
RIGENERA
Micrografting Technology
hbw srl.
human brain wave

About Our Company

HBW s.r.l. HUMAN BRAIN WAVE

- *HBW was founded in April 2012 to provide innovative medical services by producing biotechnological devices for medical applications.*
- *HBW was founded by Antonio Graziano and Riccardo D'Aquino following their research on stem cells and regenerative medicine.*
- *HBW in 2014 patented its micro-graft technology called RIGENERA®.*
- *HBW started to test a prototype of Rigenera® technology in the Italian market in January 2013 (first clinical tests started in 2006)*
- *The Rigenera® technology is based on micrografts generated from autologous tissues without enzymes and/or additives using a disposable medical device called Rigeneracons/Adipecons.*
- *The Rigeneracons is CE and FMA (Japan) certified as a disposable medical device and FDA listed for Skin surgical graft and Bone mill*

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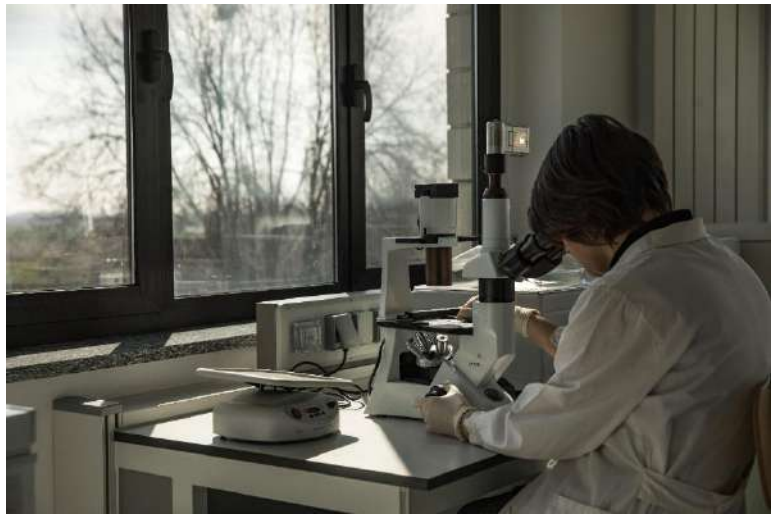
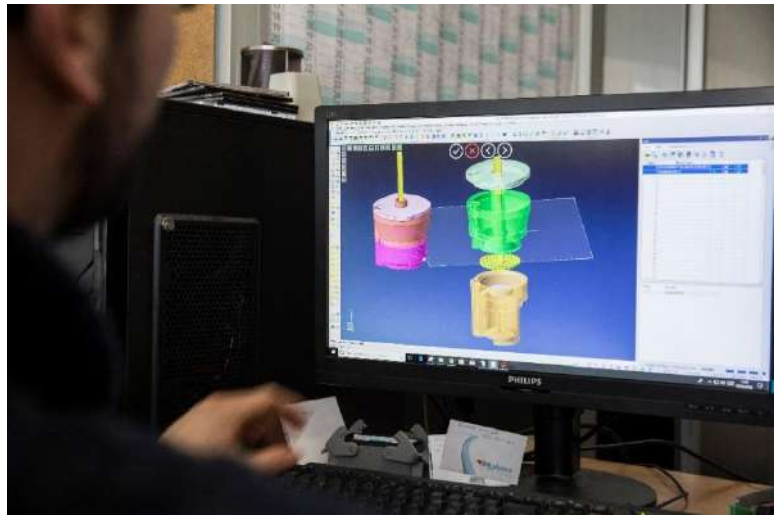




International congresses

RIGENERA Micrografting Technology hbw human brain wave

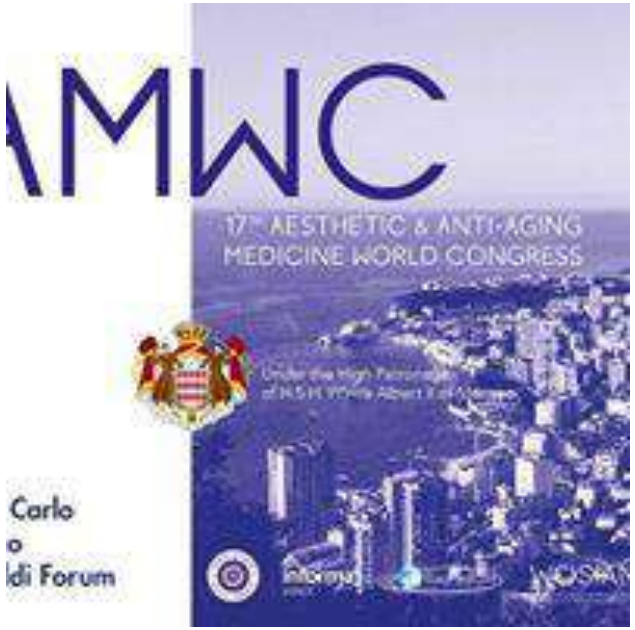
DELHI ACSICON 2019

ACSICON 2019
17th National Conference of
Association of Cutaneous Surgeons (I)

RIGENERA Micrografting Technology hbw

2019 WCHR BARCELONA

11th WORLD CONGRESS HAIR RESEARCH
Sitges, Barcelona



IN OCCASIONE DEL 67° CONGRESSO NAZIONALE SICPRE

RIGENERA Micrografting Technology hbw

VENERDÌ 12 OTTOBRE
ORE 12:30
ROME MARRIOTT PARK HOTEL **SALA CARAVAGGIO**

WORKSHOP
Rigenera Re-evolution

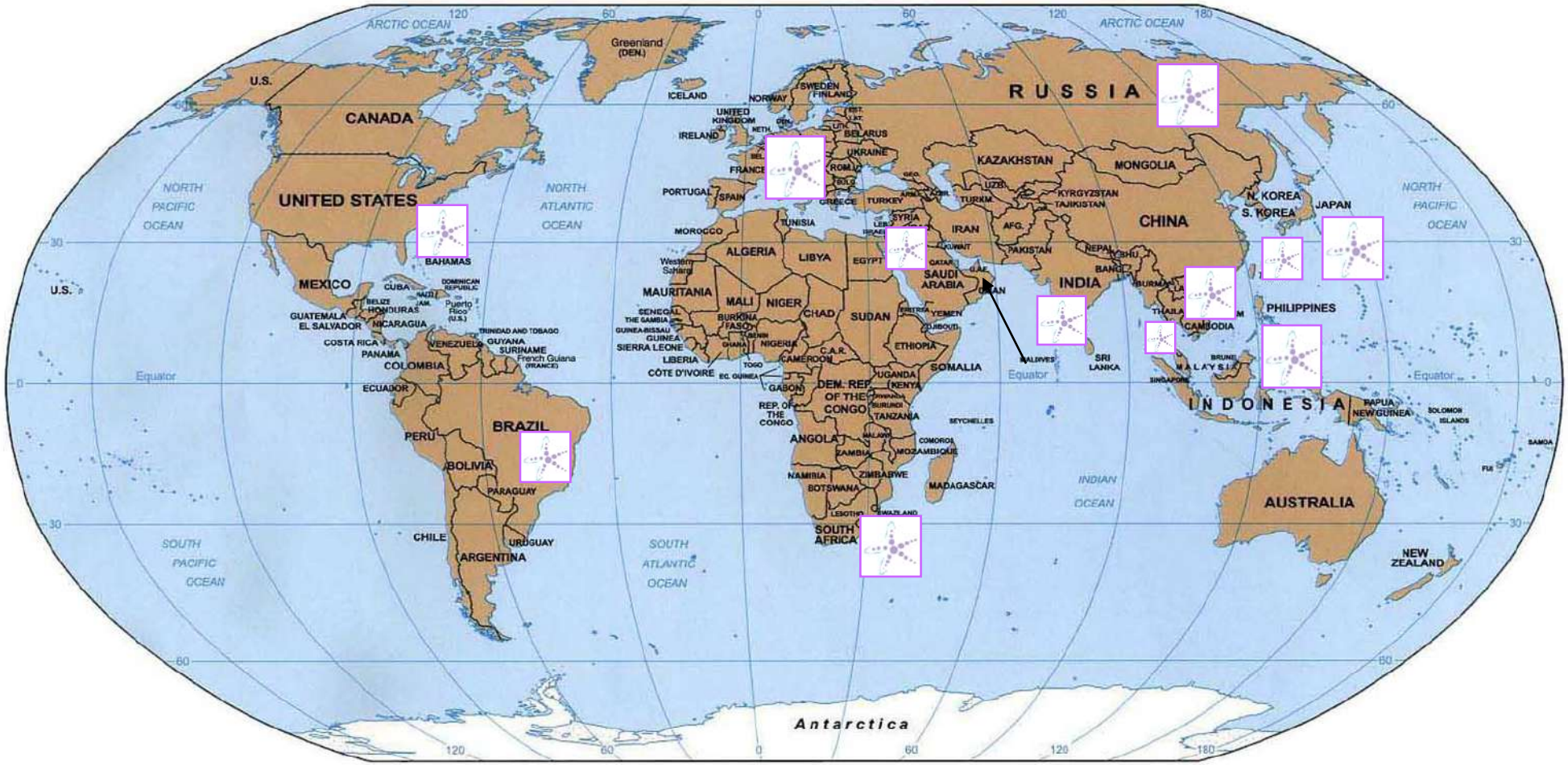
RIGENERA NAPOLI hbw

GIOVEDÌ 21 GIUGNO 2018
ORE 14:30
PRESSO SALA SAFFO - CITTÀ DELLA SCIENZA

WORKSHOP

RIGENERA HBW NAPOLI
I PROGRESSI
DELLA RIABILITAZIONE 4.0:
LE NUOVE FRONTIERE
DELLA MEDICINA
TRA INNOVAZIONE E SVILUPPO

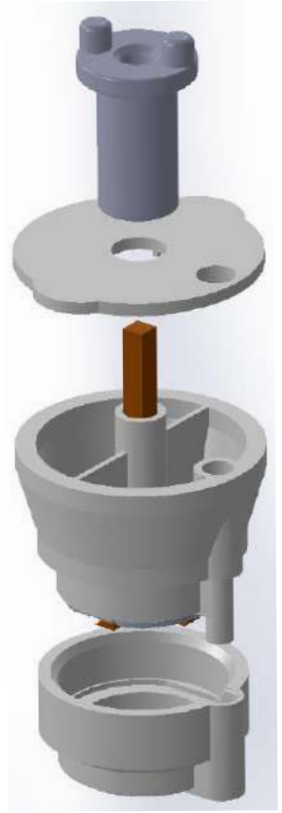
Rigenera worldwide: where we are where we'll go…



Rigenera® a HBW technology

The RIGENERACONS are surgical disposable medical devices CE, FMI approved and FDA listed in which the **autologous** tissue sample form the patient are **mechanically disaggregated** to obtain the Micrografts.

Every device owns a grid with 100 hexagonal holes. Any hole is embraced by six micro-blades designed for efficient cutting of hard and soft tissues.



How it works ?

- *After the tissue simple collection, RIGENERA allows a standard tissue disaggregation in one surgical time*

Rigenera-Definição

A tecnologia Rigenera, consiste em dispositivo descartável, chamados Rigeneracons e Adipecons, em combinação com diferentes ativadores,acionados pelo dispositivo Sicurdrill.

Os descartáveis são desagregadores mecânicos de tecidos biológicos, que permitem a obtenção de microenxertos autólogos de forma minimamente invasiva;

O dispositivo Sicurdrill ativa os descartáveis, pressionado suavemente o tecido sobre as lâminas;

Enquanto a amostra de tecido coletada é processada, os orifícios atuam como filtro, selecionando apenas as partículas e células menores que 80 microns.

Rigenera- Definição

Procedimento em tempo único, dura menos de 30 minutos;

O paciente é doador e receptor;

Estudos demonstram que a população de células obtidas tem de 70 a 90% de viabilidade celular;

Os microenxertos contém alta porcentagem de células de fração vascular estromal e células progenitoras, que desempenham um papel fundamental na regeneração de tecidos.

Diferencial do Rigenera

Possibilidade de desfragmentar diferentes tecidos, fornecendo diferente tipos celulares com alta viabilidade.

As células já estão diferenciadas no tipo de célula específica para a regeneração, exemplo:

Se o objetivo é regeneração óssea, o sítio doador é o periósteo(tecido de alta concentração de osteoblastos).

Inicio imediato do processo regenerativo e redução do tempo em até 70%

Diminuição do processo inflamatório;

Melhora importante na dor.

Células Tronco (Grau de plasticidade)

- **Totipotentes**, aquelas **células** que **são** capazes de diferenciarem-se em todos **os** 216 tecidos que formam o corpo humano, incluindo a placenta e anexos embrionários.
- **Pluripotência** refere-se a uma célula-tronco que possui o potencial de se diferenciar em qualquer um dos três tipos de folheto embrionário humano: endoderme (que origina o trato gastrointestinal e os pulmões), mesoderme (que origina os músculos, ossos, sangue e sistema urogenital) e ectoderme (que origina os tecidos epidermais e sistema nervoso).[4] Células-tronco pluripotentes podem dar origem a qualquer tipo de célula fetal ou adulta, mas não podem por si próprias desenvolver-se em um organismo fetal ou adulto porque não possuem a capacidade de criar tecido extra-embrionário, como a placenta.

Células tronco (Grau de plasticidade)

- Células progenitoras **multipotentes** são capazes de se diferenciar em um número limitado de outros tipos de células. Um exemplo de célula-tronco multipotente é a célula hematopoiética — uma célula-tronco do sangue que pode se desenvolver em diversos tipos de células sanguíneas, mas não pode se desenvolver em neurônios ou outros tipos de células. No final da longa série de divisões celulares que formam o embrião estão células que terminaram o seu processo de diferenciação, ou que se considera que se comprometeram permanentemente a um tipo específico de função. Outro exemplo são as células-tronco mesenquimatosas, que se podem diferenciar em osteoblastos, condrócitos e adipócitos.

Células tronco adultas

- Além do embrião, as células-tronco também são encontradas em vários órgãos e tecidos no indivíduo adulto, onde participam da homeostase tecidual, gerando novas células em resposta ao repovoamento celular fisiológico ou a algum tipo de injúria. Tais populações celulares indiferenciadas mantidas no organismo adulto são denominadas células-tronco adultas
- As células-tronco adultas (CTAs) estão em estado quiescente ou de baixa proliferação, predominantemente nas fases G0 e G1 do ciclo celular, localizando-se em regiões específicas essenciais para o seu desenvolvimento e a manutenção de seus atributos, particularmente a capacidade de autorrenovação (Gritti et al., 2002). Estas regiões são denominadas de nichos celulares e dentre os principais sítios estão: medula óssea (Heissig, 2005), coração (Leri et al, 2005), rins (Li, 2005), pele (Tumbar et al., 2004), fígado (Guettier, 2005), pâncreas, ovários, cordão umbilical, placenta e líquido amniótico.

CÉLULAS-TRONCO MESENQUIMAIS (CTMS)

- São consideradas células multipotentes não hematopoiéticas com propriedade de autorrenovação e capacidade de diferenciação em tecidos mesenquimais (Reiser et al., 2005). O primeiro relato das CTMs foi realizado pelo pesquisador russo Friedenstein e seus colaboradores, na década de 70, que as descreveu como sendo células aderentes, morfologicamente semelhantes aos fibroblastos e com alta capacidade de adesão à superfície plástica. Vários estudos posteriores relataram a multipotência destas células, ou seja, a capacidade de diferenciarem-se em linhagens derivadas da mesoderme embrionária: osteogênica, condrogênica e adipogênica (Prockcop, 1997).

Célula progenitora e Célula tronco

Como células-tronco, as **células progenitoras** têm a capacidade de se diferenciar em um tipo especializado de célula. Em contraste com as células-tronco, no entanto, as células progenitoras são mais diferenciadas, sendo estimuladas a se diferenciar em suas "células alvo". A diferença mais importante entre as células-tronco e as células progenitoras é que as primeiras podem se replicar indefinidamente, enquanto que as segundas podem se dividir apenas em um número limitado de vezes

Células Progenitoras

As MSC tem potencial imunomodulatório;

Células-tronco mesenquimais , exibem a capacidade de modular a resposta das células T e geralmente esses efeitos imunomoduladores são anti-inflamatórios;

As MSC são capazes de se diferenciar em:

-fibroblastos;

-osteoblasto;

-adipócitos;

-condroblastos;

-miócitos;

- **pericito** é uma célula tipo mesenquimal, associada com as paredes de vasos sanguíneos pequenos. Como é uma célula relativamente indiferenciada, serve como suporte para estes vasos, mas pode se diferenciar em um fibroblasto, célula de músculo liso ou macrófago conforme a necessidade.

Células progenitoras

Liberam fator de crescimento,fatores apoptóticos e pró angiogênico;

A função dos fatores de crescimento não é somente a de estimular a proliferação celular, iniciando a mitose, mas também de manter a sobrevivência celular, estimular a migração celular, a diferenciação celular e também apoptose (morte celular programada)

Células mesenquimais na MEDULA ÓSSEA

- A medula óssea adulta é um compartimento onde ocorrem interações entre sistemas celulares diferentes que formam um microambiente essencial (estroma) para a hematopoese (Prockop, 1997). As CTMs são encontradas primariamente imersas no estroma medular e em íntimo contato com diversos outros tipos celulares, como: adipócitos, fibroblastos, osteoblastos, células reticulares, entre outras. Sua frequência é muito baixa sendo estimada em 0,005% de todas as células mononucleadas de uma MO. Muitos fatores podem influenciar no número de células, tal como a presença de patologias, uso de medicamentos e a idade do doador.

Células mesenquimais no CORDÃO UMBILICAL

- Na última década, um número considerável de estudos comprovou que o sangue de cordão umbilical humano possui células-tronco hematopoéticas e um pool de células- tronco mesenquimais. A população de células-tronco na matriz da geléia está localizada perto da vasculatura do cordão, estas são denominadas células perivasculares do cordão umbilical humano. As CTMs apresentam potencial de proliferação e diferenciação em múltiplas linhagens, semelhantemente ao observado nas células da medula óssea. No entanto, como estas células correspondem a apenas uma pequena parcela das células mononucleares presentes em cada amostra, é necessário isolá-las e multiplicá-las in vitro para se ter um alto rendimento celular (Goodwin, 2001; Panepucci, 2004).

Células mesenquimais do Periósteo

- O periósteo é uma estrutura complexa,composta por duas camadas de tecido:

-uma camada fibrosa externa que fornece integridade estrutural, bem como fixação ao tecido mole;

-uma camada cambial que possui potencial osteogênico,contendo céluas progenitoras osteogênicas que suportam a formação óssea.

Durante o crescimento e desenvolvimento, o periósteo contribui para o alongamento e modelagem óssea, e quando o osso é lesado, participa da sua regeneração.

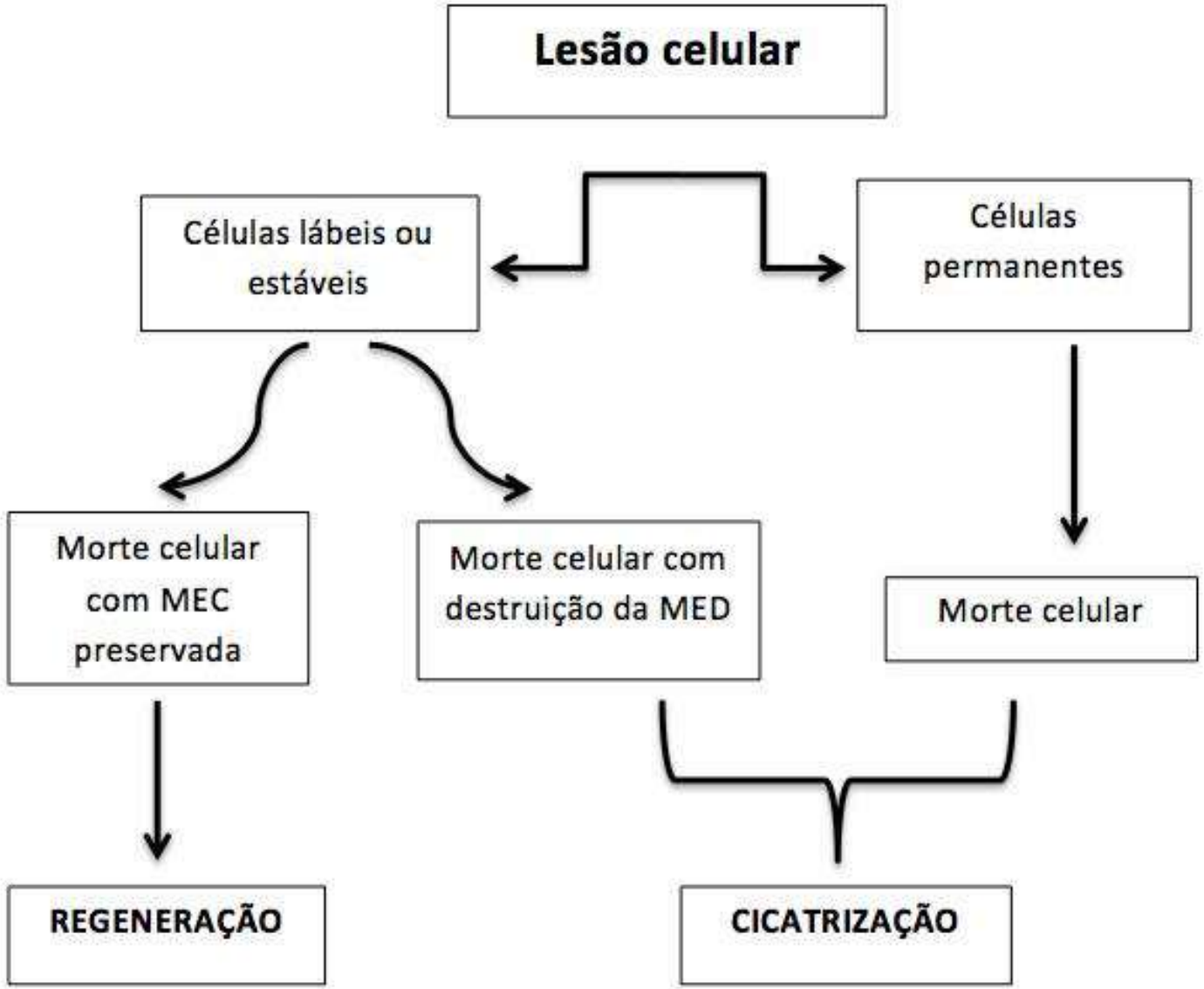
O periósteo contém células tronco mesenquimais multipotentes que são capazes de se diferenciar em osso e cartilagem, dando ao periósteo um grande potencial em aplicações na medicina regenerativa.

Tecido adiposo

No adulto, o tecido adiposo marrom é praticamente ausente,o tecido existente é o tecido adiposo branco,que se divide em tecido adiposo submucoso e tecido adiposo visceral.

O tecido adiposo submucoso de localiza entre a derme e o tecido gorduroso e é considerado um NICHO de células mesenquimais.

Nicho é um microambiente complexo e dinâmico que transmite e recebe os sinais por meio de mediadores celulares e não celulares, são considerado os reservatórios fisiológicos de células específicas.


Lesão celular
Células lábeis ou estáveis
Células permanentes
Morte celular com MEC preservada
Morte celular com destruição da MED
Morte celular
REGENERAÇÃO
CICATRIZAÇÃO

Regeneração tecidual

A regeneração se caracteriza pela restituição dos componentes teciduais idênticos aqueles removidos.

Esse tipo de reparo só é possível em tecidos que ainda possuem célula com a capacidade de se proliferar ou ainda tenham células tronco.

Assim, com base nesta habilidade de multiplicação celular, os tecidos são classificados em:

-tecidos lábeis ou de divisão contínua, exemplos: epitélios, células da medula óssea vermelha e tecidos hematopoiéticos.

-tecidos quiescentes ou estáveis, apesar de possuírem um baixo nível de replicação, quando submetidos a estímulos para divisão celular são capazes de regenerar o tecido de origem. O melhor exemplo é o tecido hepático.

-tecidos permanentes ou não divisores, são formados por células que não podem ser submetidas à divisão mitótica devido o seu grau de especificidade. Exemplos são os neurônios e as células musculares.

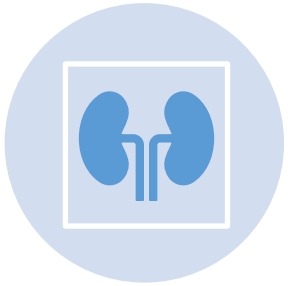
Cicatrização

É uma resposta fibroproliferativa que restaura as estruturas originais, porém envolve a deposição de colágeno e a formação da cicatriz.

Os fatores que favorecem o processo de cicatrização, são, a extensão do dano celular,o tipo de tecido afetado e a intensidade da lesão da matriz extracelular.

Fases da cicatrização

1.Resposta inflamatória a lesão inicial, com a intenção de eliminar o agente nocivo,remover o tecido lesionado e estimular a deposição de componentes da matriz extracelular;



2.Proliferação de fibroblastos e células endoteliais vasculares,formando o tecido de granulação;

3.Com o aumento do numero de fibroblastos, ocorre a síntese de matriz extracelular e deposição do colágeno, formando a cicatriz;

4.Então se inicia o processo de remodelação, que é o equilíbrio entre síntese e degradação da matriz extracelular.

Key points

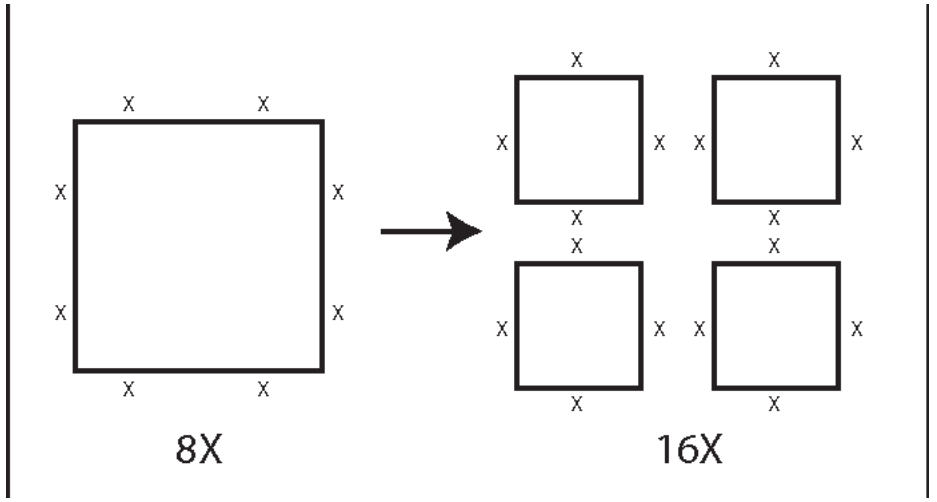
- *In just one surgical time, the patient is the donor and the acceptor of calibrated micrografts of 80 Micron.*
- *The tissue is minimally manipulated since the devices only performs mechanical cutting and filtration.*
- *The collections of tissue particles in average size of 80 Microns, after filtration, allow the collection mainly of progenitor cells, extracellular matrix and growth factors.*
- *The micrografts can be deliverable in the acceptor site with a syringe and used alone or in association with different biomaterials according the tissue to regenerate.*

AUTOLOGOUS USE **HOMOLOGOUS TISSUE** **ONE SURGICAL TIME**

Rigenera® a HBW technology a step behind:
What are the micrografts?

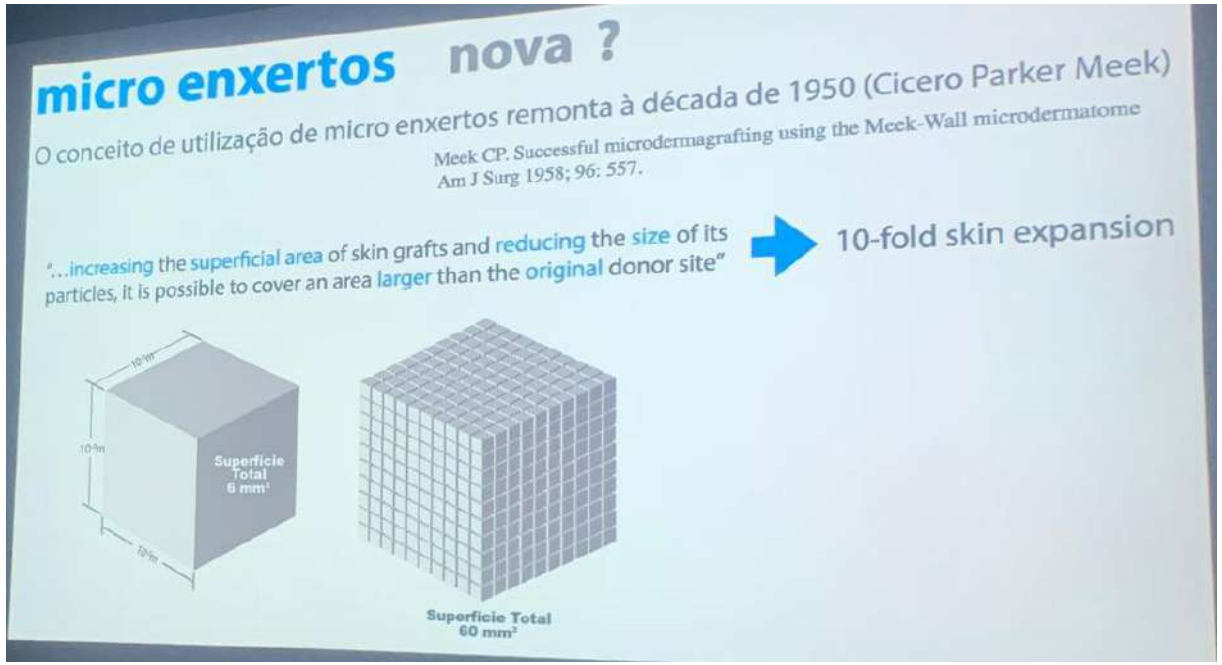
The micrografts idea is not new, Cicero Park Meek was pioneer of skin expansion techniques (1960) reaching a 10-fold skin expansion.

Proving that multiple pieces of a large graft provide more active edges for regeneration.



Microenxerto, é uma novidade?

- O conceito de utilização de microenxerto remonta à década de 1950(Cícero Parker Meek) Successful microdermagrafting using the Meek-Wall microdermatome. **Am J Surg**. **1958** Oct;96(4):557-8.



Rigenera® a HBW technology: The new Micrografts Theory

The Clinical Challenges:

To prepare viable micrografts in a fast, reliable, safe procedure without any chemical substance or tissue extensive manipulation

To reduce the size of the Micrografts particles and preserving as much as possible the cell viability

To overcome the Stem cells Legal, Ethical and Price limitations by using Micrografts-enriched in progenitor cells.

Editorial *Current Tissue Engineering, 2015, Vol. 4, No. 1* 3

Editorial

New Perspectives and Therapies in Regenerative Medicine

Letizia Trovato

Antonio Graziano

Tissue engineering is emerging as an interdisciplinary field in biomedical engineering that aims to repair diseased or damaged tissues or organs. The skin is the largest organ of the body in vertebrates and represents approximately one-tenth of the body mass in humans. It is composed of the epidermis and dermis with a complex nerve and blood supplying provides vital barrier function. Disruption of epidermal integrity due to trauma, disease, burn or surgery can be fatal, and therefore strategies are needed to enhance the physiological regenerative properties of the skin. Engineering skin substitutes represents a prospective source of advanced therapy in the clinical settings as well as valuable skin surrogates for drug permeability tests and toxicity screening. However, at the present time, there are no models of bioengineered skin that completely replicate the anatomy, physiology, biological stability or aesthetic nature of uninjured skin.

A promising alternative to tissue engineering is represented by stem cells therapy, in fact many studies have been conducted on its use to repair a damaged tissue or organ. The stem cell therapy is mainly based on the use of Mesenchymal Stem Cells (MSCs) which are multipotent adult stem cells with unique biological properties. Several in vitro studies and preclinical animal models reported that MSCs are promising for cell therapy showing the ability to home to sites of inflammation after tissue injury, to differentiate into various cell types and secrete multiple bioactive molecules capable of stimulating recovery of injured cells by inhibiting inflammation by a paracrine effect. MSCs also show the lack of immunogenicity and have the ability to exert immunomodulatory functions. Today, many pathological conditions are treated with MSCs, such as ischemic cardiovascular diseases, critical limb ischemia, bone and cartilage regeneration or neural diseases.

In this special issue, we aim to summarize some of the applications of MSCs, for example in facial aging, maxillo-facial defects and cell cardiomyoplasty. We also display a new approach to isolate specifically this cell population from human connective tissues and create autologous micro-grafts ready to clinical applications. Autologous bone grafting remains in fact a gold standard for the reconstruction for bone defects, mainly in the maxillofacial region, where dental pulp stem cells (DPSC) and bone-marrow mesenchymal stem cells (BMSC) represent the most common source of stem cells used for the building of 3D structures, due to their ability to self-renew and multi-lineage differentiation. In this context, was developed the Rigenera protocol, a new approach for regeneration of human injured tissues through the injection of autologous micro-grafts obtained by innovative medical device designed and produced for surgery. The patient is in fact the donor and acceptor of calibrated micro-grafts of 50 micron, displaying a high cell viability and an optimal regenerative potential. In the final part of this issue, we briefly show promising results obtained with Rigenera protocol mainly in the dentistry field.

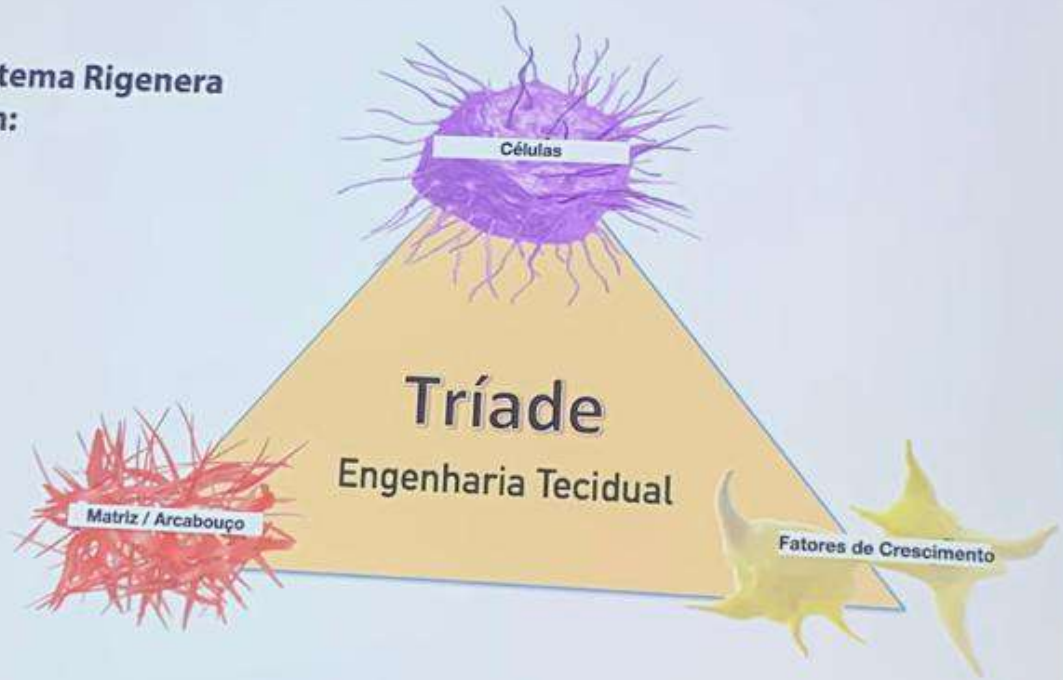
Rigenera® a HBW technology: The science behind

- *Principle 1: **The side population** .Numerous scientific papers have demonstrated that progenitor cells reside within a population with determined morphological features called side population. The main features of this side population are: 1) the size and 2) the expression of stem markers, significantly higher than in the wild population.*
- *Principle II : **The niche concept** : Preserving extra cellular matrix environment, the cells after desegregation still stand in their own physiological niche, that supports them in the grafting site.*

O que os micro enxertos possuem?

Os micro enxertos produzidos por meio do sistema Rigenera possuem cerca de 80um e contém:

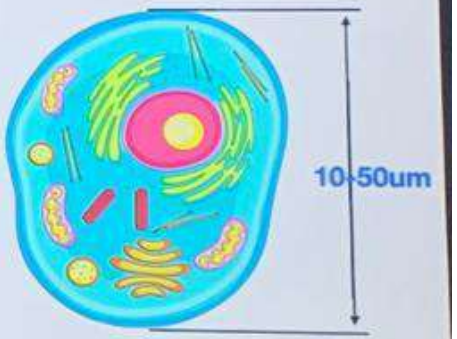
Células viáveis
Matriz extra celular
Fatores de crescimento



Estudos micro enxertos *in vitro*

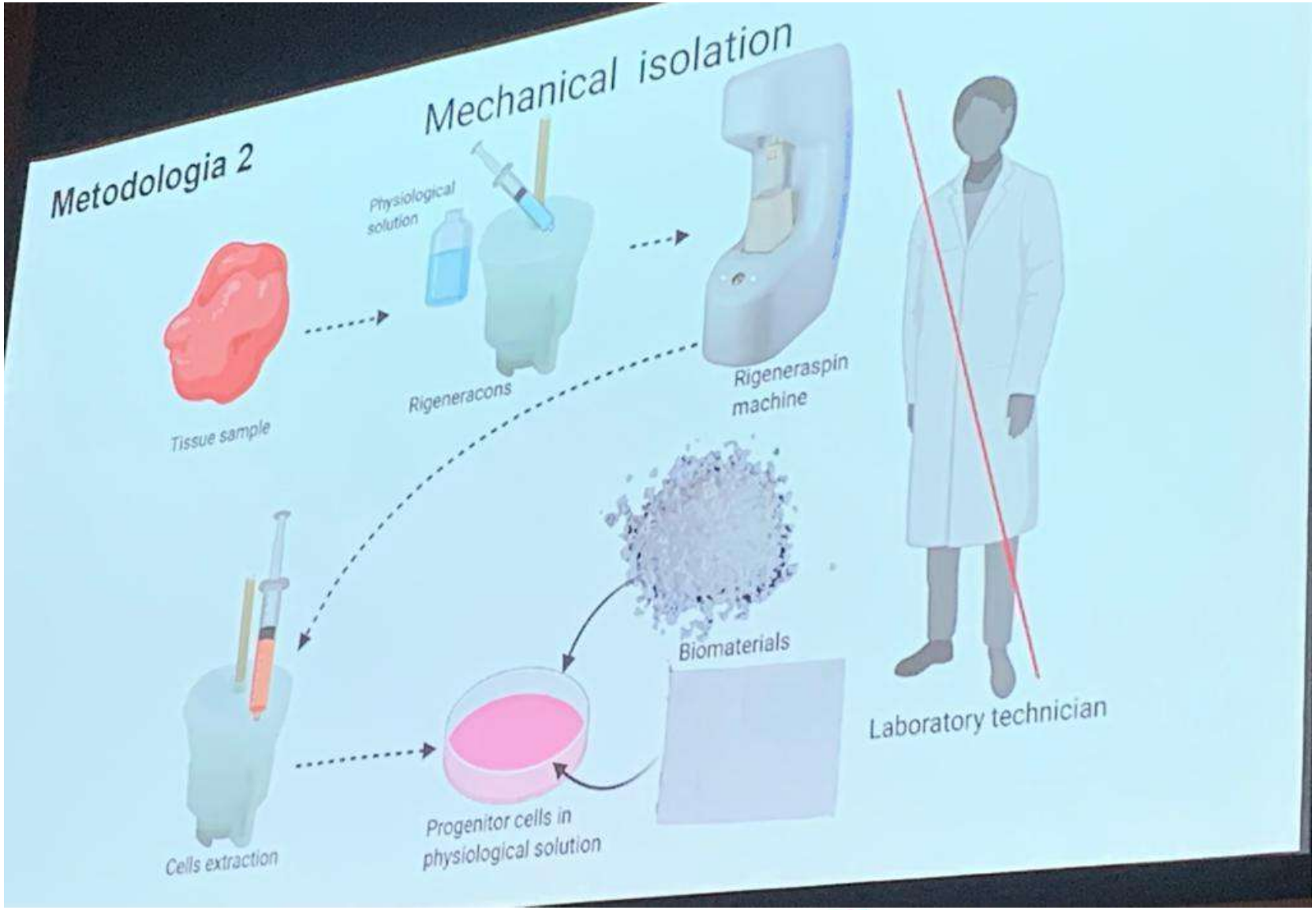
Manipulação mínima

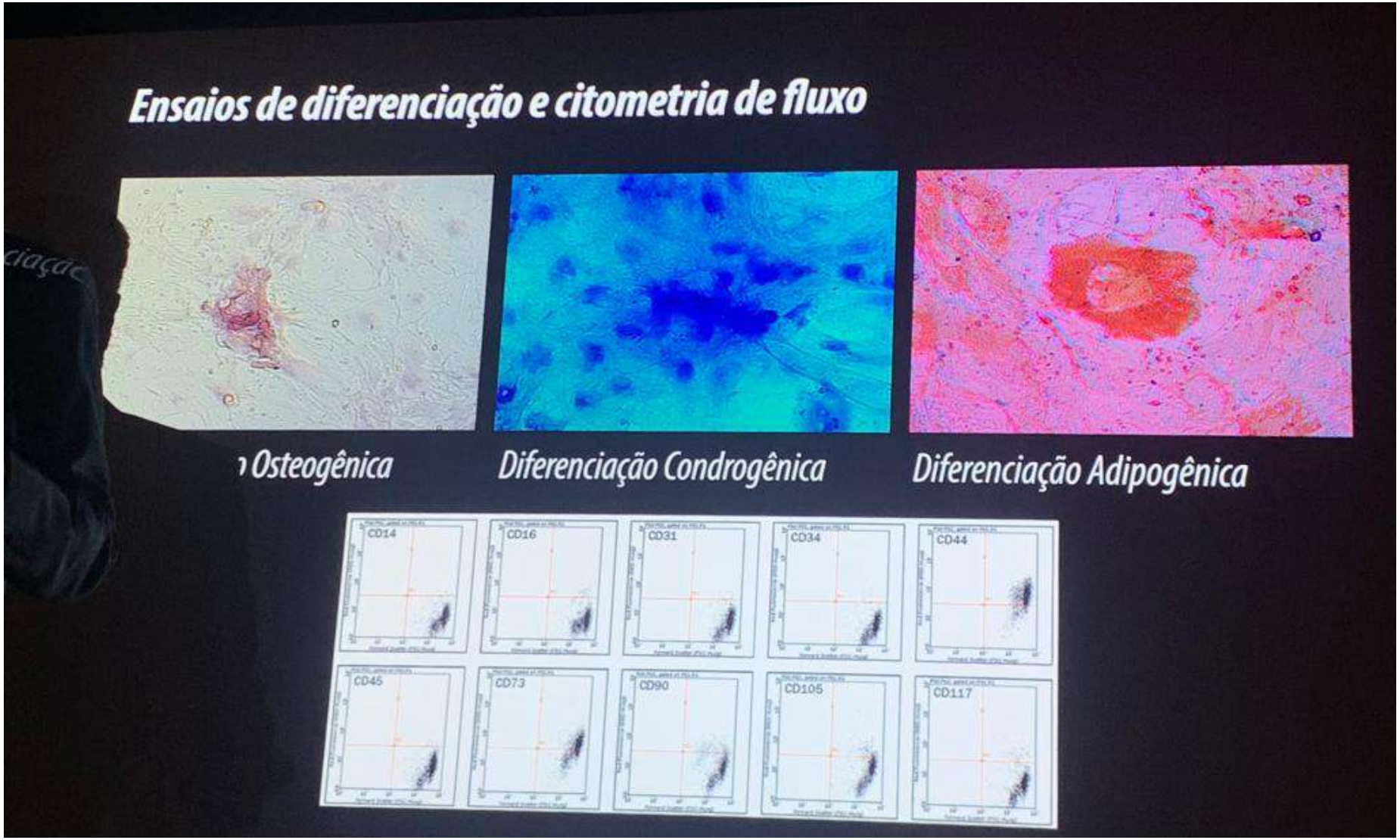
Partículas 80um



Células

Os estudos *in vitro* de micro enxertos obtidos pelo Rigenera demonstram presença de células-tronco?

