LET-dependent RBE in the skin of breast patients treated with IMPT vs 3DCRT

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ABSTRACT

Purpose: Breast patients treated with intensity-modulated proton therapy (IMPT) often experience more severe skin dose toxicity compared to those with photon 3DCRT. Here we quantitatively estimated the LET-dependent RBE (LET-RBE) for the IMPT patients.

Methods: 33 and 25 Caucasian patients treated with IMPT and 3DCRT in a single institute without chemotherapy were retrospectively analyzed in this IRB approved study. Scores for radiation dermatitis (RD) were recorded weekly. For each patient, the skin was contoured with 3 mm inside from the patient's surface, within 50% isodose line. The EQD2 of D10 of the skin was studied due to different prescriptions in proton and photon groups. Particularly, we analyzed the correlation between the RD and D10 of the course and the accumulated D10 (D10ac) when the new toxicity grades were recorded. LETd was calculated in a Monte-Carlo dose engine and 3 RBE models were employed to estimate LET-RBE. The average RBE dose from the 3 models was used for our analysis.

Results: For both proton and photon groups, no correlation between RD and the course D10 was found, however, a strong correlation was found between RD and D10ac. The mean D10ac (RBE=1.1) was 26.69 Gy, 43.71 Gy and 49.11 Gy for RD=1, 2 and 3 respectively. When LET was considered, the mean D10ac was 28.62 Gy, 46.52 Gy and 51.94 Gy for RD=1, 2 and 3 respectively. For the photon group, the mean D10ac was 28.11 Gy and 46.29 Gy for RD=1 and 2 (no photon patient had RD=3). Thus, the mean D10ac (LET-RBE) excellently agreed with photon D10 and was 7.2%, 6.4% and 5.8% higher than the mean D10ac (RBE=1.1) for RD=1, 2 and 3 respectively.

Conclusion: Breast skin toxicities show evidence of LET-RBE effect for breast patients. Currently, RBE=1.1 is used in clinic but our results indicate RBE=1.17 may be better for breast skin.

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INTRODUCTION

Breast patients treated with intensity-modulated proton therapy (IMPT) often experience more severe skin dose toxicity in the forms of radiation dermatitis and/or skin hyperpigmentation, compared to those with photon 3DCRT. It has been suggested that proton linear energy transfer (LET) increases the RBE dose. Here we quantitatively estimated the LET-dependent RBE (LET-RBE) for the IMPT patients.

METHODS AND MATERIALS

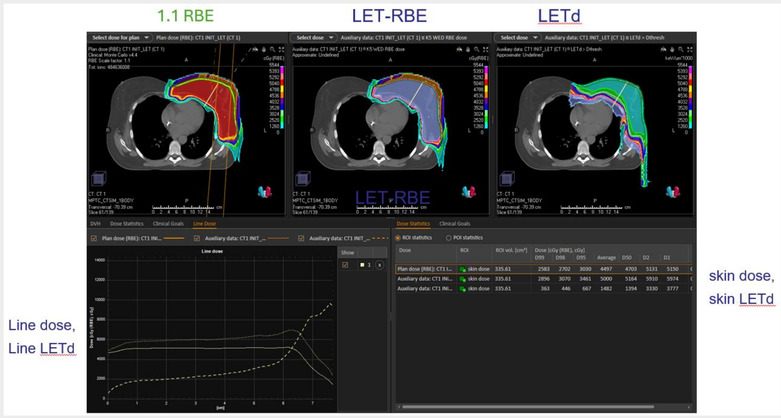
30 and 24 Caucasian patients treated with IMPT and 3DCRT in a single institute without chemotherapy were retrospectively analyzed in this IRB approved study. Scores for radiation dermatitis (RD) were recorded weekly. For each patient, the skin was contoured with 3 mm inside from the patient's surface, within 50% isodose line. The EQD2 of D10 of the skin was studied due to different prescriptions in proton and photon groups. Particularly, we analyzed the correlation between the RD and D10 of the course and the accumulated D10 (D10ac) when the new toxicity grades were recorded. LETd was calculated in a Monte-Carlo dose engine and 3 RBE models were employed to estimate LET-RBE. The average RBE dose from the 3 models (Wedenberg, Carabe-Fernandez, McNamara,) was used for our analysis.

