GENERATION REGENERATION

Biobridge European Seminar

September 20th and 21st, 2018

Santa Marta, 11 30135 Venice, ITA

Business Scientific Network

BIOBRIDGE FOUNDATION

regenlab

Dear Friends,

The 2018 seminar at our Regen Lab Venice center will focus on our company's arrival at a crossroads after 10 years of activity.

Here are the key points:

Between 2014 and 2017 Regen Lab produced a million kits of PRP medical devices for the benefit of nearly a million patients. In addition, kits of RegenExtracell Bone Marrow stem cells medical devices were produced for ten thousand orthopaedic surgeries.

A hundred thousand tubes of Cellular-Matrix, Platelet-rich plasma-Hyaluronic acid (PRP-HA) have been produced. This validates our latest patented technology. We are happy that physicians have welcomed the innovative, positive therapy and that patients have reported remarkable benefits in pain reduction and functionality.

New US FDA guidelines require structural demonstrations in clinical studies by industry experts.

In this seminar, participants will hear two reports on osteoarthritis:
- one by Dr Barac on echography evaluation
- one by Dr Renevier and Dr Marc on MRI Tesla 3 evaluation
The reports show an average of 20 percent growth of cartilage after 3 injections of Cellular-Matrix, PRP-HA.

Skin care and age management therapies Regen Lab started 10 years ago remain a main focus of our business development.

We are also proud to lead scientific and technical development in urogynecology focused on post-menopausal pelvic floor disorder, and erectile dysfunction.

Worldwide marketing data indicate a market size of $300 million with a growth potential of 15 percent a year.

As our GMP process center in Switzerland is expanded, Regen Lab will have the ability to fulfill up to 30 percent of the new markets.

The cell therapies authorized by the international regulatory bodies (PRP and combination with cells or HA) are safe and efficient in clinical practice, and we have initiated a reimbursement strategy in the major countries of the world.

Welcome to Venice, the city of Sciences, Arts and Love.

Antoine Turzi
C.E.O.

Regen Lab is certified ISO 13485 through BSI Notified Body and GMP by Swiss Agency for Therapeutic products (Swissmedic)

Medical Devices Regulation (MDR 2017/745), Article 10, requests a production quality assurance to keep production in conformity with requirements of the Regulation (ISO 13485). Good Manufacturing Practices (GMP) are requested for medicinal product manufacturing.

Production quality assurance principles

- Risk Management system in place
- Good manufacturing practices including in-process controls
- Independent Quality Control for product verification
- Product Quality Review and Post-marketing surveillance

Good Manufacturing Practice is that part of Quality Management System which ensures that Medicinal Products (*) including Medical Devices are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization or product specification (CE Mark).

Good Manufacturing Practice is concerned with both production and quality control.

Premises and equipment must be located, designed, constructed, adapted and maintained to suit the operations to be carried out. Their layout and design must aim to minimize the risk of errors and permit effective cleaning and maintenance in order to avoid unwanted mix, build up of dust or dirt and, in general, any adverse effect on the quality of products or possible misuse.

Manufacturing equipment should be designed so that it can be easily and thoroughly cleaned. It should be cleaned according to detailed and written procedures and stored only in a clean and dry condition. Repair and maintenance operations should not present any hazard to the quality of the products.

Production: All open-air treatment of raw material and primary pack filling operations need to be handled in dedicated rooms under controlled environment (Clean Rooms ISO7 class 10'000 particles/Inch cube) equipped locally with ISO5 Laminar flows (class 100 particles/Inch cube) to avoid or reduce at the lowest level particles contaminated with microorganisms and endotoxins.

The filling of sensitive OEM parts in blister packing should be operated in at least ISO8 class 100'000 particles/Inch cube) clean rooms with possible ISO5 Laminar flows on critical places.

(*) **PS: Medicinal Products** include Drugs and Medical Devices under the final responsibility of the governmental local authorities and at least European Directives. For Medical Devices the control/inspection and certification of the QM systems of Manufacturing Companies is delegated to Accredited Notified Bodies.

REGEN LAB SA QUALITY POLICY

Regen Lab develops, produces and distributes easy to use Medical Devices, ensuring safety and biological efficiency.

The clinical profits are reduction of the pain, acceleration of healing and tissue regeneration.

To date, about 1'000'000 patients received treatments distributed thanks to our products, and we wish to widen our international influence, so that maximum of patients can benefit from it. Regen Lab aspires to become world leader in modern regenerative medicine based on the autologous medical / surgical treatments by supplying Medical Devices of the highest level of quality and safety for the patient and user. It is a commitment of Public health and of respect for the well-being of the patients.

HOW SHALL WE REACH THERE?

1. System quality efficient and rigorous respect for the international regulatory frameworks

Management makes a commitment to enforce European regulatory frameworks defined by the Directive 93 / 42 / EEC, and the USA QSR 21 CFR 820, as well as the regulatory requirements of the countries with which Regen Lab collaborate.

The RegenLab Quality System responds to the requirements of ISO 13485 to provide medical devices that consistently meet customer expectations and regulatory requirements.
The Quality System is in constant improvement, managing the risks linked to the production and to the use of products.

2. The safety and the excellence of production processes

Safety is warranted by implementation, control and standardization of new technologies, which ensure a high quality product, and by developing successful production tools.

The coaching and continuous training of qualified employees ensured the quality and the safety of the end product.

3. The clinical research and the scientific promotion

Management assesses regularly the last publications and the scientific advances in the domain of autologous medical / surgical treatments.

Management ensures scientific information promotion, during an annual congress, dedicated to the doctors using our Medical Devices, and participates in numerous scientific conferences.
Regen Lab participates to spread the scientific and medical knowledge as for the beneficial effects of the autologous medical / surgical treatments. To do it, the company collaborates with numerous universities in particular the University of Economy CA ' FOSCARI for a medico-economic evaluation of the cellular therapies and well-being of the patients introduced at the end of 2013.

OBJECTIVES

Continue the improvement of the manufacturing processes and installations. Strengthen the R&D activity to meet new requests of the European Medical Device Regulation (MDR) and gather clinical data to support the intended medical purposes.

REGULATORY BACKGROUND IN EUROPE

2017/745 Medical Devices Regulation (MDR),

93/42/EEC Medical Devices Directive (MDD) and ISO 13485 certification.

The regulatory situation in European countries is standardized through the European regulations.

On May 5th, 2017, the European Commission has officially published the new Medical Devices Regulation (MDR) 2017/745 in the Official Journal of the European Union (OJEU), entry into force on May 25th, 2017. The new 2017/745 MDR replaces the existing 93/42/EEC MDD, and date of application will be May 26th, 2020.

Medical devices intended to prepare PRP fall under the scope of the new 2017/745 Medical Devices Regulation (MDR) and 93/42/EEC directive (MDD), that state on the requirements for their design, manufacturing and distribution. Many standards allow the compliance with MDR and MDD, such as ISO 13485 standard for Quality Assurance system, or ISO 10993 standards about biocompatibility requirements.

The compliance with 2017/745 regulation and 93/42/EEC directive is assessed by accredited notified bodies. This assessment leads to the ISO 13485 certification and the CE marking of medical devices, classified in a risk assessment approach (Class I, IIa, IIb or III). Notified bodies are also responsible to check the conformity of Medical Devices and Quality Assurance system with necessary standards. Except for a few countries in which medical devices are still constrained to administrative registration, the CE marking allows legally the release on the market of medical devices in all countries of Europe.

According to the 2017/745 regulation and 93/42/EEC directive, all manufacturers have to edit a Declaration of Conformity with the essential requirements of the regulation into force, which must also confirm the CE marking required for the release of their device on the market.

OTHER EUROPEAN REGULATIONS.

Devices intended to prepare PRP and the associated preparation procedure are concerned by the 2002/98/EC Directive about quality and safety requirements for the collection, testing, processing, storage and distribution of human blood and blood components. However, the Meeting of the Competent Authorities on Blood and Blood Components (2011) considers that the 2002/98/EC Directive is not applicable to PRP devices used for autologous purposes within a single procedure.

Although this comment has not been implemented yet in the directive, this recommendation of National

Competent Authorities should have priority in the application of the legislation. Cells containing products and tissues engineered products are regulated by the 1394/2007 Regulation on Advanced Therapy Medicinal Products (ATMP). The devices intended for PRP preparation are not in the scope of this regulation, while PRP itself and Bone Marrow Cells (BMC) should be discussed. Indeed, BMC might be considered as ATMP only when used in a non-homologous application, while PRP was recently excluded from ATMP classification by the EMA(*). Moreover, the paragraph 6 of the Regulation 1394/2007 clearly excludes from its scope custom-made ATMP for an individual patient, such as the non-homologous use of BMC.

Mis-compliance with IVD devices under the scope of the 2017/746 In Vitro Diagnostic Regulation and 98/79/EC Directive.

On May 5th, 2017, the European Commission has officially published the new In Vitro Diagnostic Regulation (IVDR) 2017/746 in the Official Journal of the European Union (OJEU), entry into force on May 25th, 2017. The new IVDR replaces the existing

98/79/EC directive, and date of application will be May 26th, 2020.

The new 2017/746 regulation and 98/79/EC directive state on the requirements for design, manufacturing and distribution of in vitro Diagnostic (IVD) medical devices.

Although the new regulation and the actual directive lead also to the CE marking of the devices under its scope, they do not have the same requirements in terms of safety and traceability as the new 2017/745 regulation and 93/42/EEC directive. Consequently, IVD devices that are CE marked through the 2017/746 regulation and 98/79/EC directive are not appropriate and not authorized for the same use as medical devices CE marked through MDR or MDD. Then, in regard to European legislation, the use of devices CE marked for to preparation of PRP for IVD purposes remains illegal when used for re-injection.
(*) European Medicine Agency

REGULATORY BACKGROUND IN THE US

Medical devices regulation in USA falls under the Code of Federal Regulation 21 CFR 820. Classification of Medical Devices is established according to a listing that concludes about the risk of each device category. The conformity is assessed by the US FDA that has authority to assess device safety, QA systems, and to allow or cancel their marketing authorization. The safety of medical

devices, especially biocompatibility requirements is assessed according to the ISO 10993 standards as in Europe, although some additional requirements are completed by the FDA Guidance on the Use of International Standard ISO 1993-1, issued on June 2016 (superseding the Memorandum #95).

REGULATORY AFFAIRS COMPLIANCE

To regulate Medical Devices marketing and distribution, local authorities have all developed their regulation rules for Medical Devices worldwide. Among those regulations, major regions pop out of the picture. Those are the main five Global

Harmonization Task Force (GHTF) leading countries:
- USA regulated by US FDA
- UE regulated by Notified Bodies in collaboration with Local state members authorities
- Japan regulated by MHLW
- Australia regulated by TGA
- Canada regulated by Health Canada

Those leading countries have developed several regulations that inspired one another, in order to develop an efficient international system based on basic safety rules to ensure the safety of the patients and users of the Medical Devices, as well as the performance of those types of devices. Indeed, what is the role of regulation entities, if not guaranteeing the performance of the device, its safety for the users and patients in order maintaining public health security?

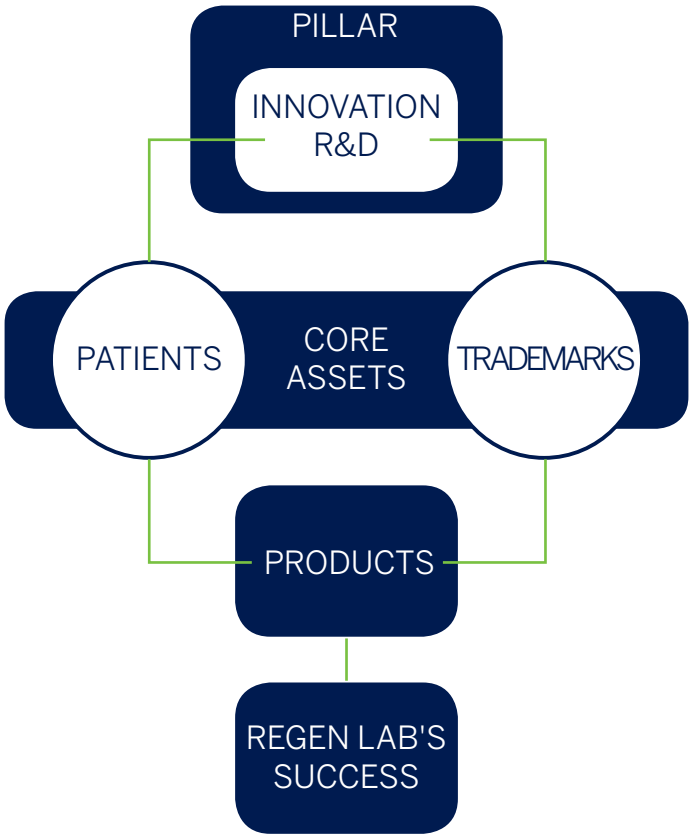
Even though regulatory compliance is varying in different countries, we can observe similarities among them, following the International Conference on Harmonization (I.C.H). Similarities between regulations make the global comprehension of the system easier to understand, but the details and variations among regulations is the challenging part.

This is the main reason why regulatory compliance for specific country requires a lot of work on the set up of technical files and huge concentration to comply with local regulations.

