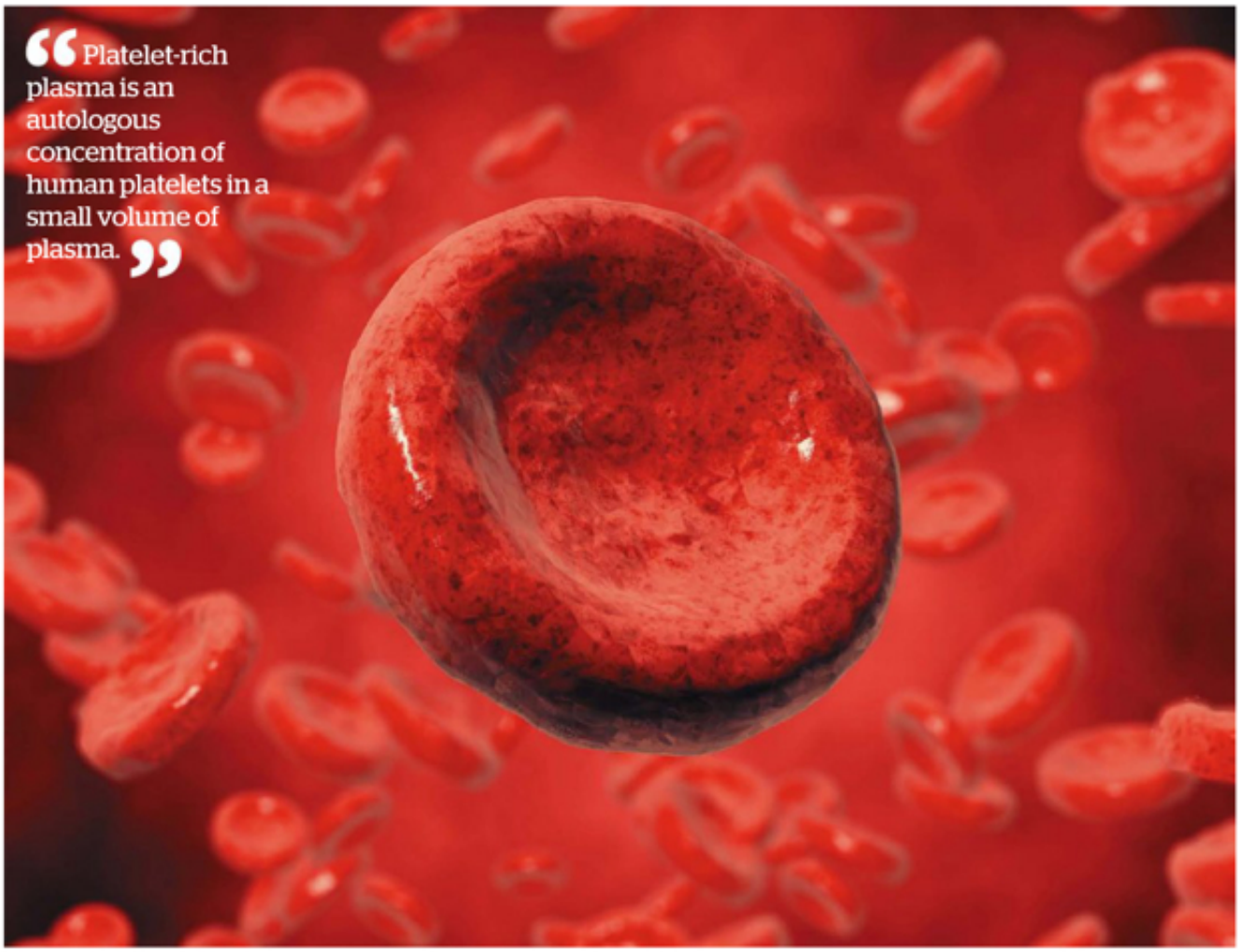


PLATELET-RICH PLASMA: NEW DEVELOPMENTS IN AESTHETIC MEDICINE

Daniel Sister reviews the literature, preparation process and mechanism of action of platelet-rich plasma formations for use in aesthetic medicine

ABSTRACT
Over the past 20 years, the demand for cosmetic procedures among our ageing population has evolved, and there has been an increasing demand for patients to seek less invasive procedures for facial rejuvenation. The improvements in knowledge and techniques, and the introduction of longer-lasting soft tissue fillers have led to an increased acceptance of cosmetic treatments. More patients are looking for less invasive procedures over surgical treatments. Platelet-rich plasma (PRP) is an autologous concentration of human platelets in a small volume of plasma. It is a safe treatment and, thanks to the included growth factors, may represent the perfect option for a large number of procedures.

THE DEMANDS OF OUR AGEING population have evolved substantially over the past few decades, with patients from the 'baby boom' generation now well into their 60s and demanding to look as young and as healthy as possible. These requirements have been coupled with the desire of the majority of patients to seek less invasive procedures for facial rejuvenation.

