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Clinical Implications of the ISC Technique for Breast Cancer Radiotherapy and Comparison with Clinical Recommendations

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Abstract. *Purpose: The present project studied the implications of using the irregular surface compensator (ISC) technique in comparison to three-dimensional conformal radiation therapy (3D-CRT) for breast cancer treatment. ISC is an electronic compensation algorithm that modulates the fluence across the radiation fields to compensate for irregularly-shaped surfaces and deliver a homogeneous dose to a compensation plane. Patients and Methods: Ten breast cancer patients (five left- and five right-sided) were planned with both techniques. The planning was done for 50 Gy in 25 fractions with 2 Gy per fraction in all patients. Physical parameters such as doses to the clinical target volume (CTV-T) and the planned target volume (PTV), heterogeneity index and doses to lung and heart were determined and compared for the treatment plans. Results: The ISC technique led to significantly better coverage of the CTV-T and PTV in almost all patients with statistically significant better homogeneity of the dose distribution. The contralateral lung and the heart receive the same dose with both ISC and 3D-CRT plans. However, ISC showed a trend towards decreasing the volumes of the ipsilateral lung irradiated with high doses. Conclusion: The ISC technique leads to an improvement of the target coverage and the radiation burden of the ipsilateral lung thus allowing better compliance with the national recommendations for breast radiotherapy and increasing the potential for improved quality of life for breast cancer patients. It should therefore be preferred over 3D-CRT for breast cases with difficult dose homogeneity to the PTV or CTV-T.*

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Breast cancer is nowadays the most frequent cancer in women in developed countries. In Sweden alone 8,490 new cases of breast carcinomas and 1,443 cases with tumours *in situ* were reported in 2012 (1). Screening programs and therapeutic developments have improved prognosis and survival rates in recent years, meaning that patients could survive for many years after treatment. Radiation therapy is an important component of the arsenal of treatment modalities to achieve long-term control of local and regional disease as well as for long-term survival (2). However, side-effects from radiation may worsen the quality of life of the patients and therefore reduce the positive contribution of radiation treatment. Among the side-effects, one could include complications of the heart and the lung and also cosmetic changes in the breast and induration from the hotspots in the dose distributions. Indeed, in some instances the use of conformal radiotherapy with multi-leaf collimators (MLC), dynamic wedges and compensating fields is not enough to achieve good target uniformity and reduction of the hotspots in the target and the organs at risk. Consequently, more advanced techniques have been proposed to improve the homogeneity of dose distributions and dose hotspots in breast radiation therapy, such as electronic compensation and inverse planning intensity modulated radiation therapy (IMRT) (3, 4). Inverse planning IMRT offers most flexibility in modulating the fluence in individual beams to achieve an optimum dose distribution in the target and the surrounding normal tissues. However, it is resource-demanding and quite sensitive to interplay effects caused by motion and setup uncertainties. Electronic compensation is a comparatively simpler method of forward planning that uses dynamic MLC to modulate individual beamlets across the radiation fields in order to improve dose distributions in cases where the body contours and the target

Table I. *Recommendations of the Swedish Beast Cancer Group (SweBCG) for the coverage of the clinical target volume (CTV-T) and the planned target volume (PTV) and dose burden to the organs at risk in breast cancer treatment with 50 Gy in 25 fractions.*

