

**Case report**

**doi:10.5633/amm.2024.0411**

**Postoperative three-dimensional conformal radiotherapy in the patient with a significant cardiovascular risk – case report**

Milica Radić<sup>1,2</sup>, Aleksandar Popović<sup>1</sup>, Katarina Krasić<sup>3</sup>, Andrija Jović<sup>4</sup>, Irena Conić<sup>1,2</sup>, Ana Cvetanović<sup>1,2</sup>,  
Ivan Petković<sup>1,2</sup>

<sup>1</sup>Clinic of Oncology, University Clinical Center Nis, Nis, Serbia

<sup>2</sup>Department of Oncology, Faculty of Medicine, University of Nis, Nis, Serbia

<sup>3</sup>Clinic of Oncology, Clinical Center Kragujevac, Kragujevac, Serbia

<sup>4</sup>Clinic of Dermatovenereology, University Clinical Center Nis, Nis, Serbia

Contact: Milica Radić

48 dr Zoran Djindjić Blvd., 18000 Niš, Serbia

E mail: milica91nis@ymail.com

AMM Paper Accepted

## **Abstract**

Radiotherapy of breast cancer represents an essential component in the overall multidisciplinary breast cancer treatment. Considering the satisfactory results of the application of the multimodal treatment as well as its role in the decrease in the mortality rate of breast cancer patients, the focus has shifted towards monitoring acute as well as chronic complications occurring as a consequence of an oncological treatment, with a view to preserving the patient's quality of life. Complications are numerous and vary from the local ones (dermatitis) to more serious forms including dysfunctions of the cardiovascular system. The application of 3D radiotherapy on the patient in this case report as the most used method in our centre points to its low acute toxic effect, while the observed negative effects in the high risk patient were removed, which resulted in satisfactory therapeutic effects despite the limited technical equipment of the centre.

**Key words:** breast cancer, cardiotoxicity, radiotherapy

AMM Paper Accepted

**Prikaz bolesnika**

**doi:10.5633/amm.2024.0411**

**Postoperativna trodimenzionalna konformalna radioterapija kod bolesnice sa signifikantnim kardiovaskularnim rizikom – prikaz slučaja**

Milica Radić<sup>1,2</sup>\*, Aleksandar Popović<sup>1</sup>, Katarina Krasić<sup>3</sup>, Andrija Jović<sup>4</sup>, Irena Conić<sup>1,2</sup>, Ana Cvetanović<sup>1,2</sup>, Ivan Petković<sup>1,2</sup>

1. Klinika za onkologiju, Univerzitetski Klinički Centar Niš, Niš, Srbija
2. Katedra za onkologiju, Medicinski fakultet, Univerzitet u Nišu, Niš, Srbija
3. Klinika za onkologiju, Klinički Centar Kragujevac, Kragujevac, Srbija
4. Klinika za dermatovenerologiju, Univerzitetski Klinički Centar Niš, Niš, Srbija

Korespondencija: Milica Radić

Bulevar dr Zorana Đinđića 48, 18000 Niš, Srbija

E mail: milica91nis@ymail.com

AMM Paper Accepted

## **Abstract**

Radioterapija raka dojke predstavlja esencijalnu komponentu u ukupnom lečenju i ranog stadijuma i lokalno uznapredovalog raka dojke. S obzirom na zadovoljavajuće rezultate, i udela u smanjenju stope mortaliteta obolelih od raka dojke, primenom multimodalnog lečenja, fokus se pomerio na praćenje akutnih, ali i hroničnih komplikacija koje nastaju kao posledica onkološkog lečenja, sa ciljem očuvanja kvaliteta života pacijenta. Komplikacije su mnogobrojne, i variraju od lokalnih (dermatitis) do nekih ozbiljnih koje obuhvataju disfunkcije kardiovaskularnog sistema. Primljena 3D zračne terapije kod pacijentkinje u ovom prikazu slučaja kao najzastupljenije metode u našem centru, ukazuje na njen nizak akutni toksični efekat, a primećeni neželjeni efekti kod visokorizičnog pacijenta su bili otklonjeni, što je rezultovalo zadovoljavajućim terapijskim efektom uprkos limitiranoj tehničkoj opremljenosti centra.

