## Measurement of Thyroid Dose by TLD arising from Radiotherapy of Breast Cancer Patients from Supraclavicular Field

# Farhood B.<sup>1, 2</sup>, Bahreyni Toossi M. T.<sup>2</sup>\*, Vosoughi H.<sup>2</sup>, Khademi S.<sup>2</sup>, Knaup C.<sup>3</sup>

## ABSTRACT

**Background:** Breast cancer is the most frequently diagnosed cancer and the leading global cause of cancer death among women worldwide. Radiotherapy plays a significant role in treatment of breast cancer and reduces locoregional recurrence and eventually improves survival. The treatment fields applied for breast cancer treatment include: tangential, axillary, supraclavicular and internal mammary fields.

**Objective:** In the present study, due to the presence of sensitive organ such as thyroid inside the supraclavicular field, thyroid dose and its effective factors were investigated.

**Materials and Methods:** Thyroid dose of 31 female patients of breast cancer with involved supraclavicular lymph nodes which had undergone radiotherapy were measured. For each patient, three TLD-100 chips were placed on their thyroid gland surface, and thyroid doses of patients were measured. The variables of the study include shield shape, the time of patient's setup, the technologists' experience and qualification. Finally, the results were analyzed by ANOVA test using SPSS 11.5 software.

**Results:** The average age of the patients was  $46\pm10$  years. The average of thyroid dose of the patients was  $140\pm45$  mGy (ranged 288.2 and 80.8) in single fraction. There was a significant relationship between the thyroid dose and shield shape. There was also a significant relationship between the thyroid dose and the patient's setup time.

**Conclusion:** Beside organ at risk such as thyroid which is in the supraclavicular field, thyroid dose possibility should be reduced. For solving this problem, an appropriate shield shape, the appropriate time of the patient's setup, etc. could be considered.

## Keywords

Thyroid Dose, Breast Cancer, Radiotherapy, Supraclavicular Field, TLD

## Introduction

B reast cancer is the most frequently diagnosed cancer and the leading global cause of cancer death among women, accounting for 23% of cancer diagnoses and 14% of cancer deaths each year, worldwide. Although breast cancer has a higher incidence in developed countries, half of new breast cancer diagnoses and an estimated 60% of breast cancer deaths are thought to occur in developing countries [1].

Risk factors of breast cancer include: sex, age, personal and family histories of breast cancer, late first parturition, early menstruation and \*Corresponding author: M. T. Bahreyni Toossi Medical Physics Department, Faculty of Medicine, Mashhad University of Medical Sciences, Pardis-e-Daneshgah, Vakil Abad Blvd., Mashhad, Iran E-mail: bahreynimt@ mums.ac.ir

# <u>Original</u>

<sup>1</sup>Student Research Committee, Department of medical physics, Faculty of medicine, Mashhad University of Medical Sciences, Mashhad, Iran <sup>2</sup>Medical Physics Research center, Mashhad University of Medical Sciences, Mashhad, Iran <sup>3</sup>Comprehensive Cancer Centers of Nevada, Las Vegas, Nevada, USA late menopause, obesity (high Body Mass Index), the patient's previous biopsy with atypical hyperplasia or hyperplasia, high-density breast tissue, radiation exposure at a young age, etc. [2].

Breast cancer treatment modalities include surgery, radiotherapy, chemotherapy and hormone therapy [3]. Factors in the selection of treatment method(s) includes: patient age, tumor size, menopausal status, tumor marker, lymph nodes status, estrogen or progesterone receptors [4] and the side effects of the selected method [5].

Radiotherapy plays a significant role in the multimodality treatment of breast cancer. It has been shown in several studies that radiotherapy reduces locoregional recurrence and improves survival [6-9]. The treatment fields of breast cancer may include: tangential, axillary, supraclavicular and internal mammary fields. The borders of the anterior supraclavicular-axillary field differ slightly for photon and electron beams. The borders of the photon beam include: the medial border is a vertical line from the second costal cartilage to the thyrocricoid groove (following the inner border of the sternocleidomastoid muscle). The lateral border is at the acromioclavicular joint and is traced among the shoulder to exclude the shoulder joint. The superior border expands laterally among the neck and the trapezius. The inferior border is a horizontal line at the level of the second costal cartilage [5].