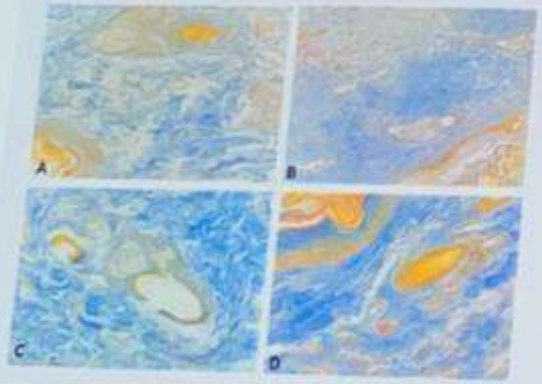

Metodologia 2
Mechanical isolation
Physiological solution
Tissue sample
Rigeneracons
Rigeneraspin machine
Biomaterials
Laboratory technician
Cells extraction
Progenitor cells in physiological solution


Ensaios de diferenciação e citometria de fluxo
Osteogênica
Diferenciação Condrogênica
Diferenciação Adipogênica
CD14
CD16
CD31
CD34
CD44
CD45
CD73
CD90
CD105
CD117

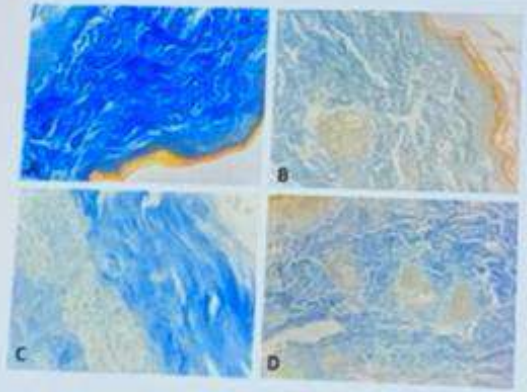
Uso da suspensão de micro enxertos no tratamento de feridas de extremidades em diabéticos

Mariza B. Palma - Anísio F. Soares (UFRPE)

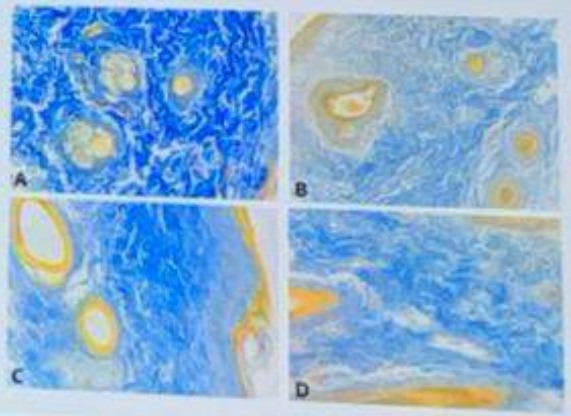
Aumento na produção de colágeno, na angiogênese e na epitelização



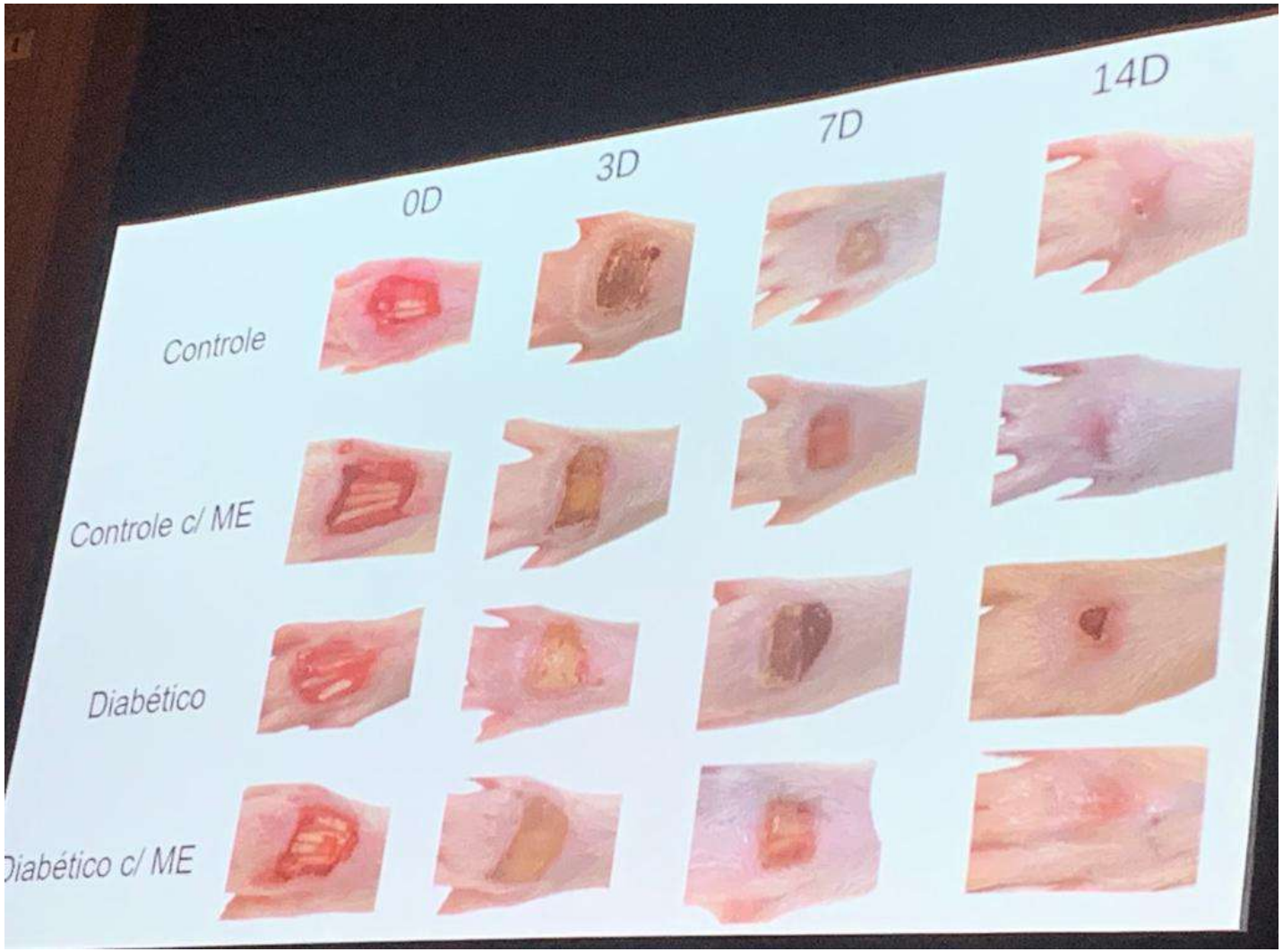
3 D

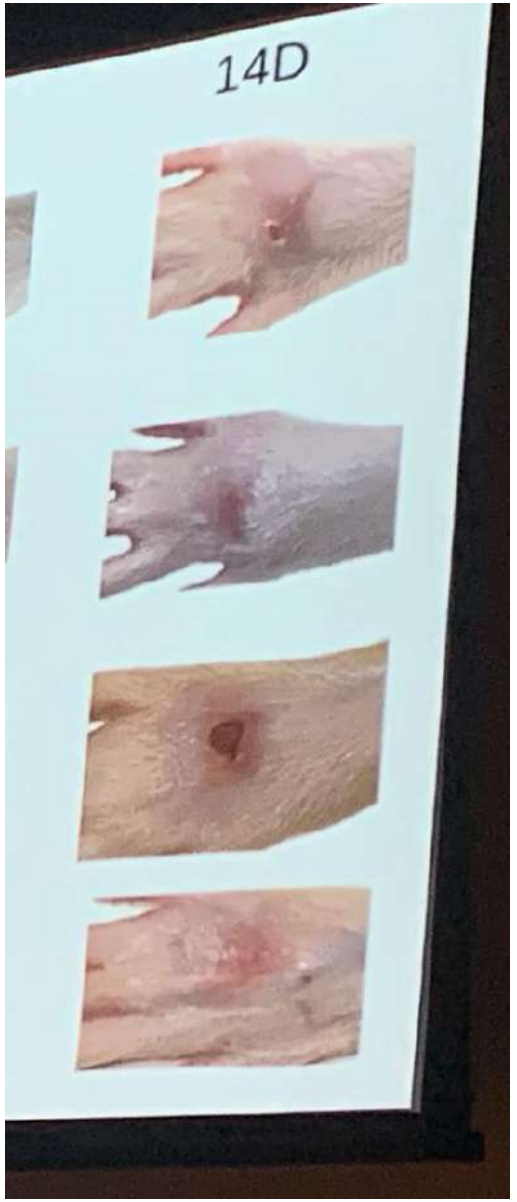


7 D



14 D

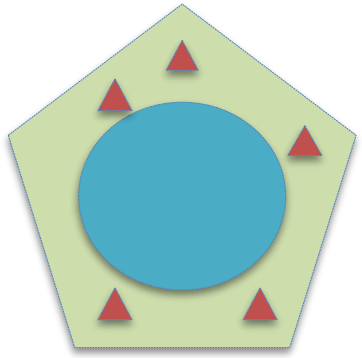

0D
3D
7D
14D
Controle
Controle c/ ME
Diabético
Diabético c/ ME

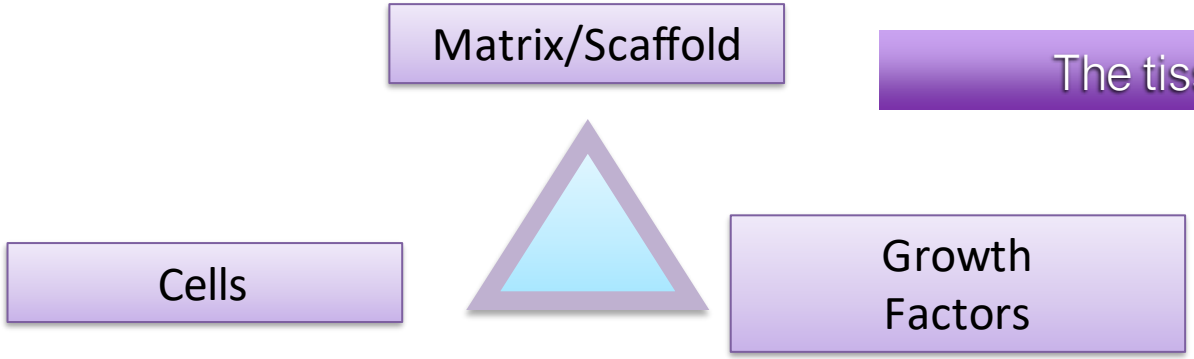

14D

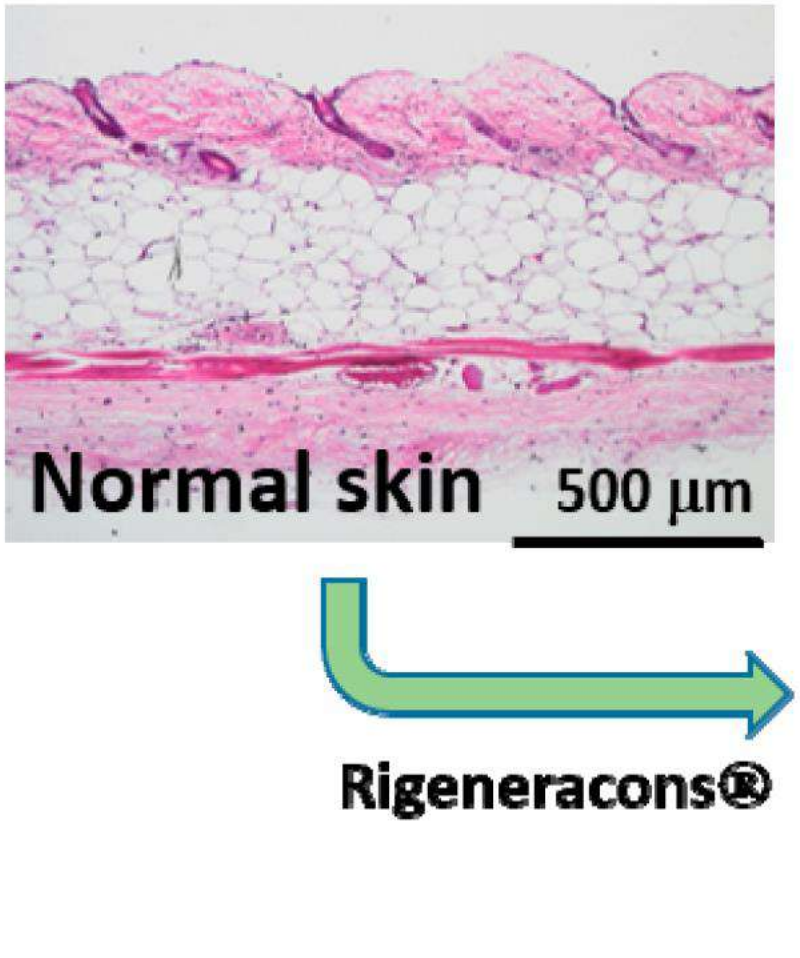
What are made of the Rigenera Micrografts?

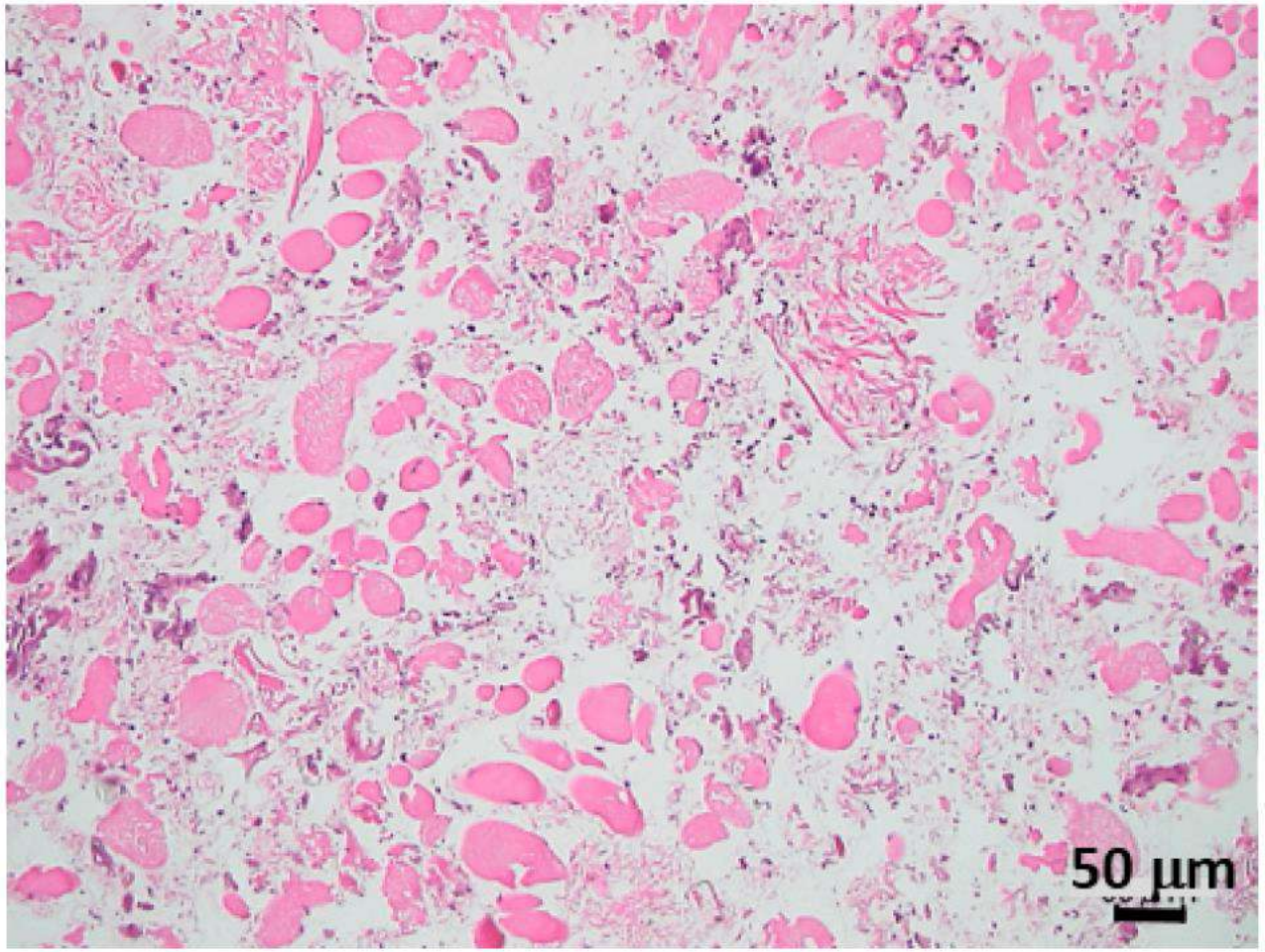
Rigenera Micro-grafts are 80/90 microns dimensions and they are made of

- **High Viable cells**
- **Extra cellular matrix**
- **Growth Factors**



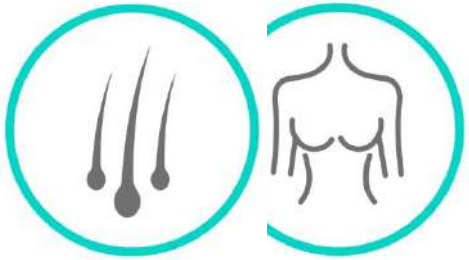






Acceleration Mechanisms of Skin Wound Healing by Autologous Micrograft in Mice
Shiro Jimi 1, *, Masahiko Kimura 2 , Francesco De Francesco 3 , Michele Riccio 3 , Shuuji Hara 2 and Hiroyuki Ohjimi 4

Micrografts clinical application



AESTHETIC MEDICINE

- Androgenetic Alopecia
- Skin Rejuvenation
- Atrophic Scars
- Vitiligo
- Body and/or Face Remodeling with lipofilling

ODONTOLOGY

- Sinus Lift augmentation
- Socket Preservation
- Ulcers
- Maxillary bone necrosis

Cleft lip and palate

WOUND HEALING

- Plastic and reconstructive surgery
- Diabetic foot
- Leg ulcers
- Non healing wound
- Burn wound
- Surgical dehiscence

ORTHOPEDICS / REHABILITATION

- Cartilaginous defect
- Chondropathies
- Osteonecrosis
- Muscle Injury
- Tendon injury Ligament injury
- Meniscus
- Pseudarthrosis

Depending on the different application the tissue is collected from the patient by different anatomical region, in any cases the sample collection is an affordable and minimally invasive procedures

Scientific and Clinical Evidence Aesthetic Medicine DIVISION

HBW s.r.l. HUMAN BRAIN WAVE

An innovative regenerative treatment of scars with dermal micrografts

Fabiano Svolacchia, MD,[1,*] Francesco De Francesco, MD,[2,*] Letizia Trovato, Bsc, PhD,[3] Antonio Graziano, BDsc, PhD,[3,4,†] & Giuseppe A. Ferraro, MD, PhD[2,†]

[1] Centre of Nanoscience, Mavi Sud, Aprilia,
[2] Multidisciplinary Department of Medical-Surgical and Dental Specialties, Second University of Naples, Naples,
[3] Human Brain Wave srl, Turin, Italy
[4] SHRO – Temple University of Philadelphia, Philadelphia, PA, USA

biomedicines

MDPI

Article

Platelet-Rich Plasma and Micrografts Enriched with Autologous Human Follicle Mesenchymal Stem Cells Improve Hair Re-Growth in Androgenetic Alopecia. Biomolecular Pathway Analysis and Clinical Evaluation

Pietro Gentile [1,*], Maria G. Scioli [2], Alessandra Bielli [2], Barbara De Angelis [1], Ciro De Sio [3], Domenico De Fazio [3], Gabriele Ceccarelli [4,5], Angelo Trivisonno [3], Augusto Orlandi [2], Valerio Cervelli [1] and Simone Garcovich [6]

Adipose Derived Stem Cells and Growth Factors Applied on Hair Transplantation. Follow-Up of Clinical Outcome

Federica Zanzottera[1*], Emilio Lavezzari[1], Letizia Trovato[2], Alessandro Icardi[2], Antonio Graziano[2]

Original Research Paper | Medical Science | Volume : 3 | Issue : 1 | Jan 2018 | e-ISSN : 2456-5040

CLINICAL AND HISTOLOGICAL EVALUATION OF THE REGENERA® METHOD FOR THE TREATMENT OF ANDROGENETIC ALOPECIA

Xavier Álvarez, MD[1], Miguel Valenzuela, MD[1], Jaume Tuffet, MD[1]

[1] Clínica Tuffet. Passeig de Gràcia, 86, 08008 Barcelona.

ABSTRACT

Androgenetic alopecia has become a more common condition in society, affecting both genders. It is a disorder of multifactorial origin, with therapeutic options both in the rise and under development. Known options include the procedures of regenerative medicine with promising results. This paper assesses clinical and histological changes in patients with AGA after applying an autologous cellular suspension obtained using the Rigenera® system. After applying treatment, an increase in the mean of hair thickness, together with reduction of its loss, have been objectified; the level of satisfaction described by patients is worth noting. Based on the results, the improvement of AGA obtained with the Rigenera system is objective; these results need to be completed with data from future studies after using this promising technique.

Scientific and Clinical Evidence Dental DIVISION

HBW s.r.l. HUMAN BRAIN WAVE

Original Article

Sinus lift tissue engineering using autologous pulp micro-grafts: A case report of bone density evaluation

Giorgio Brunelli, Alessandro Motroni,[1] Antonio Graziano,[1] Riccardo D'Aquino,[1] Ilaria Zollino,[1] Francesco Carinci[1]

Dental Clinic, Don Orione Hospital, Bergamo, [1]Department of Morphology, Surgery and Experimental Medicine, University of Ferrara, Ferrara, Italy

Testo

Abstract:

Background: Although autografts are the standard procedure for bone grafting, the use of bone regeneration by means of dental pulp stem cell is an alternative that opens a new era in this field. Rigenera Protocol is a new technique able to provide the surgeon autologous pulp micro-grafts. **Materials and Methods:** At the Department of Oral Surgery, Don Orione Hospital, Bergamo, Italy, one patient underwent to sinus lift elevation with pulp stem micro-grafts gentle poured onto collagen sponge. A CT scan control was performed after 4 month and DICOM data were processed with medical imaging software which gives the possibility to use a virtual probe to extract the bone density. Pearson's Chi-square test was used to investigate difference in bone density (BD) between native and newly formed bone. **Results:** BD in newly formed bone is about the double of native bone. **Conclusion:** This report demonstrated that micro-grafts derived from dental pulp poured onto collagen sponge are a useful method for bone regeneration in atrophic maxilla.

Key words:

Bone, homograft, jaw, reconstruction, resorption, stem cell

Journal of Translational Science

Research Article ISSN: 2059-268X

Periosteum-derived micro-grafts for tissue regeneration of human maxillary bone

Riccardo d'Aquino[1,2], Letizia Trovato[2*], Antonio Graziano[2], Gabriele Ceccarelli[3], Gabriella Cusella de Angelis[3], Angelo Marangini[4], Alessandro Nisio[5], Massimo Galli[6], Massimo Pasi[7], Marco Finotti[8], Saturnino M Lupi[9], Silvana Rizzo[9] and Ruggero Rodriguez Y Baena[9]

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[3]Department of Public Health, Experimental Medicine and Forensics, University of Pavia, Pavia, Italy

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Abstract

The bone regeneration is one of the most important challenges for regenerative medicine. In maxillo-facial area, bone resorption of the alveolar crest occurs after tooth extraction and leads to several risks for rehabilitation treatments, including dental implants procedures. Goal of our study was to demonstrate the efficacy of an innovative clinical protocol of bone tissue engineering called Rigenera protocol, aimed to create and optimize bio-complexes constituted by collagen biomaterial and human autologous periosteum-derived micro-grafts. We assessed the capacity of these bio-complexes to prevent the bone resorption in the alveolar crest with respect to simple collagen performing histological evaluations of neo-formed osseous tissue. We demonstrated that autologous bio-complexes significantly reduced the bone resorption of both horizontal and vertical dimension of alveolar crest when compared to collagen alone. We also showed that these bio-complexes accelerate the ossification process triggering the formation of new osseous tissue after 45 days from treatment and increasing the calcified matrix after 60 days and until to 120 days with respect to collagen alone. Taken together, these data showed the efficacy of bio-complexes composed by periosteum-derived micro-grafts and collagen in the alveolar ridge preservation through a reduction of bone resorption and an enhancement of new osseous tissue formation.

Scientific and Clinical Evidence Wound Healing DIVISION

HBW s.r.l. HUMAN BRAIN WAVE

Journal of Stem Cells Research, Reviews & Reports

Open Access

Austin Publishing Group

Case Report

A New Medical Device, Based on Rigenera Protocol, in the Management of Complex Wounds

Giaccone M[1,2], Brunetti M[1,2], Camandona M[1,2], Trovato L[3]* and Graziano A[3]

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[2]Department of Surgical Sciences, University of Turin, Italy

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Received: September 22, 2014; **Accepted:** October 22, 2014; **Published:** October 24, 2014

Abstract

Injury to the skin provides a unique challenge, as wound healing is a complex and intricate process. Acute wounds have the potential to move from into to chronic wounds, requiring the physician to have a thorough understanding of outside interventions to bring these wounds back into the healing cascade. The development of new and effective interventions in wound care remains an area of intense research. For this purpose, we aimed to report the use of a new medical device, called Rigeneracons® (Human Brain Wave srl, Turin), in the management of complex wounds of different etiology in two subjects where the wound healing process was very difficult. Rigeneracons® devices are based on Rigenera protocol that consists in the use of a cell population enriched of progenitor cells able to improve a tissue repair. By these case reports, we demonstrated the efficacy of Rigenera protocol in improving wound healing process through application of a cell suspension rich of progenitors cells in two different subjects that are donor and acceptor of these micro-grafts.

Keywords: Wound healing; Rigenera protocol; Rigeneracons®

jove Journal of Visualized Experiments www.jove.com

Video Article

Tissue Characterization after a New Disaggregation Method for Skin Micro-Grafts Generation

Valeria Purpura[1], Elena Bondioli[1], Antonio Graziano[2], Letizia Trovato[2], Davide Melandri[1], Martina Ghetti[1], Andrea Marchesini[3], Maria Gabriella Cusella De Angelis[4,5], Laura Benedetti[4,5], Gabriele Ceccarelli[4,5], Michele Riccio[3]

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[4]Department of Public Health, Experimental Medicine, Anatomy and Forensic, University of Pavia

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Correspondence to: Antonio Graziano at lab@hbwsrl.com

URL: http://www.jove.com/video/53579
DOI: doi:10.3791/53579

ANTICANCER RESEARCH *36*: 975-980 (2016)

Treatment of Oncological Post-surgical Wound Dehiscence with Autologous Skin Micrografts

ELISABETTA BAGLIONI[1], LETIZIA TROVATO[2], MARCO MARCARELLI[3], AMBRA FRENELLO[1] and MARIA ALESSANDRA BOCCHIOTTI[1]

[1]Department of Plastic and Reconstructive Surgery, University of Turin, San Giovanni Battista Hospital, Turin, Italy;
[2]Department of Medical Sciences, University of Turin, Turin, Italy;
[3]Unit of Orthopedics and Traumatoly, Santa Croce Hospital, Moncalieri, Italy

Scientific and Clinical Evidence

Orthopedic and Rehabilitation DIVISION

HBW s.r.l. HUMAN BRAIN WAVE

RESEARCH ARTICLE Open Access

Rationale and pre-clinical evidences for the use of autologous cartilage micrografts in cartilage repair

Marco Viganò[1†], Irene Tessaro[1†], Letizia Trovato[2*], Alessandra Colombini[1], Marco Scala[3], Alberto Magi[4], Andrea Toto[4], Giuseppe Peretti[1,5] and Laura de Girolamo[1]

OPEN

PRS GLOBAL OPEN ORIGINAL ARTICLE

Reconstructive

Reconstruction of Alar Nasal Cartilage Defects Using a Tissue Engineering Technique Based on a Combined Use of Autologous Chondrocyte Micrografts and Platelet-rich Plasma: Preliminary Clinical and Instrumental Evaluation

pharmaceuticals MDPI

Article

In Vitro and In Vivo Studies of Alar-Nasal Cartilage Using Autologous Micro-Grafts: The Use of the Rigenera® Protocol in the Treatment of an Osteochondral Lesion of the Nose

Gabriele Ceccarelli [1,2,*], Pietro Gentile [3,4], Marco Marcarelli [5], Martina Balli [1,2], Flavio Lorenzo Ronzoni [1,2], Laura Benedetti [1,2] and Maria Gabriella Cusella De Angelis [1,2,*]

Gentile et al., J Regen Med 2016, 5:2
DOI: 10.4172/2325-9620.1000129

Journal of Regenerative Medicine

Research A SCITECHNOL JOURNAL

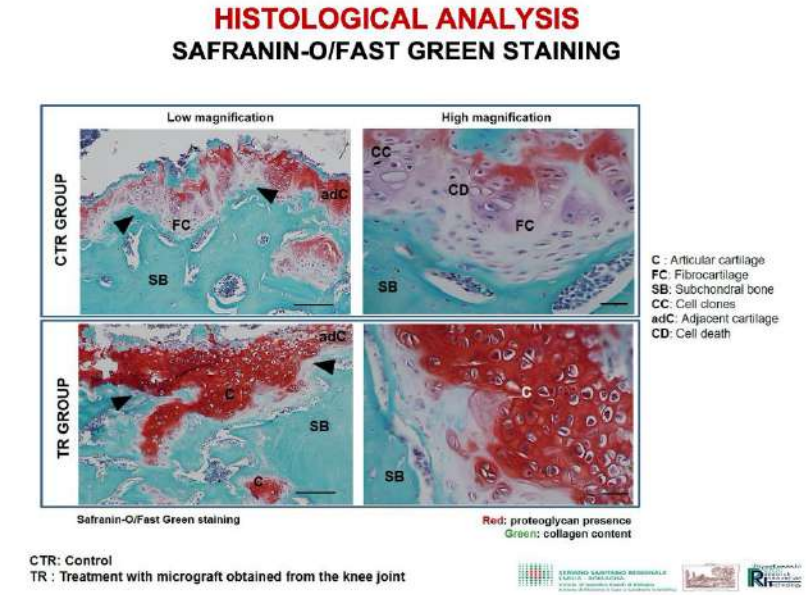
A combined use of Chondrocytes Micro Grafts (CMG) Mixed with Platelet Rich Plasma (PRP) in Patients Affected by Pinch Nose Deformity

Gentile P[1*], Scioli MG[2], Bielli A[2], Orlandi A[2] and Cervelli V[1]

medium induced proliferation and a robust chondrogenesis of adult stem cells *in vitro* [5,6]. Direct mixing of chondrocytes with PRP leads to shrinking and deformed cartilage formation in vivo [7] owing to poor mechanical stability and rapid degradability. In particular the use of chondrocytes micrografts represents a micro-invasive procedure and grafts are more flexible to fill the lesions with various shapes. Today the main problem in transferring the experimental protocols of tissue engineering in the routine clinical practice is the identification of accessible sites where an adequate amount of stem cells are collected [8,9]. In addition, the need to specifically define technical procedure and its safety is an essential factor, as occurring for stem cell application in breast reconstruction and soft tissue defects [10-13].

Nova perspectiva para lesões degenerativas

- **Cartilage Micrografts as a novel non-invasive/non- arthroscopic autograft procedure: three years follow up study**
- **Marco Marcarelli[1], Marcello Zappia[2], Lorenzo Rissolio[1], Chiara Baroni[1], Carlo Astarita[3,4]*, Letizia Trovato[4], Antonio Graziano[3, 4]**



Advantages

1. Quick and easy application method that lasts 15 min
2. No hospitalization or operating room needed
3. Can be done in a single session
4. Only local anesthesia is necessary for punch extraction
5. Closed handling system
6. No extra equipment needed
7. No nursing or specialized assistant needed
8. Rapid recovery of the injury
9. Without side effects (Autologous Tissue)
10. Affordable price for the results obtained
11. No direct competitors

Scientific and Clinical Project

HBW s.r.l. HUMAN BRAIN WAVE

- Rigenera Micrografts for the management Androgenetic alopecia: Clinical - Italy. ON GOING
- Rigenera Micrografts for VITILIGO Repigmentation: Clinical Study - Italy. PUBLISHED
- Rigenera Micrografts for Chronic Ulcer : Double blind Case-Control Clinical Trial - Israel. ON GOING – DATA ANALYSIS
- Rigenera Micrografts for VITILIGO Repigmentation : Double blind Case-Control Clinical Trial - Israel. ON GOING
- Rigenera Micrografts for Surgical Dehiscence Prevention : Clinical Study - Italy. ON GOING
- Rigenera Adipose Micrografts for Enhancing the Lipofilling implantation - Italy . COMPLETE – DATA ANALISYS
- Rigenera Cartilage Micrografts the Management of Knee Chondropathy - Italy. COMPLETE – DATA ANALISYS
- Rigenera Cartilage Micrografts the Management of Knee Chondropathy - Japan. ON GOING
- Rigenera Cartilage Micrografts the Management of Knee Chondropathy - Italy. COMPLETE – DATA ANALISYS
- Rigenera Atrial micrograft transplantation for ischemic heart failure: Clinical Trial - Finland. PARTIALLY PUBLISHED
- Rigenera Micrografts enhance the healing in patient suffering of wide burns: Clinical Study – South Africa. COMPLETE – PAPER SUBMITTED
- Rigenera periosteum micrograft support bone regeneration in Socket preservation and Sinus lifts procedure: Clinical Trial - Brazil. ON GOING

HBW is partner of national and international research's projects

And the technology has been used for more than 60 Scientific publications

Autologous atrial micrograft (AAM) transplantation for ischemic heart failure coordinated by Dr. Esko Kankuri, University of Helsinki.

European Space Agency: **Tissue Healing in Space**: *Techniques for promoting and monitoring tissue repair and regeneration*

Piemonte Region- Bando: PIATTAFORMA TECNOLOGICA "SALUTE E BENESSERE" Progetto ***Digital technology For Lung Cancer Treatment***

Rigenera Emergency Kit for military and civilian emergencies. The HBW is part of RAWINTS Project for Rapid Wound Healing, financed by NATO Science for Peace and Security Project.

EUROSTARS PROJECT : Redefine Regenerative medicine with a point of care Tissue Technology ***- GRANTED***

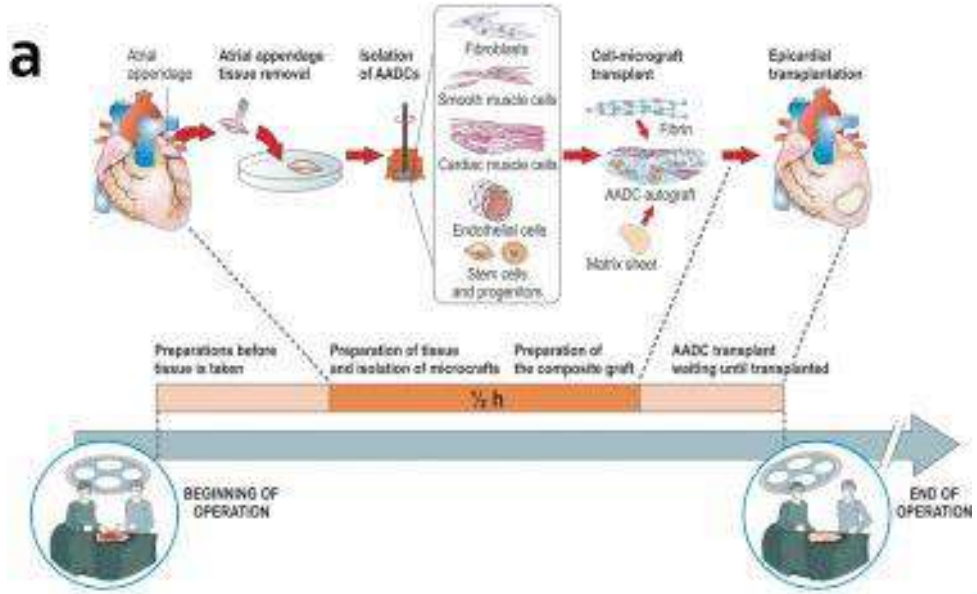
Future opportunities : heart regeneration

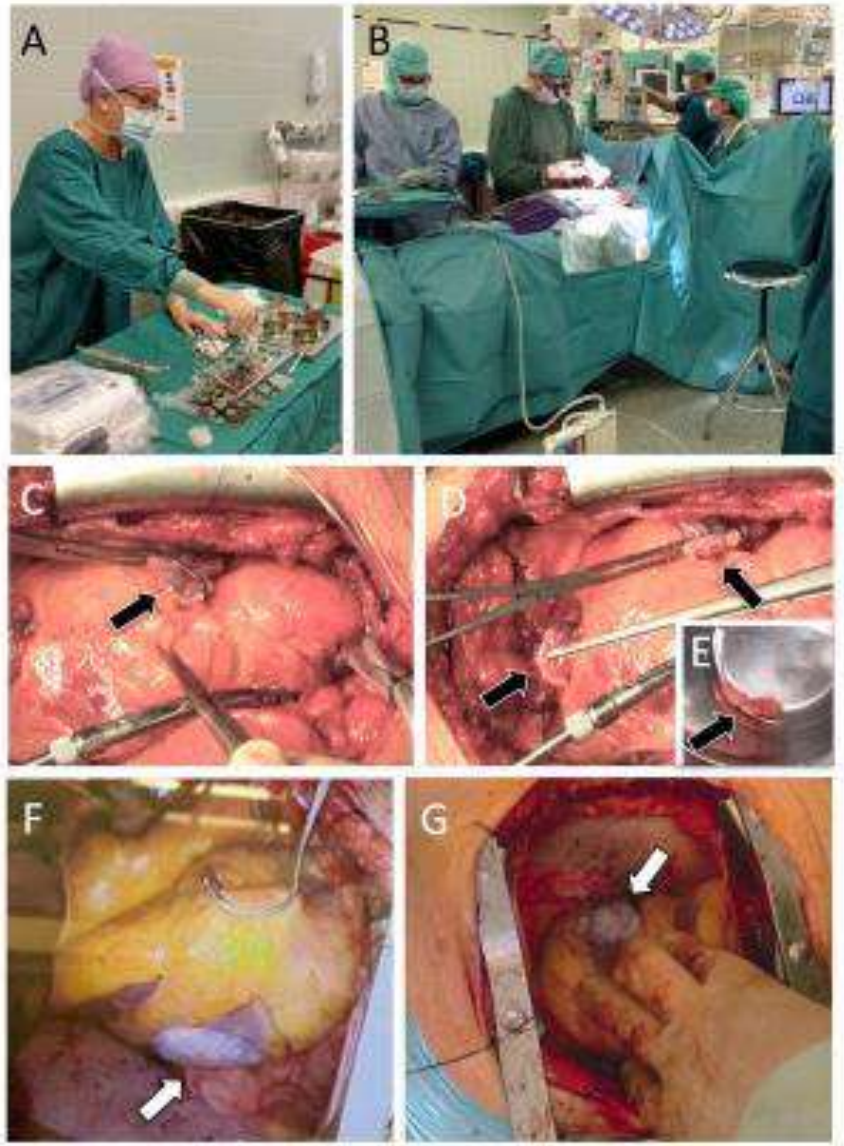
http://www.jhltonline.org

b

Intraoperative processing and epicardial transplantation of autologous atrial tissue for cardiac repairTransplantation of autologous atrial micrografts

Milla Lampinen, Annu Nummi, Tuomo Nieminen, Ari Harjula, Esko Kankuri





Future opportunities : heart regeneration

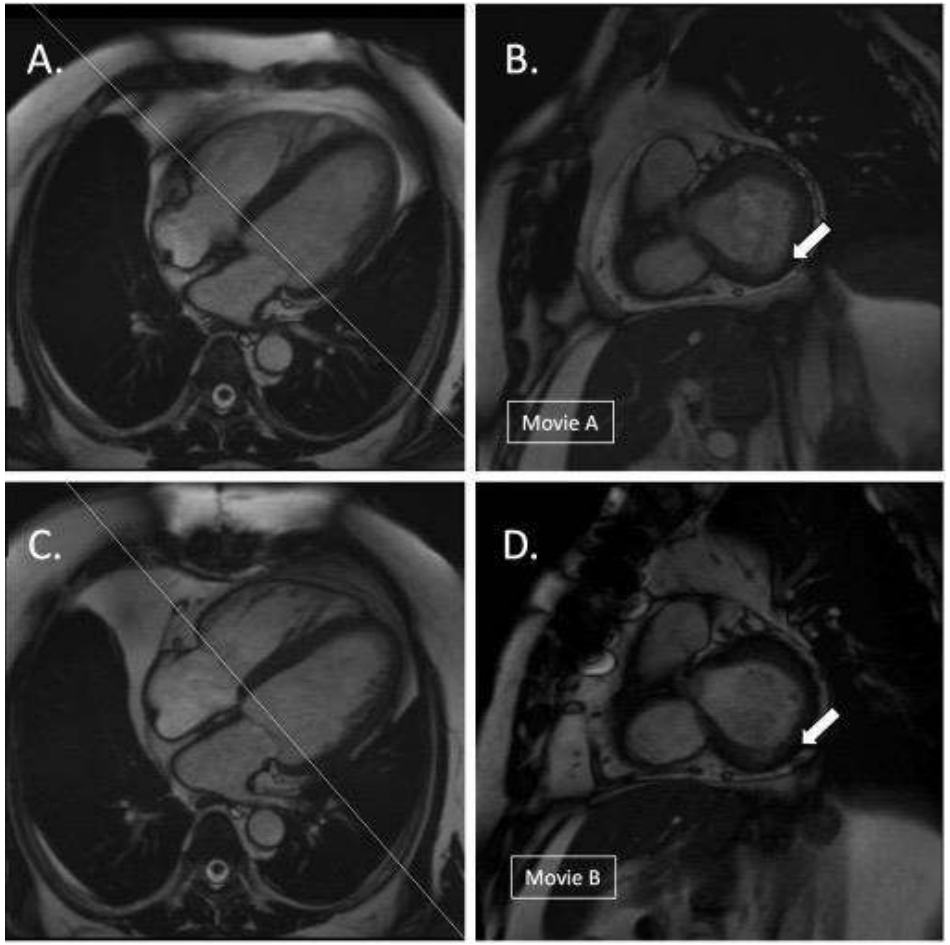
Intraoperative processing and epicardial transplantation of autologous atrial tissue for cardiac repairTransplantation of autologous atrial micrografts

Milla Lampinen, Annu Nummi, Tuomo Nieminen, Ari Harjula, Esko Kankuri

- Autologous atrial micrografts during coronary artery bypass grafting (CABG). Micrografts are isolated from the atrial appendage(AA) tissue and are combined with fibrin gel and a-decellularized small intestinal submucosa (SIS)Matrix sheet.

- The micrograft transplant was placed on the anterior wall of the left ventricle, on the scar area identified in the preoperative magnetic resonance imaging. The sheet was sutured to the myocardial surface with minimal disturbance .

- Magnetic resonance imaging at 6 months showed markedly improved movement and ventricular wall thickening in the treated infarcted scar area.



