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Radiotherapy to the Left Breast with 3DCRT, IMRT or VMAT: International Medical Center Experience

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Abstract

Radiation therapy after conservative breast surgery is an integral part of the treatment of early breast cancer. The aim of radiotherapy is to achieve the best coverage of the Planning Target Volume (PTV), while reducing the dose to the Organs at Risk (OAR). Such goals are not always achievable with the conformal three dimensions plans (3DCRT). Recently, radiation oncologist uses Intensity Modulated Radiotherapy (IMRT) and Volumetric Modulated Arc Therapy (VMAT) for irradiating the breast. In this study, we compared 3DCRT, IMRT and VMAT for left breast cancer patients in terms of PTV coverage, OAR. We also revised the different dose distribution in 1) different breast volume categories, 2) nodal irradiation versus breast only, and 3) boost versus no boost. Results: The routinely reported dose constrains for the ipsilateral lung and for the heart were not significantly different on comparing the three techniques. While for the contralateral lung, the difference in mean dose was in favor of 3DCRT. In large breast volume, 3DCRT provided a lower Max dose to the contralateral lung and the lowest mean dose to the contralateral breast when compared to IMRT $p < 0.046$. In case of no nodal irradiation, the contralateral breast mean dose was lower in 3DCRT in comparison to IMRT and VMAT $p < 0.037$. When boost dose was given, 3DCRT plans had produced a lower Max dose to the contralateral lung $p < 0.017$. Conclusion: The three techniques (3DCRT, IMRT, and VMAT) can meet the clinical dosimetry demands of radiotherapy for left breast cancer after conservative surgery, as long as the routinely OARs only (heart and ipsilateral lung) are reported. Our study showed that 3CDRT can provide a lower dose to the contralateral organs (breast and lung), specially, in case of large breast volumes, no nodal irradiation and when a boost is given.

Keywords

Left Breast Radiotherapy, 3DCRT, IMRT, VMAT, Large Breast, Nodal Irradiation, Boost

1. Introduction

Radiation therapy after conservative breast surgery is an integral part of the locoregional treatment of early breast cancer since first approved by the World Health Organization Committee of Investigators for Evaluation of Methods of Diagnosis and Treatment of Breast Cancer in 1969 [1]. Such radiotherapy proved to reduce the local recurrence and the risk of death from breast cancer. But long-term trials had shown that radiotherapy can also augment the risk of ischemic heart disease through the incidental irradiation of the heart, especially in the left sided breast cancer, which is already known to be slightly more common than the right sided carcinoma [2] [3].

The dose-volume predictors for acute and late radiation-induced toxicities are established for the lung and heart as a whole structure. An estimated linear increase of 7.4% in major coronary events and 4.1% in cardiac mortality were found per every Gy of the mean heart dose (MHD) [3] [4]. For lung toxicity, dose-volume values of the treatment plan e.g., mean dose to the whole lung and V20, are the risk factors for pneumonitis and lung fibrosis. Other factors like breast volume, nodal irradiation and boost were found to increase the MHD in a study done by Pierce *et al.* [5].

The aim of radiation planning is to achieve the best coverage of the Clinical Target Volume (CTV)/Planning Target Volume (PTV), while reducing the dose to the Organs at Risk (OAR). However, ideal plans are not always achievable with the conformal three dimensions plans (3DCRT). In the last decade, radiation oncologist started to use the Intensity Modulated Radiotherapy (IMRT) and Volumetric Modulated Arc Therapy (VMAT) for irradiating the breast, as they believe that dose distribution and target dose of both the PTV and OAR could be better achieved [6].

The aim of the study is to compare 3DCRT, IMRT and VMAT for left breast cancer patients in terms of PTV coverage, OAR constrains, homogeneity index and conformity index. The study also revised the different dose distributions in 1) different breast volume categories, 2) nodal irradiation versus breast only, and 3) boost versus no boost.

2. Patients and Method

2.1. Patients

We revised the treatment plans of 19 female patients, who received radiotherapy after conservative surgery for left breast cancer in our department of radiation oncology at the International Medical Center (IMC) Cairo, Egypt, from March

2017 and March 2020. Treatment methods were variable upon physician choice, 6 received VMAT, 7 received 3DCRT and 6 received IMRT. We created two other plans for each patient, so we could physically compare the three types of plans (3DCRT, IMRT, VMAT) for each patient.

