Brazilian Journal of Biology®

ISSN 1519-6984 (Print)
ISSN 1678-4375 (Online)

Original Article

Histomorphological evaluation of acellularized bovine pericardium in breast implant coverage

Avaliação histomorfológica do pericárdio bovino acelularizado na cobertura do implante mamário

C. Frutuoso Silva[a*], V. A. Felzemburgh[a], L. Q. Vasconcelos[a], V. L. C. Nunes[b], A. A. Barbosa Júnior[c], A. F. Giglioti[d], R. P. C. Araújo[a], F. B. Miguel[a], J. V. L. Meneses[e] and F. P. Rosa[a]

[a]Universidade Federal da Bahia – UFBA, Instituto de Ciências da Saúde – ICS, Laboratório de Bioengenharia Tecidual e Biomateriais – LBTB, Salvador, BA, Brasil

[b]Universidade Federal da Bahia - UFBA, Faculdade de Medicina da Bahia - FMB, Salvador, BA, Brasil

[c]Instituto de Patologia Geral e Cutânea – IPAC, Salvador, BA, Brasil

[d]Braile Biomédica, São José do Rio Preto, SP, Brasil

[e]Sociedade Brasileira de Cirurgia Plástica – SBCP, São Paulo, SP, Brasil

Abstract

Bovine pericardium (BP) has been used as a biomaterial for several decades in many medical applications particularly due to its mechanical properties and the high collagen content. In the acellular form it favors faster tissue repair, providing a three-dimensional support for cellular and vascular events observed during tissue repair and due, to a low elastin content, may favor its use as a breast implant cover, resulting in a low possibility of contracture of the biomaterial, preventing the appearance of irregularities during the reconstruction process. Thus, the aim of this study was to evaluate, histomorphologically, the behavior of acellularized bovine pericardium (ABP) as a mammary implant cover in rats. For this purpose, 16 animals were divided into two groups, with eight animals at each biological point: 7 and 15 days after surgery. Of the 16 animals, 32 specimens were obtained: 16 in the experimental group (EG) and 16 in the control group (CG). Throughout this study, none of the studied groups had postoperative complications. Results: The histomorphological results showed, in the two biological points, both in the EG and in the CG, chronic inflammatory infiltrate, leukocyte fibrin exudate, formation of granulation tissue and deposition of collagen fibers, more evident in the EG, regressive along the biological points. At 15 days, the implanted ABP showed initial biointegration with the fibrous capsule and surrounding tissues of the recipient bed. Conclusion: These results indicate that the due to the observed favorable tissue response ABP may be of potential use as a breast implant cover.

Keywords: biomaterials, collagen, breast implant, pericardium, rats.

Resumo

O pericárdio bovino (PB) tem sido utilizado como biomaterial há várias décadas em diversas aplicações médicas, principalmente devido às suas propriedades mecânicas e ao alto teor de colágeno. Na forma acelular, favorece a reparação tecidual mais rápida, dando um suporte tridimensional para eventos celulares e vasculares observados durante a reparação tecidual e devido ao baixo teor de elastina, pode favorecer seu uso como cobertura de implantes mamários, resultando em baixa possibilidade de contratura do biomaterial, evitando o aparecimento de irregularidades durante o processo de reconstrução. Assim, o objetivo deste estudo foi avaliar, histomorfologicamente, o comportamento do pericárdio bovino acelularizado (PBA) como cobertura de implante mamário em ratos. Dezesseis animais foram divididos em dois grupos, com oito animais em cada ponto biológico: 7 e 15 dias após a cirurgia. Dos 16 animais, 32 espécimes foram obtidos: 16 no grupo experimental (GE) e 16 no grupo controle (GC). Ao longo deste estudo, nenhum dos grupos estudados apresentou complicações pós-operatórias. Os achados histomorfológicos mostraram, nos dois pontos biológicos, tanto no GE quanto no GC, infiltrado inflamatório crônico, exsudato fibrino leucocitário, formação de tecido de granulação e deposição de fibras colágenas, mais evidentes no GE, regressivas ao longo dos pontos biológicos. Aos 15 dias, o PBA implantado apresentou biointegração inicial com a cápsula fibrosa e tecidos circundantes do leito receptor. Esses resultados indicam que, devido à resposta favorável do tecido observado, o PBA pode ser de uso potencial como cobertura de implante mamário.

Palavras-chave: biomateriais, colágeno, implante mamário, pericárdio, ratos.

*e-mail: cheniafrutuoso@gmail.com
Received: July 3, 2023 – Accepted: November 17, 2023

1. Introduction

The use of biomaterials is not recent and its application in the correction of problems related to human health dates back to antiquity. However, in recent years, technological advances in the field of tissue bioengineering (TB) have made it possible to improve and develop appropriate techniques and biomaterials for tissue replacement and regeneration (Sharma et al., 2019), in view of the limitations and disadvantages of techniques and materials currently used (Vig et al., 2017; Miguez-Pacheco et al., 2015). Thus, in recent decades, researchers in the field of BT have produced increasingly sophisticated and effective biomaterials to replace tissues that had their functions lost due to trauma, disease or as a result of the body´s natural aging process, as well as to aesthetic purposes.

These biomaterials can be produced from different sources of raw material, natural or synthetic. Among the former, type I collagen stands out mainly, the most abundant protein in the human body, which corresponds to approximately 30% of body weight, the main component of connective tissues, distributed in the extracellular matrix (ECM) where it performs different functions (Ghomi et al., 2021; Sorushanova et al., 2019), which enables wide applicability in the biomedical area, given the different structural and functional modifications that can be performed during the processing of collagen biomaterials.

Regarding the use of biomaterials in reconstructive surgeries, associated with breast implants, the literature has shown promising clinical results (Castagnetti et al., 2020; Aguilera-Sáez et al., 2015; Gubitosi et al., 2014). In this context, the use of alloplastic grafts has been an effective alternative, since it avoids the use of tissue flaps during reconstruction, which often causes tissue deformities with consequent functional and aesthetic impairments in the donor areas. There is still the possibility that some patients do not have availability of donor areas. It is worth mentioning that the use of a non-autogenous implant, such as breast silicone, induces an inflammatory response which, in turn, can lead to erosion of the surrounding tissues, fistulization and even implant extrusion (Maia et al., 2010). In these situations, the use of dermal substitutes plays an essential role in implant coverage, as it helps tissue repair by providing a fundamental three-dimensional framework for the cellular events observed after silicone implantation, which minimizes postoperative complications.