Priority	Structure	Recommendations
1	CTV-T	$V_{95\%}$=100% D_{mean}≥100%
2	PTV	$V_{93\%}$=100% (except for superficially located coldspots - see below)
3	Heart	Recommended threshold D_{mean} ≤10% (target threshold D_{mean} ≤4%) Maximum heart distance, MHD, ≤1 cm in tangential irradiation Coronary vessels should be avoided.
4	Lung	Recommended threshold D_{mean} ≤20% (target threshold D_{mean} ≤10%) for breast irradiation only Recommended threshold $V_{20\ Gy}$ ≤20% (target threshold V20 Gy ≤10%) for breast irradiation only Recommended threshold D_{mean} ≤40% (target threshold Dmean ≤20%) for irradiation of the breast and the supraclavicular lymph nodes Recommended threshold $V_{20\ Gy}$ ≤40% (target threshold $V_{20\ Gy}$ ≤20%) for irradiation of the breast and the supraclavicular lymph nodes
5	PTV	Recommended threshold $V_{105\%}$ ≤20% (target threshold $V_{105\%}$ ≤10%) In case of superficially located coldspots $V^{93\%}$ >90%, but these should be at the greatest possible distance from the CTV-T.

volumes are rounded, such as breast treatment, and where the use of simple wedges would lead to cold- or hotspots. The irregular surface compensator (ISC) is such an electronic compensation algorithm implemented in the Eclipse treatment planning system (Varian Medical Systems). Several studies have investigated the performance of electronic compensation algorithms to improve dose homogeneity in the target (4-8), but most of them date from the period of pencil beam convolution algorithms that predict more homogeneous dose distributions in heterogeneous regions like the breast and thorax than more advanced convolution-superposition algorithms for dose calculation. Furthermore, these studies were mainly concerned with the dosimetric implications of using the mentioned algorithms. The present work proposes a new approach, namely the investigation of the clinical implications of using the ISC method from the perspective of the recommendations of the Swedish Breast Cancer Group (SweBCG) for plan acceptance (9). These recommendations are followed by a large number of Swedish radiation therapy clinics and therefore represent an interesting clinical framework for plan evaluation and acceptance in breast radiation therapy. Furthermore, dose calculations are performed with the analytical anisotropic algorithm (AAA) known to provide better accuracy for heterogeneities like those in the breast and thorax region (10, 11).

Patients and Methods

Ten consecutive breast cancer patients (5 left-sided and 5 right-sided), for which the routine planning with conformal radiation therapy led to high heterogeneity in the planning target volume (PTV) or hotspots outside the PTV, were included in the analysis. The patients received radiation treatment to the whole breast only (WBO) – 4 patients – or to the breast and the supraclavicular lymph nodes (BSC) – 6 patients. The patients were CT scanned postoperatively for treatment planning with 2 mm slice thickness. The location of clinical target volume of the original tumour (CTV-T), the planning target volume (PTV) and the relevant organs at risk (lung, heart and the left anterior descending artery – LAD) were delineated or approved by experienced radiation therapy oncologists. The patients were planned according to routine practice with tangential fields for WBO patients and tangential fields plus antero-posterior fields for BSC patients with a monoisocentric technique where the isocentre was placed at the junction between the breast and the supraclavicular region. For conventional conformal radiation therapy, the choice of photon energy, dynamic wedges and compensating fields for conventional planning was determined by the individual features of the patients. Corresponding plans were also created with the tangential fields devised with the ISC technique for a user-defined transmission penetration depth of 50%. All plans were calculated with the analytical anisotropic algorithm in Eclipse TPS (version 10) and normalised so that the mean dose to the PTV was equal to 50 Gy in 25 fractions.

The resulting plans were evaluated in terms of dose to the PTV and the organs at risk (OAR) and compared to the recommendations of the SweBCG (Table I). Thus, PTV parameters included near minimum dose, $D_{98\%}$ (the dose to 98% of the PTV), near maximum dose, $D_{2\%}$ (dose to 2% of the PTV), the volume receiving at least 93% of the prescribed dose ($V_{93\%}$) and the heterogeneity index (HI) which was defined as:

$$HI=\frac{D_{2\%}-D_{98\%}}{D_{prescribed}} \qquad \text{(equation 1)}$$

where $D_{prescribed}$ is the prescription dose.

