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Evidence Based Medicine

Evidence Based Medicine

La EBM è un movimento culturale che si è progressivamente diffuso a livello internazionale, favorito da alcuni fenomeni che hanno contribuito ad una crisi dei modelli tradizionali della medicina

- la crescita esponenziale dell'informazione biomedica, che ha reso sempre più difficile l'aggiornamento professionale;
- il limitato trasferimento dei risultati della ricerca all'assistenza sanitaria documentato da: ampia variabilità della pratica professionale, utilizzo di trattamenti inefficaci, elevato livello di inappropriatezza, scarsa diffusione di trattamenti appropriati;
- la crisi economica dei sistemi sanitari (crescita della domanda e dei costi dell'assistenza);
- il maggior livello di consapevolezza degli utenti.

Evidence Based Medicine

Evidence based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients.

The practice of evidence based medicine means integrating **individual clinical expertise** with the **best available external clinical evidence** from systematic research.

Sackett DL et al. Evidence based medicine: what it is and what it isn't. BMJ 1996; 312: 71-2

Evidence Based Medicine

Evaluation of indications from the literature

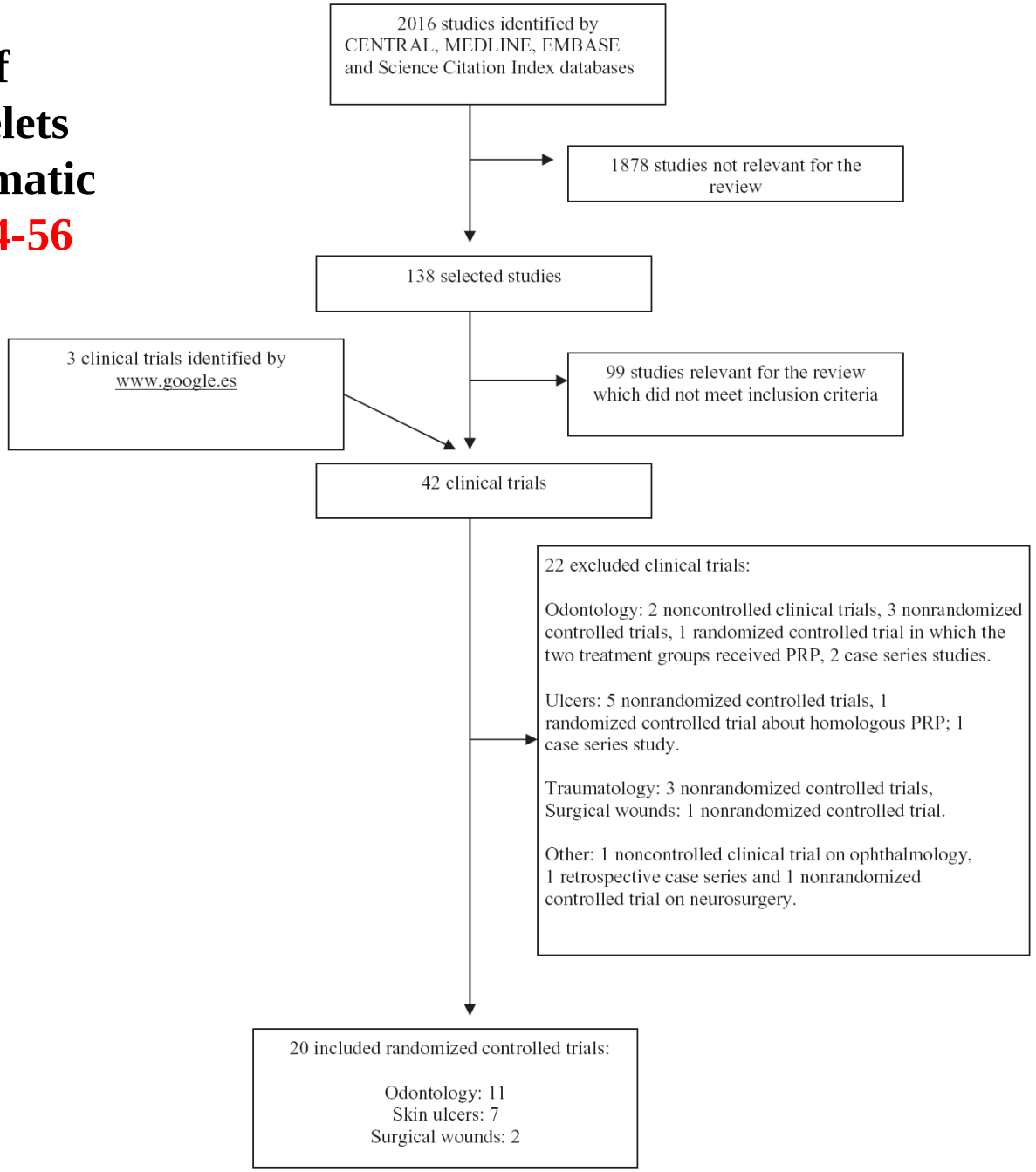
Table 1. Key to levels of evidence and grades of recommendation

Levels of evidence		Grades of recommendation	
I	Randomized controlled trials with large sample populations, clear objectives and a low or a very low risk of bias Well-conducted meta-analyses or systematic reviews	A	Supported by at least two level I studies
II	Randomized controlled trials with small sample populations, clear objectives and a moderate risk of bias	B	Supported by one level I study
III	Observational studies with contemporary controls	C	Supported by level II studies
IV	Observational studies with historical controls	D	Supported by level III studies
V	Nonanalytic studies, e.g. case reports, case series. Expert opinion	E	Supported by level IV or V studies

Martinez-Zapata MJ, et al.
Efficacy and safety of the use of autologous plasma rich in platelets for tissue regeneration: a systematic review. Transfusion 2009; 49:44-56

…all RCTs that assess the efficacy and/or safety of PRP for healing and regeneration of hard and soft tissues in any and all medical and surgical procedures.