The improvements in our knowledge and techniques, and the introduction of longer-lasting soft tissue fillers, have led to an increased acceptance of cosmetic treatments in society as a whole. A greater number of patients are now looking for less invasive procedures over surgical treatments. However, Sclafani[1] argues that 'the ideal soft tissue filler has not yet been found, one which seamlessly integrates into the surrounding tissues, is easy to place, inexpensive, readily available and persistent. Currently available soft tissue fillers may be degraded, elicit a foreign body response with encapsulation and can be quite expensive'.

It is now known that the facial ageing process is not only a result of gravity, the disappearance of the malar fat pad, and/or lack of collagen, but is a complex puzzle involving a variety of facial elements, which occurs as a cascade effect. This process affects the four main facial layers – bone, muscle, fat and skin – the changes of which fall in two directions simultaneously, from the outside skin layer inward towards the bone, and also from the bone outwards towards the skin. Any modification in one layer will affect the next to progressively impact the effects of ageing.

The most significant change in the first layer, the bony facial skeleton, occurs in the facial apertures. The nose and orbits actually increase in size with age, by as much as 20%; the eye sockets largen over time and the infraorbital bone, just under the eye, moves backwards. Consequently, all other structures (muscle, fat and skin tissues) begin to descend and slip from the surface of the receding bone. Gravity is partly the cause of this effect, but in combination with the changes to the facial skeleton.

Contrary to popular belief, the facial muscles actually tighten with age, not loosen. This can be seen in the platysmal bands of the neck, which stretch from the chin to the clavicle and become more pronounced with age, similar to the appearance of crow's feet and deep-set glabella lines. At the same time, the amount of fat present in the facial fat pads decreases with age and causes a gaunt appearance, resulting not only in volume-loss, but also a lack of efficient hydrating and elastic functions. The fibroblast cells producing elastin, collagen and hyaluronic acid (HA) work best when they're under a degree of stretch. A lessened volume of fat and stretch results in poorer skin functions and the resulting sagging effect.

Ultimately, the process of facial ageing is a complex cascade in which each facial element affects and interacts with the other.

DANIEL L. SISTER, MD, FRCM, BCAM, NYAS, is Aesthetic Doctor, Dr Sister Ltd, London, UK

email: drsister317@gmail.com

KEYWORDS
PRP, dermal rejuvenation, ageing, literature review

What is platelet-rich plasma?

Platelet-rich plasma (PRP) is an autologous concentration of human platelets in a small volume of plasma. It is a multidisciplinary procedure, with a great amount of supporting literature for the field of cosmetic surgery, as well as oral implantology, ophthalmology, orthopaedics and sports medicine.

Plasma, which comprises 55% of blood fluid, is mostly water (90% by volume), and also contains dissolved proteins, glucose, mineral ions, hormones, carbon dioxide (plasma being the main medium for excretory product transportation), platelets, and blood cells themselves. As it is a concentration of platelets, it is also a concentration of the seven fundamental protein growth factors proved to be actively secreted by platelets to initiate all wound healing (*Table 1*). These growth factors include the three isomers of platelet-derived growth factor. All of these growth factors have been documented to exist in platelets[2,3], but the platelets will need to be activated. On activation, they will release alpha granules, within which those growth factors are stored.

In addition, the activated thrombocytes have a multitude of signalisation molecules on their surface: CD9, CD-W17, CD41, CD42a-d, CD51, CD-W60, CD61, CD62P, CD63. As these concentrated platelets are suspended in a small volume of plasma, PRP is more than just a platelet concentrate; it also contains the three proteins in blood known to act as cell adhesion molecules for osteo-conduction and as a matrix for bone, connective tissue, and epithelial migration. These cell adhesion molecules are fibrin itself, fibronectin, and vitronectin.

Platelet origin, morphology and distribution

Platelets are cytoplasmic fragments of megakaryocytes (a type of white blood cell), which are formed in the marrow, are round or oval in shape, and approximately 2 µm in diameter[4]. They have a trilaminar cell membrane with a glycoprotein receptor surface overlying and partially interspersed with and penetrating a bilayer of phospholipids and cholesterol[5].

Platelets lack nuclei but contain organelles and structures such as mitochondria, microtubules, and granules (α-, δ-, and λ-)[6,7]. There are approximately 50–80 alpha granules per platelet, each bound by a unit membrane and formed during megakaryocyte maturation[8]. The granules are approximately 200–500 nm in diameter and contain over 30 bioactive proteins, many of which have a fundamental role in haemostasis and/or tissue healing[8,9]. ▷

▷ The platelet cytoplasm contains an open, canalicular system that increases the effective surface area for intake of stimulatory agonists and the discharge of effector secretions. The sub-membrane region contains microfilaments of actin and myosin that mediate morphologic alterations[3]. These cells possess a tricarboxylic acid cycle and use glucose by means of the glycolytic and hexose monophosphate shunt pathways[4]. Their function is closely linked to their metabolic activity.

