

BACTERIAL CELLULOSE REGENERATIVE DRESSING FOR TUMOR RESECTION WOUNDS
VENDAJE REGENERATIVO DE CELULOSA BACTERIANA PARA LESIONES POR RESECCIÓN TUMORAL
CURATIVO REGENERATIVO DE CELULOSE BACTERIANA PARA LESÕES POR RESSECÇÃO TUMORAL

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ABSTRACT

Introduction: Wound management remains a challenge in the healthcare field. Although there is a variety of materials available on the market, wound dressings need to be changed regularly, which can lead to debridement and pain during dressing removal. Surgeries for resection of non-melanoma skin tumors often result in complex and extensive wounds, which require treatment with appropriate dressings, preferably low-cost and that allow efficient healing. Dressings composed of biomaterials such as bacterial cellulose (BC) have been used for this purpose because they are non-toxic, biocompatible, flexible, naturally adherent and transparent materials, which allows the healing process to be monitored without removing them. **Objective:** This study was developed to evaluate the response of surgical wounds resulting from tumor resection to treatment using PolyTissue®, a BC dressing obtained through the biotechnological conversion of sugarcane molasses. **Methodology:** This was a prospective study based on a case series involving 14 adult patients (15 lesions). Wound evaluation was performed using the MEASURE methodology, along with clinical discussions among healthcare professionals (triangulation). Wounds images were recorded using the digital app imitoMeasure®, and statistical analyses were conducted using SPSS software. **Results:** The participants (14) had a mean age of 64.4±8.2 years, with the majority being male (78.6%). The predominant location of the evaluated lesions (15) was the right lower limb (40.0%, p=0.047). A reduction in the measurements of the lesions area, circumference, width, and length was observed in the final clinical evaluation (p<0.05), along with the absence of exudate in 13 of the 15 lesions evaluated (86.7%). The average healing time was 68 days. No participant reported pain during the study. **Conclusion:** The BC dressing (PolyTissue®) can aid in the healing of wounds resulting from the resection of non-melanoma skin tumors and provides comfort to patients, in addition to being low-cost.

Keywords: Bacterial Cellulose; Biopolymer; Sugarcane; Cancer; Healing; Surgical Wound.

RESUMO

Introdução: O manejo das feridas continua sendo um desafio na área da saúde, embora, exista uma variedade de materiais disponíveis no mercado, os curativos precisam ser trocados regularmente, promovendo desbridamento e dor durante sua remoção. Cirurgias para ressecção de tumores de pele do tipo não melanoma frequentemente resultam em feridas complexas e extensa, que exigem tratamento com curativos adequados, preferencialmente de baixo custo e que possibilitem uma cicatrização eficiente. Curativos compostos de biomateriais como celulose bacteriana (CB) vem sendo utilizado para esta finalidade por ser um material atóxico, biocompatível, flexível, de aderência natural e transparente, o que permite acompanhar o processo cicatricial sem sua remoção. **Objetivo:** Este estudo foi desenvolvido para avaliar a resposta de feridas cirúrgicas decorrentes de ressecção tumoral ao tratamento utilizando o PolyTissue®, curativo de CB obtido através da conversão biotecnológica do melão de cana-de-açúcar. **Metodologia:** Trata-se de um estudo prospectivo a partir de uma série de casos, incluindo 14 pacientes adultos (15 lesões). A avaliação das feridas foi realizada através da metodologia MEASURE incluindo também discussões clínicas entre profissionais da área (triangulação). Foram realizados registros das feridas usando o aplicativo digital imitoMeasure® e as análises estatísticas foram conduzidas pelo software SPSS. **Resultados:** Os participantes (14) tinham idade média de 64,4±8,2 anos, sendo a maioria homens (78,6%). A localização predominante das lesões avaliadas (15) foi no membro inferior direito (40,0%, p=0,047). Observou-se redução das medidas de área, circunferência, largura e comprimento das lesões na última avaliação clínica (p<0,05) e ausência de exsudato em 13 das 15 lesões avaliadas (86,7%). O tempo médio de cicatrização foi 68 dias. Nenhum participante referiu dor durante o estudo. **Conclusão:** Conclui-se que, o curativo de CB (PolyTissue®) pode auxiliar na cicatrização de feridas decorrentes de ressecção tumoral de câncer de pele do tipo não melanoma e proporciona conforto aos pacientes, além de ser de baixo custo.

Palavras-chave: Celulose Bacteriana; Biopolímero; Cana-de-Açúcar; Câncer; Cicatrização; Ferida Cirúrgica.

