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Contouring of the left anterior descending coronary artery in patients with breast cancer – the radiation oncologist's view

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Breast cancer is the cancer with the largest prevalence, both in Poland and worldwide. The standard treatment in patients with this disease is breast-conserving therapy (BCT), followed by whole breast radiotherapy (WBRT) with a boost dose applied to the area of the bed created after tumour resection. In women who have undergone breast amputation – in the presence of poor prognostic factors – the chest wall is irradiated with or without the irradiation of the axillary fossa and clavicular area. Radiotherapy is used as an adjuvant treatment in connection with the high rate of relapses in the area of the treated breast – as much as 20% after 10 years. Some patients, before the commencement of the irradiation, are treated systemically with the use of regimens comprising drugs with a high degree of cardiotoxicity. This effect may even be increased during the course of radiotherapy – mainly in patients after amputation of the left breast. The side-effects induced by radiotherapy depend on area of the heart within the field of irradiation. Studies suggest that the vulnerable parts of the heart are the coronary vessels, and primarily, the left anterior descending (LAD) artery, which is located close to the chest wall.

The objective of this study is to present practical guidelines concerning contouring the left anterior descending (LAD) artery in patients with cancer of the left breast, who have qualified for radiotherapy.

Contouring the LAD seems to be significant as a method of assessing the critical organ during radiotherapy. The results may cause a modification of the treatment strategy: a change to the planned radiotherapy, the quantity of the beams and/or their angle of incidence or a change in the beam weight.

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Key words: LAD, radiotherapy, breast cancer

Introduction

Breast cancer is the most frequently occurring type of cancer, both in Poland and worldwide [1]. The standard treatment in patients with this disease is the breast-conserving therapy (BCT), followed by whole breast radiotherapy (WBRT) with a boost dose applied to the area of the bed created after tumour resection. In women who have undergone breast amputation – in the presence of poor prognostic factors – the chest wall is irradiated with or without the irradiation of the axillary fossa and clavicular area. Radiotherapy is used as an adjuvant treatment in connection with the high rate of relapse in the area of the treated breast – as much as 20 % after 10 years [1, 2].

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Materials and methods

50 patients treated in the Radiotherapy Department of the Oncology Centre in Bydgoszcz were qualified to the study. All the patients had breast cancer and had been surgically treated: in 14 of them a breast had been amputated, and in 36 of them BCT (breast conserving therapy) had been applied. All the women had indications for adjuvant radiotherapy. After qualification for the treatment, a routine CT for radiotherapy planning was performed (Tab. Ia, Ib, Ic).

CT was performed in patients in the lying position with limbs abducted and rotated with the use of a Posirest support. Before assessment, a tracer was applied on the entire length of the scar. The scans were made every 3 mm, during free and gentle breathing, whilst the images were sent to an Eclipse planning system with the use of a DICOM system. In each patient apart from the standard clinical target volume (CTV) and risk organs, LAD was contoured. One examiner identified the location of the LAD on the basis of the course of the anterior interventricular sulcus, whilst the other (in an independent manner) – controlled the LAD contouring.

In the patients who had undergone breast amputation, the area of clinical target volume (CTV) comprised the entire chest wall together with the resection bed, skin, muscles, deep fascia and ribs; with a margin of 0.5 cm to the planned target volume (PTV) and adaptation to the anatomic structures with a total dose of 45 Gy in 20 fractions. In the patients who had undergone BCT, the CTV area comprised the entire breast and the tumour resection bed, sparing the lower lying muscles, ribs and skin; with a margin of 0.5 cm to PTV and adaptation to the anatomic structures with a total dose of 42.5 Gy in 17 fractions. In some patients a boost was carried out with brachytherapy, at a dose of 10 Gy in 1 fraction, whist in the remaining patients – with the use of and external beam at a total dose of 10–12 Gy in 4–6 fractions, with 2–2.5 Gy per fraction.