PRP preparation

A small volume of blood (ideally 20 ml) is taken by venipuncture from the patient and inserted into the correct size of tube to be centrifuged. Platelet concentration (growth factors) will be dependant on:

- The amount of whole-blood used
- Platelet recovery efficiency
- The final volume of plasma in which platelets are suspended.

For these reasons, to homogenate the value of the acceleration, which is of importance to the self-activation of the liquid, it is better to work with wide and short tubes. It is also important to choose a concentration factor of less than 4 to avoid a final concentration that is too high, which would be detrimental owing to a high risk of self-activation (premature). Self-activation in such cases is usually the result of an increase in concentration and platelet aggregation that follows their physical proximity.

It has been established that excessive acceleration will decrease the integrity of the platelet membrane, some of which are then activated[10]. Thus, for values of more than 400 G, 5% of platelets are activated[11], and 40–70% of platelets will be activated at 3000 G[12].

> “It is well known that the wound healing process is complex and typically divided into three phases; inflammatory, regeneration, and remodelling.”

The results obtained with systems using a double centrifugation are similar to those that use a single centrifuge, but injections are more painful and inflammatory[13], owing to the ratio between platelets, leukocytes and plasma, as well as the increased amount of manipulations. Furthermore, even if the desired concentrations are higher, the risk of self-activation will increase. PRP contains large numbers of cellular microparticles, including annexin V+ microparticles, which are lost to varying degrees when PRP is double centrifuged to remove platelets.

Platelet fragmentation during processing should be avoided, because it is the process of activation that results in the completion of the tertiary structure of some of the secretory proteins. As a result, such fragmentation during processing could result in the release of high levels of proteins with compromised bioactivity. The integrity of the platelet membrane can be preserved through the use of low gravity forces during the centrifugation process. Growth factors released from activated platelets initiate and modulate wound healing in both soft and hard tissue.

There are a number of different PRP harvesting kits available, but some contain thrombin – either from bovine or human origin – and therefore the end product cannot be categorised as autologous. Others use a chemical buffer to separate the plasma and red cells, and do not deliver pure PRP as a result. The separation should be physical, not chemical.

Table 1
Fundamental growth factors

PLATELET-DERIVED GROWTH FACTORS (PDGF)
- Chemo-attractive to mesenchymal stem cells and endothelial cells
- Differentiation for fibroblasts and osteoblasts
- Up-regulate effects of other growth factors on cells such as macrophages
- Mitogens of mesenchymal stem cells promote the synthesis of the extracellular matrix

TRANSFORMING GROWTH FACTORS (TGF) ALPHA AND BETA
- Promote cell mitosis
- Significantly increase type I collagen production in the tendons
- Favour the synthesis of collagen
- Sheath fibroblast
- Stimulation of DNA synthesis, proliferation of various types of cell

VASCULAR ENDOTHELIAL GROWTH FACTORS (VEGF)
- Stimulate angiogenesis
- Chemo-attractive for osteoblasts

EPIDERMAL GROWTH FACTORS (EGF)
- Important role in the regulation of cell growth, proliferation, and differentiation by binding to its receptor EGFR
- Induce epithelial development and promote angiogenesis
- Stimulate proliferation and differentiation of epidermis cells, co-stimulating angionegesis

INSULIN-LIKE GROWTH FACTORS (IGF) 1 AND 2
- Stimulate the proliferation and differentiation of osteoblasts

How does it work?

It is well known that the wound healing process is complex and typically divided into three phases; inflammatory, regeneration, and remodelling (*Figure 1*). A number of proteins are contained within the platelet's alpha-granules. Collectively, these proteins are members of the families of growth factors, cytokines and chemokines, which are broadly referred to as secretory proteins. They are of prime importance in the realisation of this entire process as each step of the healing cascade is under the influence of specific growth factors/cytokines[14]. Some investigators have suggested that PRP should achieve a 3- to 5-fold increase in platelet concentration over baseline[5,10,15].

Owing to the presence of high concentrations of growth factors, apart from the wide use to accelerate wound healing, PRP has been used in a wide variety of surgical procedures and clinical treatments. Indeed, there is substantial clinical evidence regarding its use in other medical fields[14,16]. The substantial concentration of platelets, compared with normal blood, certainly represents a unique source of growth factors. Following subcutaneous injection, these proteins and growth factors interact with the basal cells in the subcutaneous tissue, including fibroblasts, endothelial cells, and subcutaneous stem cells. PRP is also used in the aesthetic field for the stimulation of the superficial dermis, as well as the deep layers of the dermis. It has been proven that PRP application both augments the skin and increases its volume[17,18].

Fitzpatrick published a study proving that topical application of growth factors stimulate the rejuvenation of photoaged facial skin, improving its clinical appearance and inducing new collagen synthesis[19,20], and another research study showed that PRP actually induces increased expression of G1 cell cycle regulators, type I collagen, and matrix metalloproteinase (MMP)-1 in human dermal fibroblasts[21].