RESUMEN

Introducción: El manejo de heridas sigue siendo un desafío en el campo de la salud, aunque hay una variedad de materiales disponibles en el mercado, los apósitos deben cambiarse periódicamente, lo que promueve el desbridamiento y el dolor durante su extracción. Las cirugías de resección de tumores cutáneos no melanomas suelen dar lugar a heridas complejas y extensas, que requieren tratamiento con apósitos adecuados, preferiblemente de bajo coste y que permitan una cicatrización eficiente. Para este fin se han utilizado apósitos compuestos por biomateriales como la celulosa bacteriana (CB) por ser materiales atóxicos, biocompatibles, flexibles, naturalmente adherentes y transparentes, lo que permite monitorear el proceso de cicatrización sin necesidad de retirarlos. **Objetivo:** Este estudio fue desarrollado para evaluar la respuesta de las heridas quirúrgicas resultantes de la resección tumoral al tratamiento con PolyTissue®, un apósito de CB obtenido a través de la conversión biotecnológica de melaza de caña de azúcar. **Metodología:** Se trata de un estudio prospectivo basado en una serie de casos que incluyó a 14 pacientes adultos (15 lesiones). La evaluación de las heridas se realizó mediante la metodología MEASURE, que también incluyó discusiones clínicas entre profesionales de la salud (triangulación). Se registraron las heridas utilizando la aplicación digital imitoMeasure® y los análisis estadísticos se realizaron con el software SPSS. **Resultados:** Los participantes (14) tenían una edad media de 64,4±8,2 años, siendo la mayoría hombres (78,6%). La localización predominante de las lesiones evaluadas (15) fue en el miembro inferior derecho (40,0%, p=0,047). Se observó una reducción en las medidas de área, circunferencia, ancho y largo de las lesiones en la última evaluación clínica (p<0,05), y la ausencia de exudado en 13 de las 15 lesiones evaluadas (86,7%). El tiempo promedio de cicatrización fue de 68 días. Ningún participante informó dolor durante el estudio. **Conclusión:** Se concluye que el vendaje de CB(PolyTissue®) puede ayudar en la cicatrización de heridas resultantes de la resección de tumores de cáncer de piel no melanoma, proporcionando comodidad a los pacientes, además de ser de bajo costo.

Palabras clave: Celulosa Bacteriana; Biopolímeros; Caña de Azúcar; Câncer, Cicatrización de Heridas; Herida Quirúrgica.



INTRODUCTION

The wound healing process involves a number of factors such as time, risk of infection, tissue remodeling and pain management, which pose a challenge to healthcare professionals ⁽¹⁾. Therefore, the search for new and more effective treatments that prevent infections, in addition to helping the healing process, has increased in recent years ⁽²⁾.

When it comes to surgical wounds resulting from tumor resection, an even greater challenge is observed, as they generally present a slow healing process due to tissue loss and a high risk of infections and dehiscence. ^(3,4)

These wounds require smart dressings capable of inducing and/or leading to tissue remodeling, stimulating granulation, reducing the amount of exudate and promoting patient comfort ⁽⁵⁾. Delayed healing can also cause psychological harm to the patient, high image disturbance, as well as social and economic losses ⁽⁶⁾.

Currently, there is a wide variety of materials available on the market, coverings called special dressings, to accelerate wound healing, reduce changes and reduce the pain generated by the dressing renewal process ⁽⁷⁾, however they are expensive, and therefore are not available in the Brazilian National Health System or are difficult for some patients to acquire ⁽⁸⁾.

Wound dressings are mainly developed from natural or synthetic polymers. Synthetic polymers include polyvinylpyrrolidone (PVP), poly(ethylene oxide) (PEO), polyethylene glycol

(PEG), among others. However, some materials used have limitations such as reduced antimicrobial effect, poor mechanical performance, and inability to provide adequate moisture to accelerate the wound healing process ⁽⁹⁾.

Natural polymers that are commonly used include chitosan, cellulose, fibrin, elastin, hyaluronic acid, dextran, alginate, collagen, and gelatin ⁽¹⁰⁾. These polymers have properties suitable for wound management, such as high biocompatibility, low toxicity, biodegradability, immediate availability, and low immunogenicity. They are generally referred to as biopolymers. They tend to interact more harmoniously with tissues and cells, reducing the rejection probability, inflammation, or other adverse responses by the body, and are easily degraded by natural biological processes, meaning that after use, they break down into biologically inert components ^(11, 12).

Natural biopolymers are obtained from renewable sources such as plants, algae, animals and microorganisms, contributing to reducing dependence on finite resources and minimizing the environmental impact associated with the extraction and processing of non-renewable primary materials ^(12, 13). They are usually collected as residual by-products at manufacturing scale, where they would likely be discarded, resulting in a good cost-benefit ratio ^(12, 14).

The Bacterial Cellulose (BC) dressing is a biopolymer obtained through biotechnological synthesis using sugarcane molasses in this work ⁽¹²⁾. This product is non-toxic, biocompatible and



has the characteristics of being transparent, flexible and with good adhesion to the wound bed^(12, 13). Because the transparent characteristic, is possible observe the healing process without remove it. The dressing adheres naturally to the wound bed (self-adherent) and gradually detaches as the tissue heals. The dressing used in this study, PolyTissue® produced by POLISA®, has already been tested in experimental research protocols and is being used in different clinical protocols in the health area, with satisfactory results for the treatment of surgical, traumatic, chronic (venous ulcers) and burn wounds.⁽¹⁴⁻²⁹⁾.

BC meets the recommendations of the United States Food and Drug Administration (FDA), the US agency that regulates drugs and food, which defines that a biomaterial to be used in the health area must be biocompatible and not be toxic, carcinogenic, antigenic or mutagenic, and must not interfere with the healing of damaged tissues^(30,31). Additionally, it can be manufactured on a large scale, can be sterilized, stable during implantation, non-corrosive, and non-degradable⁽³²⁻³⁴⁾. It also complies with the regulations of the Brazilian Health Regulatory Agency (ANVISA) and qualifying as class I (RDC 185/2001)⁽³⁵⁾, Rule 4, which refers to all non-invasive medical products that come into contact with damaged skin, are intended to be used as a mechanical barrier, for compression or for absorption of exudates.

