ANTICANCER RESEARCH *41*: 3145-3152 (2021)
doi:10.21873/anticanres.15100

Inter-institutional Variation in Intensity-modulated Radiotherapy for Breast Cancer in Korea (KROG 19-01)

KYUBO KIM[1*], MINSOO CHUN[2*], HYEONGMIN JIN[2], WONGUEN JUNG[1], KYUNG HWAN SHIN[2], SEONG SOO SHIN[3], YEON JOO KIM[4#], SHIN-HYUNG PARK[5], JIN HEE KIM[6], YONG HO KIM[7], HYUN SOO SHIN[8], HAEYOUNG KIM[9], SU SSAN KIM[10], JONG HOON LEE[11], YONG BAE KIM[12], SUN YOUNG LEE[13], JINHYUN CHOI[14], DO HOON OH[15], KI MUN KANG[16], JEANNY KWON[17], MI YOUNG KIM[18], TAERYOOL KOO[19], HAE JIN PARK[20] and SUNG JA AHN[21]

[1]Department of Radiation Oncology, Ewha Womans University College of Medicine, Seoul, Republic of Korea;
[2]Department of Radiation Oncology, Seoul National University College of Medicine, Seoul, Republic of Korea;
[3]Department of Radiation Oncology, GangNeung Asan Hospital, University of Ulsan College of Medicine, Gangneung, Republic of Korea;
[4]Department of Radiation Oncology, Kangwon National University School of Medicine, Chuncheon, Republic of Korea;
[5]Department of Radiation Oncology, Kyungpook National University Hospital, Kyungpook National University School of Medicine, Daegu, Republic of Korea;
[6]Department of Radiation Oncology, Keimyung University School of Medicine, Daegu, Republic of Korea;
[7]Department of Radiation Oncology, Catholic Kwandong University, Incheon, Republic of Korea;
[8]Department of Radiation Oncology, CHA University School of Medicine, Seongnam, Republic of Korea;
[9]Department of Radiation Oncology, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea;
[10]Department of Radiation Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea;
[11]Department of Radiation Oncology, The Catholic University of Korea College of Medicine, Suwon, Republic of Korea;
[12]Department of Radiation Oncology, Yonsei University College of Medicine, Seoul, Republic of Korea;
[13]Department of Radiation Oncology, Jeonbuk National University School of Medicine, Jeonju, Republic of Korea;
[14]Department of Radiation Oncology, Jeju National University School of Medicine, Jeju, Republic of Korea;
[15]Department of Radiology, Chung-Ang University College of Medicine, Seoul, Republic of Korea;
[16]Department of Radiation Oncology, Gyeongsang National University School of Medicine, Changwon, Republic of Korea;
[17]Department of Radiation Oncology, Chungnam National University College of Medicine, Daejeon, Republic of Korea;
[18]Department of Radiation Oncology, Kyungpook National University Chilgok Hospital, Kyungpook National University School of Medicine, Daegu, Republic of Korea;
[19]Department of Radiation Oncology, Hallym University College of Medicine, Anyang, Republic of Korea;
[20]Department of Radiation Oncology, Hanyang University College of Medicine, Seoul, Republic of Korea;
[21]Department of Radiation Oncology, Chonnam National University Medical School, Gwangju, Republic of Korea

*These Authors contributed equally to this study.

[#]Current address: Department of Radiation Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea.

Correspondence to: Kyung Hwan Shin, MD, Ph.D., Department of Radiation Oncology, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 03080, Republic of Korea. Tel: +82 220722524, Fax: +82 27653317, e-mail: radiat@snu.ac.kr

Key Words: Breast cancer, dose-volume constraint, intensity-modulated radiation therapy, target volume, variation.

Abstract. *Background/Aim: To present the variations in the target delineation and the planning results of intensity-modulated radiation therapy (IMRT) for breast cancers. Patients and Methods: We requested the target volumes and organs at risk delineation for two cases of left breast cancers, and evaluated the IMRT plans including the supraclavicular and internal mammary node irradiation. Results: Twenty-one institutions participated in this study. Differences in the planning target volume among institutions reached up to three-times for breast-conserving surgery (BCS) case and five-times for mastectomy case. Mean heart*

doses ranged from 3.3 to 24.1 Gy for BCS case and from 5.0 to 26.5 Gy for mastectomy case. Ipsilateral lung volumes receiving more than 20 Gy ranged from 4.7 to 57.4% for BCS case and from 16.4 to 55.5% for mastectomy case. Conclusion: There were large variations in the target delineation and planning results of IMRT for breast cancers among institutions. Considering the increased use of breast IMRT, more standardized protocols are needed.

Intensity-modulated radiation therapy (IMRT) is an effective treatment method to limit the doses delivered to the surrounding normal tissues while delivering sufficient doses to the target volumes. IMRT has been increasingly employed in the treatment of breast cancer, especially in the setting of regional nodal irradiation in Korea (1). Recently, two randomized trials proved the survival benefit of regional nodal irradiation, including the radiation of internal mammary lymph nodes (LN) in node-positive or high-risk node-negative patients (2, 3). More patients will receive radiation therapy (RT) for the treatment of internal mammary LNs according to the guidelines (4). Additionally, IMRT has also been suggested as one of the most heart-sparing RT techniques for the treatment of left breast cancer (5). According to the many studies on the cardiotoxicity associated with left breast RT (6-8), the heart is one of the most important organs at risk (OAR). This is an important factor that should be considered in the planning process.