Cells, osteoblasts, fibroblasts, endothelial cells, and epidermal cells express the cell membrane receptors ▷

▷ to growth factors in PRP. These transmembrane receptors in turn induce an activation of an endogenous internal signal protein, which causes the expression of (unlocks) a normal gene sequence of the cell such as cellular proliferation, matrix formation, osteoid production, and collagen synthesis. The significance of this is that the PRP growth factors never enter the cell or its nucleus, are not mutagenic, and act through the stimulation of normal healing, but much faster. Therefore, PRP has no ability to induce tumour formation and has never been found to do so[22,23].

Platelet concentration

PRP must be developed in an anti-coagulated state and should be used on the graft, flap, wound, or skin within 10 minutes of clot initiation. There is a dose-response relationship between platelet concentration and the proliferation of human adult mesenchymal stem cells, the proliferation of fibroblasts, and the production of type I collagen[24,25]. This suggests that the application of autologous PRP can enhance wound healing, as has been demonstrated in controlled animal studies for both soft and hard tissues[26,27].

The next question, therefore, concerns how many platelets are enough. A sufficient cellular response to platelet concentrations first began when a 4- to 5-fold increase over baseline platelet numbers was achieved[24]. A similar study by Lui and al[25] showed that fibroblast proliferation and type I collagen production were also enhanced by increasing platelet concentrations and that much of the response was pH-dependent, with the best responses occurring at more acidic pH levels.

PRP is rapidly gaining a lot of interest worldwide, but health regulations differ from country to country, making the generalisation of the process more complicated and often more expensive. For example, in Korea it is possible to carry out a half-face study, which is not possible in the UK, and in Italy, the process can be performed only in a clinic/hospital with a haematologist on site.

> "PRP must be developed in an anti-coagulated state and should be used on the graft, flap, wound, or skin within 10 minutes of clot initiation."

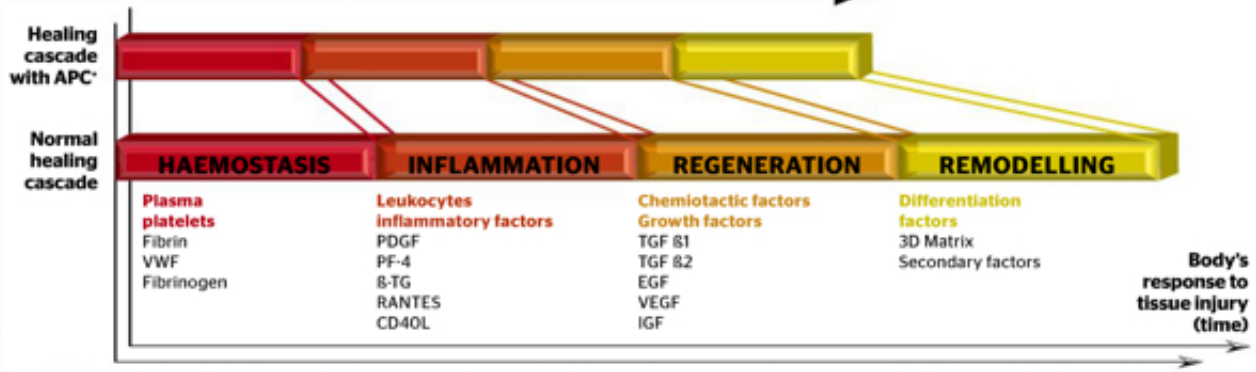
Literature review

When using PRP, the different methods used during preparation are important as they influence the quality of the product. Activation of the platelets is required for the release and enmeshment of growth factors, but the method of activation may influence the resulting matrix, growth factor availability, and healing[28]. Furthermore, some methods enrich leukocytes as well as platelets, but others are designed to be leukocyte-poor. Leukocytes have many important roles in healing and their inclusion in PRP results in increased platelet concentrations. Generally, TGF-ß1 and PDGF levels are higher in preparations that contain leukocytes compared with leukocyte-poor PRP[28].

The literature published between March 2001 and March 2011 was reviewed by Davis et al[29], and the meta-analysis of chronic wound studies revealed that PRP therapy is favoured for complete healing. This systematic review in cutaneous wounds showed complete and partial wound healing was improved compared with control wound care.

Within the eligible studies, three main types of wounds were identified and treated with PRP: open and chronic wounds, acute surgical wounds with primary closure, and acute surgical wounds with secondary closure[30,31]. The primary outcome assessed in this systematic review was complete healing[32]. In both chronic and acute wound studies, complete wound closure was more likely in wounds treated with PRP therapy. Another review concluded that the percentage of total healing in PRP-treated skin ulcers consistently increased ▷

Figure 1 Benefits reported in the healing cascade



▷ compared with controls[18]. Other reviews on PRP therapy have reached the same conclusions.

