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The Effect of Nitroglycerin Ointment, Fluorescent Angiography, and Incisional NPWT on Mastectomy Skin Flap Perfusion-Related Problems Comprehensive Cancer Center of Wake Forest University (CCCWFU)

PI: Ivo Pestana, MD IRB #00038262 NCT03716050 Date of Document: 05/07/2019

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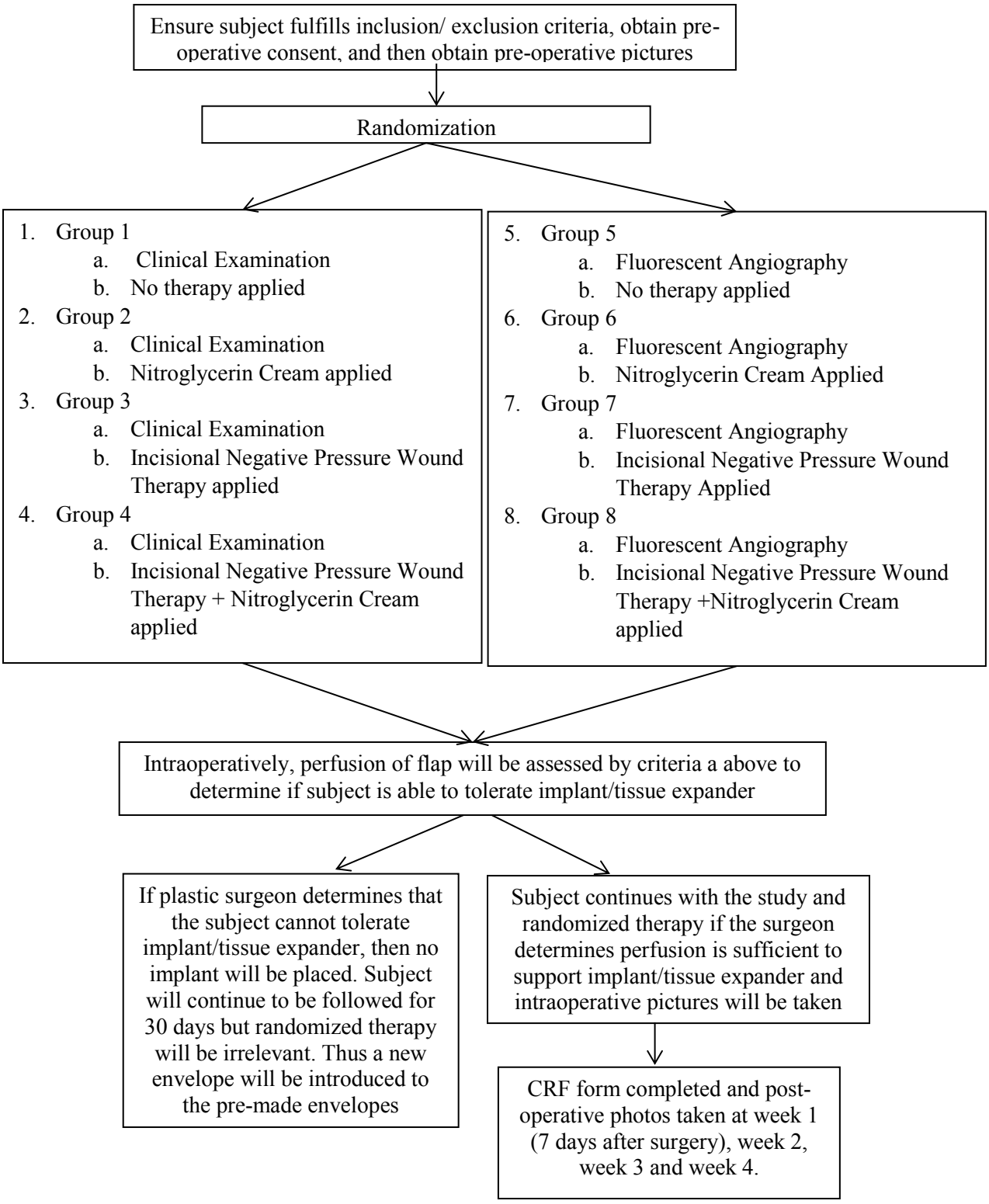
SCHEMA