…computerized literature searches for trials using the following search terms and combining them: autologous plasma, autologous platelet, rich growth factor, plasma rich in growth factors (PRGF), wound, tissue, bone, osseous, heal, and repair implant.



Gel di piastrine

Problemi aperti

- Efficacia terapeutica
- Influenza delle modalità produttive sulle proprietà biologiche
- Plt gel vs GF ricombinanti
- Competenza

Platelet Gel

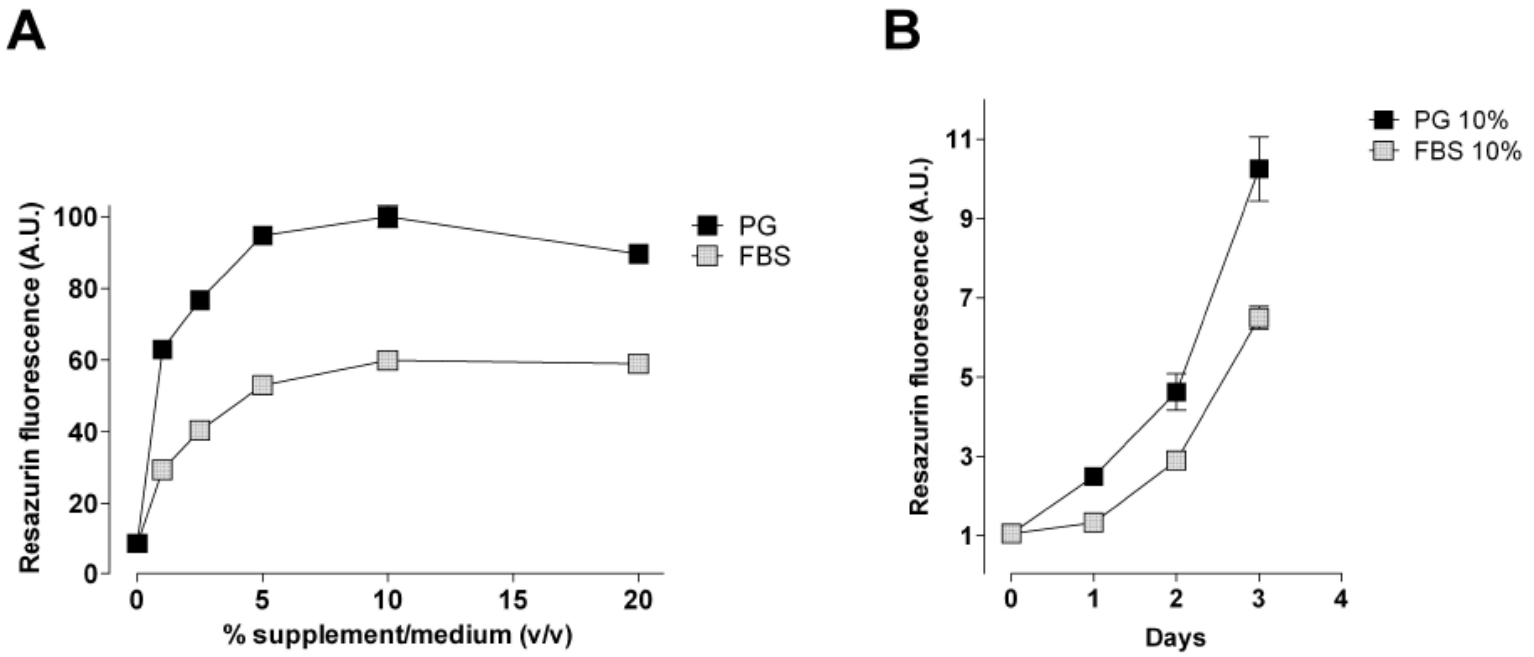
Platelet gel effect on cell proliferation

- In a study by D'Agostino et al (2002) the effect of platelet gel, obtained with different methods (from PRP, apheresis and modified apheresis) on the fibroblasts proliferation has been evaluated. Human fibroblasts derived from skin biopsies have been used.
- After routine culture in DMEM supplemented with 10% foetal calf serum for 24h, fibroblasts have been cultured in serum free DMEM with or without platelet.
- Application of platelet gel prevented cell detachment, apoptosis and increased cell proliferation in serum free medium.
- The effect of PGs was comparable for each of the different PG utilized.