One systematic review went so far as to conclude that, based on the meta-analysis and scientific evidence regarding consistent favourable outcomes, PRP is a treatment of choice for the topical care of wounds[19]. A total of 15 randomised controlled trials and 25 case-control studies were found. Thirty-six publications demonstrated favourable outcomes with the use of PRP. The included articles were divided into three topics related to cosmetic surgery: wound healing, fat grafting and bone grafting. Carter et al[19] described a substantially beneficial effect of PRP for a number of indications, including a better wound healing rate, an increased survival rate of fat grafts, and an enhancement of bone graft regeneration.

Tissue remodelling

Autologous PRP has attracted attention in a number of medical fields. In one study[34], the effects of activated PRP (aPRP) and activated platelet-poor plasma (aPPP) were investigated with regard to the remodelling of the extracellular matrix (ECM), a process that requires activation of the dermal fibroblasts – essential for the rejuvenation of aged skin. aPRP AND aPPP both stimulated cell proliferation, with peak proliferation occurring in cells grown in 5% aPRP. Additionally, aPRP and aPPP increased the expression of type I collagen, MMP-1 protein, and mRNA in human dermal fibroblasts.

aPRP and aPPP promote tissue remodelling in aged skin and may be used as adjuvant treatment to lasers for skin rejuvenation in cosmetic dermatology. Although the optimal platelet concentration is unclear, the current methods by which PRP is prepared is reported to involve approximately 300–700% enrichment, with platelet concentrations consequently increasing to greater than 1 000 000 platelets[35]. These factors are known to regulate processes including cell migration, attachment, proliferation and differentiation, and promote ECM accumulation by binding to specific cell surface receptors[36].

In the dermis, which is continually exposed to UVB, collagen degeneration and altered deposition of elastic tissue result in the impairment of the structural integrity of the dermal ECM, causing the skin to wrinkle. The skin's resilience is also reduced. Compared with the serum-treated control group in one study[37], aPRP and aPPP showed a marked increase in fibroblast proliferation. Cells exposed to 5% or 10% aPRP also exhibited significantly higher rates of proliferation than positive control cells. These results indicate that aPRP and aPPP promote the proliferation of fibroblasts. On the other hand, the expression of the α1 and α2 chains of type I collagen was increased in cells treated with 5% aPRP or aPPP (compared with negative control), suggesting that both PRP and PPP show an ability to induce collagen production.

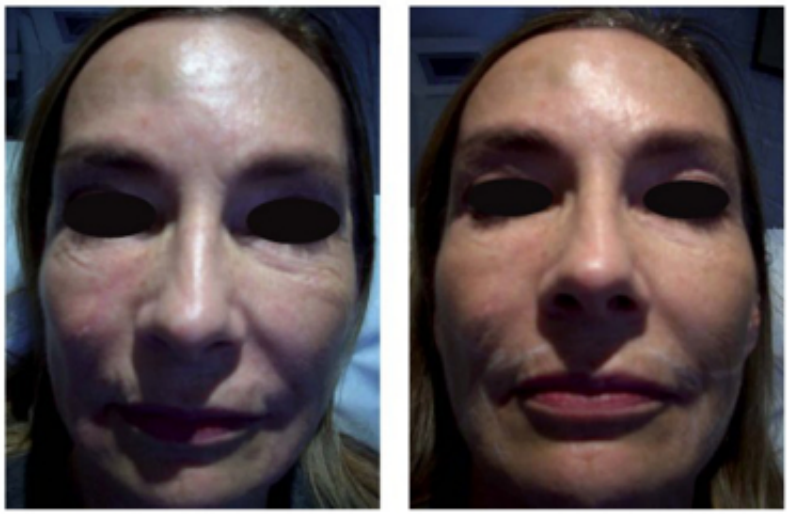


Figure 2 (A) Before and (B) after treatment with platelet-rich plasma

This stimulation of *de novo* collagen synthesis may compensate for the defects that arise as a result of the fragmentation or loss of collagen in photoaged and aged skin. Accumulation of this newly-synthesised collagen may improve the structural integrity of the dermal ECM and stimulate fibroblasts to produce more collagen. Similarly, induction of MMP-1 in photoaged skin may facilitate the removal of collagen fragments that damage the dermal matrix tissue, thus providing a better foundation for the deposition of new collagen[38]. In a more recent study, injection of PRP in the face and neck for revitalisation obtained good results[39].

> "PRP combined with fractional laser was found to increase patient satisfaction and skin elasticity, and decrease the erythema index."

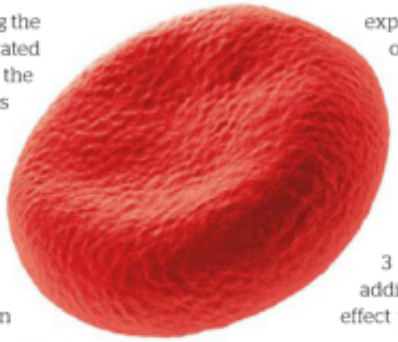
PRP treatment results

PRP combined with fractional laser was found to increase patient satisfaction and skin elasticity, and decrease the erythema index[40]. Furthermore, treatment increased the length of the dermo-epidermal junction, the amount of collagen, and the number of fibroblasts. PRP with fractional laser treatment is a good combination therapy for skin rejuvenation. Keratinocyte and fibroblast proliferation and collagen production can explain the capacity of PRP to increase dermal elasticity.