Ključne reči: karcinom dojke, kardiotoxicnost, radioterapija

## Introduction

Breast cancer represents a huge global challenge for public health considering the fact it is one of the most common neoplasmas in humans, accounting for one quarter of all cancers in women all over the world and 27% of cancers in developed countries. Breast cancer can also appear in men, but it is 100 times more frequent in women (1,2). Persons who are at a greater risk of becoming ill are those with genetic predisposition, primarily relatives, then those being on hormonal therapy for a number of years, obese people having unhealthy lifestyle. There are several types of cancer, and in clinical practice ductal is the most frequent one, then lobular, while inflammatory cancer is the rarest (3,4).

Upon receiving pathohistological verification, complete biochemical and diagnostic processing of the patient, the stage of illness as well as the plan of treatment are defined. The Medical Consilium brings the initial plan of treatment of these patients, basing its decision not only on scientifically proven facts but also taking care of maximal individualistic approach to each patient, taking into consideration his/her general health and existing comorbidities. Methods of breast cancer treatment include operative treatment, radiotherapy, chemotherapy, hormonal therapy, target therapy and immunotherapy. Depending on the type and stage of cancer, these methods of treatment can be combined, and surgical removal of cancer is most frequently followed by radiotherapy or system therapy.

Radiotherapy of breast cancer represents an essential component in the overall treatment and early stage and locally advanced breast cancer. It is based on the application of local and locoregional treatment of ionising radiation. Local refers to the radiation treatment of the rest of the breast or the scar region after radical surgery. Also, the corresponding lymphatic drainage regions can be treated by radiotherapy. The role of radiotherapy is reflected in "the sterilisation" of the treated region with a view to preventing ipsilateral recurrences, locoregional recurrences and potential dissemination of tumor cells (5).

Since the number of patients who survive breast cancer is on the increase, the focus has shifted towards monitoring and assessment of toxicity, with the emphasis put not only on acute complications of usually reversible character but also on later consequences of radiotherapy. Complications are

numerous and vary from the local ones (dermatitis) to more serious forms including dysfunctions of the cardiovascular system (6,7).

### **Case report**

At the beginning of 2022 patient D.Č. aged 54, discovered a lump the size of a walnut at the intersection of the lateral quadrants of the right breast. As part of diagnostic processing, mammography detected two stellate shadows, one next to the other, 15mm and 14mm in diameter, in the region of the right breast, at the intersection of the lateral quadrants, as well as one more stellate shadow 11x10mm in the upper lateral quadrant, which retracted the surrounding parenchyma. No abnormality was detected in the axillas and counterlateral left breast. Mammography result of the right breast was classified as Bi Rads 5, while the left breast was classified as Bi Rads 1. Taking into account Bi Rads classification, the Oncological Consilium suggested ultrasound "core" biopsy and it was pathohistologically determined that it was invasive breast cancer, with histological characteristics ER 8, PR 8, HER2 1+, Ki 67 20%.

By looking at the anamnesis and available medical documentation, it was observed that in 2017 the patient underwent surgical revascularisation of the myocard with one vein graft on RCA coronary artery, replacement of the mitral valve by the artificial mechanical valve and the plastic repair of the tricuspid valve with ring implantation. Since then she has been on the prescribed internistic therapy – application of oral anticoagulant therapy, regularly controlled hemodynamic status and regular echosonography of the heart.

Considering a significant cardiovascular disease burden as well as the multicentricity of the malignant change verified by pathohistological biopsy, the Consilium made a decision that a specific oncological treatment should begin with surgery; therefore, the patient underwent surgery in May 2022 when radical mastectomy with the dissection of the axilla was performed.

