A Primer for Partial Breast Radiation

Nathan Bennion, MD
Radiation Oncology

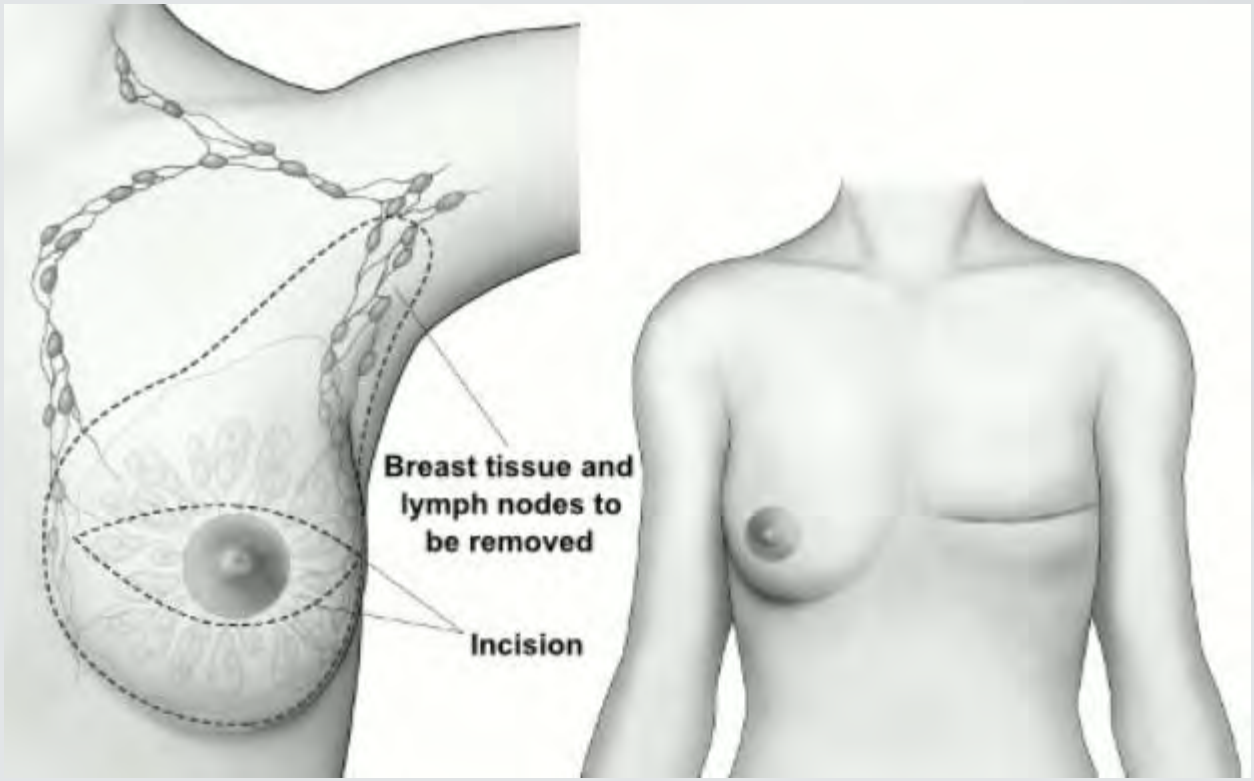
University of Nebraska Medical Center


Passion

Objective Principles

- Background/History
- Data for APBI
- Focus on EBRT techniques

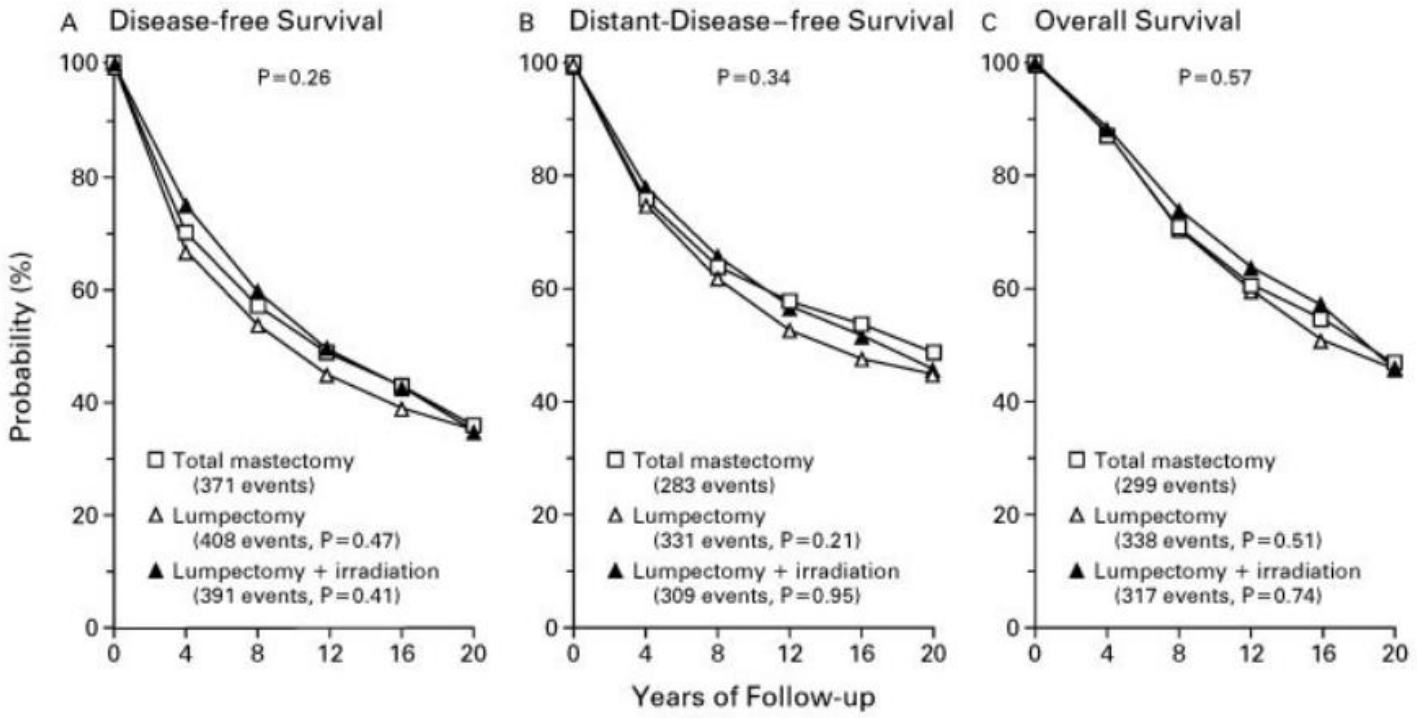
History



ORIGINAL ARTICLE

Twenty-Year Follow-up of a Randomized Trial Comparing Total Mastectomy, Lumpectomy, and Lumpectomy plus Irradiation for the Treatment of Invasive Breast Cancer

Bernard Fisher, M.D., Stewart Anderson, Ph.D., John Bryant, Ph.D., Richard G. Margolese, M.D., Melvin Deutsch, M.D., Edwin R. Fisher, M.D., Jong-Hyeon Jeong, Ph.D., and Norman Wolmark, M.D.



Fisher et al 2002

Original Investigation

May 5, 2021

Survival After Breast Conservation vs Mastectomy Adjusted for Comorbidity and Socioeconomic Status

A Swedish National 6-Year Follow-up of 48 986 Women

Jana de Boniface, PhD[1,2]; Robert Szulkin, PhD[3,4]; Anna L. V. Johansson, PhD[4,5]

- Prospective Cohort
- Adjusted for:
  - tumor characteristics
  - Treatment
  - Demographics
  - Comorbidities
  - Socioeconomic status

Original Investigation

May 5, 2021

Survival After Breast Conservation vs Mastectomy Adjusted for Comorbidity and Socioeconomic Status

