Regenera Activa AMT

AMT® protocol in Androgenetic Alopecia Management

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Leading you to the healing
power of Regenerative Science

CONTENTS

01 Regenera Activa

Regenera Activa is a worldwide company that delivers the Rigenera® technology on which the Autologous Micrografting Technology® (AMT®) procedures are based.

AMT® has been used for more than ten years since its discovery and development, by physicians worldwide who seek to stimulate and enhance self-regenerative processes on multiple conditions.

Why Regenera Activa?

Regenera Activa is the only distributor of the Rigenera® technology, now present in more than 60 countries, with doctors using it in more than 250,000 procedures procedures so far. Regenera Activa is a synonym for a high-quality standard and constant investment in R&D in an innovative technology meant to stay and continuously improve.

What is AMT®?

AMT® is a simple procedure that transfers the regenerative and self-healing potential of the body to where it is most needed. The procedure involves class I and IIa medical devices specifically intended to obtain a micrograft solution from small biopsies. This micrograft solution contains different cell types, including progenitor and multipotent stem cells, that will act to regenerate the normal function of an autologous and homologous impaired tissue. As the processed biopsies are minimally manipulated and come from the patient itself, AMT® is considered a minimally invasive and highly safe procedure[1].

02 The science behind AMT®

SIGNALLING CELLS

From embryological stages, cells replicate, differentiate, and secrete factors that develop a complete individual. Pluripotent stem cells can become any multipotent stem cell type, which in turn can differentiate into many different oligopotent stem cells (also called progenitor cells) and, finally, fully specialised cells. The difference between these cells is their options to become any cell type: the more they differentiate, the fewer options they have. However, the more specified they are, the more specific functions they have for the tissue they belong to[2].

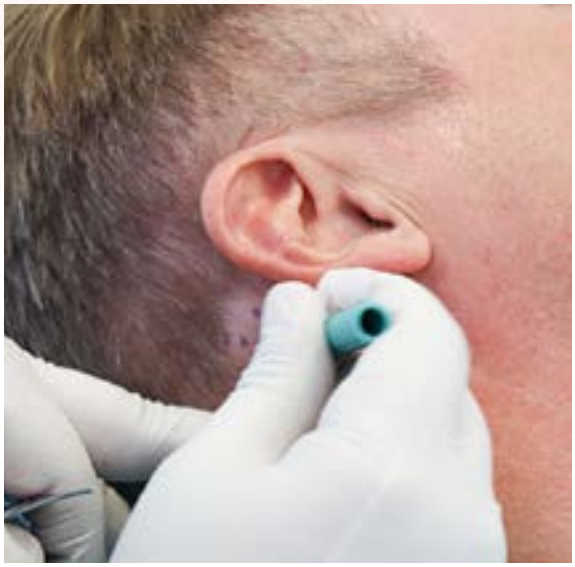
Adult stem cells can be classified in many ways: by embryologic origin, by differentiation potential, by location... Mesenchymal stem cells are multipotent stem cells that can be found widely in the human body and have their embryological origin in the mesoderm. Their main function is to keep tissue homeostasis by secreting specific signalling factors, replicating, and differentiating into specialised cells. But, when injected into an impaired tissue, their activity is basically 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. Therefore, mesenchymal stem cells (MSC) have been proposed to be called mesenchymal signalling cells (also MSC), highlighting their absence of proliferative multipotency but high regenerative potential in such conditions[3].

AUTOLOGOUS MICROGRAFTING TECHNOLOGY®

The Autologous Micrografting Technology® or AMT® is a set of procedures that brings the regenerative potential of a healthy MSC and progenitor-cells enriched tissue to restore an impaired tissue's function. In three steps, healthy homologous tissue is taken from a patient, processed to create a micrograft solution, and injected into the impaired tissue. There, signalling cells are found in a stressful environment and secrete specific factors that stimulate the normal functioning of the tissue[4-6].

Two of the keys of AMT® is that micrografts come from an autologous and homologous tissue to the one impaired, meaning they come from the same patient and from a tissue of the same embryological origin. On the one hand, this provides a good safety profile and non-rejection of the procedure. On the other hand, it ensures specificity since being homologous makes their activity tissue-specific and able to recover normal functioning through specific signalling pathways[1].

With AMT®, we bring the body's regenerative potential where it is most needed.



AMT® IN ANDROGENETIC ALOPECIA

In the hair follicle, the dermal papilla (DP) and the bulge are the main niches for mesenchymal and epithelial stem cells that regulate the homeostasis and correct functioning of the hair follicle[7]. Inside AGA-affected dermal papilla (DP) cells, androgens couple with specific receptors that unchain different signalling pathways responsible for AGA development. Some of the consequences of these pathways include a decrease in DP cell number[8], the death of epithelial progenitor cells in the bulge[9]... As a result, they affect the essential mesenchymal-epithelial interaction between the dermal papilla and the bulge that regulates the hair cycle and the onset of the anagen growth phase[8,10]. On a more macroscopic level, this leads to devascularisation, inflammation, early apoptosis and lack of nutrients reaching progenitor cells that alter the hair cycle phases[11–16], causing the hallmark of AGA: hair miniaturisation[17].

AMT®'s strategy to treat AGA is to use the signalling potential of healthy hair follicles, including its MSC, progenitor cells and signalling factors, to enrich an imbalanced environment and enhance the normal functioning of AGA hair follicles. When injected in the form of a micrograft solution into the affected scalp, these cells can signal with cytokines, chemokines and growth factors that inhibit apoptosis, regulate inflammation, and stimulate the vascularisation of hair follicles in degeneration that were not receiving enough nutrients. As this signalling is paracrine, a few injections can nourish the whole scalp. As a result, AMT® can stop hair loss and increase hair thickness, rescuing AGA hair follicles in regression[1,5,17].