Platelet gel in the treatment of cutaneous ulcers: the experience of the Immunohaematology and Transfusion Centre of Parma

Blood Transfus 2010;8:237-47

Gino Bernuzzi[1], Saverio Tardito[2], Ovidio Bussolati[2], Daniela Adorni[1], Stefano Cantarelli[1], Francesco Fagnoni[1], Angelo Rossetti[3], Matteo Azzarone[4], Elena Ficarelli[5], Edoardo Caleffi [6], Giancarlo Gazzola[2], Massimo Franchini[1]



Effects of platelet gel supernatant on the growth of human cultured fibroblasts.
Panel A: Cell viability evaluated after 72 hours at different concentration of FBS or PG.
Panel B: Cell viability evaluated at the indicated times (10% FBS vs 10% PG supernatant)

Modulation of Wound Response and Soft Tissue Ingrowth in Synthetic and Allogeneic Implants With Platelet Concentrate

Arch Facial Plast Surg. 2005;7:163-169

Anthony P. Sclafani, MD; Thomas Romo III, MD; Gennady Ukrainsky, MD, DDS; Steven A. McCormick, MD; Jason Litner, MD; Sherwin V. Kevy, MD; May S. Jacobson, PhD

Methods: Adult New Zealand white rabbits underwent phlebotomy, and the blood was used to produce nonconcentrated autologous blood clot, platelet-poor plasma (PPP), and PC for each animal. Disks of porous high-density polyethylene (PHDPE) and acellular dermal graft (ADG) were implanted into each animal in a subcutaneous location. Implants of each type were treated with isotonic sodium chloride solution, PPP, PPP followed immediately with PC, or autologous blood clot (by means of manual impregnation). Animals were killed at 2, 7, 14, and 21 days after implantation. Implants were harvested with surrounding soft tissue and examined by means of light microscopy for evidence of acute and chronic inflammatory cells and vascular and fibroblast invasion.

Modulation of Wound Response and Soft Tissue Ingrowth … With Plt Concentrate

no differences between controls and implants treated with PPP.

Table. Summary of Statistically Significant Histological Data

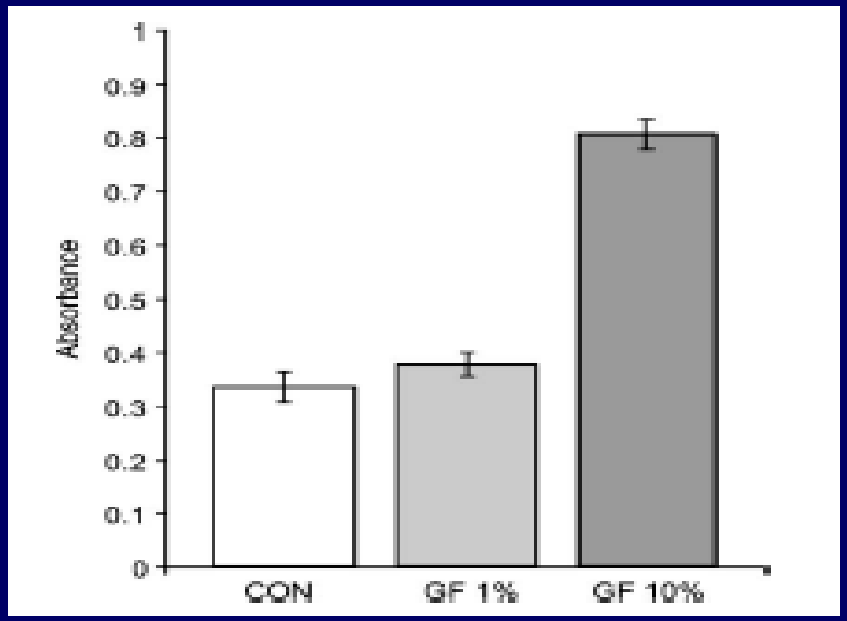
Treatment Cell Type (Postoperative Day)	Control Cell Count, Mean ± SD*	Autologous Blood Clot: Cell Count, Mean ± SD*	Autologous Blood Clot: Increase Compared With Controls, %	Autologous Blood Clot: *P* Value	Platelet Gel: Cell Count, Mean ± SD*	Platelet Gel: Increase Compared With Controls, %	Platelet Gel: *P* Value	Increase Compared With ABC, %	*P* Value
PHDPE Implants									
Neutrophils (2)	34.10 ± 8.32	59.90 ± 13.20	76	<.001	50.60 ± 8.22	48	<.05	−16	NS
Macrophages/giant cells (2)	12.60 ± 4.03	24.20 ± 4.44	92	<.001	23.40 ± 5.74	86	<.001	0	NS
Fibroblasts (7)	44.33 ± 4.38	55.00 ± 13.73	24	NS	71.33 ± 9.38	61	<.001	30	<.01
Capillaries (7)	21.67 ± 7.47	33.12 ± 20.02	53	NS	42.22 ± 19.79	95	<.05	27	<.05
Lymphocytes (7)	30.33 ± 4.92	37.62 ± 9.75	24	NS	51.89 ± 11.69	71	<.001	38	<.01
ADG Implants									
Neutrophils (2)	32.60 ± 9.13	60.20 ± 18.29	85	<.001	51.90 ± 10.67	59	<.05	−14	NS
Macrophages/giant cells (2)	11.50 ± 4.14	23.90 ± 5.38	108	<.001	23.10 ± 7.23	101	<.001	0	NS
Macrophages/giant cells (7)	12.88 ± 5.08	16.33 ± 6.80	27	NS	23.50 ± 9.27	82	<.05	44	NS
Fibroblasts (7)	40.88 ± 6.56	53.89 ± 12.24	32	<.05	62.25 ± 11.16	52	<.001	16	<.01
Capillaries (7)	17.25 ± 3.33	24.67 ± 10.10	43	NS	34.00 ± 9.34	97	<.001	38	NS
Lymphocytes (7)	25.62 ± 4.69	44.33 ± 23.55	73	NS	51.25 ± 14.66	100	<.05	16	NS

