mytocel MSK

Mytocel MSK Protocol with AMT®

FOR OSTEOARTHRITIS

ADVANCED REGENERATIVE MEDICINE FOR MUSCULOSKELETAL HEALTH

EUROPEAN PATENTED RIGENERA TECHNOLOGY

THE ONLY PROVEN AUTOLOGOUS MICROGRAFTING PROCEDURE

Index

01

Mytocel MSK

As part of Remedi, a pioneering biotechnology company specializing in regenerative medicine through autologous micrografting, Mytocel MSK is among the most advanced treatments for joint restoration and musculoskeletal health, using the revolutionary and minimally invasive Rigenera® technology.

Why Mytocel MSK?

With a presence in over 70 countries and more than 450,000 successful treatments performed worldwide, the patented Rigenera® technology used for the Mytocel MSK protocol allows us to create our AMT® solution to promote tissue healing, managing musculoskeletal pain and helping to restore joint function.

What is AMT® Solution?

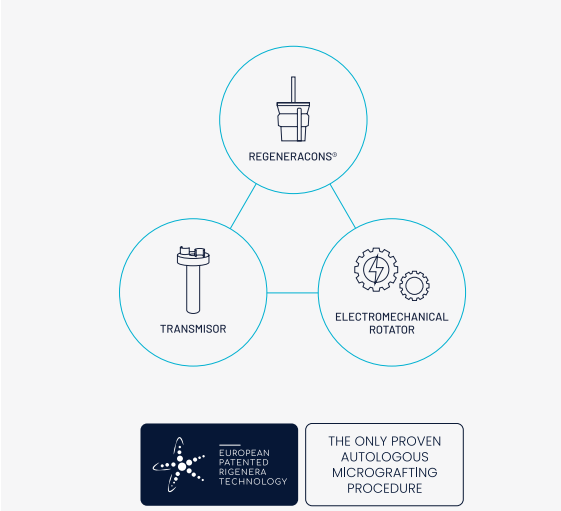
AMT® is an autologous micrograft solution that, through a simple protocol, harnesses the body's regenerative and self-healing potential, delivering it precisely where it's needed most. The procedure utilizes Class I and IIa medical devices specifically designed to create a micrograft solution from small biopsies. This solution contains various cell types, including progenitor and multipotent cells, which aid in restoring the normal function of damaged autologous and homologous tissue. Since the biopsies are minimally manipulated and sourced from the patient, **AMT®** is considered a minimally invasive and highly safe procedure.[1]

02

The science behind

THE RIGENERA® TECHNOLOGY

Our innovative patented Rigenera® technology, supported by over 80 scientific publications and registered in more than 30 countries, marks a significant advancement in regenerative medicine. This technology leverages the powerful synergy between three critical components: the **Regeneracons®**, the **Transmisor**, and the **Electromechanical Rotator**. Working together, these elements perform a precise and controlled process, disaggregating the patient's tissue into 80 µm micrografts with an impressive 90% biological components viability, maximizing the body's innate healing abilities.

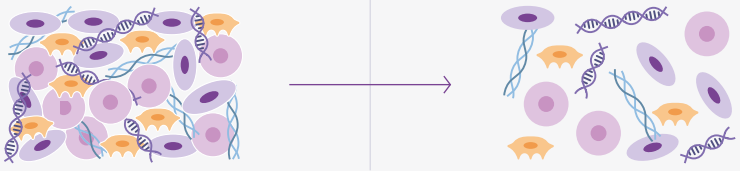


AMT® APPLIED FOR OSTEOARTHRITIS

Auricular cartilage tissues contain a surrounding layer called perichondrium, which contains a pool of mesenchymal progenitor cells called chondroblasts. Chondroblasts contribute to tissue homeostasis by replicating and differentiating into chondrocytes[7]. In the hyaline cartilage of the knee joint, chondrocytes supply the extracellular matrix (ECM) with the elements that constitute the cartilage function, such as collagen and proteoglycans[8]. However, when the joint is damaged by an injury or a degenerative disease, such as osteoarthritis, chondrocytes are unable to restore the homeostasis of the tissue[9,10]. AMT®'s strategy is to **transfer the signalling potential of chondroprogenitor cells**, chondrocytes and signalling factors together with ECM components to enhance the restoration of joint function, reducing pain and stiffness[6].

