Original Article

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Temporary Implant Irradiation: Survey of Turkish Society of Radiation Oncology Breast Cancer Study Group

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ABSTRACT

Objective: To understand the clinical approach of radiation oncologists during the treatment of patients with breast reconstruction.

Materials and Methods: A questionnaire survey was emailed to 105 active members of the Turkish Radiation Oncology Society, the Breast Cancer Study Group. The factors associated with radiation oncologists and their current practice was identified.

Results: Fifty radiation oncologists (47.6%) responded, and most of the responders (83%) were physicians who treated >50 new breast cancer patients annually. The majority of the physicians worked in academic hospitals and had more than 15 years of work experience. The early reconstruction rate was noted to be low among patients with mastectomy (<10% of the mastectomy patients) ($p<0.05$). Early implant irradiation with temporary tissue expander was noted to be a more common procedure. The majority of the respondents (68%) preferred to irradiate an inflated implant (20% total, 80% partial). In addition, 22% of the physicians declared that they routinely used bolus and that 60% of them used it only for patients at a high risk of local recurrence factors.

Conclusion: It can thus be concluded that variations exist between experienced radiation oncologists and others. Hypofractionation is not yet commonly practiced for patients with reconstruction in Turkey. A concrete consensus can be helpful to create a homogeneity in treatment decisions and practical applications.

Keywords: Breast reconstruction, post-mastectomy radiation, tissue expander, breast cancer, survey

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Introduction

Breast cancer (BC) is the most common type of cancer affecting women across the world. Cancer-related mortality rates have declined from 39% to 20% without any change in the incidence of BC. Although breast-conserving surgery (BCS) and postoperative radiotherapy (RT) are performed in most patients, mastectomy and breast reconstruction (BR) are also being applied at increasing rates (1). Even in cases with early BC, it has been shown that the rate of mastectomy and BR has increased from 15% to 30% in the last 10 years (2).

After mastectomy, organ loss can be a devastating problem for patients. The psychological effect and the quality of life of the operated patients can be improved by BR. For this purpose, the options of autologous tissues or implant reconstruction (IR) are available. In autologous reconstruction (AR), a flap can be formed with the muscles of the rectus abdominis or latissimus dorsi. The IR involves two procedures: one is a single-stage permanent silicon implantation and the other one is double-stage reconstruction after tissue expander (TE) (3). Although AR or IR decision changes with the preference of the patient and physician or the RT indication, the most common current method of BR is implant-based, as suggested by Albornoz et al. (4). Past studies have shown that post-mastectomy RT (PMRT) reduces local recurrence and provides a survival advantage to patients with lymph node involvement in BC. In addition, it remains unknown whether nipple-sparing or skin-sparing mastectomies with implant can be considered as oncologically safe as mastectomies for patients without lymph node metastases. Therefore, some of these patients with negative factors for local recurrence, such as close or positive margins or tissue flaps of >5 mm, tumors with aggressive biology should be considered for chest-wall irradiation (5).

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On the other hand, patients, particularly those with IR, have concerns such as poor cosmetic outcomes with PMRT and damage to reconstruction and implant failure (2). BR and PMRT outcomes are impacted by various factors related to patient and treatment, such as body-mass index, smoking status, implant replacement, expander or permanent implant irradiation, and multiple other factors (6). The application of RT with expander–IR is possible in multiple ways; however, there is no consensus on the best approach. Moreover, there exists no data on radiation practice globally, and there is often much heterogeneity among practitioners with respect to the radiation technique.

In this survey study, we aimed to determine the clinical approach of PMRT in patients who underwent early IR at different RT centers in Turkey.

Materials and Methods

A questionnaire was prepared by considering the problems encountered by radiation oncologists in determining early IR and postoperative RT. The survey questionnaire contained 23 questions, as detailed in the Appendix 1. The questionnaire was sent to 105 radiation oncologists who are the members of the Turkish Society of Radiation Oncology Breast Cancer Study Group. The most appropriate response signs were requested from the physicians. In addition to the demographics of the physicians from different centers, RT timing, total dose, fractionation, and technical differences in practice were questioned. This study was approved by the local institutional ethics committee (number: 2018-3/23).

