XXV CONGRESSO NAZIONALE

AIRO 2015

PALACONGRESSI - Rimini, 7-10 novembre

SIMPOSIO

Ricostruzione mammaria ed implicazioni radioterapiche

Tossicità

Fiorenza De Rose

Radioterapia e Radiochirurgia

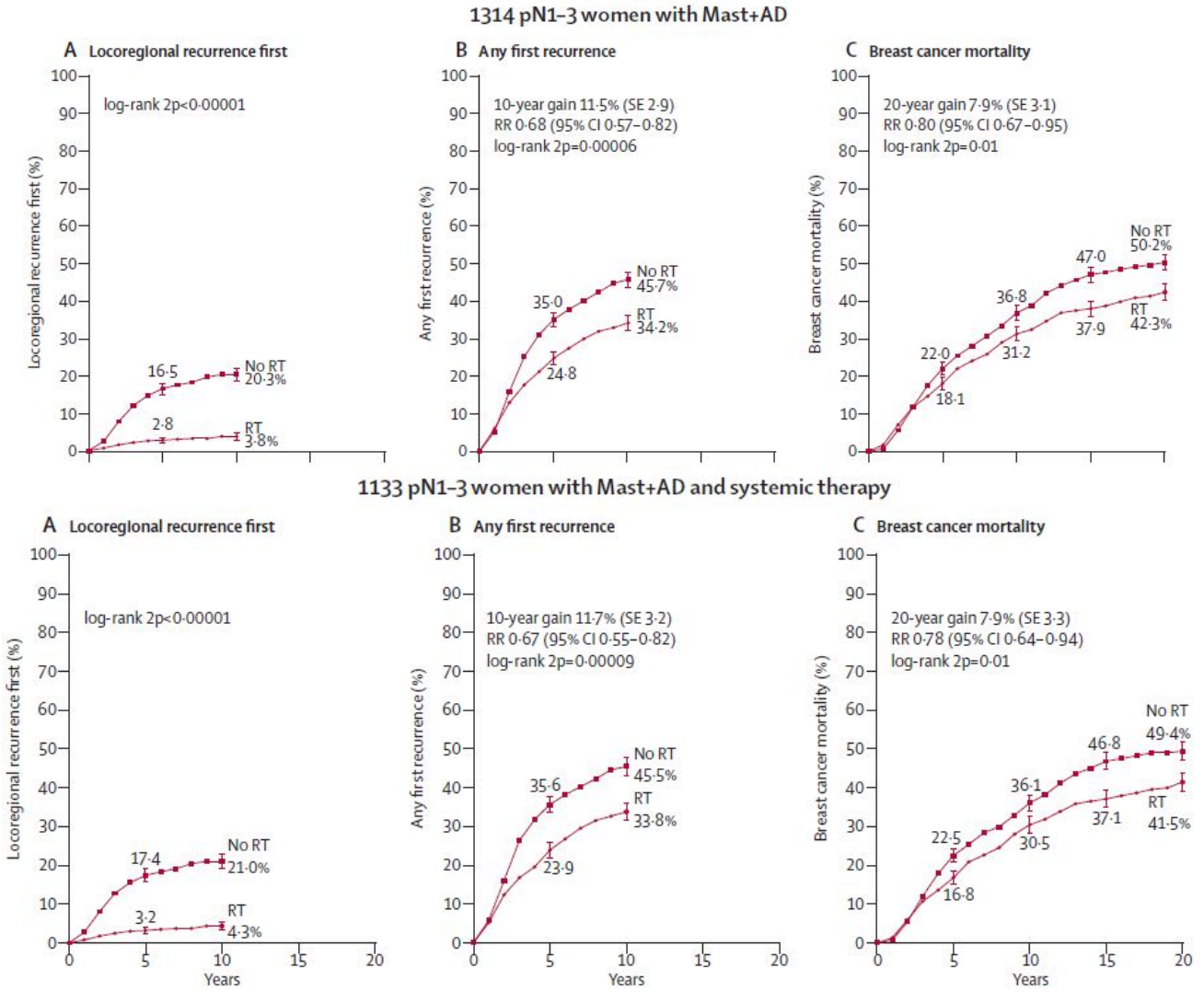
Istituto Clinico Humanitas – Rozzano (MI)

DICHIARAZIONE

Relatore: FIORENZA DE ROSE

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Consulenza ad aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Partecipazione ad Advisory Board **(NIENTE DA DICHIARARE)**
- Titolarietà di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**

Background



EBCGT, Lancet 2014

Background

"The effects of radiation therapy on the irradiated chest wall and reconstructed breast are widely feared but poorly understood"

Jagsi R et al Ann Surg 2015; 00:1-9

Toxicity and Complications

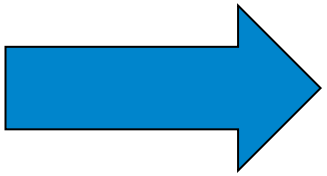
- Type of reconstruction
- Timing of radiotherapy
- Other potential risk factors
- Current attitudes

Type of Reconstruction

- Immediate Breast Reconstruction **(IBR)**
- Delayed Breast Reconstruction **(DBR)**
- “Delayed-Immediate” **(Two-stage approach)**

Immediate Breast Reconstruction

- Superior aesthetic outcome
- Single coordinated operation
- Significant cost savings



STANDARD of CARE

Immediate Breast Reconstruction: Autologous tissue

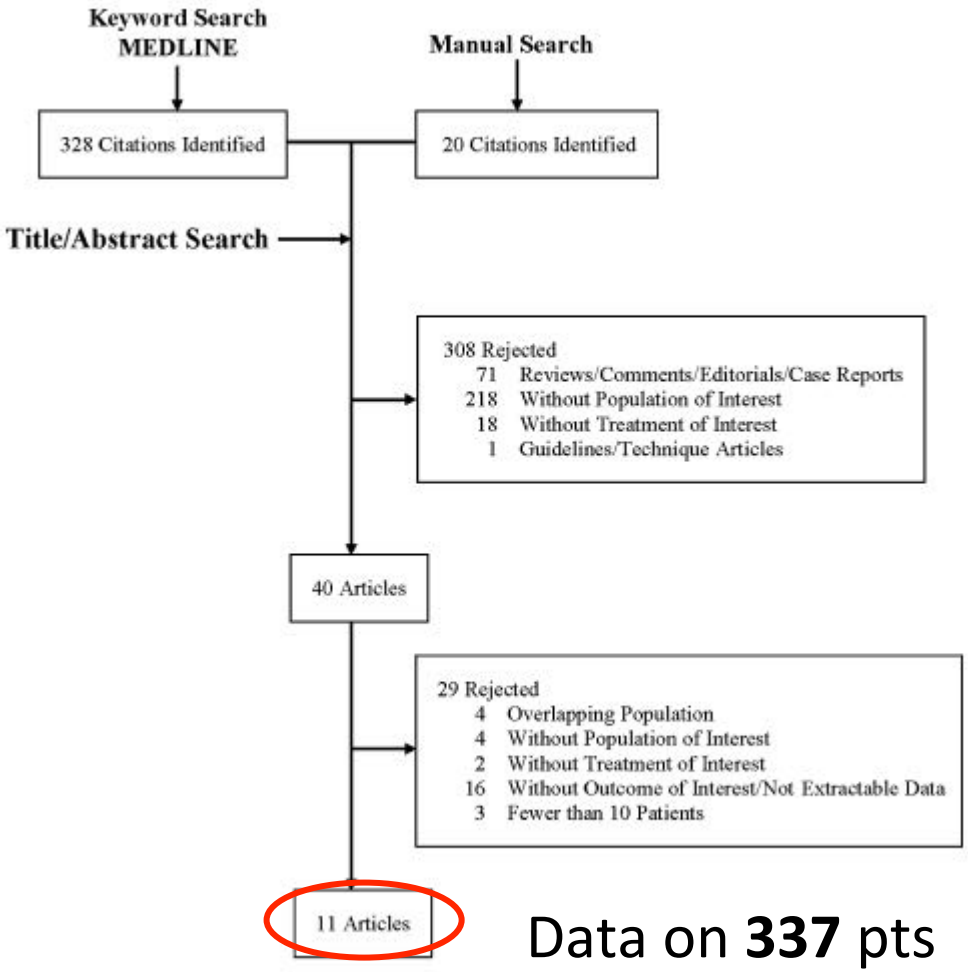
Journal of Surgical Oncology 2015;111:251–257