03 Properties

- Minimally invasive procedure[6]
- Tissue-specific[1]
- Autologous and homologous[1]
- 1 surgical time[1]
- Fast: 30 minutes
- Stop hair loss[5]
- Increase hair thickness[5]

04 Devices

AMT® Protocol in Androgenetic Alopecia involves the use of the following Regenera Activa's devices:

RIGENERACONS® DERMA

The Rigeneracons® Derma 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® Derma is composed of a grid with 100 hexagonal holes, each containing 6 calibrated microblades; a helix that rotates through an internal metal ring; and 2 arms. All these elements are thought and designed so that rotation of the helix happens at constant 80 rpm, applying a controlled due pressure especially 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 1-minute cycles, each starting by pressing the frontal button. Specially designed to offer the highest comfort in the process.

05 AMT® protocol in Androgenetic Alopecia Management

The AMT® procedure has been shown to be effective in delaying the biological evolution of AGA. This protocol is based on multiple studies that used the Rigenera® system to perform an AMT® procedure on AGA patients[1,5,17].

HANDY INFORMATION FOR USERS

Warning & Recommendations

The user physician must be familiar with the operating manual of the medical devices prior to use.

Only qualified physicians who can judge if the treatment fits the patient's condition should use the product.

Rigeneracons® Derma is a single-use disposable medical device and must be disposed of as per local guidelines.

Check the seal, possible damage, or term of validity of the product before use.

The Rigeneracons® Derma must not be resterilised, because the integrity of each microblade cannot be assured after one single use of the device.

Adverse events

Being an autologous, homologous, and minimally invasive procedure, this treatment presents no severe adverse events and, once it is done, offers fast recovery and return to everyday life within 48 hours.

Storage

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

REQUIRED MATERIALS

1. Rigenera® N4SA Machine
2. Rigeneracons® Derma
3. 2% aqueous chlorhexidine
4. 2% lidocaine without vasoconstrictors
5. Hair razor
6. Paper tape (micropore)
7. Syringe 1 ml (anaesthesia)
8. Two 3 ml Luer Slip syringes (micrografting solution collection)
9. Two 3 ml Luer Lock syringes (AMT® Solution infiltration)
10. Syringe connectors
11. Needles 30G x ½, 0.3 x 12 mm
12. Needles 21G x 1½, 0.8 x 40 mm
13. Dermal punch 2.5 mm
14. Sterile Adson Tweezers (toothless)
15. Injectable saline solution
16. Adrenalin 1mg/ml
17. Band-aids
18. Sterile gauze pads
19. Sterile gloves
20. Sterile sizes

PREVIOUS CONSIDERATIONS

1 Signed consent is required, like in any other aesthetic medicine procedure. Its characteristics will be subjected to local laws. Thus, the physician must be acquainted with them.

2 Pictures must follow a previously established guideline. Light, distance to focus, zoom, and camera from the pre-treatment photo must be the same for all the follow-up photos, so they can be compared.

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

4 Patients must be diagnosed with an ongoing process of Androgenetic Alopecia, discarding other possible concomitant causes for alopecia.

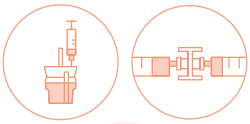
5 To achieve visible macroscopic results, trichoscopic analysis must report:

- ≥20% of thin hairs (≤30µm) in the frontal area.
- Lower cumulative hair thickness (measured in mm/cm^2 in the frontal area than in temporal and occipital areas, independently.

6 Absence of local inflammatory pathologies must be assured.

7 Grafts must be procured from a healthy hair follicle area.

DETAILED PROCEDURE



STEP 1 Diagnosis

STEP 2 Preparation & Anaesthesia

STEP 3 Extraction

STEP 4 Disaggregation & Collection

STEP 5 Infiltration

STEP 1

Diagnosis

- **In order to treat the patient** with Regenera Activa, Androgenetic Alopecia **must be diagnosed.**
  - We recommend any tool for the diagnosis that includes macro and micro pictures of the vertex, occipital and temporal area of the scalp and compare the classical parameters for AGA in the next visits.

STEP 2

Preparation & Anaesthesia

- **Prepare** the sterile field with all necessary materials.
  - Sterile conditions and surgical behaviour must always be guaranteed.
  - Leave the disposable material on an accessory table. The whole set must be ready-to-use and kept sterile.
  - Connect the Rigenera® N4SA machine to the power supply. A green and red lights will start flashing.
  - Turn on the machine by pressing the central button. Then, only a green light will flash every few seconds until activation.
  - Withdraw the protective shield from the Rigeneracons® Derma and discard it. A second cover with the activator chip keeps the Rigeneracons® in a sterile environment.
  - Activate the system by approaching the activator chip of the Rigeneracons® to the lector on the Rigenera® N4SA machine. A steady green light will indicate the system is activated for an entire hour.
  - Ensure optimal light.
  - Use sterile gloves, and goggles (optional). .
- **Disinfect** the extraction area with an antiseptic solution (alcohol 70%, chlorhexidine...). Micrografts will be extracted from the **thick-hair-follicles mastoid area**, containing entire hair follicle complexes.
- **Mark** the extraction area with a dermal marker.
- **Shave** gently to remove the stratum corneum.

