# Post-mastectomy Radiation in the setting of Breast Reconstruction

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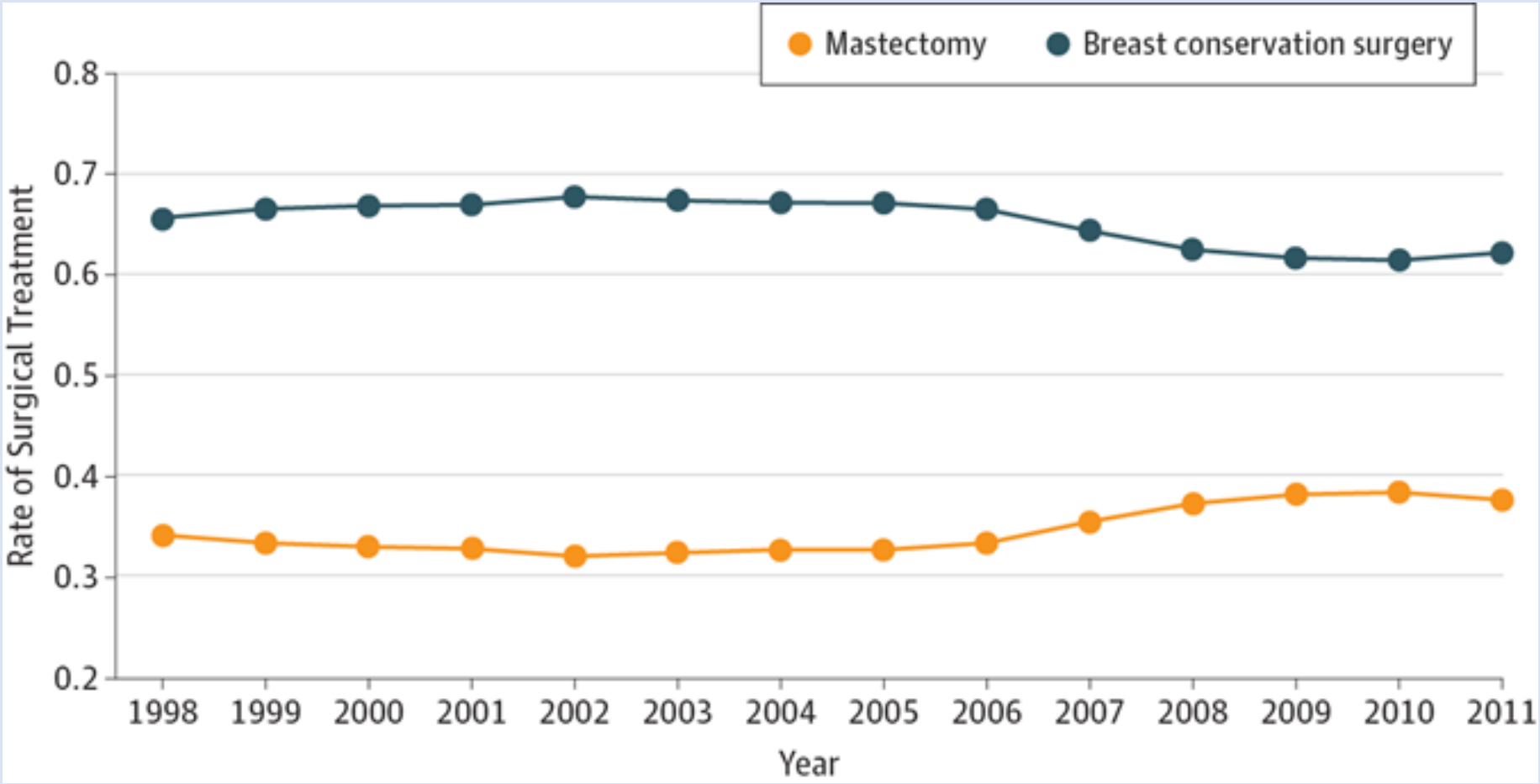
- No conflicts of interest to disclose

# Surgical trends in women with early breast cancer




Temporal Trends in Surgical Treatment of Early Breast CancerProportion of women with early breast cancer who underwent mastectomy (orange line) and breast conservation surgery (blue line) by year of diagnosis in the National Cancer Data Base. All trends are significant (P < .001).

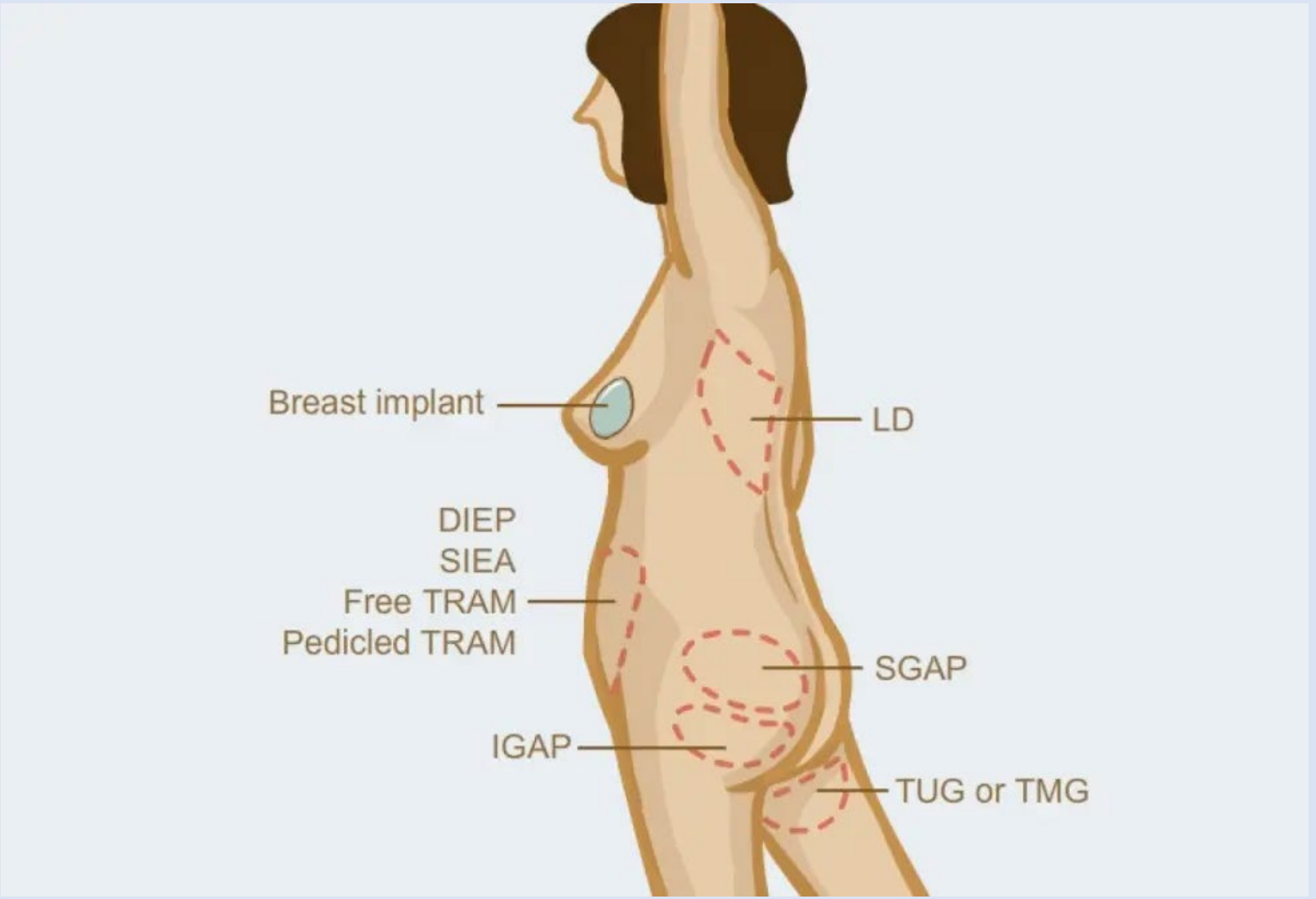
JAMA Surg. 2015;150(1):9-16. doi:10.1001/jamasurg.2014.2895

# Angelina Jolie Effect

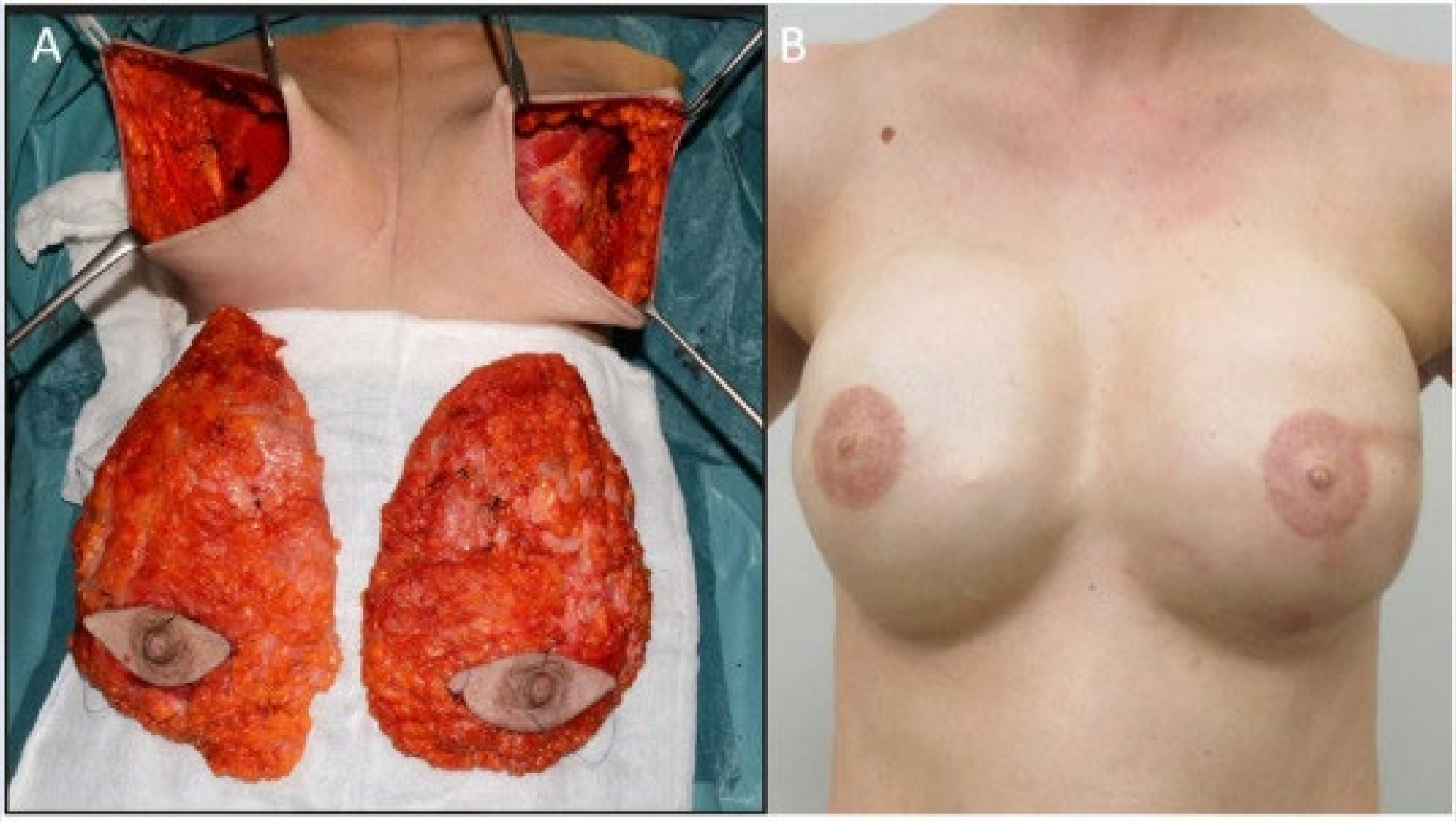
- There was an increase in testing for BRCA1/2 mutations after revelation that she had undergone a prophylactic mastectomy after finding out she was a carrier
- Jolie's announcement was published on May 14, 2013 in NY Times
- Subsequent increase in number of women with BRCA mutations undergoing prophylactic mastectomy—she increased awareness and reduced the stigma associated with the risk reducing surgery