In this scenario, the use of acellular dermal matrices (ADMs) has become one of the main options for breast reconstruction using prostheses (Urban et al., 2016), due to the possibility of improving the aesthetic result and reducing the side effects of the radiotherapy. Clinical and experimental data show that the use of matrices to cover breast implants for reconstructions contributes to a lower incidence of complications or deformities, as it improves the definition of the inframammary fold and provides a more natural breast, with less invasive procedures and a lower rate of long-term capsular contracture, common in this type of reconstruction (Lee and Mun, 2016, 2017; Schmitz et al., 2013, Mofid et al., 2012), which favors better functional and aesthetic results (Castagnetti et al., 2020; Mallikarjuna et al., 2017; Urban et al., 2016). Alternatively, the use of acellularized bovine pericardium (ABP) in silicone coverage has been researched.

The BP in its native form has been used for years as a biomaterial, mainly in the cardiovascular area, due to its mechanical and biological properties resulting from its high content of type I collagen. In its acellular form, it mimics the ECM of the host tissue, especially in the which refers to their three-dimensional organization and chemical composition. Furthermore, it presents itself as a material with wide availability and accessibility, which makes it a biomaterial with characteristics that favor wide use in the biomedical area (Soares et al., 2021; Braile-Sternieri et al., 2020; Mathapati et al., 2013; Goissis et al., 2011). The acellularization process is a procedure that removes cellular components from tissues without altering the integrity of the remaining ECM (Crapo et al., 2011), decreasing tissue antigenicity due to the elimination of cellular debris and soluble components.

The use of ABP was described in breast reconstruction surgery with implants by Mofid et al. (2012), using a biomaterial with structural characteristics similar to ADMs, but with greater ease of obtaining. And since then, it has been used as an alternative to ADM, due to the decrease in postoperative complications; faster healing, as it provides a suitable three-dimensional framework for tissue regeneration; and for presenting better functional and aesthetic results (Mallikarjuna et al., 2017).

The ABP has a lower elastin content (2.98%) when compared to ADMs (5-7%) (Giuliani et al., 2014) and has a high amount of collagen, which enables faster tissue repair (Castagnetti et al., 2020; Mallikarjuna et al., 2017; Urban et al., 2016) and may be beneficial in preventing irregularities during the breast expansion process by covering part of the soft tissues. Given the above, the objective of this study was to evaluate, histomorphologically, the use of ABP in the coverage of breast implants on the back of rats.

2. Material and Methods

2.1. ABP matrix

ABP matrices with dimensions of 3.0 x 3.5 cm that were previously treated in a phosphate buffer solution with pH in the range of 6.5 to 8.5 containing: a) Glycerol (>4 M); b) 0.1% dodecyl sulfate (SDS), for 72 hours and c) Triton X-100, in the presence of EDTA with 0,005% sodium azide, throughout the processing.

In the intervals of this treatment, the matrices were washed with water and saline solution. The reconstitution of the collagen fibril set was performed in 0.13 M phosphate buffer and pH 7.4. The volume of 0.1% SDS solutions was calculated based on the total mass of collagen present in the BP used in each experiment and on the stoichiometry of the SDS-collagen interaction. After processing, the matrices were sterilized and stored in 4% formaldehyde. The ABP used in this study was provided by Braile Biomédica® (São José do Rio Preto – SP).

2.2. Surgical procedure for biomaterial implantation

This study was developed in accordance with the Normative Resolution no. 55/2022 (Brazilian Guideline for the Care and Use of Animals in Teaching or Scientific

Research Activities – DBCA) and Normative Resolution no. 37/2018 (Guideline for the Practice of Euthanasia), both from the National Council for the Control of Animal Experimentation, after approval by the Ethics Committee on the Use of Animals of the Institute of Health Sciences of the Federal University of Bahia (Protocol nº. 115/2017).

Sixteen male Wistar rats, weighing between 250 and 350 g, were distributed into two groups: experimental (EG) - biomaterial (ABP) overlaid on the mini mammary prosthesis (MP) and control (CG) - MP without biomaterial implantation - with eight animals in each biological point (7 and 15 days). According to the principles of the 3R's (Replacement, Reduction and Refinement), was implanted the MP in the submuscular plane of all animals, on both sides of the back, right (control) and left (experiment). Thus, from the 16 animals it was possible to obtain 32 specimens, 16 with biomaterial and 16 without the biomaterial. Prior, to implantation in the animals, the ABP matrices were washed, under manual handling, for three minutes for five repetitions, in 150 mL of sterile physiological solution each wash, to remove formaldehyde.

Prior to the surgical procedures, the animals received anesthesia with ketamine hydrochloride 75 mg/kg, associated with xylazine hydrochloride 5 mg/kg, intraperitoneally, as described by Damy et al. (2010). The 2 mL MPs (Silimed®) were implanted on both sides of the animals' dorsum having as reference the mid-sagittal line and a horizontal line at the height of the lower costal ridge, as described by Schmitz et al. (2013) and Kafejian et al. (1997). On the experimental side (EG), the MP was overlapped with a ABP matrix, which covered the entire MP and was fixed with 4 points with nylon thread no. 4.0.

2.3. Histological processing

After the biological time points of 7 and 15 days, the animals were euthanized with lethal intraperitoneal injection of ketamine and xylazine, in respective dosages, 300 mg/Kg and 30 mg/kg. Then, tissue samples were obtained, with a margin of 1.0 cm from the edge of the MP and depth below the muscle plane, including the *panniculus carnosus* muscle. The specimens were fixed in 4% buffered formalin for 24 hours. After this period, the silicone MP was removed from all groups and the tissue samples were sectioned in two regions: central and peripheral, to evaluate the biomaterial interface with the MP. The specimens were then sent for routine histological processing, embedded in paraffin, cut 5 µm thick, and stained by hematoxylin and eosin (HE) and picrosirius red (PIFG). Histological sections were examined by light microscopy with a DM6B microscope (LEICA®), photographed with a DFC 7000T camera (LEICA®) and LAS V.4.12 Leica Application Suit® (LEICA®) software.

3. Results

3.1. Acellularized bovine pericardium

The photomicrograph in Figure 1 shows the effectiveness of the BP acellularization process, which demonstrates the complete absence of cells in the biomaterial structure, as well as the maintenance of the collagenous framework with waved collagen fibers in standard BP appearance.