STEP 3

Extraction

- **Inject 1 ml of Lidocaine 2% anaesthetic without vasoconstrictor** in the periphery of the donor area, blocking and avoiding flooding the donor tissue.
- Extract **3 biopsy punches** with a 2.5 mm dermal punch. While extracting place them in a sterile gauze moistened with antiseptic.*
- Place the 3 biopsies in the **Rigeneracons® Derma**, on the grid under the helix.

STEP 4

Disaggregation & Collection

- Add approximately **1.8 ml of saline solution** through the extraction hole with a Luer Slip syringe, until the solution slightly floods the biopsies.**
- Close the cap, attach the Rigeneracons® Derma to the Sicurlid and Sicurstick and place it in the **Rigenera® N4SA machine**.
- **Press the central button** in the machine front to start disaggregation. 2 consecutive minutes of mechanical disaggregation are required, and each pulse of the button equals a 1-minute cycle. Hence, after one minute has elapsed, press the button again.
- **Cure** the patient's donor area by second intention and apply a band-aid.
- **Extract the solution obtained** with a 3 ml Luer Slip syringe (syringe 1) and save it. This is a high concentration micrografts solution.
- Add again approximately 1.8 ml of saline solution in the Rigeneracons® Derma.
- Perform 1 minute cycle to collect any remaining material
- **Extract the solution obtained** with a 3 ml Luer Slip syringe (syringe 2) and save it. This is a low concentration micrografts solution.
- **Mix** syringe 1 and syringe 2 using a connector.
- **Split** the volume between the two syringes.
- **Increase** the volume up to 3 ml with saline solution in each syringe. The result is **6 ml of AMT® Solution** divided into two syringes.
- Optionally, transfer the AMT® Solution to Luer Lock syringes for a safer infiltration. *(See dilution diagram in Figure 1).*

STEP 5

Infiltration

- **Disinfect** the infiltration area with antiseptic solution.
- Injections shall be approximately **0.1 ml per cm².**
- **Inject** the AMT® Solution with a 30G x ½, 0.3 x 12 mm needle with a 45 degrees inclination to the scalp, into the deep dermis or superficial subcutaneous at most.
- **Gently massage** the scalp for one minute after the injections to distribute the solution.

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* The procedure is standard and simple, but some complication may arise related to the small size of the sample.
  - The tissue might stay inside the dermal punch. Use a needle to help extraction.
  - The tissue might get washed away by blood.
  - Second intention is enough to cure the donor area.. Exceptionally, a stitch together with Vicryl Rapid 4/0 might be required for each incision.

** The grid must be wet, and the sample must be slightly flooded, but not submerged in the saline solution. If too much saline solution has been used, with biopsies floating on it, aspirate and discard the excess solution.

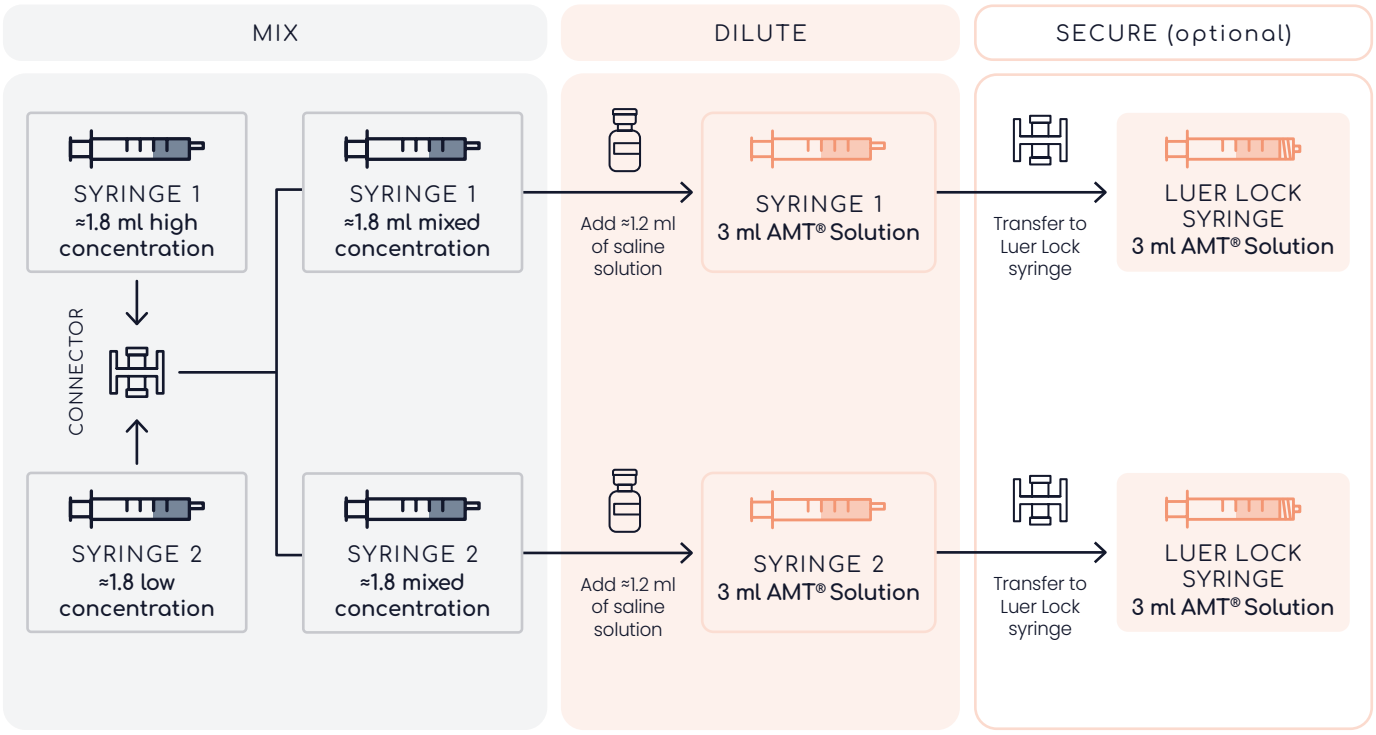


Figure 1. Dilution diagram for the obtention of the AMT® Solution.