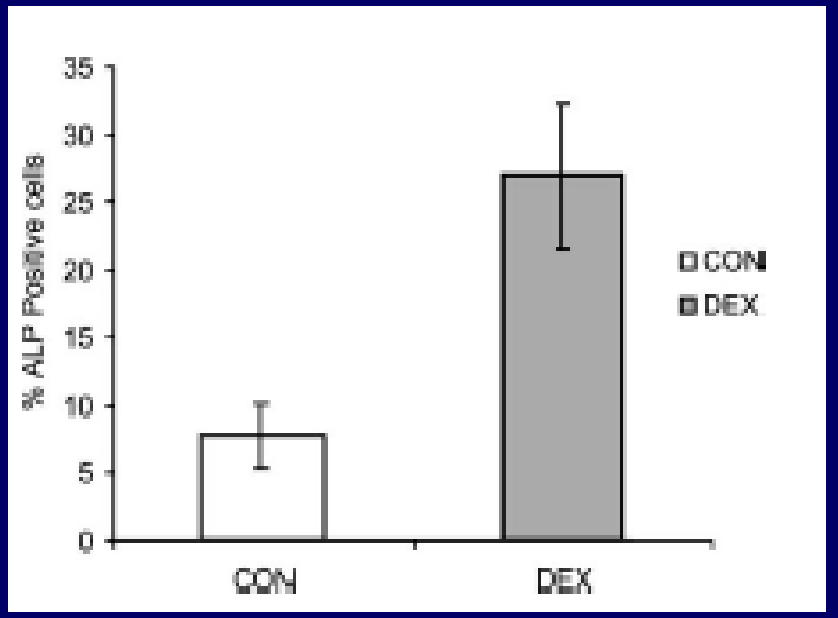
PHDPE, porous high-density polyethylene. ADG, acellular dermal graft;

Sclafani et al. Arch Facial Plast Surg. 2005;7:163-169

Platelet-derived growth factors enhance proliferation of human stromal stem cells

Lucarelli E et al, Biomaterials, 2003





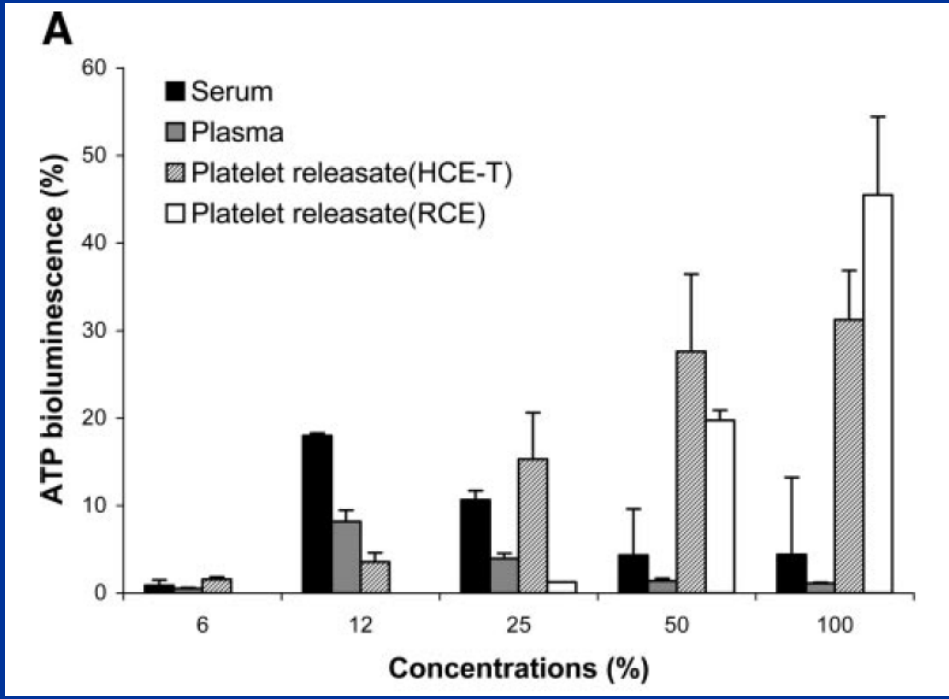
1. 10% PRP induce SSC proliferation
2. Removal of PRP restored the characteristic proliferation rate
3. Cell expanded with 10% PRP can mineralize the extracellular matrix, once PRP is withdrawn

Corneal Epitheliotrophic Capacity of Three Different Blood-Derived Preparations

Investigative Ophthalmology & Visual Science, June 2006, Vol. 47, No. 6

Lei Liu,[1] *Dirk Hartwig,*[2,3] *Susanne Harloff,*[1] *Philip Herminghaus,*[1] *Thilo Wedel,*[4] *Karsten Kasper,*[1] *and Gerd Geerling*[1]

Cell proliferation of human corneal epithelial cells and (HCE) and rabbit corneal epithelial cells (RCE) was **best supported by platelet releasate** followed by serum and FFP; however, cell migration and differentiation were better supported by serum than by platelet releasate and FFP.



