Source and Number of the Project：

Evaluation of the Cosmetic Outcome and Safety of 3D-Printed Biodegradable Biological Mesh for One-Stage Breast Reconstruction After Radical Mastectomy - A Prospective, Single-Center, Single-Arm Clinical Study

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Study Duration: 2025-12-01 – 2028-12-01

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PROTOCOL SYNOPSIS

Study Title	Evaluation of the Cosmetic Outcome and Safety of 3D-Printed Biodegradable Biological Mesh for One-Stage Breast Reconstruction After Radical Mastectomy - A Prospective, Single-Center, Single-Arm Clinical Study
Study Objective	To evaluate the clinical efficacy (cosmetic outcomes and quality of life) and safety of 3D-printed biodegradable biological mesh in breast reconstruction.
Study Design	A prospective, single-center, single-arm clinical study.
Sample Size	25 cases.
Subject Selection	**Inclusion Criteria:** 1. Female breast cancer patients aged 18 to 70 years. 2. Histopathologically confirmed invasive breast cancer, as defined by the latest ASCO/NCCN guidelines. 3. Unable to undergo breast-conserving surgery or willing to undergo total mastectomy with immediate implant-based breast reconstruction.

	4. ECOG performance status of 0-1. 5. Voluntary participation in the study and signing of the written informed consent form. **2.Exclusion Criteria:** 1. Age >70 years. 2. Metastatic breast cancer (Stage IV) at initial diagnosis. 3. Multicentric, extensive, diffuse lesions, or inflammatory breast cancer. 4. Tumor involvement of the nipple-areolar complex. 5. Breast cancer during pregnancy. 6. History of other malignancies within the past 5 years, except for cured cervical carcinoma in situ or non-melanoma skin cancer. 7. Abnormal function of vital organs such as heart, lungs, liver, or kidneys; poorly controlled diabetes, etc., rendering the patient unable to tolerate surgery. 8. Patients deemed unsuitable for participation by the investigator.
Treatment Plan	This is a prospective, single-center, single-arm clinical study. Patients will undergo

	immediate breast reconstruction with a 3D-printed biodegradable biological mesh combined with a silicone implant following total mastectomy. After providing fully informed consent and choosing the surgical method based on personal preference, and signing the informed consent form, eligible subjects will enter the trial period. The specific treatment plan is as follows: 1. **Preoperative Patient-Reported Outcome Assessment:** Complete the Chinese version of the BREAST-Q V2.0 scale for breast aesthetics and satisfaction scoring, as well as QoL (Quality of Life) scoring. **2.Imaging Assessment:** Enrolled patients will undergo a preoperative thin-slice breast MRI scan, including conventional plain scans (SE T1WI sequence) and 3D dynamic contrast-enhanced scans (FLASH sequence), to obtain three-dimensional enhanced images. **3. Preoperative Implant Size Assessment:** Estimate the implant volume using empirical methods. **4. Preparation of Biological Mesh:** Obtain 3D model data of the breast tissue to be resected via MRI scans. Use Mimics software to

	extract models of the lesion and healthy tissue to guide surgical planning. Subsequently, design the mesh model using software such as Geomagic and 3-matic. Finally, use medical-grade polycaprolactone as the material to manufacture the biodegradable breast micro-nano fiber mesh on a dedicated high-precision fused deposition modeling (FDM) 3D printing platform. The mesh is then sterilized and set aside for use. **5. Surgery:** Perform Nipple-Sparing Mastectomy (NSM) or Skin-Sparing Mastectomy (SSM) breast reconstruction surgery using the 3D-printed biodegradable biological mesh combined with a silicone implant. **6. Postoperative Follow-up:** Establish electronic health records. Follow-ups will be conducted at 1 week, 1 month, 3 months, 6 months, 12 months ， 18 months，and 24 months post-surgery，through study completion, an average of 2 year. Follow-up content includes recording complications or adverse reactions, completing the Chinese version of the BREAST-Q V2.0 scale for quality of life assessment, and checking for metastasis or recurrence.
Efficacy Evaluation	**1. Primary Efficacy Endpoints:** Patient-reported outcomes (postoperative cosmetic results) and