Postmastectomy Radiation Therapy and Immediate Autologous Breast Reconstruction: Integrating Perspectives From Surgical Oncology, Radiation Oncology, and Plastic and Reconstructive Surgery

DANIELLE H. ROCHLIN, BA,[1] AH-REUM JEONG, BA,[2] LEAH GOLDBERG, BA,[1] TIMOTHY HARRIS, MD, PhD,[3] KRITI MOHAN, MD,[4] STELLA SEAL, MLS,[5] JOE CANNER, MHS,[6] AND JUSTIN M. SACKS, MD[1]*

… the reported effect on the reconstructed breast using ***autologous tissue*** *remains imprecisely defined…*

Immediate Breast Reconstruction: Autologous tissue



Data on **337** pts

Immediate Breast Reconstruction: Autologous tissue

TABLE I. Patient and Treatment Characteristics of Studies

Source	No. of patients	Mean age (year)	Smoker (%)	Adj chemo (%)	Mean follow-up (months)	Unilateral (%)	Bilateral (%)	Mean interval (months)	Mean RT dose (Gy)	Bolus (%)
Zimmerman et al. [24]	21	47	NA	85.7	19	NA	NA	5	53.02	0
Tran et al. [19]	41	48[a]	0	95.1	36	65.9	34.1	6–12	50.99	NA
Rogers et al. [17]	30	48.2	16.7	NA	19.9	93.3	6.7	4.1	50.5	NA
Halyard et al. [22]	15	51[a]	0	80.0	26.4[a]	NA	NA	7[a]	50[a]	13.3
Soong et al. [30]	21	Patient demographics cannot be extracted								
Mehta et al. [28]	22	47[a]	0	13.6	18[a]	NA	NA	NA	50.4[a]	NA
Foster et al. [21]	35	49.5	NA	NA	48[a]	NA	NA	1[a]	NA	NA
Huang et al. [27]	82	42.7	NA	100	40[a]	98.8	1.2	6.2	50	100
Carlson et al. [20]	25	48.9	12.0	NA	NA	NA	NA	NA	NA	NA
Chatterjee et al. [29]	22	Patient demographics cannot be extracted								
Adesiyun et al. [61]	23	Patient demographics cannot be extracted								

TABLE II. Summary of Major Complication Rates

Source	Pop.	No. of flaps	Type of flap	Partial flap loss (%)	Total flap loss (%)	Fat necrosis (%)	Volume loss (%)	Fibrosis/contracture (%)	Revisional surgery (%)	Overall rate (%)
Zimmerman et al. [24]	RT	21	F TRAM	0 (0)	0 (0)	NA	NA	NA	NA	0 (0)
Tran et al. [19][a]	RT	41	9 P 32 F TRAM						NA	NA
	No RT	14	TRAM						NA	NA
Rogers et al. [17]	RT	30	DIEP						20 (66.7)	NA
	No RT	30	DIEP						26 (86.7)	NA
Halyard et al. [22]	RT	15	14 P 1 F TRAM						NA	NA
Soong et al. [30]	RT	21	TRAM						NA	NA
Mehta et al. [28]	RT	22	P TRAM						0 (0)	NA
Foster et al. [21]	RT	35	TRAM						2 (5.7)	NA
Huang et al. [27]	RT	82	TRAM						NA	NA
Carlson et al. [20]	RT	25	P TRAM						3 (12.0)	11 (44.0)
	No RT	149	P TRAM						24[c] (18.8)	54 (36.2)
Chatterjee et al. [29]	RT	22	DIEP						3 (13.6)	NA
Adesiyun et al. [61]	RT	23	21 P 2 F TRAM	0 (0)	0 (0)	NA	NA	NA	NA	8 (34.8)

Overall rate of
-Fat necrosis 16.9%
-Revisional surgery 24.1%
-Volume loss 16.9%
-Contracture 35.4%

Immediate Breast Reconstruction: Autologous tissue

TABLE III. Summary of Aesthetic Outcomes

Source		No. of flaps (total)	Method	Result
Zimmerman et al. [24]		20 (21)	Self-evaluation, rating 1–4 (poor-excellent)	Excellent: 12/20 (60%) Good: 6/20 (30%) Fair: 2/20 (10%) Poor: 0/20 (0%)
Rogers et al. [17]	RT	10 (30)	Before and after photo evaluation by 8 judges, criteria: symmetry, position of superior pole, overall aesthetic proportion, and combination rating 1–5 (worst-best). Difference between before and after analyzed.	Sym.: −0.48 Sup. Pole: −0.72 Prop.: −0.47 Comb.: −0.56
	No RT	10 (30)		Sym: +0.51 Sup. Pole: +0.38 Prop.: +0.63 Comb.: +0.50
Halyard et al. [22]		15 (15)	Self-evaluation, rating poor-excellent*	Excellent/Good: 13/15 (86.7%) Fair: 1/15 (6.7%) Poor: 1/15 (6.7%)
Huang et al. [27]		61 (82)	Self-evaluation by phone interview, rating 1–4 (excellent-poor)	Excellent: 10/61 (16.4%) Good: 33/61 (54.1%) Fair: 14/61 (23.0%) Poor: 4/61 (6.6%)
Carlson et al. [20]	RT	25 (25)	Postoperative photo evaluation by 4 blind judges, criteria: volume of breast mound, contour of breast mound, placement of breast mound, inframammary fold (IMF), rating 0–2 (worst-best). Global aesthetic score, rating 1–4 (poor-excellent).	Volume: 1.45 Placement: 1.67 Contour: 1.23 IMF: 1.52 Global: 2.56
	No RT	149 (149)		Volume: 1.51 Placement: 1.64 Contour: 1.22 IMF: 1.47 Global: 3.02
	Preop RT	15 (15)		Volume: 1.45 Placement: 1.68 Contour: 1.35 IMF: 1.43 Global: 2.32

Immediate Breast Reconstruction: Autologous tissue

… our systematic review reflects the larger opinion within the literature that there is no definitive evidence supporting or refuting immediate autologous reconstruction in patients undergoing PMRT…

