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Original research paper

THE COMPARISON OF THE RADIATION LOAD TO THE HEART AND THE LEFT ANTERIOR DESCENDING CORONARY ARTERY FOR VARIOUS MODES OF RADIATION TREATMENT OF THE BREAST CANCER PATIENTS*

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Abstract. *The aim of this paper is to compare the levels of radiation exposure in three variants of BC (breast cancer) exposure. The study involves dosimetric radiotherapeutic (RT) plans of 20 female patients with left BC. Pre-irradiation preparation included 3 sessions of CT scan: patient in standard dorsal position with tidal respiration (STR), in dorsal position with controlled breathhold on top inspiration (DBH) and in prone position with tidal respiration (PTR). 3D-plan dosimetric calculations were performed for three CT-sessions. Dose-volumetric measures for organs at risk (OAR) were assessed for every irradiation option. Contoured heart volume in all studied variants varied within 477 cm^3 - 1056 cm^3, mean volume of 769 cm^3. The best values, such as V25, average doses per heart and LAD (Left arteria descending) were received using DBH method (V25 heart 4.26%, D mean heart 3.13 Gy, DmeanLAD 13.8 Gy) as compared to STR method (V25 heart 9,49%, D mean heart 4.97Gy, DmeanLAD 19.55Gy) and PTR-position (V25 heart 12,8%, Dmean heart 9.06Gy, DmeanLAD 24.18Gy) (V25 heart P = 0.00153, D mean heart: P =0.000; D mean LAD: P = 0.00088), with the inclusion of Mamma Glandule (MG) and axillary LN in the total volume. The preferences of STR- and DBH-related dosimetric values remained unchanged followed by the inclusion of supraclavicular and infraclavicular lymph nodes (LN) in the total volume. DBH method (V25 heart 3.49%, D mean heart 3.07Gy, DmeanLAD 13.88Gy) was compared to STR method (V25 heart 7.91%, D mean heart 4.99 Gy, DmeanLAD 19.89Gy) (V25 heart P = 0.00205, D mean heart: P =0.004; D mean LAD: P = 0.03). Irradiation in dorsal position was performed with controlled breath hold while full inspiration was associated with a statistically significant decrease of the heart volume, which was exposed to more than 25 Gy (V25heart), average heart dose, average LAD dose.*

Key words: *Breast cancer, radiotherapy, heart, left anterior descending coronary artery (LAD), controlled breath hold*

1. Introduction

Conservative surgery represents the standard approach in breast cancer therapy [1]. It has been proved that adjuvant RT reduces the frequency of local relapses and increases the indices of total survival [2]. In addition, there is a probability that BC RT can induce the progression of cardiovascular diseases (CVD). Meta-analysis shows a significant predominance of death unrelated to breast cancer in the group of patients receiving adjuvant radiotherapy compared to the patients who did not receive such therapy. The main cause of death was represented by CVD [2]. However, it should be mentioned that these results are based on 2D RT findings. Advanced technologies (3D conformal RT, IMRT, VMAT) reduce heart and ipsilateral lung exposure, maintaining the adequate coverage of the target volume [3, 4, 5, 6]. But yet, the dose levels per heart and LAD in the course of dorsal RT remain rather high [7, 8]. Darby et al. have shown that the impact of ionizing radiation (IR) per heart can significantly induce the risk of delayed CAD. The authors note that every 1Gy in average dose with exposed heart increases the risk of main coronary vessel disease by 7.4% [9]. The reduction of OAR radiation exposure is of paramount importance in the setting of increased lifespan among BC patients and, thus, the rising probability of late complications.

The study of various radiation and patients' positioning options focused on the reduction of dose per organ at risk and target coverage comparison revealed that RT with controlled breath hold leads to the reduction of the heart and lung exposure, since inhalation is followed by the separation of the heart and exposed target volume and the reduction of lung tissue density [10].

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It is also considered that prone position can reduce heart and lung exposure [11, 12]. The exposure benefits in this position, with the reduced irradiation of the lung tissue among all patients and the reduced heart volume subjected to radiation exposure, are mainly applicable to patients with big mammae (≥1000 cm^3) in comparison to dorsal position [11, 13, 14, 15].

The purpose of this study resides in the prospective comparison of three various options of whole MG irradiation with/without supraclavicular and infraclavicular LN: standard dorsal position with tidal respiration (STR), dorsal position with controlled breathhold on top inspiration (DBH) and prone position with tidal respiration (PTR).