Presence of an organ at risk such as thyroid inside the supraclavicular field is the basis for using a thyroid shield in radiotherapy of the supraclavicular field as well as the beam typically tilted 15° laterally to avoid other irradiating organs such as trachea, esophagus and spinal cord [5].

Besides, in various studies thyroid dose arising from different imaging or therapeutical modalities such as angiography, CT and radiotherapy of the nasopharynx cancer have been evaluated [10-12]. The importance of this subject and the minimal relevant data in the literature were main motivations for this study to assess thyroid dose and relevant influencing factors. The authors hope that their results lead to reduced thyroid dose.

#### Material and Method

In this study, the skin entrance dose (SED) of thyroid of 31 female patients with breast cancer and involved supraclavicular lymph nodes which had undergone conformal radiotherapy (without multi leaf collimator) were measured. The patients were treated by 6 MV photon beams of Varian and Elekta linear accelerators. In this study, source axis distance (SAD) technique was used. All patients were treated with standard fractionation regimen. There were five treatment sessions per week and dose per fraction was 200 cGy. Total prescribed dose was 5000 cGy. In this study, the SED of thyroid was measured only in one session for each patient in the supraclavicular field. For the estimation of total SED of thyroid during the treatment dose, all patients were measured in a single fraction, then they were average. Finally, the average total SED of thyroid for any patient was estimated by multiplying the total number of sessions in the average SED of thyroid in single fraction. Thermoluminescent dosimeter (TLD)-100 chips were used to measure the SED of thyroid. The TLD-100 chips produced by Harshaw Company and made of LiF:Mg:Ti with the dimensions of  $3 \times 3 \times 1$ mm<sup>3</sup> which have high sensitivity and the appropriateness for radiation dosimetry. A total number of 93 dosimeters were used for dose evaluation that had a sensitivity in the range of  $\pm$  3 % from the average response. Also, many dosimeters were used to measure the background radiation. TLD reader system (Harshaw, USA) was applied for dose assessment. Before dose measurement of patients, the TLD chips were calibrated with known doses.

To have high accuracy of dosimetry results

#### www.jbpe.org

#### Measurement of Thyroid Dose in Supraclavicular Field

for each patient, three TLD chips were placed and the absorbed dose was obtained the average dose by three TLD chips.

Three TLD chips were formed as a triangle shape and were positioned on the thyroid gland of each patient and the SED of thyroid was obtained in a single fraction (Figure 1).

Figure 1 shows the arrangement of TLD chips on thyroid gland.

A questionnaire was filled for each patient including patient's name, age, the SED of thyroid in single fraction, dose per fraction, shape shield, the time of patient's set up and the technologist's experience and qualification (radiotherapy or radiology major). In terms of staff experience, the technologists were classified into two groups; one group consisted of persons who had worked fewer than 2 years in a radiotherapy department (inexperienced) and another group included persons who had worked more than 2 years in that department (experienced). The time of patient's setup was classified to the time setup of low (lower than 2 minutes), medium (2-3 minutes) and high (more than 3 minutes). The shields used for covered thyroid gland had different geometri-



Figure 1: Positioning TLD chips on thyroid gland

cal shapes (i.e. square, rectangle and triangle) as variable was considered. These shields had exact shapes and were not made for every patient specifically. They were applied as usual shields that were bought with each linear accelerator. Finally, the results were analyzed by ANOVA test using SPSS 11.5 software. Statistically p-value  $\leq 0.05$  was considered a significant level.

#### Results

In this study, the average age of the patients was  $46 \pm 10$  years and the minimum and maximum ages were 21 and 65 years, respectively. Time of the patients' setup for three groups (low, moderate and high) is illustrated in Figure 2.