Ensure subject fulfills inclusion/ exclusion criteria, obtain pre-operative consent, and then obtain pre-operative pictures
Randomization
1. Group 1
a. Clinical Examination
b. No therapy applied
2. Group 2
a. Clinical Examination
b. Nitroglycerin Cream applied
3. Group 3
a. Clinical Examination
b. Incisional Negative Pressure Wound Therapy applied
4. Group 4
a. Clinical Examination
b. Incisional Negative Pressure Wound Therapy + Nitroglycerin Cream applied
5. Group 5
a. Fluorescent Angiography
b. No therapy applied
6. Group 6
a. Fluorescent Angiography
b. Nitroglycerin Cream Applied
7. Group 7
a. Fluorescent Angiography
b. Incisional Negative Pressure Wound Therapy Applied
8. Group 8
a. Fluorescent Angiography
b. Incisional Negative Pressure Wound Therapy +Nitroglycerin Cream applied
Intraoperatively, perfusion of flap will be assessed by criteria a above to determine if subject is able to tolerate implant/tissue expander
If plastic surgeon determines that the subject cannot tolerate implant/tissue expander, then no implant will be placed. Subject will continue to be followed for 30 days but randomized therapy will be irrelevant. Thus a new envelope will be introduced to the pre-made envelopes
Subject continues with the study and randomized therapy if the surgeon determines perfusion is sufficient to support implant/tissue expander and intraoperative pictures will be taken
CRF form completed and post-operative photos taken at week 1 (7 days after surgery), week 2, week 3 and week 4.

1.0 Introduction and Background

Breast cancer changes the lives of more and more women each year. Despite its oncologic benefits, mastectomy results in disfigurement of the chest and women who undergo breast reconstruction demonstrate a profound psychosocial benefit. The outcome of breast reconstruction is highly dependent on the remnant soft tissues and skin after mastectomy. Unfortunately, vascular perfusion-related problems (PRPs) after mastectomy are common and may manifest as skin loss, wound dehiscence, delayed wound healing, or wound/ implant infections. These, in turn, may result in significant patient morbidity as they undergo the process of breast reconstruction. Medications and technologies have been developed to aid in perfusion assessment (fluorescent angiography-FA), perfusion augmentation (nitroglycerin paste-NTG), and wound healing (incisional negative pressure wound therapy-iVAC), but their use and effect in minimizing mastectomy flap skin loss remains unclear.

Indocyanine-green fluorescent angiography (FA) is a safe and efficient technology which implements laser excitation of indocyanine green (ICG) fluorescent dye to provide real-time angiography and assessment of tissue perfusion. Our plastic and reconstructive surgery department and others have utilized FA since it is an accepted technique employed to identify perfusion-related problems in breast and free tissue transfer surgery.

Nitroglycerin ointment exerts a vasodilatory effect on the soft tissue to which it is applied. Thus, nitro paste may help to prevent perfusion-related problems when used in a prophylactic fashion after immediate breast reconstruction. Most recently, a Level 1 evidenced randomized-controlled trial comparing nitroglycerin ointment to placebo in patients undergoing mastectomy with immediate reconstruction has shed new light on the use of this non-invasive treatment to decrease the incidence of potential ischemia-related complications postoperatively.

Vacuum-assisted closure (VAC) dressings, also referred to as negative-pressure wound therapy (NPWT), have been employed since the early 1990's to treat difficult open wounds, and recent evidence has elucidated their role in decreasing complications when placed over surgical closure sites (in which setting they are often referred to as "incisional NPWT" or iVAC). A recent study has demonstrated decreased rates of mastectomy skin flap necrosis when incisional NPWT was placed over the surgical closure compared to no dressing placed over the incision.

2.0 Objectives

Our aim is to evaluate and to compare the above described interventions and their effect on the incidence of PRPs in patients with breast cancer undergoing mastectomy and implant-based immediate breast reconstruction (IBR). The ability to identify, prevent and treat these PRPs can help maximize aesthetic results after breast surgery, improve patient satisfaction with both mastectomy and breast reconstruction, and reduce healthcare cost associated with mastectomy and reconstruction complications.