Rigenera micro grafts are effective in reducing the myocardial scar after infarction

Nummi et al. Pilot and Feasibility Studies (2017) 3:74
DOI 10.1186/s40814-017-0217-9

Pilot and Feasibility Studies

STUDY PROTOCOL Open Access

Epicardial delivery of autologous atrial appendage micrografts during coronary artery bypass surgery—safety and feasibility study

Annu Nummi[1*], Tuomo Nieminen[1,2], Tommi Pätilä[3], Milla Lampinen[4], Mia L. Lehtinen[1], Sari Kivistö[5], Mila Holmström[5], Erika Willman[6], Kari Teittinen[1], Mika Laine[1], Juha Sinisalo[1], Markku Kupari[1], Esko Kankuri[4], Tatu Juvonen[1], Antti Vento[1], Raili Suojaranta[6], Ari Hatjula[1] and The AADC consortium

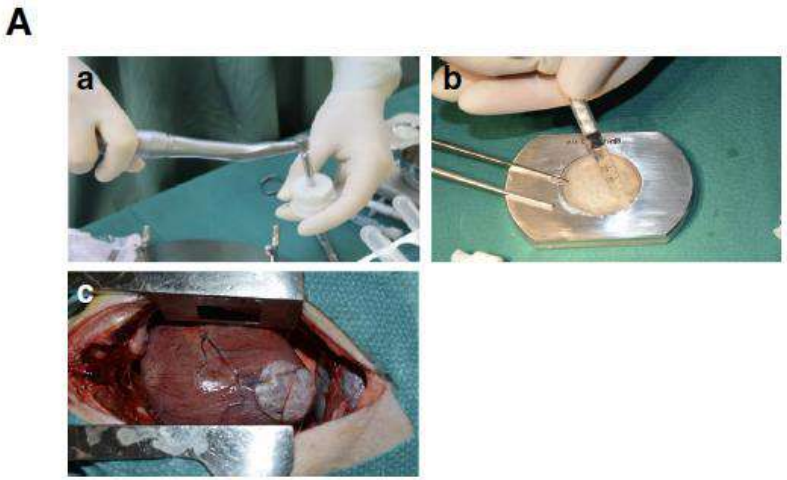


Fig. 1 a Preparing the AADC-sheet. (A) The atrial appendage tissue is processed with cell therapy tissue homogenizer (Rigenera-system). (B) The micrografts are secured to extracellular matrix sheet (Cormatrix®) by using a fibrin sealant (Tisseel™). (C) The AADC sheet is placed to the myocardium in the location of infarction scar (animal model). **b** Administration of therapy during CABG surgery. Figure reproduced from our article by Lampinen et al. (Current Gene Therapy, 2015)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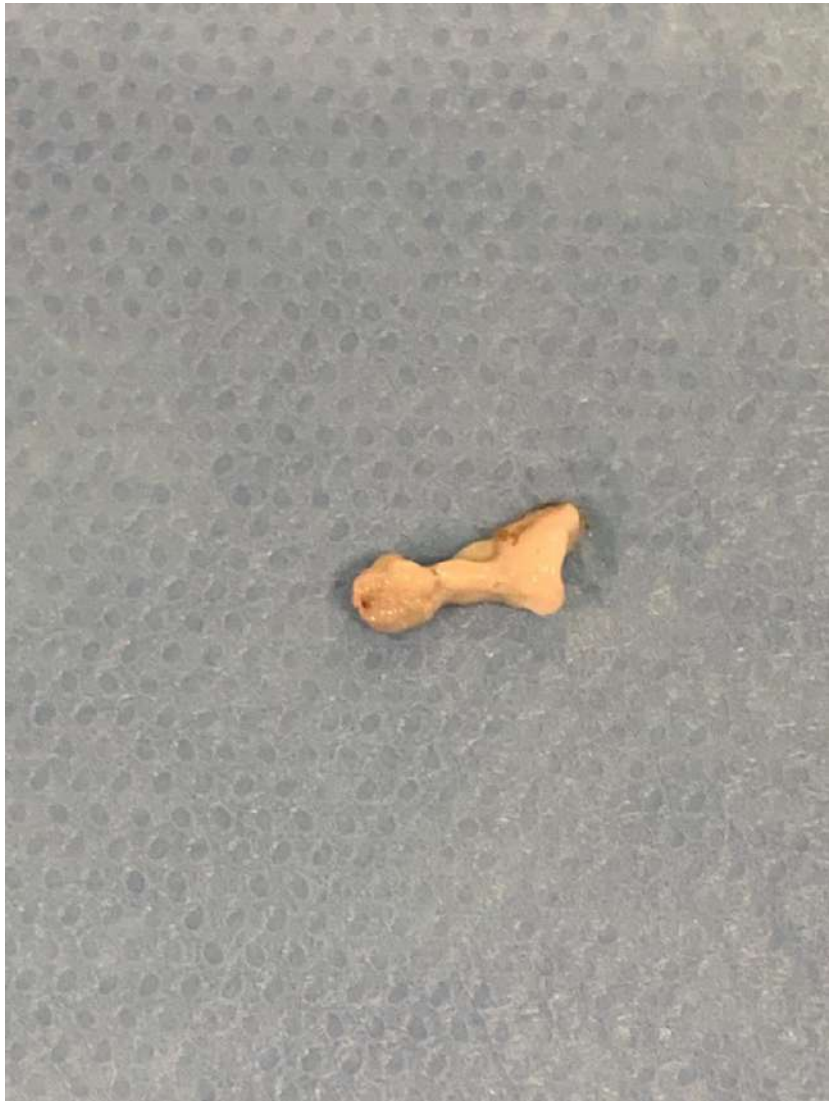

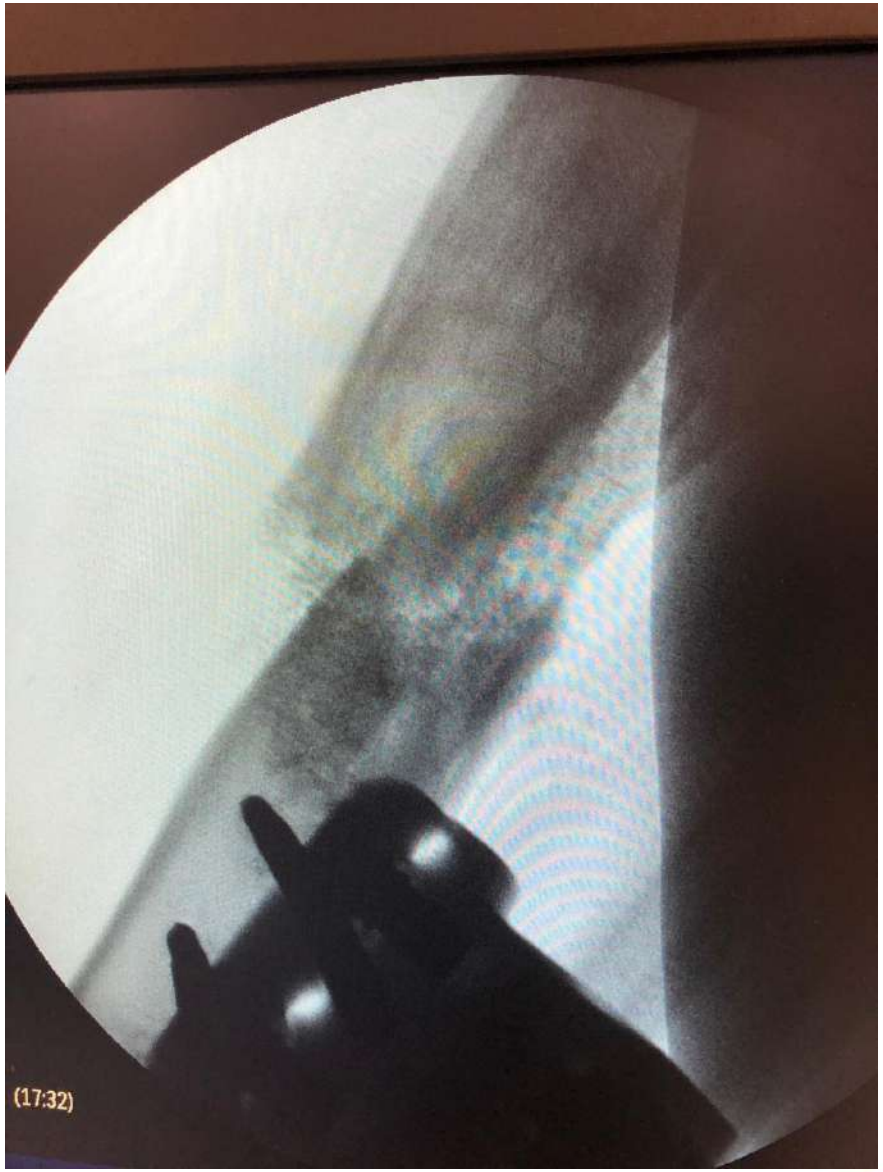
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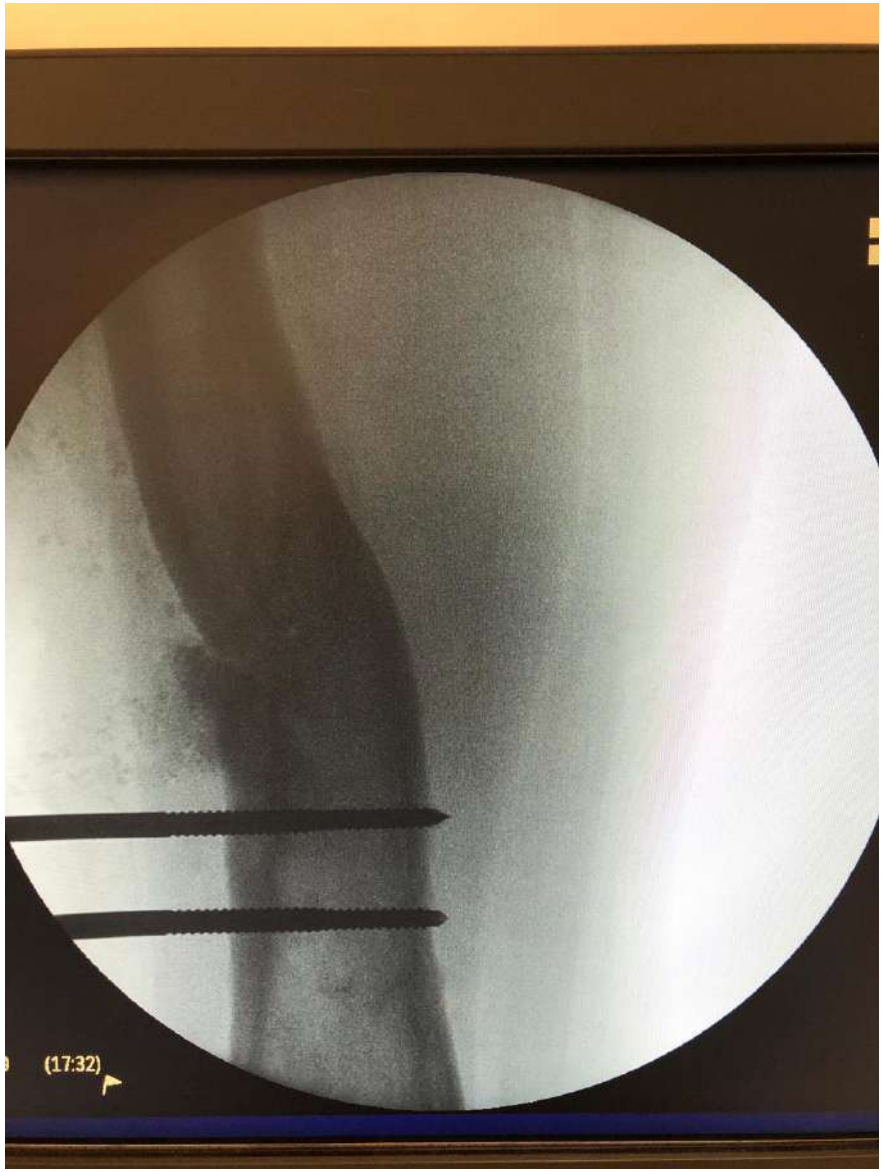
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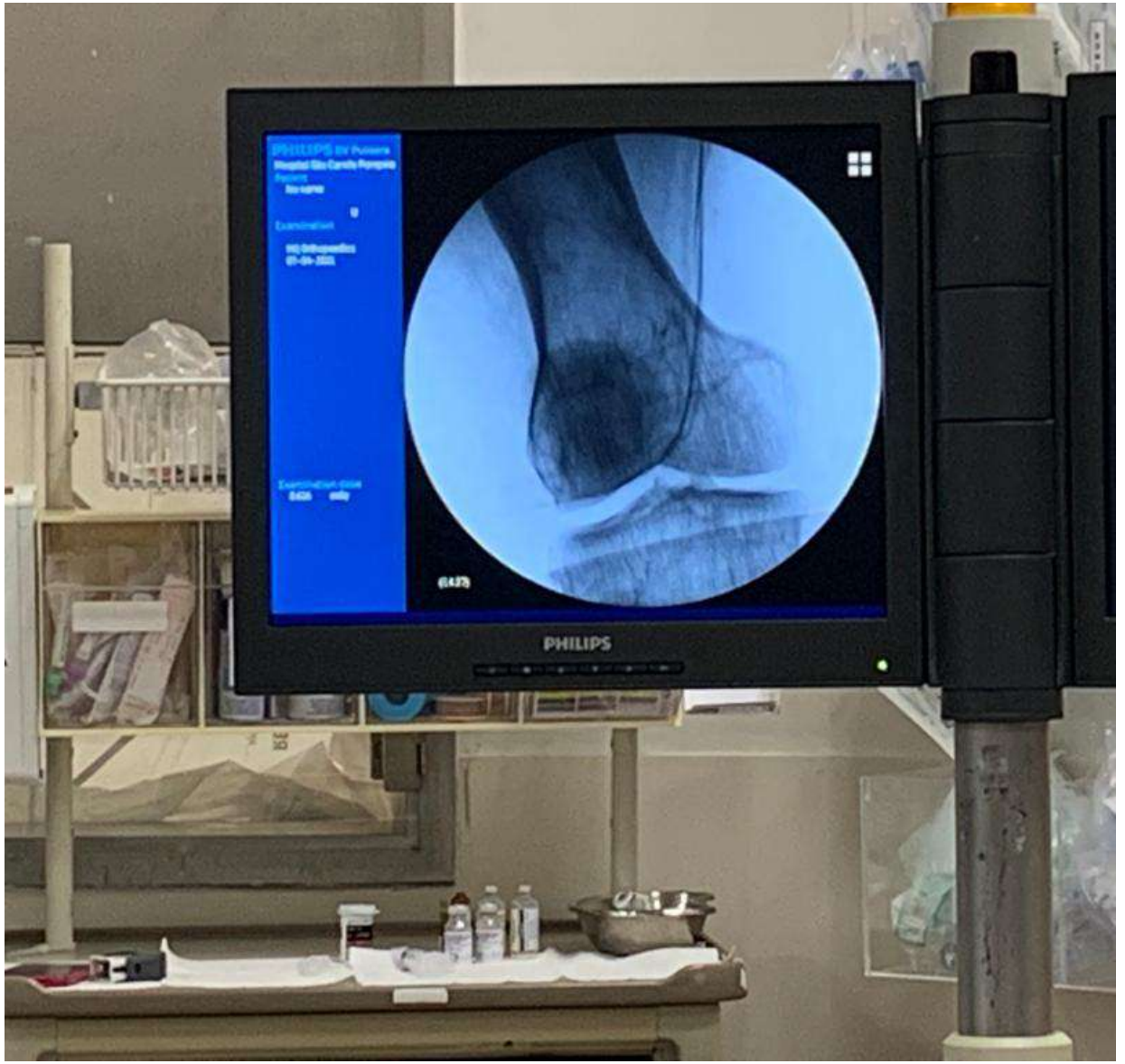
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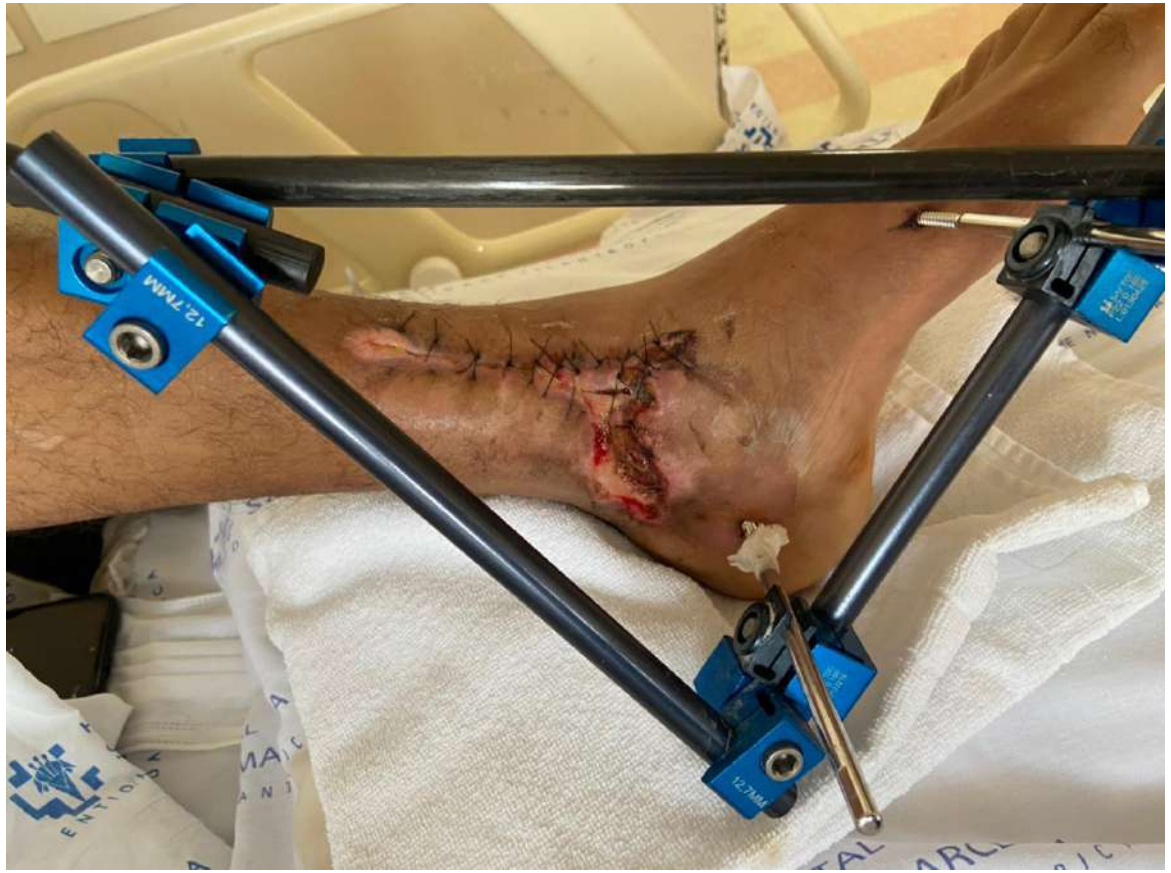
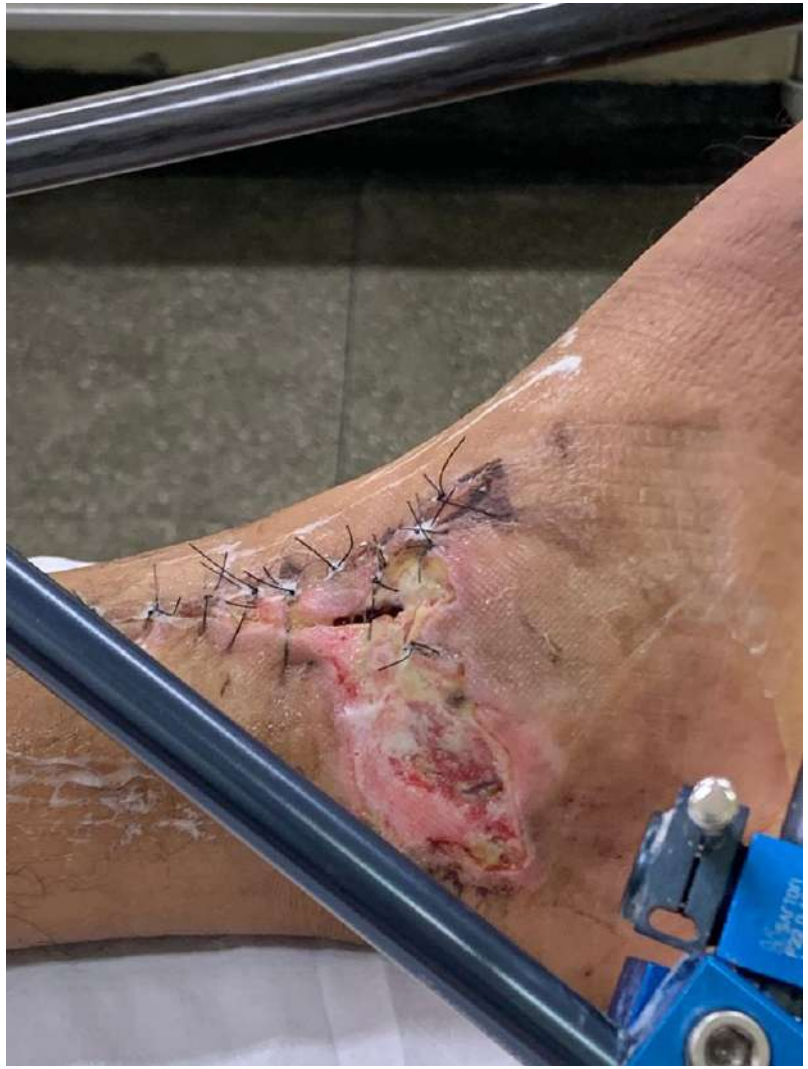
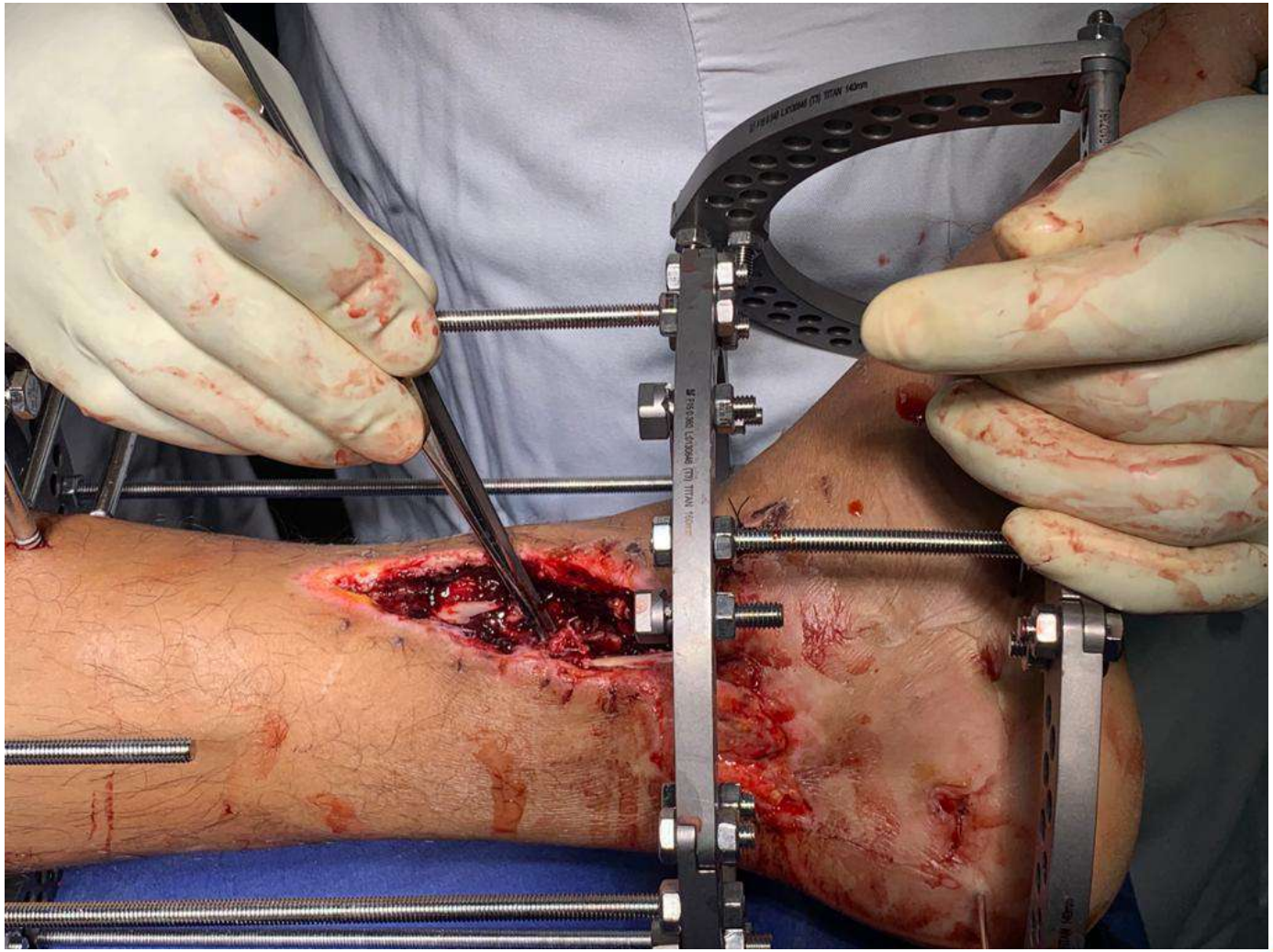
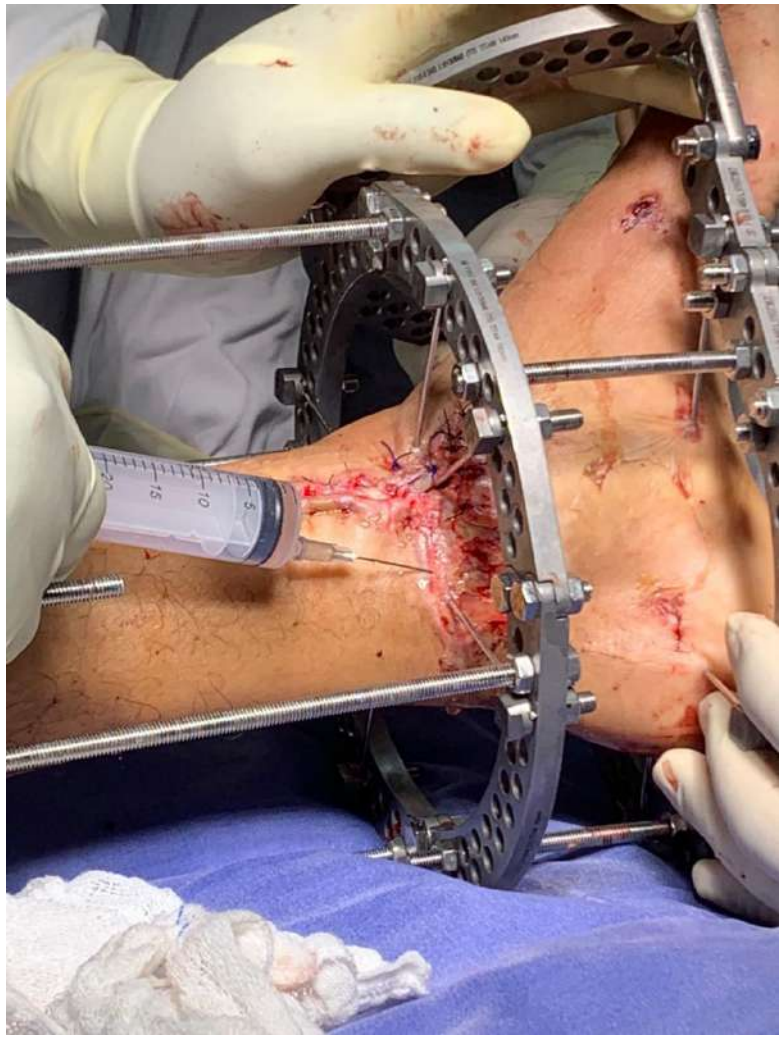
Pré operatório