2.2. Simulation

2.2.1. Positioning and CT Scanning

Patients have their both arms raised above their heads, fixed by breast board. CT scanning of 5 mm slicing, was performed (aperture of 64 spiral slices CT, GE Medical Systems). CT scans obtained from the mandible to the lower border of the thorax.

2.2.2. Clinical Target Volume (CTV) and Organ at Risk (OAR) Delineation

CTV included the left breast only or, with lymph node region, and/or boost to the tumor bed. Dedicated OAR included: ipsilateral lung, heart, the spinal cord, contralateral lung, contralateral breast, and the left anterior descending artery (LAD). All delineated by the radiation oncologist, using Varian eclipse 15.6 treatment planning system (TPS). Planning Target Volume (PTV)/CTV margin was decided to be 5 mm isotropically.

2.3. Plan Design

2.3.1. Plan Goals

PTV was prescribed to a total dose of 50 Gy, in 25 fractions. When a boost was indicated, an added 10 Gy to the tumor bed was planned, to be given sequentially. Plan goals were as follows: For the PTV, 99% of the PTV should receive at least 95% of prescription dose (47.5 Gy), maximum dose ≤ 107%, and the minimum dose ≥ 95%. For the ipsilateral lung, V20 < 30% and the mean dose (D mean) < 22 Gy. For the spinal cord, the Dmax should be < 45 Gy. For the heart, V25 < 10 Gy. For the contralateral lung V5 Gy < 26% and V15 Gy < 5%. The contralateral breast, the mean dose (D mean) < 5 Gy. The left anterior descending (LAD) artery should be less as possible.

2.3.2. Plan Arrangement

For each patient, we developed three plans using the same techniques as shown in (**Table 1**).

2.4. Plan Assessment

For each plan, we assessed the followings:

- **For the PTV:**

  PTV Max %, PTV Min %, 107% volume, PTV 100% cc (the PTV volume receiving 100% of the dose), D2, D98, D50 (dose received by the 2%, 98% and 50% of the volume, respectively). CI (Conformity Index) was defined as: Body V100% (cc)/PTV (cc), HI (Homogeneity Index) was defined as: (D2%-D98%)/D50%.

- **For the OARs:**

  For the ipsilateral lung: V10, V20, and D mean. For the contralateral lung: D

Table 1. 3DCRT, IMRT and VMAT beam arrangements.

Technique	Photon Energy allowed	Field Arrangement	Algorithm
3DCRT	6, 10 and 15 MV	Tangential field/Isocentric Gantry angles were selected using the beam's eye view of the Eclipse treatment planning system, avoiding direct exposure of the contralateral breast; supraclavicular lymph nodes were covered by 3rd anterior beam ± posterior beam, with a gantry angle chosen to avoid direct exposure of the spinal cord. In large breast field-in-field technique was used to reduce hot spots.	AAA
IMRT	6 MV only	5 - 9 fields (Isocentric, Static with tangential field setup)	
VMAT	6 MV only	Two double arcs (clockwise and antic lock wise) to disperse field, abduction of 10˚ - 25˚ by tangent field as starting and ending angle each way, with collimator angle 5˚, treatment couch angle 0˚, maximum dose rate 600 MU/min.	

mean, V5 and V10. For the contralateral breast D mean and D max. For the heart D mean and V5, V10 and V25. For the LAD, D mean, D max. For the body, V100% (the body volume receiving 100% of the dose).

3. Statistical Analysis

Data collected were analyzed using SPSS version 22. We used the paired-samples T-test to perform the comparison of dosimetry differences among 3 plans, which is based on as the statistical difference ($P < 0.05$).

4. Results

4.1. Patient and Target Volume Criteria

In our cohort the mean age was 57.37 years. All the patients received radiotherapy to the left breast, with 7 patients (36.8%) received nodal irradiation and 13 patients (68.4%) received a boost to the tumor bed. According to breast volume, patients were categorized into three categories small, intermediate, large volume (Table 2).

4.2. PTV and OAR Dosimetrics

Table 3 shows the archived dose constrains in percentage dose format, for the PTV and the routinely reported OARs.

4.2.1. PTV

Regarding the PTV coverage, there was no difference in both PTV Max and PTV Min dose in the three techniques, only the 107% cc volume was significantly lower in IMRT plans compared with VMAT (p 0.045).

