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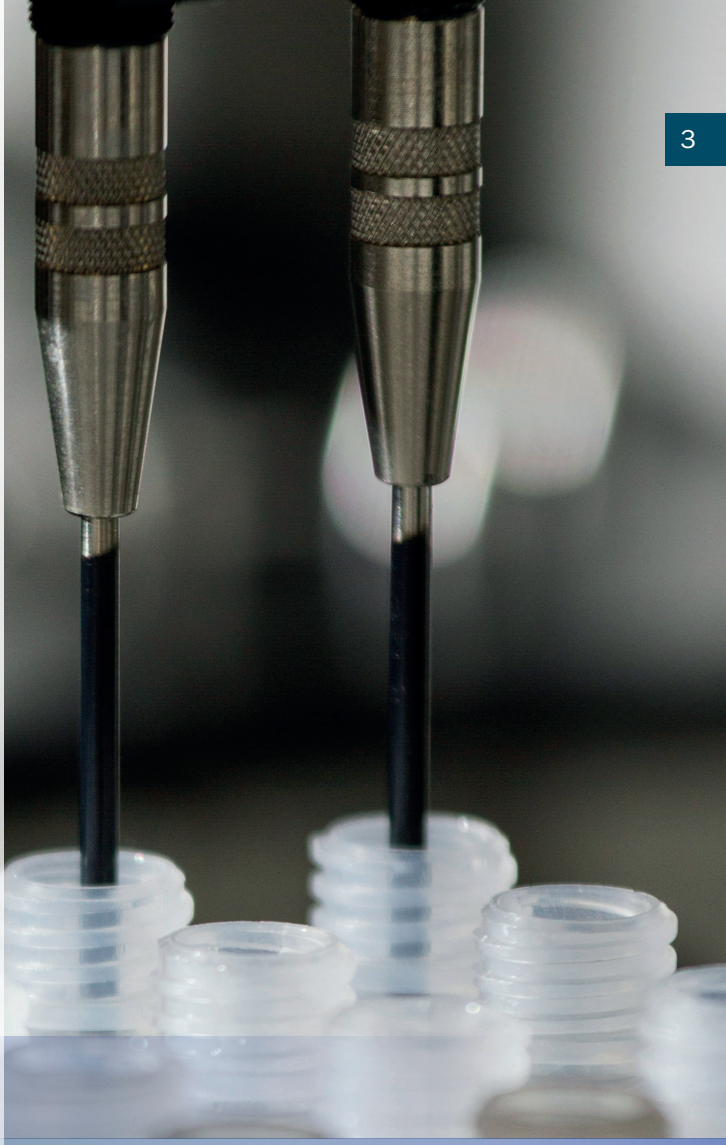

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EDITORIALS

BENEFITS OF REGENERATIVE BIOSURGERY

Prof. Albert-Claude BENHAMOU
Founding President of ARSIA,
Past-President of the French National Academy of Surgery

With the creation of the International Academy of Biosurgery (ARSIA), we want to structure an international scientific space dedicated to this new founding stage of surgery. We are ushering in the era of regenerative biosurgery, which must be combined with the structuring contributions of 4.0 surgery incorporating digital technology, robotics and artificial intelligence.

A new stage in surgical thinking

For a long time, surgery has been associated with the mechanical, often invasive, act of removing, repairing or reconstructing. Regenerative biosurgery proposes a breakthrough: intervening on living tissue by stimulating its capacity for self-repair using biological, cellular and technological devices, while reducing the aggressiveness of the surgical procedure.

This hybrid model, which respects living tissue, opens up a vast new field for the surgery of the future.

This is not an intuition. It's already an acknowledgement that scientific ideas and practices are evolving, and that a number of disciplines are moving forward, including cell therapy, bioengineering, personalised regenerative medicine, 3D bioprinting and bioactive physical agents such as lasers, ultrasound and radiofrequency.

ARSIA intends to develop the cross-disciplinary field of bio-disciplines, which will find full expansion both in experimental work and in clinical research and their industrial developments. ARSIA intends to unite all these players around an academic centre of excellence.

“Regenerative surgery is at the dawn of a major transformation of the entire ecosystem of surgical and interventional practices.”

Prof. Albert-Claude BENHAMOU

ARSIA: an international multidisciplinary vocation

ARSIA - the Actual Regenerative Surgery International Academy - has positioned itself as a scientific, multidisciplinary, multilingual think tank with an international vocation.

Our aim is clear: to bring together learned societies, clinician-researchers, bio-technological innovators and biosurgeons to discuss the major challenges facing regenerative surgical and interventional practices.

ARSIA’s mission is based on several pillars:

- Promoting less invasive, better tolerated and more effective surgical techniques.

- To stimulate research into wound healing, tissue regeneration and biological engineering.

- Encourage practical clinical applications in all medical and surgical disciplines.

- Reduce hospitalisation costs by adopting a more physiological approach to less traumatic surgical procedures.

This initiative already enjoys the support of numerous French and international learned societies.
Together, in an open, interdisciplinary approach, we must build the regenerative biosurgery of today and tomorrow.

Between the history of medicine and surgery, the evolution of life sciences and the systemic revolution of the digital age.

Cell and tissue regeneration is an ancient idea. It has its roots in mythology - Prometheus’ liver comes to mind - and in the history of surgery with Professor Reverdin, the unwitting pioneer of autologous skin grafting in the 19th century.

Today, bio-technologies are enabling us to put into practice what nature and intuition had foreseen.
Thanks to the seminal work of researchers such as William Haseltine, John Gurdon and Shinya Yamanaka - winner of the 2012 Nobel Prize for cell reprogramming - we now know that adult cells can become pluripotent again, capable of regenerating numerous human tissues.

This advance makes it possible to carry out repair and regenerative practices that were previously unthinkable, such as the introduction of bioprinting of autologous skin, layer by layer, as illustrated by the recent work of Dr Diala Haykal.

Concrete prospects for cross-disciplinary cooperation

Regenerative biosurgery has applications in almost every branch of surgery: plastic, orthopaedic, cardiovascular, digestive, urological, gynaecological, ENT, maxillofacial, aesthetic and reconstructive surgery, organ transplants and transplants, treatment of burns and chronic wounds, etc.

ARSIA is committed to transforming surgery through tissue regeneration and multidisciplinary innovation.

By mobilising ortho-biological (autologous) resources, i.e. those derived from the patient himself (such as PRP, stem cells, growth factors), and combining them with bio-energetic technological devices (lasers, radiofrequencies, ultrasound), we are entering the era of hybrid personalised regenerative therapies, with the prospect of better healing by making greater use of the regenerative potential of living organisms.

The ARSIA task force

We are calling for a broad mobilisation to integrate regenerative biosurgery into all the surgical disciplines represented within the French National Academy of Surgery.

All 13 major surgical and interventional specialities and their sub-disciplines are concerned. Each can benefit from tissue engineering, cellular reprogramming, 3D bio-printing and artificial intelligence applied to regeneration.

This is no longer a distant hope, but a reality in the making. Together, let's make this revolution a task force for integrated, rigorous surgical practices that benefit patients.

Which of the major disciplines represented by the National Academy of Surgery will be affected by regenerative biosurgery?

The National Academy of Surgery represents 13 major thematic disciplines.
Within these disciplines, there are specialised subsets, as is the case for example in trauma and orthopaedic surgery, with experts working on specific areas such as the shoulder and knee.

All disciplines and sub-disciplines should include regenerative biosurgery to promote the contributions of tissue engineering and its innovative practices, such as the support of 3D bioprinting assisted by artificial intelligence.

In the history there is not a drug or medical technology that is clinicaly efficient from the head to the toe, like PRP in combination with tissue engineering.

TO REMEMBER

Regenerative biosurgery will transform surgical practices in several significant ways:

1. **Improved tolerance and reduced aggressiveness of surgical procedures**
2. **Fewer scars and after-effects.**
3. **Fewer hospitalisations and lower costs.**
4. **Varied clinical applications and innovation :**

Biosurgery would make it possible to explore a multitude of clinical disciplines, with potential applications in numerous fields such as reconstructive, plastic and cosmetic surgery, orthopaedics, visceral, cardiac, vascular, gynaecological, urological and anti-ageing surgery, organ transplants, chronic wounds, burns and tissue defects.

5. **Exploiting self-repair capacities :**

ARSIA emphasises the importance of exploiting the body's natural self-repair mechanisms, which could transform the way surgeons approach operations.

The main aims of the new International Academy of Biosurgery (ARSIA) include:

1. **Promoting biosurgery:**

ARSIA aims to further research and development in the field of biosurgery, a fundamental field that exploits the self-repairing capabilities of the human body.

2. **International collaboration:**

ARSIA seeks to bring together leading learned societies, as well as international correspondents from various regions, to create a global academic network.

3. **Diverse clinical applications:**

ARSIA emphasises the search for varied clinical applications that improve the tolerability of surgical procedures, reduce their aggressiveness, and limit sequelae and hospitalisation times.

4. **Innovative approaches :**

ARSIA plans to use modern medical devices and regeneration techniques, including growth factors and other biological or biophysical agents, to aid tissue repair and regeneration.

MY MESSAGE FOR ARSIA

at the launch of ARSIA on May 23, 2025.

Prof. Carole MATHELIN

President of the French National Academy of Surgery

“As a surgeon with a long-standing commitment to oncology, and breast surgery in particular,I would like to emphasise my keen interest in this innovative initiative.”

Tissue regeneration in oncology: a major challenge

Breast cancer surgery is often mutilating, requiring sophisticated reconstruction strategies. Lipofilling, which restores lost volume using autologous fatty tissue, is one of the most promising techniques. It is appreciated by patients for being natural and less invasive. Some questions remain about the use of stem cells in oncology. There are fears about the possible reactivation of dormant cancer cells. These concerns underline the importance of rigorous assessments to define indications and contraindications.

A collaborative, interdisciplinary approach

ARSIA offers a unique framework for collaboration between researchers, clinicians and institutions, to conduct shared clinical work, promote the publication of robust data and encourage the emergence of new standards of practice. This approach will not only make it possible to refine therapeutic indications, but also to better identify high-risk situations.

In this respect, the International Society of Senology - which federates the learned societies in the field worldwide - has shown a keen interest in joining this initiative. It could play a key role in the evaluation of regenerative approaches, by encouraging international exchanges of experience and supporting multicentre research projects.

Strong patient expectations

This innovation meets a growing demand from patients for more natural and less invasive reconstructions, avoiding implants or foreign materials wherever possible. Many patient

“It is with confidence and enthusiasm that I welcome the birth of the International Academy of Regenerative Surgery (ARSIA).”

Prof. Carole MATHELIN

associations have expressed their desire to become actively involved in this process. Their commitment is invaluable in guiding research towards practical solutions tailored to their real needs.

In a nutshell

Regenerative biosurgery represents a major advance for reconstructive surgery in cancerology. It is based on :

- **Autologous techniques**, which are better tolerated and preferred by patients;

- **Natural tissue regeneration capabilities**, via lipofilling or stem cells;

- **A demand for safety**, requiring rigorous clinical research to validate each new application;

- **A collective approach**, involving healthcare professionals, researchers and patients.

We are proud that this first meeting is being held under the aegis of the Académie Nationale de Chirurgie. It marks a structuring step towards more personalised, ethical and innovative medicine. ARSIA will have a key role to play in this process.

Pr Carole MATHELIN Pr Hubert JOHANET

Regenerative biosurgery for reconstructive surgery

Prof. Franck Duteille
Executive Chairman of ARSIA,
Chairman of the CNU for Plastic,
Reconstructive and Aesthetic Surgery

There have been three main phases in the development of reconstructive surgery:

The first was based on the use of autologous tissue and free flaps. This period, marked by the surgery of the “Gueules cassées”, enabled major reconstructions to be carried out using the patient’s own resources.

This method remains partially mutilating: moving tissue from one area to reconstruct another inevitably leads to after-effects.

The second phase focused on biomaterials and artificial dermis. While these technical solutions have led to certain advances, their biological performance has proved inferior to that of human tissue, in terms of regeneration, integration and tolerance.

We are now entering a third phase, that of autologous regenerative biosurgery. This is based on the body’s natural ability to repair itself, stimulated by the use of stem cells, growth factors or other personalised biological devices. The aim of this approach is to reconstruct tissues as close as possible to their original integrity, after trauma, burns or tumour resection.

“The objective is clear: to improve surgical results by integrating this new biosurgery into the therapeutic tree we know.”

Prof. Franck Duteille

The structuring role of ARSIA

ARSIA’s mission is to provide a framework for the integration of these new regenerative biotechnologies into surgical practice.

It provides:
- a scientific framework for these innovations by drawing up precise recommendations on their **indications and limitations**;

- encourage **rigorous multi-centre studies** to validate their effectiveness in a variety of clinical contexts;

- help them to be **gradually integrated** into existing **therapeutic decision trees**.

This transformation also presupposes a change of culture within the surgical community. Adopting these technologies means reconsidering certain habits, embracing innovation with a critical and rigorous eye, and combining traditional approaches with these new hybrid solutions.

Advantages and limitations of regenerative approaches:

Advantages:
- Biomaterials and biological devices offer effective alternative solutions to traditional reconstructions.

- They provide improved functional and aesthetic restoration, while reducing the sequelae associated with harvesting.

- Autologous regenerative techniques promote better integration and tolerance.

Limitations:
- Their repair capacity may be inferior to that of native tissue in certain cases.

- The novelty of these technologies requires strict supervision, solid clinical studies and rigorous selection of indications.

- Acceptance by the medical profession is still under construction: changing established practices is a challenge that we need to take up collectively.

Regenerative biosurgery marks a decisive stage in the development of reconstructive surgery.

Thanks to ARSIA, we have the opportunity to support, structure and disseminate these innovations within a robust scientific framework. The objective is clear: to improve surgical results by integrating this new biosurgery into the therapeutic tree we know.

ARSIA at the crossroads of research and development

Antoine Turzi,
Co-founder of ARSIA,
CEO of RegenLab, Founder of the BioBridge Foundation

The founding of ARSIA is based on a strong conviction: medical advances in regenerative surgery require close synergy between scientific research, practitioners and industry. It was in this spirit that the BioBridge Foundation was created in 2001, to encourage transatlantic scientific exchanges, with conferences hosted at the UN in Geneva, bringing together the leading international academic institutions.

Dual expertise: research and production

At RegenLab, our mission is based on two complementary pillars: scientific innovation and industrial development.

Research enables us to devise new approaches to tissue engineering, through constant dialogue with doctors, surgeons, clinicians and biology researchers. This technical research must then be rigorously validated at clinical level. To date, more than 300 scientific publications and several collective works have documented the effectiveness of our systems. One outstanding example is the pioneering French study into Peyronie's disease, combining PRP and hyaluronic acid.

Industrial production is subject to strict standards. We design medical devices that enable living cells to be prepared, handled and injected in a closed circuit, under optimum safety conditions. These devices are used in several European university hospitals for clinical studies in orthopaedics, dermatology, gynaecology and regenerative medicine.

“ARSIA is a strategic platform for structuring the integration of regenerative medical technologies into surgical practice.”

Antoine Turzi

Clinical evaluation: an essential requirement

Clinical evaluation is the cornerstone of any credible medical technology. It guarantees the safety, therapeutic efficacy and regulatory compliance of a device.

For example, our CellularMatrix® technology - a blend of hyaluronic acid and autologous PRP - has demonstrated its effectiveness in indications as diverse as :

- Grade IV osteoarthritis of the knee, with multicentre studies (one pivotal study involving 280 patients),
- gynaecological medicine, with publications in leading international journals,
- chronic wounds (ulcers, post-surgical complications), thanks to work carried out in France, leading to FDA approval and CMS reimbursement in the United States.

These advances require years of clinical trials, conducted in accordance with Good Clinical Practice (GCP), before they can be recognised by the health authorities. Rigorous validation is therefore an essential step in any development strategy.

Closed-loop PRP: a benchmark in safety

Safety is at the heart of our commitments. PRP produced via a CE-certified, closed-circuit medical device is classified as level A (minimal risk) according to European standard NF EN 16844 A2, concerning injectable products for aesthetic medicine.

This classification places it ahead of hyaluronic acids (class B) or other complex injectable agents (classes C to E). This recognition demonstrates the reliability of a product that complies with the highest standards of quality and safety (European regulation EU-MDR 2017/745).

Towards an augmented clinic: the benefits of in silico research

To take things a step further, we are exploring innovative approaches such as in silico control models, which make it possible, in certain situations, to replace control groups with computer simulations based on existing clinical data.

Although these practices are not yet fully recognised by the FDA for all indications, they offer a promising future for streamlining evaluation protocols without compromising scientific rigour.

The industry’s commitment, when backed by scientific rigour, multi-centre studies and production in line with international standards, becomes an accelerator of innovation for the benefit of patients.

We are fully available to collaborate with all the specialists involved in this approach, in order to contribute to the emergence of regenerative biosurgery that is safe, effective and validated according to the state of the art.

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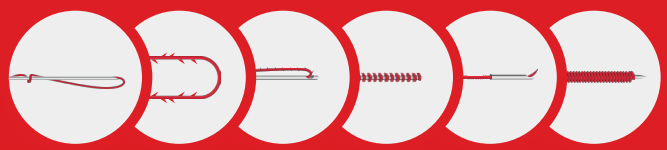


BY SWISS GROUP

ARSIA SCIENTIFIC COMMITTEE CONTRIBUTIONS

TO T**RANSDISCIPLINARY** RESEARCH AND APPLICATIONS IN **REGENERATIVE BIOSURGERY**

Concepts and strategies **Rethinking "regenerative biosurgery"**

Dr Dorina DONICI

I am a plastic surgeon and gynecologist, trained in Moldova. I have always been drawn to regenerative medicine and surgery. For over 25 years, I have worked in surgery, gynecology, and interdisciplinary preventive internal medicine.

From the very beginning, regenerative medecine has fascinated me. Because I also wanted to remain closely involved in clinical practice, I sought out countries where regenerative medicine is legally recognized, in order to work directly with patients.

That's why I founded my clinic in Moscow, which became the university clinic of the Pirogov Medical University of Russia in February 2024. In collaboration with the department of therapeutic oncology and reconstructive surgical oncology, we are now intensifying our work on stem cells and regenerative methods.

Today, I would like to share with you the concept of regenerative bio-surgery, as well as strategies and insights into bio-regeneration in plastic surgery.

Currently, when we talk about the most advanced tissue regeneration methods, cell therapy remains at the forefront—a true star. We refer to stem cells, specialized cells, and their healing potential.
Since 2009, I have extensively worked with fat grafting and mesenchymal stem cells used in various types of injections.

STEM CELL THERAPY

I also had valuable experiences with the Stem Cell Institute in Seoul, working on stem cell therapy for cardiac and other diseases.
I observed how fat behaves when injected alongside stem cells and their regenerative secretome—growth factors, exosomes, etc.

3D BIOPRINTING

Another strategy is 3D bioprinting, which involves creating complex cellular structures using bioprinters that allow for custom tissue engineering.

GROWTH FACTORS

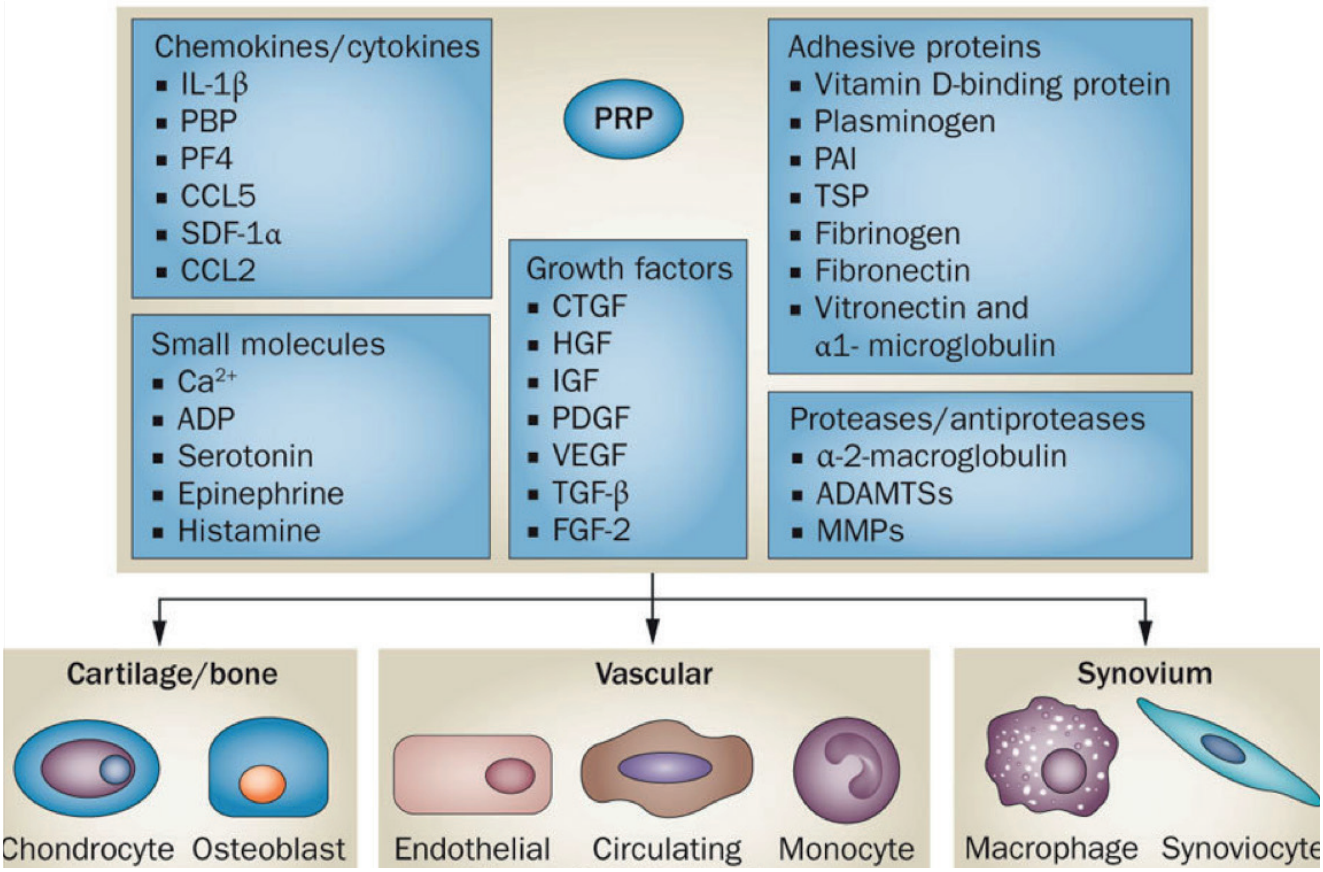
PRP (Platelet-Rich Plasma) is the star when it comes to growth factors.

SECRETOMES AND EXOSOMES

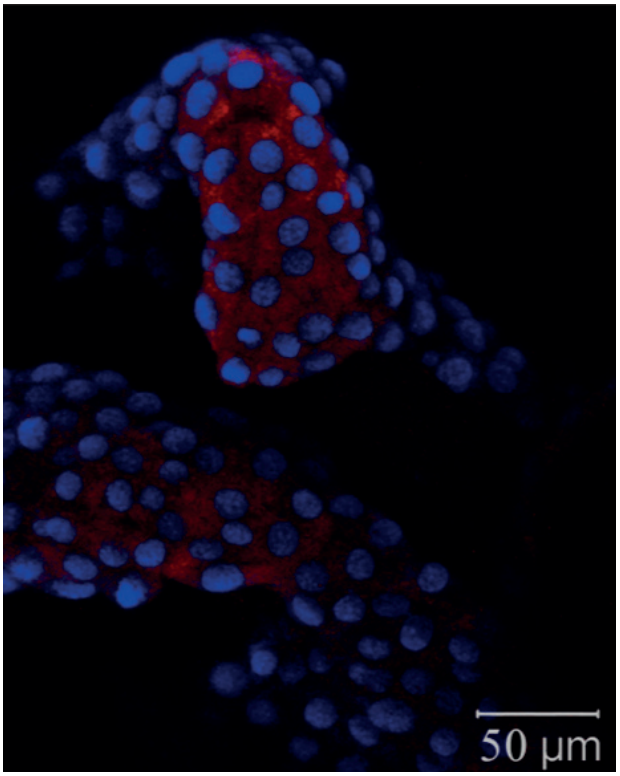
These are highly active molecules derived from stem cells or other cell types—such as bone marrow, immune cells, or lymphocytes.

Dr Dorina DONICI

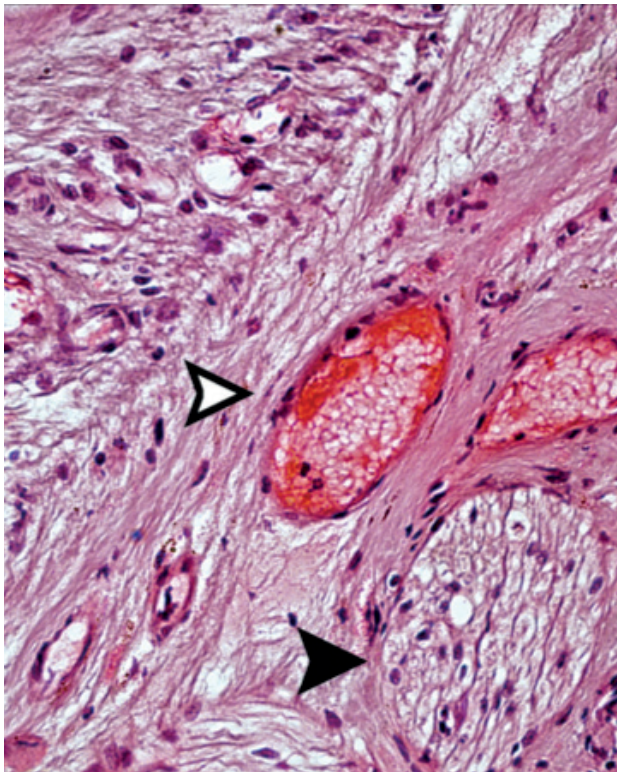
Medical Director, Swiss Group SA (Geneva, Paris)



Stimulating cell proliferation and the formation of new blood vessels is also a key method in modern tissue regeneration- visible on the surface of the matrix.



The surface of the resorbable thread serves as a substrate for cell adhesion and proliferation. The nuclei of fibroblasts are visible on the surface of the matrix.



After 60 days of implantation, the device is replaced by tissue from the experimental animal. Blood vessels (white arrows) and nerve fibers (black) are visible.

Luxeface technique, along with more than 30 types of threads (PDO, PCL, PLLA, etc.), is used for both lifting and regenerative effects on the face.

They're particularly promising because they can replace cellular therapies and offer similar regenerative results with lower immunological risks.

I believe this pathway will become an essential part of regenerative surgery.

BIOLOGICAL SCAFFOLDS

With SWISS GROUP SA, my company, I have been developing resorbable suspension threads for body and facial aesthetic procedures for over 15 years. These offer results comparable to plastic surgery—but without surgery.

This minimally invasive technology has always intrigued me. I asked myself: Can we implant materials into tissues that act like magnets to attract stem cells, stimulate their activity, and regenerate tissue—without directly injecting cells ?

Stimulating natural tissue regeneration has always been my main focus.

ANIMAL & HUMAN MODELS OF TISSUE REPAIR

In animal models, and later in human models, we observed that biomaterials can fully resorb within two months. In the implantation area, we saw the formation of new blood vessels and full tissue reconstruction, mimicking ontogenesis.

This was remarkable. Our scientific group went further by testing different models using tubes, sponges, and films. To understand the process more deeply, we also created intestinal wall defects.

One slide shows an animal model where the defect was covered with a biofilm.

Within just one week, the site was completely regenerated with intestinal tissue.

Most surprisingly, after one week, tissue started growing from the peritoneal side. The arrow indicates the mucosal side.

The film was still in place but fully covered by tissue on both sides.

After three weeks, the most impressive findings emerged: On the luminal side of the intestine, tissue regenerated fully, mimicking ontogenesis.

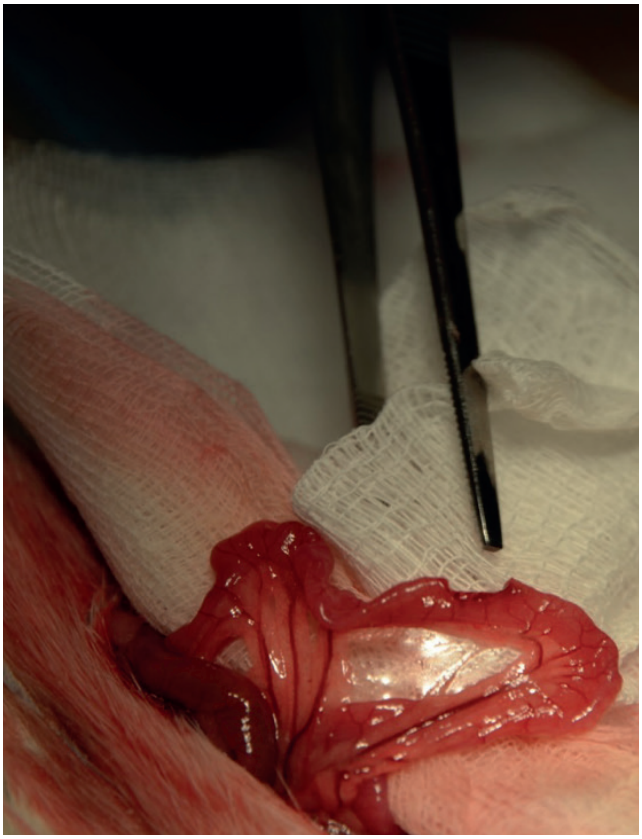
This experimental model, initially tested in animals, is now being developed for human applications.

Importantly, no side effects have been observed so far. At this stage, I cannot reveal further details, as the material is currently under patent application.

But early results show an extraordinary tissue regeneration capability using a non-cellular stimulant—no cells, no growth factors, no peptides, no secretome.

I believe that in the future, such approaches could revolutionize surgical practice—such as suture materials capable of stimulating tissue regeneration without leaving scar tissue.

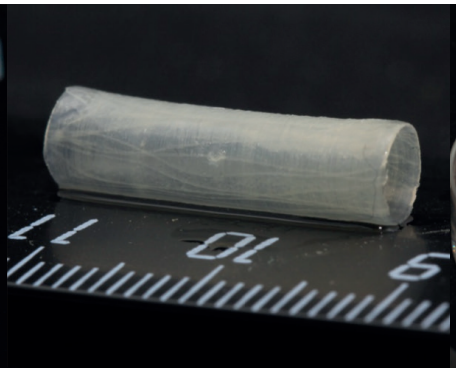
This is why I believe we are on the verge of a revolution in the field of resorbable threads. Within 3 to 5 years, we may see a major transformation—once all certifications are completed, as rightly pointed out by Antoine Turzi. This is a necessary but long process.



