

# Intra-operative Radiation Therapy versus Whole Breast External Beam Radiotherapy: A Comparison of Patient-Reported Outcomes

Jo Leatherman, MS-3<sup>1</sup>, Christina Nicholas, M.D.<sup>1,2</sup>, Therese Cusick, M.D.<sup>1,2</sup>, Ellen Cooke, M.D.<sup>1,3</sup>, Elizabeth Ablah, Ph.D.<sup>1,4</sup>, Hayrettin Okut, Ph.D.<sup>1,4,5</sup>, Diane Hunt, M.D.<sup>1,2</sup>

<sup>1</sup>University of Kansas School of Medicine-Wichita, Wichita, KS

<sup>2</sup>Department of Surgery

<sup>3</sup>Department of Radiology

<sup>4</sup>Department of Population Health

<sup>5</sup>Office of Research

Received Feb. 2, 2021; Accepted for publication April 7, 2021; Published online July 9, 2021  
<https://doi.org/10.17161/kjfm.voll415147>

## ABSTRACT

**Introduction.** This project sought to compare patient-reported outcomes between patients who received intra-operative radiation therapy (IORT) and those who qualified for IORT but received whole-breast external beam radiation therapy (EBRT) following breast-conserving surgery (BCS).

**Methods.** Three scales from the BREAST-Q Breast Cancer BCT Module Version 2.0 questionnaire were used to collect patient-reported outcomes regarding post-operative physical well-being of the chest, post-operative satisfaction with breast cosmesis, and post-operative adverse effects of radiation.

**Results.** Patients who received EBRT travelled farther on average than patients who received IORT to complete treatment. Respondents who received IORT reported better physical well-being of the chest than those who received EBRT. Regression revealed that the respondent's age was the determining factor in the difference between IORT and EBRT post-operative physical well-being scores, where younger patients report poorer well-being. There was no difference in patient-reported outcomes regarding post-operative satisfaction with breast cosmesis or adverse effects of radiation.

**Conclusions.** Patients who received IORT reported better physical well-being of the chest than patients who received EBRT. There appeared to be a relationship between age and physical well-being of chest. This study suggested that there was no difference in patient-reported outcomes concerning post-operative satisfaction with breast cosmesis or post-operative adverse effects of radiation between patients who received IORT and those who received EBRT.

*Kans J Med* 2021;14:170-175

## INTRODUCTION

In 2015, there were approximately 3,418,124 women living in the United States with breast cancer.<sup>1</sup> In 2019, approximately 268,600 new cases were diagnosed, and 41,760 U.S. women died due to breast cancer-related complications.<sup>2</sup> Among Kansans, an estimated 2,420 women were diagnosed with breast cancer in 2019, and 350 died due to breast cancer-related complications.

Since the 1990s, breast-conserving therapy (BCT), a combination of breast-conserving surgery (BCS) and radiation therapy (RT), has been the preferred treatment for patients with breast cancer.<sup>3</sup> Traditional whole-breast external beam radiation therapy (EBRT) has been

the primary form of RT following BCS. Adjuvant EBRT involves the patient receiving treatment at a radiation oncology center five days a week for three to six weeks. Up to 21% of patients who undergo BCS do not complete the prescribed RT,<sup>4</sup> and failure to complete RT is associated with higher mortality and a 25% relative increase in local recurrence.<sup>5,6</sup> Those least likely to complete this therapy included patients who are African American, resided in a rural community, or were single.<sup>7</sup> In addition, travel burden, adverse effects of treatment (e.g., fatigue, rib fractures, arm lymphedema),<sup>8</sup> and the complex multidisciplinary nature of breast cancer treatment likely contribute to failure of completion of adjuvant EBRT.<sup>4</sup>