32 percent of technologists were in inexperienced group and 68 percent were in experienced group. Additionally, 42 percent of technologists graduated in radiotherapy major and 58 percent graduated in radiology major. The percentage of different shield shapes used in supraclavicular field for covering thyroid is illustrated in Figure 3.

The most important part of our work was the measurement of SED of thyroid to patients with breast cancer and involved supraclavicular lymph nodes which had undergone radiotherapy.

Table 1 illustrates average SED of thyroid for each patient and its relevant factors in single fraction.

The average SED of thyroid from the supraclavicular field was  $140 \pm 45$  mGy, in single fraction of radiotherapy treatment and the minimum and maximum SEDs of thyroid were 80.8 and 288.2 mGy, respectively. ANO-VA test was used to assess the relationship between the SED of thyroid and variables of the time of patients' setup, shield shapes, the technologist's experience and qualification.

There was a significant relationship between the SED of thyroid and the time of patients' setup (p = 0.036). No significant relationship







Figure 3: Frequency percent of different shield shapes

was found between the SED of thyroid and technologist's experience (p = 0.559), nor between the SED of thyroid and technologist's qualification (p = 0.318). There was a significant relationship between the SED of thyroid and square shield (p = 0.048) and rectangular shield (p = 0.05).

#### Discussion

Considering the fact that thyroid gland is a radiosensitive organ [13], many studies in the fields of radiology, radiotherapy and nuclear medicine have been performed on the effects of exposure related to thyroid absorbed dose

#### Table 1: Average absorbed thyroid for each patient and its relevant factors

No. of	Age	Shield	Setup	Technologist's	Technologist's	Average absorbed
patient		shape	time *	experience **	major	dose (mGy)
1	47	rectangular	High	inexperienced	Radiotherapy	168.80
2	45	rectangular	Low	experienced	Radiology	141.3
3	36	rectangular	High	experienced	Radiology	119.8
4	38	rectangular	Low	experienced	Radiotherapy	259.2
5	52	triangle	High	experienced	Radiology	91.06
6	48	rectangular	High	experienced	Radiotherapy	135.3
7	40	square	High	inexperienced	Radiotherapy	130.4
8	52	square	Moderate	inexperienced	Radiotherapy	129.4
9	60	rectangular	Low	experienced	Radiotherapy	288.2
10	40	triangle	Moderate	experienced	Radiology	139.2
11	53	rectangular	Moderate	experienced	Radiology	90
12	43	square	Moderate	experienced	Radiology	110.93
13	59	rectangular	Moderate	experienced	Radiology	142.70
14	43	square	Moderate	inexperienced	Radiotherapy	121.73
15	57	triangle	Moderate	inexperienced	Radiotherapy	128.4
16	56	triangle	Moderate	inexperienced	Radiotherapy	175.89
17	51	triangle	Moderate	experienced	Radiology	175.63
18	40	square	Low	experienced	Radiology	183.6
19	47	square	Low	experienced	Radiology	148.03
20	21	rectangular	High	experienced	Radiology	176.02
21	48	square	Moderate	experienced	Radiology	112.7
22	44	square	High	experienced	Radiology	160
23	48	square	High	experienced	Radiology	115.6
24	65	rectangular	High	inexperienced	Radiology	167.36
25	40	rectangular	Moderate	inexperienced	Radiotherapy	120
26	43	triangle	Low	experienced	Radiology	145.65
27	56	square	Moderate	inexperienced	Radiotherapy	84.72
28	30	square	High	inexperienced	Radiotherapy	80.81
29	29	square	Moderate	experienced	Radiotherapy	109.93
30	51	square	Low	experienced	Radiology	105
31	45	rectangular	Low	experienced	Radiology	96.47

\* Low = lower than 2 minutes, Moderate = 2-3 minutes, High = more than 3 minutes

\*\* Inexperienced = to work lower than 2 years in radiotherapy department, experienced = to work more than 2 years in radiotherapy department

and its induced disorders [14-38]. The disorders can include hypothyroidism, thyroiditis, Graves' disease, euthyroid Graves' ophthalmopathy, benign adenocarcinoma, multinodular Goiter and radiation-induced thyroid carcinoma. Primary hypothyroidism, the most common radiation-induced thyroid dysfunction, affects 20–30% of patients undergoing curative radiotherapy to the neck region, with approximately half of the events occurring within the first 5 years after radiotherapy.