METHODS

Study Design

This is a prospective study including a series of cases carried out during the period from

March 2021 to April 2022, with patients referred by the Oncological Surgery Outpatient Clinic of the Pernambuco Cancer Hospital (PCH), Stomatherapy Outpatient Service for monitoring of the surgical wound.

Eligibility Criteria

All patients who participated in the study were ≥ 18 years-old, both sexes, with a histopathologically confirmed diagnosis of cancer, presenting surgical wounds resulting from tumor resection and without signs of infection. Patients who presented any sign of hypersensitivity to the dressing components, infected or cavitory wounds, pregnant or in the postpartum period were not included in the study.

Casuistry and Data Collection

Individual consultations were held in a private, air-conditioned and noise-free environment, explaining the study, risks and benefits to the patients. After listening carefully to the instructions and without any doubts, the Informed Consent Form (ICF) was signed, in accordance with resolution 466/2012 of the Brazilian National Health Council, the Declaration of Helsinki and the Nuremberg Code for human experimentation. The protocol was approved by the Research Ethics Committee of the Federal University of Pernambuco – Health Sciences Center with the CAAE number: 23402513.9.0000.5208 and of the PCH with CAAE number: 23402513.9.3002.5205.

A total of twenty-three patients were invited to participate in the study, of which eight



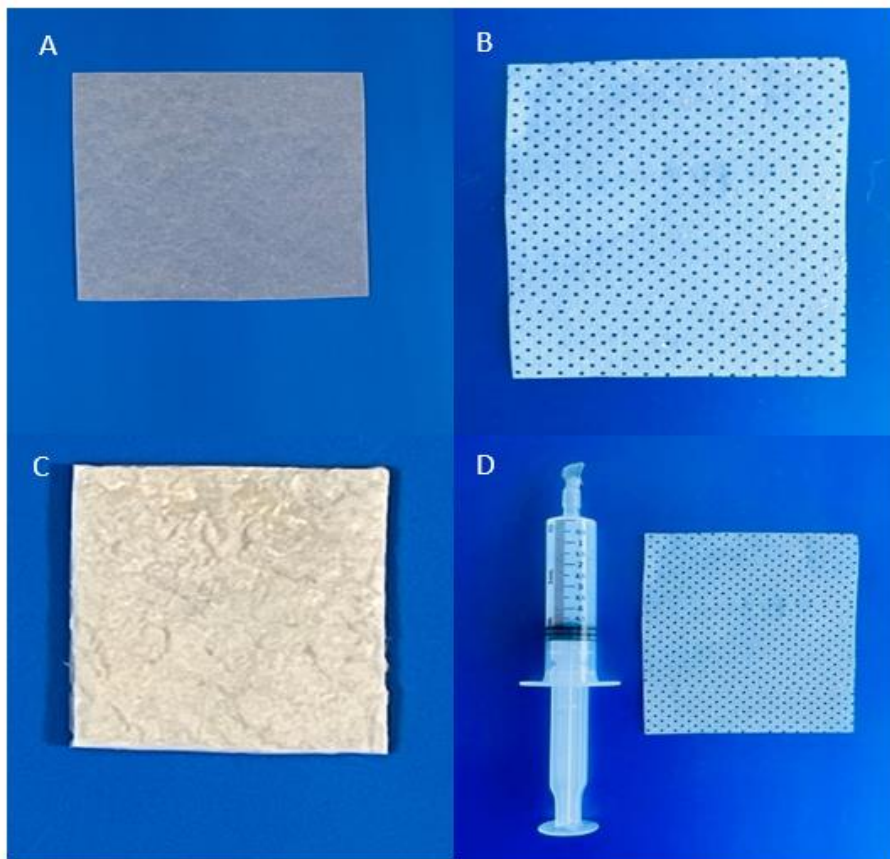
were excluded because they didn't comply with the eligibility criteria mentioned above (35%) (see methodology: eligibility criteria) or refused to participate in the study, therefore, the sample studied was made up of fourteen participants and fifteen lesions.

All participants were monitored at the PCH Stomatherapy Outpatient Clinic in weekly visits in the first two weeks to check the participant's adherence to the study and to evaluate the wound in relation to the proposed treatment with BC dressing. After this period, monitoring became biweekly for a maximum of 120 days (D120). Clinical evaluation, including replacement and adjustment of the primary dressing prescription (BC dressing) as needed, was conducted from the first month (D0), after thirty days (D30), sixty days (D60), ninety days (D90) and/or at most 120 days (D120), with a window of \pm three days.

Bacterial Cellulose (BC) Dressing

BC dressings (PolyTissue®) were produced and supplied by Polisa® Biopolymers for Health Ltd., a company dedicated to research, development, technological innovation, production and marketing of sugarcane biopolymers (a start-up within the Incubatec of the Federal Rural University of Pernambuco). The BC for dressing is obtained via biotechnology process from sugar cane molasses diluted in water without any additives⁽¹²⁾. The BC obtained is treated and purified, resulting in a pure, crystalline product made up of micro and nano cellulose fibrils intertwined with each other, with a fine texture and uniform structure⁽¹²⁾. BC film has viscoelastic properties and remains stable when packaged in a BagClean® or surgical grade®, stored at temperatures of 8-35°C⁽¹²⁾. BC is a very pure product, does not induce an immunological response, is biocompatible and non-toxic, with a wide range of clinical applications^(10,12,30,36,37).