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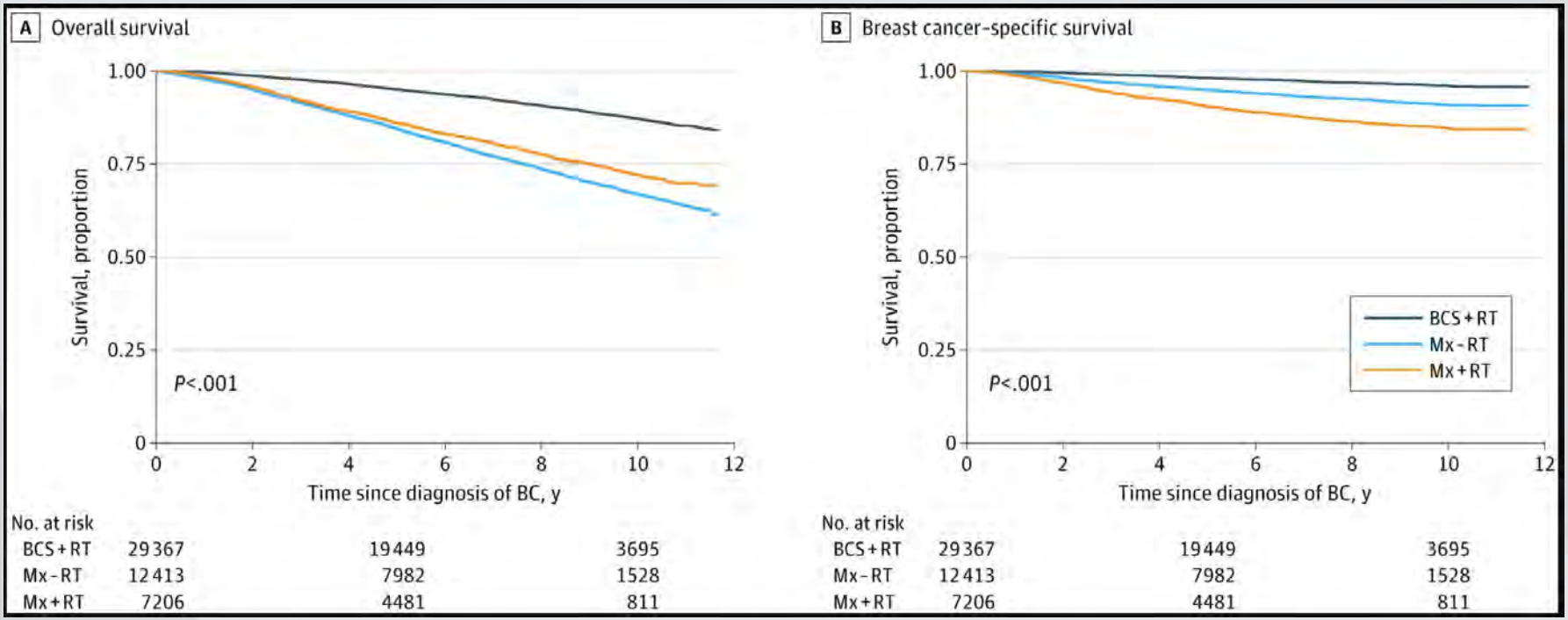
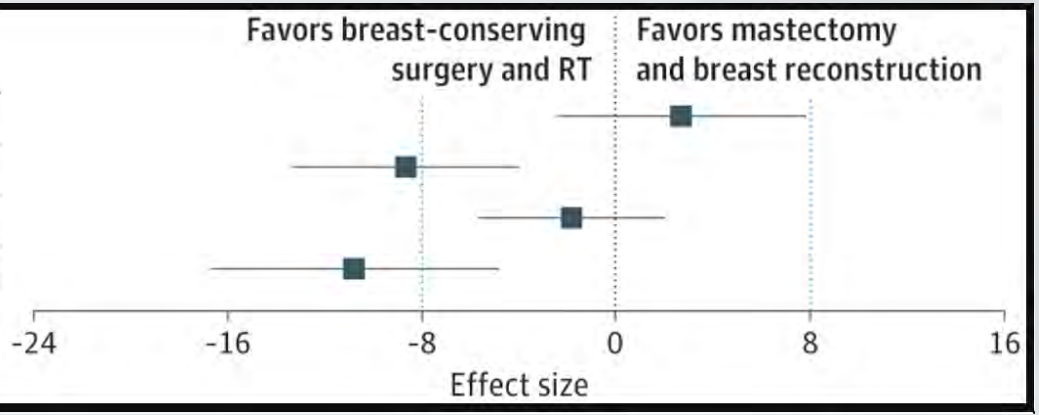


Long-term Quality of Life in Patients With Breast Cancer After Breast Conservation vs Mastectomy and Reconstruction

Summer E. Hanson, MD, PhD[1]; Xiudong Lei, PhD[2]; Margaret S. Roubaud, MD[1]; et al

- 647 women
- 10y patient reported satisfaction

Variable	Effect size (95% CI)
Satisfaction with breasts	2.71 (-2.45 to 7.88)
Psychosocial well-being	-8.61 (-13.26 to -3.95)
Physical well-being	-1.8 (-5.65 to 2.05)
Sexual well-being	-10.68 (-16.60 to -4.76)



Clinical Investigation

A Comparison of Patient- and Clinician-Reported Acute Toxic Effects During Radiation Therapy for Primary Breast Cancer

Kaitlyn Lapen MD *, Caroline King PhD †, Lior Z. Braunstein MD *, Atif J. Khan MD, MS *, Mitchell R. Kamrava MD ‡, Erin F. Gillespie MD *, [1], Kiri A. Cook MD

- Acute CTCAE
- Patient vs Physician Assessment
- 842 multi-institutional
- 14% PBI, 58% WBI, PMRT or WBI+RNI 28%

Lapen, 2022

Clinical Investigation

A Comparison of Patient- and Clinician-Reported Acute Toxic Effects During Radiation Therapy for Primary Breast Cancer

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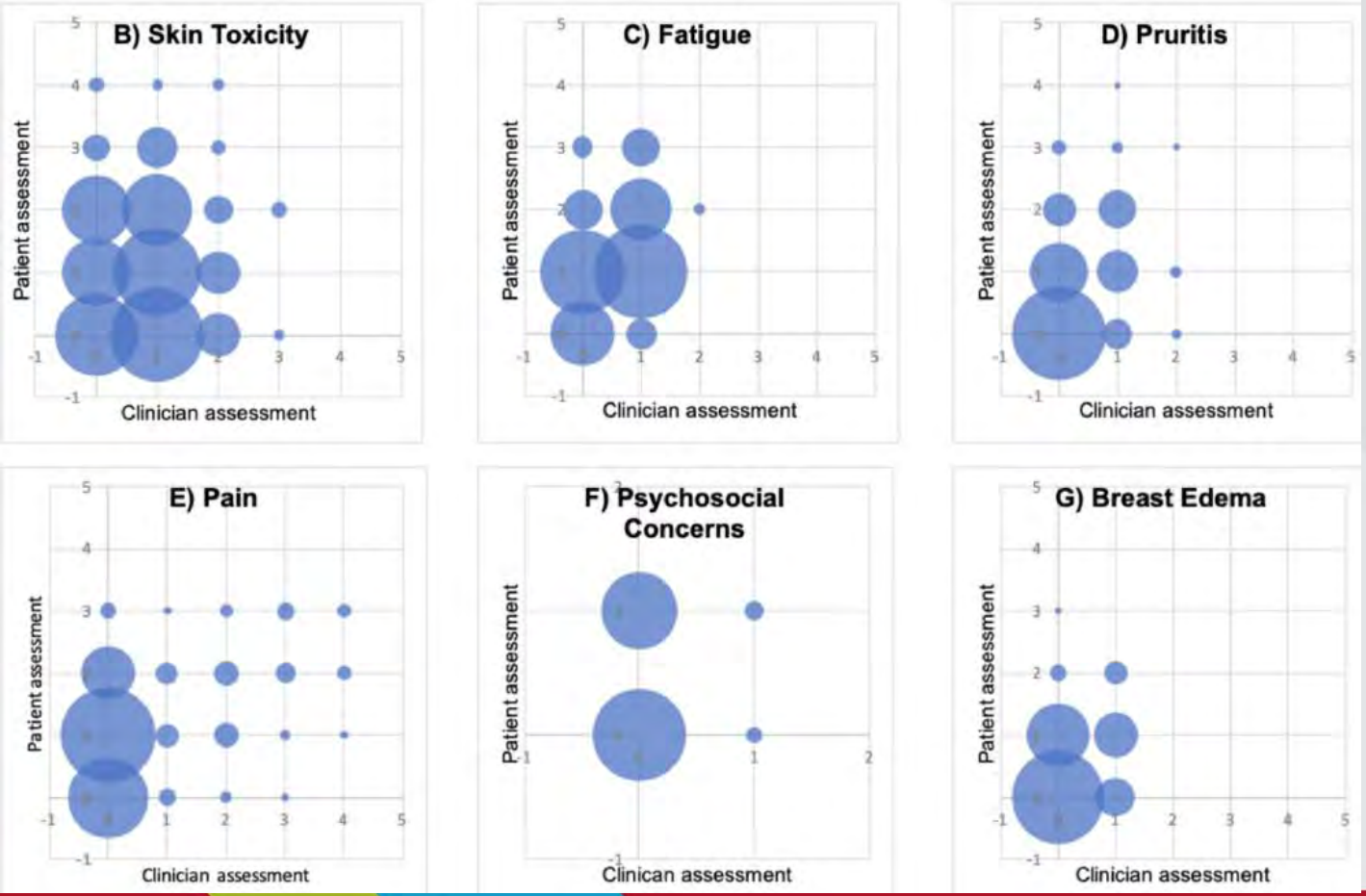

Lapen, 2022

Clinical Investigation

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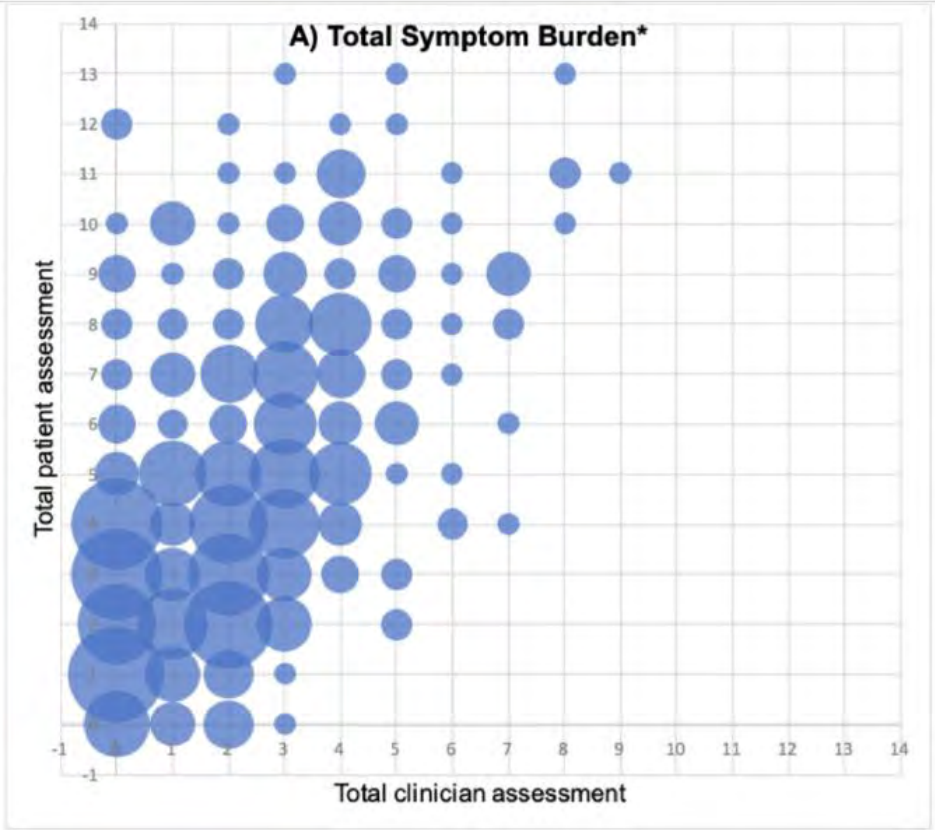