In 2000, intra-operative radiation therapy (IORT) was introduced, a technique that uses a targeted, one-time, high-dose RT performed concurrently with BCS for low-risk patients.<sup>9,10</sup> Two randomized control trials, TARGIT-A and ELIOT, suggested IORT is non-inferior to EBRT in terms of local recurrence risk for low-risk patients.<sup>9,10</sup> To be considered for IORT, the patient's tumor profile must fit the following criteria: estrogen receptor (ER) positive, human epidermal growth factor receptor 2 (Her2) negative, size less than 2 cm on pre-operative imaging, negative lymph nodes,<sup>11</sup> and no evidence of ductal carcinoma in-situ (DCIS) or invasive lobular carcinoma on initial core biopsy.<sup>12</sup> The overall toxicity profile was lower for IORT patients, and quality-adjusted life-years were improved among IORT patients compared to EBRT patients.<sup>13,14</sup> IORT patients reported excellent outcomes but did not offer comparison to EBRT patients.<sup>15</sup> Another study suggested IORT patients reported less general pain and better societal role functioning than EBRT patients,<sup>16</sup> and a third suggested IORT patients reported fewer breast symptoms and body image concerns than EBRT patients.<sup>17</sup> A lifetime cost-effectiveness analysis suggested IORT was a more valuable strategy than EBRT and was preferential among low-risk patients.<sup>18</sup>

IORT has a higher risk of ipsilateral breast tumor recurrence compared to EBRT if used inappropriately,<sup>19</sup> so it is essential to stratify patients based on risk of local recurrence and metastases before choosing this strategy.<sup>12</sup> Post-operative discovery of predefined factors (e.g., positive sentinel node) could result in the addition of EBRT (expected for approximately 15% of patients);<sup>10</sup> in this situation, IORT serves as a tumor bed boost dose and has been demonstrated to further lower the risk of local recurrence.<sup>11</sup>

More research is needed regarding the comparison of patient-reported outcomes based on RT type (IORT versus EBRT), including post-operative satisfaction with breast cosmesis, post-operative physical well-being of the chest, adverse effects of radiation, and travel burden. This project sought to compare patient-reported outcomes between patients who received IORT and patients who qualified for IORT but received EBRT.

## METHODS

**Participants.** All IORT-eligible patients of three Wichita-area surgeons from May 1, 2017 through April 17, 2019 were considered

for this study. Inclusion criteria were women 50 years or older with tumors that were ER-positive, Her2-negative, size less than 2 cm on pre-operative imaging, and without identification of DCIS or invasive lobular carcinoma on initial core biopsy. No incentive was provided for participation in this study. This case-control study was approved by the Human Subjects Committee at the University of Kansas School of Medicine-Wichita.

**Instruments.** Office staff at participating clinics used ICD-10 codes (19294, 19297, and 19301) to identify eligible patients within their respective electronic health records (EHRs). The abstracted variables included patient identifiers (e.g., name, address, phone number, date of birth, medical record number), patient demographics (e.g., race, insurance coverage), tumor information (e.g., ER and Her2 status, size), and therapy details (e.g., IORT vs. EBRT, date of surgery). Study data were collected and managed using REDCap® electronic data capture tools hosted at the University of Kansas Medical Center.<sup>20</sup>

A survey was developed to collect patient-reported outcomes including breast satisfaction, adverse effects of radiation, and travel burden. The survey included questions from the BREAST-Q Breast Cancer BCT Module Version 2.0 questionnaire,<sup>21</sup> as well as additional questions created by the research team, all of which used Likert scales.

The BREAST-Q has been used since 2009 to collect meaningful and reliable data regarding patient-reported outcomes.<sup>22,23</sup> Three scales from the BREAST-Q BCT module were used to assess outcomes at the time of the survey. The first scale included 11 questions about post-operative satisfaction with breast cosmesis (e.g., appearance when clothed, breast shape when wearing a bra, feeling normal in clothes, being able to wear fitting clothing, how the breast sits/hangs, how smoothly shaped the breast looks, the contour of the breast, whether breasts are equal in size, how normal the breast looks, whether breasts look the same, and appearance when unclothed). The second scale included nine questions about post-operative physical well-being of the chest (e.g., difficulty lifting or moving arms; difficulty sleeping because of breast discomfort; tightness, pulling, tenderness, sharp pain, or aching feeling in the breast area; difficulty lying on the side of lumpectomy breast; or swelling of the arm (lymphedema)). The third scale included six questions about post-operative adverse effects of radiation at the time of the survey (e.g., amount of bother from breast skin looking different, marks on breast skin caused by radiation, radiated breast skin feeling dry, radiated breast skin feeling sore/sensitive when touched, radiated breast skin feeling unnaturally thick, and radiated breast skin feeling irritated by clothing). Additionally, the authors modified these questions to assess adverse effects at the time of RT (n = 6) to address the discrepancy regarding time since surgery among patients in the nearly two-year study period. An additional eight of questions addressed complications related to RT. Participants were asked to provide the geographic location of their RT, the number of weeks they received RT, and the number of days per week they received RT.