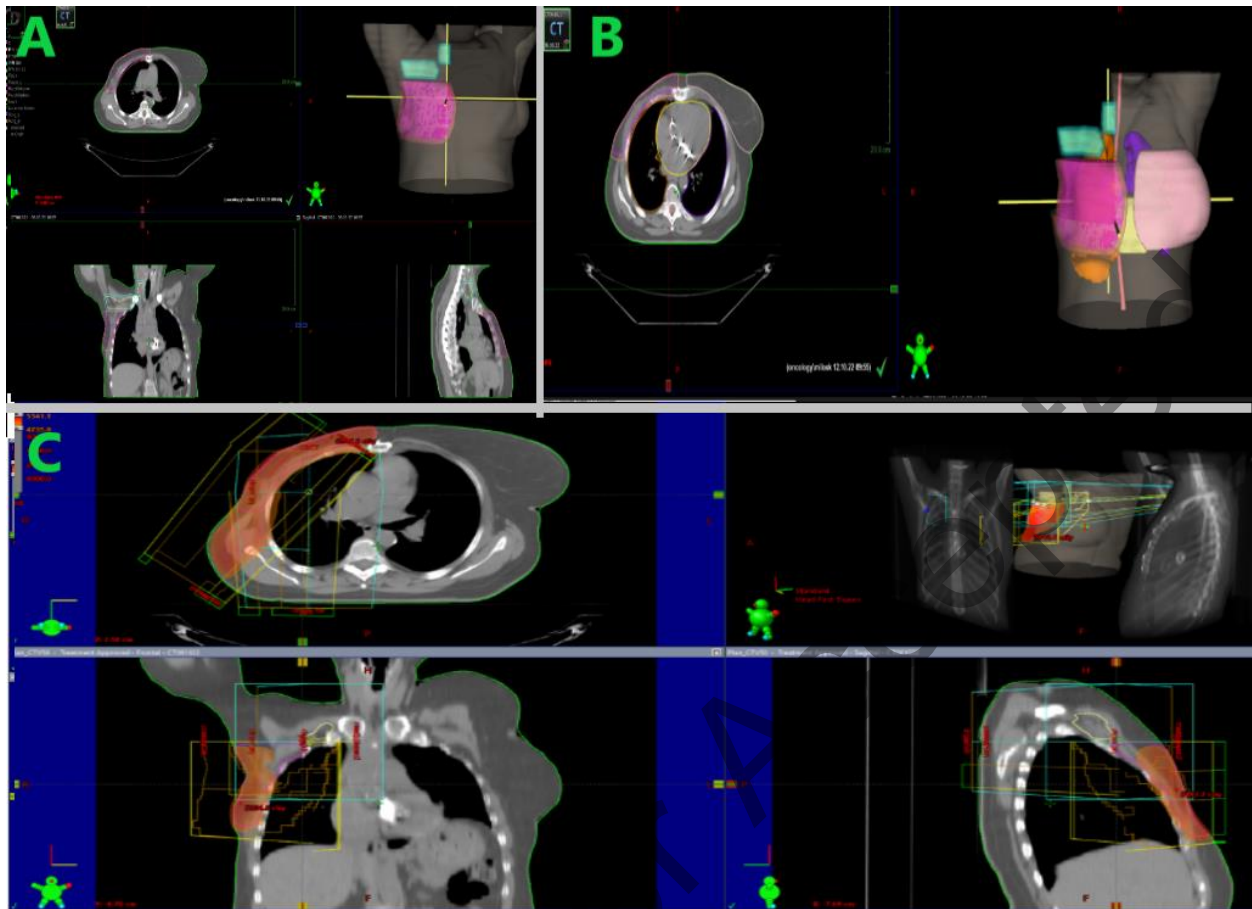
Clinical, laboratory and diagnostic processing as well as heart and lungs X-ray, MSCT of the abdomen and the lesser pelvis were done prior to the surgery in order to exclude the dissemination of the malignant process. The patient was thoroughly examined by the cardiologist, when the

echosonography of the heart was done and anticoagulant therapy was prescribed during and after the surgery so as to keep the INR in the therapeutic range between 2.5 and 3.5.

A definite pathohistological result indicated that it was micropapillary invasive breast cancer, gradus 2, dimensions 15mm and 9mm, where in 6 out of 15 extirpated lymph nodes the presence of malignant cells was detected. The disease was determined to be at stage T1cN2Mx. Biological characteristics of the tumor indicated that it was a hormone dependent breast tumor with highly positive estrogen and progesterone receptors ER 8, PR 7, Her 2 negative gene expression.

Taking this into account, in the continuation of treatment the patient was prescribed hormonal therapy with aromatase inhibitors, 1mg daily, with regular monitoring. The treatment was afterwards presented to the Consilium that indicated the continuation of the prescribed hormonal therapy with the application of locoregional radiotherapy.