3.0 Patient Selection

3.1 Inclusion Criteria

3.1.1 Patients must be female.

3.1.2 Patients must be between the ages of 18 and 99 years.

3.1.3 Patients must undergo mastectomy with our attending breast oncology surgeons followed by possible implant-based immediate breast reconstruction (IBR) performed by our attending plastic surgeons at WFBMC.

3.1.4 Patients must have the ability to understand and the willingness to sign an IRB-approved informed consent document.

3.2 Exclusion Criteria

3.2.1 Patients who are under the age of 18 or over the age of 99.

3.2.2 Patients who are undergoing mastectomy without immediate breast reconstruction including immediate breast reconstruction with autologous tissue (or combination of autologous tissue with tissue expanders or implants), or patients with a history of mastectomy presenting for delayed breast reconstruction.

3.2.3 Patients with pre-existing conditions in which use of indocyanine-green is contraindicated or must be used with caution, including those with a history of allergy to iodides or iodinated dye, those with chronic kidney disease, those with hepatic failure or cirrhosis of the liver, and females who are nursing, pregnant, or may become pregnant.

3.2.4 Pregnant women are excluded from this study because pregnancy precludes immediate breast reconstruction in our patient population.

3.2.5 Patients with pre-existing conditions in which use of nitroglycerin paste is contraindicated, including those with a history of cardiac insufficiency, hypotension, sensitivity to nitrites, severe liver impairment, glaucoma, hyperthyroidism, recent head trauma, severe anemia, or taking certain medication (i.e. alteplase, aspirin, beta-blocker, calcium channel blocker, diuretics or thiazides).

3.2.6 Patients with pre-existing conditions in whom use of incisional negative pressure wound therapy is contraindicated including those with evidence of surgical site infection (i.e. erythema, purulent drainage), clinical signs of hematoma (i.e. wound swelling, fluctuance, blood drainage), history of persistent cancer, exposed blood vessel on site of proposed therapeutic use, or allergy to acrylics and adhesives.

3.3 Inclusion of Women and Minorities

Females of any race or ethnicity who meet the above-described inclusion criteria are eligible to participate in this study.

4.0 Study Outcomes and Study Measures

We will perform a randomized pilot study comprised of eight groups. All of these groups employ accepted techniques, medications and dressings and therefore are not experimental.

Group 1: Breast skin after mastectomy will be clinically examined by the surgeon to determine if there is adequate blood flow to the skin to allow safe coverage of the breast implant. No dye study, ointment, or vacuum dressing will be applied to the breast after implant placement.

Group 2 - Breast skin after mastectomy will be clinically examined by the surgeon, and nitroglycerin (NTG) cream will be applied to the breast skin after implant placement. This cream does not have systemic effects but may improve blood flow to the remnant breast skin after mastectomy.

Group 3 - Breast skin after mastectomy will be clinically examined by the surgeon, and an incisional vacuum-assisted dressing (iVAC) will be placed over the breast incisions after implant placement, which may improve blood flow to the skin and help wound healing.

Group 4 - Breast skin after mastectomy will be clinically examined by the surgeon, and both NTG cream will be applied to the breast skin and an iVAC will be placed over the incisions after implant placement.

Group 5 - Blood flow to breast skin after mastectomy will be examined using a fluorescent dye study called fluorescent angiography (FA) to determine if there is adequate blood flow to the skin to allow safe coverage of the breast implant. No further intervention will be used after implant placement.

Group 6 - Blood flow to breast skin breast skin will be examined using FA, and NTG cream will be applied to the skin after the implant is placed.

Group 7 - Blood flow to breast skin breast skin will be examined using FA, and an iVAC will be placed over breast skin incisions after the implant is placed.

Group 8 - Blood flow to breast skin breast skin will be examined using FA, and both NTG cream and iVAC will be used as interventions after the implant is placed.

The dosage of indocyanine-green (IC-green) to be used for assessment of mastectomy flaps will be in 10 mg boluses, not to exceed 5 mg/kg.

