Trial Registration Information	
Primary registry	ClinicalTrials.gov
NCT number	TBD
Primary Sponsor	University of British Columbia
Contact for scientific and public queries	Dr. N. Van Laeken, email: Nancy@vanlaeken.com
Public Title	The BREAST Trial: a randomized comparison of the surgical outcomes from four ADM products utilized in breast reconstruction
Scientific Title	The BREAST Trial: A randomized, non-inferiority, pilot study comparing the complication profile of four commercially available acellular dermal matrixes used in alloplastic breast reconstruction
Country of recruitment	Canada
Subjects	Patients undergoing alloplastic breast reconstruction with the use of acellular dermal matrix for breast pocket creation
Intervention	Active comparators: AlloMax or DermACELL or FlexHD, Alloderm
Study Type	Interventional, randomized, parallel, single blinded, pilot study
Date of first enrolment	November 2020
Target sample size	40 participants for pilot (328 for complete trial)
Recruitment status	Actively recruiting

Participant Information and Consent Form

1. Study title:

The BREAST Trial: A randomized, non-inferiority, study comparing the complication profile of four commercially available acellular dermal matrixes used in alloplastic breast reconstruction

2. Study personnel

Principal Investigator: Nancy Van Laeken, MD, FRCSC
Site lead: Mount Saint Joseph's Hospital
Department of Surgery, Division of Plastic Surgery
University of British Columbia
Office: 604-669-1633 ext. 5

Co-Investigator(s): Esta Bovill, MD, PhD, FRCSC
Department of Surgery, Division of Plastic Surgery
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Peter Mankowski, MD
Department of Surgery, Division of Plastic Surgery
University of British Columbia
Office: 604-875-4969

Emergency Telephone Number
For all emergencies please contact your nearest hospital and ask to speak to the plastic surgery team member on call.

Vancouver General Hospital	604-875-4111
St. Paul's Hospital	604-806-9090
University of British Columbia Hospital	604-822-7121
Mount St. Joseph's Hospital	604-874-1141

Non-emergency Contact Number: For non-emergencies, please contact your primary surgeon's office to see assistance or for any additional concerns the principal study investigator Dr. Van Laeken may be contacted at 604-669-1633.

3. Invitation

You have been invited to take part in this research study because you will be having a mastectomy (def: breast removal) at the same time as a breast reconstruction with an Acellular Dermal Matrix (ADM).

4. Your participation is voluntary

Your participation is voluntary. You have the right to refuse to participate in this study. If you decide to participate, you may still choose to withdraw from the study at any time without any negative consequences to the medical care, education, or other services to which you are entitled or are presently receiving.

You should be aware that there is a difference for both you and your doctor between being a patient and being a research participant. As a patient, all medical procedures and treatments are carried out for your benefit only according to standard accepted practice. As a research participant, you and your doctor also must take into account the requirements for the research study. These may include improving procedures or using products that are not part of standard practice. This consent form describes using multiple different products used for assisting in your future surgical reconstruction for research purposes. Please review the consent document carefully when deciding whether or not you wish to be part of the research and sign this consent only if you accept being a research participant.

Please take time to read the following information carefully and to discuss it with your family, friends, and doctor before you decide.

5. Who is conducting this study?

This study is not receiving funds from an external agency or sponsor. This study is being conducted by the UBC division of Plastic surgery solely for the purposes of improving both knowledge and patient care. No additional industry or sponsors are involved in this study and there are no conflicts of interest to declare.

6. Background

After being diagnosed with breast cancer, breast reconstruction is usually done by forming new breasts using your own skin and a balloon like device called a tissue expander. To help the tissue expander make a pocket for the final breast implant, an acellular dermal matrix is placed under the skin to support the expander. This way, the tissue does not move out of place. Acellular Dermal Matrices (ADMs) are material made from treated human skin to avoid patient reactions. ADMs where first used in breast surgery in 2001 and have been

allowed in Canada since 2009. Now they are very popular and commonly used in breast reconstruction surgery. AlloDerm was one of the first ADMs to be developed followed by other brands such as DermACELL, Flex HD, and AlloMax. Each have been shown to be safe for use in breast reconstruction but these four products have not been compared to each other.

7. What is the purpose of the study?

The goal of this study is to compare four different acellular dermal matrices used in breast reconstruction to see if they have the same results. Also, the final appearance of the breast reconstruction will be graded by both you (the patient) and other plastic surgeons in this study.