3.2. CG - 7 days - MP without ABP implant

At this biological point, was noted the presence of diffuse mononuclear inflammatory infiltration and granulation tissue (Figures 2a and 2c) subjacent to the fibrous capsule formed around the MP (Figures 2a and 2b). The beginning of collagen fiber deposition was observed near the region where the MP was implanted, evidenced by PIFG (Figure 2d). Peripherally to the fibrous capsule, the presence of blood vessels was noted.

3.3. CG - 15 days - MP without ABP implant

At 15 days, a moderate chronic inflammatory infiltrate was noted with a decrease in edema and more organized granulation tissue in relation to the previous biological point (Figures 3a and 3c). The fibrous capsule was thin and with the collagen fibers organized in a parallel fashion, in relation to the 7 days (Figure 3b), better evidenced in the staining with PIFG (Figures 3b and 3d).

3.4. EG - 7 days – MP with ABP implant

At this biological point, we observed chronic inflammatory infiltrate, more intense when compared to the CG, and granulation tissue surrounding the ABP and MP (Figures 4a and 4c). In some histological sections, this finding extended to the hypodermis. Fibrous capsule formation was more evident than in the CG (Figure 4b), which was seen in the early stages of biointegration with the ABP and adjacent tissues (Figure 4d).

3.5. EG - 15 days - MP with ABP implant

At 15 days, the mononuclear inflammatory infiltrate was still notoriously observed with edema and granulation tissue, more evident than at seven days (Figure 5a). It was also noted the presence of fibrin, evident collagen deposition (Figure 5b) and fibrous capsule formation, on both sides of the biomaterial, more evident on the external side to the ABP (Figure 5c). At higher magnification, we observed the integration of the ABP with the neoformed collagen tissue (Figure 5d).

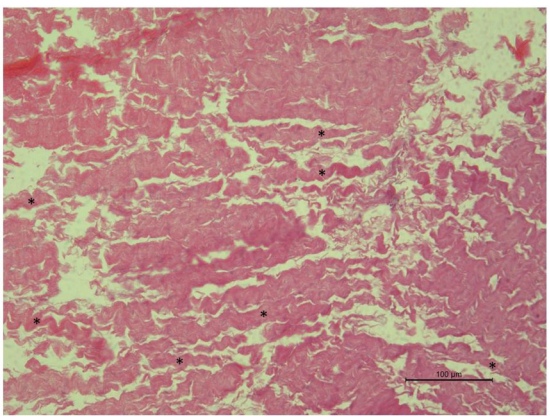

Figure 1. ABP structure. Note the absence of cells and the maintenance of collagen fibers (*) and the native structure of the BP matrix after the acellularization process. H.E. **Source:** Authors' elaboration.

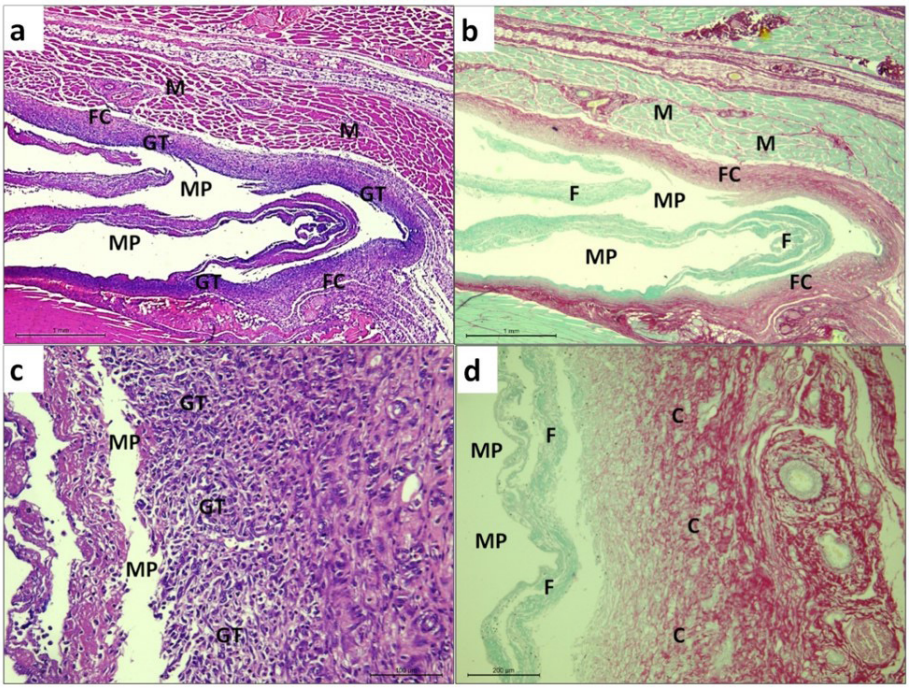

Figure 2. Photomicrographs of the CG at the 7-day biological point. After 7 days, GC shows: (a) Diffuse mononuclear inflammatory infiltrate and granulation tissue, contiguous to the fibrous capsule, surrounding the MP. HE. Bar: 1mm; (b) Fibrous capsule formation so circumjacent to the MP. PIFG. Bar: 1mm; (c) Granulation tissue adjacent to the MP. HE. Bar: 100 µm; (d) Deposition of collagen and fibrin fibers adjacent to the PM. PIFG. Bar: 200 µm. Collagen (C), Fibrin (F), Fibrous Capsule (FC), Granulation Tissue (GT), Mini Prosthesis (MP), Muscle (M).
Source: Elaborated by the authors.