# Breast reconstruction

- As of 2016, 40% of women who underwent mastectomy had reconstruction
- Implant based reconstruction accounts for majority (80%) of breast reconstructions
- Autologous reconstruction most commonly involves tissue from the abdomen (TRAM or DIEP flap)or back (latissimus dorsi)



# Bilateral SSM with nipple reconstruction



# Post-mastectomy radiation indications

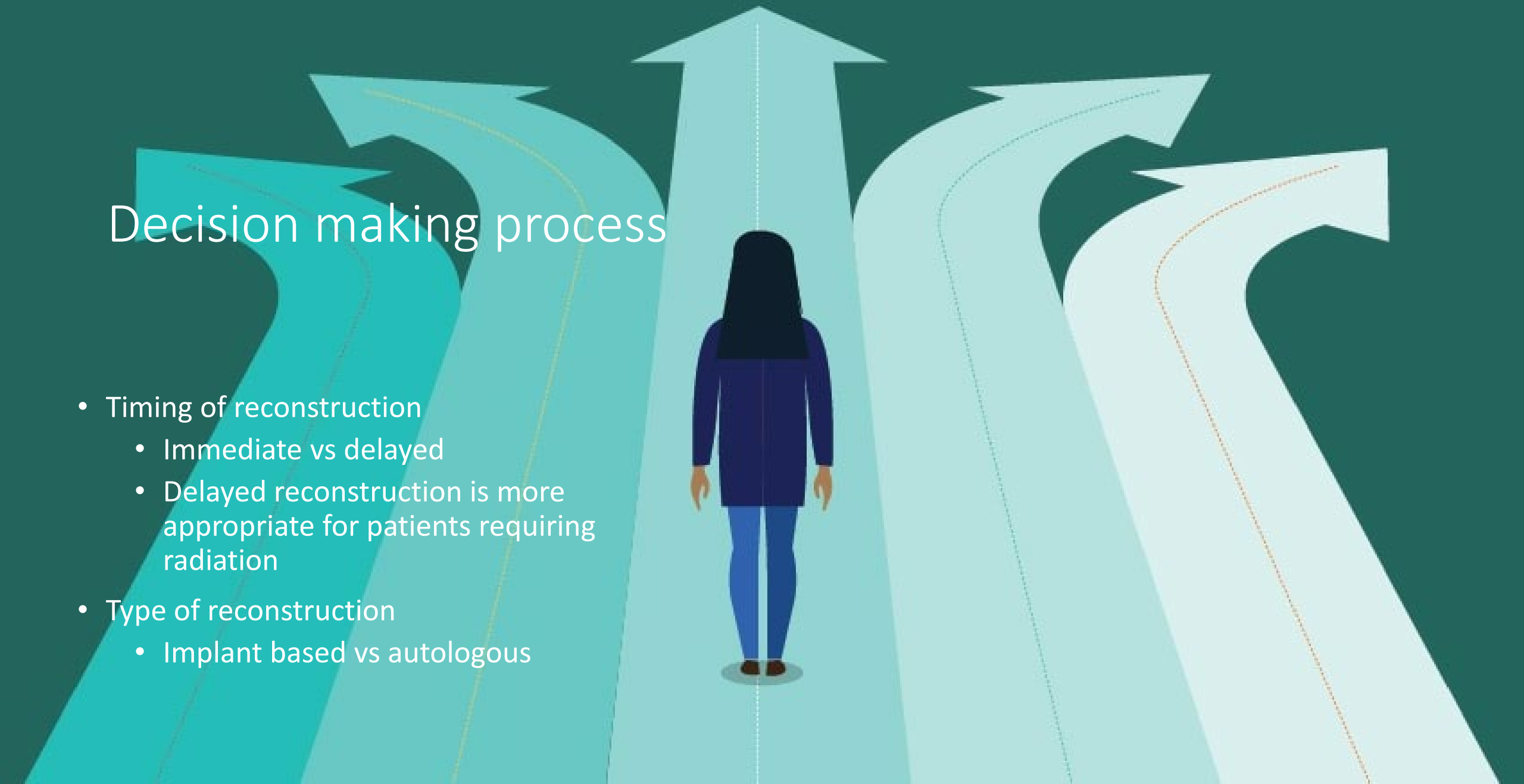
**High risk**

- T3/4, N2

**Intermediate risk**

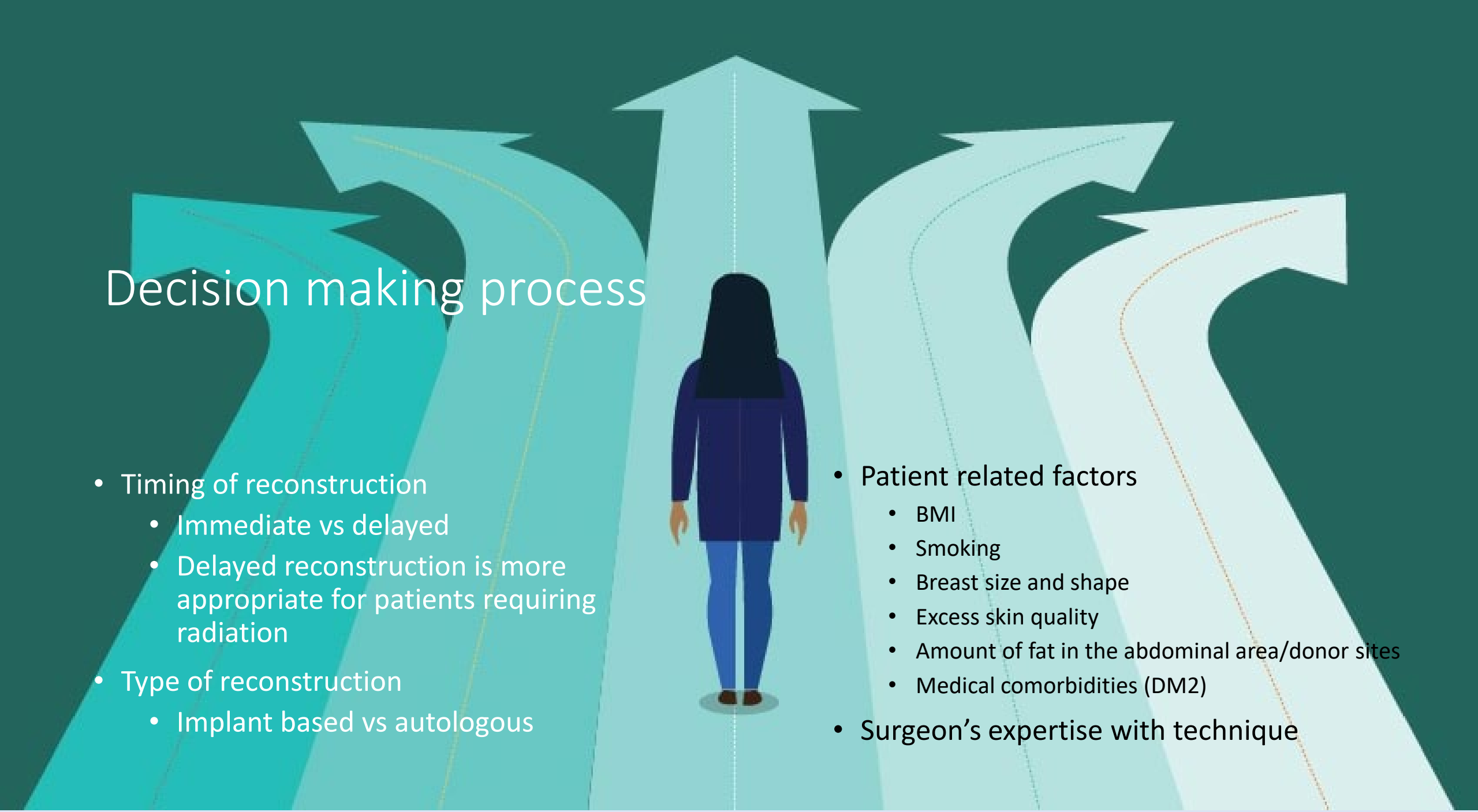
- T1/2N1 or T3N0
- Axillary radiation being offered in lieu of ALND in cN0 with positive sentinel node
  - AMAROS
  - Z0011
- Benefit to RT in N1
  - MA20, EORTC 22922-10925
  - EBCTG meta-analysis

# Decision making process



- Timing of reconstruction
  - Immediate vs delayed
  - Delayed reconstruction is more appropriate for patients requiring radiation
- Type of reconstruction
  - Implant based vs autologous

# Decision making process



- Timing of reconstruction
  - Immediate vs delayed
  - Delayed reconstruction is more appropriate for patients requiring radiation
- Type of reconstruction
  - Implant based vs autologous

- Patient related factors
  - BMI
  - Smoking
  - Breast size and shape
  - Excess skin quality
  - Amount of fat in the abdominal area/donor sites
  - Medical comorbidities (DM2)
- Surgeon’s expertise with technique

# Immediate reconstruction

**Pros**

- Awaken with reconstructed breast →less distress and better psychosocial well-being
- Avoid external prosthesis
- Preserve native skin envelope
- Smaller scars
- Fewer procedures under anesthesia

**Cons**

- Final pathology not available
- May introduce technical challenges with RT treatment planning
- Complications may delay the start of radiation

# Immediate implant-based reconstruction

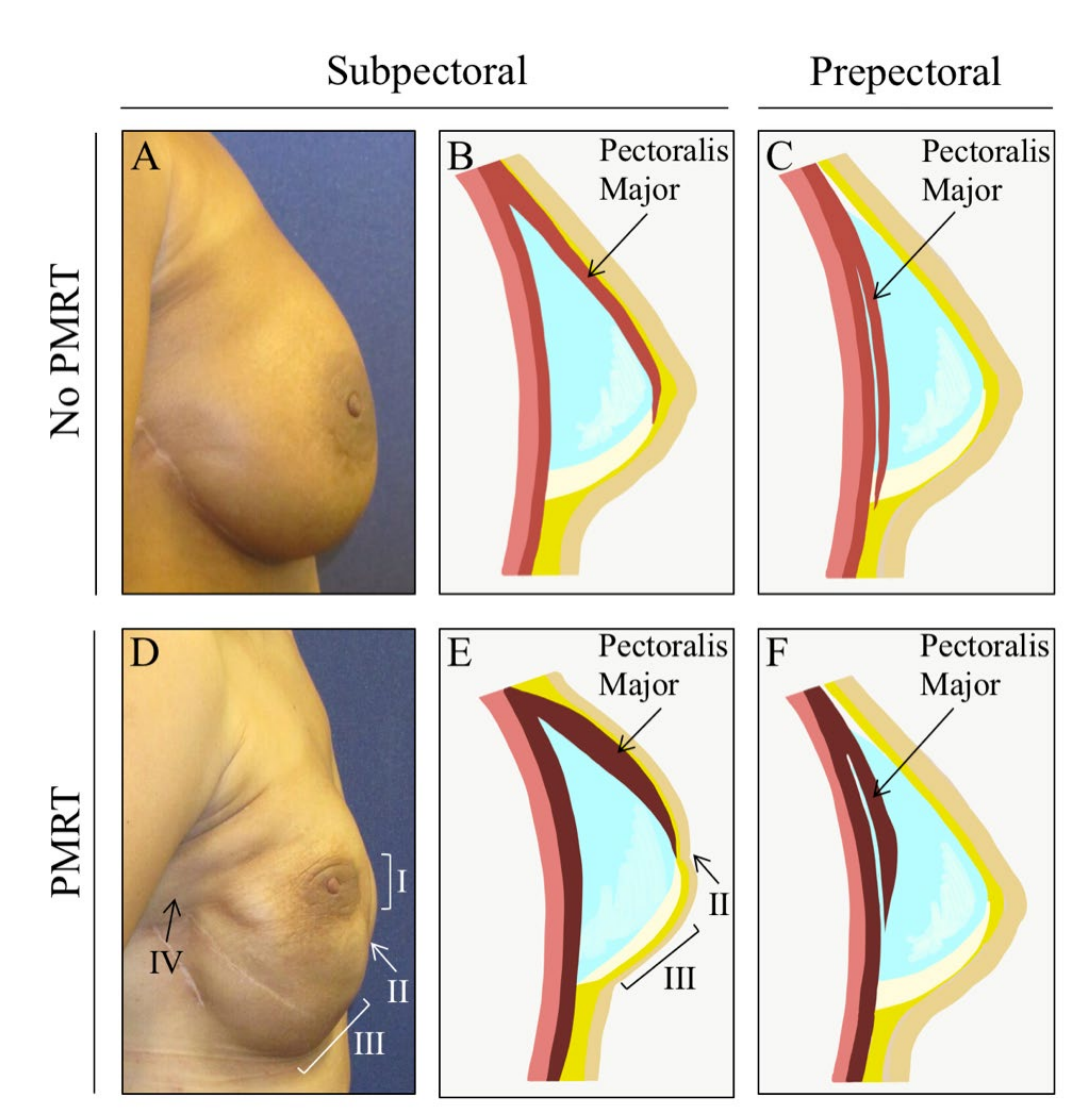
**Pros**

- Most cost effective in the short term
- Best aesthetic outcome if radiation is not involved
- Single procedure