**Procedures.** Case sample size was limited to the 23 patients

receiving IORT from May 1, 2017 through April 17, 2019. All patients who qualified for IORT but instead received EBRT during the same time period were identified as possible controls. These patients were matched to the IORT study arm by age and surgeon, then randomized, using a random number generator to create a control arm of equal size.

After the study and control arms were established, patients were called and invited to participate in the study. A maximum of three attempts were made, including voicemails. Upon agreement to participate, patients were given the option to complete the questionnaire over the phone, through the mail, or through an online survey. A REDCap® database was used to log completed calls and collect additional information (e.g., best time to call, current mailing address, e-mail address). All participants gave informed consent.

Likert scale responses to the BREAST-Q were summed and converted into an equivalent Rasch-transformed score (0-100). Higher equivalent Rasch-transformed scores reflect a better outcome. To determine travel burden, the roundtrip distance from each patient's home address at the time of BCT to the patient's radiation oncology center was calculated using Google Maps.<sup>14</sup> The shortest roundtrip route was recorded in miles as the patient's travel distance. The travel distance was multiplied by the number of radiation treatments completed to determine the total number of miles traveled for RT.

**Statistical Analysis.** SAS version 9.4 was used to generate descriptive statistics for nominal, categorical, and continuous variables (SAS Int. Inc., Cary, NC). Prior to data analysis, outcomes were tested for normal distribution using Shapiro-Wilk's method. Comparisons across the two groups were made using t-tests and analysis of variance (ANOVA) tests for normally distributed variables. For non-normal distribution with appropriate transformation operations, non-parametric approaches such as Mann-Whitney U test and Kruskal-Wallis test were conducted. Data were reported as frequencies, percentages, means, standard deviations, observed t's, F and Likelihood Ratio Chi-square values, and corresponding significance levels (p).

Multiple linear regression was used to model the relationship between post-operative physical well-being, and immediate adverse effects of radiation with age, tumor size, RT type, and surgeon by fitting a linear equation to observed data. All statistical tests at  $p \leq 0.05$  were considered significant.

## RESULTS

Of the 155 women who had BCS during the study time period, 54.8% (n = 85) were excluded due to not meeting IORT criteria (Figure 1). The 70 remaining patients were given the option to choose IORT or EBRT based on their preferences. Of the 70 patients who were candidates for IORT based on their tumor characteristics, 32.9% (n = 23) received IORT (identified from ICD codes 19294 and 19297) and were invited to participate by completing a survey. Those who received EBRT during the same period (67.1%, n = 47) were matched to the study arm and invited to participate (n = 22). One patient declined participation, one was ineligible as she was undergoing chemotherapy prior to radiation, and 10 did not respond. Six participants elected not to undergo RT (five EBRT and one IORT due to technical difficulties) and were not asked to complete the survey. Altogether, 27 of the 45 surveys were returned, for a response rate of 60%.

One patient who received IORT had positive margins and subsequently underwent 25 EBRT treatments; she was included in the analysis of the IORT group on an intent-to-treat basis. This singular exception representing 6% of the IORT group remains well below the expected 15% of patients who require addition of EBRT after IORT.<sup>10</sup>

Participants ranged from 51 to 81 years, with a mean age of 64.0 years (SD = 6.8). Caucasians accounted for the majority of the population (94% of IORT participants and 100% of EBRT participants, n = 27; Table 1). Most IORT patients were insured by Medicare (83%, n = 15), and the largest insurer of EBRT patients was Blue Cross and Blue Shield of Kansas (44%, n = 4). Table 2 provides an age comparison by radiation therapy type.