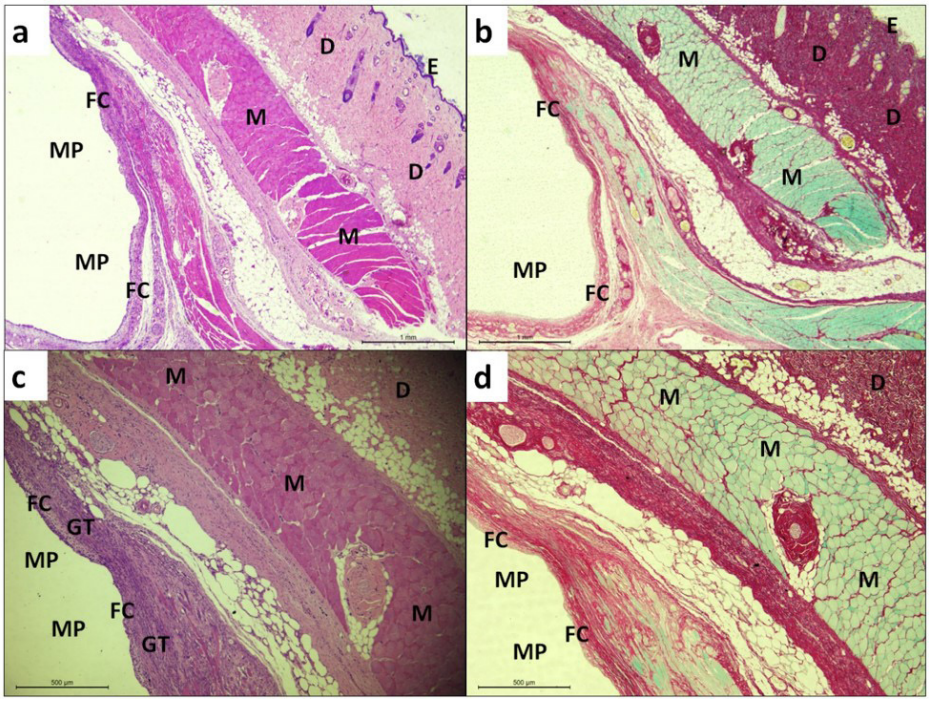

Figure 3. Photomicrographs of the CG at the 15-day biological point. At 15 days the CG shows: (a) Chronic inflammatory infiltrate with decreased edema and more organized granulation tissue than at 7 days. HE. Bar: 1mm; (b) Thinner fibrous capsule than at the 7-day biological point. PIFG. Bar: 1mm; (c) More organized granulation tissue. HE. Bar: 500 µm; (d) Parallel organized collagen fibers in the fibrous capsule. PIFG. Bar: 500 µm. Dermis (D), Epidermis (E), Fibrous Capsule (FC), Granulation Tissue (GT), Mini Prosthesis (MP), Muscle (M).
Source: Authors' elaboration.

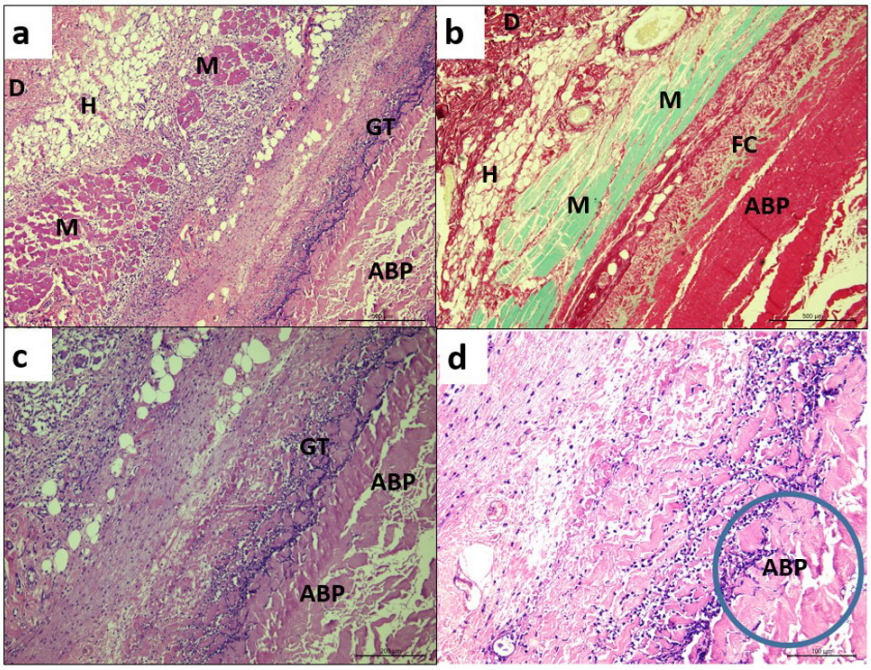

Figure 4. Photomicrographs of the EG at the 7-day biological point. At 7 days EG shows: (a) Chronic inflammatory infiltrate and granulation tissue surrounding the ABP and MP. HE. Bar: 500 µm; (b) Fibrous capsule formed contiguously to the ABP. PIFG. Bar: 500 µm; (c) Initial biointegration of the acellularized bovine pericardium to the surrounding tissues. HE. Bar: 200 µm; (d) Acellularized bovine pericardium in an initial process of biointegration more evident. Initial biointegration of the acellularized bovine pericardium with collagen fibers. PIFG. Bar: 100 µm. Acellularized Bovine Pericardium (ABP), Dermis (D), Fibrous Capsule (FC), Granulation Tissue (GT), Hypoderm (H), Muscle (M).
Source: Elaborated by the authors.

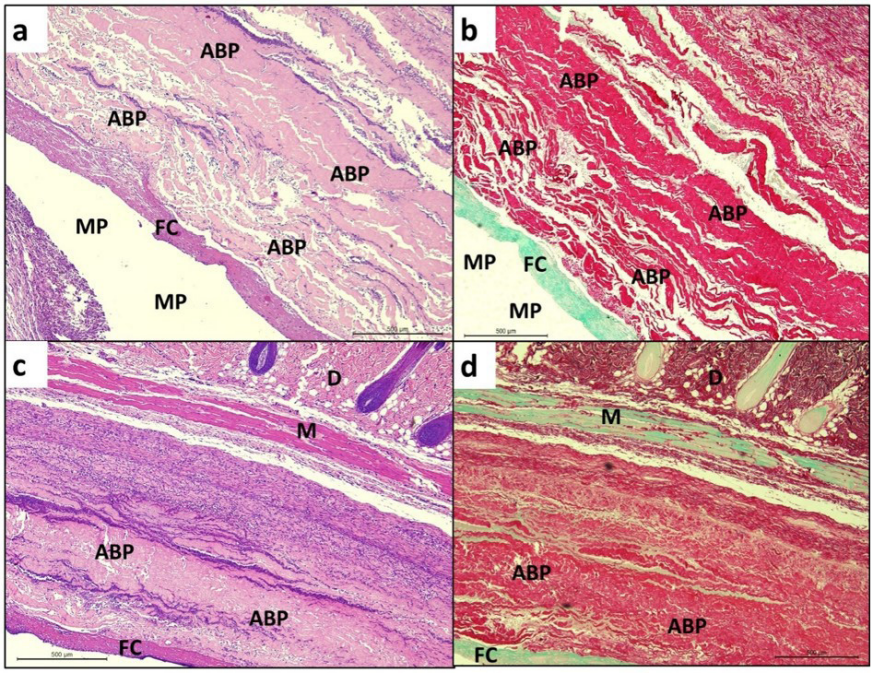

Figure 5. Photomicrographs of the EG at the 15-day biological point. After 15 days it is evident in the EG: (a) ABP surrounded by mixed inflammatory infiltrate. HE. Bar: 500 µm; (b) ABP being integrated to the surrounding tissues. PIFG. Bar: 500 µm; (c) ABP surrounded by inflammatory fibrinous exudate. HE. Bar: 500 µm; (d) ABP integrated to the fibrous capsule more evident. PIFG. Bar: 200 µm. Acellularized Bovine Pericardium (ABP), Dermis (D), Fibrous Capsule (FC), Mini Prosthesis (MP), Muscle (M). Fibrous Capsule (FC), Dermis (D), Mini Prosthesis (P), Muscle (M), Acellularized Bovine Pericardium (ABP).
Source: Elaborated by the authors.