**Cons**

- Higher risk of complications compared to autologous
- Complications: capsular contracture most common with PMRT
- Lymph node dissection associated with increased risk of implant loss

# Capsular contracture




- Skeletal muscle fibrosis results in (I) superolateral displacement of NAC (II) dimpling or creasing of the soft tissue at the level of pec major muscle (III)flattening of inferior pole projection (IV) axillary fold crease
- Results in pain, poor cosmesis and reoperations

# Immediate autologous reconstruction

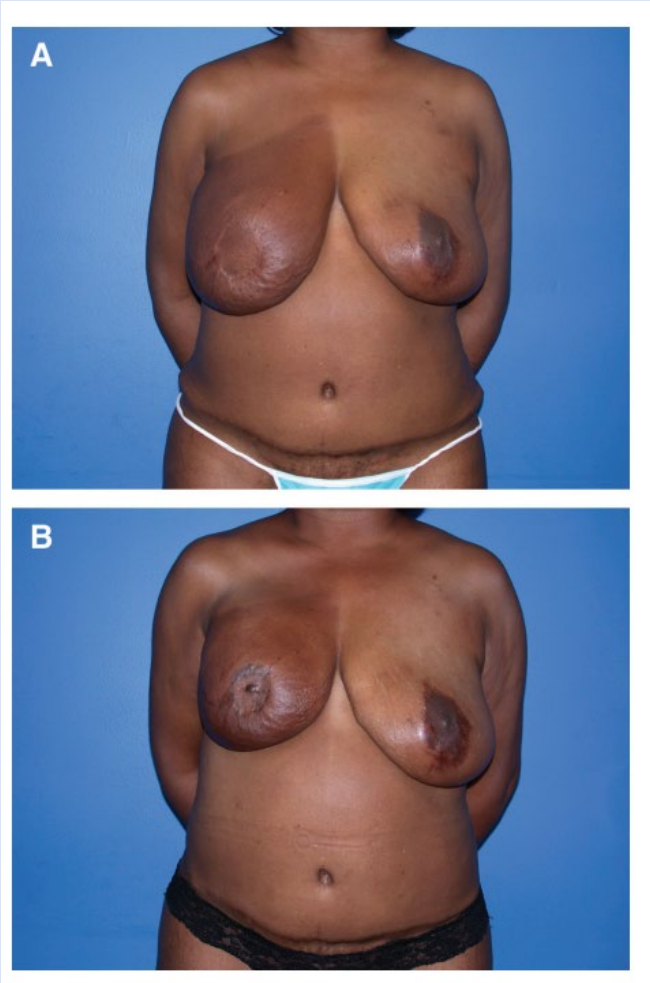
**Pros**

- More cost-effective long term
- Fewer complications in setting of PMRT when compared to implant based
- Better cosmesis when compared to implant
- Better skin sensation recovery after PMRT

**Cons**

- Initially more expensive
- Scarring across donor site
- Complications: PMRT can result in wound contracture, volume loss, and fat necrosis

# Immediate autologous breast reconstruction




Immediate reconstruction of right breast with free muscle-sparing TRAM flap, 3 months post radiation

The late effects of radiation have made the right breast smaller, more firm and fibrotic, less ptotic, and asymmetric compared to the left breast

Chevray, P. M. (2008). Timing of Breast Reconstruction: Immediate versus Delayed. *The Cancer Journal, 14* (4), 223-229. doi: 10.1097/PPO.0b013e3181824e37.

# Delayed reconstruction

**Pros**

- Simplify RT treatment planning
- Minimize the incidence of autologous flap fibrosis
- Minimize the incidence of mastectomy flap necrosis

**Cons**

- Temporary loss of breast →lower patient reported satisfaction, psychosocial, and sexual well-being
- Requires autologous tissue
- Second operation required
- Greater technical difficulty to operate of radiated tissues/vessels

# Delayed autologous reconstruction

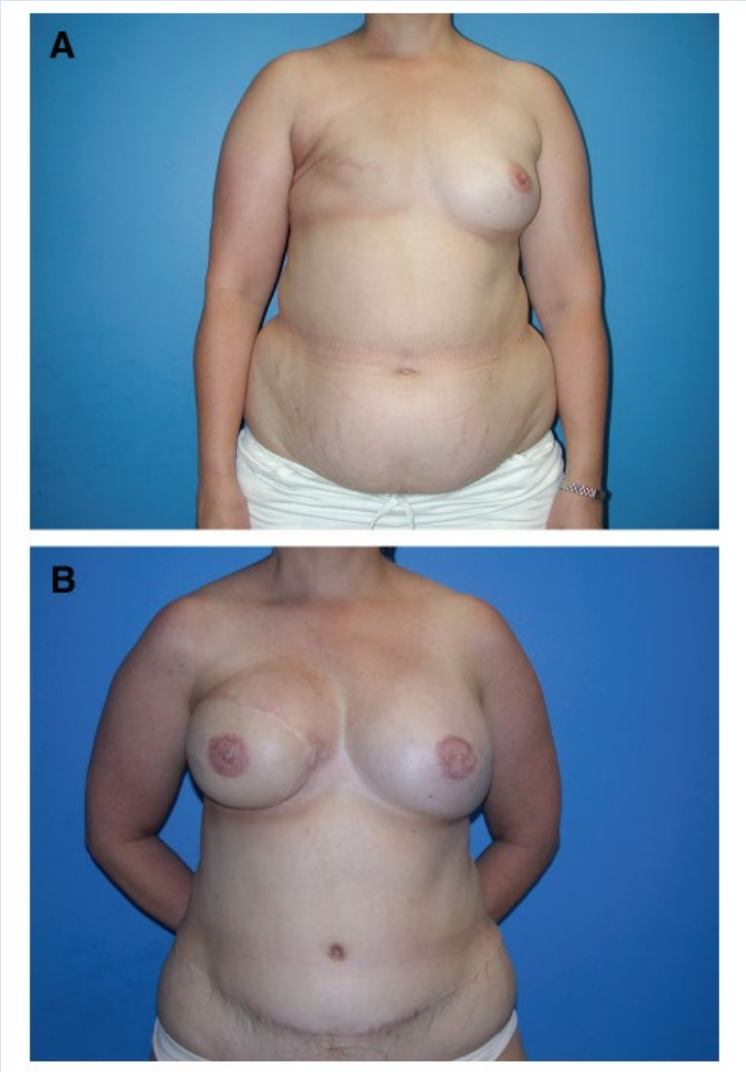
**Pros**

- Less wound contracture, volume loss, fat necrosis, and revision surgeries compared to immediate autologous

**Cons**

- Initially, more expensive
- Two procedures
- Ideal time from PMRT to reconstruction is unknown

# Delayed autologous breast reconstruction




- Pt s/p right mastectomy and radiation
- Inadequate skin surface to envelope a reconstructed breast
- Delayed right breast reconstruction and immediate left breast reconstruction with bilateral DIEP flaps (21 months post-op)

Chevray, P. M. (2008). Timing of Breast Reconstruction: Immediate versus Delayed. *The Cancer Journal, 14* (4), 223-229. doi: 10.1097/PPO.0b013e3181824e37.

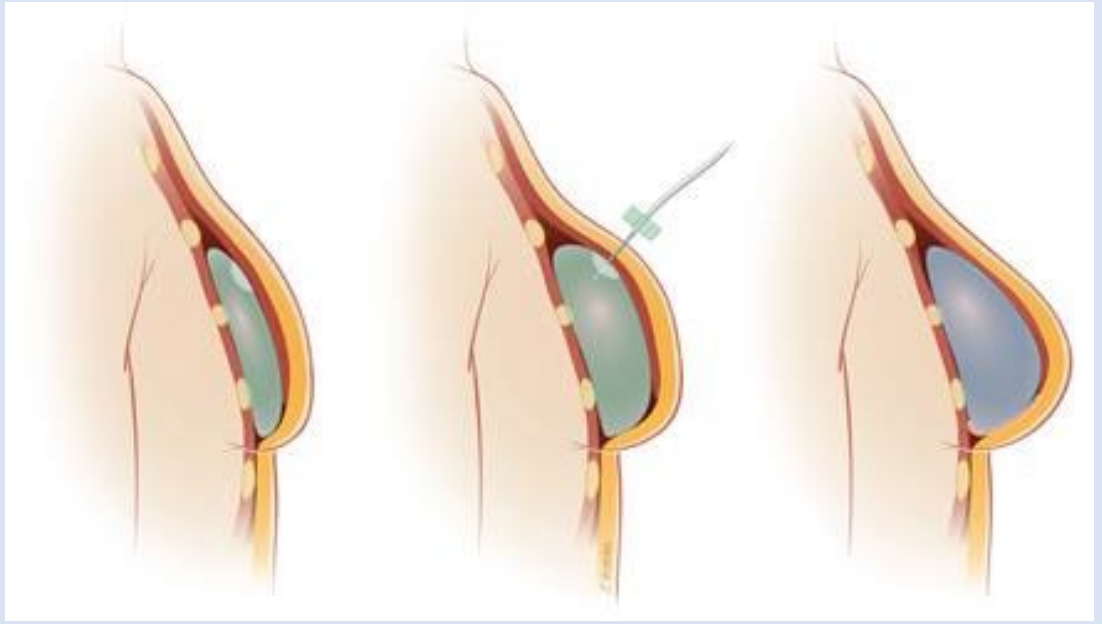
# Delayed Expander Implant reconstruction

**Pros**

- Allows more time for patients to choose between an implant replacement or autologous reconstruction
- Ability to revise any asymmetries or radiation effects at the time of tissue expander removal

**Cons**

- Long term expander use associated with rupture



# MROC Study: Mastectomy Reconstruction Outcomes Consortium

- Prospective observational study of 2247 women who underwent various forms of reconstruction
  - 622 irradiated patients
  - 1625 unirradiated
- 11 different centers
- 5 plastic surgeons
- Treated between 2012-2015

Jagsi, JNCI (2018) 110(2)