During the first visit to the radiotherapy ambulance, the patient submitted control MSCT result of the thorax and abdomen, a cardiologist report with the consent to perform radiotherapy, after which she was clinically examined. The results corresponded to the performed procedures, no abnormality was detected regarding the scar tissue, and also no subjective symptoms were reported. She was processed on MSCT simulator in order to perform postoperative radiotherapy of the right hemitorax and regional lymphatics. Following the recommendations of the national radiotherapeutic protocol for the treatment of malignant illnesses by the Ministry of the Republic of Serbia from 2022, on the series of CT slices, a careful delineation of target volumes and organs form risk defined the contours encompassing the scar region with surrounding skin, where the upper and the lower boundary were at the level of tissue projection of the collateral breast. The contours of regional lymphatics included all three levels of the same side axilla as well as supra and infraclavicular regions (Figure 1).



**Figure 1.** Delineation of the target volumes (A and B); Dose distribution to target volumes (C).

Technical equipment of the radiotherapy centre in Niš referred to the application of 3D conformal radiotherapy, using the techniques of beforehand directed planning, when by combining two lateral fields with two added segment fields with a view to optimization, a satisfactory distribution of the dose was achieved. The patient was processed and was to receive TD 50 Gy in 25 fractions. By arranging the fields and using the experience of the medical physicist, it was attempted to maximally exclude the heart volume from the radiation volume, therefore, based on the Quanteq constraints determined at V10% <10 Gy, the heart in our case received on 10% of the volume only 2.88 Gy.



## Discussion

Current options for the protection / avoidance of heart in order to decrease cardiotoxicity of radiation include maneuvers which transfer the heart from the field, such as coordination of the breathing cycles or positioning of the patient in the supine position. Technological advancement enabled the therapies such as intensity modulated radiation therapy (IMRT) or proton beam therapy (PBT) and techniques treating lesser volume around the lumpectomy cavity, such as accelerated partial breast irradiation (APBI) or intraoperative radiation therapy (IORT) (7). Although these techniques have dosimetrically proven to be promising, there are limited possibilities of their application (8,9). They are primarily related to the limited technical equipment of the centres, and on the other hand, there are insufficient data regarding later heart attacks due to difficulties related to long-term monitoring. The application of 3D conformal radiotherapy represents a standard in the radiotherapeutic treatment of patients, within which a precise delineation of target volumes is done on CT slices, not only because it is based on the recommendations but also because it is the only available treatment in our centre. Therefore, the purpose of this review is to assess how the applied technique can lead to the decrease of heart dose in the patient with a significant cardiological burden. Future studies are necessary in order to confirm the efficiency of the advanced techniques which spare the heart dose and can use surrogates for heart attacks such as biomarkers or perfusion scanning.

The most common heart problems during radiotherapy are acute pericarditis, pericardial hemorrhage and arrhythmia. Acute damage of pericardial and intimal coronary endocytosis caused by radiation results in ischemia of myocytes and fibrosis. It seems that the risk of coronary diseases increases decades after radiation therapy (10). Majority of heart diseases was noticed in patients who underwent the radiation of the left thoracic wall after the left-side mastectomy, but present-day radiotherapy techniques expose the heart to lesser radiation than those 30 years ago, even in those patients with tumors on the left side (11). Earlier epidemiological cohort studies noticed a greater risk of death due to heart failure among the patients having cancer on the left breast as compared to those having cancer on the right breast, with the risk more increasing, the more time after treatment passes (10,11). However, the analysis of results of epidemiological surveillance of the patients who had radiation of the left breast as compared to those who had radiation of the right breast did not

show that the passage of time made a significant difference regarding the hospitalisation due to heart diseases or heart insufficiency (12), suggesting that the occurrence of complications is independent of the side on which the tumor change is present.

In our case, the patient with a high cardiovascular risk (burden) did not develop acute serious complications related to the cardiovascular or respiratory systems after the application of 3D conformal radiotherapy. The complications that developed in the patient included skin changes such as erythema (gradus I) which was locally treated with corticosteroids. The incidence of skin toxicity caused by radiation is an important clinical problem which affects majority of patients with breast cancer who were subjected to the adjuvant therapy. This problem is related to the radiation technique, dose homogeneity, PTV receiving the dose bigger than 100% of the prescribed dose and prophylactic use of the local therapy (13) and is present in almost all patients exposed to radiotherapy, going up to 70%-100% (14). The fluctuation of values of INR are common among oncological patients, and it was also noticed during the radiotherapeutic treatment of the patient, thus it can be viewed as one more complication of this therapeutic protocol (15). On the other hand, this can be regarded as deterioration i.e. change of the basic illness in the patient.