The answers were categorized using the Statistical Package for Social Sciences system (version 20.0). The frequencies and percentages of the answers for each question were calculated. The chi-square test was used for the statistical analyses of the answers. P<0.05 was considered to be statistically significant.

Results

The questionnaire survey was answered by 50 of the 105 physicians, and the response rate was 47.6%. The majority of the responders (n=40) were from academic institutions, while the others were from (n=10) private institutions. A total of 26 radiation oncology specialists, 14 associate professors, and 10 professors answered the questionnaire. The expertise of the responding physicians ranged from 5 to 10 years to >20 years. When evaluated according to the duration of the specialization, 17 physicians had been working for 5–10 years, nine physicians for 10–15 years, 11 physicians for 15–20 years, and 13 physicians for >20 years as radiation oncologists (Table 1).

The majority of the respondents (70%) treated >50 new BC cases every year. One-third of the respondents (76%) reported that the rate of patients who underwent early reconstruction in the patient group receiving PMRT were <10%. Almost all respondents (96%) performed PMRT after implant-based reconstruction when compared to AR. RT was mostly performed on the TE, and 26 respondents (52%) reported that the percentage of cases with permanent implant irradiation in their daily practice was <10%. Irradiation on the permanent implant was performed by radiation oncologist with more experience, and 83% of the respondents were physicians who treated 50 new patients annually (p=0.05).

The majority of the radiation oncologists (68%) reported that they needed intervention to the ipsilateral TE prior to RT planning, but they did not prefer full deflation when an intervention was required (80%). After the intervention to the expander, half of the respondents indicated that they waited before the initiation of RT, and 88% of them chose to wait for 1 week. Moreover, there was a statistically significant correlation between the physicians who selected 2-week waiting period and those who preferred full deflation (p=0.002).

The percentage of responders who routinely applied bolus after BR was 22%. Moreover, 60% of the responders indicated that they preferred to use bolus in case of risk factors such as skin involvement or anterior surgical margin positivity. The majority of physicians (73%) dictated that the bolus was used during half of the RT schedule. Sixteen physicians preferred to apply the bolus during the first half of the treatment, while 14 physicians preferred it in the second half. Four physicians replied that they used bolus throughout the RT. All responders used customized bolus in their practice.

The results revealed that 30 physicians (60%) did not prescribe chest-wall boost dose in any case after BR, while 38% physicians applied the boost in cases with high local recurrence risk factors or at pathological T4-stage. Only two physicians preferred mild hypofractionation (40–42.5 Gy in 15–16 fractions), while the majority preferred conventional fractionation (50–50.4 Gy in 25–28 fractions; 86%).

In target volume delineation, 84% of the radiation oncologists included the whole implant or TE into the clinical target volume (CTV). Physicians who did not include the whole implant or TE to the CTV were those with an extensive experience in treating patients with IR (p=0.01). The majority of the responders (54%) indicated that they did not attempt to keep the expander port out of the CTV in patients with TE.

Most respondents agreed that they could provide an optimal planning with 3-dimensional (3D) and field-in-field technique; conversely, 13 physicians preferred dynamic-intensity modulated RT (IMRT) in cases with BR. For patients with internal mammary chain irradiation, 78% of the physicians dictated that they could obtain a good coverage with wide tangential field technique with acceptable organ at risk doses. In addition, 34% of the physicians did not use deep inspiration breath-hold (DIBH) technique for the left BC treatment in their clinics. At the centers at which DIBH was routinely applied, the rate of patients irradiated after BC with a DIBH was 52%. The majority of the physicians (80%) who preferred the DIBH with BR were significantly found to have >50 new diagnosed BC patients annually (p=0.01).