We are looking for patients from the University of British Columbia hospital, Vancouver General Hospital, and Mount Saint Joseph Hospital. You will randomly receive one ADM with your breast reconstruction surgery, either AlloDerm, DermACELL, Flex HD, or AlloMax. In the study we hope to compare and make meaningful conclusions between these ADMs, how they effect patient results and their possible complications.

First, we are doing a “pilot study”. A “pilot study” is done to make sure that that this study can be continued for a long time and that we will be able to get enough patients to participate. A pilot study starts with a small number of participants. We run the study with these few patients and then reflect on if the study has any problems that need to be fixed. This does not allow us to prove that the four ADMs are similar. Instead, the pilot study guide how we do a larger study in the future.

For this pilot study we hope to invite 40 women into the study. Once the pilot study is finished, we hope to start the larger study in the future where we are planning to enroll hundreds of patients to study all four ADM products.

8. Who can participate in this study?

You may be able to participate in this study if*:*

All woman aged 21 years or older but less than 65 undergoing mastectomy and breast reconstruction with a tissue expander and ADM will be invited to participate.

9. Who should not participate in this study?

You will not be eligible to participate in this study if:

1. Patients you chose to have a different type of breast reconstruction that doesn't include a tissue expander
2. Patients who had previously breast reconstruction procedures.
3. Patients who had radiation treatments to the breast in the past.
4. Patients who needed lymph node dissections for their breast cancer treatment (determined by your General surgeon).
5. Patients who cannot take Nitroglycerine for reasons such as:

Acute circulatory failure accompanied by clear hypotension, Myocardial insufficiency related to obstruction, Use of sildenafil, vardenafil & tadalafil, Use of beta-blockers, calcium channel blockers, diuretics, or phenothiazides, Salicylates (ASA), Alteplase, Recent history of MI or cardiac insufficiency, Anemia, severe, Cerebral hemorrhage or recent head trauma, Glaucoma, Hepatic function impairment, severe Hyperthyroidism, Hypotension, Sensitivity to nitrites.

6. Patients with an allergy to polysporin or any of its ingredients.
7. Patients with allergies to the following antibiotics:
    - Gentamicin, Vancomycin

8. The surgeon performing the breast reconstruction may also deem a patient ineligible if they deem it not safe to proceed with their originally planned reconstruction.

Please note: Your surgeon will review these criteria with you to make sure you are safe to participate in this study.

10. What does the study involve?

Overall design of the study:

- The skin-saving or nipple-saving mastectomy surgery and the immediate breast reconstruction technique (with an implant or tissue expander) will follow a standard procedure, which means that it will be performed in exactly the same way on patients who do not participate in this study.

- Whether you get the AlloDerm, DermACELL, Flex HD, or Allomax acellular dermal matrix will be decided randomly (by chance) like flipping a coin or rolling dice, which means that you have a 25% chance of getting each option.

- To strengthen the results of the study, you will not be told which ADM you have received until after the study is over.

If You Decide to Join this study, these are the specific procedures involved:

Study staff will meet you in person if you are eligible and interested in participating to review the study consent form in detail and to answer any questions you might have about these procedures or study details. Written informed consent will be obtained 1 to 2 weeks following this meeting.

Baseline assessment: If you are eligible and willing to participate in the study, your surgeon will document your medical history before surgery. All information will be kept anonymous so that the people conducting the study will not know the information is collected from your experiences. The pre-operative BREAST-Q questionnaire will be filled out by you at this time.

Randomization: Randomization of the type of acellular dermal matrix will occur at the time of ordering the acellular dermal matrix product. This does not require a study visit.

Surgery: The skin-saving or nipple-saving mastectomy surgery will follow a standard procedure performed by general surgery. The reconstructive surgery you discussed with your surgeon will also follow standard procedure and a biopsy of your ADM will be collected to check how well it is healing. The dressing will remain in place for a minimum of 48 hours.

Follow-up: All women will attend standard post-surgical follow up appointments to have their breasts examined. Follow up visits will be scheduled after surgery at 1-2 weeks, 4 weeks, 6 – 8 weeks, and then at 3, 6, 12 and 24 months. The duration of these follow ups will be consistent will a routine clinic visit (approx. 45mins) No additional visits are required for the study unless required by the patient.

Study Questionnaire: As part of the study, your surgeon will document your healing and will note if there are any areas of concern or any other complications will need to be documented. Before and after your surgery at the 1-year visit, we ask that you complete a short questionnaire called the BREAST-Q. This questionnaire takes about 10-15 mins to complete. It will ask you questions about your satisfaction and experiences with their breast reconstruction.

Examples include:

“How happy are you with how your bra fits?”