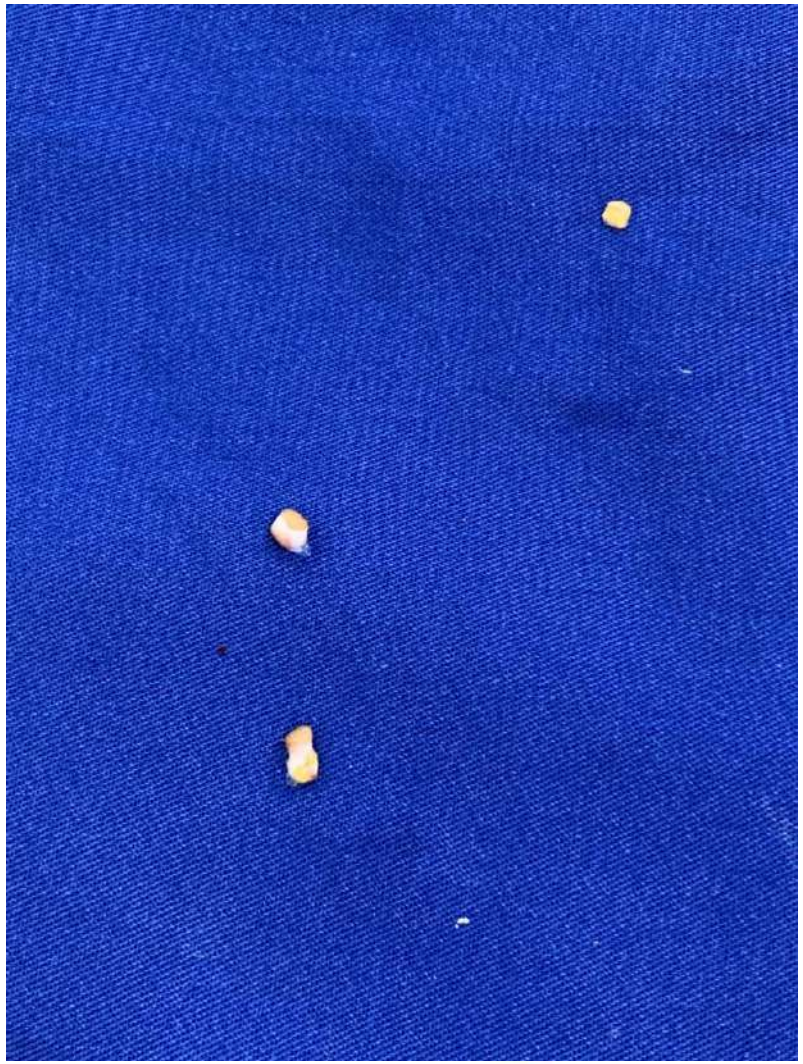




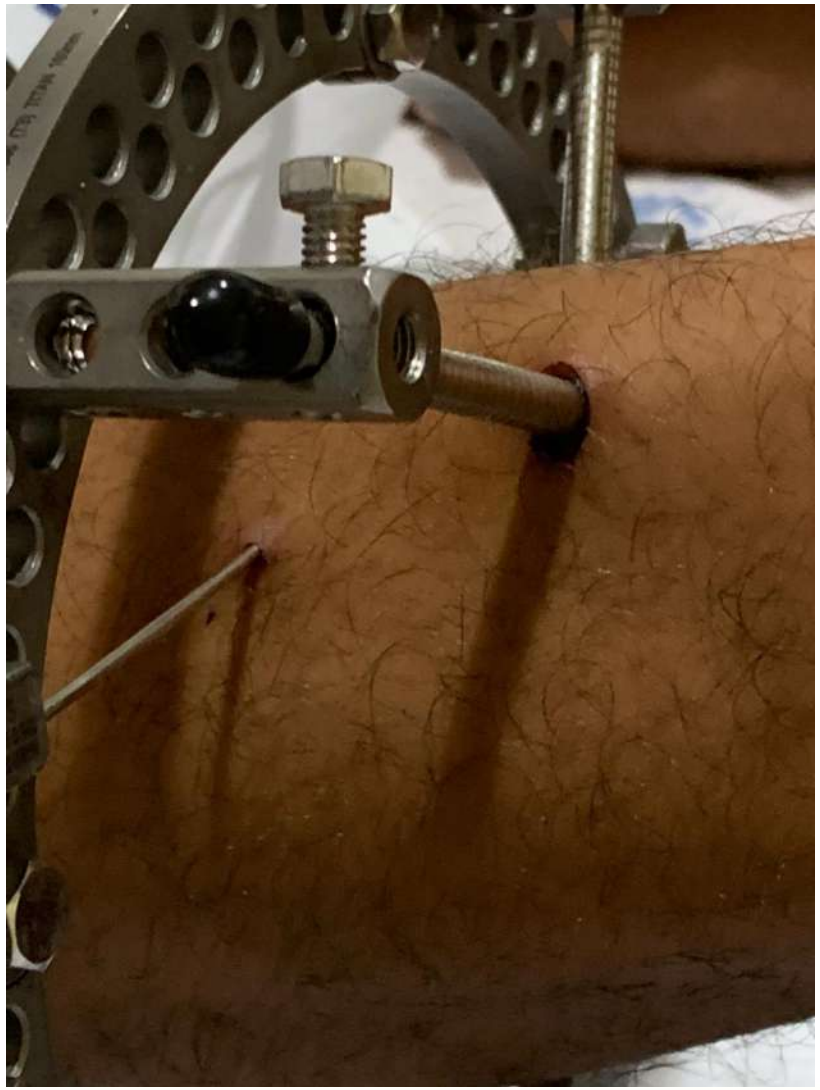
Transoperatório

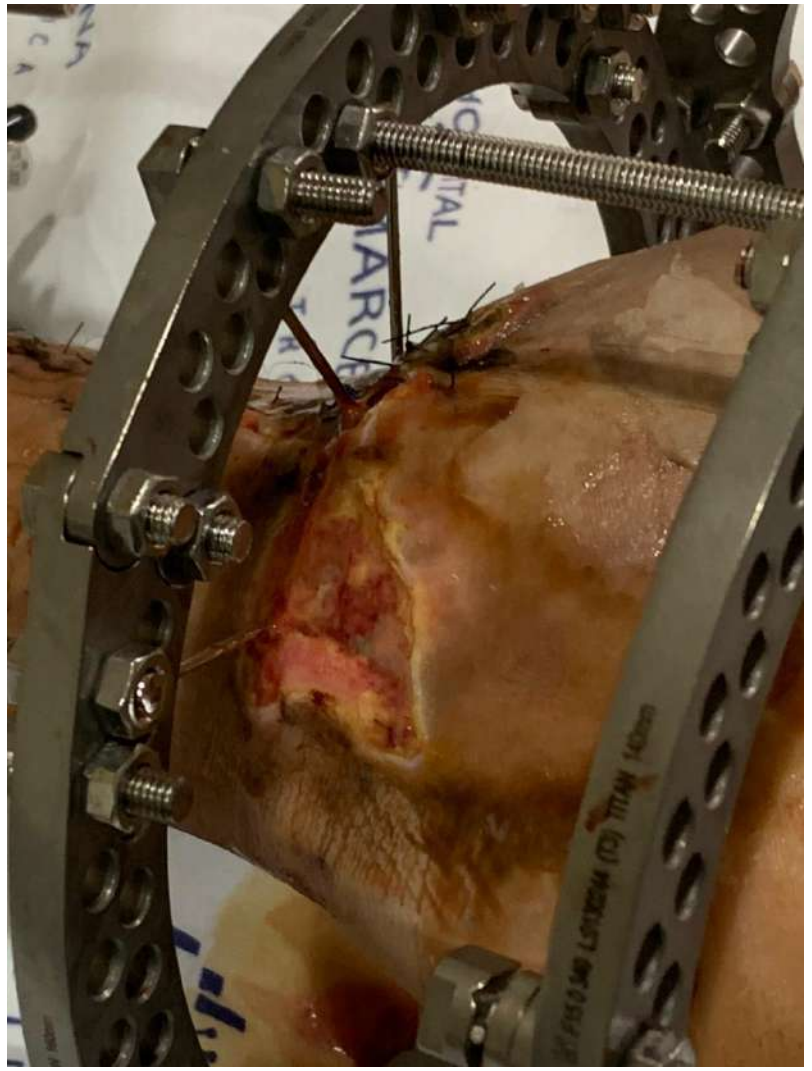




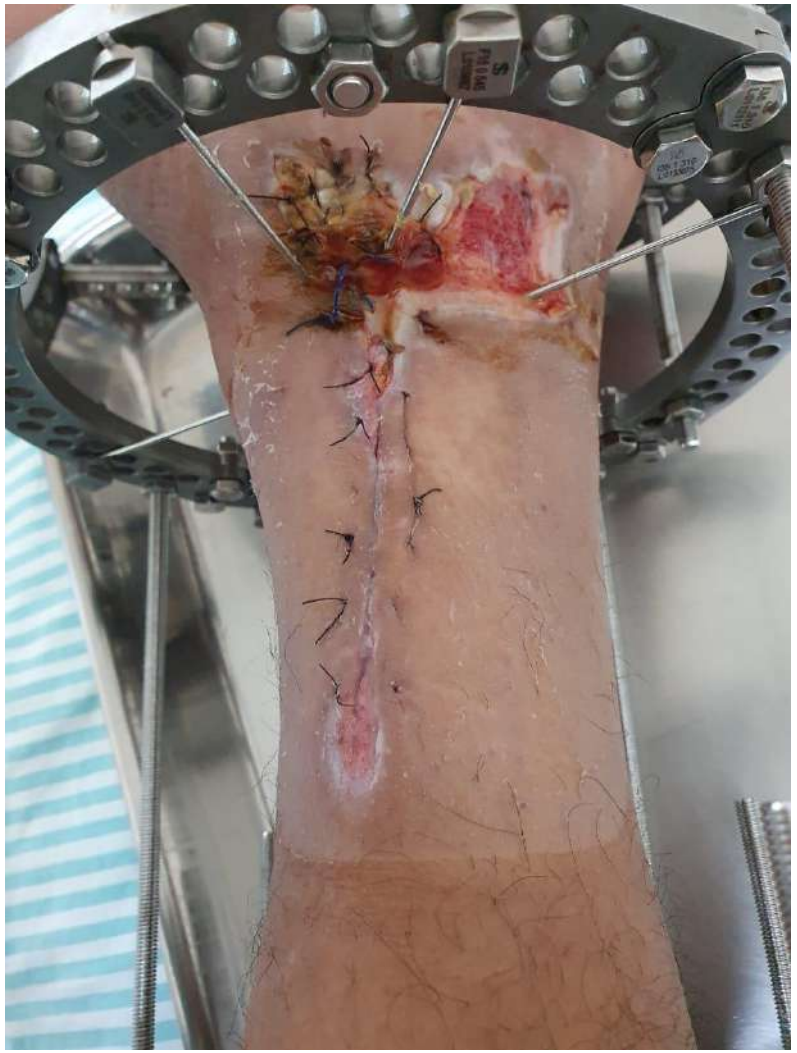


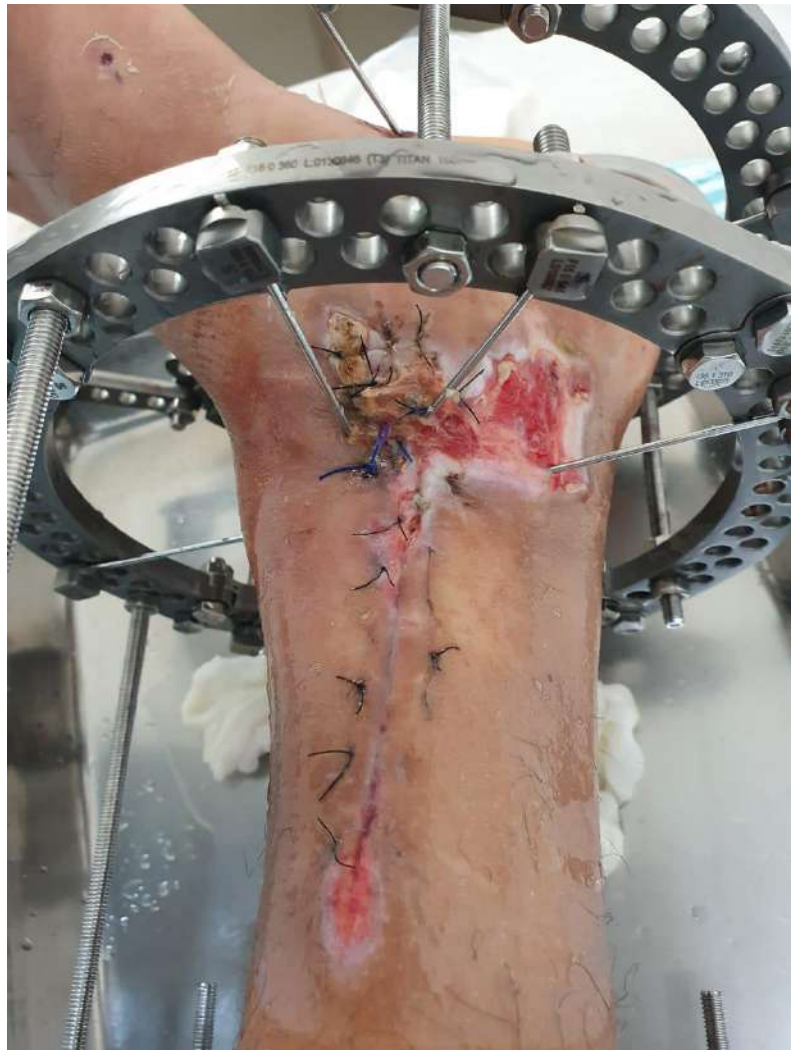
Pós de 4 dias



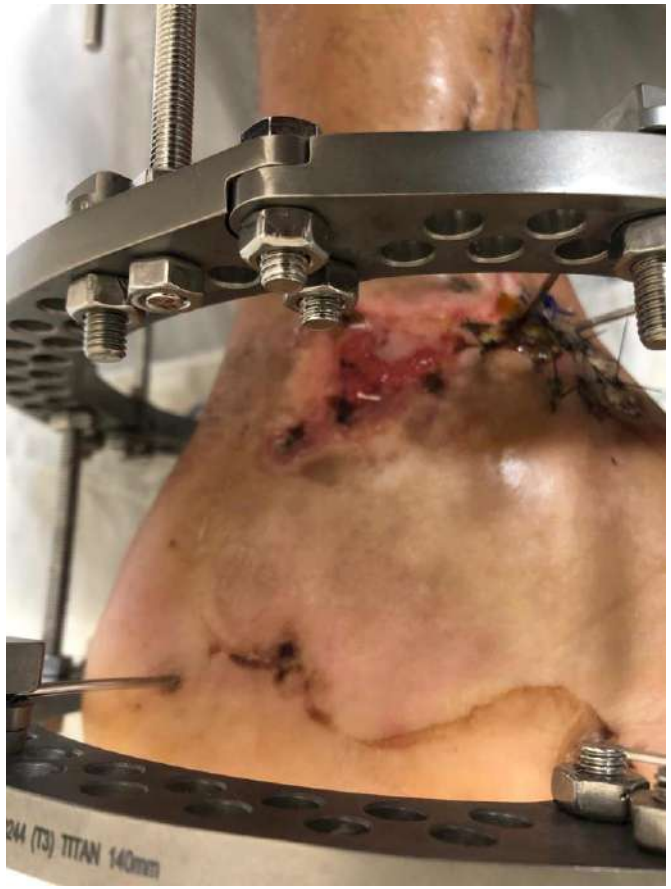


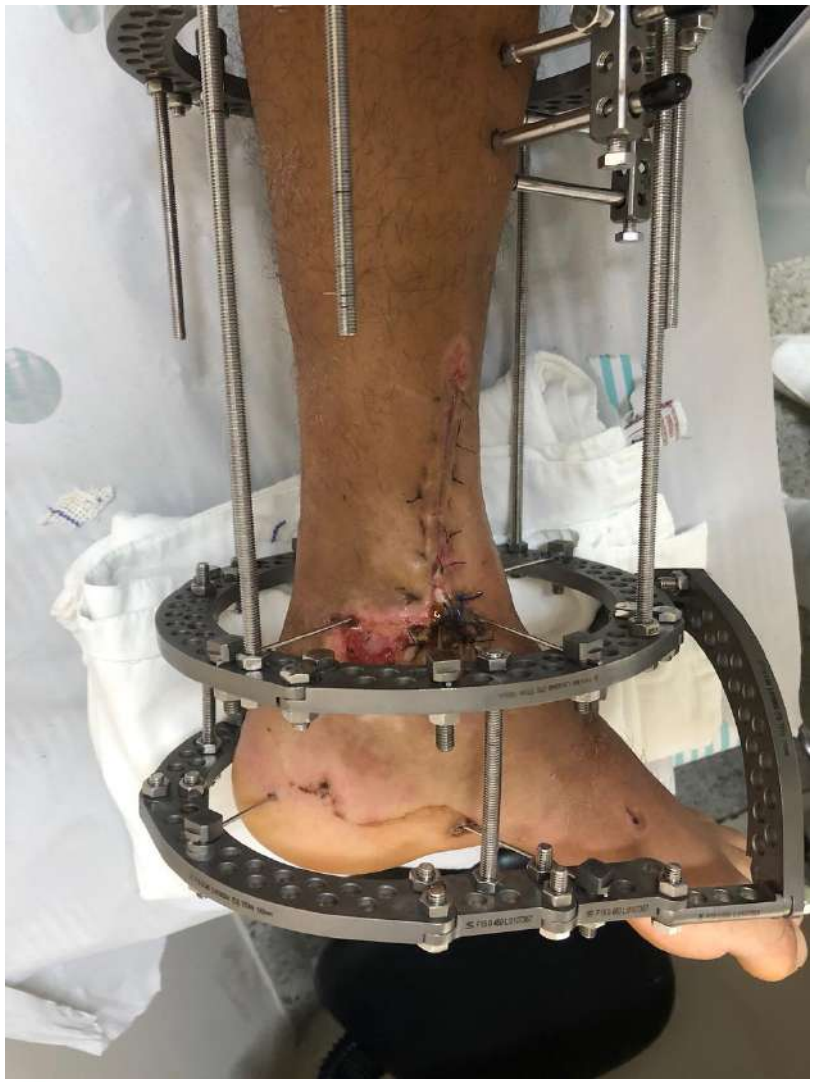
Pós de 11 dias



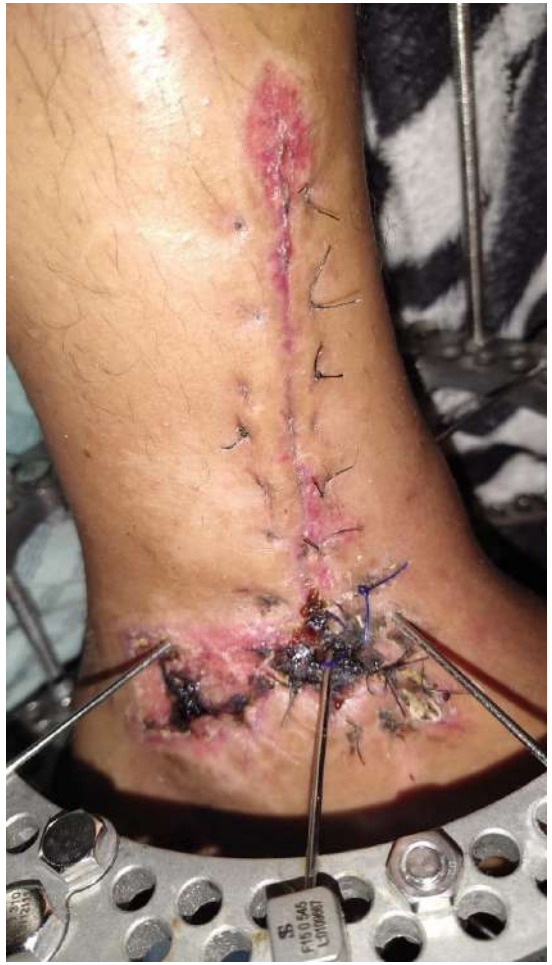


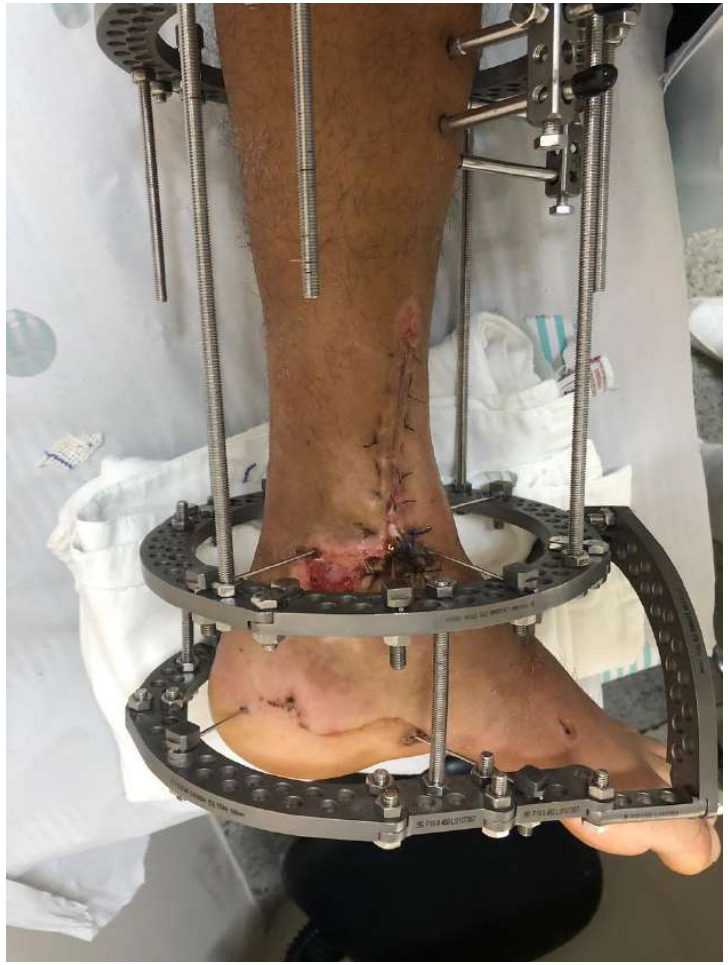
Pós de 18 dias

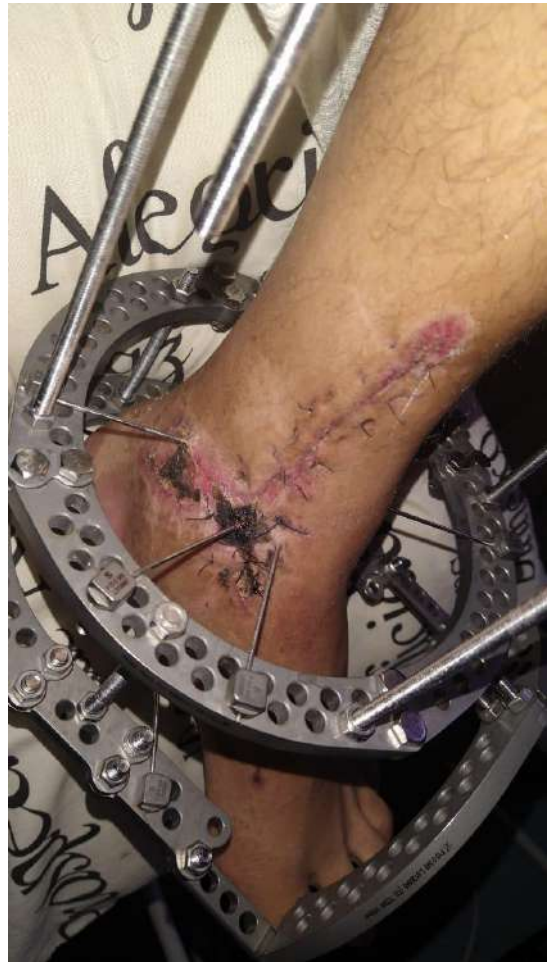


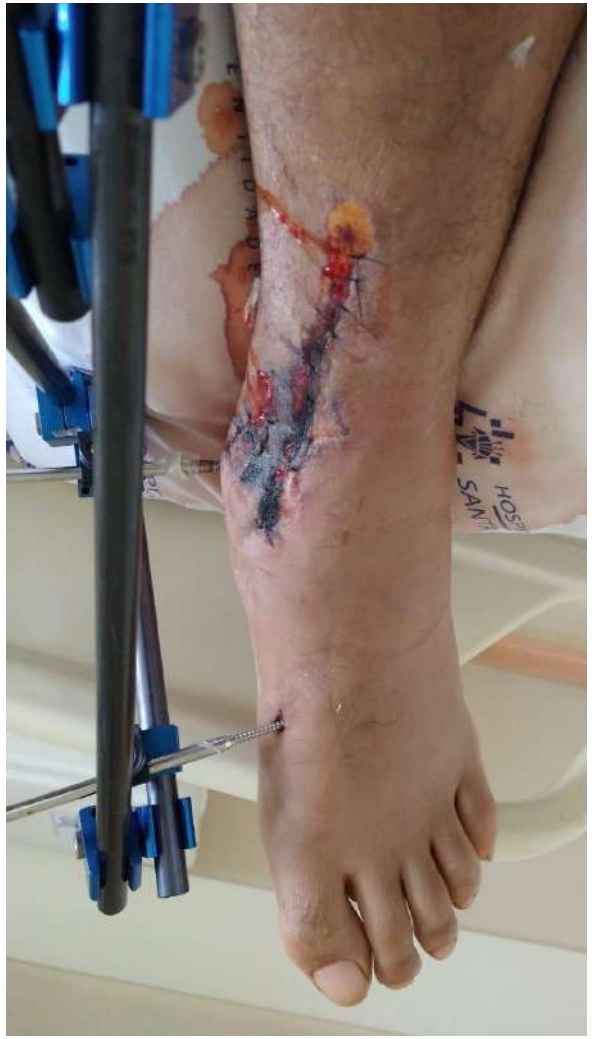


Pós de 25 dias

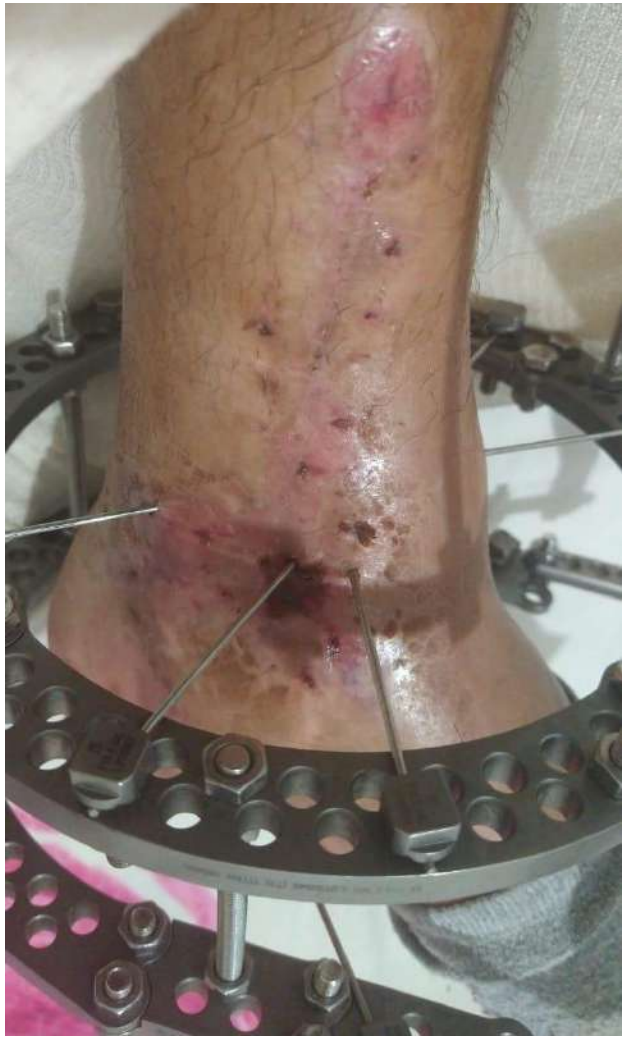




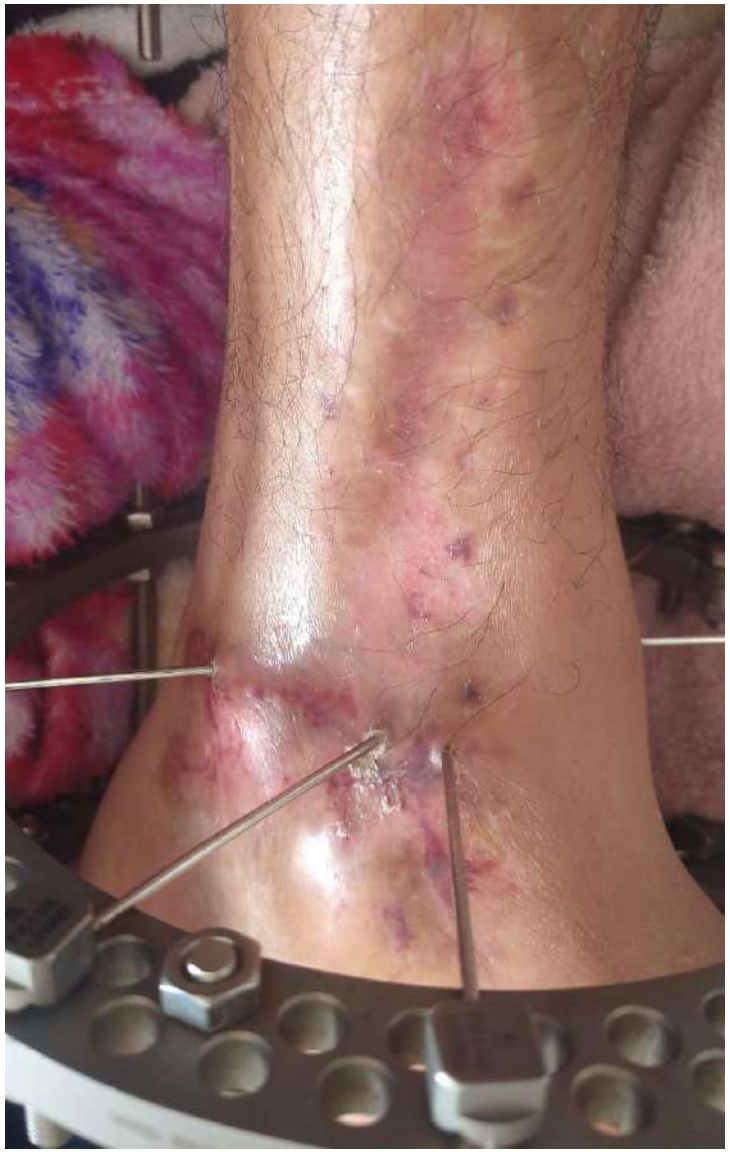




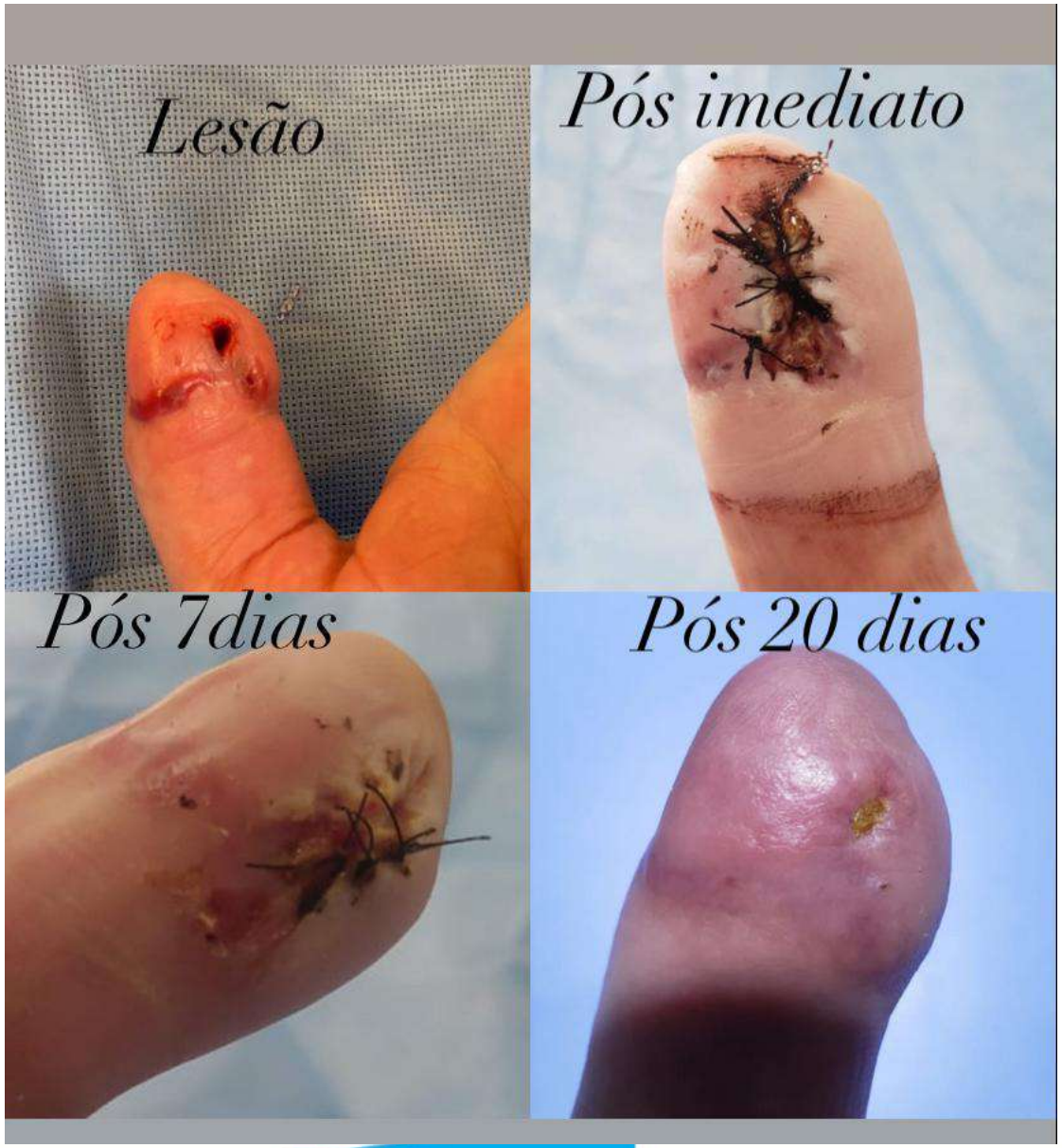
Pré operatório



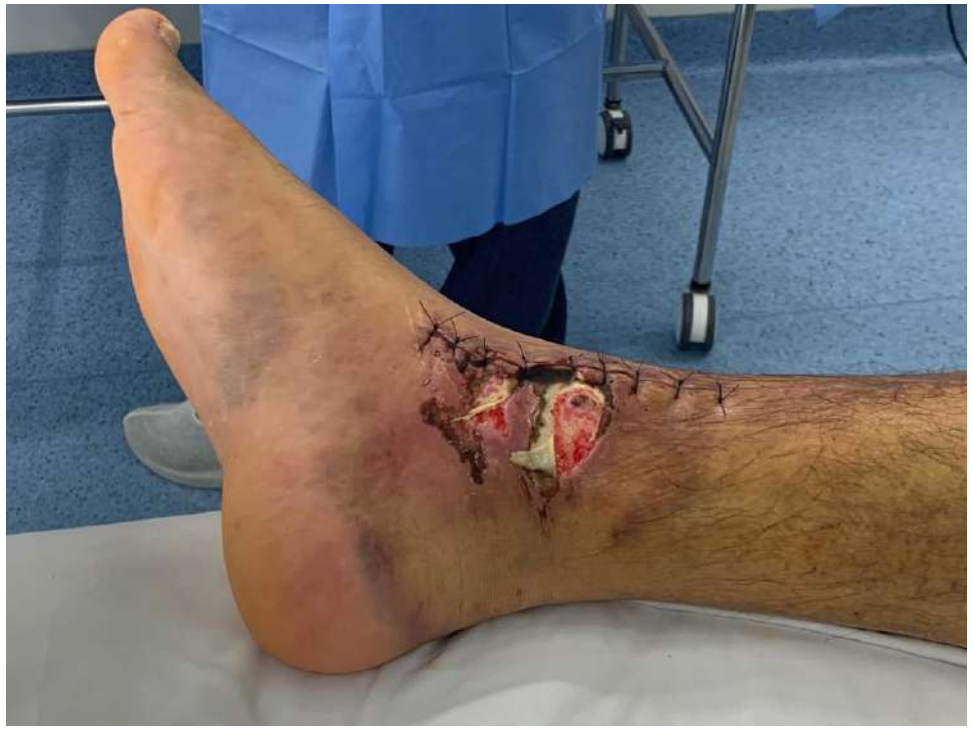
Pós operatório de 35 dias

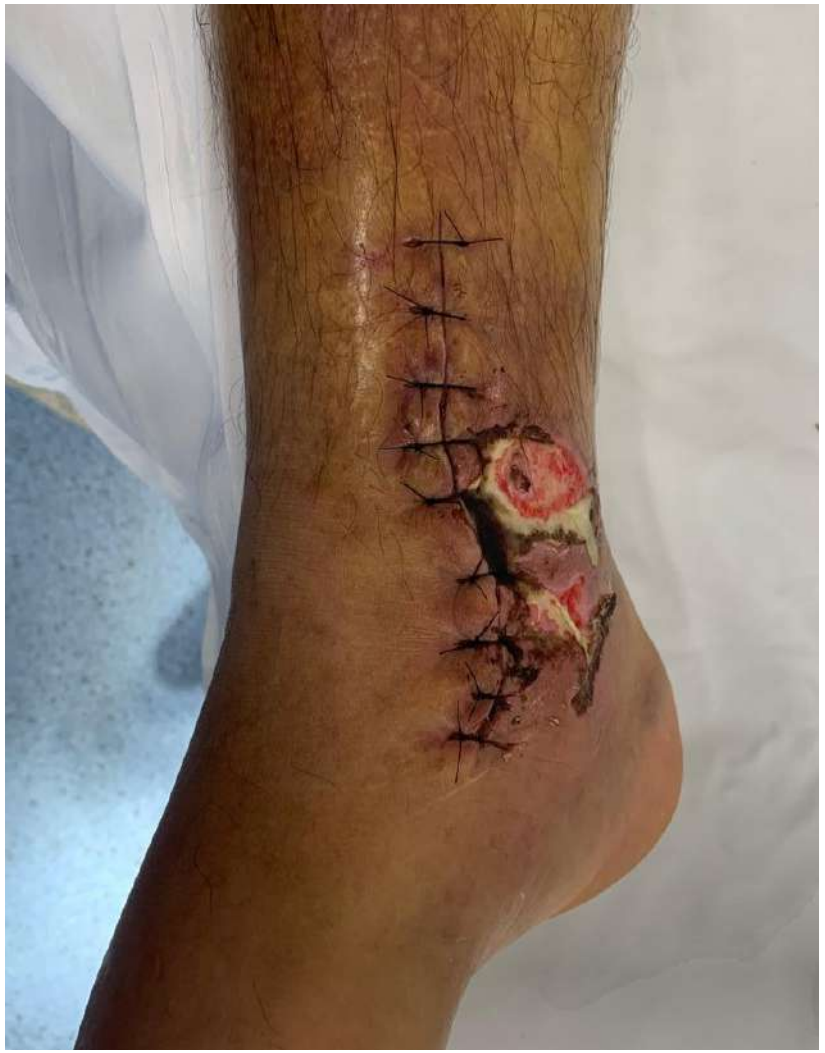


Pós de 60 dias

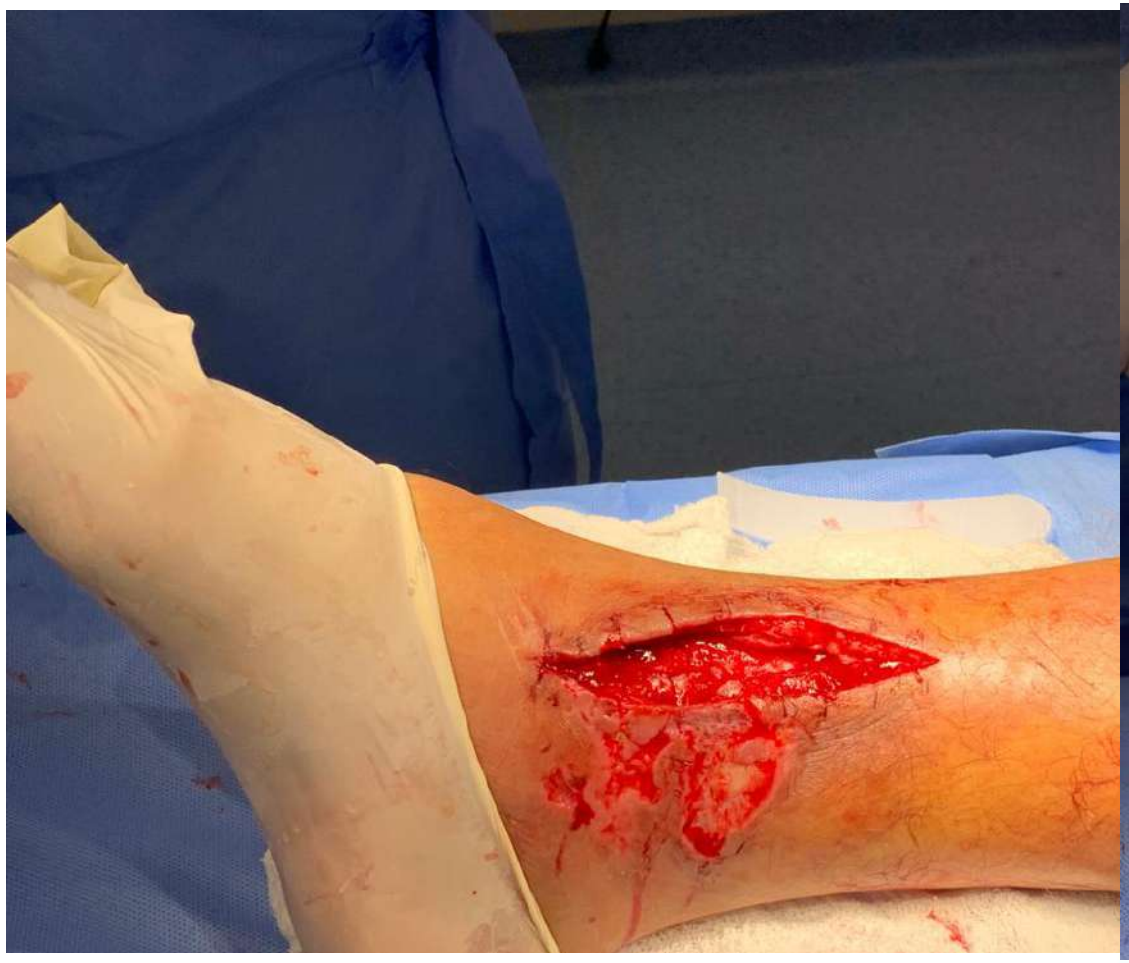

Lesão
Pós imediato
Pós 7dias
Pós 20 dias

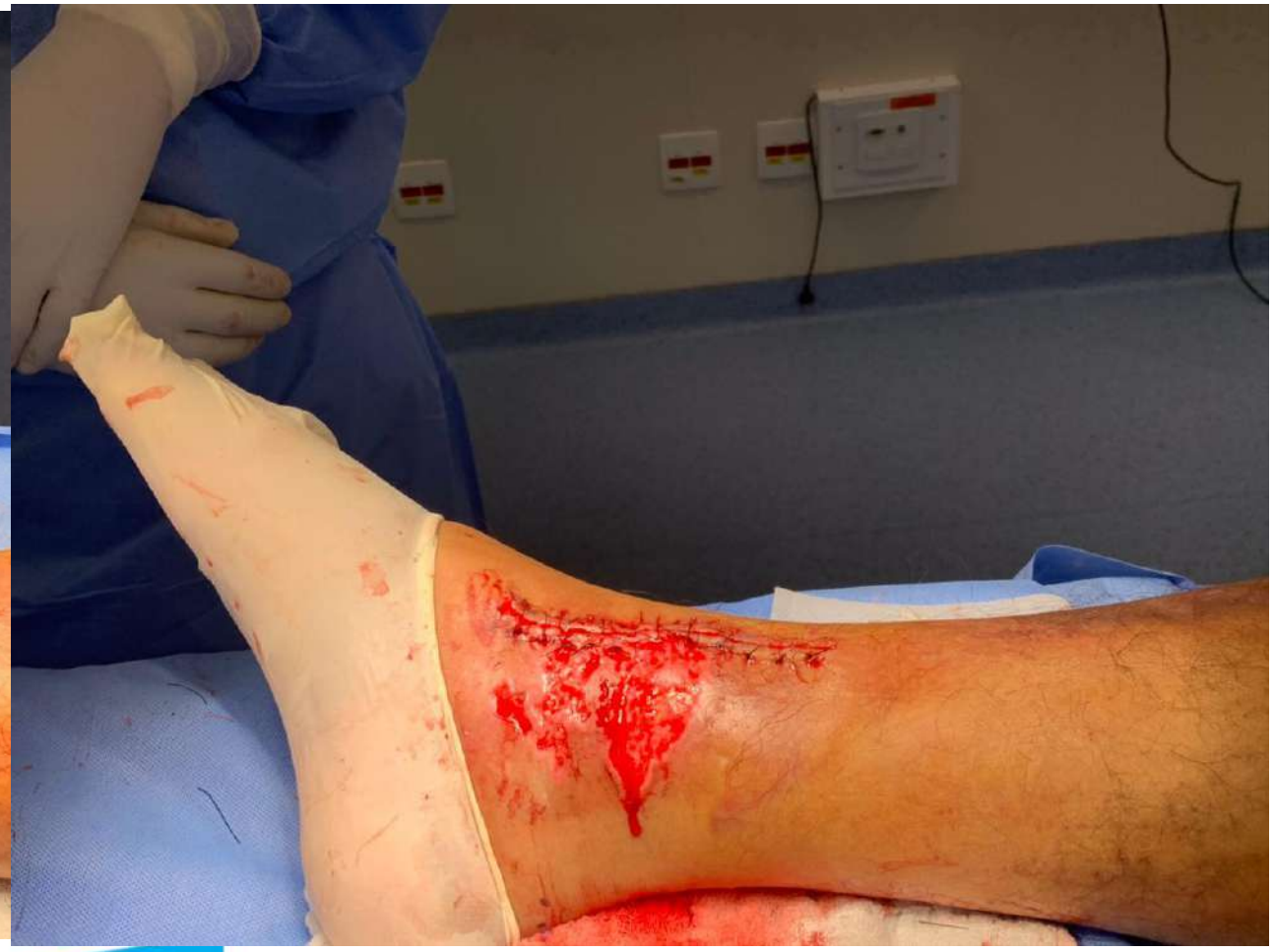
Pré operatório



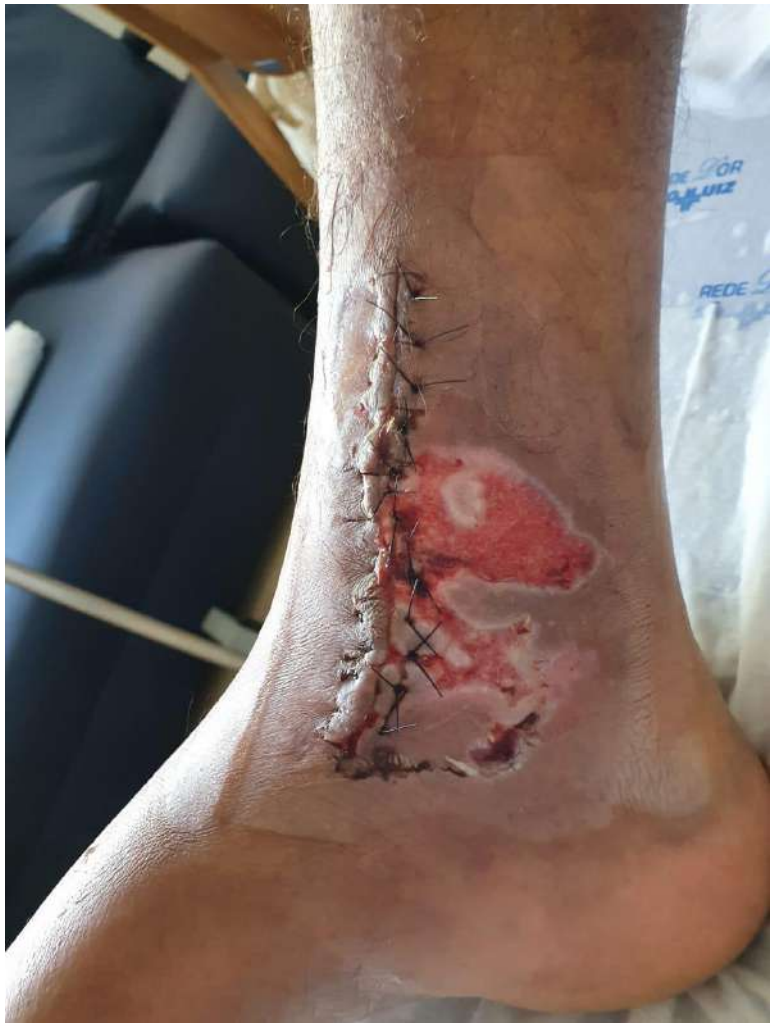


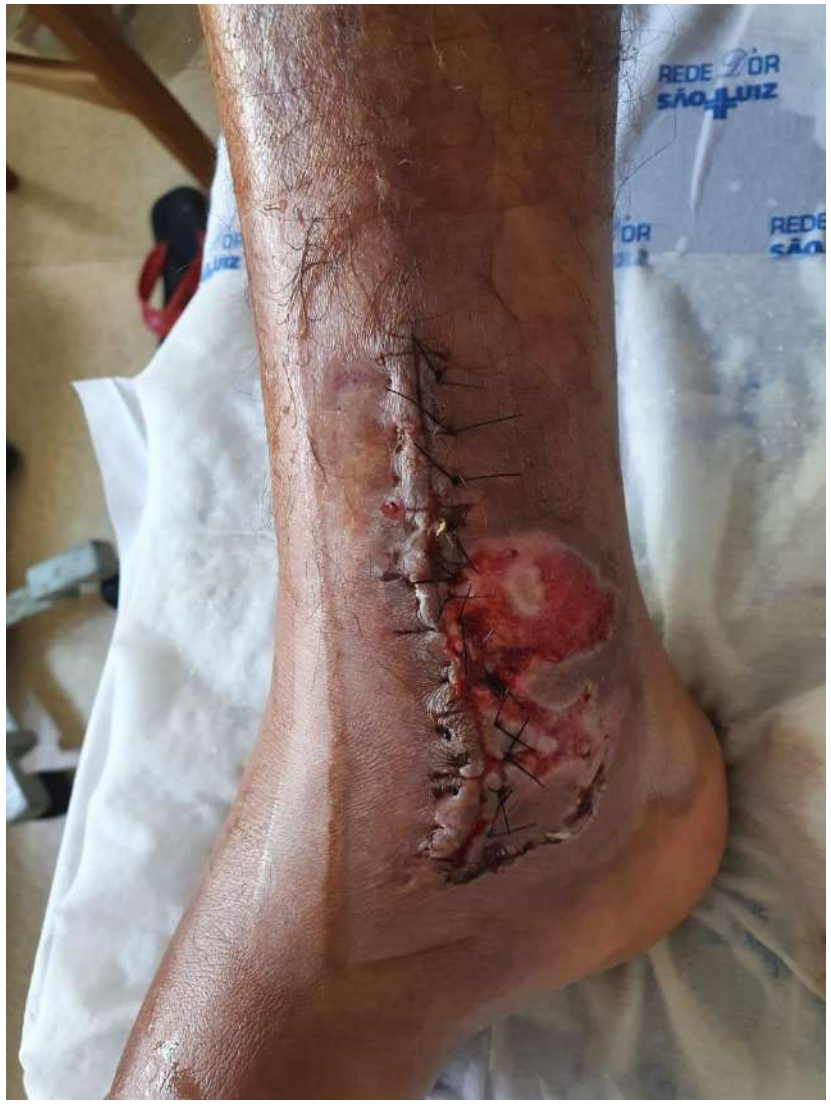