Table 2. Patient and target volume.

		Number	%
Breast Volume Categories	Small Volume: less than 975 cc	5	26.3%
	Intermediate Volmue: 975 - 1600 cc	10	52.6%
	Large Volume: More than 1600 cc	4	21.1%
Nodal Irradiation	Yes	7	36.8%
	No	12	63.2%
Boost	Boost	13	68.4%
	No Boost	6	31.6%

4.2.2. OAR

The routinely reported dose constrains for the ipsilateral lung (mean dose, V10 and V20), and for the heart (mean dose, V5, V10 and V25,) were not significantly different on comparing the three techniques. While for the contralateral lung, the difference in mean dose was statistically significant and generally in favor of 3DCRT: (p 0.001 3D vs IMRT vs VMAT), (p 0.002 3D vs IMRT in favor of 3D), (p 0.001 3D vs VMAT in favor of 3D). Regarding the Max dose, 3DCRT provided the lowest dose in comparison with VMAT ($p < 0.041$). Similarly, the contralateral breast mean dose constrains had a better profile in favor of 3DCRT: (p 0.002 3D vs VMAT in favor of 3D), (p 0.006 (3D vs IMRT in favor of 3D), (p 0.002 (3D vs VMAT in favor of 3D). Contrarily, in our cohort, IMRT provided lower LAD mean dose when compared with 3DCRT ($p < 0.001$).

4.2.3. The Effect of Breast Volume, Nodal Irradiation and Boost

The three techniques showed almost the same dose constrains (Table 4) except for:

1) In large breast volume, 3DCRT provided a lower Max dose to the contralateral lungand lowest mean dose to the contralateral breast when compared to IMRT ($p < 0.046$ 3D vs IMRT).

2) In case of No nodal irradiation, the contralateral breast mean dose was lower in 3DCRT in comparison to IMRT and VMAT ($p < 0.037$ 3DCRT vs IMRT vs VMAT). Also, Body Volume receiving 100% cc was lower in VMAT ($p < 0.031$ VMAT vs 3DCRT). And IMRT provided higher homogeneity index compared with VMAT ($p < 0.046$ IMRT vs VMAT).

3) When boost dose was given, 3DCRT plans had produced a lower Max dose to the contralateral lung ($p < 0.017$ 3D vs IMRT) and lower mean dose to the contralateral breast ($p < 0.006$ 3D vs IMRT).

5. Discussion

Radiotherapy in breast cancer is challenging due to the geometric differences in the breast tissue structures which may have an impact on the dose distribution so the selection of the radiotherapy technique is crucial for safe treatment delivery [7]. A number of studies have demonstrated the dosimetric benefit of IMRT

Table 3. Percentage dose constrains for PTV, OAR.

	3DCRT	IMRT	VMAT	P value
		Mean ± SD		
PTV Max %	109.37 ± 2.08	108.32 ± 2.88	111.26 ± 4.27	NS
PTV Min %	28.33 ± 22.44	61.48 ± 16.29	67.34 ± 12.33	NS
Volume 107% (cc)	48.94 ± 105.22	4.29 ± 12.84	39.27 ± 61.08	0.045 (IMRT vs VMAT in favor of IMRT)
LAD Mean %	22.28 ± 14.55	21.83 ± 8.29	22.29 ± 9.24	0.001 (3D vs IMRT vs VMAT) 0.029 (3D vs IMRT in favor of IMRT)
LAD Max %	45.02 ± 8.22	39.93 ± 7.65	38.69 ± 7.49	NS
Heart Mean %	4.05 ± 2.02	7.39 ± 2.45	7.40 ± 2.75	NS
Heart V5 %	12.24 ± 6.18	53.74 ± 22.38	55.82 ± 16.47	NS
Heart V10 %	6.72 ± 4.74	21.82 ± 15.93	155.83 ± 567.83	NS
Heart V25 %	7.76 ± 15.48	5.66 ± 8.58	13.41 ± 27.44	NS
Ipsilateral Lung Mean %	8.66 ± 3.57	11.55 ± 3.54	11.85 ± 2.89	NS
Ipsilateral Lung V10 %	20.28 ± 8.14	41.76 ± 15.22	267.47 ± 976.62	NS
Ipsilateral Lung V20 %	16.08 ± 7.26	15.54 ± 3.87	17.11 ± 7.92	NS
Contralateral Lung mean %	0.34 ± 0.33	3.09 ± 1.34	2.96 ± 0.99	0.001 (3D vs IMRT vs VMAT) 0.002 (3D vs IMRT in favor of 3D) 0.001 (3D vs VMAT in favor of 3D)
Contralateral Lung Max %	4.03 ± 5.28	16.82 ± 7.94	16.82 ± 7.49	0.041 (3D vs VMAT in favor of 3D)
Contralateral Breast mean %	0.28 ± 0.21	2.55 ± 1.79	2.79 ± 1.15	0.002 (3D vs VMAT in favor of 3D) 0.006 (3D vs IMRT in favor of 3D) 0.002 (3D vs VMAT in favor of 3D)
Contralateral Breast Max %	13.07 ± 15.43	23.91 ± 9.74	20.36 ± 5.87	NS
Body Volume 100% cc	1036 ± 585	937 ± 849	932 ± 593	NS
PTV 100% cc	1036.36 ± 584.78	937.36 ± 849.36	931.68 ± 593.22	0.029 (IMRT vs VMAT in favor of IMRT)
CI	1.23 ± 0.16	1.05 ± 0.08	1.03 ± 0.03	NS
HI	0.18 ± 0.08	0.10 ± 0.076	0.15 ± 0.05	0.016 (3D vs IMRT vs VMAT) 0.043 (3D vs IMRT in favor of IMRT)