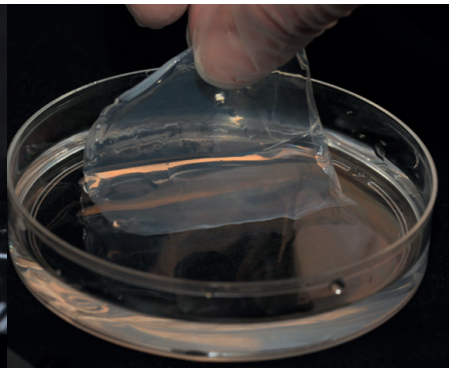
Artificial defect of the small intestine (location of the defect indicated by an arrow)

The defect is covered by the device/film

Biodegradable materials with varying porosities

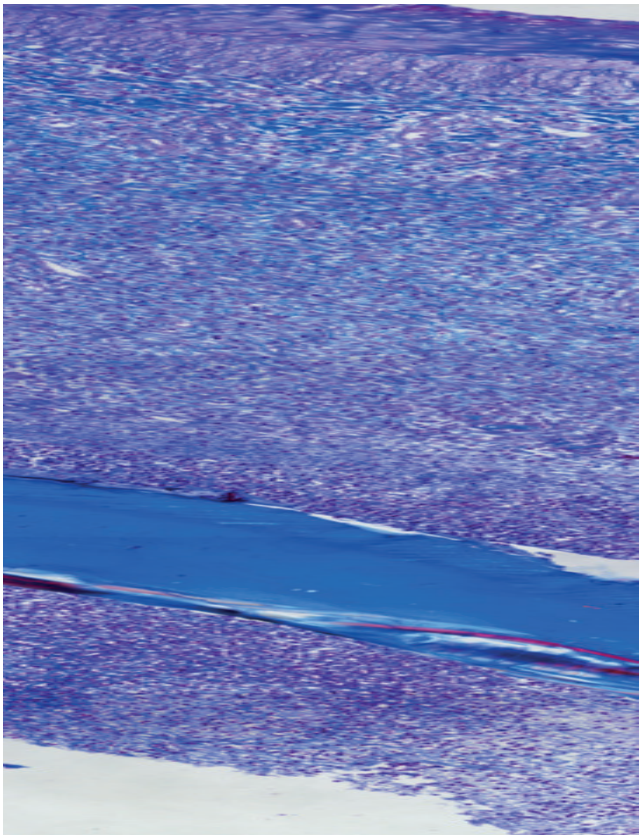


Tubes for the regeneration of hollow organs

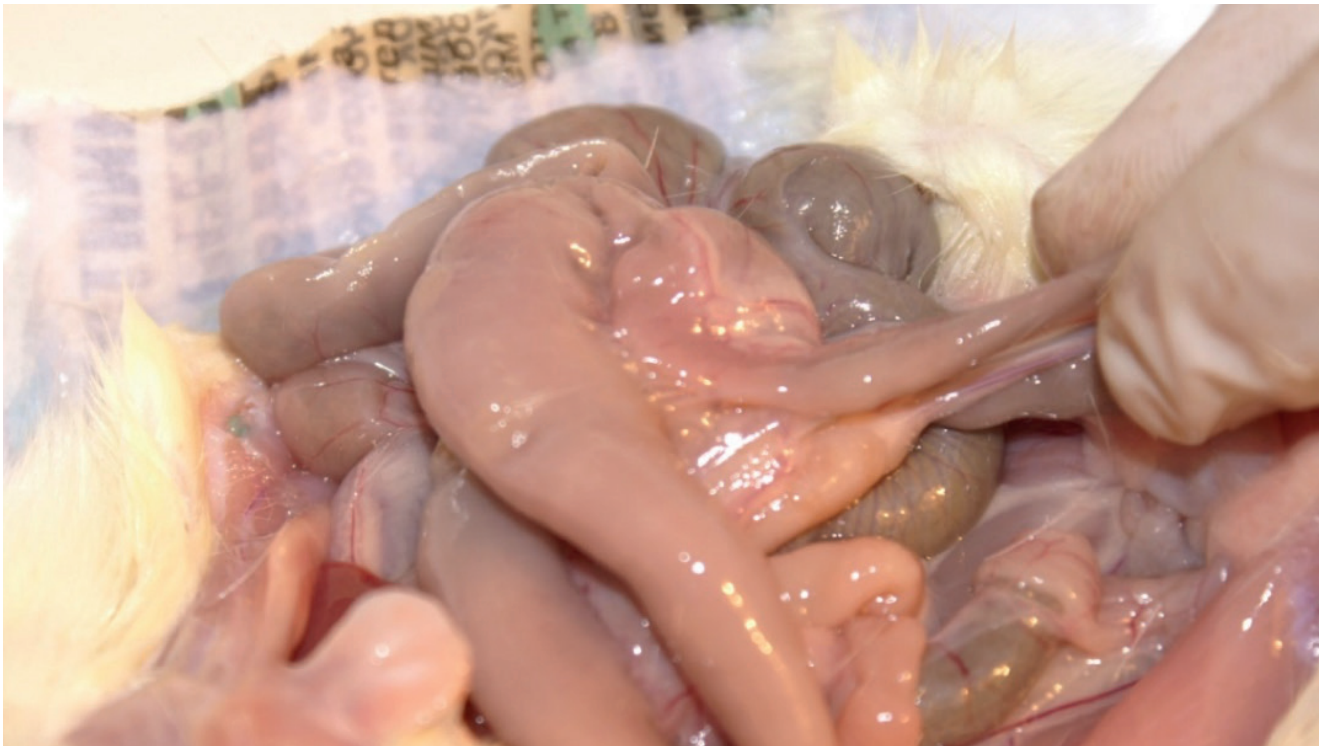


Films – a key component in the creation and modification of biodegradable structures

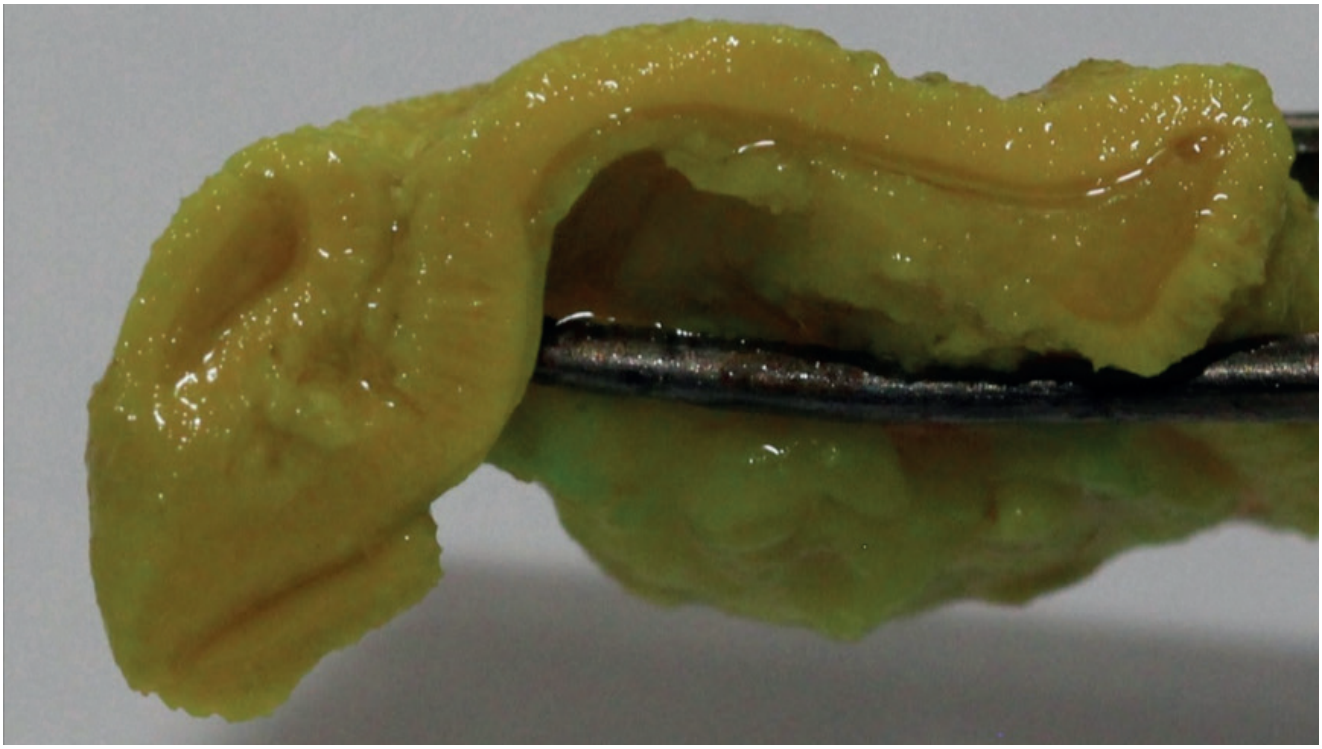
One week after implantation, the device can be found in the intestinal wall.



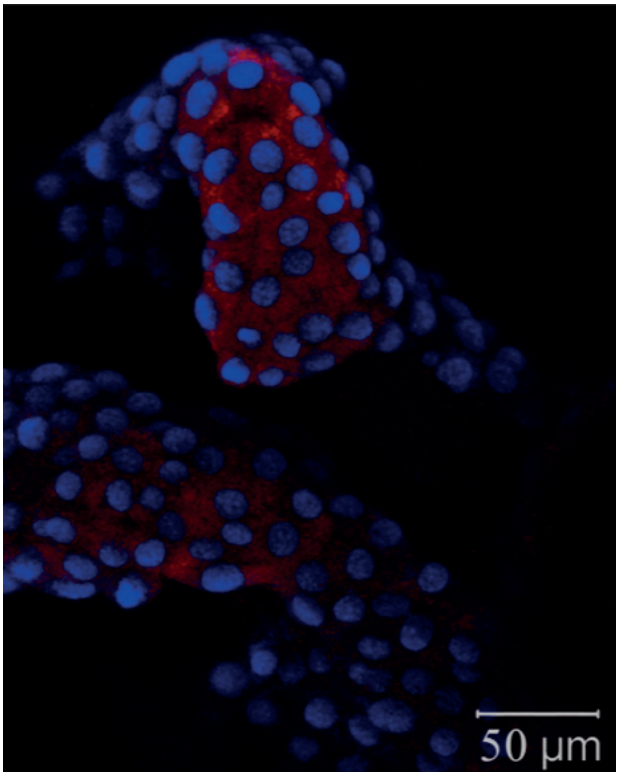
Histological section of the intestinal area containing remnants of the implant.



Intestine of the experimental animal one week after implantation



After 3 weeks, the mucosa and the muscular wall are fully formed.



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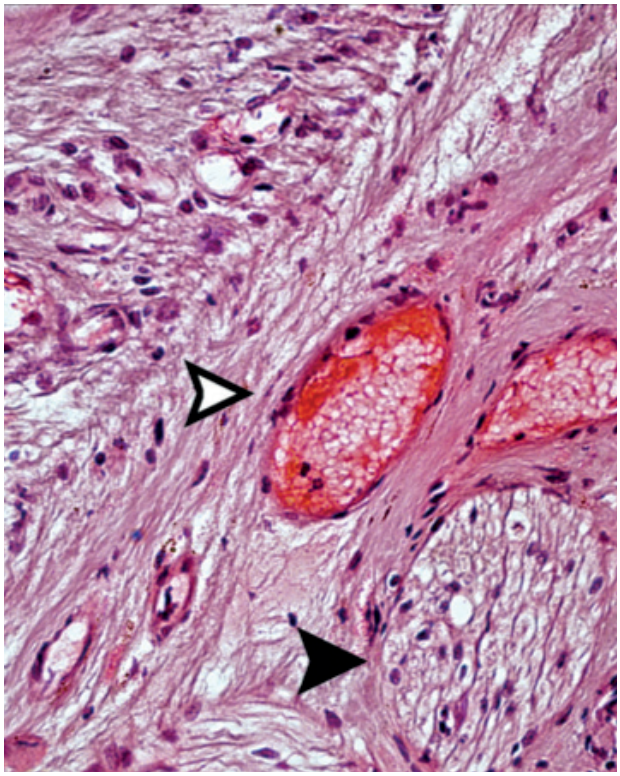

After 60 days of implantation, the device is replaced by tissue from the experimental animal. Blood vessels (white arrows) and nerve fibers (black) are visible.

Hyaluronic Acid in Wound Repair: Biological Foundations and Evidence-Based Perspectives

Dr Denis COUCHOUREL

This article aims to provide a comprehensive overview of the biological roles of HA in wound healing, structured around the phases of tissue repair. Particular attention is given to HA's molecular properties and their clinical translation in surgical and chronic wound management.

1. INTRODUCTION

Wound healing is a dynamic, tightly regulated biological process involving multiple overlapping phases—hemostasis, inflammation, proliferation, and remodeling—aimed at restoring tissue integrity following injury.

Clinically, wounds can be classified as **acute** (e.g., surgical incisions, burns) or **chronic**, with the latter often associated with comorbidities such as diabetes mellitus or peripheral vascular disease.

Chronic wounds represent a significant burden on healthcare systems worldwide, with impaired healing leading to prolonged morbidity, increased risk of infection, and substantial costs (Voigt & Driver, 2012).

Hyaluronic acid (HA), a glycosaminoglycan naturally present in the extracellular matrix (ECM), has gained considerable interest in recent years for its multifaceted role in wound repair. Due to its high biocompatibility, hygroscopic properties, and involvement in cell migration and signaling, HA is not only a passive component of the ECM but also an active modulator of the healing process.

It is used in various medical-grade formulations, including topical dressings, injectable gels, and hydrogel-based delivery systems, particularly in the management of difficult-to-heal wounds (Parmar et al., 2025).

2. FUNDAMENTAL BIOLOGY OF HYALURONIC ACID IN THE WOUND HEALING CONTEXT

Hyaluronic acid (HA) is a **non-sulfated glycosaminoglycan (GAG)** composed of repeating disaccharide units of **D-glucuronic acid and N-acetyl-D-glucosamine**, linked by -1,3 and -1,4 glycosidic bonds. Unlike other GAGs, HA is **not synthesized in the Golgi apparatus**, but rather at the plasma membrane by three isoforms of **hyaluronan**

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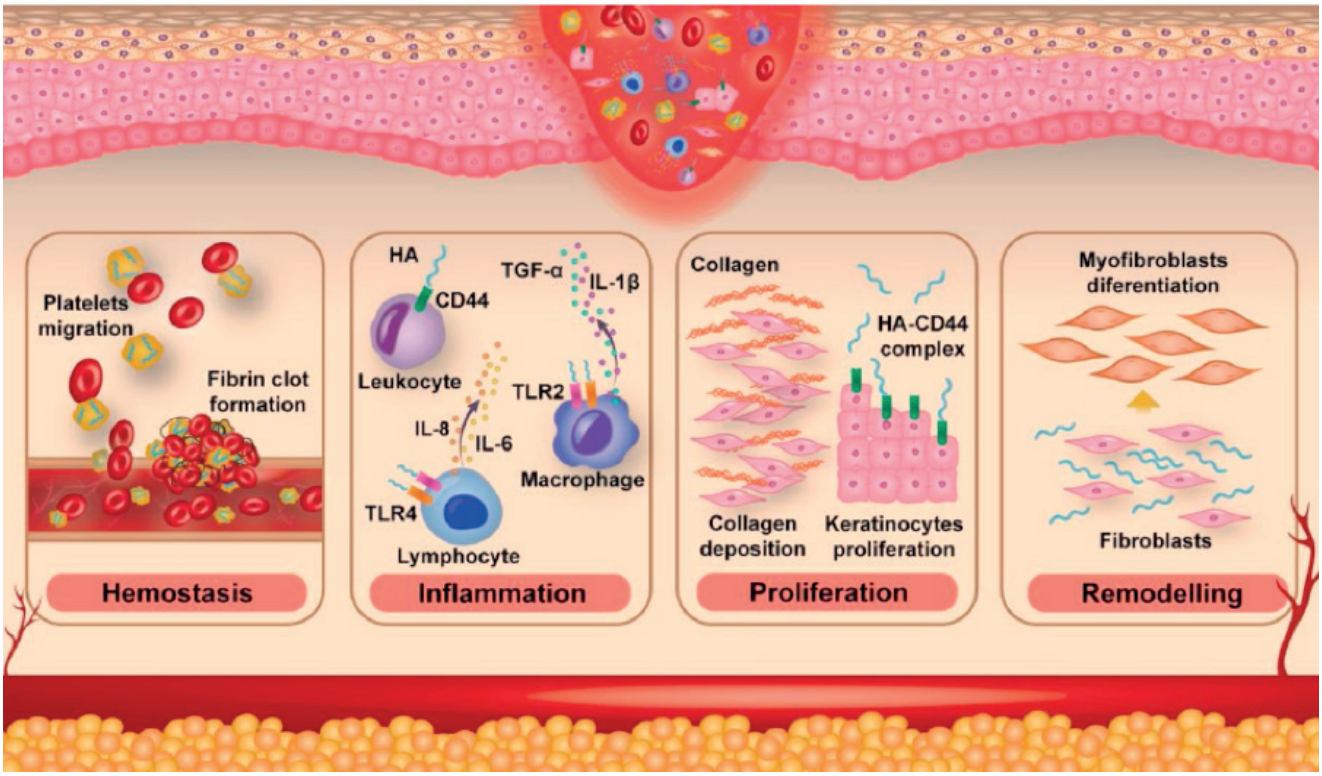

Figure 1: Illustration of HA main roles in the wound healing process (Graca et al, 2020)

synthase (HAS1, HAS2, HAS3) (Parmar et al., 2025). It is ubiquitously distributed in the skin, synovial fluid, vitreous humor, and connective tissues, where it contributes to tissue hydration, structural scaffolding, and biochemical signaling.

A key determinant of HA's biological function is its molecular weight. **High molecular weight HA (HMW-HA)**, typically >1,000 kDa, is associated with **anti-inflammatory, immunosuppressive**, and anti-angiogenic properties, whereas **low molecular weight HA (LMW-HA)** fragments, usually <500 kDa, tend to exhibit **pro-inflammatory and pro-angiogenic effects.** This duality underlies its phase-specific roles in wound repair.

Immediately after the formation of the lesion, the healing process begins, striving to restore tissue architecture as quickly as possible and to stop the bleeding. To accomplish this task, **platelets secrete a large quantity of HMW-HA**, enabling the early accumulation of fibrinogen in order to form an initial clot **(Figure 1, step 1).**

At the same time, HA, also an important component of edematous fluid, **is involved in the recruitment of neutrophils**. This cell type plays a crucial role in the healing process as it ensures, among other functions, the phagocytosis of tissue debris and the **massive secretion of TNF-, IL-1, and IL-8** (pro-inflammatory cytokines).

Figure 1, step 2: the establishment of a pro-inflammatory environment also involves the emergence of **significant oxidative stress**. It is also known that hyaluronidases (notably HYAL2) can be activated by reactive oxygen species (ROS) through a p38 MAPK-dependent pathway (Monzon et al., 2010).

The HMW-HA present in the lesion environment is gradually transformed into LMW-HA, which in turn amplifies the local inflammatory response by further increasing the production of IL-1, as well as inducing IL-6, IL-8, and MCP-1 (Quero et al., 2013).

It is worth noting that hyaluronidases are not the only mechanism by which HMW-HA is converted into LMW-HA, as **ROS themselves can also induce this transformation.**

Thus, it becomes clear that hyaluronic acid plays a central role in the molecular and cellular machinery that is essential for the transition from step 2 to step 3 in Figure 1.

HA acts as a multiplier of beneficial and necessary inflammatory processes that allow the progression to the proliferative phase.

Figure 1, step 3: as the LMW-HA fragments generated during the inflammatory phase (via enzymatic or oxidative fragmentation) begin to disappear, **HMW-HA becomes predominant.** It binds to CD44 expressed on the surface of keratinocytes and fibroblasts, **stimulating their proliferation and migration toward the injured site, thereby contributing to re-epithelialization and matrix reorganization** (Hoarau et al., 2022; Kawano et al., 2021).

The role of LMW-HA diminishes as an anti-inflammatory environment is established, orchestrated by HMW-HA, which also promotes the **polarization of macrophages toward the M2 phenotype, conducive to resolving inflammation.**

In parallel, fibroblasts activated by HMW-HA/CD44 binding become highly productive: **they abundantly synthesize type I and III collagen, structuring the newly formed tissue, while also producing fibronectin and other extracellular matrix components** (Kawano et al., 2021).

Additionally, HMW-HA creates a highly **hydrated and viscoelastic microenvironment**, facilitating cell migration, proliferation, and the extracellular matrix reorganization necessary for dermal reconstruction (Lee et al., 2021).

Figure 1, step 4: during the **remodeling phase** of wound healing, **fibroblasts** continue synthesizing extracellular matrix components and differentiate into **myofibroblasts**, which express **a-smooth muscle actin (a-SMA)**, generate contractile forces, and deposit dense bundles of collagen I/III to promote wound contraction and tensile strength.

Importantly, the **production of endogenous HMW HA** by fibroblasts is essential for this differentiation process (Webber J et al, 2009). Hence, during remodeling, HMW HA orchestrates the **balance between matrix deposition and resolution**, preventing unchecked fibrosis while enabling appropriate **myofibroblast-mediated ECM compaction and wound closure** (Sapudom J et al, 2020).

From a mechanical standpoint, HA possesses remarkable **viscoelastic and water-retentive properties**, forming a hydrated pericellular matrix that facilitates cell movement and serves as a reservoir for growth factors and cytokines. This characteristic is particularly beneficial in maintaining a moist wound environment.

Thus, HA should not be viewed as a static ECM component but rather as a dynamic **bioactive molecule** whose function evolves throughout the wound healing process, dictated largely by its molecular size and interactions with specific receptors.

3. PRECLINICAL AND CLINICAL EVIDENCE FROM SYSTEMATIC REVIEWS AND META-ANALYSES

The clinical application of hyaluronic acid (HA) in wound management has been increasingly investigated through systematic reviews and meta-analyses, yielding **encouraging but heterogeneous results**.

A meta-analysis by Voigt and Driver (2012) evaluated nine randomized controlled trials (RCTs) involving both acute and chronic wounds (including burns, surgical incisions, and diabetic foot ulcers) **found that HA significantly improved healing outcomes in 8 out of 9 trials**, demonstrating consistent efficacy in accelerating wound closure and tissue regeneration, particularly in diabetic ulcers.

Supporting this, Chen et al. (2014) conducted a meta-analysis focused specifically on diabetic patients' conditions and reported a **statistically significant increase in complete wound healing at 12 weeks among patients treated with topical HA**, with an odds ratio of 1.71 ($p = 0.047$; 95%CI:1.01–2.91) across a pooled sample of 328 patients.

However, other reviews have called for caution in interpreting these outcomes. Shaharudin and Aziz (2016) systematically reviewed nine RCTs totaling 865 patients with chronic wounds and concluded that while the evidence for improved healing rates was limited, HA

dressings showed more consistent benefit in terms of **pain reduction**, a critical parameter in patient-centered care strategies.

More recently, a comprehensive Cochrane review by Roehrs et al. (2023) assessed HA-containing dressings for chronic wounds and concluded that the **clinical benefit remains uncertain**, citing low-certainty evidence and highlighting the urgent need for well-designed, large-scale RCTs to determine HA's true therapeutic value in chronic wound care.

Taken together, while preclinical models and early-phase trials indicate promising pro-healing and analgesic effects of HA, **the current clinical evidence remains questionable**, particularly for chronic wounds.

The discrepancy among reviews underscores the need to standardize HA formulations and dosing regimens, and to stratify patients based on wound etiology and severity in future studies.

CONCLUSION

Hyaluronic acid emerges as a **dynamic and phase-specific modulator of wound healing, influencing inflammation, cell migration, and extracellular matrix remodeling through its molecular weight-dependent actions.**

Preclinical data consistently support its biological relevance, yet clinical evidence - though promising **-remains mixed and context-dependent.**

While certain studies highlight its potential in accelerating healing and reducing pain, particularly in diabetic and chronic wounds, **the heterogeneity of results underscores the need for standardized formulations and robust clinical trials.**

Future research should focus on optimizing HA application strategies to fully harness its therapeutic potential in targeted wound care.

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Lasers, artificial intelligence, regenerative surgery research

Dr Diala HAYKAL

Ever since Hippocrates, our body's capacity for self-regeneration has been at the heart of medical thinking. He wrote that the human body possesses within itself the resources to repair itself. Today, this biological intelligence is combined with another: that of artificial intelligence.

THE ADVANTAGES OF USING FRACTIONATED LASERS

As a doctor specialising in lasers, I have had the opportunity to explore, through numerous publications, the potential of non-ablative fractional lasers in tissue regeneration.

1. Activation of youth genes: Fractional lasers can help to 'switch' genes associated with youth, leading to regeneration of the dermis and collagen fibres.

2. Personalised treatments: Thanks to technological advances and artificial intelligence, it is now possible to personalise treatments according to the unique characteristics of each patient, optimising the effectiveness of care.

3. Improved tissue regeneration: Lasers can improve tissue regeneration, which is particularly beneficial when treating burns, scars or ulcers.

4. Reduced rejection: By using autologous techniques (based on the patient's own cells), fractionated lasers reduce the risk of rejection and the use of immunosuppressive drugs.

These points highlight the growing importance of laser technologies in the field of regenerative medicine.

THE IMPORTANCE OF ARTIFICIAL INTELLIGENCE AND TISSUE ENGINEERING: TOMORROW'S MEDICINE IS BEING CODED TODAY

1. Cell selection and optimisation: AI can help to choose the most appropriate cell types for optimum efficiency in tissue regeneration. This includes the ability to classify and modulate cells according to the specific needs of each patient.

2. Culture Conditioning: Using advanced algorithms, AI can determine the best culture conditions, such as temperature and growth factors, enabling more precise and efficient tissue development.

3. Personalised treatments: Using predictive models, AI can create bespoke care for each patient,

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Aesthetic Medicine, Healthcare Management Degree - Harvard Medical School (SFME)

taking into account their unique situation, which can significantly reduce the risk of rejection and the need for immunosuppressive drugs.

4. Accelerating Research: AI facilitates faster research on organoids, allowing the behaviour of tissues under various conditions to be simulated and predicted. This increases the effectiveness of tests and the development of treatments.

5. Refinement of surgical techniques: In surgery, AI and tissue engineering can provide more aesthetic (in cosmetic and reconstructive surgery) and functional grafts, by adapting the size and thickness of grafts to the specific needs of surgical procedures.

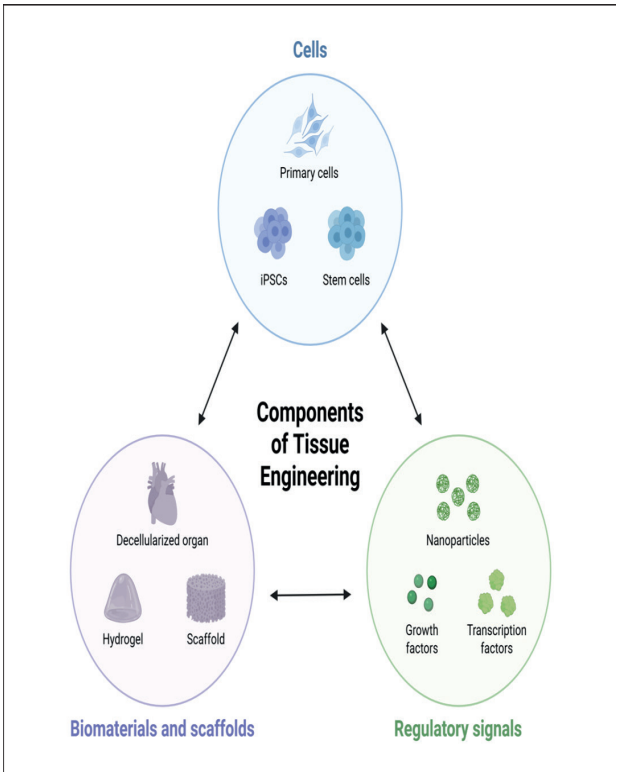
In short, the integration of AI in these fields offers immense potential to transform patient treatment, making regenerative medicine more effective and personalised.

THE CHALLENGES OF FUNDING SCIENTIFIC RESEARCH IN EUROPE :

1. Access to funding: In the United States, access to funding for research projects is much easier. The United States has instruments such as small federal loans (SBA Loans) that facilitate the launch of innovative projects, whereas such mechanisms are lacking in Europe, which significantly penalises research initiatives on the continent.

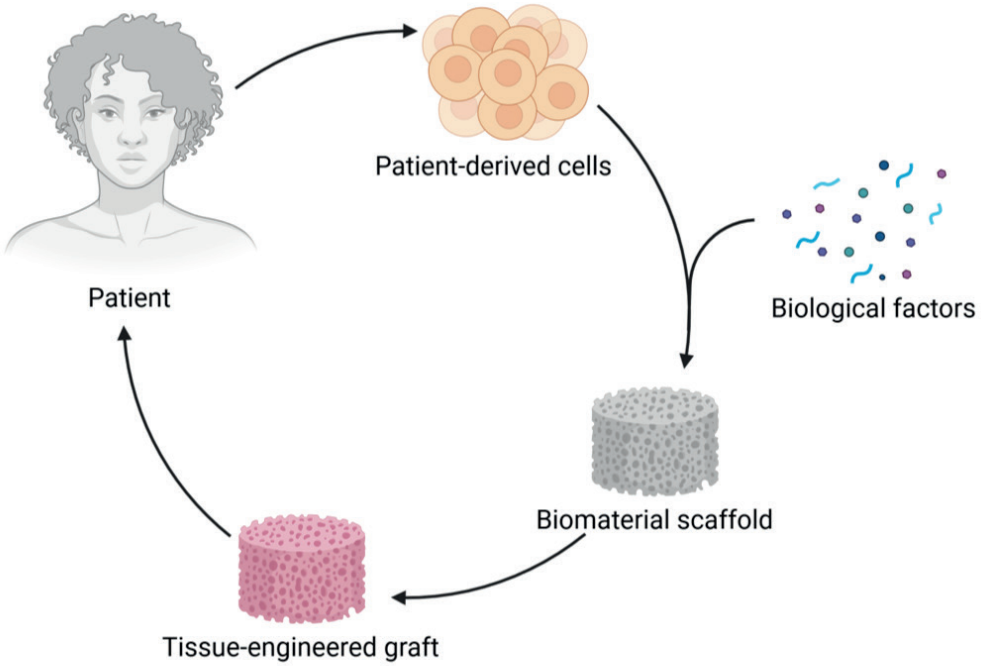
2. Percentage of government funding: It was mentioned that 95% of research in Germany is funded by the US government, which shows the extent of US involvement in funding European research, in stark contrast to the lower percentage of direct funding by European governments.

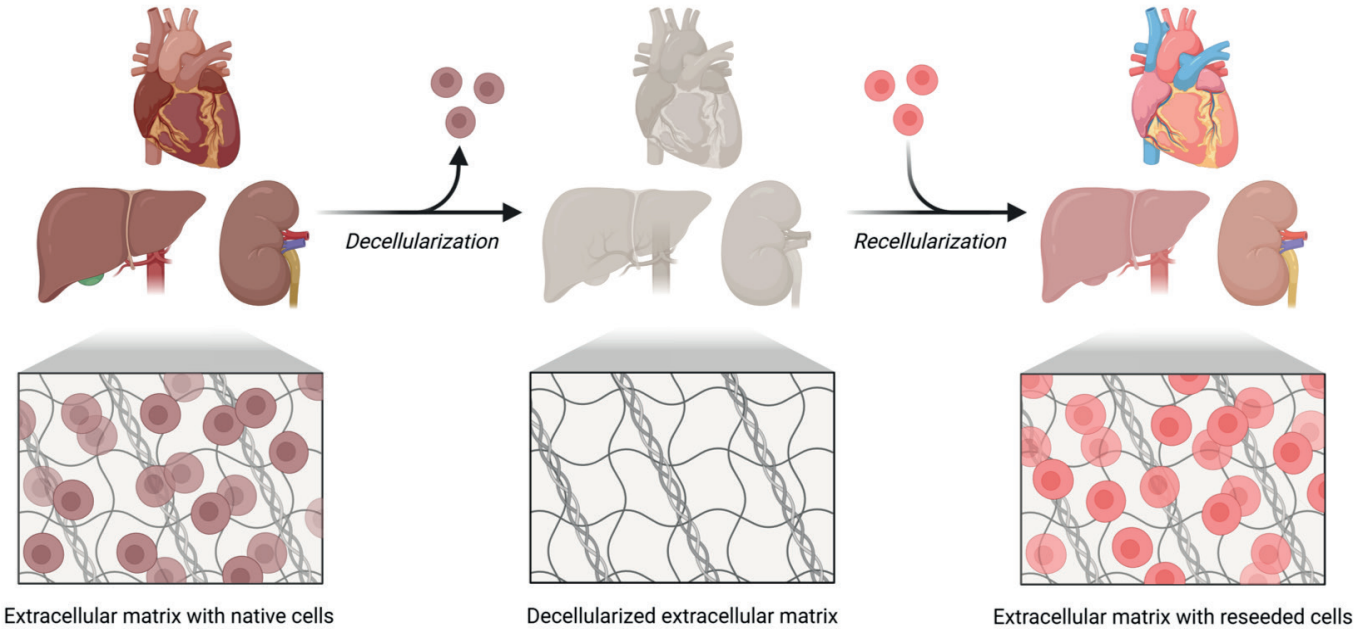
3. Innovation comparison: Despite innovative initiatives in France, such as certain collaborations supported by local organisations, the level of funding and innovation in general fails to match that observed in the United States. This indicates a need to strengthen funding mechanisms to support such initiatives in Europe.



These points highlight the structural challenges that Europe must overcome to improve support for scientific research and remain competitive in the face of innovations that are often better funded in the United States.

Traditional Tissue Engineering
Ex vivo Conditioning and endogenous regeneration





Regenerative biosurgery will prevail in the future

Prof. David BOCCARA

Prof. David BOCCARA
Plastic and Reconstructive Surgery (APHP Paris)
Francophone Society of Burn Treatment (SFB)

Prof. David Boccara

Our mission as surgeons is to repair, reconstruct and heal.

But doesn't the future lie elsewhere?

Aren't we now witnessing the beginnings of a new era: that of tissue regeneration?

Trained to restore what already exists, we may still be in the infancy stage of our discipline.

As head of the post-graduate diploma in flap anatomy, I often remind residents that one day we may be able to laugh about the days when we harvested flaps, because we will be able to create everything in the laboratory, using the patient's own cells, without having to transpose. This reality is not yet within our grasp, but it is on the horizon.

DEFINITION: WHAT IS REGENERATION?

It is the ability to create and produce human tissue using biological or alternative means. How can we imagine building a strip of tissue, building an avatar? We all dream of having our avatar in the fridge and of one day being able to open a fridge and say to ourselves, rather than having your colon repaired when you have colon cancer, or your pancreas, or whatever, we'll take it, throw it away and put on a new one. Regenerative surgery is a bit like that, and there are a lot of teams working on it.

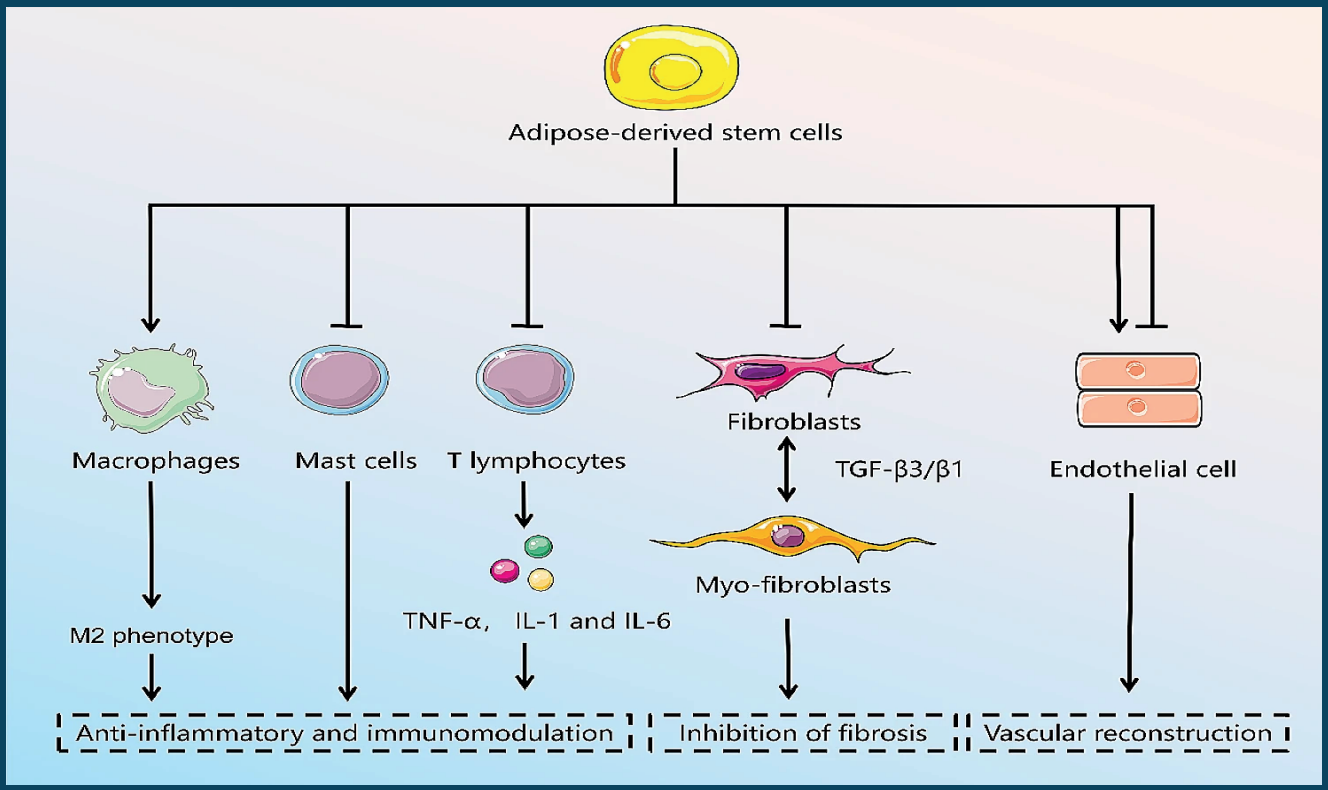
MAIN APPLICATIONS

Plastic surgery is a cross-disciplinary field with a huge range of applications: wounds, breast reconstruction, burns, bone and nerve regeneration, post-trauma, skin ageing, etc. The aim is to repair diseased or ageing tissue. Several techniques are already in use, some of which are still being perfected, but others are showing real potential. In France, plastic surgery research is dynamic. At Saint-Louis Hospital, as elsewhere, we are working with gene and cell therapy laboratories and tissue banks. This field will only progress through cooperation: researchers, doctors, surgeons, engineers and computer scientists need to work together.