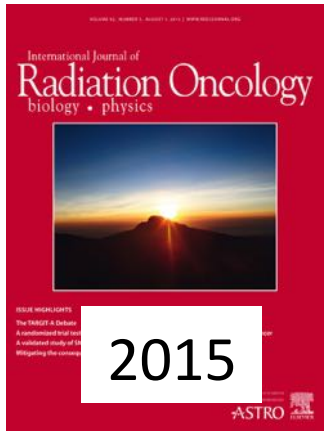
*We recommend **delayed-immediate reconstruction**, in which the placement of tissue expanders during radiation therapy promotes a superior aesthetic result without interfering with the delivery of PMRT*

Immediate Breast Reconstruction: TE/I

Clinical Investigation

Rates of Reconstruction Failure in Patients Undergoing Immediate Reconstruction With Tissue Expanders and/or Implants and Postmastectomy Radiation Therapy

Barbara Fowble, MD,* Catherine Park, MD,* Frederick Wang, MD,† Anne Peled, MD,† Michael Alvarado, MD,‡ Cheryl Ewing, MD,‡ Laura Esserman, MD, MBA,‡ Robert Foster, MD,† Hani Sbitany, MD,† and Alex Hanlon, PhD§



From 2004 to 2012
99 pts (86 TE, 13 PI)
Immediate TE/I reconstruction
Fully expanded prior to radiation

Immediate Breast Reconstruction: TE/I

Table 2 Reconstruction failure rates in a series of tissue expander or implant reconstructions with postmastectomy radiation

Study series (ref)	Study period	No. of patients	Mastectomy type	RT and reconstruction	% of RF	Follow-up
Ho et al (18)	1996-2006	151	SSM	PI	13%	7 y
Berry et al (10)	2000-2006	72	NS	TE	16.5%	NS
Baschnagel et al (19)	2006-2011	94	NS	TE in 90 patients; PI in 4 patients	18% all pts.	2 y
Ho et al (9)	1998-2011	113	SSM or TSSM	TE	21.3%	1 y minimum
Anderson et al (20)	1987-2006	74	MRM	TE in 62 patients PI in 12 patients	5% TE 0% PI	median of 4 y
Cowen et al (21)	1998-2006	141	MRM	TE	22.7%	mean of 3.1 y
Nava et al (8)	2003-2007	159	NS	TE in 50 patients PI in 109 patients	40% TE 6.4% PI	NS
Seth et al (22)	2006-2008	123	SSM or TSSM	TE	14%	mean of 2 y
Jhaveri et al (23)	1998-2005	69	MRM	TE and/or PI	19%	3.2 y
Pestana et al (24)	1996-2011	89	NS	TE and/or PI	42% TE 25% PI	mean of 6 y
Spear et al (25)	2004-2010	56	NS	TE	21%	NS
Hvilsom et al (5)	1999-2006	125	NS	TE in 76 patients; PI in 49 patients	13% TE 4% PI	NS
Burdge et al (26)	2001-2012	60	SSM in 21 patients; TSSM in 39 patients	TE and/or PI	5% all pts	2.1 y for TSSM; 3.2 y for SSM
Present series	2004-2012	99	TSSM in 62 patients; SSM in 37 patients	TE in 86 patients; PI in 13 patients	18% for all patients; 21% received TSSM; 13.5% received SSM; 19.8% received TE; 7.7% received PI	Median of 3.8 y

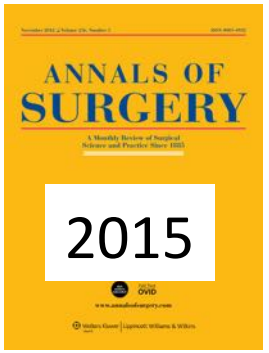
Infection was the most common cause

Immediate Breast Reconstruction

Complications After Mastectomy and Immediate Breast Reconstruction for Breast Cancer

A Claims-based Analysis

Reshma Jagsi, MD, DPhil, Jing Jiang, MS,† Adeyiza O. Momoh, MD,‡ Amy Alderman, MD, MPH,§ Sharon H. Giordano, MD, MPH,¶ Thomas A. Buchholz, MD,‖ Lori J. Pierce, MD,* Steven J. Kronowitz, MD,** and Benjamin D. Smith, MD‖*



