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RIGENERA TECHNOLOGY

The Rigenera Technology consists of disposable devices named Rigeneracons and Adipecons in combination with different activators, such as the Sicurdrill device. This technology has obtained CE, FDA, and FMA certification. Rigeneracons and Adipecons devices are mechanical disruptors of biological tissues, respectively skin and fat, that allow to obtain micrografts in an autologous, homologous, and minimally invasive manner. The main difference between the devices is the ability of disaggregating different kinds of tissue (also cartilage and bone) and the obtained volume of micrografts suspensions, 3.5ml, and 16 ml, respectively.

The Rigenera Technology is currently applied in aesthetic medicine, dermatology, dentistry, orthopedics, and wound care application. More specifically, the use of Rigenera in Wound Care refers to the treatment of: (1) non-healing wounds (acute and chronic), (2) post-surgical dehiscence, (3) post-traumatic wounds, (4) vascular or diabetic ulcers and (5) burns. Recent evidence suggests its use also in the field of cardiac regeneration, such application is still at the R&D stage.

The Rigeneracons and Adipecons technologies consist of a grid with 100 hexagonal holes, each hole is 80 Microns in size and equipped with six microblades, responsible for the tissue disaggregation.

The Sicurdrill Device activates the Rigeneracons/Adipecons by pressing smoothly the tissue on the microblades. Lastly while the sample is processed, the calibrated holes act as a filter by selecting only the particles and cells smaller than 80 microns which are collected in a reservoir and later collected by the doctors as a Micrograft. The entire procedure (disaggregation and grafting) occurs in one surgical time, that lasts about 30 minutes and the patient is both donor and acceptor of the tissue.

Scientific studies have shown that the cellular population obtained after the mechanical disaggregation is positive for mesenchymal stem cells markers identifying those cells as progenitor cells (PC) and have shown a viability above 90% (Trovato L, et al. J Cell Physiol. 2015). Moreover, subsequent analysis displays that micrografts contain a high percentage of Stromal Vascular Fraction Cell (SVF) which play a key role in tissue regeneration by promoting revascularization and regrowth. Based on clinical experience and tests performed on patients suffering of non-healing wounds, with Rigenera it takes approximately 8 weeks to heal completely. The reduction of the therapeutic time by the reactivation of the healing mechanisms leads to a reduction in admission times and/or the number of outpatient accesses.

The procedure does not require special preparations for the patient and does not require a period of convalescence or rehabilitation. The Rigenera technology does not present any type of risk to the patient, as it is minimally invasive and involves the collection of a small fragment of skin, even in the case of large lesions. Likewise, there are no risks for the personnel, as the use is simple and possible even in private practice (for non-hospitalized patients).
The patient’s quality of life improves drastically, as well as the compliance, because the check-up at the hospital or private practice are few or none since the management of dressings can be delivered at home. The use is simple and intuitive, training is short, comprises in a demonstration of the method by the product specialist. No installations are required that involve building and plant modifications and no adjustments are made to consumables other than those used in common advanced dressings.

FAT MICROGRAFTING

Adipose tissue or fat is a connective tissue consisting mostly of adipocytes. These cells are collected in groups and organized in small lobules arranged along the path of blood vessels. Using Rigenera–HBW technology the obtained adipose-derived micrografts help dermatologists, plastic surgeons and orthopedic surgeons to achieve effective results in the many procedures, where the fat is used (e.g.: lipofilling, wound healing). Adipecons allows the mechanical disruption and filtration of small samples of adipose tissue to obtain a calibrated and injectable micrograft solution.

MICRO-GRAFTS THEORY
Rigenera Technology is based on two fundamental pillars of regenerative biology:

- **Principle 1: The side population.**
  Numerous scientific papers have demonstrated that progenitor cells (PC) reside within the adult tissue but have determined morphological features. The main features of these cells are: (1) the size, and (2) a significantly higher stem cell marker expression.