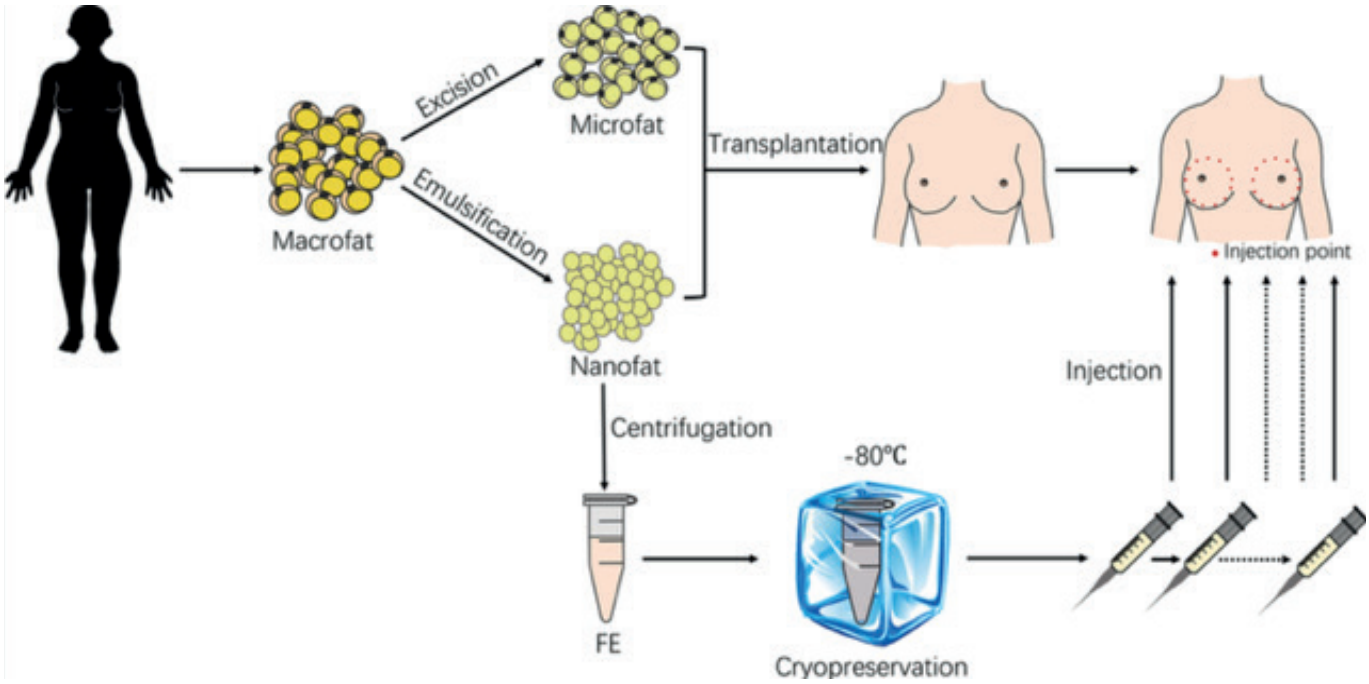
THE BLACK GOLD OF REGENERATIVE SURGERY: ADIPOSE TISSUE

One of the most promising resources is fat. Long perceived as a problem, it is in fact a rich reserve of stem cells. Adipose transplants are attracting a great deal of interest, as is PRP, which is still poorly understood because it is sometimes misused.

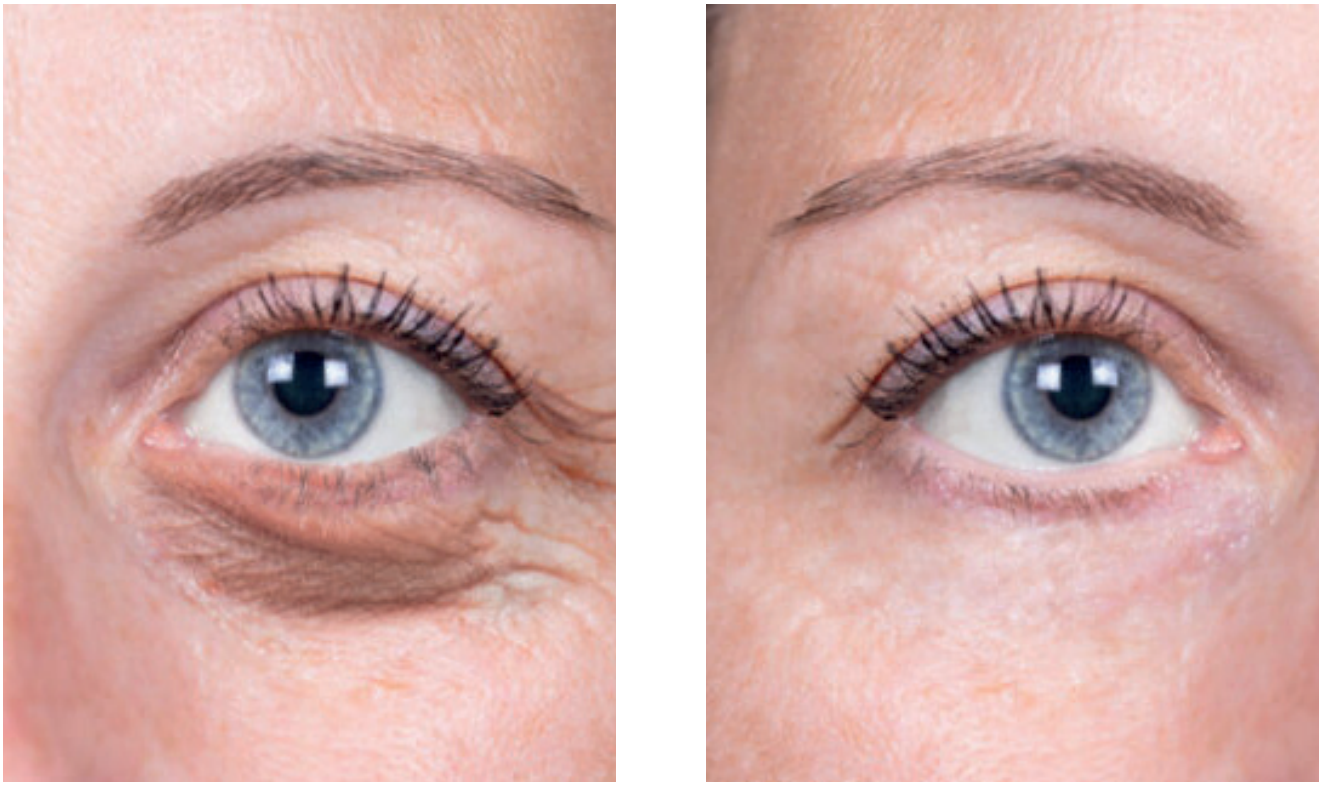
Other technologies are well established, such as extracellular matrices (Matriderm®, Integra®), which are widely used in burns, both acute and reconstruction. Their use in hand and breast surgery is increasing.



The mechanism of the treatment of adipose stem cells for hypertrophic scarring.



Macro Micro and Nano fat for Lipofilling



Nano lipofilling

A crucial issue in plastic surgery is three-dimensional reconstruction. 3D printing makes it possible to design synthetic skins and structures to be colonised by cells, particularly adipocytes. Several French laboratories, both public and private, are very active in these areas.

RECONSTRUCTING WITHOUT DESTROYING

The great advantage of regeneration is the ability to reconstruct without removal: 'reconstruct without destroying'. This avoids the functional or aesthetic losses associated with removal.

Skin remains a major challenge: along with the brain, it is one of the few organs that cannot be transplanted without perfect compatibility. The rare case of a transplant between identical twins at Saint-Louis clearly illustrates this limitation. Current solutions (cadaver, pig and fish skins) are still imperfect.

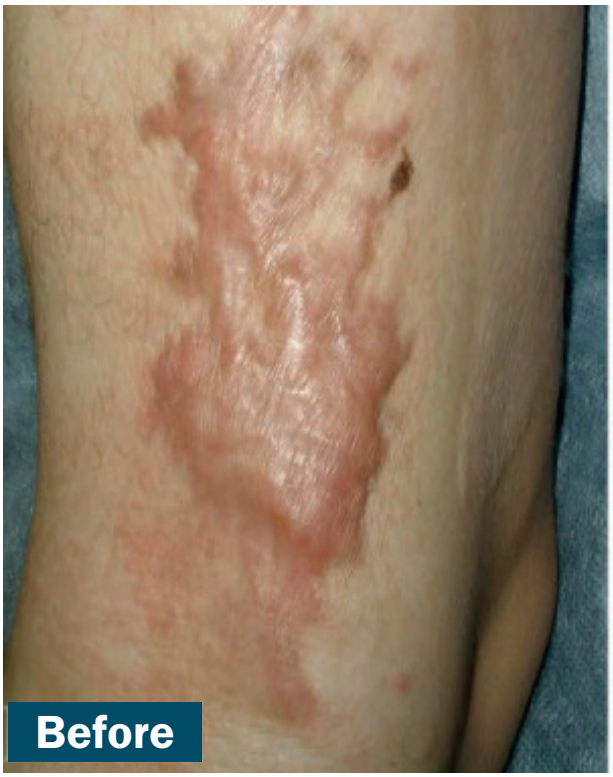
Developing a universal skin tissue bank could save lives. It would also avoid the use of foreign implants, which are poorly tolerated from a psychological or immune point of view, as in breast reconstruction.

CURRENT OBSTACLES AND LIMITATIONS

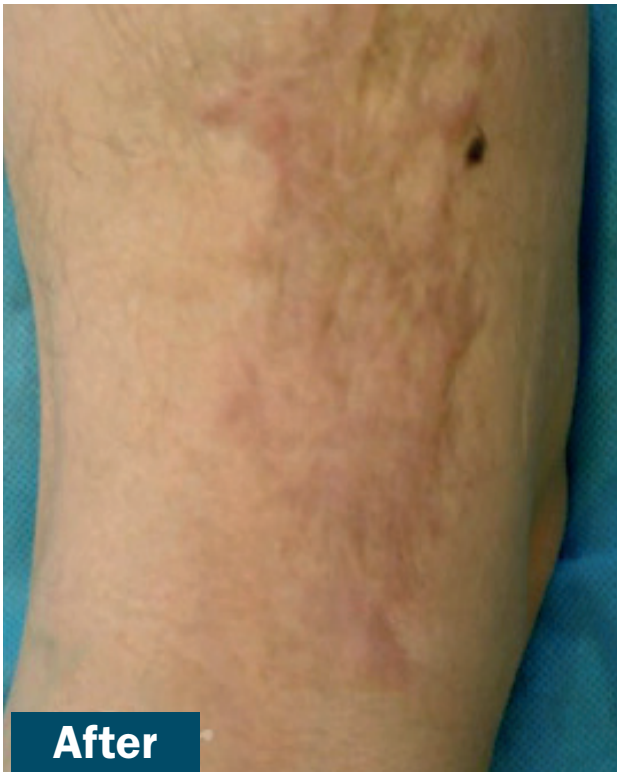
But there are real limitations: in France, regulations are often a brake. Investment is insufficient. Many laboratories conduct their clinical trials abroad. There is a need to create joint teams and genuine clinical research structures. Without concrete applications, a discovery remains a dead letter. And without researchers, surgeons' ideas cannot become reality.

The AP-HP is fortunate to have this dual expertise. We need to encourage young people to get involved in the laboratory. Too many projects are aborted for lack of support, resources and time.

The creation of the ARSIA Chair is a strong signal, a message of hope for the emergence of genuine regenerative surgery in France.



Microneedling with PRP



Microneedling with PRP

Regenerative surgery for induced Alopecia by chemotherapy and endocrine therapy

Dr Anthony ROSSI

Thank you for allowing me to present our work at Memorial School and Kettering using platelet rich plasma for the treatment of chemotherapy and endocrine therapy induced alopecia.

This was one of the first of its kind clinical trials at Memorial because we really wanted to see the efficacy of this in our cancer patients. We did have support from the region for this trial as well as a Memorial Spoon Kettering grant to conduct this work.

We know a lot about regenerative medicine for alopecia, stem cell culture, but there's more in the research phase. We have platelet rich plasma, and this is plasma-based growth factors, and we also have exosomes now that are coming out around the world.

However, we're focusing on platelet rich plasma because that has the most tested and rigorous studies associated with it and efficacy. And in our patients, we really want to make sure that we are doing right by them.

WHAT IS THE MECHANISM BY WHICH PLATELET RICH PLASMA (PRP) IS BELIEVED TO STIMULATE HAIR GROWTH IN CHEMOTHERAPY AND ENDOCRINE THERAPY INDUCED ALOPECIA?

It's an autologous solution of plasma containing four to seven times the baseline concentration of platelets and plasma proteins.these growth factors help modulate tissue repair and regeneration and the positive proteins acts as a scaffold for connective tissue and epithelial migration.

When we inject it in the scalp, the theory is that these growth factors help stimulate the hair follicles to go into the antigen phase.

Platelet-rich plasma (PRP) is believed to stimulate hair growth in cases of chemotherapy and endocrine therapy-induced alopecia through several mechanisms. The key points regarding its mechanism of action include:

1. Growth Factors: PRP contains a high concentration of growth factors that are essential for tissue repair and regeneration. These growth factors help modulate the healing process and act as a scaffold for connective tissue and epithelial migration.

2. Activation of Hair Follicles: When PRP is injected into the scalp, the growth factors are thought to stimulate hair follicles to enter the anagen (growth) phase. This is crucial for promoting hair regrowth.

3. Wnt/-catenin Pathway: A significant aspect of PRP's action is its ability to activate the Wnt/-catenin signaling pathway in the dermal papilla of hair follicles. This pathway is critical for hair follicle development and cycling. PRP may help overcome the signaling disruptions caused by conditions such as androgen receptor binding, which can inhibit hair growth.

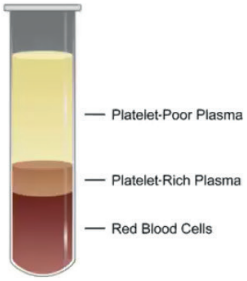
Dr Anthony ROSSI

Dermatology, Memorial Sloan Kettering Cancer Center, New York (USA)

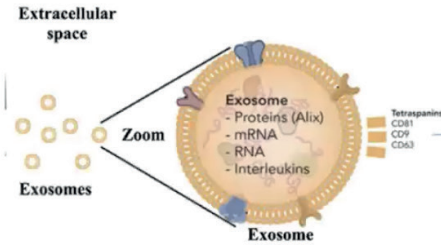
Regenerative Surgery for Alopecia

Mesenchymal stem cell (MSC)

Aditya K. Gupta, H elen J. Renaud, Jeffrey A. Rapaport. Platelet-rich Plasma and Cell Therapy. The New Horizon in Hair Loss Treatment . Dermatol Clin 39 (2021) 429–445



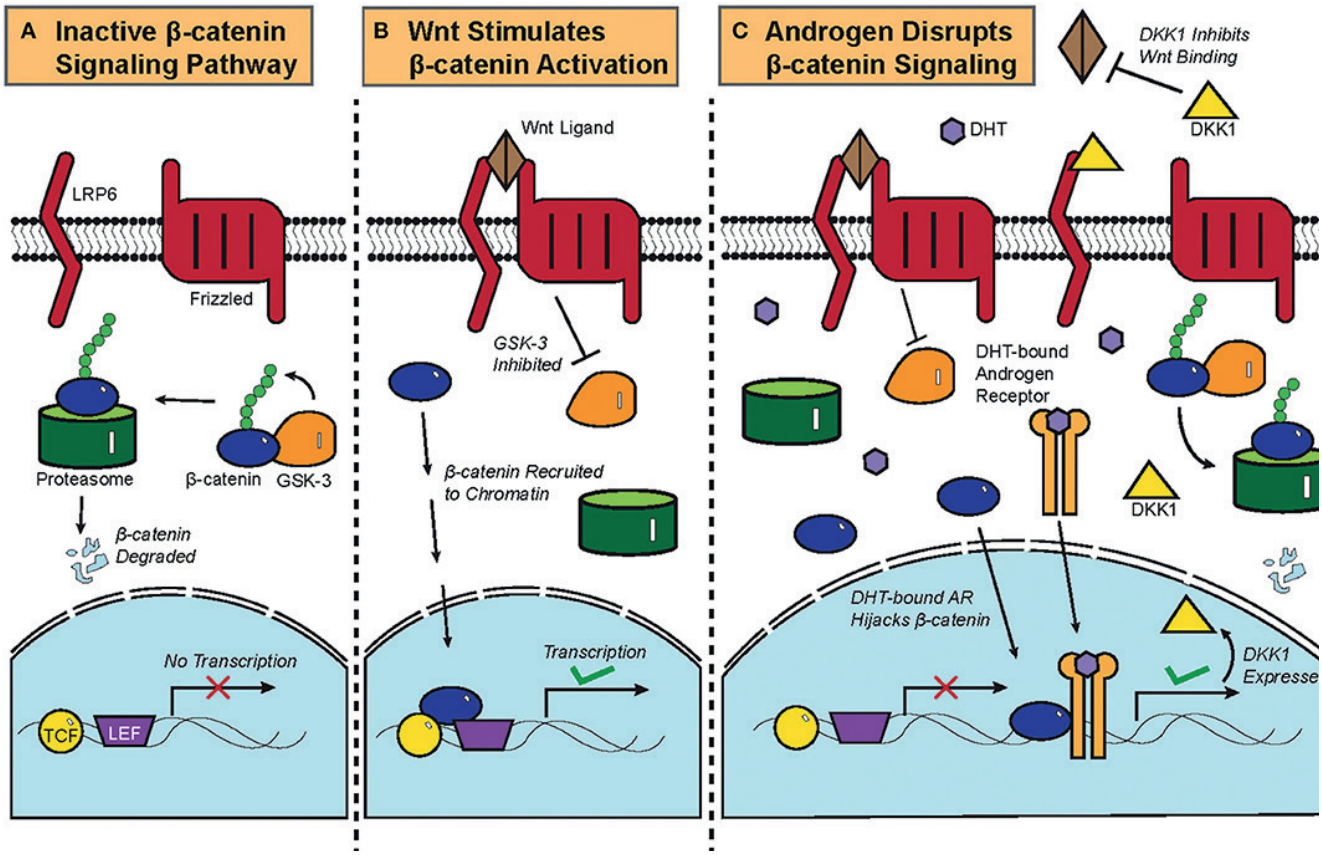
Plasma with growth factors (platelet rich plasma or PRP)



Exosomes

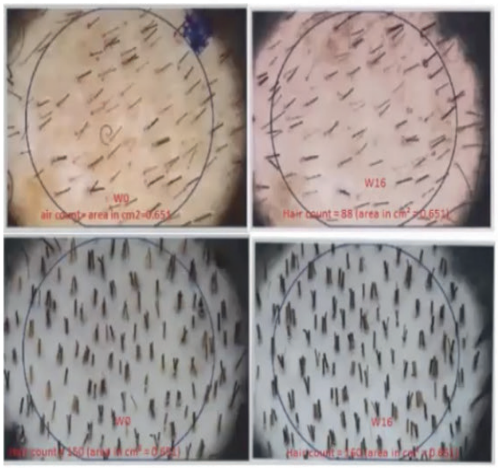
Ajit, A., Nair, M.D. & Venugopal, B. Exploring the Potential of Mesenchymal Stem Cell–Derived Exosomes for the Treatment of Alopecia. Regen. Eng. Transl. Med. 7, 119–128 (2021). https://doi.org/10.1007/s40883-021-00204-3

PRP for the treatment of chemotherapy and endocrine therapy induced alopecia

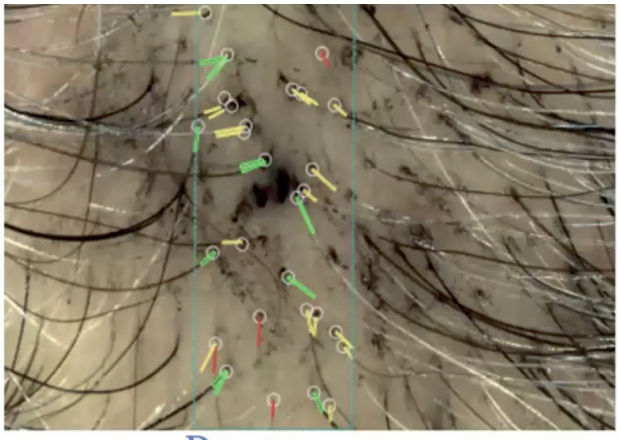


Biochemistry of the Wnt/βcatenin signaling pathway and its crosstalk with androgen.

Each patient received 4 series of injections (4 to 5 ml per session) of PRP non-activated (PRPn).
Patients were treated at **W0, W3, W6 and W12** (every 3 weeks for 3 first injections and 6 weeks for the last injection).
The assessment was done at W16, 4 weeks after the last session.



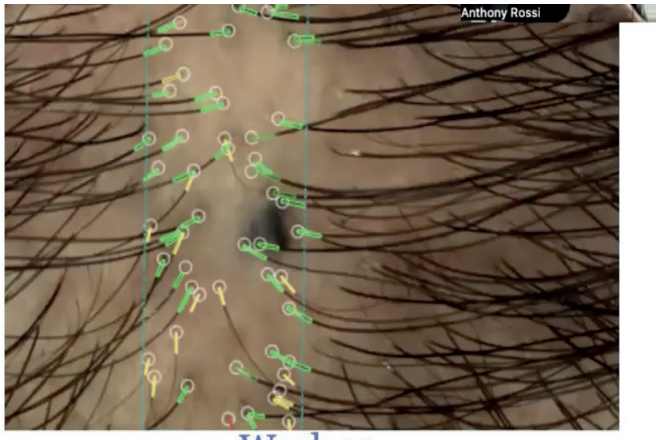
An improvement in hair density was observed in 11 cases while a cosmetic i mprovement on the vertex was noticed in 2 cases.



Day 0

Intrafollicular distance: - 22.73%
Follicle count per cm2: +79.3%
Hair count per cm2: +70.2%

Sum of hair widths per cm2: +117.2%
Average hair width: +27.5%



Week 12

Ludwig scale: Grade 3 → Grade 2

Global Assessment Scale
Blinded assessor: No change from baseline on
Patient: No change from baseline

4. Collagen Remodeling: PRP promotes collagen remodeling and increases fibroblast proliferation, which can enhance the structural integrity of the dermal matrix surrounding hair follicles. This remodeling is evident in histological assessments and contributes to improved hair quality and density.

5. Clinical Evidence: Studies have shown that repeated PRP injections can lead to significant improvements in hair density and quality, with many patients experiencing reduced hair shedding and increased hair growth.

Overall, the combination of growth factor delivery, activation of critical signaling pathways, and enhancement of the scalp's structural environment contributes to the efficacy of PRP in treating hair loss associated with chemotherapy and endocrine therapies.

THE CLINICAL TRIAL DESIGNED TO TEST THE EFFICACY AND SAFETY OF PLATELET-RICH PLASMA (PRP) TREATMENT IN BREAST CANCER PATIENTS WITH ALOPECIA WAS STRUCTURED AS FOLLOWS:

1. Design: It was a randomized split-scalp study where one side of the scalp received PRP treatment while the other side received no treatment. This arrangement allowed for direct comparison within the same individual, minimizing variability from external factors.

2. Treatment Protocol: Treatments were spaced 4 weeks apart, and after a series of sessions, there was a break before switching the treatment assignment between the scalp sides. This helped in assessing both the efficacy and safety of PRP without leaving the untreated side at a disadvantage for too long.

4. Primary Endpoint: The main measure of efficacy was assessed via trichoscopic evaluations conducted at 12 and 24 weeks post-treatment. This included metrics like hair density and the health of hair follicles.

5. Secondary Endpoints: These addressed the patients' quality of life related to their alopecia, and global assessments of hair growth by investigators were also included.

6. Safety Measures: The study focused on monitoring adverse events to determine the safety of PRP in patients who had undergone cancer treatments.

The study aimed to establish whether PRP could provide significant improvement in hair regrowth for patients suffering from chemotherapy-induced and endocrine-induced alopecia, which are common concerns for breast cancer patients.

WHAT ARE THE DIFFERENCES IN TREATMENT RESPONSE BETWEEN ENDOCRINE INDUCED ALOPECIA (EIA) AND PERSISTENT CHEMOTHERAPY INDUCED ALOPECIA (PCIA) ACCORDING TO THE STUDY?

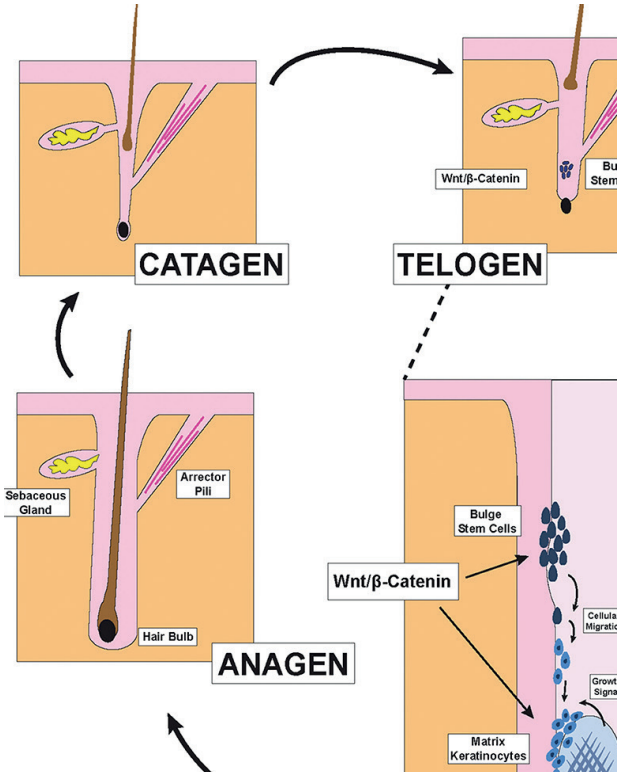
The treatment responses between endocrine induced alopecia (EIA) and persistent chemotherapy induced alopecia (PCIA) differ significantly according to the study:

- **Effectiveness**: EIA showed better improvement in treatment responses compared to PCIA. The study indicated that patients with EIA experienced a more favourable outcome from treatments, with significant hair growth observed.

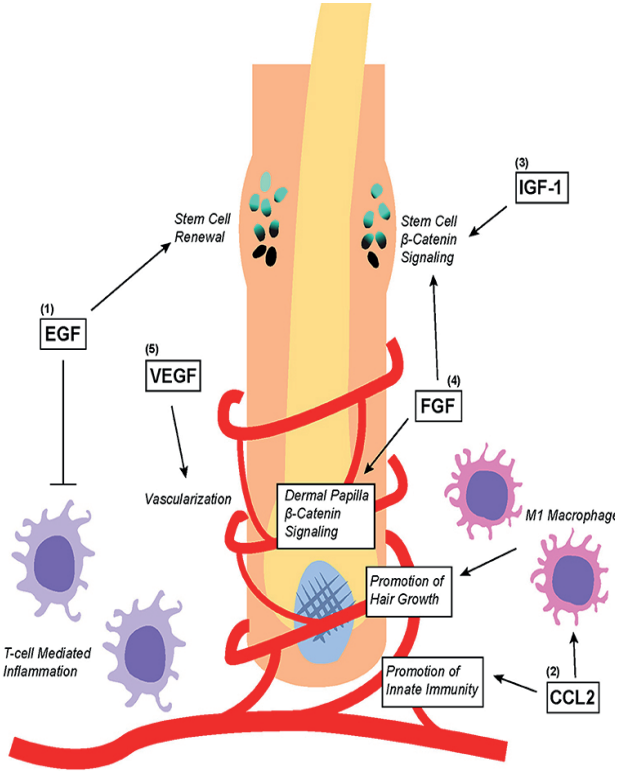
- **Condition Severity**: PCIA is characterized as having worse baseline trichoscopic assessments, indicating a more advanced and damaged state of hair follicles, making it more challenging to treat. The PCIA condition is compounded by incomplete hair growth around six months after ceasing cytotoxic chemotherapy.

- **Treatment Outcomes**: Although both conditions show statistically significant improvements, PCIA patients demonstrate less effective responses due to the more severe state of hair loss they experience. In essence, the study suggests that EIA is easier to manage therapeutically, whereas PCIA is more challenging and considered a "burned-out" condition.

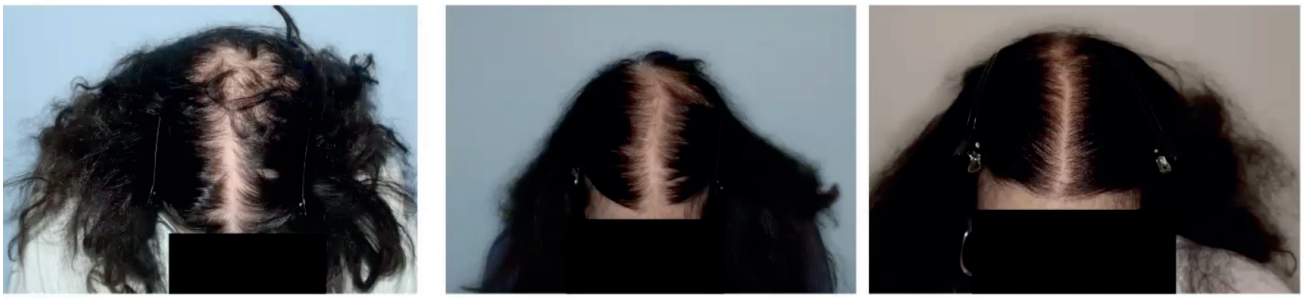
This highlights the importance of early intervention in both types of alopecia to optimize treatment efficacy.



Hair Follicle structures and phases of the hair cycle.



Overview of PRP-associated growth factors and chemokines as well as their effects on hair follicle biology.



Baseline
Treated side: 103
Untreated side: 103

Week 12
Treated side: 113
Untreated side: 110

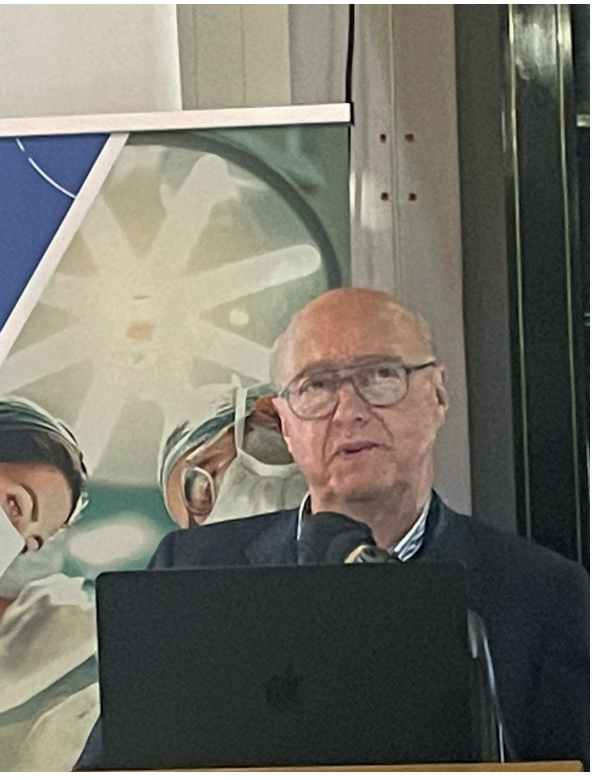
Week 24
Treated side: 134
Untreated side: 123

Global Photos - pCIA Example

Orthobiological injections (PRP) for the treatment of osteoarthritis of the knee

Dr Philippe ADAM

Dr Philippe ADAM
Radiologist, Médipôle Clinic of Toulouse, France



Dr Philippe Adam

In a clinic where surgeons implant a lot of prostheses,

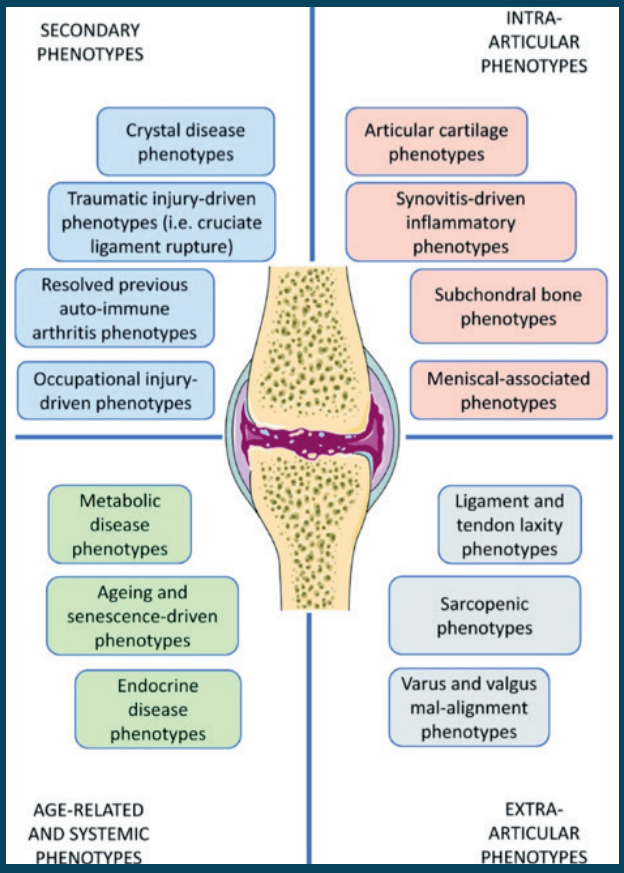
I have succeeded in proposing and then finding a place for bio-surgery, which has gone from being a potential 'enemy' of orthopaedic surgeons to becoming a complementary 'friend' in the proposed therapeutic tree.