	safety. **2. Secondary Efficacy Endpoints:** Quality of life; breast cancer-free interval (recurrence- free survival, disease-free survival, overall survival).
Statistical Methods	Professional statisticians will be responsible for the statistical analysis and will be involved throughout the entire process, from trial design and implementation to analysis and summary. A statistical analysis plan will be developed after the trial protocol and case report forms are finalized, with necessary modifications made during the trial as needed. A statistical analysis report will be provided upon completion of data analysis.
Study Duration	December 2025– December2028

1. Background

Breast cancer has become the most common malignancy among women globally and is the number one threat to the physical and mental health of women in China [1]. In recent years, there has been a trend of younger onset of breast cancer worldwide, with patients aged 35-45 accounting for 20%-30% in China. Fortunately, significant advances in early screening and comprehensive treatment over the past three decades have markedly improved the overall survival rate of breast cancer [2]. Surgery remains the cornerstone of comprehensive breast cancer treatment. However, while total mastectomy can effectively control local tumors, the subsequent loss of the breast inflicts immense physical and psychological trauma on patients, severely impacting their quality of life. Consequently, breast reconstruction has become an essential component of breast cancer surgery [3,4]. Currently, nipple-sparing subcutaneous mastectomy followed by immediate pre-pectoral one-stage breast reconstruction has gained consensus both domestically and internationally due to its advantages of concealed incisions, minimal trauma, and rapid recovery. Literature reports that the rate of immediate implant-based reconstruction for early-stage breast cancer patients in Europe and the United States has reached 40%-60%, and this proportion has exceeded 30% in major medical centers in China's first-tier cities. However, in clinical practice, the shape of the cavity formed after subcutaneous mastectomy exhibits significant individual heterogeneity, influenced by tumor location, resection scope, and the patient's thoracic anatomy. Existing standardized implants cannot perfectly match the cavity shape, leading to issues such as implant displacement, rotation, and ptosis, which not only affect the aesthetic outcome of the reconstruction but may also increase the risk of capsular contracture. Therefore,

mesh-assisted fixation has become a key technique to address implant stability. Its core functions include: supporting the implant and maintaining the breast contour, filling the dead space in the surgical cavity, isolating the implant from surrounding tissues to reduce inflammatory reactions, and guiding local tissue regeneration.

Currently, the commonly used mesh materials in clinical practice are mainly divided into two categories: biological meshes and synthetic meshes. Among them, biological meshes, such as acellular dermal matrix (ADM), are biosynthetic materials derived from human, bovine, or porcine sources. After decellularization, they retain the three-dimensional structure of the extracellular matrix, exhibit excellent biocompatibility, can induce host tissue cell ingrowth, reduce the rate of capsular contracture, and decrease local inflammation. They have been rapidly and widely adopted in post-mastectomy breast reconstruction. However, they are costly, have limited sources, and are associated with risks of absorption, deformation, and rejection. Moreover, their remodeling process is uncontrollable, leading to unstable long-term support [5,6,7]. Synthetic meshes, centered on non-degradable polymer materials, include the titanium-coated polypropylene mesh (TCPM/TiLOOP® Bra), which is considered a potential alternative to ADM. It is made of non-absorbable, titanium-coated, lightweight polypropylene with a monofilament structure [8,9]. It is soft, thin, has excellent mechanical properties, and is inexpensive,providing effective support for the implant. This mesh was approved for breast reconstruction in Europe in 2008 and is now widely used clinically. Studies have shown that the TiLOOP mesh is currently the most commonly used mesh material in China. A retrospective observational analysis of 276 patients who underwent mastectomy (a total of 328 procedures) confirmed that the titanium mesh

integrates well into the tissue, demonstrating normal tissue repair and healing processes, good oncological safety, and bio- integration with natural tissue. It ensures a more natural and aesthetically pleasing breast appearance and is highly recognized in terms of quality of life [10]. However, its firm texture and poor feel can cause chronic pain, displacement, and exposure. Long-term retention in the body poses risks associated with foreign materials and may interfere with postoperative radiotherapy and imaging follow-up. Therefore, both biological and synthetic meshes generally have shortcomings such as lack of personalization, unnatural feel, poor integration with autologous tissue, and potential interference with subsequent treatments (like radiotherapy) or long-term complications, urgently requiring innovative solutions.