“How happy are you with how your abdomen looks when exposed?”

Photographs and Physical examination: A routine physical examination will be performed by the attending surgeon and photographic documentation (5 standardized photographs) of your breasts will be obtained at pre-operatively and at each follow-up visit. The photographs will not include your face and will only include your neck, torso and abdomen. The images will be blinded and identified with an alphanumeric code. Your

photographs may be selected for an external reviewer to assess cosmetic success. Some body features such as tattoos, piercings, or specific skin features (e.g. unique moles) may allow people to identify you in the photos. Every effort to minimize possible identification from the photos will be made. These photos may still be used in the aesthetic evaluation but efforts will be made to ensure that that these photos are not shared publicly in any way (e.g. final study report, published paper, presentation etc.). The images will be stored in a secure location along with the other study documents and will be destroyed according to University guidelines following completion of the study. Your photo may be used in presentations or publications but will not identify you in any way.

11. What are the possible harms and discomforts?

Risks Related to Being in the Study:

The risks and side-effects of the standard or usual treatment of breast reconstruction using an ADM will be explained to you as part of your standard care. If you are unclear about what is standard of care and what is specifically part of this study, please discuss this with your study doctor.

Currently, it is unknown if all four ADMs have the same risk of red breast syndrome. Red breast syndrome is a reaction to the ADM that causes your breasts to become large, red and swollen. This problem usually goes away with time and anti-inflammatory treatments and sometimes antibiotics. It is possible that you may receive an ADM that has a higher risk of red breast syndrome. This is something the study will be monitoring and your doctor will treat this potential problem if it occurs.

12. What are the potential benefits of participating?

You may or may not receive any direct benefit from being in this study. Information learned from this study may help other women receiving a mastectomy with breast reconstruction in the future.

13. What are the alternatives to the study treatment?

If you choose not to participate in this study or to withdraw at a later date, the treatment of receive immediate skin-saving or nipple-saving mastectomy and breast reconstruction with an ADM will still be available to you. Selection of the ADM product will then be performed by your surgeon. You can discuss these options with your doctor before deciding whether or not to participate in this research project.

The following are approved alterative surgical procedures of breast reconstruction are also available and may be discussed with your doctors:

- Immediate two-stage tissue expander/ implant breast reconstruction
- Immediate Autologous tissue reconstruction (using your own body tissue)
- Combined implant and autologous tissue reconstruction

14. After the study is finished

The use of any of the acellular dermal matrices involved in this study, will not have an impact on any of your future treatment options.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

15. What happens if I decide to withdraw my consent to participate?

You may withdraw from this study at any time without giving reasons. If you choose to enter the study and then decide to withdraw at a later time, the study team will have a discussion with you about what will happen to the information about you *breast tissue samples* already collected. You have the right to request the destruction of your information *breast tissue samples* collected during the study, or you may choose to leave the study and allow the investigators to keep the information already collected about you until that point.

If you choose to have the data collected about you destroyed, this request will be respected to the extent possible. ADM biopsy specimens will have been sent to pathology for microscopy assessment and to evaluate ADM integration. Normally, these specimens will be stored within the routine practices of the pathology department for oncological specimens (2 years for paraffin blocks) then will be disposed of by standard tissue disposal. Should the study be terminated early, the specimens will be disposed of. There is no future plan for utilization of these specimens.

Please note however that there may be exceptions where the data will not be able to be withdrawn for example where the data is no longer identifiable (meaning it cannot be linked in any way back to your identity) or where the data has been merged with other data. If you would like to request the withdrawal of your data, please let your study doctor know.

16. Can I be asked to leave the study?

It is unlikely that you will be asked to leave the study. Instead, the study be stopped early or at any time by the Research Ethics Board or the division of Plastic surgery research team, if new information rises about these ADM products or their safety. The reasons for study stoppage will be explained to you by the study doctor. If the study stops early you will still proceed with your breast reconstruction as planned by your surgeon.

17. How will my taking part in this study be kept confidential?

Your confidentiality will be respected. However, research records and health or other source records may be inspected in the presence of the Investigator or his or her designate by representatives of the UBC Providence Health Care Research Ethics Board for the purpose of monitoring the research. No information or records that disclose your identity will be published without your consent, nor will any information or records that disclose your identity be removed or released without your consent unless required by law.

You will be assigned a unique study number as a participant in this study. This number will not include any personal information that could identify you (e.g., it will not include your Personal Health Number, SIN, or your initials, etc.). Only this number will be used on any research-related information collected about you during the course of this study, so that your identity will be kept confidential. Information that contains your identity will remain only with the Principal Investigator and/or designate. The list that matches your name to the unique study number that is used on your research-related information will not be removed or released without your consent unless required by law.