2. Materials and techniques

RT plans of 20 patients with left BC were prepared for analysis in the Federal state budgetary institution “Russian Research Center of Radiology and Surgical Technologies” of the Ministry of Health of the Russian Federation. 8 dosimetric plans were calculated for every studied case based on three CT-scan sessions without intravenous contrast:

1. In dorsal position, using an individually modified breast-board with tidal respiration, with/without the inclusion of supraclavicular and infraclavicular LN (plan 1/2), Fig. 1A;

2. In prone position, using a prone-board without/with the inclusion of axillary LN (plan 3/4), Fig.1B;

3. In dorsal position, using an individually modified breast-board with controlled breathhold, with/without the inclusion of supraclavicular and infraclavicular LN (ptv 1.0 cm) (plan 5/6), Fig.1C;

4. In dorsal position, using an individually modified breast-board with controlled breathhold, with/without the inclusion of supraclavicular and infraclavicular LN (ptv 0.5 cm) (plan 7/8), Fig.1C.

ABC device (Elekta, Sweden) was used for the active control over breathhold on top inspiration – its construction was comprised of a personal computer with specific software installed, a spirometer, and a respiratory tube (for patient’s breathing during the entire procedure of RT). After the passage of the threshold air volume through the spirometer (set individually in the training course), the valve built in the respiratory tube interrupts the respiratory cycle at a given value.

The average fractionation was applied. The fraction dose was 3Gy, the physical total boost dose (TBD_{phys}) per mammary gland was 42Gy, whereas in case of supraclavicular and infraclavicular LN inclusion – it was 39Gy. The planning was performed using standard opposing fields with the addition of 2-3 segments to every field. Irradiation was performed by high-energy photons MeV (Fig. 2.).

DVH (dose-volume histogram) was generated for all contoured structures within all plans per every patient. The following values were calculated for the ipsilateral lung: exposed volume percent ≥28Gy (V_{28lung} α/β 9) for early pulmonitis and exposed volume percent ≥ 25Gy (V_{25lung} α/β 3.1) for late complications – pulmonary fibrosis.

A

B

C

Figure 1. 1a-in dorsal position with tidal respiration, 1b-in prone position using prone-board, 1c-in dorsal position with controlled breathhold

CT findings were transferred to the station of dosimetric planning (Xio, Elekta). Heart and LAD were contoured based on the recommendations of Feng et al., who developed the atlas of heart and coronary artery contouring [14]. All stages of pre-irradiation preparation were performed by the same team, which included a topometrist and a radiotherapist (Fig. 2).

DVH (dose-volume histogram) was generated for all contoured structures within all plans per every patient. The assessment of Dmean and Dmax per heart and LAD and also the volume rate (in %) was performed for doses ≥8.33 Gy (V 8.33), 12.5Gy (V 12.5), 16.67Gy (V 16.67), 20.83Gy (V 20.83), 25Gy (V 25) and re-estimated for the standard fractionation mode when heart α/β was equal to 3.

The statistical analysis was performed using the program STATISTICA 12.

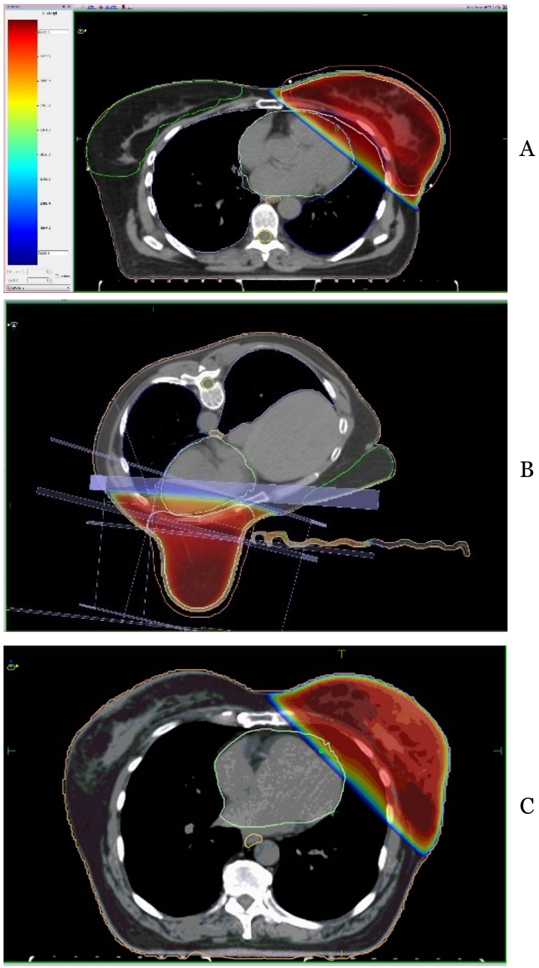

Figure 2. 2a-in dorsal position with tidal respiration, 2b-in prone position using prone-board, 2c-in dorsal position with controlled breathhold