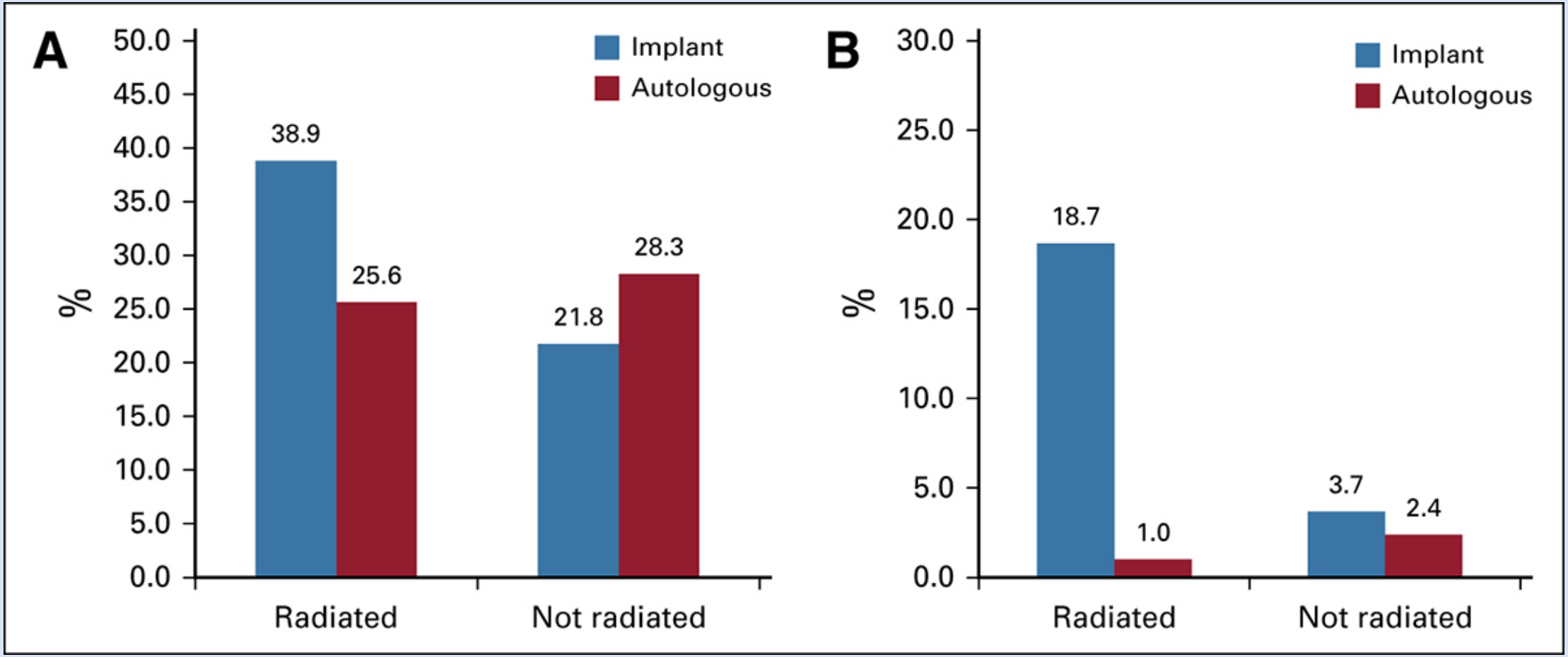
# MROC Study: Mastectomy Reconstruction Outcomes Consortium

- Measured outcomes
  - Breast complications
    - Hematoma, wound infection, wound dehiscence, flap necrosis, flap loss, capsular contracture, implant malposition, implant leakage, seroma
    - “major complication” defined as requiring hospitalization or re-operation
  - Reconstruction failure
  - 4 patient reported outcomes
    - Satisfaction with breasts
    - Satisfaction with outcome
    - Psychosocial well-being
    - Physical well-being

Jagsi, JNCI (2018) 110(2)

# MROC – Mastectomy Reconstruction Outcomes Consortium

Incidence of (A) any breast complication (B) reconstruction failure after 2 years

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# Postoperative Complication by RT status and Procedure type

| Complication | One year post-op, No. (%) | | | | Two years post-op*, No. (%) | | | |
|---|---|---|---|---|---|---|---|---|
| | Radiated | | Not radiated | | Radiated | | Not radiated | |
| | Implant | Autologous | Implant | Autologous | Implant | Autologous | Implant | Autologous |
| No. patients | 386 | 236 | 1218 | 407 | 283 | 199 | 964 | 332 |
| Hematoma | 17 (4.4) | 9 (3.8) | 42 (3.4) | 27 (6.6) | 12 (4.2) | 8 (4.0) | 35 (3.6) | 21 (6.3) |
| Wound dehiscence | 11 (2.8) | 12 (5.1) | 12 (1.0) | 8 (2.0) | 21 (7.4) | 11 (5.5) | 10 (1.0) | 8 (2.4) |
| Wound infection requiring oral antibiotics | 18 (4.7) | 4 (1.7) | 44 (3.6) | 7 (1.7) | 20 (7.1) | 3 (1.5) | 48 (5.0) | 5 (1.5) |
| Wound infection requiring IV antibiotics | 30 (7.8) | 5 (2.1) | 43 (3.5) | 3 (0.7) | 25 (8.8) | 3 (1.5) | 36 (3.7) | 3 (0.9) |
| Wound infection requiring surgical repair | 7 (1.8) | 5 (2.1) | 10 (0.8) | 4 (1.0) | 7 (2.5) | 3 (1.5) | 6 (0.6) | 3 (0.9) |
| Mastectomy skin flap necrosis | 28 (7.3) | 16 (6.8) | 76 (6.2) | 32 (7.9) | 19 (6.7) | 15 (7.5) | 52 (5.4) | 25 (7.5) |
| Acute partial flap necrosis | - | 6 (2.5) | - | 19 (4.7) | - | 5 (2.5) | - | 12 (3.6) |
| Total flap loss | - | 1 (0.4) | - | 8 (2.0) | - | 1 (0.5) | - | 6 (1.8) |
| Chronic fat necrosis | - | 11 (4.7) | - | 33 (8.1) | - | 14 (7.0) | - | 29 (8.7) |
| Capsular contracture | 6 (1.6) | - | 6 (0.5) | - | 15 (5.3) | - | 10 (1.0) | - |
| Implant malposition | 0 (0.0) | - | 9 (0.7) | - | 3 (1.1) | - | 8 (0.8) | - |
| Seroma | 20 (5.2) | 2 (0.8) | 27 (2.2) | 7 (1.7) | 14 (4.9) | 2 (1.0) | 20 (2.1) | 5 (1.5) |
| Implant leakeage, rupture and/or deflation | 7 (1.8) | - | 12 (1.0) | - | 6 (2.1) | - | 12 (1.2) | - |

* Complication rates are cumulative for the entire two year postoperative period.

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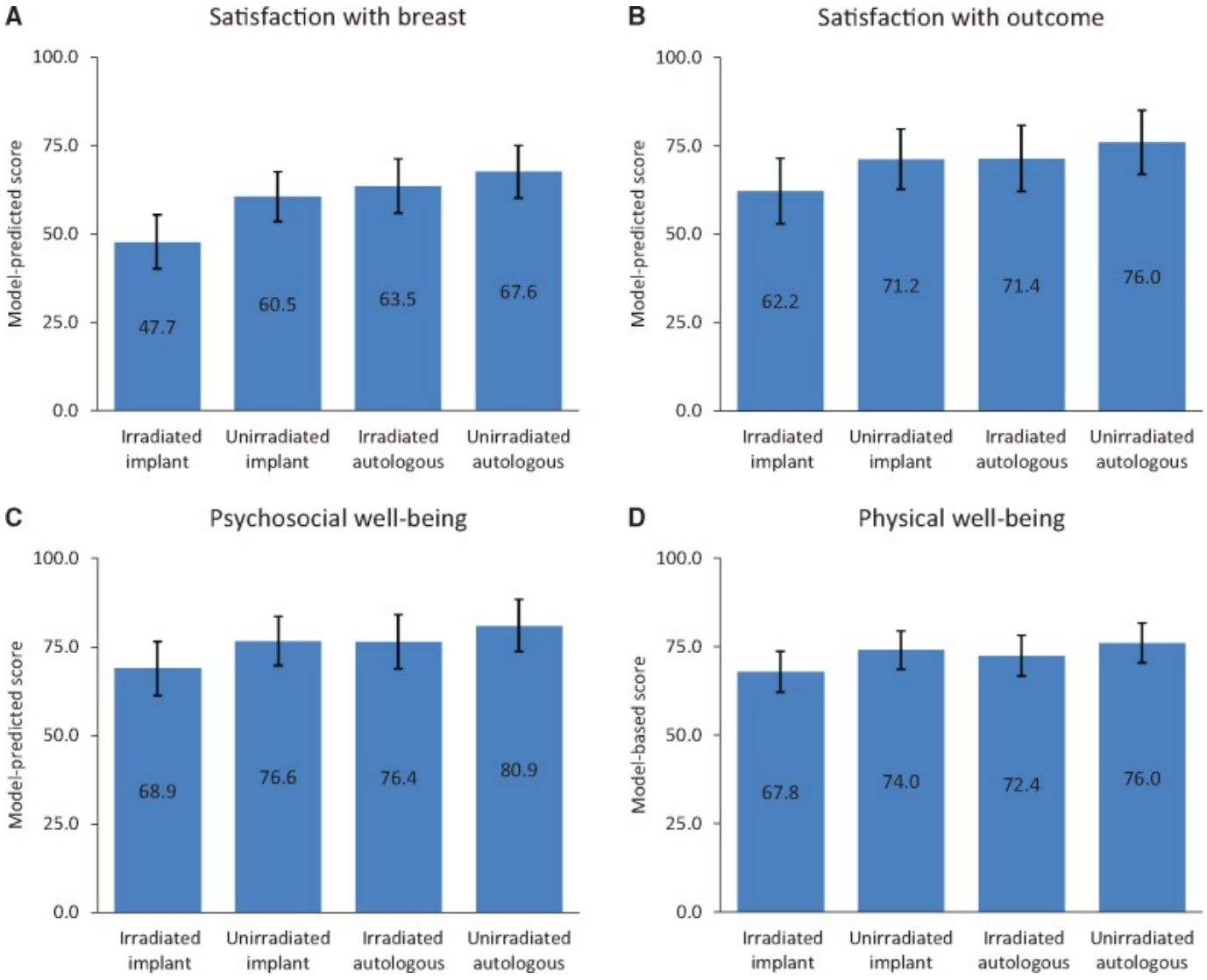
# MROC: Patient reported outcomes

- Model-predicted scores for BREAST-Q domains
- Results for women who had not experienced reconstruction failure




Jagsi, JNCI (2018) 110(2)

# MROC Study: Mastectomy Reconstruction Outcomes Consortium

- RT increased complications in patients undergoing implant reconstruction but not autologous reconstruction
- At 2 years, major breast complications
  - 33.2% of irradiated implant
  - 17.6% of irradiated autologous
  - 15.6% of no RT implant
  - 22.9% of no RT autologous
- Rates of reconstruction failure at 2 years
  - 18.7% irradiated implant
  - 1% irradiated autologous
  - 3.7% no RT implant
  - 2.4% no RT autologous

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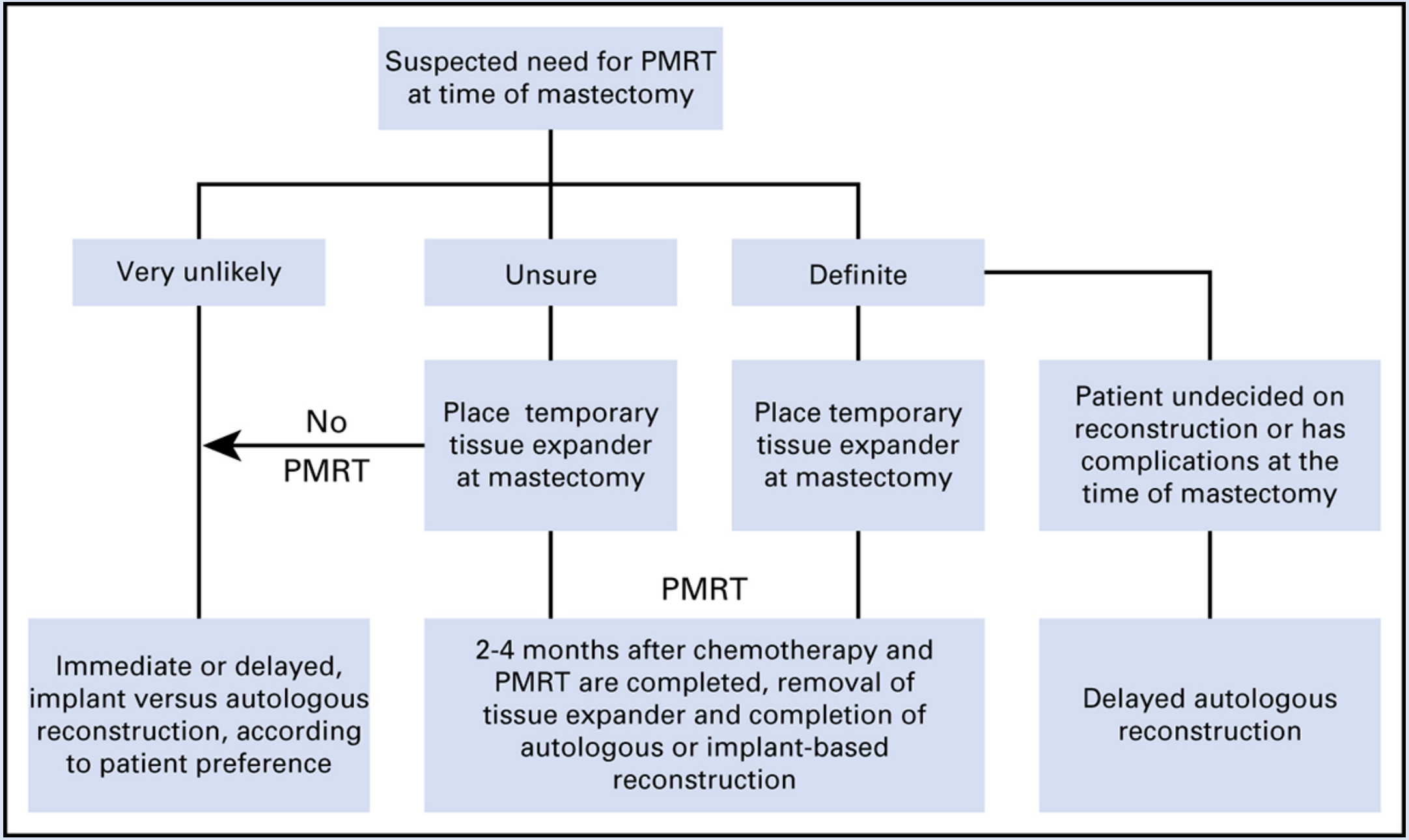



Poppe, M. M. & Agarwal, J. P. (2017). *Journal of Clinical Oncology*, *35* (22), 2467-2470. doi: 10.1200/JCO.2017.72.7388.