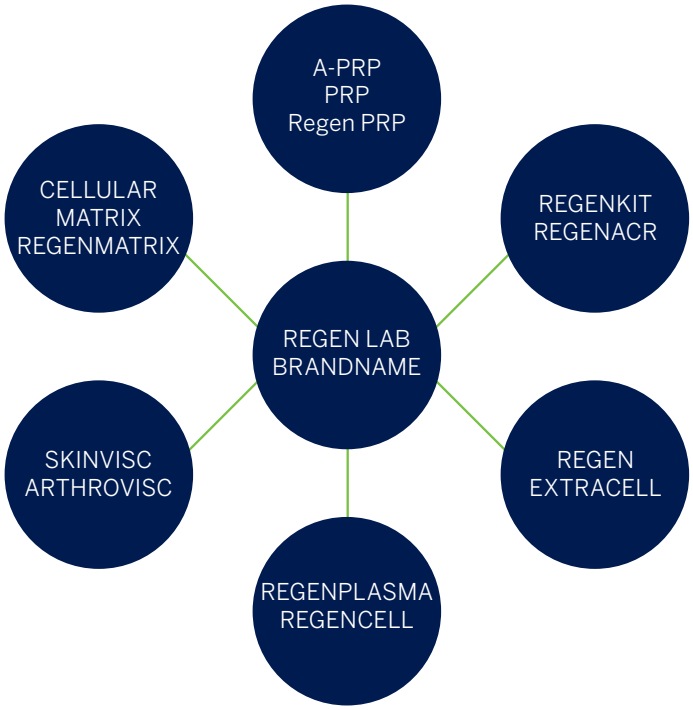
INNOVATION AND INTELLECTUAL PROPERTY

Intellectual Property Rights (IPRs) as Core Assets
As a leader in the PRP&HA regenerative field and as an innovation-driven company, Regen Lab SA has devoted important resources since 2004 to put on the market pioneering and diversified products constituting a complete set of tools/technologies for the medical community. Innovation represents one of the strongest pillar of the company with more than 30 in-house scientists and a unique network of talented and renowned medical doctors contributing to Regen Lab's Research & Development.

Over more than 10 years, this innovation has been secured by building substantial patent & trademarks portfolios making Regen Lab a major actor and indispensable partner in the regenerative field. Intellectual Property Rights (IPRs) therefore represent core assets of the company protecting its unique products against potential infringers and forging Regen Lab's renowned brandname



Trademarks
Regen Lab owns nearly twenty international trademarks constituting a large and diversified portfolio including general trademarks protecting the company and its products overall like RegenLab®, RegenKit® or A-PRP®, and others used for specific lines of products like RegenACR® for aesthetics or CellularMatrix® for the "all in one" PRP+HA product.



Patents - Technologies covered

We understand the investment you have made in selecting and marketing our products, even developing specific protocols & techniques around them for patients' satisfaction. Our strong patent portfolio represents the best guarantee for Freedom To Operate (FTO) ensuring that you will not be hindered in any way to continuously market/use our range of products for decades.

The patent portfolio covers several key technologies as summarized in the Figure with patent references. As securing innovation and building an efficient portfolio is a continuous endeavour, protection may cover other technologies including suturable membranes with the addition of calcium gluconate, or PRP in combination with TCP/chitosan.

The purpose of our patent portfolio is to provide monopolistic positions for the company in the PRP&HA field and beyond. Evidently, the aim is to block competitors from developing and marketing similar products. On the other hand, we want to prevent any risk of infringement for our clients/ distributors, to ensure their FTO and to restrict it as much as possible for competitors.

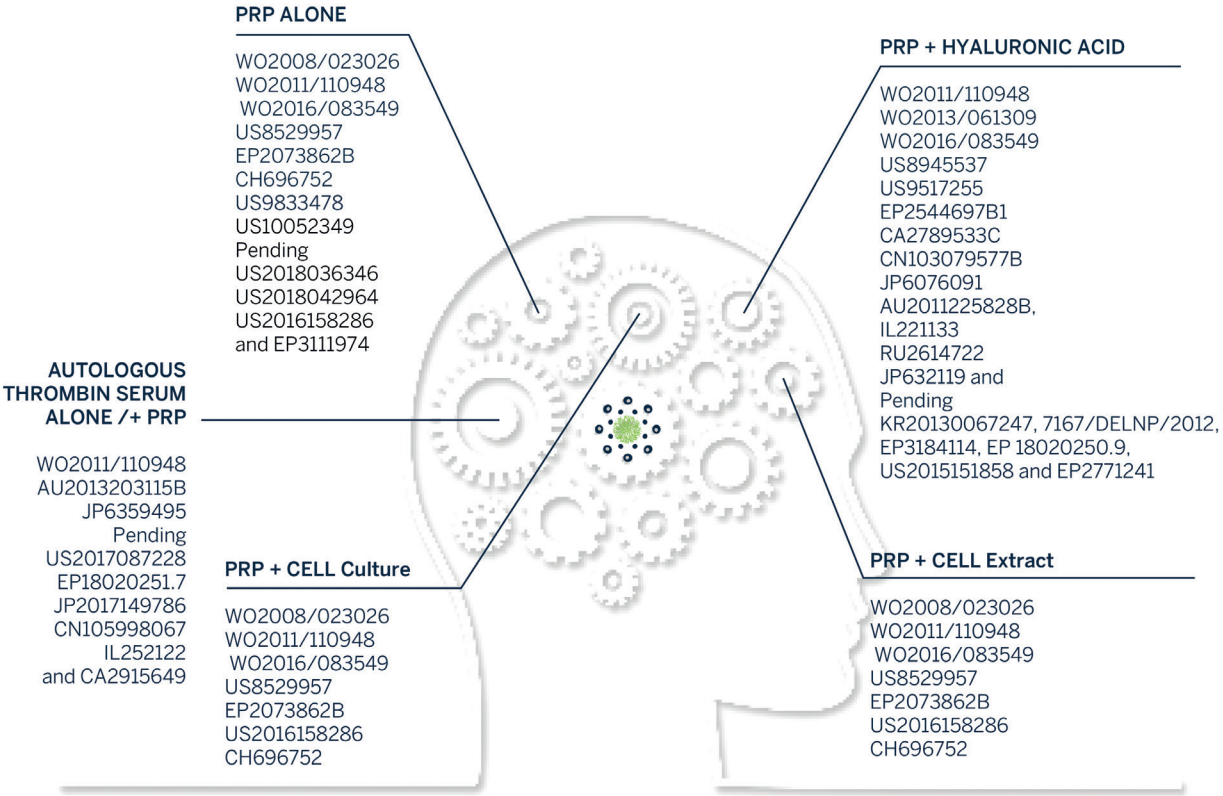
The IP message

As a leading innovator of medical products in the PRP&HA regenerative field for more than 15 years, which it markets under the well-recognized REGENLAB® and RegenKit® brands, Regen Lab and its founder Mr. Antoine Turzi have developed a substantial patent portfolio.

Innovation represents one of the strongest pillars of the company with more than 60 in-house scientists and a unique network of talented and renowned medical doctors contributing to Regen Lab's Research & Development.

The patent portfolio relates to the protection of tubes & methods for the preparation of Platelet Rich Plasma, biological glue/gel, Autologous Thrombin Serum (ATS), combination of PRP with cell extracts like Bone Marrow Concentrate (BMC) and fat tissue as well as the major/breakthrough technological innovation Cellular Matrix® which combines PRP and hyaluronic acid (HA).

Additional information about Regen Lab's patents can be found at https://www.regenlab.com/patents



CLINICAL EVALUATION AS PLATFORM FOR NEW CLINICAL STUDIES

Because reinforcement of the regulatory requirements for clinical data has become the universal rule during the past few years, clinical evaluation is nowadays a prerequisite for placing medical devices on the market, irrespective of their classification. Clinical evaluation aims at assessing clinical safety and performance/effectiveness as well as the overall benefit-to risk ratio of a medical device within the scope of its intended use.

In Europe, except for implantable and class III medical devices for which clinical studies are mandatory (unless an exemption can be justified), clinical evaluation as part of the CE-marking process can be based either on data specific to the device itself (clinical investigations, published data, post-marketing surveillance data) or on published data relating to a device deemed as equivalent by the manufacturer (the so-called "equivalence route"). The new Medical Device Regulation (MDR), however, imposes stricter requirements, such as the basis for establishing equivalence with another device and the quality of data considered in the clinical evaluation. Practically, this implies that (1) the equivalence route will be made less accessible, especially for high risk devices, and (2) clinical data collected from clinical investigations lacking Good Clinical Practice (GCP) compliance might not be accepted anymore.

Even though conducting clinical studies may appear as a constraint at first sight – as they often take long time to organize and represent a huge expense item - Regen Lab SA rather saw in these new requirements the opportunity to collect valuable clinical data that could be useful as part of post-marketing activities or in the framework of reimbursement procedures for some indications.

Therefore, for a couple of years, Regen Lab has committed to invest on clinical investigations in order to provide high-quality clinical data relating to its products, ensuring this way to make the difference on the market.

Up to now, Regen Lab products have been evaluated in more than 160 published clinical trials, reviews or in vitro studies covering a broad spectrum of therapeutic areas, ranging from skin care, plastic surgery, ophthalmology, orthopedics, sports medicine and cardiac surgery. Even though they greatly vary in terms of quality, they all demonstrate safety and efficacy of RegenPRP and PRP prepared in presence of hyaluronic acid with Cellular Matrix.

In order to get reimbursement of our products, Regen Lab strives to design clinical studies according to gold standards (i.e. controlled and randomized trials enrolling an appropriate number of patients, which have been approved by Ethics Committees and notified to Competent Authorities of involved countries), with a special focus on Cellular Matrix as a treatment for osteoarthritis.

As part of these reimbursement procedures, Regen Lab is currently also conducting medico-economic evaluation of PRP for the treatment of diabetic foot ulcers in collaboration with the Ca'Foscari University of Venice, Italy.

Finally, in order to improve our post-marketing surveillance to comply with the new MDR, various tools are currently being implemented to enable physicians to directly report their experience (adverse reactions, outcomes, complaints) with Regen Lab products.

A-PRP TECHNOLOGY

Platelet rich plasma (PRP) is a biological product prepared from the blood of the patient (autologous) for therapeutical applications. Platelets are small entities produced in the bone marrow by fragmentation of huge cells called megakaryocytes. Although they have no nucleus and are ten times smaller than other cells, they are alive and functional. They are involved in hemostasis and tissue healing. Until recently they were considered only as big vesicles full of coagulation factors and growth factors, however their role is more complex. They are active players in all the steps of the healing process, but also in the control of infection and inflammation and pain.

Although numerous (around 200 million by ml), platelets represent only 0.2 % of the blood volume. Consequently specific devices have been designed to isolate them from other blood components. The Regen Lab separating gel technology allows the easiest and fastest preparation of 6 to 6 ml of PRP from only 10 ml of blood, in a completely closed system insuring the sterility of the product. The specific density of our separating gels ensures optimal platelet recovery (>80%) in the full volume of plasma. The process is operator independent, therefore guarantees reproducible performances. The collected platelets are of highest quality and fully functional. Undesired contaminants, red blood cells and pro-inflammatory white blood cells, are efficiently removed while still recovering the largest and densest platelets, which have the highest content in growth factors, thus producing an optimal PRP.

RegenPRP is used for injections in damaged tissues. Platelets are activated by the contact with extra cellular matrix proteins, such as collagen and form micro-clots at the site of injection. When more localized action is desired, RegenPRP can be naturally activated with autologous serum rich in activated thrombin, prepared with the RegenATS tube. This combination allows the formation of platelet gel but also of fully autologous fibrin glue that can be used for all surgical applications. Compared to pharmaceutical glues, it is not only safest, with no risk of contamination with transmissible disease or allergic reaction to allogenic components, but also, thanks to the presence of active platelets, this glue will accelerate the healing of treated tissues and prevent infection.

RegenPRP is also designed to improve cell therapies and graft bio-integration. It is the ideal media to insure bone marrow stem cell survival, differentiation and proliferation during orthopedic reconstructive surgery. Regen Lab produces kits designed for bone marrow cell preparation, using the separating gel technology for optimal stem cell isolation.
RegenPRP sustains the survival of fat graft during soft tissue reconstruction. In addition, it is successfully used to improve skin and hair graft and biointegration of prosthesis and implants.
Cellular Matrix is the latest Regen Lab innovation. It is the sole device that allows the rapid preparation of RegenPRP combined with a high quality hyaluronic gel in conformity with regulations for medical devices and for the use of autologous cells. The natural (no chemical modification) hyaluronic acid (HA) produced by fermentation, creates a cell friendly matrix in which the platelets are in suspension. This product ensures the synergy of the biological action of PRP with the hydration and visco-supplementation effects of HA. This biologically enriched network facilitates cell migration and proliferation on the treated site.

GOOD PRACTICES

GOOD PRACTiCES WiTH REGEN LAB A-PRP® KiTS

• Users must be **trained for the procedure** before starting using Regen Lab kits.

• **Patient must be informed** of the general risks associated with the treatment and of possible adverse effects.

• **Integrity of the packaging** must be checked before kit opening.

• Treatments are registered in the patient file, using the removable stickers to **record reference and lot number** of the kit used.

• Document **any undesired events** and report them to our quality affairs department.

• Use **surgical aseptic technique throughout the procedure** (blood draw, A-PRP collection, injection).

• Use **appropriate safety precautions** to protect yourself from needles and beveled cannulas.

• Throw away the entire kit after use, using the appropriate method of elimination for **potentially contaminated blood products**.

• Use **Regen Lab centrifuge**. Centrifuges from other manufacturers can be used only if they have a **centrifugation angle of 45°or spin the tubes horizontally**. Cellular Matrix tubes should be centrifuged preferentially in a 45° fixed angle rotor.

• Tube holders must **correctly fit** Regen Lab tubes.

