A Double-Blind Randomized Controlled Trial on the Efficacy of Hydrocolloid Dressing vs. Topical Antibiotic on Wound Healing of Post-Punch Biopsy Wounds Among Patients in a Tertiary Hospital in Manila

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PROJECT SUMMARY

Rationale:

Objectives: The main objective of this study is to determine the efficacy of using hydrocolloid dressing on wound healing of post-punch biopsy wounds vs topical antibiotic. Specifically, it aims to measure the following parameters: the presence or absence of infection, the clinical estimate of reepithelialization, the clinical estimate of wound closure, scar formation, pigmentation of scar, and the cosmetic appearance of the wound.

Methodology and Population: The study is a double-blind randomized controlled trial which will be conducted at the Dermatology outpatient department and the private clinics of dermatology consultants of the University of Santo Tomas Hospital. Patients who will be included are those who are 18 to 64 years of age with clean cutaneous lesions. Excluded from this study are those who have infected wounds, those who have conditions with poor tendency to heal including diabetes mellitus, peripheral vascular disease, history of keloid formation, those currently receiving anticoagulation therapy or systemic corticosteroids, and those known to have hypersensitivity to topical antibiotics.

Time Frame: 6 months

Expected Outcomes: The primary outcome measure is the proportion of patients who achieved better overall healing when treated with hydrocolloid dressing.

GENERAL INFORMATION

PROTOCOL TITLE:

A DOUBLE-BLIND RANDOMIZED CONTROLLED TRIAL ON THE EFFICACY OF HYDROCOLLOID DRESSING VS. TOPICAL ANTIBIOTIC ON WOUND HEALING OF POST-PUNCH BIOPSY WOUNDS AMONG PATIENTS IN A TERTIARY HOSPITAL IN MANILA

NAME AND ADDRESS OF SPONSOR/FUNDER:

NOT APPLICABLE

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BACKGROUND

Skin biopsies play an essential role in the verification or confirmation of the diagnosis of patients with dermatologic disorders. The punch biopsy, one of the frequently performed types of skin biopsies, is an incisional method that makes use of a cylindrical blade to obtain a specimen with a fuller thickness of the skin as compared to a shave biopsy. It is a procedure that has a low-risk of developing surgical site infections due to the short operative time and shallow wound depth. The most commonly used skin punch sizes range from 2 mm to 6 mm in diameter. Punch biopsies of less than 4 mm in size do not need to be closed with sutures. Obtaining an adequate tissue sample for histopathologic evaluation while preventing patient disfigurement is important.[1]

Wound healing is a complex biological process where the main goal of clinical intervention is the promotion of tissue restoration.[2] Acute wounds are wounds that follow a predictable and timely repair process which results in the restoration of sufficient anatomical and functional integrity if healing proceeds normally.[3] In the pathophysiology of acute wound healing, there are four overlapping phases of the normal wound healing process namely coagulation, inflammation, granulation tissue formation, and remodeling phase. Neutrophils, macrophages, and platelets provide growth factors and provisional matrices that are required for the recruitment of epidermal and dermal cells into the wound bed during the coagulation and inflammatory phases of healing. The proliferative phase begins 3 days after injury and is characterized by increased keratinocyte and fibroblast proliferation, migration, and extracellular membrane synthesis. During this stage, angiogenesis or neovascularization also occurs. The tissue has a granular appearance due to the presence of blood vessels (granulation tissue). Finally, 1 to 2 weeks after injury,

differentiated fibroblastic cells (myofibroblasts) present in the granulation tissue begin to remodel the extracellular matrix. Acellular scar formation is caused by extracellular matrix remodeling followed by apoptosis of resident cells.[4]

Hydrocolloid is a type of dressing in which a "hydrophilic gelable mass is applied in a semisolid form to a flexible semipermeable carrier." Hydrocolloids were originally made as small square pieces in 1985. In 1989, a "thin" version was developed wherein these dressings have little or no fluid retention ability and are less permeable than the standard films and are used as post-operative dressings or as secondary retention products over primary dressings. Hydrocolloid dressings are most commonly utilized with the treatment of chronic wounds such as leg ulcers and pressure ulcers, however they can also be used with good effect for the treatment of a variety of acute wounds where their ability to facilitate debridement, absorb excess fluid and provide a barrier to infection is equally valuable.[5]

Locally, in the Philippines, due to high rates of infection, topical antibiotics are routinely applied as wound care and prophylaxis despite obtaining clean wounds. In this study, we will investigate whether hydrocolloid dressings can be used as a treatment modality for the healing and care of post-punch biopsy sites.