According to the recommendations of the SweBCG, the mean dose to the CTV-T and the CTV-T volume covered by at least 95% of the prescribed dose were also included in the analysis. For the OARs, clinically relevant parameters were determined from the dose volume histograms (DVH) and included mean as well as near maximum dose to the lung, the heart and the LAD.

Table II. *Mean values and the corresponding standard deviations (SD) for dosimetric parameters for the clinical with target volume (CTV-T), the planned target volume (PTV) and the organs at risk included in the analysis*

	Conventional plan		ISC plan		
	Mean value	SD	Mean value	SD	*p*-Value
CTV-T					
D_{mean}	101.1	1.6	100.8	1.4	0.5
$V_{95\%}$	99.0	3.0	99.7	0.8	0.5
PTV					
D_{mean}	100.0	0.0	100.0	0.0	-
$V_{93\%}$	97.5	2.0	98.3	1.2	0.2
$V_{105\%}$	8.8	4.1	4.7	3.4	0.001
$D_{98\%}$	92.5	2.5	93.3	1.0	0.2
$D_{2\%}$	107.3	1.2	106.0	1.7	0.02
HI	14.8	3.4	12.6	2.3	0.02
Heart					
D_{mean}	2.3	2.6	2.6	2.7	0.1
$D_{2\%}$	18.4	29.7	19.6	29.9	0.3
Lung (ipsilateral)					
D_{mean}	16.1	7.3	15.3	7.6	0.1
$D_{2\%}$	87.5	8.6	85.9	7.8	0.1
$V_{20\ Gy}$	13.8	8.1	12.8	8.3	0.07
$V_{10\ Gy}$	19.4	10.4	18.3	10.6	0.1
Lung (contralateral)					
D_{mean}	0.3	0.2	0.3	0.2	0.7

The dosimetric parameters in the conventional and ISC plans were evaluated for statistically significant differences with a paired, two-tailed Student's *t*-test.

Results

A summary of the dosimetric parameters for all ten patients are summarised in Table II. The ISC technique was shown to improve homogeneity of the dose distribution in the CTV-T and PTV for all the patients. Thus, the hotspots were significantly reduced in the ISC plans in comparison to the conventional plans (p=0.001 for $V_{105\%}$ and 0.02 for $D_{2\%}$). Similarly, the heterogeneity index was significantly smaller for ISC plans (p=0.02). Figure 1 illustrates these differences with the dose volume histograms for a representative patient.

The difference in coverage of the PTV with the 93% isodose did not reach statistical significance if all the patients were pooled together (p=0.2). A subgroup analysis on left-sided patients and for BSC treatments showed an improvement of target coverage (Figure 2), but without reaching statistical significance. The trend toward improving target coverage is illustrated in Figure 3 for a left-sided BSC patient. These results are however quite promising and show that the ISC technique could improve target coverage for individual difficult cases.

With respect to the normal tissues, there was no significant difference in the doses to the contralateral lung and the heart from the two techniques. There was a trend of increasing the radiation burden to the LAD and the heart with ISC, especially for left-sided patients, but this was however not statistically significant (p-values in the range 0.12-0.33).

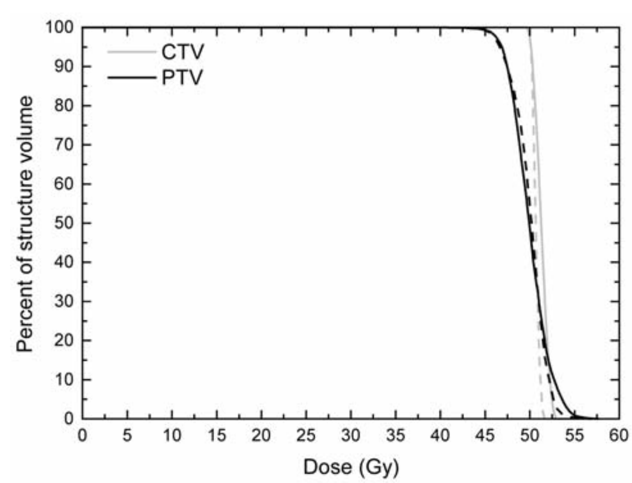

Figure 1. *Dose volume histograms for the clinical target volume (CTV) and the planning target volume (PTV) for a conventional plan (solid lines) and for the corresponding irregular surface compensator (ISC) plan (dashed lines) for one patient included in the analysis.*