Addressing the limitations of existing meshes, 3D-printed biodegradable breast meshes offer a new path for personalized and precise breast reconstruction. Biodegradable materials, such as medical-grade polycaprolactone (mPCL), are a research hotspot. mPCL is FDA-approved for clinical use, possesses good biocompatibility, and can biodegrade in the body over a period of 2-4 years, with degradation products being carbon dioxide and water, leaving no foreign material behind. It also has good mechanical properties, being flexible yet moderately strong, capable of mimicking the elasticity of soft tissue and providing effective support. 3D printing technology can accurately replicate the patient's breast anatomy based on preoperative imaging data to manufacture implants that perfectly match the defect shape [11]. Furthermore, processing mPCL into complex microstructures, such as micropores and channels, using 3D printing technology can promote vascularization, cell infiltration, and adipose tissue survival [12]. In our preliminary research, our team developed a 3D-printed, multi-layered,

porous, degradable PCL breast scaffold. Basic research revealed that this scaffold provides stable support and has mechanical properties matching those of the breast. Animal studies showed that the scaffold has excellent biocompatibility and creates an immune microenvironment conducive to local tissue repair and regeneration. In clinical trials, we not only completed the world's first application of a 3D-printed PCL scaffold in breast reconstruction in 2017 [13] but also found in a follow-up of 30 patients that the 3D- printed PCL scaffold has good oncological safety and meets the needs of post-lumpectomy breast reshaping [14].

Therefore, based on our previous work, this project aims to further develop a 3D-printed biodegradable biological mesh that better conforms to the implant's shape. We will explore the application of this 3D-printed biodegradable biological mesh in implant-based breast reconstruction, evaluate the effect of the degradable mesh on tissue regeneration, postoperative cosmetic outcomes, and postoperative complications. By establishing a novel surgical model, we aim to fill the gap in domestic and international markets for a more personalized, physiological, and safer innovative technology for breast reconstruction using degradable personalized meshes, thereby promoting the implementation of precision medicine and regenerative medicine concepts in the field of breast cancer rehabilitation.

2. **Study Objectives**

2.1 Primary Objective: To evaluate the clinical efficacy and safety of breast reconstruction using a 3D- printed biodegradable biological mesh.

2.2 Secondary Objective: To evaluate the postoperative quality of life and breast cancer-free interval after breast reconstruction with a 3D-printed biodegradable biological mesh.

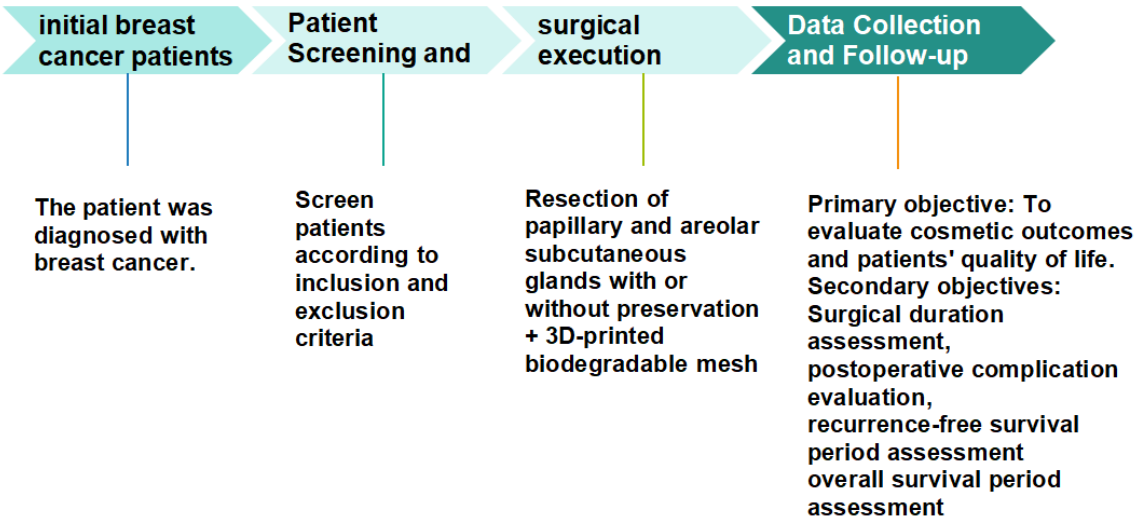
3. Study Design, Principles, and Procedures