REVIEW OF RELATED LITERATURE

Surgical Wounds

In the management of surgical wounds, hydrocolloid dressings have been used as primary and secondary dressings for sutured wounds and wounds with secondary intention healing.[5]

The use of hydrocolloids following excision of pilonidal sinuses have been reported by Viciano *et al*. through a prospective randomized trial involving 38 patients in which the researchers compared a hydrocolloid (Comfeel with Varihesive/Duoderm) and conventional gauze. Median healing time in the control group was 68 days in comparison to the experimental group which was 65 days. One-third of the cultures in the control group developed pathogens compared with 1 out of 23 patients with the hydrocolloid group, however these results were deemed statistically insignificant. Pain was assessed as significantly less in the hydrocolloid group in the first four weeks post-operation compared with those in the control group in which the conclusion was made that the use of hydrocolloid dressings leads to a reduction in pain but no effect on healing times.[6]

A study by Estienne and Di Bella compared Granuflex/Duoderm with traditional dressings which made use of hypochlorite irrigation and packing with paraffin gauze in 40 patients for pilonidal fistula. The hydrocolloid dressing was first applied on the third postoperative day after an iodoform gauze pack was removed which was applied in theater. Dressings were changed on alternate days, but was extended to 3-5 days later on and results showed that wounds with hydrocolloid dressings had complete healing in an average of 6 weeks compared with 10 weeks with the traditional dressings.[7]

Michie and Hugill compared Granuflex/Duoderm Extra Thin hydrocolloid dressing with an impregnated gauze (Xeroform) in 28 patients with 40 wounds after an elective surgery to assess the effects of the dressings on incisional healing. One-half of every incision was covered with each of the dressings under investigation as each patient served as their own control. Wounds were assessed after a period of 2 to 3 days, 7 to 10 days, 4 weeks, and 7 months postoperatively. No incision showed any evidence of infection and during suture removal, hydrocolloid dressings were assessed to contain exudate, protect the wound, and facilitate mobility and personal hygiene more effectively compared with the impregnated gauze dressing. When assessment was done after 4 weeks, scar segments covered with hydrocolloid dressings showed better appearance in terms of color, evenness, and suppleness compared with the Xeroform gauze, however these differences were no longer observed 7 months after the elective surgery.[8]

A study by Hulten showed that soiling which commonly occurs with wounds dressed with traditional gauze were not observed in 89% of 340 patients who had undergone colorectal surgery with stoma creation and dressed with hydrocolloid. The study also showed that 92% of the patients studied had no wound infections encountered.[9]

Burns

A report on the use of hydrocolloid dressing in the treatment of burns by Hermans and Hermans in 1984 showed that the use of Granuflex/Duoderm in 24 patients had favorable healing rates compared with those treated with silver sulfadiazine cream in both superficial and deep partial thickness burns.[10]

In a study by Wright *et al*, 67 patients with partial thickness burns managed as outpatients were treated with hydrocolloid dressings (Granuflex/Duoderm) versus conventional dressing (Bactigras) to compare the two products. The healing time (median 12 days) were comparable for both products in this study, however the quality of healing was rated “excellent” in 56% of the participants treated with Granuflex/Duoderm versus 11% in the group treated with Bactigras. The authors in this study suggested to use Granuflex/Duoderm as “first-choice dressing in the management of partial skin thickness burns”.[11]

Traumatic Wounds

A study done by Heffernan and Martin compared Granuflex/Duoderm Extra Thin with a perforated film absorbent dressing in managing 96 patients with lacerations, abrasions and minor operation incisions. The study showed similar results for healing time for both interventions; however, those patients using hydrocolloid dressings experienced less pain, required less analgesia, and were able to carry out activities of daily living without their wounds getting affected.[12]

Pediatric Wounds

A study done by Schmitt et al. compared hydrocolloid dressing with adhesive skin tapes on post-operative wounds in 170 children. Effective skin closure was comparable in both interventions but hydrocolloids were observed to be more secure, remaining in place in 69 children compared with adhesive skin tapes.[13]

SIGNIFICANCE OF THE STUDY

This study can provide a potential option to promote faster healing of post-operative wounds particularly for skin punch biopsy used in the field of Dermatology.

It will encourage Filipino dermatologists to reduce the routine use of prophylactic topical antibiotics as post-biopsy care heralding better antibiotic stewardship practices.