Experience the AMT® Procedure step by step
Scan the QR code now!

POST-PROCEDURE

1. Pictures must be taken in the exact same conditions as in the pre-procedure.
2. Patient must avoid activities that increase hydrostatic blood pressure in the first 48 hours: sports, yoga, sauna, etc.
3. Avoid showering during the first 24 hours.
4. Wound hygiene must be controlled.
5. Sun protection is mandatory.

TIPS & TRICKS

1 Choosing the hair follicles

Ideally, choose the thicker hair follicles. If the first line of the retroauricular mastoid area is too thin, you can go a bit further in your follicle selection.

2 How to punch

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

If the skin 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.

3 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.

4 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.

5 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.

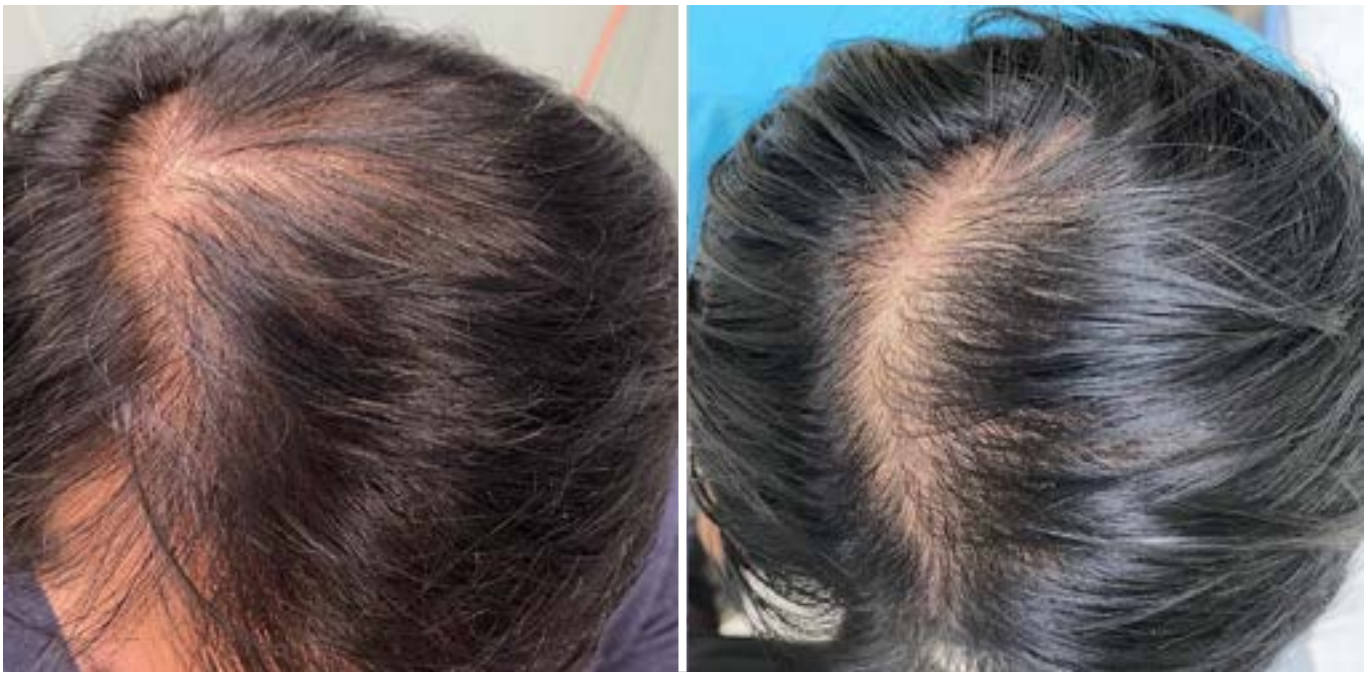
6 Haemostasia and use of vasoconstrictors