• Speed in round per minutes (RPM) should be set to reach the desired relative centrifugal force **(RCF) of 1500 x g** (1600 x g for bone Marrow aspirate). Use manufacturer instructions and RCF to RPM converter **to calculate the appropriate speed in RPM**.

• Tubes must be correctly **balanced**. If necessary, fill a **counterbalance tube** with water until it reaches the same volume as the blood filled tube it will counterbalance.

• Respect the **centrifugation protocol** (time, centrifugal force). Any modifications will lead to lowering the device performances.

• Regen PRP is prepared and kept until used at **room temperature**. Never refrigerate. Use **within four hours** after blood collection.

• **Take time to resuspend well** the platelets in the plasma before PRP collection. Always perform a **visual control** that platelets are well detached from the separating gel.

• If a cell and platelet count is desired, dedicate a full tube for this evaluation. Ensure that **all aggregates**, **even the microscopic ones**, **are well disrupted** before performing the automated cell counting.

• Respect injection or application protocol. **Avoid injecting too high volumes** that would distend tissues.

GENERATION REGENERATION

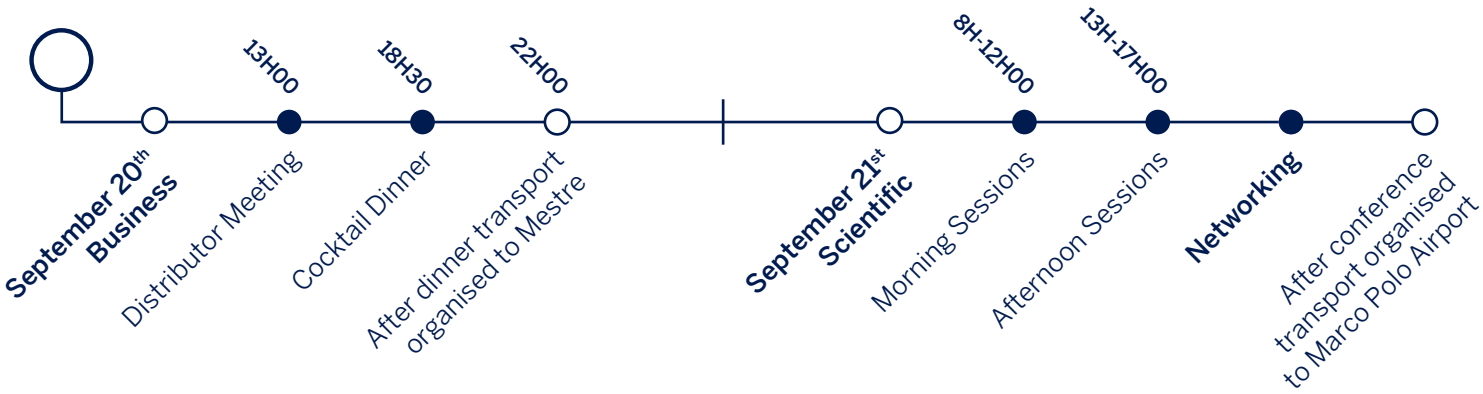
European Conference

September 20th and 21st, 2018

- V E N E Z I A - San Basilio,11 30135 Venice,ITA

Business Scientific Network

PROGRAM OUTLINES



ROOM 1
Dermal

- **Dermatology, Scars & Ageing Management**
- **Dermatology, Scars & Ageing Management**
- Lunch Break
- **Plastic Surgery, Adipocytes**
- **Wound Management**
- END

ROOM 2
Urogenital

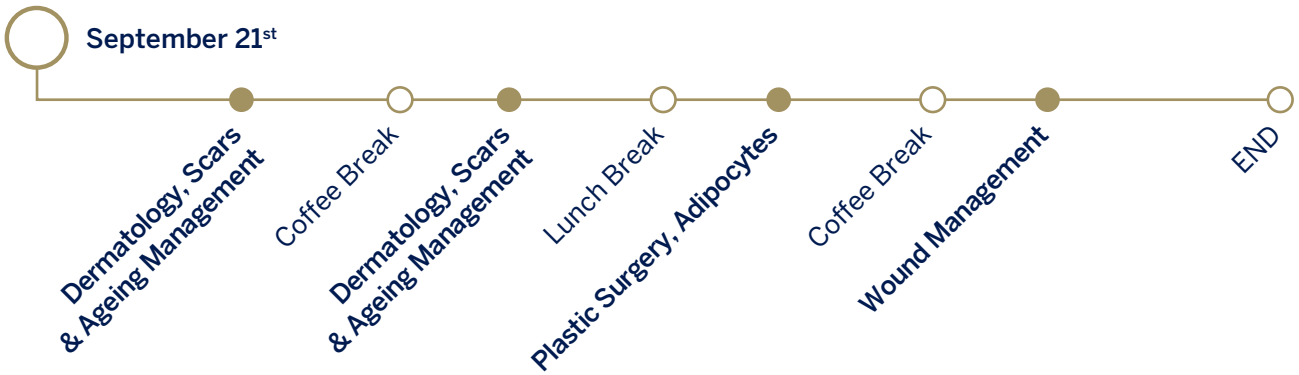
- **Key Challenges in Gynaecology**
- **GSM Management**
- Lunch Break
- **Urology & Male E.D.**
- **Urology & Gynecology**
- END

ROOM 3
Musculoskeletal

- **OA Management with CellularMatrix**
- **MSK Pain Management**
- Lunch Break
- **Orhopaedic & Sports Surgery**
- **MSK Pain Management**
- END

ROOM 1

Dermal



DERMAL

OPENING	**DERMATOLOGY, SCARS & AGEING MANAGEMENT**
9h00	PRP plasma rich platelet therapy: Our over 15 years' experience in Dermatology, Trichology, Plastic surgery & sexual medicine **Emiliano Betti Italy**
9h15	Autologous biological culture system with A-PRP to boost human fibroblast expansion in vitro. **Sarah Berndt Switzerland**
9h30	Trichologic response of platelet rich plasma in androgenetic alopecia is maintained during combination therapy. **Jerry Shapiro USA**
10h00	Platelet-rich plasma in androgenetic alopecia: where do we stand? **Maria-Angeliki Gkini UK**
10h15	Discussion & Questions
10h30	Coffee Break
	DERMATOLOGY, SCARS & AGEING MANAGEMENT
11h00	Fundamentals of A-PRP & Cellular-Matrix in anti-ageing **Ghislaine Beilin France**
11h20	Research of clinical effectiveness of Cellular-Matrix technology in therapy of skin aging, practical aspects of 3D-modeling of the face, neck and décolleté **Inna Sharypova Russia**
11h40	Combined use of RegenLab A-PRP with micro-needling RF-treatment in aesthetic medicine. **Andrey Alenichev Russia**
12h00	Discussion & Questions
12h30	**Lunch Break**
	PLASTIC SURGERY, ADIPOCYTES
13h40	RegenKit Extracell Adipocytes, activated PRP in fat grafts In vivo study **Barbara Hersant France**
14h00	RegenKit Extracell Adipocyte for facial rejuvenation **Aleksandr Babych UA**
14h15	PRP application to prevent wound complications after cardiac surgery **Giuseppe Filiberto Serraino Italy**
14h30	Discussion & Questions
14h40	A preliminary economic evaluation on the care management of diabetic foot ulcers **Salvatore Russo/ Landi Italy** Regulatory / MDR / Patent / I.P. **Antoine Turzi**
15h00	Coffee Break
	WOUND MANAGEMENT
15h30	Treatment of cutaneous skin lesions of the diabetic foot with PRP: clinical protocol **Antonino Grasso Italia traducteur**
15h50	A-PRP plus ATS in Public Health Care diabetic foot patients wound management **Vladimir Jovanovic, Voja Pavlovic, Serbia**
16h05	RegenBCT PRP + ATS: A new approach for the treatment of chronic diabetic foot ulcer **Renaud Heraud France**
16h20	Effect of Autologous Platelet Rich Plasma/Thrombin gel (RegenACR®Plus) on the repair of complicated infected pluri-tissular wounds. **El-Khatib Karim Morocco**
16h35	New Healing options for diabetic foot ulcers **Alaoui Mustapha Morocco**
16h50	Autologous Platelet-Rich Plasma for Treatment of Chronic Leg Wounds **Domantas Rainys Lithuania**
17h05	Discussion & Questions
17h15	**END**

PRP plasma rich platelet therapy: Our over 15 years' experience in Dermatology, Trichology, Plastic surgery & sexual medicine

Dr. Emiliano Betti

Biography: Dr. Emilio Betti dermatologist and aesthetic surgeon is a pioneer of regenerative medicine in Italy, well known as the creator of original techniques and protocols in aesthetic medicine and in dermatology. He has been coordinating a group of highly specialized plastic surgeons and dermatologists for over 10 years.

Abstract: We have used the PRP safely for over 15 years in many therapeutic areas such as dermatology, aesthetic medicine, plastic surgery, orthopedics and pain therapy, hair loss and sexual medicine for both male and female. We started in 2002 at the University of Pisa for the treatment of injuries and vascular and pressure ulcers and we continued to perform treatments in private clinics for many indications, during the years more and more new and more interesting indications and uses. Platelet Rich Plasma (PRP) therapy is a natural and safe treatment which reinjects platelets and growth factors into your body. PRP produces a healing response in the body to repair and rejuvenate an area. For example, PRP is a simple and effective procedure for male and female pattern baldness but also for newer application such as to treat Peyronie's disease, erectile dysfunction in male and to improve sexual satisfaction and reduce vaginal dryness in female. We record brilliant and successful results in every indication with PRP therapies, not only for the PRP alone but also in the more recent combination of the PRP with hyaluronic acid or with the fat grafts. Present and recent future show excellent perspectives of new development of standardized and effective therapies.

NOTES

Autologous biological culture system with PRP to boost human fibroblast expansion in vitro.

Dr Sarah Berndt

Biography: PhD in Biomedical and Pharmaceutical Sciences focused on experimental cancerology and gynecological research in Belgium. To extend her expertise in trophoblast research, she moved to Paris Descartes University and then to Collège de France to concentrate on vascular biology and tissue engineering. Since 2013, she is working in tissue engineering and cell therapy research in Switzerland. She is now R&D project leader for Regenlab, focusing on the use of PRP for cell therapy research in collaboration with physicians of the Geneva University hospitals in Plastic Surgery, Gynecology and Orthopedic Surgery.

Abstract: The purpose of this study was to build up a 100% autologous culture system to expand human skin cells cultures in vitro with the patient's own Platelet-rich-plasma (PRP) and to compare it with classical culture settings where fetal bovine serum (FBS) is used as the main source of growth factors.

Normal human dermal Fibroblasts (NHDF) were retrieved from patients undergoing abdominoplasty. Blood was collected on the same day and PRP was prepared with the CuteCell PRP medical device. The cultures were followed up to 7 days in the presence of FBS or PRP as the source of nutritive and growth factors supplements. The following cellular parameters were assessed: morphology, proliferation and cell cycle, migration, adhesion, differentiation and genomic stability.

NHDF cultured with their own PRP showed significantly higher proliferation rates compared to FBS supplemented medium. The PRP treatment triggers DNA synthesis and a higher mitosis rate. NHDF are activated directly after PRP treatment: their adhesion properties to laminin and collagen are decreased and they initiated collective migration in a wound healing model. A one week PRP treatment at high concentration is affecting NHDF morphology with a cytoskeleton rearrangement and a switch to a myofibroblast phenotype as evidenced by an increase in alpha-SMA expression and a decrease in vimentin expression. Comparative genomic hybridization demonstrated no unbalanced chromosomal rearrangements in cells cultured in the presence of PRP.

PRP prepared with the CuteCell device is a better and a safer alternative as a supplement for cell culture media used for in vitro cell expansion with a clinical cell therapy purpose.

NOTES

Platelet-rich plasma in androgenetic alopecia: where do we stand?

Dr Maria-Angeliki Gkini

Biography: MD, MSc, PhD. Dr. Maria-Angeliki Gkini qualified from Aristotle University Medical School in Greece. She started her training in Dermatology at Athens, Greece, while she completed her PhD on the safety and efficacy of PRP in the management of androgenetic alopecia. Currently, she is a clinical research fellow at Barts Health NHS Trust, London, UK, where she treats dermatology patients as well as being a sub-investigator in numerous large multicentre commercial and academic studies. Her special interests include hair disorders, psychodermatology and dermatologic surgery, including aesthetics.

Abstract: Platelet-rich plasma (PRP) is defined as an autologous concentration of plasma with a greater count of platelets than that of whole blood. It has been investigated in numerous fields of aesthetic medicine. During the last 8 years, it has attracted significant attention as treatment for androgenetic alopecia. Aim of the lecture is to assess the level of evidence regarding PRP as treatment in male and female pattern baldness, through a systematic literature review, trying to provide a guidance in its use. Other factors that may affect its efficacy are going to be reviewed, such as activation, and preparation methods. The potential use of PRP in other types of alopecia is also explored. PRP injections appear to be effective in the increase of hair density and thickness, with no significant adverse events, in the majority of studies. Nevertheless, the available meta-analyses seem to be inconclusive and the level of evidence of most trials is low. Contributing factors seem to be different protocols, different PRP preparation kits, small studies and presence of few randomized controlled trials. In conclusion, from clinical practice PRP seems to be a promising treatment for androgenetic alopecia, either as monotherapy or as concomitant treatment. Nevertheless, further larger, randomized, double-blind, controlled studies are required to objectively assess its safety and efficacy through a standardized protocol.

NOTES

Trichologic response of platelet rich plasma in androgenetic alopecia is maintained during combination therapy.