Transoperatório



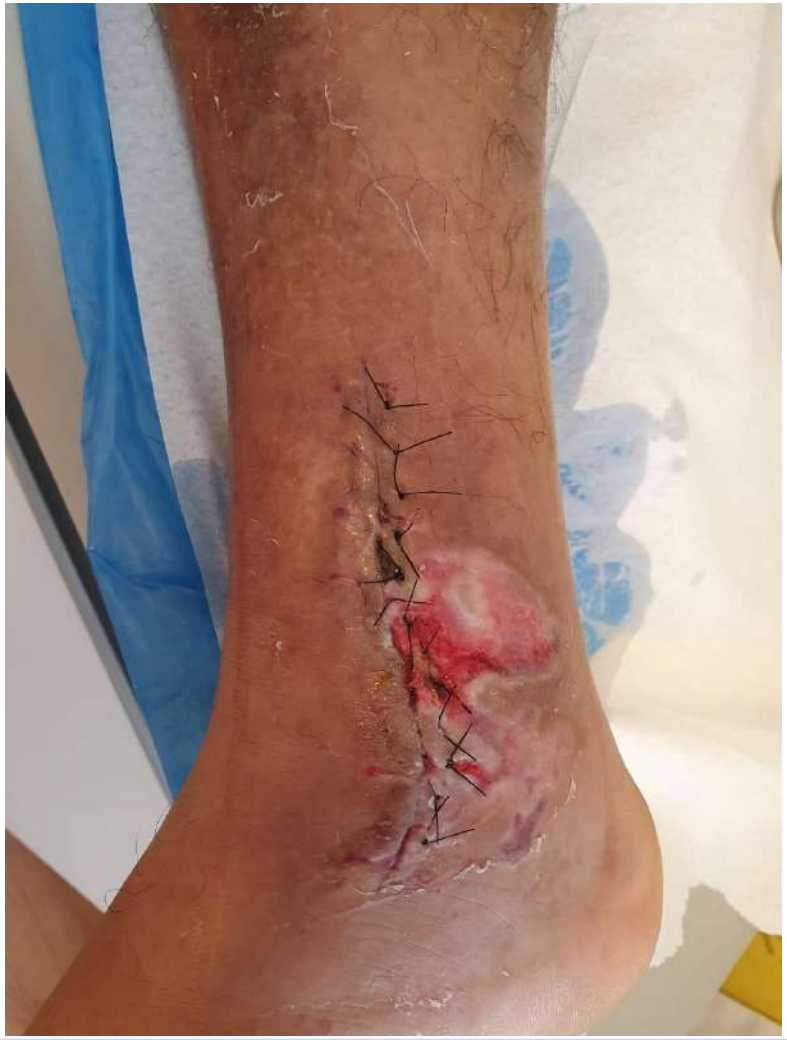


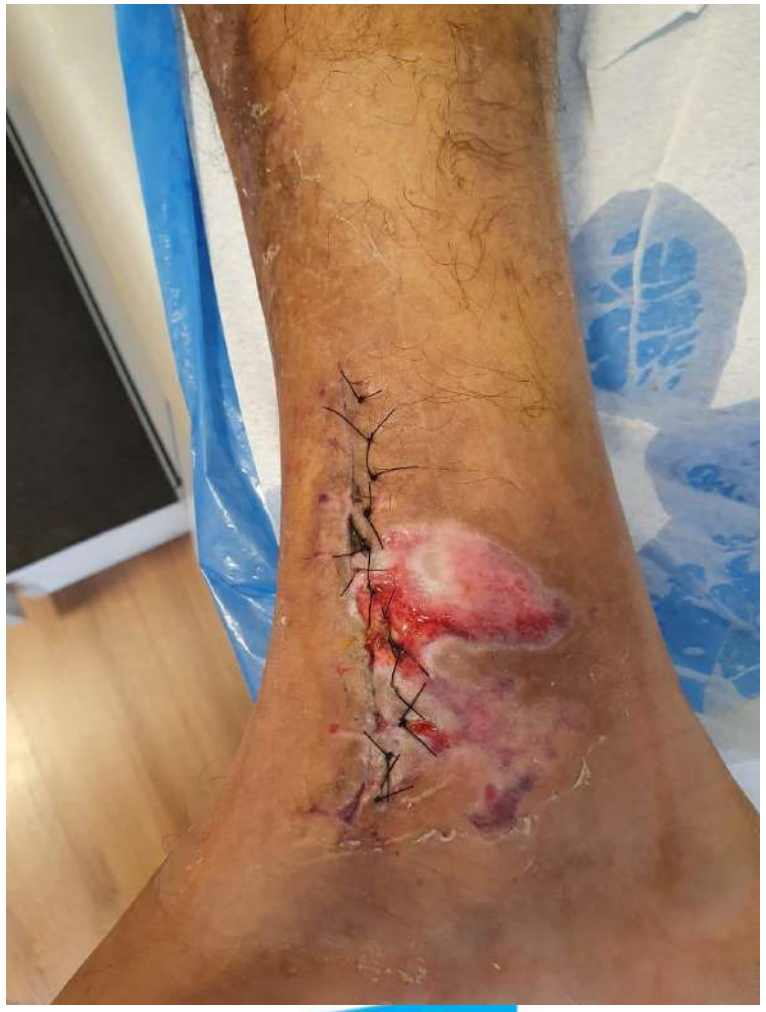
Pós de 4 dias

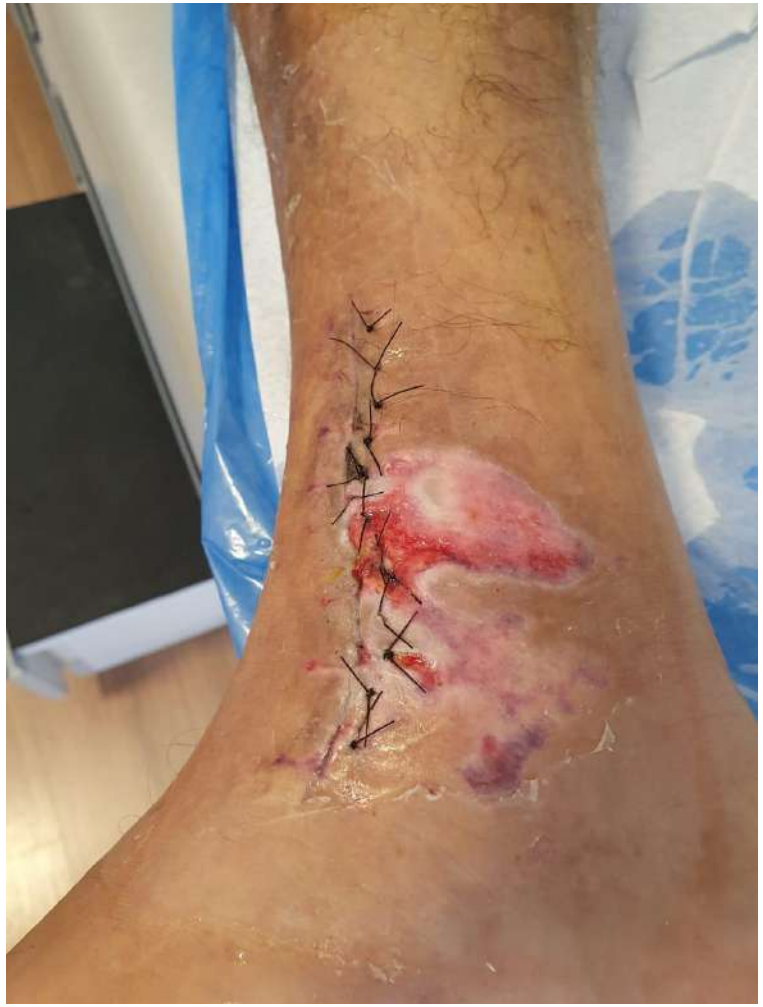




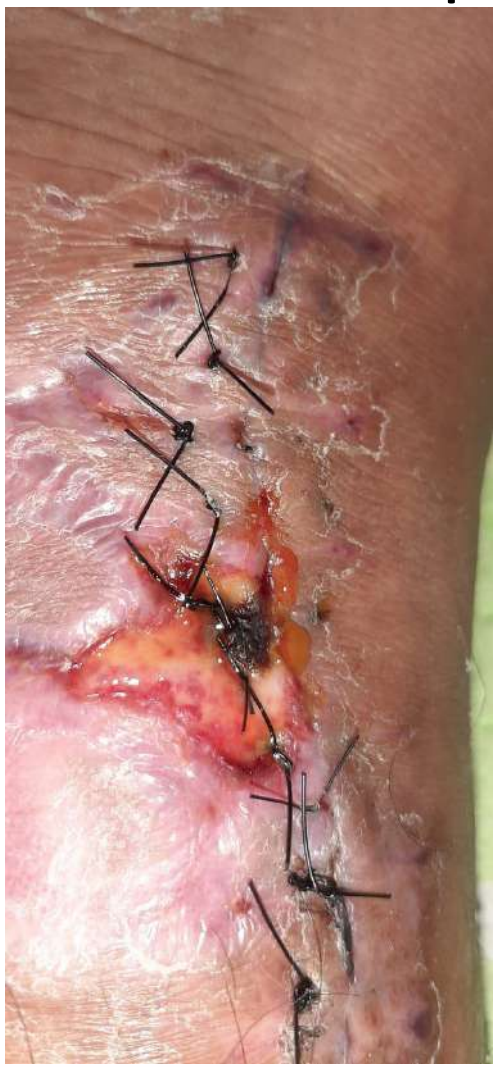
Pós de 11 dias

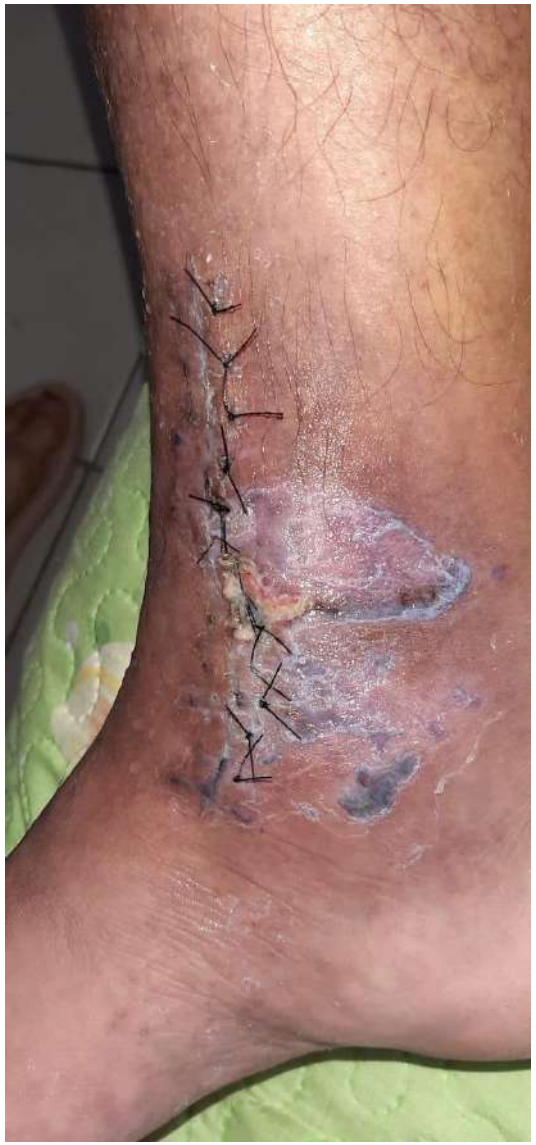




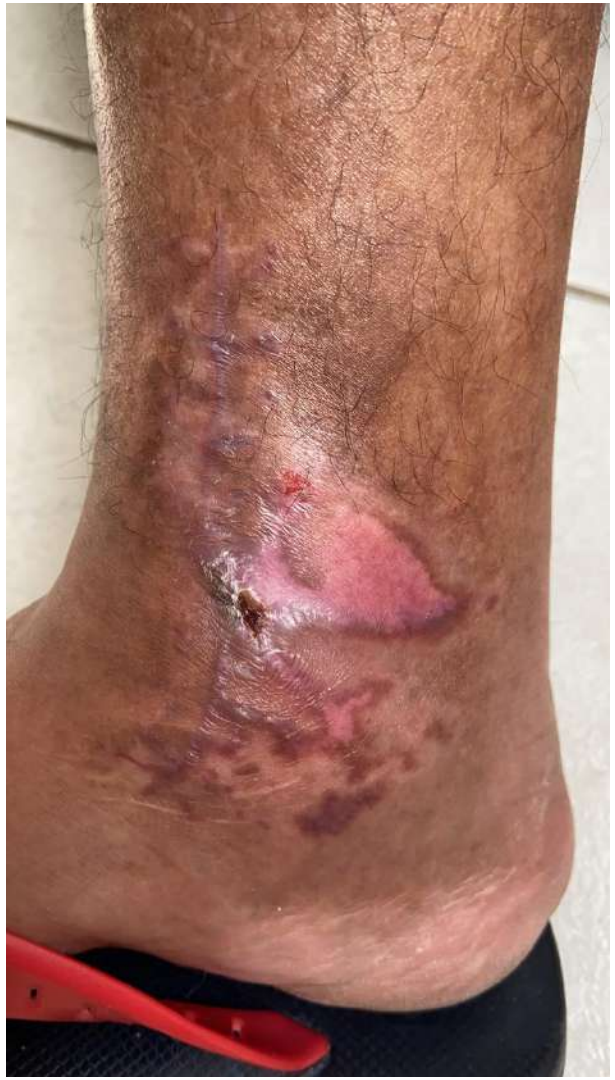


Pós de 15 dias

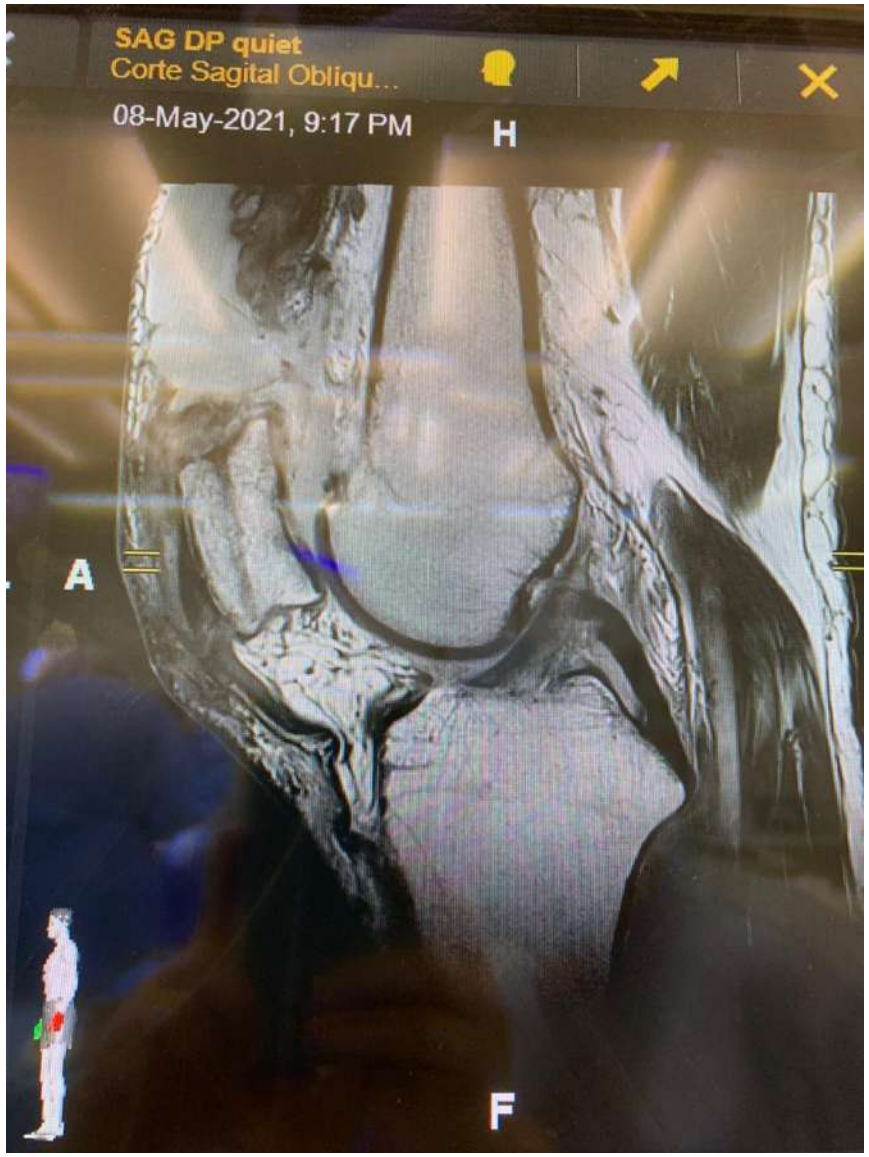




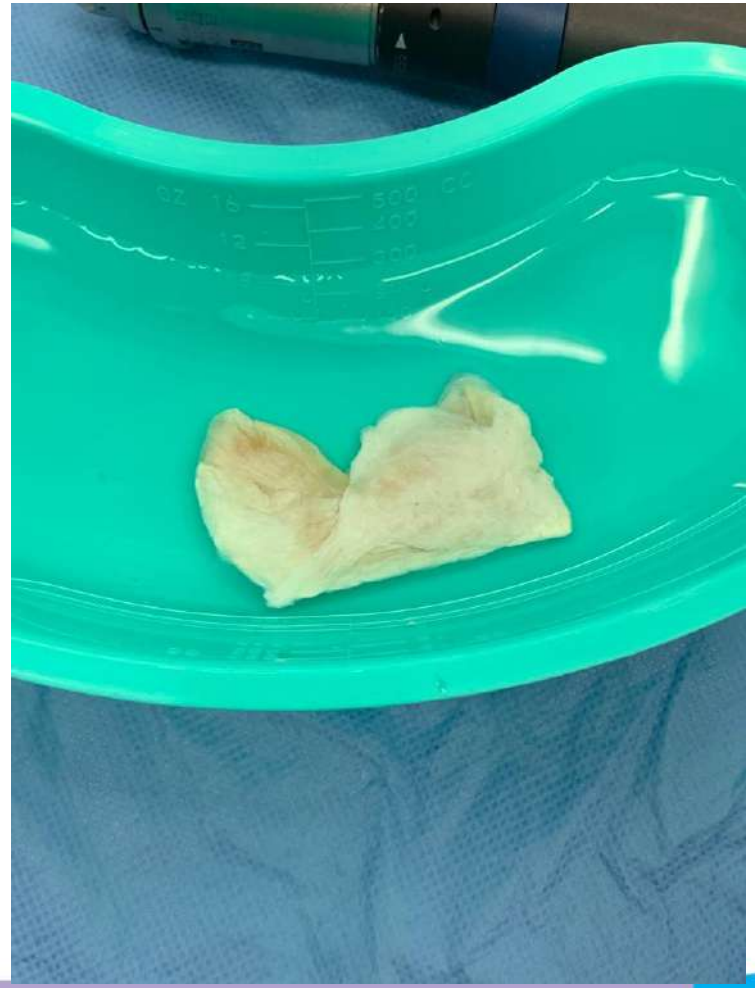
Pós de 35 dias



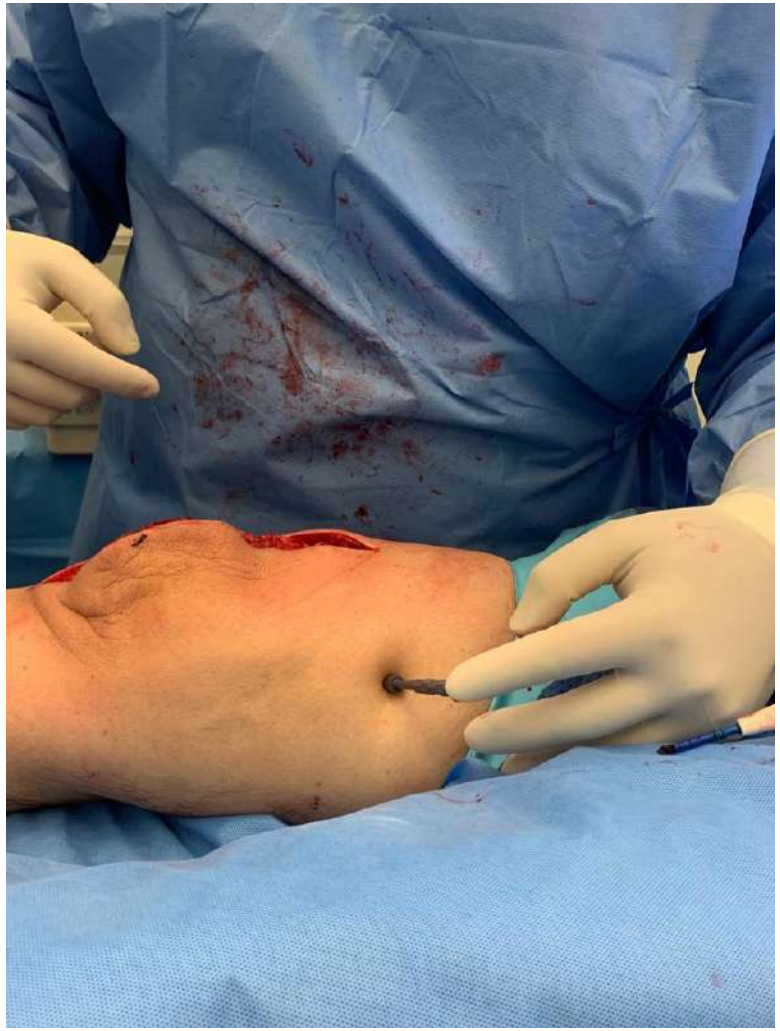
Pré operatório

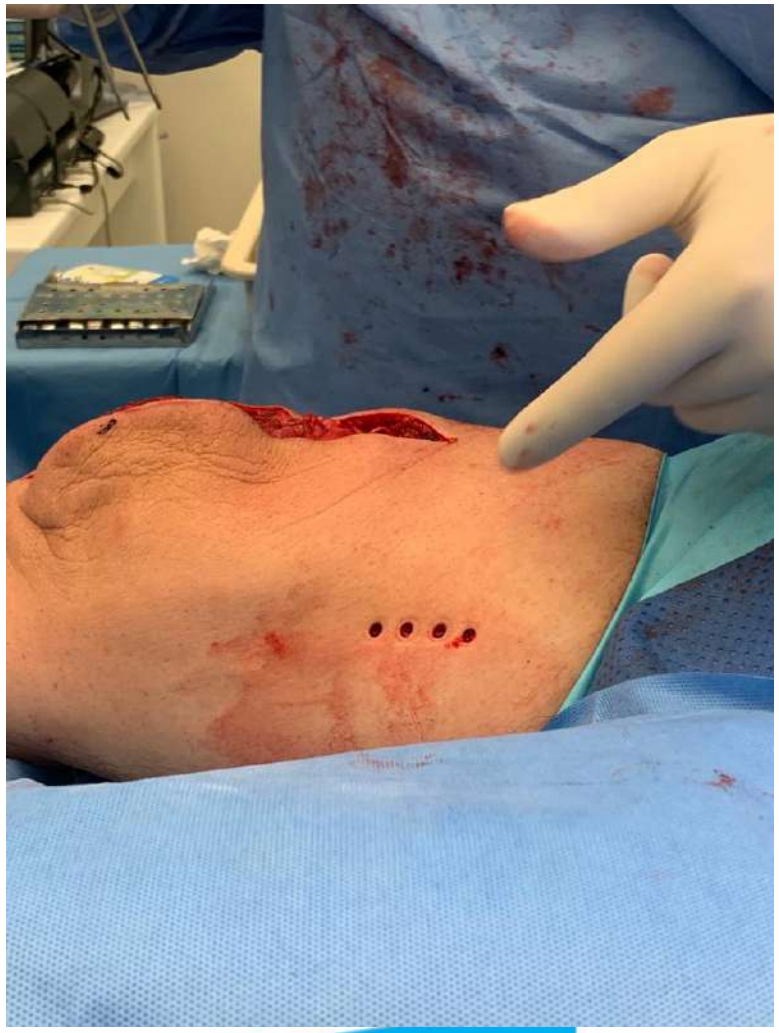


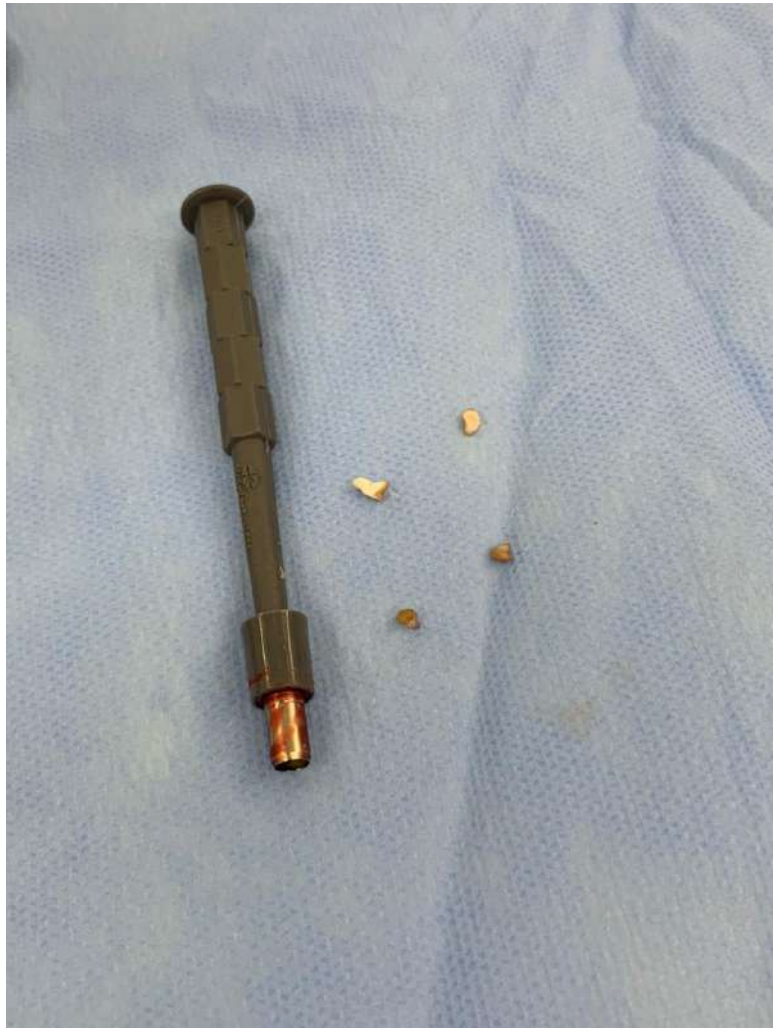
Transoperatório



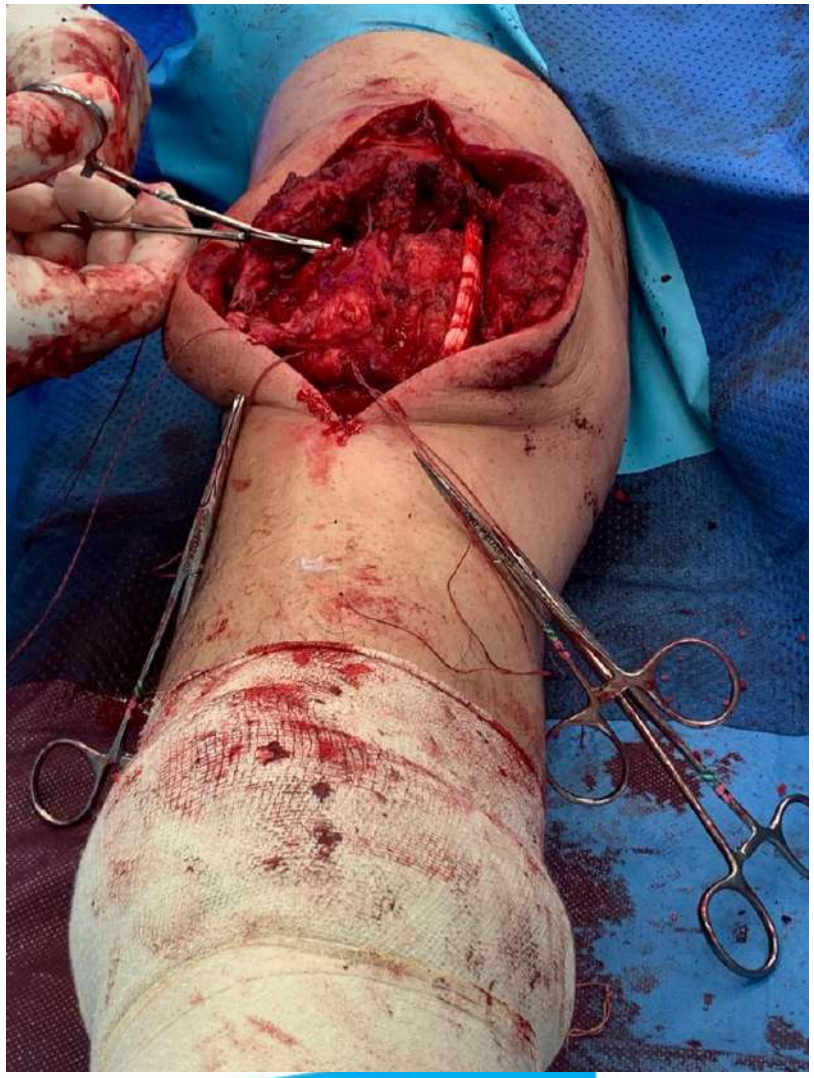
Transoperatório

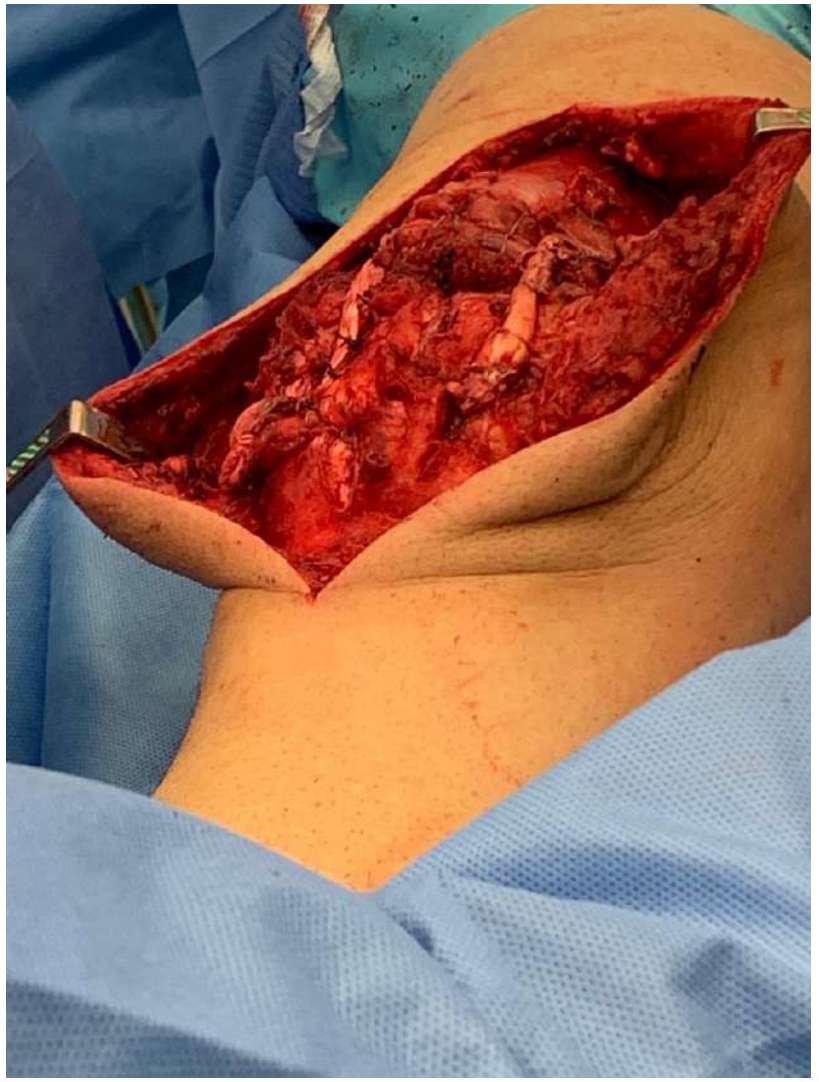




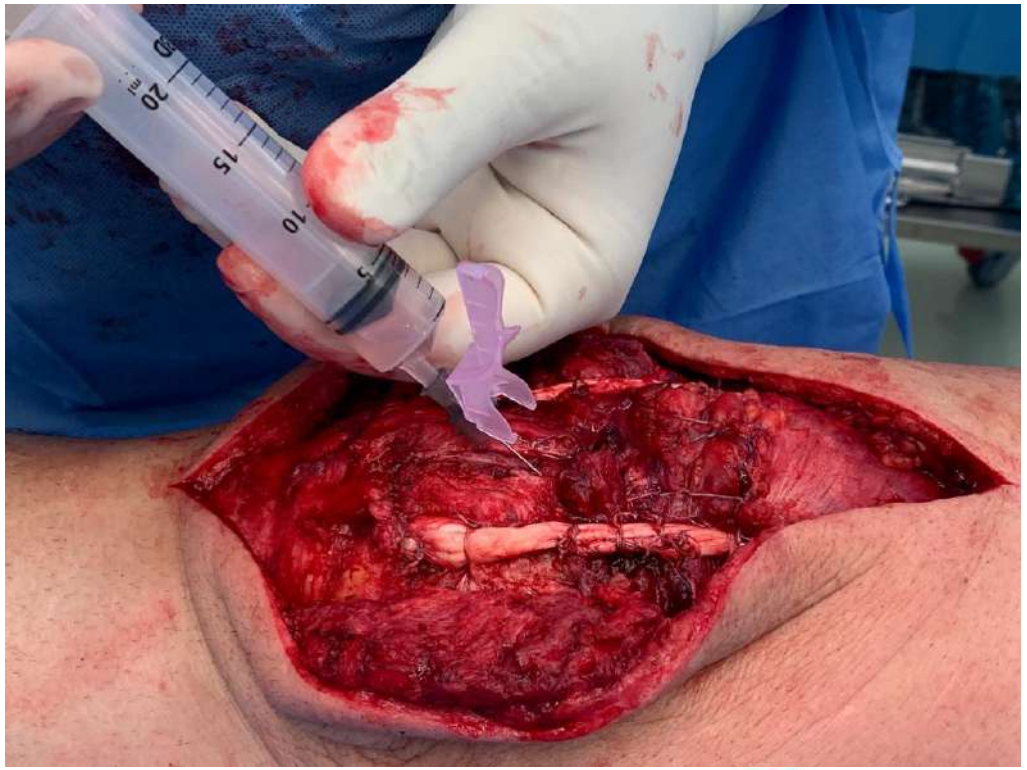


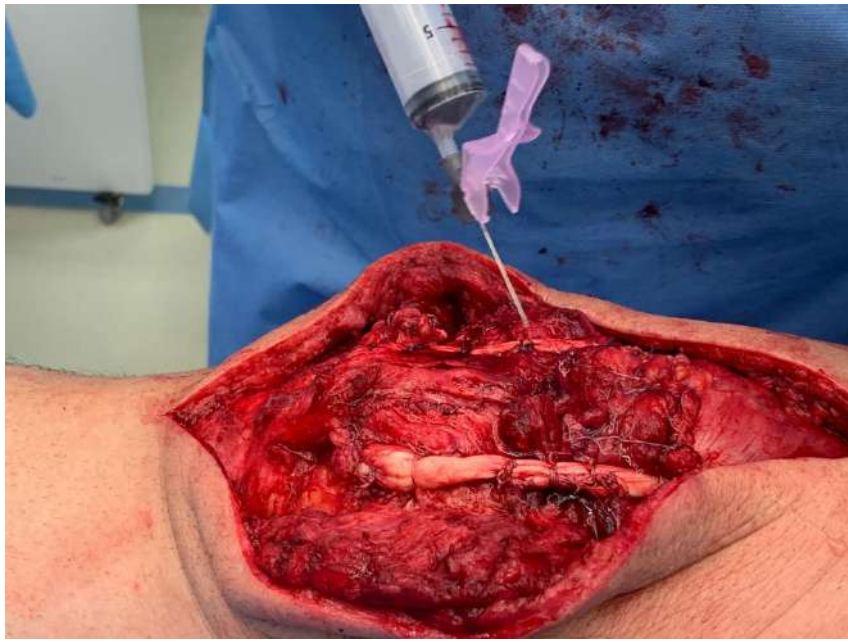
Transoperatório





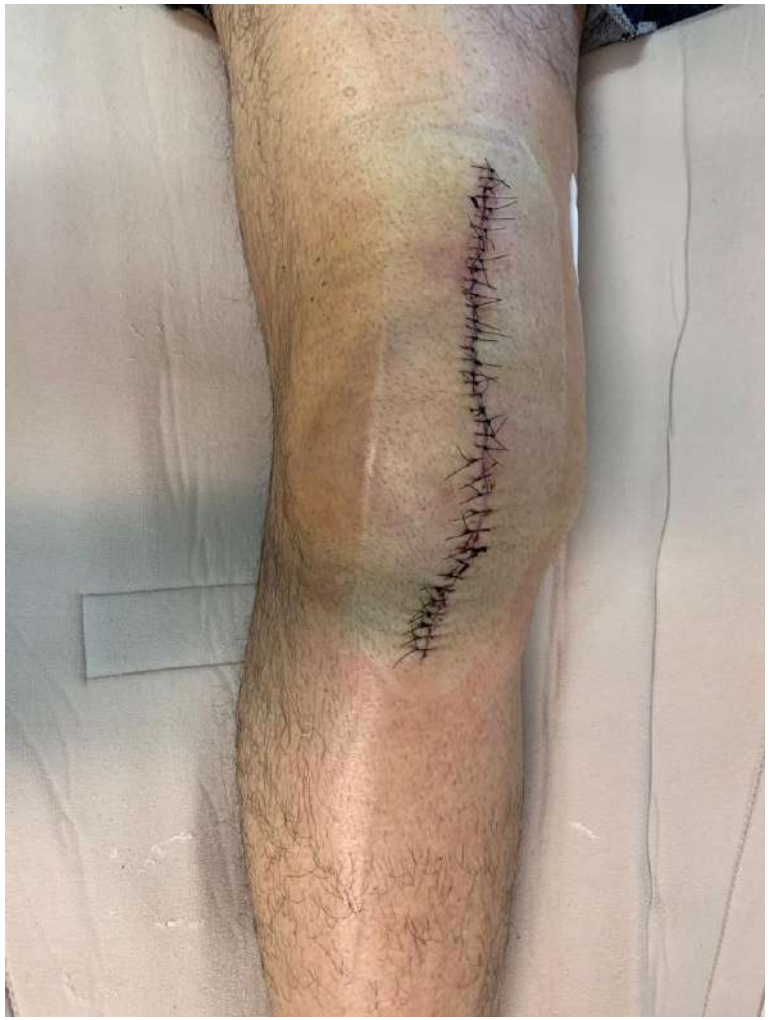
Transoperatório



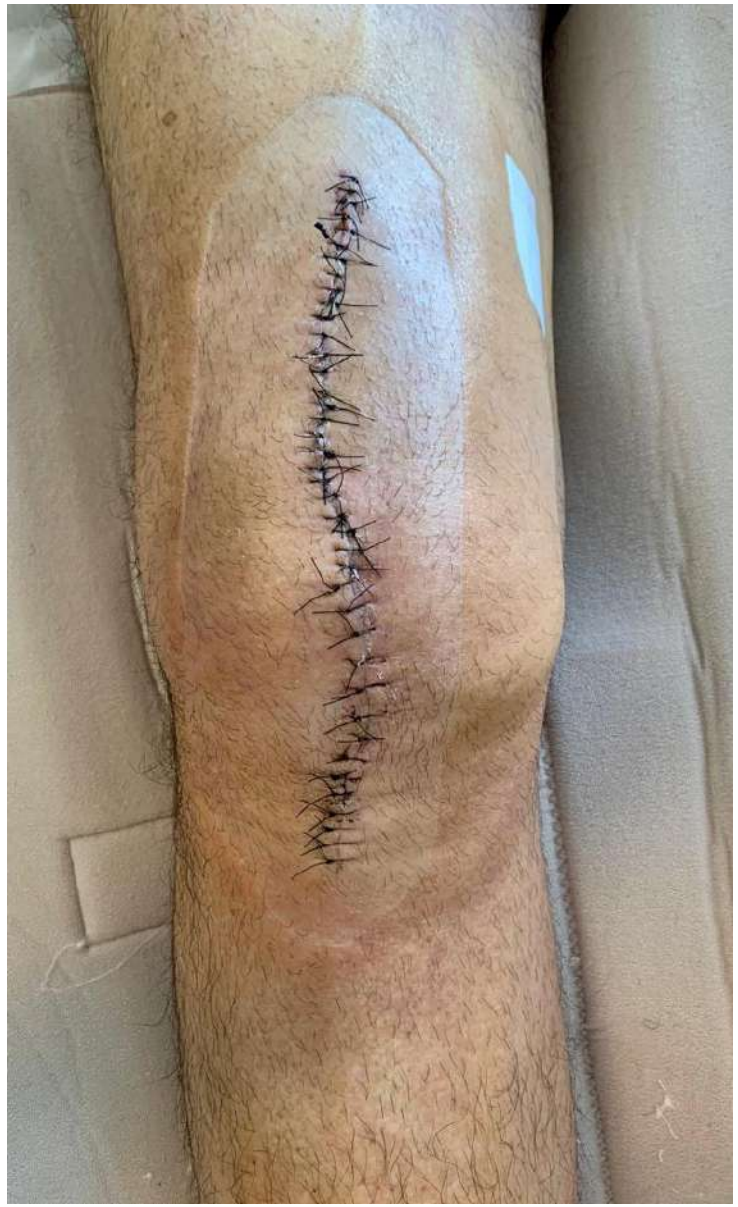


Pós de 4 dias

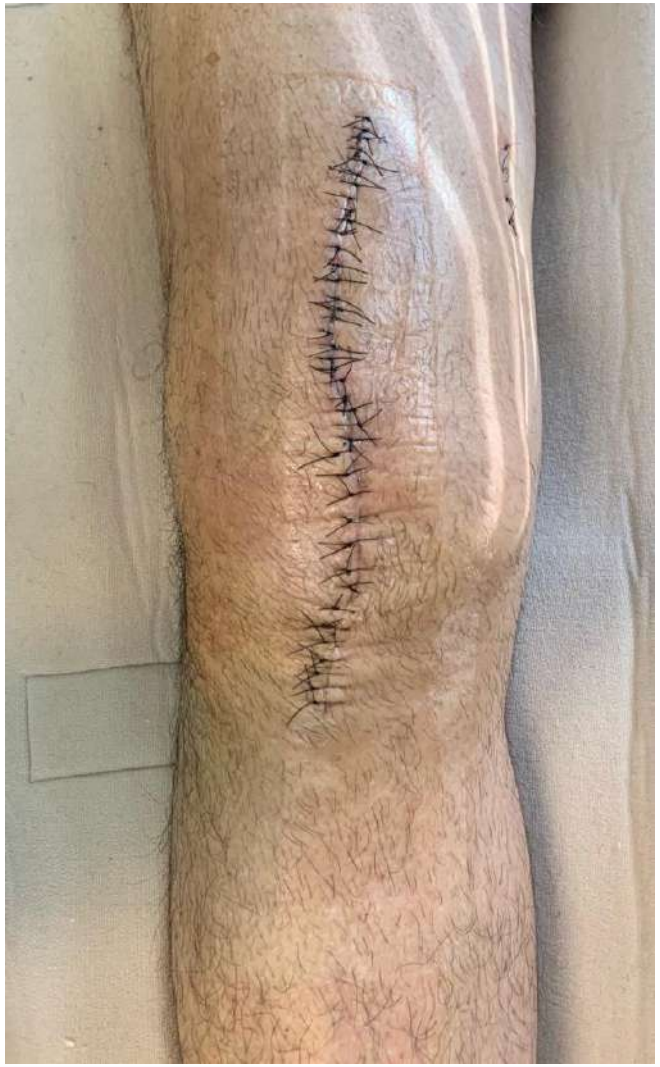
- Ausência de dor;
- Ausência de exsudato;
- Ausência de edema.