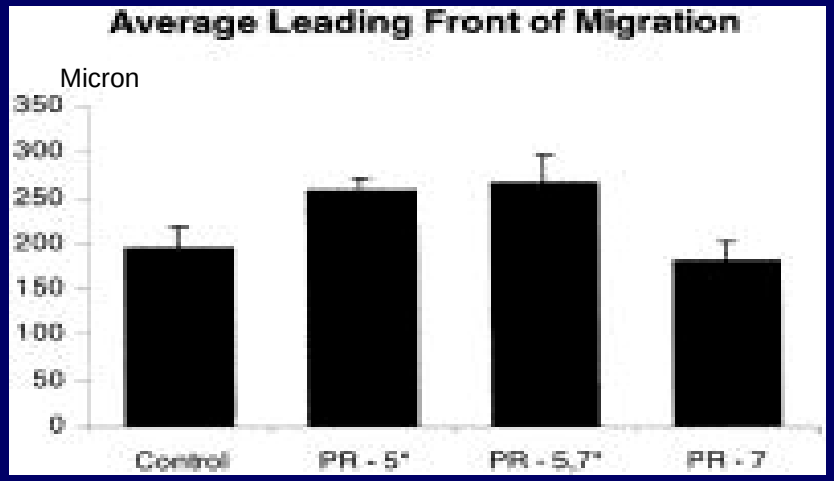
Involvement of platelets in stimulating osteogenic activity

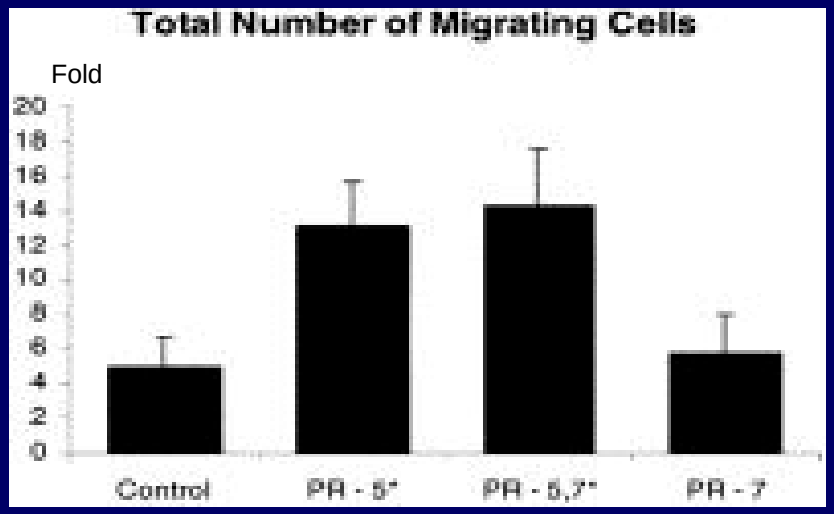
Slater M, Journal of Orthopaedic Surgery, 1995

Platelet-supplemented medium stimulates proliferation and maintains the differentiated function of human osteoblast-like cells.

Effect of platelet releasate on bone cell migration and recruitment in vitro

Oprea WE et al, The Journal of craniofacial Surgery, 2003





Cultures of primary rat bone marrow cells were overlaid with a fibrin matrix, and the number of cells migrating within the three-dimensional matrix and the leading front of migration were quantified. The addition of PR to the top of the fibrin gels at different time points caused a 25% increase in the leading front of migration and a 3.5-fold increase in the number of migrating cells. Platelet releasate was also shown to have a mitogenic effect on bone cells in proliferation studies.

Platelet-rich plasma

Oral Surg Oral Meal Oral Pathol Oral Radiol Endod
1998;85:638-46

Growth factor enhancement for bone grafts

Robert E. Marx, DDS,[a] Eric R. Carlson, DMD,[b] Ralph M. Eichstaedt, DDS,[c] Steven R. Schimmele, DDS,[d] James E. Strauss, DMD,[e] and Karen R. Georgeff, RN,[f] Miami, Fla.
UNIVERSITY OF MIAMI SCHOOL OF MEDICINE

- **88 Pts** had elective cancellous cellular marrow bone graft reconstructions of mandibular continuity defects > 5 cm
- Pts divided in 2 groups. One group received cancellous cellular marrow grafts without added PRP. The 2nd group received grafts with PRP added during the bone-milling phase of graft preparation and applied topically after bone placement into the defect.
- Autologous bone was used, harvested from posterior iliac crest.
- **Panoramic radiograph were taken after 2, 4 and 6 months and "graft maturity index" was calculated by 2 blinded investigators**
- **After 6 months computerized histomorphometry to calculate % of trabecular bone area vs marrow space area.**