Dr Jerry Shapiro

Biography:Professor Shapiro is the only dermatologist in the USA who practices only medical hair restoration. He has trained over 29 Hair Fellows from all over the world. He has published over 150 peer reviewed articles, five books in three languages and has one of the busiest hair clinics in the world in New York City at the Ronald O. Perelman Department of Dermatology, New York School of Medicine.

Abstract: With institutional review board approval, we assembled records of 24 patients with androgenetic alopecia (19F, 5M) who received platelet rich plasma (PRP) while using concomitant medical hair restoration therapy. PRP was prepared by venipuncture of 8 ml of blood and then centrifuged for 5 minutes at 1500 g (RegenKit-BCT-1) The supernatant harvested contained 1.6 times normal blood concentration of platelets (total 5 ml) and injected into the scalp as 50 injections of 0.1 cc. Folliscope measurements were taken at the anterior crown 12 cms from the glabella. Hair density with PRP increased over 10% from baseline in 62.5% of patients and over 20% in 33.3% of patients. One patient had an increase in hair density of over 50%. These findings represent real-world outcomes that can be used to inform patients' decision on pursuing PRP. There was no shock loss in any of these patients.

NOTES

Fundamentals of A-PRP & Cellular-Matrix in anti-ageing

Dr Ghislaine Beilin

Biography: MD and Clinic Vendome Medical Director. She is president of the ESAAM (European Society of AntiAging and regenerative Medicine), and vice-president of the SNME (Syndicat National de Médecine Esthétique). Paris medical university assistant Professor; Key opinion leader in aesthetic and antiaging medicine and Scientific committee in main international congress.

Abstract: Platelet-rich plasma becomes the goal standard in regenerative medicine. Since the last 10 years Regent Lab research and development have standardized and valided truth multiple clinical studies all the technics and protocol treatments in the field orthopaedic rheumatology, stomatology, gynaecology, skin care, burns, alopecia and surgery.

Adding hyaluronic acid to autologous growth factor in "CELLULAR-MATRIX" and combination with the stem cells activation we can achieve a truth tissue restoration. The indication is not only in pathologic but also in a preventive and regenerative approach in anti-aging to maintain our physiological functionality of all our cells, the tissues and organs. The revolution of PRP and cellular-matrix give us a huge application from deep tissue to superficial dermis from youth sportsman and athlete to older patients, from post-partum to post-menopausal women, from wrinkle to skin graft. Helping us to provide to our patients solution to maintain the optimal physiological status in all our cells and tissues. We can delete aging.

It's a real break though in anti-aging; cutting age and even reversing time.

We will present the fundamentals basics of Regen Lab PRP and CELLULAR-MATRIX and focus of skin care, alopecia, dermatology, wound healing and age relating skin disorder.

NOTES

Research of clinical effectiveness of Cellular-Matrix technology in therapy of skin aging, practical aspects of 3D-modeling of the face, neck and décolleté

Dr. Inna Sharypova

Biography: MD, PhD, President of Anti-aging Medicine Corporation and CEO of the Clinical Institute of Anti-aging Medicine. Dr. Sharypova has 25 years of extended clinical experience, one of the recognized leaders in the Russian aesthetic medicine. Lecturer at the chairs of dermatology and cosmetology, speaker at International congresses and conferences. Takes part in international scientific projects. Regen Lab coach in aesthetic medicine.

Abstract: In the study, we estimated the efficacy of HA enriched with platelet's growth factors in treatment of laxity, wrinkles and other aspects of chrono- and photoaging.

Using a Global aesthetic improvement scale (GAIS), corneometery and digital dermatoscopy as well as quantitative analysis of changes in two groups of patients with indications for rejuvenation, we assessed the effect of triple injection procedures of combined preparation Cellular-Matrix. We conducted procedures within the period of 3 months with 30 days intervals. During each visit, we injected preparation in bolus and vector technique into deep derma and on the border with superficial fat avoiding orbital area. We adapted lifting and remodeling approach, as well as the spot volume of the injected Cellular-Matrix according to the type of aging of each patient.

Therapy in both subgroups resulted in mean 33.5% (30-37%) improvement in hydration of derma according to corneometry, depth and width of wrinkles decreased in both groups and we registered high self-assessment scores on GAIS. In more than 55% of patients, aesthetic result was persistent up to 12 months.

The assessed approach that combines autologous platelet rich plasma (A-PRP) with hyaluronic acid (HA) proved to be a desirable solution for skin rejuvenation.

NOTES

Combined use of RegenLab A-PRP with micro-needling RF-treatment in aesthetic medicine.

Dr. Andrey Alenichev

Biography: MD, PhD, Vice President of Anti-aging Medicine Corporation and Director of the Clinical Institute of Anti-aging Medicine.

He has 17 years of extended clinical experience, recognized as an expert level specialist in rejuvenation medicine. Lecturer at the chairs of dermatology and cosmetology, speaker at Russian and International conferences. RegenLab coach in aesthetic medicine.

Abstract: We studied the clinical efficiency of combined treatment of age-related skin changes using micro-needle RF and PRP.

Scarlet micro-needle RF device and RegenLab kit Plus. 39 patients aged 35-65 y/o underwent procedures according to a developed protocol: Group A (n=20, ≤ 49 y/o) and Group B (n=19, ≥ 50 y/o). Severity of signs of skin aging was assessed using VAS, GAIS, dermatoscopy, ultrasound and Laser Doppler Flowmetry.

LDF data showed increased blood flow and decreased blood retention in the microcirculation system with the integral index of microcirculation efficiency improved by 1.8. The ultrasound assessment demonstrated improved skin morphostructure, increased dermal acoustic density and thickness. VAS and GAIS showed a significant decrease in signs of skin chronoaging. Hydration improved 1.6-1.9 times.

The combined therapy using A-PRP RegenLab and micro-needle RF is a highly effective method for correction of age-related skin changes. It eliminates spasms of arterioles and stagnation in venules, which is confirmed by the increased integral index of microcirculation. The method improves skin's morphological structure. The rejuvenation effect in most patients lasts up to 1.5 years.

NOTES

RegenKit Extracell Adipocytes, activated PRP in fat grafts In vivo study

Dr Barbara Hersant

Biography: Barbara Hersant is a plastic surgeon in the department of plastic, reconstructrive, aesthetic and maxillo facial surgery of a university hospital near Paris (Henri Mondor Hospital, Creteil). She is assistant professor and she is the co-director of a the DUMEG (Diplome universitaire de médecine esthétique génitale). Her practice is specialized in vulvo vaginal, penis, bottom and breast surgery. She is also a researcher in the field of adiposed steam cells and platelets rich plasma for skin and nerve rejuvenation.

Abstract: The adjunction of platelet-rich plasma with graft fat has been the subject of a few clinical trials which have demonstrated its value in adipocyte survival. The aim of this study was to assess the different efficacies between activated and non-activated PRP on adipose cells in vitro and for adipose tissue graft survival in vivo. We also used the RegnKit Extracell adipocyte to improve the preparation of micofat for various surgical and aesthetic applications.

The in vitro study assessed the effects of PRP on both the proliferation and adipocyte differentiation of adipose cells. For the in vivo study, 8 nude rats received 3 human fat injections as follows: 0.8 mL of fat + 0.2 mL of normal saline; 0.8 mL of fat + 0.2 mL of non-activated PRP; and 0.8 mL of fat + 0.2 mL of PRP activated with calcium chloride (CaCl2). The quantitative assessment of adipocyte survival was implemented after 3 months using histomorphometric analysis. Histological and immunohistochemical analysis were also performed to evaluate angiogenesis, inflammation and quality of adipocytes in the grafted tissue.

We showed that activated PRP stimulated, in vitro, proliferation and differentiation of adipose cells. In vivo experiments indicated that CaCl2-activated PRP was more efficient than nonactivated to prolong the survival of fat grafts in nude rats. The mean percentage areas occupied by viable adipocytes in the PRP-free group, non-activated PRP group and activated PRP group were 13%, 14% and 24% ($p = 0.05\%$), respectively. Histological and immunohistochemical analysis revealed protective effect of activated PRP on inflammation and adipocyte death.

This study showed that activation by CaCl2 improves the beneficial effects of PRP for fat graft maintenance.

NOTES

RegenKit Extracell Adipocyte for facial rejuvenation

Dr Aleksandr Babych

Biography: Graduated from National Medical University (Ukraine) in 2000, he became General surgeon in 2004. Since 2004 Urologist (Institute of Urology of the Academy of Medical Sciences of Ukraine). Since 2016 Thread lift & dermal fillers injection techniques trainer. Since 2017 Trainer in "Avicenna" (Regen Lab, Ukraine).

Abstract: Progressive loss of elasticity of soft tissues and facial volume are the main causes of age-related changes of the face.

It is becoming increasingly obvious that autologous fat transfer is the optimal method to correct aging face. In addition to the volumetric effect, adipose tissue has a regenerative effect due to the presence of stromal-vascular fraction (SVF). Combination of fat grafting and PRP increase the survival of adipocytes and differentiation of stem cells.

RegenKit Extracell Adipocytes allows to reduce the time of harvesting, processing and mixing fat grafting with PRP. Adding of PRP to fat grafting leads to a better fat grafts survival, less bruising and inflammation reaction.

Resume. Autologous fat transfer using this new closed system offers many advantages as a fast, simple and safe method.

NOTES

PRP application to prevent wound complications after cardiac surgery

Pr. Giuseppe Filiberto Serraino

Biography: M.D., PhD. Dr. Serraino is a Professor of Cardiac Surgery at School of Medicine at the University Magna Graecia in Catanzaro, Italy. Over the past two decades, his clinical practice has focused on surgical repair of mitral valve disease, aortic valve replacement with minimally invasive approaches and coronary artery bypass graft surgery. His research is focused on basic research as inflammatory response after cardiac surgery and regenerative medicine. He is a member of the Italian Society of Cardiac Surgery, the European Society of Cardiac Surgery and the American Association of Thoracic Surgeons.

Abstract: Despite the large choice of wide-spectrum antibiotic therapy, deep sternal wound infection (DSWI) following cardiac surgery is a life-threatening complication world- wide. This study evaluated that the use of platelet-rich plasma (PRP) applied inside the sternotomy wound would reduce the effect of sternal wound infections and leg wound infections after bypass surgery, both superficial and deep. Between January 2007 and January 2012, 1093 consecutive patients underwent cardiac surgery through median sternotomy. Patients were divided into two groups. Group B, the study group, included those who received the PRP applied inside the sternotomy wound before closure. Group A, the control group, included patients who received a median sternotomy but without the application of PRP. Antibiotic prophylaxis remained unchanged across the study and between the two groups. Occurrence of DSWI was significantly higher in group A than in group B [10 of 671 (1.5%) versus 1 of 422 (0.20%), P=0.043]. Also, superficial sternal wound infections (SSWIs) were significantly higher in group A than in group B [19 of 671 (2.8%) versus 2 of 422 (0.5%), P = 0.006]. Moreover, we performed a 5 years follow-up for 187 enrolled patients: none of them results in DSWI or SSWI. The use of PRP can significantly prevent the occurrence of DSWI and SSWI in cardiac surgery.

NOTES

A preliminary economic evaluation on the care management of diabetic foot ulcers

Dr Salvatore Russo & Dr Stefano Landi

Biography: Department of Management, University "Ca' Foscari" Venice, Venice-Italy
Dr Stefano Landi
Master Degree in Statistics and economics in University Bicocca, Milan and PhD in Health economics at University of Genoa
From February 2016 to now: Research Fellow in "Health technology innovation and sustainability of health systems" University Cà Foscari Venice
Field of interest: Health inequalities, Pharmacoeconomics analysis, Health Technology Assessment.

Abstract: It is estimated that 15% of diabetics develop at least one foot ulcer in their lifetime. Diabetic foot exhibits rapid and complex progression, leading to neuropathy, infection, and gangrene, which may require lower extremity amputation. Foot ulcers are one of the most complicated conditions to manage in diabetics, as the ulcers attract infections which lead to further complications. Eighty-five percent of amputations in diabetics are preceded by an ulcer. While diabetes itself doubles the rate of mortality by all causes as compared to non-diabetics, foot ulceration imposes an even higher morbidity. Developing countries spend almost 40% of their health expenditure on diabetics; in developed countries, it accounts for approximately 12–15% of health spend.

The goal of diabetic foot ulcer treatment is to obtain wound closure as expeditiously as possible. Accepted therapeutic objectives and standards of care for diabetic foot ulcers include wound debridement, pressure relief in the wound are a, appropriate wound management (eg, moist wound healing), infection management, ischemia management, medical management of comorbidities, and surgical management as needed. Emerging cellular therapies such as platelet – rich plasma (PRP) can have an adjunctive role in a standardized, quality treatment plan.

It has been demonstrated that plasma growth factor (PGF) such as platelet derived growth factor (PDGF) significantly shortens treatment duration.

A review of the literature on costs and therapies effectiveness will be presented with a preliminary introduction on the modelling for the economic evaluation of the treatment of diabetic foot ulcers with PRP.

NOTES

Treatment of cutaneous skin lesions of the diabetic foot with PRP: clinical protocol

Pr Antonino Grasso

Biography: Researcher – Professor - Medical Director and Manager of the Vulnology Service and the Ecocolordoppler Section and coordinator of the Master in Vulnology and Diabetic Foot at University Hospital "Policlinico - Vittorio Emanuele", Catania (Italy).