Nitro-Bid® (nitroglycerin ointment, 2%) at a dose of 45 mg (equal to 7.5 cm on the measuring strip provided with packaging) will be used. The paste will be applied to remnant breast skin after skin closure and surgical dressings placed over top.

Incisional negative pressure wound therapy will consist of a standard sponge dressing with adhesive drape, either Ioban® 2 (3M ™) or KCI-V.A.C.® Drape (KCI®), to continuous suction at 125 mm Hg while the patient is in hospital and not to exceed 4 days.

A physician will see the subjects on a regular weekly basis for up to 30 days once the procedure has been completed. These clinical visits are standard of care and the subject's health and well-being will be monitored rigorously during these visits. If during any of these visits, the physician deems a therapy necessary to prevent impairment/damage and improve well-being, the subject will be treated appropriately.

At no point during this study will the needs of the randomized arm/research take priority over the subject's health and well-being.

Study Risks

Risks of surgery may include bleeding, infection, hematoma/seroma formation, risks of anesthesia, implant/tissue expander failure, extrusion, or tissue necrosis.

Risks with ICGLA may include a potential risk for anaphylaxis/urticarial reaction. Caution must be taken with patients with iodine/iodinated contrast allergy. There have been no studies performed to evaluate carcinogenicity, mutagenicity, or impairment of fertility.

Risks associated with the use of nitroglycerin paste may include dizziness, light-headedness, blurred vision, fainting, increased risk of alcohol toxicity if consumed in conjunction with nitroglycerin use, headaches, severe allergic reactions (rash, hives, itching, difficulty breathing, tightness in chest, swelling of mouth, face, lips, throat or tongue), flushing and red, swollen, blistered or peeling skin.

Vacuum-assisted closure is routinely used in the medical setting for various types of traumatic, surgically-created, or chronic wounds. The use of NPWT therapy is contraindicated when the system is in direct contact with vital structures (i.e. exposed vessels, anastomoses, organs, or nerves), or when the following are present in the wound: malignancy, untreated osteomyelitis, non-enteric and unexplored fistulas, or necrotic tissue with eschar present.Use of Ioban® drape is contraindicated in patients with a known sensitivity to iodine. In these instances, the KCI-V.A.C.® drape will be used. Patients with known allergy to acrylics or adhesives may develop an adverse hypersensitivity reaction to the KCI drape and will be excluded from the study.

4.1 Primary Outcomes

4.1.1 The primary outcomes will be the following perfusion-related problems:

- Soft tissue ischemia/loss (i.e. partial and full thickness soft tissue defects identified postoperatively in clinic follow up)
- Surgical site infection (i.e. soft tissue cellulitis or abscess identified postoperatively either clinically or with wound culture)
- Delayed wound healing (manifesting as suture dehiscence and opening of an incisional wound)

4.2 Secondary Outcomes

4.2.1 The secondary outcomes will be the following:

- Rate of operative intervention secondary to perfusion related problems as listed in "Primary Outcomes" above, and surgical outcome with regards to mastectomy flaps
- Rate of prescribing of outpatient antibiotics or admission for inpatient IV antibiotics for treatment of surgical site infection

- Wound care management modalities for treatment of delayed wound healing complications as listed in "Primary Outcomes" above, and wound healing outcomes

5.0 Treatment Plan

	Pre-Operative Visit	Day of Surgery	Week 1 Postop	Week 2 Postop	Week 3 Postop	Week 4 Postop
Enrollment and informed consent	X					
Clinical assessment to determine whether implant/tissue expander can be placed without compromising perfusion		X				
Clinical photos of surgical site	X	X	X	X	X	X
Data sheet documenting outcome			X	X	X	X

5.1 Study Related Activities

Potential subjects will be identified by the physician, advanced practice provider, or research coordinator. This individual will discuss the study with the patient and answer any questions or concerns they may have. This will take place in an exam room, hospital room, or by phone depending on whether or not the patient is inpatient or a clinic patient.