Lapen, 2022

Toward Improving Patients' Experiences of Acute Toxicity From Breast Radiotherapy: Insights From the Analysis of Patient-Reported Outcomes in a Large Multicenter Cohort

Reshma Jagsi, MD, DPhil[1]; Kent A. Griffith, MPH, MS[1]; Frank Vicini, MD[2]; Thomas Boike, MD, MMM[2]; Jacob Burmeister, PhD[3]; Michael M. Dominello, DO[3]; Inga Grills, MD[4]; James A. Hayman, MD[1]; Jean M. Moran, PhD[1]; Peter Paximadis, MD[5]; Jeffrey D. Radawski, MD[6]; Eleanor M. Walker, PhD[7]; and Lori J. Pierce, MD[1] on behalf of the Michigan Radiation Oncology Quality Consortium

	Hypofractionation	Conventional
Severe pain	9%	20%
Pruritis	24%	40%
Stinging	19%	40%
Swelling	20%	29%
Any Breast Symptom	41%	60%
Severe Fatigue	19%	27%

Jagsi, 2020

Necessity is the mother of invention

- 5-6 weeks
- Cost
- Irritant
- Cosmesis

Necessity is the mother of invention

Long-Term Results of Hypofractionated Radiation Therapy for Breast Cancer

Timothy J. Whelan, B.M., B.Ch., Jean-Philippe Pignol, M.D., Mark N. Levine, M.D., Jim A. Julian, Ph.D., Robert MacKenzie, M.D., Sameer Parpia, M.Sc., Wendy Shelley, M.D., Laval Grimard, M.D., Julie Bowen, M.D., Himu Lukka, M.D., Francisco Perera, M.D., Anthony Fyles, M.D., et al.

The UK Standardisation of Breast Radiotherapy (START) trials of radiotherapy hypofractionation for treatment of early breast cancer: 10-year follow-up results of two randomised controlled trials

Joanne S Haviland, MSc • J Roger Owen, FRCR • Prof John A Dewar, FRCR • Rajiv K Agrawal, FRCR • Jane Barrett, FRCR • Prof Peter J Barrett-Lee, MD • et al. Show all authors • Show footnotes

Published: September 19, 2013 • DOI: https://doi.org/10.1016/S1470-2045(13)70386-3 • Check for updates

Birth of Partial Breast Radiation

1985:

Histologic Multifocality of Tis, T1-2 Breast Carcinomas

Implications for Clinical Trials of Breast-Conserving Surgery

ROLAND HOLLAND, MD,* SOLKE H. J. VELING, MSc,† MARCEL MRAVUNAC, MD§
AND JAN H. C. L. HENDRIKS, MD‡

- 282 invasive, 32 DCIS
- Clinically unifocal T1-2

  - 37% had no tumor outside of the reference mass
  - 20% had additional foci within 2 cm
  - 43% had additional foci > 2cm from reference mass

Radiotherapy after breast-conserving surgery in small breast carcinoma: Long-term results of a randomized trial

U. Veronesi,[1] E. Marubini,[2] L. Mariani,[2] V. Galimberti,[1] A. Luini,[1] P. Veronesi,[1]
B. Salvadori[3] & R. Zucali[4]

[1]*Department of Senology, European Institute of Oncology,* [2]*Department of Biometrics, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milano,*
[3]*Department of Oncology, Policlinico San Marco, Zingonia, Bergamo,* [4]*Department of Radiotherapy, Ospedale Clinicizzato, Milano, Italy*

Sector Resection With or Without Postoperative Radiotherapy for Stage I Breast Cancer: Five-Year Results of a Randomized Trial

Get access >

G. Liljegren, L. Holmberg ✉, H.-O. Adami, G. Westman, S. Graffman, J. Bergh,
Uppsala-Örebro Breast Cancer study Group

JNCI: Journal of the National Cancer Institute, Volume 86, Issue 9, 4 May 1994, Pages 717–722, https://doi.org/10.1093/jnci/86.9.717

Published: 04 May 1994 **Article history** ▾

- Tumor bed recurrences predominated in-breast failures with < 5% occurring elsewhere

Volume

Defining the clinical target volume for patients with early-stage breast cancer treated with lumpectomy and accelerated partial breast irradiation: A pathologic analysis

Frank A. Vicini, M.D. • Larry L. Kestin, M.D. • Neal S. Goldstein, M.D.

- Re-excision after lumpectomy
- >90% of R0 resections had no additional tumor beyond 1 cm from initial lumpectomy bed.

Dose

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Breast radiobiology

Is α/β for breast cancer really low?

X. Sharon Qi [a,b,*], Julia White [b], X. Allen Li [b]

[a] Department of Radiation Oncology, University of Colorado Denver, Aurora, CO, USA; [b] Department of Radiation Oncology, Medical College of Wisconsin, Milwaukee, WI, USA

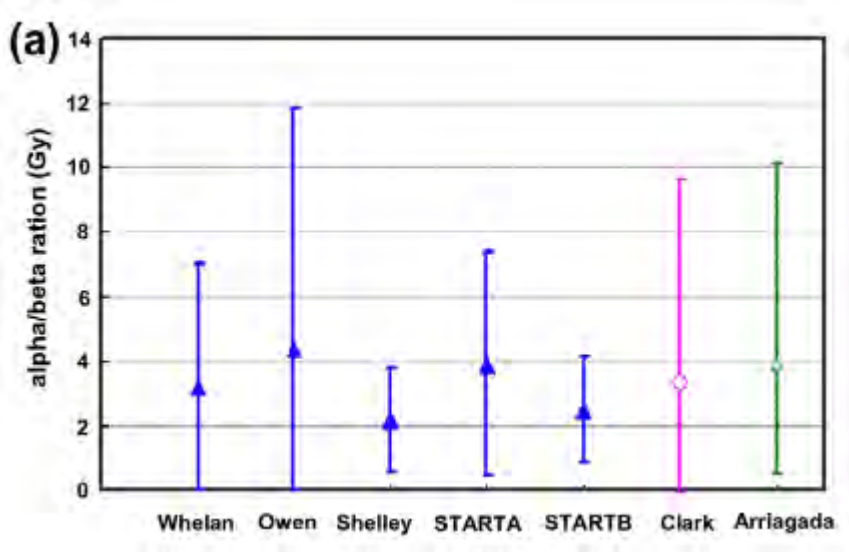


Table 2
The estimated radiobiological parameters from different clinical data (95% CL).

	α/β (Gy)	$\Delta(\alpha/\beta)$	α (Gy $^{-1}$)	$\Delta(\alpha)$	T_d (day)	$\Delta(T_d)$
Whelan	3.21	3.86	0.16	0.10	10.4	17.1
Owen	4.39	7.45	0.05	0.04	12.2	26.2
Shelley	2.21	1.59	0.13	0.06	21.3	71.5
START A	3.91	3.47	0.02	0.06	17.1	58.5
START B	2.49	1.63	0.09	0.02	15.9	9.7
Clark	1.44	1.27	0.03	0.10	10.8	48.6
Arriagada	3.89	6.25	0.04	0.04	11.0	12.2

Dose

Equivalent to 50 Gy in 25 fractions

- Brachytherapy: 34 Gy in 10 fractions
- EBRT: 38.5 Gy in 10 fractions

Patient Selection

Thorough work up

Patient: reliable for follow-up, comorbidities, genetics

Tumor: size, margin, histology, grade, nodal status, focality, LVSI

Treatment: BCT candidate, breast size to tumor ratio, distance from tumor to skin

Modality: Interstitial

Breast-Conserving Surgery Followed by Partial or Whole Breast Irradiation: Twenty-Year Results of a Phase 3 Clinical Study

Csaba Polgár, MD, PhD, MSc, DSc,*,† Tibor Major, PhD, DSc,*,† Zoltán Takácsi-Nagy, MD, PhD,*,† and János Fodor, MD, PhD, DSc†

*Center of Radiotherapy, National Institute of Oncology, Budapest, Hungary; †Department of Oncology, Semmelweis University, Budapest, Hungary

Received Aug 12, 2020. Accepted for publication Nov 2, 2020.

- T1N0-1mi, G1-2, non lobular, R0
- 36.4 Gy in 7 BID fractions
- 20y LR 9.6% APBI vs 7.9% WBI
- Cosmesis favored APBI

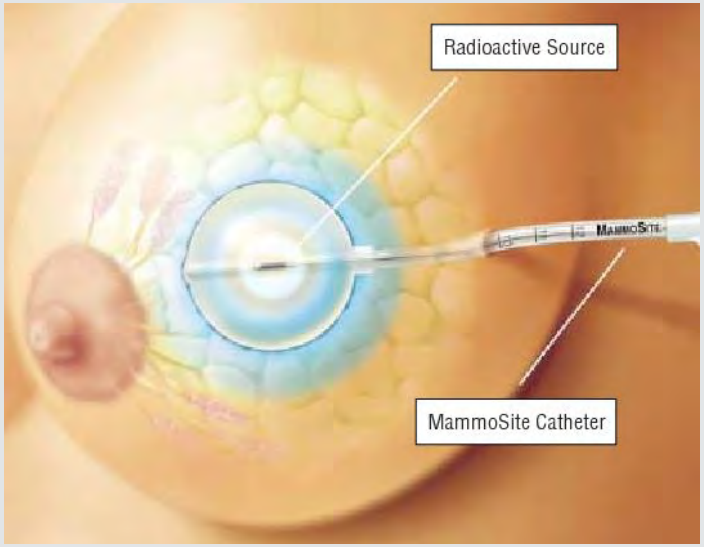
Modality: Balloon-based

PRESENTATION | VOLUME 194, ISSUE 4, P456-462, OCTOBER 01, 2007

Five-year results: the initial clinical trial of Mammosite balloon brachytherapy for partial breast irradiation in early-stage breast cancer

Pamela R. Benitez, M.D. • Martin E. Keisch, M.D. • Frank Vicini, M.D. • ... Coral Quiet, M.D. • Oscar Streeter, M.D. • Mel Silverstein, M.D. • Show all authors

