Acellular Dermal Matrix in Immediate Implant-Based Breast Reconstruction

Findings from the Mastectomy Reconstruction Outcomes Consortium (MROC) Study

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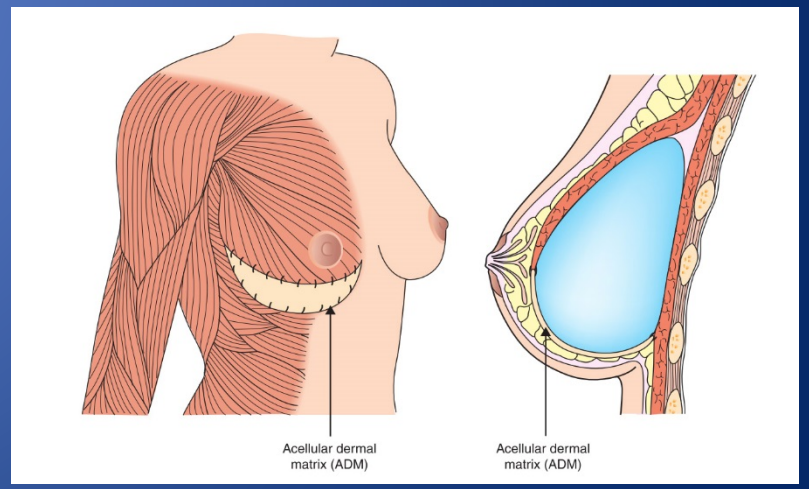
No conflicts of interest to disclose

Acellular Dermal Matrix (ADM) in Mastectomy Reconstruction

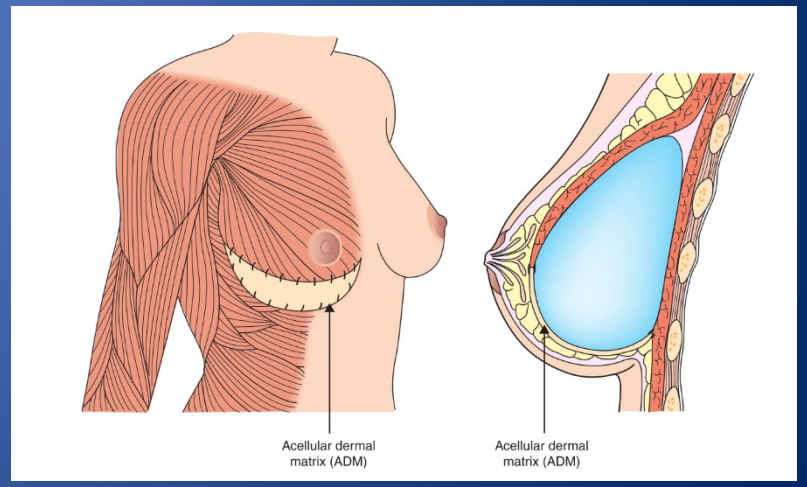
- Over 74,000 implant-based breast reconstructions performed every year
- ADM used in 80%
- Improved aesthetic outcomes (?)
- Superior expansion dynamics (?)



Potter et al., BJS 2015

Acellular Dermal Matrix (ADM) in Mastectomy Reconstruction

- **Previous studies limited by**
  - Retrospective designs
  - Single center, single surgeon populations
  - Small patient numbers
  - Inadequate controls
- **Patient reported outcomes (PROs) poorly assessed**