DIAGNOSIS OF OSTEOARTHRITIS

Imaging is essential not only for diagnosing the location and quantification of osteoarthritis, but also for monitoring its progress and planning treatment.

The earlier osteoarthritis is effectively treated in its initial stages, the more effective it will be in preventing the disease from progressing, by avoiding the most destructive and advanced stages, such as grade 4 osteoarthritis with total pinching.

There are several phenotypes of knee osteoarthritis, which play a crucial role in the choice of treatment. Here is a summary of the phenotypes identified:



There is a clear overlap of phenotypes and structural and molecular alterations

1. Rheumatological phenotype:
Characterised by inflammatory flare-ups. In this case, the synovium, which plays an important role in the patient's pain, is of key importance.
2. Traumatological phenotype:
Common in sportspeople, it is mainly associated with premature wear and tear factors, in particular meniscus damage and ligament instability. Repair of ruptured ligaments is often necessary before considering other treatments.

3. Degenerative phenotype:
This form is usually linked to factors such as weight and age, but can also include deformities such as varus and valgus.

4. Biological Phenotypes :
Recognition of variations in the types of macrophages present in the joint, suggesting a link with changes at the molecular level.
ontogenesis.

Phenotypes directly influence the treatment options to be considered.

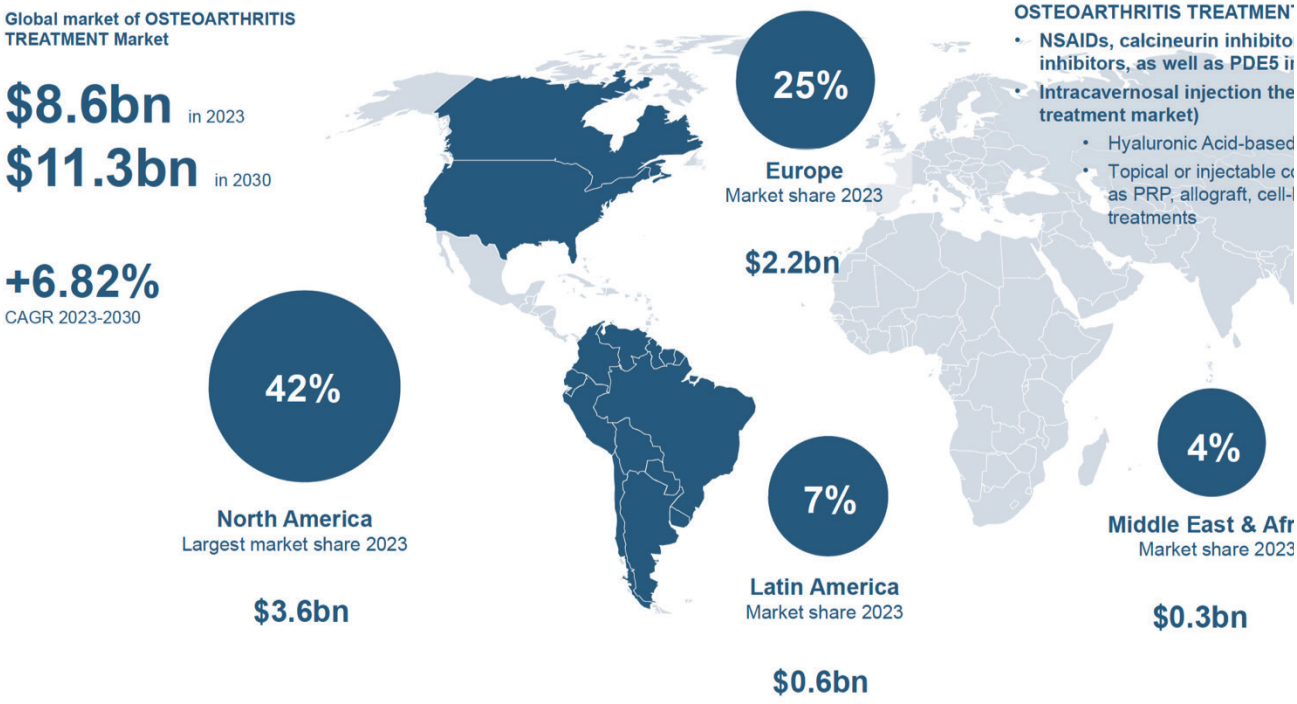
For example:
- Early treatment is essential for rheumatological forms to avoid progression to destructive stages of osteoarthritis.

- For the traumatological phenotype, it is crucial to first treat ligament instabilities before considering regenerative treatments.

- Therapeutic approaches vary according to the nature and severity of the phenotypes, requiring detailed assessment and an individualised treatment plan.

In short, understanding the different phenotypes of knee osteoarthritis enables the most appropriate treatments to be chosen, thereby optimising patient outcomes.

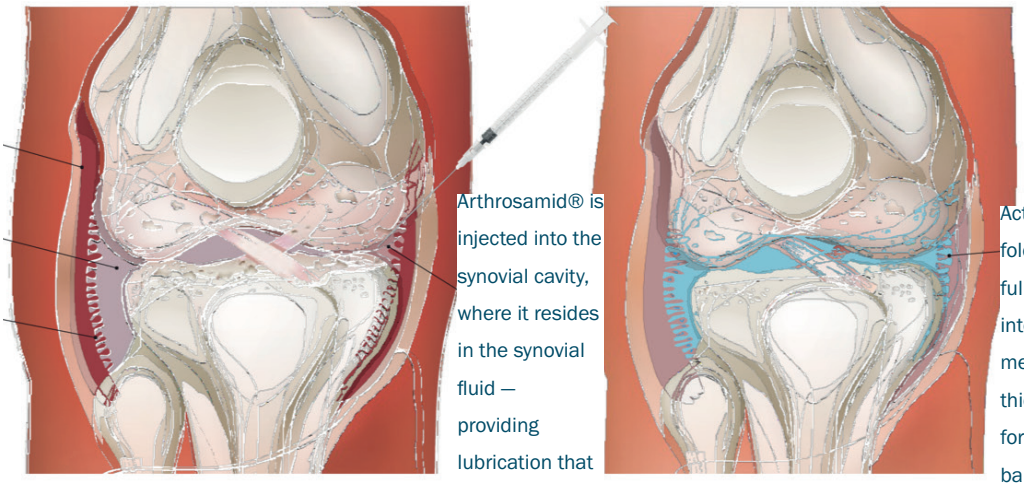
MARKET OVERVIEW OF OSTEOARTHRITIS TREATMENT



Viscoelastic hydrogel for intra-articular injection (integration into the synovial tissue)
How does Arthrosamid® (iPAAG) work?

Arthrosamid® is the only iPAAG treatment in the world approved for permanent integration into the synovial tissue of the inner capsule.
It decreases joint stiffness, thereby reducing pain and improving the function of the knee affected by osteoarthritis.
Its durability means it can provide long-term pain relief in the treatment of knee osteoarthritis.

BEFORE injection
Joint capsule
Joint cavity containing synovial fluid
Synovial membrane (covered with synovial villi) with multiple inflammatory cells

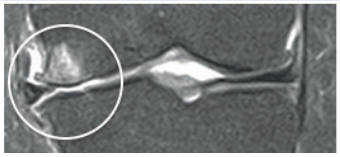


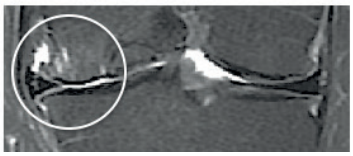
iPAAG: Injectable polyacrylamide hydrogel

Arthrosamid® is injected into the synovial cavity, where it resides in the synovial fluid — providing lubrication that cushions the inner capsule of the joint.

Acting as a scaffold, Arthrosamid® fully integrates into the synovial membrane, thickening it and forming a physical barrier that interrupts the inflammatory cycle – thus reducing pain.

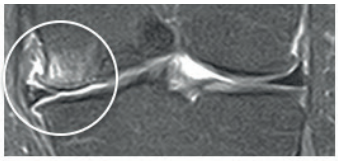
Primary Knee Osteoarthritis: “White” hypersignal on MRI (fat-sat) indicating subchondral bone lesions, with signal intensity correlated to pain severity
“Bone Marrow Edema concept” and “Bone Marrow Lesions” – Davies-Tuck et al.

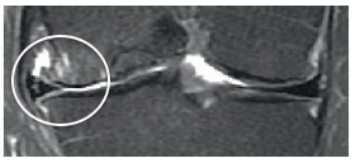


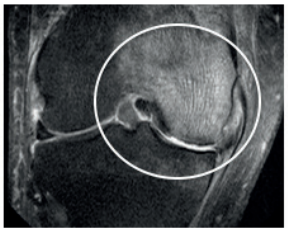


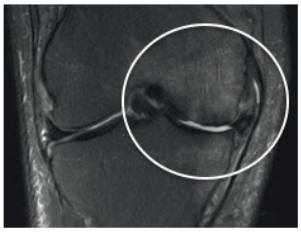
Before intra-articular PRP-HA injection and internal perimeniscal PRP injection

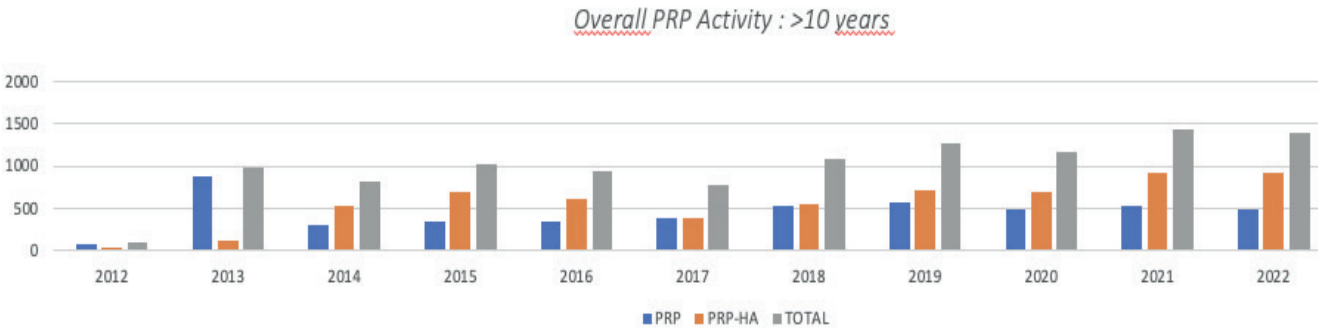
One and a half months after injection

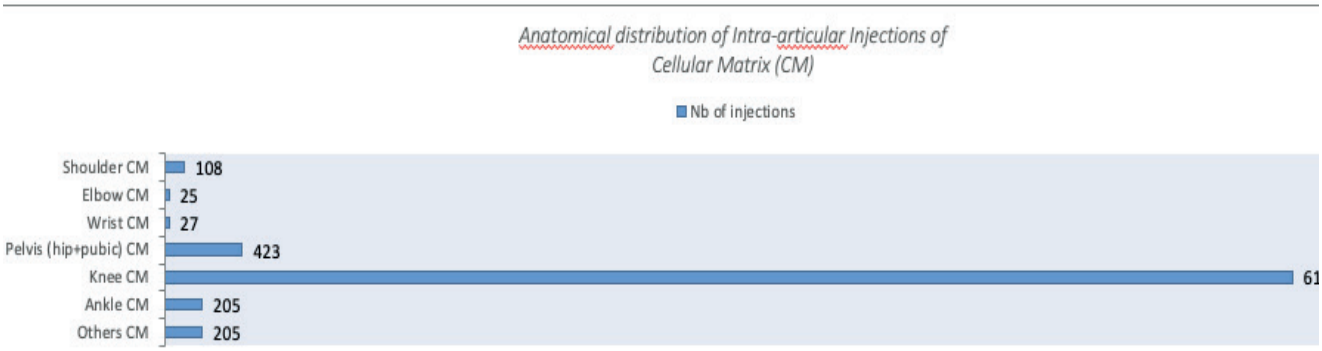












Report – Clinical Imaging Department, Médipole Garonne, Dr. ADAM

8134 “All-in-One” PRP-HA injections (Cellular Matrix) performed at Médipole Garonne

(between August 2012 and December 2023, plus 1010 in 2024; 80% for Knee Osteoarthritis)

OSTEOARTHRITIS ARE FINANCIAL

It would be interesting to compare (cost balance) effective and early treatments at reasonable cost with ineffective treatments that are too costly and too late. So why not Orthobiology, mainly autologous injections of platelet-rich plasma? This type of treatment is not reimbursed in France, but it is in the USA. And yet it generates substantial savings, given the economic burden of osteoarthritis.

THE ADVANTAGES OF PLATELET-RICH PLASMA (PRP) IN THE TREATMENT OF OSTEOARTHRITIS

- **Effectiveness on pain and inflammation**: PRP has intrinsic analgesic and anti-inflammatory properties thanks to its growth factors. This helps to reduce the pain and inflammation associated with osteoarthritis.

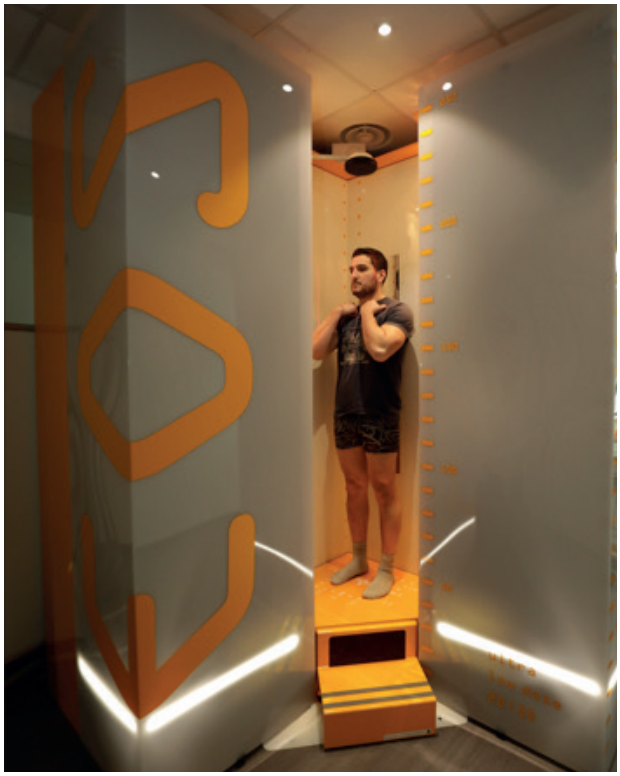
- **Tissue regeneration:** It promotes healing and angiogenesis, which can help cartilage regeneration. PRP can slow the progression of osteoarthritis, especially when administered at an early stage.

- **Synergy with other treatments**: PRP can be used in combination with other treatments, such as hyaluronic acid, thereby increasing their effectiveness and reducing the frequency of injections. more precise and more respectful of natural biological processes. The framework proposed by ARSIA will be decisive in framing, validating and disseminating these innovations on an international scale.

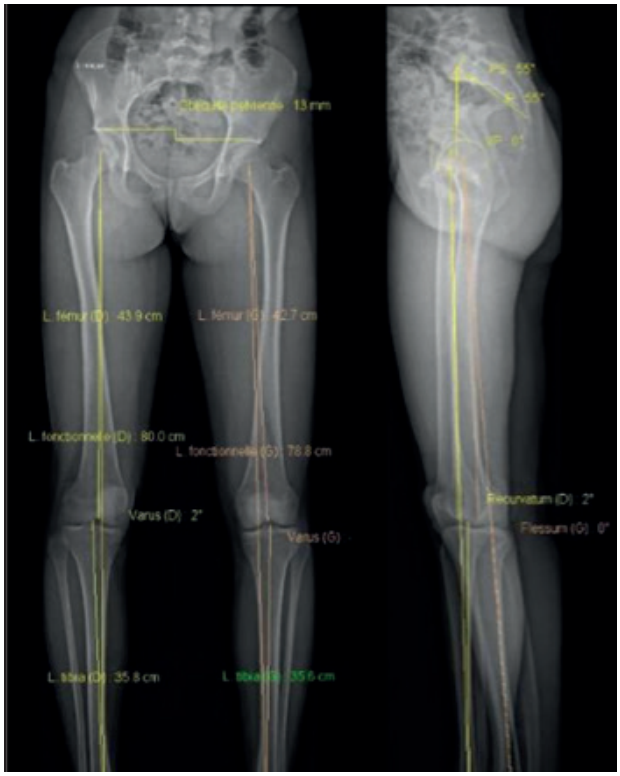
PRECAUTIONS TO BE TAKEN WHEN USING PRP

1. Specialist consultation: It is essential to have a specialist consultation beforehand to ensure that PRP is appropriate for the patient. This includes a biological work-up to confirm a sufficient concentration of platelets (at least 50,000 platelets per microlitre).

2. Avoid incompatible drugs: Anti-inflammatory drugs and anti-platelet aggregation agents should be avoided before PRP is injected, as they may reduce its effectiveness.



Radiological Staging of Knee Osteoarthritis



frontal view – Kellgren-Lawrence grades, lateral view, Rosenberg view, femoropatellar skyline view) + EOS Postural Study (pangonogram)

carried out under strict aseptic conditions to minimise the risk of infection. In addition, the patient's medical history should be examined to ensure that there are no bleeding risk factors.

4. Assessment of contraindications: Care should be taken if there is a history of cancer or infection, as PRP may not be appropriate in these cases. Precautions should be taken if osteoarthritic fluid is present, which should be evacuated before injection.

Taking these benefits and precautions into account, platelet-rich plasma may be a promising option for the treatment of osteoarthritis, but requires a rigorous approach to ensure the efficacy and safety of the treatment.

THE CONSENSUS OF SCIENTIFIC EXPERTS

PRP for osteoarthritis should preferably be used before the surgical stages, but it can be used pre-operatively during arthroscopy, and especially post-operatively, following joint lavage or post-meniscectomy or post-meniscal suture.
A certain number of patients refuse prosthesis, and PRP will be an alternative. There are also patients at high risk of surgery, and those too young to receive a total prosthesis

iNNOVATIONS IN THE TREATMENT OF OSTEOARTHRITIS OF THE KNEE, IN TERMS OF REGENERATIVE SURGERY?

The prospects and innovations in the treatment of osteoarthritis of the knee, particularly in the field of regenerative surgery, include a number of promising approaches and technologies:

Stem cells: Treatments based on stem cells are being considered, often used as a second-line treatment after other methods such as PRP (Platelet Rich Plasma). These cells could help repair cartilage tissue.

Bioprinting: The bioprinting technique, which makes it possible to create personalised biological implants, is seen as an essential development in the field of regenerative medicine.
This includes bioprinting and bioimplants, which could revolutionise the treatment of cartilage lesions.

Viscoelastic hydrogel: This new therapy, which attaches to the synovium, is still under study but could have a significant impact on the treatment of osteoarthritis.
Geniculate artery embolisation: Although primarily a technique for treating pain, embolisation could be considered in osteoarthritis as a complementary approach.

Robotic prostheses: The use of robotically implantable prostheses is increasing rapidly, representing an important technological advance for patients with severe osteoarthritis.

Integration of orthobiological treatments: Researchers are proposing a mix of orthobiological and surgical techniques, adapting treatments according to the patient's clinical profile, which could improve the effectiveness of care.

These innovations represent a move towards more personalised and less invasive treatments for patients suffering from osteoarthritis of the knee, promising a better quality of life and a reduction in the need for major surgery.

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CELLULAR MATRIX®

The exclusive **PRP & HA technology**

Breaking the vicious circle of knee osteoarthritis

regenlab™ TISSUE ENGINEERING SPECIALISTS

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ESSKA Consensus on PRP in knee osteoarthritis

Dr Laura DE GIROLAMO

The ESKKA formal consensus methodology is a structured approach designed to formulate clinical recommendations based on the aggregation of expert clinical knowledge and opinions, particularly in fields where literature may be lacking.

Beyond sitting on the ESSKA board, I'm also co-chair with Doctor Lior Laver the ORBIT initiative, which is the orthobiologic initiative of ESSKA, which is aimed indeed to try to provide recommendations to the daily clinicians, to the daily practitioners.

With the doctor Beaufils and following the ESSKA formal consensus we provide, we prepare 2 consensus documents, both about the use of injectable orthobiologics for knee osteo-arthritis.
Here are the key features and differences from surveys or academic research:

ESSKA FORMAL CONSENSUS METHODOLOGY

The ESSKA formal consensus methodology is an adapted version of the formal consensus described by the French Haute Autorité de Santé. All the 8 consensus documents that you finally listed here follow this consensus methodology as well as all the five incoming consensus documents that will be presented in Prague next year at the ESSKA Congress follow the same methodology as well. And you can find more information if you like in this very interesting paper written by Professor Beaufils.

1. Purpose: It aims to provide practical recommendations for clinicians based on daily practice expectations and expert opinion, rather than pure academic inquiry.

Structure: Involves independent groups, including a steering group to outline questions, a rating group to evaluate the statements, and a peer review group to ensure geographic adaptability.

2. Process: The methodology includes multiple rounds of voting and feedback from different experts, emphasizing the collective judgment of diverse specialists rather than individual opinions.

3. Recommendations: Focuses on providing clinical practice guidelines even when scientific literature is sparse, incorporating both available evidence and clinical expertise.

DIFFERENCES FROM SURVEYS OR ACADEMIC RESEARCH

1. Not Hypothesis-Driven: Unlike academic research, ESSKA consensus does not originate from a hypothesis but is based on the real-world needs of practitioners.

2. Collective Judgment vs. Individual Response: Surveys often collect individual opinions without the iterative and collective evaluation seen in consensus methods. The consensus methodology values group judgment over isolated responses.

Dr Laura DE GIROLAMO

Director of the Orthopedic Biotechnology Laboratory and of the Regain Galeazzi Institute. Galeazzi Santa Maria Hospital. Milan. Italy.

3. Focus on Education: The ESCA methodology is oriented towards guiding clinical practice rather than contributing to theoretical knowledge.

In summary, the ESSKA formal consensus methodology aims to harmonize clinical practices through expert collaboration, differentiating itself from traditional surveys and academic research by focusing on practical implications rather than theoretical exploration.

FINDINGS OF THE ESSKA CONSENSUS REGARDING THE USE OF PRP FOR TREATING OSTEOARTHRITIS?

1. Effectiveness: The consensus supports the use of PRP in patients with mild to moderate osteoarthritis (grade A recommendation, agreement score of 8.1) based on several Level 1 and 2 clinical studies demonstrating its safety and clinical benefits.

2. Comparison with Other Treatments: PRP is deemed safer and more effective compared to corticosteroids, providing longer-term clinical improvement. The agreement about PRP's superiority over corticosteroids received a very high score (8.7). Additionally, PRP is favored over hyaluronic acid (HA) for its overall clinical improvement and longer-lasting effects, though with a slightly lower agreement score (B, 8.1).

3. Administration Protocol: For optimal results, the consensus suggests 2 to 4 injections per treatment cycle, spaced one to two weeks apart, is more effective than a single injection.

4. Leukocyte Content: There are no significant differences in clinical outcomes between leukocyte-poor and leukocyte-rich PRP, indicating flexibility in PRP preparation choices.

5. Patient Demographics: While there is no specific age range identified, the consensus indicates that PRP can be used across diverse age groups.

6. Independent Consensus Methodology: The consensus process involved a diverse group of experts from 27 European countries, enhancing its robustness and geographic adaptability.

These findings emphasize the clinical utility of PRP in treating osteoarthritis, advocating for its use as an effective and safer alternative to traditional injectables.

STRENGTHS AND LIMITATIONS OF THE ESCA CONSENSUS ON INJECTABLE ORTHOBIOLOGICS FOR OSTEOARTHRITIS?

Strengths

1. First Comprehensive Effort: This is the first major European consensus following a rigorous methodology, reflecting a strong commitment to addressing the field of orthobiologics.

2. Diverse Participation: The process involved 77 experts from 27 European countries, ensuring a pluralistic approach and a wide range of perspectives.

3. Structured Methodology: The consensus was developed through a well-defined process that included various independent groups, promoting credibility and thoroughness.

4. Clinical Relevance: The consensus aims to provide clinically relevant recommendations even when scientific literature is limited, combining evidence from studies with clinical expertise.

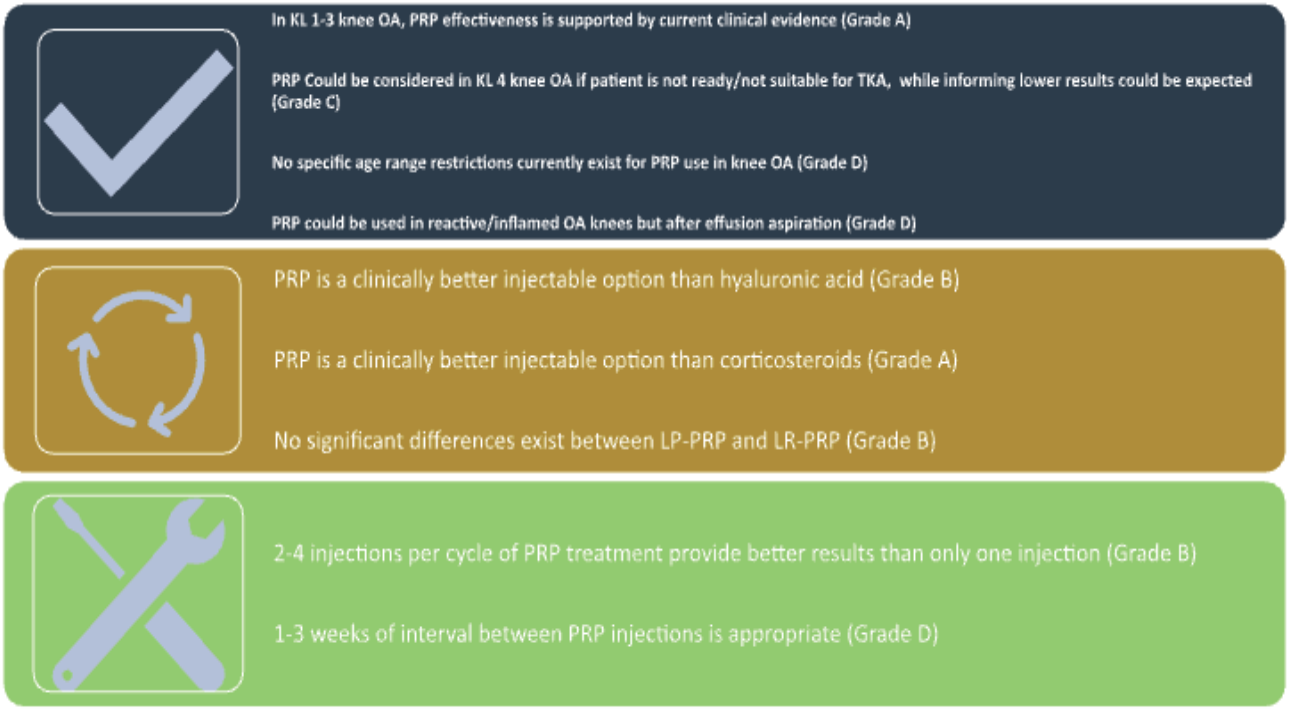
Limitations

1. Variable Scientific Evidence: Some topics within the consensus rely on low-quality studies, which might affect the reliability of certain recommendations.

2. Unclear Candidate Selection: The consensus does not clearly identify the ideal candidates for injectable treatments, which can lead to confusion in clinical applications.

3. Geographic Variability: The diversity among European countries means that the findings may not be universally applicable, and local practice might differ significantly.

4. Potential Biases: Differences in formulations of injectable products like PRP and hyaluronic acid may introduce bias in conclusions from meta-analyses.



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European Society for Sports Traumatology,Knee Surgery and Arthroscopy

The clinical contribution of adipose tissue and the stromal vascular fraction

Prof. Isabelle Auquit-Auckbur

Prof. Isabelle AUQUIT-AUCKBUR
Plastic and Hand Surgery, Rouen, France
First Vice-President of the French Society of Hand Surgery (SFCM)

Pr Isabelle AUQUIT-AUCKBUR

We are very familiar with adipose tissue, which is widely used in plastic surgery for its volumising effect, but we have realised that within this adipose tissue there are not only adipocytes involved in this volumising effect, but also mesenchymal stem cells.

I work a lot on the vascular stromal fraction in Rouen, in very close collaboration with biologists.

We extract the stromal vascular fraction, which is this cellular soup that contains both the cells of the supporting adipose tissue, but which are not adipocytes; these are the cells of the blood line, the famous mesenchymal stem cells, the ADSCs.

APPLICATIONS OF STROMAL VASCULAR FRACTION IN HAND SURGERY

The stromal vascular fraction (SVF) has several interesting applications in hand surgery:

1. Skin rejuvenation: SVF contributes to hand rejuvenation by improving tissue trophicity and filling the inter-metacarpal valleys thanks to its volumising effect.

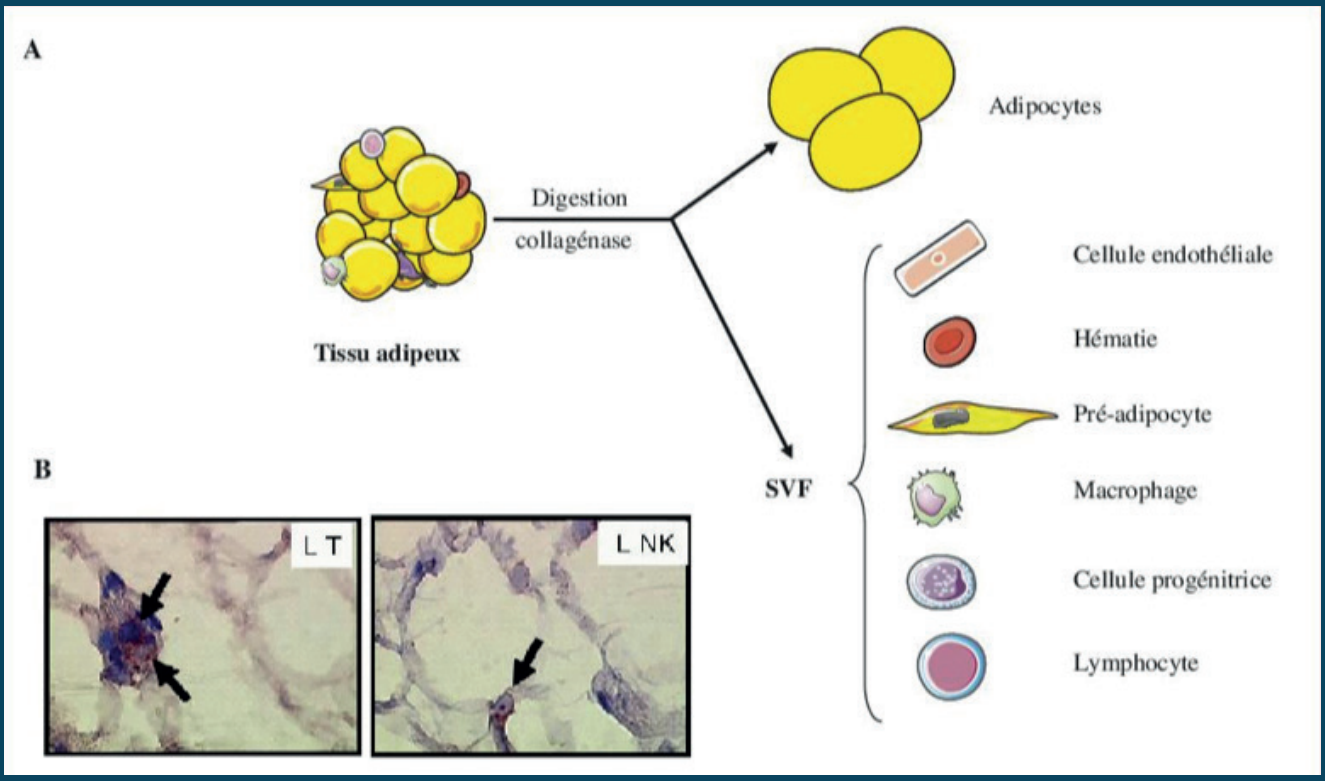
2. Treatment of scleroderma: Its use has been shown to be effective in reducing pain and digital ulcers in patients suffering from scleroderma. Specific protocols have been put in place for injecting FVS into patients' fingers.

3. Dupuytren's disease: FVS is used during procedures such as aponeurotomies. It helps to reduce post-operative retractions, thereby promoting better recovery.

4. Tissue regeneration: Because of its neo-angiogenesis, immunomodulation and anti-inflammatory properties, FVS can support the healing and regeneration of damaged tissue.

5. Bone and cartilage regeneration: Although exploratory, FVS could have potential applications in the regeneration of bone and cartilage tissue for specific pathologies.

These applications show the potential of FVS to improve results in hand surgery, both in aesthetic and functional procedures.