The most important factors contributing to hypothyroidism include total radiotherapy dose, irradiated volume of the thyroid gland and the extent of thyroid resection [39].

Although induced thyroid dysfunction arising from radiotherapy is well established, there have been fewer studies related to thyroid dose evaluation during radiotherapy of cancer patients [40].

There are some studies that show the differences between radiation-induced thyroid disorders and threshold dose. Wartofsky, et al. have reported that a dose about 400 mGy can increase benign and malignant thyroid tumors [41]. Hancock et al. [42] reported that doses to the thyroid gland that exceeded 26 Gy produce hypothyroidism. Turner et al. [17] reported that vascular damage and follicular cell damage followed radiation doses as low as 2.25 Gy.

In the present study, the average SED of thyroid of the patients was 140 mGy in a single fraction (7% of prescribed dose of supraclavicular field). The average SED of thyroid was 350 cGy during total treatment, so it is possible that some patients will develop thyroid disorders after irradiation. According to Radiation Therapy Oncology Group (RTOG) protocols [43-44], the maximum thyroid absorbed dose should be less than 3% prescribed dose, but in this study, the thyroid absorbed dose was about 7%. So, according to the significant relationship between the SED of thyroid and various shield shapes (Figure 4), and also significant relationship between the SED of thyroid and the time of patient's setup (Figure 5), care should be taken when using differ-



Figure 4: Thyroid absorbed dose (mGy) and various forms of used shields





ent shields and with patient setup.

## Conclusion

Doses to organ at risk such as thyroid which is in the supraclavicular field, should be carefully evaluated. The dose to the thyroid is dependent on appropriate shield shape and the appropriate time of the patient's setup.

## Acknowledgments

The authors would like to thank student research committee of Mashhad University of Medical Sciences for financial support of this work. We are also thankful to the staff of "Omid and Imam Reza" radiotherapy departments (Mashhad, Iran) who collaborated sincerely in this project.

## Conflict of Interest

None

#### References

1. Jemal A, Bray F, Center MM, Ferlay J, Ward E,

Forman D. Global cancer statistics. *CA Cancer J Clin.* 2011;**61**:69-90. doi.org/10.3322/caac.20107. PubMed PMID: 21296855.

- 2. Halperin EC, Perez CA, Brady LW. Perez and Brady's principles and practice of radiation oncology: Lippincott Williams & Wilkins; 2008.
- 3. Jalilian M, Arbabi F. Cutaneous complication after electron beam therapy in breast cancer. *Journal* of Research in Medical Sciences. 2005;**10**:368-70.
- Tobler M, Leavitt DD. Design and production of wax compensators for electron treatments of the chest wall. *Med Dosim.* 1996;**21**:199-206. doi. org/10.1016/S0958-3947(96)00126-4. PubMed PMID: 8985924.
- 5. Levitt SH, Purdy JA, Perez CA, Vijayakumar S. Technical Basis of Radiation Therapy Practical Clinical Applications. 4th ed. Germany: Springer-Verlag Berlin Heidelberg; 2006. p. 492.
- Darby S, McGale P, Correa C, Taylor C, Arriagada R, Clarke M, et al. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomised trials. *Lancet.* 2011;**378**:1707-16. doi. org/10.1016/S0140-6736(11)61629-2. PubMed PMID: 22019144. PubMed PMCID: 3254252.