Descriptive statistics were used for dose-volumetric parameters using the analysis of variance, focused on the correlation search among experimental data via diversity investigation of differences in average values, which enabled the comparison between three and more groups. This approach was developed by Fisher and it focused on the outcome analysis of experimental studies. For all statistical tests, P<0.05 was statistically significant.

3. Results

The comparison of Dmeanheart revealed that the best results were achieved in the DBH group, the worst – in prone position (Table 1, Fig. 3).

During the comparison of STR, DBH and PTR plans, with only the exposition of MG and axillary LN, the least Dmean of heart values were recorded in dorsal position with controlled breathhold, the worst – in prone position (p=0.000) (Fig. 4, Table 1).

Dosage analysis per heart in STR, DBH and PTR plans with the inclusion of supraclavicular and infraclavicular LN (STR versus DBH positions) shows that the lowest Dmean values per heart were recorded in dorsal position with controlled breathhold (p=0.004), (Fig. 5, Table 1). Substantial irradiation of supraclavicular and infraclavicular LN in prone position does not seem technically possible.

Table 1. The comparison of Dmeanheart

Group	№	Mean Dose,cGy	Median, cGy	MinDose, cGy	Max Dose, cGy	Std Dev	Stan dard
All series CT	**160**	464.08	421.5	82.0	1395.7	307.23	27.37
STR+LN	20	499.52	480.0	219.2	806.2	158.30	39.58
STR-LN	20	496.63	476.95	200.8	821.70	164.45	41.11
PTR-LNAx	20	805.6	778.2	417.3	1316.5	272.3	70.49
PTR+LNAx	20	906.31	857.4	511.3	1395.7	274.66	70.92
DBH+LN ptv 1.0cm	20	307.74	256.55	100.2	759.6	188.84	47.21
DBH-LN ptv 1.0cm	20	313.27	270.45	110.7	701.3	173.76	43.44
DBH+LN ptv 0.5 cm	20	213.66	153.05	82.0	532.3	133.10	33.28
DBH-LN ptv 0.5 cm	20	218.86	167.0	87.6	486.9	122.05	30.51

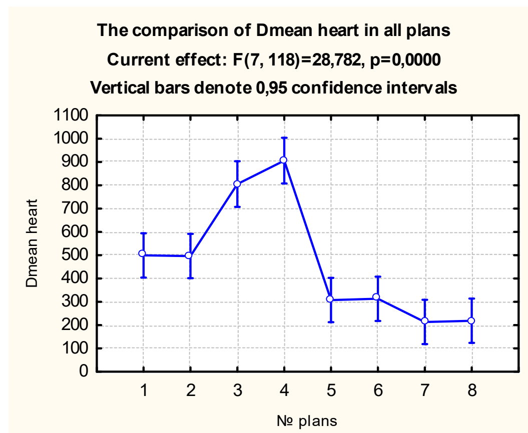

Figure 3. The comparison of Dmean heart in all plans

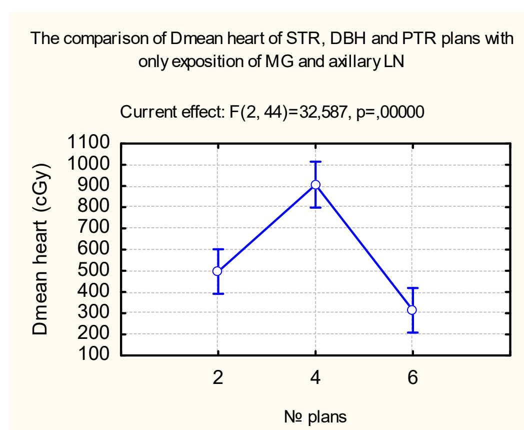

Figure 4. The comparison of D mean heart of STR. DBH and PTR plans with only exposition of MG and axillary LN