3.1 Study Design

1) This is a prospective, single-center, single-arm clinical trial.
2) This study is led by the First Affiliated Hospital of the Air Force Medical University, with participation from the State Key Laboratory for Manufacturing Systems Engineering at Xi'an Jiaotong University.
3) Experimental Group: Immediate one-stage breast reconstruction using a 3D-printed biodegradable mesh combined with a silicone implant after total mastectomy.
4) Sample Size Estimation: 25 cases.

3.2 Study Procedures

This is a prospective, single-center, single-arm clinical study where enrolled patients will undergo breast reconstruction using a 3D-printed biodegradable biological mesh. The overall design of the study is shown in the figure below:



4.Subject Selection

4.1 Inclusion Criteria

1) Female breast cancer patients aged 18 to 70 years.
2) Histopathologically confirmed invasive breast cancer, as defined by the latest ASCO/CAP guidelines.
3) Unable to undergo breast-conserving surgery or willing to undergo total mastectomy with implant- based breast reconstruction.
4) ECOG performance status of 0-1.
5) Voluntary participation in the study and signing of the written informed consent form.

4.2 Exclusion Criteria

1) Age >70 years.
2) Metastatic breast cancer (Stage IV) at initial diagnosis.
3) Multicentric, extensive, diffuse lesions, or inflammatory breast cancer.
4) Tumor involvement of the nipple-areolar complex.
5) Breast cancer during pregnancy.
6) History of other malignancies within the past 5 years, except for cured cervical carcinoma in situ or non-melanoma skin cancer.
7) Abnormal function of vital organs such as heart, lungs, liver, or kidneys; poorly controlled diabetes, etc., rendering the patient unable to tolerate surgery.
8) Patients deemed unsuitable for participation in the study by the investigator.

5. Study Methods and Technical Route

5.1 Investigational Product Name and Specification (if applicable)

This study does not involve investigational drugs.

5.2 Treatment Plan

1) Study Enrollment and Informed Consent: All subjects will sign the relevant informed consent forms before surgery.
2) Preoperative Assessment: Patients will complete the Chinese version of the BREAST-Q V2.0 scale and the QoL (Quality of Life) scale.
3) Preoperative Imaging Assessment:

Enrolled patients will undergo a preoperative thin-slice breast MRI (3.0T) using a multi-channel phased-array dedicated breast coil. The patient will be in a prone position, head-first. The operator will assist in placing the breast in the center of the coil, allowing it to hang naturally without compression to maintain its natural shape. The prone position also helps reduce respiratory motion artifacts. The patient's arms will be placed naturally in front of their head, avoiding the scan field to reduce artifacts. A high-pressure injector will be connected to an intravenous catheter. An axial three-dimensional thin-slice scan will be selected to display both breasts simultaneously, showing the radially arranged ducts converging towards the nipple and the glandular tissue in the axillary tail. The 3D thin-slice scan facilitates sagittal and coronal reconstructions. The scan range will cover the superior and inferior borders of both breasts.

Conventional Plain Scan: A SE T1WI sequence will be used to obtain T1-weighted transverse images. Scan parameters: TR 500ms, TE 15ms, slice thickness 2.8mm, FOV for both breasts 360mm, matrix 256x320, NEX 2.