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

06 Case Reports

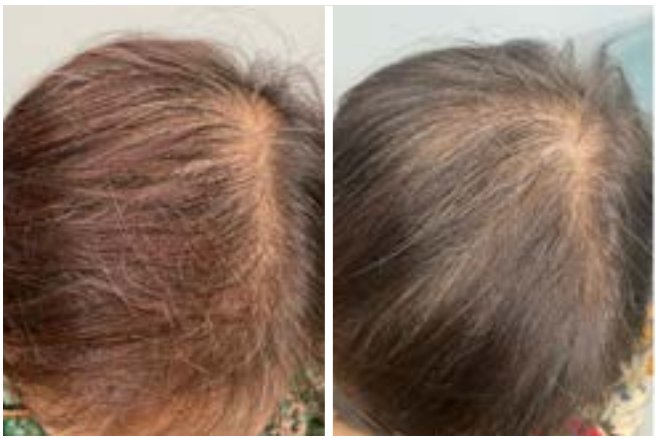
Dr. Tina Fang
Australia

BEFORE AFTER



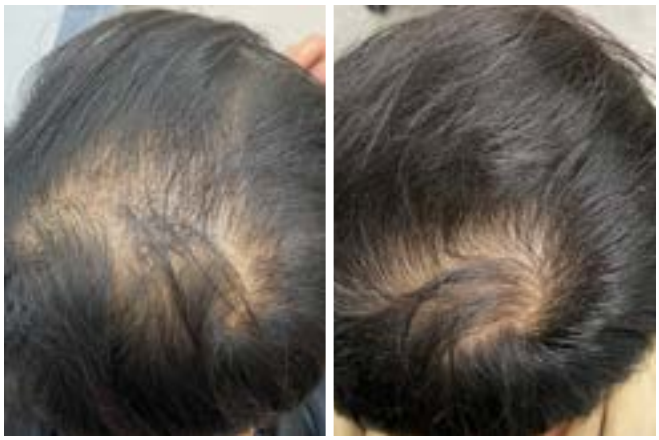
3 months
after AMT® procedure

BEFORE AFTER



3 months
after AMT® procedure

BEFORE AFTER

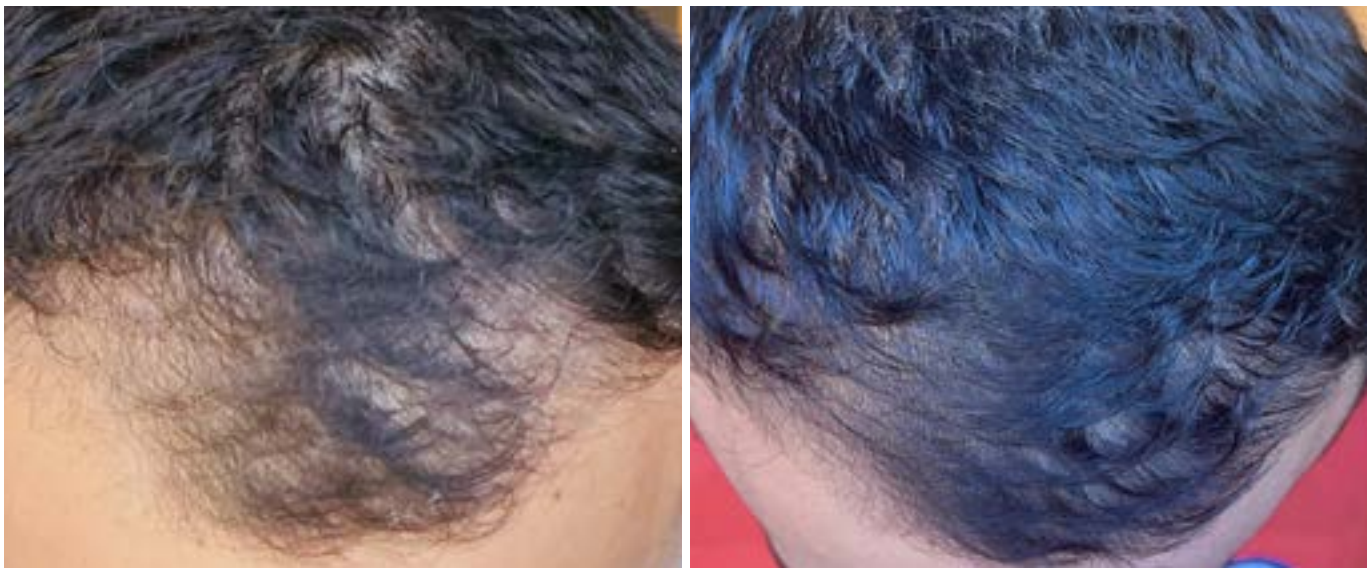


3 months
after AMT® procedure

Dr. Adel Elmodir

Lybia

BEFORE AFTER

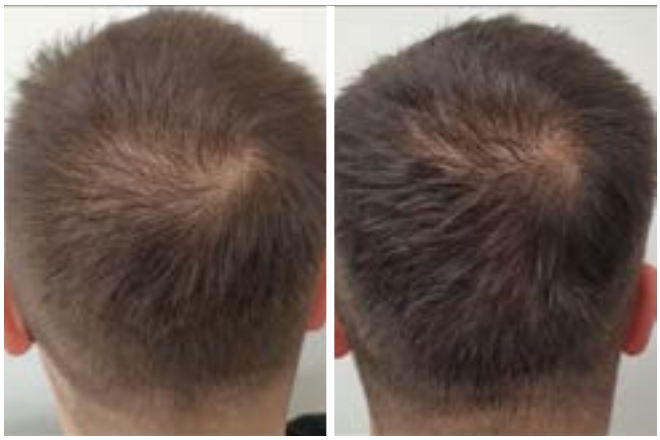


6 months
after AMT® procedure

Dr. Emel Ertürk Özdemir

Turkey

BEFORE AFTER



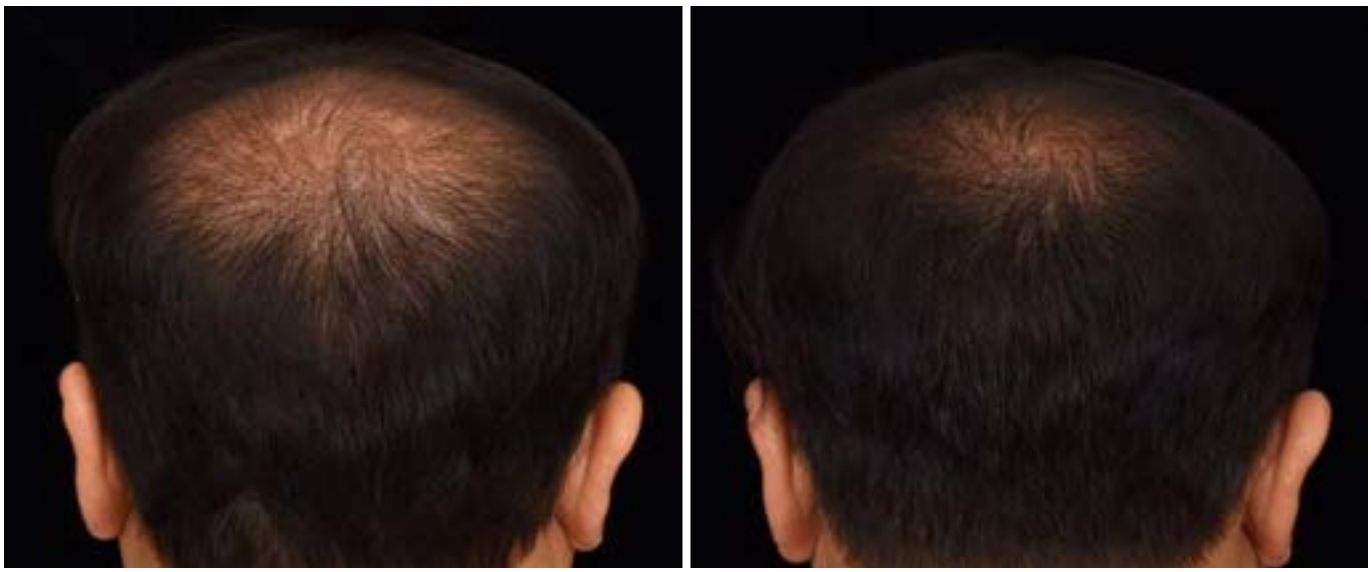
2 months
after AMT® procedure

BEFORE AFTER

2 months
after AMT® procedure

Dra. Panchaprateep
Thailand

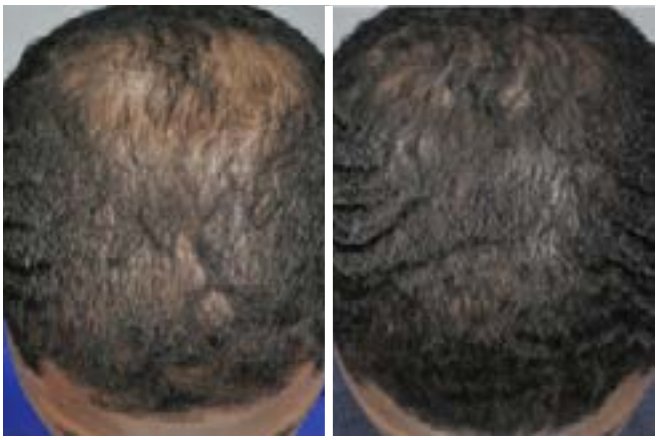
BEFORE AFTER



3 months
after AMT® procedure

Dr. Jerry Cooley
EUA

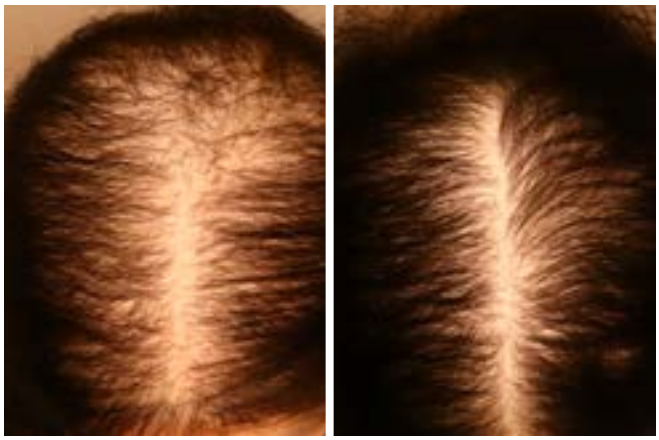
BEFORE AFTER



1 month
after AMT® procedure

Dr. Fahad Almutawa
Kuwait

BEFORE AFTER

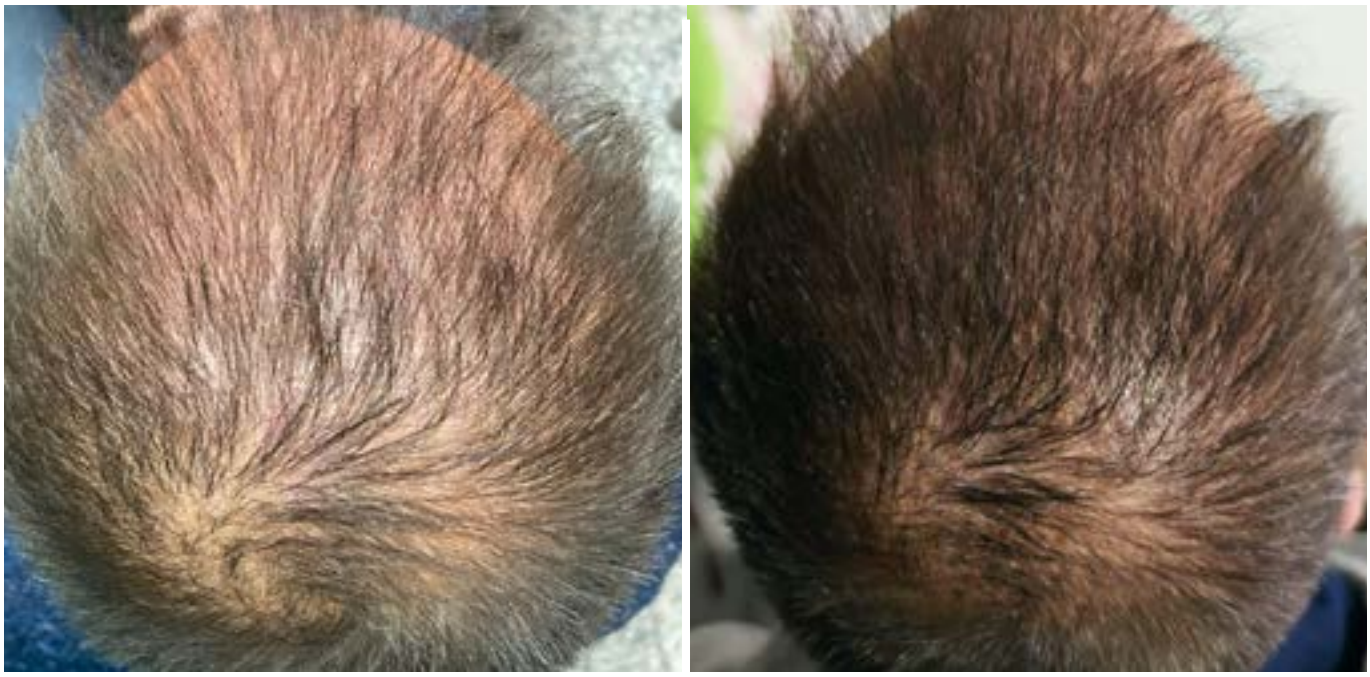


9 months
after AMT® procedure

Dr. Nur Masbout

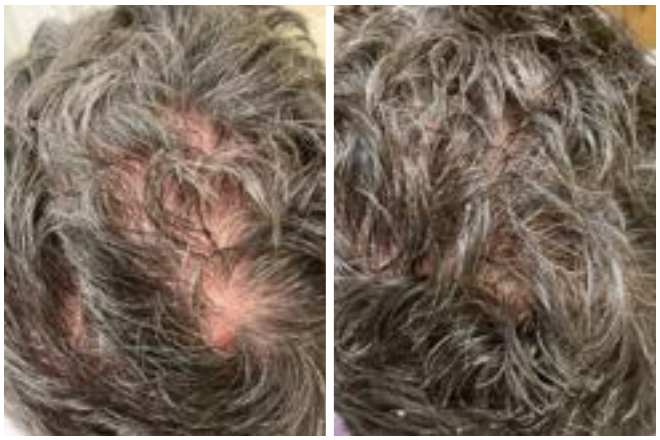
Spain

BEFORE AFTER



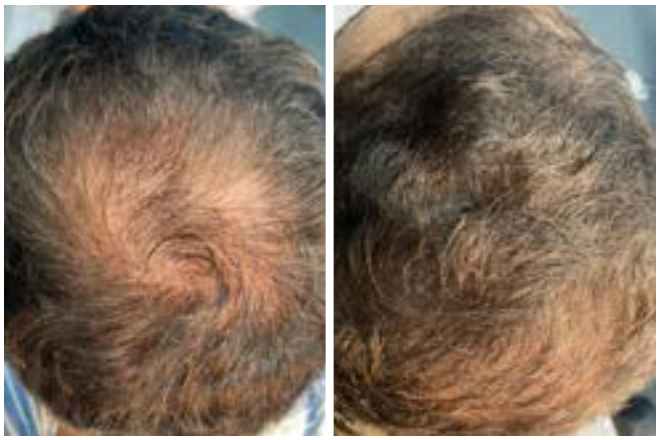
5 months
after AMT® procedure

BEFORE AFTER



3 months
after AMT® procedure