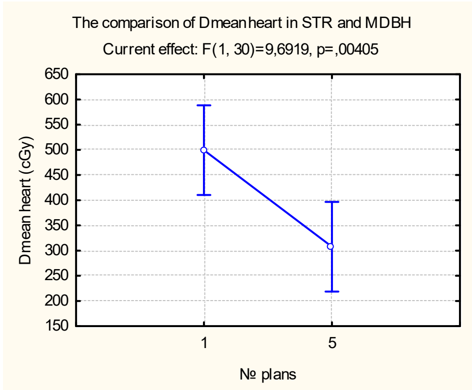

Figure 5. The comparison of Dmean heart in STR and MDBH techniques with exposition of MG. supraclavicular, infraclavicular and axillary LN

The same pattern was observed during the estimation of V25 values per heart. The greatest doses per V25 of the heart were received in prone position, where the lowest – in dorsal position, with/without the exposition of supraclavicular and infraclavicular LN. These differences were statistically significant (Fig. 6,7; Table 2).

Table 2. The comparison of V heart in all plans

Heart α/β 3	$V_{8.33}$	$V_{12.5}$	$V_{16.67}$	$V_{20.83}$	$V_{25.00}$
All series CT	13.25063	10.70147	9.211587	7.808254	6.669151
STR+LN	12.67687	10.88750	9.715000	8.773750	7.917063
STR-LN	17.08000	12.77188	11.49125	10.45437	9.495625
PTR-LNAx	25.93067	21.60600	18.38000	15.09800	12.82267
PTR+LNAx	27.63667	22.26067	18.91200	15.33000	12.69867
DBH+LN ptv 1.0cm	6.935000	5.557188	4.740625	4.082500	3.496250
DBH-LN ptv 1.0cm	9.320000	7.726250	6.591250	5.490000	4.256875
DBH+LN ptv 0.5 cm	4.063750	3.110625	2.526250	2.083750	1.715000
DBH-LN ptv 0.5 cm	4.053750	3.095625	2.515625	2.079375	1.712500

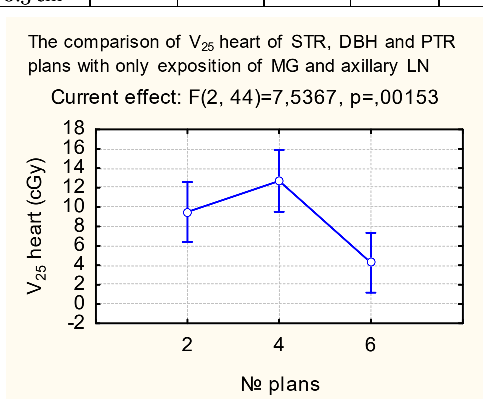

Figure 6. The comparison of V25heart of STR, DBH and PTR plans with only exposition of MG and axillary LN

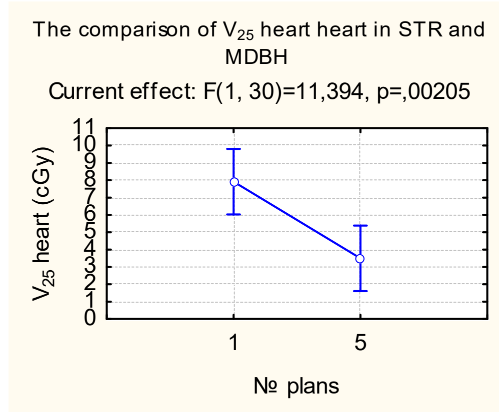

Figure 7. The comparison of V25 heart in STR and DBH techniques with exposition of MG, supraclavicular, infraclavicular and axillary LN

Table 3. The comparison of Dmean LADin all plans

Group	№	Mean Dose. cGy	Median cGy	Min Dose. cGy	Max Dose. cGy	Std Dev	Standard
All series CT	160	1669.563	1852.400	212.0000	3671.200	883.9735	78.75062
STR+LN	20	1989.331	2131.700	737.5000	2826.700	626.1240	156.5310
STR-LN	20	1955.694	2076.250	735.3000	2817.800	615.4277	153.8569
PTR-LNAx	20	2309.400	2334.400	1170.000	3172.600	576.6749	148.8968
PTR+LNAx	20	2418.633	2394.200	1305.300	3244.600	595.7888	153.8320
DBH+LN ptv 1.0cm	20	1388.456	1306.750	314.2000	3671.200	870.9292	217.7323
DBH-LN ptv 1.0cm	20	1380.856	1291.500	335.7000	3655.700	855.0114	213.7529
DBH+LN ptv 0.5 cm	20	988.8750	743.4000	212.0000	3271.700	804.1131	201.0283
DBH-LN ptv 0.5 cm	20	1012.069	749.3500	216.0000	3359.400	817.1166	204.2792