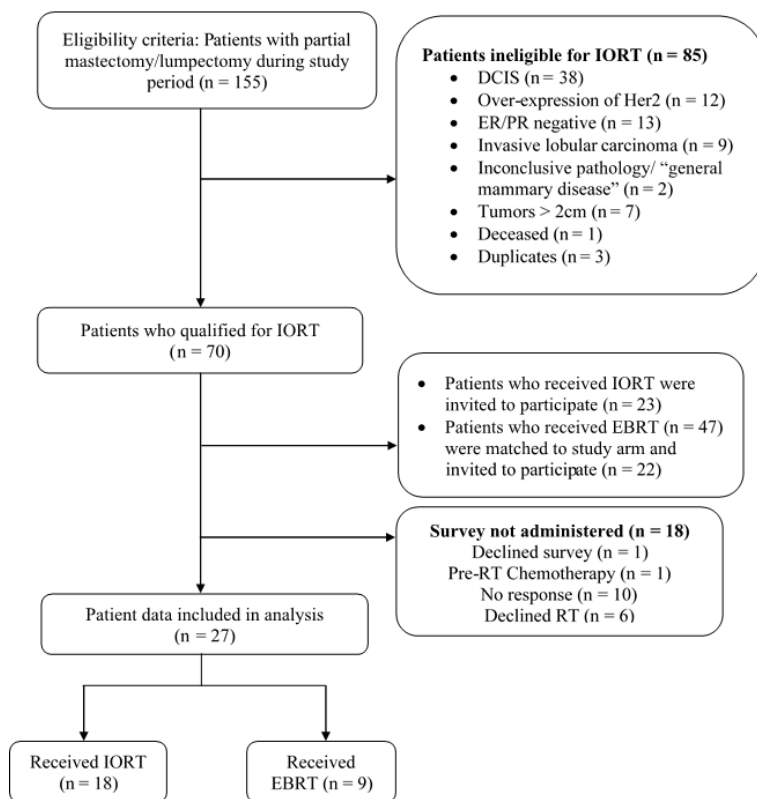


Figure 1. Flow diagram.

More participants who received IORT (11.8%, n = 2) reported being bothered “a lot” by the necessity to limit work or activity than those who received EBRT (0%, n = 0),  $\chi^2(3, n = 27) = 8.9, p = 0.03$ . The number of respondents who required additional therapies to address the side effects of their radiation therapy (e.g., topical moisturizers) was greater among those who received EBRT (22.2%, n = 6) than those who received IORT (7.4%, n = 2),  $\chi^2(1, n = 27) = 7.04, p < 0.01$ .

Of the four BREAST-Q scales used, only post-operative physical well-being equivalent Rasch-transformed scores were associated with RT type (Table 3). Respondents who received IORT reported better physical well-being of the chest (mean = 86.2) than those who received EBRT (mean = 66.4),  $Z = -1.73, p = 0.05$ .

Table 1. Participant demographics.

	IORT		EBRT		p value
	Frequency	%	Frequency	%	
Age					0.25
50 - 59 years	2	11%	3	33%	
60 - 69 years	11	61%	6	67%	
70 - 79 years	3	17%	0	0%	
80 years or older	2	11%	0	0%	
Race					0.47
White/Caucasian	17	94%	9	100%	
Black/African American	1	6%	0	0%	
Ethnicity					0.29
Not Hispanic or Latino	16	89%	9	100%	
Hispanic or Latino	2	11%	0	0%	
Insurance					0.01
Medicare	15	83%	2	22%	
Blue Cross Blue Shield of Kansas	0	0%	4	44%	
Aetna	1	6%	1	11%	
Miscellaneous	1	6%	0	0%	
United Healthcare	1	6%	1	11%	
Ascension	0	0%	1	11%	

Table 2. Age comparison by radiation therapy type.

