradiation, has been increasingly reported especially for head and neck cancer patients [9,10]. Gujral et al. reported the radiation related stroke and transient ischemic attack is mediated by radiation-induced atherosclerosis, which is characterized by increased of carotid intima-media thickness and plague development, subsequent with stenosis. They also suggested that risk for cerebrovascular injuries could be further increased in patients who have any risk factors for atherosclerosis [11].

The conventional radiotherapy technique, which is used in breast cancer treatment, two opposed tangential field technique with or without one anterior supraclavicular field creates a uniform dose distribution on the beam pathway. However, this feature may cause significant incidental doses of radiation in unnecessary

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areas. In breast cancer patients treated with adjuvant RT, the risk of adverse effects can be increased in organ lying in the beam pathway such as heart or vessels like coronary arteries, brachiocephalic trunk, subclavian artery, and common carotid arteries. Nilsson et al. showed a significant increase of stroke after irradiation of supraclavicular lymph nodes in a large Swedish breast cancer cohort [6,7]. Recently, Vallerio et al. showed the arterial stiffness on the site of previous RT treatment in breast cancer patients [5]. The increased atherosclerotic changes and arterial stiffness stresses the importance of currents improvement of RT techniques. The idea of organ sparing RT is really attractive for clinicians to prevent cardiovascular risk factors of radiation, especially for patients who are more vulnerable to develop a late side effect on heart and vessels. The modern patient positioning systems and radioherapy planning and treatment techniques such as intensity modulated radiotherapy (IMRT) or volumetric modulated arc therapy (VMAT) allow to achieve highly conformed dose distributions on the target volume and to spare the adjacent normal tissues and organs at risk (OAR) [12,13]. The feasibility of carotid sparing RT techniques instead of conventional techniques in order to reduce the carotid artery dose for early stage glottis cancer has recently been shown [14–16].

The aim of this study was to investigate to the dosimetry and feasibility of CS-IMRT technique to minimize the radiation dose to carotid arteries for comprehensive irradiation of breast cancer patients who have risk factors for atherosclerosis. The virtual dosimetric comparison of the CS-IMRT technique and the conventional irradiation technique were also evaluated.

2. Materials and methods

All patients received conventional RT using 3DCRT. Inclusion criteria for the study were that: 1) Histologically proven breast cancer 2) The patients who underwent breast conserving surgery and axillary dissection 3) TanyN1-3 (Stage II/III) patients according to seventh edition of American Joint Committee on Cancer Staging criteria 4) Left breast, axillary lymph node and supraclavicular lymph nodes irradiated patients 5) The patients with at least one of the following risk factors for atherosclerosis: age over 70 years, obesity, hypertension, diabetes mellitus, hyperlipidemia, smoking, or previous coronary heart disease. Ten patients with breast cancer were selected from our departmental database that met with the inclusion criteria. Clinical characteristics of patients were shown in Table 1.

2.1. Original 3DCRT plans

In each patient, a treatment planning computed tomography (CT) scan with a 5 mm slice thickness was obtained, while the patients were immobilized in breast board with the ipsilateral arm-up and head turned to the contralateral side. Clinical target volume (CTV: left breast, axillary lymph nodes and supraclavicular lymph nodes) was contoured using the Radiation Therapy Oncology Group breast cancer atlas for radiation therapy planning [17]. The planning target volume (PTV) was defined as the CTV plus a 5-mm margin. All relevant normal tissues including the heart, lung, spinal cord, brachial plexus, contralateral breast and lung were delineated. The plans were performed using standard forward planning methods. The prescription dose was 50 Gy at 2 Gy per fraction. The dose was prescribed to the ICRU reference that was usually the isocenter located in the PTV. Every plan was normalized so that ⩾95% of the PTV received 100% of the prescription dose. The dose delivered to 5% of the volume (D05) of PTV was <110% of the prescribed dose to PTV. The energy of 6 MV was used for treatments. All patients received conventional three fields (two tangential fields and one anterior supraclavicular field) RT. A standard conventional tangential technique consists of two-opposed tangential fields were used to cover the PTV breast. Lateral wedges were used to improve dose inhomogeneity without increasing the dose to opposite breast. Field collimation was adjusted to follow the slope of the chest wall. Gantry angles were adjusted to make the deep tangential beams coplanar to limit the volume of lung. A supraclavicular/axillary apex field was matched to the tangential field at the level of the caudal edge of the sternoclavicular junction. Divergence was prevented at the abutment of the tangential and supraclavicular/axillary apex field by modifying the couch rotation angle and collimator angel. The gantry angle was rotated 350 degrees to spare the spinal cord. The humeral head was shielded.

2.2. Carotid artery contouring and virtual CS-IMRT plans

Archival treatment plans and CT simulation data were extracted as DICOM-RT files. The CTV and PTV DICOM-RT structure set of 3DCRT planning was used. The left common carotid arteries were retrospectively contoured for each patient with a radiologist. Since the anatomy of the left and right carotid arteries are different and to prevent bias for interrupting results, patients with left breast cancer were selected for the study. Although the right common carotid artery starts from the brachiocephalic trunk, the left common carotid artery directly arises from the arch of the aorta. From the sternoclavicular joints, both common carotid arteries ascend to upper border of thyroid cartilage at the level of C3-4 vertebras where it divides into internal and external branches [18]. The contouring of the left carotid artery was performed according to anatomy as described above. Fig. 1 demonstrates the localization of ipsilateral common carotid artery in the supraclavicular field. The dose constraints such as dmax < 50 Gy and V50 < 1% were used

Table 1
Clinical characteristics of patients.

Variables	Patients (n = 10)
Age (years)*	68 ± 4.7
Previous chemotherapy	9 (90%)
Previous hormonal therapy	7 (70%)
BMI (kg/m^2)*	23.4 ± 3
Diabetes Mellitus	3 (%30)
Hypertension	5 (%50)
Dyslipidemia	2 (%20)
Coronary artery disease	1 (%10)
Current/ex smoker	4 (%40)

* Data are shown as mean ± standard deviation.

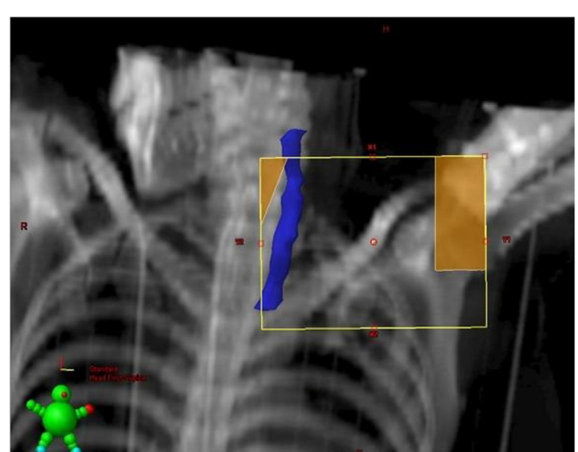

Fig. 1. The localization of ipsilateral common carotid artery in supraclavicular field.