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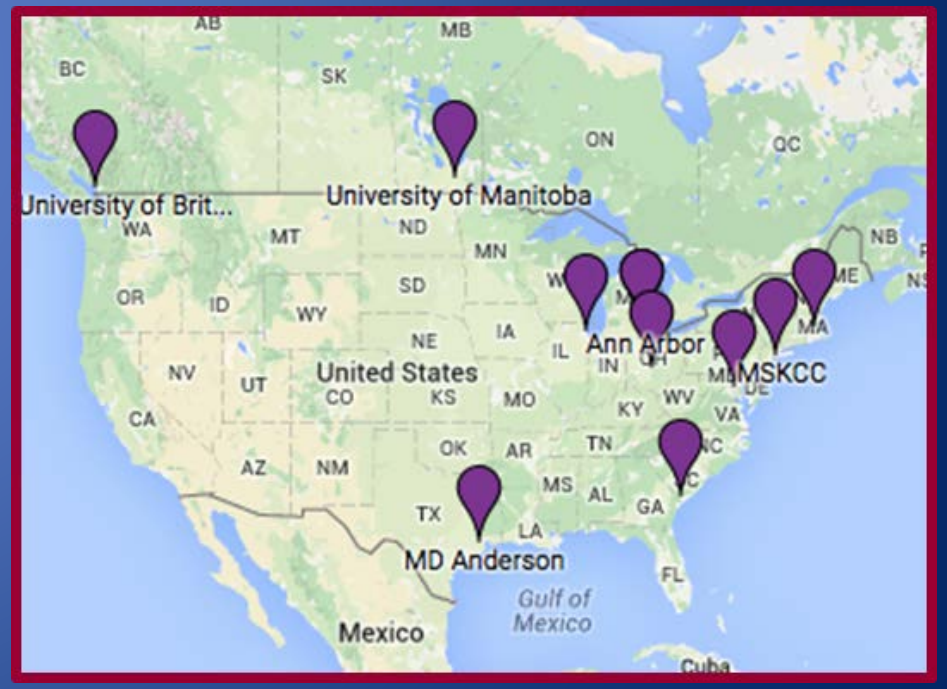
The Mastectomy Reconstruction Outcomes Consortium (MROC) Study *(2012-2017)*

- Eleven leading U.S. centers in post-mastectomy breast reconstruction
- 5 plastic surgeons



MROC Study
Specific Aims

- Compare long-term outcomes for commonly used breast reconstruction techniques
- Evaluate complications and patient-reported outcomes (PROs)

MROC Study
Design

- Prospective cohort design (pre-/post-op measures)
- Funded by the U.S. National Cancer Institute in 2011 (1R01CA152192)
- Patients recruited 2012-2015
- Data collection concluded December, 2017

MROC Study

Inclusion Criteria

- First time reconstructions
- Immediate or delayed procedures
- Mastectomies for cancer treatment or prophylaxis
- Procedure Types
  - Expander/Implant
  - Latissimus Dorsi (LD)
  - Pedicle TRAM (PTRAM)
  - Free TRAM (FTRAM)
  - DIEP
  - SIEA

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MROC Study

Measures

- **Complications**
- **Patient-Reported Outcomes**
  - Patient satisfaction
  - Psychosocial well-being
  - Anxiety/Depression
  - Body image
  - Physical well-being
  - Sexual well-being
  - Pain
  - Fatigue

MROC Study
Data Collection

- **Electronic medical records (EMRs)**
- **PRO Survey panel**
  - *BREAST-Q*: QOL for breast reconstruction
  - *EORTC QLQ BR23*: QOL for breast cancer
  - *PROMIS 29*: Generic QOL
  - *NPRS*: Pain
  - *McGill Pain Questionnaire (Short Form)*
  - *PHQ*: Depression
  - *GAD*: Anxiety

BREAST-Q Survey

- **Seven domains assessing satisfaction, psychosocial/physical well-being**
- **Satisfaction with Breast Subscale**
  - –Size, shape, symmetry
  - –“Natural” appearance
  - –Softness
  - –Functioning in bras/clothing

MROC Study
Data Collection

- **EMR Reviews**
- **Patient Survey Panel**
  - Pre-reconstruction
  - Post-reconstruction at 1 week, 3 months, one year and two years

MROC Study

Patient Population

- Total enrolled: 4436
- Withdrawn: 1313 (29.6%)
- **Active participants: 3123**
- 92.7% immediate reconstructions

MROC Analyses
(2014-Present)

- 1 and 2 Year complications
- 1 and 2 Year PROs
- Effects of reconstruction timing, radiation
- Effects of patient BMI, age, race/ethnicity
- Outcomes of fat grafting
- Evaluation of risks/benefits of acellular dermal matrix (ADM)
- Impact of contralateral prophylactic mastectomy/reconstruction

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BREAST

Outcomes Article

Acellular Dermal Matrix in Immediate Expander/Implant Breast Reconstruction: A Multicenter Assessment of Risks and Benefits

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Background: Acellular dermal matrix has gained widespread acceptance in immediate expander/implant reconstruction because of perceived benefits, including improved expansion dynamics and superior aesthetic results. Although previous investigators have evaluated its risks, few studies have assessed the impact of acellular dermal matrix on other outcomes, including patient-reported measures.