Figure 1 - Presentations of BC dressing. Compact film (A); Perforated film (B); Sponge (C); Hydrogel in the syringe and Perforated film (D).



Source: Images provided by the company POLISA® Biopolymers for Health LTD.

The dressing used, PolyTissue® (Figure 1), acts as a mechanical barrier, protecting the wound and surrounded skin, facilitating the healing process^(12,14,32,38). The physical-chemical product characteristics allow the natural moisture of the tissues to be maintained, promoting tissue regeneration, epithelialization, and reducing healing time^(12,23,31). The PolyTissue® dressings were used in different sizes (5.0 X 5.0 cm; 6.0 X 7.0 cm; 10 X 16 cm) and, when necessary, were customized to adapt more precisely to the wounds.

Technical Procedures

All participants included underwent wound cleaning with 0.9% saline solution, followed by drying using sterile gauze to reduce moisture. Next, the wound was clinically

assessed and the primary PolyTissue® dressing was directly applied. The dressing was kept moist with saline solution to facilitate handling, increase flexibility and better accommodate wound irregularities. The dressings were finished with gauze and wrapped with bandages. PolyTissue® dressing tends to naturally detach from the injured site after healing, which usually occurs in less than 30 days. In wounds where the healing time exceeded 30 days, the dressings were removed by the researcher for detailed evaluation of the wound and to respect the 30-day period of permanence recommended in the protocol.

Participants were instructed to only remove the secondary dressing, when performing their personal routine hygiene during the bath. They were also instructed to clean the

primary BC dressing, removing excess moisture with sterile gauze and covering the primary dressing with a new secondary dressing.

Data Analysis

The wound assessment was performed using the MEASURE methodology (39), clinical discussions between an oncology nurse and a stoma care nurse (triangulation). Images were captured by the imitoMeasure® digital application, which provided circumference, length and width dimensions in cm and the wound area in cm², and from digital photographic records with a cell phone camera. All lesions were photographed with the same camera on the iPhone® 12 Pro Max mobile device at a fixed distance.

The MEASURE system provides an overview of the principles and practices of chronic wound assessment. This system includes the evaluation of the wound in relation to size, width, length, depth, area, exudate (quantity and quality), pain, type of edge, detachment (absent or present) and the appearance of the wound, with the description of the inspection, type of tissue involved and coloration.

The imitoMeasure® application is an FDA-approved digital method developed for healthcare professionals to calculate wound dimensions (length, width, area and circumference) through a visual map obtained from photographic records made by a cell phone and which also allows electronic recording (40). The application was used in digital image mode with manual calibration.

To ensure data accuracy, a photograph of the wound must be recorded with a ruler next to it to serve as a size reference, i.e. calibration. The edges of the wound are then outlined in the image and the dimensions are calculated in this way (41). In this study, wounds were classified by size. A small wound was considered when the total wound area was ≤ 10 cm². A medium wound was considered when the area was between > 10 cm² and ≤ 50 cm², and a large wound was considered when the area was greater than > 50 cm².² (42).

Comparisons between categorical variables were performed using the Chi-square test or Fisher's exact test (when applicable), while Kruskal-Wallis and Mann-Whitney tests were used for the nonparametric data. For continuous variables test with paired samples, was used the Friedman test with the *pairwise* Wilcoxon Signed Ranks as *post-hoc* analysis. For the tests of categorical variables with paired samples, the marginal homogeneity test was used. All p-values were adjusted for both sides with a significance level of 0.05. When necessary, the Bonferroni correction was applied for multiple hypothesis comparisons. When necessary, the odds ratio (OR) and 95% confidence interval (95% CI) were considered. The analyses were performed using the SPSS (Statistical Package for Social Sciences) Statistics 19.0 software (IBM corporation).

The sociodemographic, clinical and oncological characteristics of the patients were detailed descriptively.

RESULTS



Sociodemographic Data

Among the fourteen participants evaluated, the average age was 64.4 ± 8.2 years, with eleven being male (78.6%). Six patients declared themselves to be brown (42.9%), nine were married (64.3%), nine lived in the metropolitan region (64.3%), six had secondary education (42.9%) and seven were retired (50.0%). There was no statistical difference between the variables analyzed ($p > 0.05$).

Oncological Data and Healing Outcomes

The histological lesions data obtained in this study indicated that the majority of patients had squamous cell carcinoma (73%) and in smaller proportions having basal cell carcinoma (13.3%), epidermoid carcinoma (6.7%) and infiltrating ductal carcinoma (6.7%). When analyzing the histological type of lesions with the healing outcome, no statistical difference was observed ($p > 0.05$). Concerning the areas of the body affected by lesions, one patient had a lesion on the breast (6.7%), two on the right upper limb (13.3%), four on the left upper limb (26.7%), six on the right lower limb (40.0%), and two on the left lower limb (13.3%).

A correlation was identified between the healing outcome and the specific body area affected, showing a statistical significance ($p > 0.047$). Patients with left upper limb injuries had

less favorable healing outcomes compared to those with right lower limb injuries. While injury location may influence healing process, causality cannot be determined from this analysis, and other factors may affected the outcomes.