Signed informed consent will be obtained from each subject who will be undergoing mastectomy with immediate breast reconstruction using breast implants during a pre-operative appointment in the General Surgery (Breast Oncology) or Plastic Surgery clinic. After the subject has been identified as meeting the inclusion criteria by the clinician or research coordinator, the study coordinator will obtain the signed informed consent. A signed copy of the consent form will be given to the subject. Once the patient has agreed to take part in the study and sign the consent form, pre-operative photos of the breast will be taken. Pregnancy tests performed 15 days apart (prior to surgery) is done as standard of care for all women of childbearing age potentially undergoing this surgery.

Twenty subjects will be randomized to each arm of the study using sealed instructions provided by the study coordinator who will inform the clinician of the arm prior to surgery. The envelopes will be filled prior to the study with envelopes containing a document indicating to which group the patient will be a part of. The envelopes will be sealed and shuffled and then labeled from subject 1 through 160.

Once the subject is randomized to an arm of the study, the operating surgeon will be informed of the arm prior to the surgery. On the day of surgery, the surgeon will decide intraoperatively whether an implant/tissue expander can be safely placed without compromising perfusion of the flap. If the surgeon determines that an implant/tissue expander cannot be safely placed, they will continue to be followed as that indicates a perfusion related problem. At that point, another envelope will be introduced into the pre-made envelopes with that subject's assigned arm. Pictures will be take pre-

operatively, intraoperatively, and at week 1,2,3, and 4 post-operatively. In addition to these pictures, the data collecting sheet will be completed by the physician, advanced practice provider or study coordinator at week 1, 2,3 and 4 post-operatively.

This is not an intent-to-treat trial. In order to ensure that we are able to gather the most information from this study, we want to be able to closely monitor our enrolled subjects and remove any subjects that are non-compliant with their randomized arm. The study coordinator will be responsible for keeping a detailed Excel spreadsheet of the enrolled subjects and their respective arms of the study. If a subject comes off the study prematurely, another envelope will be introduced to the pre-made envelopes with the withdrawn subject's arm – in this way the arms will never be unbalanced.

This study will be monitored by the Cancer Center's Safety and Toxicity Review (STRC) for SAEs and will also be monitored for accrual by the Clinical Research Oversight Committee (CROC) since this is an institutional intervention study. The standard operating procedures for the STRC can be found below in appendix c.

5.2 Duration of Follow-up

Patients will be followed for a minimum of 30 days after the procedure. Clinical assessments will occur weekly.

6.0 Adverse Events List and Reporting Requirements

Any unanticipated problems, serious and unexpected adverse events, deviations or protocol changes will be promptly reported by the principal investigator or designated member of the research team to the IRB and sponsor or appropriate government agency if appropriate.

6.1 Adverse Event Characteristics

Adverse events may include, but are not limited to: anaphylaxis/urticarial reaction, dizziness, light-headedness, blurred vision, fainting, severe allergic reactions (rash, hives, itching, difficulty breathing, tightness in chest, swelling of mouth, face, lips, throat or tongue), flushing and red, swollen, blistered or peeling skin, intraoperative or immediately postoperative/post-procedure death.

6.2 WFUHS IRB AE Reporting Requirements

Any unanticipated problems involving risks to subjects or others and adverse events shall be promptly reported to the IRB, according to institutional policy. Reporting to the IRB is required regardless of the funding source, study sponsor, or whether the event involves an investigational or marketed drug, biologic or device. Reportable events are not limited to physical injury, but include psychological, economic and social harm. Reportable events may arise as a result of drugs, biological agents, devices, procedures or other interventions, or as a result of questionnaires, surveys, observations or other interactions with research subjects.

All members of the research team are responsible for the appropriate reporting to the IRB and other applicable parties of unanticipated problems involving risk to subjects or others. The Principal Investigator, however, is ultimately responsible for ensuring the prompt reporting of unanticipated problems involving risk to subjects or others to the IRB. The Principal Investigator is also responsible for ensuring that all reported unanticipated risks to subjects and others which they receive are reviewed to determine whether the report represents a change in the risks and/or benefits to study participants, and whether any changes in the informed consent, protocol or other study-related documents are required.

Any unanticipated problems involving risks to subjects or others occurring at a site where the study has been approved by the WFUHS IRB (internal events) must be reported to the WFUHS IRB within 7 calendar days of the investigator or other members of the study team becoming aware of the event.