The use of IMRT in the routine clinical practice could help balance the survival benefit and the potentially increased cardiotoxicity of internal mammary LN RT, especially for the treatment of left breast cancer. However, we observed significant variations in the application of IMRT to breast cancer patients. Although several target volume delineation guidelines for breast cancer have been published (9-11), guidelines discrepancies promote variations across institutions (12). Also, the use of various IMRT techniques may further contribute to the heterogeneity of breast IMRT (13-16).

This study aimed to describe the variations in the target volume delineation and planning results of IMRT, including the regional nodal irradiation in Korea.

Patients and Methods

Study design. We collected the institutional policies on computed tomography (CT) simulation, dose prescription, normal tissue dose-volume constraints, and planning process from the participating investigators.

Furthermore, we selected two cases of breast cancer. The first patient displayed a stage IIB left breast cancer (pT2N1, 2 out of 3 nodes were positive). She underwent breast-conserving surgery (BCS) and sentinel lymph node biopsy. The second patient displayed a stage IIIA left breast cancer (pT3N1, 3 out of 20 nodes were positive). She underwent a total mastectomy and axillary lymph node dissection.

The participating investigators were requested to delineate the clinical target volume (CTV) and OARs on the same CT images. We ignored the differences in dose distributions caused by the different electron densities to Hounsfield unit tables. The components of the CTV and OAR were not specified but allowed to follow each institutional policy.

Regarding the IMRT planning, each institution was also requested to follow its policy regarding any specific IMRT techniques. However, the forward-planned IMRT (*i.e.*, the field-in-field technique) was not accepted in this study. Additionally, the elective regional nodal irradiation of supraclavicular and internal mammary LNs was mandatory, while tumor bed boost (*e.g.*, sequential or simultaneous integrated boost) was not included. The institutional review board approved this study (approval no. EUMC 2019-02-019) and waived the requirement of informed consent.

Dosimetric analysis. For planning evaluation, we calculated the conformity index (CI) and the homogeneity index (HI) according to the Report 62 of the International Commission on Radiation Units and Measurements as follows (17, 18):

CI=(Volume of PTV covered by the reference dose)/
(Volume of PTV)
HI=(Minimum dose delivered to the 5% of PTV)/
(Minimum dose delivered to the 95% of PTV)

We also performed a dose-volume histogram (DVH) analysis for the heart, the ipsilateral lung, the contralateral lung, and the contralateral breast. We evaluated the mean heart dose (MHD) and volume receiving more than 30 Gy (V_{30Gy}). We also measured the ipsilateral and contralateral lung volumes receiving more than 5 Gy (V_{5Gy}) and 20 Gy (V_{20Gy}), respectively. The contralateral breast was not delineated in all institutions and we only evaluated the maximal dose (D_{max}, dose receiving less than 0.3 ml).

Results

Institutional policies on breast IMRT. A total of 21 radiation oncologists from 21 institutions participated in this study. During the CT simulation, most institutions (n=16) used a breast board alone for immobilization but none used breath control. The planning target volume (PTV) was expanded by 2-10 mm from the CTV in all but two institutions. Nineteen institutions applied skin-sparing and subtracted an average of 1-5 mm of skin from the surface.

Regarding the IMRT techniques, 13 institutions employed fixed-field IMRT (dynamic or static), 7 employed volumetric modulated arc therapy (VMAT), and one employed helical tomotherapy (HT). All institutions used 6 MV photon beams. Thirteen institutions used conventional fractionation and 8 used hypofractionation.

The planning goal was usually delivering 95% (n=8) or 100% (n=7) of the prescribed dose to at least 95% of the PTV. The detailed dose prescriptions for PTV and normalization are summarized in Table I. For the dose-volume constraints of the ipsilateral lung, V_{20Gy} was the most commonly used (n=13) and its limit ranged from 20% to 40%. Only 5 institutions

Table I. *Dose prescriptions for planning target volume (PTV) and normalization goal.*

	No. of institutions
Dose prescription	
50 Gy/25fx	8
50.4 Gy/28fx	5
43.2 Gy/16fx	3
40.05 Gy/15fx	2
42.72 Gy/16fx	1
42.4 Gy/16fx	1
41.6 Gy/16fx	1
Normalization goal	
95% dose to 95% of PTV	8
100% dose to 95% of PTV	7
90% dose to 100% of PTV	2
97% dose to 95% of PTV	1
96% dose to 95% of PTV	1
95% dose to 100% of PTV	1
90% dose to 90% of PTV	1

applied constraints for the contralateral lung or both lungs. Only 12 institutions out of 9 considered the contralateral breast in the planning process. The mean heart dose was the most commonly used dose-volume constraint to limit the cardiac dose (n=10) but its limit ranged from 4 Gy to 15 Gy. Nineteen institutions applied an inhomogeneity correction algorithm in the dose calculation.