DOI: https://doi.org/10.1016/j.amjsurg.2007.06.010



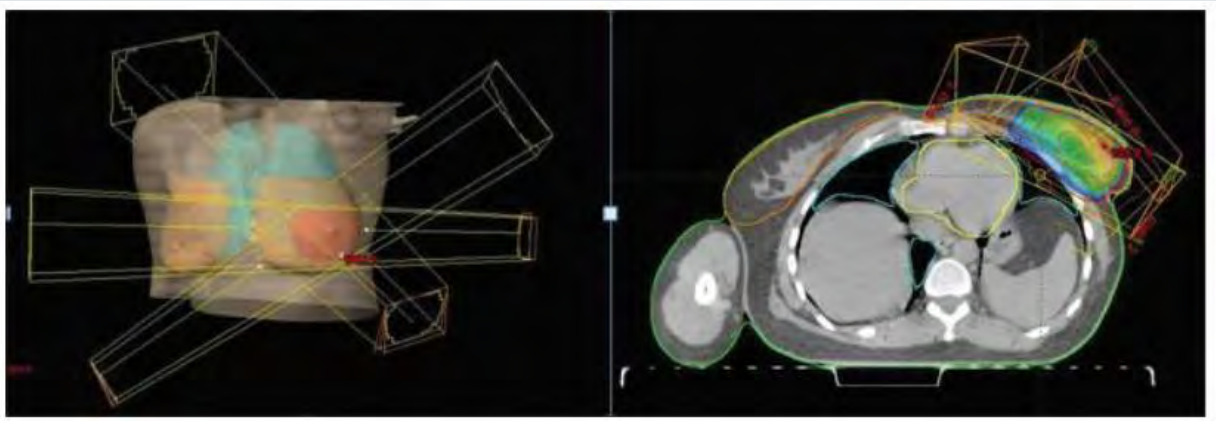
Dowlatshahi 2004

Modality: EBRT

Ongoing clinical experience utilizing 3D conformal external beam radiotherapy to deliver partial-breast irradiation in patients with early-stage breast cancer treated with breast-conserving therapy

Frank A Vicini, M.D. • Vincent Remouchamps, M.D. • Michelle Wallace, R.N. • ... Jane Pettinga, M.D. • Neal S Goldstein, M.D. • John Wong, Ph.D. • Show all authors

DOI: https://doi.org/10.1016/S0360-3016(03)01573-6



- 31 pts
- Technically feasible and good acute tolerance

EBRT Timeline Highlights

Date	Institution	Technique	Good-Excellent Cosmesis
2003	Beaumont	34 or 38.5 Gy in 10 BID	90%

EBRT Timeline Highlights

Date	Institution	Technique	Good-Excellent Cosmesis
2003	Beaumont	34 or 38.5 Gy in 10 BID	90%
2004	NYU	30 Gy in 5 fractions over 10 days. Prone	100%

EBRT Timeline Highlights

Date	Institution	Technique	Good-Excellent Cosmesis
2003	Beaumont	34 or 38.5 Gy in 10 BID	90%
2004	NYU	30 Gy in 5 fractions over 10 days. Prone	100%
Many phase II studies with positive outcomes			

EBRT Timeline Highlights

Date	Institution	Technique	Good-Excellent Cosmesis
2003	Beaumont	34 or 38.5 Gy in 10 BID	90%
2004	NYU	30 Gy in 5 fractions over 10 days. Prone	100%
Many phase II studies with positive outcomes			
2010	Michigan	3.85 Gy x 10 BID; ABC & IMRT	73%

EBRT Timeline Highlights

Date	Institution	Technique	Good-Excellent Cosmesis
2003	Beaumont	34 or 38.5 Gy in 10 BID	90%
2004	NYU	30 Gy in 5 fractions over 10 days. Prone	100%
Many phase II studies with positive outcomes			
2010	Michigan	3.85 Gy x 10 BID; ABC & IMRT	73%
2013	RTOG 0319	3.85 Gy x 10 BID	64%

EBRT Timeline Highlights

Date	Institution	Technique	Good-Excellent Cosmesis
2003	Beaumont	34 or 38.5 Gy in 10 BID	90%
2004	NYU	30 Gy in 5 fractions over 10 days. Prone	100%
Many phase II studies with positive outcomes			
2010	Michigan	3.85 Gy x 10 BID; ABC & IMRT	73%
2013	RTOG 0319	3.85 Gy x 10 BID	64%
2013	Canadian Rapid	3.85 Gy x 10 BID	65%

EBRT Timeline Highlights

Date	Institution	Technique	Good-Excellent Cosmesis
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Many phase II studies with positive outcomes			
2010	Michigan	3.85 Gy x 10 BID; ABC & IMRT	73%
2013	RTOG 0319	3.85 Gy x 10 BID	64%
2013	Canadian Rapid	3.85 Gy x 10 BID	65%
Many phase II studies with positive outcomes			

EBRT Issues

- Michigan:
  - V50% and V100% correlated with cosmesis
  - Larger V20%, V50%, V80%, and V100%
  - Breathing control decreased inherent feathering?
- RAPID:
  - Dose had higher biologic effect than WBI arm
  - 6-hour interval may not be adequate

EBRT Timeline Highlights

Date	Institution	Technique	Good-Excellent Cosmesis
2011	Canadian (Berrang)	35 or 38.5 Gy in 10 BID	85%

EBRT Timeline Highlights

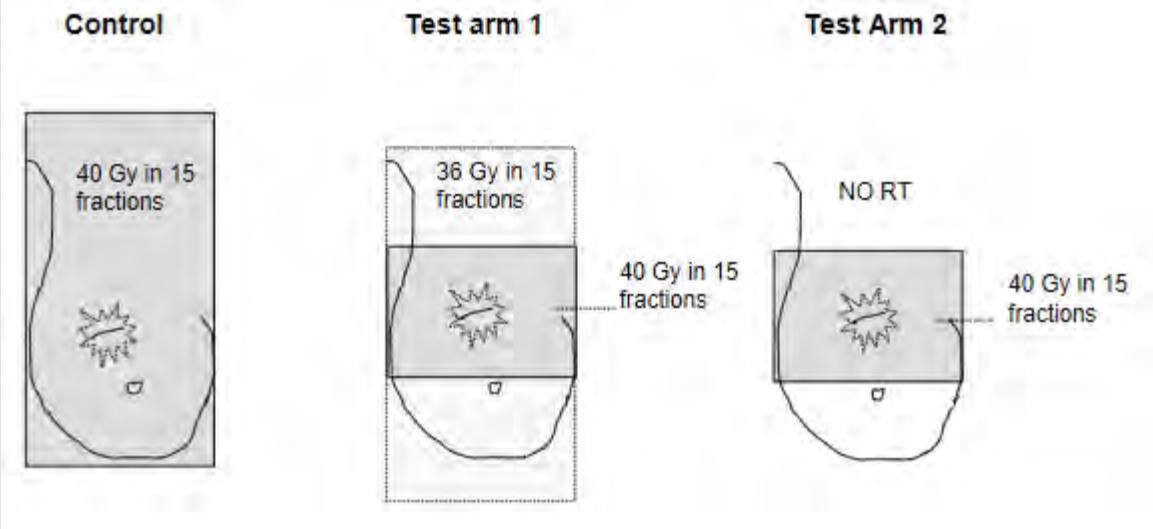
Date	Institution	Technique	Good-Excellent Cosmesis
2011	Canadian (Berrang)	35 or 38.5 Gy in 10 BID	85%
2012	Mass Gen	3.2 Gy x 10 BID	97%

EBRT Timeline Highlights

Date	Institution	Technique	Good-Excellent Cosmesis
2011	Canadian (Berrang)	35 or 38.5 Gy in 10 BID	85%
2012	Mass Gen	3.2 Gy x 10 BID	97%
2013	APBIMRT	3.85 Gy x 10 BID	90%

Partial-breast radiotherapy after breast conservation surgery for patients with early breast cancer (UK IMPORT LOW trial): 5-year results from a multicentre, randomised, controlled, phase 3, non-inferiority trial

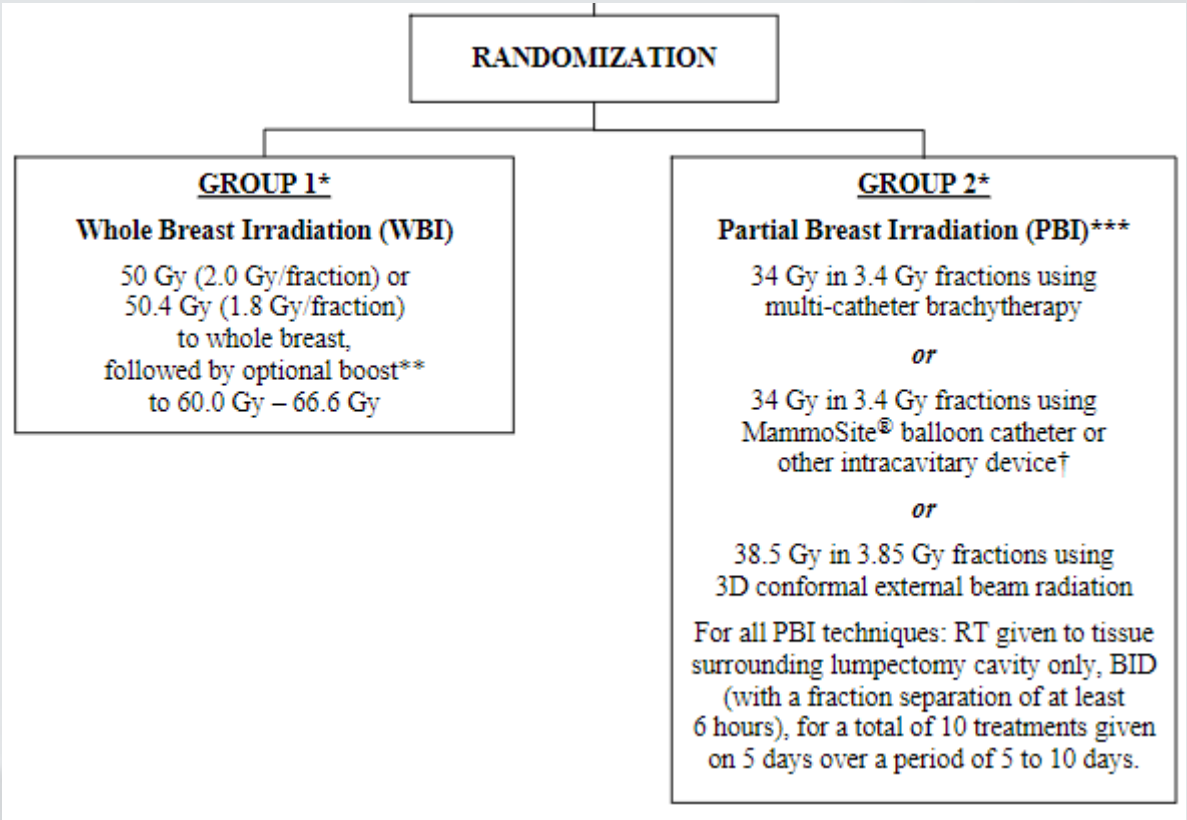
Dr Charlotte E Coles, PhD • Clare L Griffin, MSc • Anna M Kirby, MD • Jenny Titley, BSc • Rajiv K Agrawal, FRCR • Abdulla Alhasso, FRCR • et al. Show all authors • Show footnotes



