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Breast radiotherapy

Inter-observer variation in delineating the coronary arteries as organs at risk

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ABSTRACT

Purpose: To determine the inter-observer variation in delineating the coronary arteries as organs at risk (OAR) in breast cancer (BC) radiotherapy (RT) and how this variation affects the estimated coronary artery radiation dose.

Method: Delineation of the left main and the left anterior descending coronary artery (LMCA and LAD), and the right coronary artery (RCA), by using the heart atlas by Feng et al., was performed by three radiation oncologists in 32 women who had received adjuvant RT for BC. Centres of the arteries were calculated and distances between artery centres were measured and the artery radiation doses were estimated. The intraclass correlation coefficient (ICC) was used to quantify the variability in doses.

Results: Along the extent of RCA, the median distance between centres of arteries varied from 2 to 9 mm with similar patterns over pairs of oncologists. For the LMCA-LAD the median distance varied from 1 to 4 mm. The estimated maximum radiation doses showed an ICC variation from 0.82 to 0.97.

Conclusion: The coronary arteries can be reliably identified and delineated as OARs in BC RT. The spatial variance is limited and the total variation in radiation dose is almost completely determined by the between patient variation.

Breast cancer (BC) is the most common cancer form and cause of cancer death in women [1]. Adjuvant radiotherapy (RT) is a standard treatment after breast conserving surgery (BCS) and in the case of lymph node metastases [2]. Large meta-analysis shows significant benefits in terms of reducing local recurrences and breast cancer deaths [3,4]. In node-negative, and node-positive diseases, respectively, an absolute 5-year risk reduction of 16.1%, and 30.1% for local recurrences, and an absolute risk reduction in 15-year-breast cancer mortality of 5.1%, and 7.1% were shown, when RT was given after BCS. In patients undergoing mastectomy and axillary clearance and with lymph node metastasis, an absolute 5-year risk reduction of 17.1% for local recurrence, and 5.4% for 15-year breast cancer mortality, was shown after RT to the chest wall and regional lymph nodes [3,4].

RT on the other hand increases the risk for heart disease due to incidental irradiation of the heart [5]. Trials have shown an increase in cardiac mortality and morbidity, and a relationship between higher absorbed radiation dose and a higher incidence of ischemic heart disease (IHD) [5–7]. In some studies, RT to the left breast is associated with higher risk of IHD than RT to the right breast, probably due to the localization of the heart [8,9]. Dosimetry studies have shown that the left anterior descending artery (LAD) receives the highest radiation doses [10,11] and a higher incidence of coronary artery stenosis in the LAD has also been shown after RT of left-sided BC [12,13].

The relationship between absorbed radiation dose to the coronary arteries and IHD has raised the question whether coronary arteries should be regarded as separate organs at risk (OAR) in RT. Historically the heart has been regarded as an OAR. The radiation tolerance for the coronary arteries may however be different from other cardiac structures, and there are no current models for normal tissue complication probability (NTCP) concerning coronary artery toxicity [14]. The radiation volumes and doses to the heart have changed during the last decades due to the development of new radiation techniques but radiation doses to the most anterior part of the heart may still be high [11,15].

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A better understanding of radiation tolerance of the coronary arteries is important in order to form recommendations concerning dose constraints and consistent clinical guidelines. Modern three-dimensional (3 D) RT is based on the delineation of target volumes and OARs in the computerized tomography (CT) scan. Consistency in delineation is crucial in further development of NTCP models for coronary arteries and in the clinical practice to optimize the RT plan for each patient. Several studies have documented significant inter-observer variation in delineation of target volumes and OARs [16–18]. One previously published study on reproducibility of delineating coronary arteries showed a substantial inter-observer variation in estimated dose [19].

The aim of the present study was to determine the degree of inter-observer variation in delineating the coronary arteries as OARs, and to assess the relationship between inter-observer and inter-patient variability in estimated radiation doses to the coronary arteries.

Patients and methods

Patients

The patients were defined from a larger cohort of irradiated women with BC who subsequently developed coronary artery stenosis requiring percutaneous coronary intervention. To identify the cohort, we selected women diagnosed with BC in three health care cancer regions of Sweden (Uppsala-Örebro, Stockholm and the Northern region) during the period 1992–2012 who had received adjuvant RT according to the Breast Cancer Quality of Care registers. This BC cohort was then linked to the Swedish Coronary Angiography and Angioplasty Register, a part of the nationwide Swedish cardiac register SWEDEHEART [20]. For the present study all women treated at one of the radiotherapy departments, the Department of Oncology at the hospital of Gävle, were selected. Information concerning BC surgery, adjuvant endocrine therapy, chemotherapy, and tumour characteristics (invasive cancer or cancer in situ, size, grade, and nodal status) were obtained from the Breast cancer quality of care registers.