Target delineation. The variations in the PTV delineation between institutions are presented in Figure 1 (BCS case) and Figure 2 (mastectomy case). The volumetric data of the PTV, heart, and ipsilateral lung are presented in Table II. Because this study did not specify the components of the CTV, such as the supraclavicular LN and the internal mammary LN, the specific comparisons between these components among institutions were unavailable.

Dosimetric data

1) Planning target volume. For the BCS case, the mean values of $D_{95\%}$ and $D_{5\%}$ were 45.0±4.5 Gy and 49.3±5.2 Gy, respectively. The mean values of CI and HI were 0.80±0.24 and 1.10±0.04, respectively. For the mastectomy case, the mean values of $D_{95\%}$ and $D_{5\%}$ were 43.4±6.6 Gy and 48.1±7.2 Gy, respectively. The mean values of CI and HI were 0.98±0.31 and 1.11±0.04, respectively.

2) Heart. Figure 3A and B showed the DVHs obtained from the contours by different investigators for the heart of the BCS and mastectomy cases, respectively.

The MHD ranged from 3.3 Gy to 24.1 Gy (median, 12.5 Gy) and the V_{30Gy} from 0% to 28.1% (median, 4.7%) for the BCS case. For the mastectomy case, the MHD ranged from 5.0 Gy to 26.5 Gy (median, 12.1 Gy) and V_{30Gy} from 0% to 35.6% (median, 6.7%) (Table III).

3) Ipsilateral lung. Figure 4A and B shows the DVHs obtained from the contours by different investigators for the ipsilateral lung of the BCS and mastectomy cases, respectively.

For the BCS case, the median value of V_{20Gy} was 29.5% (range=4.4-57.4%) and the median value of V_{5Gy} was 90.2% (range=37.9-100.0%). For the mastectomy case, the median value of V_{20Gy} was 30.9% (range=16.4-55.5%) and the mean value of V_{5Gy} was 92.5% (range=45.4-100.0%) (Table III).

4) Contralateral lung and contralateral breast. The V_{20Gy} for the contralateral lung ranged from 0% to 59.8% (median, 0.1%) and from 0% to 4.1% (median=0.6%) for the BCS and the mastectomy cases, respectively. The mean value of V_{5Gy} was 34.4% (range=0.7-91.7%) and 47.0% (range=2.1-85.4%) for the BCS and the mastectomy cases, respectively (Table III).

For the BCS case, the D_{max} for the contralateral breast ranged from 5.5 Gy to 30.6 Gy (median, 17.8 Gy). For the mastectomy case, it ranged from 12.0 Gy to 32.6 Gy (median, 20.3 Gy) (Table III).

Discussion

In this study, the CTV delineation was allowed to follow each institutional policy. The PTV margin ranged from 0 mm to 10 mm. With a 0-5 mm subtraction from the skin surface, the PTV volumes were different by up to three- and five-times for the BCS and the mastectomy cases, respectively, among institutions. In addition to these variations in the target volume delineation, we observed large variations in the dose-volume constraints for the OAR, which resulted in a wide range of OAR doses among institutions.

A similar finding was also reported in the United States (19). Nine different radiation oncologists compared the target volumes. They found that the breast volume of the node-positive BCS patient ranged from 413.5 cm^3 to 1070.6 cm^3 and the chest wall volume of the mastectomy patient ranged from 361.5 cm^3 to 949.9 cm^3. They observed a greater variation in the delineation of the regional nodes, although the absolute volume and their differences were relatively small. Because they did not apply a PTV margin except for the boost PTV, the overall PTV difference might be greater. Based on these results, the Radiation Therapy Oncology Group suggested an atlas for breast cancer RT (9). A similar guideline was also suggested by the European Society for Radiotherapy and Oncology (10) and the Danish Breast Cancer Cooperative group (11). However, these guidelines displayed discrepancies especially for the extent of the nodal target volumes (12). Therefore, a large difference can still be observed in the target volume of node-positive cases requiring regional nodal irradiation.