MAIN OBJECTIVE

The main objective of this study is to determine the efficacy of using hydrocolloid dressing on wound healing of non-sutured post-punch biopsy sites in comparison to gauze dressing impregnated with topical antibiotics (mupirocin ointment) at the Dermatology outpatient department and the private clinics of dermatology consultants of the University of Santo Tomas Hospital.

SPECIFIC OBJECTIVES

Specifically, this study aims to compare the efficacy of hydrocolloid dressing after 5 days post-punch biopsy by measuring the following parameters: absence or presence of infection, clinical estimate of reepithelialization, clinical estimate of wound closure, scar formation, pigmentation of scar and cosmetic appearance of wound.

METHODOLOGY

A. Study Design

This is a double blind randomized controlled trial that will be conducted at the outpatient department of the University of Santo Tomas Hospital Department of Dermatology. Permission letters from the Head of Ambulatory Care Services (ACS), the Data Privacy Officer (DPO), and the Medical Director of UST Hospital will be obtained prior to the implementation of this study. Permission letters from the USTH Dermatology consultants for their private patients will be obtained prior to the implementation of this study.

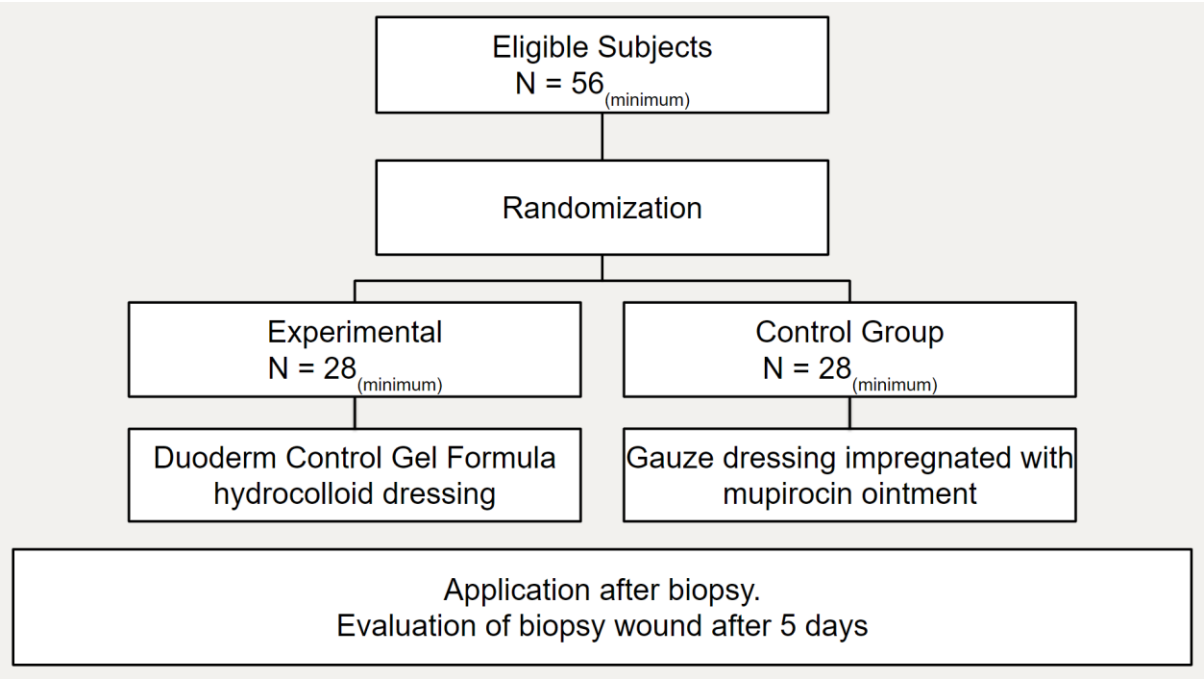

Figure 1. Schematic diagram of the study design

B. Patient Selection, Recruitment and Withdrawal

Adult patients 18 to 64 years old with clean cutaneous lesions who will undergo skin punch biopsy using a 3-mm disposable biopsy puncher shall be included in the study.

Patients will be recruited from the UST Hospital outpatient department and from the private clinics of the UST Hospital Dermatology consultants. Patients who have infected wounds, patients who have conditions with poor tendency to heal including diabetes mellitus, peripheral vascular disease, history of keloid formation, patients currently receiving anticoagulation therapy or systemic corticosteroids, and patients known to have hypersensitivity to topical antibiotics shall be excluded from the study.

