Radiotherapy and Oncology 122 (2017) 423–430

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Coronary artery delineation

Development of delineation for the left anterior descending coronary artery region in left breast cancer radiotherapy: An optimized organ at risk

Jie Lee [a,b,c], Kai-Lung Hua [d], Shih-Ming Hsu [c], Jhen-Bin Lin [e], Chou-Hsien Lee [f], Kuo-Wei Lu [a], Kun-Yao Dai [a], Xu-Nian Huang [a], Jun-Zhao Huang [g], Meng-Hao Wu [a,b,*], Yu-Jen Chen [a,b,*]

[a] *Department of Radiation Oncology, MacKay Memorial Hospital, Taipei;* [b] *Department of Medicine, MacKay Medical College;* [c] *Department of Biomedical Imaging and Radiological Sciences, National Yang-Ming University;* [d] *Department of Computer Science and Information Engineering, National Taiwan University of Science and Technology, Taipei;* [e] *Department of Radiation Oncology, Changhua Christian Hospital;* [f] *Department of Radiation Oncology, E-Da Cancer Hospital, Kaohsiung; and* [g] *Department of Radiology, MacKay Memorial Hospital, Taipei, Taiwan*

ARTICLE INFO

Article history:
Received 19 May 2016
Received in revised form 27 November 2016
Accepted 23 December 2016
Available online 10 January 2017

Keywords:
Left breast cancer
Coronary artery
Radiotherapy

ABSTRACT

Background and purpose: The left anterior descending coronary artery (LAD) and diagonal branches (DBs) are blurred on computed tomography (CT). We aimed to define the LAD region (LADR) with adequate inclusion of the LAD and DBs and contouring consistency.

Methods and materials: The LADR was defined using coronary CT angiograms. The inclusion ratio was used to assess the LAD and DBs inclusion by the LADR. Four radiation oncologists delineated the LAD and LADR, using contrast-enhanced CT of 15 patients undergoing left breast radiotherapy. The Sørensen–Dice similarity index (DSI), Jaccard similarity index (JSI), and Hausdorff distance (HD) were calculated to assess similarity. The mean dose (D_{mean}) and maximum dose (D_{max}) to the LAD and LADR were calculated to compare consistency. Correlations were evaluated using Pearson's correlation coefficient.

Results: The inclusion ratio of the LAD by the LADR was 96%. The mean DSI, JSI, and HD values were respectively 27.9%, 16.7%, and 0.42 mm for the LAD, and 83.1%, 73.0%, and 0.18 mm for the LADR. The D_{mean} between the LAD and LADR were strongly correlated ($r = 0.93$).

Conclusion: Delineation of the LADR significantly improved contouring similarity and consistency for dose reporting. This could optimize dose estimation for breast radiotherapy.

Current standard treatment for early-stage breast cancer consists of breast-conserving surgery, followed by adjuvant radiotherapy. Data from the Early Breast Cancer Trialists' Collaborative Group's most recent meta-analysis suggest that adjuvant radiotherapy for breast cancer reduces a woman's relative risk of breast cancer recurrence by nearly 50% [1]. In addition, there is an absolute reduction of approximately 4% in breast cancer mortality at 15 years. However, patients undergoing left breast radiotherapy also receive radiation to the heart and left anterior descending coronary artery (LAD). Consequently, women who undergo left breast radiotherapy have increased cardiac morbidity [2] and mortality [3], compared to women who undergo right breast radiotherapy for right-sided breast cancer. Studies have established the heart dose as an indicator of cardiac morbidity in long-term cancer patient survivors [4–12]. However, compared to the whole heart dose, the coronary artery dose has been suggested as a superior predictor of potential radiation-induced cardiac toxicity [7,13–17]. Recent studies have suggested that the LAD is more sensitive to a radiation dose, compared to myocardial tissue, which constitutes the majority of the cardiac tissue [4,5,18]. Therefore, the LAD should be regarded as an organ at risk during left breast radiotherapy.

Feng et al. developed a cardiac atlas that estimates radiation dose [19]. However, in standard computed tomography (CT)-based simulation, the LAD may not be entirely visible, resulting in variation of LAD delineation and dose evaluation (Supplementary Fig. 1) [19,20]. Without visualization of the coronary artery, dose constraints on the LAD delineated by prior anatomic knowledge would probably be meaningless. Coronary computed tomography angiography (CTA) could be used to visualize the LAD better. However, it is not routinely performed and not available for breast cancer patients worldwide. In addition, the LAD

* Corresponding authors at: Department of Radiation Oncology, MacKay Memorial Hospital, 92, Section 2, Chung Shan North Road, Taipei 10449, Taiwan (M.-H. Wu). Department of Radiation Oncology, MacKay Memorial Hospital, 92, Section 2, Chung Shan North Road, Taipei 104, Taiwan (Y.-J. Chen).

E-mail addresses: radionc1@gmail.com (M.-H. Wu), chenmdphd@gmail.com (Y.-J. Chen).

http://dx.doi.org/10.1016/j.radonc.2016.12.029
0167-8140/

can have 1–3 diagonal branches (DBs) along its course above the level where the LAD branches from the left main coronary artery to the level of the cardiac apex, which also supplies the anterolateral wall of the left ventricle [21]. Nilsson et al. reported increased stenosis in the mid and distal LAD, including the distal DB, in irradiated left-sided breast cancer [5]. Contouring the LAD alone for dose reporting or optimization of radiotherapy planning is insufficient to minimize radiotherapy-induced cardiac morbidity and mortality.

