Chronic skin toxicities and quality of life in breast cancer survivors after adjuvant radiotherapy: a systematic review and meta-analysis of different radiotherapy techniques

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Introduction

- Radiotherapy (RT) techniques influence acute skin reactions; however, their impact on chronic skin reactions and quality of life (QoL) is less understood.
- This review evaluates long-term skin toxicities and quality of life (QoL) in patients receiving adjuvant RT to the breast and/or regional lymph nodes via 3-dimensional conformal RT (3DCRT) compared to modern techniques including Intensity-modulated RT (IMRT), volumetric arc therapy (VMAT)

Methods

- Comprehensive literature search in Embase, MEDLINE, and Cochrane CENTRAL from inception to June 29, 2023, updated April 26, 2024.
- Included human studies in English comparing conventional RT with alternative techniques for adjuvant breast cancer treatment.
- Exclusions: intraoperative and partial breast RT techniques, studies without chronic toxicity or QoL outcomes.
- Data synthesis involved pooled risk ratios (RR) with 95% confidence intervals (CI) using a random-effects model.
- Heterogeneity assessed with Cochran Q and I^2 statistics.
- Two-tailed p values of <0.05 considered statistically significant.
- The meta-analyses and graphs were generated using Review Manager (RevMan), version 5.4.
- Review registered with PROSPERO (CRD42023443169).

Table 1. Cosmetic outcomes reported by the studies.

Study	Scores	Cosmetic effect		Results		p-value
				3DCRT (%)	IMRT (%)	
Donovan et al. (2007)	Photographic assessment of change in breast appearance	1-year	None	64.1	74.2	0.008*
			Mild	28.2	21.0	
			Marked	7.6	4.8	
		2-year	None	56.6	65.1	
			Mild	38.0	30.2	
			Marked	5.4	4.7	
		5-year	None	41.8	60.2	
			Mild	44.3	29.7	
			Marked	13.9	10.2	
Harsolia et al. (2007)	Harvard 4-point Scale	NR	Good to excellent	97.0	99.0	0.60
Mukesh et al. (2013)	Three-point score	5-year	Good	36.7	42.6	0.038
			Moderate	41.5	45.7	
			Poor	21.8	11.7	
Pignol et al. (2016)	EORTC cosmetic rating system	10-year	Good to excellent	82.7	82.0	NR†

IMRT may reduce selected chronic skin toxicities compared to 3DCRT with no consistent long-term differences in cosmetic outcomes or QoL

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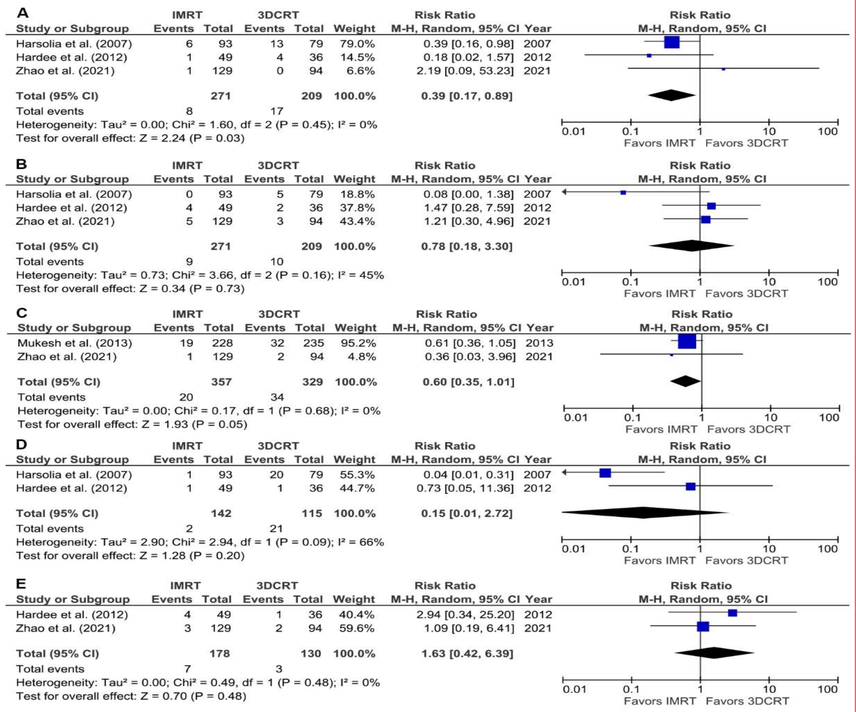
Results

- From 1,305 screened studies, nine articles representing seven studies (2,418 patients) met criteria, including three RCTs.
- Predominant use of conventional fractionation (1.8–2 Gy per fraction); one study used moderate hypofractionation (40 Gy in 15 fractions). All compared IMRT versus 3DCRT
- **IMRT associated with significantly lower incidence of grade ≥2 hyperpigmentation (RR: 0.39, 95% CI: 0.17–0.89). (Figure 1)**
- No significant differences for grade ≥2 breast fibrosis (RR: 0.78), telangiectasia (RR: 0.60), edema (RR: 0.15), and atrophy/retraction (RR: 1.63). **(Figure 1)**
- **Short-term cosmetic outcomes favored IMRT**; no long-term differences observed. **(Table 1)**
- Three studies utilizing EORTC QLQ-C30 and QLQ-BR23 reported **no significant differences in QoL between IMRT and 3DCRT**.

Figure 1. Forest plots of risk ratios comparing IMRT and 3DCRT: Grade ≥2 (A) hyperpigmentation, (B) breast fibrosis/induration, (C) telangiectasia, (D) breast edema, (E) breast atrophy/retraction. Abbreviations: IMRT, intensity-modulated radiotherapy; 3DCRT, 3-dimensional conformal radiotherapy.



Limitations

- Interpretation is limited by the small number of studies and variability in reporting standards, underscoring the need for uniform outcome measures in future research.