It has been reported that the frequency and severity of skin reactions did not increase in BR patients than in patients without reconstruction (90%). Two of the five physicians who observed an increase in acute skin toxicity were those who needed intervention to the expander (p=0.006).

Discussion and Conclusion

The aim of the present study was to evaluate the variation in the management of implant irradiation in Turkey. Among patients treated by physicians in this survey, the number of cases with BR was found to be low (10%).

In this study, it was observed that 96% of the physicians treated patients with TEs after mastectomy. Similarly, a worldwide survey was conducted by Chen et al. (7) and an American survey was conducted by Thomas et al. (8). Thomas et al. (8) reported the rate of reconstruction

Table 1. Statistical analyses

		p-value
Rate of irradiation on the temporary implant	**Number of breast cancer patients**	
100% of physicians who answered “more than 50%”	> 50 new patients annually	**0.11**
Rate of irradiation on the permanent implant	**Number of breast cancer patients**	
83% of physicians who answered “more than 50%”	> 50 new patients annually	**0.05**
Intervention to the ipsilateral tissue expander	**Number of breast cancer patients**	
75% of physicians who answered “almost never”	> 50 new patients annually	
63.6% of physicians who answered “less than 10% of cases”	> 50 new patients annually	**0.41**
Full deflation of the tissue expander	**Number of breast cancer patients**	
62.5% of physicians who answered “yes”	>50 new patients annually	**0.92**
72.5% of physicians who answered “no”	>50 new patients annually	
Selected a 2-weeks waiting period	**Number of breast cancer patients**	
100% of physicians who selected “2 weeks”	> 50 new patients annually	**0.33**
	Full deflation of the tissue expander	
66.7% of physicians who selected “2 weeks”	Select full deflation of the tissue expander	**0.01**
Bolus utilization	**Number of breast cancer patients**	
76.9% of physicians who answered “presence of high risk”	> 50 new patients annually	
72.8% of physicians who answered “almost every case”	> 50 new patients annually	**0.53**
Apply the bolus throughout the	**Number of breast cancer patients**	
100% of physicians who answered “whole treatment”	> 50 new patients annually	
100% of physicians who answered “every other day”	> 50 new patients annually	
63.4% of physicians who answered “half of the treatment period”	> 50 new patients annually	**0.004**
Prescribe a boost dose	**Number of breast cancer patients**	
80% of physicians who answered “never”	> 50 new patients annually	**0.36**
52.7% of physicians who answered “presence of high risk”	>50 new patients annually	
CTV delineation	**Number of breast cancer patients**	
61.1% of physicians who include the whole implant into the CTV	> 50 new patients annually	**0.9**
66.6% of physicians who include a part of the implant into the CTV	> 50 new patients annually	
	Rate of reconstructed case	**0.01**
81% of physicians who include the whole implant into the CTV	Rate of reconstructed case <10%	
Radiotherapy technique	**Number of breast cancer patients**	
77% of physicians who preferred IMRT technique	> 50 new patients annually	
68.5% of physicians who preferred 3D treatment	> 50 new patients annually	**0.89**
Expander port	**Number of breast cancer patients**	
68.2% of physicians who try to keep the port out of the CTV	> 50 new patients annually	
73.1% of physicians who don”t try to keep the port out of the CTV	> 50 new patients annually	**0.53**
Deep breath-hold technique	**Number of breast cancer patients**	
80.8% of physicians who preferred treatment with breath hold	> 50 new patients annually	**0.01**
Early side-effects	**Number of breast cancer patients**	**0.08**
60% of physicians who observed an increase in early side-effects	> 50 new patients annually	
	Intervention to the tissue expander	**0.006**
100% of physicians who observed an increase in early side-effects	Who needed intervention to the expander	
	Full deflation of the tissue expander	**0.18**
40% of physicians who observed an increase in early side-effects	Select full deflation of the tissue expander	
	Waiting period	**0.63**
60% of physicians who observed an increase in early side-effects	Who preferred no waiting period	
	Bolus utilization	**0.08**
100% of physicians who observed an increase in early side-effects	Select treatment with bolus	
	Prescribe a boost dose	**0.53**
60% of physicians who observed an increase in early side-effects	Select treatment with boost	