4. Discussion

This study analyzed the tissue response of ABP in the coverage of breast implant, since collagen has been widely researched in the development of biomaterials for different biomedical applications. The inflammatory response observed after implantation of the ABP matrix was of the chronic type, with a predominance of mononuclear cellular infiltrate, compatible with the type of inflammation observed in the evaluation of biomaterials in vivo (Santos et al., 2021; Al-Maawi et al., 2017; Miguel et al., 2013; Anderson et al., 2008). This finding is in line with the study of Bernardini et al. (2020) who also observed chronic inflammation after ABP implantation. However, these authors studied this biomaterial with different analysis periods than our study.

According to Kim et al. (2012) and Heyer et al. (2010), the presence of the matrices in the host tissue can act as a foreign body, susceptible to inflammatory response, especially, chronic, given that macrophages respond rapidly to the implantation of biomaterials in living tissue (Anderson et al., 2008; Sheikh et al., 2015; Zaveri et al., 2014). The tissue injury observed as a consequence of the surgical procedure for the implantation of a biomaterial triggers chemical signaling cascades that initially culminate in the migration of neutrophil like leukocytes to the region of injury, which degranulate and initiate the acute phase of the inflammatory response (Anderson et al., 2008). In sequence, the leukocyte predominance is of macrophages, primarily type 1 (M1), classically activated by the newly synthesized chemical mediators at the implantation site - histamine, interleukin 4 (IL-4), interleukin 8 (IL-8) and interleukin 13 (IL-13) (Klopfleisch and Jung, 2017; Klopfleisch, 2016; Anderson et al., 2008). These cells are responsible for effecting the locally observed immune response, thus characterizing the chronic phase of the inflammatory response (Anderson et al., 2008). The release of IL-4 and IL-13 stimulates polarization of type 2 (M2) macrophages that secrete chemical mediators, which modulate cellular and vascular events that favor the formation of multinucleated giant cells to increase phagocytic capacity at the biomaterial implantation site (Zhou and Groth, 2018), and tissue repair (Rahmati et al., 2020; Klopfleisch and Jung, 2017; Klopfleisch, 2016; Sheikh et al., 2015) Soon, angiogenesis, granulation tissue development, fibroblast infiltration, collagen synthesis, and connective tissue formation occur (Rahmati et al., 2020). In our study we noted the formation of blood vessels both in the periphery and permeating the ABP fibers in the two periods studied. Regarding vascular neoformation, Bernardini et al. (2020) observed a greater number of blood vessels from 3 weeks after ABP implantation, which according to Kalaba et al. (2016) is considered a positive response and indicates integration of the biomaterial with the surrounding tissue, probably favors the production of non-fibrotic dermal tissue.

These responses occur due to the immediate adsorption of proteins on the surfaces of biomaterials after tissue implantation, before the host cells interact with the material. With this, there is the formation of a provisional matrix rich in fibrin on and around the biomaterial. In parallel, the acute phase of the inflammatory response initially arises, which may take a few hours to even days (Rahmati et al., 2020; Anderson et al., 2008). Over time, this phase is gradually replaced by the chronic one, which lasts from approximately two weeks to months (Anderson et al., 2008). The types, levels and conformation of adsorbed proteins are dependent on the physicochemical characteristics of biomaterials (Sheikh et al., 2015; Das et al., 2011). In this sense, modulation of macrophage responses through modifications of surface chemistry and roughness is an alternative that can be used to mitigate the chronic inflammation observed after biomaterial implantation, since an exacerbated inflammatory reaction limits the functional performance of numerous biomaterials, for example, pacemaker electrodes and breast implants (Zaveri et al., 2014; Siggelkow et al., 2003; Kamel et al., 2001). Our histological findings evidenced, in both groups studied, the aforementioned events presence of fibrin, granulation tissue, collagen synthesis and fibrous capsule formation (Bernardini et al., 2020; Das et al., 2011; Xu et al., 2009; Gamba et al., 2002; Santillán-Doherty et al., 1995), important for biomaterial integration and tissue repair. In the experimental group, since the first period of analysis, we noticed connective tissue deposition permeating the collagen fibers of the ABP matrix and circumjacent to the biomaterial with fibrous capsule formation, which presented itself more organized at 15 days, suggesting initial biointegration of the biomaterial (Bernardini et al., 2020; Ludolph et al., 2019; Schmitz et al., 2013). In the CG, the formation of the fibrous capsule was less thick compared to the experimental group, probably due to the presence of ABP and more noticeable inflammatory response in the EG. In the study by Schmitz et al. (2013), the use of ADM evidenced, at 3 and 12 weeks, the presence of myofibroblasts arranged circumjacently to the implant, which, according to Bernardini et al. (2020), in moderate quantity is considered positive for biomaterial integration and accommodation of the prosthesis.

Knowing that the biocompatibility of the biomaterial is directly related to its immunogenic potential, that is, with the type and intensity of the observed inflammatory response, which should preferably be chronic and discrete (De Paula, 2017), the results of our study allow us to state that the evaluated ABP proved to be biocompatible throughout the studied period. These findings are in line with what was observed by Bernardini et al. (2020), who demonstrated regressive chronic inflammatory response over time, suggesting good biocompatibility of the evaluated dermal matrix. Furthermore, macroscopically, at all biological points, none of the groups studied showed local adverse effects, such as hematoma, abscess, seroma, wound dehiscence, or extrusion of the mini prostheses. These findings ratify the results found by Bernardini et al. (2020) who also used ABP as a mini breast prosthesis cover in rats. Seroma formation in reconstructive surgery is a common problem that can distend the skin and culminate in negative aesthetic outcome (Mallikarjuna et al., 2017), as well as cause extrusion of the prosthesis.