Nationwide, employment-based database

Data from 1998 to 2009

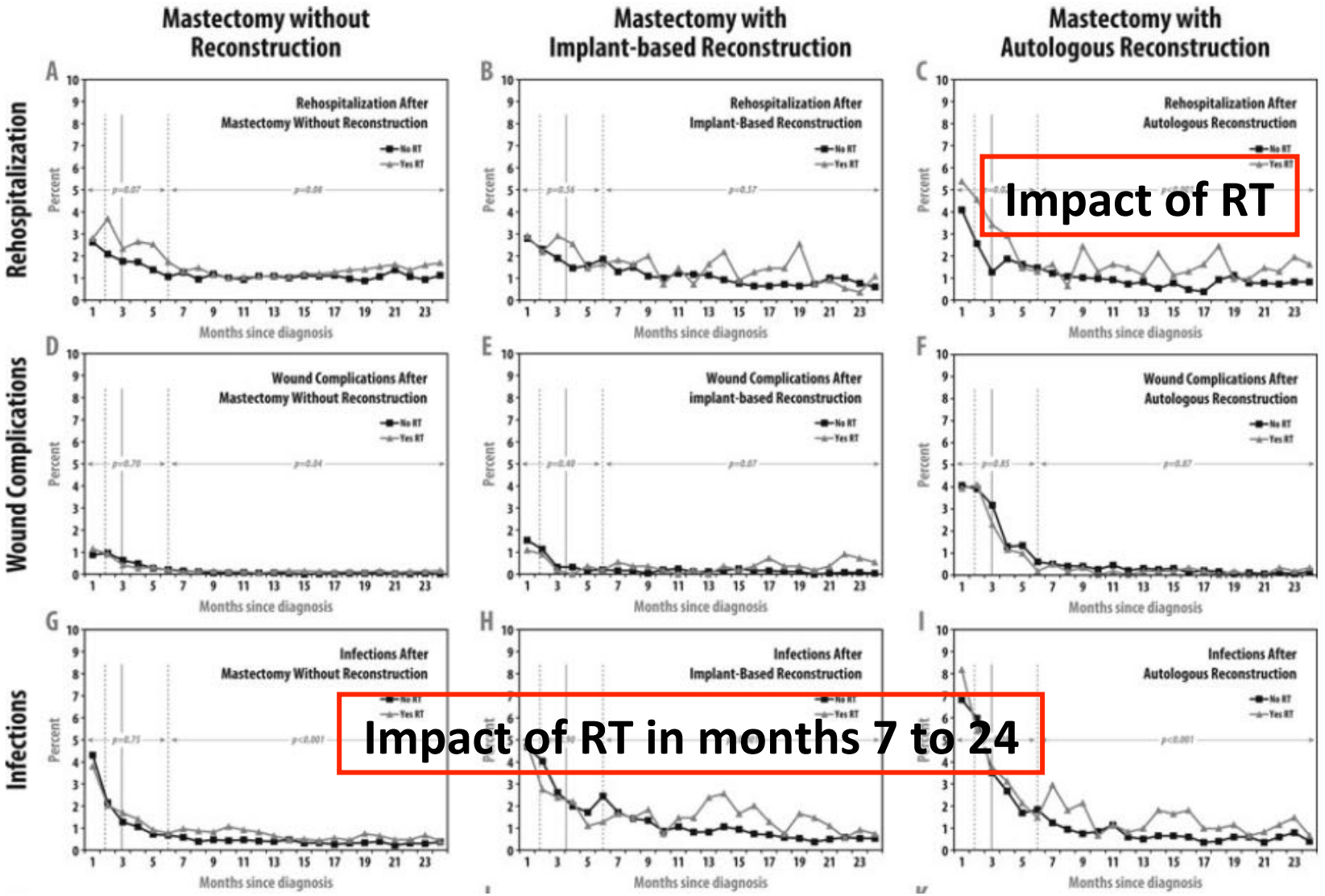
14894 pts

Mastectomy and IBR (autologous tissue or TE/I) ± PMRT

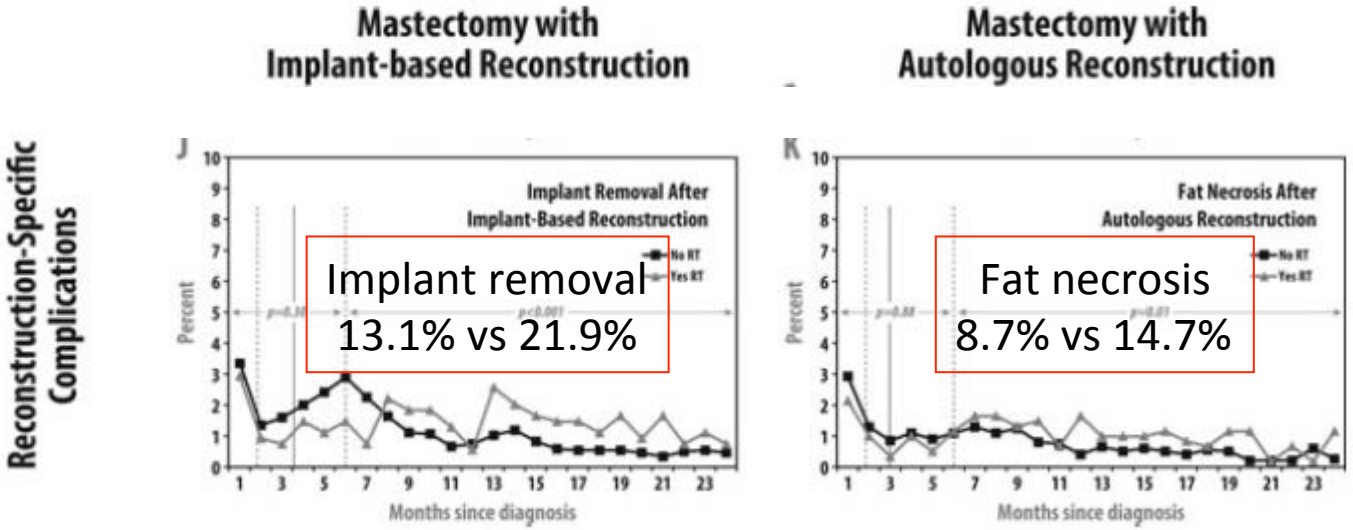
3 general outcomes:

- 30-day rehospitalization
- wound complication (first 2 postoperative years)
- skin or soft-tissue infections (first 2 postoperative years)

Immediate Breast Reconstruction



Immediate Breast Reconstruction



Impact of RT in months 7 to 24

Immediate Breast Reconstruction

… The current study suggests that the complications of immediate breast reconstruction do differ depending on approach and that radiation therapy seems to modestly increase certain risks. ***Further research is necessary*** *to determine whether the increasing use of acellular dermal matrices and autologous fat grafting in implant-based reconstruction or the use of delayed reconstruction approaches (including a staged, "delayed-immediate" approach to autologous reconstruction with transfer ofthe flap after radiation) may alter these risks.*

IBR vs DBR

Comparison of Delayed and Immediate Tissue Expander Breast Reconstruction in the Setting of Postmastectomy Radiation Therapy

Akhil K. Seth, MD, Hayley R. Silver, BS, Elliot M. Hirsch, MD, John Y.S. Kim, MD, and Neil A. Fine, MD

TABLE 5. Two-Stage Success Rate, DTER and ITER Breasts Stratified by PMRT

Stage	All Patients	*P*	No PMRT	*P*	PMRT	*P*
TE placement						
DTER	67 (90.5)	0.65	46 (90.2)	0.24	21 (91.3)	0.75
ITER	1039 (92.2)		826 (94.0)		213 (85.9)	
TE exchange						
DTER	63 (94)	0.54	44 (95.6)	0.39	19 (90.5)	0.54
ITER	923 (95.5)		760 (96.9)		149 (81.9)	
Overall						
DTER	63 (85.1)	0.54	44 (86.3)	1.00	**19 (82.6)**	**0.04**
ITER	923 (81.9)		760 (86.5)		**149 (60.0)**	
Operative		1 (2.0)		1 (4.4)		0.53
ECF		4 (7.8)		2 (8.7)		1.00
Complication		**ITER (n = 1127 breasts) (834 patients)**				***P***
		No PMRT (n = 879 Breasts) (626 Patients)		**PMRT (n = 248 Breasts) (208 Patients)**		
Total complications*		132 (15.0)		66 (26.6)		<0.0001
Exposure		8 (0.90)		9 (3.6)		0.005
Infection		36 (4.1)		20 (8.1)		0.02
Pain/tightness		10 (1.1)		28 (11.3)		<0.0001
Hematoma		21 (2.4)		7 (2.8)		0.65
Seroma		30 (3.4)		9 (3.6)		0.85
Mastectomy flap necrosis		67 (7.7)		27 (10.9)		0.12
Nonoperative		69 (7.9)		30 (12.1)		0.04
Operative		97 (11.0)		42 (16.9)		0.02
ECF		53 (6.0)		35 (14.1)		<0.0001

IBR vs DBR

Comparison of Delayed and Immediate Tissue Expander Breast Reconstruction in the Setting of Postmastectomy Radiation Therapy

Akhil K. Seth, MD, Hayley R. Silver, BS, Elliot M. Hirsch, MD, John Y.S. Kim, MD, and Neil A. Fine, MD

Limitations

-Size of delayed cohort
-Retrospective nature
-No analysis of aesthetic outcomes or medical costs

*… Therefore, we **do not use DTER as our first-line reconstructive option**, but rather as a **viable alternative in a multistep process** that involves continued discussion between patient and surgeon.*

Toxicity and Complications

- Type of reconstruction
- Timing of radiotherapy
- Other potential risk factors
- Current attitudes

Timing of Radiotherapy

Kelley et al (Ann Surg Oncol, 2014)

1994-2012
20 studies (at least 10 pts)
No RCTs
Only Autologous (1580)
Including studies on recurrences

Momoh et al (Ann Surg Oncol, 2014)

1992-2012
26 studies (at least > 10 pts)
No RCTs
Only Definite Implant (1489)
Including studies on recurrences

Berbers et al (Eur J Cancer, 2014)