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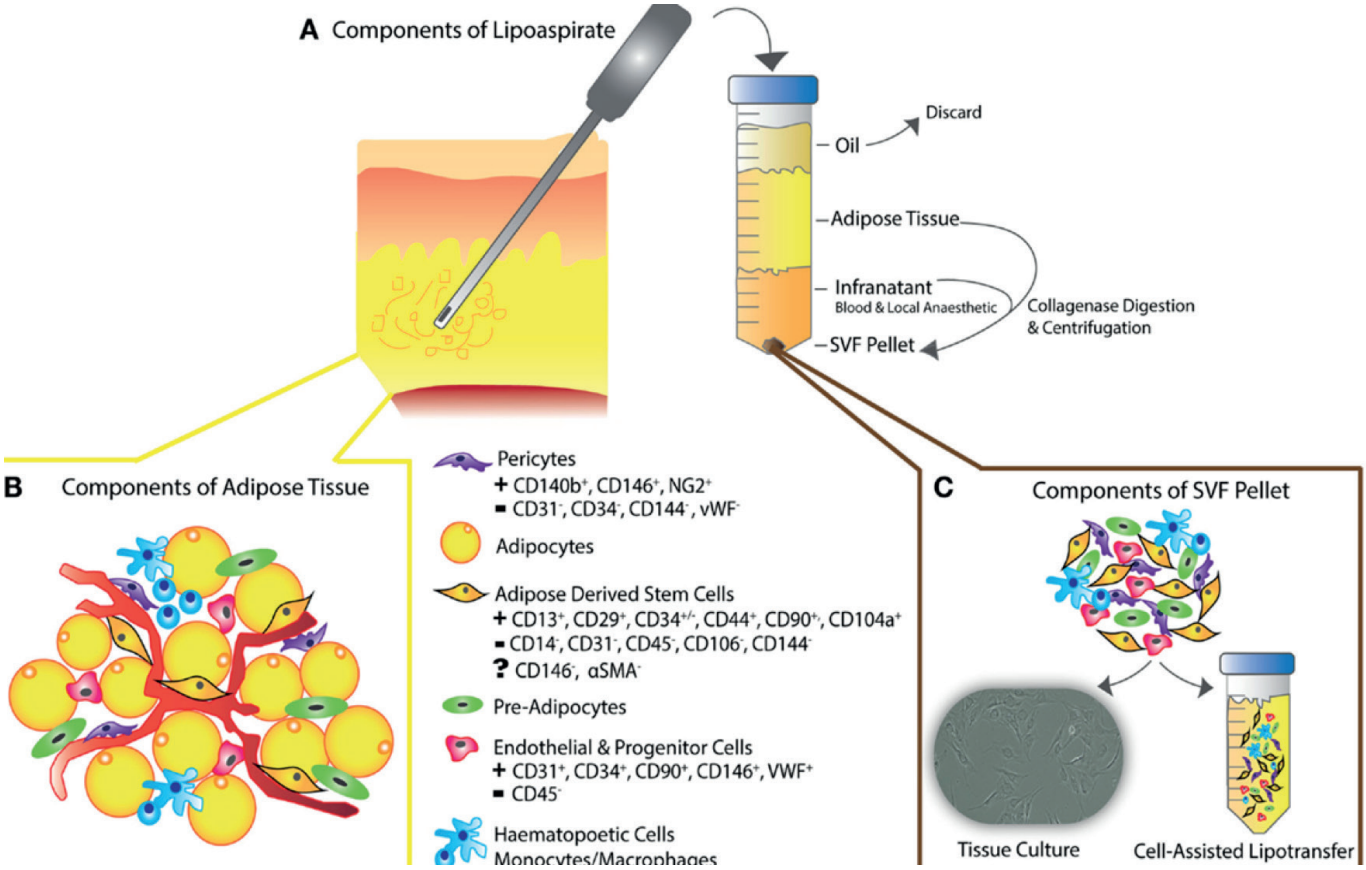


STROMAL VASCULAR FRACTION EXTRACTED FROM ADIPOSE TISSUE

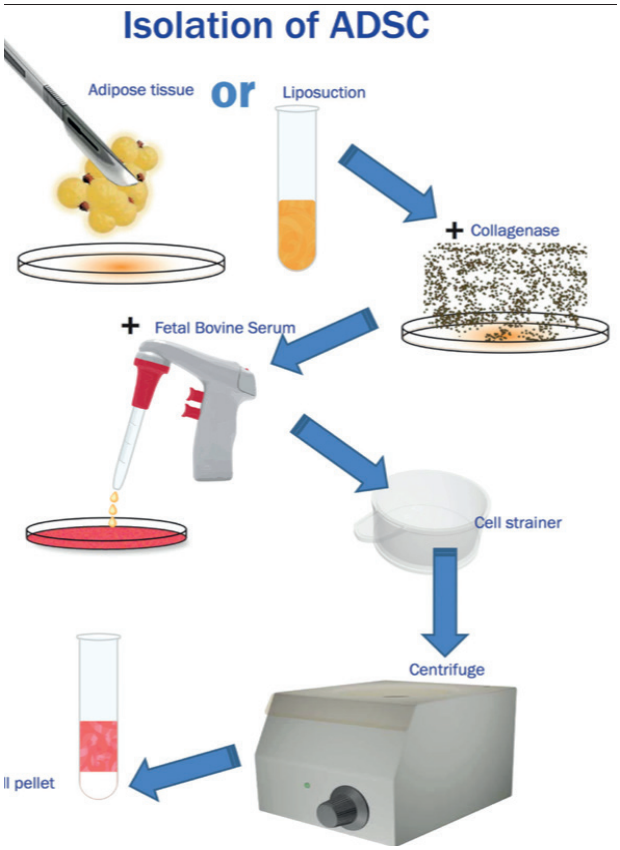
Adipose-Derived Stem/Stromal Cell (ADSC)
By IFATS – International Federation of Adipose Therapeutics and Science

Mesenchymal stem cells:

- **Able to adhere to plastic under standard culture conditions,**
- **Positive for non-hematopoietic markers CD105, CD73, and CD90, and negative for hematopoietic markers CD45, CD34, CD14 or CD11b, CD79βor CD19, and HLA class II,**
- **Capable of differentiating into chondrocytes, osteoblasts, and adipocytes under standard in vitro differentiation conditions.**

Adipose tissue: a promising alternative source of cells to bone marrow,

- **Exhibits properties comparable to those of bone marrow-derived stem cells (BMSC),**
- **Has the advantage of being more easily harvested through less invasive techniques such as liposuction or abdominoplasty.**



Isolation of ADSC Adipose-Derived Stem/Stromal Cell (ADSC)

HOW IS THE STROMAL VASCULAR FRACTION EXTRACTED FROM ADIPOSE TISSUE?

The stromal vascular fraction (SVF) is extracted from adipose tissue via a methodical process to preserve cell viability. Here are the key stages:

Atraumatic collection: Adipose tissue is collected using a syringe rather than a conventional lipo-aspirator. This method minimises damage to the supporting cells and ensures gentler extraction.

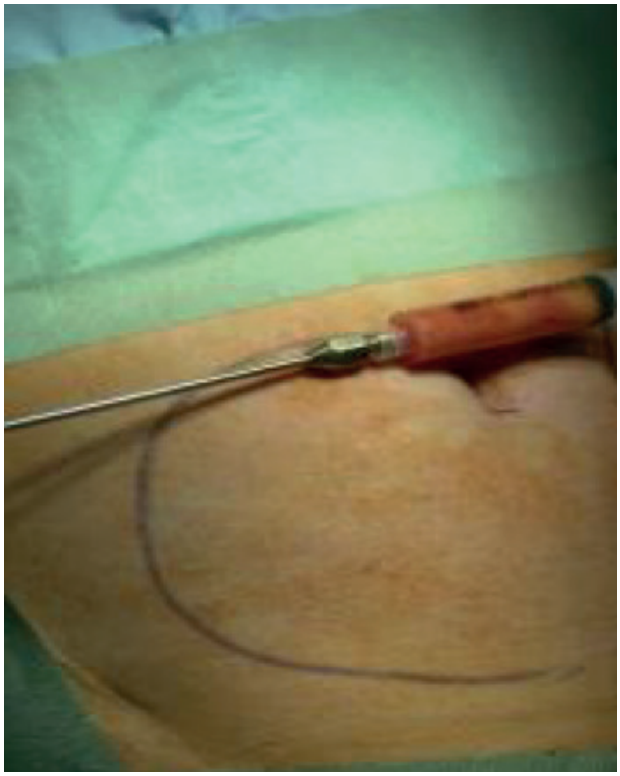
Use of specific cannulas: Cannulas with precise orifices are used for better calibration and vacuum control, enabling safe and effective aspiration.

Laboratory processing: After extraction, the stromal vascular fraction can be isolated either by centrifugation or by sending the tissue to a specialist laboratory that complies with strict regulations on human biological tissue. This includes the use of MTPI-certified laboratories.

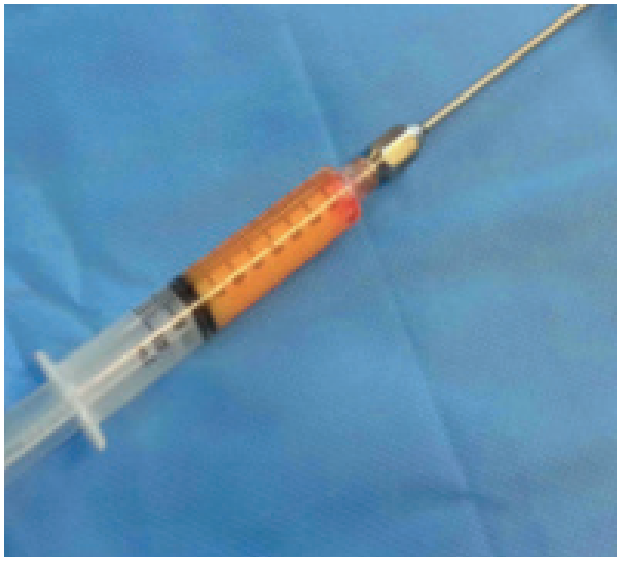
Regulations: Once the tissue has been processed in the laboratory, it is considered to be a medicine, subject to the same laws and regulations as any other medical therapy.

This process guarantees not only the quality and efficacy of the stromal vascular fraction, but also that it remains compliant with the numerous regulatory requirements.

Extraction by Centrifugation: initially 3000 rpm for 3 minutes, now less. Washing and decantation.



Donor sites: abdomen, trochanteric areas, inner thighs or knees.Infiltration with adrenaline-containing saline solution, with or without local anesthesia.



Reinjection: In retrograde fashion.
17-gauge cannulas (or 20, 23, or 25 depending on the recipient site).

THE OBSERVED BENEFITS OF USING STROMAL VASCULAR FRACTION

The use of stromal vascular fraction (SVF) in the treatment of Dupuytren's disease and scleroderma has demonstrated a number of benefits:

Dupuytren's disease

Reduced retraction: Studies have shown that reinjection of VSF after fasciotomies can reduce tissue retraction, thereby improving hand function.

Beneficial effects on healing and regeneration: FVS contains mesenchymal stem cells, which contribute to neo-angiogenesis and tissue regeneration, promoting better healing.

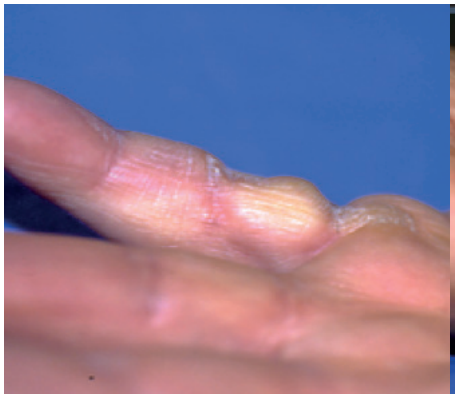
ADSCs have demonstrated a role in reducing:
- Fibrosis: pulmonary, hepatic, renal, and cardiac in animal models,
- Immune and inflammatory responses.

In vitro: In Dupuytren's disease, ADSCs (through direct contact and via multiple secreted factors):
- Decrease the proliferation and contractility of myofibroblasts,
- Decrease the expression of -smooth muscle actin protein.

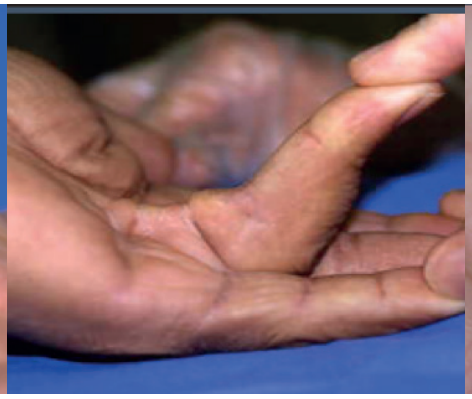
Jennifer S. N. Verhoekx et al., "Adipose-Derived Stem Cells Inhibit the Contractile Myofibroblast in Dupuytren's Disease:," Plastic and Reconstructive Surgery 132, no. 5 (November 2013)

R. Khoury, 2011: Technique of multiple percutaneous aponeurotomies combined with adipose tissue transfer:
- Reduction of flexion contracture:
- MCP: from 61° to 27°
- PIP: from 37° to –5°
- Improved skin trophicity,
- No major complications.

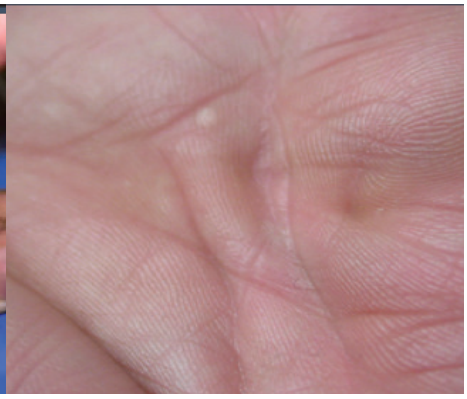
Steven E. R. Hovius et al., "Extensive Percutaneous Aponeurotomy and Lipografting: A New Treatment for Dupuytren Disease:," Plastic and Reconstructive Surgery 128, no. 1 (July 2011)



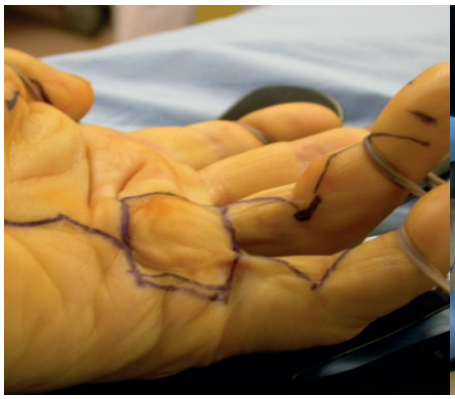
Fibromatosis



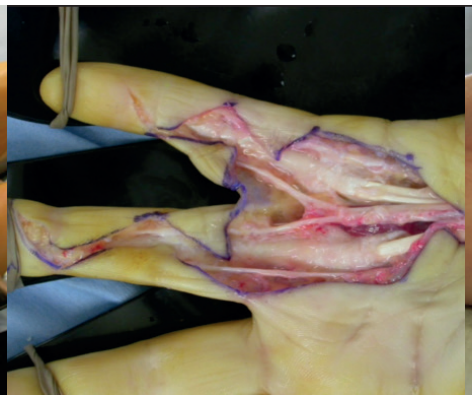
Flexion contractures of the MCP and PIP joints



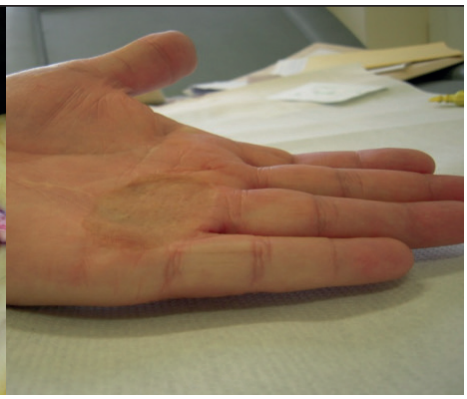
Involvement of the palmar aponeurosis



Medical treatment: Needle aponeurotomy



Surgical treatment: Aponeurectomy with reconstruction



Scleroderma

Hand involvement:
- Raynaud's phenomenon and acrocyanosis
- Ischemic digital ulcers
- Subcutaneous calcinosis
- Skin fibrosis with retraction

Hand disability accounts for 75% of the overall disability rate.
→ Significant functional improvement of the sclerodermic hand
→ Importance of the regenerative effects of SVF (stromal vascular fraction) and ADSCs (adipose-derived stem/ stromal cells)

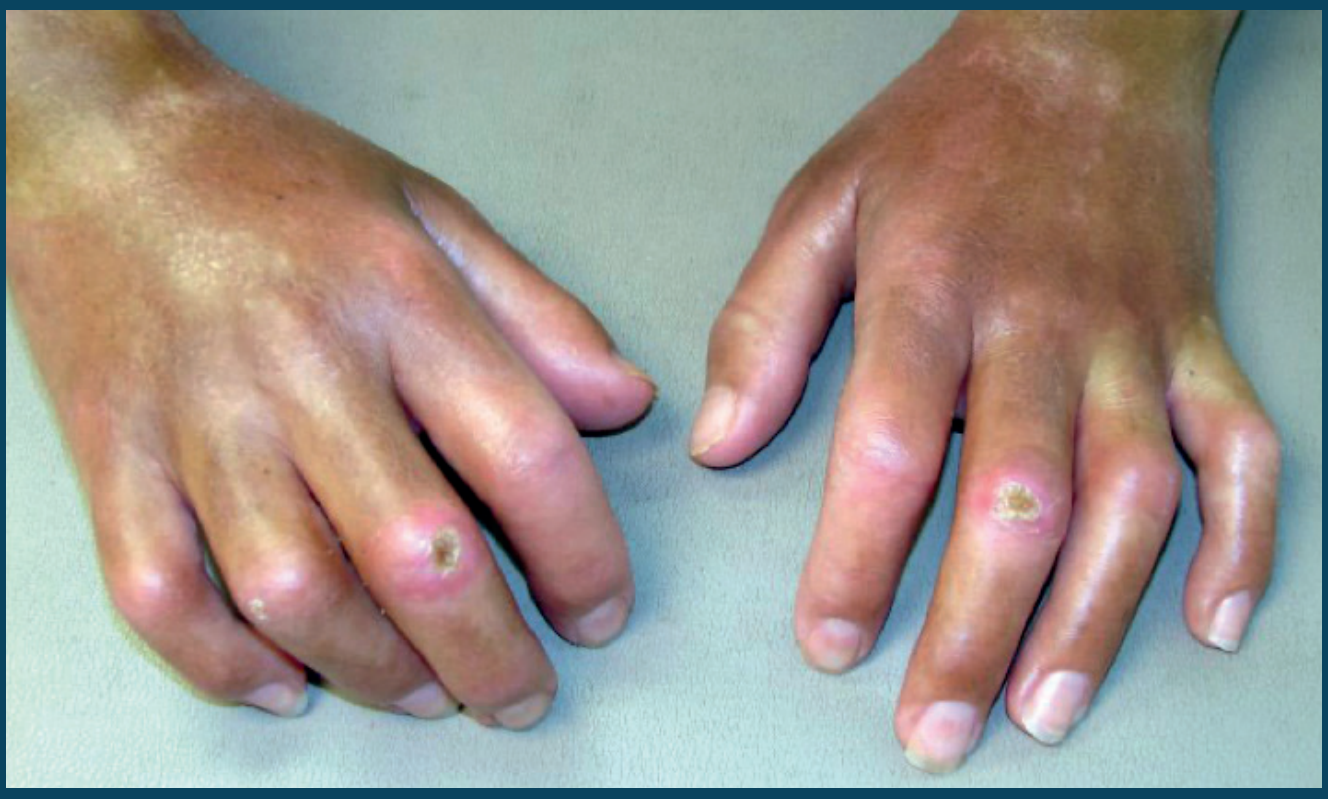
Reduced digital pain and ulcers: In clinical trials, injecting FVS into the fingers of scleroderma patients was significantly effective, reducing digital pain and ulcers. Reduction of skin fibrosis and increased local vascularization after fat and SVF (stromal vascular fraction) injection in mice with bleomycin-induced scleroderma.

Nicolas Serratrice et al., "New Fat-Derived Products for Treating Skin-Induced Lesions of Scleroderma in Nude Mice," Stem Cell Research & Therapy 5, no. 6 (2014)

Improved quality of life: The results of the treatment were considered conclusive, leading to an improvement in patients' quality of life, linked to a reduction in symptoms. Reduction in pain, frequency, duration, and severity of cold-related attacks after adipose tissue injection in 12 sclerodermic hands.

Jonathan Bank et al., "Fat Grafting to the Hand in Patients with Raynaud Phenomenon: A Novel Therapeutic Modality," Plastic and Reconstructive Surgery 133, no. 5 (May 2014)

These benefits are largely attributed to the anti-inflammatory and regenerative properties of the cells present in FVS, as well as their ability to modulate the tissue microenvironment.



Scleroderma

Clinical Experience with over 2000 patients using Regen PRP

For the prevention of sternal and venous access infection in cardiac surgery

Prof. G.Filiberto SERRAINO
Cardiac Surgery, Magna Græcia University of Catanzaro (Italy)

As a cardiothoracic surgeon, most of our procedures involve a median sternotomy - we open the chest to access the heart.

After performing a life-saving operation on a patient who was at the brink of death, the very first question they often ask upon waking is:
"How is my wound?"

One of the most serious postoperative complications is a chest wound infection known as mediastinitis. Its incidence, while variable, can be significant, and when it occurs, hospital mortality rates are alarmingly high.

Beyond the human toll, mediastinitis also imposes a substantial financial burden on both hospitals and healthcare systems.

Prof G.Filiberto SERRAINO

Magna Græcia University of Catanzaro (Italy)

BENEFITS OF USING PRP (PLATELET-RICH PLASMA) IN CARDIAC SURGERY

According to the studies presented, the benefits of using Platelet-Rich Plasma (PRP) in cardiac surgery include:

1. Reduction in Infection Rates:
The application of PRP significantly decreases the incidence of both deep and superficial sternal infections in patients undergoing cardiac surgeries, such as coronary artery bypass grafting.

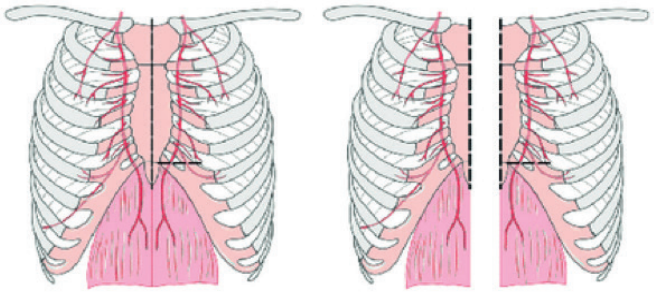
2. Enhanced Quality of Life:
By preventing infections that could lead to complications, the use of PRP contributes positively to patient quality of life; patients experience fewer postoperative issues that would require hospitalization or lead to prolonged recovery.

3. Cost Efficiency:
The studies highlighted a substantial reduction in postoperative costs associated with complications related to infections. This suggests that PRP could lead to lower healthcare expenditures by minimizing the need for additional treatments and hospital stays.

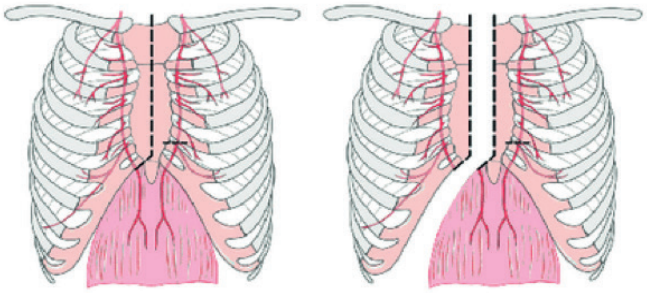
4. Safe Application:
The research indicates no adverse events were reported with the topical application of PRP in cardiac surgery settings, making it a safe option for enhancing recovery.

5. Specific Benefits in Diabetic Patients:
PRP application appears particularly beneficial for diabetic patients, reducing the incidence of infections at surgical sites more than in non-diabetic patients. Overall, the studies support PRP as a promising adjunctive treatment in cardiac surgery for improving surgical outcomes and reducing the risk of infection.

I) Standard midline sternotomy without sparing of the xiphoid process. The left thoracic internal artery was harvested to the level below its bifurcation.

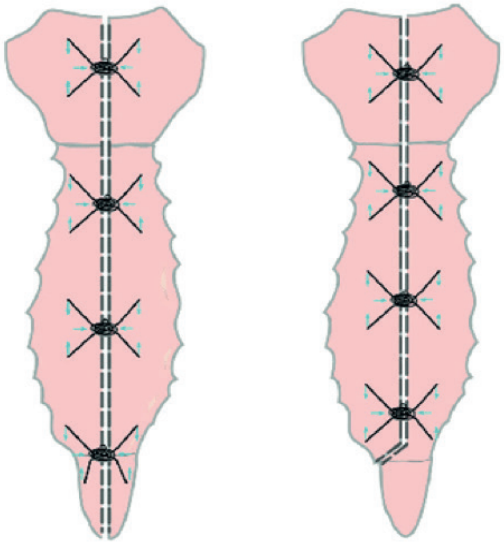


II) Xiphoid-sparing sternotomy. The left thoracic internal artery was harvested to the level just above its bifurcation.



III) criss-cross sternal wiring with the involvement of the xiphoid process.

IV) criss-cross sternal wiring with sparing of the xiphoid process.



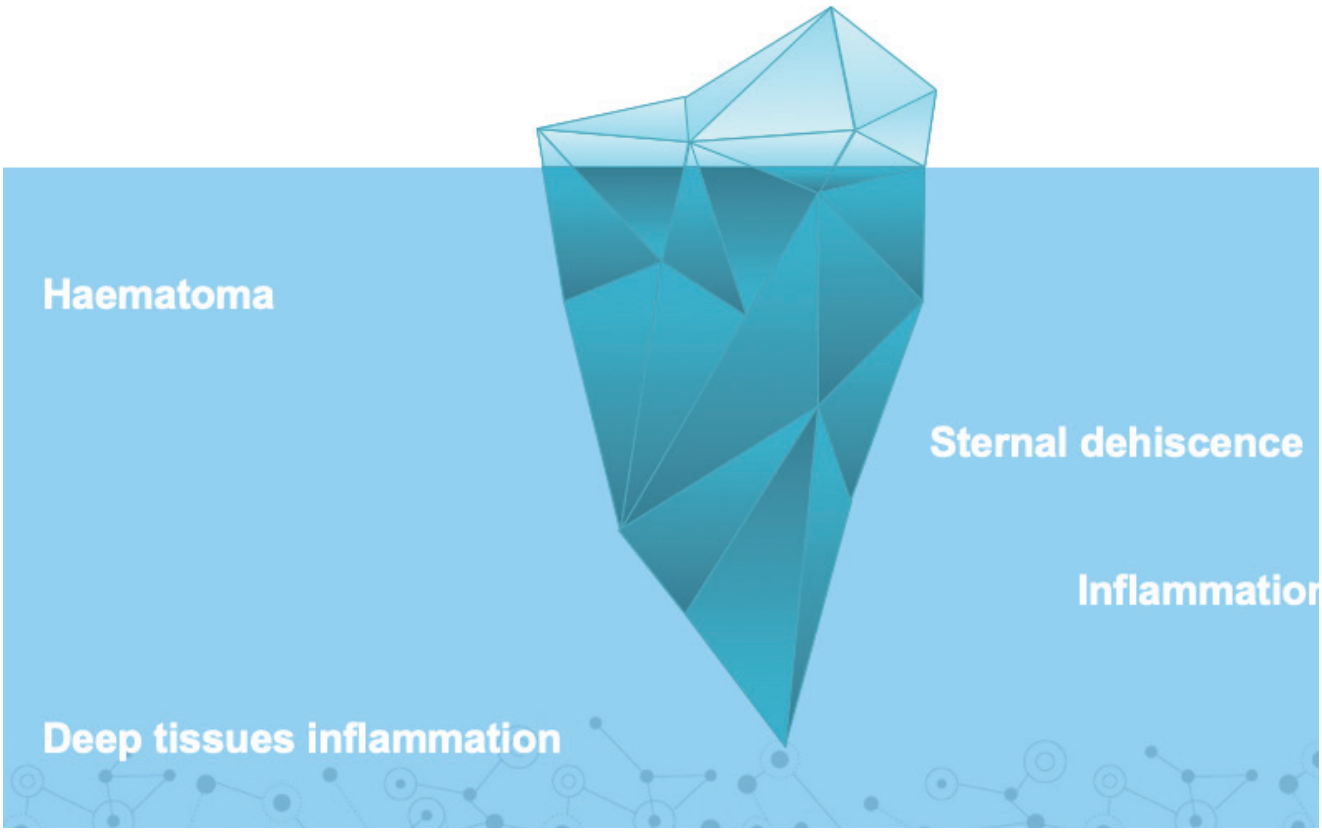
OPEN HEART SURGERY: 80 % WITH MEDIAN STERNOTOMY

Cost and efficiency

0.3 to 3.4 %
Mediastinitis post cardiac surgery

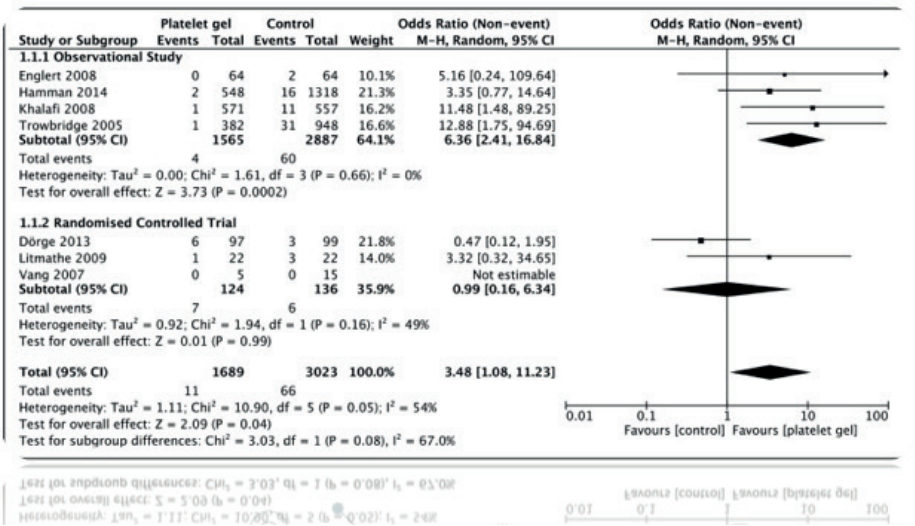
1.1 to 19%
In-hospital mortality

1.300.000$
Costs per patient



Deep or Superficial Wound Infection after Cardiac Surgery

A meta-analysis of platelet gel for prevention of sternal wound infections following cardiac surgery



Study or Subgroup	Platelet gel Events	Total	Control Events	Total	Weight	Odds Ratio (Non-event) M-H, Random, 95% CI
1.1.1 Observational Study						
Englert 2008	0	64	2	64	10.1%	5.16 [0.24, 109.64]
Hamman 2014	2	548	16	1318	21.3%	3.35 [0.77, 14.64]
Khalafi 2008	1	571	11	557	16.2%	11.48 [1.48, 89.25]
Trowbridge 2005	1	382	31	948	16.6%	12.88 [1.75, 94.69]
Subtotal (95% CI)		**1565**		**2887**	**64.1%**	**6.36 [2.41, 16.84]**
Total events	4		60			
Heterogeneity: Tau² = 0.00; Chi² = 1.61, df = 3 (P = 0.66); I² = 0%						
Test for overall effect: Z = 3.73 (P = 0.0002)						
1.1.2 Randomised Controlled Trial						
Dörge 2013	6	97	3	99	21.8%	0.47 [0.12, 1.95]
Litmathe 2009	1	22	3	22	14.0%	3.32 [0.32, 34.65]
Vang 2007	0	5	0	15		Not estimable
Subtotal (95% CI)		**124**		**136**	**35.9%**	**0.99 [0.16, 6.34]**
Total events	7		6			
Heterogeneity: Tau² = 0.92; Chi² = 1.94, df = 1 (P = 0.16); I² = 49%						
Test for overall effect: Z = 0.01 (P = 0.99)						
Total (95% CI)		**1689**		**3023**	**100.0%**	**3.48 [1.08, 11.23]**
Total events	11		66			
Heterogeneity: Tau² = 1.11; Chi² = 10.90, df = 5 (P = 0.05); I² = 54%						
Test for overall effect: Z = 2.09 (P = 0.04)						
Test for subgroup differences: Chi² = 3.03, df = 1 (P = 0.08), I² = 67.0%						

Odds Ratio (Non-event) M-H, Random, 95% CI

0.01 0.1 1 10 100

Favours [control] Favours [platelet gel]

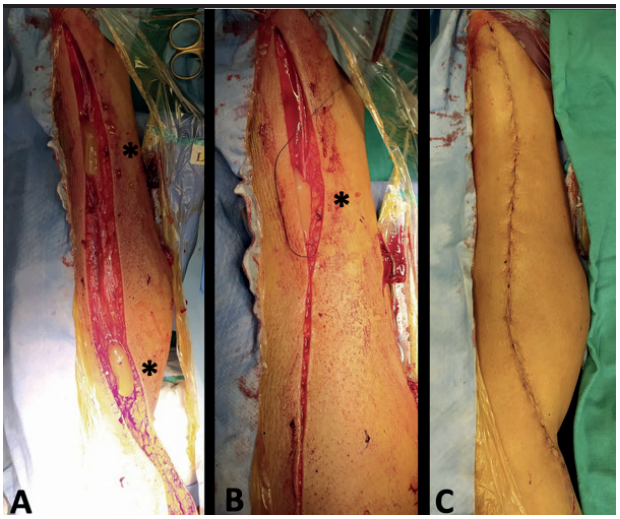
HOW DOES PRP APPLICATION AFFECT THE INCIDENCE OF DEEP STERNAL WOUND INFECTIONS AND LEG INFECTIONS AFTER CORONARY ARTERY BYPASS GRAFT SURGERY?

The application of Platelet-Rich Plasma (PRP) in coronary artery bypass graft surgery (CABG) has demonstrated a significant impact on reducing the incidence of deep sternal wound infections (DSWIs).