Participants may request to withdraw from the study at any time. A participant may also be withdrawn from the study if the primary investigator believes that the participant was non-compliant with the treatment guidelines or develops severe and intolerable adverse effects (e.g. hypersensitivity reaction) secondary to the treatment given.

C. Randomization and Blinding

Randomization

Assignment of participants to the experimental (hydrocolloid dressing) or control group (topical antibiotic) will be done using the fishbowl method by a research assistant.

Blinding

Participants and the physician assessors will be blinded with the treatment assigned.

D. Baseline Data Collection

On the first visit, informed consent will be obtained from the patient. Afterwards, the following data will be recorded by the primary investigator on the baseline general information sheet: study code assigned to each individual patient, age, sex, and anatomic sites involved.

Photographs will be limited to the skin punch biopsy sites and will be taken at baseline using a DSLR camera with uniform distance (3 inches) and lighting.

On the 5th day after the skin punch biopsy procedure, the following data will be recorded by the physician assessors: the presence or absence of infection, the clinical estimate of reepithelialization, the clinical estimate of wound closure, scar formation, pigmentation of scar, and the cosmetic appearance of the wound. The primary investigator will then collect the wound evaluation sheets from the physician assessors. Photographs of the biopsy site will also be taken.

E. Intervention

Before the biopsies will be performed, the sites will be cleansed with 70% isopropyl alcohol and anesthetized intradermally with 1% lidocaine hydrochloride.

No suture, electrocautery, aluminum chloride or other hemostatic agents will be applied to the biopsy sites to avoid inhibition of wound healing inherent with these agents.

Once bleeding will be controlled by pressure, wounds will be dressed with either a 1-inch size Duoderm Control Gel Formula hydrocolloid dressing or gauze dressing impregnated with mupirocin ointment covered by a transparent dressing (Tegaderm). Dressings will be left in place for 5 days, after which the dressings will be removed and will be cleansed with water to remove any exudate.

F. Assessment

For this study, wound assessment will be done after 5 days. Dermoscopy and photographs of the wounds will be taken for every evaluation.

According to a study entitled “Pathophysiology of Acute Wound Healing” by Jie Li, PhD et. al. published in Elsevier Clinics in Dermatology in 2007, there are three phases of wound repair that overlap in time. These are the inflammatory reaction phase, proliferation phase, and remodeling phase. Days after initial injury, the wound would be in the proliferative phase where there would be reepithelialization of the wound, the establishment of appropriate blood supply, and reinforcement of the injured dermal tissue.[14]

Three physician assessors who will be trained in the evaluation of skin punch biopsy wounds and the scoring criteria that will be used in this study will assess the wound and record their evaluations individually.

SAMPLE SIZE AND STATISTICAL ANALYSIS

Using G*Power 3.1.9.7, a minimum of 56 patients or 28 per group are required for this study based on the 8.38 mean Scar appearance score on Hydrocolloid

dressing versus 7.23 mean Scar appearance score on Conventional daily dressing.[15] This computation also accounts for desired 1.5 common standard deviation, 5% level of significance and 80% power.

Descriptive statistics will be used to summarize the demographic and clinical characteristics of the patients. Frequency and proportion will be used for categorical variables and mean and SD for normally distributed continuous variables. Independent Sample T-test and Fisher's Exact/Chi-square test will be used to determine the difference of mean and frequency, respectively, between patients undergoing Hydrocolloid Dressing versus Topical Antibiotic. All statistical tests will be two tailed tests. Shapiro-Wilk test will be used to test the normality of the continuous variables. Missing values will neither be replaced nor estimated. Null hypotheses will be rejected at 0.05α-level of significance. STATA 13.1 will be used for data analysis.

Inter-rater and Intra-rater reliability will also be conducted.

SAFETY EVALUATION

Assessment of possible adverse effects due to the hydrocolloid dressing or the topical antibiotics will be done on follow-up visit. Complaints of pruritus, burning, or stinging sensation will be asked from participants, while other physical signs and symptoms of adverse effects to the treatment applied will be checked by the primary investigator.

ETHICAL CONSIDERATIONS

This study will be conducted in accordance with the accepted ethical research practices of the ICH Good Clinical Practice regulations and guidelines. The study will

be explained thoroughly to the eligible patients prior to enrollment. Free and informed written consent will be obtained.