2000-2012
37 studies (at least 20 pts)
No RCTs
Autologous (1635)/Definite Implant (1048)
No studies on recurrences

Timing of Radiotherapy

TABLE 2 Summary of overall estimates and 95 % CI for complication rates

Complication	Pre- or post-reconstruction XRT flaps	No. of studies	No. of flaps	Weighted point estimate and 95 % CI	I^2	Test of heterogeneity *p*-value
Total flap loss	Pre	11	1011	0.01 (0.00–0.02)	6.8 (0–62.9)	0.38
	Post	12	426	0.04 (0.00–0.04)	0	1.0
Partial flap loss	Pre	9	728	0.06 (0.03–0.11)	64.9 (28.3–82.8)	0.004
	Post	5	162	0.00 (0.00–0.02)	0	1.0
Thrombosis	Pre	3	515	0.04 (0.03–0.06)	0 (0–88.4)	0.41
	Post	3	81	0.00 (0.00–0.02)	0	0.98
Would healing	Pre				(86.0–95.8)	<0.0001
	Pos				(74.5–95.3)	<0.0001
Infection	Pre				–64.9)	0.24
	Post				8.8 (0–73.4)	0.36
Hematoma	Pre	4	375	0.02 (0.01–0.04)	0 (0–82.3)	0.46
	Post	5	160	0.01 (0.01–0.04)	22.7 (0–68.0)	0.27
Seroma	Pre	6	583	0.04 (0.02–0.05)	0 (0–69.6)	0.53
	Post	4	135	0.04 (0.00–0.12)	61.9 (0–87.2)	0.049
Fat necrosis	Pre	9	872	0.10 (0.06–0.14)	68.9 (37.7–84.4)	0.001
	Post	12	463	0.13 (0.07–0.20)	73.1 (52.1–84.9)	<0.0001
Contracture/fibrosis	Pre	–	–	–	–	–
	Post	9	368	0.27 (0.12–0.45)	92.2 (87.4–95.2)	<0.0001

No significant differences

Kelley et al (Ann Surg Oncol, 2014)

Timing of Radiotherapy

TABLE 2 Summary of overall estimates and 95 % CI for complication rates

Complication rate	Pre- or post-XRT reconstruction	No. of studies	No. of breasts	Weighted point estimate (95 % CI)	Test of heterogeneity *P* value	I^2
Minor complications	Pre	4	150	0.18 (0.05–0.36)	0.0036	77.9 (40.2–91.8)
	Post	4	246	0.31 (0.17–0.463)	0.0003	81 (55.8–91.9)
Major complications	Pre	8	252	0.49 (0.25–0.72)	<0.0001	92.4 (87.4–95.4)
	Post	14	708	0.39 (0.24–0.55)	<0.0001	94.2 (91.9–95.9)
CC I and II	Pre					94.8 (89.7–97.4)
	Pos					95.4 (93.1–97)
CC III and IV	Pre					62.9 (0–89.4)
	Post	10	818	0.32 (0.20–0.46)	<0.0001	93.2 (89.4–95.6)
Failure/need for flap	Pre	10	377	0.19 (0.10–0.29)	<0.0001	75.1 (53.6–86.6)
	Post	16	977	0.20 (0.15–0.25)	<0.0001	67.7 (45.7–80.8)
Completion	Pre	6	311	0.83 (0.68–0.94)	<0.0001	87.8 (75.8–93.8)
	Post	5	321	0.80 (0.68–0.90)	0.0037	74.3 (36.2–89.6)

No significant differences

Momoh et al (Ann Surg Oncol, 2014)

Timing of Radiotherapy

'Reconstruction: Before or after postmastectomy radiotherapy?' A systematic review of the literature

Judith Berbers [a], Angela van Baardwijk [b], Ruud Houben [b], Esther Heuts [c], Marjolein Smidt [c], Kristien Keymeulen [c], Maud Bessems [c,1], Stefania Tuinder [d] Liesbeth J. Boersma [b,*]

Table 2
Complication rate and cosmetic outcome categorised by the timing of radiotherapy and subdivided in autologous and implant reconstructions.*

Complications	Radiotherapy first				Reconstruction first			
	Autologous		Implant		Autologous		Implant	
	Reported incidences	Weighted mean (95%-CI)**	Reported incidences	Weighted mean (95%-CI)**	Reported incidences	Weighted mean (95%-CI)**	Reported incidences	Weighted mean (95%-CI)**
Haematoma	0 [34], 3.2 [28]	3.0 (1.4–4.6)	0 [28], 0 [33], 1.8 [35], 19.1 [38]	4.5 (0–13.1)	0 [34], 5.3 [36], 7.0 [37]	3.6 (0–7.7)	/	/
Infection	0 [34], 2.1 [29], 3.7 [28], 7.0 [41]	3.6 (1.4–5.8)	4.8 [40], 5.0 [31], 5.4 [13], 6.4 [38], 7.5 [35], 7.7 [44], 9.1 [28], 10.3 [33]	6.8 (5.2–8.4)	0 [34], 5.3 [36], 7.0 [37], 8.5 [42], 16.7 [43]	8.1 (2.8–13.4)	0.9 [39], 3.7 [11], 30.0 [44]	3.5 (0–12.1)
Seroma	3.0 [41], 5.8 [28]	4.8 (2.2–7.4)	0 [28], 2.7 [13], 3.6 [35]	2.6 (0.7–4.5)	8.5 [42], 10.5 [36]	9.2 (7.4–11.0)	/	/
Open wound	7.0 [45], 11.0 [41], 11.6 [29]	10.7 (8.4–13.0)	0 [45], 8.2 [33], 16.2 [13]	10.3 (5.2–15.4)	5.3 [36], 36.7 [43]	23.1 (0–53.6)	20.0 [46]	20.0 (/)
Fibrosis (capsular contracture (implant)/ parenchymal fibrosis (autologous))	0 [50], 3.7 [28]	2.7 (0–5.9)	3.2 [40], 12.5 [35], 13.6 [28], 14.9 [38], 21.6 [13], 22.7 [33], 32.5 [31]	20.8 (12.8–28.8)	17.0 [47], 23.5 [48], 36.0 [51], 56.7 [43], 75.0 [50]	36.0 (17.1–54.9)	0 [48], 19.3 [12], 39.0 [10], 39.7 [11], 55.0 [52], 57.8 [39]	39.8 (21.6–58.0)
Revision surgery	0 [34], 9.0 [29], 14.9 [28]	11.5 (6.4–16.6)	27.7 [38], 40.9 [28], 45.5 [33], 54.0 [13]	42.4 (32.3–52.5)	0 [55], 0 [57], 0 [58], 2.9 [53], 9.6 [42], 12.0 [34], 47.0 [47], 66.7 [43]	23.6 (5.7–41.5)	6.4 [39], 10.0 [46], 11.1 [11]	8.5 (5.3–11.7)

Timing of Radiotherapy

Overall complication rate 37% (range 8.7 – 70)

	AFTER PMRT	BEFORE PMRT
Implant reconstruction	48.7%	19.6%
Autologous reconstruction	NS	NS

Table 2
Complication rate and cosmetic outcome categorised by the timing of radiotherapy and subdivided in autologous and implant reconstructions.*