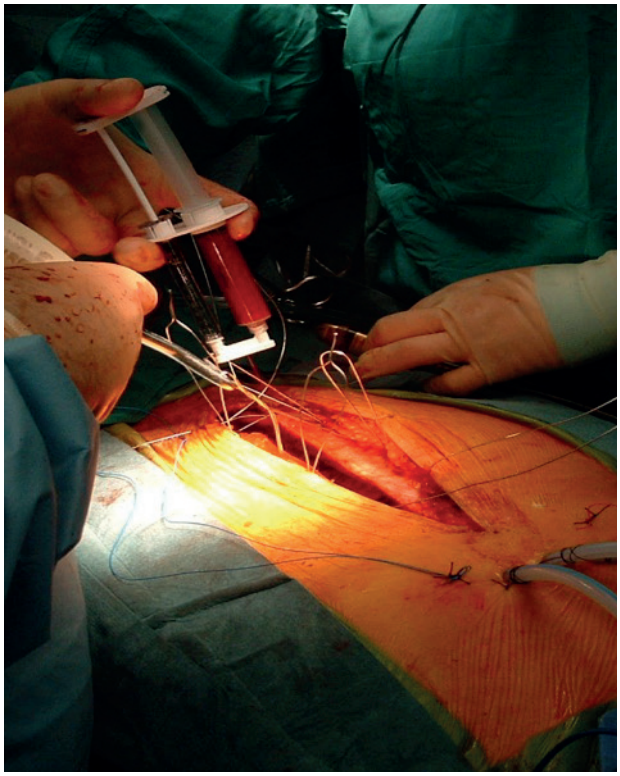
In one study, it was found that the use of PRP effectively prevented the recurrence of both deep and superficial infections post-surgery, leading to improved quality of life for patients. Additionally, a similar beneficial effect was observed regarding leg infections, particularly in diabetic patients.

The topical application of PRP on the surgical site resulted in a notable reduction of infections not only in the sternum but also in areas where leg veins were harvested. This approach significantly minimizes the risk of postoperative complications, which is critical considering that patients undergoing CABG often share common risk factors such as obesity and diabetes.

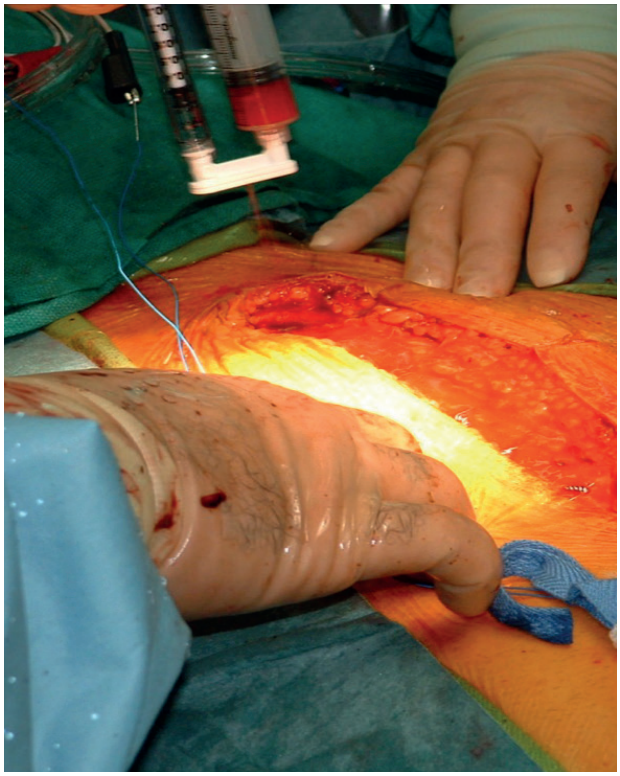
Overall, the use of PRP appears to be a promising strategy for reducing infection rates and improving patient outcomes following CABG surgery.



Saphenous vein is harvested to be used for coronary artery bypass graft



PRP is sprayed along the exposed sternal edges



PRP is sprayed over the subcutaneous tissue

THE ECONOMIC IMPLICATIONS OF PREVENTING POST-OPERATIVE INFECTIONS WITH PRP FOR HOSPITALS AND PUBLIC HEALTH SYSTEMS

The economic implications of preventing post-operative infections with Platelet-Rich Plasma (PRP) for hospitals and public health systems are significant. Key points include:

1. Reduction in Infection Rates:
The application of PRP, especially in high-risk patients (e.g., those with diabetes), has been associated with reduced rates of surgical site infections (SSIs). This is crucial given that SSIs can lead to extended hospital stays and higher medical costs.

2. Cost Savings from Reduced Length of Stay:
By preventing infections, hospitals can reduce the length of stay for patients. For instance, managing infections in intensive care units can incur costs as high as $10,000 per day. Therefore, preventing these infections can translate into substantial savings.

3. Improvement in Patient Quality of Life:
Reduced infections can also lead to improved patient outcomes and quality of life. Avoiding complications associated with infections can enhance recovery and reduce follow-up care costs.

4. Economic Studies and Cost-Benefit Analysis:
Economic evaluations, such as the mentioned medical economic studies, suggest that using PRP can cut postoperative care costs significantly, potentially by a factor of ten in certain cases. These findings could encourage more hospitals to adopt PRP treatment protocols.

5. Broader Public Health Impacts:
Widespread adoption of PRP could reduce the burden on public health systems by alleviating the incidence of SSIs, leading to lower healthcare costs overall and better allocation of resources.

Through these avenues, preventing post-operative infections with PRP holds considerable potential not only for individual hospitals but also for the healthcare system as a whole, suggesting a compelling case for its integration into standard surgical practices.

Results

Risk factors	Group A 671 patients	Group B 422 patients	*P* value
Operation			
Isolated CABG	271 (40·4%)	187 (44·3%)	0·299
Single IMA	261	184	0·352
Double IMA	10	3	0·187
Isolated valvular operation	219 (32·6%)	111 (26·3%)	1·000
Other than isolated CABG isolated valvular operation	181 (27·0%)	124 (29·4%)	1·000
Operation time (incision to closure) > 300 minutes	101 (15·1%)	55 (13·0%)	0·353
Blood transfusion (number of patients)	305 (45·5%)	209 (49·5%)	0·189
Packed red blood cells (U)	2·74 ± 0·99	2·32 ± 1·09	0·094
Postoperative bleeding (ml)	630·42 ± 361·200	693·27 ± 333·802	0·721
Platelet ($n \times 10^3$ cells/mm^3) (48 hours postoperative)	125·32 ± 46·738	131·66 ± 49·738	0·153
Acute renal failure	21 (3·1%)	14 (3·3%)	0·864
Postoperative delirium	75 (11·2%)	52 (12·3%)	0·565
Respiratory failure (hypoxia)	22 (3·1%)	10 (2·4%)	0·386
Reopening	35 (5·2%)	15 (3·6%)	0·201
Hospital mortality	32 (4·8%)	16 (3·8%)	0·443

CABG, coronary artery bypass graft; IMA, internal mammary artery; BMI, body mass index; COPD, chronic obstructive pulmonary disease.

Serraino et al Int Wound Journal

Regenerative Surgery and current management of vaginal dryness at all ages

Dr Fabienne MARCHAND LAMIRAUD
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Prof. Philippe DESCAMPS
Gynecologic surgeon, Head of Department, University Hospital of Angers, Member of the French National Academy of Surgery and the CNGOF.
Past Vice-President of FIGO (2021–2023). ARSIA MEMBER.

***THE AUTHORS DECLARE NO CONFLICTS OF INTEREST IN RELATION TO THIS ARTICLE.

Dr. Fabienne MARCHAND LAMIRAUD

Prof. Philippe DESCAMPS

INTRODUCTION AND OVERVIEW

Vaginal dryness is a frequent symptom that can occur throughout a woman's life and is most often linked to estrogen deficiency. This hormonal deficiency is responsible for daily intimate discomfort and always has an impact on sexual life.

Estrogen deficiency creates a menopausal state and causes genito-urinary disorders called Genitourinary Syndrome of Menopause (GSM). It is a very frequent pathology, most often underestimated because the subject remains taboo. Women find it difficult to talk about it and practitioners tend to minimize the patients' words or do not wish to speak about sexuality, which delays the management of vulvo-vaginal dryness.

More than 1 in 2 women will one day be affected in their lifetime by a disorder of the genito-urinary organs responsible for intimate discomfort.
It occurs most often after natural menopause or is secondary to anti-cancer treatment:

- 60% to 70% of menopausal women suffer from vulvo-vaginal dryness

- 70% of women treated for hormone-dependent breast cancer present signs of intimate discomfort

But not only: YOUNG women can also suffer from vaginal dryness. This results in a greater feeling of incomprehension, malaise, guilt, shame, with significant personal impact and always a MAJOR impact on sexuality with sometimes social consequences all the more frequent the younger the woman (infidelity, couple separation).

CLINICAL PRESENTATION

The diagnosis of vulvovaginal dryness is clinical and includes three categories of symptoms:

- **Vulvovaginal symptoms:**
irritation, itching, burning, pain, post-coital bleeding, recurrent vaginal infections

• **Sexual symptoms:**
insertional dyspareunia, vaginal pain described as “knife or razor blade” sensations

• **Urinary symptoms:**
urgency, day/night frequency, stress urinary incontinence, painful urination, recurrent urinary infections especially post-coital

To describe all of these associated symptoms, we speak of **Genitourinary Syndrome of Menopause or GSM**, new terminology for vulvo-vaginal atrophy since 2014 (1). 60 to 70% of menopausal women present at least 1 of these symptoms, which generally begin 4 to 5 years after menopause.

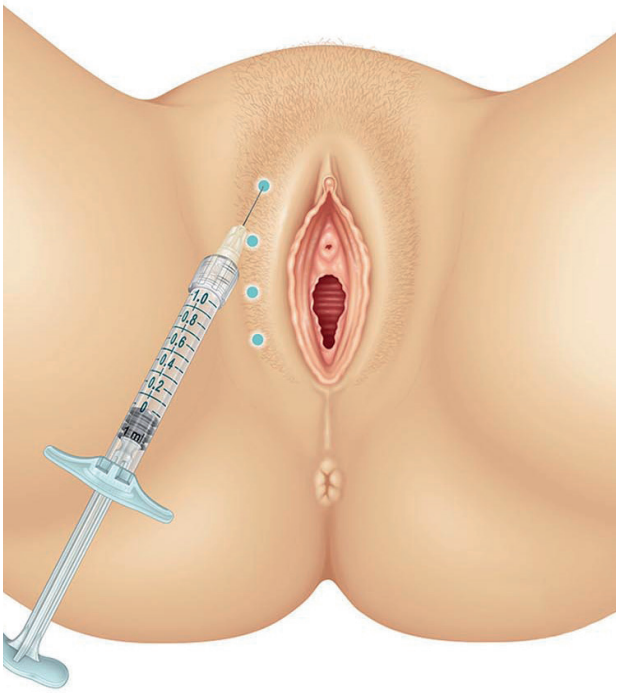
TREATMENT OF VAGINAL DRYNESS

If the GSM is early or moderate, rehydration of the vaginal mucosa is proposed as a first intention using aqueous gels or those based on hyaluronic acid (HA) or polycarbophils. These local treatments relieve more than they treat and suffer from poor long-term adherence due to the constraint of bi- or tri-weekly use and the discharges they cause, most often requiring the wearing of protection, a source of irritation.

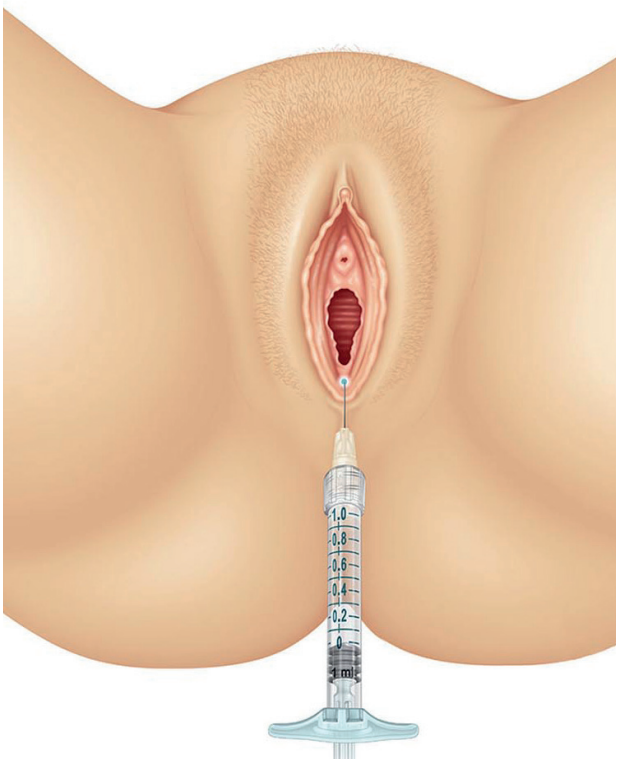
TOPICAL HORMONAL TREATMENTS (E.G., ESTRIOL OR PROMESTRIENE) on the other hand have a certain effectiveness but also suffer from poor adherence for the same reasons. Their prescription is still debated for women treated for breast cancer, even in patients on Tamoxifen. However, a recent study has just rehabilitated their prescription (2) (3).

ALL ESTROGENS, ESTRADIOL OR ESTRIOL, BY VAGINAL ROUTE AT LOW DOSE IMPROVE THE SYMPTOMS OF GSM (4) (5).
It is therefore recommended to consider in the evaluation of the individualized benefit–risk balance and in the shared decision-making process.

VAGINAL HYALURONIC ACID is associated with a significant improvement in GSM symptoms but the effectiveness is lower than that of local estrogen therapy (4) (5).



Injection Techniques of Genital Hyaluronic Acid



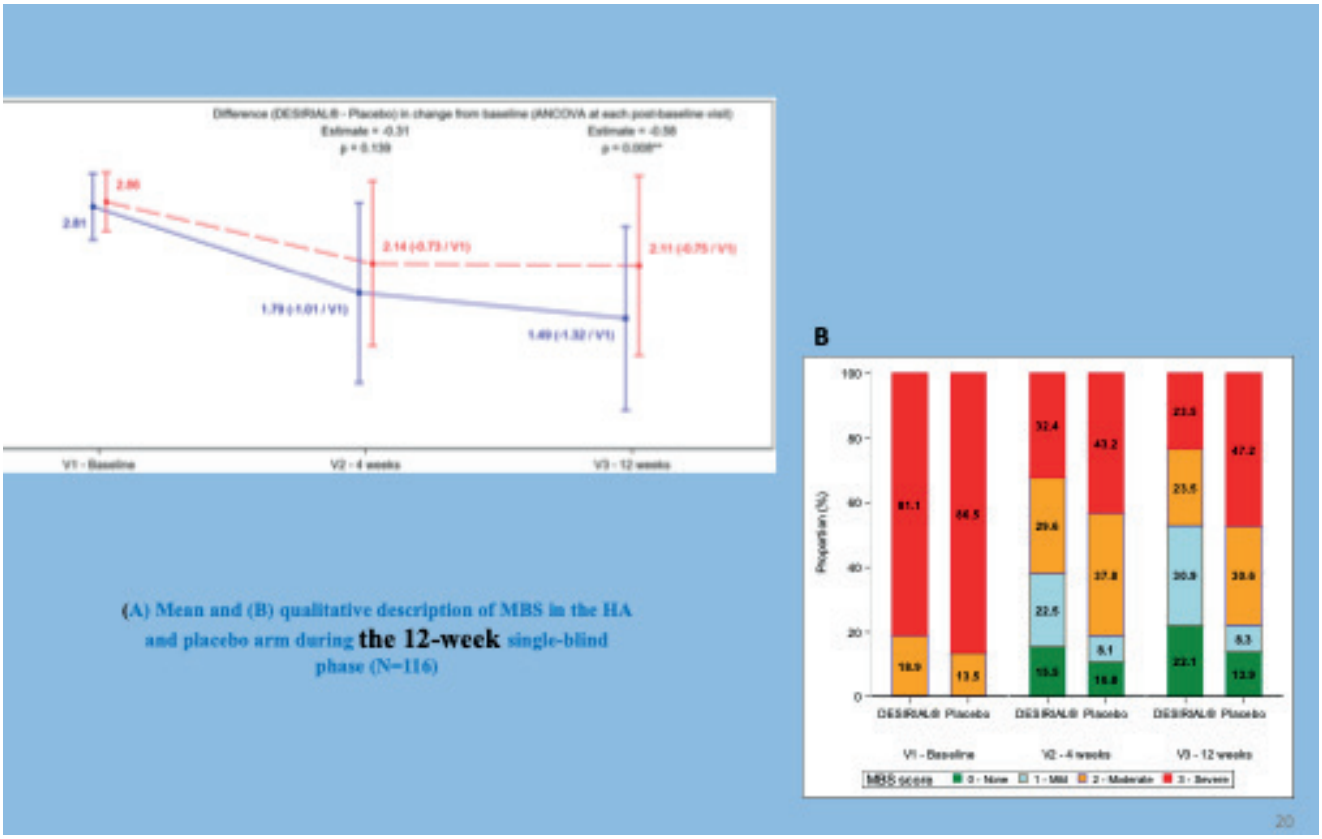


Figure 2: Evaluation of the effectiveness of genital HA injection on AVV at 12 weeks

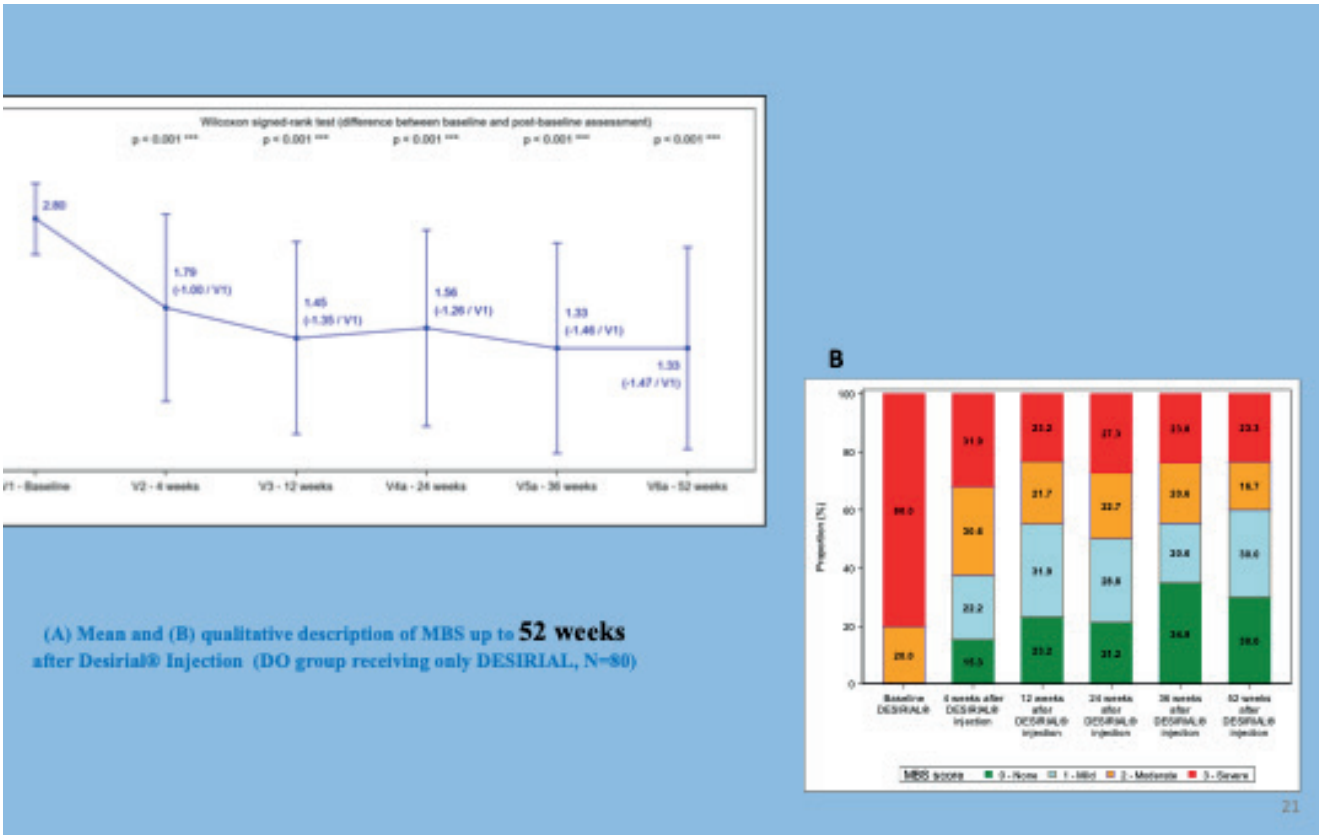


Figure 3: Evaluation of the effectiveness of HA injection on AVV at 52 weeks

NON-HORMONAL REGENERATIVE AESTHETIC SURGERY TECHNIQUES ADAPTED TO GYNECOLOGY

These provide simple, effective non-hormonal therapeutic alternatives, such as:

- **Injectables:** Genital hyaluronic acid (Desirial*), Platelet-Rich Plasma (PRP), lipofilling, or nanofat
- **Physical methods**: laser, radiofrequency, vulvovaginal photobiomodulation, HIFU

INJECTABLE GENITAL HYALURONIC ACID (HA)

Thanks to the French company Vivacy, which originally manufactured HA for aesthetic purposes, an injectable, non-volumizing, resorbable cross-linked HA gel adapted to the genital area was developed. It is the only HA product approved for use in the genital area with CE marking.

It has significant hygroscopicity as it can capture up to 1,000 times its molecular weight in water. It is associated with mannitol, an antioxidant, which enhances the action of HA by ensuring its protection. Thanks to this protocol, the injection is almost painless and the gel is well distributed without bolus, even in case of significant atrophy, the injection of lidocaine having performed a hydrodissection of the planes (figure 1). Resumption of activity is immediate [6) (7).

Contraindications include:

- Pregnancy or breastfeeding
- Known allergy to HA or mannitol
- Ongoing vulvovaginal infections (bacterial, viral, fungal)
- Autoimmune diseases (e.g., lichen sclerosus)
- Immunosuppressive treatment
- Coagulation disorders or anticoagulant use
- History of vulvovaginal neoplasia

The results obtained show an optimal effect of the product 3 months after injection, particularly on hydration, elasticity, tone and sensitivity of the vulvo-vaginal region. A new treatment is recommended 6 to 8 months after the first injection depending on the chronicity of the dryness, the taking or not of treatments responsible for the dryness, followed by 1 injection per year on average. But, as injections progress, the interval between each injection increases over time especially if a regular sexual life has resumed, sexual intercourse maintaining the beneficial effect of genital HA. The feeling of well-being and intimate comfort begins around the 15th day to be maximal at 3 months which allows a rapid recovery of intimate quality of life and painless sexual intercourse (6) (7) (8).

A MULTICENTER RANDOMIZED PLACEBO-CONTROLLED STUDY

A randomized, placebo-controlled, multicenter study was recently published in Maturitas (9).
In the **SYLIVA study,** 120 menopausal women were included from French and European centers.

At D0, the recruited patient received either a genital HA injection or a placebo injection. At 3 months, the placebo group received a genital HA injection. MBS scores (vulvo-vaginal atrophy) and FSFI (sexuality) were evaluated at 1 month, 3 months, 6 months, 9 months and 1 year.

This study shows that at 12 weeks, a single injection of 1ml of genital HA is effective versus placebo, that it reduces even severe AVV symptomatology (figure 2), improves sexual function and that at 52 weeks the effects are durable (figure 3).
No major adverse events were reported in this study.

PLATELET-RICH PLASMA (PRP)

has a reparative and regenerative action due to the presence of growth factors contained in the plasma and platelets. Its use for aesthetic purposes is not authorized in France. It is authorized only for therapeutic purposes since September 2023.

PRP injections are known and used in the treatment of androgenic alopecia. Its gynecological application is therefore recent and has its full place in the management of lichen sclerosus atrophy of the vulva, an autoimmune disease and where, therefore, Desirial* is not indicated (due to the presence of mannitol).
It is a self-regeneration since it is one's own plasma.

LIPOFILLING & NANOFAT

The reparative and volumizing effect can be done by lipofilling or nanofat associated or not with PRP. This technique is less commonly used in the management of dryness because it requires anesthesia, thus an operating room for the harvesting of autologous fat followed by reinjection after centrifugation and/or filtration.

A short outpatient hospitalization is therefore necessary as well as a work stoppage. The injection is done: in the vulvar region to treat insertional dyspareunia, fill retractile scars from episiotomy or tears, resistant fissures of the perineal fork to other therapies and can treat at the same time vulvar gaps secondary to childbirth, or in the vaginal walls in the submucosa.

Indications:
- Introital dyspareunia
- Scars from episiotomy or tears
- Perineal fissures
- Vulvar gaping

PHYSICAL REGENERATIVE TREATMENTS

They are more recent in use. By their thermal effect, these treatments increase blood circulation by promoting neovascularization and stimulate fibroblasts which will produce collagen (thickening of the mucosa), elastin (flexibility of the mucosa) and HA (hydration of the mucosa).

The mucosa thus regains thickness, flexibility and hydration. Thus, physical treatments restore the mucosa and normalize vaginal pH and flora.

Several techniques are used to achieve this result:
- **Laser**
- **Radiofrequency**
- **Focused Ultrasound (HIFU)**
- **Photobiomodulation (LED)**

Vaginal dryness is a frequent symptom that is underestimated and undertreated, the subject remaining taboo. Patients do not always dare to mention it during a consultation and the medical profession is not always attentive.

Yet, if the woman were informed of the risk of dryness before menopause or anti-cancer treatment, the treatment would be initiated early and a single injection of genital hyaluronic acid Desirial* would most often be sufficient to treat the patient and prevent the worsening of the dryness which, if untreated, will become permanent.

When GSM is more advanced and affects the vulva and the entire vaginal cavity, physical treatments such as Laser, Radiofrequency, Photobiomodulation then have their full place, LED should be associated. But the result is longer to obtain and requires several sessions.

It is therefore urgent to take into account this symptom which leaves women in misunderstanding of their pain to which is added a feeling of guilt and devaluation.
It is our duty to inform our patients and to direct them quickly to practitioners trained in these techniques.

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*VIVACY Internal Data – Preclinical evaluation of 2 HA-based fillers on an aged reconstructed skin model.

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PARIS

Regenerative Biosurgery in genital reconstruction surgery

Prof. Barbara HERSANT

I began my academic career in the Department of Plastic, Reconstructive, Maxillofacial and Aesthetic Surgery at Hôpital Henri Mondor, APHP, Université Paris Est Créteil, under the direction of Professor Jean-Paul Méningaud

Through him, I met Antoine Turzi, who promoted a lot of the research I was able to do (with CPP and ANSM authorisation) in the field of regenerative plastic surgery and wound healing.

I've been lucky enough to spend my entire research career on the subject of regenerative medicine and surgery (PRP and fat mesenchymal stem cells).

WHAT ARE THE ADVANTAGES OF USING PLATELET-RICH PLASMA (PRP) IN GYNAECOLOGICAL REGENERATIVE SURGERY?

The aim of regenerative medicine is to stimulate fibroblasts, in our sphere of competence of the dermis, and in the mucous membranes of the lamina propria.

By stimulating these fibroblasts, there will be a secretion of collagen, endogenous hyaluronic acid and elastin, and therefore an improvement in tissue suppleness and tissue regeneration through neo angiogenesis and the creation of extra-cellular matrix.

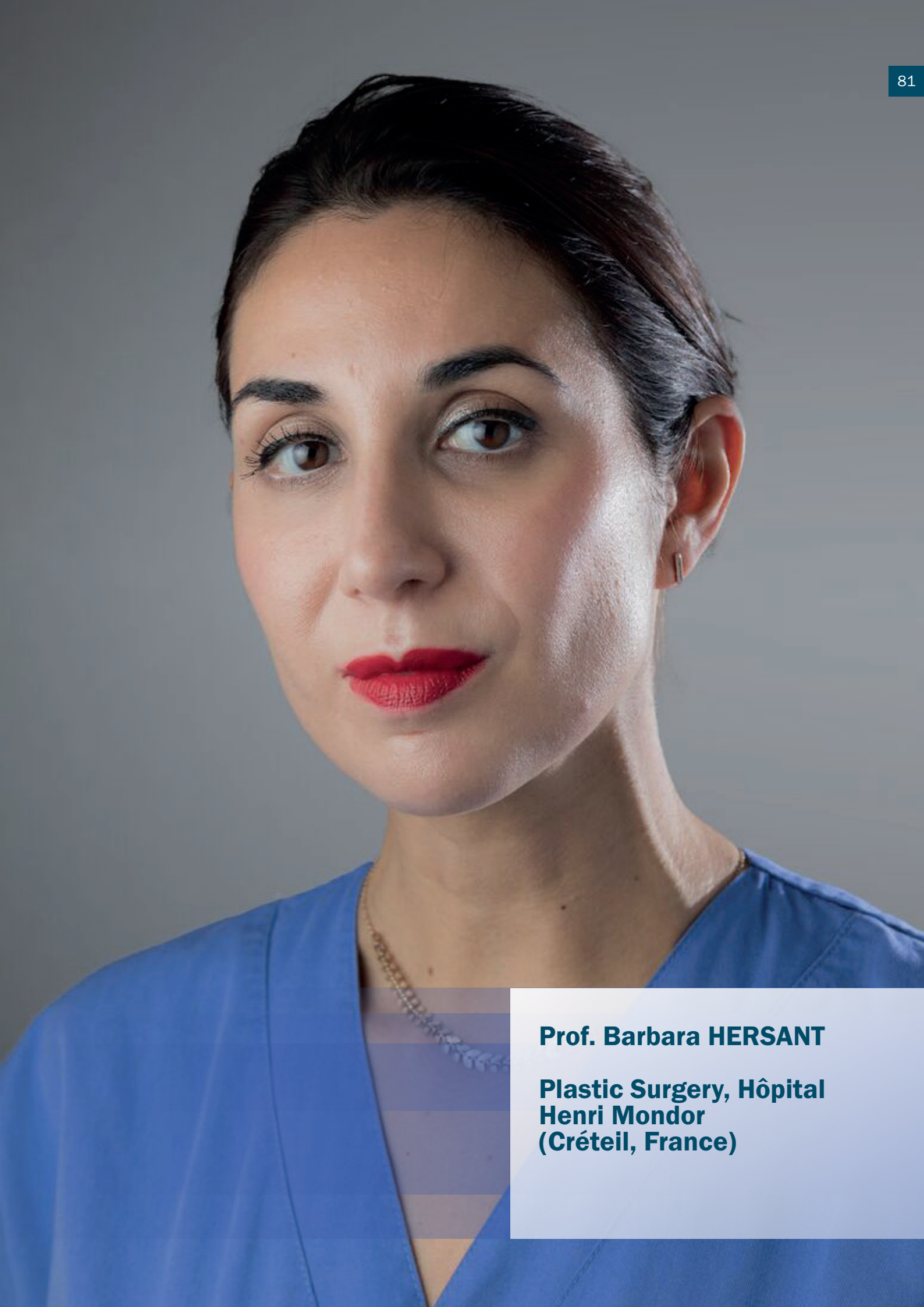
There is also an immunomodulating effect, which calms the inflammatory response, which is of interest in inflammatory diseases such as psoriasis, scleratrophic lichen, etc.

The main advantages of using platelet-rich plasma (PRP) in gynaecological regenerative surgery are:

Fibroblast stimulation:
PRP has a paracrine effect that stimulates fibroblasts, promoting the production of collagen, hyaluronic acid and elastin, which improves tissue suppleness.

Pro-angiogenic effect:
It promotes neoangiogenesis, which is essential for tissue regeneration.

Immunomodulation:
PRP helps to regulate the immune response and calm inflammation, which is particularly beneficial for conditions such as lichen scleratrophica, which are often resistant to conventional treatments such as corticosteroids.



Prof. Barbara HERSANT

Plastic Surgery, Hôpital Henri Mondor (Créteil, France)

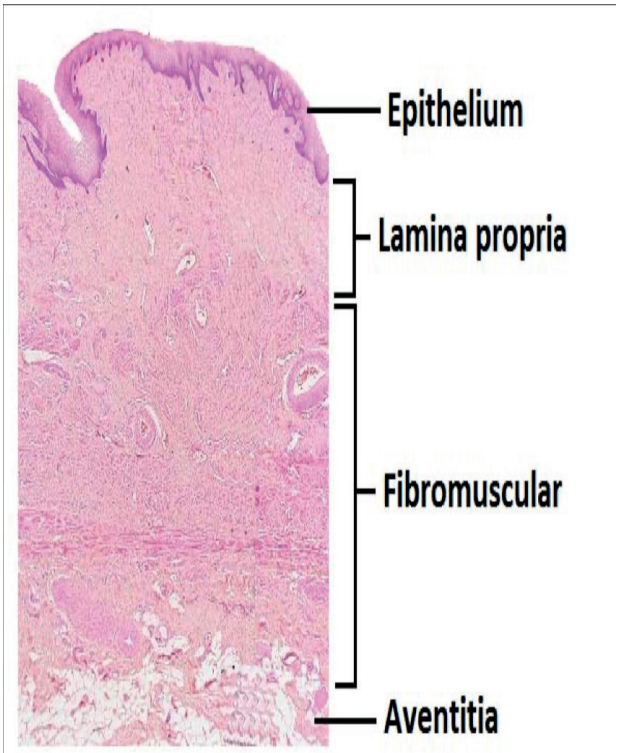
Improved quality of life:
The use of PRP has been shown to improve patients' sexual quality of life, particularly after surgery or in cases of post-operative pain in the vulvovaginal area.

Ease of use:
PRP injections can be carried out in the clinic, making it a practical option for patients.