With respect to the ipsilateral lung, there was a trend of reducing the radiation burden to this organ with ISC, on the borderline of statistical significance (p=0.07 for $V_{20\ Gy}$),

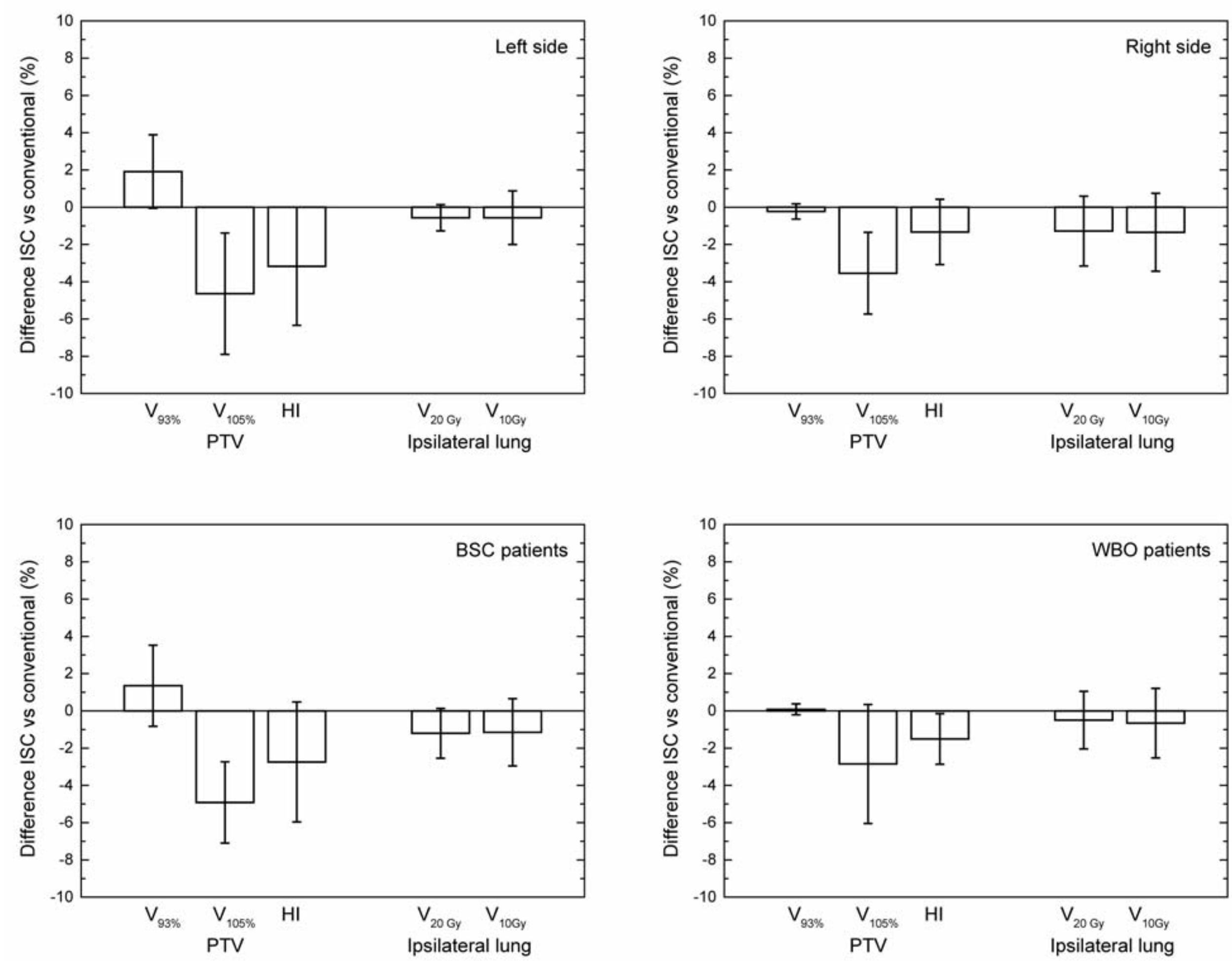

Figure 2. *Subgroup comparisons of dosimetric parameters for the planned target volume (PTV) and the ipsilateral lung.*

indicating that the ISC technique has potential for lowering the dose to the ipsilateral lung, towards better compliance with the national recommendations for breast radiotherapy and also for improved quality of life of the patients after radiation therapy.

Discussion

Modulating individual beamlets with dynamic multileaf collimators has been proposed several years ago as an intermediate step between conventional fields with wedges and full IMRT to improve dose distributions in breast radiation therapy (4). Several studies have been published on the effectiveness of this method to improve dose homogeneity in comparison to other planning methods for breast irradiation (4-8). However, relatively little attention has been paid to the clinical implications of the potential improvement or the choice of the algorithm for dose calculation. Therefore, this study aimed to investigate the clinical implications of using ISC planning compared with conventional 3D-CRT planning from the perspective of the recommendations of the Swedish Breast Cancer Group (9), currently used for plan evaluation in Sweden. It used the analytical anisotropic algorithm that is particularly suited for dose calculation in breast radiotherapy as it better takes into account the lateral energy transport in heterogeneous media. Furthermore, the study included both WBO and BSC patients in order to investigate the clinical impact on both these subgroups of breast cancer patients, an aspect that has not been covered in previous studies. For the BSC patients it is essential to know the real dose distribution in the target and in the lungs as they involve a larger irradiated volume than patients with only the whole breast. Thus, the use of AAA for dose calculation has been associated with increased heterogeneity in the target compared to PBC calculations (12). Consequently, attempting to increase dose homogeneity