INFORMED CONSENT

All participants involved in the study will not be compromised in terms of treatment. All possible benefits and side effects of the treatment will be fully explained and must be understood by the patients prior to enrollment into the study.

The primary investigator will explain the study objectives, procedure, risks, and benefits to the eligible patients. Patients will be encouraged to ask questions regarding the study. In order to affirm voluntary participation, the patients will be asked to sign a written informed consent form (ICF) available in both English and Filipino versions (attached separately). One copy of the ICF will be given to the patient for reference. Another consent taker will be provided if the participant is a patient of the primary investigator.

CONFLICT OF INTEREST

This study is investigator-initiated and not industry funded or company sponsored. There is no potential conflict of interest.

PRIVACY AND CONFIDENTIALITY

All data will be handled in compliance to the Data Privacy Act of 2012 and its implementing rules and regulations in 2016.

The identity, personal data, and other medical information of patients will remain confidential. In the event of any publication regarding the study, the identity of the patients will remain confidential.

Physical data will be securely filed and electronic data will be stored in an encrypted hard drive by the principal investigator. Both forms of data will be protected from illegal or inadvertent access. Only the primary investigators, study coordinators, and the statistician will have access to the information collected for this study.

Physical data will be shredded and securely disposed of one year after the completion of this study. Electronic data will be stored for a maximum of three years after completion of this study after which all data will be permanently deleted.

The records, to the extent of the applicable laws and regulations, will not be made publicly available. However, the UST Hospital – Research Ethics Committee (USTH-REC) will be granted direct access to the participant's original medical records to check study procedures and data, without making any of the information public. The informed consent form that patients will sign prior to participation in the study will include a section that they are authorizing such access to the study and medical records.

VULNERABILITY

Patients aged 18 years old to 64 years old with clean cutaneous lesions who will undergo skin punch biopsy will be recruited in this study. No patients aged below 18 years old or above 64 years old, prisoners, mentally handicapped, or those with incurable diseases will be included.

RISKS

The possible side effect of hydrocolloid dressing is irritation of the skin. Treatment on patients who will experience any adverse side effects will be immediately stopped.

To minimize the risk of COVID-19 exposure, all safety measures in accordance with the IATF guidelines will be observed.

BENEFITS

The benefit that the patient will acquire from this study is better clinical outcomes of the post-biopsy site. This study can also help reduce medical costs and patients are suggested with alternative options which can be potentially used as one of the treatment modalities for post-biopsy sites.

INCENTIVES AND COMPENSATION

All of the dermatologic consultations and medications of the participants for the duration of the study will be free of charge. Transportation allowance of PHP 100.00 will be provided to the participant on their visit on the 5th day. Management, consultation, and treatment of adverse effects resulting from the participation in this study will be free of charge. No other form of monetary compensation will be provided to the patients for their participation. Patients will be informed of the results of the study once it has been completed.

SCORING CRITERIA FOR EVALUATION OF WOUND

Objective assessment is based on a study by Armstrong et. al. in 1986 entitled "Punch biopsy wounds treated with Monsel's solution or a collagen matrix".[16] For this study, the assessment will be done as follows:

(1) infection (absent, millimeters of surrounding erythema or equivocal findings; or present, as inferred by indurated erythema or purulent discharge);

(2) clinical estimate of reepithelialization (rated on a scale of (a) 0% to 25%, (6) 26% to 50%, (c) 51% to 75%, and (d) 76% to 100%);

(3) clinical estimate of wound closure (rated on a scale of (a) 0% to 25%, (b) 26% to 50%, (c) 51% to 75%, and (d) 76% to 100%)

(4) scar formation (unhealed; depressed or atrophied; normal fine-line scar; or hypertrophied scar or keloid);

(5) pigmentation of scar (indeterminate or unhealed; normal; hyperpigmented; or hypopigmented);

(6) cosmetic appearance of wound (acceptance of patient: indeterminate or unhealed; poor; fair; good; excellent)

DUMMY TABLES

Table 1. Baseline demographic and clinical characteristics

	Total	Hydrocolloid Dressing	Topical Antibiotic	P-value
	Frequency (%); Mean ± SD			
Age, years				
Sex				
Male				
Female				
Indications for Skin				
Punch Biopsy				
…				