We hypothesized that inconsistencies in LAD contouring were primarily because of inadequate imaging quality provided by current imaging techniques. We also hypothesized that this clinical difficulty could be overcome by combining anatomical knowledge and current practical contouring tools. This study aimed to establish anatomical boundary-based delineation definition for the LAD region (LADR) to determine the optimized organ at risk volume with adequate inclusion of the LAD and DBs and to evaluate contouring consistency.

Materials and methods

Patients

Fifteen patients with early-stage left-sided breast cancer were randomly selected from the CT planning database, retrospectively. All patients had undergone breast-conserving surgery, followed by left breast radiotherapy, between August 2012 and October 2013. Patient characteristics are shown in Supplementary Table 1.

Development of the definition of the left anterior descending coronary artery region

We randomly reviewed coronary CT angiograms of 15 analogous female patients from our institute database because CTA was not routinely performed for breast cancer radiotherapy planning. The definition of the LADR (Table 1 and Supplementary Table 2) was developed, based on coronary topology on CTA by radiologists and radiation oncologists. An example of the LAD and LADR contours on CTA are illustrated in Fig. 1. The inclusion ratio was calculated to evaluate the inclusion of the LAD and its DBs by the LADR. The inclusion ratio was defined as follows:

$$\text{Inclusion Ratio} = \frac{V_{\text{LAD+Diagonal branches}} \cap V_{\text{LADR}}}{V_{\text{LAD}}}$$

in which $V_{\text{LAD+Diagonal branches}}$ and V_{LADR} represent the volume of the LAD and its DBs and the LADR, respectively. The ∩ symbol represents the intersection of the contours. A value of 1 indicates a perfect overlap.

Table 1
Definition of the LAD region.

	Description
Cranial	The level above where the LAD branches from the left main coronary artery
Caudal	The level of the heart's apex
Left	Upper: Left auricle and pericardium Lower (when the interventricular wall can be detected): Junction of the parietal and visceral pericardium; alternatively (if detection is difficult on CT images), along the extrapolation line of the interventricular wall left edge or apex (white arrow in Figs. 1C and D, respectively)
Right	Upper: Virtual line along the left and posterior border of the pulmonary trunk (blue line in Fig. 1(A and B)) Lower (when the interventricular wall can be detected): Along the extrapolation line of the interventricular wall right edge (blue line in Fig. 1(C and D))
Anterior	Parietal pericardium
Posterior	Upper: Virtual line between the pulmonary trunk and aorta, or if the myocardium can be detected on CT images, the anterior border of the myocardium (red lines in Fig. 1(A and B)) Lower (when the interventricular wall can be detected): Heart or myocardium

Abbreviations: CT, computed tomography; LAD, left anterior descending coronary artery.

Patient positioning and image acquisition

All patients undergoing breast radiotherapy were scanned in the supine position on the Alpha Cradle, and with their arms extended above their heads in supports. Markers were placed ipsilaterally 2 cm lateral to all palpable breast tissue along the midaxillary line and midsternal line. Surgical scars and all visible breast tissue were circled with wires. Patients were scanned using the Philips Brilliance CT Big Bore scanner (Philips Healthcare, Amsterdam, Netherlands). The CT images were acquired during free-breathing immediately after an intravenous bolus injection (100 mL) of a non-ionic intravenous contrast agent (Ultravist 300™, Schering AG, Berlin, Germany), from the C6 vertebral body to the diaphragm using 3-mm slice intervals.

Delineation of target tissues and organs at risk

The clinical target volume (CTV) encompassed the breast tissue visualized on CT. The CTV was limited by the pectoral fascia. The planning target volume was generated by adding a 5-mm margin around the CTV, except for at the skin surface. Mammary chain or supraclavicular fossa irradiation was not performed. The assessed organs at risk included the heart and LAD, which were delineated based on the guidelines previously published by Feng et al. [19], and the LADR, as defined in the present study.

Plan design

All plans were performed using a three-dimensional treatment planning system (Eclipse, version 7.3; Varian Medical Systems, Inc., Palo Alto, CA, USA). Patients were treated using 6-MV photons with 50 Gy in 25 fractions over 5 weeks. The tangential wedge-based field plans were applied, and ⩾90% of the whole breast CTV was encompassed by the 95% isodose. For cardiac shielding, the percentage of the heart volume irradiated with ⩾40 Gy was <5%, and that irradiated with ⩾20 Gy was <10%. The constraint for the ipsilateral lung was that the percentage of lung volume irradiated ⩾20 Gy was <20%. The LAD was not routinely used as an avoidance structure. The priority to spare the organs at risk was as follows: heart > lung > CTV-breast.

Evaluation of delineations

The LAD and LADR were contoured by 4 experienced radiation oncologists from 3 cancer centres. Each observer received the CT scans of the patients in Digital Imaging and Communications in Medicine (DICOM) format and was asked to perform delineations independently. The delineations were imported and analysed in Matlab version R2014a software (The Mathworks Inc., Natick, MA, USA).

Volume and spatial overlap

For each patient, the mean volume and spatial overlaps of all LAD and LADR delineations were calculated. For ease of comparison with previous studies, 2 commonly used indices of spatial overlap, the Sørensen–Dice similarity index (DSI) and the Jaccard similarity index (JSI), were calculated. They were defined, as follows: