

Postmastectomy Radiation Therapy after Breast Reconstruction

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Introduction

- Oncologic results of BCT is comparable to mastectomy.
- Mastectomy is still inevitable in some patients.
- Psychosocial impact of surgery type - body image and feelings of attractiveness

	Lumpectomy	Mastectomy with reconstruction	Mastectomy alone	Two-sided <i>P</i> †
CARES body image				
Mean (SD)‡	0.65 (0.92)	1.24 (1.25)	1.37 (1.32)	.0001
CI	0.59–0.70	1.11–1.38	1.25–1.48	
Uncomfortable with changes in body, %§				
Not at all/a little	78.5	64.4	64.6	.0001
Fair amount to very much	21.5	35.6	35.4	
CI	19.2–23.9	30.4–40.8	31.2–35.5	
Don't feel sexually attractive, %§				
Not at all/a little	73.5	65.9	60.6	.0001
Fair amount to very much	26.5	34.1	39.4	
CI	23.9–29.1	28.9–39.2	35.2–43.7	
Unattractive to partner, %§				
Not at all/a little	85.2	82.3	79.8	.034
Fair amount to very much				
Mean (SD)	14.8	17.7	20.2	
CI	12.7–16.9	13.5–21.9	16.7–23.7	
14-item RDAS (for partnered only)				
Mean (SD)‡	49.8 (8.7)	49.1 (9.5)	50.4 (8.8)	.302
CI	49.2–50.4	47.9–50.2	49.5–51.4	
Impact of breast cancer on sex life, %§				
None/positive	70.2	54.6	58.7	.0001
Negative	29.8	45.4	41.3	
CI	27.1–32.5	39.9–50.9	36.9–45.6	

Introduction



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[Breast Cancer Table of Contents](#)
[Staging, Discussion](#)

- Type of reconstruction
 - Implants, autologous tissue (“flaps”) or a combination
- Time of reconstruction
 - Immediate (at the same time as mastectomy) or
 - Delayed (some time following the completion of cancer treatment)
- SSM – equivalent risk of local and regional cancer recurrence



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Type of Reconstruction

Advantages and disadvantages

Implant-based reconstructions	TRAM (Pedicle/free flap)	Lattisimus flap	Perforator flap surgery DIEP/SIEP/SGAP/IGAP/TUG
<i>Minimally invasive</i>	No implant	More natural tissue and natural results, but usually still needs/requires implant	No implant
<i>Shorter operation, shorter recovery</i>	<i>Very natural looking</i>	Decreases risk associated with implant and radiation	<i>Very natural looking</i>
Minimal scarring	<i>Ages with patient</i> Less fat necrosis-better blood supply	Longer initial surgery	<i>Ages with patient</i> Minimal abdominal weakness and abdominal hernia
Overall complication rate 10.5%: infection (4%), malposition (3.5%), rupture (1.7%), extrusion (0.6%), and capsular contracture (0.6%)	Altered tension on thoracolumbar fascia-back pain <i>Decreased abdominal strength,</i> especially pronounced with bilateral procedure	<i>Lose muscle function-initial shoulder weakness 15-20%</i> Synergistic muscle compensation (teres major, subscapularis, pectoralis major)	Longer operation <i>Technically difficult</i> operation Risks associated with microsurgery

Reconstruction with Implant



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Results of Reconstruction

- Capsular contracture (CC)
 - the leading long-term complication that occurs after breast implantation
 - soft deformable implant → formation of an acellular collagenous sheath → formation of hard spherical mass
 - PMRT can increase the risk of severe CC.

Appearance
Contracture
Firmness

Panel 2: Baker classification of capsular contracture¹⁵⁰

Grade I

Breast absolutely natural; no one could tell breast was augmented

Grade II

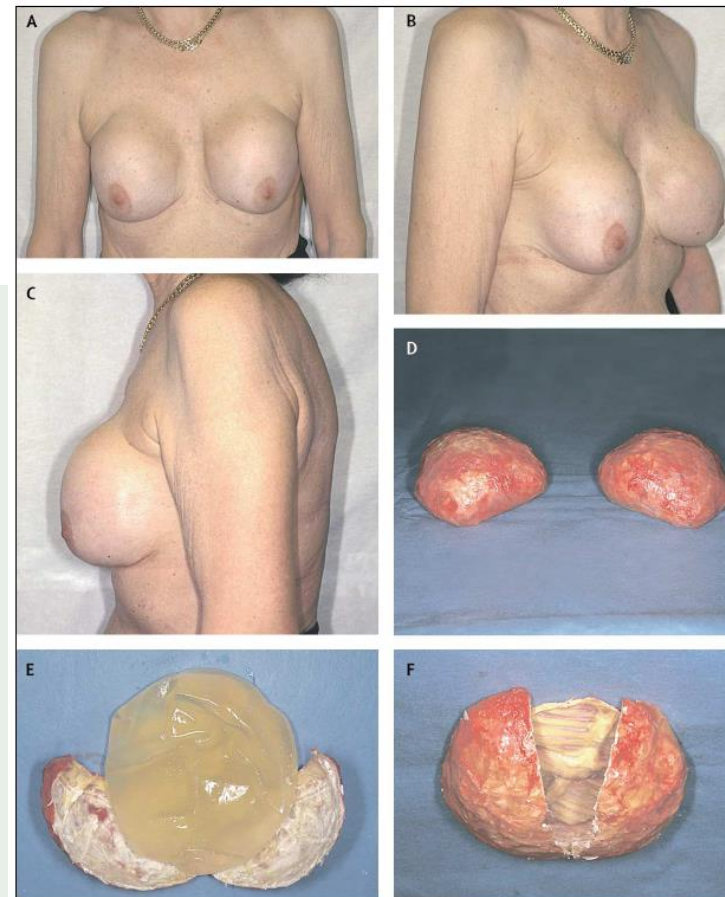
Minimum contracture; I can tell surgery was done, but patient has no complaint

Grade III

Moderate contracture; patient feels some firmness

Grade IV

Severe contracture; obvious just from observation



Results of Reconstruction



Baker IV capsular contracture

-> s/p implant change

-> for free fat injection

- F/41 at op
- Rt breast cancer cT3N1M0 (2009/9/4)
IDC HG 2/3 ER 7/7 PR 4/7 c-erbB2 (3/3)
- s/p neoadj AC #4 --> docetaxel #4
- s/p SSM/immediate implant,
ypT1b(0.8cm)N0(0/12)M0)
- s/p adjuvant RT 50.4 Gy / 28 factions
- s/p adjuvant herceptin 1 year
- On adjuvant tamoplex

- 2010/03/09 lt SSM/implant – TRAM 실패
- 2010/05/17 Irrigation, debridement, TEI
- 2011/01/24 Implant change
- 2011/05/17 Primary closure, Rt. breast
- 2011/06/03 Debridement, irrigation
- **2012/02/20 Free fat injection**
- 2012/05/31 Starlux laser



Results of Reconstruction

The clinical course of immediate breast implant reconstruction after breast cancer

- Danish Registry for Plastic Surgery of the Breast, 1999-2006, 1418 reconstructions
- 189 *immediate reconstructions with implant - no RT*, no prophylactic mastectomy
149 two-stage procedures, 40 one-stage procedures
- 353 delayed two-stage procedures with implant- no RT, no prophylactic mastectomy

Table II. Cumulative incidence of complications adjusted for competing risks according to time since operation for all immediate implant reconstructions (Implant level, n = 189).

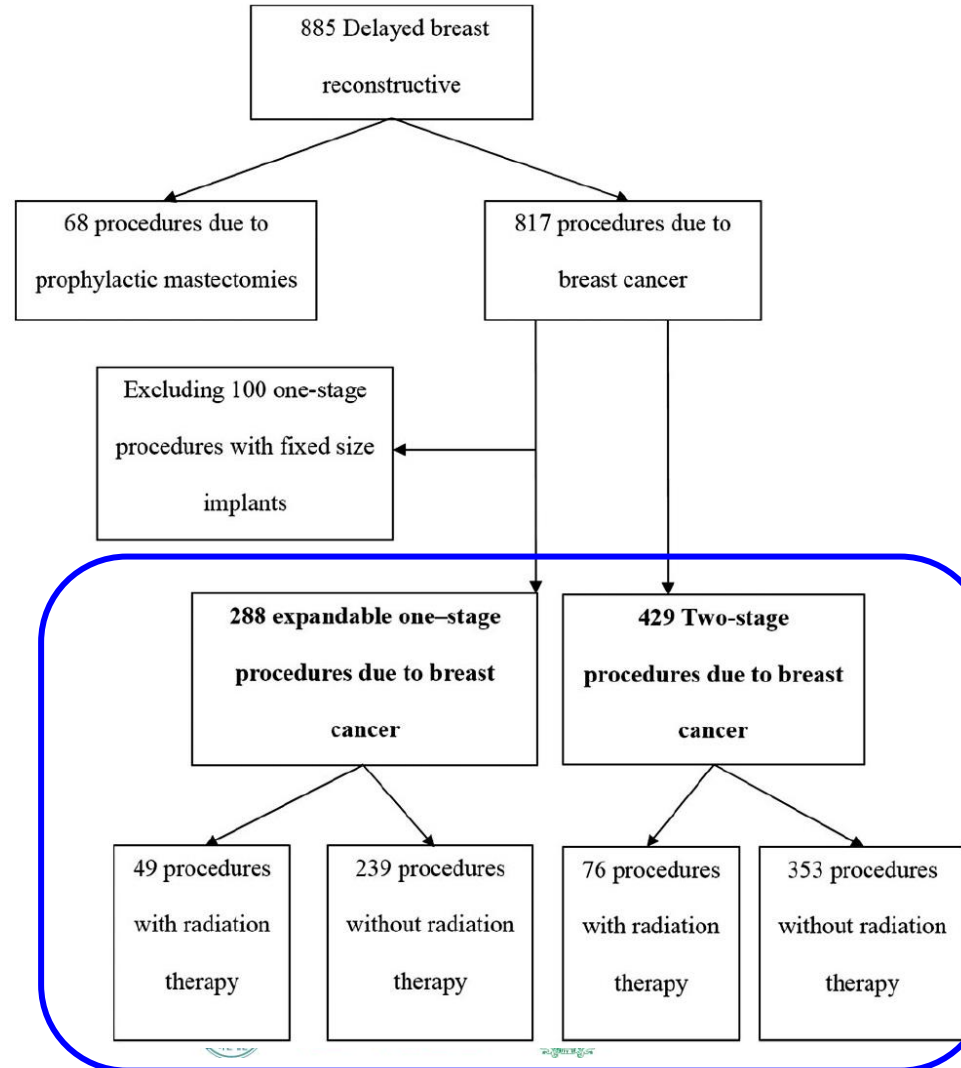
Outcome	N [§]	1 Year Risk (95% CI)	2 Year Risk (95% CI)	5 Year Risk (95% CI)	8 Year Risk (95% CI)
Any complication**	144	52.4 (48.7;56.0)	67.2 (63.8;70.6)	75.7 (72.6;78.8)	76.4 (73.3;79.5)
Infection [¶]	38	19.0 (16.2;21.9)	19.6 (16.7;22.5)	20.1 (17.2;23.0)	20.1 (17.2;23.0)
Hematoma	23	11.1 (8.8;13.4)	12.2 (9.8;14.6)	12.2 (9.8;14.6)	12.2 (9.8;14.6)
Seroma	23	12.2 (9.8;14.5)	12.2 (9.8;14.5)	12.2 (9.8;14.5)	12.2 (9.8;14.5)
Capsular Contracture#	10	2.1 (1.1;3.2)	4.2 (2.8;5.7)	5.3 (3.7;7.0)	5.3 (3.7;7.0)
Extrusion of the implant	11	5.8 (4.1;7.5)	5.8 (4.1;7.5)	5.8 (4.1;7.5)	5.8 (4.1;7.5)
Rupture [@]	3	1.6 (0.7;2.5)	1.6 (0.7;2.5)	1.6 (0.7;2.5)	1.6 (0.7;2.5)
Displacement/asymmetry	55	14.8 (12.2;17.4)	23.8 (20.7;26.9)	28.7 (25.4;32.0)	29.5 (26.1;32.9)

PMRT after Reconstruction

Delayed Breast Implant Reconstruction

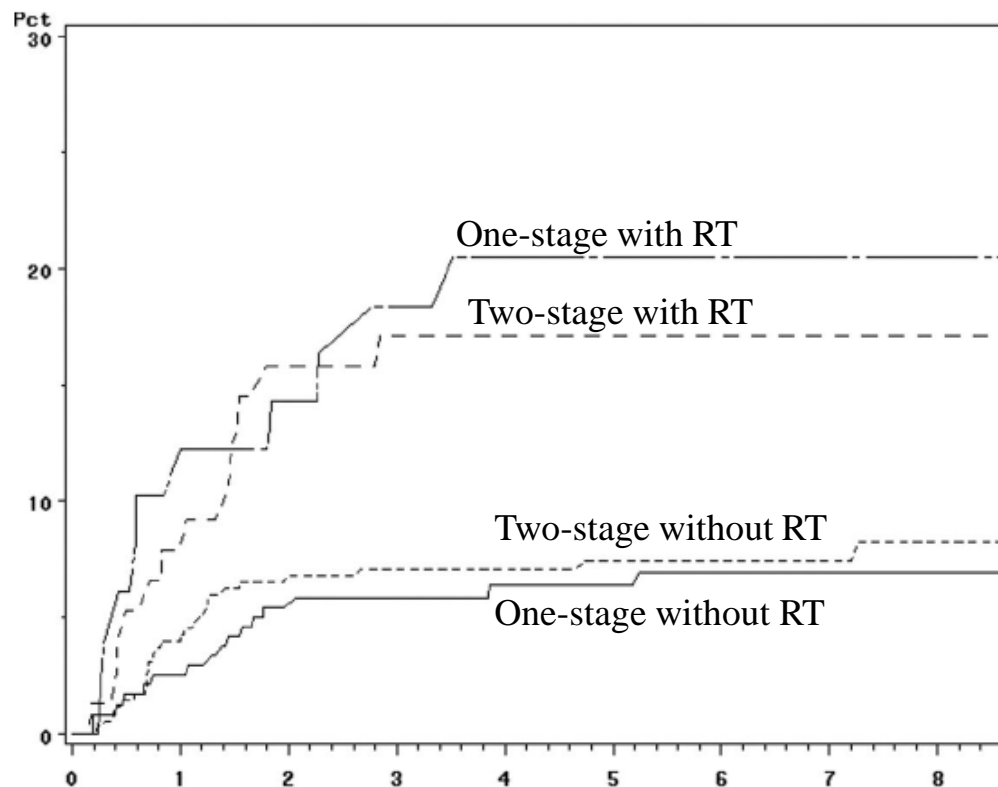
Is Radiation Therapy Associated With Capsular Contracture or Reoperations?

- Danish Registry for Plastic Surgery of the Breast, 1999-2006
- 717 reconstructions of expandable procedures
- 288 one-stage, 429 two-stage
- 99.5% of the implants: submuscular
- 99% of permanent implants: silicone gel



PMRT after Reconstruction

Severe capsular contracture



	N*	Crude HR (95% CI)	Adjusted HR (95% CI) Including All Women [†]
1-stage procedures			
Without radiation therapy	16	1.0	1.0
With radiation therapy	10	3.3 (1.5; 7.3)	5.2 (1.9; 14.2)
2-stage procedures			
Without radiation therapy	27	1.0	1.0
With radiation therapy	13	2.7 (1.4; 5.1)	5.0 (2.2; 11.4)

PMRT after Reconstruction

- Retrospective review
- Cleveland Clinic, 2000-2006
- TE/I group: 733 reconstructions
- Irradiated patients: 13.2%
- Total complication rate: 31.8%
- **Major complication rate: 24.4%**
21.2% (no RT) vs 45.4% (RT)
- 10.3% of patients: TE/I to ABR
- Infection
10.1% (overall) vs 10.3% (RT)
- Implant extrusion
4% (overall) vs 16.5% (RT)
- **Capsular contracture**
9.6% (overall) vs 23% (RT)

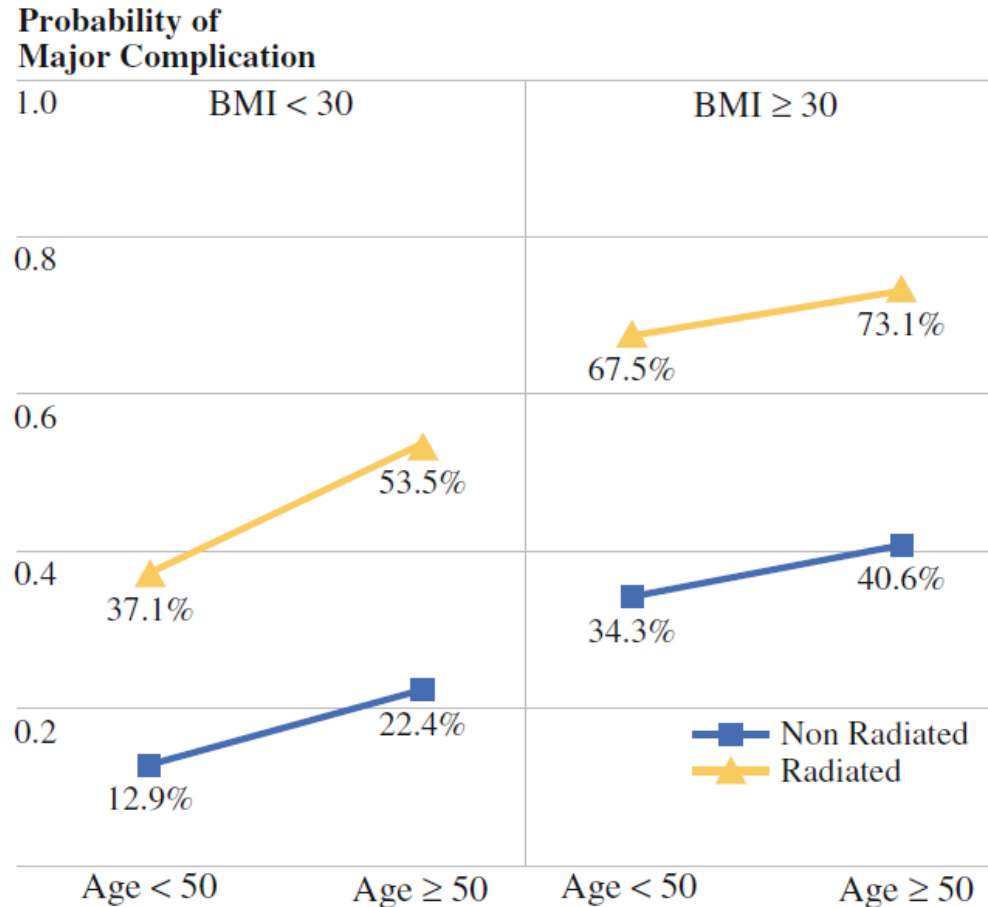


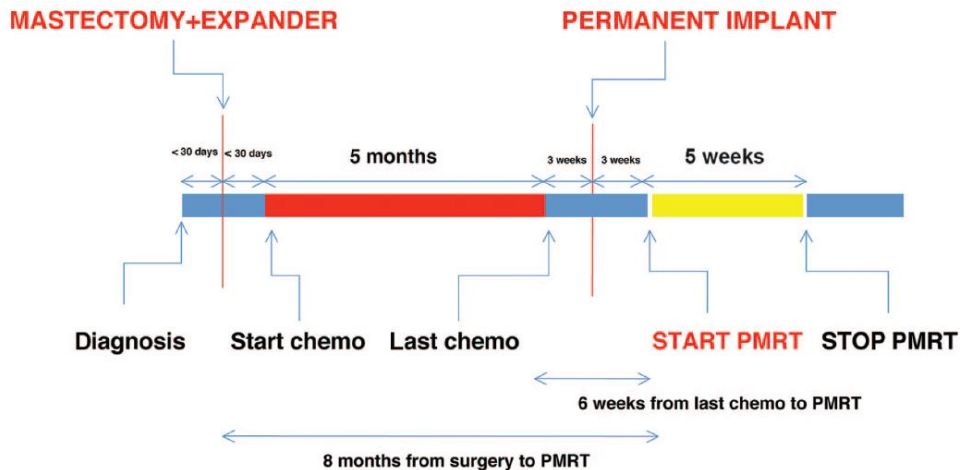
FIG. 1 Incidence of major complication rates for tissue expander/implant reconstruction for BMI and age controlling for radiation

PMRT after Reconstruction

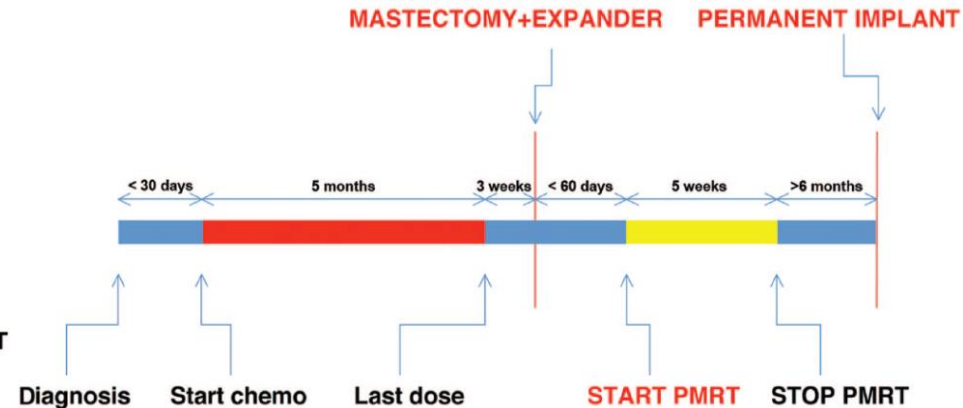
Outcome of Different Timings of Radiotherapy in Implant-Based Breast Reconstructions

- Italian study comparing toxicities according to the timing of radiation therapy
- 2003-2007, 257 patients
- Group 1: RT after second-stage insertion of permanent implant (n=109 patients)
- Group 2: RT to tissue expanders before insertion of permanent implant (n=50 patients)
- Group 3: randomly selected patients of no RT (n=98 patients)

Group 1: RT to PI



Group 2: RT to TE



PMRT after Reconstruction

Failure: implant removal, flat chest wall, or requirement of flap-based technique

Removal of device: exposure/infection/poor results/severe capsular contracture (Baker Gr IV)

Table 1. Total Failure Rates*

	RT and PI (Group 1) (%)	RT and TE (Group 2) (%)	Control (%)
Failed	7 (6.4)	20 (40)	2 (2.3)
Successful	102 (93.5)	30 (60)	96 (97.6)
Total	109	50	98

Table 3. Shape Evaluation by Surgeons*

Shape	RT and PI (Group 1) (%)	RT and TE (Group 2) (%)	Control (%)
Good	37 (58.7)	8 (30.8)	68 (74.2)
Medium	21 (33.3)	16 (61.5)	21 (23)
Bad	5 (7.9)	2 (7.6)	2 (2.19)

PMRT after Reconstruction

Systematic review

Stage 2 (RT to implant) vs Stage 1 (RT to tissue expander)

Failure rate : 5.6% (RT to implant) vs 22.9% (RT to tissue expander)

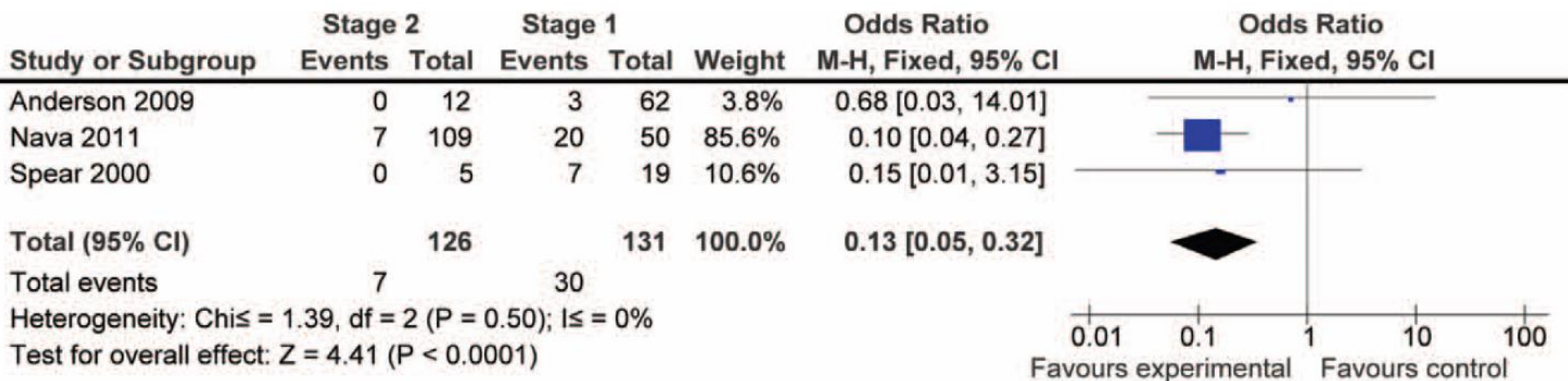


Fig. 5. Odds ratio forest plot of stage 2 (after implant) (5.6 percent) versus stage 1 (after expander) (22.9 percent) immediate breast reconstruction plus adjuvant radiotherapy for failure (prosthesis loss).

PMRT after Reconstruction



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[Breast Cancer Table of Contents](#)
[Staging, Discussion](#)

- PMRT can cause severe capsular contracture and reconstruction failure after implant based reconstruction.
- Implant reconstruction - preferable immediate reconstruction
 - Tissue expansion of irradiated skin can increase risk of capsular contracture, malposition, poor cosmesis, and implant exposure



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Reconstruction with Autologous Tissue



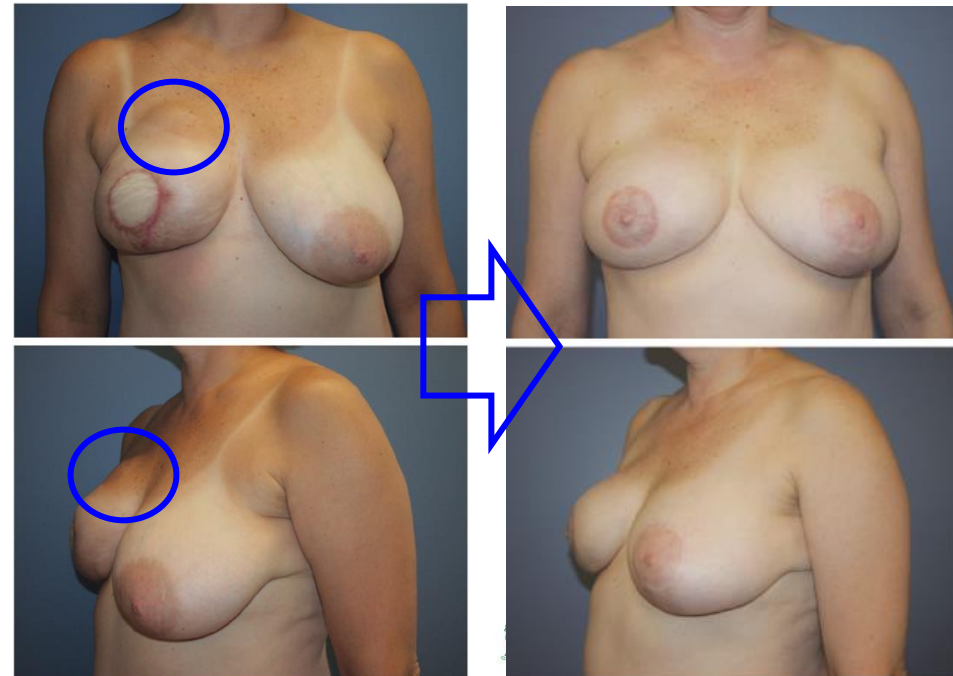
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Results of Reconstruction

- Fat necrosis
 - Minor complication following autologous reconstruction
 - Defined as an area of hardness within the adipose tissue, usually at the periphery of the flap
 - Devitalized tissue causes by insufficient perfusion
 - Adversely impact aesthetic outcome/patient discomfort/concerns of cancer recurrence
 - 6-17% following TRAM/DIEP flap reconstructions
 - 35% - USG-based studies
 - Small sizes (<2cm) often resolves
 - Surgical excision: contour irregularity
 - (USG-guided) liposuction



Results of Reconstruction

Evolution of the **Pedicled TRAM Flap**

A Prospective Study of 500 Consecutive Cases by a Single Surgeon in Asian Patients

Eun Key Kim, MD, Jin Sup Eom, MD, PhD,* Sei Hyun Ahn, MD, PhD,† Byung Ho Son, MD, PhD,† and Taik Jong Lee, MD, PhD**

TABLE 2. Breast Complications

- AMC, July 2001- May 2006
- SSM 368 breasts (73%)
- NASSM 115 breasts (23%)
- Adj CTx (58%)
 - HRT (56%)
 - RT (9%)

Breast Complication	Incidence
Major flap loss	0.2%
Fat necrosis/partial flap necrosis	14.2%
Skin envelope necrosis	15%
Nipple-areolar necrosis	5.2%
Wound dehiscence	1%
Infection	0.8%
Bleeding/hematoma	2%
Seroma	1%
Hypertrophic scar	2.6%
Total incidence	24.6%

Results of Reconstruction

500 Consecutive Patients with Free TRAM Flap Breast Reconstruction: A Single Surgeon's Experience

- Univ. of Penn., 1992-2003
- Experiences using muscle-sparing free-TRAM flap, inferior epigastric vessels
- Median F/U:14.2 months
- Immediate (78%), delayed (22%)

Table 2. Summary of Results*

	Value (%)
Type of reconstruction (no. of patients)	
Immediate	389 (77.8)
Delayed	111 (22.2)
Hospital setting (no. of flaps)	
Community	381 (67.0)
University	188 (33.0)
Recipient vessels (no. of flaps)	
Thoracodorsal	477 (83.8)
Internal mammary	55 (9.7)
Other	37 (6.5)†
Average operative time (hr)	
Immediate unilateral	5.9
Immediate bilateral	7.8
Delayed unilateral	6.1
Delayed bilateral	8.0
Average hospital stay (days)	5

*n = 500 patients; n = 569 flaps.

†Subscapular, lateral thoracic, and thoracoacromial vessels.

Results of Reconstruction

Table 4. Summary of Nonthrombotic Complications*

Complication	No. (%)
Hematoma requiring operative intervention	4 (0.8)
Significant mastectomy flap loss	4 (0.8)
Wound infection	16 (3.2)
Delayed healing	13 (2.6)
Partial free flap loss	7 (1.4)
Fat necrosis	15 (3.0)
Total number of nonthrombotic complications	67 (13.4)
Revision procedures required	72 (14.4)

* $n = 500$ patients.

PMRT after Reconstruction

Feasibility of Postmastectomy Radiation Therapy After TRAM Flap Breast Reconstruction

- MDACC, TRAM flap and PORT 1988-1994, 19 patients
- Recurrent or high-risk for local recurrences
- 1/19 local recurrences

Cosmetic result	Patient evaluation (%)	Physician evaluation (%)
Excellent	7 (37)	9 (47)
Good	9 (47)	9 (47)
Fair	0 (0)	0 (0)
Poor	1 (5)	0 (0)
Not evaluuable	2 (11)	1 (5)
Total	19 (100)	19 (100)

PMRT after Reconstruction

A Prospective Longitudinal Study of Cosmetic Outcome in **Immediate Latissimus Dorsi Breast Reconstruction** and the Influence of Radiotherapy

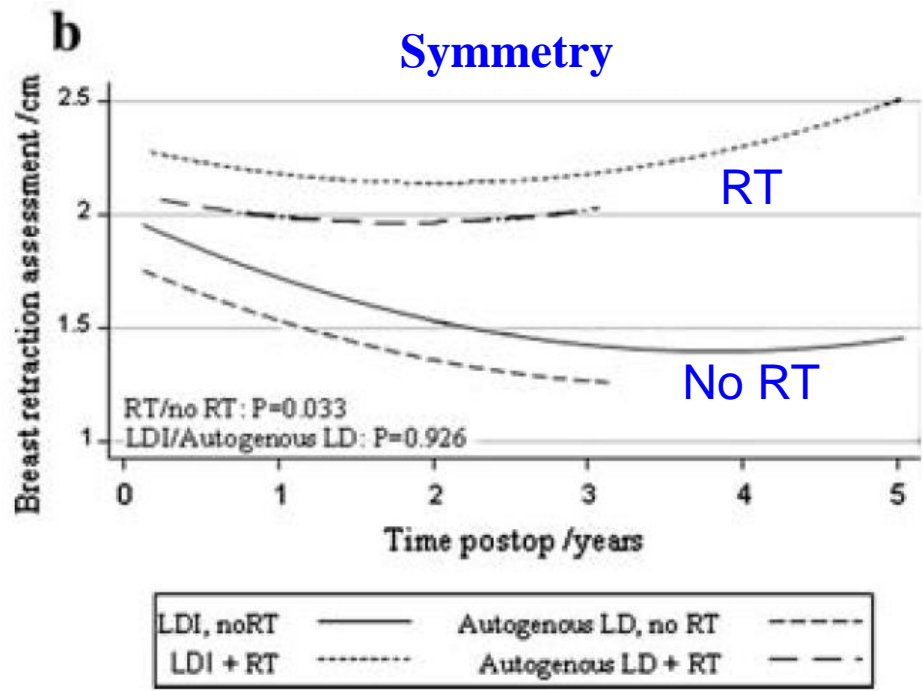
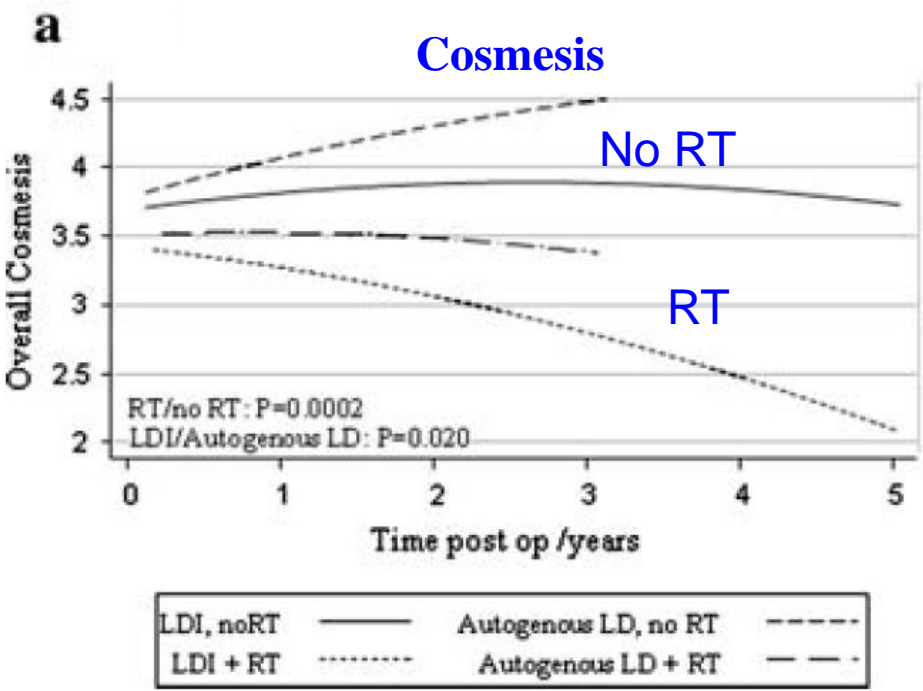
- LD flap – easily adopted, but small volume, need of additional implant
- UK study, 2000-2007, 73 women
- PMRT (42%)

	No Radiotherapy			Radiotherapy ^a			P
	Mean (SD)	n	(%)	Mean (SD)	N	(%)	
Age at time of surgery (years)	48.00 (8.01)	42	100.0	49.26 (7.23)	31	100.0	0.635 ^t
Body mass index (kg m ⁻²)	24.52 (3.56)	42	100.0	25.18 (3.95)	31	100.0	0.513 ^t
Length of follow-up (years)	2.58 (1.41)	42	100.0	2.71 (1.45)	31	100.0	0.345 ^t
Smokers		6	14.3		7	22.6	0.375 ^f
Operation							0.032 ^f
Implant-based LD		35	83.3		18	58.1	
Autogenous LD		7	16.7		13	41.9	
Contralateral surgery		2	4.8		3	9.68	0.645 ^f
Nipple reconstruction		10	23.8		6	19.4	0.778 ^f

PMRT after Reconstruction

TABLE 2. Morbidity data for the 73 women in the study

For LD implant cases	No radiotherapy <i>n</i> = 35 (%)	Radiotherapy <i>n</i> = 18 (%)	<i>P</i>
Capsular contracture	4 (10.8)	7 (33.3)	0.048
Implant revision			0.286
capsule	3 (8.6)	4 (22.2)	
aesthetics	7 (20.0)	1 (5.6)	
fat necrosis of LD flap	1 (2.9)	0	



PMRT after Reconstruction

- Retrospective review
 - Cleveland Clinic, 2002-2007
 - ABR: 528 reconstructions
 - Irradiated patients: 41.5%
 - Total complication rate: 31.5%
- 32.5% (no RT) vs 28.5% (RT)**

TABLE 4 Univariate analysis of risk factors for total complications in autologous reconstruction

Factor and level	Total	No complications		Complication(s)		P value
		N	Percentage	N	Percentage	
BMI						<.001C
<30	302	226	74.8	76	25.2	
>30	139	72	51.8	67	48.2	
Radiation therapy						.51C
None	274	185	67.5	89	32.5	
Preoperative	101	70	69.3	31	30.7	
Postoperative	78	58	74.4	20	25.6	
Chemotherapy						.04C
None	193	121	62.7	72	37.3	
Preoperative	80	62	77.5	18	22.5	
Postoperative	181	128	70.7	53	29.3	

PMRT after Reconstruction

Autologous Breast Reconstruction: The Vanderbilt Experience (1998 to 2005) of Independent Predictors of Displeasing Outcomes

Vanderbilt Medical Center, 1998-2005, 200 autologous tissue flaps

Prereconstruction local RT: 28%

Table 1. Novel Classification System for Noninfectious Wound Complications

Class	Complication and treatment
1	Epidermolysis or loss of tissue and/or necrosis confined to mastectomy skin only; +/- need for debridement; flap skin preserved; no operative revision needed
2	Tissue loss or necrosis requiring local wound care including office debridement; no operative revision needed
3	Any flap tissue loss, necrosis, or both, requiring operative debridement; no operative revision needed
4	Any flap tissue loss, necrosis, or both, requiring operative debridement and operative revision
5	Complete flap loss requiring salvage procedure

Total flaps	200 [‡]	
TRAM	171	86
Unipedicled	148	74
Bipedicled	12	6
Free	8	4
Delayed	3	1
Latissimus dorsi	29	14
Total NIWC classes	76	38
1	23	11
2	10	5
3	18	9
4	22	11
5	3	1
Infections	19	9
Hematomas	14	7
Donor-site hernia [§]	11	6
Fat necrosis	36	18

PMRT after Reconstruction

Table 7. Results of Multiple Logistic Regression Analysis for the Outcomes of Any Class of Noninfectious Wound Complication

Variable	Hazards ratio	95% CI	p Value
Type of autologous flap used	0.49	0.18–1.31	0.160
Concomitant breast resection	0.7	0.33–1.46	0.340
Local radiation therapy	1.54	0.73–3.25	0.260
Smoker	1.64	0.67–4.00	0.280
BMI $\geq 25 < 30$ = overweight*	3.66	1.60–8.34	0.002
BMI > 30 = obese*	6.58	2.85–15.18	0.000
Age	1.01	0.97–1.04	0.060

Table 8. Results of Multiple Logistic Regression Analysis for the Outcomes of Noninfectious Wound Complications Requiring Operative Intervention

Variable	Hazards ratio	95% CI	p Value
Type of autologous flap used	0.76	0.26–2.34	0.65
Concomitant breast resection	1.33	0.58–3.04	0.50
Local radiation therapy	0.75	0.31–1.81	0.52
Smoker	0.71	0.24–2.12	0.54
BMI $\geq 25 < 30$ = overweight*	3.74	1.27–11.02	0.02
BMI > 30 = obese*	6.23	2.15–18.05	< 0.00
Age	1.01	0.97–1.05	0.67

PMRT after Reconstruction

Autologous tissue reconstruction

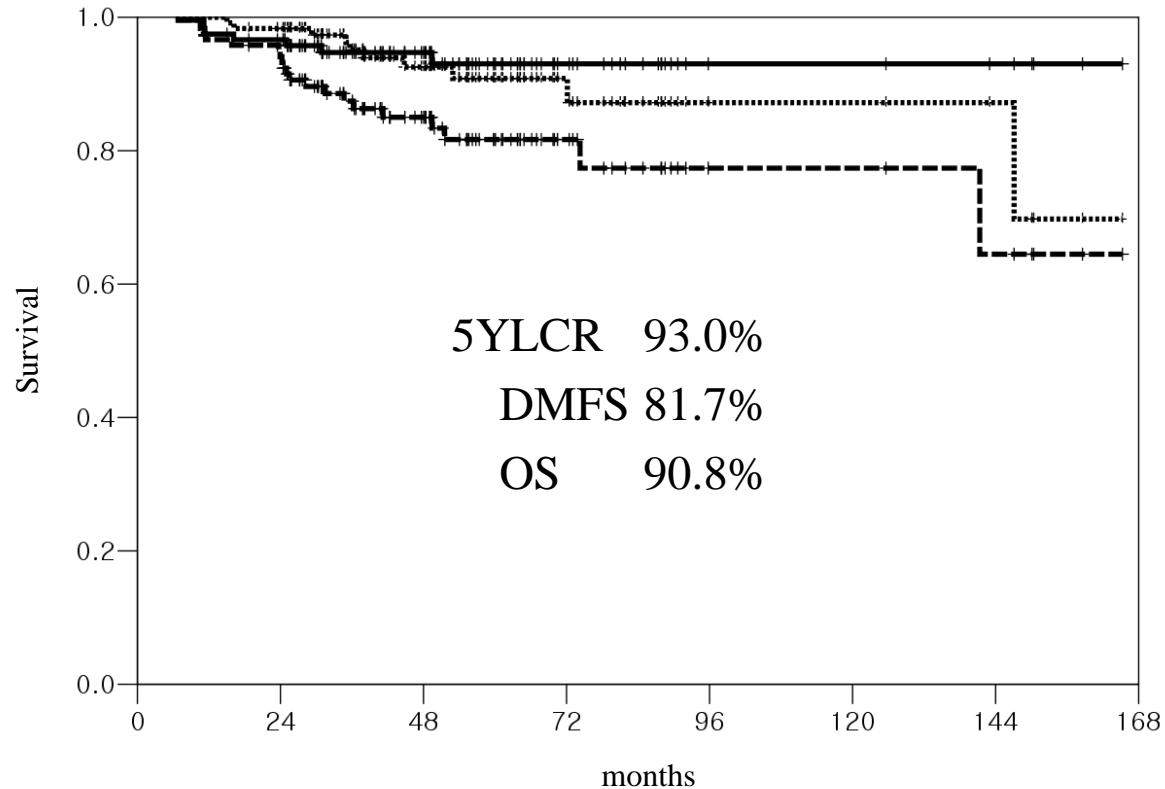
- PMRT after recon → reduces cosmetic results → preferable delayed reconstruction
- Some experienced breast cancer teams have employed protocols in which immediate reconstructions are followed by radiation therapy (category 2B).

AMC Experience

- 1999-2010, IBR and PMRT, 119 patients
- F/U period: 15-165 months (median 49)
- Age: 25-68 yrs (median 42)
- NCT 22 patients (18.5%)
- Reconstruction method

LD	1
f-TRAM	23
p-TRAM	89
Implant	6
- Stage (cStage of NCT cases)

II	13
IIIA	80
IIIB	9
IIIC	17
- Radiation therapy
 - dose: 49.0-60.4 Gy (median 50.4)
 - volume: reconstructed breast/sc/axilla



AMC Experience

- The incidence of complications which required surgical interventions 15/119 (12.6%)

Minor	10 (8.4%)
Liposuction	3
Free fat injection	7

Major	5 (4.2%)
Fat necrosis removal	2
I&D d/t flap cellulitis	1
implant change	1
reconstruction with a-flap	1

AMC Experience

Subgroup analysis for cosmesis

- 2008-2012.8, IBR and PMRT, 91 patients
- F/U period: 12-58 months (median 33)
- Age: 29-63 yrs (median 43)
- Reconstruction method
 - f-TRAM 33 (36.3%)
 - p-TRAM 58 (63.7%)
- NAC preserved 50 (54.9%)
- Weight of mastectomy specimen (g)
 - Mean 434.1
 - Range 160-1186
- Stage (cStage of NCT cases)
 - II 8 (8.8%)
 - IIIA 54 (59.3%)
 - IIIC 23 (25.3%)
- NCT 23 patients (25.3%)
- Radiation therapy
 - dose: 50.0-60.4 Gy (median 50.4)
 - volume: reconstructed breast/scl/axilla
 - technique: single isocenter, forward
 - IMRT technique using 4-6 segments per each beam

AMC Experience

- Subgroup analysis for cosmesis
 - Subjective cosmetic evaluation - four grades – excellent, good, fair, poor
 - symmetry, deformity, and surface appearance



- Excellent cosmesis, F/31 at op, 3 years after RT



- Good cosmesis, F/47 at op, 4 years after RT

AMC Experience

- Subgroup analysis for cosmesis



- Fair cosmesis, F/46 at op, 2.8 years after RT



- F/47 at op, 10 months after RT
- Fair/poor cosmesis

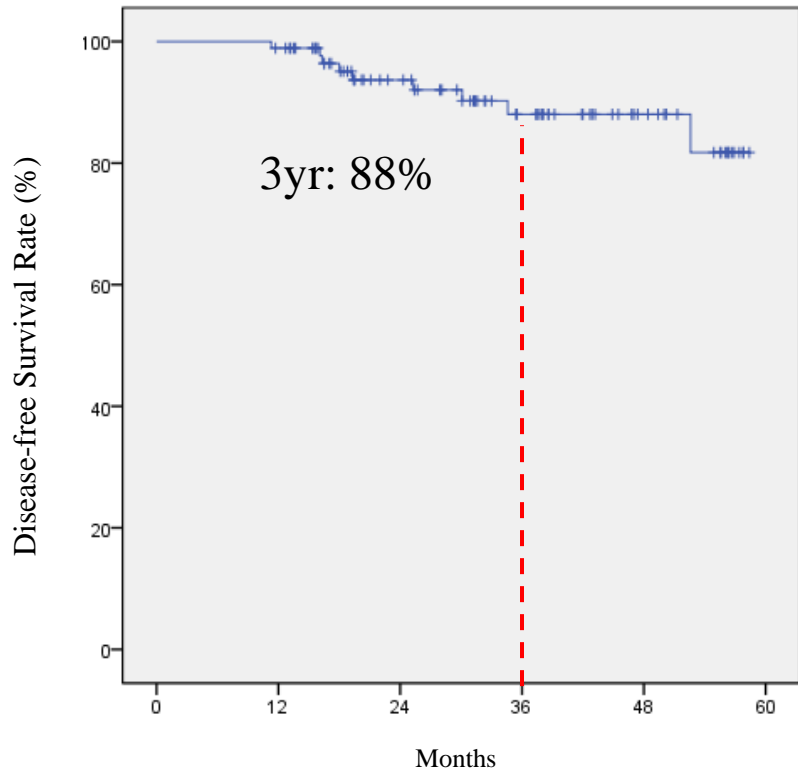
AMC Experience

	3D-wedge	IMRT	p-value
Homogeneity index	1.12±0.18	1.07±0.17	<0.001
Conformity index	1.40±0.27	1.29±0.24	<0.001

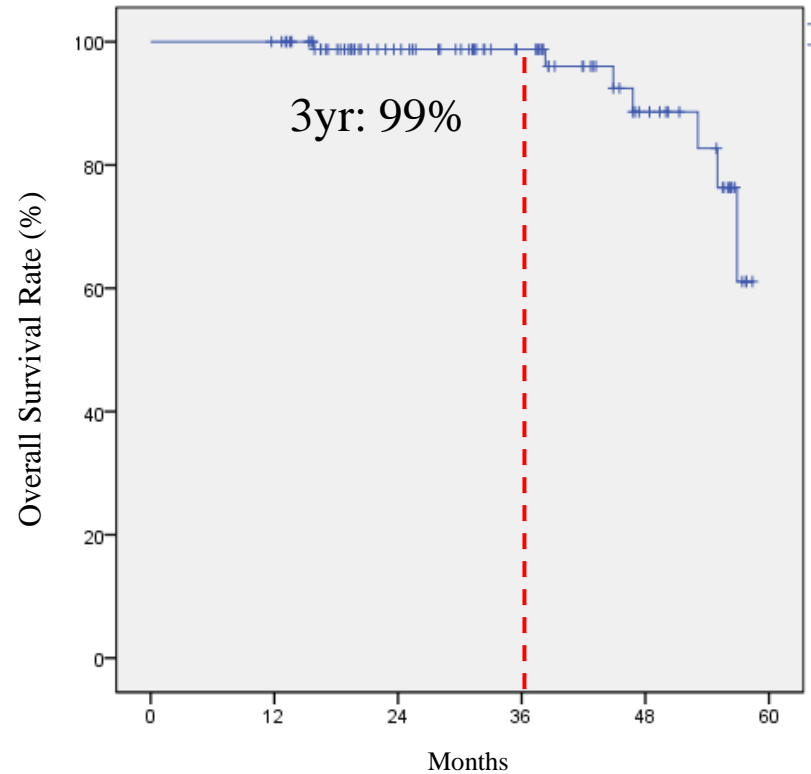
- All patients treated with f-IMRT
- Improved target homogeneity and conformity over rival 3D wedge plan

AMC Experience

Local recurrence	1
Regional recurrence	0
Distant metastasis	8



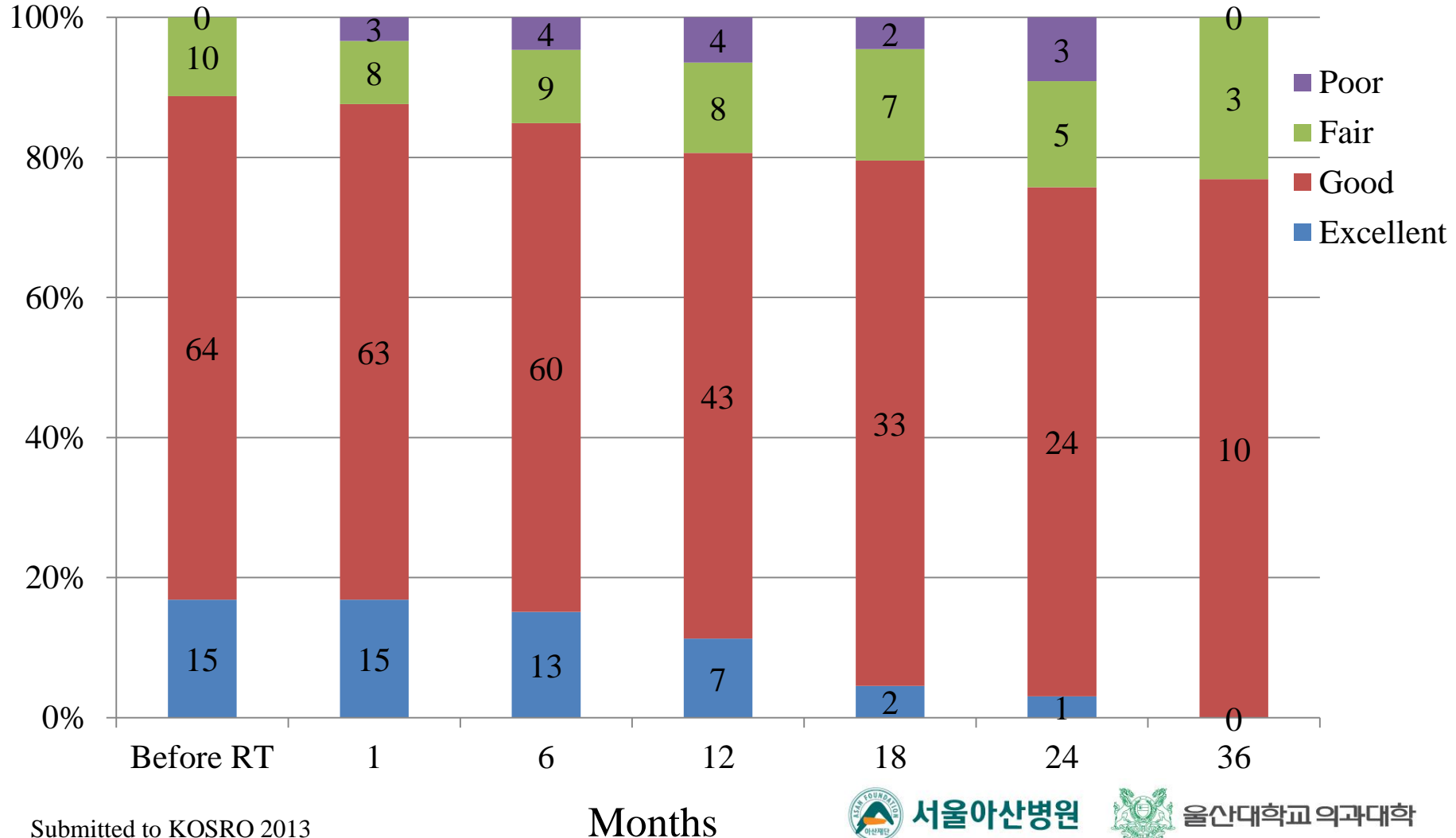
Disease-free Survival



Overall Survival

AMC Experience

Proportions of each grade of cosmetic results according to the follow-up period



AMC Experience

Univariate analysis of risk factors for fair-to-poor cosmesis

	Odd ratio	p value
Age	1.04	0.29
Smoking	0.00	1.00
Alcohol	2.42	0.12
BMI	1.01	0.97
Breast size	1.00	0.33
<i>Poor cosmesis before RT</i>	18.95	0.00
<i>Fat necrosis before RT</i>	6.22	0.00
<i>OP method (pedicled flap)</i>	0.13	0.01
Neoadjuvant CTx	0.25	0.08
Adjuvant CTx	4.35	0.06
RT boost	3.10	0.06

Multi-variate analysis of risk factors for fair-to-poor cosmesis

	Odd ratio	p value
<i>Neoadjuvant CTx</i>	0.012	0.003
OP method (pedicled flap)	0.209	0.166
<i>Poor cosmesis before RT</i>	27.1	0.002
<i>Fat necrosis before RT</i>	19.7	0.002
<i>RT boost</i>	15.8	0.006

Summary

- Breast reconstruction is beneficial to psychosocial confidence of patients.
- Cosmetic results of PMRT after IBR are correlated with the type and time of reconstruction.
- PMRT after IBR could result in unacceptable cosmetic results infrequently.
- Acceptable oncologic and cosmetic outcome were achieved with a robust forward IMRT after IBR with autologous tissue.
- Future studies
 - Dynamic nature of cosmetic results
 - PMRT technique and cosmetic results
 - Pathogenesis of poor cosmesis
 - NCT/IBR and PMRT
 - Necessity of objective parameter to compare complications and cosmetic results