Abstract: In the world more than 346 million people suffer from diabetes and it is estimated that in 2030 this value will be 366 million. In Italy, there are 3 million diabetics, equal to 4.9% of the population. 25% of patients with diabetes develop ulcers during their lifetime which are the most frequent cause of amputation of the body extremities and require a long procedure, with patient pain and huge health expenses. The goal of wound management is to promote a quick and complete recovery of the wound in order to reduce the risk of infections, but often, the treatments are very expensive and require continuous entry by the patient in the hospital or in health facilities. Unfortunately, among patients with good vascularization, less than 2/3 respond positively to standard care. There are several alternative treatments available. PRP is a blood component for topical, autologous and non-transfusional use; it's easy to 'find' and easy to use: once the gel is created, it is placed on the lesion and it is supported by the final use of advanced dressings.

The mechanisms that produce the beneficial effects are not perfectly clear, but they are surely linked to the presence of growth factors and chemical mediators in large quantities.

There are several fields of application: diabetic ulcers; venous ulcers; pressure lesions; dehiscence of surgical wounds; traumatic injuries.

STUDY POPULATION: diabetic patients suffering from an "HARD TO HEAL" cutaneous ulcer (a chronic skin lesion unable to heal not only with the aid of traditional but also advanced dressings, remaining blocked in the inflammatory phase for more than 8 weeks, without complete closure, although in the presence of a good blood perfusion).

From January to August 2018, 14 patients with diabetic lesions were treated in our clinic; 8 have reached full recovery while the remaining 7 showed clear sign of improvements. All the recovered patients were subjected to three sessions of PRP with an interval of 15 days, while for the remaining patients a second cycle is planed (still ongoing).

The technique is painless, easy to find and compliant with the patient (it doesn't require hospitalization or preliminary assessments and the day of the procedure the patient returns to his home). The next access to the clinic takes place on the fifth day for the first dressing.

NOTES

A-PRP plus ATS in Public Health Care diabetic foot patients wound management

Dr Vladimir Jovanovic & Dr Voja Pavlovic

Biography:
Vladimir Jovanovic
Doctor of Medicine, Specialist of Orthopedics, Clinic for Orthopedics, Clinical Center of Nis.
Work experience: Started 1,5 year in Emergency squad and continue the following 20 years in Clinic for Orthopedics, University Clinical Center of Nis. Private practice: NAISSA, Polyclinic for Internal Medicine, Orthopedics, and Physical Medicine and Rehabilitation

Voja Pavlovic
MD, PhD is Assistant Profesor at the Institute of Physiology at Medical Faculty, University in Nis, Serbia, and as a PhD of Physiology and Researcher, he is working at the Department of Physiology, Medical Faculty in the last 18 years.

Abstract: Platelet rich plasma (PRP) therapy has accumulated considerable attention in last decades due to its potential ability in wound healing and tissue regeneration. The use of PRP speeds up the neovascularization and therefore increase the blood supply and nutrients influx necessary for cell regeneration in damaged tissue. Also, by increasing the blood supply, PRP stimulates the requirement, proliferation and differentiation of the cells, which are involved in the healing process. In the current study, we present 5 diabetes mellitus type 2 patients (2 males and 3 females) with developed foot ulcers over 1 to 3 years, hospitalized at Orthopedic Clinic, Clinical Centre in Nis, Serbia. In all patients, chronic infection was detected and all undergo hyperbaric oxygen therapy but without any success. Following the debridement, PRP (Regen Kit BCT 2A) was applied together with fibrin glue patch in all diabetic patients. In a period of 60 days, wound healing was complete in all treated patients. Also, wound healing was followed with complete eradication of bacterial infection in all evaluated diabetic patients. Obtained results may indicate a PRP as a promising agent for tissue regeneration in patients with diabetic foot ulcers.

NOTES

Platelet Gel, a new approach in wound care of chronical diabetic foot ulcers

Dr Renaud Heraud

Biography: MD, GP and emergency doctor, 3 years of bio-chemical study. Actually Medical Science Liaison for RegenLab in France, takes place in the wound care development project of RegenLab.

Abstract: Diabetes is a major health problem in developed countries, especially one of the diabetic complications is the diabetic foot chronical ulcers.

For example, in France, the diabetes prevalence was 5 % of the population in 2015, 3,3 million people, and it is still growing up. The occurrence of a foot ulcer in the diabetic people is estimated between 15 and 25 % in the course of their lives.

This complication gives rise to a major alteration of patients' quality of life and elevated health cost. Now the best of our knowledge, there is no treatment that permits a significative reduction of healing delay and management cost.

In this study, we tried to demonstrate that platelet gel produced with RegenBCT kit could be a great alternative to treat effectively diabetic foot ulcerations, permitting a significative reduction in healing delay and management cost.

The study was driven in Le Creusot, France, on 100 patients with neuropathic ulcers, 50 were treated with the usual treatment of the hospital, and 50 with RegenBCT platelet gel. Intermediary results showed a significant decrease in the healing delay and management costs.

NOTES

Effect of Autologous Platelet Rich Plasma/Thrombin gel (ACR®Plus) on the repair of complicated infected pluri-tissular wounds

Pr el-KHATIB Karim

Biography: Army Colonel. Associate Professor of the Val de Grâce, Paris. Head of pole of maxillofacial and reconstructive and plastic surgery at Mohamed V military hospital. Active member of several learned societies in Morocco, England and France. PES at the Faculty of Medicine of Rabat.

Abstract: Chronic wounds are defined by multiple pathophysiological and biochemical abnormalities that ultimately alter the normal healing process in Fragile patients with co-morbidities or inappropriate care after a traumatic or surgical wound.
A wound is considered chronic if it is not healed after 6 weeks.
They represent a problem for patients as
• they become disabling for health professionals
• they are facing a therapeutic impasse. The cost of their care, within the actual health system is very high due to the duration of the treatment.

All research aims to either heal chronic wounds that do not heal naturally or accelerate their healing.

In this work, we present our prospective study on the healing of infected multi-site wound wounds or chronic wounds in patients with comorbidities that affect the normal healing process and who are at therapeutic stalemate using the biological glue technique (A-PRP / thrombin gel) by evaluating the duration and quality of this healing.

NOTES

New Healing options for diabetic foot ulcers

Dr Oussama Almaghraoui

Biography: Army Colonel. Head of vascular surgery department at the Avicenne Marrakech Military Hospital. Vice President of the Moroccan Society of Vascular Surgery. Teacher at the Faculty of Medicine of Marrakech.

Abstract: Diabetic foot is a real health problem, 15% of diabetic person will have a diabetic foot with chronic wound which the healing is very difficult with a major risk of amputation. Platelet rich plasma is a potential wound healing treatment containing fibrin and high concentrations of growth factors that are supposed to accelerate the healing process. Many studies try to prove the efficiency of PRP with a very encouraging results.

We noticed a notable decrement in wound size over a relatively short time using the platelet-rich plasma technique with a very significate limb rescue. PRP is a safe and efficient option of diabetic foot ulcers healing.

NOTES

Autologous Platelet-Rich Plasma for Treatment of Chronic Leg Wounds

Dr Domantas Rainys

Authors: D.Rainys, A.Cepas, M.Kievisas, R.Rimdeika
Lithuanian University of Health Sciences

Biography: MD and Plastic surgeon at the Department of Plastic Surgery in the Hospital of Lithuanian University of Health Sciences Kaunas Clinics.

Abstract: We aimed to evaluate the effectiveness of autologous PRP gel in the treatment of chronic leg wounds compared to conventional treatment.

A prospective randomized study included 70 adult patients with chronic leg wounds. Patients were randomized into either PRP or control groups. Patients were followed up every two weeks until complete wound closure (CWC) or the end of the study (at 8 weeks). The primary endpoint of a study was the proportion of completely healed chronic. Secondary endpoints included the evaluation of healing progress and patient's satisfaction with the received treatment.

There were no significant differences in the rates of CWC – 29.03% of the PRP group patients and 29.63% of the control group (P = 0.960). Mean wound area size in PRP group decreased by 69.84%±36.35, whereas in control group – by 50.38%±49.40 (P = 0.116).

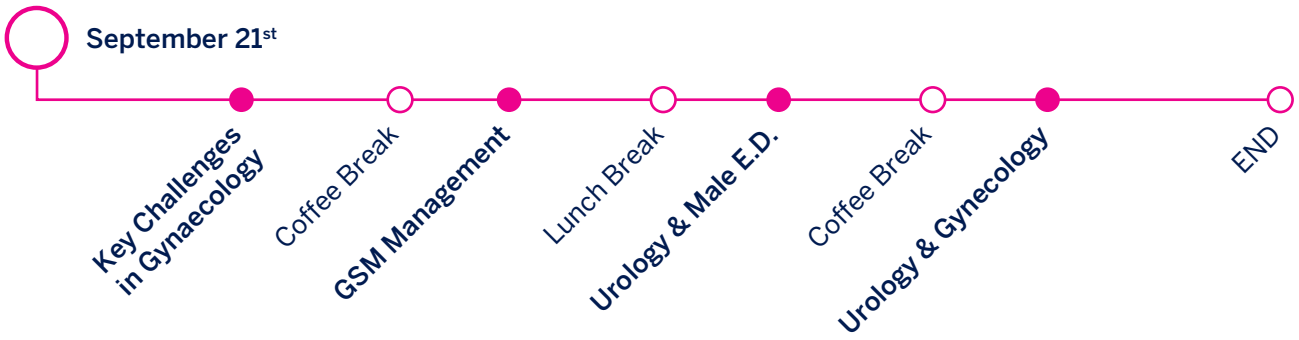
PRP group patients were more satisfied with the received treatment (VAS 4.71 vs 3.96, P =0.001).

PRP may improve the healing of chronic leg ulcers and relieve related symptoms. Treatment with PRP is well tolerated and highly rated by the patients.

NOTES

ROOM 2

Urogynecology



UROGYNECOLOGY

OPENING — **KEY CHALLENGES IN GYNECOLOGY**

9h00 Economic evaluation **Salvatore Russo/ Landi Italy**
Regulatory / MDR / Patent / I.P. **Antoine Turzi**

9h30 Non-invasive novel approach to challenging pelvic floor disorders for the Modern Women. Choice, Chance, Change. **Fariba Behnia Willison Australia**

9h50 Non-invasive novel approach to Women's Sexual Health. Every man needs a gynecologist! **Fariba Behnia Willison Australia**

10h00 Rational for Cellular-Matrix evaluation for the treatment of lichen sclerosus: biology, technology, pilot cases and the design of a clinical study protocol. **Agnieszka Nalewczynska Poland**

10h20 Discussion & Questions

10h30 Coffee Break

GSM MANAGEMENT

11h00 Cellular-Matrix for female sexual dysfunction **Ksenija _elih Martinec Slovenia**

11h20 Clinical experience in the treatment of atrophic vaginitis and "thin" endometrium with CellularMatrix and Regen A-PRP **Elena Ivanova Russia**

11h40 Efficacy of injecting platelet concentrate combined with hyaluronic acid for the treatment of vulvovaginal atrophy in postmenopausal women with history of breast cancer: a phase 2 pilot study. **Barbara Hersant France**

12h00 Discussion & Questions

12h30 **Lunch Break**

UROLOGY & GYNECOLOGY

13h40 Regen Lab A-PRP and cellular Matrix in male ED and female SD **Lina Ciaplinskiene Lithuania**

14h00 A-PRP as an eminent therapy for balanitis xerotica obliterans **Laura Lasinger Serbia**

14h20 PRP in Cosmetic Plastic Gynecology after C-section and laparotomy **Michael Barwijuk Poland**

14h40 Discussion & Questions

15h00 Coffee Break

UROLOGY & MALE E.D.

15h30 PRP in male sexual medicine: the search for scientific evidence **Ronald Virag France**

15h50 PRP in Erectile Dysfunction & Urology **Aleksandr Babych Ukraine**

16h10 Erectile Deficit Therapy by PRP in 50 patients **Nicola Maria Ilacqua Italy**

16h30 Discussion & Questions

17h00 **END**

Non-invasive novel approach to challenging pelvic floor disorders for the Modern Women. Choice, Chance, Change.

Dr Fariba Behnia-Willison

Biography: Gynecologist sub- specialised in minimally invasive surgery and advanced laparoscopy, with a special interest in utero-vaginal prolapse and urinary incontinence.

Senior consultant at Flinders Medical Centre and senior lecturer at Flinders University. She is a pioneer in the use of MonaLisa Touch laser, Platelet Rich Plasma (PRP), and vaginal stem cell use in Australia.

Abstract: It is estimated that up to 70% of women may experience prolapse or stress incontinence in their lifetime, 30-40% of whom are symptomatic, requiring treatment to improve their quality of life. Pelvic floor surgery is challenging; physically, socially and economically and modern women are searching for non-hormonal and non-invasive treatment options. Despite the growing evidence base for CO2 laser and PRP as safe, feasible and effective alternatives, reluctance to their use as a treatment modality is still present within the gynaecological and wider medical community.

The contemporary woman deserves choice and autonomy in their treatment decisions. As clinician-scientists, gynaecologists should embrace and encourage research into novel technologies that have the potential to enhance their patient's quality of life. In this new and changing environment, larger-scale studies investigating the long-term effects of CO2 laser and PRP in the treatment of pelvic floor and sexual disorders is essential. Many women are unwilling, or unable to have surgery, and they deserve choices, and changes in the current standard of care.

NOTES

Non-invasive novel approach to Women's Sexual Health. Every man needs a gynecologist !

Dr Fariba Behnia-Willison

Biography: Gynecologist sub- specialised in minimally invasive surgery and advanced laparoscopy, with a special interest in utero-vaginal prolapse and urinary incontinence.

Senior consultant at Flinders Medical Centre and senior lecturer at Flinders University. She is a pioneer in the use of MonaLisa Touch laser, Platelet Rich Plasma (PRP), and vaginal stem cell use in Australia.