CTV: Clinical target volume; IMRT: Intensity modulated radiotherapy

with TE to be 96%. The number of BC patients with reconstruction in America was higher than that in Europe (40% versus 10%). The rate of reconstruction using TE was 52% in America, while AR was preferred at the rate of 36% in Europe (8).

The 2-stage BR (TE placement followed by implant placement) is an alternative to AR (6). This technique offers the advantages of shorter duration of surgery, less technically demanding operations, and acceptable cosmetic outcomes (3). After the TE placement, the necessity of intervention to the implant or expander prior to the RT was observed depending on the patient characteristics. There is no consensus among the physicians about the expander deflation before the RT, and this decision is take on a case-by-case basis (2). In the American study, the frequency of expander deflation was 11.5% prior to RT, and the majority of the physicians (75%) did not prefer intervention routinely (8). It was emphasized that this difference in intervention was due to the geographical location. The physicians preferred the deflation for the improvement of the nodal coverage. Similarly, Chen et al. (7) showed that the total deflation rate of the expander was low (13%), while 47% of the physicians preferred to reduce the volume of 150–200 cc to decrease the dose to the heart and the ipsilateral lung (7). In our survey, the rate of intervention was found to be higher (68%) when compared with others. Nevertheless, 80% of the physicians do not prefer a complete deflation in expander intervention. Physicians who did not prefer complete deflation in this study were more experienced with implanted patient irradiation, although the difference was not statistically significant (p=0.92). Immediate total expander deflation prior to RT can affect the RT cosmetic outcomes. In an animal model, Celet Ozden et al. (9) determined complete TE deflation immediately before RT increased the radiosensitization with a consequence of increased blood pooling and oxygenation (9). In our study, the respondents did not initiate the RT immediately after the expander intervention, and 50% of them waited for 1 week to start the irradiation. It was statistically significant that the physicians who waited for 2 weeks after the intervention were those who preferred a complete deflated expander (p=0.01). It may thus be considered to reduce the side-effects by allowing tissue repair by adding a 2-week waiting period after the full deflation of TE.

Bolus is applied to the chest wall after mastectomy for increasing the dosage to skin (3). There are differences regarding the utilization of bolus in patients with mastectomy among radiation oncologists, which is more pronounced in patients undergoing BR. In their study, Thomas et al. (8) reported that 52.2% of the respondents used bolus routinely while treating BC patients with TEs. In addition, 11.1% of the participants reported that the bolus utilization differed from patient to patient. In a worldwide survey study, bolus was not used routinely in PMRT with BR. Especially, high-volume BC physicians did not prefer to use a bolus. Asper the literature, bolus utilization was 62% in America and 24% in Europe (7). In Turkey, the routine use of bolus is 22%, and the majority of physicians (60%) prefer using bolus in the presence of skin involvement or anterior surgical margin positivity. Although 76.9% of the physicians who preferred to use bolus in the presence of high-risk factors and who treated >50 new BC patient annually, this correlation was not significant (p=0.53). Regarding the timing of bolus, in America, the most preferred bolus application was every other day at the rate of 53.2%. In the same study, 37.2% of the responders reported that they applied bolus until the patient could tolerate it (8). We observed that, 73% of the physicians preferred to use bolus in any half of RT and that only four physicians treated using bolus during the entire treatment process.