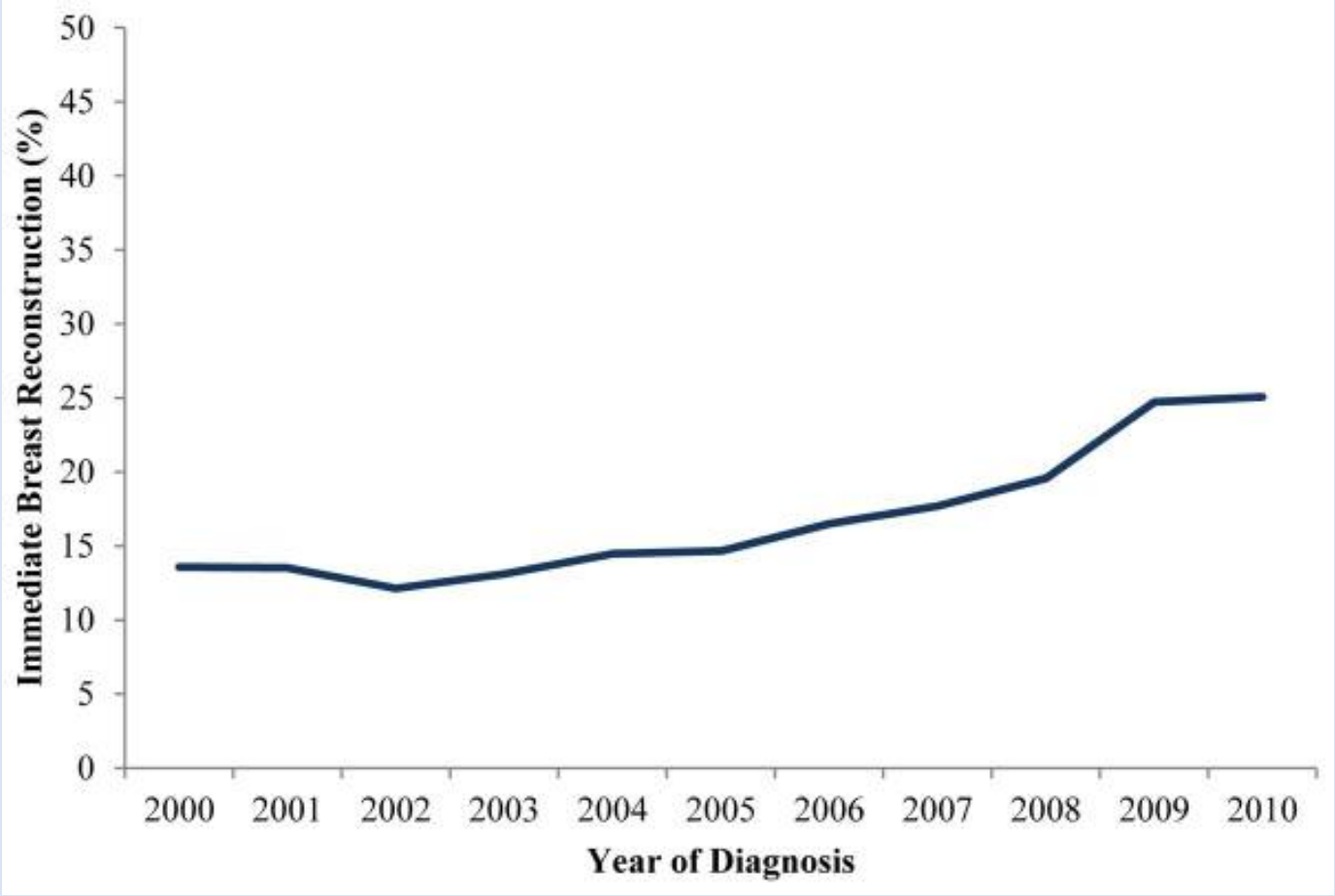
# Immediate Breast Reconstruction Rate in patients requiring radiation

SEER database study 2000-2010

Included 5,481 women who underwent RT and reconstruction

Captures information on breast reconstruction up to 4 months after initial mastectomy

**Immediate implant-based reconstruction has increased among patients requiring PMRT**



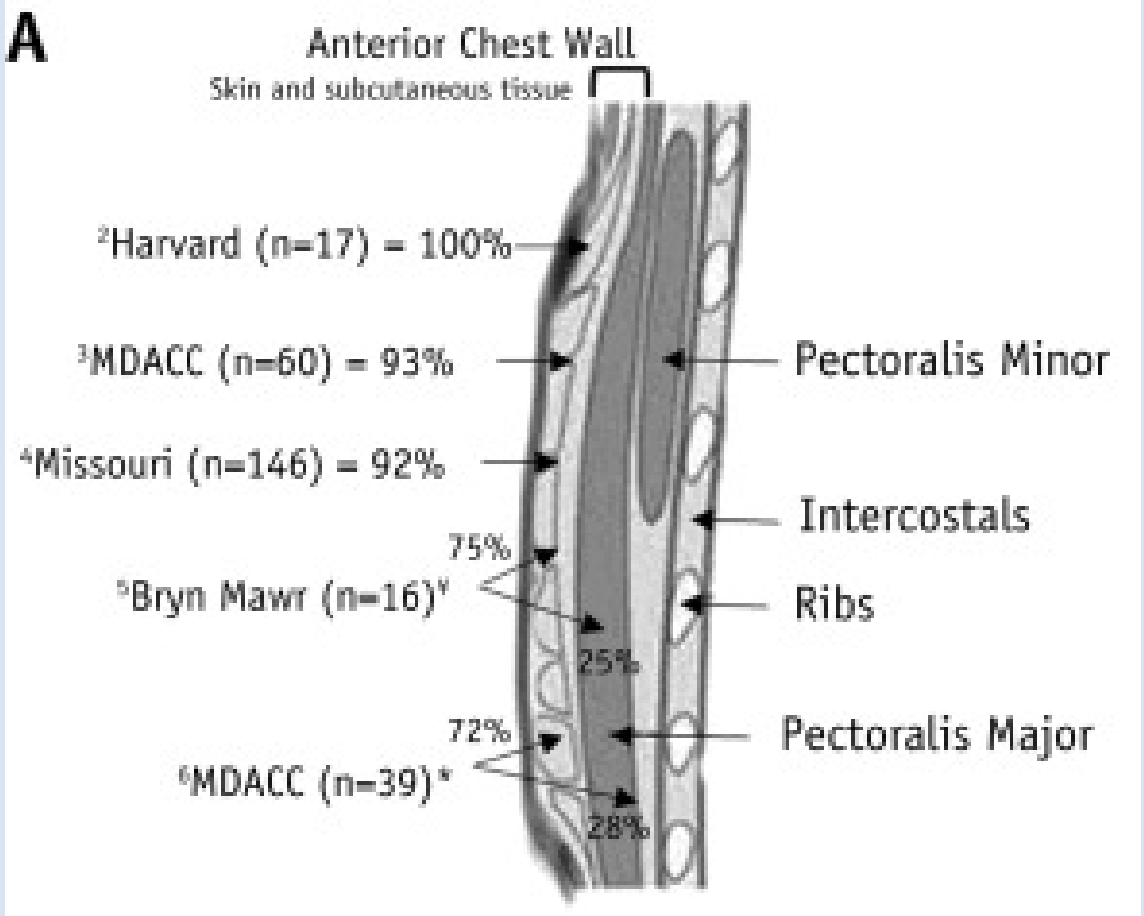

Agarwal. Ann Surg Oncol. 2015 Aug

# PMRT Treatment planning

- Target volume
- Techniques
- Dose fractionation
- Use of bolus

# Patterns of failure

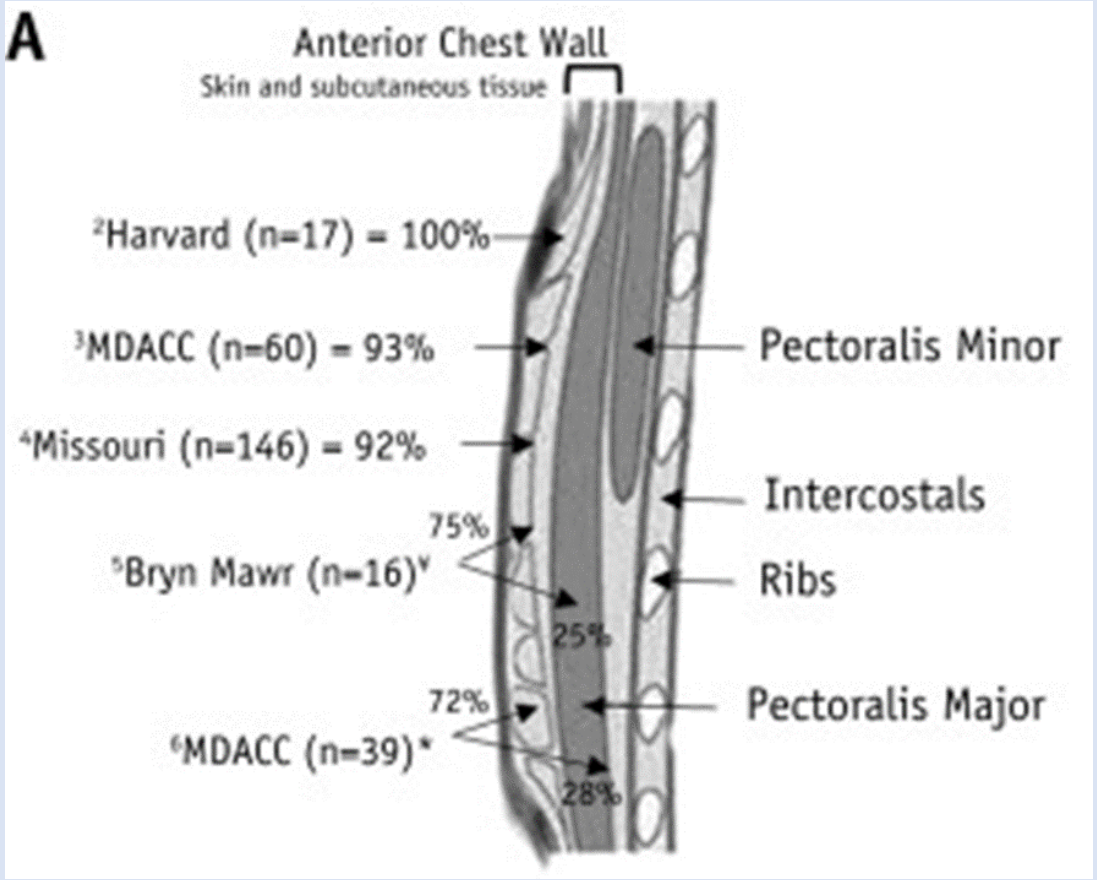
- Most recurrences (72-100%) occur in the skin/subcutaneous tissue
- 2nd most common site is within the pectoralis major
- Few occur posterior to the pectoralis major (deep chest wall)