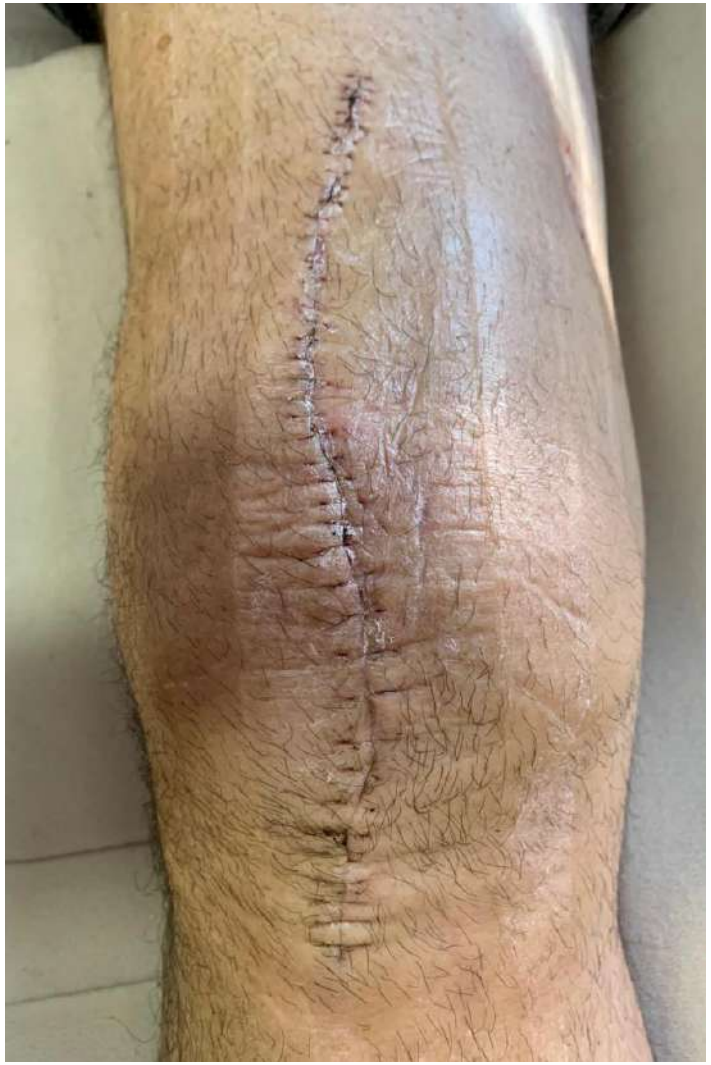


Pós de 07 dias

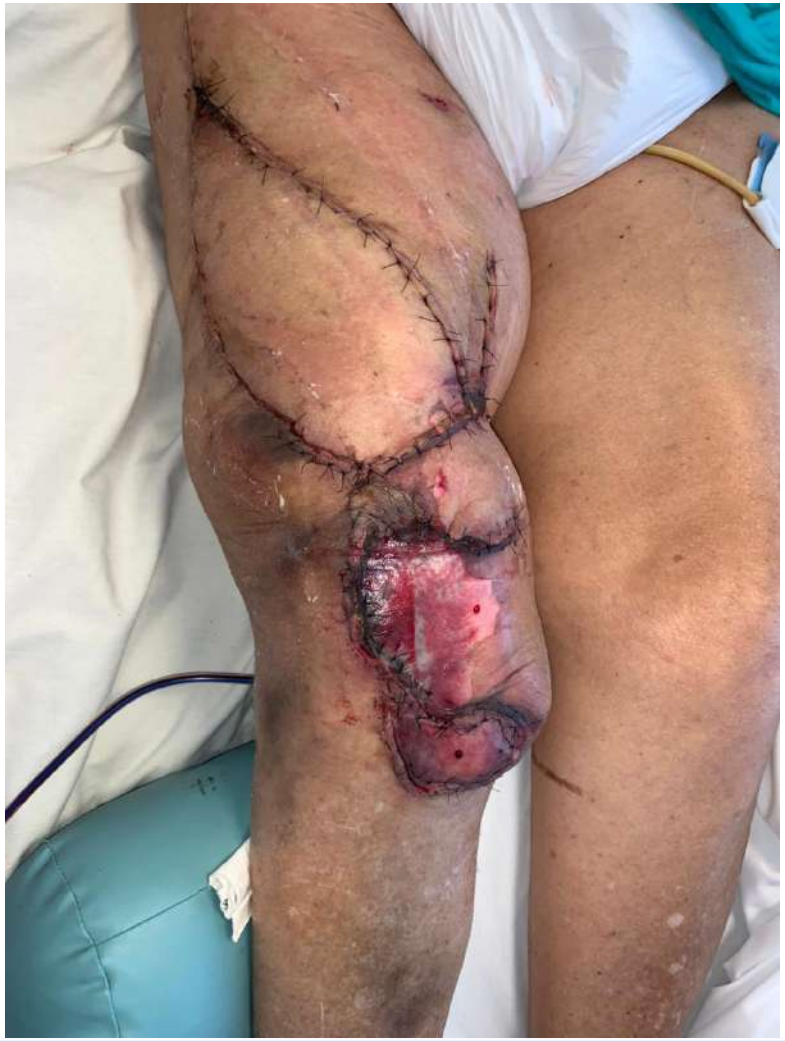


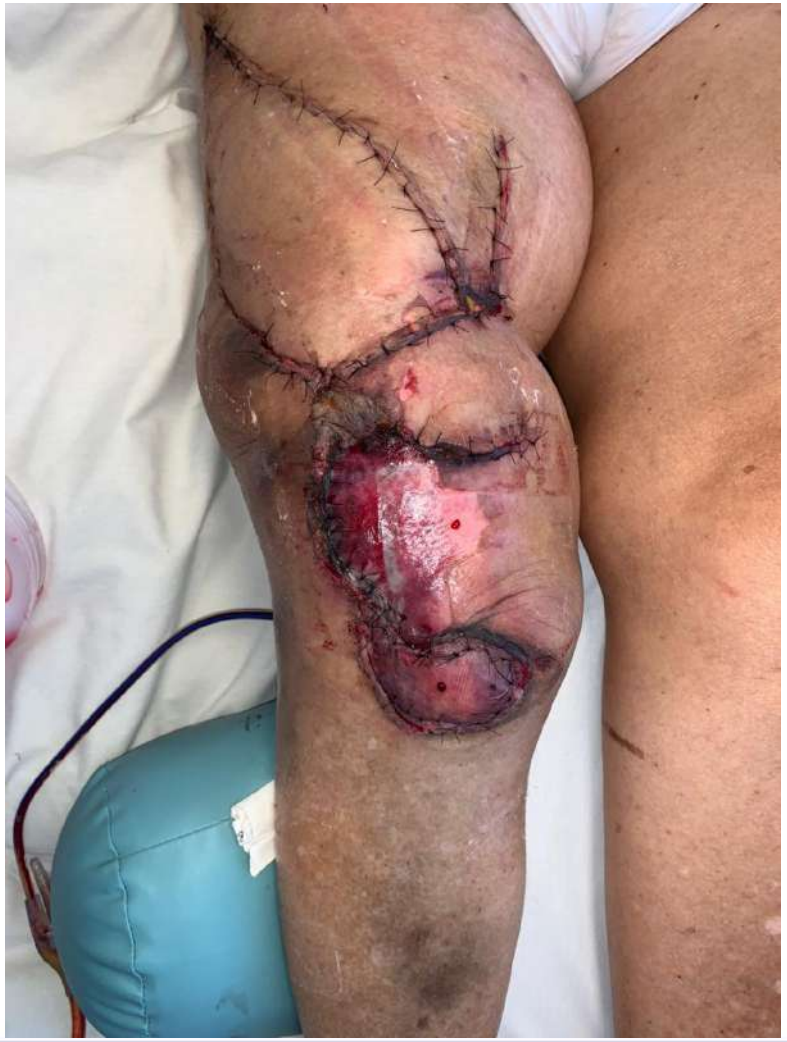
Pós de 15 dias



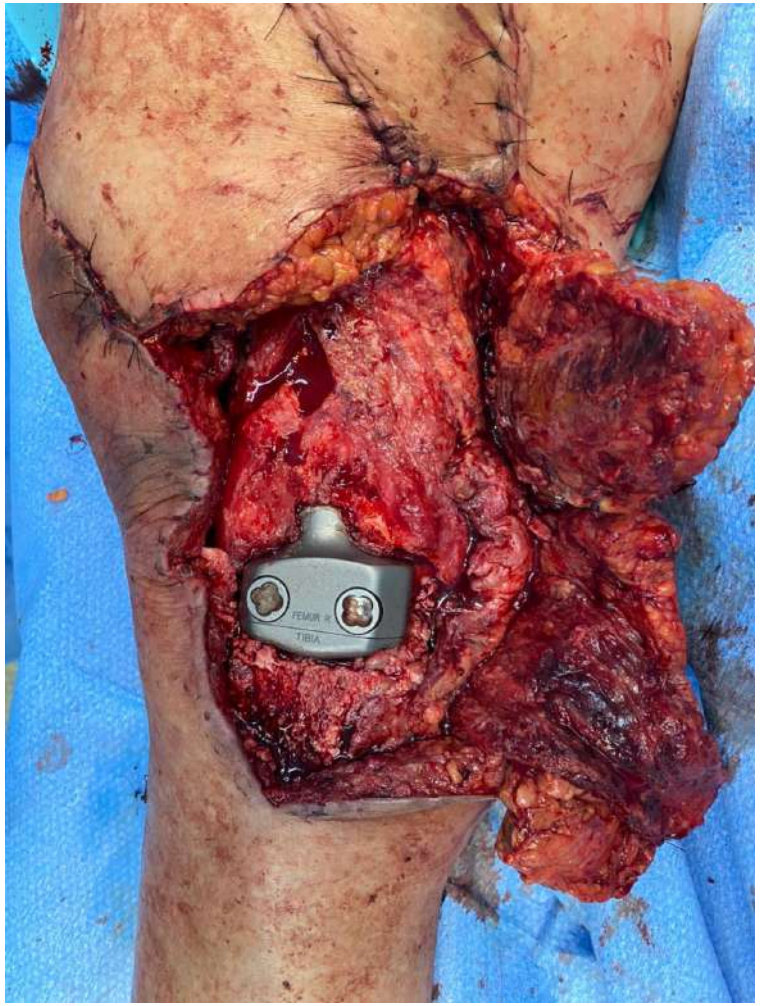


Pré operatório

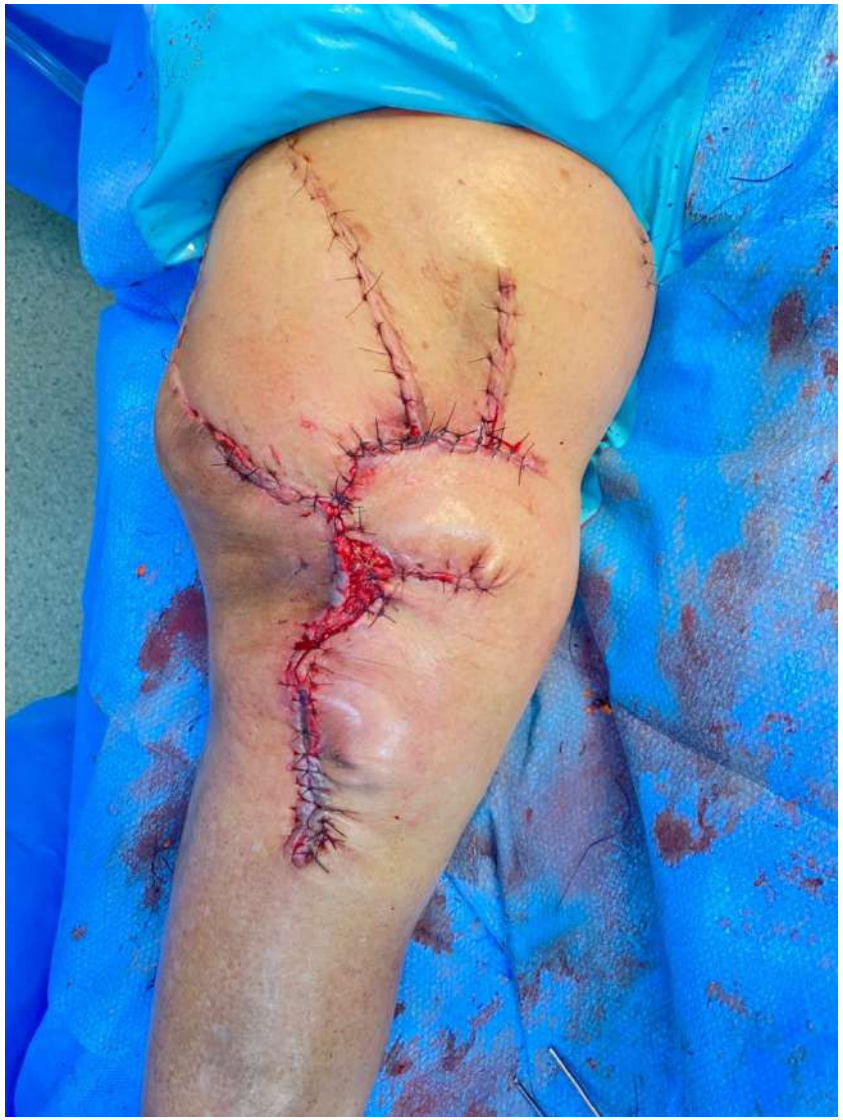




Transoperatório

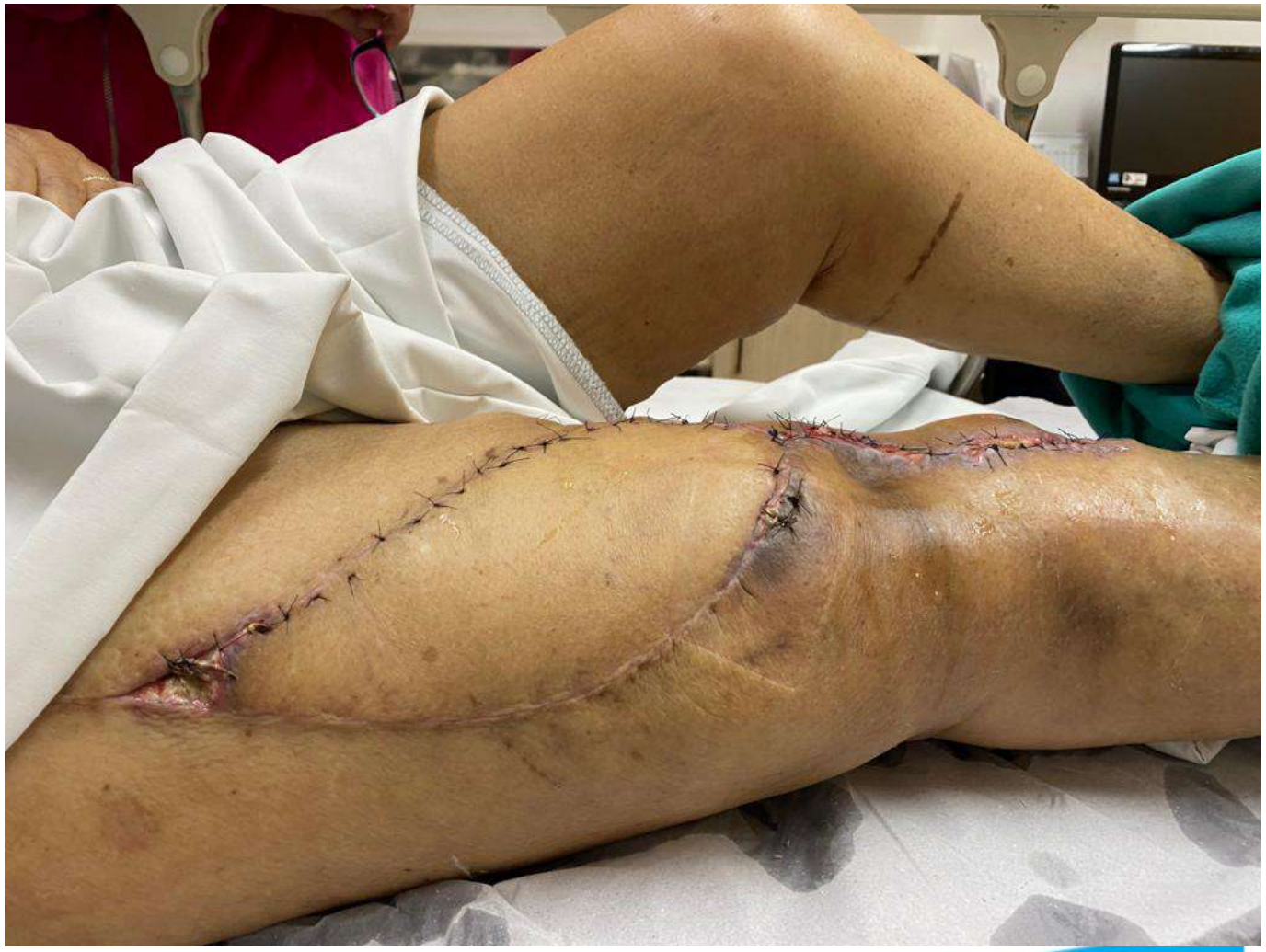


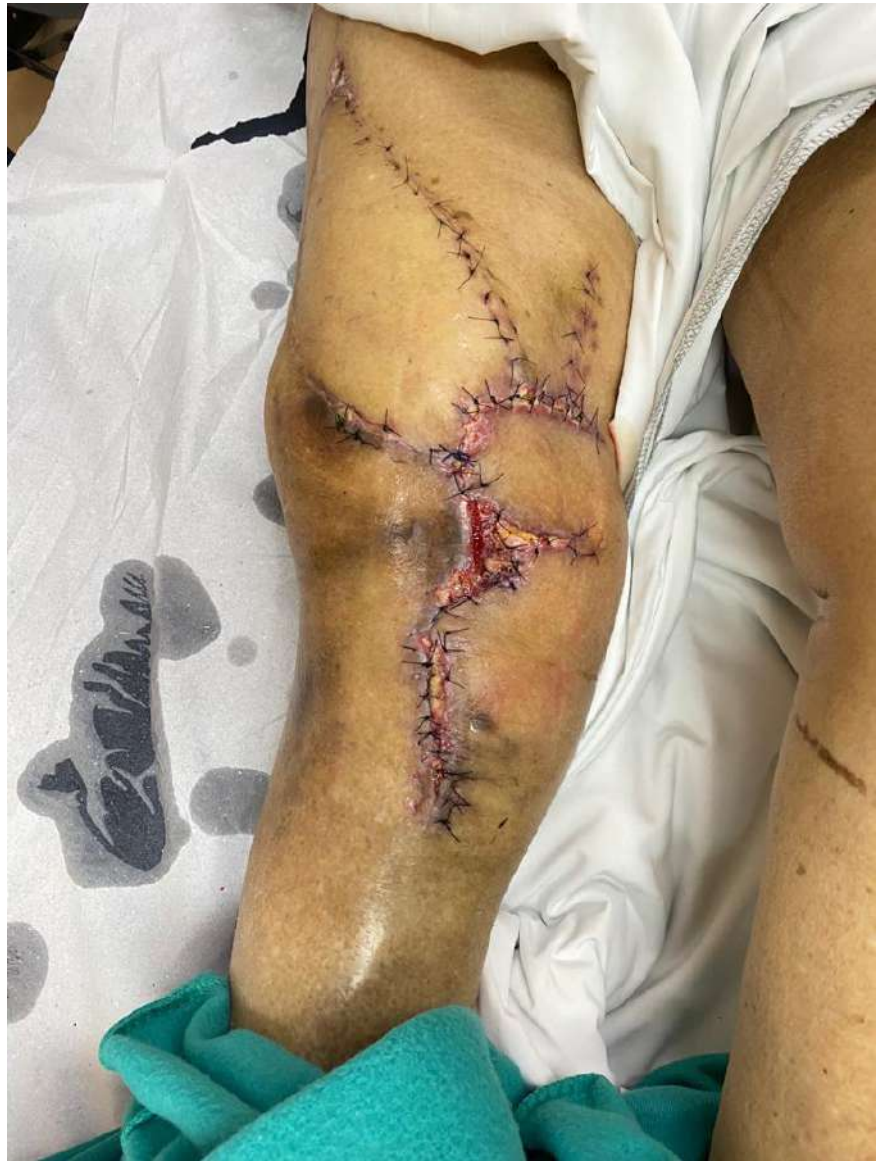
Pós de 4 dias



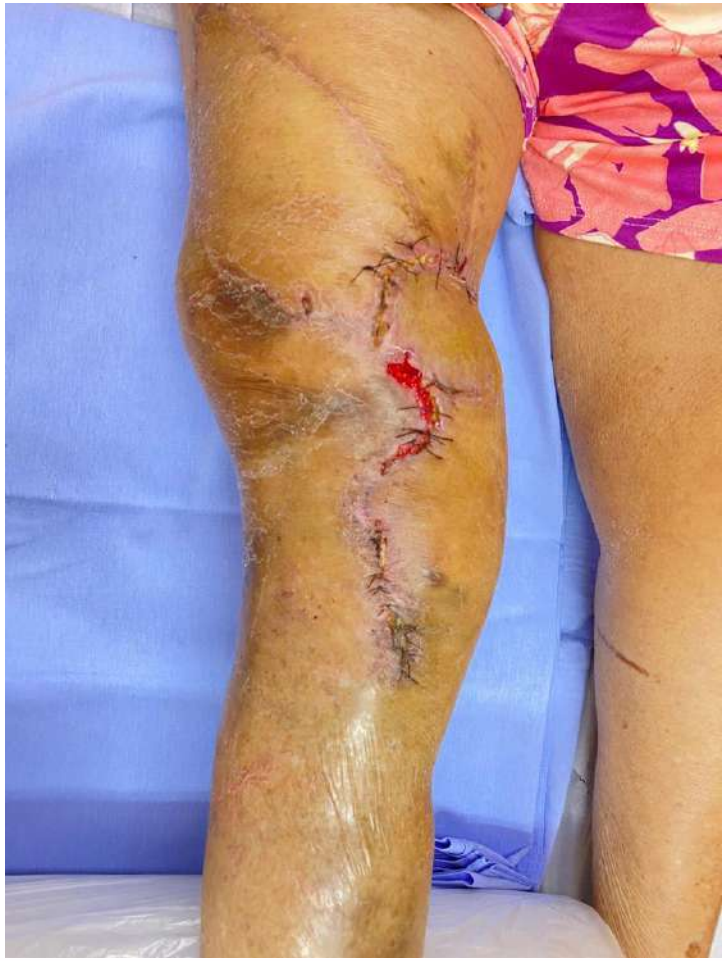
Pós de 7 dias

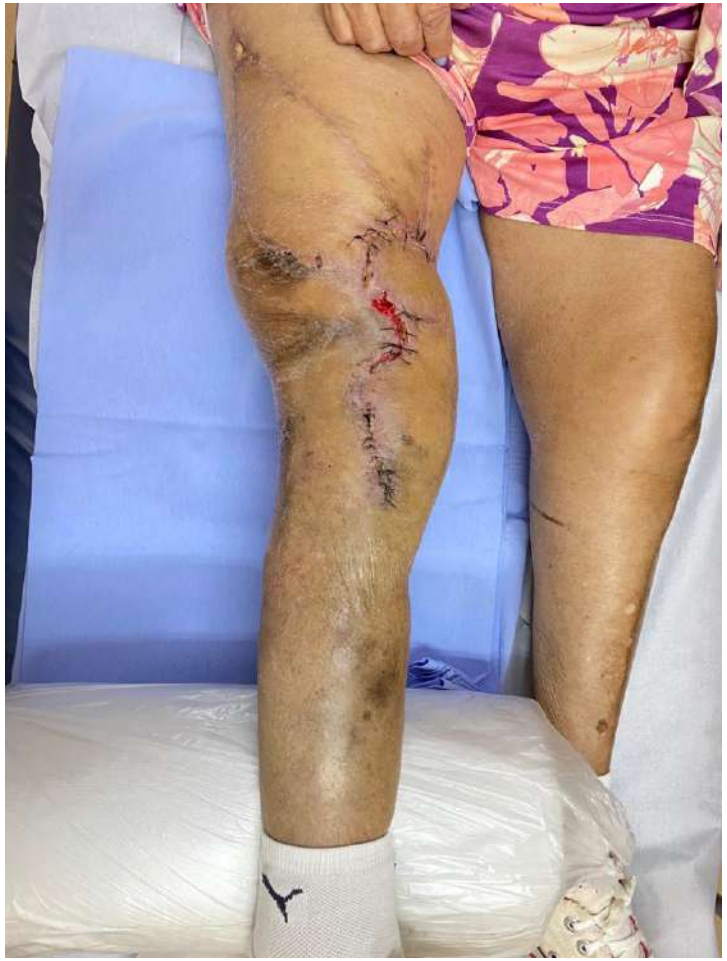
Pós de 11 dias



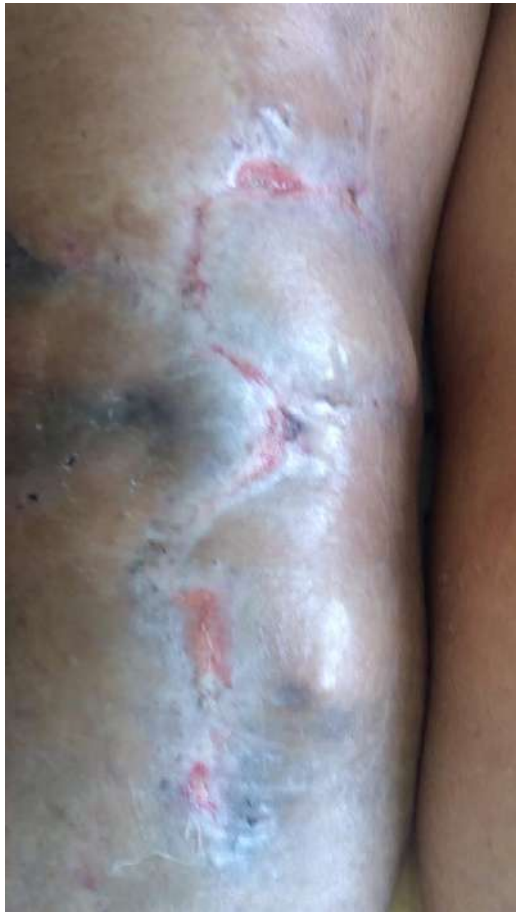


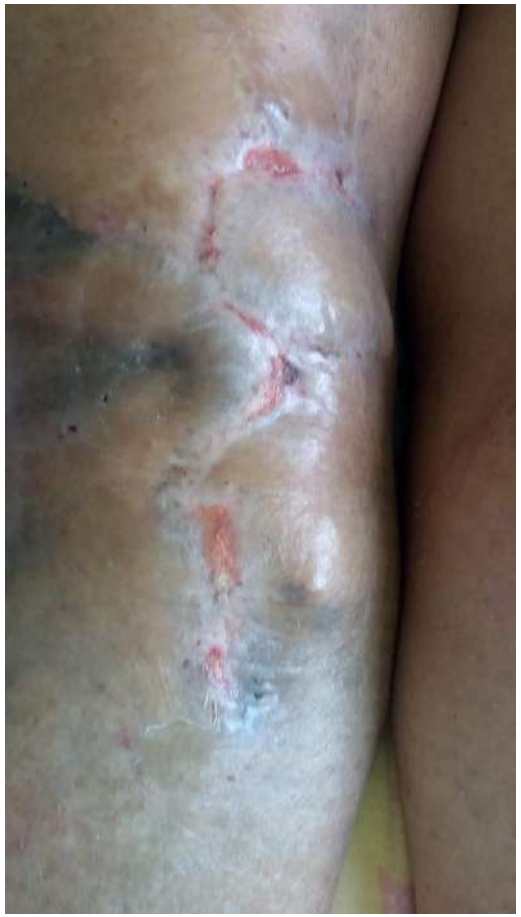
Pós de 21 dias



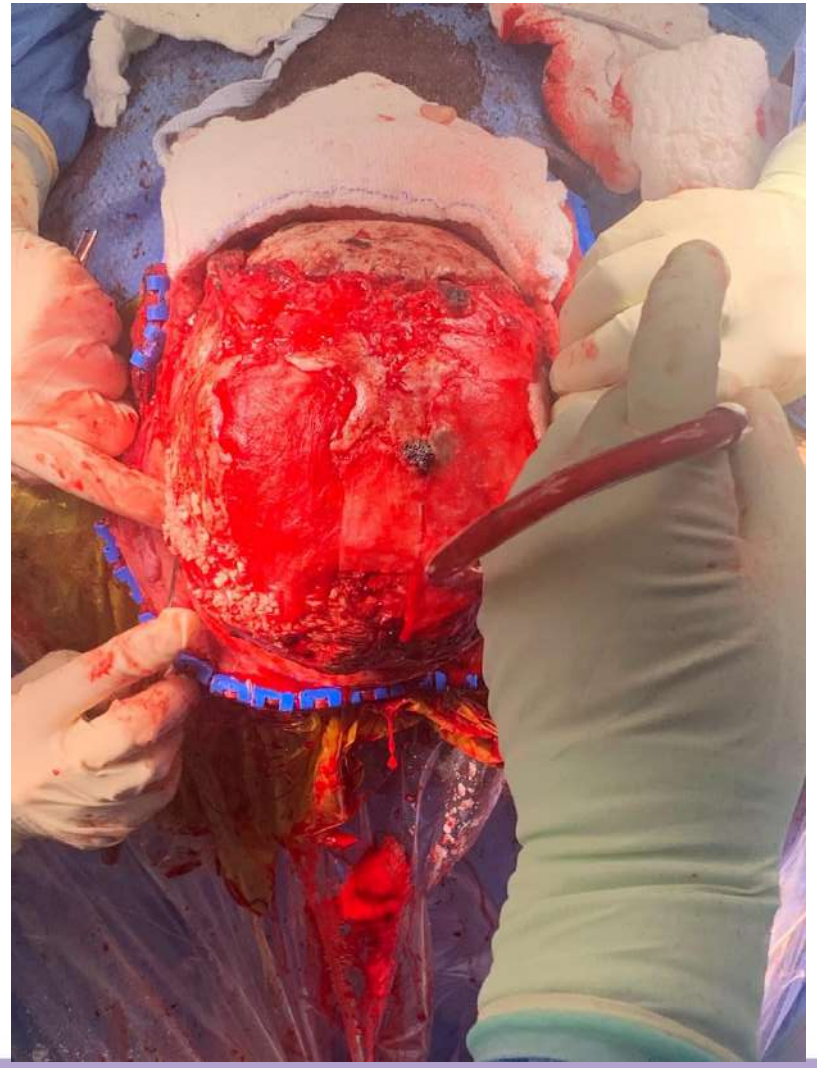


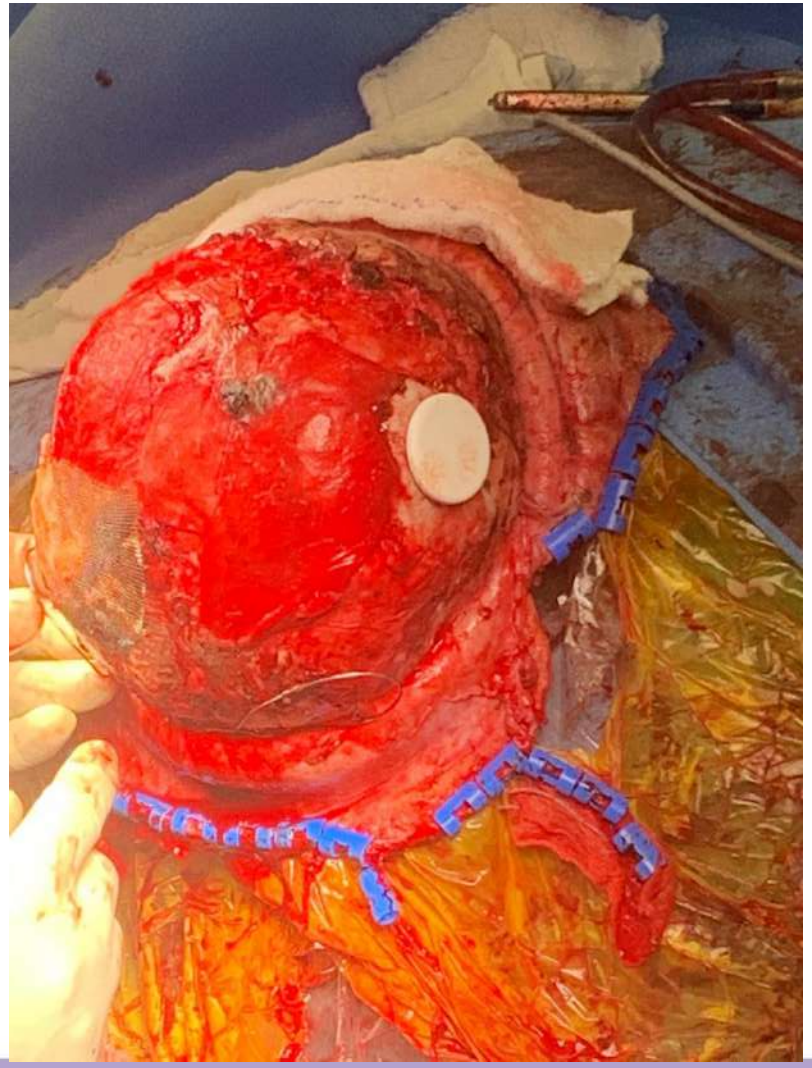
Pós de 40 dias



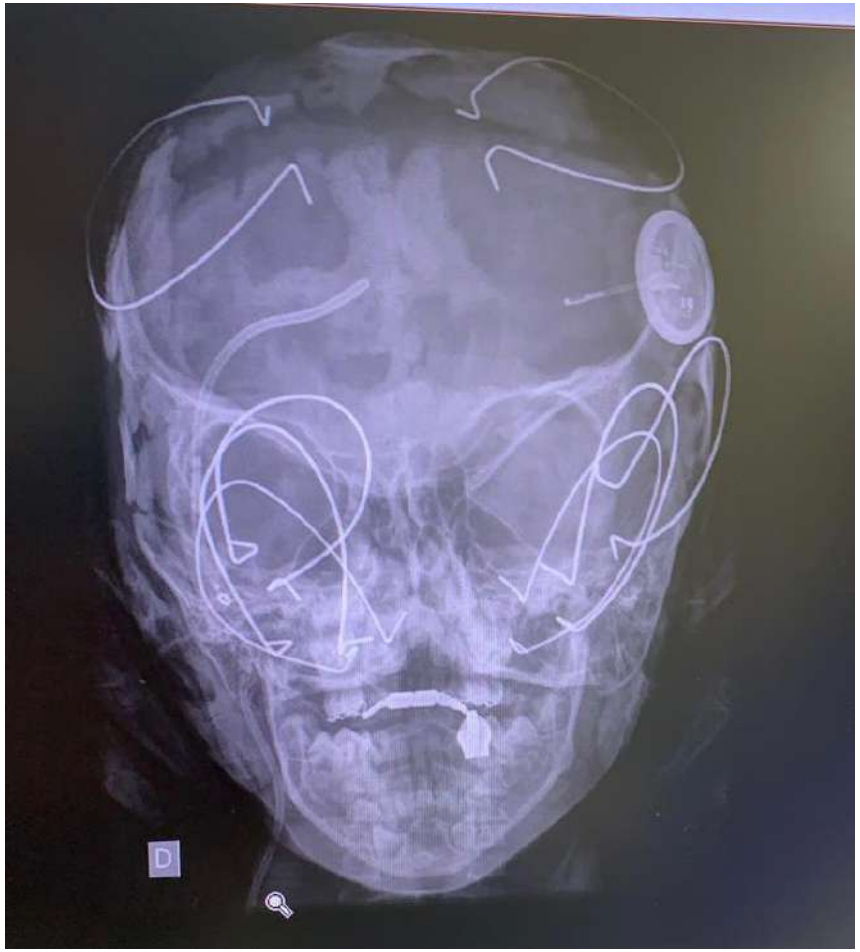


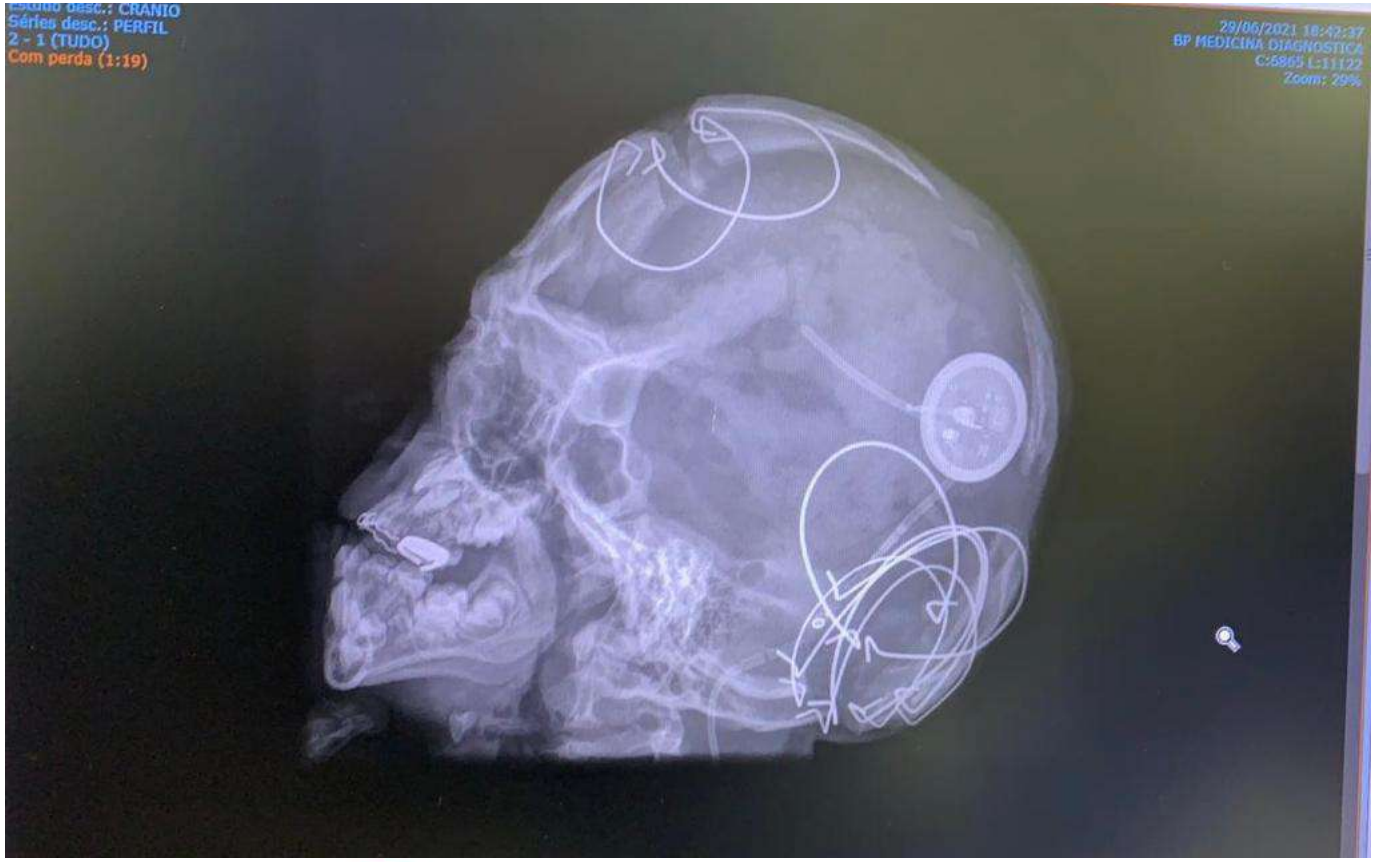
Transoperatório cranioestenose



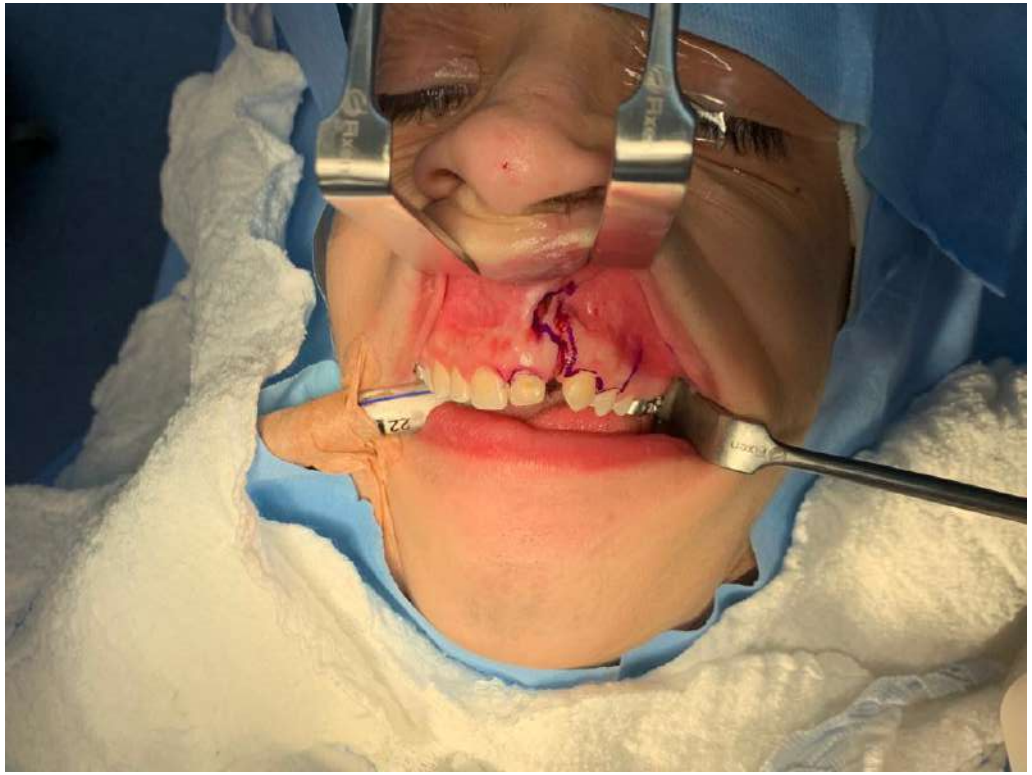


Pós de 30 dias de cranioestenose

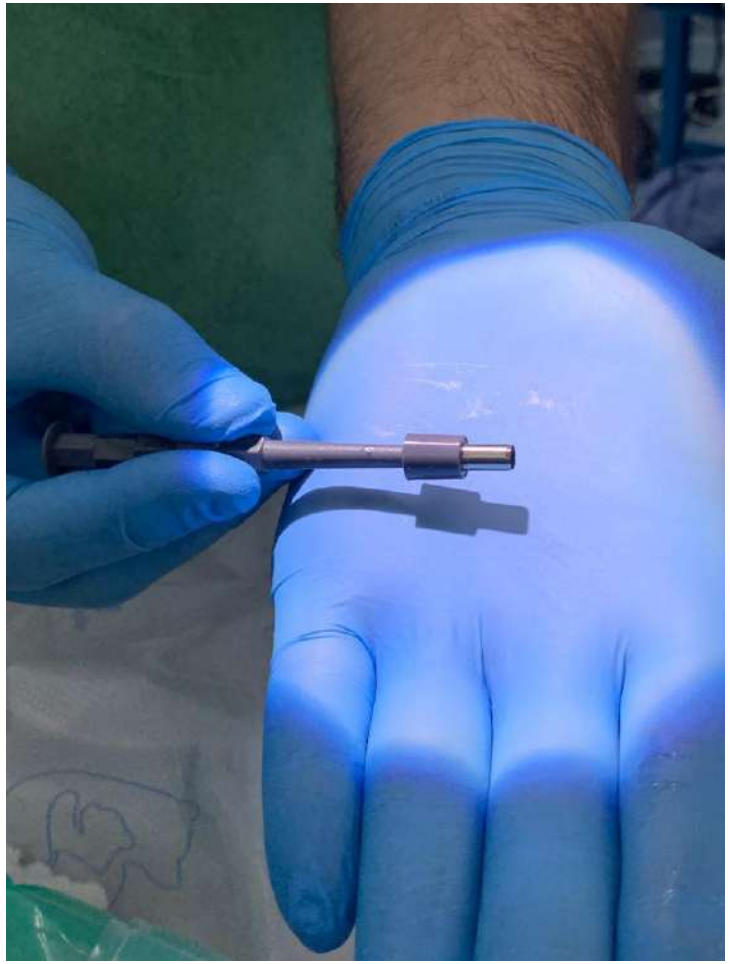


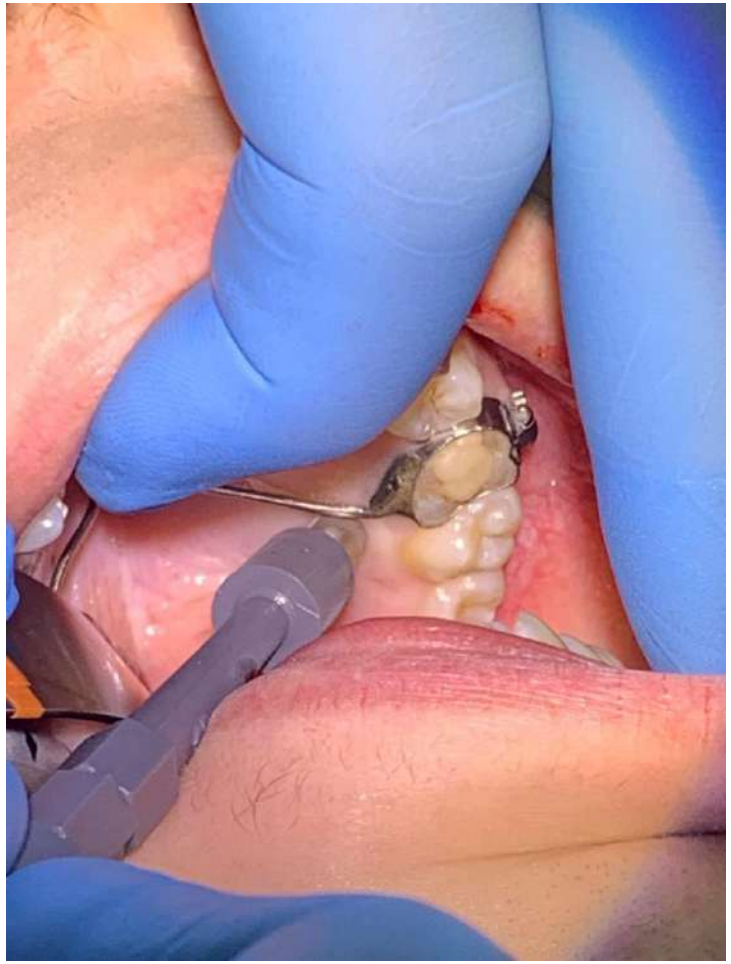


Pré operatório de fissura palatina

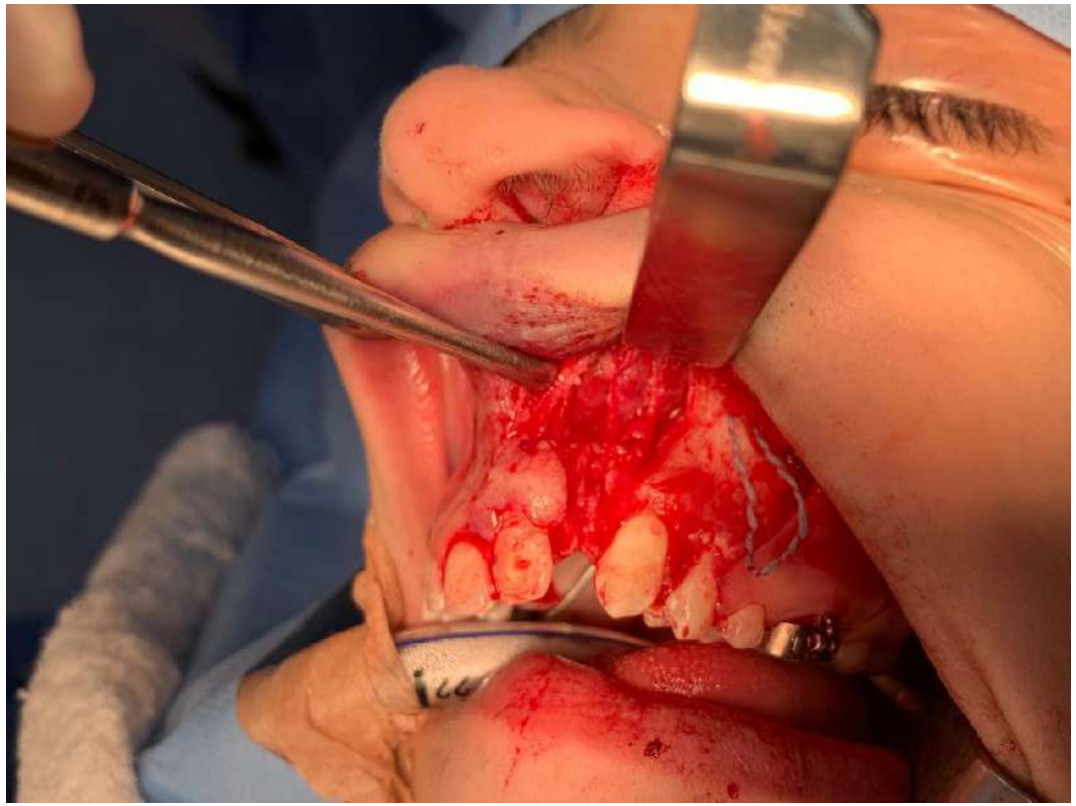


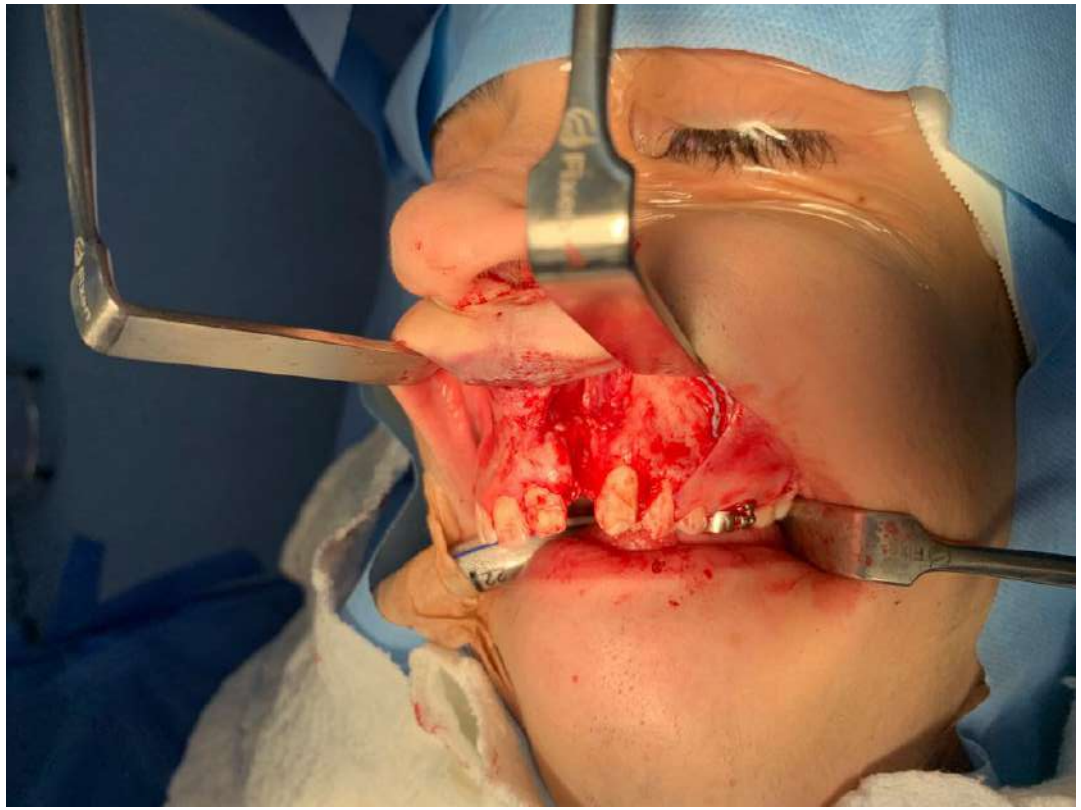
Transoperatório de fissura palatina





Transoperatório de fissura palatina

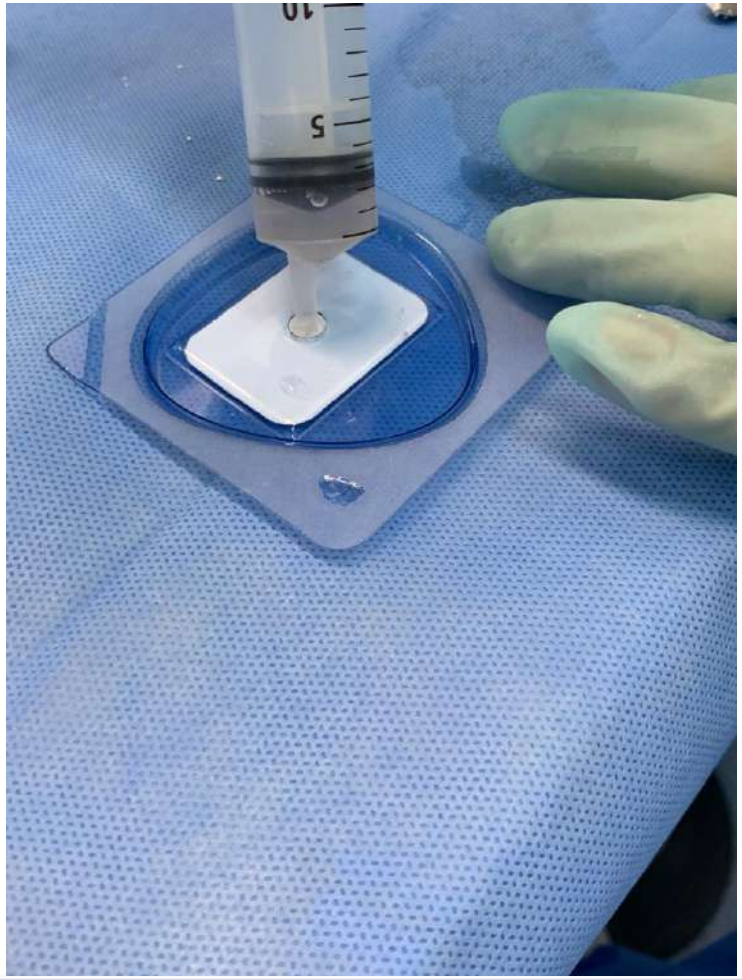


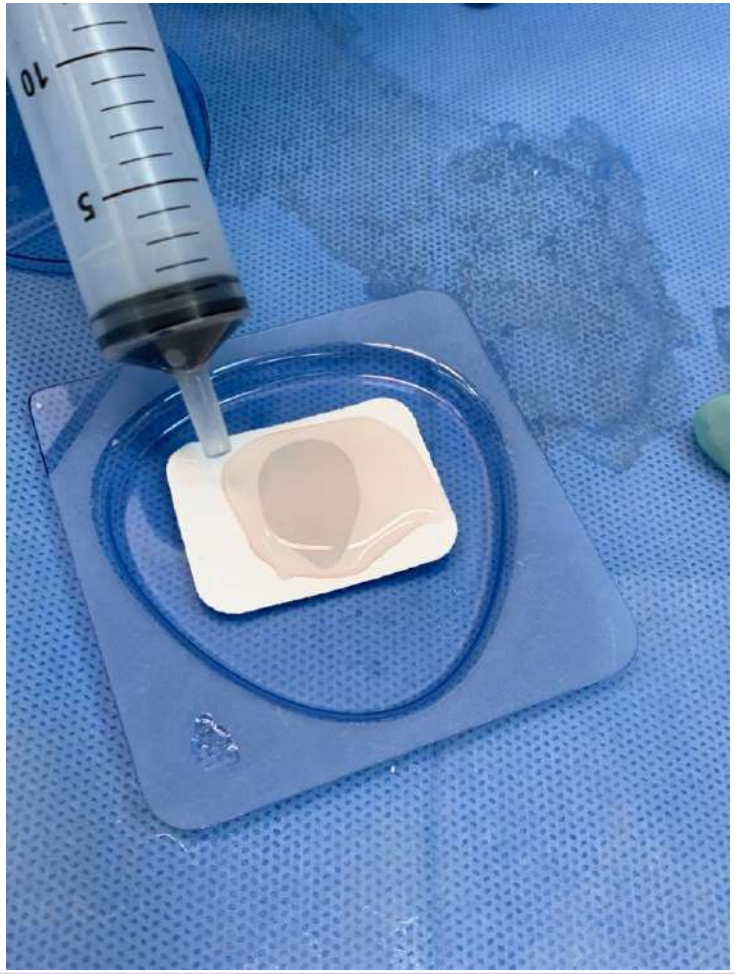


Transoperatório de fissura palatina

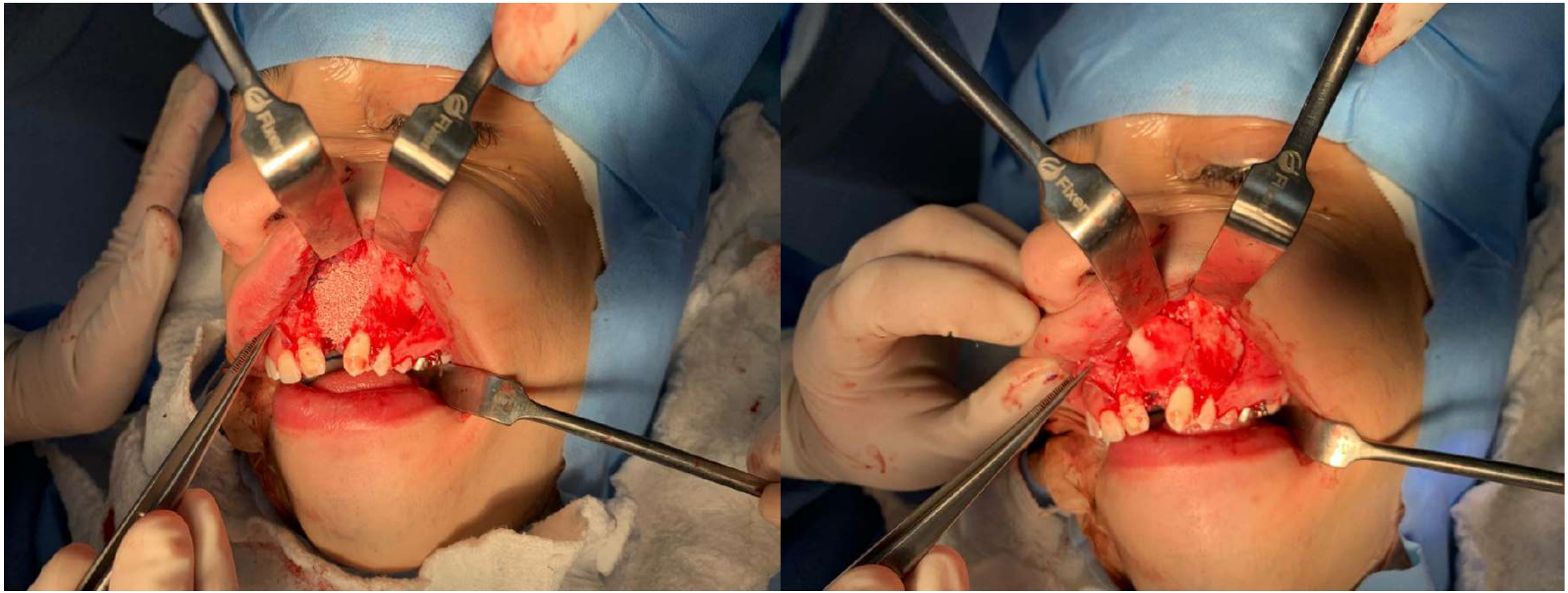
Associação com substituto ósseo

Associação com membrana de PDO

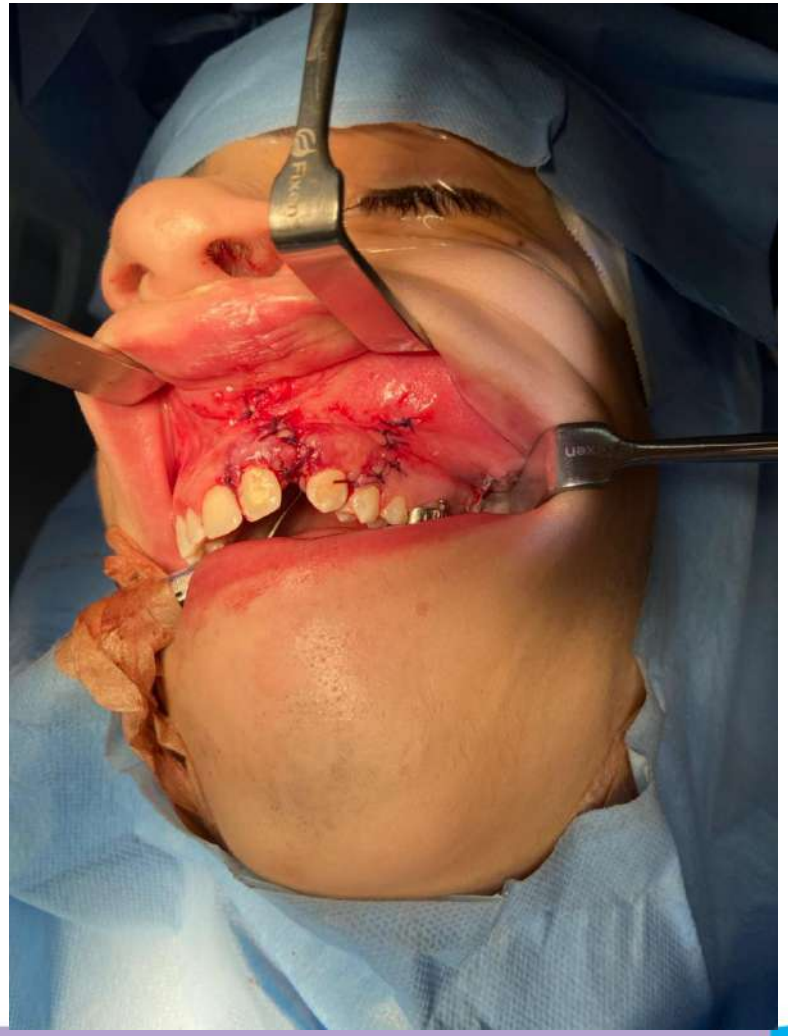




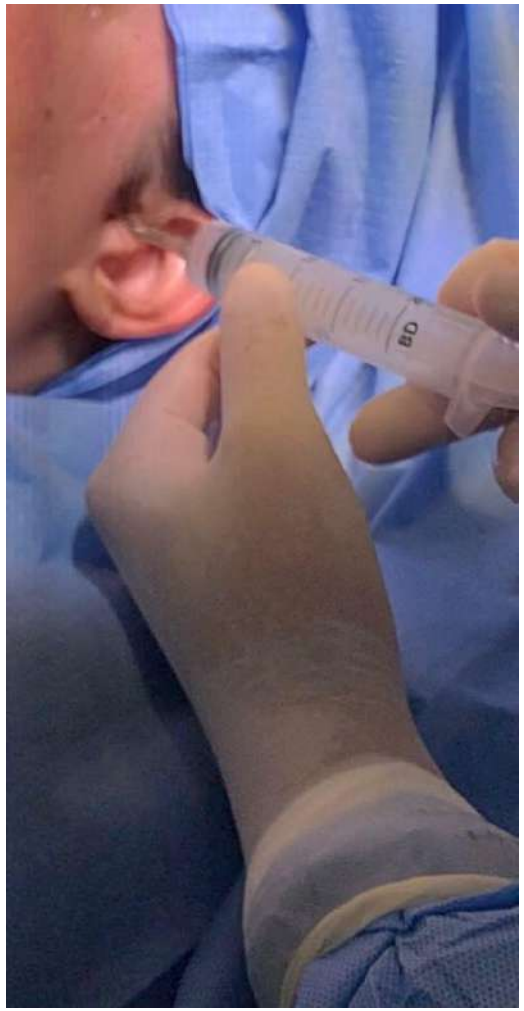
Transoperatório com utilização de substituto ósseo+ membrana de PDO