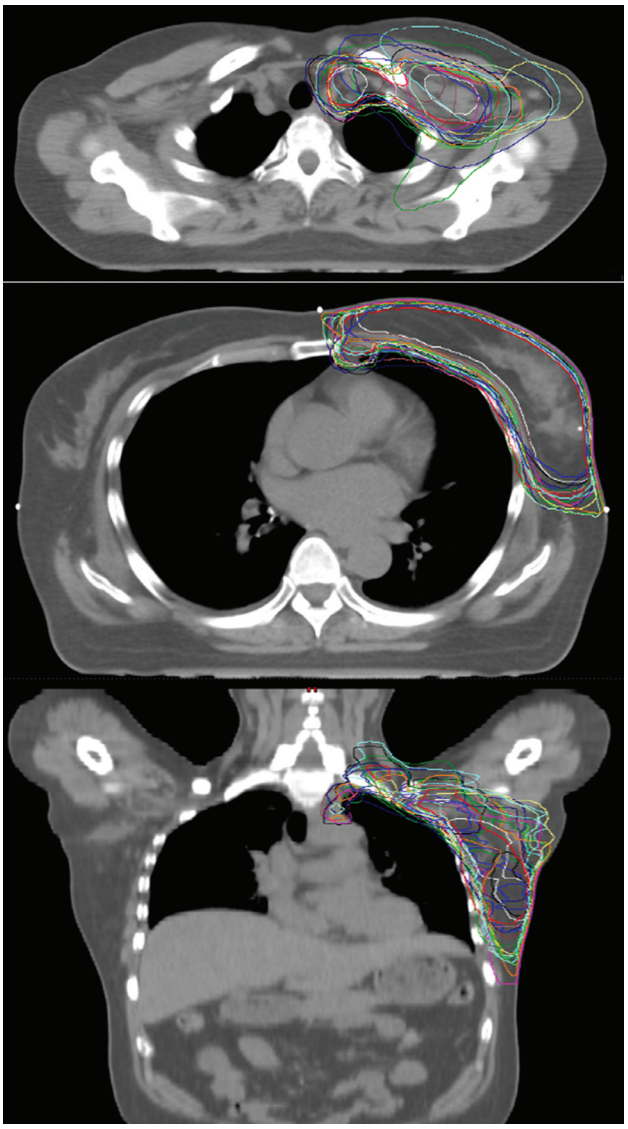

Figure 1. *Contours of planning target volumes in the level of claviclular head (upper) and of mid-breast (middle) in an axial plane and in a coronal plane (lower) for a breast conserving surgery case.*

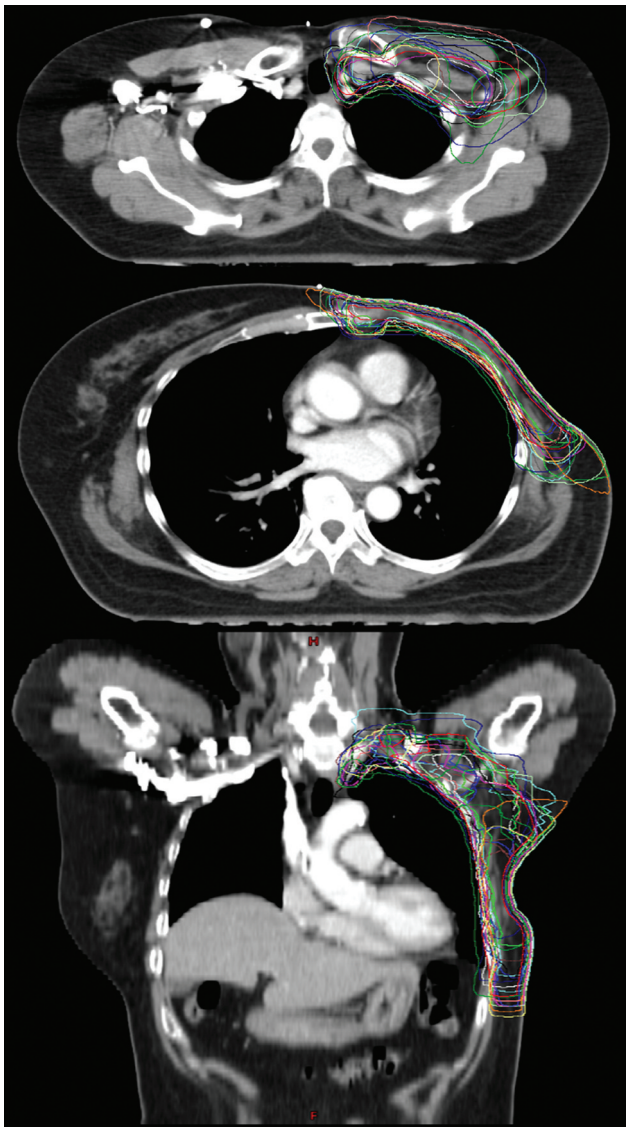

Figure 2. *Contours of planning target volumes in the level of claviclular head (upper) and of mid-breast (middle) in an axial plane and in a coronal plane (lower) for a mastectomy case.*

Inter-observer variation in the target volume delineation is not a new issue regarding the standardization of RT in several other primary sites (20-22). However, such a discrepancy is still observed even in head and neck cancer cases that have a long history of IMRT application (23). Recently, it was noted that an atlas-based auto-segmentation could reduce the inter-observer variation in target volumes (24). Additionally, a deep learning-based auto-segmentation is more consistent compared with an atlas-based one (25). Moreover, a digital platform such as Anatom-e, which provides an atlas as well as guidelines and protocols, could facilitate target contouring and decrease the inter-observer variability (26).

The aforementioned study performed in the United States already showed that the variability in target delineation can result in dramatic variations in the dosimetric results even after applying the same planning goal (19). Besides the difference in the target delineation, various IMRT techniques are also employed among institutions. In our study, a fixed-filed IMRT was more commonly used than a VMAT or HT. Because the aim of our study was not to prove the superiority of a specific IMRT technique over

Table II. *Volumetric data of planning target volume (PTV) and organs at risk.*

	Breast conserving surgery		Mastectomy	
	Median	Range	Median	Range
PTV (cm^3)	1092.3	(502.3-1550.1)	953.7	(243.3-1347)
Heart (cm^3)	597.3	(390.6-735.7)	672.7	(477.6-798.7)
Ipsilateral lung (cm^3)	732.2	(716.8-814.8)	1024.2	(998.0-1116.3)