RT type	N	Mean age (years)	SD	Median	Quartile range	p value
IORT	18	66.6	7.1	67.2	4.7	0.008
EBRT	9	61.5	5.2	61.9	7.4	

Table 3. Comparison of BREAST-Q mean equivalent Rasch-transformed scores between IORT and EBRT participants.<sup>a</sup>

BREAST-Q Scale	IORT (SD)	EBRT (SD)	p value
Post-op satisfaction with breast cosmesis	85.9 (16.4)	70.5 (26.8)	0.10
Post-op physical well being: Chest	86.2 (19.6)	66.4 (30.9)	0.05
Post-op adverse effects of radiation at treatment time	88.2 (16.6)	84.6 (9.3)	0.18
Post-op adverse effects of radiation at survey time	84.7 (23.8)	82.2 (28.6)	0.49

<sup>a</sup>Higher equivalent Rasch-transformed scores denote better outcome.

**Table 4. Questions included in the BREAST-Q Version 2.0 for Physical Well-Being: Chest.**

In the past week, how often have you experienced:	None of the time	Some of the time	All of the time
a. Difficulty lifting or moving your arms?	1	2	3
b. Difficulty sleeping because of discomfort in your breast area?	1	2	3
c. Tightness in your breast area?	1	2	3
d. Pulling in your breast area?	1	2	3
e. Tenderness in your breast area?	1	2	3
f. Share pains in your breast area?	1	2	3
g. Aching feeling in your breast area?	1	2	3
h. Difficulty laying on the side of your lumpectomy breast?	1	2	3
i. Swelling of the arm (lymphedema) on the side(s) that you had your breast surgery?	1	2	3

All patients who received IORT (100%, n = 18) were insured by companies that cover IORT (e.g., Medicare, UnitedHealthcare), whereas 44% (n = 4) of those who received EBRT were insured by companies that cover IORT,  $\chi^2(1, n = 27) = 12.3, p < 0.01$ . More patients who received EBRT (18%, n = 6) did not complete RT as prescribed by their physician. One patient who was prescribed IORT (3%) did not receive her treatment due to equipment malfunction, and she thereafter elected not to complete EBRT,  $\chi^2(1, n = 33) = 6.19, p = 0.01$ . The average age of patients who elected to forgo EBRT was 65.7 years.

For all patients, the median total travel distance to complete RT was 100 miles, with a mean of 598 miles (SD = 1778.39) and a range of three to 9,520 miles. Participants who received EBRT travelled farther (mean = 1351 miles  $\pm$  2783.52) than participants who received IORT (mean = 138 miles  $\pm$  247),  $Z = 2.99, p < 0.01$  to complete treatment.

Age, tumor size, RT type, and surgeon explained the 39% variability in post-operative well-being of chest. After adjusting for tumor size, RT type, and surgeon, only age ( $\beta = 1.93, SE = 0.64, t = 2.99$  and  $p = 0.007$ ) was associated significantly with this variability, with younger patients reporting poorer well-being,  $F(4,22) = 3.48, p = 0.02, R^2 = 0.39$ . Though the model was not significant ( $F(4,22) = 1.14, p = 0.36$ ), immediate adverse effects of radiation as defined by the Rasch-transformed score were associated solely with the participant's age ( $p = 0.05$ ).

**DISCUSSION**

The current study suggested that IORT patients reported better post-operative physical well-being than EBRT patients. This was an expected outcome as IORT has minimal chest wall and pulmonary radiation exposure. While tangential beams are used with EBRT, often the physical shape of the chest wall requires inclusion of the underlying ribs, superficial lung, and more rarely, portions of the anterior aspect of the heart within the treatment fields to deliver dose to all of the breast tissue adequately. There are well-documented secondary effects of this