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Baseline Plt count 232.000 (111.000-523.000) **PRP Plt count 785.000** (595.000 -1.100.000)

Table II. Graft maturity index

Time (mo)	*Grafts*	*Graft + PRP*	P
2	0.92	2.16	0.001
4	0.88	1.88	0.001
6	1.06	1.62	0.001

Table III. Histomorphometric findings at 6 months

	TBA	P
Native mandible (10)	38.9% ± 6%	-
Bone grafts (44)	55.1% ± 8%	0.005
Bone grafts with PRP (44)	74.0% ± 11%	0.005

Other RCT studies in oral and maxillofacial surgery

Positive results

- Anitua E. Plasma rich in growth factors: preliminary results of use in the preparation of future sites for implants. ***Int J Oral Maxillofacial Implants 1999;14:529-35***.
- Wiltfang J, Schlegel KA, Schultze-Mosgau S, Nkenke E, Zimmermann R, Kessler P. Sinus floor augmentation with beta-tricalciumphosphate (beta-TCP): does platelet-rich plasma promote its osseous integration and degradation? ***Clin Oral Implants Res 2003;14:213-8***.
- Cheung WS, Griffin TJ. A comparative study of root coverage with connective tissue and platelet concentrate grafts: 8-month results. ***J Periodontol 2004;75:1678-87***.
- Simon D, Manuel S, Geetha V, Naik BR. Potential for osseous regeneration of platelet-rich plasma—acomparative study in mandibular third molar sockets. ***Indian J Dent Res 2004;15:133-6***.

From: Martinez-Zapata et al. Transfusion 2009; 49: 44-56

Other RCT studies in oral and maxillofacial surgery

- Huang LH, Neiva RE, Soehren SE, Giannobile WV, Wang HL. The effect of platelet-rich plasma on the coronally advanced flap root coverage procedure: a pilot human trial. ***J Periodontol 2005;76:1768-77***.
- Okuda K, Tai H, Tanabe K, Suzuki H, Sato T, Kawase T, Saito Y, Wolff LF, Yoshiex H. Platelet-rich plasma combined with a porous hydroxyapatite graft for the treatment of intrabony periodontal defects in humans: a comparative controlled clinical study. ***J Periodontol 2005;76:890-8***.
- Steigmann M, Garg AK. A comparative study of bilateraln sinus lifts performed with platelet-rich plasma alone versus alloplastic graft material reconstituted with blood. ***Implant Dent 2005;14:261-6***.

Negative results

- Raghoebar GM, Schortinghuis J, Liem RS, Ruben JL, van derWal JE, Vissink A. Does platelet-rich plasma promote remodeling of autologous bone grafts used for augmentation of the maxillary sinus floor? *Clin Oral Implants Res 2005;16:349-56*.

From: Martinez-Zapata et al. Transfusion 2009; 49: 44-56

Enhanced Tibial Osteotomy Healing with Use of Bone Grafts Supplemented with Platelet Gel or Platelet Gel and Bone Marrow Stromal Cells

D. Dallari, L. Savarino, C. Stagni, E. Cenni, A. Cenacchi, P.M. Fornasari, U. Albisinni, E. Rimondi, N. Baldini and A. Giunti

J Bone Joint Surg Am. 2007;89:2413-2420. doi:10.2106/JBJS.F.01026

33 Pts undergoing tibial osteotomy to treat genu varum were assigned to 3 groups.

Group A, lyophilized bone chips + PLT gel;

Group B, lyophilized bone chips with platelet gel and bone marrow stromal cells;

Group C, lyophilized bone chips alone.