All types of elastic and hyaline cartilage, except the one in articulations, are surrounded by the perichondrium[11]. AMT® takes small cartilage biopsies from the auricular concha and disaggregates them to obtain a micrograft solution. When injected into the affected joint, these elements restore the cartilage function in the affected area, significantly reducing pain and stiffness. Therefore, a degenerative joint condition can be stabilised with the AMT® procedure[6].

Components of auricular cartilage



AMT® SOLUTION Dissagregated

Tissue disaggregation with Rigenera® Technology

- Progenitor cells
- Chondrocytes
- Perycites
- ECM component
- Genet icinformation

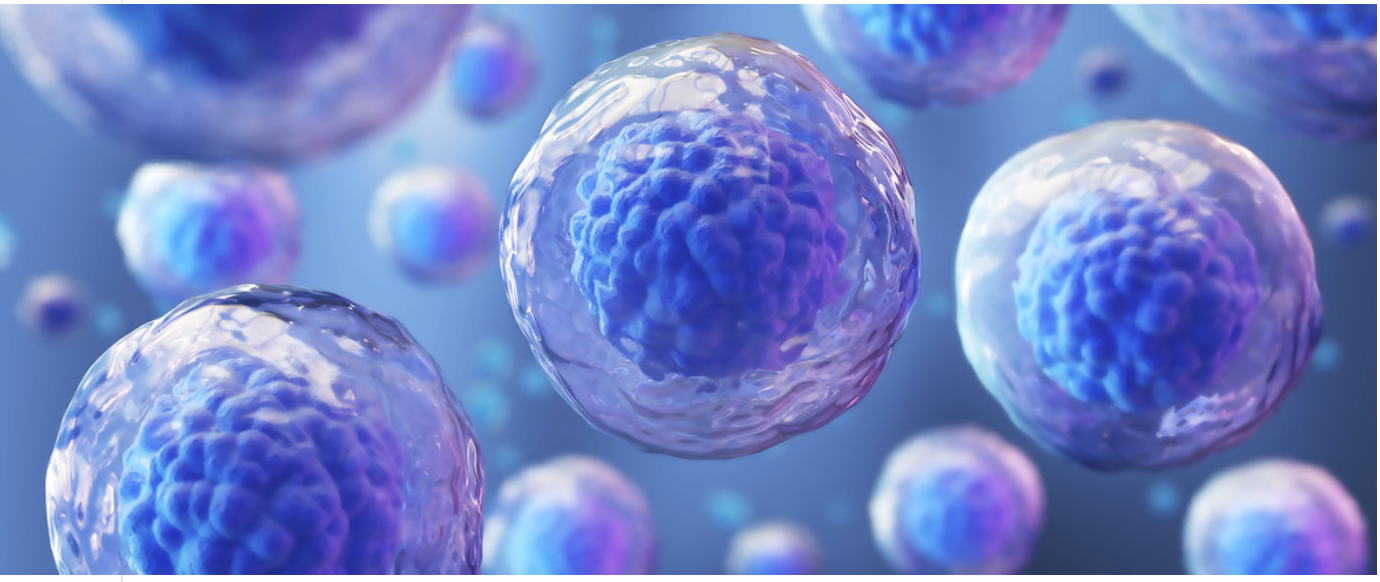
SIGNALLING CELLS

From the earliest embryonic stages, the journey of cellular development begins. Cells replicate, differentiate, and secrete vital factors that contribute to the creation of a complete individual.

Stem cells are the origin of all ours cells. Their primary function is to maintain tissue homeostasis by secreting specific signaling factors, replicating, and differentiating into specialized cells. Among these remarkable cells are pluripotent stem cells, which have the extraordinary ability to transform into one multipotent stem cell, and then differentiate into one of many types of progenitor cells and ultimately evolve into fully specialized cells. As cells differentiate, their potential to become any cell type diminishes, but their specific functions within their respective tissues become increasingly specialized and critical.

When the progenitors cells are injected into an impaired or damaged tissue, their activity is importanly therapeutical by secreting trophic and immunomodulatory factors that can: regulate the immune response, stimulate intrinsic progenitor cells and angiogenesis, and inhibit apoptosis and scar formation, among other activities. This is why they are also called signalling cells.

The therapeutic potential and the dynamic interplay of these cells underscore the critical importance of progenitor cells in advancing regenerative medicine, offering innovative solutions for tissue repair and healing.