Abstract: In part due to sexual empowerment through feminism, we are living in a culture that is beginning to embrace female sexuality, dissolving the stigma and shedding light on a once taboo subject. In line with this, gynaecological medicine is entering into a new era of being able to deliver more non-invasive, non-hormonal therapies to woman than ever before. This is not only good news for women, but for couple's sexual health. Men can experience erectile dysfunction (often undiagnosed), and this may be related to a lack of intimacy within the relationship with the woman experiencing pain. Regaining and sustaining intimacy for both sexes can reduce stress, improve sleep quality, minimise pain, boost the immune system and improve mental health.

For many women whom may have previously opted to abandon sexual activity, or put up with the pain associated, the increasing acceptance and availability of novel treatments offer innovative solutions. In one recent study, almost all 28 patients previously unresponsive to conservative management for Lichen Sclerosus (LS) saw clinical improvement in the size of their lesions with the use of PRP. PRP may offer minimally invasive, non-surgical, low risk and efficacious alternative treatments – that both men and women can reap the benefit from.

NOTES

Rational for Cellular-Matrix evaluation for the treatment of lichen sclerosus: biology, technology, pilot cases and the design of a clinical study protocol.

Dr Agnieszka Nalewczynska

Biography: She graduated from the Medical University in Warsaw (Poland) in 2006. Specialist in Obstetrics and Gynecology and general Aesthetic Medicine as well. Member of the Polish Society of Plastic Gynecology. Instructor in the treatment of gynecological problems with hyaluronic acid filler and PRP and CO2 laser.

Abstract: Lichen sclerosus is an inflammatory dermatosis with autoimmune pathogenesis. Its true incidence is unknown and likely underestimated. Administration of topical corticosteroids is the mainstay of medical treatment. Injection of platelet-rich plasma (PRP) into affected areas has been reported to result in the regeneration of normal skin. We performed the pilot study to evaluate the safety, efficacy and symptom improvement in patients with lichen sclerosus after treatment with PRP Cellular-Matrix.

PRP was prepared from autologous blood using the Regen Cellular Matrix Kit. PRP was administered twice over two months. We estimated symptoms and signs of the disease. In our opinion PRP+HA is a new treatment option for lichen sclerosus.

NOTES

Cellular-Matrix for female sexual dysfunction

Dr Ksenija Šelih Martinec

Biography: OBGYN is founder and works in Kalliste Medical Center in Slovenia. After finishing specialisation of Obstetrics and gynecology in 1992, she dedicated her work for helping women getting back their confidence and feeling feminine again also after deliveries and in postmenopause.

She is certified for Aesthetic Vaginal surgery by ECAMS. In her clinic she developed nonsurgical treatment for female urinary incontinence (SUI, OAB and UUI) and Female Sexual Disfunction by using EBDs and PRP. She brought O shot procedure in Europe in 2012 and is the pioneer in using PRP for treating Lichen Sclerosus.

Abstract: WHO describes sexuality as a central aspect of being human throughout life. But 25-63% of women of all ages and more than 80% of postmenopausal women have some degree of female sexual dysfunction. Treatment options were until recently not very promising. Last years there has been a great improvement in treating FSD with energy based devices and injectables. In 2012, Charles Runnels MD the first time injected Platelet Rich Plasma (PRP) into female sexual organs for improving sexual function. He invented an OShot® procedure where a doctor injects patient` own blood into clitoris and suburethraly into Skene`s glands to improve sexual wellbeing in women. Since then the procedure spreads through all the world and amazing results are shown.

PRP is an easy, low cost, and minimally invasive procedure to deliver high concentration of autologous growth factors and cytokines into injured tissue in physiological proportions. It has become a very important part of regenerative medicine and it helped to develop also regenerative gynecology where we got a new option for treating some very common gynecological problems like dry vagina, sexual dysfunction, Lichen sclerosus, urinary incontinence.

NOTES

Clinical experience in the treatment of atrophic vaginitis and “thin” endometrium with Cellular-matrix and Regen A-PRP

Dr Elena Ivanova

Biography: MD, PhD. Clinical Institute of Anti-aging Medicine. The Dr Ivanova has 9 years of extended clinical practice in gynecology-endocrinology and aesthetic gynecology. Speaker at Russian and International conferences. Regen Lab and laser treatments coach in aesthetic gynecology.

Abstract: Atrophic vaginitis is a consequence of decreased estrogen levels in postmenopausal women and premature ovarian insufficiency. The use of Cellular-matrix improves the blood supply to the mucosa, stimulates neocollagenesis. The «thin endometrium» is an actual problem at the present time. Intrauterine injection of the A-PRP allows stimulating the growth of the endometrium and improves the blood supply of tissues.

There were 15 patients with atrophic vaginitis, 9 of them in menopause and 2 with premature ovarian insufficiency.

There was one patient with a thin endometrium. Poor endometrial response (<7 mm) was even after the standard hormone replacement therapy (HRT). Intrauterine infusion of Regen A-PRP was performed. PRP was infused into the uterine cavity on the 7th day of menstrual cycle.

15 patients with atrophic vaginitis and vaginal dryness after 7 days of the application Cellular-matrix have noticed improvement in the moistening of the vaginal walls and increase sensitivity during sexual intercourse. The growth of endometrium after single intrauterine injection of the PRP was more than 8 mm. No patients experienced complications at follow-up.

Cellular-matrix appears to be a safe and feasible treatment of atrophic vaginitis. Regen A-PRP appears to be a safe and effective treatment of thin endometrium.

NOTES

Efficacy of injecting platelet concentrate combined with hyaluronic acid for the treatment of vulvovaginal atrophy in postmenopausal women with history of breast cancer: a phase 2 pilot study.

Dr Barbara Hersant

Biography: Barbara Hersant is a plastic surgeon in the department of plastic, reconstructrive, aesthetic and maxillo facial surgery of a university hospital near Paris (Henri Mondor Hospital, Creteil). She is assistant professor and she is the co-director of a the DUMEG (Diplome universitaire de médecine esthétique génitale). Her practice is specialized in vulvo vaginal, penis, bottom and breast surgery. She is also a researcher in the field of adiposed steam cells and platelets rich plasma for skin and nerve rejuvenation.

Abstract: Approximately 50% to 70% of breast cancer survivors are affected by one or more symptoms of vulvovaginal atrophy (VVA). For those who cannot take hormone therapy, autologous platelet-rich plasma combined with hyaluronic acid (A-PRP-HA) may provide a new alternative therapy for the treatment of VVA in postmenopausal women with history of breast cancer.

We enrolled 20 postmenopausal breast cancers survivors with VVA and a score of <15 on the Gloria Bachman Vaginal Health Index (VHI) comprised of five items including: vaginal pH, elasticity, fluid volume (secretions), epithelial integrity, and moisture.We administered intramucosal injections of A-PRP combined with HA (Regenkit) and performed clinical evaluations at 0, 1, 3, and 6 months. Primary endpoint: evaluation of vulvovaginal mucosa changes using the VHI; secondary endpoint: evaluation of dyspareunia and sexual dysfunction based on the Female Sexual Distress (FSD) score.

All participants (20 women) showed improvement in the clinical symptoms of vaginal dryness and dyspareunia. The VHI score showed a significant increase at 6 months, going from a total baseline score (pretreatment) of 10.7±2.12 to 20.75±4.8 ($P<0.0001$) at 6 months. Improvement in hydration and vaginal epithelial integrity was reported. A VHI score of > 15 showed a successful treatment outcome. The FSD score decreased significantly during the study, from a baseline score of 36.35±2.53 pretreatment to 30.15±2.47 6 months after treatment, representing improvement of 17% ($P<0.0001$, respectively). No adverse events were reported.

The injection of A-PRP-HA appeared to be a promising method to improve the trophicity and hydration of vaginal mucosa for the treatment of VVA in postmenopausal breast cancer survivors with contraindications to hormone therapy.

NOTES

Regen Lab A-PRP and Cellular-Matrix in male ED and female SD

Dr Lina Ciaplinskiene

Biography: PhD, Obstetrician- gynecologist, aesthetic gynecology specialist, sexual medicine doctor since 2011. The dissertation was defended on the topic of sexual medicine in 2015. Since 2017 working with man sexual problems including ED and peyronie's disease. In 2017 passed training courses with doctor Ronald Virag, Paris. Councle member of Lithuanian Society of sexual medicine.

Abstract: Sexual distress is an important factor in the etiology, maintenance, and treatment of sexual difficulties. A limitation in treatment of distressing sexual difficulties has been the lack of reliable methods. It has been shown that PRP therapy gives good results treating both man and women sexual problems. During the presentation evidence based information will be given about man erectile dysfunction and women sexual dysfunction including etiology, pathology and treatment using RegenKit A-PRP and Cellular-Matrix.

NOTES

A-PRP as an eminent therapy for balanitis xerotica obliterans

Dr Laura Lasinger

Biography: Medical Doctor, dermatovenerologist. Resort of dermatolovenerology and dermatosurgery. General manager at Medic Policlinic Subotica, Serbia. PRP therapy training Belgrade, 2016. Membership of World Society Interdisciplinary of Anti-Aging Medicine (WOSIAM)/WOSAAM, International Dermoscopy Society/IDS, Biobridge Foundation Knowledge Platform and Serbian Medical Chamber.

Abstract: The aim is to evaluate the functional, perceptive and aesthetic benefits of A-PRP therapy for balanitis xerotica obliterans. Facing a well-known, but not explored to the final edge of it's possibilities this autologous transplantation modality can offer, we are to give a clinical evidence with a case report.

Our patients were evidented with photodocumentation containing JPEG files taken before the procedure and 1 months postprocedure to testify for the success of intralesional A-PRP injections. Lichen sclerosus localised on male genital region as Balanitis xerotica obliterans is often missdiagnosed, not treated well or not treated at all, leaving the disease progress on its own and leads to disabilty of having normal sexual activity, causes physiological disturbance and provokes psychologic side effects noticed in male patients coping with it. A-PRP therapy performed in mild or middle severity balanitis xerotica obliterans, can likely establish an eminent position among other non-surgical procedures, providing good results, seen as the regression of sclerotic areas, restored sensibilty of the treated region of glans, tissue regeneration and improved foreskin elasticity.

NOTES

PRP in aesthetic Gynecology, after c-section and laparotomy

Dr Michael Barwijuk

Biography: Currently working in the Central Clinical Hospital of Ministry of the Interior and Administration in Warsaw at Clinical Department of Obstetrics, Female Diseases and Gynecological Oncology. Founder and member of the Polish Society of Plastic Gynecology (PTGP) and of the Polish Society of Aesthetic and Reconstructive Gynecology (PTGEiR). He performs equally highly effective treatments of aesthetic gynecology, as well as the minimally and micro invasive treatments using: laser, radiorequency, HIFU and PRP.

Abstract: PRP effects and indications in aesthetic medicine and dermatology have been known for many years.

What can we provide using PRP in intimate areas? Revitalization and rejuvenation of intimate skin, improvement of labia majora flexibility, tension and density as well as collagen remodeling in vagina, scar reconstruction after gynecological oncological procedures such as vulvar cancer, regeneration of vaginal mucosa, increasing its tension and flexibility and decreasing dryness of vagina and number of infections. Last but not least, due to injecting PRP we can accelerate wound-healing process after aesthetic gynecological procedures. There are new indications for which we are still developing the methodology in the middle of clinical trials waiting for publications. We have big hopes using PRP in Lichen sclerosus, vaginal atrophy and dyspareunia/vulvodynia according to what patients report but there is still a need of EBM standard. Aim of our clinical study (80 women) is to assess the impact of PRP on wound healing and its dehiscence in high-risk oncological women undergoing laparotomy because of ovarian/uterus cancer.

The second aim of the study is to assess the impact of PRP on reducing pain and sensation after cesarean section and laparotomy. Preliminary results are showing lower risk of dehiscence and lower pain after surgery.

NOTES

PRP in male sexual medicine: the search for scientific evidence

Dr Ronald Virag, MD & Hélène Sussman MD. CETI, Paris, France

Biography: Between 1972 and 1977 he was private practitioner in general and cardio-vascular surgery (creating one of the first private units in cardiac surgery). Since that time, Dr Virag's activity has been dedicated to the diagnosis and treatment of erectile dysfunction. Retired from his surgical duties, he his consultant at CETI.

Abstract: Our purpose in this presentation is to emphasize the potential role of PRP in the treatment of male sexual disorders, i.e. erectile dysfunction (ED) and Peyronie's disease (PD), excluding cosmetic use of PRP for the "so-called" locker's syndrome. Based on our experience with PD (250 patients) as well ED (150 patients) and a survey of the scientific literature we shall draw some directions to have specific guidelines to evaluate our results. For PD, for example, (Sex Health issue, 2017 doi: 1015761/SHI.1000102) we have shown in a series of 90 patients a 72% improvement rate based on the reduction of the angulation and or deformity and the decrease of the thickness of the albuginea, with a combination of PRP and HA obtained with Cellular-Matrix BCT-HA. In addition to these results based on objective data, some patients reported an improvement of their erectile function. Scientific evaluation of the results of PRP injections for ED is much more difficult. It is a multifactorial disease. Precise diagnosis is scarcely present. Patients try multiple therapies and encounter unfortunately fantasist use of PRP. Moreover, we need to better precise what we inject in terms of quality and quantity of PRP. We are testing the results of an increased quantity of PRP in both ED and PD. We shall propose to all experts to validate a scale of results based on these data.