Any unanticipated problems involving risks to subjects or others occurring at another site conducting the same study that has been approved by the WFUHS IRB (external events) must be reported to the WFUHS IRB within 7 calendar days of the investigator or other members of the study team becoming aware of the event.

Any event, incident, experience, or outcome that alters the risk versus potential benefit of the research and as a result warrants a substantive change in the research protocol or informed consent process/document in order to insure the safety, rights or welfare of research subjects.

7.0 Data Management

Race Verification Form	ORIS
Protocol registration form	ORIS
Data Collection	REDCap

8.0 Statistical Considerations

This investigation will be designed as a pilot study, in which patients will be randomized to one of the eight groups described. Once enrollment goals are met, outcomes data will be calculated for each of the primary and secondary measures. Using these estimates, a larger randomized clinical trial will be designed to assess differences between study groups. It is anticipated that the rate of study completion will be uniformly high across the study groups, with low rates of attrition. For use in designing a future trial, we will calculate the rate of dropout for each group. Reasons for dropout will be recorded and reported.

8.1 Estimated Accrual Rate

8.1.1 We anticipate enrolling approximately 70-80 patients per year; With 8 study groups, with 20 subjects per group, the study will need 160 subjects to meet recruitment goals. We will allow for attrition in our enrollment estimates, as our goal is to have 20 completed subjects in each arm. Assuming a 15% dropout rate,

the study would need approximately 184 subjects. Study recruitment should be completed within 2.5 years.

8.2 Estimated Study Length

8.2.1 The time Follow up time for each patient will be thirty days, which will allow enough time for mastectomy flap necrosis to develop.

8.3 Statistical Analyses

8.3.1 Estimates of all primary outcomes (Soft tissue ischemia/loss, surgical site infection, delayed wound healing) and secondary outcomes (rate of operative intervention, rate of prescribing antibiotics or admission for IV antibiotic therapy, wound care management modalities and outcomes) will be calculated. These data will provide estimates of rates for each outcome that will allow planning for future studies. The rates of the primary outcomes will be reported, along with corresponding 95% confidence intervals. With an anticipated sample size of 20 in each group, the width of the exact 95% confidence interval would be approximately +/- 22.8 if the observed rate was 50%. The table below shows the power for testing against an observed rate of 10% (the anticipated average rate in the 8 study groups) in group 1 versus 20%, 30%, 40%, and 50% in other groups with an alpha of 0.20. With group sample sizes of 20 in each of the 2 groups, the study would have 84% power to detect a difference of 30%.

Numeric Results of Tests Based on the Difference: P1 - P2
H0: P1 - P2 = 0. H1: P1 - P2 = D1 ≠ 0. Test Statistic: Z test with pooled variance

Power	N1	N2	N	Trt|H1 P1	Cntrl P2	Diff D1	Target Alpha	Actual Alpha
0.36453	20	20	40	0.10	0.20	-0.10	0.2000	0.1966
0.62930	20	20	40	0.10	0.30	-0.20	0.2000	0.2228
0.84713	20	20	40	0.10	0.40	-0.30	0.2000	0.2172
0.95746	20	20	40	0.10	0.50	-0.40	0.2000	0.1920

The table below shows the target and actual alpha and power if groups are combined to have 80 subjects in each one.

Numeric Results of Tests Based on the Difference: P1 - P2
H0: P1 - P2 = 0. H1: P1 - P2 = D1 ≠ 0. Test Statistic: Z test with pooled variance

Power	N1	N2	N	Trt|H1 P1	Cntrl P2	Diff D1	Target Alpha	Actual Alpha
0.42287	80	80	160	0.10	0.20	-0.10	0.05	0.0503
0.71633	80	80	160	0.10	0.25	-0.15	0.05	0.0518
0.90284	80	80	160	0.10	0.30	-0.20	0.05	0.0513
0.97682	80	80	160	0.10	0.35	-0.25	0.05	0.0507
0.99617	80	80	160	0.10	0.40	-0.30	0.05	0.0472

With group sample sizes of 80 in each of the 2 groups, being compared, the study would have 90% power to detect a difference of 20%.