03

Benefits

	Minimally invasive procedure[6]
	Tissue-specific[6]
	Autologous[6]
	1 single intervention[6]
	30 minutes procedure
	Reduce pain and stiffness[6]
	Long-term results[6]

04

Patented Rigenera Technology Devices

Mytocel MSK protocol with AMT® on Orthopedics involves the use of the following devices:

EUROPEAN PATENTED RIGENERA TECHNOLOGY

THE ONLY PROVEN AUTOLOGOUS MICROGRAFTING PROCEDURE

Rigeneracons® RS

The Rigeneracons® RS is a sterile disposable class IIa medical device designed to mechanically disaggregate solid human tissue to obtain soluble autologous micrografts in a minimally invasive procedure, without manipulating the biological tissue. The Rigeneracons® RS comprises a grid with 100 hexagonal holes, each containing 6 calibrated microblades; a helix that rotates through an internal metal ring; and 3 arms. All these elements are thought and designed so that rotation of the helix happens at constant 80rpm, applying a controlled due pressure specially meant to disaggregate biopsies while preventing cellular disruption, keeping their viability, and resulting in an injectable micrografts solution, the AMT® Solution.

Rigenera® N4SA Machine 2.0

The Rigenera® N4SA Machine is a class I medical device with a motor that provides the electromechanical impulse to rotate the helix of the Rigeneracons® at a constant calibrated speed of 80 rpm. The assembly ensures that mechanical disaggregation is performed without damaging the cellular structure of the disaggregated tissue with an 80 microns cut-off. It operates in 6 minute cycles, each starting by pressing the frontal button. Specially designed to offer the highest comfort in the process.

05

Mytocel MSK step by step Protocol with AMT® for Osteoarthritis

The Autologous Micrografting Technology® has been shown to be effective in delaying the the pathophisiology of Osteoarthritis and knee joint injuries. This protocol is based on multiple studies that used the Rigenera® system to perform an AMT® procedure on patients with different conditions, including knee-joint-degeneration patients[1,4,6].

HANDY INFORMATION FOR USERS

Warning & Recommendations

- Unseal the product just before treatment and ensure that the device does not touch other objects; the sterile conditions of the device must always be guaranteed.
- Only qualified physicians who can judge if the treatment fits the patient's condition should use the product.
- Rigeneracons® is a single-use disposable device, and the entire kit must be disposed of as per local guidelines.
- Check the seal, possible damage, or term of validity of the product before use.
- The Rigeneracons® must not be resterilised because the integrity of each microblade cannot be ensured after one single use of the device.

Adverse events

Being an autologous, homologous, and minimally invasive procedure, this procedure presents no severe adverse events and, once it is done, offers fast recovery and return to everyday life less than 2 weeks.

Storage

Store the product in a well-ventilated and dry place at room temperature.

REQUIRED MATERIALS

1. N4SA 2.0
2. Rigeneracons® RS
3. 2% aqueous chlorhexidine
4. 2% lidocaine without vasoconstrictor
5. Adrenaline
6. Injectable physiological saline solution
7. Nobecutan®
8. 3 ml syringe (for anaesthesia)
9. 5 ml syringes (for infiltration)
10. 30G x ½, 0.3 x 12 mm needle
11. 21G x 1½, 0.8 x 40 mm needle
12. 2.5 mm dermal punch
13. Sterile Adson Tweezers
14. Round sticking plasters
15. Sterile gloves
16. Surgical drapes

PREVIOUS CONSIDERATIONS

01 **Patient exclusion criteria:**

- It is recommended to conduct a pre-operative analysis with a complete blood count (glycated haemoglobin, ESR, levels of vitamin D3, B12 and cholesterol with their fractions and triglycerides). Patients with low levels of vitamin D3 and B12 should be treated with supplements of these vitamins.
- Patients with inflammatory diseases: familial inflammatory arthrosis, positive antinuclear antibodies, ASLO>150, positive rheumatoid factor, and a history of inflammatory rheumatism cannot be treated with this protocol.
- Patients with morbid obesity, unbalanced diabetes or a severe metabolic pathology should also be excluded.
- Patients must be diagnosed with osteoarthritis grade III or inferior, meaning that the joint preserves at least part of the articular cartilage.
- Patients who have received any corticosteroid medication or local intra articular injection in the last 3 months.