Proton cases

	Median Age (y)	# patients with RD scores			
		0	1	2	3
Mastectomy	44	0	6	13	0
Lumpectomy /Intact	54	0	3	6	2

Photon cases

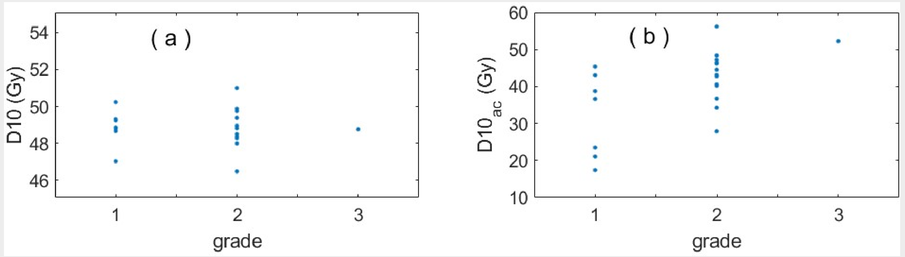
	Median age (y)	# patients with RD scores			
		0	1	2	3
Mastectomy	46.5	2	5	2	0
Lumpectomy/Intact	62	3	11	0	1



RESULTS

For both proton and photon groups, no correlation between RD and the course D10 was found, however, a strong correlation was found between RD and D10ac. The mean D10ac (RBE=1.1) was 26.69 Gy, 43.71 Gy and 49.11 Gy for RD=1, 2 and 3 respectively. When LET was considered, the mean D10ac was 28.62 Gy, 46.52 Gy and 51.94 Gy for RD=1, 2 and 3 respectively. For the photon group, the mean D10ac was 28.11 Gy and 46.29 Gy for RD=1 and 2 (no photon patient had RD=3). Thus, the mean D10ac (LET-RBE) excellently agreed with photon D10 and was 7.2%, 6.4% and 5.8% higher than the mean D10ac (RBE=1.1) for RD=1, 2 and 3 respectively.

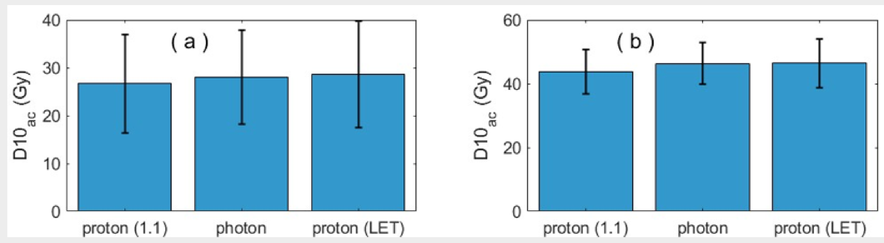
The figures below display (a) the course D10 and (b) accumulated D10 vs RD toxicity. No correlation between the course D10 and toxicity but strong correlation between the accumulated D10 and toxicity.



The table below lists the correlation coefficients between D10 and RD grade, with and without LET dependence. D10 (1.1) is the D10 with fixed RBE=1.1, D10 (LET) is the D10 with LET-dependent RBE, D10ac is the accumulated D10 at the fraction in which the RD grade was first-time reported. D103mm and D105mm stand for D10 in the groups of skin 3 mm and 5 mm removed. For photon, RBE=1.0.

modality	quantity vs RD grades	Correlation coefficient	quantity vs RD grades	Correlation coefficient
proton	D10 (1.1)	-0.060	D10 (LET)	-0.256
	$D10_{ac}$ (1.1)	0.606	$D10_{ac}$(LET)	0.582
	$D10_{3mm}$ (1.1)	-0.017	$D10_{3mm}$ (LET)	-0.311
	$D10_{3mm\ ac}$ (1.1)	0.569	$D10_{3mm\ ac}$ (LET)	0.530
	$D10_{5mm}$ (1.1)	-0.134	$D10_{5mm}$ (LET)	-0.179
	$D10_{5mm\ ac}$ (1.1)	0.658	$D10_{5mm\ ac}$ (LET)	0.653
photon	D10 (1.0)	0.05	-	-
	$D10_{ac}$ (1.0)	0.684	-	-

The figures below show the mean D10ac with RBE=1.1, LET-dependent RBE and photon D10. (a) RD = 1 and (b) RD = 2. The bar shows the mean, and the line stands for the standard deviation.



DISCUSSION

Radiation-induced skin toxicity, in the forms of radiation dermatitis and/or skin hyperpigmentation is an important endpoint affecting quality of life. Our results suggest that for breast skin the RBE=1.17 is more reasonable than the clinically used RBE=1.1. The increased 6% RBE may explain the higher dose toxicity in proton breast patients. In general, RBE=1.1 is related to the average LET in SOBP, but for breast SOBP that consists of lower energy layers the average LET is relatively large.

CONCLUSIONS

Breast skin toxicities show evidence of LET-RBE effect for breast patients. Currently, RBE=1.1 is used in clinic but our results indicate RBE=1.17 may be better for breast skin.

REFERENCES

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