## **Conclusion**

This case report indicates the applicability of 3D conformal radiotherapy in patients after the breast cancer surgery with a high cardiovascular risk. Since the application of this technique is the most frequent at our centre, despite the implementation of new techniques, this case report confirms its safety and applicability in high-risk patients. The applied radiation therapy in the patient in this case report points to its low toxic effect, while the noticed negative effects in high-risk patients were removed. The therapeutic treatment was finished a few months ago and since then there have not been delayed complications, and in the future monitoring they will be noted.

References:

1. Lakhani SR, Ellis IO, Schnitt SJ, Tan PH, Van de Vijver MJ, editors. WHO Classification of Tumours of the Breast. Fourth ed. IARC; Lyon: 2012. ISBN.13.
2. M. Morrow, H.J. Burstein, J.R. Harris. Malignant tumors of the breast. V.T. DeVita Jr., T.S. Lawrence, S.A. Rosenberg (Eds.), Cancer: Principles and Practice of Oncology (tenth ed.), vol. 79, Wolters Kluwer Health/Lippincott Williams & Wilkins, Philadelphia 2015; 1117-1156.
3. M. Akram, M. Iqbal, M. Daniyal, A.U. Khan. Awareness and current knowledge of breast cancer. Biol. Res. 2017; 50 (1):33.
4. Shah R, Rosso K, Nathanson SD. Pathogenesis, prevention, diagnosis and treatment of breast cancer. World J Clin Oncol. 2014; 5:283-8.
5. EBCTCG (Early Breast Cancer Trialists' Collaborative Group), McGale P, Taylor C, Correa C, Cutter D, Duane F, et al. Effect of radiotherapy after mastectomy and axillary surgery on 10- year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data from 8135 women in 22 randomised trials. Lancet 2014; 383:2127-35.
6. Rietman JS, Dijkstra PU, Hoekstra HJ, Eisma WH, Szabo BG, Groothoff JW, et al. Late morbidity after treatment of breast cancer in relation to daily activities and quality of life: a systematic review. Eur J Surg Oncol 2003; 29: 229-238.
7. Bergom C, Bradley JA, Ng AK, Samson P, Robinson C, Lopez-Mattei J, et al. Past, Present, and Future of Radiation-Induced Cardiotoxicity: Refinements in Targeting, Surveillance, and Risk Stratification. JACC Cardio Oncol 2021; 3: 343-359.
8. Shah C, Badiyan S, Berry S, Khan AJ, Goyal S, Schulte K, et al. Cardiac dose sparing and avoidance techniques in breast cancer radiotherapy. Radiother Oncol 2014; 112(1):9-16.
9. Stowe HB, Andruska ND, Reynoso F, Thomas M, Bergom C. Heart Sparing Radiotherapy Techniques in Breast Cancer: A Focus on Deep Inspiration Breath Hold. Breast Cancer (Dove Med Press) 2022; 14:175-186.

10. Díaz-Gavela AA, Figueiras-Graillet L, Luis ÁM, Salas Segura J, Ciérvide R, Del Cerro Peñalver E, et al. Breast radiotherapy-related cardiotoxicity. when, how, why. risk prevention and control strategies. *Cancers (Basel)* 2021; 13 (7):1712.
11. Bird BR, Swain SM. Cardiac toxicity in breast cancer survivors: review of potential cardiac problems. *Clin Cancer Res* 2008; 14(1):14–24.
12. Soumarová R, Rušinová L. Cardiotoxicity of breast cancer radiotherapy - overview of current results. *Rep Pract Oncol Radiother* 2020; 25(2):182-186.
13. Di Franco R, Calvanese M, Murino P, Manzo R, Guida C, Di Gennaro D, et al. Skin toxicity from external beam radiation therapy in breast cancer patients: protective effects of Resveratrol, Lycopene, Vitamin C and anthocianin (Ixor®). *Radiat Oncol* 2012; 30;7:12.
14. Andersen ER, Eilertsen G, Myklebust AM, Eriksen S. Women's experience of acute skin toxicity following radiation therapy in breast cancer. *J Multidiscip Healthc* 2018; 23;11:139-148.15.
15. Zhu Z, Li L, Ye Z, Fu T, Du Y, Shi A, et al. Prognostic value of routine laboratory variables in prediction of breast cancer recurrence. *Sci Rep* 2017; 7:8135.