compared to 3DCRT; some of these trials have reported lower doses to the ipsilateral lung, heart, and left anterior descending artery [5]. Meanwhile VMAT has a great advantage in reducing the treatment time and the number of MU without reducing dose distribution [8]. In this study we had compared the dosimetric parameters of 3DCRT, IMRT and VMAT in order to select the best technique for post-operative radiotherapy delivery to left breast ± draining lymph nodes ± boost irradiation, after breast conservative surgery. Also, breast volume categories were challenged against the three techniques.

In our cohort, with three plans (3DCRT, IMRT and VMAT) generated for each patient, there was no significant difference neither in PTV Max nor in Min dose. Only the 107% volume in PTV was lower in IMRT plans. These results were comparable to Vasudevan *et al.* [9], who reported that the PTV volume

Table 4. Breast volume, nodal irradiation and boost dosimetrics.

		3DCRT	IMRT	VMAT	p values
		Mean ± SD			
Large Breast Volume	Contralateral Lung Max dose %	2 ± 0.81	15 ± 2.16	16.75 ± 7.08	• 0.046 (3D vs IMRT in favor of 3D)
	Contralateral Breast mean dose %	0.20 ± 0.14	1.22 ± 0.51	3 ± 1.41	• 0.046 (3D vs IMRT in favor of 3D)
No Nodal Irradiation	Contralateral Breast mean dose %	0.28 ± 0.22	2.3 ± 1.71	2.76 ± 0.93	• 0.037 (3D vs IMRT vs VMAT) • 0.02 (3D vs IMRT in favor of 3D) • 0.013 (3D vs VMAT in favor of 3D)
	Body Volume receiving 100% cc	1058.75 ± 698.91	911.75 ± 953.52	926.58 ± 725.50	• 0.031 (3D vs VMAT in favor of VMAT)
	Homogeneity Index	0.19 ± 0.08	0.09 ± 0.03	0.15 ± 0.05	• 0.04 (3D vs IMRT vs VMAT) • 0.046 (IMRT vs VMAT in favor of IMRT)
Boost Irradiation	Contralateral Lung Max dose %	5.96 ± 7.46	20.15 ± 12.15	18.91 ± 9.62	• 0.017 (3D vs IMRT in favor of 3D)
	Contralateral Breast mean dose %	0.43 ± 0.2	1.95 ± 0.64	2.53 ± 0.51	• 0.006 (3D vs VMAT in favor of 3D)
	Homogeneity Index	0.21 ± 0.12	0.08 ± 0.03	0.13 ± 0.07	• 0.01 (3D vs IMRT vs VMAT) • 0.038 (IMRT vs VMAT in favor of IMRT))

received 107% of the prescribed dose was higher for VMAT and 3DCRT compared to IMRT. Conversely, Lancellotta *et al.* [10], reported that 3DCRT provided the poorest target coverage in comparison with IMRT.