8.3.2 The rate of attrition and reason for dropout will be reported for each of the study groups; these data will be used in adjusting the needed sample size for a larger study. The rate of attrition and its corresponding 95% confidence interval will be calculated; attrition will be defined as the number of subjects who do not attend the final assessment, divided by the number accrued into the treatment group.

9.0 Registration Procedures

All patients entered on any CCCWFU trial, whether treatment, companion, or cancer control trial, **must** be registered with the CCCWFU Protocol Registrar or entered into ORIS Screening Log. Patients **must** be registered prior to the initiation of treatment.

You must perform the following steps in order to ensure prompt registration of your patient:

1. Complete the Reduced Review Registration Form (Appendix A)
2. Complete the Race Verification Form (Appendix B)
3. Send the Reduced Review Protocol Registration Form and the Race Verification Form to the registrar, either by fax or email.

Contact Information:
Protocol Registrar PHONE (336) 713-6767
Protocol Registrar FAX (336) 713-6772
Protocol Registrar E-MAIL (registra@wakehealth.edu)

*Protocol Registration is open from 8:30 AM - 4:00 PM, Monday-Friday.

To complete the registration process, the Registrar will:

- register the patient on the study and assign the PID number

References

Burnier P, et al. Indocyanine green applications in plastic surgery: A review of the literature. J Plast Reconstr Aesthet Surg. 2017 Jun;70(6): 814-27.

Dent BL, Small K, Swistel A, Talmor M. Nipple-areolar complex ischemia after nipple-sparing mastectomy with immediate implant-based breast reconstruction: risk factors and the success of conservative treatment. Aesth Surg J. 2014;34(4): 560-70.

Duggal CS, Madni T, Losken A. An outcome analysis of intraoperative angiography for postmastectomy breast reconstruction. Aesthet Surg J. 2014 Jan;34(1): 61-5.

Fan Z, He J. Preventing necrosis of the skin flaps with nitroglycerin after radical resection for breast cancer. J Surg Oncol. 1993 Jul;53(3): 210.

Foglia E, et al. Economic and organizational sustainability of a negative-pressure portable device for the prevention of surgical-site complications. Clinicoecon Outcomes Res. 2017 Jun;12(9): 343-51.

Gdalevitch P, et al. Effects of nitroglycerin ointment on mastectomy flap necrosis in immediate breast reconstruction: a randomized controlled trial. Plast Reconstr Surg. 2015 Jun;135(6): 1530-9.

Gorai K, et al. Prediction of skin necrosis after mastectomy for breast cancer using indocyanine green angiography imaging. Plast Reconstr Surg Glob Open 2017 Apr;5(4): e1321.

Griffiths M, Chae MP, Rozen WM. Indocyanine green-based fluorescent angiography in breast reconstruction. Gland Surg. 2016;5(2): 133-49.

Harless CA, Jacobson SR. Tailoring through technology: A retrospective review of a single surgeon's experience with implant-based breast reconstruction before and after implementation of laser-assisted indocyanine green angiography. Breast J. 2016 May;22(3): 274-81.

Kim, DY, Park SJ, Bang SI, Mun GH, Pyon JK. Does the use of incisional negative-pressure wound therapy prevent mastectomy flap necrosis in immediate expander-based breast reconstruction? Plast Reconstr Surg. 2016 Sept;138(5): 558-66.

Komorowska-Timek E, Gurtner GC. Intraoperative perfusion mapping with laser-assisted indocyanine green imaging can predict and prevent complications in immediate breast reconstruction. Plast Reconstr Surg. 2010 Apr;125(4): 1065-73.

Kutun S, et al. Is transdermal nitroglycerin application effective in preventing and healing flap ischaemia after modified radical mastectomy? S Afr J Surg. 2010 Nov;48(4): 119-21.

Matsen CB, et al. Skin flap necrosis after mastectomy with reconstruction: A prospective study. Ann Surg Oncol. 2016 Jan;23(1): 257-64.

Munabi NCO, et al. The ability of intra-operative perfusion mapping with laser-assisted indocyanine green angiography to predict mastectomy flap necrosis in breast reconstruction: A prospective trial. J Plast Reconstr Aesthet Surg. 2014 Apr;67(4): 449-55.