Methods: The Mastectomy Reconstruction Outcomes Consortium Study used a prospective cohort design to evaluate patients undergoing postmastectomy reconstruction from 10 centers and 58 participating surgeons between 2012 and 2015. The analysis focused on women undergoing immediate tissue expander reconstruction following mastectomies for cancer treatment or prophylaxis. Medical records and patient-reported outcome data, using the BREAST-Q and

Plastic & Reconstructive Surgery. 140(6):1091-1100, 2017.

Objective of ADM Analysis

- Prospectively evaluate the effects of ADM on complication rates and patient-reported outcomes in immediate expander/implant breast reconstruction

Inclusion Criteria

Patients Undergoing Immediate Two-Staged Breast Reconstruction (Cancer Treatment/Prophylaxis)

↓

Two Years of Follow-up

↓

ADM

No ADM

Study Design

Independent variables

- ADM
- Demographics
- Indication (Prophylactic vs. Therapeutic)
- Mastectomy Type (Simple vs nipple-sparing)
- Age
- BMI
- Smoking Status (Current, Previous, or None)
- Nodal Management (SNBx, ALND, or None)
- Radiation
- Chemotherapy

Study Design

Dependent Variables

- **Complications**
  - Any/all
  - Major
  - Failure
  - Infection
- **Time to expander/implant exchange**
- **Patient Reported Outcomes (PROs)**
  - Satisfaction with breast
  - Physical, sexual, psychosocial well-being
  - Postoperative pain

Study Methods

Analyses

- Bivariate and mixed effects regression analyses for complications and PROs
- Adjusted for site and surgeon
- Multiple imputations with chained equations for missing PRO data (60% 2-yr response rate)

Results:
Patient Population

- **Total Patients : 1297**
  - ADM: 655
  - No ADM: 642
- **Significant cohort differences ($p<0.05$) for…**
  - Indications for mastectomy (therapeutic vs. prophylactic)
  - Mastectomy type (simple vs. nipple-sparing)
  - Lymph node management (SLNB, ALND, or none)
  - Radiation
  - Chemotherapy

Results:

Complication Rates at Two Years

Complication		ADM (n=655)	No ADM (n=642)	Overall (n=1297)	P Value
Any (Total)		183 (27.9%)	157 (24.5%)	340 (26.2%)	0.184
Major		147 (22.4%)	101 (15.7%)	248 (19.1%)	0.052
Infection		74 (11.3%)	61 (9.5%)	135 (10.4%)	0.112
Failure		60 (9.2%)	37 (5.8%)	97 (7.5%)	0.126

Results:

Mixed Effects Regressions for Two Year Complications

	Any Complication			Major Complication			Wound Infection			Failure		
	OR	95% CI	P-Value	OR	95% CI	p-Value	OR	95% CI	P-Value	OR	95% CI	P-Value
No ADM	Reference			Reference			Reference			Reference		
ADM	1.21	(0.86, 1.70)	0.263	1.43	(1.00, 2.05)	0.052	1.49	(0.90, 2.44)	0.118	1.55	(0.93, 2.58)	0.089

- Controlled for age, BMI, laterality, mastectomy indication, mastectomy type, smoking history, diabetes, lymph node management, radiation, and chemotherapy
- Adjusted for site and surgeon

Results:

Did ADM Brand Make a Difference in Complications?

- Brand A : 416 patients
- Brand B: 107 patients
- Brand C: 47 patients
- Brand D: 71

Results:

Did ADM Brand Make a Difference in Complications?