As regards to the routinely used OARs, the heart and ipsilateral lung dose were the same among the three techniques but LAD mean dose was lower in IMRT. These findings are opposed to what Aras *et al.* [6] reported, that at lower doses, the dose to the left lung and the heart, were lower with the 3D-CRT technique. Differently, Vasudevan *et al.* [9], reported that the mean heart and lung doses were higher with VMAT and IMRT compared to 3DCRT.

In literature, the risk of second malignancy is related to the low dose regions rather than the high dose regions in the OARs [11]. Unfortunately, the dose constrains of the contralateral lung and breast are not routinely reported. These constrains of the contralateral organs may be one of the areas of difference, and debate, between the three techniques. In our study, 3DCRT provided a lower mean and Max doses to the contralateral lung breast. On the other side Vasudevan *et al.* [9], documented that the mean dose to contra lateral breast and lung were similar for IMRT and 3DCRT, but higher with VMAT.

Regarding the definition of different breast volumes, some of the studies used the bra size [12], others used the distance between the edges of the lateral and medial fields *i.e.*, separation. [13]. But more conveniently to the modern radiation techniques, breast volume (in cc) is better used to categorize the clinical target volumes (CTV) volumes. One of the commonly used categorizations, suggested by Michalski A *et al*., is as follows: Large volume ≥ 1.600 cm^3, Intermediate 975 - 1.600 cm^3, and Small ≤ 500 - 975 cm^3 [14]. In large breast volume category, the 3DCRT showed an advantage over IMRT and VMAT, in terms of achieving a better constrains to the contralateral organs e.g., a lower Max dose to the contralateral lung and lower mean dose to the contralateral breast.

Also, the 3DCRT had been shown to be more protective to the contralateral breast in patients who received breast only irradiation, as it provided a lower mean dose. Conversely, in those patients with no nodal irradiation, IMRT provided higher HI. Additionally, 3DCRT provided lower Max dose to the contralateral lung and lower mean dose to the contralateral breast, when we added boost dose 10 Gy/5fx [15].

6. Conclusion

The choice of radiotherapy in breast cancer treatment is a very important factor in the protection of normal tissue and in providing proper coverage of the target. The three techniques (3DCRT, IMRT, and VMAT) can meet the clinical dosimetry demands of radiotherapy for left breast cancer after conservative surgery, as long as the routinely OARs only (heart and ipsilateral lung) are reported. Our study showed that 3CDRT can provide a lower dose to the contralateral organs (breast and lung), specially, in case of large breast volumes, no nodal irradiation and when a boost is given.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Fisher, B., Anderson, S., Bryant, J., Margolese, R.G., Deutsch, M., Fisher, E.R., Jeong, J.H. and Wolmark, N. (2002) Twenty-Year Follow-Up of a Randomized Trial Comparing Total Mastectomy, Lumpectomy, and Lumpectomy plus Irradiation for the Treatment of Invasive Breast Cancer. *The New England Journal of Medicine*, **347**, 1233-1241. https://doi.org/10.1056/NEJMoa022152

[2] Clarke, M., Collins, R., Darby, S., Davies, C., Elphinstone, P., Evans, V., Godwin, J., Gray, R., Hicks, C., James, S., MacKinnon, E., McGale, P., McHugh, T., Peto, R., Taylor, C. and Wang, Y. (2005) 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. *The Lancet*, **366**, 2087-2106. https://doi.org/10.1016/S0140-6736(05)67887-7

[3] Darby, S.C., Ewertz, M., McGale, P., Bennet, A.M., Blom-Goldman, U., Brønnum, D., Correa, C., Cutter, D., Gagliardi, G., Gigante, B., Jensen, M.B., Nisbet, A., Peto, R., Rahimi, K., Taylor, C. and Hall, P. (2013) Risk of Ischemic Heart Disease in Women after Radiotherapy for Breast Cancer. *The New England Journal of Medicine*, **368**, 987-998. https://doi.org/10.1056/NEJMoa1209825

[4] Tulinius, H., Sigvaldason, H. and Olafsdóttir, G. (1990) Left and Right Sided Breast

Cancer. *Pathology—Research and Practice*, **186**, 92-94.
https://doi.org/10.1016/S0344-0338(11)81015-0

[5] Pierce, L.J., Feng, M., Griffith, K.A., Jagsi, R., Boike, T., Dryden, D., Gustafson, G.S., Benedetti, L., Matuszak, M.M., Nurushev, T.S., Haywood, J., Radawski, J.D., Speers, C., Walker, E.M., Hayman, J.A. and Moran, J.M. (2017) Michigan Radiation Oncology Quality Consortium. Recent Time Trends and Predictors of Heart Dose from Breast Radiation Therapy in a Large Quality Consortium of Radiation Oncology Practices. *International Journal of Radiation Oncology*, *Biology*, *Physics*, **99**, 1154-1161.