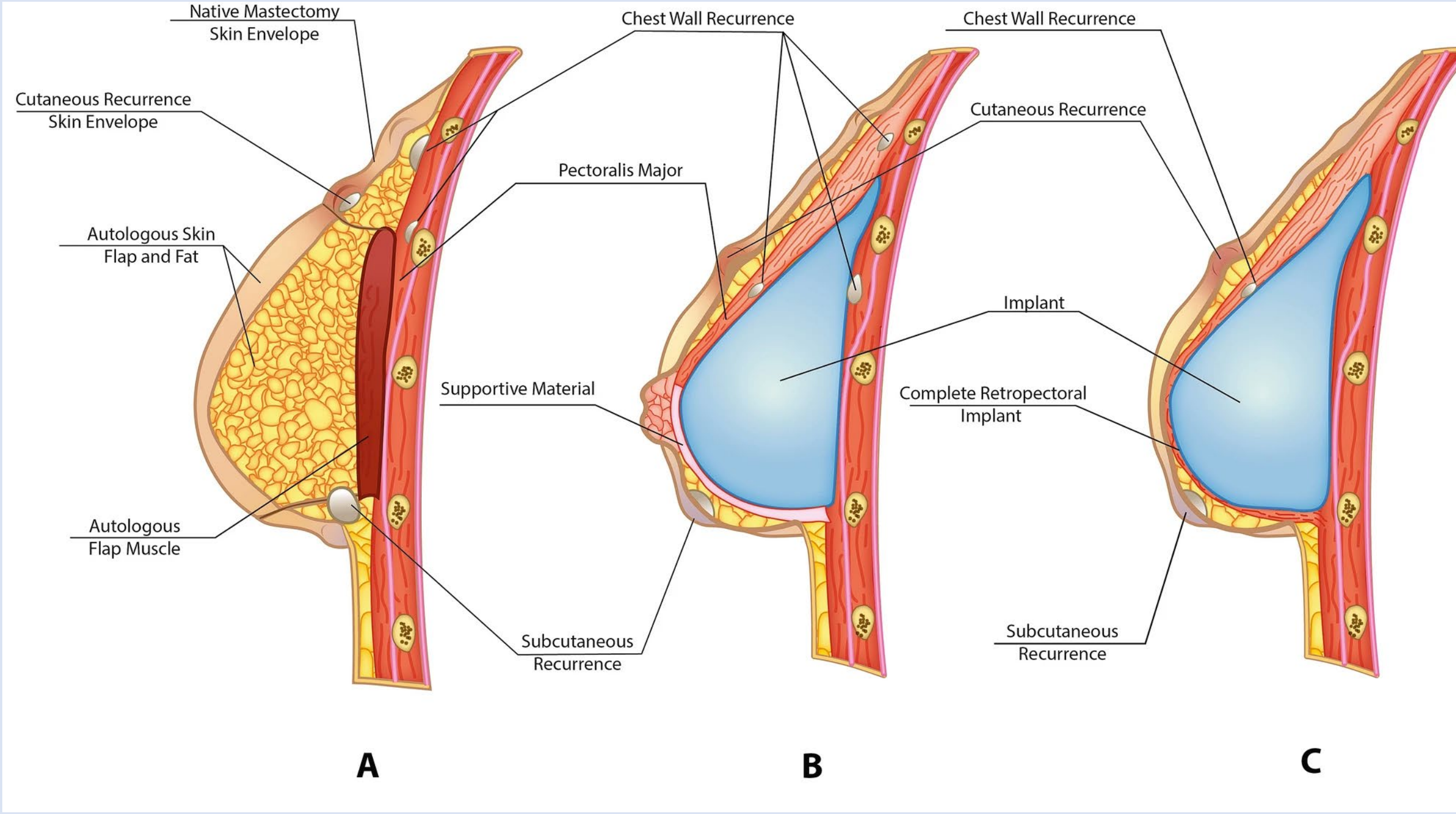

Vargo et al., IJROBP 2015

# Patterns of failure

- Exclusion of the deep chest wall from the radiation field may reduce implant failure, capsular contracture, cardiac and lung toxicity

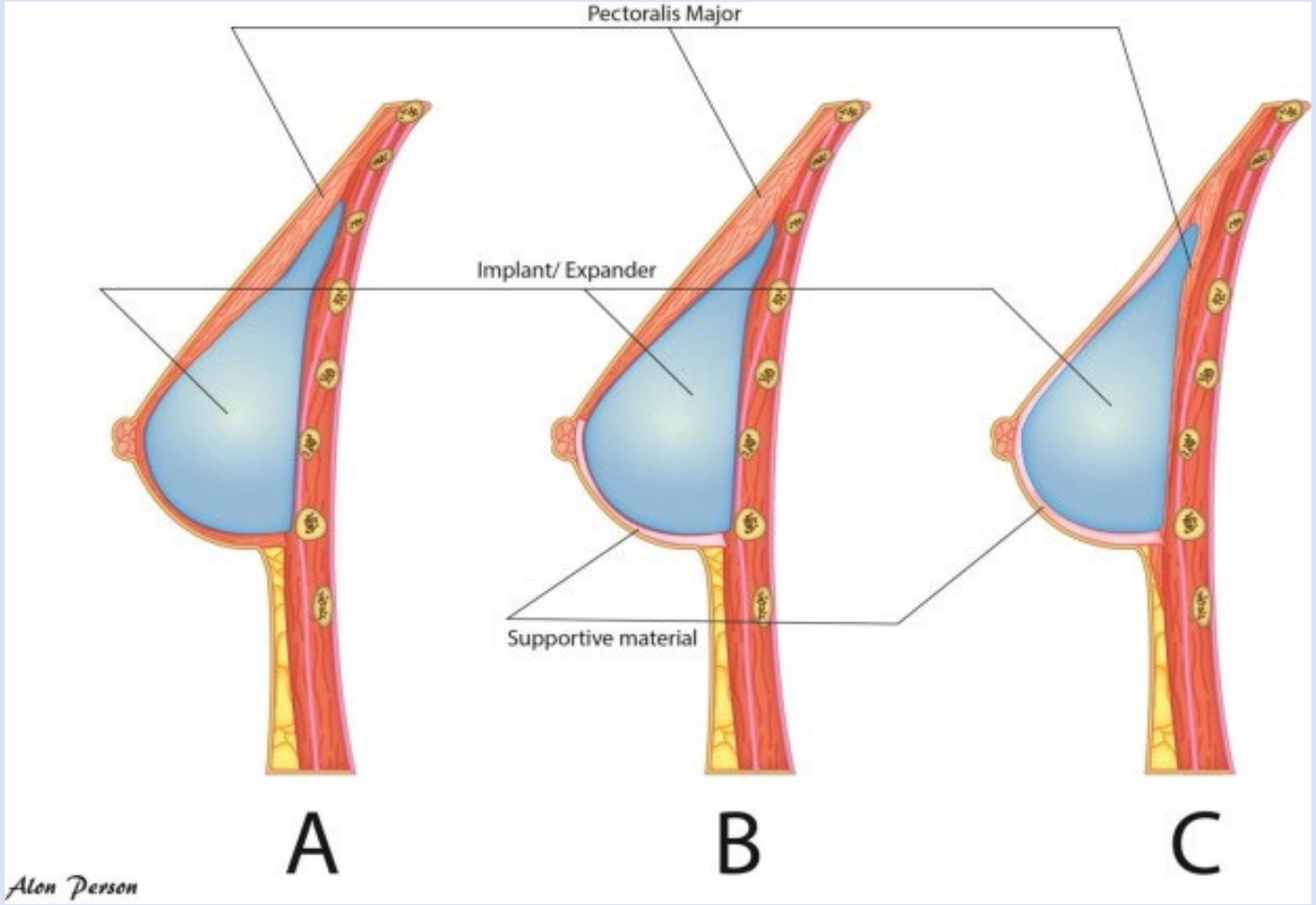


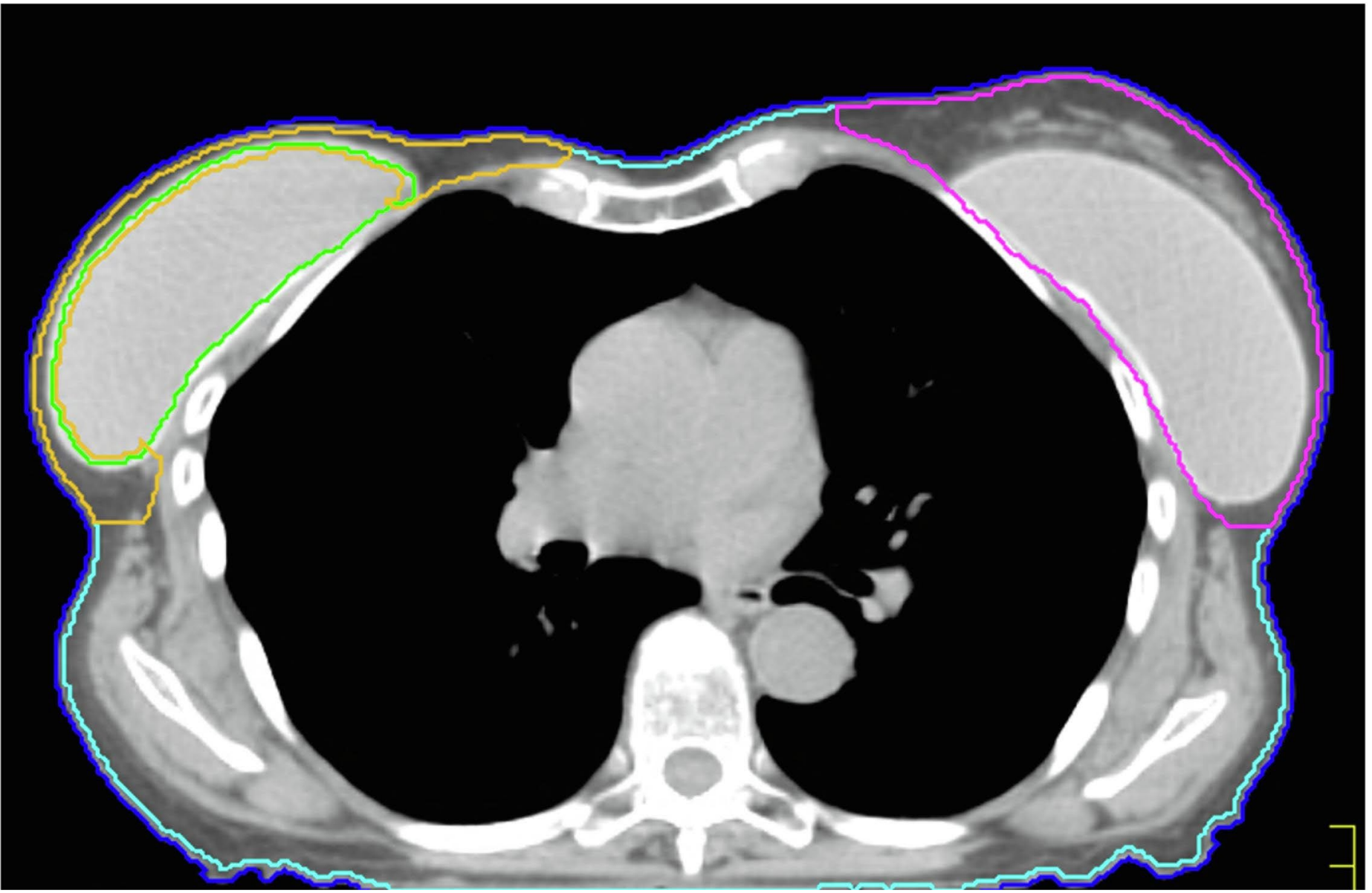

Vargo et al., IJROBP 2015


Native Mastectomy Skin Envelope
Cutaneous Recurrence Skin Envelope
Autologous Skin Flap and Fat
Autologous Flap Muscle
Chest Wall Recurrence
Pectoralis Major
Supportive Material
Subcutaneous Recurrence
Chest Wall Recurrence
Cutaneous Recurrence
Implant
Complete Retropectoral Implant
Subcutaneous Recurrence
A
B
C

# ESTRO Guidelines for implant-based reconstruction

- Typically, implants are placed anterior to the pectoralis minor and posterior to the pectoralis major
- Implant positioning. (A) retropectoral with full coverage by the pectoral muscle; (B) retro-pectoral with partial coverage by the pectoral muscle and supportive material in the lower part; (C) pre-pectoral with full coverage by supportive material.