potential exposure of these organs.<sup>24,25</sup>

There were no differences between patients who received IORT or EBRT in post-operative satisfaction with breast cosmesis or post-operative adverse effects of radiation. This was consistent with one study which suggested that IORT patients have a comparable quality of life to EBRT patients,<sup>17</sup> but inconsistent with another study which suggested that IORT patients reported better quality of life than EBRT patients.<sup>13</sup> This variability may be due to the different tools used to assess patient-reported outcomes; other studies have used the European Organization for the Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire-Core 30 and Breast 23 (QLQ-C30 and BR23).<sup>13,17</sup> The current study used the BREAST-Q because the scales were more specific to the adverse effects of radiation, which was more pertinent to the research question, and fewer questions were included, requiring less time commitment for participants.

The current study suggested that fewer women who are prescribed adjuvant EBRT complete their RT than those who are prescribed IORT. Participants reported a mean difference of 1,000 miles of traveling between EBRT and IORT patients to complete RT. This was consistent with previous studies that reported that travel distance to a radiation center was inversely related to prescribed RT receipt.<sup>7,26</sup> If a woman is not willing to undergo radiation, she often will select a mastectomy over driving that many miles and potentially losing her job (according to participating surgeons, email communication, August 2020). A previous study suggested one-step IORT is associated with an advantage in work resumption.<sup>27</sup> This is particularly relevant in a state such as Kansas with concerns surrounding rural patients' access to treatment. Among the 18% of EBRT patients in this study who chose not to receive adjuvant EBRT after surgery, the average age was 65.7 years. Patients aged 70 and over are typically not offered EBRT, however, particularly healthy patients in this age range may be considered for IORT as a single dose may be considered more reasonable. It also should be considered that a one-time visit rather than multiple appointments limits possible SARS-CoV-2 exposure for patients.

The current study suggested that IORT recipients were bothered "a lot" by the necessity to limit work or activity at the time of their treatment, more than EBRT recipients. The wording of this question may have been confusing as to whether patients were bothered by travel, radiation, or post-operative restrictions. This likely was motivation for the patient choice for a single dose of radiation (IORT) over multiple trips to a radiation center (EBRT) over many weeks in a rural state.

The current study suggested that the number of respondents who required additional therapies to address the side effects of their RT (e.g., topical emu oil, Cetaphil® lotion) was greater among those who received EBRT. When given the option (i.e., their insurance covers the treatment), the current study suggested that women will choose IORT over EBRT. This was consistent with a previous study that indicated that patients chose IORT, and they were willing to travel for it.<sup>28</sup> The current study showed that women who receive EBRT travel farther over the course of their treatment than patients who receive IORT. This was consistent with a previous study done in the UK correlating the greater distance with more time travelled and higher CO<sub>2</sub> emissions.<sup>29</sup> IORT's one-time nature could ease treatment burden on patients substantially, particularly those who live in rural areas and must travel long

distances to the nearest radiation oncology center for repeated EBRT treatments.

**Limitations.** Recall bias may have contributed to participants' responses regarding adverse effects of radiation at the time of surgery, further amplified for participants who had surgery at the beginning of the study period. Sample size was limited by the number of patients who received IORT. Risk-adapted criteria necessarily limited the patient pool, as only 45% of BCS patients were considered eligible for IORT. Whereas 78% (18/23) of IORT patients responded to the survey, only 41% (9/22) of EBRT patients responded. This discrepancy further limited the comparison of the data. The small sample size also can be attributed partly to some private insurers considering IORT to be experimental or investigational. In this study, only 32% (23/70) of IORT-eligible patients had insurance coverage for IORT. Most of the surveyed patients who qualified for IORT but received EBRT had insurance through Blue Cross and Blue Shield of Kansas (54.5%, n = 12), the largest insurance carrier in Kansas. Medicare and private insurers in several states have concluded that IORT is reasonable and medically necessary for suitable patients and cover this treatment.<sup>30-32</sup>

## CONCLUSIONS

Most patients who had insurance coverage for IORT chose IORT over EBRT. This study showed that patients who received EBRT travelled farther on average than patients who received IORT to complete treatment. Patients who received IORT reported better physical well-being of the chest than patients who received EBRT. There was no difference in patient-reported outcomes concerning post-operative satisfaction with breast cosmesis or adverse effects of radiation between patients who received IORT and those who received EBRT.