Lesion Evolution Assessment

A statistically significant difference was observed in the measurements of area, circumference, length and width of the lesions throughout the three evaluations ($p < 0.05$) (Table 1). *Post hoc* analysis with the Wilcoxon *signed-rank* test was performed with Bonferroni correction applied, resulting in a significance level set at $p < 0.017$. Significant reductions in lesion area measurements were observed between the first and second evaluations ($p = 0.001$), the second and third evaluations ($p = 0.017$), and the first and third evaluations ($p = 0.012$). A similar significant decrease was noted in lesion circumference across all evaluation points ($p < 0.017$). For lesion length measurements, there was a significant reduction observed between the first and second evaluation ($p = 0.005$) as well as between the first and third evaluation ($p = 0.012$). Similarly, lesion width data demonstrated a significant reduction between the first and second evaluations ($p = 0.001$) and between the first and third evaluations ($p = 0.012$).

Table 1 - Measurements evaluation of the lesions remaining areas (unhealed regions).

| Evaluation / Measurement | First (1) | Second (2) | Third (3) | P-value ¹ | P- value ² | P- value ³ | P- value ⁴ |
|----------------------------------|--------------|---------------|--------------|----------------------|-----------------------|-----------------------|-----------------------|
| Area (cm ²), average | 22.25 | 17.36 | 6.71 | 0.001 | 0.001 | 0.017 | 0.012 |
| Range | 3.2 – 134.6 | 1.6 – 119.6 | 1.2 – 10.2 | | | | |
| Circumference (cm), average | 13.4 | 13.42 | 9.75 | 0.001 | 0.011 | 0.017 | 0.012 |
| Range | 3.0 – 43.8 | 5.11 – 40.5 | 4.5 – 12.7 | | | | |
| Length (cm), average | 5.82 | 5.27 | 3.73 | 0.001 | 0.005 | 0.018 | 0.012 |
| Range | 2.20 – 15.4 | 1.90 – 14.9 | 1.80 – 5.5 | | | | |
| Width (cm), average | 3.80 | 3.17 | 2.40 | 0.002 | 0.001 | 0.050 | 0.012 |
| Range | 1.70 – 12.10 | 1.02 – 11.40 | 0.90 – 3.20 | | | | |

¹ Friedman Test. Comparison between 1 vs 2 vs 3.

² Wilcoxon Signed Ranks Test. Comparison between 1 vs 2.

³ Wilcoxon Signed Ranks Test. Comparison between 2 vs 3.

⁴ Wilcoxon Signed Ranks Test. Comparison between 1 vs 3.

Description of wound healing time

Table 2 shows the initial area of fifteen lesions at the first and last evaluation, and the total healed area in square centimeters (cm²) and percentage (%) by the end of follow-up. The

shortest follow-up was 14 days with a 70.49 cm² starting area and 27% healed. The longest was 93 days with a 134.63 cm² starting area and 100% healed, using 2 and 3 dressings, respectively. Most lesions were small (8/15), followed by medium (5/15) and large (2/15).

Table 2 - Area of lesions, follow-up time, number of dressings used and mean wound size assessments.

| Patient | Initial Area (cm ²) | Final Area (cm ²) | Healed Area (cm ²) | Follow-up time (days) | Dressings used |
|---------|---------------------------------|-------------------------------|--------------------------------|-----------------------|----------------|
| 001 | 3.59 | 3.2 | 0.39 (11%) | 93 | 4 |
| 002 | 6.38 | 0 | 6.38 (100%) | 60 | 2 |
| 003 | 13.66 | 0 | 13.66 (100%) | 92 | 3 |
| 004 | 5.06 | 0 | 5.06 (100%) | 63 | 2 |
| 005a | 17.8 | 0 | 17.8 (100%) | 90 | 3 |
| 005b | 13.0 | 0 | 13.0 (100%) | 90 | 3 |
| 006 | 28.33 | 9.33 | 19.0 (67%) | 61 | 3 |
| 007 | 7.67 | 0 | 7.67 (100%) | 60 | 2 |



| | | | | | | |
|---------------------|--|-------|-------|--------------|-------|------|
| | 008 | 8.53 | 0 | 8.53 (100%) | 61 | 2 |
| | 009 | 5,08 | 0 | 5.08 (100%) | 58 | 2 |
| | 010 | 3.26 | 1.26 | 2.0 (61%) | 63 | 3 |
| | 011 | 3.24 | 0 | 3.24 (100%) | 59 | 2 |
| | 012 | 13.03 | 9.36 | 3.67 (28%) | 58 | 3 |
| | 013 | 70.49 | 51.35 | 19.14 (27%) | 14 | 2 |
| | 014 | 134.6 | 0 | 134.6 (100%) | 93 | 3 |
| Average lesion size | Small (>10 cm ²) | 5.35 | 0.56 | 4.79 (84%) | 64.63 | 2.38 |
| | Medium (entre >10 e ≤ 50 cm ²) | 17.16 | 3.74 | 13.43 (79%) | 78.20 | 3 |
| | Large (> 50 cm ²) | 102.5 | 25.68 | 76.89 (64%) | 53.50 | 2.50 |

In Figure 2, the cases of patients 14 and 09 respectively can be seen, where a total healed area of 100% was obtained using PolyTissue® dressings. As seen in Figure 2A, patient 14 presented an Operative Wound (OW) containing a medium amount of exudate, non-adhered edges and slightly granular tissue. In this case, the PolyTissue® dressing was used in the spongy presentation, providing greater comfort to the patient, who was monitored for 90 days until complete healing of the OW was achieved (Figure 2B).