[6] Aras, S., İkizceli, T. and Aktan, M. (2019) Dosimetric Comparison of Three Dimensional Conformal Radiotherapy (3D-CRT) and Intensity Modulated Radiotherapy Techniques (IMRT) with Radiotherapy Dose Simulations for Left-Sided Mastectomy Patients. *European Journal of Breast Health*, **15**, 85-89.
https://doi.org/10.5152/ejbh.2019.4619

[7] Fiorentino, A., Ruggieri, R., Giaj-Levra, N., Sicignano, G., Di Paola, G., Nac-carato, S., Fersino, S., Mazzola, R., Tebano, U., Ricchetti, F. and Alongi, F. (2017) Three Dimensional Conformal versus Intensity Modulated Radiotherapy in Breast Cancer Treatment: Is Necessary a Medical Reversal? *La Radiologia Medica*, **122**, 146-153.
https://doi.org/10.1007/s11547-016-0700-z

[8] Li, J.B., Wang, J.G., Lu, J., *et al*. (2009) Influence of Active Breathing Control on the Dose Distribution in the Target of Forward Whole-Breast Intensity-Modulated Radiotherapy after Breast Conserving Surgery. *Chinese Clinical Oncology*, **31**, 617-621.

[9] Vasudevan, A., Kariyarambath, S., Bhasi, S., *et al*. (2015) Comparative Dosimetric Study of 3DCRT, IMRT and VMAT for Whole Breast Irradiation Following Breast Conservation: A Single Institution Experience. *International Journal of Radiation Oncology*, *Biology*, *Physics*, **93**, E13-E14.
https://doi.org/10.1016/j.ijrobp.2015.07.578

[10] Lancellotta, V., Iacco, M., Perrucci, E., *et al*. (2018) Comparing Four Radiotherapy Techniques for Treating the Chest Wall plus Levels III-IV Draining Nodes after Breast Reconstruction. *The British Journal of Radiology*, **91**, Article ID: 20160874.
https://doi.org/10.1259/bjr.20160874

[11] Zurl, B., Stranzl, H., Winkler, P., *et al*. (2013) Quantification of Contralateral Breast Dose and Risk Estimate of Radiation-Induced Contralateral Breast Cancer among Young Women Using Tangential Fields and Different Modes of Breathing. *International Journal of Radiation Oncology*, *Biology*, *Physics*, **85**, 500-505.
https://doi.org/10.1016/j.ijrobp.2012.04.016

[12] Dundas, K.L., Atyeo, J. and Cox, J. (2007) What Is a Large Breast? Measuring and Categorizing Breast Size for Tangential Breast Radiation Therapy. *Australasian Radiology*, **51**, 589-593. https://doi.org/10.1111/j.1440-1673.2007.01898.x

[13] Back, M., Guerrieri, M., Wratten, C., *et al*. (2004) Impact of Radiation Therapy on Acute Toxicity in Breast Conservation Therapy for Early Breast Cancer. *Clinical Oncology*, **16**, 12-16. https://doi.org/10.1016/j.clon.2003.08.005

[14] Michalski, A., Atyeo, J., Cox, J., *et al*. (2014) A Dosimetric Comparison of 3D-CRT, IMRT, and Static Tomotherapy with an SIB for Large and Small Breast Volumes. *Medical Dosimetry*, **39**, 163-168. https://doi.org/10.1016/j.meddos.2013.12.003

[15] Bartelink, H., Maingon, P., Poortmans, P., *et al*. (2015) Whole-Breast Irradiation with or without a Boost for Patients Treated with Breast-Conserving Surgery for Early Breast Cancer: 20-Year Follow-Up of a Randomised Phase 3 Trial. *The Lancet Oncology*, **16**, 47-56. https://doi.org/10.1016/S1470-2045(14)71156-8