We will include your exact consultation and reconstructive dates fon research records or materials forwarded to others. It is unusual to include personal information on documents sent to others. Most studies submit information identified by code numbers or letters only. However, this information is necessary for this study as it allows us to calculate time related outcomes associated with your post-operative care (e.g. drain duration).

Your rights to privacy are legally protected by federal and provincial laws that require safeguards to ensure that your privacy is respected. You also have the legal right of access to the information about you that has been provided to the sponsor and, if need be, an opportunity to correct any errors in this information. Further details about these laws are available on request to your study doctor.

Because this is a treatment study, your signed consent form will be included in your electronic medical record, and your healthcare team will be alerted that you are on a study. This is to ensure your healthcare team has a little information about the study so that they can treat you safely according to the study protocol.

Disclosure of Race/Ethnicity

Studies involving humans now routinely collect information on race and ethnic origin as well as other characteristics of individuals because these characteristics may influence

how people respond to different medications. You should be aware that providing this information is not mandatory.

19. What happens if something goes wrong?

By signing this form, you do not give up any of your legal rights and you do not release the study doctor, participating institutions, or anyone else from their legal and professional duties. If you become ill or physically injured as a result of participation in this study, medical treatment will be provided at no additional cost to you. The costs of your medical treatment will be paid by your provincial medical plan.

In case of a serious medical event, please report to an emergency room and inform them that you are participating in a clinical study and that the following person can then be contacted for further information: Dr. Nancy Van Laeken at telephone number: 604-669-1633.

20. What will the study cost me?

All research-related medical care and treatment and any related tests that you will receive during your participation in this study will be provided at no cost to you. As enrolling within the study will not result in participant activities beyond their expected standard of care, no reimbursement or remuneration is planning upon enrollment.

21. If I have questions about the study procedures during my participation, who should I speak to?

If you have any questions or desire further information about this study before or during participation, or if you experience any adverse effects, you can Dr. Nancy Van Laeken at telephone number: 604-669-1633 ext. 5.

22. Who do I contact if I have any questions or concerns about my rights as a participant?

If you have any concerns or complaints about your rights as a research participant and/or your experiences while participating in this study, contact the Research Participant Complaint Line in the University of British Columbia Office of Research Ethics by e-mail at RSIL@ors.ubc.ca or by phone at 604-822-8598 (Toll Free: 1-877-822-8598.) Please reference the study number (H18-02052) when calling so the Complaint Line staff can better assist you.

23. Signatures

The BREAST Trial: A randomized, non-inferiority, pilot study comparing the complication profile of four commercially available acellular dermal matrixes used in alloplastic breast reconstruction

Participant Consent

My signature on this consent form means:

- I have read and understood the information in this consent form.
- I have had enough time to think about the information provided.
- I have been able to ask for advice if needed.
- I have been able to ask questions and have had satisfactory responses to my questions.
- I understand that all of the information collected will be kept confidential and that the results will only be used for scientific purposes.
- I understand that my participation in this study is voluntary.
- I understand that I am completely free at any time to refuse to participate or to withdraw from this study at any time, and that this will not change the quality of care that I receive.
- I understand that I am not waiving any of my legal rights as a result of signing this consent form.
- I authorize access to my health records **and tissue samples associated with my breast reconstruction procedures** as described in this consent form.

I will receive a signed and dated copy of this consent form for my own records.

I consent to participate in this study.

Participant's Signature	Printed name	Date

Signature of Person Obtaining Consent	Printed name	Study Role	Date

Future Contact

- ☐ Yes, I would like to contacted for inquiry about future opportunities to be involved in breast reconstruction research
- ☐ No, I am not interested in being contacted at this time.

If this consent process has been done in a language other than that on this written form, with the assistance of an interpreter/translator, indicate:

Language: _____

Was the participant assisted during the consent process in one of ways listed below?

Yes No [Note: For typical situations where the person conducting the consent discussion simply reads the consent with the participant to ensure that informed consent is properly obtained, check “no”.]

If yes, please check the relevant box and complete the signature space below:

The consent form was read to the participant, and the person signing below attests that the study was accurately explained to, and apparently understood by, the participant (please check if participant is unable to read).

The person signing below acted as an interpreter/translator for the participant, during the consent process (please check if an interpreter/translator assisted during the consent process).

Signature of Person Assisting Printed Name Date

in the Consent Discussion”