Its possible observe in Figure 2C, patient 09 presented a moist OW, with regular and adherent edges. In this case, the PolyTissue® dressing in the microperforated presentation was used, providing a mechanical barrier between the wound and the external environment, allowing monitoring of the healing stage without removing the dressing. The patient was followed for 60 days until complete healing of the OW was achieved (Figure 2D).

Figure 2 - Assessment of wound appearance (Patients 14 and 09 at 90 days and 60 days of follow-up, respectively). (A) D0, moist wound with medium amounts of seropurulent exudate, with edges not

adhered to the wound bed, little predominant granulation tissue, slough, fibrotic tissue, wound treated with CB in the spongy presentation; (B) D90, healed wound; (C) D0, moist wound with regular and adhered edges, with granulation tissue, slough, wound treated with CB in the microperforated film presentation; (D) D60, healed wound.



Source: Researcher's personal collection.

Clinical Progression of Lesions

The lesions' morphological characteristics and the pain parameters were compared based on MEASURE, considering two specific points in time: the initial (D0) and the final evaluation. In the initial evaluation, 53.3% of the wounds were classified as small. However, in the final evaluation, this proportion increased to 86.7%. Medium-sized wounds were present in 33.3% of initial cases and dropped to 6.7% by the final evaluation. Large wounds were found in 13.3% of cases initially and 6.7% by the final evaluation. A statistically significant

difference was observed in the evolution of lesion sizes between the two time points ($p = 0.034$).

Regarding bacterial content, all wounds at both time points were classified as clean. Tissue analysis indicated that the necrosis was present in 6.7% of wounds during the initial evaluation, but none were observed in the last. Epithelialization was absent at any time point. Slough appeared in 40% of wounds initially and decreased to 6.7% by the final evaluation. Granulation increased from 53.3% at the first evaluation to 93.3% at the last, indicating higher tendência for granulation at the final point. There

was a statistically significant difference in tissue characteristics ($p = 0.046$).

In the exudate amount analysis, 53.3% of responses showed no exudate in the initial evaluation increasing to 86.7% in the final. Small amounts of exudate were observed in 26.7% of the responses in the initial assessment, decreased to 13.3% in the last. The mean amount of exudate was documented in 20% of responses during the initial assessment, with no occurrences noted in the final assessment. A statistically significant difference in the amount of exudate was also observed in relation to the progression of the lesions ($p = 0.046$).

The exudate characteristics showed that 26.7% of the wounds initially had serous exudate, but it was absent in the final evaluation. Sanguineous exudate was present in 13.3% of the cases, decreasing to 6.7% by the final evaluation. In the final assessment, serosanguineous exudate was observed in 6.7% of the cases. Furthermore, seropurulent exudate was noted in 6.7% of the cases initially, with no instances of purulent or fibrous exudate recorded at any time.

The evaluation of wound edges showed that 80% of the wounds in the first assessment had adhered edges, while this characteristic was observed in 100% of the wounds in the final. Non-adhered edges were present in 6.7% of the wounds during the first evaluation, but there were no cases in the final. No indistinct, macerated, thickened, or fibrotic edges were observed at any time points, and hyperkeratin was detected in 13.3% of the wounds in the initial assessment but was absent in the final one.

Additionally, no patients reported pain throughout the evaluations.

DISCUSSION

The study evaluated fourteen patients, with a majority being males (78.6%). This data differs from the Brazilian National Cancer Institute's (INCA) estimate for each year of the 2020/2022 triennium, which predicts 176,930 new cases of basal cell and squamous cell skin cancer in Brazil, comprising 83,770 men and 93,160 women ⁽⁴³⁾.

The average age was 64.4 years, with 66% (10 individuals) being over the age of 60. According to data from the World Health Organization (WHO), non-melanoma skin cancers (NMSC) are common malignant tumors in Brazil. They mainly occur in individuals over 60 years of age and constitute approximately 10% of all new cancer cases diagnosed in this age group, following prostate, breast, and gastrointestinal cancers ⁽⁴⁴⁾.

In terms of marital status, it was found that 9 out of 14 participants (64.3%) in this study were married, and among these, 5 individuals (55.6%) experienced complete healing of the lesion. While married individuals may tend to adopt healthier lifestyle habits, such as greater attention to health and increased social support, the relationship between marital status and non-melanoma skin cancer remains unclear ⁽⁴⁵⁾. Emotional and social support, along with shared responsibility, directly influence seeking specialized health care. Partners encourage routine checkups, attending medical



appointments, and seeking treatment for health issues⁽⁴⁶⁾.

The majority of participants (64.3%) resided in the metropolitan area, with five of these individuals (55.6%) achieving complete healing of the lesion. Residence in Recife and/or the metropolitan region likely facilitated continuous treatment and consistent evaluations, owing to the availability of transportation and proximity to the treatment facility⁽⁴⁷⁾.