02 Signed consent is required; its characteristics will be subjected to local laws. Thus, the physician must be acquainted with them.

03 Clinical record is mandatory in accordance with local laws and requirements, despite this being a minimally invasive medical procedure.

04 Carry out a WOMAC or KOOS questionnaire recommended by the International Knee Documentation Committee (IKDC) for assessing pain, stiffness, and function before and after the procedure. Also, an MRI can be performed to evaluate the extent of the injury and post-procedure results.

05 Read the user manuals for the devices. Make sure the N4SA 2.0 is connected. If the green LED is blinking, it means the machine is ready to scan the RFID chip. Use the RFID chip to activate the machine and perform the disaggregation.

PROCEDURE

STEP 1
Preparation & Anaesthesia

STEP 2
Extraction

STEP 3
Disaggregation & Collection

STEP 4
Infiltration

STEP 1

Preparation & Anaesthesia

- **Prepare** the sterile field with all necessary materials:
  - · Sterile conditions and surgical behaviour must always be guaranteed.
  - · Connect the N4SA 2.0 and get ready the RFID chip for its activation.
  - · Leave the disposable material on an accessory table. The whole set must be ready to use and kept sterile.
  - · Ensure optimal light.
  - · Use goggles (optional).
  - · Use sterile gloves.
- **Disinfect** the auricular concha of the ear with chlorhexidine.
- **Delimit** the work area where the biopsy will be extracted with a dermal marker.
- **Anaesthetise** with 2.5 ml of Lidocaine 2% without vasoconstrictors. Use 0.5 ml in the retroauricular nerve to anaesthetise and the rest on both sides of the auricular concha to hydroseparate the skin from the cartilage.

STEP 2

Extraction

- **Extract** 3 biopsy punches with a 2.5 mm dermal punch.
- **Separate** skin from cartilage.
- Place the 3 biopsies in the Rigeneracons® RS on the grid and rotate manually to cover them under the helix.
- Press the extraction site with gauze for about 5-10 minutes.

STEP 3

Disaggregation & Collection

- **Add** approximately 4 ml of saline solution through the extraction hole with a Luer Slip syringe until the solution slightly embeds the biopsies.
- **Close** the cap, insert the Sicurstick in the Rigeneracons® RS, and place it into the Sicurlid and place it in the Rigenera® N4SA machine.
- **Press** the button in the machine to start disaggregation. A 6 consecutive minutes mechanical disaggregation cycle will start.
- **Cure** the patient's donor area and apply a band-aid.
- **Collect** 4 ml of the AMT® Solution with a Luer Slip syringe.
- While disaggregating, heal the donor site area
- Retire the gauze and check if bleeding has stopped.
- If bleeding persists after mechanical pressure, apply diluted adrenaline (0.8 lido/0.1 adrenaline) with saline solution in each extraction hole, 0.1 ml.
- Once the bleeding stops, apply adhesive bandages to protect the area.

STEP 4

Infiltration

- **Disinfect** the external femorotibial compartment area with chlorhexidine.
- **Inject** the AMT® Solution with a 21G ½, 0.8x4 mm needle, into the external femorotibial compartment.
- **Mobilize** the joint to distribute the injected AMT® Solution evenly across the treated area.

POST-PROCEDURE

01

Joint inflammation is common in the first 24-72 hours post-procedure. Using analgesics is recommended, avoiding NSAIDs, which may interfere with the micrografts' effectiveness.

02

Resting positions that do not overstain the joint are recommended for at least 7 days post-procedure. Once the inflammation has diminished, some physical exercise and rehabilitative physiotherapy are recommended.

03

The WOMAC or KOOS questionnaire should be repeated after 1, 6 and 12 months post-procedure.

04

If an MRI to evaluate cartilage thickness was performed before the procedure, a follow-up MRI can be performed 12 months after the intervention.

05

Wound hygiene must be controlled.

06

Avoid washing the wound on the ear for 24 hours.

TIPS & TRICKS

01 HOW TO PERFORM

You can use some pressure and rotations to extract a skin biopsy with the dermal punch. Once reached the maximum depth, leverage the dermal punch to help the extraction.

Ensure there is enough distance (2mm) between each punch to avoid wound fusion.

If the cartilage biopsy remains internally attached, you can use some Adson Tweezers.