It is important to prescribe a boost dose in early BC patient for the local recurrence after BCS (10, 11). Increased negative cosmetic outcomes have been reported with high boost doses, even in non-mastectomy BC patients (12). The utility of boost varies between physicians in patients with BR. Chen et al. (7) reported that, 40% of the physicians did not prescribe the boost doses in treatment of BC patients with reconstruction. However, they found that physicians aged ≥50 years defined boost doses to be more statistically significant than young physicians (69% vs 55%). Although geographic differences exist in the USA, 33.5% of the physicians do not prescribe boost doses, while 42.9% of the physicians deliver a boost to only selected reconstructed BC cases (8). In Turkey, while 60% of the physicians do not define a chest-wall boost in the RT of patients with BR, 38% add a boost treatment in the presence of high-risk factors for local recurrence. Although 80% of the physicians who never prescribe a boost for patients with BR treated >50 new BC patients annually, we could not determine any statistically significant correlation between the number of patients with annual treatment and the definition of boost (p=0.36).

Hypofractionation has been accepted as a new standard for BC radiation therapy (13, 14). In addition, increasing evidence has been provided regarding the use of hypofractionation after BR (15, 16). In the current survey, only two responders declared that they used hypofractionation for implant irradiation. Most of the physicians (86%) preferred 2 Gy as the daily fraction dose in conventional RT.

There exists no guideline for target volume delineation in patients undergoing BR during our survey, and most physicians (84%) defined the whole implant or TE as the CTV. More experienced physicians sometimes do not include the entire implant in CTV. In addition, we noticed a statistically significant relationship between 81% of the physicians who included the whole implant into the CTV and those who treated <10% of the reconstructed patients annually (p=0.01).

Another conflict among the radiation oncologists was regarding the optimal radiation technique for patients with BR. Both IMRT and volumetric modulated arc therapy are preferred in addition to field-in-field and 3-D conformal RT (2). In Turkey, 74% of the physicians prefer 3D technique for patients with BR. The DIBH technique is commonly used for left-sided BC patients, and the rate of preference is 52% in our survey. In particular, the physicians who treated >50 new BC patients annually used this technique more frequently, and this correlation was statistically significant (p=0.01).

The side-effects of reconstructed breast irradiation depend on multiple factors such as the surgery type, timing, and RT dose (17). In our study, most of the physicians did not observe any difference between the early side-effects of reconstructed and non-reconstructed patients after the PMRT. Physicians who needed an intervention to TE declared that they experienced more early side-effects (p=0.006).

In the two survey studies that have been previously published, the participation rate of the physicians was 8% and 19.2% (7, 8). Our study was organized by the Turkish Radiation Oncology Society Breast Cancer Study Group at the participation rate of 47.6%. In addition, the majority of respondents (88%) treated >50 newly diagnosed BC patients annually. On the other hand, the number of patients treated with PMRT after BR in Turkey was quite low, with a ratio of 10%. Although there is an extensive questionnaire prepared with 23 questions, it has not been previously validated, and no physicians could fully reflect their daily practice because of the limited number of questions and answers. However, this document serves as a baseline of

practice in reconstructed BC patients with PMRT in Turkey and was created for promoting awareness among radiation oncologists.

In conclusion, as in other countries, treatment practice for PMRT after BR differs among the physicians in Turkey. However, this difference was found to be less among experienced physicians. PMRT remains the most common approach with TE, and the number of cases with AR is rare. In Turkey, hypofractionation is not preferred after BR. Treatment with boost and bolus is generally preferred in high-risk patients. No increase in early RT side-effects was observed by the respondents for patients with BR.

Key Points

- This is a questionnaire study about the increasing cases of implant irradiation in Turkey as well as across the world.
- Different practices among radiation oncologists regarding implant irradiation have been introduced, but only a limited number of studies have investigated this topic in Turkey.
- The questionnaire was filled only by physicians interested in breast irradiation who were members of the Turkish Radiation Oncology Breast Cancer Study Group. Thus, more specific results were achieved.
- Having a higher participation rate compared to other survey studies increases the statistical power of the study.