NOTES

PRP in Erectile Dysfunction & Urology

Dr Aleksandr Babych

Biography: Graduated from National Medical University (Ukraine) in 2000, he became General surgeon in 2004. Since 2004 Urologist (Institute of Urology of the Academy of Medical Sciences of Ukraine). Since 2016 Thread lift & dermal fillers injection techniques trainer. Since 2017 Trainer in "Avicenna" (Regen Lab, Ukraine).

Abstract: As is known, male erectile function is a multistage cascade mechanism.

The penile hemodynamic and the smooth muscles relaxation of penile erectile tissue plays a key role in the erectile process. Structural changes of the smooth muscles of the walls of arterioles, fibrous envelope, fibroelastic components of the trabeculae, cavernous smooth muscle and endothelium leads to a decrease of penile perfusion, as well as to a violation of the mechanism of erection response. This results in the emergence of vasculogenic erectile dysfunction (ED).

PRP-therapy is justified and could be an option a method for treating ED due to the regenerative effect of PRP on the structural elements of erectile tissue.

Patients with a vasculogenic ED confirmed by Penile Doppler Sonography (PDS) underwent a course of intracavernous injections of PRP. Outcomes have been evaluated by means of questionnaire and PDS method before the treatment and at the different observation stages. Serious side effects associated with the treatment were not observed.

Obtained data indicate that PRP-therapy is an effective and safe method of treatment of ED. Platelets-rich plasma alone could be an option for treatment of ED.

NOTES

Erectile Deficit Therapy by PRP in 50 patients.

Dr Nicola Ilacqua

Biography: Graduated in Medicine and Surgery and specialized in Nephrology and Urology. Previously researcher at the Institute of Urological Sciences of the University of Messina; director of a center affiliated with the Calabria Region for ESWL and president for 9 editions of the National Congress of Progress in Andrology held in Reggio Calabria. Today, director of the «Multidisciplinary Andrology Surgery» unit of the ASP of Reggio Calabria since 2002. Co-author of 2 books and author of thirty-five works of publication.

Abstract: The purpose of the research is to treat the erectile deficit (ED) diagnosed by questionnaire IIEF 5 and Dynamic Penile Ecocolordoppler (EPD), using Platelet-rich plasma (PRP) and evaluate its effectiveness.

PRP prepared using RegenKit was used to treat 50 patients affected by ED diagnosed from IIEF 5 score less than 11 and by means of EPD with values of VPS less than 20 cm/sec. The age of the patients ranged from 26 to 61 years. We performed 4 sessions of PRP followed by FIC of 10 mg of PGE1, spaced from 7 to 14 days. From the first session, 4 months of treatment with Phosphodiesterase 5 Inhibitors (IPDE5) at full dose plus 3 g of Citrulline for OS have been prescribed. IIEF 5 questionnaire and EPD were evaluated after the last PRP injection and at 4 months and 6 months from the first PRP injection.

After a follow-up of 12 to 18 months, 41 patients presented clinical remission of ED symptoms, accompanied by improvement of the final EPD with VPS values between 27 and 35 cm/sec and improvement of the final IIEF5 score between 21 and 25. The 9 patients who did not benefit fully presented, however, an improvement of the parameters of IIEF5 and EPD at the final control. Patient follow-up continues with new clinical control after another 6 months.

The treatment of ED by PRP proves to be effective in a large percentage of patients. The clinical remission of the disease is observed in patients under conditions inserted in a therapeutic route. The best results were observed in younger patients, and in patients without cardiovascular diseases and diabetes. In this study, we chose not to include patients with advanced post-surgical ED because we considered that PRP is most indicated for vascular forms of ED.

In perspective, we would like to complete the protocol by analyzing means of biopsy of the cavernous bodies with NitrOxydosynthetase histochemical examination which highlights the functional activity of endothelial cells.

NOTES

ROOM 3

Musculoskeletal

MUSCULOSKELETAL

OPENING	**OA MANAGEMENT WITH CELLULARMATRIX**
9h00	Cellular-Matrix PRP-HA for patients with osteoarthritis having had an unsatisfactory clinical response to hyaluronic acid alone. Result of a pilot study, multicenter French study with long-term follow-up. **Jean-Luc Renevier Jean-François Marc France**
9h30	Therapeutic application of Cellular matrix /PRP+HA/, compared with two different types of Hyaluronic Acid /HA/ in Knee Osteoarthritis. Prospective, Double- Blind, Randomized, Controlled Study **Branko Barac Serbia**
9h50	Midterm clinical experience with Cellular-Matrix in the treatment of osteoarthritis **Michele Abate Italy**
10h10	Discussion & Questions
10h30	Coffee Break
	OA MANAGEMENT WITH CELLULARMATRIX
11h00	Indications for Cellular Matrix (PRP-HA): Big Joints (meniscal healing, arthritis, bone marrow edema) and Small Joints (talar dome injury, other). **Philippe Adam France**
11h20	Use of PRP and PRP-HA (ACP-HA) in the athletic and degenerative foot and ankle joints **Berend-Tüge Berendsen Germany**
11h40	Autologous Platelet Rich Plasma and Hyaluronic Acid combined single injection in the treatment of osteoarthritis of the knee **Gorav Datta UK**
12h00	Platelet rich plasma mix with hyaluronic acid in knee osteoarthritis treatment, 12 months follow-up **Valdis Goncars Latvia**
12h20	Discussion & Questions
12h30	**Lunch Break**
	TENDONS & SPINE SURGERY
13h40	Use of Platelet Rich Plasma in Tendons and Muscular Lesions **Philippe Peetrons, Jean-Marc Grison Belgium**
14h00	A-PRP/PRP ATS/Cellular-Matrix Atlas for conservative therapies and surgery treatments **Christian Hendrich Germany**
14h20	From intervertebral disc degeneration to regeneration **Gianluca Vadalà Italy**
14h40	Discussion & Questions
15h00	Coffee Break
	ORTHOPAEDIC - DENTAL SURGERY & MEDICO-ECONOMIC
15h30	Use of Platelet Rich Plasma (PRP) and Bone Marrow Derived Stem Cells (BMSC) in tissue regeneration. **Alberto Gobbi Italy**
15h50	A-PRP ATS for Bone Augmentation in dental implant surgery **Federica Isaia Italy**
16h10	The potential economic role of regenerative therapy in the treatment of knee osteoarthritis. Scenario analysis: the clinical outcomes thresholds needed to handle the growth of socioeconomic costs of knee OA. **Salvatore Russo/ Landi Italy** Regulatory / MDR / Patent / I.P. **Antoine Turzi**
16h40	Discussion & Questions
17h00	**END**

Cellular-Matrix PRP-HA for patients with osteoarthritis having had an unsatisfactory clinical response to hyaluronic acid alone. Result of a pilot study, multicenter French study with long-term follow-up.

Dr JL Renevier, Dr JF Marc, Dr Philippe Adam, Dr J Le Coz, Dr Y Prothoy, Pr N Sans

Biography:
Jean-Luc Renevier
Rheumatologist. Former expert for the HAS (Haute Autorité de Santé). Assistant physician at the APARC Rehabilitation Center in Rosny-sur-Seine, Yvelines. Diploma of legal compensation of bodily injury. Diploma of aptitude for medical expertise.

Jean-François Marc
Rheumatologist, MD, PhD. Since 2014, CEO AGCOSS SAS, Health Consulting Agency & Medical Research. Titular Member of Rheumatology French Society (SFR), Member of national office of Professional postgraduate training, Member of national office of Fundraising for research in rheumatology and Member of the editorial board of the International journal of clinical rheumatology.

Abstract: French multicenter study, prospective 9 months with 3 injections of 2 ml of PRP + 2 ml of non-crosslinked HA in joint knee following a very simple procedure.

There is a significant difference in the change in the average WOMAC A1 before the start of treatment and pain 36 weeks after starting treatment. This difference was also significant between the first and the second injection and between the second and third injection. There is no significant difference in pain scores as the radiological grade (II-III). No significant side effects reported.

The response to the primary efficacy endpoint showed a decrease in the average WOMAC A1 from 5.87 at baseline to 1.89 at 9 months, statistically significant.

During the follow-up for 4 years, almost 60% of patients still had benefit 2 years after the end of treatment and at 4 years only 21% of patients had knee remplacement…

NOTES

Therapeutic application of Cellular matrix /PRP+HA/, compared with two different types of Hyaluronic Acid /HA/ in Knee Osteoarthritis. Prospective, Double- Blind, Randomized, Controlled Study

Dr Branko Barac

Biography: MD, PhD Subspecialization in Rheumatology, Institute of Rheumatology, Belgrade Serbia. Member of ethical committee, "Institute of Rheumatology, Serbia"; Member of the International Society of the Study of the Aging male; member of the International Society of Gynecological Endocrinology; member of the Serbian Multidisciplinary Society for Menopause and Andropause; member of the Serbian Society of Rheumatology and member of the Serbian Society of Endocrinology.

Abstract: The aim of this study was to compare the efficiency of Platelet rich Plasma combined with Hyaluronic Acid (Cellular-Matrix (CM)) injections, versus two different types of Hyaluronic Acid injections in treatment of knee osteoarthritis. Study design: prospective, randomized, double-blind, controlled study that includes: 90 patients suffering from knee osteoarthris divided in III groups: I Group 30 knees treated with CM, 3 injections (one injection/2nd week), II Group 30 knees treated with 2% non cross linked sodium hyaluronate (Arthrovisc, AV), 3 injections (one injection/week) and III Group 30 knees treated with 2% non cross linked sodium hyaluronate with manitol (Ostenil plus, OP), 3 injections (one injection/week). We measured VAS of pain, WOMAC, KOOS, IKDC scores and cartilage thickness for each patient on every visit at 0,2,6,12 months after the last application of injection. Blood sample is taken from each patient before the treatment starts. Each injection is administrated under the sonography control, by one sonographer. Included and blinded patients were > 30 years with history of chronic (at least 4 months) pain or swelling of the knee and imaging findings of degenerative changes of the joint (Kellgren-Lawrence Score up to 3) at X-ray evaluation or US findings of degenerative changes and VAS > 50. The independent rheumatologist, blinded for the treatment option, examined the patients and measured the cartilage thickness by US at each visit.

There were statically significant differences, $p<0.05$, in CM groups comparing to AV and OP group in VAS, WOMAC, KOOS and IKDC score after 2 months, even in all groups we found improvement in all these parameters. There were high statiscally significant differeneces, $p<0.01$, in CM group compering to AV and OP group in VAS, WOMAC, KOOS and IKDC score after 6 and 12 months. In both groups treated with hyaluronic acid we found deterioaration in VAS, WOMAC, KOOS and IKDC score after second month. In group terated with CM, we found statistically significant improvement in cartilage thicknes , $p<0.05$, after 2 and also after 6 and 12 months in medial and high statistically significant improvement, $p<0.01$, in lateral compartments.

NOTES

Midterm clinical experience with Cellular-Matrix in the treatment of osteoarthritis

Dr Michele Abate

Biography: MD, PhD and Specialist in Physical Medicine and Rehabilitation. He is a medical researcher with experience in rehabilitation (mostly orthopaedic and sport patients) and ultrasound diagnosis of musculoskeletal disorders.

Abstract: In our Unit we have been using during the last years different treatments for the OA management. Among them, there is growing interest for therapies (HA and PRP) able to stimulate the biological articular milieu and therefore favour a better healing response.

Here we report our experience with the use of Cellular-Matrix (PRP+HA) for the treatment of large joint OA.

More than 200 patients suffering from mild-moderate OA have been treated. Different dosing schedules have been used. Clinical and functional evaluations were performed at baseline and after 3 and 6 months. The same data were collected among patients previously treated with HA or PRP alone.

In the treatment of knee and ankle OA positive results were observed in younger patients with low degree OA. The higher amount of PRP showed slighlty significant improvement. The infra-group comparison showed mixed results between groups in all the clinical evaluations.

Patients suffering from hip and shoulder OA did not experience significant clinical results. In the management of hip OA better outcomes were observed with HA.

In conclusion Cellular-Matrix exhibit better therapeutic activity in the treatment of knee and ankle OA while the effects on hip and shoulder joint should be evaluated by controlled trials.

NOTES

Indications for Cellular Matrix (CM, PRP-HA): Big Joints (meniscal healing, arthritis, bone marrow edema) and Small Joints (talar dome injury, other).

Dr Philippe Adam

Biography: Imaging Physician Interventional Radiology. Member of European Society of Radiology. Regenlab Doctor Consultant for Musculo-Skeletal Pathology and Sport Medicine. INSEP PRP Expert, PRP Board / French Society of Rheumatology. Imaging and Regenerative Medicine Department at Medipole Garonne Sports Clinic, France.

Abstract: CM Big Joints: meniscal and labral healing, arthritis, bone marrow edema. CM Small Joints: talar dome injury, arthritis, acromio-clavicular conflict, TFCC. 7 years of use in Medipole Garonne with a score of 2328 procedures (knees 1957, hip 140, ankle 114).

Early medical treatment of cartilaginous and fibrocartilaginous lesions but also BME by CM was preventive for arthritis with a real slowdown, and efficient for pain management. US guided CM injections into the joints can replace HA alone after failure and limit in the future the use of prosthetic devices. Therapeutic effects of CM were much more sustainable by modification of joint environment owing to the biological synergy of PRP and HA.
In a French multicentric study including patients of Medipole Garonne (KL 2 and 3, knee) we were able to collect long-term data for 62 out of 77 study participants (80.5%). 59.7% of the them still perceived substantial clinical benefit 2 years after the treatment, while 50% were still satisfied with it at the time of the survey (4 years after the treatment). For 79% of them, the treatment allowed avoiding surgery.