Proposed CTV

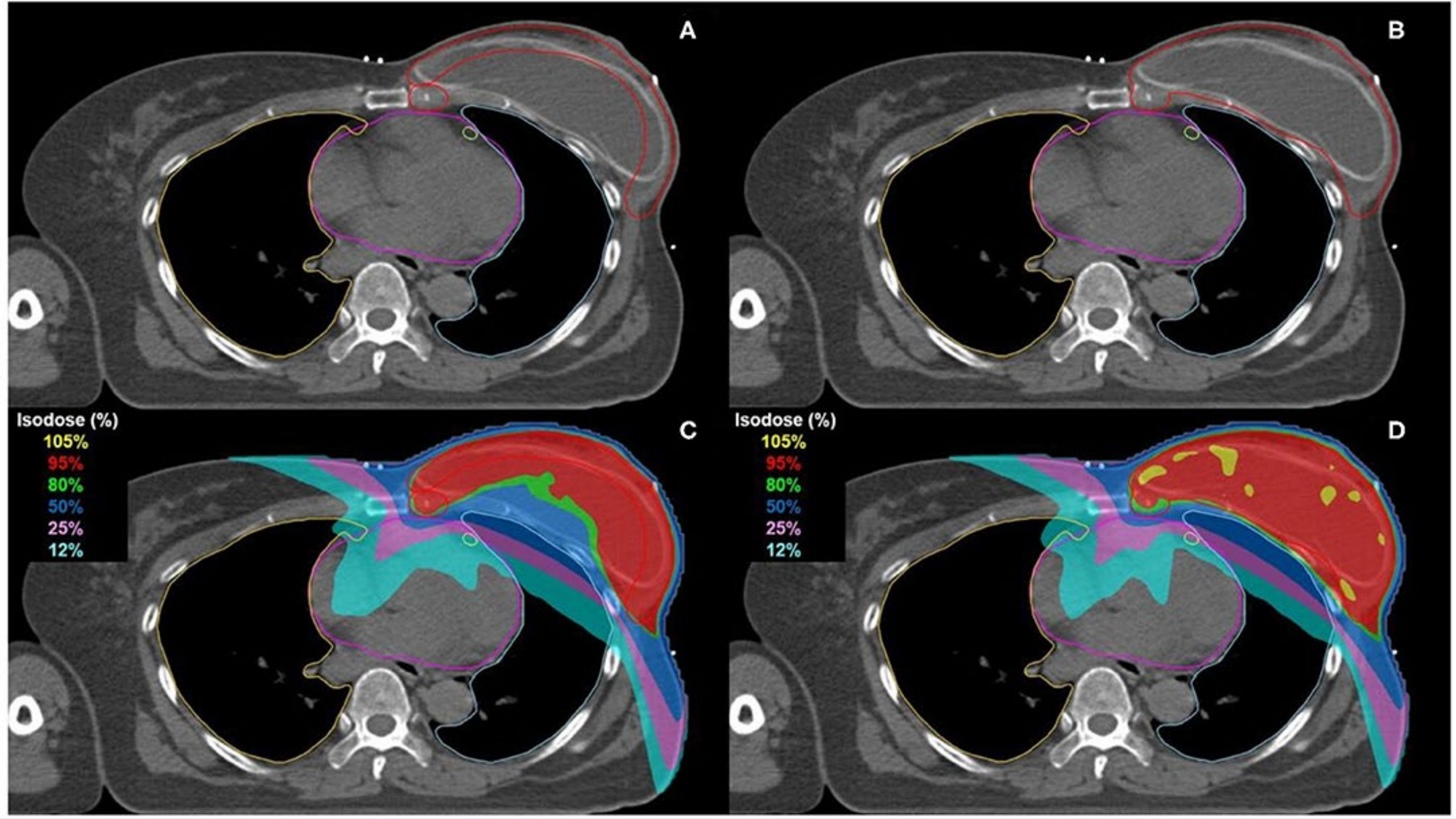
Implant

Skin – 2mm

External contour

Standard CTV

ESTRO guidelines for implant-based reconstruction

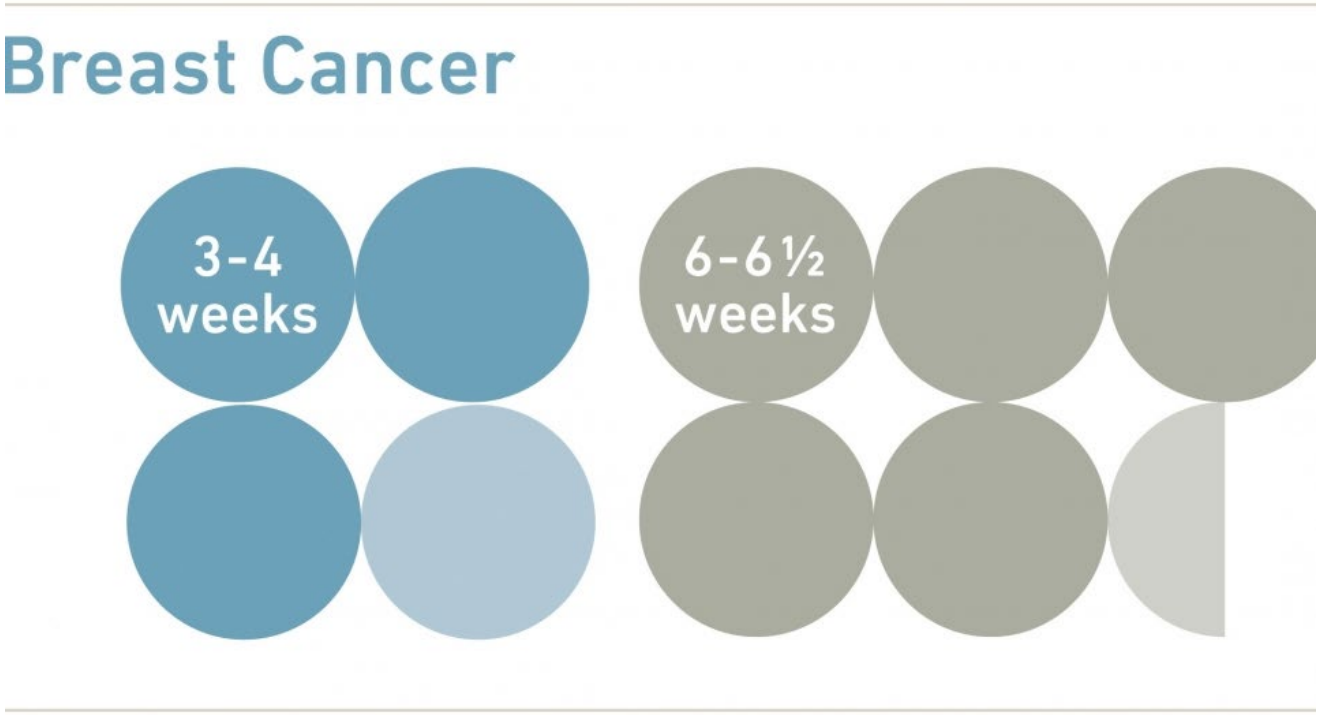

A
B
C
D
Isodose (%)
105%
95%
80%
50%
25%
12%
Isodose (%)
105%
95%
80%
50%
25%
12%

# ESTRO guidelines: Indications for including volume posterior to implant

- Pre-pectoral implant
- Large primary breast cancer (T3)
- LABC with non-pathological complete response to primary systemic therapy
- Invasion of the pectoralis major muscle and/or chest wall

Radiotherapy and Oncology, 2019-08-01, Volume 137, Pages 159-166

# Hypofractionation




- In setting of breast conservation, hypofractionated breast radiation resulted in similar or better cosmetic outcomes such as breast shrinkage, telangiectasia, dyspigmentation, and breast edema
  - Canadian hypofx – Whelan
  - START trials

# Randomized trials of Hypofractionated PMRT and regional nodal irradiation

| First Author | Year | No. of Patients | Follow-Up, Median (months) | Treatment Arms, Total Dose/Dose per Fraction (Gy) | LRR (%) | DFS (%) | OS (%) |
|---|---|---|---|---|---|---|---|
| Baillet[32] | 1990 | 91[a] | 48 | 45/1.8 *v* 23/5.75 | 5 *v* 7 | NR | 85 *v* 85 |
| Shahid[33] | 2009 | 300 | 60 | 27/5.4 *v* 35/3.5 *v* 40/2.67 | 11 *v* 12 *v* 10 | 71 *v* 72 *v* 71 | 87 *v* 83 *v* 82 |
| Haviland[34] (UKSTART A) | 2013 | 336[a] | 111.6 | 50/2 *v* 41.6/3.2 *v* 39/3 | 7.4 *v* 6.3 *v* 8.8 | 77.4 *v* 77.3 *v* 75.7 | 80.2 *v* 81.6 *v* 79.7 |
| Haviland[34] (UK START B) | 2013 | 177[a] | 118.8 | 50/2 *v* 40/2.67 | 5.5 *v* 4.3 | 77.8 *v* 81.7 | 80.8 *v* 84.1 |
| Wang[36] | 2019 | 820 | 58.5 | 50/2 *v* 43.5/2.9 | 8.1 *v* 8.3 | 70 *v* 74 | 86 *v* 84 |
| Atef[37] | 2019 | 35[a] | 26.8 | 50/2 *v* 42.56/2.66 | NR | 90 *v* 87 | 87 *v* 87 |

NOTE. No significant differences in the reported oncologic end points were observed in any of the randomized trials.

Abbreviations: DFS, disease-free survival; LRR, locoregional recurrence rate; NR, not reported; OS, overall survival.

[a]Subset of patients treated with mastectomy in these trials. Note that the reported LRR, DFS, and OS within the table are for the entire cohort of patients (both breast-conserving surgery and mastectomy patients) but that these end points did not differ significantly based on surgery type.

Torres, M. A. , Horst, K. C. & Freedman, G. M. (2020). *Journal of Clinical Oncology, 38* (20), 2299-2309. doi: 10.1200/JCO.19.02908.

# Ongoing trials

- Alliance A221505 RT CHARM: Hypofractionated PMRT in women undergoing reconstruction
- FABREC trial: Dana Farber Cancer Institute, evaluating hypofractionation in women undergoing immediate breast reconstruction
- DBCG RT Recon trial: randomized trial of delayed immediate (expander placement) vs delayed reconstruction
  - Utilizes ESTRO guidelines for target volumes

# Alliance A221505: RT CHARM: Phase III Randomized Trial of Hypofractionated Post Mastectomy Radiation with Breast Reconstruction

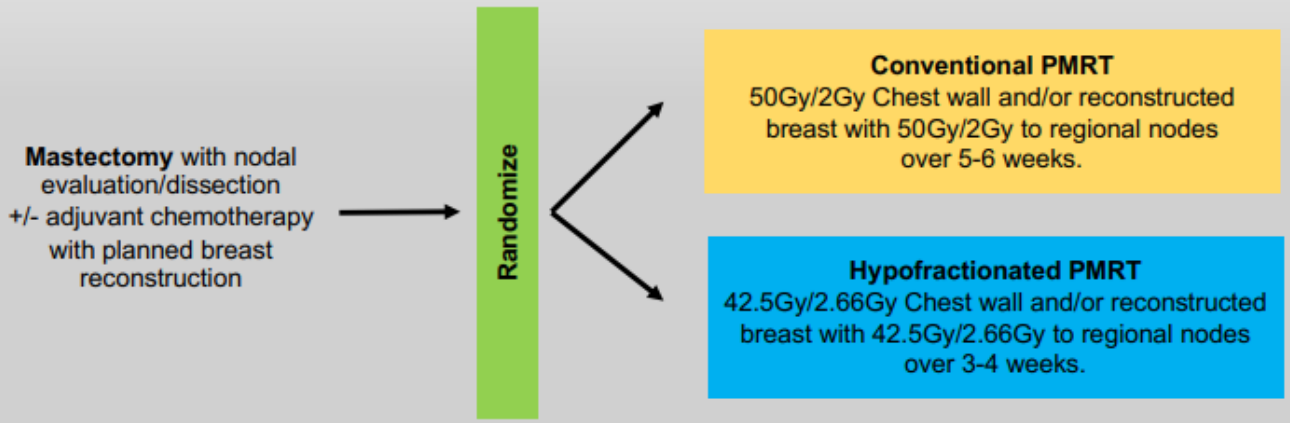
Matthew M. Poppe, MD

Huntsman Cancer Hospital, University of Utah

TAP TO RETURN TO KIOSK MENU



## Study Schema




Regional Nodes will include axilla (Level I, II, III), supraclavicular fossa and internal mammary nodes. If an axillary dissection has been performed. RT will only be directed to the un-dissected axilla.