Table 2. Scoring Criteria for Evaluation of Wound

	Total	Hydrocolloid Dressing	Topical Antibiotic	P-value
	Frequency (%)			
Infection				
Absent				
Present				
Re-epithelialization estimate				
0 to 25%				
26 to 50%				
51 to 75%				
76 to 100%				
Wound closure				
0 to 25%				
26 to 50%				
51 to 75%				
76 to 100%				
Scar Formation				
Unhealed				

Depressed or Atrophied
Normal Fine-Line Scar
Hypertrophied Scar or
Keloid
Scar Pigmentation
Indeterminate or Unhealed
Normal
Hyperpigmented
Hypopigmented
Cosmetic Appearance
Indeterminate or Unhealed
Poor
Fair
Good
Excellent

REFERENCES

1. Ramsey ML, Rostami S. Skin Biopsy. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; September 9, 2022.
2. Mendonça RJ de, Coutinho-Netto J. Cellular aspects of wound healing. *Anais Brasileiros de Dermatologia*. 2009;84(3):257-262. doi:https://doi.org/10.1590/s0365-05962009000300007
3. Lazarus GS. Definitions and Guidelines for Assessment of Wounds and Evaluation of Healing. *Archives of Dermatology*. 1994;130(4):489. doi:https://doi.org/10.1001/archderm.1994.01690040093015
4. Demidova-Rice TN, Hamblin MR, Herman IM. Acute and Impaired Wound Healing. *Advances in Skin & Wound Care*. 2012;25(7):304-314. doi:https://doi.org/10.1097/01.asw.0000416006.55218.d0
5. Thomas S. Hydrocolloid dressings in the management of acute wounds: a review of the literature. *International Wound Journal*. 2008;5(5):602-613. doi:https://doi.org/10.1111/j.1742-481x.2008.00541.x
6. Viciano, José E. Castera, J V. Effect of Hydrocolloid Dressings on Healing by Second Intention after Excision of Pilonidal Sinus. *The European Journal of Surgery*. 2000;166(3):229-232. doi:https://doi.org/10.1080/110241500750009339
7. Estienne G, Bella D. L'impiego del "DuoDerm" nella ferita operatoria dopo trattamento chirurgico delle fistole pilonidali col metodo aperto [The use of DuoDerm in the surgical wound after surgical treatment of pilonidal fistulae using the open method]. *Minerva Chir*. 1989;44(19):2089-2092.

8. Michie DD, Hugill JV. Influence of Occlusive and Impregnated Gauze Dressings on Incisional Healing. *Annals of Plastic Surgery*. 1994;32(1):57-64. doi:https://doi.org/10.1097/00000637-199401000-00011
9. Hultén L. Dressings for surgical wounds. *The American Journal of Surgery*. 1994;167(1A):S42-S45. doi:https://doi.org/10.1016/0002-9610(94)90010-8
10. Hermans MHE, Hermans RP. Preliminary report on the use of a new hydrocolloid dressing in the treatment of burns. *Burns Incl Therm Inj*. 1984;11(2):125-129. doi:https://doi.org/10.1016/0305-4179(84)90135-9
11. Wright A, MacKechnie DWM, Paskins JR. Management of partial thickness burns with Granuflex “E” dressings. *Burns*. 1993;19(2):128-130. doi:https://doi.org/10.1016/0305-4179(93)90034-6
12. Heffernan A, Martin AJ. A comparison of a modified form of Granuflex (Granuflex Extra Thin) and a conventional dressing in the management of lacerations, abrasions and minor operation wounds in an accident and emergency department. *Emergency Medicine Journal*. 1994;11(4):227-230. doi:https://doi.org/10.1136/emj.11.4.227
13. Schmitt M, Vergnes N P., Canarelli JP, et al. Evaluation of a hydrocolloid dressing. *Journal of Wound Care*. 1996;5(9):396-399. doi:https://doi.org/10.12968/jowc.1996.5.9.396
14. Li J, Chen J, Kirsner R. Pathophysiology of acute wound healing. *Clinics in dermatology*. 2007;25(1):9-18. doi:https://doi.org/10.1016/j.clindermatol.2006.09.007
15. Holmes SP, Rivera S, Hooper PB, Slaven JE, Que SKT. Hydrocolloid dressing versus conventional wound care after dermatologic surgery. *JAAD International*. 2021;6:37-42. doi:https://doi.org/10.1016/j.jdin.2021.11.002

16. Armstrong RB. Punch Biopsy Wounds Treated With Monsel's Solution or a Collagen Matrix. *Archives of Dermatology*. 1986;122(5):546. doi:https://doi.org/10.1001/archderm.1986.01660170076023