Complications	Radiotherapy first				Reconstruction first			
	Autologous		Implant		Autologous		Implant	
	Reported incidences	Weighted mean (95%-CI)**	Reported incidences	Weighted mean (95%-CI)**	Reported incidences	Weighted mean (95%-CI)**	Reported incidences	Weighted mean (95%-CI)**
Patient satisfaction	69.2 [12]					86.6)	42,9 [12], 67.0 [11], 80.0 [40], 88.9 [39]	78.2 (64.1–92.3)
Physician satisfaction	51.3 [12]		92.3 [39]		[47]	87.2)	42,9 [12], 80.0 [11], 92.1 [39]	83.7 (68.2–99.2)

No significant differences

Timing of Radiotherapy

Limitations

-NO RCTs
-Retrospective nature (Heterogeneity)
-Different personal/Institutional experience
-NO analysis of FU length

*Placing of a **definite implant** after radiotherapy seems to lead to a higher complication rate, with clearly more implant failures. Thus, if implant reconstruction is chosen, **it is advised to be performed prior to radiotherapy**.*
*If **autologous reconstruction** is chosen, it seems slightly better to apply it **after radiotherapy**, since radiotherapy on an autologous flap may yield radiation-induced fibrosis with impaired cosmetic outcome.*

Berbers et al EJC 2014

Timing of Radiotherapy

What Is the Optimum Timing of Postmastectomy Radiotherapy in Two-Stage Prosthetic Reconstruction: Radiation to the Tissue Expander or Permanent Implant?

TE-XRT 94	IMPLANT-XRT 210
Neoadjuvant chemotherapy	Mastectomy and TE placement
Mastectomy and TE placement 3-4 weeks post completion of chemotherapy	Expansion starting 10-14 days postop
Rapid expansion starting 10-14 days postop. Expansion completed by 6 weeks	Expansion during chemotherapy
Radiation 8 weeks after TE placement	Exchange for permanent implant 4 weeks after chemotherapy
Exchange for permanent implant 6 months after completion of radiotherapy	Radiation 4 weeks after exchange

Cordeiro et al Plast. Reconstr. Surg. 2015

Timing of Radiotherapy

Table 2. Failure Rates

	Non-XRT	TE-XRT	Implant-XRT	*p*	*p**
No.	1486	94	210		
TE removal	54 (3.6)	8 (8.5)	2 (1.0)	<0.01	<0.01
Implant removal	14 (1.0)	9 (9.6)	24 (11.4)	<0.01	NS
Reconstructive failure	68 (4.6)	17 (18.1)	26 (12.4)	<0.01	NS

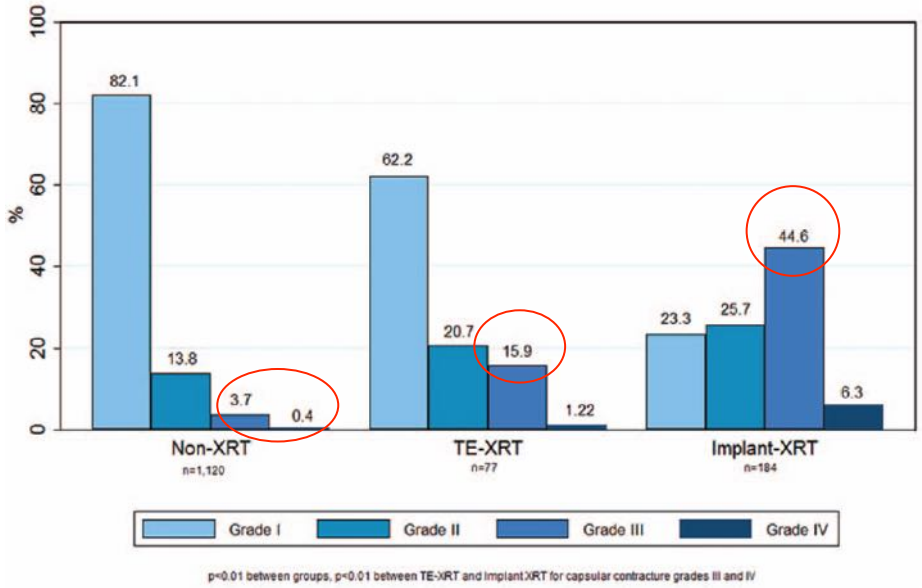


Table 4. Adjusted Median BREAST-Q Scores*

	Non-XRT	TE-XRT	Implant-XRT	*p*	*p*†
No.	520	22	84		
BREAST-Q scale					
Satisfaction with breasts (SD)				<0.01	NS
Satisfaction with outco				<0.01	0.02
Psychosocial well-being				<0.01	<0.01
Sexual well-being (SD)				<0.01	<0.01
Physical well-being (SD)	78.5 (2.4)	73.4 (1.9)	72.5 (2.6)	<0.01	NS

No significant differences

Cordeiro et al Plast. Reconstr. Surg. 2015

Nipple-sparing Mastectomy

Nipple-Sparing Mastectomy in Irradiated Breasts: Selecting Patients to Minimize Complications

Rong Tang, MD[1,2], Suzanne B. Coopey, MD[1], Amy S. Colwell, MD[3], Michelle C. Specht, MD[1], Michele A. Gadd, MD[1], Kari Kansal, MD[1], Maureen P. McEvoy, MD[1], Andrea L. Merrill, MD[1], Upahvan Rai, MD[1], Alphonse Taghian, MD, PhD[4], William G. Austen, MD[3], and Barbara L. Smith, MD, PhD[1]

TABLE 2 Surgical complications of nipple-sparing mastectomy with and without radiotherapy

	Cohort 1, no RT ($n = 816$)	Cohort 2, prior RT ($n = 69$)	Cohort 3, PMRT ($n = 97$)	p values for cohort comparison		
				1:2	1:3	2:3
Overall unplanned surgery	184 (22.5 %)	23 (33.3 %)	22 (22.7 %)	0.04*	1.00	0.13
Cosmetic revision	112 (13.7 %)	12 (17.4 %)	8 (8.2 %)	0.40	0.13	0.07
Overall complications	83 (10.2 %)	15 (21.7 %)	17 (17.5 %)	0.003*	0.03*	0.50
Early complications[a]	58 (7.1 %)	13 (18.8 %)	10 (10.3 %)	<0.001*	0.26	0.12
Late complications[b]	28 (3.4 %)	2 (2.9 %)	7 (7.2 %)	1.00	0.06	0.31
Overall skin necrosis	37 (4.5 %)	8 (11.6 %)	10 (10.3 %)	0.02*	0.02*	0.79
Breast skin necrosis	20 (2.4 %)	5 (7.2 %)	7 (7.2 %)	0.04*	0.02*	1.00
Nipple/areola necrosis[c]	18 (2.2 %)	5 (7.2 %)	4 (4.1 %)	0.03*	0.29	0.49
Nipple loss	7 (0.9 %)	3 (4.3 %)	4 (4.1 %)	0.04*	0.02*	1.00
Reconstruction failure	18 (2.2 %)	2 (2.9 %)	8 (8.2 %)	0.47	0.003*	0.19

Toxicity and Complications

- Type of reconstruction
- Timing of radiotherapy
- Other potential risk factors
- Current attitudes