Table III. *Dosimetric data of organs at risk.*

	Breast conserving surgery		Mastectomy	
	Median	Range	Median	Range
Heart				
Mean heart dose (Gy)	12.5	(3.3-24.1)	12.1	(5.0-26.5)
V_{30Gy} (%)	4.7	(0.0-28.1)	6.7	(0.0-35.6)
Ipsilateral lung				
V_{20Gy} (%)	29.5	(4.4-57.4)	30.9	(16.4-55.5)
V_{5Gy} (%)	90.2	(37.9-100.0)	92.5	(45.4-100.0)
Contralateral lung				
V_{20Gy} (%)	0.1	(0.0-59.8)	0.6	(0-4.1)
V_{5Gy} (%)	34.4	(0.7-91.7)	47.0	(2.1-85.4)
Contralateral breast				
D_{max} (Gy)	17.8	(5.5-30.6)	20.3	(12.0-32.6)

others, we did not give any detailed guidelines to the investigators regarding the planning process, such as dose fractionation, dose prescription, and dose-volume constraints. Considering the target and OAR volumes as well as the planning process were different among institutions, our ability to compare the dosimetric data among the different IMRT techniques was somewhat limited. Many dosimetric studies have been published regarding optimal IMRT techniques for breast cancer (13-16). In our study, we also used different targets and planning goals, therefore, the direct comparison of the dosimetric data across studies should be performed with caution.

MHD is an important dose-volume parameter that was reported to predict acute coronary events in a study by Darby *et al*. (8) In our study, MHD was the most commonly used dose-volume constraint. However, optimal constraints for the heart, including the internal mammary LN, are not yet established in the IMRT planning. In a single institutional prospective study from the Memorial Sloan Kettering Cancer Center, the average MHD by fixed-filed IMRT, including internal mammary LN, was 13.2 Gy (27), which was similar to our results. To further decrease MHD, the breath-hold technique combined with IMRT could be considered for eligible patients (28), although the institutions in our study did not employ any breath controls.

For the ipsilateral lung, the V_{20Gy} was the most commonly used dose-volume constraint in this study. According to the Danish Breast Cancer Cooperative Group, the ipsilateral lung V_{20Gy} is recommended to limit less than 35% in cases including the periclavicular LN. However, no specification is provided when an internal mammary LN RT is also given (11). The median ipsilateral lung V_{20Gy} was 29% in the study performed at the Memorial Sloan Kettering Cancer Center (20), which was again similar to our results. The researchers also reported that the long-term pulmonary outcomes were acceptable, justifying the use of fixed-field IMRT in node-positive breast cancer.

Recently, Verbakel *et al*. reported the results of a quality improvement program in the RT planning for head and neck cancer (29). They compared the planning results based on the same target volumes and planning goals among the participating institutions and distributed all anonymized plans. The authors also shared the optimization strategy of the best plan in terms of OAR sparing and requested to repeat this plan for the same case. They observed an improved OAR sparing through this intervention. Given the

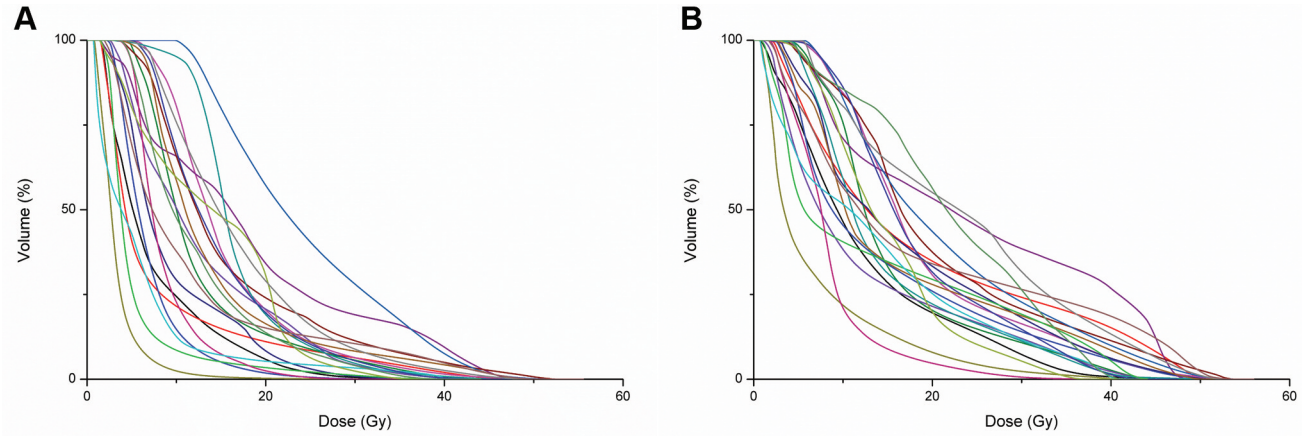

Figure 3. *Dose-volume histograms for the heart (A) and left lung (B) for a breast conserving surgery case.*