## ACKNOWLEDGEMENTS

The authors thank to Rosalee Zackula for her assistance with REDCap®.

## DATA AVAILABILITY STATEMENT

The datasets generated during and analyzed during the current study are not publicly available as these data were abstracted from medical charts and contain information that could compromise research participant privacy.

## REFERENCES

- National Cancer Institute, DCCPS, Surveillance Research Program. Surveillance, Epidemiology, and End Results (SEER) Program Populations (1969-2016). December 2017. [www.seer.cancer.gov/popdata](http://www.seer.cancer.gov/popdata).
- Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. *CA Cancer J Clin* 2019; 69(1):7-34. PMID: 30620402.
- No authors. NIH consensus conference. Treatment of early-stage breast cancer. *JAMA* 1991; 265(3):391-395. PMID: 1984541.
- Tuttle TM, Jarosek S, Habermann EB, Yee D, Yuan J, Virnig BA. Omission of radiation therapy after breast-conserving surgery in the United States: A population-based analysis of clinicopathologic factors. *Cancer* 2012; 118(8):2004-2013. PMID: 21952948.
- Fisher B, Anderson S, Bryant J, 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(16):1233-1241. PMID: 12393820.
- Clarke M, Collins R, Darby S, et al. Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: An overview of the randomised trials. *Lancet* 2005; 366(9503):2087-2106. PMID: 16360786.
- Hershman DL, Buono D, McBride RB, et al. Surgeon characteristics and receipt of adjuvant radiotherapy in women with breast cancer. *J Natl Cancer Inst* 2008; 100(3):199-206. PMID: 18230795.

- Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, Abeloff MD. *Abeloff's Clinical Oncology*. Fifth edition. Philadelphia: Elsevier, 2014. ISBN: 1455728659.

- Veronesi U, Orecchia R, Maisonneuve P, et al. Intraoperative radiotherapy versus external radiotherapy for early breast cancer (ELIOT): A randomised controlled equivalence trial. *Lancet Oncol* 2013; 14(13):1269-1277. PMID: 24225155.

- Vaidya JS, Joseph DJ, Tobias JS, et al. Targeted intraoperative radiotherapy versus whole breast radiotherapy for breast cancer (TARGIT-A trial): An international, prospective, randomised, non-inferiority phase 3 trial. *Lancet* 2010; 376(9735):91-102. PMID: 20570343.

- Harris EER, Small W Jr. Intraoperative radiotherapy for breast cancer. *Front Oncol* 2017; 7:317. PMID: 29312887.

- Vaidya JS, Wenz F, Bulsara M, et al. Risk-adapted targeted intraoperative radiotherapy versus whole-breast radiotherapy for breast cancer: 5-year results for local control and overall survival from the TARGIT-A randomised trial. *Lancet* 2014; 383(9917):603-613. PMID: 24224997.

- Corica T, Nowak AK, Saunders CM, et al. Cosmesis and breast-related quality of life outcomes after intraoperative radiation therapy for early breast cancer: A substudy of the TARGIT-A Trial. *Int J Radiat Oncol Biol Phys* 2016; 96(1):55-64. PMID: 27511847.

- Sosin M, Gupta SS, Wang JS, et al. A prospective analysis of quality of life and toxicity outcomes in treating early breast cancer with breast conservation therapy and intraoperative radiation therapy. *Front Oncol* 2018; 8:545. PMID: 30560085.

- Olsen JR, Ridings JW, Dickinson J, et al. Patient reported outcomes from a prospective risk-adapted breast IORT registry trial. *Int J Radiat Oncol* 2018; 102(3):E591-E592.

- Welzel G, Boch A, Sperk E, et al. Radiation-related quality of life parameters after targeted intraoperative radiotherapy versus whole breast radiotherapy in patients with breast cancer: Results from the randomized phase III trial TARGIT-A. *Radiat Oncol* 2013; 8:9. PMID: 23294485.