Based on the results found in this study, it is suggested that the ABP has the potential to be used in surgeries with breast prostheses safely. However, it is necessary to develop further research involving a longer observation period to show biological responses of ABP after long periods of implantation, in order to support the understanding of biomaterial integration, specifically at the interface with the host tissue.

5. Conclusion

According to the experimental conditions of this study, we conclude that the ABP was biocompatible and showed initial integration to the surrounding tissues in the two biological points evaluated. Thus, it has the potential to be used clinically in surgeries with breast prostheses safely.

Acknowledgements

The authors thank Braile Biomédica for supplying the acellularized bovine pericardium; Silimed for donating the mini prostheses; the Instituto de Patologia Geral e Cutânea for making the histological processing of the samples possible; and the Coordenação de Aperfeiçoamento de Pessoa de Nível Superior/CAPES for granting a scholarship to Chenia Frutuoso Silva.

References

AGUILERA-SÁEZ, J., BOSACOMA-ROURA, P., GARRIDO-FERRER, A. and GUINOT-MADRIDEJOS, A., 2015. Experiencia en reconstrucción mamaria inmediata con implante y matriz acelular de pericardio bovino tras mastectomía ahorradora de piel. *Cirúgia Plástica Ibero-latinoamericana*, vol. 41, no. 4, pp. 385-392. http://dx.doi.org/10.4321/S0376-78922015000400005.

AL-MAAWI, S., ORLOWSKA, A., SADER, R., JAMES KIRKPATRICK, C. and GHANAATI, S., 2017. In vivo cellular reactions to different biomaterials: physiological and pathological aspects and their consequences. *Seminars in Immunology*, vol. 29, pp. 49-61. http://dx.doi.org/10.1016/j.smim.2017.06.001. PMid:28647227.

ANDERSON, J.M., RODRIGUEZ, A. and CHANG, D.T., 2008. Foreign body reaction to biomaterials. *Seminars in Immunology*, vol. 20, no. 2, pp. 86-100. http://dx.doi.org/10.1016/j.smim.2007.11.004. PMid:18162407.

BERNARDINI, R., VARVARAS, D., D'AMICO, F., BIELLI, A., SCIOLI, M.G., CONIGLIONE, F., ROSSI, P., BUONOMO, O.C., PETRELLA, G., MATTEI, M. and ORLANDI, A., 2020. Biological acellular pericardial mesh regulated tissue integration and remodeling in a rat model of breast prosthetic implantation. *Journal of Biomedical Materials Research. Part B, Applied Biomaterials*, vol. 108, no. 2, pp. 577. http://dx.doi.org/10.1002/jbm.b.34413. PMid:31094057.

BRAILE-STERNIERI, M.C.V.B., GOISSIS, G., GIGLIOTI, A.F., RAMIREZ, V.D.A., PEREIRA, N.P., DE VASCONCELLOS, A., BASSO-FRAZZATO, G.G. and BRAILE, D.M., 2020. In vivo evaluation of vivere bovine pericardium valvular bioprosthesis with a new anti-calcifying treatment. *Artificial Organs*, vol. 44, no. 11, pp. E482-E493. http://dx.doi.org/10.1111/aor.13718. PMid:32364253.

CASTAGNETTI, F., BERTANI, C., FORONI, M., FALCO, G., CENINI, E., DE BONIS, F. and FERRARI, G., 2020. The Bovine pericardium matrix in immediate implant-based breast reconstruction. *Aesthetic Plastic Surgery*, vol. 44, no. 6, pp. 2051-2060. http://dx.doi.org/10.1007/s00266-020-01651-z. PMid:32112193.

CRAPO, P.M., GILBERT, T.W. and BADYLAK, S.F., 2011. An overview of tissue and whole organ decellularization processes. *Biomaterials*, vol. 32, no. 12, pp. 3233-3243. http://dx.doi.org/10.1016/j.biomaterials.2011.01.057. PMid:21296410.

DAMY, S.B., CAMARGO, R.S., CHAMMAS, R. and FIGUEIREDO, L.F., 2010. Aspectos fundamentais da experimentação animal: aplicações em cirurgia experimental. *Revista da Associação Médica Brasileira*, vol. 56, no. 1, pp. 103-111. http://dx.doi.org/10.1590/S0104-42302010000100024. PMid:20339795.

DAS, D., ZHANG, Z., WINKLER, T., MOUR, M., GUNTER, C., MORLOCK, M., MACHENS, H.G. and SCHILLING, A.F., 2011. Bioresorption and degradation of biomaterials. *Advances in Biochemical Engineering/Biotechnology*, vol. 126, pp. 317-333. http://dx.doi.org/10.1007/10_2011_119. PMid:21975956.

DE PAULA, B.L., 2017. *Análise histomorfométrica da resposta inflamatória e reparo tecidual frente à implantação de matriz colágena suína no tecido subcutâneo de camundongos.* Bauru: Universidade do Sagrado Coração, 65 p. Dissertação de Mestrado em Biologia Oral.

GAMBA, P.G., CONCONI, M.T., LO PICCOLO, R., ZARA, G., SPINAZZI, R. and PARNIGOTTO, P.P., 2002. Experimental abdominal wall defect repaired with acellular matrix. *Pediatric Surgery International*, vol. 18, no. 5-6, pp. 327-331. http://dx.doi.org/10.1007/s00383-002-0849-5. PMid:12415348.

GHOMI, E.R., NOURBAKHSH, N., KENARI, M.A., ZARE, M. and RAMAKRISHNA, S., 2021. Collagen-based biomaterials for biomedical applications. *Journal of Biomedical Materials Research. Part B, Applied Biomaterials*, vol. 109, no. 12, pp. 1986-1999. http://dx.doi.org/10.1002/jbm.b.34881. PMid:34028179.

GIULIANI, A., MANESCU, A., LARSSON, E., TROMBA, G., LUONGO, G., PIATTELLI, A., MANGANO, F., IEZZI, G. and MANGANO, C., 2014. In vivo regenerative properties of coralline-derived (Biocoral) scaffold grafts in human maxillary defects: demonstrative and comparative study with beta-tricalciumphosphateand biphasic calcium phosphate by synchrotron radiation X-Ray microtomography. *Clinical Implant Dentistry and Related Research*, vol. 16, no. 5, pp. 736-750. http://dx.doi.org/10.1111/cid.12039. PMid:23350548.