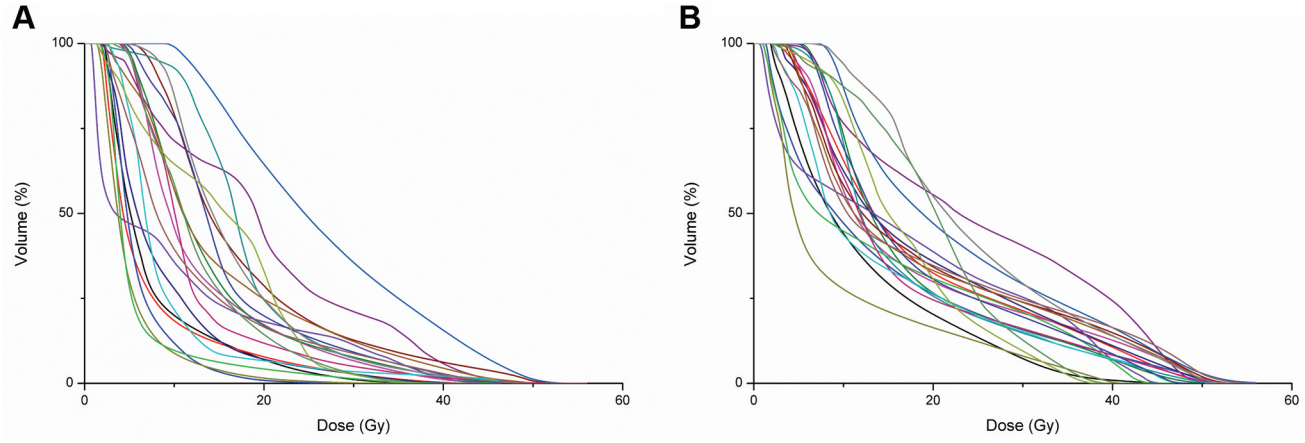

Figure 4. *Dose-volume histograms for the heart (A) and left lung (B) for a mastectomy case.*

large variations in the target volumes and planning results in our study, a similar approach could improve the quality of breast IMRT.

There are several limitations to this study. We did not request to follow any specific contouring guidelines and the components of the CTV were not identical among institutions. Therefore, we could not determine which components of the CTV mainly contributed to the variation. The dose-volume constraints were also dependent on the institutional policy, which partly resulted in a wide range of OAR doses. However, the aim of our study was not to select the best answer among several contouring guidelines, dose-volume constraints, or IMRT techniques but to describe the current status of breast IMRT among institutions. Given the large variations observed in this study, a prospective interventional study to improve the quality of breast IMRT, both in the target volume consistency and OAR sparing, is being planned.

In conclusion, we observed large variations in the target delineation and planning results of IMRT for breast cancer among Korean institutions. Considering the increased use of breast IMRT, more standardized protocols are needed.

Conflicts of Interest

There were no conflicts of interest related to this article.

Authors' Contributions

Conception and design: SKH; Provision of study materials: all Authors; Collection and assembly of data: KK, CM and JH; Data analysis and interpretation: KK and CM; Manuscript writing: all authors; Final approval of manuscript: all Authors.

References

1 Park HJ, Oh DH, Shin KH, Kim JH, Choi DH, Park W, Suh CO, Kim YB, Ahn SD, Kim SS and Division for Breast Cancer, Korean Radiation Oncology Group: Patterns of practice in radiotherapy for breast cancer in Korea. J Breast Cancer *21(3)*: 244-250, 2018. PMID: 30275852. DOI: 10.4048/jbc.2018.21.e37

2 Poortmans PM, Collette S, Kirkove C, Van Limbergen E, Budach V, Struikmans H, Collette L, Fourquet A, Maingon P, Valli M, De Winter K, Marnitz S, Barillot I, Scandolaro L, Vonk E, Rodenhuis C, Marsiglia H, Weidner N, van Tienhoven G, Glanzmann C, Kuten A, Arriagada R, Bartelink H, Van den Bogaert W and EORTC Radiation Oncology and Breast Cancer Groups: Internal mammary and medial supraclavicular irradiation in breast cancer. N Engl J Med *373(4)*: 317-327, 2015. PMID: 26200978. DOI: 10.1056/NEJMoa1415369

3 Whelan TJ, Olivotto IA, Parulekar WR, Ackerman I, Chua BH, Nabid A, Vallis KA, White JR, Rousseau P, Fortin A, Pierce LJ, Manchul L, Chafe S, Nolan MC, Craighead P, Bowen J, McCready DR, Pritchard KI, Gelmon K, Murray Y, Chapman JA, Chen BE, Levine MN and MA.20 Study Investigators: Regional nodal irradiation in early-stage breast cancer. N Engl J Med *373(4)*: 307-316, 2015. PMID: 26200977. DOI: 10.1056/NEJMoa1415340

4 National Comprehensive Cancer Network. Breast Cancer (Version 4.2021). Available at: http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf [Last accessed on April 29, 2021]

5 Nanavati A, Lynch M and Vicini FA: Cardiac dose sparing and avoidance techniques in breast cancer radiotherapy. Radiother Oncol *112(1)*: 9-16, 2014. PMID: 24813095. DOI: 10.1016/j.radonc.2014.04.009

6 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, Wang Y and Early Breast Cancer Trialists' Collaborative Group (EBCTCG): 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 *366(9503)*: 2087-2106, 2005. PMID: 16360786. DOI: 10.1016/S0140-6736(05)67887-7