- **Principle 2: The niche concept.**
  Preserving the extracellular matrix (ECM) allows the cells to maintain their physiological niche. This specific environment not only improves cell viability, but also gives the progenitor cells the appropriate growth factors that support their role in the regenerative process.
CLINICAL PROCOTOL FOR WOUNDS TREATMENT: DERMIS MICROGRAFTING WITH RIGENERACONS

The use of Rigenera in Wound Care refers to the treatment of:
- Non-healing wounds (acute and chronic)
- Post-surgical dehiscence
- Post-traumatic wounds
- Vascular or diabetic ulcers
- Burns

PROCEDURE

A. Disinfect the wound area using a non-aggressive disinfectant (no alcoholic, no iodine derivate).

B. Disinfect and anesthetize, without vasoconstrictor, the area where the sample will be collected. De-epithelize the choose area with a scraper.

C. Harvest the tissue sample using a biopsy punch:
   I. It is suggested to collect the sample from the retro-auricular area, however other sites can be selected (trunk, the arms and legs)
   II. 1 mm² of sample is adequate to heal maximum 2cm²-sized wound

D. Add 3.5ml of saline solution, using a syringe through the hole on the edge of the device (The syringe does not need a needle)

E. Place the harvested tissue sample on the grid inside the Rigeneracons. Manually turn the device helix in order to cover the tissue sample.

F. Connect the Rigeneracons, with the adapter, to the Sicurdrill Device. Activate the Sicurdrill Device for 2 cycle (each cycle last 1min.)

G. Collect the micro-graft suspension with syringe from the same hole in which was previously injected the saline solution (the syringe does not need needle).
   I. If necessary, repeat from Step E to Step G if more tissue sample were collected. Each Rigeneracons allows the disaggregation of maximum 12mm² of tissue (equal to n.3 2.5mm Biopsy punch).
   II. Inject ½ of the obtained micrograft solution in the wound bed and wound edges (4mm deep).
      Inject the remaining ½ of the obtained micrograft solution in a collagen scaffold (or different) and place it onto the wound bed.
   III. In case of burns, the Micrograft can be also sprayed on the injured area.

H. Do not add-secondary dressing (eventually cover also with a polyurethane dressing to manage the exudate), use normal gauzes to dress (not too tight)

POST TREATMENT

First control after 7-10 days, then every 7 days.
The use of Rigenera might induce the exudate production to increase
- Clean the wound only with saline solution
- Do not scrape the wound, if appropriate clean the peri-injured area
- Do not use Silver dressing
- Do not use NPTW for the first month after the procedure
Rigenera-HBW® technology protocols

**CLINICAL PROTOCOL FOR WOUNDS TREATMENT: FAT AND/OR DERMIS MICROGRAFTING WITH ADIPECONS**

The use of Rigenera in Wound Care refers to the treatment of:
- Non-healing wounds (acute and chronic)
- Post-surgical dehiscence
- Post-traumatic wounds
- Vascular or diabetic ulcers
- Burns

The use of the Adipecons device is suggested in the following cases:
1. **There is a need to disaggregate more than 12mm² of dermal tissue (equal to n.3 2.5mm Biopsy punch).**
   - In this particular case the clinical protocol will be the same as described before in "CLINICAL PROTOCOL FOR WOUNDS TREATMENT: DERMIS MICROGRAFTING WITH RIGENERACONS", but the device will need 16ml of saline solution instead of 3.5ml.
2. **There is a need to disaggregate Adipose tissue instead of dermal tissue.**
3. **There is a need to disaggregate Adipose tissue + Dermal tissue.**

**THE PROTOCOL DESCRIBED HEREAFTER REFERS TO CASE N.2 AND N.3**

**PROCEDURE**

A. **This passage is only for Adipose tissue + Dermal tissue disaggregation (case n.3)**

   Collect a dermis sample using 2.5 mm or 3 mm punch from the from the retroarticular region, trunk, the arms and legs (1 punch every 10ml of Lipoaspirate):
   1. Disinfect the retrieval area with the antiseptic solution of your choice.
   2. Anesthesia application in the periphery area without embedding the donor tissue [e.g.: 2% lidocaine without vasoconstrictor]. Shave gently to remove the outermost layer of keratinocyte.
   3. Extract the samples with a 2.5 mm or 3 mm diameter dermal punch.
   4. Place the sample on a clean firm surface (generally we perform this step on the cover disc of the Adipecons® device). Place the biopsies inside the Adipecons® device. Pay special attention to the site where you leave the sample: over the hollowed disc not over the rotor.