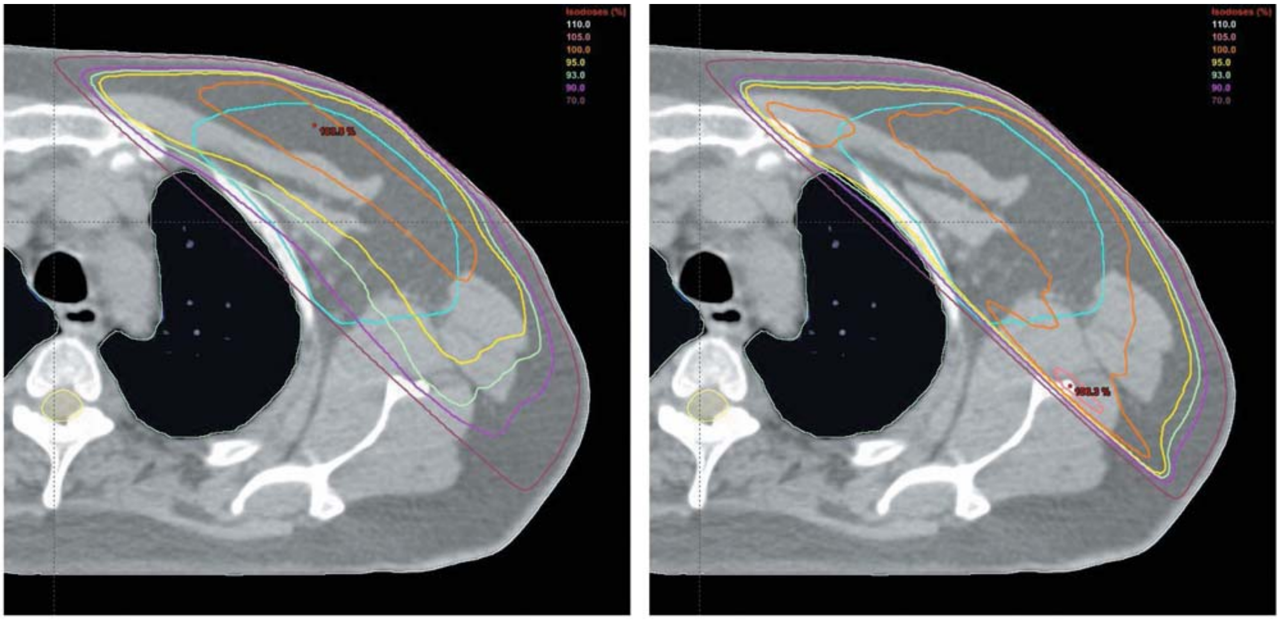

Figure 3. *Axial section showing the dose distributions from a conventional plan (left panel) and the corresponding irregular surface compensator plan (right panel) for a left-sided patient receiving treatment to the breast and the supraclavicular lymph nodes.*

in the target could lead to increased lung doses and hotspots that may result in higher fibrosis rates and even skin problems. Although only a few BSC patients have been included in our analysis, this population subgroup showed important trends for the irradiation of the lung, where the dose reduction with ISC was on the borderline of statistical significance (p=0.08).

The results of this study showed that the ISC technique is capable of improving target coverage and reducing dose heterogeneity and hotspots for breast cancer patients. This was shown to be particularly important for BSC patients that have a larger PTV. These results complement the findings of Hideki et al (8) who also used AAA for dose calculation, but investigated only WBO patients. Improving target coverage is particularly important for patients with multifocal or lobular disease for which cold spots in the PTV should be avoided. Furthermore, decreasing the hotspots could lead to a reduction of the toxicity. From this point of view, ISC should be considered for hypofractionated schedules where hotspots could increase the biological effect much more than the percent increase in physical dose. Indeed, schedules with 2.66 Gy per fraction have been shown to lead to the same clinical outcome as schedules with fractional doses of 2 Gy (13) and might be favoured by some radiation therapy departments to decrease waiting times or increase patient throughput.

Promising trends were also seen for ISC for reducing the radiation burden of the lung, also in line with the findings of other studies. This is especially important for AAA-planning as this algorithm was found to predict larger burden to this organ than PBC (12, 14). However, in two out of ten cases for which there were difficulties in fulfilling the SweBCG-recommended thresholds for lung irradiation ($V_{20Gy} \leq 20\%$) with conventional plans, the situation did not significantly improve with ISC-devised plans.

Our results also indicated a trend to increase the dose to the heart and the LAD in left-sided patients, but this was not found to be statistically significant. Hideki et al (8) reported that ISC could be used to significantly reduce the dose to the heart and therefore our findings might be an artefact of the small number of patients included in the analysis. Nevertheless, further reduction of the dose to the heart could be achieved by using respiratory gating to increase the distance between the heart and the radiation beams.

Modulation of the beam fluence with the dynamic MLC introduces a certain degree of complexity in the treatment of the breast that might raise a question on possible interaction with uncertainties due to respiratory motion and setup errors. However, it has been shown that the clinical implications of the dosimetric changes thus introduced are relatively small and hence clinically acceptable (15).

Conclusion

The ISC technique should be considered as a clinically useful alternative for breast cancer cases that require particularly high homogeneity of the dose to the target, such as patients with multifocal or lobular cancer and especially the subgroup that requires irradiation of the supraclavicular lymph nodes. It is also a useful alternative for hypofractionated treatment schedules as it could decrease the hotspots outside the target and lower the dose to organs at risk, thus having potential to improve the quality of life of the patients after radiation therapy.

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