7 Giordano SH, Kuo YF, Freeman JL, Buchholz TA, Hortobagyi GN and Goodwin JS: Risk of cardiac death after adjuvant radiotherapy for breast cancer. J Natl Cancer Inst *97(6)*: 419-424, 2005. PMID: 15770005. DOI: 10.1093/jnci/dji067

8 Darby SC, Ewertz M, McGale P, Bennet AM, Blom-Goldman U, Brønnum D, Correa C, Cutter D, Gagliardi G, Gigante B, Jensen MB, Nisbet A, Peto R, Rahimi K, Taylor C and Hall P: Risk of ischemic heart disease in women after radiotherapy for breast cancer. N Engl J Med *368(11)*: 987-998, 2013. PMID: 23484825. DOI: 10.1056/NEJMoa1209825

9 White J, Tai A, Arthur D, Buchholz T, MacDonald S, Marks L, Pierce L, Recht A, Rabinovitch R, Taghian A, Vicini F, Woodward W and Li A: Breast cancer atlas for radiation therapy planning: consensus definitions. Available at: https://www.nrgoncology.org/Portals/0/Scientific%20Program/CIRO/Atlases/BreastCancerAtlas_corr.pdf?ver=2018-04-18-144201-270 [Last accessed on April 29, 2021]

10 Offersen BV, Boersma LJ, Kirkove C, Hol S, Aznar MC, Sola AB, Kirova YM, Pignol JP, Remouchamps V, Verhoeven K, Weltens C, Arenas M, Gabrys D, Kopek N, Krause M, Lundstedt D, Marinko T, Montero A, Yarnold J and Poortmans P: ESTRO consensus guideline on target volume delineation for elective radiation therapy of early stage breast cancer, version 1.1. Radiother Oncol *118(1)*: 205-208, 2016. PMID: 26791404. DOI: 10.1016/j.radonc.2015.12.027

11 Nielsen MH, Berg M, Pedersen AN, Andersen K, Glavicic V, Jakobsen EH, Jensen I, Josipovic M, Lorenzen EL, Nielsen HM, Stenbygaard L, Thomsen MS, Vallentin S, Zimmermann S, Offersen BV and Danish Breast Cancer Cooperative Group Radiotherapy Committee: Delineation of target volumes and organs at risk in adjuvant radiotherapy of early breast cancer: national guidelines and contouring atlas by the Danish Breast Cancer Cooperative Group. Acta Oncol *52(4)*: 703-710, 2013. PMID: 23421926. DOI: 10.3109/0284186X.2013.765064

12 Gee HE, Moses L, Stuart K, Nahar N, Tiver K, Wang T, Ward R and Ahern V: Contouring consensus guidelines in breast cancer radiotherapy: Comparison and systematic review of patterns of failure. J Med Imaging Radiat Oncol *63(1)*: 102-115, 2019. PMID: 30267561. DOI: 10.1111/1754-9485.12804

13 Xu Y, Wang J, Hu Z, Tian Y, Ma P, Li S, Dai J and Wang S: Locoregional irradiation including internal mammary nodal region for left-sided breast cancer after breast conserving surgery: Dosimetric evaluation of 4 techniques. Med Dosim *44(4)*: e13-e18, 2019. PMID: 30529304. DOI: 10.1016/j.meddos.2018.09.004

14 Zhang F, Wang Y, Xu W, Jiang H, Liu Q, Gao J, Yao B, Hou J and He H: Dosimetric evaluation of different intensity-modulated radiotherapy techniques for breast cancer after conservative surgery. Technol Cancer Res Treat *14(5)*: 515-523, 2015. PMID: 25311257. DOI: 10.1177/1533034614551873

15 Haciislamoglu E, Colak F, Canyilmaz E, Dirican B, Gurdalli S, Yilmaz AH, Yoney A and Bahat Z: Dosimetric comparison of left-sided whole-breast irradiation with 3DCRT, forward-planned IMRT, inverse-planned IMRT, helical tomotherapy, and volumetric arc therapy. Phys Med *31(4)*: 360-367, 2015. PMID: 25733372. DOI: 10.1016/j.ejmp.2015.02.005

16 Mo JC, Huang J, Gu WD, Gao M, Ning ZH, Mu JM, Li QL and Pei HL: A dosimetric comparison of double-arc volumetric arc therapy, step-shoot intensity modulated radiotherapy and 3D-CRT for left-sided breast cancer radiotherapy after breast-conserving surgery. Technol Health Care *25(5)*: 851-858, 2017. PMID: 29103057. DOI: 10.3233/THC-160746

17 International Commission on Radiation Units and Measurements: Prescribing, recording, and reporting photon beam therapy. Bethesda, MD, USA, ICRU, 1999.