In radiotherapy planning, most frequently, 2 tangential fields with adaptation of the posterior border were applied, with the use of mechanical and/or dynamic wedges of 15–30 degrees and photon radiation with the energy of 6 and 15 MeV. In the majority of patients who had undergone mastectomy, a tissue-like bolus was required, whilst some patients who had undergone BCT needed a strip of tissue-like bolus in the midline.

Results

After analysis of the contouring of LAD in 50 patients by 2 independent examiners and after comparison of their drawings, the following conclusions were drawn:

1. The LAD is invisible in some places and its location should be interpolated from the previous scans.
2. The LAD is best visible in women with coronary atherosclerosis.
3. Coronary vessels are best visible for contouring in the windows from +600 to 800 and –150 to –200 Hausfield units (HU).
4. The easiest way to identify the LAD is to begin with the upper part of the heart, where this artery is located between the left and right heart ventricle and to right of the descending aorta – i.e. in the place where the LAD

Table Ia. Mean maximum dose (Dmax), mean minimum dose (Dmin), mean average dose (Dmean) and mean median dose (Dmed) for the heart and LAD in all patients

	Dmax (Gy)	Dmin (Gy)	Dmean (Gy)	Dmed (Gy)
Heart	42.10	0.57	5.08	1. 87
LAD	41.46	3.21	30.03	32.22

Table Ib. Mean maximum dose (Dmax), mean minimum dose (Dmin), mean average dose (Dmean) and mean median dose (Dmed) for the heart and LAD for the patients who had undergone BCT

	Dmax (Gy)	Dmin (Gy)	Dmean (Gy)	Dmed (Gy)
Heart	42.62	0.58	5.96	2.34
LAD	40.94	3.91	32.11	35.45

Table Ic. Mean maximum dose (Dmax), mean minimum dose (Dmin), mean average dose (Dmean) and mean median dose (Dmed) for the heart and LAD for the patients who had undergone mastectomy

	Dmax (Gy)	Dmin (Gy)	Dmean (Gy)	Dmed (Gy)
Heart	41.39	0.42	5.45	1.48
LAD	41.31	3.46	31.05	32.63

branches away from the main left coronary artery, and then runs towards the front and down towards the heart apex.

5. There were significant differences observed between specific CT scans with regards to the location of the LAD, which were connected to its tortuous course, and which led to significant difficulties in interpolating its location on the next scans.
6. The vessel is so small near the heart apex that it is rarely visible.
7. In about 1/3 of the upper part of the heart LAD is poorly visible; the anterior interventricular sulcus must be located as the artery runs in this area.
8. During contouring, it was observed that the LAD in 1/2 or 1/3 of the heart length is adjacent to the chest wall from the inside (this concerned the majority of the patients).
9. The area in which the LAD was adjacent to the chest wall was largest in women with heart disease and the vessel did not have a circular cross-section,
10. In the group of young and very slim patients, there were cases in which the LAD and the entire heart were not adjacent to the chest wall so the dose applied to these structures was minimal and, moreover, the cross-section of vessel in these patients was circular, which significantly facilitated its identification.
11. In patients with a lower body mass index, a thinner chest wall and/or a small amount of fatty tissue in the pericardium, the dose per LAD was higher than in patients with a larger amount of the pericardial fatty tissue, which isolated the LAD from the chest wall, thus increasing the distance between them.
12. A comparison of the contouring of the left anterior descending (LAD) artery made by two independent examiners did not reveal any significant differences, and these differences decreased even more with an increase in the experience in locating the vessel and in precision in contouring,
13. When, in accordance with the suggestions of other authors, a 1 cm margin was added around the vessel with regard to difficulties in contouring and the respiratory mobility of the heart, all the patients then had the LAD located in this area, irrespective of the person who performed the contouring of the risk organ; and when the examiners had more experience in contouring, a margin of 0.5 cm was sufficient.

Discussion

Clinical studies carried out among patients with breast cancer point to the benefits in adjuvant radiotherapy, after both BCT and breast amputation, where the risk of recurrence is high. The side-effect connected with radiotherapy is an increase in cardiological incidents, which might lead to death [3–5].