- 674 pts
- 5y LR 1.1% - 0.2% - 0.5%
- SS improved breast appearance and breast firmness in Test arm 2

Long-term primary results of accelerated partial breast irradiation after breast-conserving surgery for early-stage breast cancer: a randomised, phase 3, equivalence trial

Frank A Vicini, Reena S Cecchini, Julia R White, Douglas W Arthur, Thomas B Julian, Rachel A Rabinovitch, Robert R Kuske, Patricia A Ganz, David S Parda, Michael F Scheier, Kathryn A Winter, Soonmyung Paik, Henry M Kuerer, Laura A Vallow, Lori J Pierce, Eleftherios P Mamounas, Beryl McCormick, Joseph P Costantino, Harry D Bear, Isabelle Germain, Gregory Gustafson, Linda Grossheim, Ivy A Petersen, Richard S Hudes, Walter J Curran Jr, John L Bryant, Norman Wolmark*



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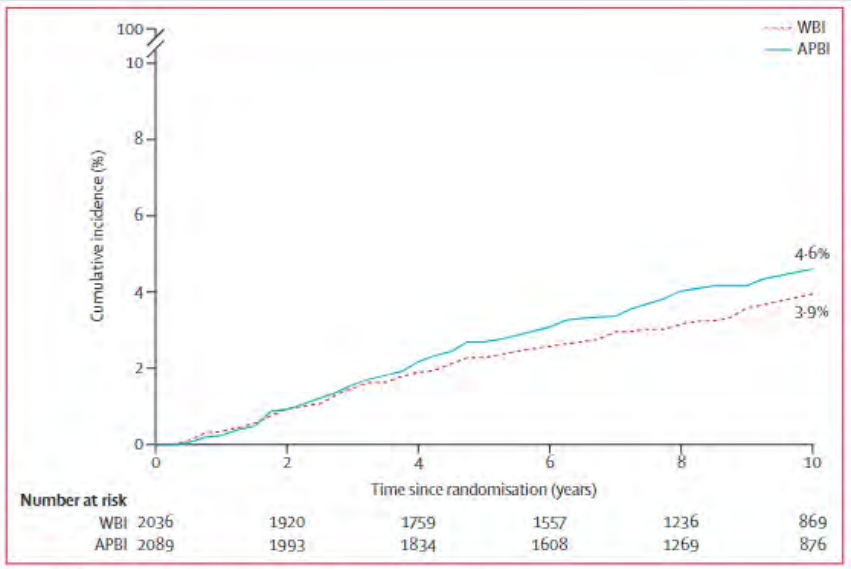


Figure 2: **Cumulative incidence of in-breast tumour recurrence**
APBI=accelerated partial breast irradiation. WBI=whole-breast irradiation.

- PRO: equivalent cosmesis
- MD: worse cosmesis for PBI
- Central Review: PBI worse for CT group, better in no-CT group

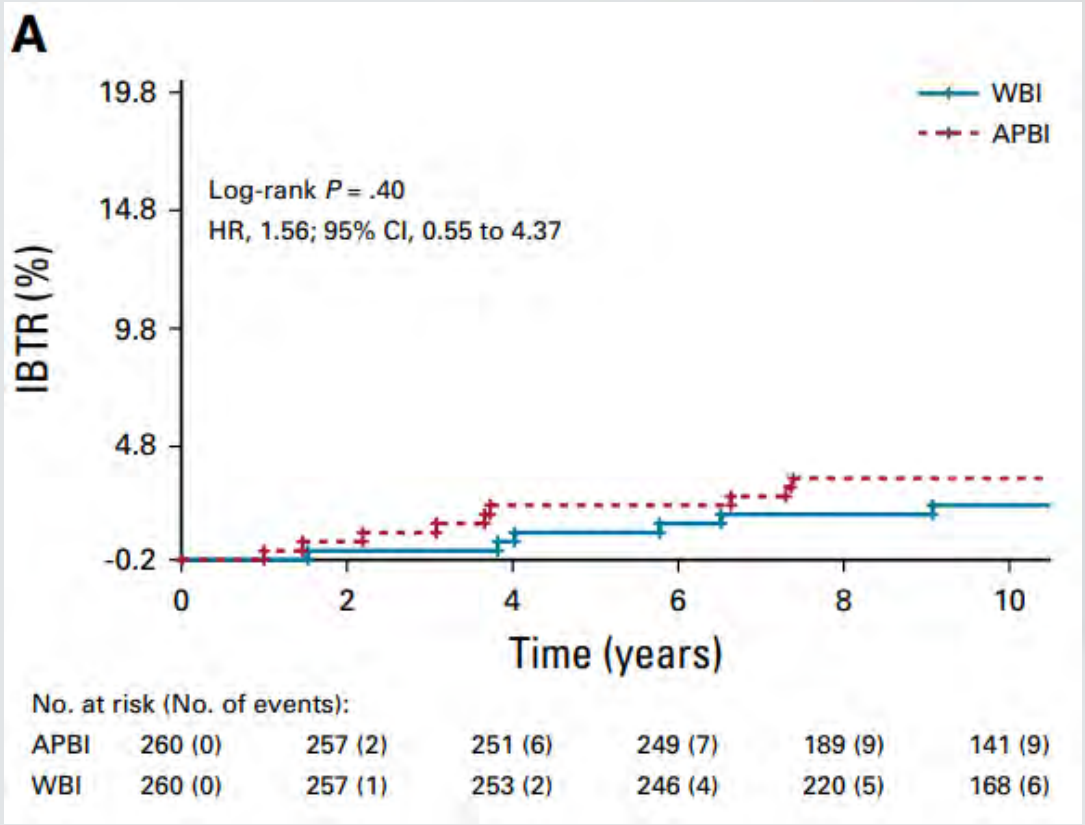
ASTRO 2019

Lancet 2019

Accelerated Partial-Breast Irradiation Compared With Whole-Breast Irradiation for Early Breast Cancer: Long-Term Results of the Randomized Phase III APBI-IMRT-Florence Trial

Icro Meattini, MD[1,2]; Livia Marrazzo, MS[2]; Calogero Saieva, MD[3]; Isacco Desideri, MD[1,2]; Vieri Scotti, MD[2]; Gabriele Simontacchi, MD[2]; Pierluigi Bonomo, MD[2]; Daniela Greto, MD[2]; Monica Mangoni, MD, PhD[1,2]; Silvia Scoccianti, MD[2]; Sara Lucidi, MD[1]; Lisa Paoletti, MD[4]; Massimiliano Fambrini, MD[1,2]; Marco Bernini, MD, PhD[2]; Luis Sanchez, MD[2]; Lorenzo Orzalesi, MD[1,2]; Jacopo Nori, MD[2]; Simonetta Bianchi, MD[1,2]; Stefania Pallotta, MS[1,2]; and Lorenzo Livi, MD[1,2]

- 520 pts randomized
- WBI 50/25 vs 30/5 EOD IMRT PBI



- APBI had more favorable G1-2 acute tox, G1 late tox
- APBI had more favorable physician and patient cosmetic scores

Assessment	APBI (n = 246)	WBI (n = 260)	P
Acute period adverse events[a]			
None	194 (78.9)	87 (33.5)	.0001
Yes, any grade	52 (21.1)	173 (66.5)	
Grade 1	47 (19.1)	75 (28.8)	.0001
Grade 2	5 (2.0)	81 (31.2)	
Grade 3	—	17 (6.5)	
Grade 4	—	—	
Grade 0-1	241 (98.0)	162 (62.3)	.0001
Grade ≥ 2	5 (2.0)	98 (37.7)	.0001
Late period adverse events[a]			
None	235 (95.5)	182 (70.0)	.0001
Yes, any grade	11 (4.5)	78 (30.0)	.0001
Grade 1	11 (4.5)	71 (27.3)	.0001
Grade 2	—	7 (2.7)	
Grade 3	—	—	
Grade 4	—	—	
Grade 0-1	246 (100)	253 (97.3)	.015
Grade ≥ 2	0	7 (2.7)	
Physician-rated cosmesis[b]			
Excellent	233 (94.7)	189 (72.7)	.0001
Good	13 (5.3)	66 (25.4)	
Fair	—	5 (1.9)	
Poor	—	—	
Patient-rated cosmesis[b]			
Excellent	44 (17.9)	13 (5.1)	.0001
Good	200 (81.3)	209 (80.3)	
Fair	2 (0.8)	38 (14.6)	
Poor	—	—	

Efficacy, Improved Quality of Life, and Cost-effectiveness of Partial Breast Irradiation
A Triple-Threat Approach

Table. Outcomes With Partial Breast Irradiation From Randomized Trials

Trial	No. of patients	Follow-up, y	PBI technique	Local recurrence
National Institute of Oncology (Hungary)[4]	258	10.2	Interstitial	5.9% vs 5.1%
NSABP B39/RTOG 0413[2]	4216	10.2	Interstitial, applicator, 3D-CRT	4.8% vs 4.1%
RAPID[3]	2135	8.6	3D-CRT	3.0% vs 2.3%
GEC-ESTRO[5]	1184	6.6	Interstitial	1.4% vs 0.9%
IMPORT LOW[6]	2018	6.0	IMRT	0.5% PBI vs 1.1% HWBI vs 0.2% reduced dose
University of Florence[7]	520	5.0	IMRT	1.5% Both arms

Abbreviations: 3D-CRT, 3-dimensional conformal radiotherapy; GEC-ESTRO, Groupe Européen de Curiethérapie-European Society for Radiotherapy; HWBI, hypofractionated whole-breast irradiation; IMPORT LOW, Intensity Modulated Partial Organ Radiotherapy; IMRT, intensity-modulated radiotherapy; NSABP, National Surgical Adjuvant Breast and Bowel Project; PBI, partial breast irradiation; RAPID, Randomized Trial of Accelerated Partial Breast Irradiation Using 3-Dimensional Conformal Radiotherapy; RTOG, Radiation Therapy Oncology Group.