18 Shaw E, Kline R, Gillin M, Souhami L, Hirschfeld A, Dinapoli R and Martin L: Radiation Therapy Oncology Group: radiosurgery quality assurance guidelines. Int J Radiat Oncol Biol Phys *27(5)*: 1231-1239, 1993. PMID: 8262852. DOI: 10.1016/0360-3016(93)90548-a

19 Li XA, Tai A, Arthur DW, Buchholz TA, Macdonald S, Marks LB, Moran JM, Pierce LJ, Rabinovitch R, Taghian A, Vicini F, Woodward W, White JR and Radiation Therapy Oncology Group Multi-Institutional and Multiobserver Study: Variability of target and normal structure delineation for breast cancer radiotherapy: an RTOG Multi-Institutional and Multiobserver Study. Int J Radiat Oncol Biol Phys *73(3)*: 944-951, 2009. PMID: 19215827. DOI: 10.1016/j.ijrobp.2008.10.034

20 Leunens G, Menten J, Weltens C, Verstraete J and van der Schueren E: Quality assessment of medical decision making in radiation oncology: variability in target volume delineation for brain tumours. Radiother Oncol *29(2)*: 169-175, 1993. PMID: 8310142. DOI: 10.1016/0167-8140(93)90243-2

21 Tai P, Van Dyk J, Yu E, Battista J, Stitt L and Coad T: Variability of target volume delineation in cervical esophageal cancer. Int J Radiat Oncol Biol Phys *42(2)*: 277-288, 1998. PMID: 9788405. DOI: 10.1016/s0360-3016(98)00216-8

22 Lee E, Park W, Ahn SH, Cho JH, Kim JH, Cho KH, Choi YM, Kim JS, Kim JH, Jang HS, Kim YS and Nam TK: Interobserver variation in target volume for salvage radiotherapy in recurrent prostate cancer patients after radical prostatectomy using CT *versus* combined CT and MRI: a multicenter study (KROG 13-11). Radiat Oncol J *36(1)*: 11-16, 2018. PMID: 29207866. DOI: 10.3857/roj.2017.00080

23 van der Veen J, Gulyban A and Nuyts S: Interobserver variability in delineation of target volumes in head and neck cancer. Radiother Oncol *137*: 9-15, 2019. PMID: 31048235. DOI: 10.1016/j.radonc.2019.04.006

24 Tao CJ, Yi JL, Chen NY, Ren W, Cheng J, Tung S, Kong L, Lin SJ, Pan JJ, Zhang GS, Hu J, Qi ZY, Ma J, Lu JD, Yan D and Sun Y: Multi-subject atlas-based auto-segmentation reduces interobserver variation and improves dosimetric parameter consistency for organs at risk in nasopharyngeal carcinoma: A multi-institution clinical study. Radiother Oncol *115(3)*: 407-411, 2015. PMID: 26025546. DOI: 10.1016/j.radonc.2015.05.012

25 Choi MS, Choi BS, Chung SY, Kim N, Chun J, Kim YB, Chang JS and Kim JS: Clinical evaluation of atlas- and deep learning-based automatic segmentation of multiple organs and clinical target volumes for breast cancer. Radiother Oncol *153*: 139-145, 2020. PMID: 32991916. DOI: 10.1016/j.radonc.2020.09.045

26 Franco P, Arcadipane F, Trino E, Gallio E, Martini S, Iorio GC, Piva C, Moretto F, Ruo Redda MG, Verna R, Tseroni V, Bona C, Pozzi G, Fiandra C, Ragona R, Bertetto O and Ricardi U: Variability of clinical target volume delineation for rectal cancer patients planned for neoadjuvant radiotherapy with the aid of the platform Anatom-e. Clin Transl Radiat Oncol *11*: 33-39, 2018. PMID: 29928706. DOI: 10.1016/j.ctro.2018.06.002

27 Ho AY, Ballangrud A, Li G, Gupta GP, McCormick B, Gewanter R, Gelblum D, Zinovoy M, Mueller B, Mychalczak B, Dutta P, Borofsky K, Parhar P, Reyngold M, Braunstein LZ, Chawla M, Krause K, Freeman N, Siu CT, Cost Z, Arnold BB, Zhang Z and Powell SN: Long-term pulmonary outcomes of a feasibility study of inverse-planned, multibeam intensity modulated radiation therapy in node-positive breast cancer patients receiving regional nodal irradiation. Int J Radiat Oncol Biol Phys *103(5)*: 1100-1108, 2019. PMID: 30508620. DOI: 10.1016/j.ijrobp.2018.11.045

28 Duma MN, Baumann R, Budach W, Dunst J, Feyer P, Fietkau R, Haase W, Harms W, Hehr T, Krug D, Piroth MD, Sedlmayer F, Souchon R, Sauer R and Breast Cancer Expert Panel of the German Society of Radiation Oncology (DEGRO): Heart-sparing radiotherapy techniques in breast cancer patients: a recommendation of the breast cancer expert panel of the German society of radiation oncology (DEGRO). Strahlenther Onkol *195(10)*: 861-871, 2019. PMID: 31321461. DOI: 10.1007/s00066-019-01495-w

29 Verbakel WFAR, Doornaert PAH, Raaijmakers CPJ, Bos LJ, Essers M, van de Kamer JB, Dahele M, Terhaard CHJ and Kaanders JHAM: Targeted intervention to improve the quality of head and neck radiation therapy treatment planning in the netherlands: short and long-term impact. Int J Radiat Oncol Biol Phys *105(3)*: 514-524, 2019. PMID: 31306734. DOI: 10.1016/j.ijrobp.2019.07.005

Received April 20, 2021
Revised April 28, 2021
Accepted April 29, 2021