Among the participants identified as smokers, five individuals (35.7%) achieved complete healing of their lesions during the study period. Research conducted at the University of Leeds involving 700 melanoma patients indicates that smokers have a 40% reduced probability of surviving skin cancer, as smoking exacerbates the condition⁽⁴⁸⁾. Furthermore, several factors influence wound healing, including smoking⁽⁴⁹⁾. Smoking is correlated with delayed healing, increased risk of wound infection, and dehiscence⁽⁵⁰⁾.

Regarding the identified comorbidities, 42.9% of patients presented with arterial hypertension, and 21.4% had diabetes mellitus. Notably, only one patient achieved complete healing of the lesion. Patients with diabetes often experience delayed tissue repair in wounds due to excessive production of reactive oxygen species, reduced nitric oxide levels, and decreased responsiveness to growth factors and proteins involved in the insulin signaling pathway. This condition, coupled with the wound's location, further slows the healing process due to the increased probability of mechanical trauma to which the lower limbs are

prone and their specific circulatory characteristics^(49,51).

The study observed that 11 out of 14 participants (73.3%) had NMSC of the histological type squamous cell carcinoma (SCC). As reported by INCA (2022), NMSC represents the most common type of cancer in Brazil, constituting approximately 30% of all documented malignant tumors within the country. Basal cell carcinoma (BCC) and SCC represent 95% of all skin cancer cases. Specifically, SCC accounts for 21.7% of malignant skin tumor cases. Although it is the least common type, SCC is the most aggressive and, if not properly treated, can result in significant mutilations^(43,45,52).

No statistical difference was found between the histological type of lesions and the healing outcome ($p > 0.05$). However, the area of the body affected was associated with the healing outcome ($p < 0.047$). It is important to note that this study's sample size was limited, so conclusions should be drawn cautiously. Among the six participants (40%) with lesions on the right lower limb, four (66.7%) achieved complete healing, possibly due to factors like sun exposure. For instance, the legs are often exposed to sunlight in warmer environments or during outdoor activities.

Excessive sun exposure is one of the main risk factors for the development of skin cancer⁽⁴⁷⁾. However, the lower limbs generally do not receive the same attention in terms of sun protection, compared to more visible areas of the body, such as the face and arms. As a result, legs receive less sunscreen and protective clothing,



leading to more sun exposure ⁽⁴⁵⁾. Additionally, people tend to pay less attention to skin care on the legs compared to other body regions, which may contribute to the prevalence of non-melanoma skin cancer in this area ⁽⁵²⁾.

There was a statistically significant difference in the reduction of the area, circumference, length and width of the lesions, comparing the measurements of the initial and final evaluations of the lesions (Table 1). Similar data were found in the study by Silva et al. (2021), where 20 patients in the experimental group with active chronic venous ulcers were treated with BC dressing in hydrogel and microperforated film forms ⁽⁵³⁾. The results showed a 28% reduction in the mean total area of the lesions ($p=0.029$) and increased

epithelialization, along with a decrease in the amount of exudate ⁽⁵³⁾.

In the study carried out by Maia et al. (2020), the BC dressing was applied to patients with lower limb wounds, and the authors indicated a reduction in the wounded area and pain decreased ⁽⁵⁴⁾. BC dressings have been employed in treating various wound types, demonstrating significant benefits in tissue regeneration, epithelialization, and pain management. Clinical trials involving different wound categories have shown that BC dressings can effectively induce granulation tissue formation, reduce wound depth, and promote re-epithelialization ⁽⁵³⁻⁵⁵⁾. Table 3 shows the results of using BC dressings for treating various types of wounds, evaluated according to the MEASURE system.

Table 3 - Efficacy of BC dressings in different wound types

| Reference | Type and Location of Wound | Treatment (BC Presentation) | N° patients | Results | |
|------------------------|------------------------------------|------------------------------|-------------|---|---------|
| | | | | Characteristics and Healing Time | p-value |
| Correia et al., 2024 | Infected wounds (in vitro) | Hydrogel | N/R* | Prevention of biofilm formation | N/R* |
| Silva, et al., 2021 | Lower limbs wound | Perforated film and Hydrogel | 39 | Increased epithelialization, reduction of wound area | < 0.001 |
| Magalhães et al., 2020 | Wound coverage for skin autografts | Perforated film | 20 | Decreased pruritus and pain, good adhesion, wound epithelialization in 15.8 days | ≤ 0.05 |
| Oliveira et al., 2020 | Nail bed after avulsion | Sponge and Perforated film | 26 | Decreased pruritus and pain, adhesion re-epithelialization and preservation of the nail bed after an observation period of 180 days | ≤ 0.05 |

| | | | | | |
|--------------------------|----------------------|--|----|--|-------------|
| Oliveira et al., 2019 | Wounds in general | Sponge and Hydrogel | 10 | Granulation tissue induction and wound depth reduction in 30 days | ≤ 0.05 |
| Maia et al., 2019 | Lower limbs wounds | Perforated film and Hydrogel | 24 | Wound area reduction, epithelialization increased, amount of exudate decreased in 30 to 180 days of observation. | ≤ 0.05 |
| Silveira F. et al., 2016 | Tympanic perforation | Compact film | 40 | Reepithelialization and closure of the tympanic membrane over a period of 30 days | ≤ 0.05 |
| Cavalcanti et al., 2017 | Lower limbs wound | Perforated film | 25 | Wound area and pain reduction | ≤ 0.05 |
| Martins et al., 2013 | Operative wounds | Perforated film | 60 | Tissue regeneration, wound protection and complete healing between the 8th and 10th day | N/R* |
| This Work | Operative wounds | Perforated film, Compact film, Hydrogel and Sponge | 14 | Wound area reduction and pain decreased. Complete healing within 120 days | ≤ 0.05 |

*N/R Data not reported in the study

The shortest follow-up for lesions was 14 days, starting with an area of 70.49 cm² and achieving 27% healing. The longest follow-up was 93 days, beginning with an area of 134.63 cm² and achieving 100% healing. Out of the 14 patients, 5 did not complete the follow-up due to death, tumor recurrence, or treatment abandonment. Data from these patients were analyzed based on their participation period.