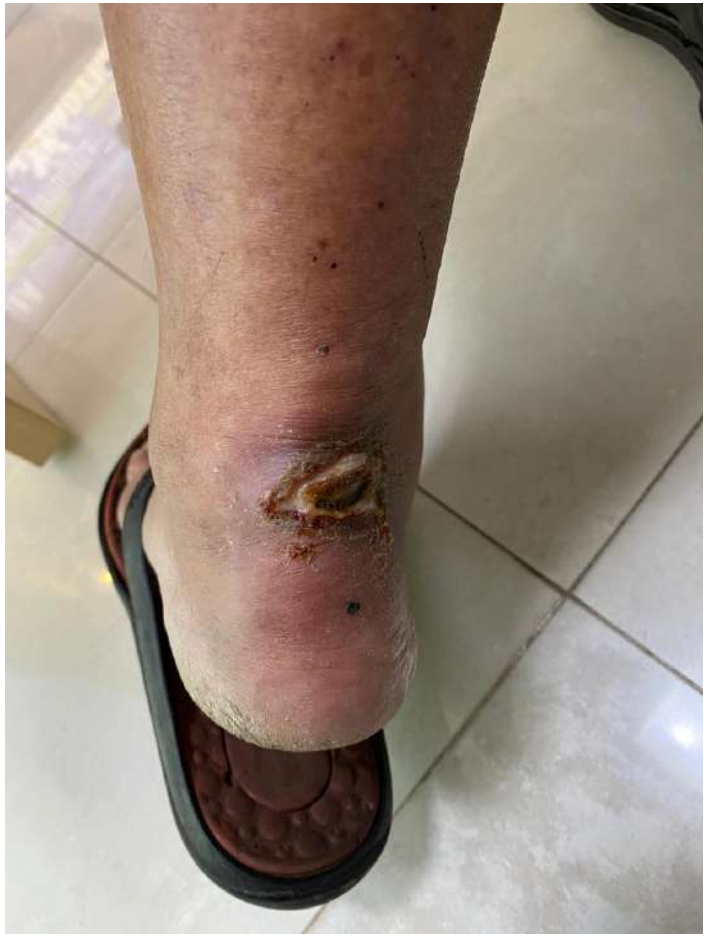
Fechamento de fissura palatina

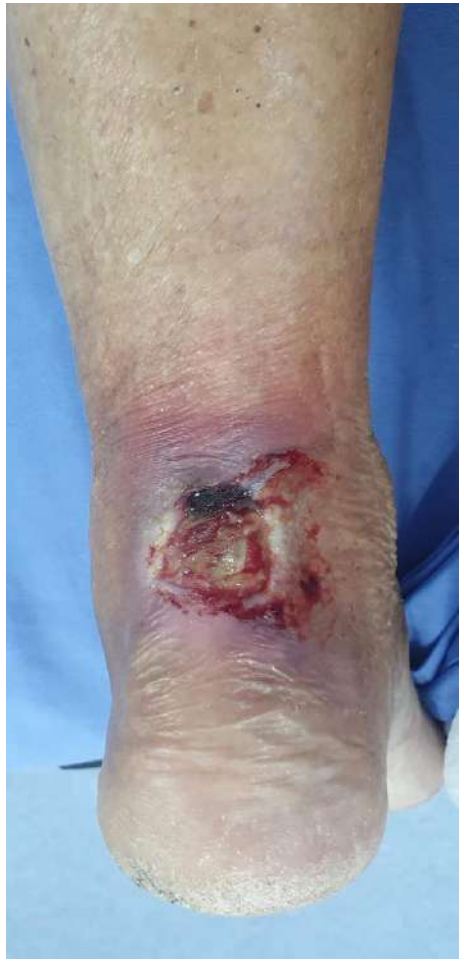


Alteração degenerativa do côndilo mandibular

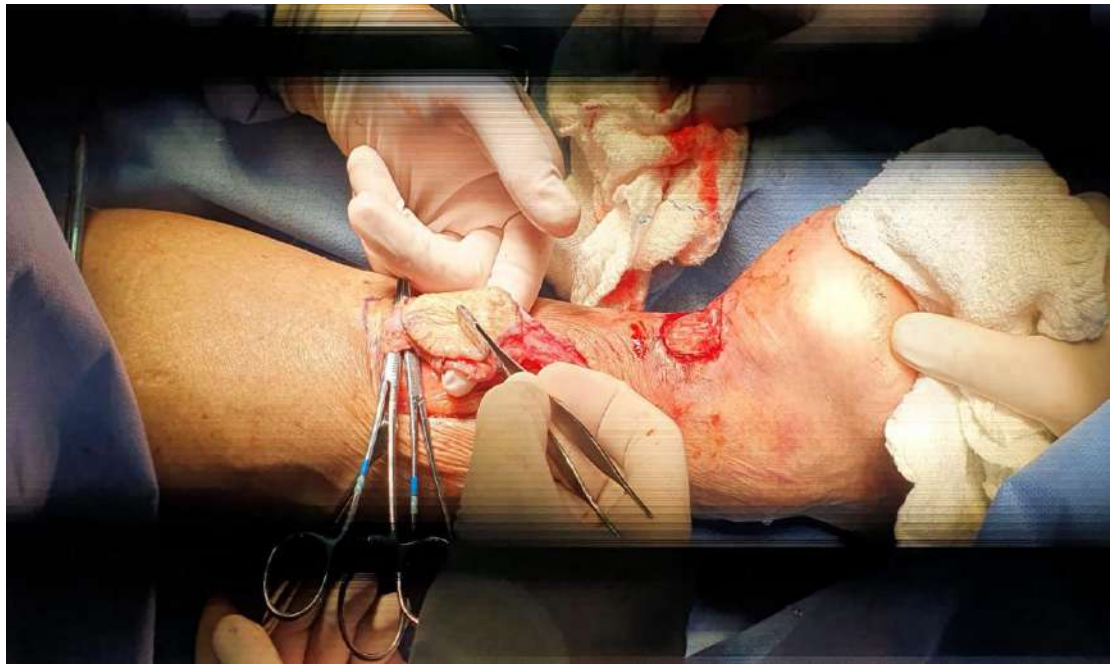


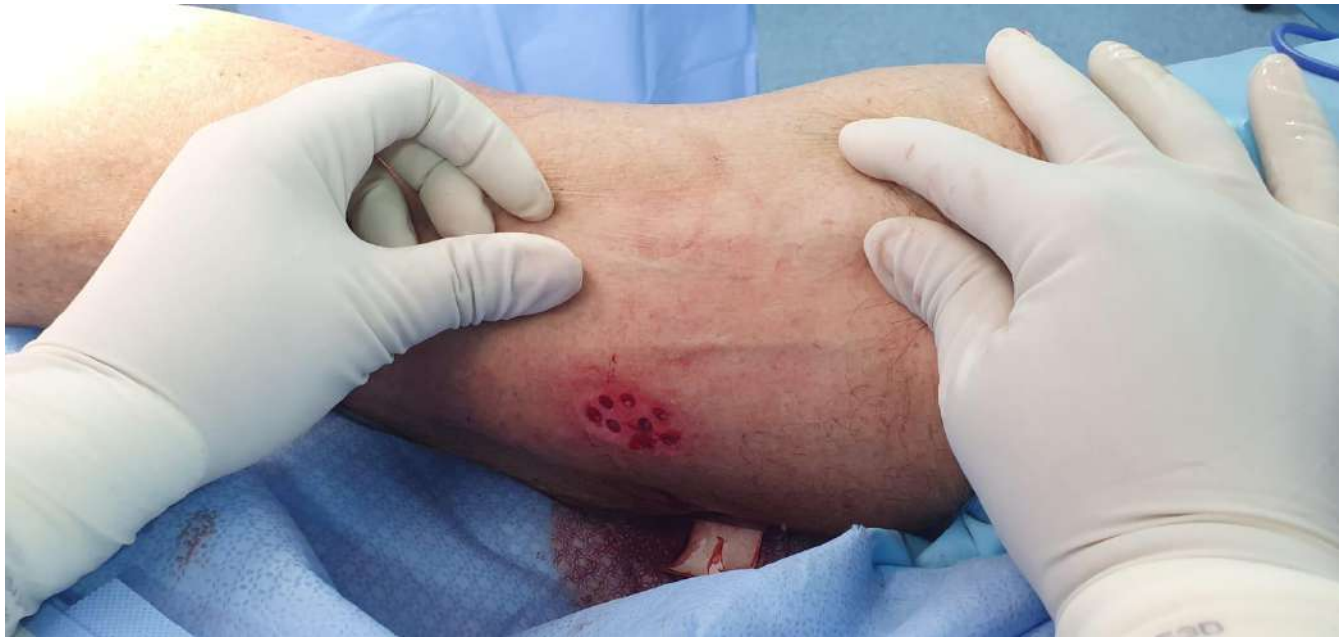
Pré operatório de deiscência cirúrgica



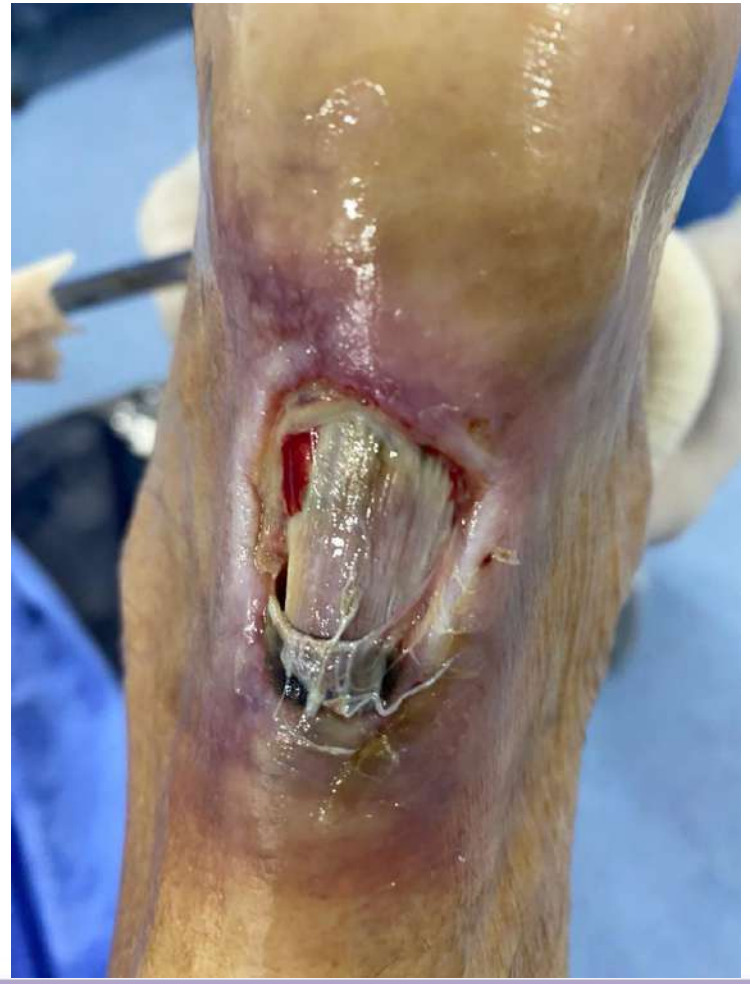


Transoperatório de deiscência cirúrgica

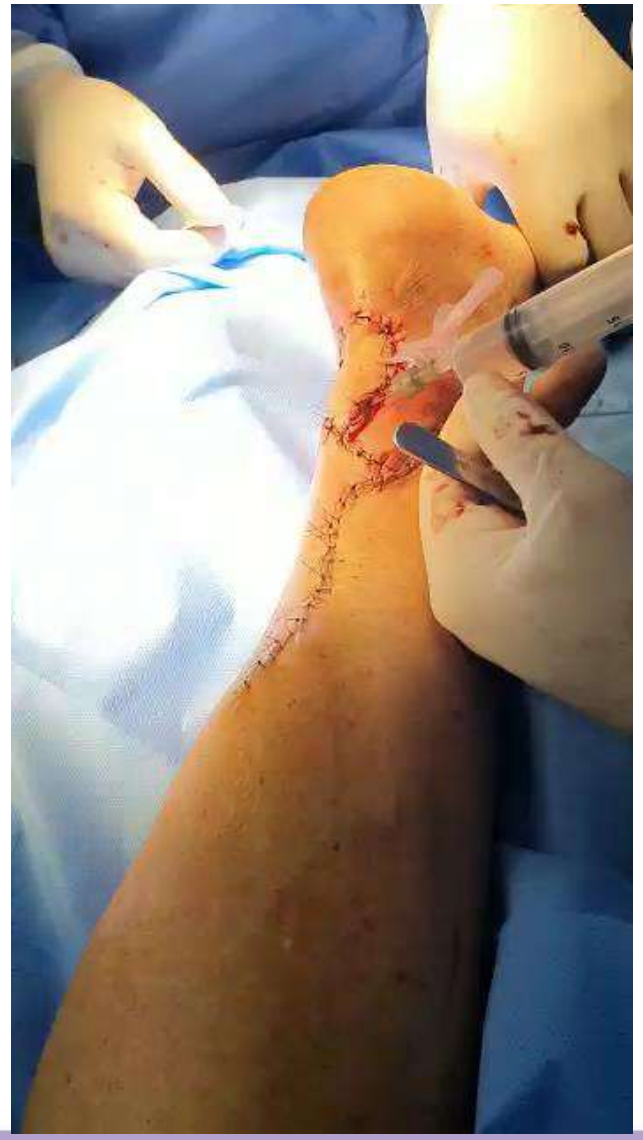




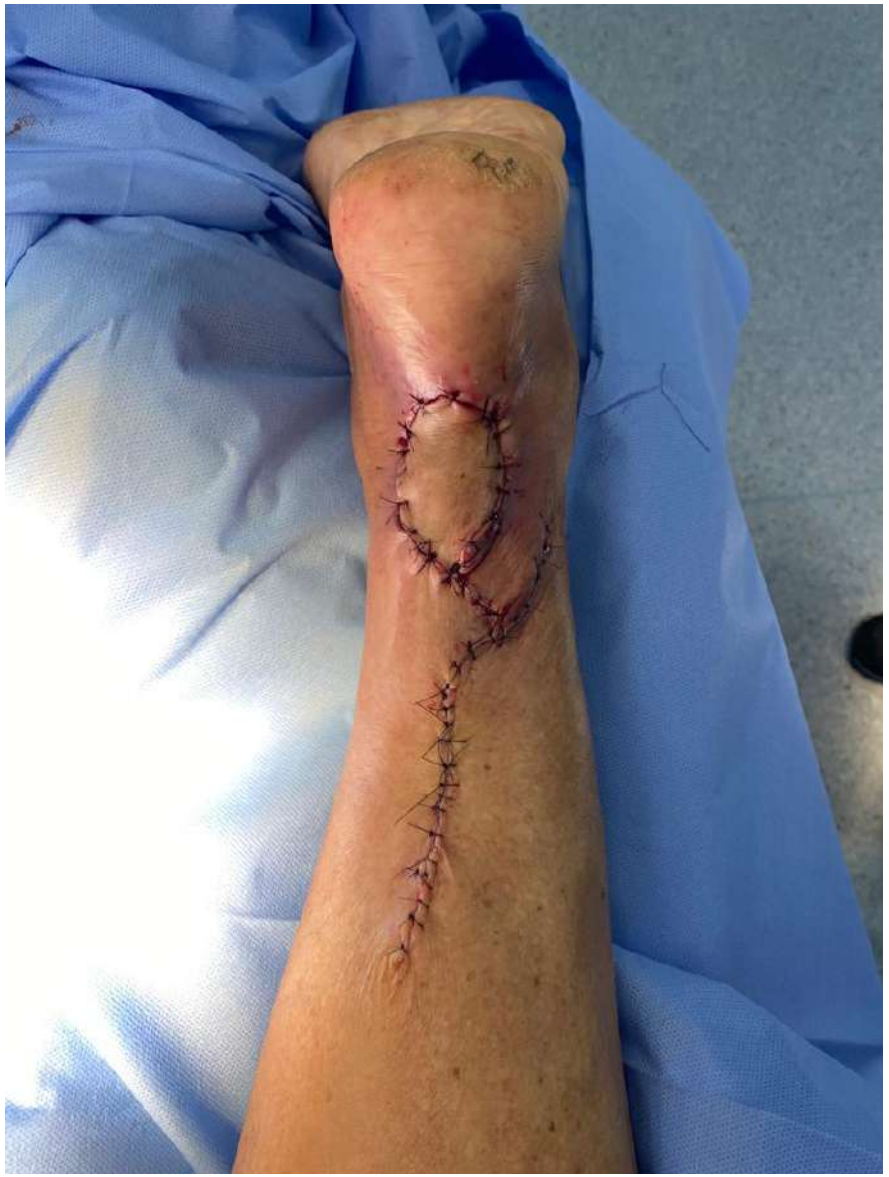
Transoperatório de deiscência cirúrgica



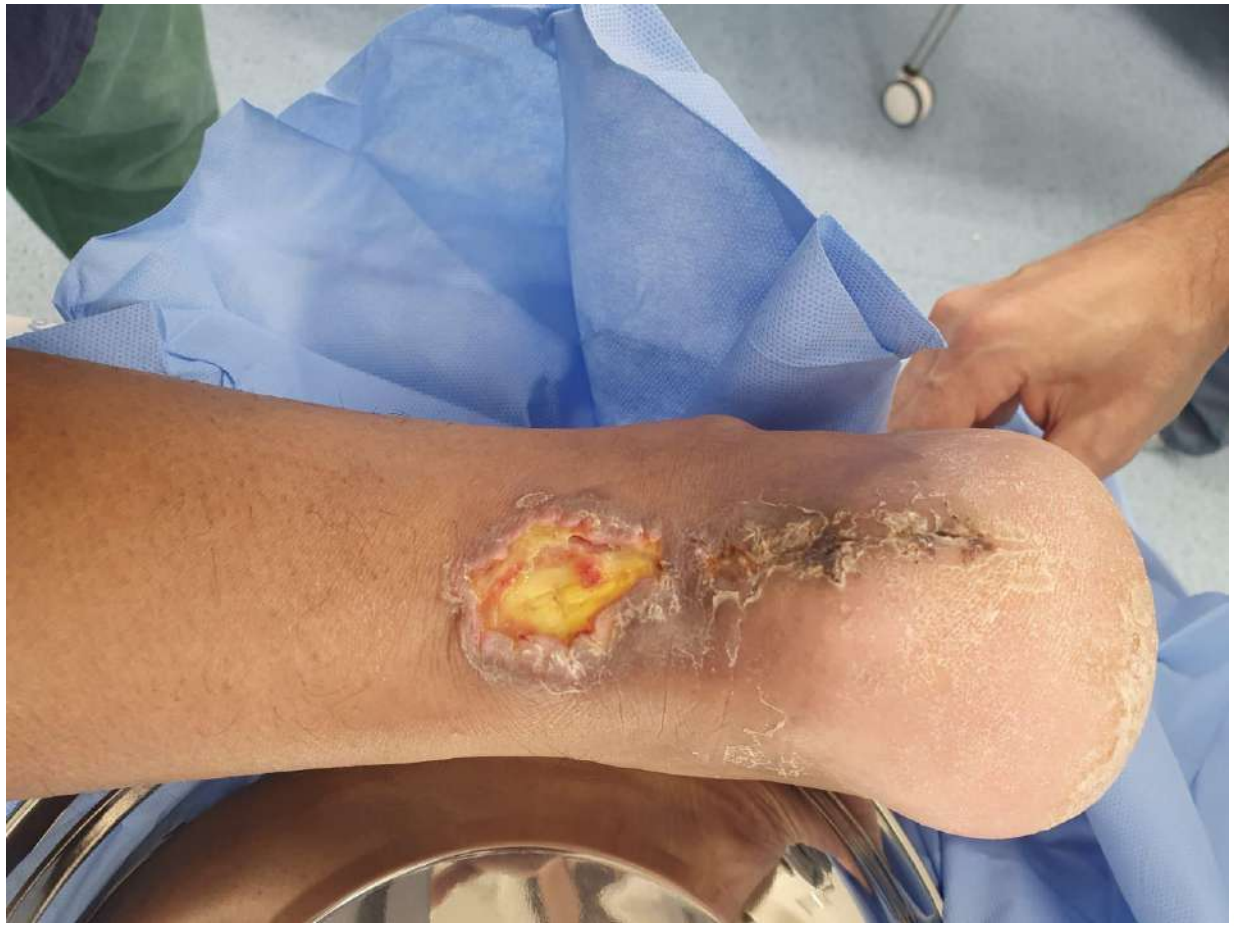
Transoperatório de deiscência cirúrgica



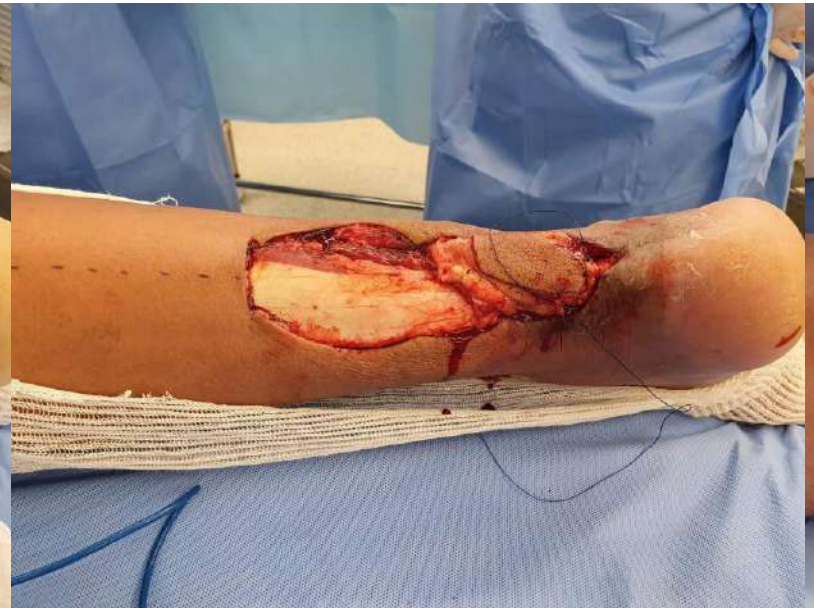
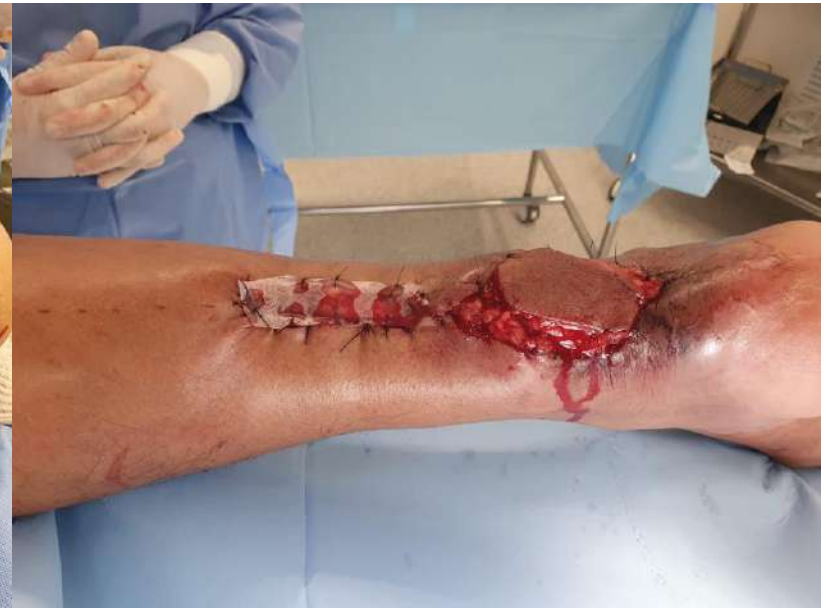
Transoperatório de deiscência cirúrgica



Pré operatório de deiscência de sutura



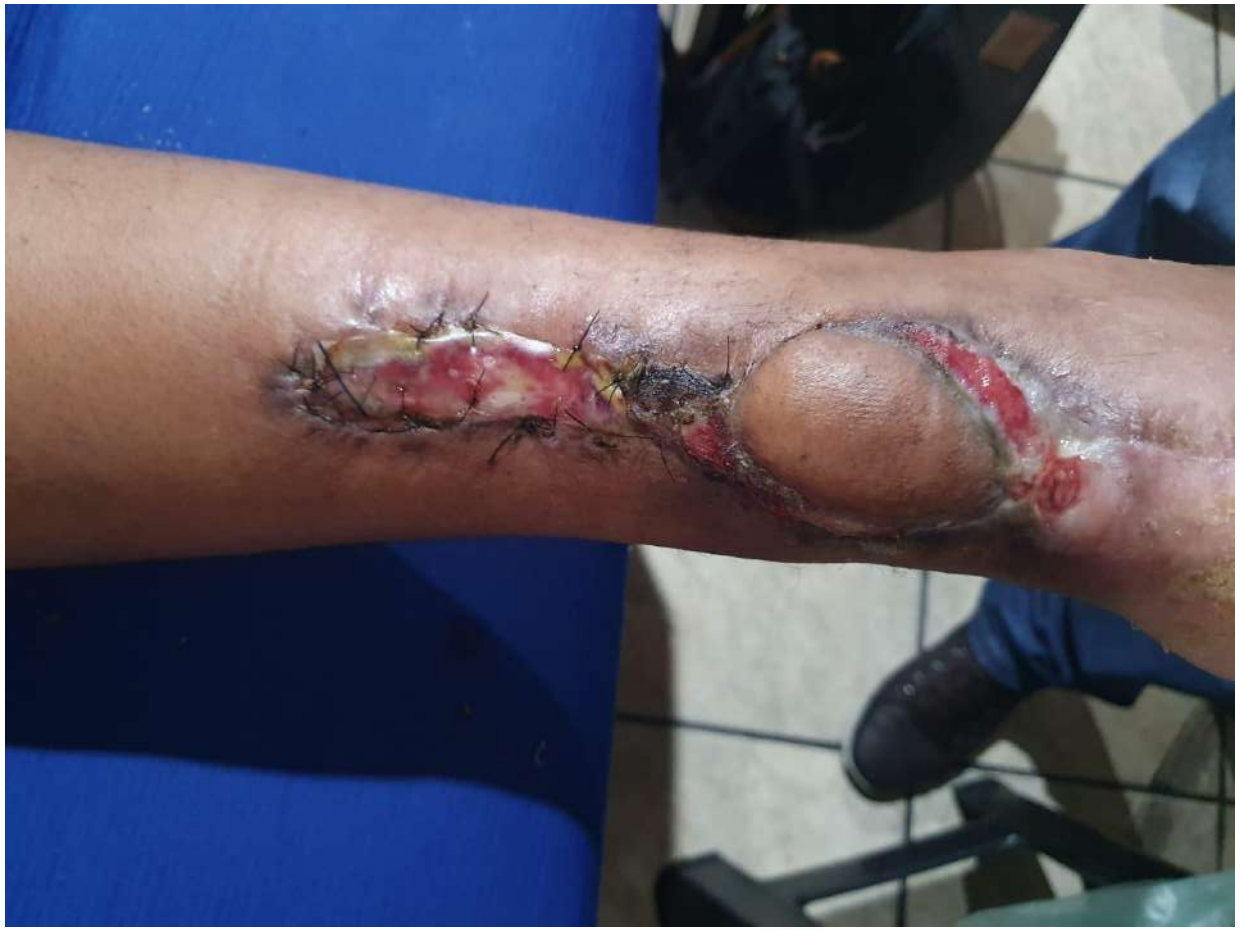
Transoperatório

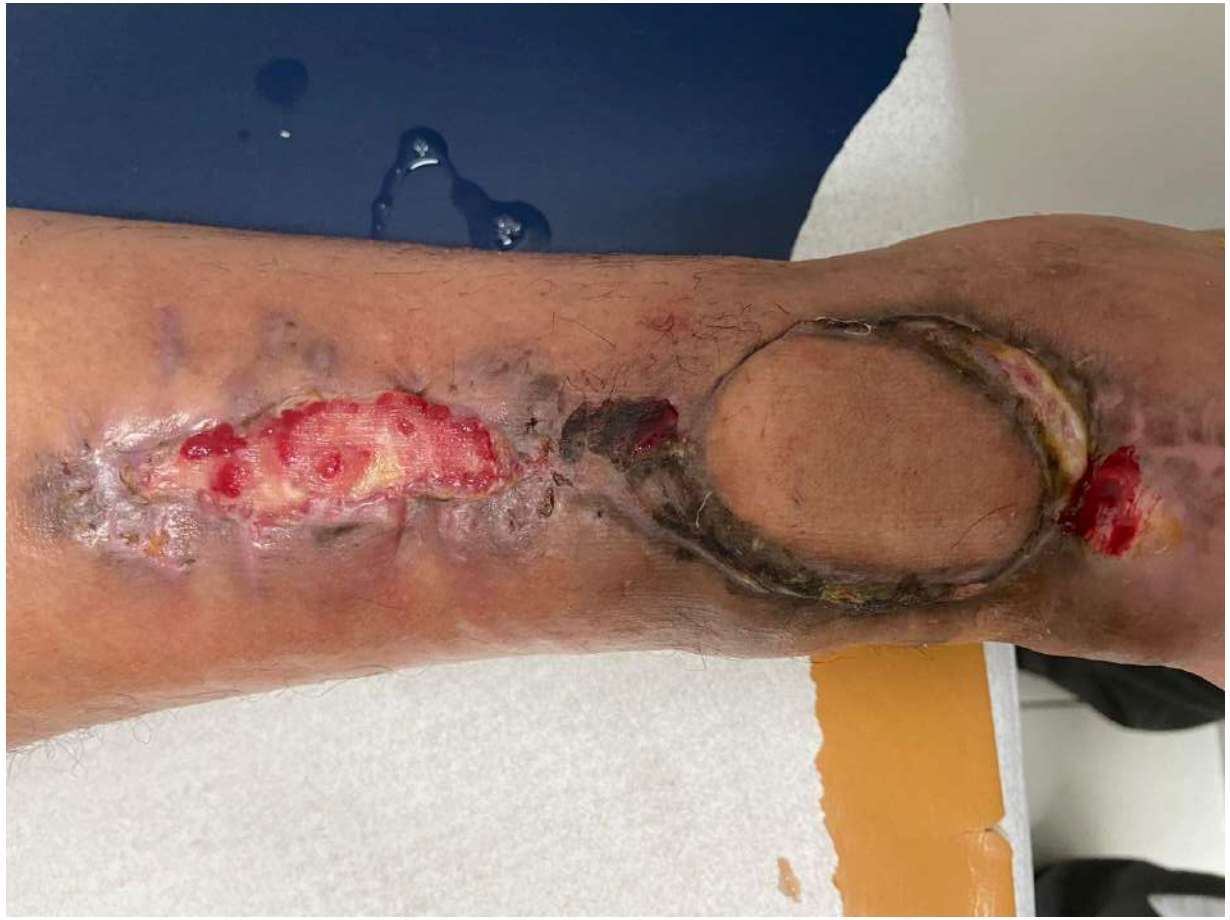
Pós de 4 dias

Pós de 11 dias

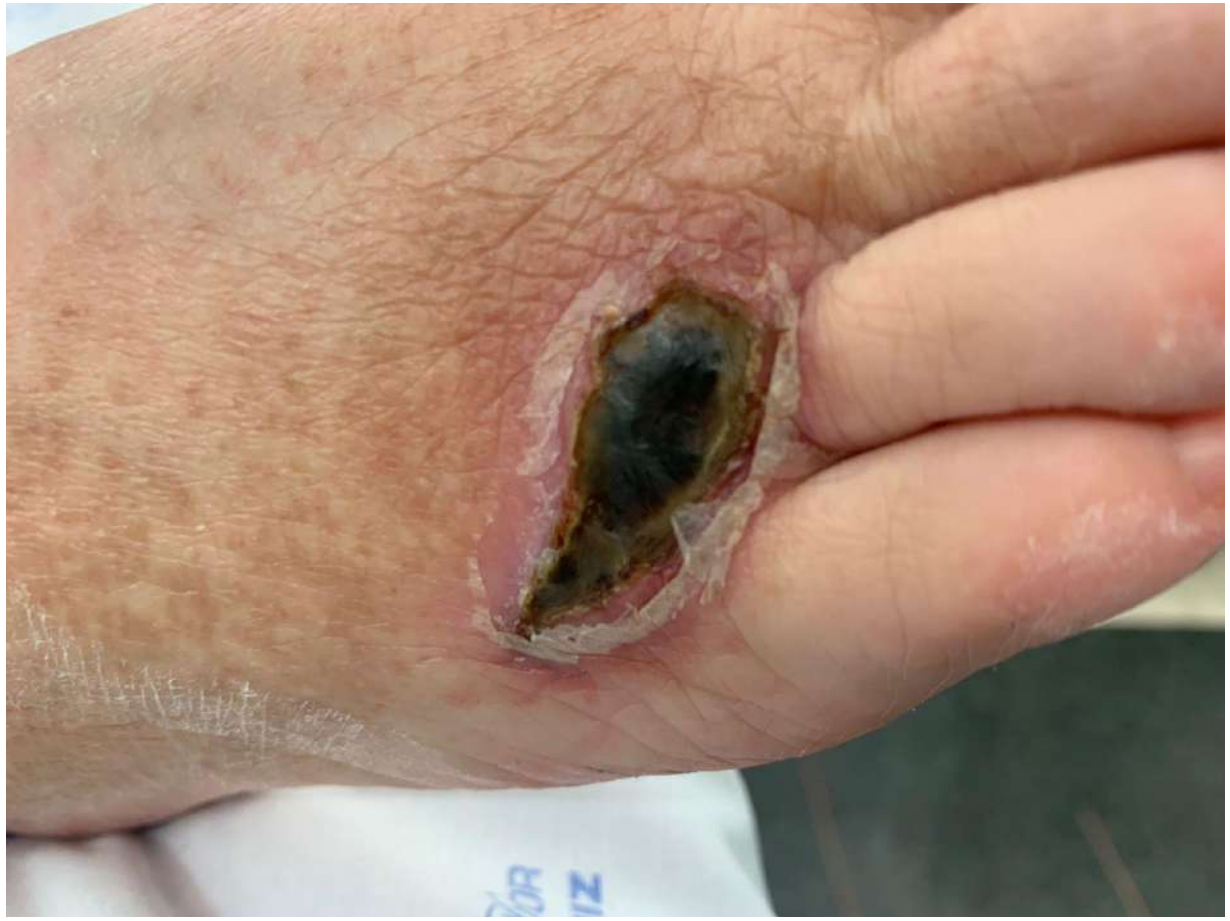
18 dias de PO

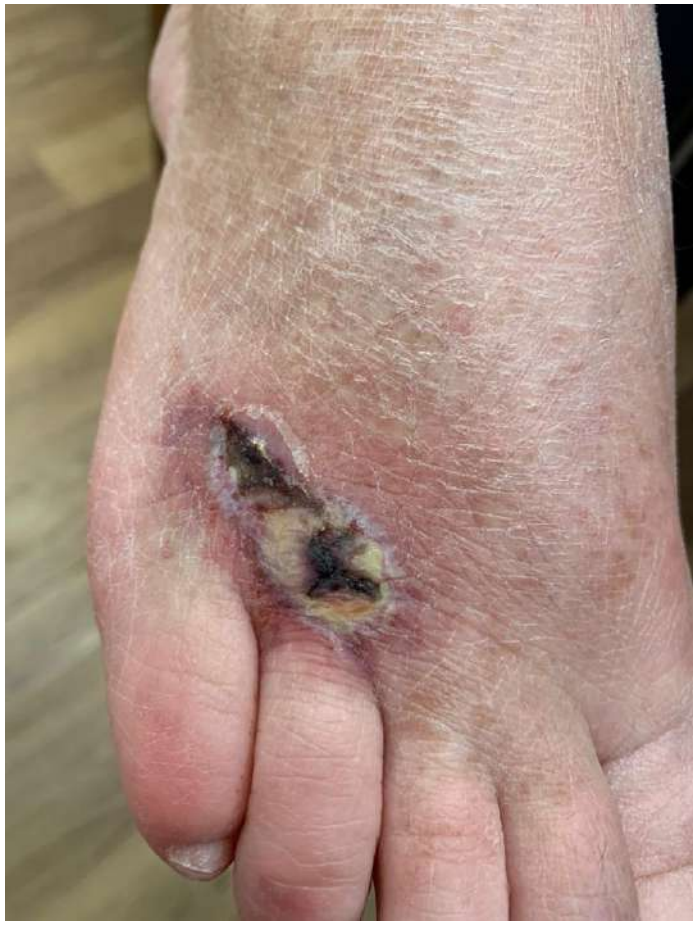


28 dias de PO



Úlcera de pé diabético





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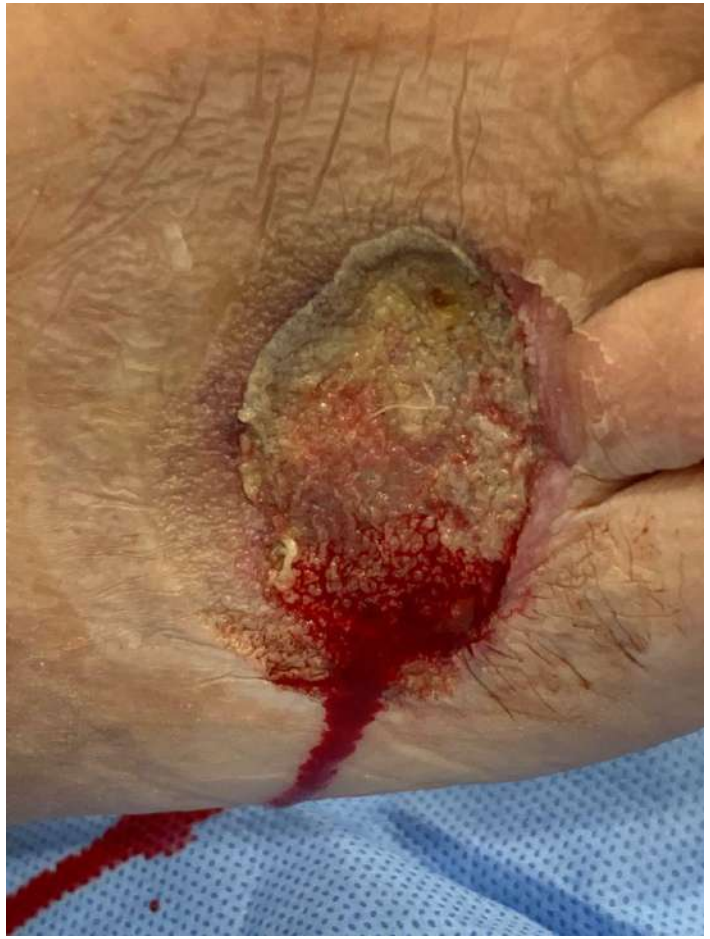
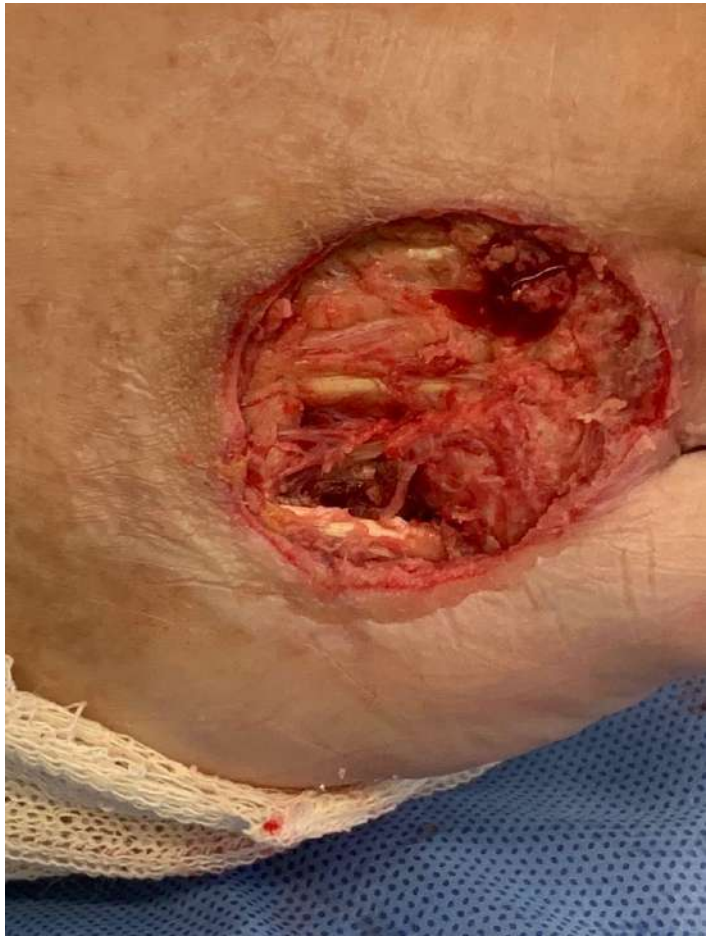
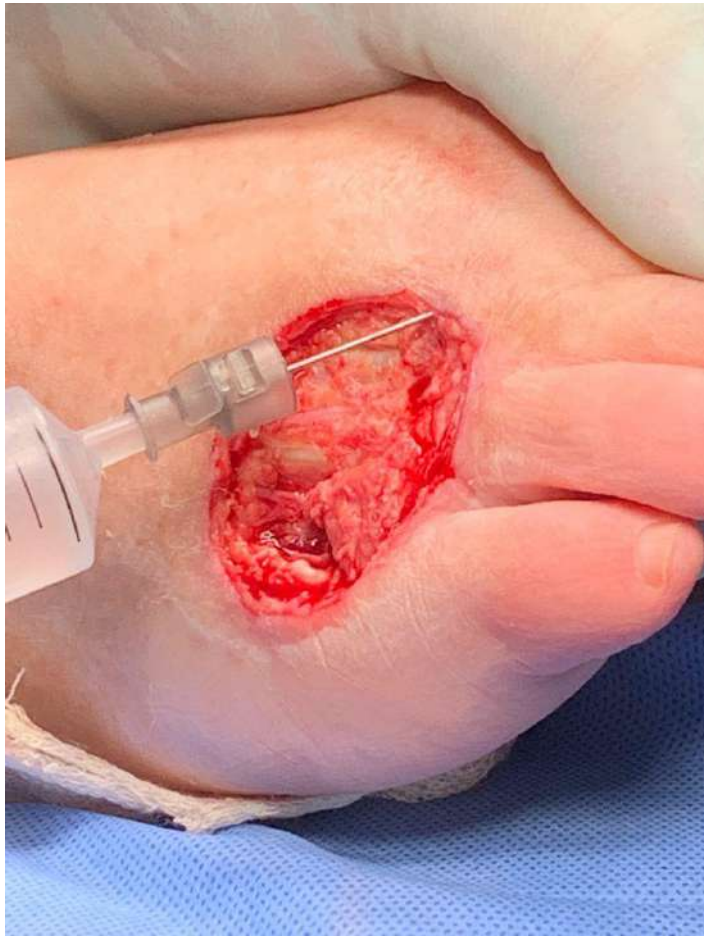
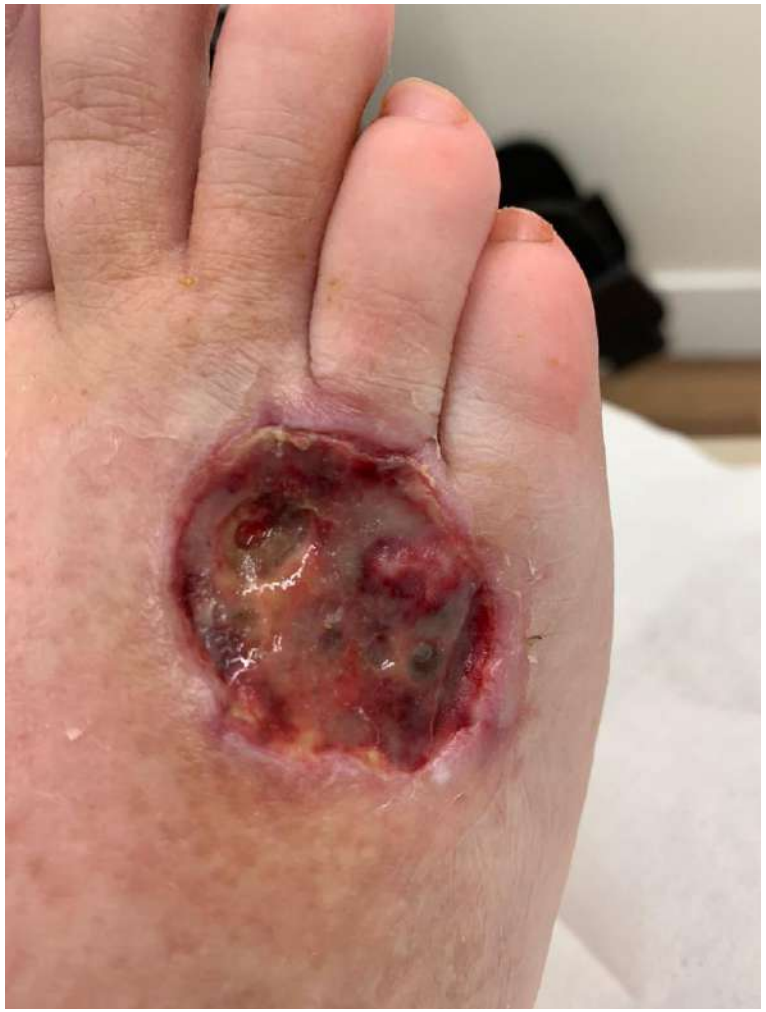
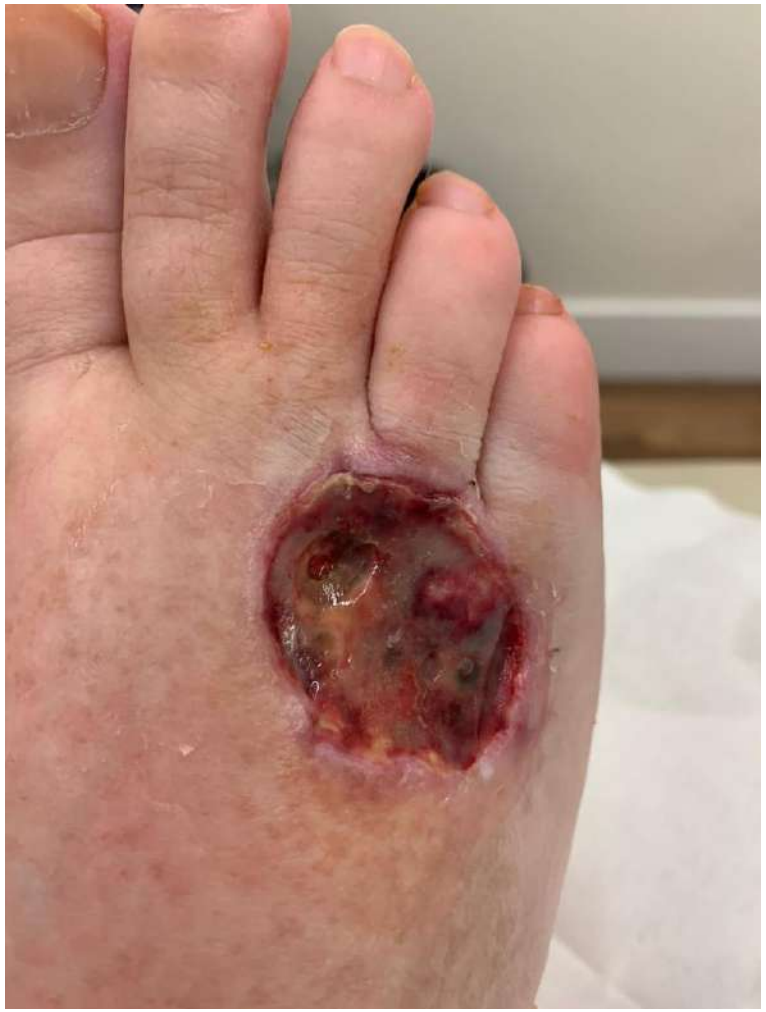