Other potential risk factors: IBR TE/I

Table 8 Significant predictive factors of IPMR failure/complications with the TE/I technique followed by external radiotherapy (univariate analysis)

Institution/first author	Variable	Failure/complication	*P*
Fox Chase/Anderson [2]	Bolus type	Major complications	0.05
IPC/Tallet [27]	Chemotherapy	Failure	0.04
	Smoking	Failure	0.01
Massachusetts/Chawla [8]	IPMR type	Failure	<0.01
Columbia/Ascherman [3]	Chemotherapy	All complications	<0.01
University of Michigan/Krueger [16]	Tamoxifen	Failure	0.03
Long Island/Jhaveri [13]	IPMR type	Failure	0.007
Memorial/Cordeiro [10]	Not tested	Not tested	Not tested
Bordet/Vanderweyer [28]	Not tested	Not tested	Not tested
Present study	Smoking	Failure	0.0009
	Tumor size	Failure	0.0000016
	pN+	Failure	0.037

Cowen et al Breast Cancer Res Treat 2010

Other potential risk factors: IBR TE/I

-Expander/Implant size

Recommended checklist

Patient weight
Thickness of skin envelope
Presence of ADM or serratus coverage
Location of mastectomy scar
Use of targeted therapies and endocrine therapy
Interval to exchange

-Interval exchange

-BMI

-Scar location inframammary

Fowble et al Int. J. Radiat. Oncol. Biol. Phys. 2015

Other potential risk factors: NSM

TABLE 3 Univariable and multivariable logistic regression analysis of factors associated with complications requiring surgical revision

Predictors	Complication requiring surgical revision		Univariable analysis		Multivariable analysis	
	No	Yes	OR (95 % CI)	*p*	OR (95 % CI)	*p*
RT						
No RT ($n = 816$)	733	83	1 (Ref.)		1 (Ref.)	
Prior RT ($n = 69$)	54	15	2.45 (1.33–4.54)	0.004	2.53 (1.32–4.91)	0.006
PMRT ($n = 97$)	80	17	1.88 (1.06–3.32)	0.03	2.29 (1.17–4.47)	0.015
Age at surgery						

TABLE 4 Number of risk factors and complication rates in all breasts and in irradiated breasts

No. of risk factors	0	1	2	≥3	*p*
No. of breasts ($N = 982$)	471	368	118	25	
No. of breasts with complication	33 (7.0 %)	50 (13.6 %)	22 (18.6 %)	11 (44 %)	<0.001
RT with no. of risk factors	**RT only**	**RT + 1**	**RT + 2**	**RT + ≥ 3**	***p***
Breasts with RT ($n = 166$)	82	63	18	3	
No. of breasts with complications	11 (13.4 %)	11 (17.5 %)	9 (50 %)	2 (66.7 %)	<0.001

Smoking status						
No ($n = 902$)	806	96	1 (Ref.)		1 (Ref.)	
Yes ($n = 80$)	61	19	2.62 (1.50–4.56)	0.001	2.62 (1.46–4.69)	0.001
Reconstruction						
TE to implant ($n = 329$)	289	40	1 (Ref.)		1 (Ref.)	
Direct implant ($n = 625$)	558	67	0.87 (0.57–1.32)	0.50	0.78 (0.51–1.21)	0.27
Autologous flap ($n = 28$)	20	8	2.89 (1.19–7.00)	0.02	2.12 (0.83–5.42)	0.12
Incision						
Nonperiareolar ($n = 829$)	740	91	1 (Ref.)		1 (Ref.)	
Periareolar ($n = 151$)	127	24	1.54 (0.94–2.50)	0.08	1.74 (1.04–2.90)	0.03
Chemotherapy						
No ($n = 652$)	576	76	1 (Ref.)		1 (Ref.)	
Yes ($n = 330$)	291	39	0.99 (0.65–1.49)	0.94	0.77 (0.48–1.26)	0.30

Tang et al Ann. Surg. Oncol. 2015

Toxicity and Complications

- Type of reconstruction
- Timing of radiotherapy
- Other potential risk factors
- Current attitudes

Current attitudes: Survey

Current attitudes to breast reconstruction surgery for women at risk of post-mastectomy radiotherapy: A survey of UK breast surgeons

Paula J. Duxbury*, Ashu Gandhi, Cliona C. Kirwan, Yogesh Jain, James R. Harvey

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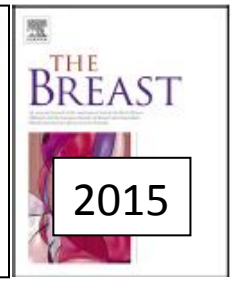


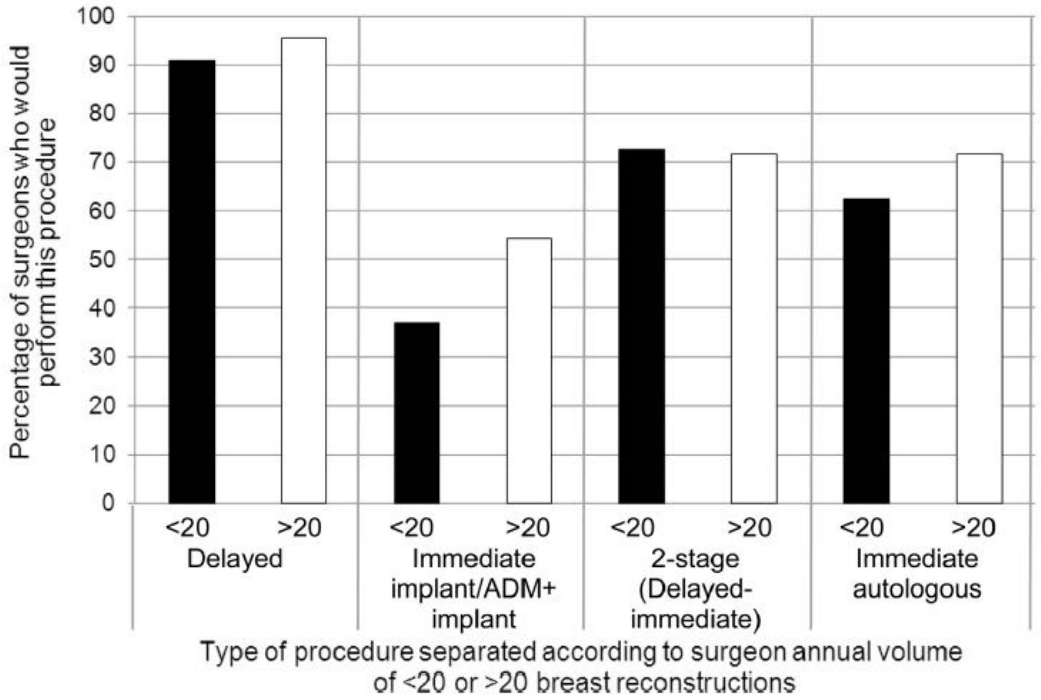
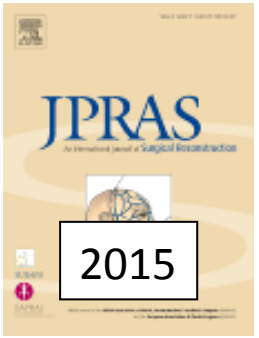


Fig. 2. Surgeons' preference for a patient potentially requiring PMRT-effect of annual surgical volume.