In medium and large lesions, BC film was used with BC hydrogel and it improved dressing fixation, allowing for longer stays and fewer changes⁽³⁴⁾. Additionally, coverings that remain on the lesion for longer can reduce treatment costs⁽⁵³⁾.

Pain during dressing changes is noted as a common issue⁽³²⁾. In this study, patients reported no pain during dressing changes. Reducing pain during dressing changes can

enhance patients' quality of life by providing a greater sense of control over their treatment and lessening the injury's impact on their daily activities⁽⁵⁶⁾.

Previous research suggests that pain episodes can substantially affect patient adherence to treatment. Another investigation utilizing BC dressings in patients with ischemic wounds reported pain episodes associated with distress, particularly during dressing changes⁽⁵⁵⁾.

No adverse events related to PolyTissue® dressings were reported in this study. However, literature describes dermatitis and pain from special dressings in skin wound treatment, which concerns health professionals and patients⁽⁵⁷⁾. Special dressings are designed to promote healing and protect wounds, but they can cause skin irritation and discomfort if not selected and applied properly. Therefore, it is



important to evaluate the patient's skin carefully before applying the dressing ⁽⁵⁷⁾. When selecting the appropriate dressing and presentation for a wound, it is important to consider the type of wound, its location, and the individual needs of the patient. The skin around the dressing should be regularly monitored, and gentle techniques should be used for its removal to minimize trauma and reduce pain associated with the treatment ^(57, 58, 59).

Palácio et al. (2024) highlighted in their systematic review that BC dressings excel over conventional ones due to their biocompatibility, biodegradability, and exudate absorption, which maintains a moist environment and allows gas exchange. They also protect the wound bed by serving as a mechanical barrier, supporting cells, inducing cell migration and proliferation, and promoting effective tissue regeneration ⁽⁵⁷⁾.

In a previous study conducted by Carvalho et al. (2025), BC dressing confirmed be highly pure, crystalline, and thermally stable. Key properties such as nanofibril content, transparency, porosity, tensile strength, water vapor permeability, and in vitro degradation indicated that this material is ideal for medical applications, particularly as a dressing after sterilized by irradiation ⁽¹²⁾.

As this study represents a pioneering investigation into the application of cellulose dressings (PolyTissue®) for surgical wounds following tumor resection, each assessment of the dressing during participant follow-up also entailed evaluating the suitability of the presentation used to address the wound's requirements. At each dressing change,

additional instructions were given to participants to ensure consistent home treatment with the PolyTissue® presentations. This process helped determine the most suitable presentation based on the specific wounds characteristics. These findings offer valuable insights for future studies with the same population, indicating potential directions for further research. This approach enabled a detailed observation of the wounds' responses to different dressing presentations.

CONCLUSIONS

Based on the obtained results, it can be concluded that the BC dressing (PolyTissue®), available in presentations smooth, perforated, hydrogel, and spongy forms, facilitated the healing process of lesions resulting from tumor resection of non-melanoma skin cancer. This dressing effectively covered the wound area, including its extension, width, and length, fully healing the wounds in an average of 68 days. Additionally, there were no reports of pain during the application and removal of the dressing. The Wilcoxon signed-rank test for wound healing progression showed statistical significance for all evaluations conducted, rejecting the null hypotheses and indicating a statistical difference between the averages obtained.

In previous research, the physical and chemical characteristics of PolyTissue® were analyzed and scientifically detailed, confirming BC as an ideal candidate for applications in regenerative medicine, aiding in the re-epithelialization of surgical wounds after tumor



resection, thus supporting the findings of the present study.

These findings suggest that BC dressings could be a promising option for treating surgical wounds from non-melanoma skin tumor resections. PolyTissue® ability to reduce wound size and provide patient comfort may enhance clinical practice, leading to a more effective and less painful recovery after skin cancer-related surgeries.

However, since this is a pioneering research in the use of PolyTissue® in surgical wounds resulting from tumor resection, there is still a need for complementary studies, which should aim to expand the application of the dressings, through multicenter clinical research and increase the sample size to confirm the results obtained.

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Authorship criteria (authors' contributions)

Santos KM designed the study, collected data, analyzed and interpreted the data, and wrote the manuscript. Mahnke LC analyzed and interpreted the data, wrote and revised the manuscript. Arcoverde MM participated in the technical development and therapeutic innovation of the tested product. Aguiar JLA critically reviewed the work and approved the final version of the manuscript. Pinto FCM supervised the research, analyzed and interpreted the data, critically reviewed the work, and approved the final version of the manuscript.

Declaration of conflict of interest

Nothing to declare.

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