	Any Complication			Major Complication			Wound infection			Reconstructive Failure		
	OR	95% CI	p-Value	OR	95% CI	p-Value	OR	95% CI	p-Value	OR	95% CI	p-Value
No ADM	reference			reference			reference			reference		
Brand A	0.91	(0.62, 1.34)	0.637	1.03	(0.69, 1.54)	0.892	1.41	(0.81, 2.45)	0.230	1.25	(0.70, 2.24)	0.444
Brand B	1.61	(0.91, 2.84)	0.102	2.47	(1.42, 4.29)	0.001	1.99	(0.84, 4.70)	0.118	1.81	(0.79, 4.16)	0.159
Brand C	4.06	(1.91, 8.62)	<.001	3.09	(1.47, 6.50)	0.003	1.84	(0.68, 4.99)	0.227	3.16	(1.17, 8.52)	0.023
Brand D	0.88	(0.40, 1.94)	0.753	1.19	(0.56, 2.53)	0.660	0.52	(0.10, 2.68)	0.433	1.46	(0.45, 4.77)	0.527

- Controlled for age, BMI, laterality, mastectomy indication, mastectomy type, smoking history, diabetes, lymph node management, radiation, and chemotherapy
- Adjusted for site and surgeon

Results:
Patient-Reported Outcomes

	Satisfaction with Breasts			Psychosocial Well-Being			Sexual well-Being		
	Beta	95% CI	P-Value	Beta	95% CI	P-Value	Beta	95% CI	P-Value
No ADM	Reference			Reference			Reference		
ADM	-0.86	-4.02, 2.31	0.588	0.31	-2.98, 3.61	0.846	-1.71	-4.71, 1.28	0.258

- Controlled for age, BMI, laterality, mastectomy indication, mastectomy type, smoking history, diabetes, lymph node management, radiation, and chemotherapy
- Adjusted for site and surgeon

Results:
Patient-Reported Outcomes

	Physical Well-Being			Post-Operative Pain		
	Beta	95% CI	P-Value	Beta	95% CI	P-Value
No ADM	Reference			Reference		
ADM	-0.70	-2.04, 0.63	0.300	-0.01	-0.16, 0.13	0.851

- Controlled for age, BMI, laterality, mastectomy indication, mastectomy type, smoking history, diabetes, lymph node management, radiation, and chemotherapy
- Adjusted for site and surgeon

Results:

Did ADM Brand Make a Difference in Patient-Reported Outcomes?