Graph showing the mean osseointegration percentage levels on radiographs

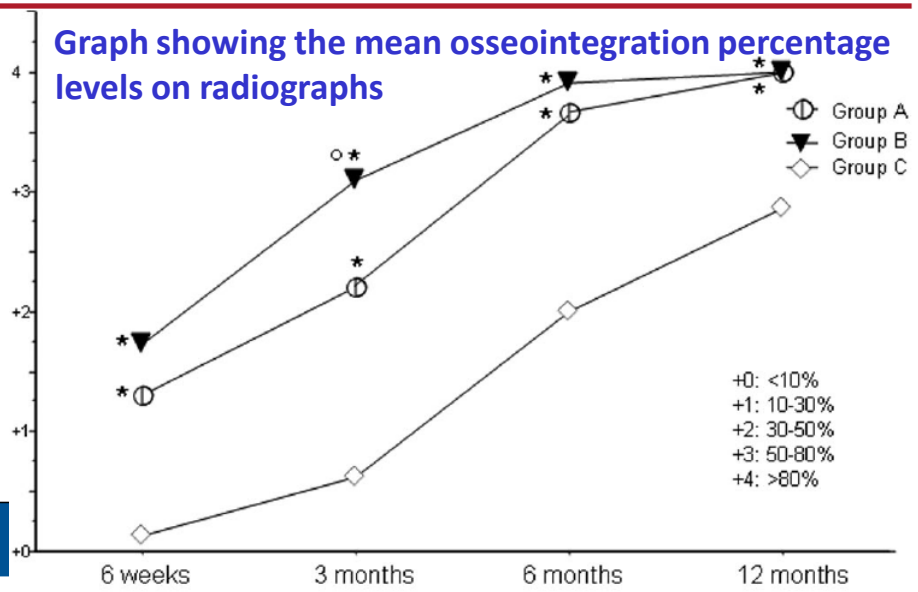


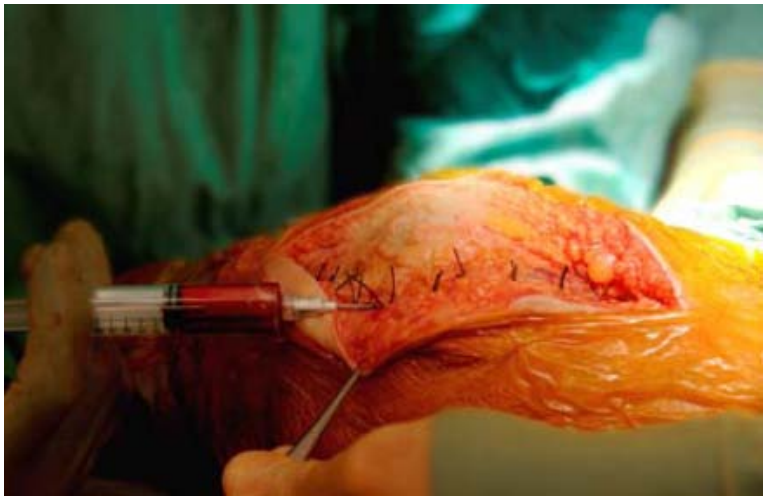
TABLE III Histomorphometric Results

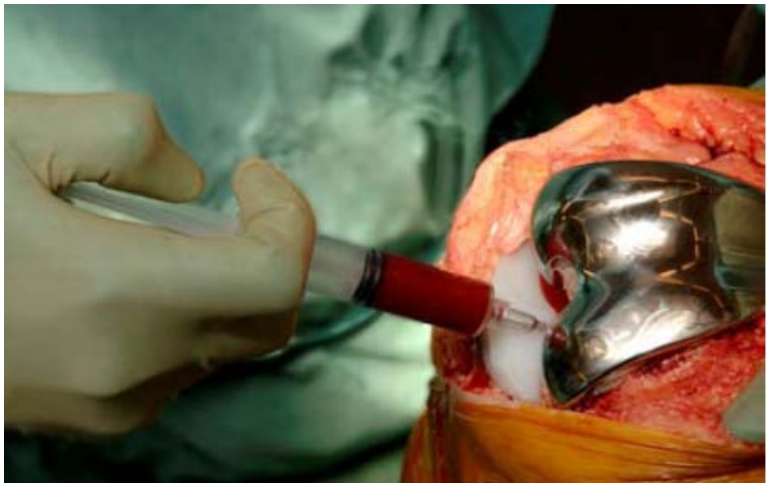
Histomorphometric Parameters	Group A			Group B			Group C		
	Mean and Standard Error	Median	Range	Mean and Standard Error	Median	Range	Mean and Standard Error	Median	Range
No. of osteoblasts	9.8 ± 1.3	8.0	0-40	11.1 ± 1.5	9.0	0-38	1.9 ± 0.4	1.0	0-8
No. of osteoid areas	3.8 ± 1.1	2.0	0.0-18.0	9.5 ± 0.8	9.0	1.0-25.0	1.7 ± 0.5	1.0	0.0-7.0
Percentage of bone apposition on chips	16.9 ± 3.1	16.0	5.0-33.0	36.2 ± 8.4	35.0	10.0-70.0	5.7 ± 1.3	6.0	0.0-10.0
No. of vascular buds	10.1 ± 6.3	3.0	0.0-58.6	5.9 ± 2.1	3.2	0.0-35.0	1.2 ± 0.2	1.2	0.0-2.0
No. of osteoclasts	0.07 ± 0.05	0.0	0.0-0.4	0.2 ± 0.1	0.0	0.0-1.0	0.4 ± 0.1	0.0	0.0-1.2
Percentage of defect filled with fibrous tissue	13.7 ± 7.1	2.5	0.0-50.0	7.7 ± 5.5	2.0	0.0-40.0	11.6 ± 4.4	8.0	0.0-30.0

Autologous platelet gel and fibrin sealant enhance the efficacy of total knee arthroplasty: improved range of motion, decreased length of stay and a reduced incidence of arthrofibrosis