Functional Imaging: A FLASH (Fast Low Angle Shot) sequence will be used for 3D dynamic contrast-enhanced scanning. Scan parameters: TR 4.42ms, TE 1.41ms, flip angle 12 degrees, FOV for both breasts 360mm, matrix 512x384, slice thickness 1.2mm, 6 acquisitions, total time 6 minutes 19 seconds, one acquisition 55 seconds. The contrast agent will be Gd-DTPA at a dose of 0.2 mmol/kg, administered as a bolus injection via an antecubital or dorsal hand vein at a rate of 3 ml/s, followed by a 20 ml saline flush at the same rate. After the first scan, the automatic high-pressure injector will be activated to inject the Gd-DTPA contrast agent and saline. The enhanced scan will be initiated simultaneously with the injection and repeated 5 times. The post-enhancement images will be subtracted from the initial plain scan images to obtain 5 sets of subtracted images. These subtracted images will then be reconstructed using the Maximum Intensity Projection (MIP) method to generate 5 three-dimensional enhanced images.

4) Preoperative Implant Size Assessment: The implant volume will be estimated using empirical methods to determine the proposed implant size.

5) Surgical Simulation, Design, and 3D Printing of PCL Mesh:

Using medical-grade polycaprolactone (PCL) microspheres as the printing material, the optimized breast mesh model will be manufactured using Selective Laser Sintering (SLS) technology. The model data will be processed by slicing software, and the processed data will be input into the SLS printer. The SLS printer will control the laser scanning path according to the contour and filling structure of the current layer to sinter the PCL powder. This process is repeated layer by layer to print the model structure. After printing, the structure

is removed, residual powder on the surface is cleaned off, and the final product is sterilized with low-temperature ethylene oxide for 48 hours before use.

6) Surgery:

Nipple-sparing subcutaneous mastectomy combined with an implant for immediate breastreconstruction will be performed according to standard clinical practice. The choice of incision will be at the surgeon's discretion. Intraoperatively, tissue from behind the nipple will be sent for frozen

section histopathological examination. If the margin is positive, the nipple-areolar complex will be resected following safety principles. The 3D-printed biodegradable biological mesh will be used to wrap the silicone implant, which is then placed in the subcutaneous tissue. The wound will be soaked and irrigated with sterile distilled water and normal saline. After achieving thorough hemostasis, a drain will be placed, and the skin will be closed in layers.

7) Postoperative Management:

Electronic health records will be established. Follow-ups will be conducted at 1 week, 1 month, 3 months, 6 months, 12 months ， 18 months， and 24 months post-surgery， through study completion, an average of 2 year. Follow-up content includes recording complications or adverse reactions, completing the Chinese version of the BREAST-Q V2.0 scale for breast aesthetics, satisfaction, and QoL assessment, and monitoring for metastasis or recurrence.

5.3 Concomitant Medication

This study does not involve concomitant medication.

6. Observation Items and Timepoints

Clinical observation and laboratory examination items will be designed around the primary and secondary efficacy endpoints of the study. Safety assessment indicators will also be considered, and the detection timepoints will be specified.

Postoperative Management: Dressings will be changed at 3, 7, 10, and 14 days post-surgery to observe the wound for redness, swelling, exudate, infection, and skin flap necrosis. The VAS pain scale will be used to record the patient's postoperative pain, assessed once daily for two consecutive weeks. Patient-reported numbness, swelling, or other sensations will also be recorded. Daily drainage volume will be recorded, and the drain will be removed when the volume is <10ml/24h. The occurrence of complications such as infection or adverse reactions will be recorded.

Long-term Postoperative Follow-up: Electronic health records will be established. Follow-ups will be conducted at 1 week, 1 month, 3 months, 6 months, 12 months ， 18 months，and 24 months post-surgery，through study completion, an average of 2 year. During follow-ups, the Chinese version of the BREAST-Q V2.0 scale will be completed to assess breast aesthetics, satisfaction, and QoL. The presence of metastasis or recurrence will also be recorded.