>10,000 pts randomized

- Equivalent Efficacy
- Improved Quality of Life
- More Cost Effective

Shah, Arthur, Vicini 2020

Current ASTRO Guidelines

Table 2 Current ASTRO guidelines for accelerated partial breast irradiation (63,64)

Consideration	Suitable	Cautionary	Unsuitable
Age	≥50 years of age	40–49 years of age if meet all other "suitable" criteria or ≥50 years of age with one or more other cautionary feature	<40 years of age or 40–49 years of age and not meeting all other criteria
Genetics	BRCA 1/2 negative	–	BRCA 1/2 positive
Margins	≥2 mm	<2 mm	Positive
DCIS	≤2.5 cm, screen-detected, low-intermediate grade, margins ≥3 mm	≤3.0 cm not meeting criteria for "suitable"	>3.0 cm
Size	≤2.0 cm	2.0–3.0 cm	>3.0 cm
LVSI	None	Limited/focal	Extensive
Hormone-receptor status	ER positive	ER negative	–
Histology	Invasive ductal	Invasive lobular	–
Extensive intraductal component	None	≤3 cm	>3 cm
Focality	Clinically unifocal	–	Clinically multifocal or microscopically multifocal with total size >3.0 cm
Centricity	Unicentric	–	Multicentric
Nodal status	pN0	–	pN+
Neoadjuvant therapy	None	–	Any

DCIS, ductal carcinoma in situ; LVSI, lymphovascular space invasion; pN0, pathologically node-negative; ER, estrogen receptor; pN+, pathologically node-positive.

American Society of Breast Surgeons (ASBrS), Suitable Criteria (2018)	• Age ≥ 45 years • Tumor size ≤ 3 cm • All invasive subtypes and DCIS • Estrogen receptor positive or negative • Surgical Margins negative (no ink on tumor for invasive tumor and ≥ 2 mm for DCIS) • Node negative • Focal LVSI accepted • Multifocal accepted (if span of tumors is ≤ 3 cm) • No genetic mutation

Groupe Européen de Curiethérapie/European Society for Therapeutic Radiology and Oncology (GEC/ESTRO), low-risk/good candidates (2010)	Age ≥ 50 years • Tumor size ≤ 3 cm • Invasive carcinoma (excluding invasive lobular carcinoma or DCIS) • Margins ≥ 2 mm • Estrogen receptor positive or negative • Node negative • Unifocal • Unicentric • No LVSI • No EIC • No neoadjuvant chemotherapy

Study	Trial design	Enrollment	Age (years)	Tumor size (cm)	ER status	Histology	Margin (mm)	Arms	Status
RAPID (41)	Phase III	2,135	≥40	≤3.0	–	Non-lobular invasive or DCIS	Negative	(I) Standard fractionated whole breast RT (II) APBI (3D-CRT; 38.5 Gy delivered over 10 twice-daily fractions)	Closed to accrual in 2011; pending results
NSABP B39 and (40)	Phase III	4,216	≥18	≤3.0	–	Non-lobular invasive or DCIS	Negative	(I) Standard fractionated whole breast RT (II) APBI (3D-CRT; 38.5 Gy delivered over 10 twice-daily fractions)	Closed to accrual in 2013; pending results
Nurnburg (65)	Phase III	1,300	≥40	≤3.0	–	All invasive or DCIS	≥2; ≥5 if DCIS or lobular histology	(I) Standard fractionated whole breast RT (II) APBI (interstitial)	Closed to accrual in 2016; pending results
SHARE (66)	Phase III	1,006	≥50	≤2.0	–	All invasive	>2	(I) Standard fractionated or hypofractionated whole breast RT (II) APBI (3D-CRT; 38.5 Gy delivered over 10 twice-daily fractions)	Closed to accrual in 2017; pending results
IRMA (67)	Phase III	3,302	49–85	<3.0	–	All invasive	≥2	(I) Standard fractionated whole breast RT (II) APBI (interstitial or balloon-based or external beam)	Recruiting
Budapest (68)	Phase II	90	≥40	≤3.0	Positive; cannot overexpress HER2	Non-lobular invasive	≥2	3D-CRT or IMRT-based APBI; 36.9 Gy delivered over 9 twice-daily fractions	Closed to accrual in 2014; pending results
Ontario (69)	Phase II	280	≥50	≤3.0	–	Non-lobular invasive or DCIS	–	3D-CRT APBI; 27.5 or 30 Gy delivered over 5 daily fractions	Closed to accrual in 2017; pending results
TRIUMPH-T (70)	Phase II	200	≥45	≤3.0	Positive	All invasive or DCIS	Negative	Balloon-based APBI	Closed to accrual in 2017; pending results
Mayo (71)	Phase II	168	≥50	≤2.5	Positive (unless DCIS)	Non-lobular invasive or DCIS	Negative	(I) 3D-CRT APBI (II) APBI using protons (III) Interstitial APBI	Closed to accrual in 2018; pending results
Milano (72)	Phase II	700	55–70	≤2.0	Positive	–	>5	(I) Hypofractionated whole breast RT with integrated boost (II) APBI (3D-CRT; 30 Gy delivered over 5 fractions over 10 days)	Recruiting
Alberta (73)	Phase II	274	≥50	≤3.0	–	All invasive or DCIS	≥2	3D-CRT APBI; 27 Gy delivered over 5 daily fractions	Recruiting
U Penn (74)	Phase II	57	≥50	≤3.0	Positive	All invasive or DCIS	≥2	APBI using protons	Recruiting
TROG 06.02 and (75)	Single arm	48	≥50	≤2.0	–	Non-lobular invasive	≥2	3D-CRT APBI; 38.5 Gy delivered over 10 twice-daily fractions	Closed to accrual in 2017; pending results
Yale (76)	Single arm	30	> 50	≤2.0	–	Non-lobular invasive or DCIS	>2	4D-CRT APBI	Closed to accrual in 2017; pending results
NYU (77)	Single arm	310	18-65	≤2.0	–	All invasive	Negative	Image-guided external beam APBI; 30 Gy delivered over 5 daily fractions, treated prone	Closed to accrual in 2017; pending results

Planning

	Coverage	Ipsilateral Breast	Heart	Lung	Contralateral Breast	Volumes
Florence						CTV: GTV+ 1cm (3mm skin subtraction) PTV: CTV+1cm (allowed 4mm into lung but 3 mm skin subtraction)
B39						CTV=GTV+ 15 mm PTV=CTV+10 mm PTVeval = PTV – 5mm from skin
IMPORT-LOW						CTV= GTV + 15mm PTV+ CTV + 10 mm 5mm skin subtraction

Planning

	Coverage	Ipsilateral Breast	Heart	Lung	Contralateral Breast	Volumes
Florence	PTV: V95%>100% Dmax <105% Dmin 28 Gy					CTV: GTV+ 1cm (3mm skin subtraction) PTV: CTV+1cm (allowed 4mm into lung but 3 mm skin subtraction)
B39	PTVeval: V90%>90% Dmax < 120%					CTV=GTV+ 15 mm PTV=CTV+10 mm PTVeval = PTV – 5mm from skin
IMPORT-LOW	PTV V95>95%					CTV= GTV + 15mm PTV+ CTV + 10 mm 5mm skin subtraction

Planning

	Coverage	Ipsilateral Breast	Heart	Lung	Contralateral Breast	Volumes
Florence	PTV: V95%>100% Dmax <105% Dmin 28 Gy	V15Gy<50%				CTV: GTV+ 1cm (3mm skin subtraction) PTV: CTV+1cm (allowed 4mm into lung but 3 mm skin subtraction)
B39	PTVeval: V90%>90% Dmax < 120%	V50%<60% V100<35%				CTV=GTV+ 15 mm PTV=CTV+10 mm PTVeval = PTV – 5mm from skin
IMPORT-LOW	PTV V95>95%					CTV= GTV + 15mm PTV+ CTV + 10 mm 5mm skin subtraction

Planning

	Coverage	Ipsilateral Breast	Heart	Lung	Contralateral Breast	Volumes
Florence	PTV: V95%>100% Dmax <105% Dmin 28 Gy	V15Gy<50%	V3Gy<10%			CTV: GTV+ 1cm (3mm skin subtraction) PTV: CTV+1cm (allowed 4mm into lung but 3 mm skin subtraction)
B39	PTVeval: V90%>90% Dmax < 120%	V50%<60% V100<35%	Left sided: V5<40% Right sided: V5%<5%			CTV=GTV+ 15 mm PTV=CTV+10 mm PTVeval = PTV – 5mm from skin
IMPORT-LOW	PTV V95>95%					CTV= GTV + 15mm PTV+ CTV + 10 mm 5mm skin subtraction