Current attitudes: Survey

Surgeon motivations behind the timing of breast reconstruction in patients requiring postmastectomy radiation therapy

Ming Lee [a], Erik Reinertsen [a,b], Evan McClure [a,c], Shuling Liu [d], Laura Kruper [e], Neil Tanna [f], J. Brian Boyd [g], Jay W. Granzow [g,*]



Preference toward timing of reconstruction involving PMRT

	PRS	SO
Immediate Reconstruction	54 (16.7%)	58 (16.8%)
Delayed Reconstruction	152 (46.9%)	148 (42.8%)
Delayed Immediate Reconstruction	118 (36.4%)	140 (40.5%)

Preferred type of immediate reconstruction with PMRT

	PRS	SO	P-value
Tissue expander/implant	128 (39.5%)	180 (52.6%)	<0.01
Latissimus dorsi flap with or without implant	26 (8.0%)	21 (6.1%)	0.34
Pedicled TRAM flap	57 (17.6%)	39 (11.4%)	0.024
Free TRAM flap	15 (4.6%)	14 (4.1%)	0.74
DIEP/SIEA	14 (4.3%)	18 (5.3%)	0.57
GAP/ other perforator	0 (0.0%)	1 (0.3%)	0.99
Overall			0.034

Current attitudes: Survey

Primary reasons for ***immediated reconstruction*** in patients who will require PMRT

	PRS	SO	P-value
Patient-driven desire to have immediate reconstruction	77 (71.3%)	82 (65.6%)	0.94
Mainly due to the opinion of surgical oncologist performing mastectomy	8 (7.4%)	36 (28.8%)	<0.01
Mainly due to the opinion of the plastic surgeon performing the reconstruction	40 (37.0%)	42 (33.6%)	0.98
Believe the reconstructive outcome is not greatly affected by radiation	21 (19.4%)	29 (23.2%)	0.33
Other (please specify)	17 (15.7%)	12 (9.6%)	0.27
Skipped Question	222	223	
All reasons			<0.01

Primary reasons for ***delayed reconstruction*** in patients who will require PMRT

	PRS	SO	P-value
Patient-driven desire to have delayed reconstruction	20 (10.2%)	20 (9.8%)	0.86
Mainly due to the opinion of surgical oncologist performing mastectomy	18 (9.2%)	53 (26.0%)	<0.01
Mainly due to the opinion of plastic surgeon performing the reconstruction	77 (39.3%)	128 (62.7%)	<0.01
Believe the reconstructive outcome is significantly and adversely affected by radiation	155 (79.1%)	81 (39.7%)	<0.01
Other (please specify)	5 (2.6%)	24 (11.8%)	<0.01
All reasons			<0.01

Take Home

- Delayed/immediate approach vs IBR/DBR
  (Two stage is better than one?)

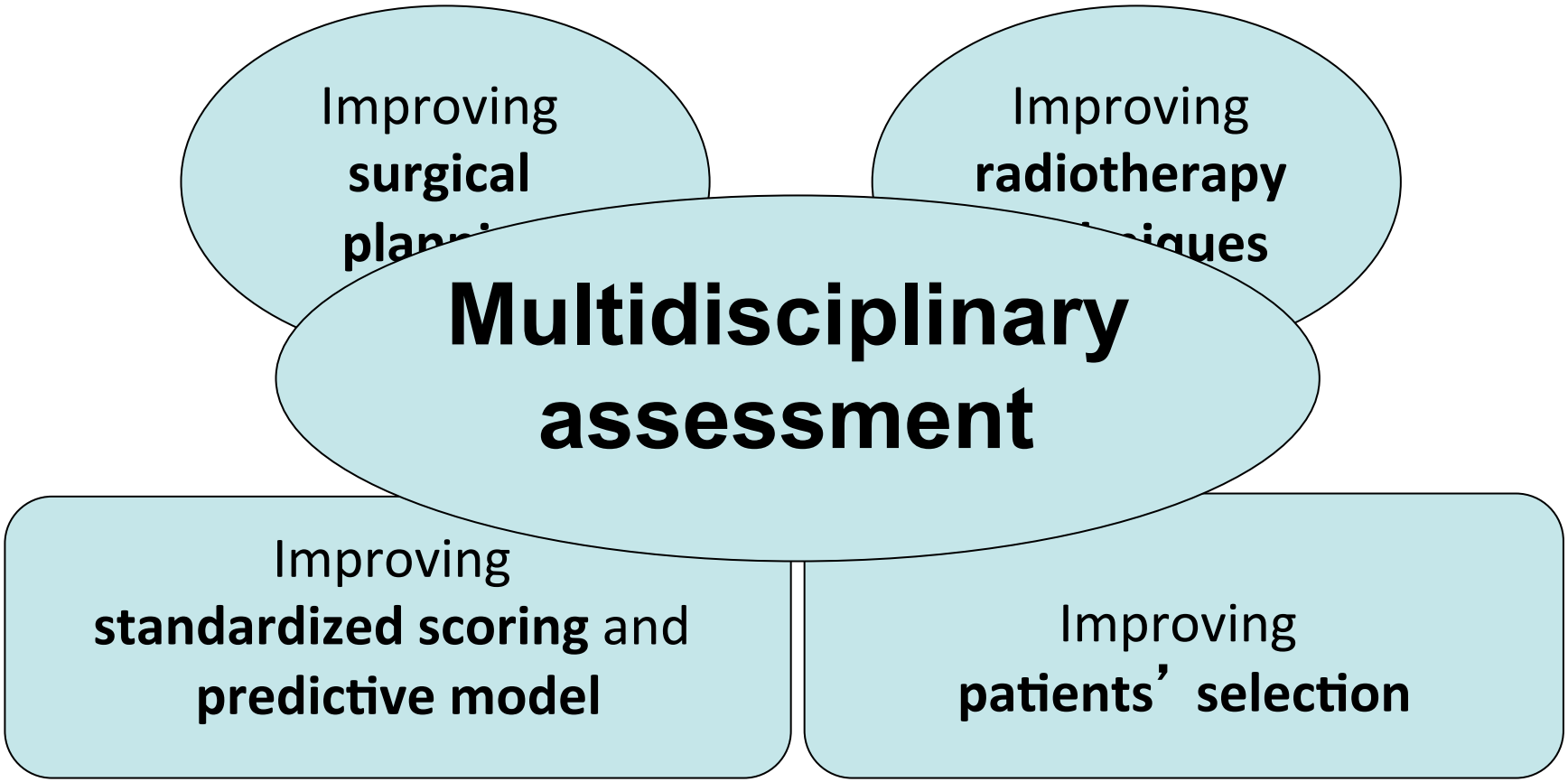
- Timing TE/I: Placing of a definite implant is advised to be performed prior to radiotherapy

- Timing Autologous: no statistical differences were found between total complication rates or revision surgery

- Timing is driven primarily by patient preference and PRS concern for optimal aesthetic outcome

- Other potential risk factors independently increase the overall complication rate

Take Home


Improving
surgical
Improving
radiotherapy
Multidisciplinary
assessment
Improving
standardized scoring and
predictive model
Improving
patients' selection