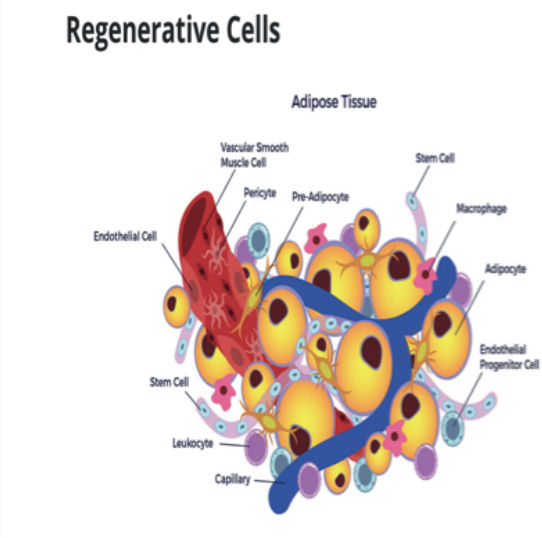
These advantages make PRP a valuable tool in regenerative medicine applied to gynaecology.

Stimulation of the fibroblats
- In the dermis
- In the Lamina propria

Endogenous collagen
Endogenous hyaluronic acid
Elastin
Neo angiogenesis
Immunomodulation



Regenerative medicine for vulva-vagina



- Adipocytes (30-60%)
- Blood cells

After centrifugation :

Stroma VascularFraction (SVF)

- Endothelial cells
- Endothelial progenitor cells
- Hematopoietic Stem cells
- Fibroblast
- Pericytes
- **Adipose-Derived stem cells:**

ADSCs (2-10% of SVF)

DOES THE COMBINATION OF FAT AND PRP IMPROVE RESULTS IN GENITAL RECONSTRUCTIVE SURGERY?

The combination of fat (which contains mesenchymal stem cells) and platelet-rich plasma (PRP) offers significant benefits in genital reconstructive surgery. Here are some key points about this synergy:

Stimulation of local cells:
Injected stem cells, particularly when combined with PRP, help to stimulate local cells in pain. This promotes tissue regeneration by improving trophicity and stimulating collagen and elastin production.

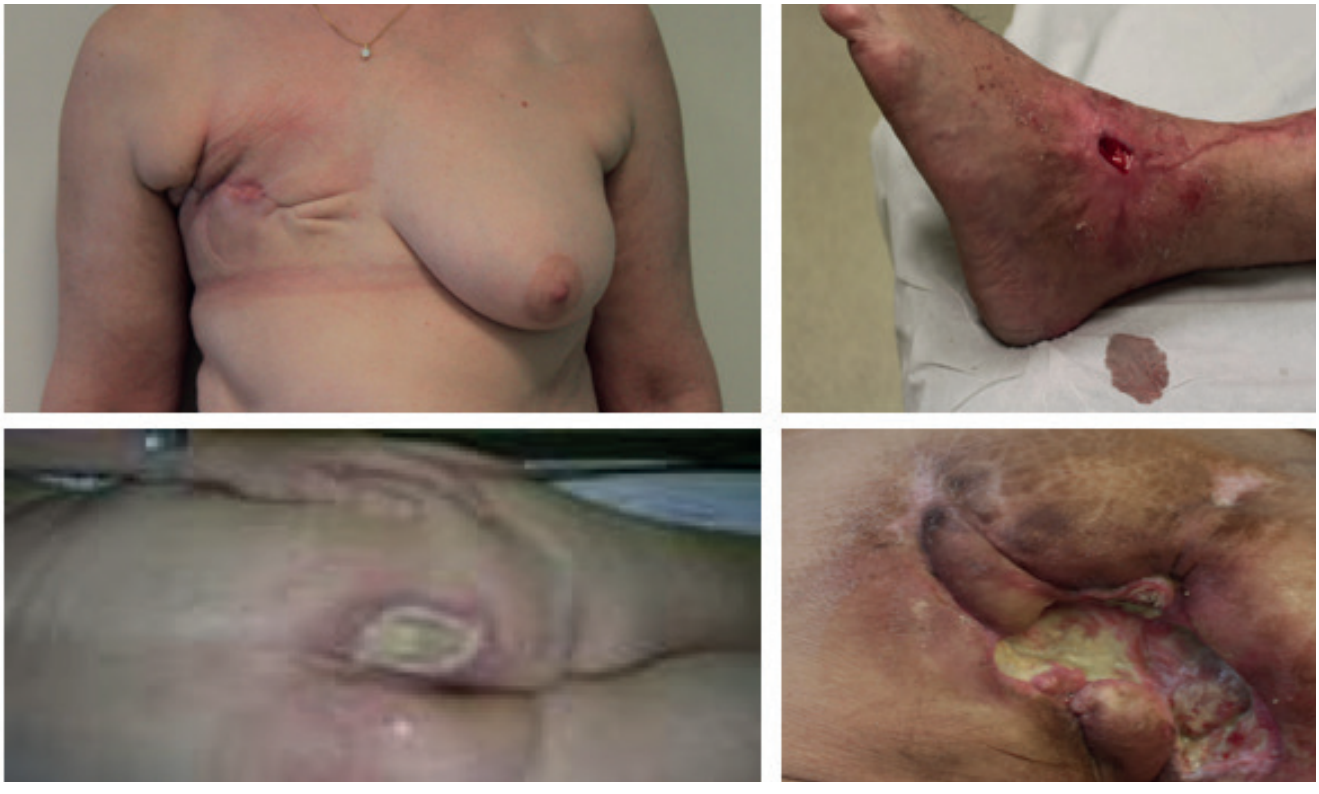
Immunomodulatory effect:
PRP has a pro-angiogenic effect and helps to modulate the immune response, which is particularly useful in the management of tissues undergoing inflammation or oxidative stress, as is often the case after surgical procedures or trauma.

Scar improvement:
This combination is proving effective in treating scarring sequelae, for example after episiotomies or genital mutilation. Regeneration treatments with fat and PRP can significantly improve the quality of life of affected patients.

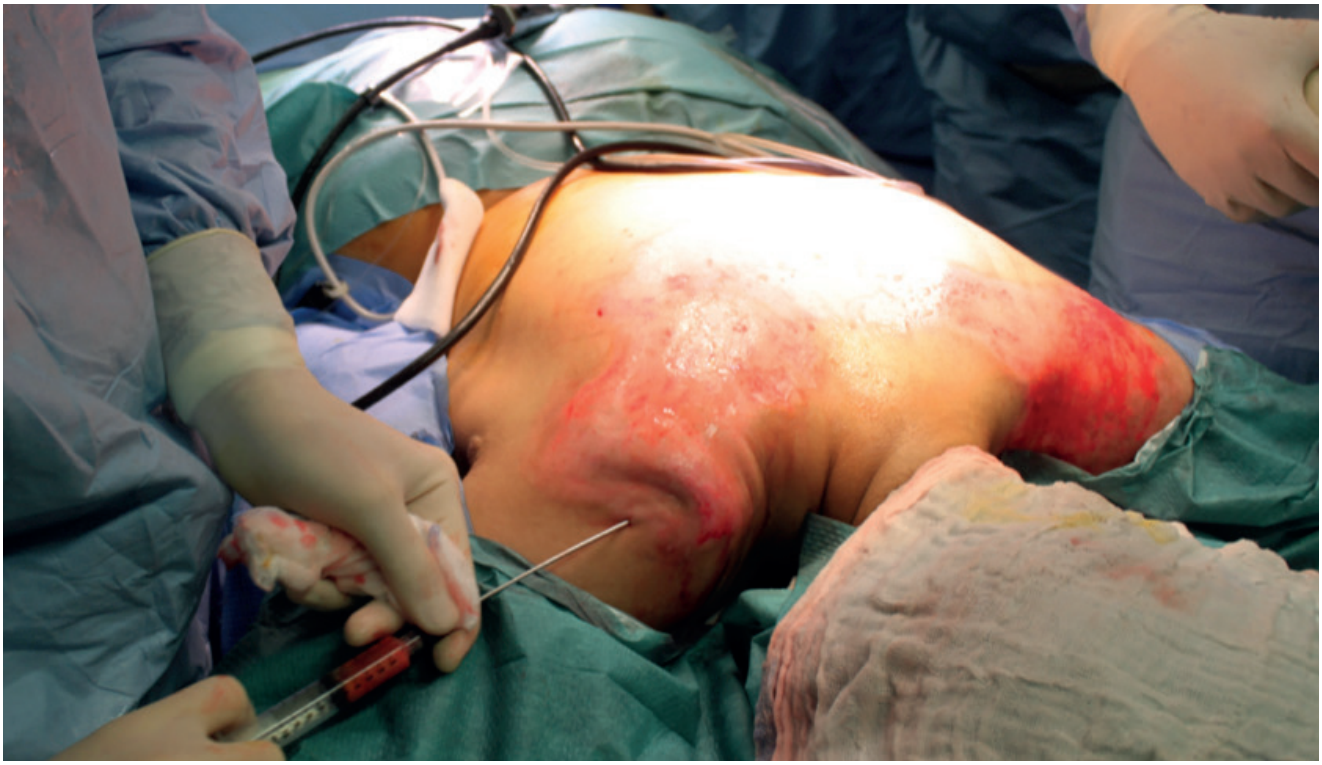
Natural results:
Aesthetic and functional results are often considered natural and are associated with an improvement in sexual quality of life. The use of these techniques makes it possible to adopt a conservative approach while offering satisfactory results.

Varied applications:
This method can be beneficial for a variety of genital pathologies, including after-effects of cancer treatment, helping to improve patients' physical and psychological well-being.

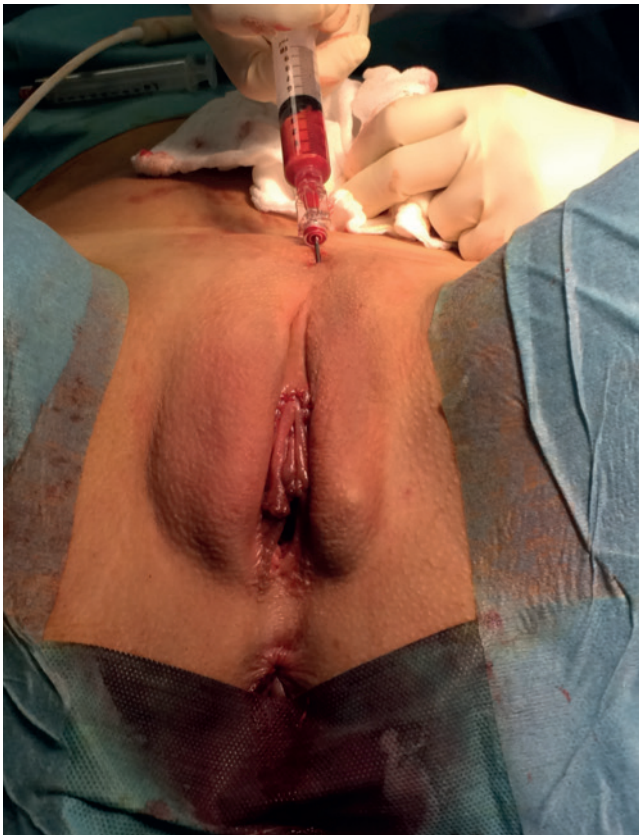
The combined use of fat and PRP in genital reconstructive surgery is therefore a promising approach, capable of improving not only clinical results but also patients' satisfaction with their bodies and their sex lives.

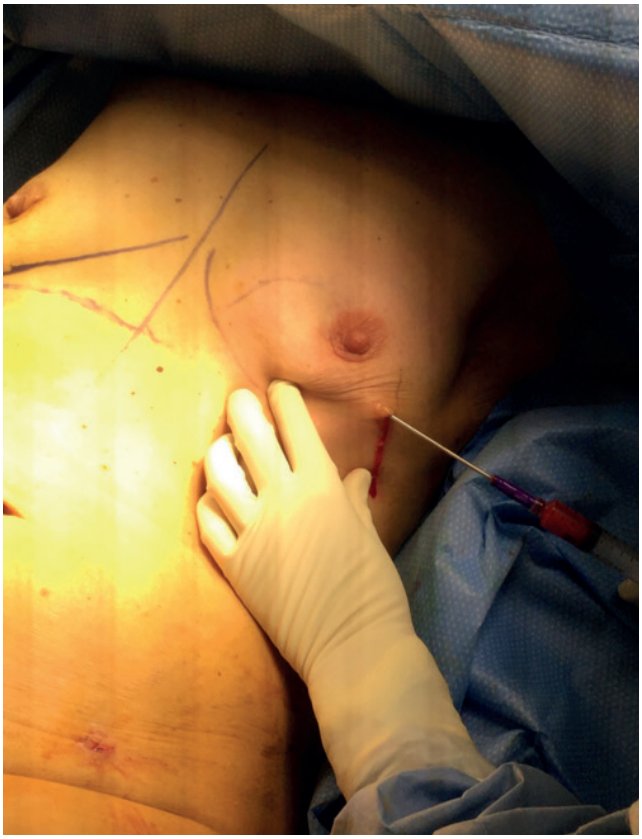


Multiple indications: The adipocyte graft for trophic purposes



Trophic adipose tissue





Adipocyte transplantation, volume restoration

Autologous fat transfer or “lipofilling” or “Fat grafting”

- A revolution in plastic surgery
- Dr Fournier in 1989
- Pr Coleman Plast Reconst Surg 2006 Sep;118(3 Suppl):108S-120S.

Different techniques of liposuction and preparations:
Tonnard P et al,Plast Reconstr Surg 2013; 132:1017-26

- Macro-lipofilling
- Micro-lipofilling
- Nano-lipofilling/ TVS

Evolution of lipofilling from 1997 to 2023

- Coleman technique to Microlipofilling/milli/Nano/ Emusifiedfat/SVT
- Decantation to Filtration
- Opened system to closed system:

Avoid infections
Avoid fat oxidation

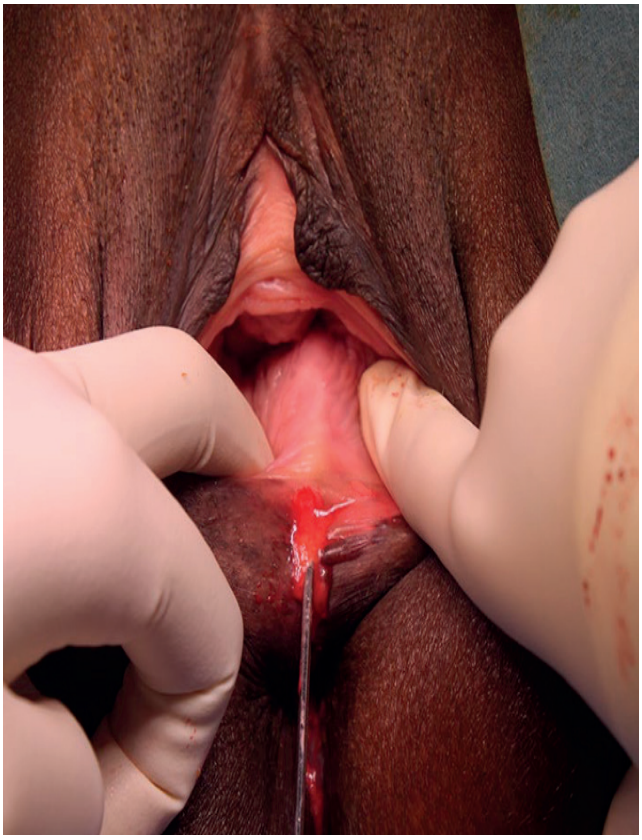
Autologous PRP and growth factors

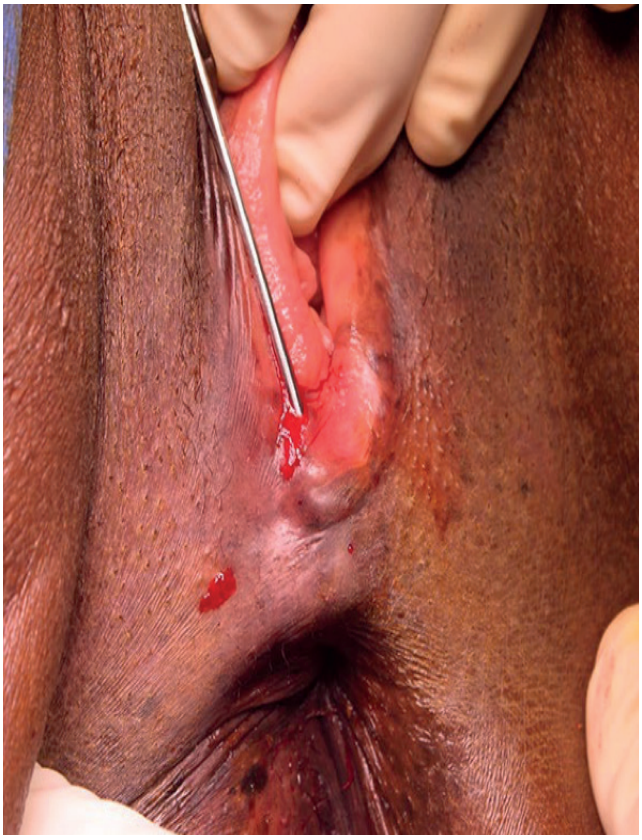
> 3000 bioactive molecules
Growth factors:
- platelet-derived growth factor (PDGF),
- transforming fibroblast growth factor (FGF),
- transforming growth factor (TGF-),
- epidermal growth factor (EGF), vascular
- endothelial growth factor (VEGF),
- insulin-like growth factor (IGF)

PRP preparation: 8ml of blood with a separating gel and a citrated anticoagulant then 5mn of centrifugation at 1500 RPM.

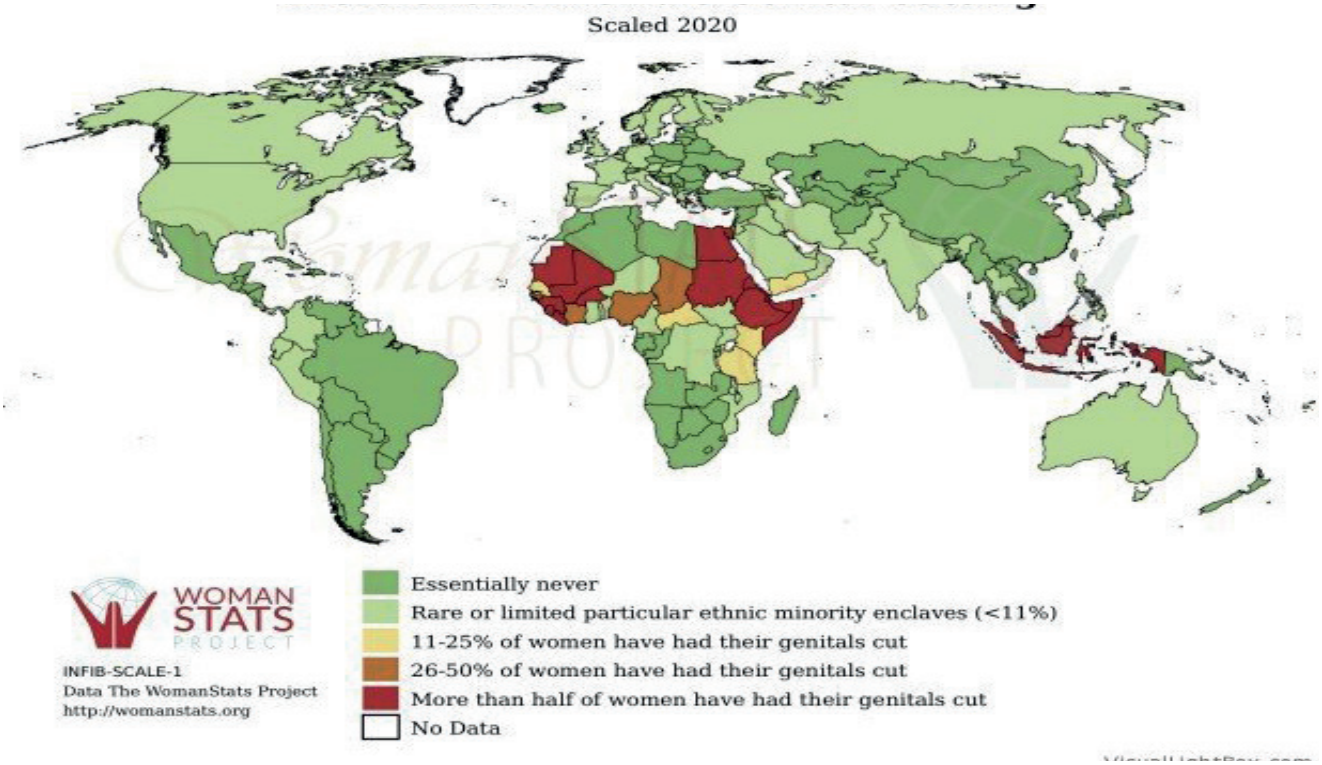
Hyaluronic Acid « HA »

HA is an important component of skin and extracellular matrix. Its functions are: Hydration, modulation of cellular microenvironnement
Tissue regeneration processes: as scaffold facilitating the entry of a large number of cells into the injured area
In practice: Cellular matrix, Regen Lab

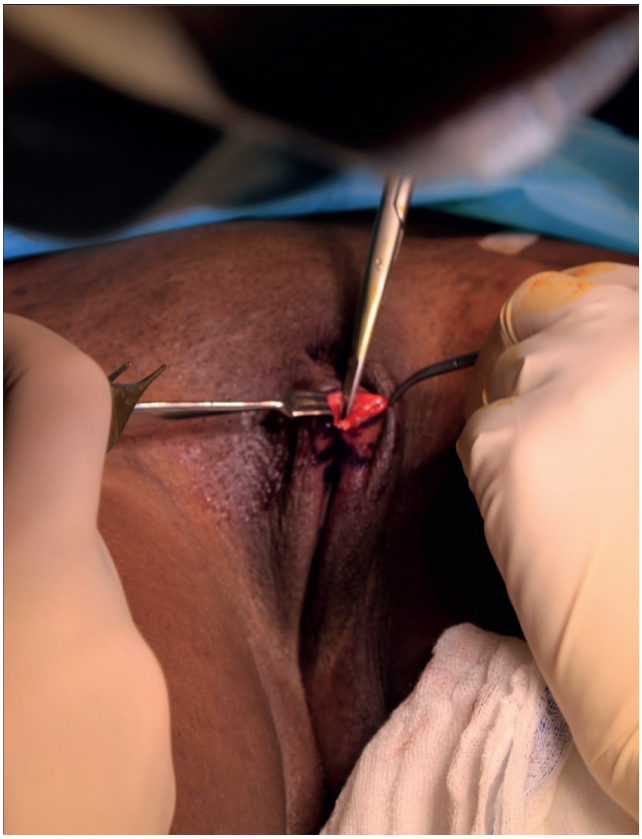




The nanofat or vascular stromal tissu for the vulvo-vaginal trophicity



130 million women have had Female Genital Mutilation (FGM)



TYPE 2

BREAST CANCER AND VAGINAL HEALTH

- 55- 75% = vulvo-vaginal atrophy (VVA) due to Estrogen deficiency
- Decreasing quality of sexual life and FSD (femal sexual distress)
- No hormonal supplementation
- Less than 50% use of treatment
- Poor information

More than 30% of patients do not complete the planned adjuvant hormone therapy. Discontinuation of hormone therapy is associated with a higher risk of breast cancer recurrence. Better knowledge and rapid and sustained management of side effects could improve compliance.

CHALLENGES AND PRECAUTIONS ASSOCIATED WITH THE USE OF LASERS IN THE TREATMENT OF VULVOVAGINAL PATHOLOGIES

In the discussion on the use of lasers in the treatment of vulvovaginal pathologies, a number of challenges and precautions were raised:

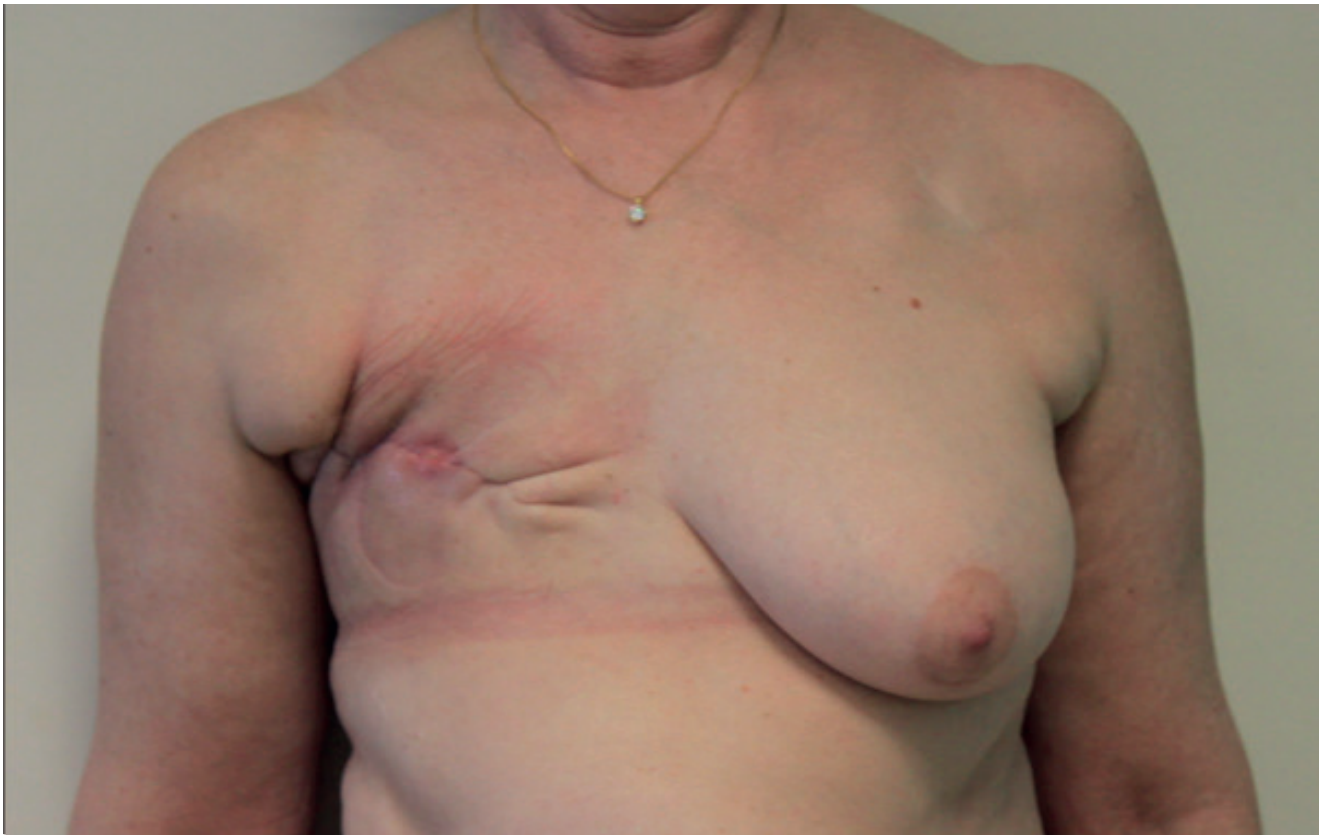
1. State of the mucosa: Thinning of the vulvovaginal mucosa can pose problems when lasers are used. It is crucial to take this thinning into account to avoid complications.

2. Potential complications: Negative examples have been reported, such as fistulas occurring in patients who have undergone laser treatment for severe prolapse. This underlines the importance of caution when using this technology.

3. Types of laser: Two main types of laser are mentioned for these treatments: the CO2 laser and the Erbium-YAG laser. Research seems to favour the CO2 laser because of its published results.

4. Importance of preparation: Before applying laser treatment, it is recommended that the mucosa be prepared using regenerative medicine approaches, which could improve the overall treatment results.

Although laser treatment can offer promising results, it is essential to carefully assess the patient's condition and be aware of the risks associated with its use.



Treatment: breast surgery

Regenerative biosurgery: new perspectives with ARSIA

Dr Ghyslaine BEILIN, former President of ESAAM (European Society for Regenerative and Anti-Aging Medicine)

I have the great honor of being part of this scientific committee. Four years as president of the ESAAM European Society of Regenerative and Anti-Aging Medicine allowed me to assess and highlight the complex field of regenerative medicine from the Atlantic to the Ural Mountains; from telomere repair and the use of stem cells to neurobiology and age-related degenerative or autoimmune diseases.

BIOSURGERY

Current REGENERATIVE BIO SURGERY has surpassed the tissue surgical act using a scalpel, expanding it to minimally invasive techniques, using various interventional surgical systems ranging from the endoscopy, to robots, to cannulas, to microneedling and techniques based on laser energy, radiofrequency, ultrasounds.

These approaches combined with contributions from artificial intelligence and the digital transformation of surgical acts are increasingly often associated with innovative biological methods known as cellular and tissue regenerative techniques that mark the advent of the new bio-surgery.

This HYBRID BIO-SURGERY allows targeting the cell to even reprogram it using stem cells, or regenerate it via tissue-inducing thread lifts, hyaluronic acid injections, PRP (platelet-rich plasma) or tissue inducers and other bio-revitalizers.

REGENERATIVE BIO-SURGERY: NEW PERSPECTIVES TO ADDRESS AESTHETIC CHALLENGES RELATED TO AGING

The skin is a major organ: we cannot live without skin! But it is also a very accessible organ. For 40 years all the techniques were first developed and applied to the skin, integuments, and external mucous membranes.

It is easy to biopsy them, check tissue biointegration, and ensure the safety of all regenerative techniques developed in dermatology and plastic and aesthetic surgery with injections of hyaluronic acid, bio-lasers, LEDs, radiofrequency, HIFU, and other physical or chemical agents.

The applications were then evident for internal mucous membranes, and all other surgical specialties that have simultaneously developed surgical bio-research in ophthalmology, rheumatology and orthopedic surgery or gynecologic surgery for intimate rejuvenation.

Dr Ghyslaine BEILIN

Former President of ESAAM (European Society for Regenerative and Anti-Aging Medicine)

Regenerative bio-surgery techniques to combat facial aging encompass innovative approaches that stimulate the natural regeneration of tissues using stem cells, growth factors, and advanced physical processes. These methods aim to achieve sustainable, natural, and personalized rejuvenation.

THE MAIN TECHNIQUES USED IN BIOSURGERY

• **PRP (Platelet Rich Plasma):** extracted and concentrated from the patient's own blood, PRP is reinjected to stimulate collagen production, improve skin texture, reduce wrinkles and pigmentation spots, and accelerate natural healing.

• **Microneedling:** performing micro-perforations in the skin to activate the production of new collagen (neo-collagenesis), often combined with the application of active ingredients (vitamins,peptides, fluid hyaluronic acid) to boost regeneration and skin uniformity.

• **Stem cell injections:** using cells from the patient or specific cultures, capable of transforming into skin cells and thus repairing, densifying, and restructuring tissues affected by dermatoporosis.

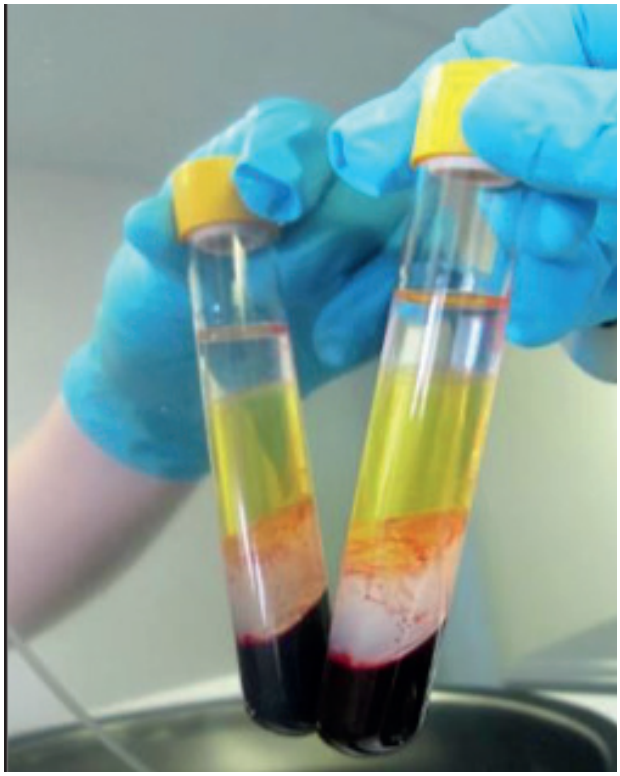
• **Biostimulation (radiofrequency, ultrasound, HIFU, tightening threads) without incisions)**: these physical techniques stimulate collagen and skin elasticity without surgery, acting deeply to lift, firm, and redefine the contours of the face while maintaining a natural effect.

• **Lipofilling / Nanofat:** grafts of autologous fat enriched with regenerative cells from the patient PRP to restore volume, smooth features, and improve skin quality, with a visible effect lasting several years.

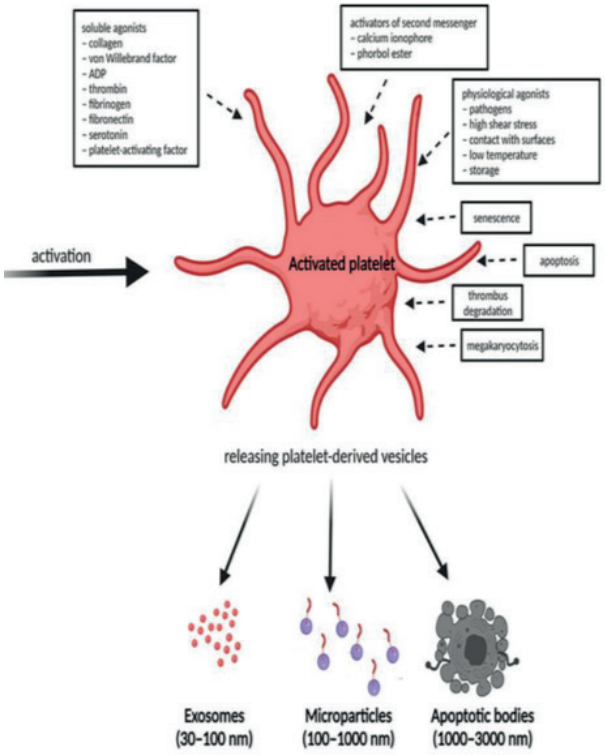
• **Biorevitalization through microinjections of hyaluronic acid**: use of non-crosslinked hyaluronic acid microinjections to hydrate, plump, and improve dermal structure.