Planning

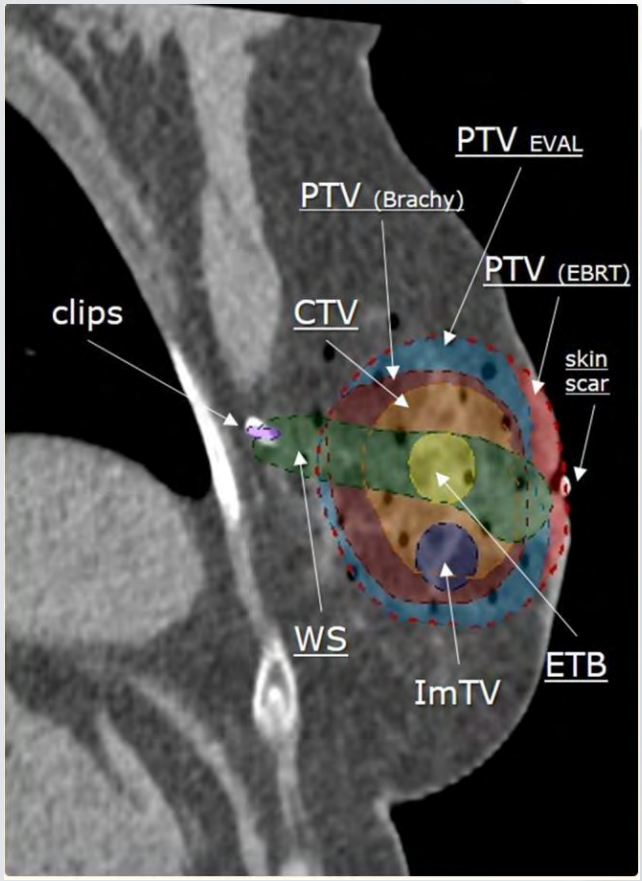
	Coverage	Ipsilateral Breast	Heart	Lung	Contralateral Breast	Volumes
Florence	PTV: V95%>100% Dmax <105% Dmin 28 Gy	V15Gy<50%	V3Gy<10%	Ipsi:V10<20% Contra: V5<10%		CTV: GTV+ 1cm (3mm skin subtraction) PTV: CTV+1cm (allowed 4mm into lung but 3 mm skin subtraction)
B39	PTVeval: V90%>90% Dmax < 120%	V50%<60% V100<35%	Left sided: V5<40% Right sided: V5%<5%	Ipsi: V30%<15% Contra: V5%<15%		CTV=GTV+ 15 mm PTV=CTV+10 mm PTVeval = PTV – 5mm from skin
IMPORT-LOW	PTV V95>95%					CTV= GTV + 15mm PTV+ CTV + 10 mm 5mm skin subtraction

Planning

	Coverage	Ipsilateral Breast	Heart	Lung	Contralateral Breast	Volumes
Florence	PTV: V95%>100% Dmax <105% Dmin 28 Gy	V15Gy<50%	V3Gy<10%	Ipsi:V10<20% Contra: V5<10%	Dmax < 1Gy	CTV: GTV+ 1cm (3mm skin subtraction) PTV: CTV+1cm (allowed 4mm into lung but 3 mm skin subtraction)
B39	PTVeval: V90%>90% Dmax < 120%	V50%<60% V100<35%	Left sided: V5<40% Right sided: V5%<5%	Ipsi: V30%<15% Contra: V5%<15%	Dmax<3%	CTV=GTV+ 15 mm PTV=CTV+10 mm PTVeval = PTV – 5mm from skin
IMPORT-LOW	PTV V95>95%					CTV= GTV + 15mm PTV+ CTV + 10 mm 5mm skin subtraction

DEGRO Guidelines

- Patient selection
- Target definition
- Techniques
- Constraints



1. Coverage index (CI): $V_{100} \geq 90–95\%$ (i.e., at least 90% of the PTV had to receive the PD)
2. $V_{150} < 65\ cm^3$
3. $V_{200} < 15\ cm^3$
4. Absolute volume irradiated by prescription dose—$D_{PD} \leq 300\ cm^3$
5. Dose non-uniformity ratio—DNR ≤35 (only for brachytherapy)
6. Conformal index—COIN ≥65 (only for brachytherapy)
7. Dose homogeneity—maximal dose should not exceed 110% of prescribed dose (only for EBRT)

DEGRO Guidelines

Recommended dose–volume limits for organ at risk. (Modified according [84])

Organ	Constraints
Ipsilateral non-target breast	V_{90} <10%
	V_{50} <40(50)%
Skin	D_{1cm3} <90%
Rib	
Heart	Mean heart dose, MHD <8% (<2.5 Gy)
	$D_{0.1cm3}$ <50%
Lung	Mean lung dose, MLD <8% (<3–4 Gy)
	$D_{0.1cm3}$ <60%
	stochastic effects: MLD <1–1.5 Gy

The recommended schedules with EBRT are:

1. Total dose 40 Gy, 2.66 Gy in 1 fraction/day ~15 fraction over 3 weeks
2. Total dose 38.5 Gy, 3.85 Gy in 1 fraction/day ~10 fraction over 10 days

Tips

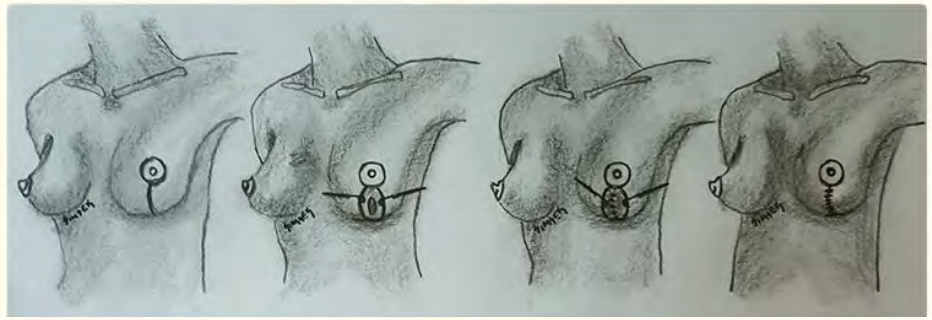
- Discuss with surgeon
  - Likelihood of post-surgical candidacy
  - Request clips
- Degree of oncoplastics

Oncoplastics

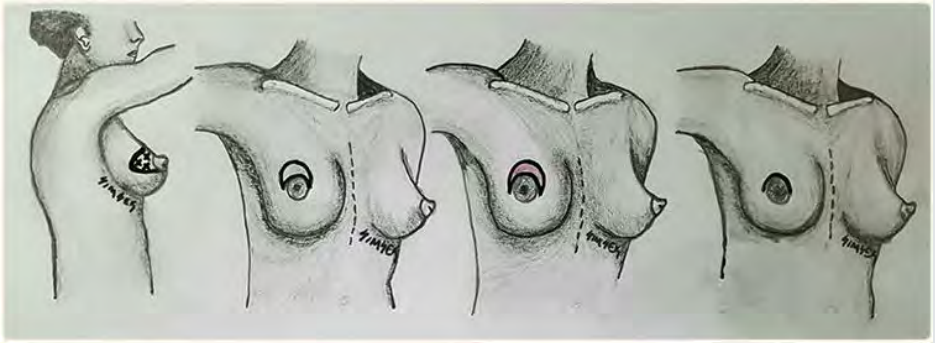
- Level I Oncoplastics: excision of < 20% of Breast
- Level II Oncoplastics: 20-50% of breast

Quadrant per quadrant techniques preferred

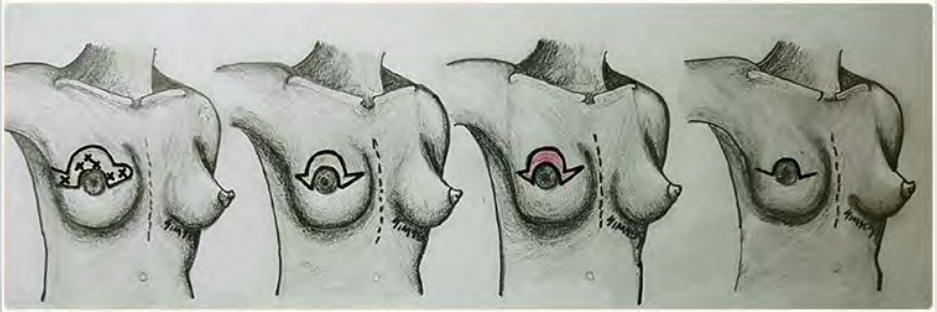
	Size of breast		
Location	**Small**	**Medium**	**Large**
Upper			
• Outer quadrant	Round block	Round block, inferior pedicle reduction	Round block, inferior pedicle reduction
• Middle quadrant	Round block Batwing	Round block, inferior pedicle reduction Batwing	Round block, inferior pedicle reduction
• Inner quadrant	Round block	Round block, inferior pedicle reduction	Round block, inferior pedicle reduction
Lower			
• Outer quadrant	Grisotti	Superior pedicle reduction, Grisotti, J mammoplasty	Superior pedicle reduction, inferior pedicle reduction
• Middle quadrant	Superior pedicle reduction, Grisotti	Superior pedicle reduction, Grisotti, triangular resection	Superior pedicle reduction, Grisotti, triangular resection
• Inner quadrant	Grisotti, triangular resection, inframammarian resection	Superior pedicle reduction, Grisotti, V mammoplasty	Superior pedicle reduction, inferior pedicle reduction, inframammarian resection
Central	Batwing, central, quadranectomy	Grisotti, Batwing, inferior pedicle reduction	Inferior pedicle reduction, inverted T resection, Grisotti