In a study to evaluate the efficacy of a single injection of autologous platelet-rich fibrin matrix (PRFM) for the correction of deep nasolabial folds (NLFs), whole blood was obtained from 15 adults, and an activated autologous platelet-rich fibrin matrix produced using a proprietary system[1]. It was then injected into the dermis and immediate subdermis below the nasolabial folds. Subjects were photographed before and after treatment; folds were rated by the ▷

▷ treating physician before and after treatment using the Wrinkle Assessment Scale (WAS), and patients rated their appearance at each post-treatment visit using the Global Aesthetic Improvement Scale (GAIS). Patients were evaluated at 1, 2, 6, and 12 weeks post-treatment.

All patients were treated to maximal (no over-) correction, with a mean reduction in WAS score of 2.12 +/- 0.56. No patient noted any fibrosis, irregularity, hardness, restricted movement, or lumpiness. The author of the study concluded that PRFM can provide significant long-term diminution of deep nasolabial folds without the use of foreign materials. PRFM holds significant potential for stimulated dermal augmentation. (NB. The system used in this study uses thrombine to get a stronger fibrin mesh and therefore cannot be defined as 100% autologous.)



> "With the accumulated knowledge on this procedure, we now have the most complete, versatile and active treatment for skin rejuvenation and anti-ageing."

Objective results

A study by Amgar et al[41] is one of the very few studies concentrating only on the objective results of PRP. It uses biometric parameters for scientifically measurable means of assessing the results from the PRP injections. Skin hydration was made after compensating for the ambient humidity level. The hydration was expressed by a standard index. Anisotropy measures the distribution of micro-lines in 360°, and is expressed as a percentage. Following marked swelling of the skin, a number of micro-lines on the surface of the skin can be observed. The projection and distribution of these micro-lines, two-dimensionally in all directions (360°), is indicative of young skin. The older the skin, the more these lines will change orientation and become parallel.

The study tracked 37 patients for a period of 3 weeks following PRP treatment, and 27 for an additional 10 weeks post-treatment. A good anti-ageing effect was assessed by measured anisotropy values of -24.1% and -16.9%., respectively. Additionally, a cross-analysis involving the initial anisotropy readings demonstrated further improvement. The anisotropy correlates were -33% and -39.7%, respectively, if the treatment is provided to patients who would mostly benefit from it (anisotropy >30%). The study also demonstrated that the effects of one PRP treatment could last for up to 10 months.

In another study which combined PRP with fractional laser therapy for dermal rejuvenation[42], a high concentration of PRP induced an up-regulation of type I collagen, MMP-1, and MMP-2 expression in human skin fibroblasts. Taken together, PRP treatment induced an increase in expression of G1 cell cycle