Irradiation may cause 2 types of cardiovascular disease: micro- and macrovascular diseases. The first group is characterised with a decrease in the density of the vessels within the heart leading to chronic heart ischemic disease and myocardial infraction secondary to focal degeneration. In macrovascular diseases, in turn, irradiation accelerates and/or intensifies the development of coronary atherosclerosis [6].

Currently, many strategies are applied in order to minimize the effects of systemic treatment and/or radiotherapy. Modern methods of reducing cardiotoxicity comprise radiotherapy planning techniques: the use of coplanar beams, megavolt energy, intensity-modulated radiotherapy (IMRT), deep inspiration breath hold (DIBH), spiral tomotherapy or irradiation with the use of special immobilisation used when a patient is in the prone position – for women after breast conserving surgery [2, 6].

Retrospective studies carried out among women with breast cancer showed a significant effect of irradiation on the heart and, consequently, an increase in the cardiotoxicity of this type of treatment; some correlation was observed between the mortality rate and the dose-volume histogram (DVH) in this critical organ, namely the heart [3–5].

Radiotherapy-induced adverse effects depend on the region of the heart which is contained in the field of irradiation. Studies suggest that these important areas are made up of the coronary vessels, and, primarily the LAD, which is located in close proximity to the chest wall. The LAD contouring seems, therefore, significant for the assessment of the critical organ during radiotherapy. The results of contouring may influence the modification of the treatment strategy: a change of the technique of the planned radiotherapy, the quantity of the beams and/or their angle of incidence or a change of the beam weight [7, 8].

The results of many clinical studies suggest that patients with cancer of the left breast are exposed to a larger risk of cardiovascular complications than those with cancer located in the right breast [2, 4, 5]. Tanaka states that in patients with breast cancer receiving radiotherapy, the mortality rate connected with heart disease was between 1.27 and 1.76 times higher than in patients without radiotherapy [9]. Borger et al. estimated that for patients with left breast cancer who received radiotherapy with the use of tangential fields, the rate of cardiological complications was 1.38 (95% confidence interval: 1.09–2.15) in comparison with a location in the right breast [10].

It must also be remembered that patients with breast cancer make up a group in whom radiotherapy planning is very difficult – in particular in women after mastectomy, in whom the chest wall thickness is very low, which increases the quantity of the irradiation deposited in soft tissue. This leads to the fact that a larger dose is administered to the lung and/or heart parenchyma, and that dose is also administered onto a larger area [2]. Studies clearly show that each dose increase by 1 Gy for the heart, results in an increase of mortality rate by 3% within 20 years [2]. In patients with chest wall radiotherapy, asymptomatic disorders of the perfusion of the heart vessels, occurring within 6 to 24 months of the completion of radiotherapy are observed [11, 12]. There are some individual reports which exclude the effect of radiation dose on the heart, yet these reports were published in the last century, where treatment planning and realisation were completely different so now it is difficult to make any reference to these reports [2].

The largest difficulty in contouring the LAD is the fact that in the majority of centres no contrast agent is administered for the CT when planning radiotherapy. This significantly deteriorates the visibility of the course of the vessel, in particular given the fact that this artery is very small and has a tortuous course, and its diameter is usually 3 mm (and at the apex – about 1 mm) [13].

Venarini et al. used computed tomography with optimum image resolution obtained thanks to a detector measuring 0.5 mm, yet the patients' breath and the kinetics of circulation led to blurring of the image, which made imaging of the LAD very difficult [13]. During the contouring process it was observed that the left anterior descending artery, in 1/2 or 1/3 of its length, is most frequently adjacent to the chest wall from inside. In this very place, the LAD is also located close to the sternum, and, because of this location and the necessity of irradiating the whole chest wall in patients who have undergone breast amputation, when adding a margin to clinical target volume (CTV), the LAD lies within the planned target volume (PTV). This allowed the clinicians to draw conclusions and introduce corrections while contouring and treatment planning. Much more attention was paid to the correctness of the LAD contouring and target volumes so that the part of the artery within the field of the therapeutic beam could be limited and/or the creation of "hot spots" i.e. areas of high dose could be reduced.