The great question will be the good frequency of CM for further improving clinical benefits.

NOTES

Use of PRP and PRP-HA (A-CP-HA) in the athletic and degenerative foot and ankle joints.

Dr Berend-Tüge Berendsen

Biography: MD, PhD at the Christian-Albrechts-University of Kiel and University of Alabama (USA) and University of South Alabama (USA). Training as a specialist in orthopaedics and rheumatology at the Medical University of Lübeck, Hanover Medical School and Bavarian Rheumatology Centre Bad Abbach. Specialist in sports medicine with several years of experience as team physician of the National German Athletics Association (DLV) including the support of the U23 national team, junior elite team (DLV) and running team at international and national championships. Team physician of the National Cheerleader and Cheerdance Team Germany. Highly experienced in conservative and surgical treatment of osteoarthritis.

Abstract: The athletic foot and ankle joint can develop symptoms similar to the degenerative joint. Pain with or without movement, swelling and limited range of motion. The cartilage shows changes in the quality and quantity.

The patients and the athletes wish to be pain free and free in motion as soon as possible and without time limitation.

The treatment with PRP/PRP-HA of 145 foot and ankle joints in athletes and 155 foot and ankle joints in degenerative patients over 1 year now shows us promising results.

results: excellent	85 (athletes)	/	90 (degenerative patients)
good	45	/	47
fair	10	/	9
Non-responders	5	/	9
Complications:	pain over 1 day:		1 (3 days) / 3 (2 and 3 days)
	no infection.		

The details will be presented. The treatment with PRP/PRP-HA in the foot and ankle joint seems to be a good conservative method with less side effects.

NOTES

Autologous Platelet Rich Plasma and Hyaluronic Acid combined single injection in the treatment of osteoarthritis of the knee.

Dr Gorav Datta

Biography: Dr Datta is a consultant orthopaedic surgeon specialising in hip and knee surgery, stem cell therapy and regenerative orthopaedics. He is actively involved in research and has run a number of clinical trials investigating joint preservation treatments.

NOTES

Platelet rich plasma mix with hyaluronic acid in knee osteoarthritis treatment, 12 months follow-up

Dr Valdis Goncars

Kristaps Blums1, Valdis Goncars2,3
1 Riga East Clinical University hospital, Riga, Latvia
2 Riga Hospital of Traumatology and Orthopedics, Duntes str 22, Latvia
3University of Latvia, Raina blvd 19, Riga, Latvia

Biography: Trauma and Orthopaedic surgeon. Since 2011 he is researcher at the Latvian University and he is part of the teaching staff for Traumatology and Orthopaedic. He works on clinical studies on arthroplasty evacuated tissue as source for the mononuclear cells and on the use of bone marrow mononuclear cells in the treatment of knee or hip osteoarthritis.

Abstract: This is a prospective case series study conducted in Latvian state hospital of traumatology and orthopaedics during years 2016 and 2017. Patients were included in the study according to the following inclusion criteria: Kellgren Lawrence grade I-III knee OA and age from 18 – 65 years. The patients received PRP and HA mixture prepared with the Cellular-Matrix, manufactured by Regen Lab. The treatment protocol consists of 3 injections into the patient's knee while using aseptic technique. First injection is performed at beginning of the study and then repeated after 2 and 6 months. Patients were evaluated with the KOOS score (5 subscales: pain, symptoms, activity and daily living, sports and recreation, quality of life) before and 1, 2, 6 and 12 months after intra articular injections. The results of 30 knee joints were evaluated.

Statistically significant improvement was observed in all subscales in various time points. After 2 months peak effect was achieved that lasted at least 6 months. At 12 months effect starts to diminish, as statistically significant improvement was no longer observed in the pain and activity and daily living subscales. Exception can be seen in quality of life subscale where improvement continued to increase during all follow up period.

This is a safe method for treating knee OA patients without any serious side effects over 12 months time period. Approximately half of the patients can reach minimal important change in KOOS score after PRP and HA mixture injections after 12 months.

NOTES

Use of Platelet Rich Plasma in Tendons and Muscular Lesions

Dr Philippe Peetrons & Dr Jean-Marc Grison

Biography:
Dr Philippe Peetrons
Head of medical imaging department in Hopital IRIS SUD, in Brussels, Belgium, he is actually Professor in medical imaging in the Free University of Brussels. He is a member of European Society for Skeletal Radiology and board trustee of the ultrasound subcommittee of this society, member of the International Skeletal Society and member of many reviewing committees in ultrasound and radiology literature. His name is now associated to a grading system of muscular injuries using Ultrasound and MRI, which is widely used in sports medicine literature.

Abstract: PRP injections in tendons and muscles gained popularity from 2011 when the World AntiDoping Agency (WADA) accepted this treatment for athletes. Since March 2011, our team performed around 1200 injections mainly in tendons, more rarely in muscles. The reason of this difference is due to the treatment difficulty in tendinopathies with patients still complaining after months or even years after other conservative treatments, including physiotherapy, laser therapy, oral NSAID treatment, steroid injections and shock wave therapy, whereas muscle tears are in the vast majority cured within 5 to 6 weeks of resting and physiotherapy.

We inject only one time in the vast majority of the cases, 1 ml (up to 2 in some cases) inside the tendon, always under echoscopic guidance, inserting the needle near the clefts seen in the tendons and in a region wher microvascular Color Doppler shows the majority of the neo-vessels typical of the tendinopathy.

It's important to remember that tendonitis doesn't exist ? The lesions in the tendons are not inflammatory but degenerative. Therefore a regenerative treatment such as PRP finds all its place in this pathology.

As we don't perform fenestrations of the tendon with the needle, in opposition to other teams, we don't need to ask the patient to use crutches or to wear a cast or any other method of contention, except in the plantar fascia injections where it may be advisable to discharge the foot for 2 or 3 weeks.

We don't send the patient back to the physiotherapist as a study performed in our department on 33 high level athletes shows no benefit for physiotherapy after the injection of PRP.

We ask the patient to stop any athletic or sports or work activity involving the injected tendon, for 3 to 4 weeks depending of the severity of the lesions shown by ultrasound.

The main questions still debated for tendon therapy with PRP are due to the heterogeneity of what is injected, using different devices. Poor or rich concentration ? Leucocyte free or rich plasma ? Number of injections ? Tendon fenestration or not ? Analysis of the literature still shows no real consensus on many of these questions.

NOTES

A-PRP/PRP ATS/Cellular-Matrix Atlas for conservative therapies and surgery treatments

Dr Christian Hendrich

Biography: Specialist for Orthopaedics and Trauma Surgery, Sports Medicine, Special Orthopaedic Surgery, Medical - Hospital – Manager. He works on hip and knee using minimally invasive endoprosthetics with development of own special instruments and prosthesis replacement operations. He is specialized in shoulder surgery, sports medicine with joint endoscopies, cartilage and cruciate ligament surgery, spinal pain therapy, osteoporosis, aesthetic foot surgery, stem cell transplantation for orthopaedic diseases.

NOTES

From intervertebral disc degeneration to regeneration

Dr Gianluca Vadalà

Biography: Dr. Gianluca Vadala is currently employed at the Campus Bio-Medico University (UCBM) Hospital of Rome in the division of Orthopaedic Surgery. He obtained the PhD in Tissue Regeneration in 2012. In 2013 he received the prestigious AOSpine Young Research Award for his enthusiastic research in spine surgery and regenerative medicine. Dr. Gianluca Vadala's clinical activity is mainly focused on Regenerative medicine in the orthopedic, Spine Surgery and Trauma fields.

Abstract: Low-back pain (BP) is one of the major health problems in western society and is a leading source of disability in people under 45 years of age. Intervertebral disc degeneration (IDD) has been identified as the main cause of this problem. Stem cells therapy might support disc (IVD) regeneration by overcoming the limitation of self-regeneration, which is considered the main cause of degeneration-mediated functional loss of the IVD. The potential use undifferentiated bone marrow mesenchymal stem/stromal cells (MSC) has been described with promising perspectives. Recent evidences showed that intradiscal injection of MSC effectively alter the course of IDD in vivo and is clinically safe. However, many unanswered questions remain in the translation to the clinical phase, such as the most reliable transplantation method including the carrier choice and the optimal cell dose.

We developed a novel transpedicular approach as a potential new route for IVD regeneration and, whilst maintaining an intact AF. Using this approach, we demonstrated that an effective MSCs dose delivered with a clinical relevant hydrogel through the end-plate route effective alters the course of IDD in a transpedicular nucleotomy model in large size animal. This study brings a significant contribution towards the translation of regenerative therapies for the biological restoration of degenerative changes in the IVD, which is crucial to improve present clinical treatment and life quality of several patients.

NOTES

Use of Platelet Rich Plasma (PRP) and Bone Marrow Derived Stem Cells (BMSC) in tissue regeneration.

Dr Alberto Gobbi

Alberto Gobbi M.D.1, Graeme P Whyte M.D., MSC, FRSC1, 2, Katarzyna Herman M.D.1
1. OASI Bioresearch Foundation, Via Amadeo, G.A., 24-20133 Milano – Italy
2. Cornell University, Weill Medical College; New York Presbyterian Hospital, Queens, New York, NY, USA

Biography: Doctor Alberto Gobbi is an Orthopaedics and Traumatology and Sports Medicine specialist. He is the Director and President of O.A.S.I. Bioresearch Foundation NPO and serving as President of International Cartilage Regeneration Joint Preservation Society (ICRS).

Abstract: Stem cells are considered to be undifferentiated precursor cells that have potential for self-renewal and are capable of differentiating into a wide variety of cell types and may be found in blood, bone marrow and adipose tissue. These cells may be used in injectable form i.e. multipotent cells sourced from bone marrow aspirate.

When used with enhancement such as growth factors found in platelet rich plasma (PRP), stem cells can stimulate healing in damaged tissue. It has been shown that this kind of therapy provides good long-term results in anterior cruciate ligament primary repair. What is more stem cells can be used in conjunction with biologic scaffolds for more directed therapy of osteochondral lesions? Repair of high grade chondral lesions using a hyaluronic acid-based scaffold with activated bone marrow aspirate concentrate has proven to provide good to excellent clinical outcomes, and durable cartilage repair, at medium and long-term follow-up that is superior to marrow stimulation, and comparable to autologous chondrocyte implantation.

Further research is necessary to better elucidate the expected benefits of each of these biologic therapies, and to what extent these therapies may alter the natural history of musculoskeletal pathology.

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A-PRP ATS for Bone Augmentation in dental implant surgery

Dr Federica Isaia & Dr Leonardo Isaia

Biography:

FEDERICA ISAIA

Dentist graduated from University Alfonso X el Sabio (Madrid) in 2013 and specialized in Periodontology and Implantology from Tufts University School of Dental Medicine (Boston) in 2017. Diplomate of the American Board of Periodontology 2018. Registered with the SIDP (Italian Society of Periodontology), AAP (American Academy of Periodontology), in the National Association of Italian Dentists, and at the IAO (Italian Academy of Osseointegration).

LEONARDO ISAIA

Medical doctor from University of Padova in 1979 and specialized in Dentistry in 1982. Private practice for 40 years in Padova mainly on Mucogingival surgery, Esthetics, ATM disorders and Implantology. He attended national and international courses in Orthodontics, Mucogingival Surgery and Aesthetic Surgery, Gnathology and Implantology. Registered in the Professional Register of Dentists of Padua, to the Medical Association Member of the SIDP (Italian Society of Periodontology) and in the National Association of Italian Dentists.

Abstract: PRP gel can be successfully used in dentistry alone or mixed with biomaterials in order to achieve bone regeneration and soft tissue maturation. In this presentation we will show the results obtained in our scientific study. We demonstrated the advantage of using PRP in hard tissue reconstruction before the placement of dental implants when compared with traditional techniques.

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The potential economic role of regenerative therapy in the treatment of knee osteoarthritis. Scenario analysis: the clinical outcomes thresholds needed to handle the growth of socioeconomic costs of knee OA.

Dr Salvatore Russo & Dr Stefano Landi

Biography:
Dr Stefano Landi
Master Degree in Statistics and economics in University Bicocca, Milan and PhD in Health economics at University of Genoa
From February 2016 to now: Research Fellow in "Health technology innovation and sustainability of health systems" University Cà Foscari Venice
Field of interest: Health inequalities, Pharmacoeconomics analysis, Health Technology Assessment.

Abstract: Osteoarthritis (OA) is a chronic and degenerative pathology affecting joints. OA incidence is steeply increasing because of the ageing of the population and the increasing presence of risk factors such as obesity. OA burden of disease is correlated to a high economic impact, in terms of both direct health-related costs and indirect costs. (between 0.25% and 0.50% of a western country gross domestic product (GDP). The main direct health-related cost driver is the cost for joint replacement surgery (arthroplasty). The steady increasing of surgery incidence will make the costs grow in the foreseeable future. Both OA epidemiologic and economic trend are putting under pressure the quality of life of the individuals and the resources of the health systems. A possible solution is slowing down the progression of the pathology in order to delay (or to avoid) the surgery. In this scenario regenerative therapies can play a crucial role to improve the quality of life of the people affected by OA and to restrain the growth of socioeconomic costs, helping the sustainability of our healthcare systems.

The presentation will show a scenario analysis with different level of ability to delay the surgery. A Montecarlo simulation have been used to create different scenarios.

Simulations aimed to point out the clinical outcomes thresholds needed to handle the growth of socioeconomic costs of knee OA. Since regenerative therapy may help to lower the burden of the joint replacement surgeries, this preliminary simulation represents a first attempt to estimate potential savings, which may increase the NHS willingness to pay for the acquisition of regenerative therapies.

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