References

1. Sclafani AP. Platelet-rich fibrin matrix for improvement of deep nasolabial folds. J Cosmet Dermatol 2010; 9(1): 66-71
2. Marx RE, Carlson ER, Eichstaedt RM, Schimmele SR, Strauss JE, Georgeff KR. Platelet-rich plasma: Growth factor enhancement for bone grafts. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998; 85(6): 638-46
3. Kevy S, Jacobson M. Preparation of growth factors enriched autologous platelet gel. Proceedings of the 27th Annual Meeting of Service Biomaterials, April 2001
4. Conley CL. Hemostasis. In: Mountcastle VB. ed, Medical Physiology. St. Louis: Mosby, 2004
5. Welsh WJ. Autologous platelet gel: Clinical function and usage in plastic surgery. Cosmetic Derm 2000; 11: 13
6. Marx RE. Platelet concentrate: A strategy for accelerating and improving bone regeneration. In: Davies JE. ed, Bone Engineering. Toronto: University of Toronto, 2000
7. Caro CD, Pedley TJ, Schroter RC et al. The Mechanics of the Circulation. Oxford: Oxford University Press, 1978
8. Harrison P, Cramer EM. Platelet alpha-granules. Blood Rev 1993; 7: 52-62
9. Anitua E, Andia I, Ardanza B, Nurden P, Nurden AT. Autologous platelets as a source of proteins for healing and tissue regeneration. Thromb Haemost 2004; 91(1): 4-15
10. Bagamery K, Kvell K, Barnet M, Landau R, Graham J. Are platelets activated after a rapid, one-step density gradient centrifugation? Evidence from flow cytometric analysis. Clin Lab Haematol 2005; 27(1): 75-7
11. Gonshor A. Technique for producing platelet-rich plasma and platelet concentrate: background and process. Int J Periodontics Restorative Dent 2002; 22(6): 547-57
12. Zimmermann R, Jakubietz R, Jakubietz M et al. Different preparation methods to obtain platelet components as a source of growth factors for local application. Transfusion 2001; 41(10): 1217-24
13. Filardo G, Kon E, Pereira Ruiz MT et al. Platelet-rich plasma intra-articular injections for cartilage degeneration and osteoarthritis: single- versus double-spinning approach. Knee Surg Sports Traumatol Arthrosc 2012; 20(10): 2082-91
14. Bhanot S, Alex JC. Current applications of platelet gels in facial plastic surgery. Facial Plast Surg 2002; 18(1): 27-33
15. Kevy SV, Jacobson MS. Comparison of methods for point of care preparation of autologous platelet gel. J Extra Corpor Technol 2004; 36(1): 28-35
16. Man D, Plosker H, Winland-Brown JE. The use of autologous platelet-rich plasma (platelet gel) and autologous platelet-poor plasma (fibrin glue) in cosmetic surgery. Plast Reconstr Surg 2001; 107(1): 229-37
17. Ebisawa K, Kato R, Okada M. Cell therapy for facial anti-aging. Med J Malaysia 2008; 63 Supp A: 41
18. Martínez-Zapata MJ, Martí-Carvajal A, Solà I et al. Efficacy and safety of the use of autologous plasma rich in platelets for tissue regeneration: a systematic review. Transfusion 2009; 49(1): 44-56
19. Fitzpatrick RE, Rostan EF. Reversal of photodamage with topical growth factors: a pilot study. J Cosmet Laser Ther 2003; 5(1): 25-34
20. Kakudo N, Minakata T, Mitsui T, Kushida S, Notodihardjo FZ, Kusumoto K. Proliferation-promoting effect of platelet-rich plasma on human adipose-derived stem cells and human dermal fibroblasts. Plast Reconstr Surg 2008; 122(5): 1352-60
21. Cho JW, Kim SA, Lee KS. Platelet-rich plasma induces increased expression of G1 cell cycle regulators, type I collagen, and matrix metalloproteinase-1 in human skin fibroblasts. Int J Mol Med 2012; 29(1): 32-6
22. Schmitz JP, Hollinger JO. The biology of platelet-rich plasma. J Oral Maxillofac Surg 2001; 59(9): 1119-21
23. Marx RE. The biology of platelet-rich plasma. J Oral Maxillofac Surg 2001; 59(9): 1120
24. Haynesworth SE, Kadiyala S, Liang L et al. Mitogenic stimulation of human mesenchymal stem cells by platelet releasate suggest a mechanism for enhancement of bone repair by platelet concentrates (Poster no. 462). Transactions of the 48th Annual Meeting of the Orthopaedic Research Society, Dallas, Texas, 10-13 February, 2002
25. Liu Y, Kalén A, Risto O, Wahlström O. Fibroblast proliferation due to exposure to a platelet concentrate in vitro is pH dependent. Wound Repair Regen 2002; 10(5): 336-40
26. Carter CA, Jolly DG, Worden CE Sr, Hendren DG, Kane CJ. Platelet-rich plasma gel promotes differentiation and regeneration during equine wound healing. Exp Mol Pathol 2003; 74(3): 244-55
27. Fennis JP, Stoelinga PJ, Jansen JA. Mandibular reconstruction: a clinical and radiographic animal study on the use of autogenous scaffolds and platelet-rich plasma. Int J Oral Maxillofac Surg 2002; 31(3): 281-6
28. Sommeling CE, Heyneman A, Hoeksema H, Verbelen J, Stillaert FB, Monstrey S. The use of platelet-rich plasma in plastic surgery: a systematic review. J Plast Reconstr Aesthet Surg 2013; 66(3): 301-11
29. Davis VL, Abukabda AB, Radio NM et al. Platelet-Rich Preparations to Improve Healing, Parts I and II. J Oral Implantol 2012; [Epub ahead of print]
30. Kazakos K, Lyras DN, Verettas D, Tilkeridis K, Tryfonidis M. The use of autologous PRP gel as an aid in the management of acute trauma wounds. Injury 2009; 40(8): 801-5
31. Hom DB, Linzie BM, Huang TC. The healing effects of autologous platelet gel on acute human skin wounds. Arch Facial Plast Surg 2007; 9(3): 174-83
32. Villela DL, Santos VL. Topical therapy of chronic leg ulcers with platelet-rich plasma: a systematic review of the literature. Presented at: WOCN 2010 Conference of the Wound Ostomy Continence Nurse Society. 12-16 June, 2010
33. Carter MJ, Fylling CP, Parnell LK. Use of platelet rich plasma gel on wound healing: a systematic review and meta-analysis. Eplasty 2011; 11: e38
34. Kim DH, Je YJ, Kim CD et al. Can Platelet-rich Plasma Be Used for Skin Rejuvenation? Evaluation of Effects of Platelet-rich Plasma on Human Dermal Fibroblast. Ann Dermatol 2011; 23(4): 424-31
35. Landesberg R, Roy M, Glickman RS. Quantification of growth factor levels using a simplified method of platelet-rich plasma gel preparation. J Oral Maxillofac Surg 2000; 58(3): 297-300
36. Freymiller EG. Platelet-rich plasma: evidence to support its use. J Oral Maxillofac Surg 2004; 62(8): 1046
37. Cho JM, Lee YH, Baek RM, Lee SW. Effect of platelet-rich plasma on ultraviolet b-induced skin wrinkles in nude mice. J Plas Reconstr Aesthet Surg 2011; 64(2): e31-9
38. Almeida Issa MC, Piñeiro-Maceira J, Farias RE, Pureza M, Raggio Luiz R, Manela-Azulay M. Immunohistochemical expression of matrix metalloproteinases in photodamaged skin by photodynamic therapy. Br J Dermatol 2009; 161(3): 647-53
39. Redaelli A, Romano D, Marcianó A. Face and neck revitalization with platelet-rich plasma (PRP): clinical outcome in a series of 23 consecutively treated patients. J Drugs Dermatol 2010; 9(5): 466-72
40. Kim DH, Je YJ, Kim CD et al. Can Platelet-rich Plasma Be Used for Skin Rejuvenation? Evaluation of Effects of Platelet-rich Plasma on Human Dermal Fibroblast. Ann Dermatol 2011; 23(4): 424-31
41. Amgar G, Bonnet C, Butnaru A, Herault-Bardin F. Using objective criteria to evaluate cosmetic effects of platelet rich plasma. PRIME 2011; 1(6): 30-41
42. Shin MK, Lee JH, Lee SJ, Kim NI. Platelet-Rich Plasma Combined with Fractional Laser Therapy for Skin Rejuvenation. Dermatol Surg 2012 [Epub ahead of print]
43. Na JI, Choi JW, Choi HR et al. Rapid healing and reduced erythema after ablative fractional carbon dioxide laser resurfacing combined with the application of autologous platelet-rich plasma. Dermatol Surg 2011; 37(4): 463-8
44. Lee JW, Kim BJ, Kim MN, Mun SK. The efficacy of autologous platelet rich plasma combined with ablative carbon dioxide fractional resurfacing for acne scars: a simultaneous split-face trial. Dermatol Surg 2011; 37(7): 931-8
45. Sclafani AP, Romo T 3rd, Ukrainsky G. Modulation of wound response and soft tissue ingrowth in synthetic and allogeneic implants with platelet concentrate. Arch Facial Plast Surg 2005; 7(3): 163-9