Venarini et al. assessed the location of the left anterior descending artery in 25 breast cancer patients and presented practical guidelines for contouring this structure. They emphasised that the location of the LAD is, in some places, invisible, and therefore must be interpolated from previous scans, whereas the visibility of the vessel is also negatively affected by artefacts created by breathing and the heartbeat [13].

Jagsi et al. [14] in turn, evaluated the size of the relocation of the left anterior descending artery in a group of 10 patients and observed that the largest movements of the LAD occur in the vertical (up and down) plane. At the same time, they stressed that a good visualisation and the possibility of contouring allowed for the exclusion of the LAD from the irradiated volume. Venarini et al. in their study, specified the doses for critical organs, and found that the observance of these doses may have some influence on the protection of those organs. They calculated the maximum admissible dose for the LAD, being for D2% from 2.7 to 41.7 Gy, and V 25 Gy for the heart should be lower than 6%, and most frequently it was 1.5% with standard deviation being +/–2.1% [13].

Di Franco et al. [6] pointed to difficulties in LAD contouring, observing, at the same time, that with regards to the difficulties in contouring and the respiratory mobility of the heart, a 1 cm margin should be added around the vessel [6]. In our opinion, a 0.5 cm margin is sufficient around the LAD, provided that the examiner has gained practical skills in contouring. Certainly, in patients with large respiratory mobility of the heart and with difficulties in vessel visualisation, adding a 1 cm margin might turn out to be necessary.

In the case of patients with a burden of cardiological comorbidities, a selection of other radiotherapy planning and realisation techniques must be taken into consideration. The DIBH technique is one of the ways of minimising the dose of radiation for the heart and coronary vessels [15–18]. Thanks to this technique the Dmax and Dmean for the LAD decrease by approximately 50–60%. This is a very useful form of therapy, but also very time consuming and the capacity is lower as well. Moreover, this form of therapy forces a patient to maintain strict cooperation during the entire treatment process, which is sometimes difficult or even impossible.

Blank et al. [19] reported that the time span between entering the apparatus and administering the first fraction of treatment with slow breathing was, on average, 42 minutes, whilst the time span of conventional treatment was 15 minutes [19].

Our observations show that in patients with a larger quantity of fatty tissue and a thicker chest wall, the dose deposited on the LAD area was lower than in the case of persons with a thin chest wall and/or smaller amount of the fatty tissue. Similar observations were made by Tanaka et al. [9]. In patients with a lower body mass index, a thinner chest wall and a small amount of fatty tissue in the pericardium, the irradiation dose for the LAD was higher than in patients with larger amounts of pericardial fatty tissue which isolated the LAD from the chest wall, increasing the distance between them. In multivariant analysis, BMI was significantly correlated with Dmax, V 20 Gy and V 30 Gy. In patients with BMI ≤22 kg/m^2 and with BMI >22 kg/m^2 there were significant differences in the Dmean and V 40 Gy doses[9].

In the study of Niedere et al. [20] the average LAD volume was 1.94 cm (1.28–2.86). Planning was carried out with the use of 3D and IMRT techniques. As in some patients, PTV was very close to the LAD, it was not possible to reduce the dose of irradiation there. In the case of planning with the use of the IMRT technique, the deposited radiation was much lower in comparison with the 3D technique. And thus, in the case of a small LAD volume, 100% of the vessel received the prescribed dose, and with the IMRT technique the reduction of the mean dose was 44%. Maximum accepted doses and volumes for the LAD, adopted by the authors of the study were: a maximum 60% dose for any LAD volume, a 20% dose for 75% LAD volume, a 40% dose for 50% LAD volume and a 50% dose for 20% LAD volume [20].

Conclusions

The contouring of the left anterior descending artery is always difficult, but may reduce the post-radiation side effects, and therefore may allow for a lower rate of cardiological incidents. Thanks to this process, the treatment planning and execution may be modified on the basis of the LAD location. However, further prospective studies carried out on larger groups of patients are necessary.

Conflict of interest: none declared

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