THE ADVANTAGES OF BIO-SURGERY

• Minimally invasive approaches, without heavy surgery, with low social eviction.



PRP (Platelet Rich Plasma)



Activated platelets are a source of Growth Factors, along with hundreds of other molecules secreted by alpha granules and vesicles (exosomes) that together constitute the "Secretome."

• Prevention and correction of aging with natural, gradual effects without artificial transformation of features.
• Use of autologous techniques (from the patient), with no risk of allergy or rejection.

In summary, regenerative facial bio-surgery is based on personalized strategies, combining cellular stimulation, biotechnologies and physical processes, to sustainably rejuvenate the face while respecting the nature and expressiveness of each patient.

Research and clinical practice are directed towards innovations targeting the natural stimulation of skin repair and regeneration processes: notably through biostimulators, injections of peptides and exosomes, regenerative mesotherapy, as well as techniques combining precision and customization of treatments.

Regenerative bio-surgery techniques to combat facial aging group approaches personalization and naturalness: patients and practitioners now favor subtle and natural results, with minimally invasive interventions focused on regeneration rather than simple correction or camouflage of aging signs.

MAJOR ADVANCES IN BIOSURGERY TREATMENTS

They are based on exosomes, PRP(platelet-rich plasma), and targeted injections of next-generation peptides or hyaluronic acidpromote collagen production, improve skin texture and firmness, and align with a sustainable rejuvenation approach without artificial transformation.

EMERGING PROCEDURES: lipofilling, focused ultrasounds, radiofrequency, biomimetic peptides, and tissue inductors are also highlighted among regenerative bio-surgery techniques, allowing for effective action against facial aging while minimizing recovery time and optimizing patient comfort.

CONCLUSION

Regenerative bio-surgery incorporates a vision of time into the surgical technical act: moving from repair to regeneration and even prevention, which is what the Millennial generation calls prejuvenation.

The ARSIA draws its roots from our history of medicine and surgery. Our past and our culture allow us to forge the future of bio-surgery. Generation X has already exhausted its life expectancy from birth. We have gained a generation of life: 20 years.

Aging well is a societal challenge. The heart of life is at the heart of the cell. By repairing a cell in its environment within its homeostasis, it is a tissue that is regenerated, an organ whose function is restored.

Regenerative bio-surgery, which integrates various techniques of biostimulation and tissue and cell repair, is minimally invasive. It allows us to push the limits of surgery on a body free from age-related pathologies, it erases the marks of time, it is the era of rejuvenation.

Thanks to Professor Albert-Claude Benhamou and his brilliant scientific committee for bringing us together and wanting to push our limits to create a NEW GENERATION - REGENERATION with ARSIA.

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MD_POSTER_PRP_ATS_W_ENG_V2021

ARSIA PROJECT

A Multicenter randomized study on the use of PRP for the prevention of mediastinitis in coronary surgery

Dr Gabriel SAIYDOUN
Vice-President of ARSIA, Cardiac Surgery,
French National Academy of Surgery

Dr Gabriel SAIYDOUN

The ARSIA Project is a prospective multicentre randomised study designed to assess the efficacy of platelet-rich plasma (PRP) in preventing post-operative mediastinitis.

The study will begin in the Île-de-France region before being extended nationwide.

As a cardiac surgeon at the Pitié-Salpêtrière Hospital and President of the Conseil National des Jeunes Chirurgiens (National Council of Young Surgeons) - a federation representing the 13 surgical specialities, whose headquarters are at the Académie Nationale de Chirurgie - I also have the honour of being Vice-President of ARSIA.

I'm really proud to be part of this human adventure, which is focused above all on our patients. Our ambition is clear: to offer practical, innovative solutions to certain diseases that are still all too common.

Background: a serious complication of cardiac surgery

Coronary artery bypass surgery is one of the procedures most at risk of mediastinitis. Mediastinitis - an infection of the mediastinum following cardiac surgery - is a formidable complication. Its incidence is estimated at around 1.5%, with an increased risk in patients with co-morbidities such as diabetes or obesity.

This infection is associated with a particularly high morbidity and mortality rate, which can be as high as 23% post-operatively. The pathogens most frequently implicated are staphylococci, in particular Staphylococcus aureus and Staphylococcus epidermidis.

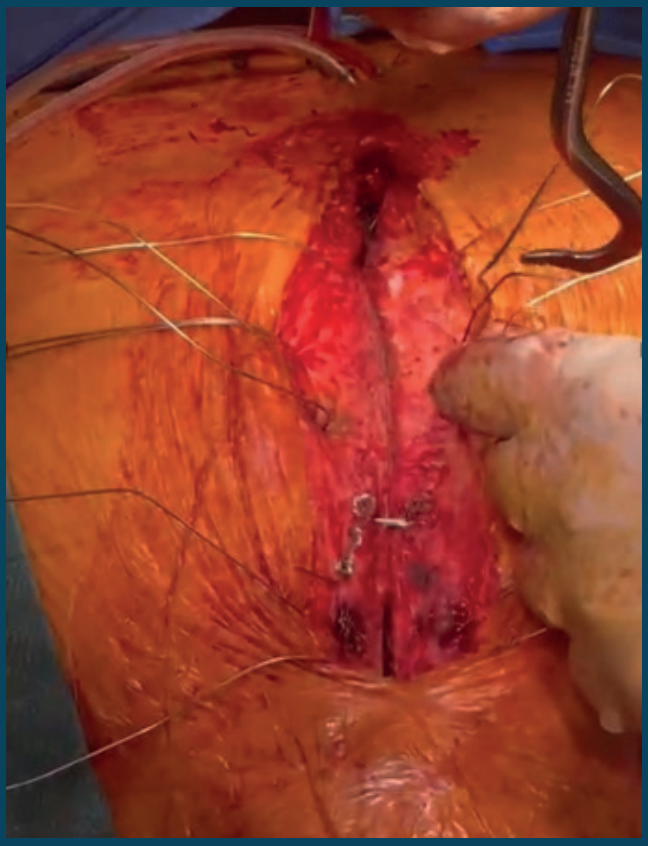
We are aiming for publication in a major international journal through this first national randomised study dedicated to the prevention of mediastinitis following coronary surgery.

This is an essential step towards scientifically validating the potential role of PRP in reducing this severe complication.

RISK FACTORS IDENTIFIED FOR POSTOPERATIVE MEDIASTINITIS IN CARDIAC SURGERY

The risk factors identified for postoperative mediastinitis in cardiac surgery include:

1. Clinical circumstances of patients:
- Obesity
- Diabetes, especially in cases of poor glycaemic control
- COPD (chronic obstructive pulmonary disease)
- Renal insufficiency



Sternal Closure
Essential to prevent dehiscence and secondary infections
Standard technique: traditional steel wire cerclage
Alternatives: rigid wires, improved materials under investigation

- Smoking
- malnutrition.

2.Linked to surgery:
- Prolonged duration of surgery (at least 2 to 3 hours)
- Immediate post-operative reinterventions due to complications such as haemorrhage. In particular, coronary artery bypass grafts, especially those with double breast harvesting, present an increased risk of mediastinitis.

THE MAIN OBJECTIVE OF THE MULTICENTRE RANDOMISED TRIAL

The main objective of the multicentre randomised trial is to evaluate the efficacy of perioperative PRP (platelet-rich plasma) in preventing mediastinitis in patients undergoing coronary artery bypass surgery.

The aim of this study is to compare a group of patients receiving sternal closure with the application of PRP with a control group using standard closure without PRP.

MATERIALS AND METHODS

Study Design and Population

- Prospective study
- Randomized & Controlled
- Multicenter (AP-HP) / University Hospital of Pitié-Salpêtrière
- October 2025 – January 2026
- Coronary artery bypass grafting – Adults – History of cardiac surgery: exclusion criteria

Patient Groups

Control Group:
- 100 patients
– Standard closure with conventional steel wires
– no application of PRP.

PRP Group:
- 100 patients
– sternal closure with the same conventional steel wires

HOW IS PRP PREPARED AND APPLIED IN THIS STUDY TO PREVENT MEDIASTINITIS?

In this study to prevent mediastinitis, PRP (Platelet Rich Plasma) is prepared and applied as follows:

Preparation:

Blood is drawn into tubes (red and blue).
The blood is centrifuged for 5 minutes at 1500G to separate the components.

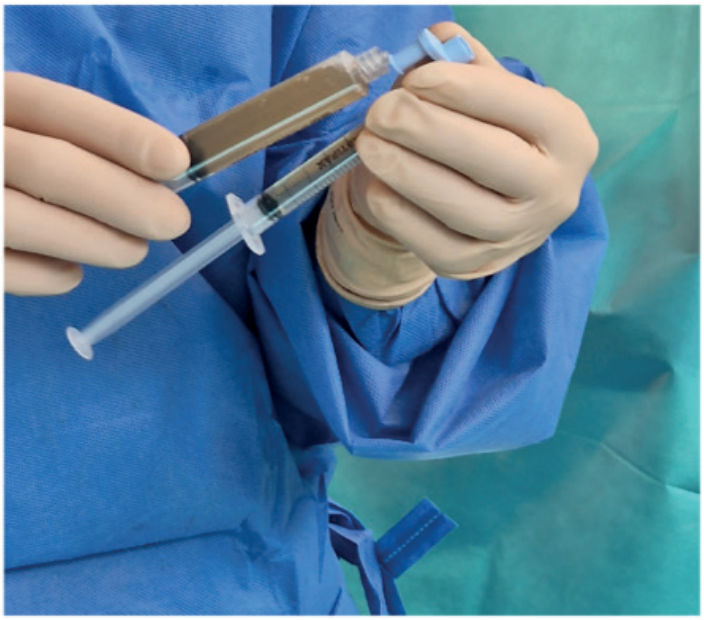
After centrifugation, the platelets are resuspended in the acellular plasma, giving the PRP a turbid colour.

Application:

Three types of PRP are used:
- Regen PRP, RegenBCT tube: injected into the edges of

The PRP Glue Procedure

PRP collection



Assembly of the Spray Applicator: PRP syringe and autologous thrombin serum syringe

the scar.
- PRP gel: applied directly to the sternal wound.
- PRP glue: prepared by the ACR-C Plus (RegenBCT and

RegenATS + Spray applicator) injected into and onto the wound after suturing.

In the study, after coronary artery bypass surgery, the surgeon injects the PRP prior to subcutaneous and intradermal closure.

The aim of this approach is to reduce the incidence of post-operative sternal infections and mediastinitis, particularly in patients identified as being at risk.

THE ECONOMIC IMPLICATIONS OF PREVENTING POST-OPERATIVE INFECTIONS WITH PRP FOR HOSPITALS AND PUBLIC HEALTH SYSTEMS

The economic implications of preventing post-operative infections with Platelet-Rich Plasma (PRP) for hospitals and public health systems are significant. Key points include:

1. Reduction in Infection Rates:
The application of PRP, especially in high-risk patients (e.g., those with diabetes), has been associated with reduced rates of surgical site infections (SSIs). This is crucial given that SSIs can lead to extended hospital stays and higher medical costs.

2. Cost Savings from Reduced Length of Stay:
By preventing infections, hospitals can reduce the length of stay for patients. For instance, managing infections in intensive care units can incur costs as high as $10,000 per day.
Therefore, preventing these infections can translate into substantial savings.

3. Improvement in Patient Quality of Life:
Reduced infections can also lead to improved patient outcomes and quality of life. Avoiding complications associated with infections can enhance recovery and reduce follow-up care costs.

4. Economic Studies and Cost-Benefit Analysis:
Economic evaluations, such as the mentioned medical economic studies, suggest that using PRP can cut postoperative care costs significantly, potentially by a factor of ten in certain cases. These findings could encourage more hospitals to adopt PRP treatment protocols.

5. Broader Public Health Impacts:
Widespread adoption of PRP could reduce the burden on public health systems by alleviating the incidence of SSIs, leading to lower healthcare costs overall and better allocation of resources.

Through these avenues, preventing post-operative infections with PRP holds considerable potential not only for individual hospitals but also for the healthcare system as a whole, suggesting a compelling case for its integration into standard surgical practices.

**Assembled Spray Applicator:
PRP glue ready for injection**

With ARSIA, let's launch the festival of regenerative biosurgery

Dr Jean-Claude COUFFINHAL
Vice-President of ARSIA,
Thoracic and Cardiovascular Surgery,
Pdt of the Innovation Committee of the French National Academy of Surgery

Jean-Claude Couffinhal is a thoracic surgeon and a leading member of the French National Academy of Surgery. He chairs the Academy's innovation commission and is responsible for setting up the digital surgery think tank, Chirurgie 4.0. Surgery 4.0 and biosurgery are two major areas on which the Académie nationale de chirurgie will be focusing over the coming years.

THE FUNDAMENTALS OF MODERN SURGERY

ARSIA represents an incredible challenge. We can already see the extent to which the use of PRP has developed in many surgical specialties, and that all our practices and disciplines are concerned by the potential of biosurgery.
We are at the dawn of the use of bioengineering, a veritable terra incognita of incredible richness, the action of the living on the living, self-repair and self-healing.

Modern surgery is :

- **The human being**
- **Robots**
- **Artificial intelligence**
- **Biology**

These elements reflect a paradigm shift in the surgical field, integrating technological and biological advances to improve practices and results.
With ARSIA, we are truly working towards a trans-specialty approach that brings these elements together.

“Regenerative surgery is not a discipline in itself; it encompasses a range of heterogeneous, multidisciplinary practices.”

Dr Jean-Claude COUFFINHAL

WHY IS THE CODIFICATION OF SURGICAL PROCEDURES ESSENTIAL FOR THE FUTURE OF SURGERY?

Precise coding of surgical procedures, particularly in biosurgery, is essential for several crucial reasons:

1. Medical sovereignty:
Codification enables the development of autonomy in the evaluation of surgical procedures, which is fundamental for personalised medicine and innovation. As discussed in the results, the Haut Conseil de la nomenclature and the CNAM are in favour of introducing specific codes for each medical device and associated procedure, to ensure traceability and systematic evaluation.

As discussed in the results, the High Council for Nomenclature and the French National Health Insurance Fund (CNAM) support the implementation of specific codes for each medical device and associated procedure, in order to ensure traceability and systematic evaluation.

2. Evaluation of practices:

Clear coding facilitates the evaluation of surgical practices and provides access to accurate data, which is essential for improving surgical techniques and assessing their effectiveness over time. This is particularly important in the age of artificial intelligence, which relies on reliable data to optimise surgical outcomes.

This is particularly important in the era of artificial intelligence, which relies on algorithms that must process reliable and structured data to optimize the benefits of AI and support advancements in surgical procedures.

3. Identifying innovations:
Coding provides better visibility into ongoing innovations and helps identify emerging practices in the fields of surgical and interventional procedures. This enables healthcare professionals to stay up to date and adapt to the rapid evolution of technologies.

4. Education and Training:
It serves as a basis for the training and education of future practitioners, ensuring that they have up-to-date knowledge of coded procedures and innovations in biosurgery.

5. International harmonisation:
In the context of the globalisation of healthcare, standardised codification helps to harmonise practices at international level, facilitating collaboration and exchanges between countries, which is crucial when it comes to solving global health problems.

Precise coding not only strengthens the future of surgery by improving the quality of care, but it is also essential to ensure the safety and effectiveness of surgical and interventional practices.

HOW WILL ARTIFICIAL INTELLIGENCE AND BIOLOGY TRANSFORM PERSONALISED SURGERY ACCORDING TO THE VICE-PRESIDENT OF THE ACADEMY OF SURGERY?

The introduction of artificial intelligence (AI) and biology into personalised surgery is seen as a significant paradigm shift.

Here are the key points:

1. Paradigm Shift:
A fundamental transformation in surgery, particularly through digital surgery, which includes AI and robotics.

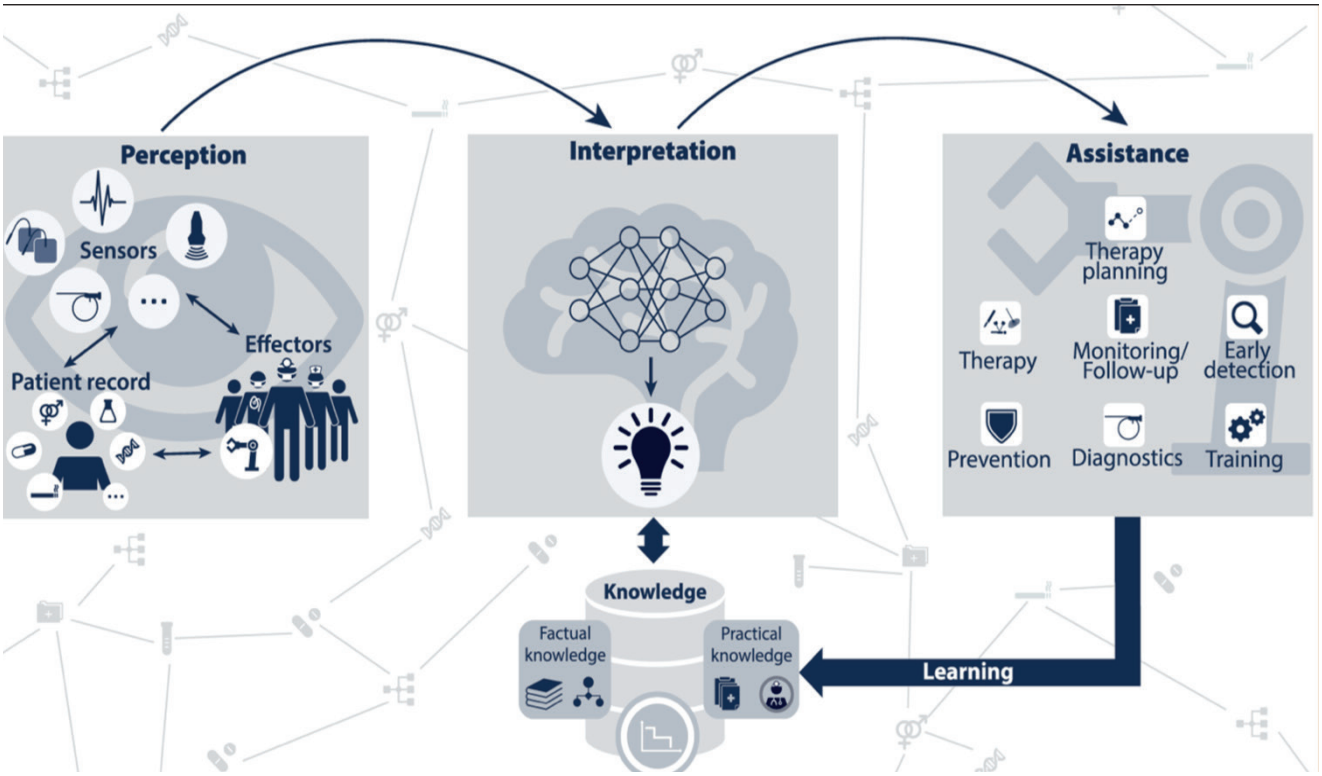
2. Importance of Biology:
Beyond AI, the growing significance of biological research—which also benefits from AI—is becoming central to personalized medicine. Autologous regenerative biology holds immense potential to transform medical treatments.

3. Integration of Technologies:
Emphasizes the need to integrate both digital and orthobiological technologies throughout the surgical pathway, including during the procedure itself. This allows for real-time recommendations and decision-making, making surgical and interventional processes far more dynamic.

4. Training and Nomenclature:
Highlights the need for improved coding of surgical procedures and the implementation of registries to integrate these innovations and ensure their proper development and evaluation.

This calls for a concerted effort in training and informing stakeholders about regulatory data—a role to be led by ARSIA—by disseminating innovative clinical insights and regulatory information.

This will enhance the understanding of coding and the characterization of both standard interventional procedures and devices, as well as those specific to regenerative bio-surgery.



The medical knowledge required for 5P medicine demands connection and networked collaboration among all operators.

Operators 4.0 are back at the center of the game:
– Evaluators of practices and innovations
– Producers of medical knowledge
Clinical research for all :
Currently, only 15% of operators are involved in clinical research!

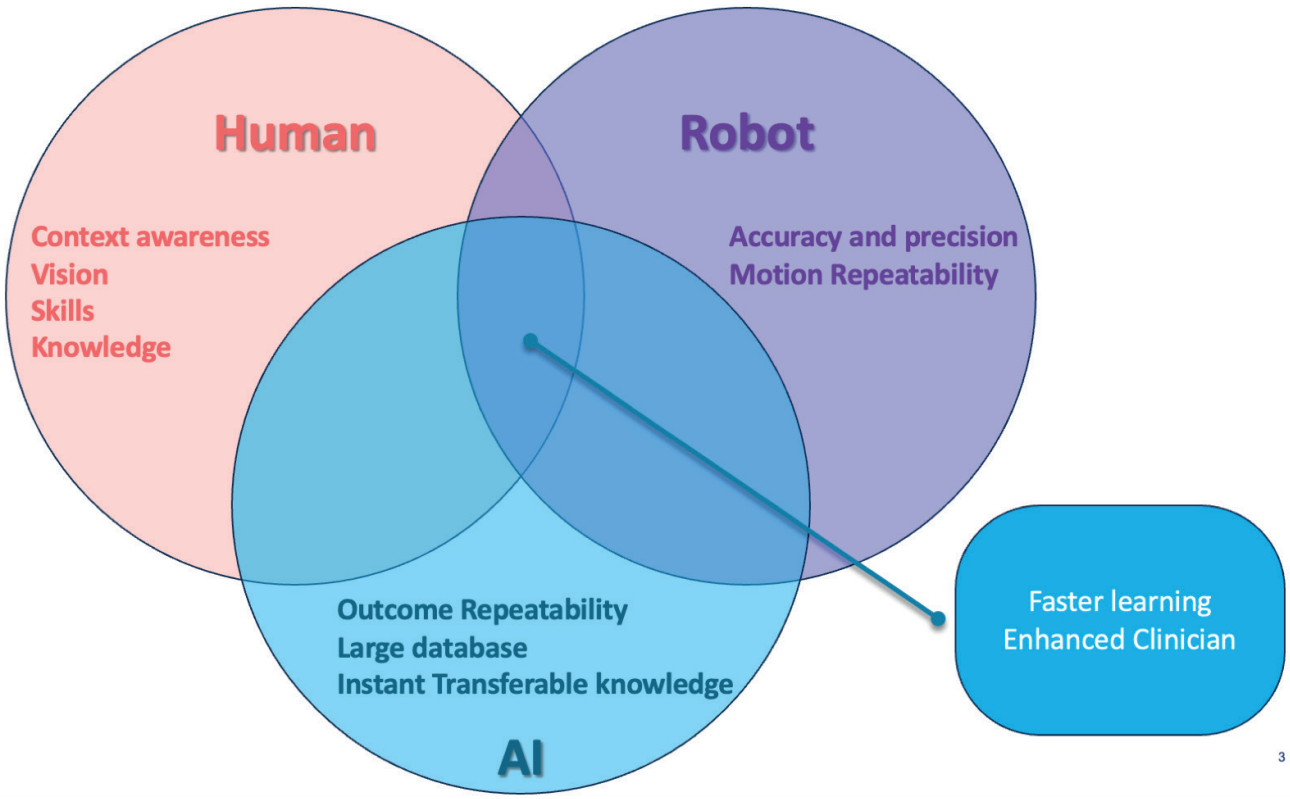
Regenerative surgery is not a discipline in itself; it brings together heterogeneous, multidisciplinary practices. Its structuring requires:

Legitimacy
- A community of practice
- Collective identity
- Institutional recognition

Practices and Innovations
- Traced
- Evaluated
- Shared

University & Education
- Undergraduate – Continuing – Postgraduate

Visibility
- Inventory
- A common language
- A standardized* framework
- A legalized framework



Surgical regenerative biotechnologies represent the greatest potential for innovation and transformation of clinical practices.

Pdt Antoine Turzi, Dr Karol Chakkour, Dr Charles Volpei, P
Pr Albert Claude Benhamou, Dr Ghyslaine Beilin, Dr Jean-
Olivier Jardé, Dr Gabriel Saiydoun, Dr Philippe Adam, Dr J
Fabrice Blum, Pr Isabelle Auquit Auckburn, Dr Dorina Dor

r Franck Duteille, Pr Barbara Hersant, Dr Diala Haykal,
-Claude Couffinhal, Pr David Boccara, Dr Ronald Virag, Pr
ean-Pierre Rozenbaum, Mr Aziz Rehouma, Dr Georges-
nici, Dr Abderrhamane Ameur

LAUNCH EVENT
ARSIA ACADEMY

May 23, 2025 – 2:30 PM to 6:30 PM (CET)

ARSIA PRESENTATION

The **Actual Regenerative Surgery International Academy (ARSIA)** is a new international academic structure dedicated to the formalization, research, and dissemination of innovative practices in regenerative surgery.

Launched through a joint initiative of the **Biobridge Foundation** and the **French National Academy of Surgery**, ARSIA's objective is to validate and share research and clinical developments in Regenerative Surgery 4.0 across all surgical disciplines.

Cellular and tissue regeneration represents the new frontier of future surgery—one that ARSIA aims to make accessible to surgical and interventional practitioners worldwide.

ARSIA's missions include:

- Structuring a high-level, transdisciplinary academic framework for regenerative surgery
- Promoting international scientific collaboration
- Sharing data and best practices
- Defining validated protocols
- Familiarizing young surgeons with these new paradigms

On May 23, 2025, the official launch of ARSIA will take place at the headquarters of the French National Academy of Surgery in Paris.

arsia · Académie Nationale de Chirurgie et des pratiques opératoires innovantes · BIOBRIDGE FOUNDATION

ARSIA supports and drives the development of regenerative surgery by promoting scientific excellence, clinical rigor, and compliance with international standards.

OPENING REMARKS

PROF. ALBERT-CLAUDE BENHAMOU, PAST PRESIDENT OF THE ACADÉMIE NATIONALE DE CHIRURGIE

A surgeon and academic, Prof. Benhamou is one of France's pioneers in integrating regenerative medicine into surgical practice. Founder and President of ARSIA, he advocates for a rigorous scientific structure for this emerging discipline.

"WHY AN INTERNATIONAL THINK TANK ON REGENERATIVE SURGERY?"

PROF. FRANCK DUTEILLE, PLASTIC AND RECONSTRUCTIVE SURGERY, EXECUTIVE PRESIDENT OF ARSIA

Head of the hospital-university department at CHU Nantes, Prof. Duteille is recognized for his expertise in tissue regeneration and transplantation.

"THE ORGANIZATION OF THE ARSIA EXECUTIVE BOARD"

PROF. CAROLE METHELIN, PRESIDENT OF THE ACADÉMIE NATIONALE DE CHIRURGIE

Specialist in gynecologic and breast surgery, Prof. Mathelin is a professor at the University of Strasbourg and active in several international medical societies. She promotes an integrated approach to regenerative surgery in the treatment of breast pathologies.

PROF. HUBERT JOHANET, VICE-PRESIDENT OF THE ACADÉMIE NATIONALE DE CHIRURGIE

A visceral surgeon and expert in clinical immunology, Prof. Johanet has held various roles within the Academy. He actively supports scientific oversight and clinical rigor in the development of regenerative surgical practices.

"SUPPORT FROM THE ACADÉMIE NATIONALE DE CHIRURGIE"

ANTOINE TURZI, PRESIDENT OF THE BIOBRIDGE FOUNDATION

A biomedical entrepreneur, Antoine Turzi is the founder of the Biobridge Foundation and co-founder of ARSIA. He is committed to fostering innovation, clinical research, and societal engagement within a structured international ecosystem for regenerative medicine.

"FROM INNOVATION TO R&D"

ROUND TABLE 1

The Role of Regenerative Surgery

in Plastic, Reconstructive, and Aesthetic Surgery

Panelists

- **Dr Ghyslaine Beilin**, Aesthetic Medicine, Vice President of SNME
- **Dr Dorina Donici**, Plastic and Aesthetic Surgery
- **Prof. Franck Duteille**, Plastic and Reconstructive Surgery, Executive President ARSIA
- **Dr Diala Haykal**, Aesthetic Medicine, Harvard Medical School
- **Prof. Jean-Paul Meningaud**, Plastic and Reconstructive Surgery, SoFCPRE, ANC
- **Dr Luc Téot**, President of the SFFPC
- **Dr Charles Volpei**, Plastic and Reconstructive Surgery, SoFCPE

Guest Speakers

PROF. DAVID BOCCARA, PLASTIC AND RECONSTRUCTIVE SURGERY, FRANCOPHONE SOCIETY OF BURNOLOGY

An expert in managing severe burns, Prof. Boccara actively applies regenerative approaches to optimize healing and complex reconstructions.

DR ANTHONY ROSSI, DERMATOLOGY, MEMORIAL SLOAN KETTERING CANCER CENTER, NEW YORK (USA)

Dr. Rossi is a dermatologist and researcher focused on dermatologic side effects of cancer treatments. He studies the use of PRP and PRP-HA for treating post-chemotherapy alopecia in breast cancer patients.

ROUND TABLE 2

The Role of Regenerative Surgery

in Orthopedic Surgery and Rheumatology

Panelists

- **Prof. Isabelle Auquit-Auckbur,** Hand Surgery, Vice-President of SFCM
- **Prof. Olivier Jardé,** Orthopedic Surgery, Past-President of SOFCOT
- **Prof. Patrice Mertl,** Orthopedic Surgery, President of SOFCOT

Guest Speakers

DR PHILIPPE ADAM, RADIOLOGIST, MÉDIPÔLE CLINIC, TOULOUSE

Specializing in interventional imaging with a focus on tracking and evaluating regenerative treatments, especially PRP and autologous cell-based protocols for musculoskeletal disorders.

DR LAURA DE GIROLAMO, ORTHOPEDIC BIOTECHNOLOGY, SAN DONATO GROUP (ITALY)

Head of the orthopedic biotechnology lab at the Galeazzi Institute in Milan, Dr. De Girolamo works on mesenchymal stem cells and tissue regeneration. She contributed to the ESSKA position paper on PRP for knee osteoarthritis.

ROUND TABLE 3

The Role of Regenerative Surgery

in Other Surgical Disciplines

Panelists

- **Dr Kahina Betroune,** Interventional Phlebology, SFP, ANC
- **Prof. Philippe Descamps,** Gynecological Surgery, CNGOF, ANC
- **Prof. Carole Mathelin,** Gynecologic and Breast Surgery, President of ANC
- **Dr Guillaume Pourcher,** Bariatric Surgery, ANC
- **Dr Jean-Pierre Rozenbaum,** Ophthalmologic Surgery, ANC
- **Dr Frédéric Vin,** Interventional Phlebology, SFP, ANC
- **Dr Ronald Virag,** Cardiovascular Surgery, Andrology, ANC
- **Prof. Antoine Watrelot,** Gynecological Surgery, CNGOF, ANC
- **Dr Sami Zerrouk,** Interventional Phlebology, SFP, ANC

Guest Speakers

PR FILIBERTO SERRAINO, CARDIAC SURGERY, MAGNA GRÆCIA UNIVERSITY OF CATANZARO (ITALY)

Prof. Serraino led a landmark clinical study on over 2,000 patients demonstrating the efficacy of PRP in preventing post-operative sternal and venous infections.

PROF BARBARA HERSANT, PLASTIC RECONSTRUCTIVE SURGERY, SOFCPRE, ANC

A plastic surgeon and professor at the University of Paris-Est Créteil, Prof. Hersant is a pioneer in clinical regenerative therapies, especially using stem cells.

ROUND TABLE 4

ARSIA PROJECT

Multidisciplinary Observational Data Platform

The ARSIA Project is a structured initiative led by ARSIA to implement a multidisciplinary longitudinal observational study on regenerative surgery.

The project includes the creation of a secure digital registry, the organization of clinical and technical training, and the integration of hospital teams (surgeons, nurses, researchers) within a standardized protocol. With an initial target of 100 documented cases, the project is supported by a young surgeons task force and centralized documentation, aiming for academic recognition through publications and integration into university diplomas.

DR GABRIEL SAIYDOUN, VICE-PRESIDENT OF ARSIA

Dr. Saiydoun plays a key role in integrating scientific data from regenerative practices into clinical protocols and in developing a dedicated observational data platform.

DR JEAN-CLAUDE COUFFINHAL, VICE-PRESIDENT OF ARSIA

Dr. Couffinhal is actively involved in shaping the scientific governance of regenerative surgery and establishing clinical data standards for international consensus.

Prof. Albert-Claude Benhamou

Pdt Antoine Turzi

Prof. Albert-Claude Benhamou

Pdt Antoine Turzi

Prof. Isabelle Auquit Auckburn

Dr Diala Haykal

Prof. Barbara Hersant, Pdt Antoine Turzi, Prof.Philippes Descamps, Dr Georges Fabrice Blum, Prof Olivier Jardé, Dr Jean-Pierre Rozenbaum

BIOBRIDGE FOUNDATION

In partnership with

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“The future of surgical regeneration begins here : with the biosurgery”

“Biosurgery does much more than replace diseased or worn-out cells and tissues: it ’regenerates them”.

Pr Albert Claude BENHAMOU

The Biobridge foundation & Regenlab medical industry

Have been dedicated since their inception to autologous cell therapies and tissue engineering research and development

The biobridge foundation is pleased to participate in the emergence of the surgical revolution of the 21st century : **“The biosurgery”**

In paris on 23 may 2025 at the impetus of the french national academy of surgery and of its former president, professor Albert Claude Benhamou, with the support of the biobridge foundation **they launched the creation of “Arsia”, the Actual Regenerative Surgery International Academy.**

arsia

Actual **R**egenerative **S**urgery **I**nternational **A**cademy

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BIOBRIDGE FOUNDATION

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French Academy of Surgery

VIVACY PARIS

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SOCIÉTÉ FRANÇAISE ET FRANCOPHONE DES PLAIES ET CICATRISATIONS

SOCIÉTÉ FRANÇAISE DE CHIRURGIE DE LA MAIN

SOCPRE

CNJC CONSEIL NATIONAL DES JEUNES CHIRURGIENS

CNOF

SOFCOT Société Française de Chirurgie Orthopédique et Traumatologique