7. Efficacy Evaluation Criteria

7.1 Primary Efficacy Endpoints

Postoperative Cosmetic Outcome and Safety: Patient satisfaction will be scored using the reconstruction module of the Breast-Q questionnaire, which includes satisfaction with breasts, satisfaction with surgical outcome, and satisfaction with treatment. Satisfaction with breasts will be the primary endpoint of this study. After the

BREAST-Q questionnaire is completed, its score, known as the Q-SCORE, will be calculated. The specific evaluation requires the use of Q-SCORE scoring software. The Breast-Q scale also includes scores for satisfaction with surgery, satisfaction with treatment, and health-related quality of life (QOL), covering physical, psychosocial, and sexual well-being. For all dimensions, a higher patient-reported score indicates higher satisfaction and better quality of life.In outcome of BREAST-Q questionnaire, a higher score indicates better efficacy, while a lower score indicates poorer efficacy.

7.2 Secondary Efficacy Endpoints

1) Recurrence-Free Survival (RFS):

Recurrence in the ipsilateral breast, chest wall, skin, or surgical scar confirmed by imaging is defined as "local recurrence day" on the date of the earliest imaging finding. If local recurrence is diagnosed based on clinical history and physical examination, the date of clinical determination is the "local recurrence day." If diagnosed by cytology or histopathology, the date of the earliest examination is the "local recurrence day." RFS is the time from the date of surgery to the date of disease recurrence or death. For patients with no observed recurrence or death, the follow-up is censored at the date of the last confirmation of no recurrence. An increase in tumor markers such as CEA alone is not sufficient to diagnose recurrence.

2) Disease-Free Survival (DFS):

The time from the date of surgery to the date of tumor recurrence (if the specific date of recurrence is unknown, the date of death due to the tumor is used). For patients with no observed recurrence or death, the follow-up is censored at the date of the last confirmation of no recurrence (last date of no recurrence confirmation: the last date of outpatient visit or examination).

3) Overall Survival (OS):

The time from the date of surgery to death from any cause (if death has not occurred, the time to the last follow-up). For surviving patients, the follow-up is censored at the date of the last confirmation of survival. For patients lost to follow-up, it is censored at the last date of confirmed survival before being lost.

4) Surgical Technical Safety (Complication Rate):

Intraoperative complications: Including but not limited to: intraoperative bleeding, major vessel injury, subcutaneous emphysema, hypercapnia, etc. The rate is calculated as the number of patients with any intraoperative complication divided by the total number of patients who underwent surgery.

Postoperative complications: Including but not limited to: infection, skin flap or nipple-areolar complex necrosis, sensory abnormalities in the surgical area, mesh-related complications, etc. The rate is calculated as the number of patients with any postoperative complication divided by the total number of patients who underwent surgery.

Unplanned reoperation rate: The proportion calculated as the number of patients undergoing unplanned reoperation divided by the total number of patients who underwent surgery.

8. Observation of Adverse Events

8.1 Definition

An Adverse Event (AE) is any untoward medical occurrence in a clinical trial subject after undergoing breast reconstruction with a 3D-printed PCL mesh. It is temporarily associated with the surgical treatment but does not necessarily have a causal relationship with it.

8.2 Adverse Event Reporting Period

All subjects will undergo postoperative safety management and assessment after surgery. The investigator should diligently observe any adverse events that occur during the clinical study period and ask subjects to truthfully report changes in their condition after treatment, avoiding leading questions.While observing efficacy, attention should be paid to adverse reactions or unexpected toxic side effects (including symptoms, signs, and laboratory findings). All adverse events, whether related to theexperimental treatment or not, should be recorded in detail in the CRF, including the time of onset, symptoms, signs, severity, duration, laboratory test results, treatment methods, course, outcome, and follow-up time. Concomitant medications should also be recorded in detail to analyze the correlation between the adverse event and the investigational product. The record should be signed and dated.

Upon discovering an adverse reaction, the investigator may take necessary measures based on the patient's condition and decide whether to terminate the trial. In the event of a serious adverse event, the institution conducting the trial must immediately take necessary measures to protect the subject's safety. All adverse events should be followed up until they resolve or return to baseline to ensure the subject's safety. The follow-up method can be chosen based on the severity of the adverse reaction, including hospitalization, outpatient visits, home visits, phone calls, or correspondence.