It is recommended to start from bottom to top, so the blood falling does not interfere with the next punch.

02 AMT® SOLUTION EXTRACTION

Use the Luer Slip syringe without a needle to extract the AMT® Solution from the Rigeneracons® in a very smooth manner so as not to disrupt the progenitor cells.

03 HOW TO CHECK THE AMT® SOLUTION

Always check the blurriness in the extracted AMT® Solution; it is a hallmark of the presence of micrografts in it. If it does not appear blurry, it may mean that disaggregation has not been efficiently performed.

04 TISSUE REMAINS

Always check that there are no remains of any tissue on the grid. Otherwise, you can add one more cycle of disaggregation. However, white fibres can be found on the grid as a white mass and must be discarded, since they are not part of the AMT® Solution. This tissue is called ghost tissue.

05 HAEMOSTASIA AND USE OF VASOCONSTRICTORS

Adrenaline can be injected to stop the wound's bleeding in case it has not stopped after 5 minutes of haemostatic pressure.

06

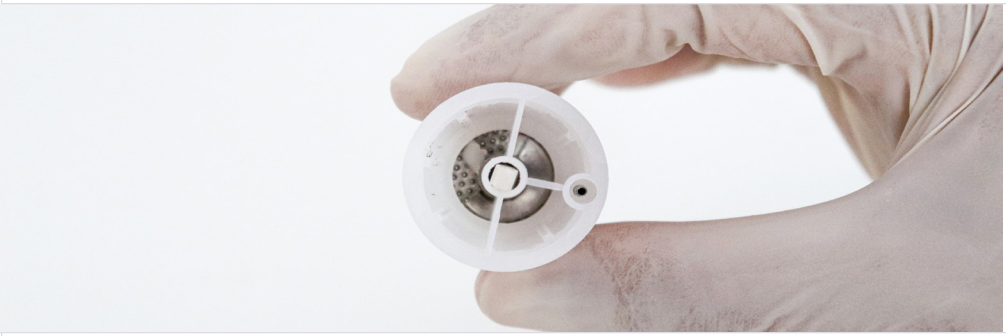
Frequently Asked Questions

Why are the biopsies taken from the auricular cartilage?

The auricular cartilage encompasses a series of advantages that make it the ideal donor site for the biopsies. In the first place, the auricular cartilage is formed by elastic cartilage which is the most similar cartilage to the hyaline one found in movable joints (knee for example). Moreover, micrografts from the auricular cartilage are easy to collect which makes AMT® easy to perform. And most importantly, ear's inner layer of perichondrium contains a high number of chondroprogenitor cells, key to the success of the AMT® in Orthopaedics.

What kind of sports-related injuries can we treat with AMT®?

A thorough history of prior injuries, treatments, and procedures can be conducted. Locking, catching, clicking, or popping are common complaints from the knee and are suggestive of concomitant pathology. Acute injury, as opposed to chronic, is a relatively better prognostic factor for outcomes. Thus, AMT® could be particularly beneficial in post-traumatic sports injuries in athletes. Moreover, the protocol could be extended to other articulations besides the knee joint, such as the hip, shoulder and ankle.



What kind of results could be expected after performing this treatment?

In the context of knee chondropathy and osteoarthritis up to grade 3, with a single AMT® procedure we could expect a high reduction in pain and stiffness, resulting in an improvement in the patients' quality of life (QoL) for as long as 3 years. In addition to improving QoL, there can be formation of new cartilage. This novel autologous micrograft procedure represents an innovative and accessible approach to the management of chondropathy. This approach could be expanded to different joints over the human body, it has been successfully used on the hip joint and ankle joint by using the same criteria.

Is this treatment effective for grade 4 osteoarthritis?

Grade 4 osteoarthritis is the most severe stage in osteoarthritis, cartilage is almost completely gone and decreased synovial fluid results in joint stiffness and highly reduced mobility. In these cases where there is no cartilage, AMT® might not be as effective as in lower grades of osteoarthritis, and treatment would need a more conventional approach. Nevertheless, an AMT® procedure could help with pain management in this kind of osteoarthritis.

When will the patient see the results?

Depending on the condition and degree of joint degeneration, results can be seen within the first month and are sustained over time, with a significant reduction in joint pain and stiffness, improving knee-related mobility in patients with osteoarthritis and sports injuries.

07

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