- Level I Oncoplastic

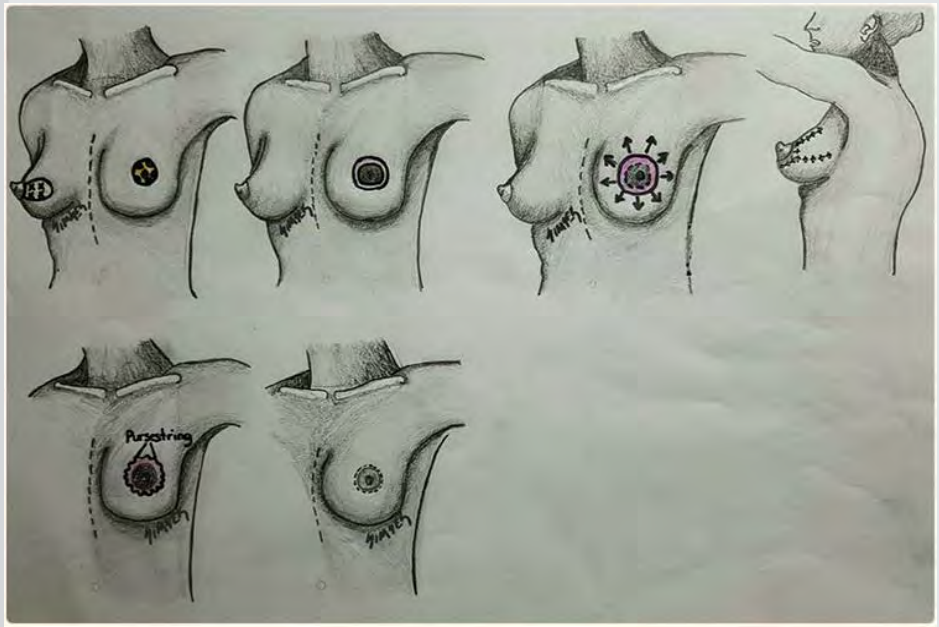


- Crescent Mastopexy

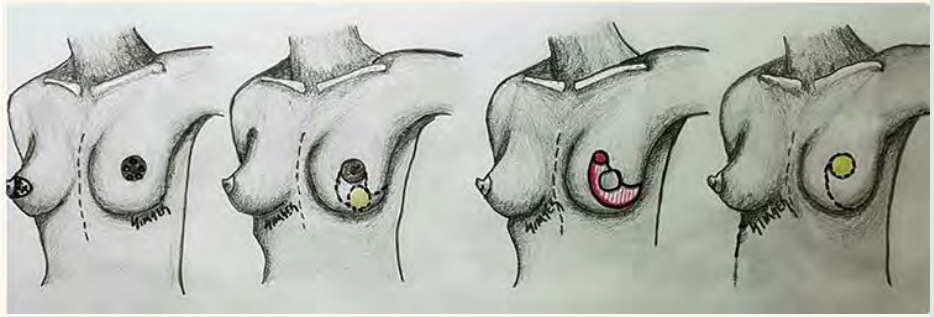


- Batwing Mammoplasty

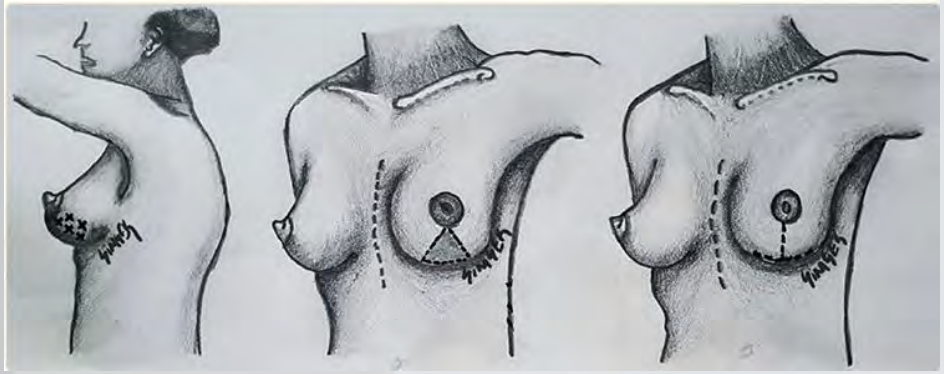
- Hemi-Batwing Mammoplasty



- Donut Mastopexy

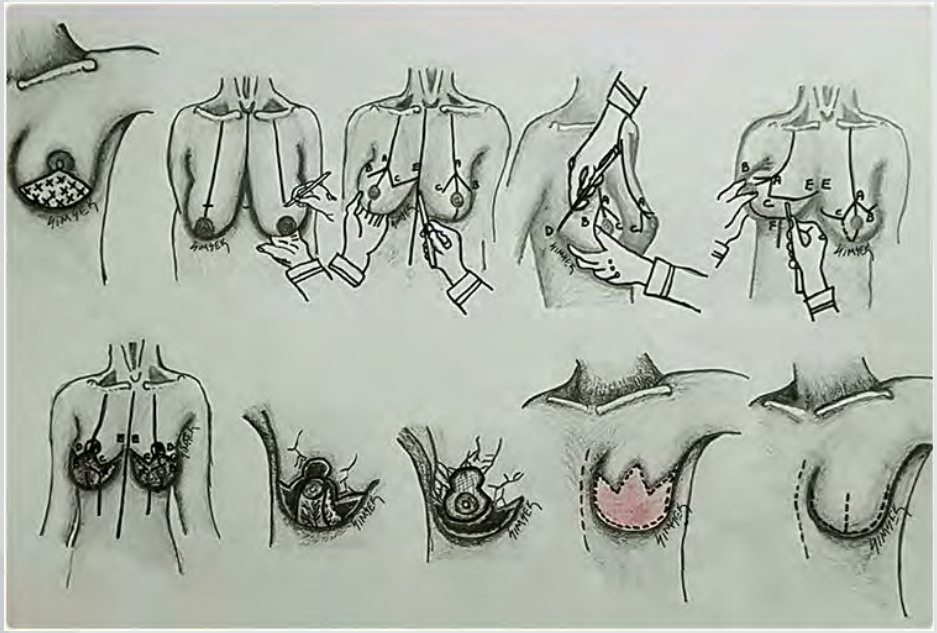


- Grisotti Flap



- Triangular Resection

- Inframmamary Resection



- Reduction Mammoplasty

Tips

- Discuss with surgeon
  - Likelihood of post-surgical candidacy
  - Request clips
- Degree of oncoplastics
- Be upfront with the patient
- Patient Selection

Selection

- Eligible for CALGB: consider omission
- <70, HER2+, luminal B, >2cm but <3 cm
- 45-50y
- TNBC, NAC, >3cm, multifocal

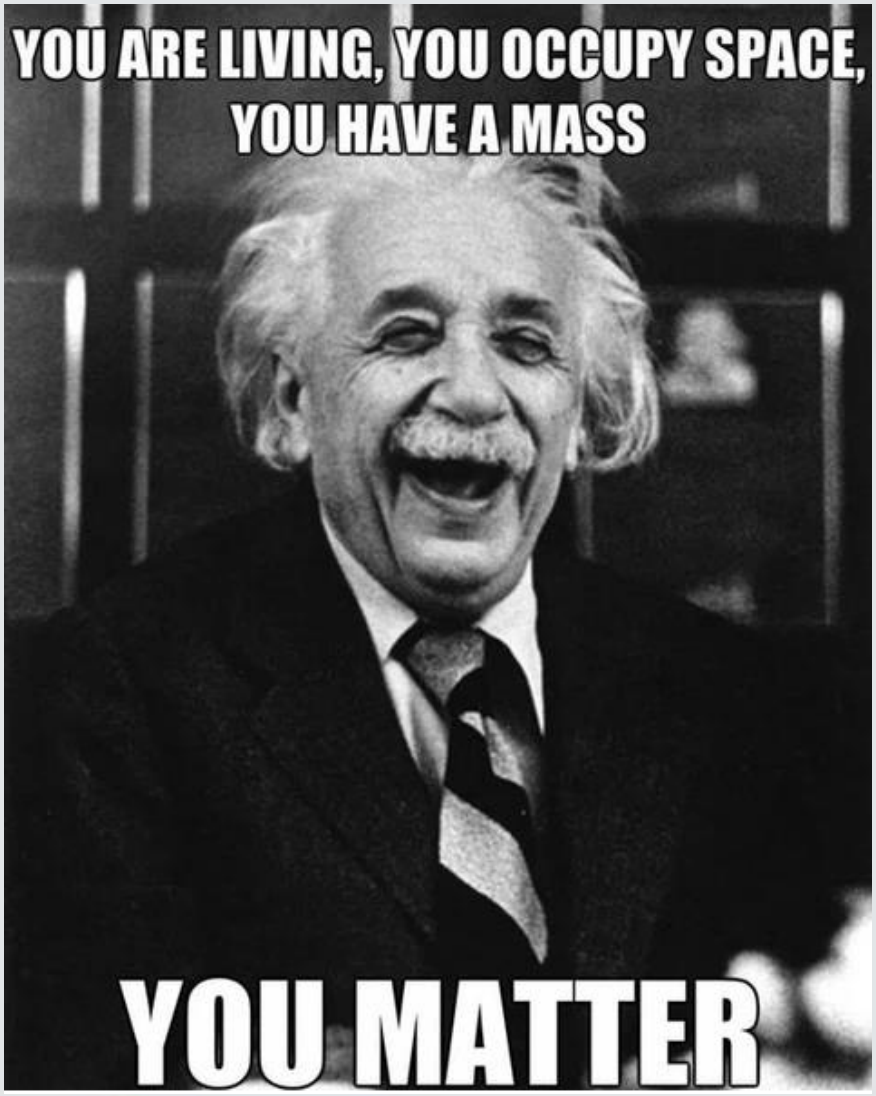
Tips

- Discuss with surgeon
  - Likelihood of post-surgical candidacy
  - Request clips
- Degree of oncoplastics
- Be upfront with the patient
- Patient Selection
- Sim: Supine vs prone, DIBH
- Plan: consider CTV and PTV margins separately in context of GTV confidence, fractionation, patient reliability

Tips Cont'd

- Plan:
  - consider CTV and PTV margins separately in context of GTV confidence, fractionation, patient reliability
  - Consider daily or EOD schemes
  - Subtraction for skin is for eval
  - Consider heart mean dose and LAD
- Treatment:
  - CBCT
  - Contour clips

Thank You



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