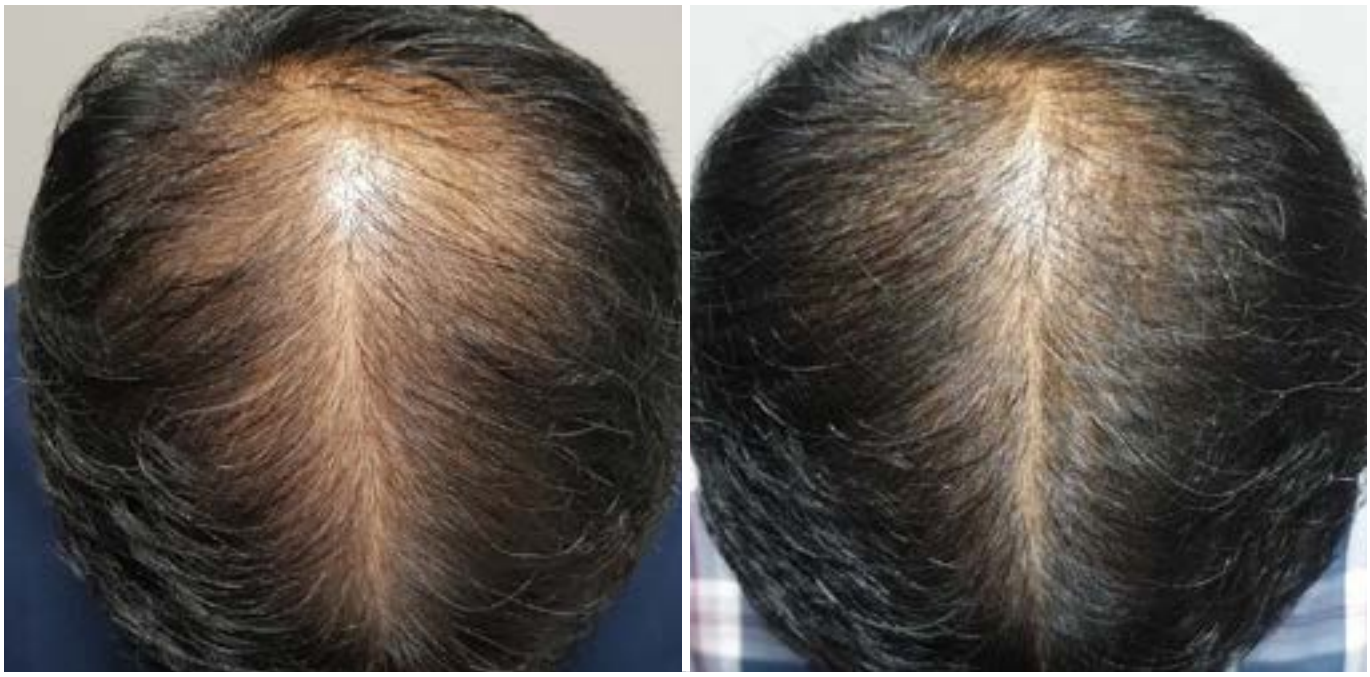
BEFORE AFTER



5 months
after AMT® procedure

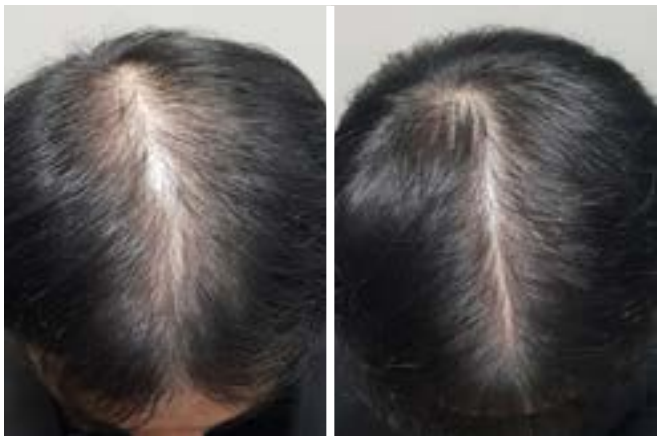
Dr. Joshua Chong
Singapore

BEFORE AFTER



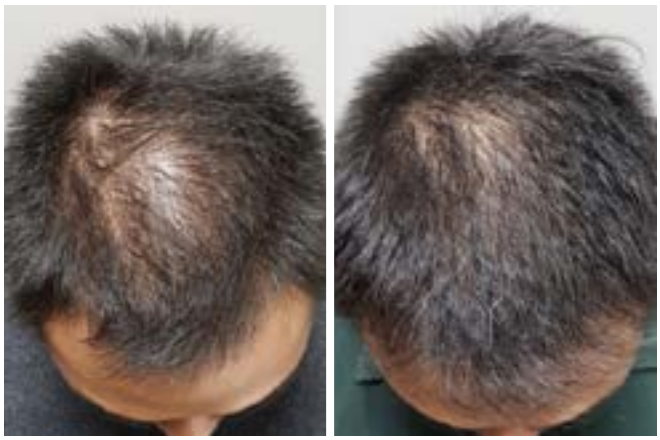
1 month
after AMT® procedure

BEFORE AFTER



3 months
after AMT® procedure

BEFORE AFTER



1 month
after AMT® procedure

07 Frequently Asked Questions

When will I see the results?

It depends on each case: age, concomitant diseases, and genetic factors... as AGA is a multifactorial condition. Microscopically, a significant reduction in the number of miniaturized hairs can be observed within three months. By the fourth month, changes in the quality and number of hairs are visible to the naked eye, as well as a high hair density. It is important to stress the importance of diagnosing AGA as the cause of hair loss for the protocol to be effective.

Does AMT® work for all kinds of alopecia?

The diagnosis is essential, as indicated by the protocol. AMT® has only proved efficacy on the AGA kind of alopecia. For this reason, it is important to know whether your patient's AGA is accompanied by another pathology such as telogen effluvium, an inflamed