- Wetzel G, Hofmann F, Blank E, et al. Health-related quality of life after breast-conserving surgery and intraoperative radiotherapy for breast cancer using low-kilovoltage x-rays. *Ann Surg Oncol* 2010; 17(Suppl 3):S359-S367. PMID: 20853059.

- Patel R, Ivanov O, Voigt J. Lifetime cost-effectiveness analysis of intraoperative radiation therapy versus external beam radiation therapy for early stage breast cancer. *Cost Eff Resour Alloc* 2017; 15:22. PMID: 29151818.

- Zhang L, Zhou Z, Mei X, et al. Intraoperative radiotherapy versus whole-breast external beam radiotherapy in early-stage breast cancer: A systematic review and meta-analysis. *Medicine (Baltimore)* 2015; 94(27):e1143. PMID: 26166124.

- Harris PA, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap) – A metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 2009; 42(2):377-381. PMID: 18929686.

- Google Maps. Google Maps. 2019. <https://maps.google.com>.

- Cohen WA, Mundy LR, Ballard TNS, et al. The BREAST-Q in surgical research: A review of the literature 2009-2015. *J Plast Reconstr Aesthet Surg* 2016; 69(2):149-162. PMID: 26740288.

- Pusic AL, Klassen AF, Scott AM, Klok JA, Cordeiro PG, Cano SJ. Development of a new patient-reported outcome measure for breast surgery: The BREAST-Q. *Plast Reconstr Surg* 2009; 124(2):345-353. PMID: 19644246.

- Taylor C, Correa C, Duane FK, et al. Estimating the risks of breast cancer radiotherapy: Evidence from modern radiation doses to the lungs and heart and from previous randomized trials. *J Clin Oncol* 2017; 35(15):1641-1649. PMID: 28319436.

- Yi A, Kim HH, Shin HJ, Huh MO, Ahn SD, Seo BK. Radiation-induced complications after breast cancer radiation therapy: A pictorial review of multimodality imaging findings. *Korean J Radiol* 2009; 10(5):496-507. PMID: 19721835.

- Athas WF, Adams-Cameron M, Hunt WC, Amir-Fazli A, Key CR. Travel distance to radiation therapy and receipt of radiotherapy following breast-conserving surgery. *J Natl Cancer Inst* 2000; 92(3):269-271. PMID: 10655446.

- Sorrentino L, Fissi S, Meaglia I, et al. One-step intraoperative radiotherapy optimizes conservative treatment of breast cancer with advantages in quality of life and work resumption. *Breast* 2018; 39:123-130. PMID: 29674010.

<sup>28</sup> Larson KE, Valente SA, Shah C, et al. Are patients traveling for intraoperative radiation therapy? *Int J Breast Cancer* 2017; 2017:6395712. PMID: 29130001.

<sup>29</sup> Coombs NJ, Coombs JM, Vaidya UJ, et al. Environmental and social benefits of the targeted intraoperative radiotherapy for breast cancer: Data from UK TARGIT-A trial centres and two UK NHS hospitals offering TARGIT IORT. *BMJ Open* 2016; 6(5):e010703. PMID: 27160842.

<sup>30</sup> IntraOp. Medicare Increases Coverage for IORT. September 20, 2018. <https://intraop.com/news-events/medicare-increases-coverage-for-iort/>. Accessed May 21, 2019.

<sup>31</sup> IntraOp. AETNA adds single treatment Electron IORT to its Medical Policy. October 02, 2018. <https://intraop.com/news-events/aetna-adds-single-treatment-electron-iort-to-its-medical-policy/>. Accessed May 21, 2019.

<sup>32</sup> IntraOp. Anthem Blue Cross and Blue Shield coverage update increases access to electron IORT. January 30, 2018. <https://intraop.com/news-events/anthem-blue-cross-blue-shield-coverage-update-increases-access-electron-iort/>. Accessed May 21, 2019.

*Keywords: breast cancer, radiation therapy, patient-reported outcomes*