regulators, type I collagen and MMP-1, thereby accelerating the wound healing process. Ablative CO_2 fractional resurfacing is a promising therapeutic intervention for the treatment of acne scars, although this technique is associated with prolonged surgical site erythema and oedema, which may affect the daily lives of patients. Treatment with PRP after ablative CO_2 fractional resurfacing enhances recovery of laser-damaged skin and synergistically improves the clinical appearance of acne scarring[43,44].

Significantly faster recovery of TEWL (transepidermal water loss) was seen on the PRP-treated side. The erythema index and melanin index on the PRP-treated side were lower than on the control side. Biopsy specimens from the PRP-treated side showed thicker collagen bundles than those from the control side.

Findings from a histological examination by Sclafani et al[45] support the clinical observations of soft-tissue augmentation. As early as 7 days post-treatment, activated fibroblasts and new collagen deposition were noted and continued to be evident throughout the course of the study. Development of new blood vessels was noted by day 19; also at this time, intradermal collections of adipocytes and stimulation of subdermal adipocytes were noted. Injection of PRFM into the deep dermis and subdermis of the skin stimulates a number of cellular changes that can be harnessed for use.

Key points

- Platelet-rich plasma (PRP) is based on the healing and regenerative effects of growth factors in the patient's own plasma product
- There are more than 6500 medical publications related to PRP listed on Medline
- The quality of PRP is definitely linked to specific harvesting kits and preparation protocols
- PRP is the safest and most versatile treatment in aesthetic medicine (e.g. deep injections, subdermal injections, with or without dermaroller, with or without fractional laser, with needles or cannulas, mixed or not with hyaluronic acid)

Conclusions

Since 1950 and the discovery of growth factors, and the fast developments of aesthetic medicine, there have been increasing numbers of research and study publications. As doctors, we are always looking for safe and effective treatments. With the accumulated knowledge on this procedure, we now have the most complete, versatile and active treatment for skin rejuvenation and anti-ageing.

Dermal fillers will replace the lost volume that comes with ageing, and lasers will act on collagen. However, as the facial ageing process involves more than just collagen depletion and gravity, but also bone resorption, with PRP a natural, safe, and efficient treatment is available to act on all aspects of ageing compartments (including bone loss).

▶ ***Declaration of interest*** *Dr Sister works in private practice, and is consultant speaker and tutor for Health Technology. This article received no funding source and is written purely from Dr Sister's experience.*

▶ ***Figure 2*** *©Dr Daniel Sister*