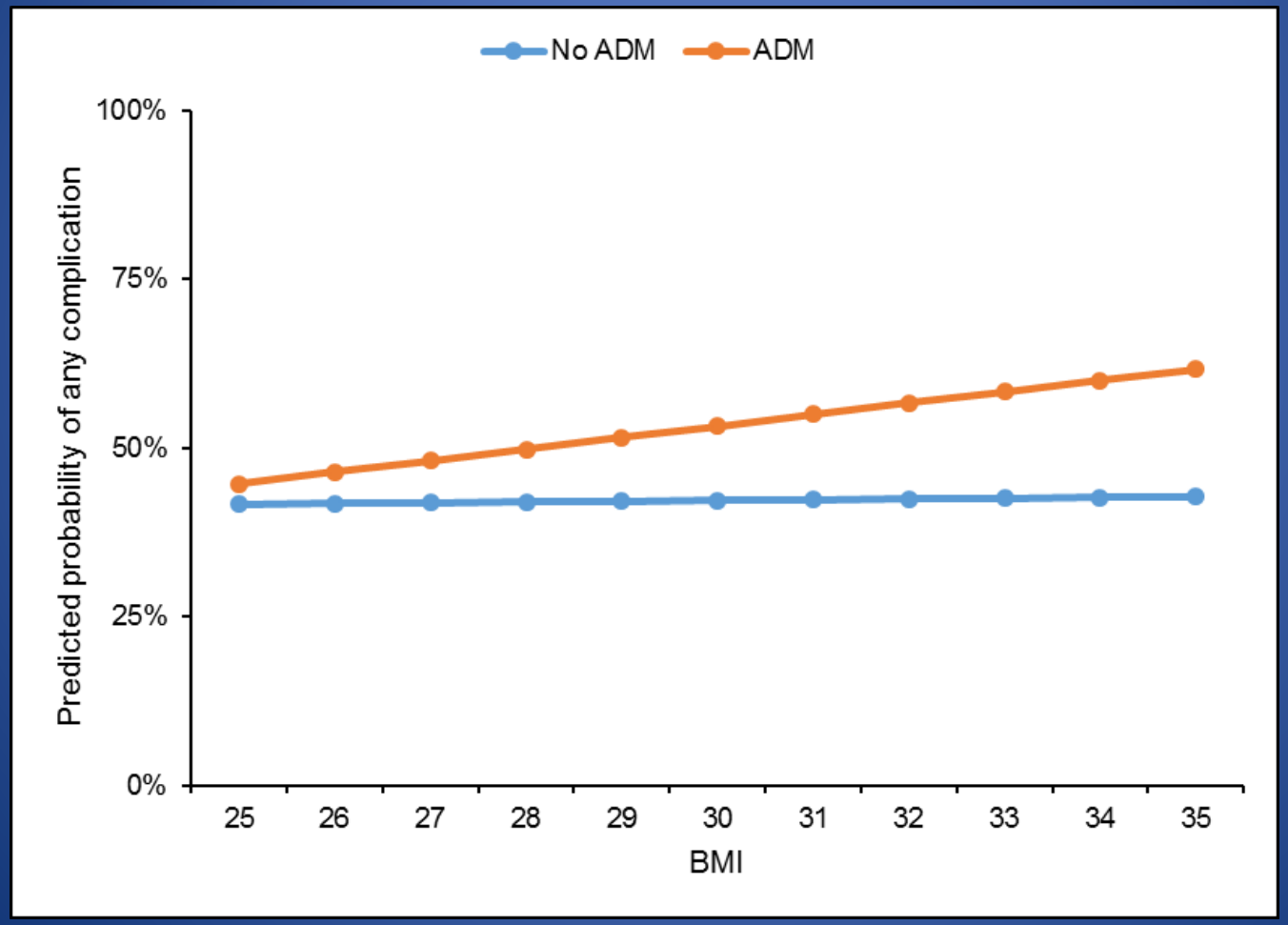
- No statistically significant differences for any PRO measure between the four ADM brands and the non-ADM cohort.

Results:

Were There Patient Subgroups in Which ADM Produced Better Outcomes?

- Subgroup analyses evaluated interactions between clinical variables and ADM use, and their effects on complications and PROs
- Included age, BMI, laterality, mastectomy indication, mastectomy type, smoking history, diabetes, lymph node management, radiation, and chemotherapy
- No subgroups identified in which ADM use was associated with better outcomes, compared with non-ADM cases

Effect of BMI on Complication Rate by ADM Usage



Results:
Did ADM Shorten Time to Exchange?

- Mean time from expander placement to expander/implant exchange
  - Non-ADM Cohort: 5.6 months
  - ADM Cohort: 5.4 months (p=0.780)

Conclusions

- Use of ADM in immediate expander/implant reconstruction was associated with a marginally higher complication rate, but had no significant effects on patient-reported outcomes, compared with non-ADM cases
- Brand differences were observed for complications, but not for PROs
- ADM had no significant effect on time to exchange

Limitations

- **MROC was not an RCT**
  - Selection bias (?)
  - Confounding by variables not controlled for (?)
- **Products have evolved since 2012-2015 (?)**
- **Our analyses did not evaluate…**
  - Direct-to-implant reconstructions (Few patients without ADM)
  - Pre-pectoral expanders or implants (Not recorded)

Points to Consider

- Why do plastic surgeons perceive aesthetically superior results with ADM in immediate expander/implant reconstruction, while patients don't?
  - Are PRO measures sufficiently sensitive? (Probably)
  - Are plastic surgeons more critical of results? (Probably)
- Since ADM offers clearer technical advantages in direct-to-implant and pre-pectoral reconstructions, are there PRO benefits in these procedures?

Acknowledgements

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NATIONAL CANCER INSTITUTE