- Santiago RJ, Wu L, Harris E, Fox K, Schultz D, Glick J, et al. Fifteen-year results of breast-conserving surgery and definitive irradiation for Stage I and II breast carcinoma: the University of Pennsylvania experience. *Int J Radiat Oncol Biol Phys.* 2004;**58**:233-40. doi.org/10.1016/S0360-3016(03)01460-3. PubMed PMID: 14697443.
- Veronesi U, Cascinelli N, Mariani L, Greco M, Saccozzi R, Luini A, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *N Engl J Med.* 2002;**347**:1227-32. doi. org/10.1056/NEJMoa020989. PubMed PMID: 12393819.
- Fisher B, Anderson S, Bryant J, Margolese RG, Deutsch M, Fisher ER, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med.* 2002;**347**:1233-41. doi.org/10.1056/NEJ-Moa022152. PubMed PMID: 12393820.
- Johansen S, Reinertsen KV, Knutstad K, Olsen DR, Fossa SD. Dose distribution in the thyroid gland following radiation therapy of breast cancer--a retrospective study. *Radiat Oncol.* 2011;6:68. doi. org/10.1186/1748-717X-6-68. PubMed PMID: 21651829. PubMed PMCID: 3128838.
- Shortt CP, Malone L, Thornton J, Brennan P, Lee MJ. Radiation protection to the eye and thyroid during diagnostic cerebral angiography: a phantom study. *J Med Imaging Radiat Oncol.* 2008;**52**:365-9. doi.org/10.1111/j.1440-1673.2008.01970.x. PubMed PMID: 18811760.
- Hopper KD, King SH, Lobell ME, TenHave TR, Weaver JS. The breast: in-plane x-ray protection during diagnostic thoracic CT--shielding with bismuth radioprotective garments. *Radiology*. 1997;**205**:853-8. doi.org/10.1148/radiology.205.3.9393547. PubMed PMID: 9393547.
- Ron E, Brenner A. Non-malignant thyroid diseases after a wide range of radiation exposures. *Radiat Res.* 2010;**174**:877-88. doi.org/10.1667/ RR1953.1. PubMed PMID: 21128812. PubMed PMCID: 3927789.
- Cannon CR. Hypothyroidism in head and neck cancer patients: experimental and clinical observations. *Laryngoscope*. 1994;**104**:1-21. doi. org/10.1288/00005537-199411001-00001. PubMed PMID: 7968176.
- 15. Markson JL, Flatman GE. Myxoedema after deep x-ray therapy to the neck. *Br Med J*. 1965;**1**:1228-

30. doi.org/10.1136/bmj.1.5444.1228. PubMed PMID: 14275023. PubMed PMCID: 2166568.

- Sinard RJ, Tobin EJ, Mazzaferri EL, Hodgson SE, Young DC, Kunz AL, et al. Hypothyroidism after treatment for nonthyroid head and neck cancer. *Arch Otolaryngol Head Neck Surg.* 2000;**126**:652-7. doi.org/10.1001/archotol.126.5.652. PubMed PMID: 10807335.
- Turner SL, Tiver KW, Boyages SC. Thyroid dysfunction following radiotherapy for head and neck cancer. *Int J Radiat Oncol Biol Phys.* 1995;**31**:279-83. doi.org/10.1016/0360-3016(93)E0112-J. PubMed PMID: 7836081.
- Zohar Y, Tovim RB, Laurian N, Laurian L. Thyroid function following radiation and surgical therapy in head and neck malignancy. *Head Neck Surg.* 1984;6:948-52. doi.org/10.1002/hed.2890060509. PubMed PMID: 6724961.
- Thorp MA, Levitt NS, Mortimore S, Isaacs S. Parathyroid and thyroid function five years after treatment of laryngeal and hypopharyngeal carcinoma. *Clin Otolaryngol Allied Sci.* 1999;**24**:104-8. doi. org/10.1046/j.1365-2273.1999.00214.x. PubMed PMID: 10225153.
- Liao Z, Ha CS, Vlachaki MT, Hagemeister F, Cabanillas F, Hess M, et al. Mantle irradiation alone for pathologic stage I and II Hodgkin's disease: long-term follow-up and patterns of failure. *Int J Radiat Oncol Biol Phys.* 2001;**50**:971-7. doi. org/10.1016/S0360-3016(01)01525-5. PubMed PMID: 11429225.
- 21. Kumpulainen EJ, Hirvikoski PP, Virtaniemi JA, Johansson RT, Simonen PM, Terava MT, et al. Hypothyroidism after radiotherapy for laryngeal cancer. *Radiother Oncol.* 2000;**57**:97-101. doi. org/10.1016/S0167-8140(00)00276-0. PubMed PMID: 11033194.
- Illes A, Biro E, Miltenyi Z, Keresztes K, Varoczy L, Andras C, et al. Hypothyroidism and thyroiditis after therapy for Hodgkin's disease. *Acta Haematol.* 2003;**109**:11-7. doi.org/10.1159/000067269. PubMed PMID: 12486317.
- Murtha AD, Rupnow BA, Hansosn J, Knox SJ, Hoppe R. Long-term follow-up of patients with Stage III follicular lymphoma treated with primary radiotherapy at Stanford University. *Int J Radiat Oncol Biol Phys.* 2001;**49**:3-15. doi.org/10.1016/ S0360-3016(00)00780-X. PubMed PMID: 11163492.
- 24. Thomas O, Mahe M, Campion L, Bourdin S, Milpied N, Brunet G, et al. Long-term complications of total