B. **Lipoaspiration of 20 ml of Fat:**
   - It is suggested a low concentration of lidocaine (0.4/0.8 mg/ml) and low pressure of aspiration, in order to preserve the vitality of the Progenitor Cells.

C. **After fat collection, the lipoaspirate should be left for decantation (3 min.)**

D. **The fat tissue will be inserted into the Adipecons (on top of the dermal tissue only for case n.3) and differently form the other protocol there is no need to add saline solution during the disaggregation. The device will allow to disaggregate max. 16ml of adipose tissue.**

E. **Connect the Adipecons, with the adapter, to the Sicurdrill Device. Activate the Sicurdrill Device for 6 cycle (each cycle lasts 1min.)**
F. Collect the micro-graft suspension with syringe (the syringe does not need needle):
   I. Inject ½ of the obtained micrograft solution in the wound bed and wound edges (4mm deep).
   II. Inject the remaining ½ of the obtained micrograft solution in a collagen scaffold (or different) and place it onto the wound bed.
   III. In case of burns, the Micrograft can also be sprayed on the injured area.

G. Do not add-secondary dressing [eventually cover also with a polyurethane dressing to manage the exudate], use normal gauzes to dress (not too tight)

POST TREATMENT
First control after 7-10 days, then every 7 days.
The use of Rigenera might induce the exudate production to increase:
- Clean the wound only with saline solution
- Do not scrape the wound, if appropriate, clean the peri-injured area
- Do not use Silver dressing
- Do not use NPTW for the first month after the procedure
Rigenera protocol in the treatment of surgical wound dehiscence

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Key words
Autologous; Dehiscence; Micro-grafts; Tissue regeneration; Wound healing

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Abstract
The effective management of post-operative wounds is important to prevent potential complications such as surgical-site infections and wound dehiscence. The purpose of this study was to treat wound dehiscence in elderly patients who were subjected to orthopaedic surgical interventions. The dehisced wounds were treated with autologous micro-grafts obtained using a promising CE-certified medical device called Rigeneracons. This instrument is a biological disruptor of human tissues able to specifically select progenitor cells that, as already reported in previous studies, maintain high cell viability but mainly have a high regenerative potential, allowing the repair of damaged tissues. Autologous micro-grafts obtained by Rigeneracons are ready to use and can be applied alone or in combination with biological scaffolds directly on the injured area. We observed in our patients a complete remission of dehisced wounds, on average, after 30 days from micro-grafts application and a total wound re-epithelialisation after 1 year from the surgical intervention. In conclusion, although we reported only three patients, autologous micro-grafts can be considered a promising approach for the treatment of dehisced wounds, improving the wound-healing process and in general the patient’s quality of life without using other dressings.

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Rigenera protocol in the treatment of surgical wound dehiscence:

Case history:
- Man 78 years old, with hypertension
- Dehiscence of dorsal medial area of foot, caused by forefoot alignment
- Rigenera technology, collection of one dermis fragment (1x1,5cm) by trochanteric region, 6 ml of micro-graft suspension, 1 ml used to create a biocomplex with a collagen sponge, 5 ml directly injected into the edges of the dehiscence
- Complete closure after 15 days

Figure 2

A Regenerative Approach with Dermal Micrografts in the Treatment of Chronic Ulcers

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Abstract

Background The etiology of non-healing ulcers depends on both systemic and local factors. The introduction of advanced dressing, negative wound therapy and compression therapy have undoubtedly improved clinical outcomes. The principal aim of study was to demonstrate the efficacy of dermal micrografts in the treatment of ulcers with different etiologies. The second aim was to investigate in vitro the action of micrografts in the regenerative process.