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Ethics Committee Approval: This study was approved by the local institutional ethics committee (Acıbadem University and Acıbadem Healthcare Institutions Medical Research Ethics Committee) (code number 2018-3/23).

Informed Consent: Voluntary nature of participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: N.B.; Design: G.A.; Data Collection or Processing: N.K.; Analysis or Interpretation: M.Ş.Ş., N.K.; Literature Search: N.K., G.A.; Writing: N.K., G.A., N.B.

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Appendix 1. Survey questions

1. What is your level of expertise in radiation oncology?
- a) Assistant Physician
- b) Specialist Physician
- c) Associate Professor
- d) Professor

2. How many years of radiation oncology practice do you have?
- a) 2 years and less
- b) 2–5 years
- c) 5–10 years
- d) 10–15 years
- e) 15 –20 years
- f) More than 20 years

3. Which institution do you work for?
- a) Government-based education - research hospital or university hospital
- b) Private university and the affiliated hospital
- c) Private center or freelance physician

4. What is the number of patients diagnosed with a new breast cancer within 1 year?
- a) 10 and fewer
- b) Between 10–50
- c) 50–100
- d) More than 100

5. Do you have any published publications on breast reconstruction and radiotherapy?
- a) Yes
- b) No

6. How many patients did you treat after mastectomy was temporary reconstructed?
- a) 10% and less
- b) Less than 50%
- c) More than 50%

7. The type of major cases in which you applied radiotherapy;
- a) Cases with autologous reconstruction.
- b) Cases with implant reconstruction.

8. What is the proportion of patients who underwent permanent implant before radiotherapy? (the remaining cases are considered as tissue expander irradiation):
- a) 10% and less
- b) Less than 50%
- c) More than 50%

9. To what extent do you interfere with the tissue expander for a good planning in expander irradiation?
- a) Almost never.
- b) In less than 10% of the cases.
- c) Almost half of the cases I have treated needed intervention.
- d) Almost all cases I have treated needed intervention.

10. Do you prefer full deflation if the expander needs to be intervened?
- a) Yes
- b) No

11. Do you wait for a certain time to start radiotherapy after interfering with the expander?
- a) Yes
- b) No

12. If the answer to the above question is "Yes", what is the duration time?
- a) I wait for a week
- b) I wait for at least 2 weeks.

Appendix 1. Survey questions

13. Do you apply bolus during radiotherapy in reconstructed cases?
a) Yes
b) No
c) I apply bolus in the presence of high-risk factors such as skin involvement or anterior surgery margin proximity.

14. What is your practical approach to cases in which you have a bolus?
a) In each fraction during the whole treatment
b) In the first half of the whole treatment period
c) In the last half of the whole treatment period
d) One day with bolus, and one day without bolus

15. Do you prescribe boost dose to chest wall after external irradiation in reconstructed cases?
a) Almost every case
b) Almost never
c) In high-risk cases of chest-wall recurrence

16. Are there any cases treated with hypofractionation after reconstruction (fraction dose >2 Gy/day)?
a) Yes
b) No

17. What is your preferred daily fractionation dose in reconstructed patients?
a) 1.8 Gy/day
b) 2 Gy/day

18. Do you include the entire implant or expander in the CTV volume?
a) Yes
b) No
c) I did not include the whole implant or tissue expander in CTV in some cases.

19. Do you prefer especially dynamic IMRT in reconstructed cases?
a) Yes
b) I can provide a good planning with 3D and field-in-field technique.

20. Do you try to keep it out of the radiotherapy area if there is an expander inflation port?
a) Yes
b) No

21. Do you prefer deep breath-hold technique in reconstructed cases?
a) Yes
b) No
c) Deep breath-hold technique is not done routinely in our clinic.

22. Do you irradiate the mamaria-interna area with wide tangential field technique in reconstructed cases?
a) Yes
b) No

23. Do you observe an increase in the frequency and severity of skin reactions compared to those without reconstruction?
a) Yes
b) No