body irradiation in adults. *Int J Radiat Oncol Biol Phys.* 2001;**49**:125-31. doi.org/10.1016/S0360-3016(00)01373-0. PubMed PMID: 11163505.

- Hancock SL, Cox RS, McDougall IR. Thyroid diseases after treatment of Hodgkin's disease. N Engl J Med. 1991;325:599-605. doi.org/10.1056/ NEJM199108293250902. PubMed PMID: 1861693.
- 26. Leon X, Gras JR, Perez A, Rodriguez J, de Andres L, Orus C, et al. Hypothyroidism in patients treated with total laryngectomy. *A multivariate study. Eur Arch Otorhinolaryngol.* 2002;**259**:193-6. doi. org/10.1007/s00405-001-0418-x. PubMed PMID: 12064507.
- 27. Shafford EA, Kingston JE, Healy JC, Webb JA, Plowman PN, Reznek RH. Thyroid nodular disease after radiotherapy to the neck for childhood Hodgkin's disease. *Br J Cancer*. 1999;**80**:808-14. doi.org/10.1038/sj.bjc.6690425. PubMed PMID: 10360659.
- Petersen M, Keeling CA, McDougall IR. Hyperthyroidism with low radioiodine uptake after head and neck irradiation for Hodgkin's disease. *J Nucl Med.* 1989;**30**:255-7. PubMed PMID: 2738654.
- 29. Tamura K, Shimaoka K, Friedman M. Thyroid abnormalities associated with treatment of malignant lymphoma. *Cancer.* 1981;**47**:2704-11. doi.org/10.1002/1097-0142(19810601)47:11<2704::AID-CNCR2820471129>3.0.CO;2-G. PubMed PMID: 7260863.
- Constine LS, Woolf PD, Cann D, Mick G, McCormick K, Raubertas RF, et al. Hypothalamic-pituitary dysfunction after radiation for brain tumors. *N Engl J Med.* 1993;**328**:87-94. doi.org/10.1056/ NEJM199301143280203. PubMed PMID: 8416438.
- Ogilvy-Stuart AL, Shalet SM, Gattamaneni HR. Thyroid function after treatment of brain tumors in children. *J Pediatr*. 1991;**119**:733-7. doi. org/10.1016/S0022-3476(05)80288-4. PubMed PMID: 1941379.
- 32. Brada M, Rajan B, Traish D, Ashley S, Holmes-Sellors PJ, Nussey S, et al. The long-term efficacy of conservative surgery and radiotherapy in the control of pituitary adenomas. *Clin Endocrinol* (Oxf). 1993;**38**:571-8. doi. org/10.1111/j.1365-2265.1993.tb02137.x. PubMed PMID: 8334743.
- 33. Oberfield SE, Allen JC, Pollack J, New MI, Levine LS. Long-term endocrine sequelae after treatment

of medulloblastoma: prospective study of growth and thyroid function. *J Pediatr*. 1986;**108**:219-23. doi.org/10.1016/S0022-3476(86)80986-6. PubMed PMID: 3944706.