Methods The dermal micrografts were obtained from mechanical disaggregation of small pieces of skin tissue through a medical device called Rigeneracons.

Results We observed in vivo the ability of dermal autologous micrografts to improve the healing of venous, diabetic, pressure and post-traumatic ulcers after few week of treatment accomplished in general with a better quality of life for the patients. In vitro results showed that these micrografts express mesenchymal stem cells (MSCS) marker such as CD34, CD73, CD90 and CD105, and are able to form a viable and proliferative biocomplex with collagen sponge. Finally, the site of ulcers displayed a different expression of epidermal growth factors, insulin-like growth factors, platelet-derived growth factors and their receptors and tumor necrosis factor-β with respect to healthy skin samples.

Conclusion We reported a good outcome for the treatment of chronic ulcers using dermal autologous micrografts. Finally, we suggest that the positivity to MSCs markers and the ability to interact with a scaffold can play a key role in their regenerative properties.

M. Riccio and G. A. Ferraro contributed equally to this work.

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Post traumatic venous ulcer

Case history:
- Man 75 years old with vascular deficit in the lower limbs
- Post traumatic venous ulcer (2 cm²) on the right malleolus (6 week old)
- Ultrasound debridement, the collection of two 4 mm punch of skin sample from healthy skin, digested with **Rigenera Technology**
- Total of 2 ml of micrografts solution: 1 ml was directly injected into the edges of the ulcer and 1 ml was used to soak a scaffold of Condress®
- Complete closure after 31 days

De Francesco et al. *A Regenerative Approach with Dermal Micrografts in the Treatment of Chronic Ulcers*  
Regenerative Surgery in the Management of the Leg Ulcers

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Abstract

The causes of non-healing leg ulcers are multi-factorial, and include both systemic and local factors. The beginning of advanced dressings or the negative pressure wound therapy and compression therapy, certainly improved clinical outcomes. In this paper, we showed the efficacy of autologous micro-grafts to improve wound healing of leg ulcers of different etiology. These micro-grafts are obtained through a disposable medical device and are constituted by viable progenitor cells and growth factors deriving from autologous tissue which was disaggregated. A total of 7 different leg ulcers from 5 patients were analyzed, and after the treatment with autologous micro-grafts, in all lesions it was observed an enhancement of wound healing process after the first week that lasted up to one month from micro-grafts injection. Furthermore, for all the lesions, the patients reported a pain disappearance. In conclusion, these preliminary results showed that leg ulcers previously treated with routine approach with no results, when treated with autologous micro-grafts quickly improve their wound healing in addition to reduction and/or disappearance of pain.

Diabetic ulcer

Case history:

- Man 65 years old, with diabetes
- Diabetic ulcer on the right heel [1.5cm]
- Ultrasound debridement and collection of two skin sample with a 3 mm punch
- Rigenera Technology®, obtained 2 ml of micro-graft solution 1 ml was directly injected into the edges of the ulcer and 1 ml was used to soak a scaffold of Condress®
- Closure after 1 month
- Complete closure after 31 days

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Surgical dehiscence post mastoplasty surgery

**Case history:**
- Woman 25 years old, surgical dehiscence post mastoplasty surgery on the left chest on a radiotherapy treated skin
- Collection of a 1cm² of dermis, **Rigenera Technology**
- Total of 4 ml of micro-grafts solution: 3 ml directly injected into the wound and 1 ml to soak one scaffold of Condress®
- Complete closure after 21 days

Ulcer wound

**Case history:**
- Woman, 37 years old with 1 cm ulcer located on the tibial crest, with bone exposition and inflamed skin
- Rigenera technology collecting 5 small pieces of dermis
- 6 ml of suspension micro-graft that was injected directly in all the wound edges and in a collagen dressing that was positioned over the wound floor
- About 60 days after micro-grafts application closure of the ulcer and reepitelization

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