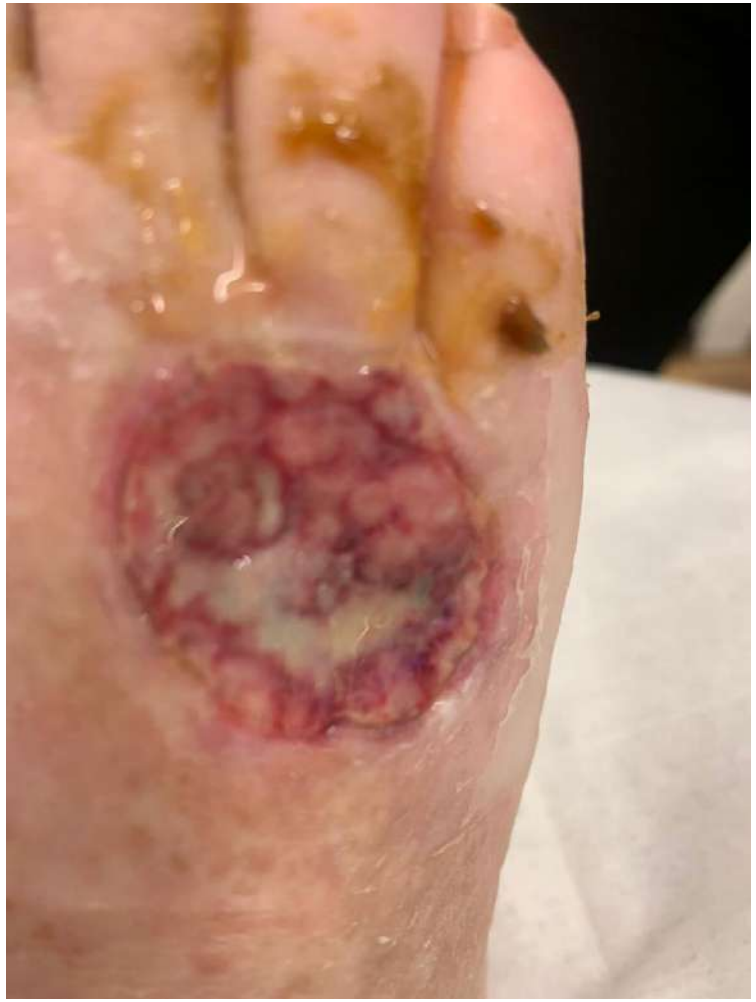


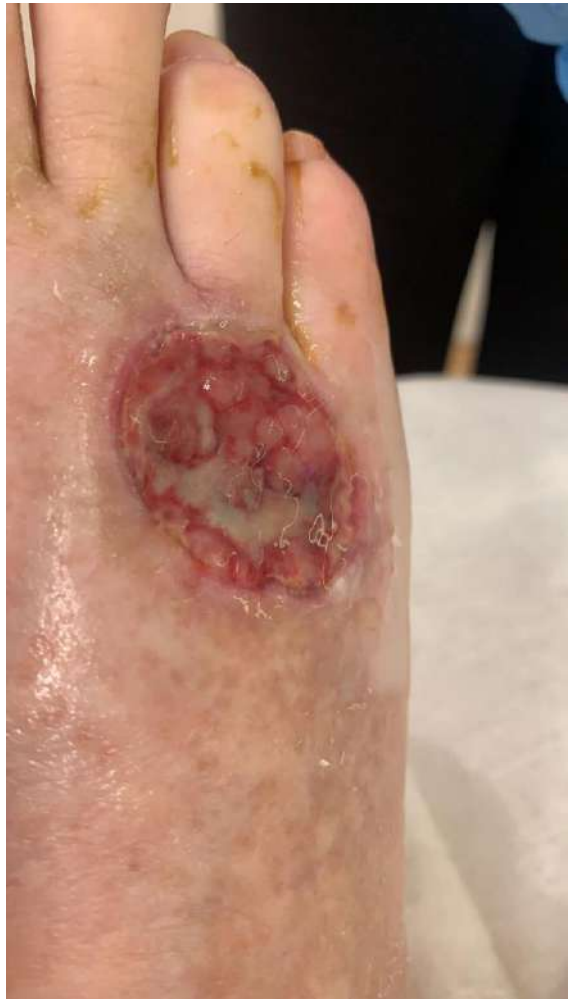
Úlcera de pé diabético /Pós de 4 dias



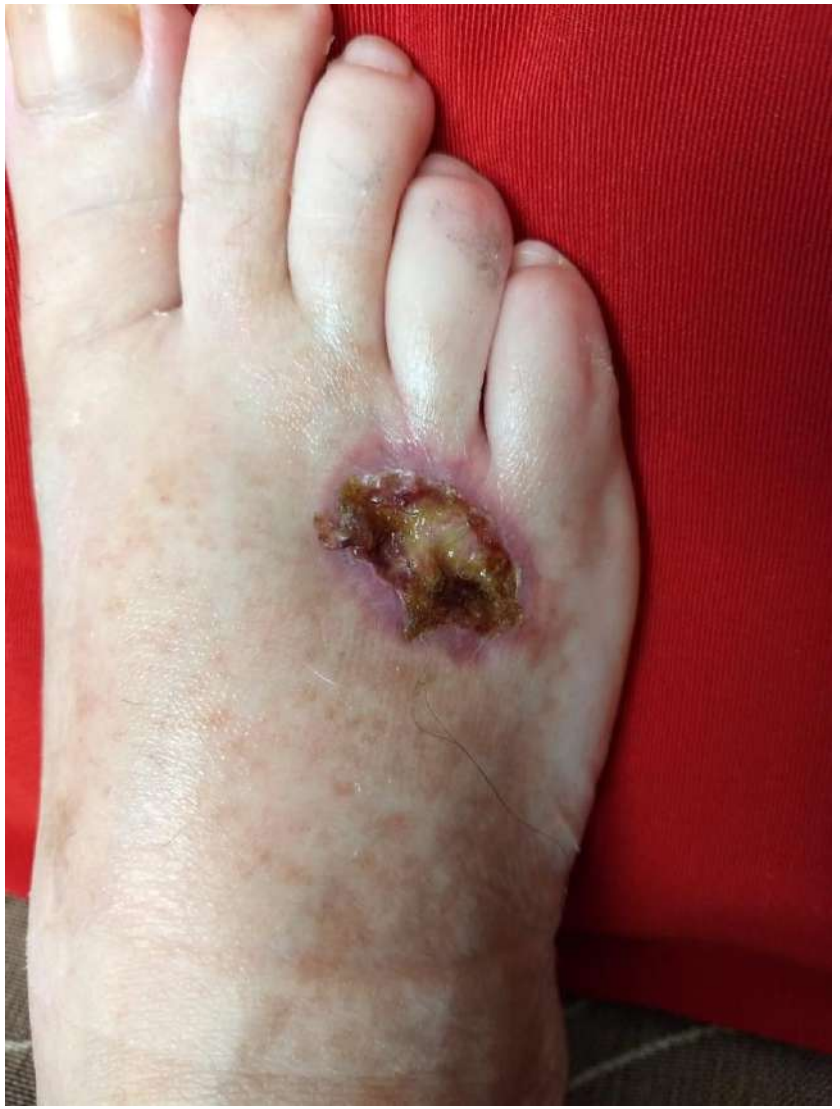


11 dias PO

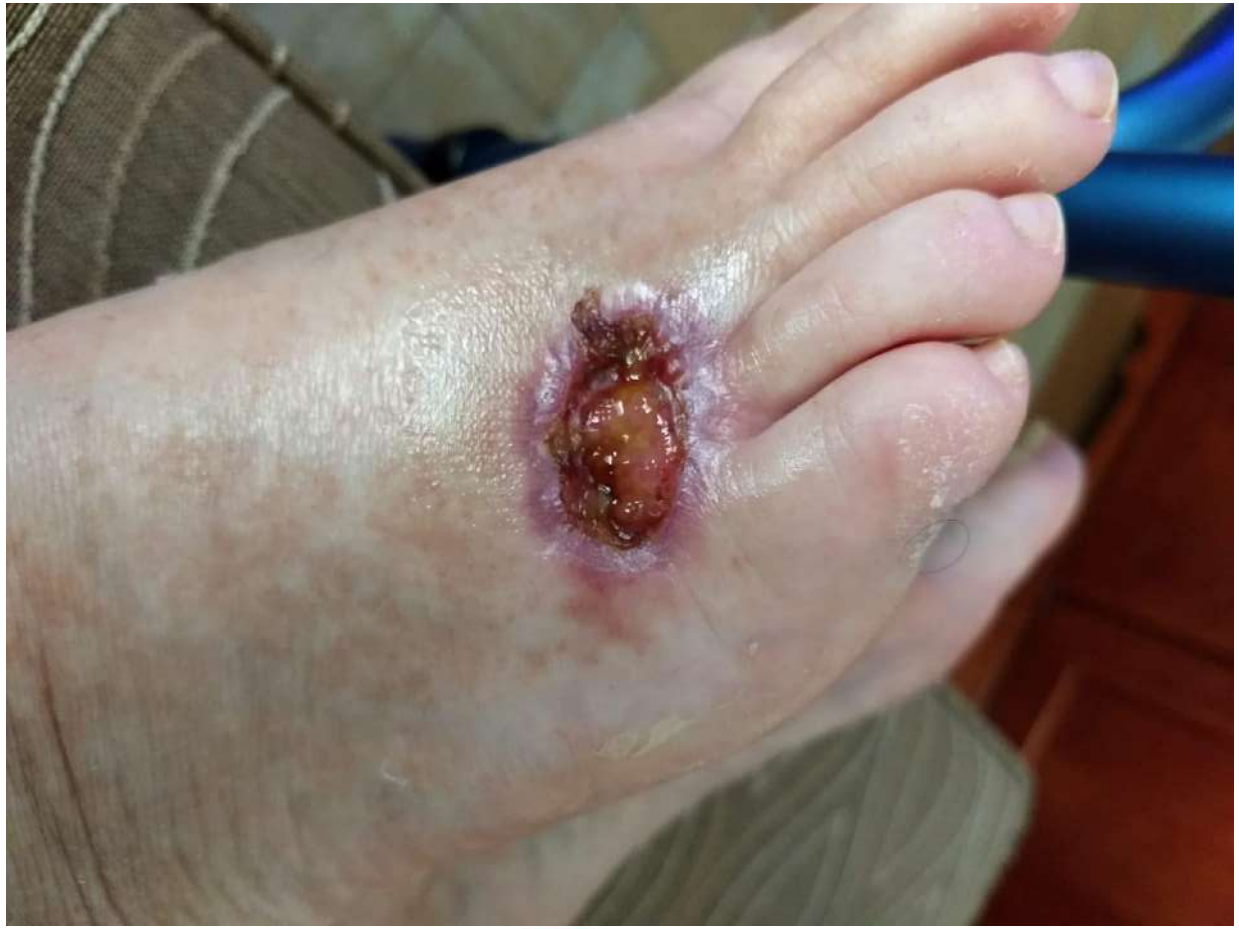




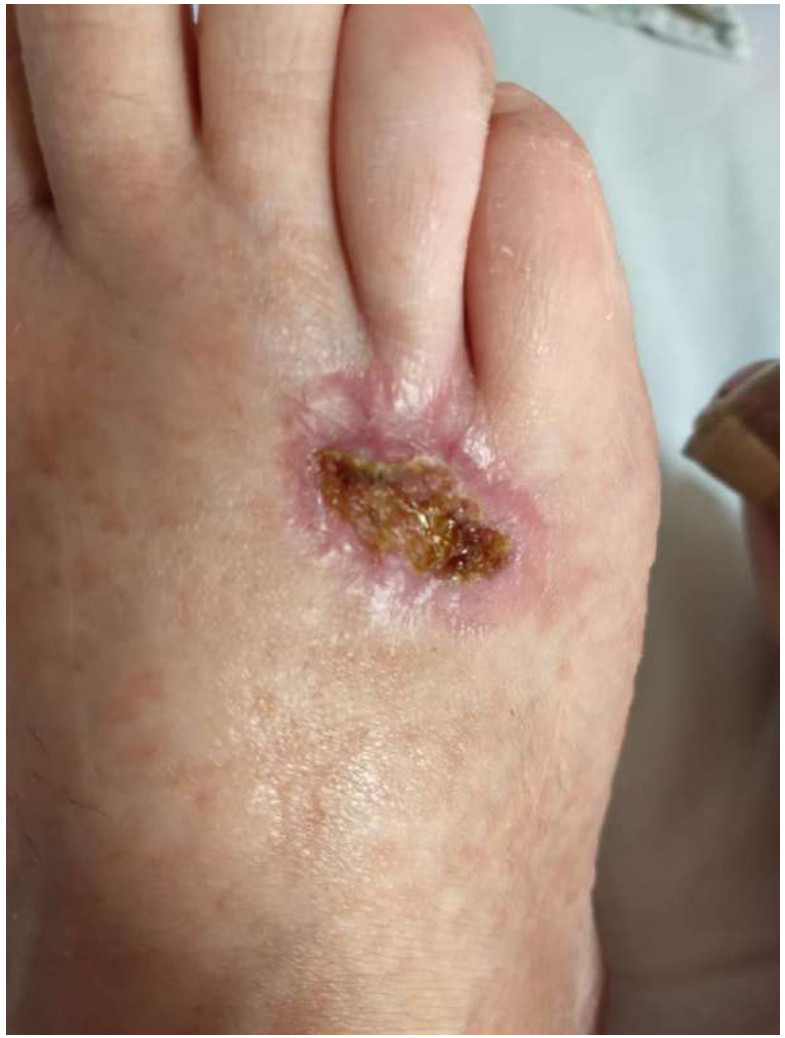
18 dias PO



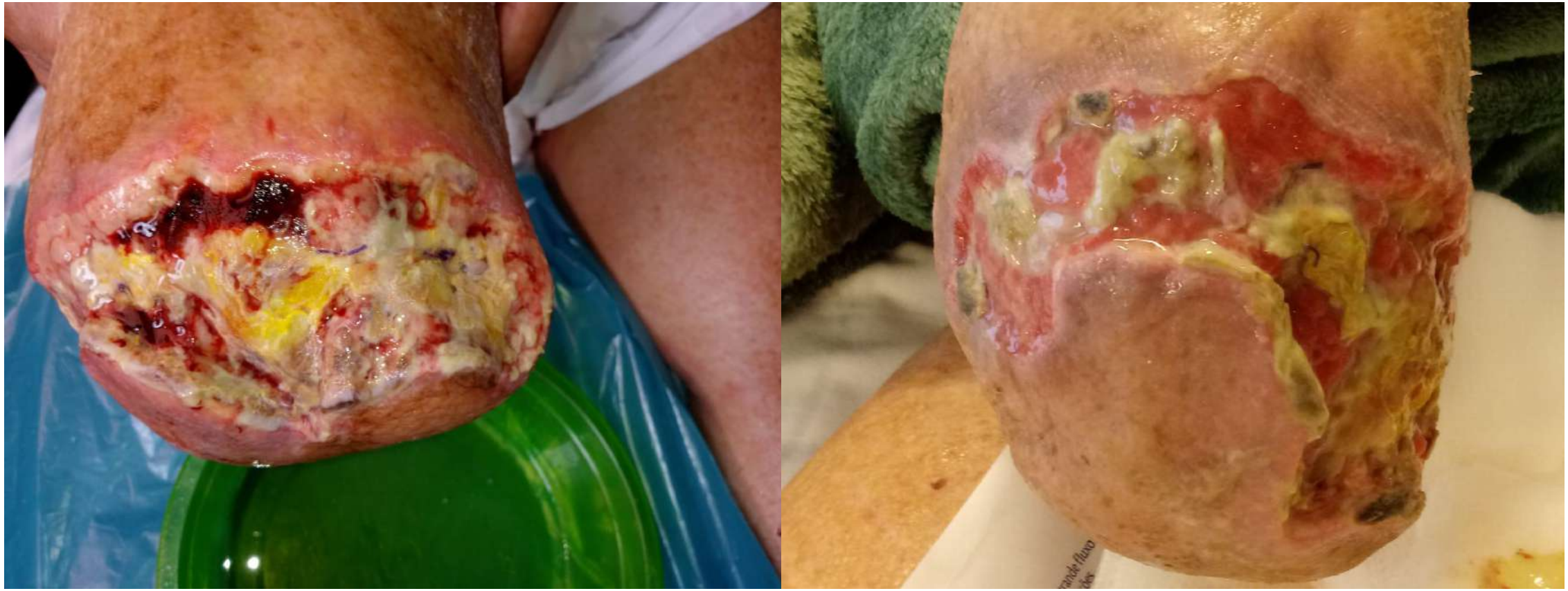
25 dias PO



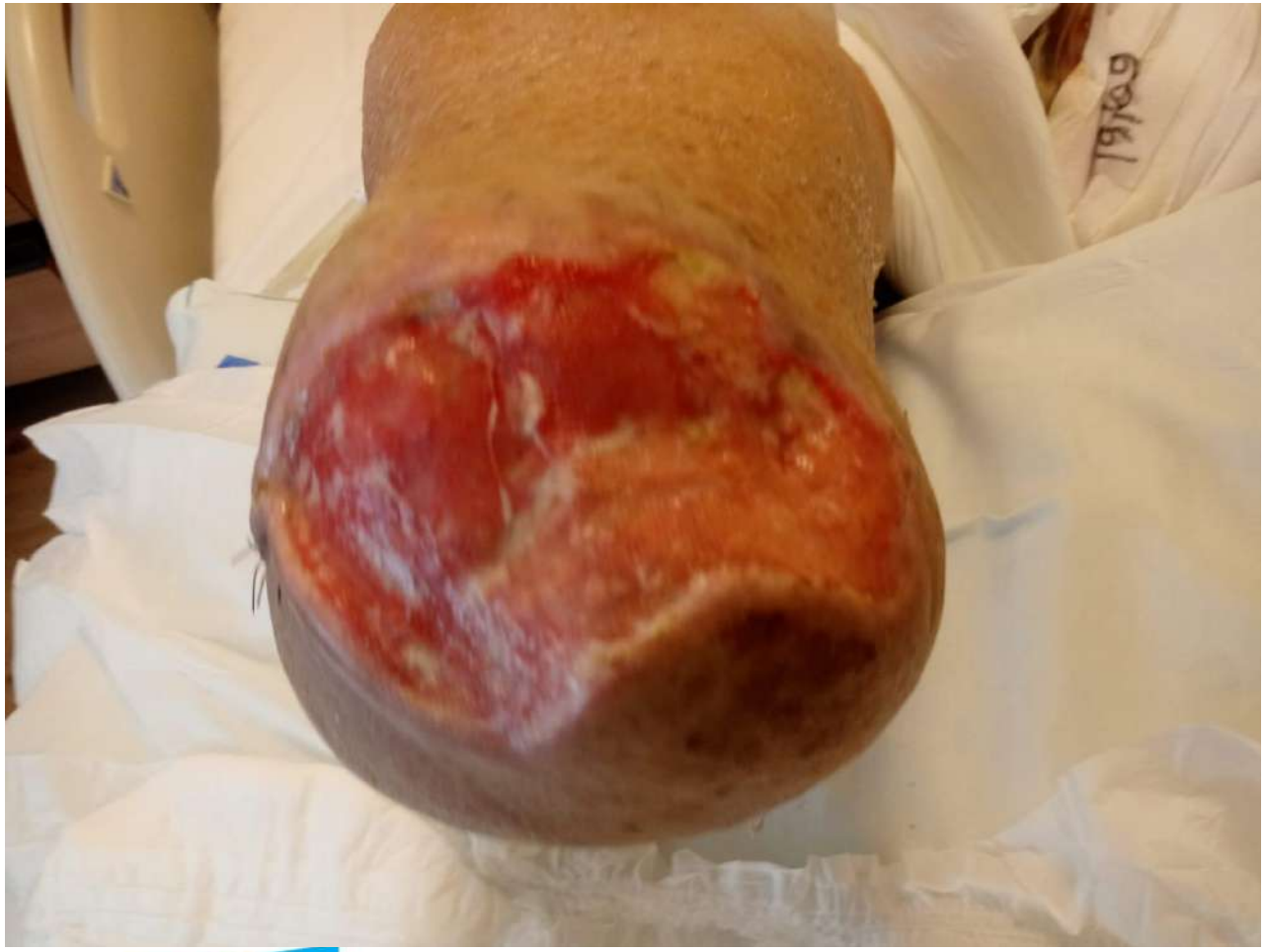
35 dias de PO



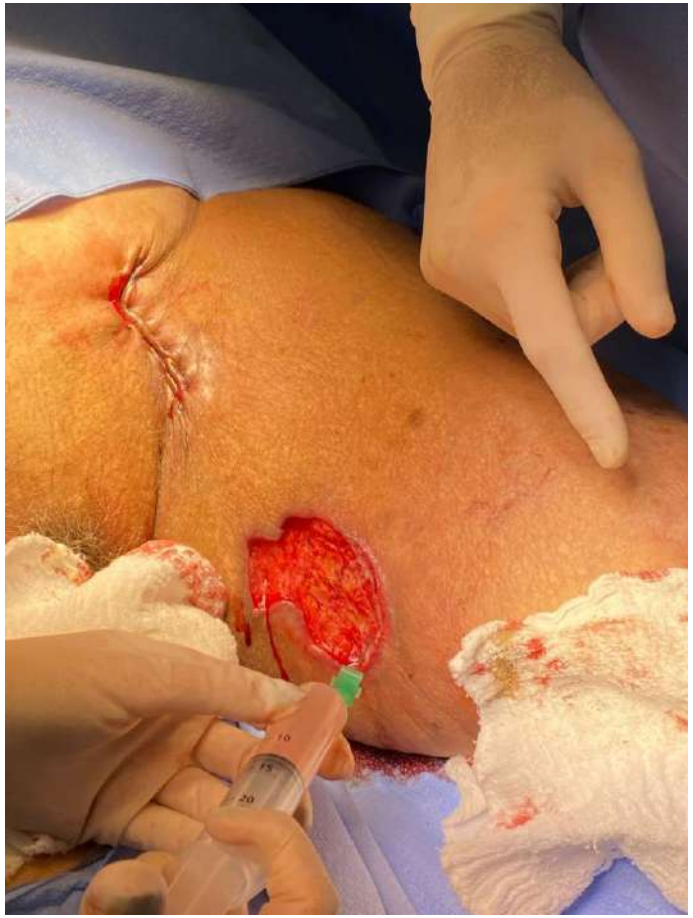
Coto de amputação Pré e Pós de 4 dias

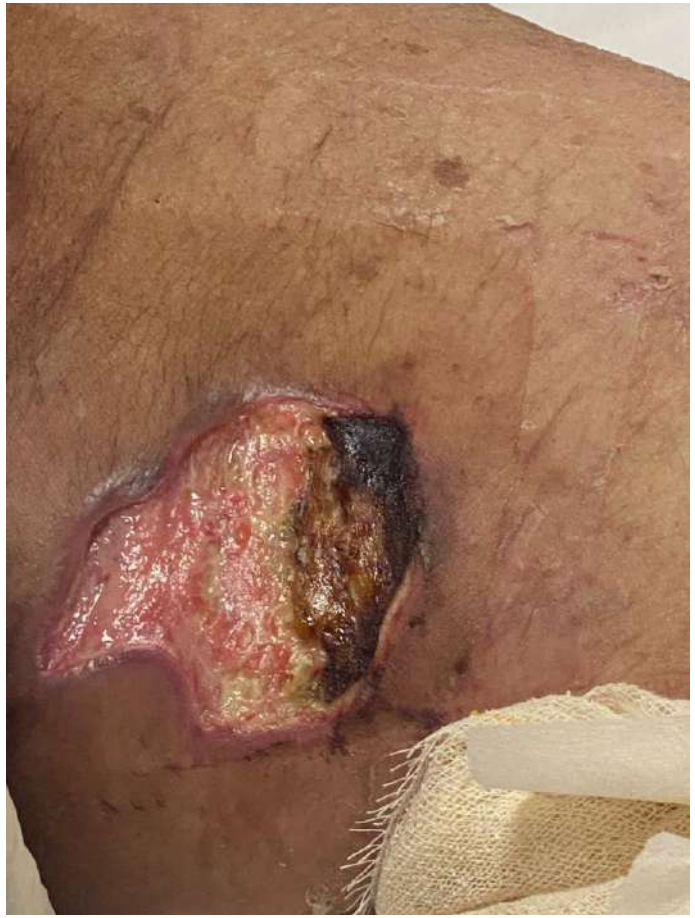


40 dias de PO

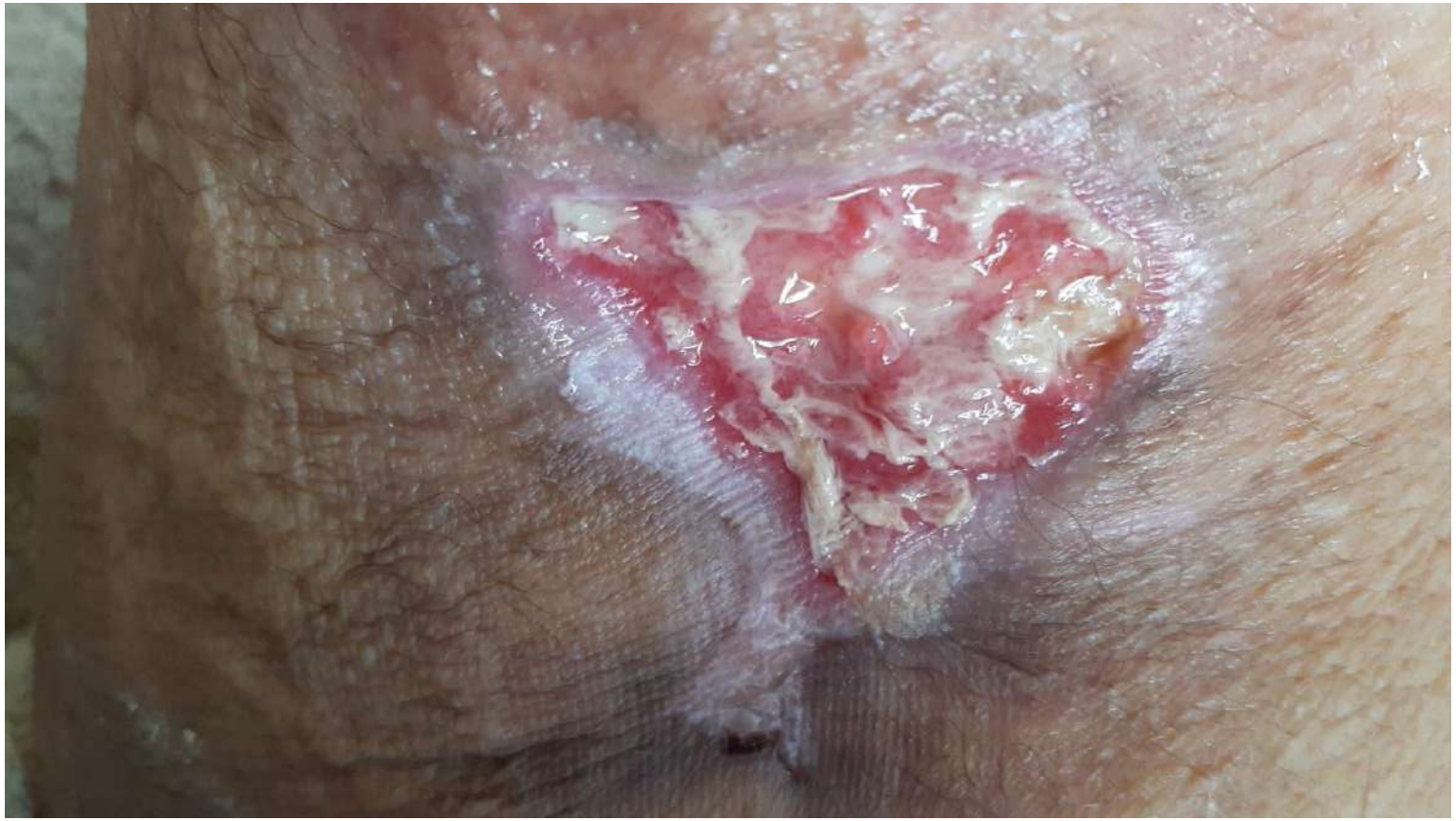


Úlcera de pressão Transoperatório e Pós de 4 dias



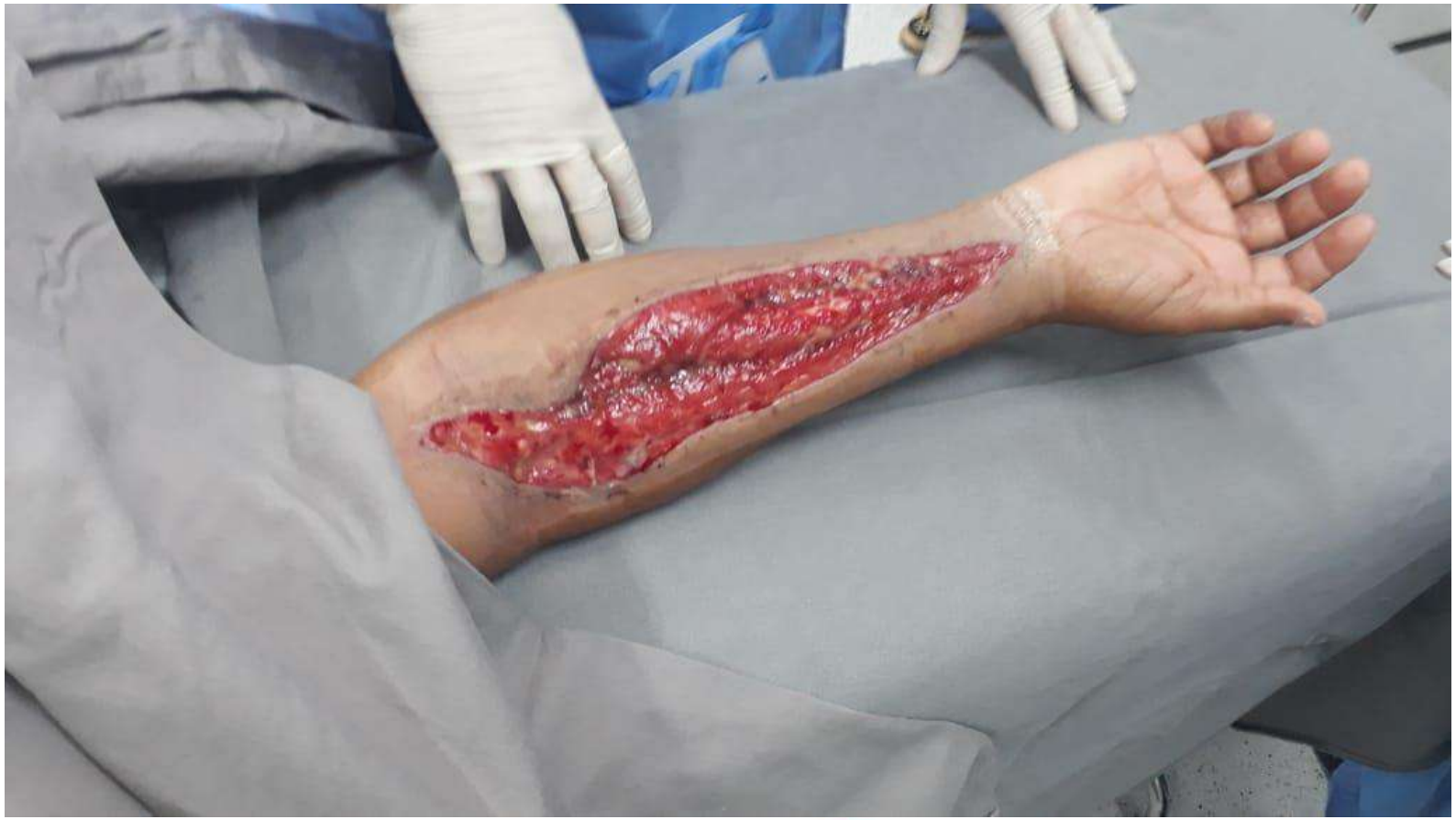


35 dias de PO

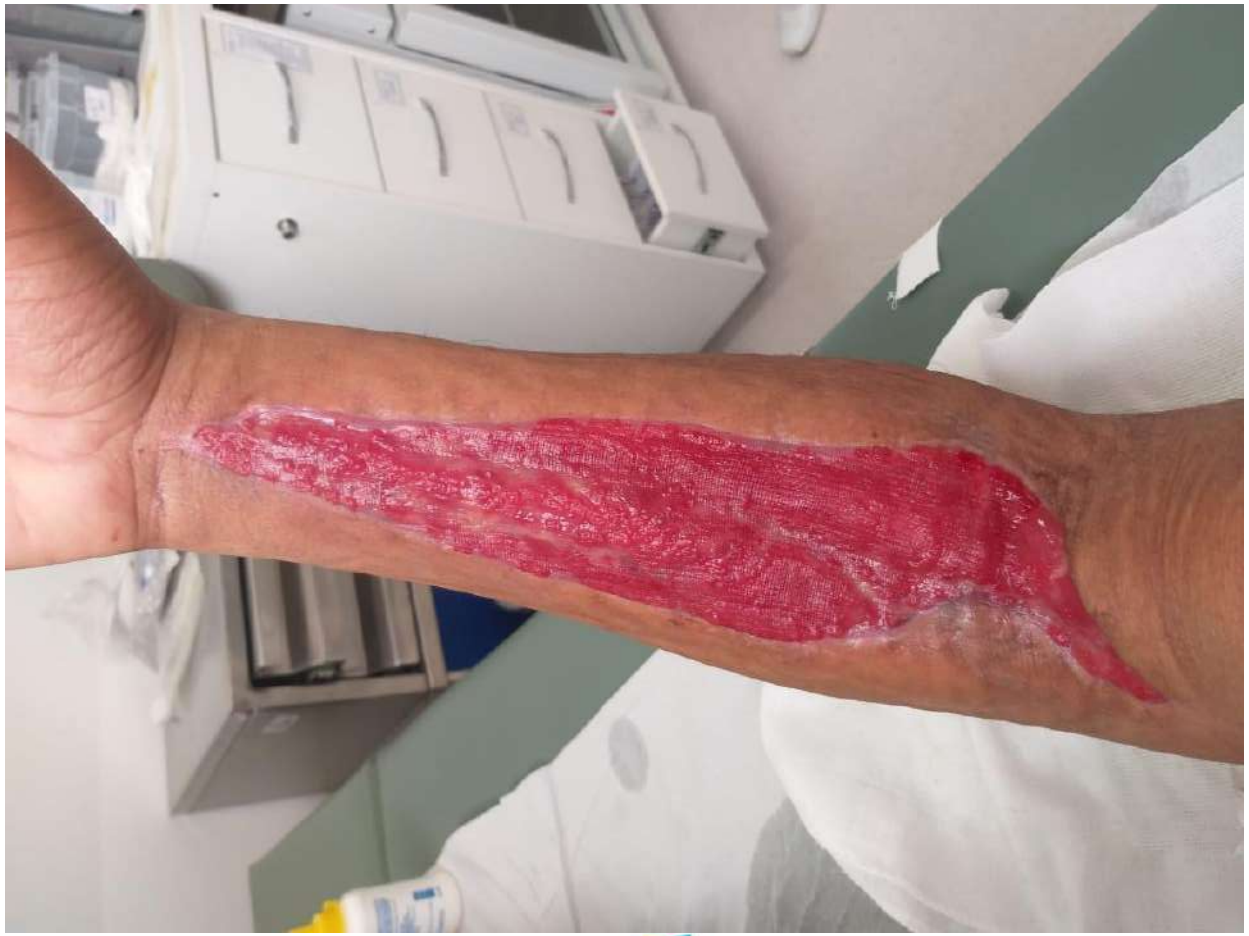


Síndrome compartimental Transoperatório

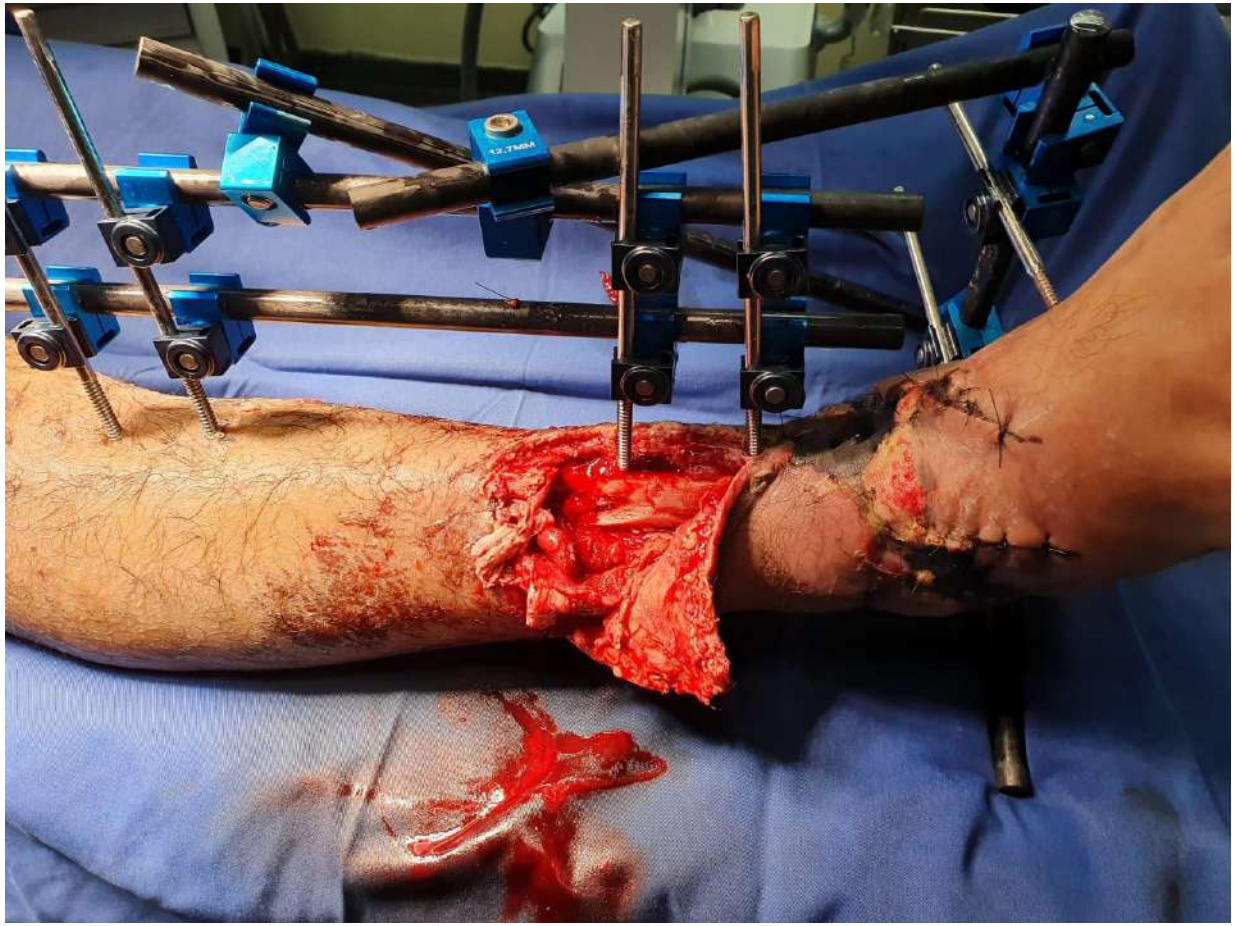
4 dias de PO



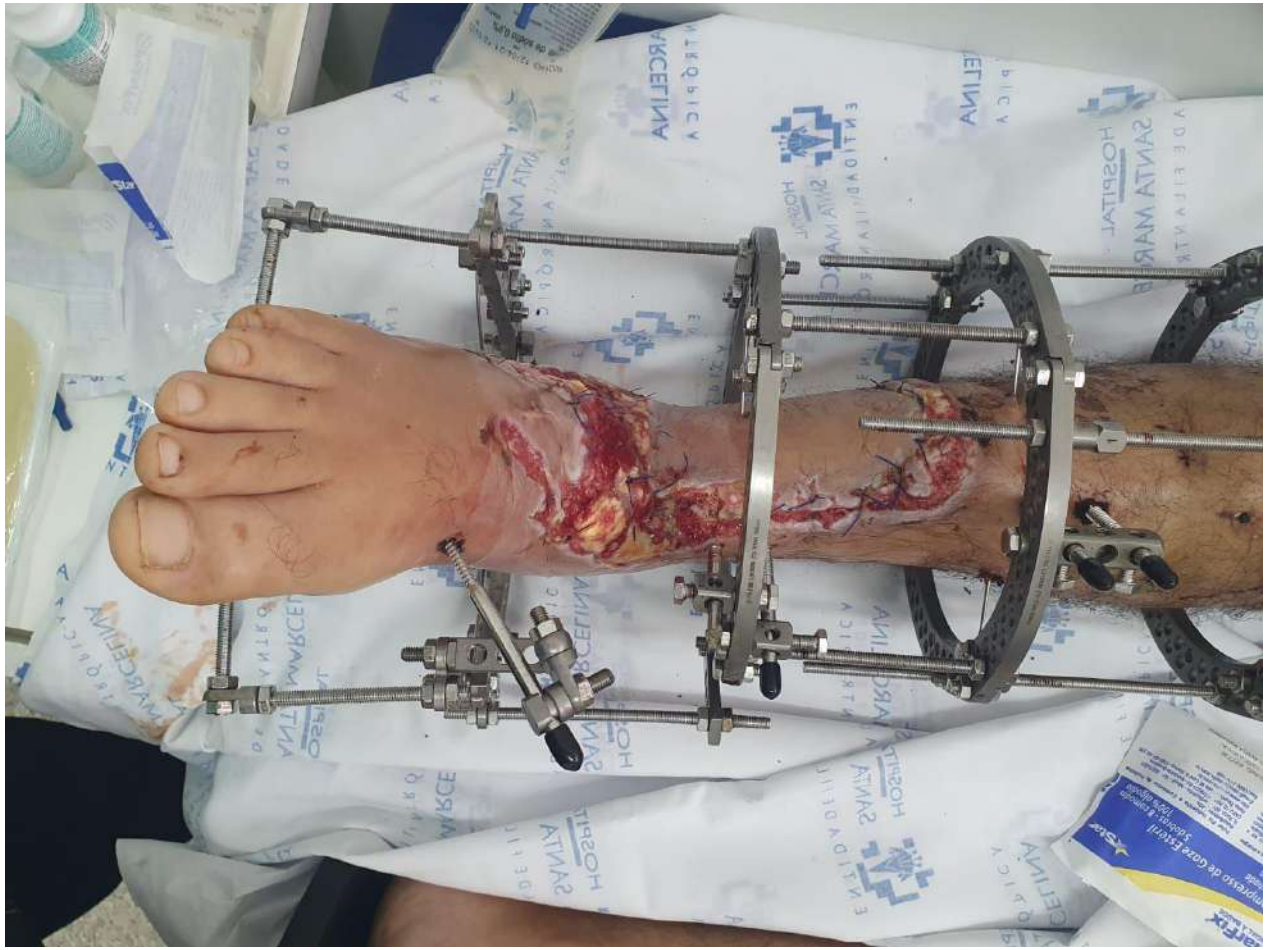
11 dias de PO



Paciente Politrauma



11 dias de PO



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