Information regarding radiation targets, fractionation, total radiation dose, and CT slice thickness was retrieved from the radiotherapy charts. For dose estimation, the dose distribution from the treatment plans was used and all dose estimation was done in the Eclipse® treatment planning system (Varian Medical Systems Inc., Palo Alto, California USA) using the analytical anisotropic algorithm (AAA). Patients treated from 1997 to 2005 were planned with the older system TMS® (Helax AB, Uppsala, Sweden) and for study purpose their treatment plans and CT scans were imported to the Eclipse system for delineation and dose calculation. The ethics committee (EPN) of Northern Sweden approved the study.

Delineation

The contouring of the coronary arteries was performed in the Eclipse dose planning system by three clinically experienced radiation oncologists from different centres in Sweden, independently of each other. The validated heart atlas by Feng et al. was used as a guideline for the delineation of the coronary arteries and delineation was attempted in each CT slice [21]. The left main coronary artery (LMCA), the left anterior descending artery (LAD), and the right coronary artery (RCA) were delineated and the arteries were divided into segments corresponding to the proximal, mid, and distal parts of the arteries (Fig. 1). In the majority of the CT slices, the coronary arteries were visible but in difficult cases anatomical landmarks such as the left interventricular, left atrioventricular, and the right atrioventricular grooves were followed and the interpolation function in the target planning system was used. No extra margin was added to the contours.

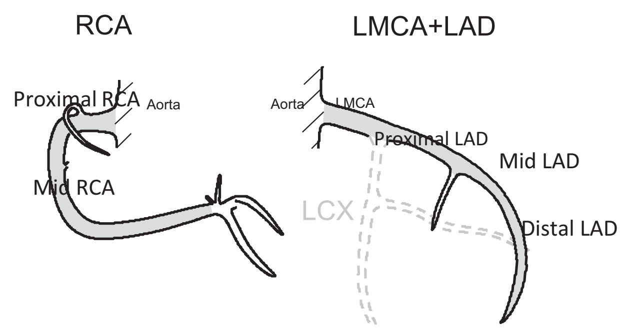

Fig. 1. Coronary arteries: the right coronary artery (RCA), the left main coronary artery (LMCA), the left anterior descending artery (LAD), and the left circumflex artery (LCX). RCA and LAD further subdivide into three segments: Proximal, Mid, and Distal.

Evaluation of inter-observer variation in spatial distance

In order to evaluate the spatial variation, the x-, y-, and z-coordinates of the centre of the arteries LMCA-LAD and RCA were determined for each of the 96 combinations of the 32 patients and the three radiation oncologists. The CT-slices determined the z-coordinate, whereas the x- and y-coordinates were determined using the centres of mass of the contoured area. For the sections of the arteries running in the same plane as the CT slices, the artery centre point was determined as a weighted average of the centres of mass of the contoured areas. The weights were proportional to the contour areas. By applying this procedure sequences of n

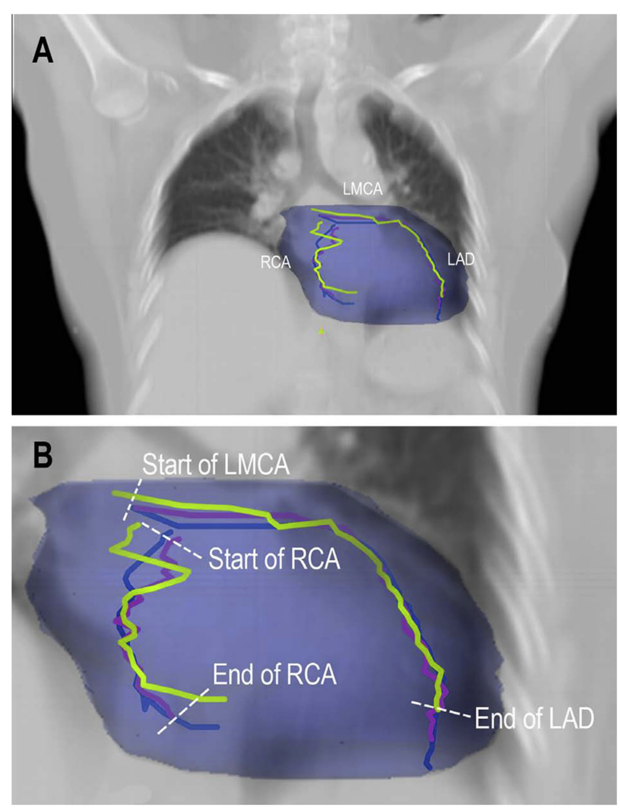

Fig. 2. (A) CT-scan of a representative patient, in which the three different radiation oncologists LMCA-LAD and RCA-curves are plotted. (B) The definition of the start and end points of the curves.