scalp or another pathology, since it can fully affect the success of the procedure. It is relevant not to have advanced evolutionary alopecia, as well as a normal blood test.

It is under these conditions that AMT® helps to slow down the evolution of androgenetic alopecia in a biological way.

Are there any risks regarding the procedure?

The procedure has no complications if performed under sterile conditions and strictly complies with the protocol, since it is an autologous (tissue from the same patient) and homologous (tissue from the same embryonical origin) micrografting procedure. AMT® stands out for being a minimally invasive and fast procedure that takes no more than 30 minutes to perform.

How is AMT® different to a PRP Treatment?

With AMT® doctors obtain a micrograft solution that comes from skin biopsies that have the same embryological origin as the receptor site (homologous), meaning that the pathways activated with this procedure are much more specific than in a PRP treatment. Unlike PRP, AMT® generates a solution which contains not only growth factors, but also progenitor cells that remain in the patient's scalp. Those cells will be continuously delivering cytokines, chemokines and growth factors to enhance regenerative properties of the affected area, for years. As a result, the healing will be much more efficient, and the results will be better and last longer.

What AGA stages are eligible for an AMT® procedure?

AMT® can be useful in all stages of an AGA process in different ways. In an initial stage, it can be used as a preventive immunotherapy procedure thanks to the numerous cytokines, chemokines and growth factors that will nourish hair follicles. In mild-moderate stages, it can be useful in combination with other therapies to help rescuing hair follicles in severe states of miniaturization. In advanced stages of AGA, it can be used in combination with a hair transplant, to both accelerate healing and enhance the success rate of transplanted UFCs.

What can you combine an AMT® procedure with?

Being AMT® an autologous and homologous procedure, it can be combined with any therapy, without any risks of cross-reaction, since the whole process is done with cells from the own patient and saline solution, with no extra chemicals added.

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