- 34. Ogilvy-Stuart AL, Clark DJ, Wallace WH, Gibson BE, Stevens RF, Shalet SM, et al. Endocrine deficit after fractionated total body irradiation. *Arch Dis Child*. 1992;67:1107-10. doi.org/10.1136/adc.67.9.1107. PubMed PMID: 1417055. PubMed PMCID: 1793609.
- Sklar CA, Kim TH, Ramsay NK. Thyroid dysfunction among long-term survivors of bone marrow transplantation. *Am J Med.* 1982;**73**:688-94. doi. org/10.1016/0002-9343(82)90411-9. PubMed PMID: 6753576.
- 36. Sandhu A, Constine LS, O'Mara RE, Hinkle A, Muhs AG, Woolf PD. Subclinical thyroid disease after radiation therapy detected by radionuclide scanning. *Int J Radiat Oncol Biol Phys.* 2000;48:181-8. doi. org/10.1016/S0360-3016(00)00592-7. PubMed PMID: 10924988.
- Kuten A, Lubochitski R, Fishman G, Dale J, Stein ME. Postradiotherapy hypothyroidism: radiation dose response and chemotherapeutic radiosensitization at less than 40 Gy. *J Surg Oncol.* 1996;61:281-3. doi.org/10.1002/(SICI)1096-9098(199604)61:4<281::AID-JSO10>3.0.CO;2-9. PubMed PMID: 8627999.
- Schneider AB, Recant W, Pinsky SM, Ryo UY, Bekerman C, Shore-Freedman E. Radiation-induced thyroid carcinoma. Clinical course and results of therapy in 296 patients. *Ann Intern Med.* 1986;**105**:405-12. doi.org/10.7326/0003-4819-105-3-405. PubMed PMID: 3740680.
- Jereczek-Fossa BA, Alterio D, Jassem J, Gibelli B, Tradati N, Orecchia R. Radiotherapy-induced thyroid disorders. *Cancer Treat Rev.* 2004;**30**:369-84. doi.org/10.1016/j.ctrv.2003.12.003. PubMed PMID: 15145511.
- 40. Gul A, Faaruq S, Abbasi NZ, Siddique T, Ali A, Shehzadi NN, et al. Estimation of absorbed dose to thyroid in patients treated with radiotherapy for various cancers. *Radiat Prot Dosimetry.* 2013;**156**:37-41. doi.org/10.1093/rpd/nct043. PubMed PMID: 23520201.
- Wartofsky L. Increasing world incidence of thyroid cancer: increased detection or higher radiation exposure? *Hormones* (Athens). 2010;9:103-8. doi. org/10.14310/horm.2002.1260. PubMed PMID: 20687393.
- 42. Hancock SL, McDougall IR, Constine LS. Thyroid

abnormalities after therapeutic external radiation. *Int J Radiat Oncol Biol Phys.* 1995;**31**:1165-70. doi.org/10.1016/0360-3016(95)00019-U. PubMed PMID: 7713780.

43. Vicini F, Winter K, Straube W, Wong J, Pass H, Rabinovitch R, et al. A phase I/II trial to evaluate three-dimensional conformal radiation therapy confined to the region of the lumpectomy cavity for Stage I/II breast carcinoma: initial report of feasibility and reproducibility of Radiation Therapy Oncology Group (RTOG) Study 0319. *Int J Radiat Oncol Biol Phys.* 2005;**63**:1531-7. doi.org/10.1016/j. ijrobp.2005.06.024. PubMed PMID: 16198508.

44. Vicini F, White J, Arthur D, Kuske R, Rabinovitch R. NSABP protocol B-39/RTOG protocol 0413: a randomized phase III study of conventional whole breast irradiation (WBI) versus partial breast irradiation (PBI) for women with stage 0, I, or II breast cancer. I, or II breast cancer. 2004.