GOISSIS, G., GIGLIOTI, A.F. and BRAILE, D.M., 2011. Preparation and characterization of an acellular bovine pericardium intended for manufacture of valve bioprostheses. *Artificial Organs*, vol. 35, no. 5, pp. 484-489. http://dx.doi.org/10.1111/j.1525-1594.2011.01264.x. PMid:21595716.

GUBITOSI, A., DOCIMO, G., PARMEGGIANI, D., PIROZZI, R., VITIELLO, C., SCHETTINO, P., AVELLINO, M., CASALINO, G., AMATO, M., RUGGIERO, R. and DOCIMO, L., 2014. Acellular bovine pericardium dermal matrix in immediate breast reconstruction after skin sparing mastectomy. *International Journal of Surgery*, vol. 12, suppl. 1, pp. S205-S208. http://dx.doi.org/10.1016/j.ijsu.2014.05.007. PMid:24859403.

HEYER, K., BUCK II, D.W., KATO, C., KHAN, S.A., ALAM, M. and KIM, J.Y.S., 2010. Reversed acellular dermis: failure of graft incorporation in primary tissue expander breast reconstruction resulting in recurrent breast cellulitis. *Plastic and Reconstructive Surgery*, vol. 125, no. 2, pp. 66e-68e. http://dx.doi.org/10.1097/PRS.0b013e3181c7264e. PMid:20124811.

KAFEJIAN, A.P., HADDAD FILHO, D., GUIDUGLI NETO, J. and GOLDENBERG, S., 1997. Estudo comparativo das reações teciduais à implantação de silicone e politetrafluoroetileno no dorso de ratos. *Acta Cirurgica Brasileira*, vol. 12, no. 3, pp. 182-188. http://dx.doi.org/10.1590/S0102-86501997000300009.

KALABA, S., GERHARD, E., WINDER, J.S., PAULI, E.M., HALUCK, R.S. and YANG, J., 2016. Design strategies and applications of biomaterials and devices for hernia repair. *Bioactive Materials*, vol. 1, no. 1, pp. 2-17. http://dx.doi.org/10.1016/j.bioactmat.2016.05.002. PMid:28349130.

KAMEL, M., PROTZNER, K., FORNASIER, V., PETERS, W., SMITH, D. and IBANEZ, D., 2001. The peri-implant breast capsule: an immunophenotypic study of capsules taken at explantation surgery. *Journal of Biomedical Materials Research*, vol. 58, no. 1, pp. 88-96. http://dx.doi.org/10.1002/1097-4636(2001)58:1<88::AID-JBM130>3.0.CO;2-7. PMid:11153003.

KIM, J.Y.S., DAVILA, A.A., PERSING, S., CONNOR, C.M., JOVANOVIC, B., KHAN, S.A., FINE, N. and RAWLANI, V., 2012. A meta-analysis of human acellular dermis and submuscular tissue expander breast reconstruction. *Plastic and Reconstructive Surgery*, vol. 129, no. 1, pp. 28-41. http://dx.doi.org/10.1097/PRS.0b013e3182361fd6. PMid:22186498.

KLOPFLEISCH, R. and JUNG, F., 2017. The pathology of the foreign body reaction against biomaterials. *Journal of Biomedical Materials Research. Part A*, vol. 105, no. 3, pp. 927-940. http://dx.doi.org/10.1002/jbm.a.35958. PMid:27813288.

KLOPFLEISCH, R., 2016. Macrophage reaction against biomaterials in the mouse model: phenotypes, functions and markers. *Acta Biomaterialia*, vol. 43, pp. 3-13. http://dx.doi.org/10.1016/j.actbio.2016.07.003. PMid:27395828.

LEE, K.T. and MUN, G.H., 2016. Updated evidence of acellular dermal matrix use for implant-based breast reconstruction: a meta-analysis. *Annals of Surgical Oncology*, vol. 23, no. 2, pp. 600-610. http://dx.doi.org/10.1245/s10434-015-4873-9. PMid:26438439.

LEE, K.T. and MUN, G.H., 2017. A meta-analysis of studies comparing outcomes of diverse acellular dermal matrices for implant-based breast reconstruction. *Annals of Plastic Surgery*, vol. 79, no. 1, pp. 115-123. http://dx.doi.org/10.1097/SAP.0000000000001085. PMid:28509698.

LUDOLPH, I., GRUENER, J.S., KENGELBACH-WEIGAND, A., FIESSLER, C., HORCH, R.E. and SCHMITZ, M., 2019. Long-term studies on the integration of acellular porcine dermis as an implant shell and the effect on capsular fibrosis around silicone implants in a rat model. *Journal of Plastic, Reconstructive & Aesthetic Surgery*, vol. 72, no. 9, pp. 1555-1563. http://dx.doi.org/10.1016/j.bjps.2019.04.015. PMid:31202696.

MAIA, M., KLEIN, E.S., MONJE, T.V. and PAGLIOSA, C., 2010. Reconstrução da estrutura facial por biomateriais: revisão de literatura. *Revista Brasileira de Cirurgia Plástica*, vol. 25, no. 3, pp. 566-572. http://dx.doi.org/10.1590/S1983-51752010000300029.

MALLIKARJUNA, U., MUJAHID, M., PILKINGTON, R., SHAHEER, M. and MUJAHID, P., 2017. Acellular bovine pericardium in implant-based breast reconstruction: a systematic review of the literature. *European Journal of Plastic Surgery*, vol. 40, no. 4, pp. 265-270. http://dx.doi.org/10.1007/s00238-017-1284-0.

MATHAPATI, S., BISHI, D.K., GUHATHAKURTA, S., CHERIAN, K.M., VENUGOPAL, J.R., RAMAKRISHNA, S. and VERMA, R.S., 2013. Biomimetic acellular detoxified glutaraldehyde cross-linked bovine pericardium for tissue engineering. *Materials Science and Engineering C*, vol. 33, no. 3, pp. 1561-1572. http://dx.doi.org/10.1016/j.msec.2012.12.062. PMid:23827609.

MIGUEL, F.B., BARBOSA JÚNIOR, A.A., DE PAULA, F.L., BARRETO, I.C., GOISSIS, G. and ROSA, F.P., 2013. Regeneration of critical bone defects with anionic collagen matrix as scaffolds. *Journal of Materials Science. Materials in Medicine*, vol. 24, no. 11, pp. 2567-2575. http://dx.doi.org/10.1007/s10856-013-4980-8. PMid:23784007.