Similar results were achieved for Dmean LAD – certain lower doses per LAD are observed in dorsal position with controlled breathhold versus dorsal position with tidal respiration and prone position without the inclusion of supraclavicular and infraclavicular LN (p=.00088) (Table 3.4). In the setting of supraclavicular and infraclavicular LN inclusion, the preferences of DBH versus STR methods were also observed (p=0.03260) (Table 3.5).

Table 4. The comparison of Dmean heart. Dmean LAD, V25 of STR, DBH and PTR plans with only exposition of MG and axillary LN

	STR	PTR	DBH	P-value
$D_{mean\ heart}$. cGy	496.62	906.3	313.27	p=.00000**
$D_{mean\ LAD}$cGy	1955.69	2418.6	1380.85	p=.00088**
V_{25}	9.49	12.82	4.25	p=.00153*

Table 5. The comparison of Dmean heart, Dmean LAD, V25 heart in STR and MDBH techniques with exposition of MG, supraclavicular, infraclavicular and axillary LN

	STR	DBH	P-value
$D_{mean\ heart}$. cGy	499.5188	307.7375	p=.00405*
$D_{mean\ LAD}$cGy	1989.331	1388.456	p=.03260*
V_{25}	7.917063	3.496250	p=.00205*

The comparison of these outlined indices: Dmean LAD was performed. Dmean and V25 per heart outlined the following patterns: 1. the dorsal position with controlled breathhold including only MG and axillary LN is the most preferable in the context of heart and LAD irradiation reduction; 2. PTR method was the worst according to all indices – Dmean LAD, Dmean and V25 of the heart. All results were statistically significant (Table 4).

The analysis of Dmean LAD, Dmean and V25 values using STR and DBH methods performed with the field inclusion of supraclavicular and infraclavicular LN also reveals the benefits of DBH positioning based on all indices (Table 5).

4. Discussion

Low doses per OAR and sufficient target coverage represent the indispensable prerequisites for reduced RT toxicity among BC patients, the life span of which can be increased due to the use of advanced combined methods of therapy.

The lowest doses per heart and LAD within our study were recorded in dorsal position with the active breathing technique in comparison to dorsal and prone positions with tidal respiration. All these results for controlled breathhold on top inspiration match the findings of other studies [11, 15, 16, 17, 18, 19, 20, 21, 22, 23]. As it has been demonstrated by Chino et al., the maximum doses per heart were recorded in prone position, which is explained by 19 mm of anterior heart extrusion [2].

This is the first Russian comparative study based on the distribution of dose-volumetric measures per OAR using three methods. In contrast to the published foreign works, we also compared STR and DBH methods with the additional irradiation of supraclavicular and infraclavicular LN.

The main benefit of the active breathing technique during the course of RT in dorsal position is maintained by the reduction of heart and LAD exposure. This technique can also be applied for supplementary RT in the area of regional LN [24], which has been confirmed within our study. The limitation of RT with active breathing technique resides in patient's preliminary education and training. Patients should be in good physical shape and master the technique of thoracic breathing instead of abdominal. The application of the breathing technique expands the RT procedure due to the reduction of the operating cycle [19,25,26]. The comparison of these methods should include both doses per OAR and technical repeatability.

Pronounced perspectives: we believe that further reduction of radiation exposure per OAR can be achieved via the improvement of target control (due to the extrusion of the thoracic wall during the respiratory cycle) and corresponding gain reduction of planned target volume (PTV).

All therapeutic interventions are characterized by certain benefits and drawbacks. We recommend considering an individual solution in every specific case during the development of the RT plan.

5. Conclusions

Dose decline per OAR can be achieved via the performance RT in dorsal position with controlled breathhold on top inspiration. Radiotherapy in dorsal position with controlled breathhold on top inspiration is the best of the studied techniques for reduced heart and LAD exposition.

RT in prone position has not measured up to our expectations related to the reduced heart and LAD exposition and it conversely resulted in the worst indices of dose-volumetric distribution over the studied OAT.

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