Please use the headings above to navigate through the different sections of the poster

# Alliance A221505: RT CHARM: Phase III Randomized Trial of Hypofractionated Post Mastectomy Radiation with Breast Reconstruction

Matthew M. Poppe, MD

Huntsman Cancer Hospital, University of Utah

TAP TO RETURN TO KIOSK MENU



Please use the headings above to navigate through the different sections of the poster

## Objective

### Primary

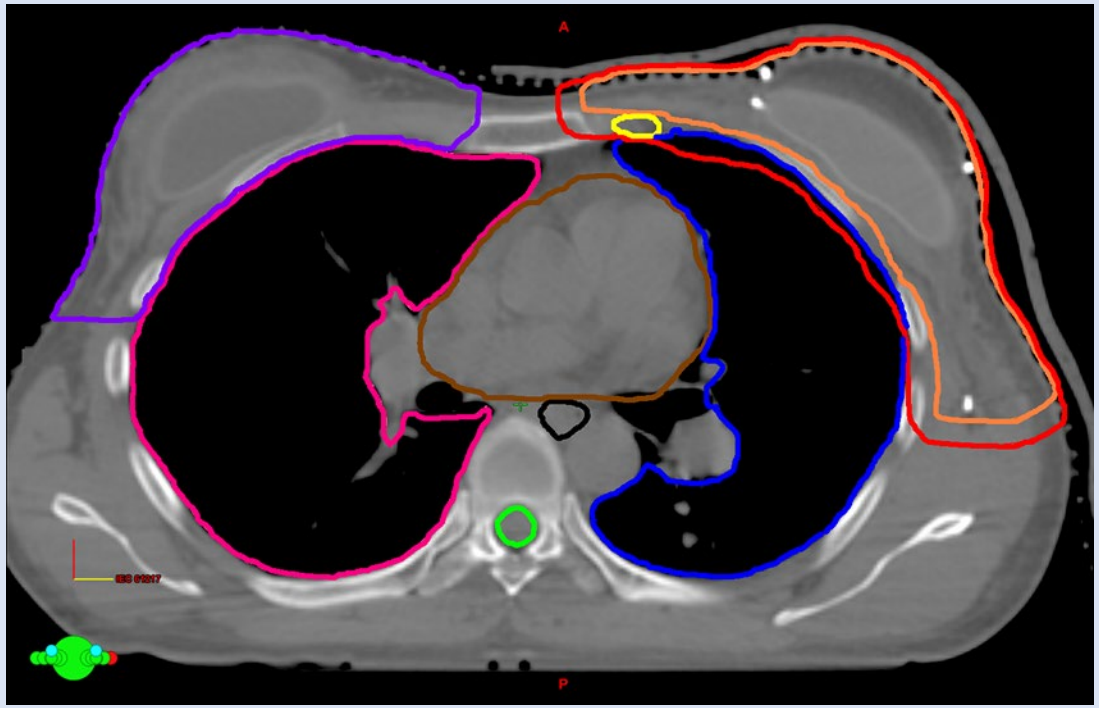
- **Non-inferior reconstruction complication rate at 24 months post radiation with hypofractionation.**
- Complications will include any re-operation or hospitalization considered as non-routine, as well any baker 3 or 4 contracture

### Secondary

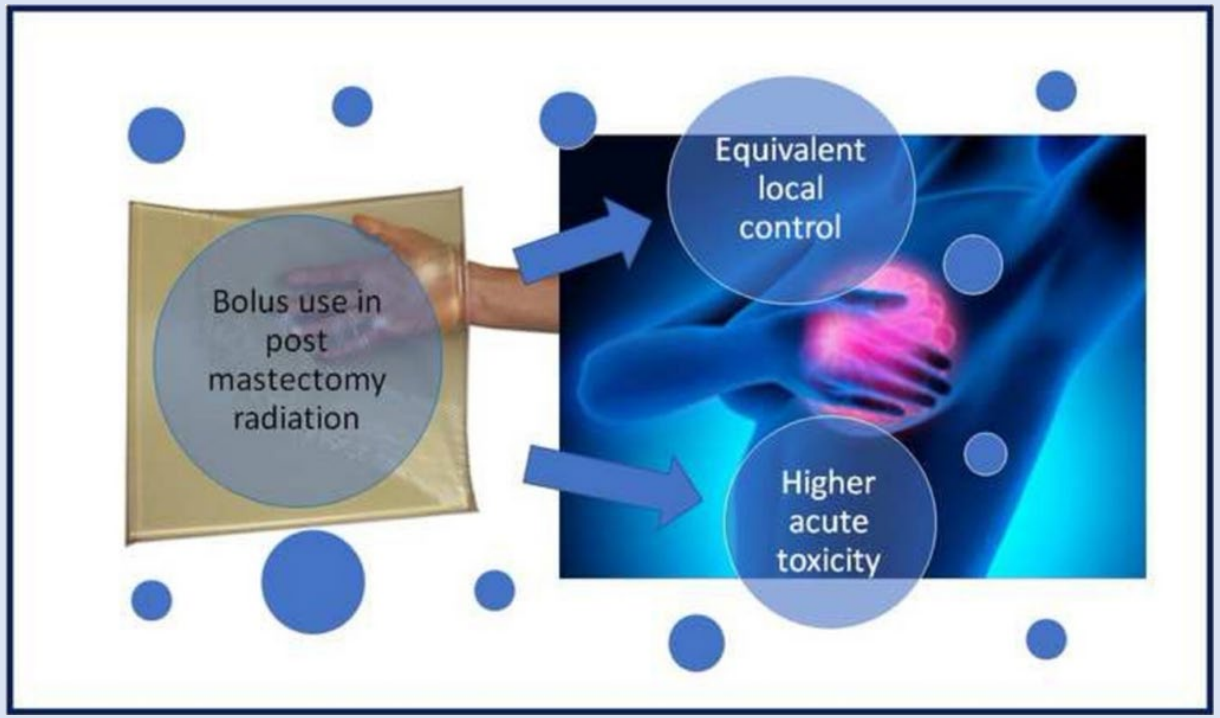
- Acute and late radiation complications, based on CTCAE 4.0 toxicity.
- Local and local regional recurrence rate.
- Photographic cosmesis 24 months after radiation.
- Lymphedema at 24 months after radiation.
- Patient satisfaction and well-being at 24 months after radiation (Breast Q)
- Compare reconstruction complication rates based on reconstruction method and timing of reconstruction.
- Cost and healthcare utilization based on hypofractionation and reconstruction technique

# To bolus or not to bolus

- In past, moist desquamation was intentional goal of PMRT and to elicit this reaction bolus was used to increase skin dose
- There is no consensus on bolus use
  - Width (3,5,10 mm)
  - Frequency (daily vs every other day)
- Bolus associated with higher rate of treatment breaks and early cessation of radiation
  - Associated with higher LR



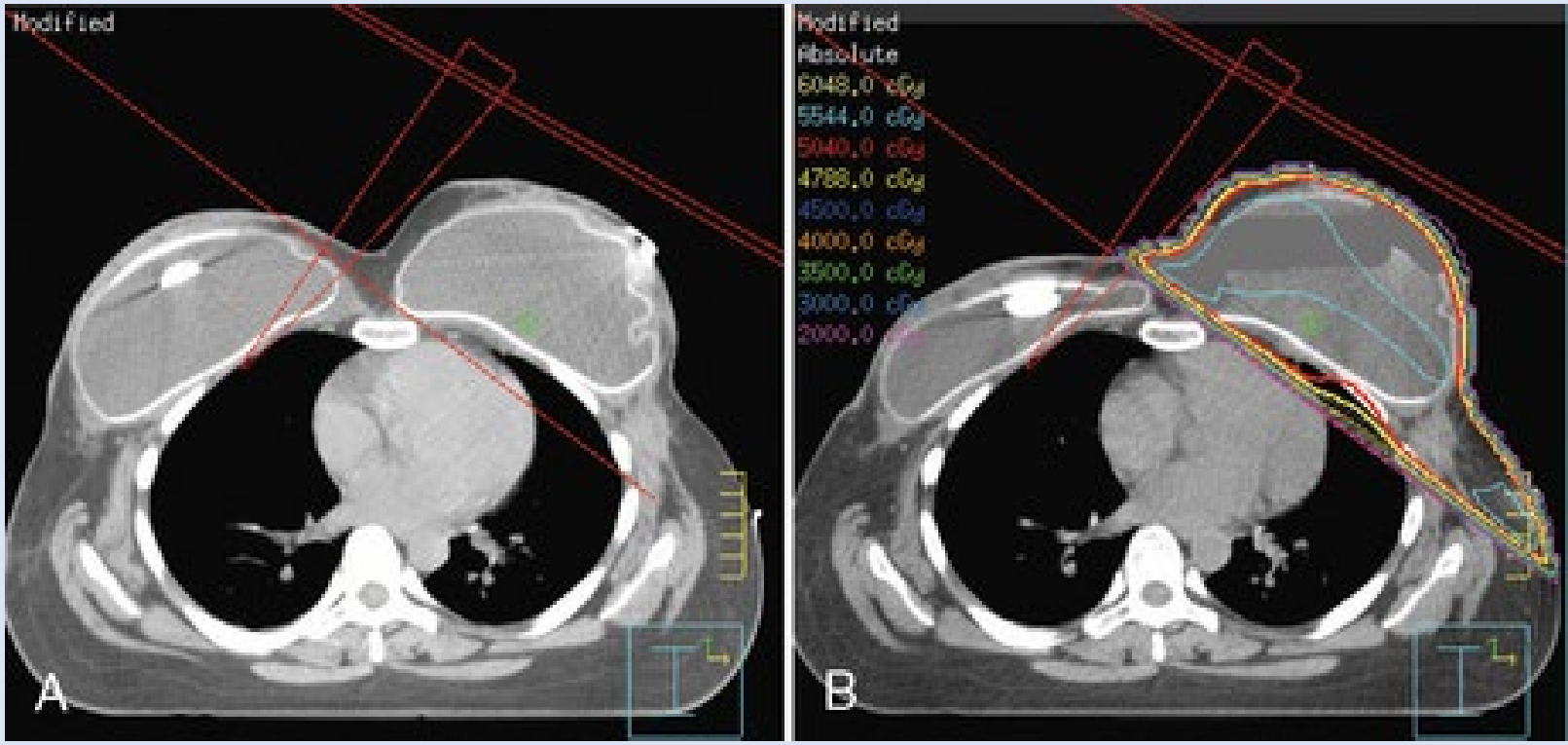
# To bolus or not to bolus




- Consider bolus for high-risk groups
  - Skin involvement or multiple high risk features for LR (positive margins, extensive LVI, triple negative subtype)
- Use of bolus in clinical trials A221505 is up to treating physician's discretion

# RT technical considerations

- Bilateral tissue expanders can potentially put restrictions on treatment planning
- Increase dose to the contralateral breast mound
- Solution: partially deflate the contralateral expander during treatment



Thank you!