MIGUEZ-PACHECO, V., HENCH, L.L. and BOCCACCINI, A.R., 2015. Bioactive glasses beyond bone and teeth: emerging applications in contact with soft tissues. *Acta Biomaterialia*, vol. 13, pp. 1-15. http://dx.doi.org/10.1016/j.actbio.2014.11.004. PMid:25462853.

MOFID, M.M., MEININGER, M.S. and LACEY, M.S., 2012. Veritas® bovine pericardium for immediate breast reconstruction: a xenograft alternative to acellular dermal matrix products. *European Journal of Plastic Surgery*, vol. 35, no. 10, pp. 717-722. http://dx.doi.org/10.1007/s00238-012-0736-9. PMid:23002328.

RAHMATI, M., SILVA, E.A., RESELAND, J.E., A HEYWARD, C. and HAUGEN, H.J., 2020. Biological responses to physicochemical properties of biomaterial surface. *Chemical Society Reviews*, vol. 49, no. 15, pp. 5178-5224. http://dx.doi.org/10.1039/D0CS00103A. PMid:32642749.

SANTILLÁN-DOHERTY, P., JASSO-VICTORIA, R., SOTRES-VEGA, A., OLMOS, R., ARREOLA, J.L., GARC-IA, D., VANDA, B. and GAXIOLA, M., 1995. Repair of thoracoabdominal wall defects in dogs using a bovine pericardial bioprothesis. *Revista de Investigacion Clinica*, vol. 47, no. 6, pp. 439-446. PMid:8850141.

SANTOS, G.G., NUNES, V.L.C., MARINHO, S.M.O.C., SANTOS, S.R.A., ROSSI, A.M. and MIGUEL, F.B., 2021. Biological behavior of magnesium-substituted hydroxyapatite during bone repair. *Brazilian Journal of Biology = Revista Brasileira de Biologia*, vol. 81, no. 1, pp. 53-61. http://dx.doi.org/10.1590/1519-6984.217769. PMid:32074171.

SCHMITZ, M., BERTRAM, M., KNESER, U., KELLER, A.K. and HORCH, R.E., 2013. Experimental total wrapping of breast implants with acellular dermal matrix: A preventive tool against capsular contracture in breast surgery? *Journal of Plastic, Reconstructive & Aesthetic Surgery*, vol. 66, no. 10, pp. 1382-1389. http://dx.doi.org/10.1016/j.bjps.2013.05.020. PMid:23764323.

SHARMA, P., KUMAR, P., SHARMA, R., BHATT, V.D. and DHOT, P.S., 2019. Tissue engineering: current status & futuristic scope. *Journal of Medicine and Life*, vol. 12, no. 3, pp. 225-229. http://dx.doi.org/10.25122/jml-2019-0032. PMid:31666821.

SHEIKH, Z., BROOKS, P.J., BARZILAY, O., FINE, N. and GLOGAUER, M., 2015. Macrophages, foreign body giant cells and their response to implantable biomaterials. *Materials (Basel)*, vol. 8, no. 9, pp. 5671-5701. http://dx.doi.org/10.3390/ma8095269. PMid:28793529.

SIGGELKOW, W., FARIDI, A., SPIRITUS, K., KLINGE, U., RATH, W. and KLOSTERHALFEN, B., 2003. Histological analysis of silicone breast implant capsules and correlation with capsular contracture. *Biomaterials*, vol. 24, no. 6, pp. 1101-1109. http://dx.doi.org/10.1016/S0142-9612(02)00429-5. PMid:12504533.

SOARES, L.G., DE OLIVEIRA, F.S., QUEIROZ, A.B.P.S., DE MEDEIROS, A.C.S.R., BARIANI JUNIOR, A.F., FECHIS, A.D.S. and ROCHA, T.A.S.S., 2021. Biomechanics of the fresh and conserved bovine pericardium. *Anatomia, Histologia, Embryologia*, vol. 50, no. 3, pp. 588-593. http://dx.doi.org/10.1111/ahe.12665. PMid:33620085.

SORUSHANOVA, A., DELGADO, L.M., WU, Z., SHOLOGU, N., KSHIRSAGAR, A., RAGHUNATH, R., MULLEN, A.M., BAYON, Y., PANDIT, A., RAGHUNATH, M. and ZEUGOLIS, D.I., 2019. The collagen suprafamily: from biosynthesis to advanced biomaterial development. *Advanced Materials*, vol. 31, no. 1, e1801651. http://dx.doi.org/10.1002/adma.201801651. PMid:30126066.

URBAN, C., FACCENDA, P.H., VELOSO, M.L.C.P.B., ARAÚJO-FILHO, A.M., MENDES, E. and LIMA, R.S., 2016. Uso de pericárdio bovino na reconstrução mamária imediata com prótese definitiva em paciente previamente irradiada. *Revista Brasileira de Mastologia*, vol. 26, no. 2, pp. 83-86. http://dx.doi.org/10.5327/Z2016000200011RBM.

VIG, K., CHAUDHARI, A., TRIPATHI, S., DIXIT, S., SAHU, R., PILLAI, S., DENNIS, V.A. and SINGH, S.R., 2017. Advances in skin regeneration using tissue engineering. *International Journal of Molecular Sciences*, vol. 18, no. 4, pp. 789. http://dx.doi.org/10.3390/ijms18040789. PMid:28387714.

XU, H., WAN, H., ZUO, W., SUN, W., OWENS, R.T., HARPER, J.R., AYARES, D.L. and MCQUILLAN, D.J., 2009. A porcine-derived acellular dermal scaffold that supports soft tissue regeneration: removal of terminal galactose-α-(1,3)-galactose and retention of matrix structure. *Tissue Engineering. Part A*, vol. 15, no. 7, pp. 1807-1819. http://dx.doi.org/10.1089/ten.tea.2008.0384. PMid:19196142.

ZAVERI, T.D., LEWIS, J.S., DOLGOVA, N.V., CLARE-SALZLER, M.J. and KESELOWSKY, B.G., 2014. Integrin-directed modulation of macrophage responses to biomaterials. *Biomaterials*, vol. 35, no. 11, pp. 3504-3515. http://dx.doi.org/10.1016/j.biomaterials.2014.01.007. PMid:24462356.

ZHOU, G. and GROTH, T., 2018. Host responses to biomaterials and anti-inflammatory design: a brief review. *Macromolecular Bioscience*, vol. 18, no. 8, e1800112. http://dx.doi.org/10.1002/mabi.201800112. PMid:29920937.