8.3 Serious Adverse Events (SAE)

An adverse event is defined as a Serious Adverse Event (SAE) if it meets one or more of the following criteria:

. Results in death

. Is life-threatening

. Requires inpatient hospitalization or prolongation of existing hospitalization

· Results in persistent or significant disability/incapacity

8.4 Reporting of Serious Adverse Events

Any serious adverse event that occurs during the trial, regardless of its relationship to the experimental treatment, must be promptly managed by the investigator with emergency treatment. The investigator must notify the ethics committee of the clinical trial responsible unit by phone/fax within 24 hours and report it to the hospital's adverse reaction monitoring center. A written report must be submitted within 72 hours. The sponsor should promptly investigate the serious adverse event with the investigator and take necessary measures to ensure the safety and rights of the subjects. All relevant medical documents, including laboratory test reports, should be recorded in the source documents.

8.5 Recording and Reporting

The investigator should explain in detail to the patient, requesting them to truthfully report any changes in their condition. The physician should avoid leading questions. While observing efficacy, close attention should be paid to observing adverse events, analyzing their causes, making judgments, and tracking, observing, and recording them, as well as calculating the incidence of adverse reactions.

For adverse events occurring during the trial, the time of onset, symptoms, severity, duration, treatment measures, and outcome should be recorded in the case report form. The relationship with the trial should be evaluated, and the investigator should record it in detail, sign, and date it. The severity of adverse events should be graded. For each symptom, the highest grade of the adverse event that occurred since the last follow-up should be reported.

9. Quality Control and Quality Assurance

The quality control and supervision of the study will be described in terms of laboratory indicator testing, adherence to relevant SOPs, investigator training, subject compliance, and study monitoring.

Adherence to relevant SOPs: New patients are diagnosed by biopsy. If they meet the criteria, they are enrolled.Baseline data of patient is collected. Surgery is performed. Collect data and conduct postoperative follow - up.

Investigator Qualifications: The responsible surgeons participating in this study must be proficient in conventional breast cancer reconstruction surgery and have independently completed at least 30 breast cancer reconstruction procedures.

Study Monitoring: The monitor will periodically check the informed consent and screening/enrollment of subjects during the trial. They will confirm that all case report forms are filled out correctly and are consistent with the source data. All errors or omissions must be corrected or noted, signed, and dated by the investigator. Any changes in treatment, intercurrent illnesses, etc., for each subject must be confirmed and recorded. The withdrawal and loss to follow-up of enrolled subjects must be explained in the case report forms. It must be confirmed that all adverse events are recorded, and serious adverse events are reported and documented.

10. Statistical Methods

Sample Size: 25 cases.

The study will use SAS 9.1.3 statistical software for statistical analysis. Measurement data will be described using mean, median, standard deviation, maximum, and minimum values. Count data or

ranked data will be described using counts and percentages. The completion of the trial will be described, and excluded and dropped-out cases will be described individually. Demographic and other baseline indicators will be described, and their significance will be tested using one-way analysis of variance. Kaplan-Meier method will be used to plot survival curves.

11. Ethics of Clinical Research

The clinical research will adhere to the relevant provisions of the World Medical Association's Declaration of Helsinki. The study protocol must be approved by the Ethics Committee before the clinical research can be initiated. Before each subject is enrolled in this study, the investigator is responsible for fully and comprehensively explaining the purpose, procedures, and potential benefits and risks of the study to the subject or their legal representative. A written informed consent form must be signed. Subjects should be informed that they have the right to withdraw from the study at any time. The informed consent form should be retained as a clinical research document for inspection. The personal privacy and data confidentiality of the subjects will be protected throughout the research process.

12. Study Schedule

2026.01.01 - 2027.12.01: Trial initiation, case enrollment.

2027.12.01 - 2028.12.01: Case follow-up, completion of primary and secondary endpoint assessments, data organization, manuscript writing, and project conclusion.

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