Newman MI, Samson MC, Tamburrino JF, Swartz KA. Intraoperative laser-assisted indocyanine green angiography for the evaluation of mastectomy flaps in immediate breast reconstruction. J Reconstr Microsurg. 2010 Sep;26(7): 487-92.

Pestana IA, Campbell DC, Bharti G, Thompson JT. Factors affecting complications in radiated breast reconstruction. Ann Plast Surg. 2013 May;70(5):542-5.

Phillips BT, et al. Intraoperative perfusion techniques can accurately predict mastectomy skin flap necrosis in breast reconstruction: Results of a prospective trial. Plast Reconstr Surg. 2012 May;129(5): 778e-788e.

Robertson SA, Jeevaratnam JA, Agrawal A, Cutress RI. Mastectomy skin flap necrosis: challenges and solutions. Breast Cancer. 2017 Mar;9: 141-52.

Xu K, Tzankova V, Li C, Sharma S. Intravenous fluorescein angiography-associated adverse reactions. Can J Ophthalmol. 2016 Oct;51(5): 321-5.

Zenn M, et al. Optimizing outcomes of postmastectomy breast reconstruction with acellular dermal matrix: A review of recent clinical data. Eplasty 2017;17(18): 156-71.

The following Appendices are required for all CCCWFU cancer treatment protocols.

Add additional appendices as needed.

***ALL** data collection forms must be included as protocol appendices at the time the protocol is submitted to the CCCWFU Protocol Review Committee (PRC) for review.*

APPENDIX A: REDUCED REVIEW REGISTRATION FORM**

Protocol#: 00038262 *Required Field

Protocol Title: The Effect of Nitroglycerin Ointment, Fluorescent Angiography, and Incisional NPWT on Mastectomy Skin Flap Perfusion-Related Problems CCCWFU#00038262

DEMOGRAPHICS

Name (last, first) : _____, _____
(or initials)

UNIT # (MRN): _____ (required if exists) Zip Code:_____ (required if no MRN)

*SEX { } MALE ( ) FEMALE

*ETHNICITY (choose one): ( ) HISPANIC { } NON-HISPANIC

*RACE (choose all that apply): □ WHITE □ ASIAN

□ AFRICAN-AMERICAN □ PACIFIC ISLANDER (HAWAIIAN)

□ NATIVE AMERICAN (ALASKAN) □ Unknown (Other, Refused}

*DIAGNOSIS : _____

BIRTH DATE: _____(include if no MRN is provided)

*MD Name (last, first): _____

*DATE CONSENT WAS SIGNED: _____

Date of Registration (if different): _____

PID#: _____ (to be completed by Registrar)

The Comprehensive Cancer Center requires that all registrations be sent to the CCCWFU Centralized Registrar the day the patient is consented; if this is not possible we require that all registrations be communicated to the Centralized Registrar within 72 hours of consent.
**Reduced review means eligibility and other review are not performed by CRM registrar. Questions: call 713-6767

Submit by Email*** Print Form

*** If not using the full wfubmc edu outlook client (full outlook, not web outlook), save this file and attach to an email to regjstra@wfubmc .edu
Submitter of this form is responsible for insuring that all regulatory and eligibility requirements are met for this registration.

Appendix B – Race Verification Form

Thank you so much for helping us to verify your race and ethnicity to ensure the quality of our information. As a brief reminder, the information you provide today will be kept confidential.

1. Are you:

☐Hispanic or Latino/a

☐Not Hispanic or Latino/a

2. What is your race? One or more categories may be selected.

☐White or Caucasian

☐Black or African American American

Indian or ☐Alaskan Native Asian

☐Native Hawaiian or Other Pacific Islander

☐Other, Please Specify: _____

Internal use only:

Was the self-reported race and ethnicity of the participant verified at the time of consent?

☐Yes ☐ No

Was a discrepancy found? **☐Yes ☐ No**

If yes, please provide what is currently indicated in the EMR:

Ethnicity: _____ Race: _____

Additional comments: _____

_____

_____