Knee Surg Sports Traumatol Arthrosc 2007; 15:888–894

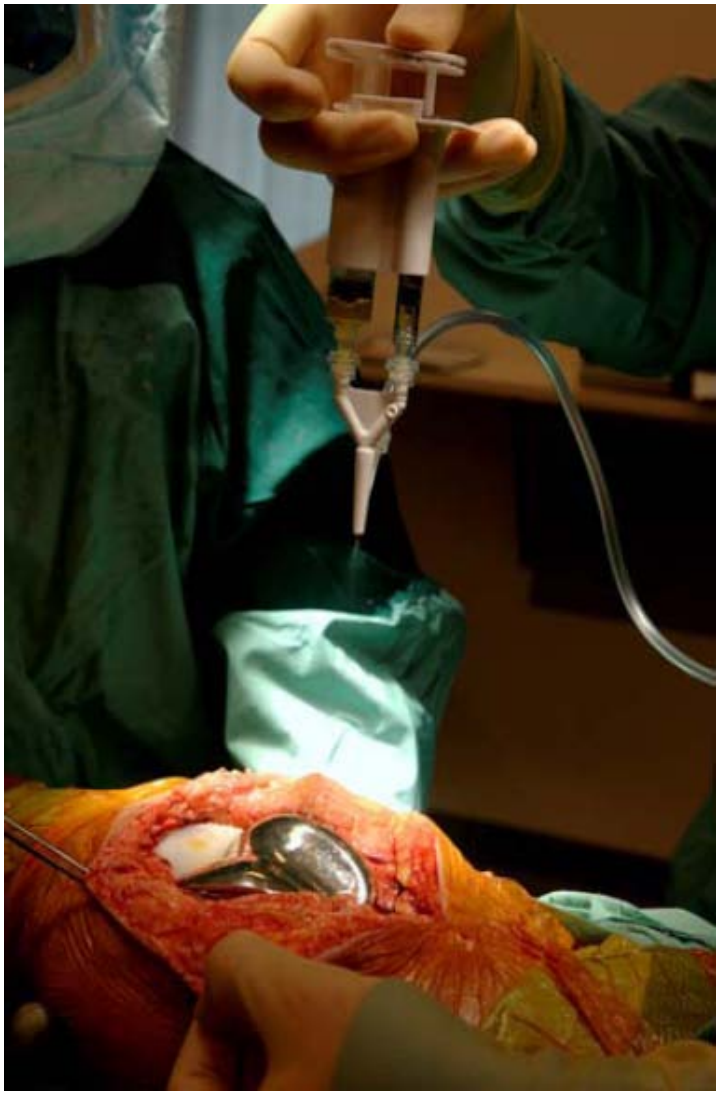
Peter A. M. Everts · Roger J. J. Devilee · Cornelis J. M. Oosterbos · Christine Brown Mahoney · Maarten Eeftinck Schattenkerk · Johannes T. A. Knape · André van Zundert





165 Pts

PRP from unit of whole blood treated by cell separat.



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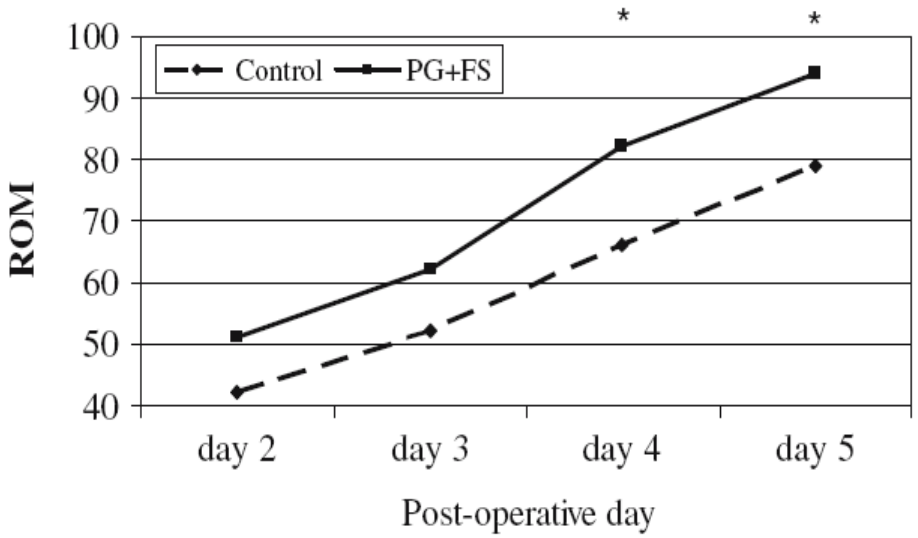
Knee Surg Sports Traumatol Arthrosc 2007; 15:888–894

Table 1 Patient characteristics and type of knee prosthesis

Description	Treatment group (n = 85)	Control group (n = 80)
Age (years)	69.4 ± 9.1	67.4 ± 9.9
Gender (F/M)	58/27	58/22
% Cemented	74	73
Pre-op hemoglobin (g/dl)	13.6 ± 1.1	13.7 ± 1.1
Post-op EC-T (Units)	0.17 ± 0.6	0.52 ± 0.9*
Discharge hemoglobin (g/dl)	10.9 ± 1.0	10.5 ± 1.1



No positive effect of autologous platelet gel after total knee arthroplasty

A double-blind randomized controlled trial: 102 patients with a 3-month follow-up

Acta Orthopaedica 2009; 80 (5): 557–562

Joost C Peerbooms[1], Gideon S de Wolf[2], Joost W Colaris[1], Daniël J Bruijn[1], and Jan A N Verhaar[3]

- Double-blind randomized controlled study in 102 pts undergoing TKA
- Primary aim was to evaluate wound healing, but the effects on knee function, use of analgesics, and Hb were also evaluated.
- A specially designed wound scoring system was used.
- Using a spray tip at a distance of 10–15 cm with the knee flexed at 90 degrees, 6 mL PRP was applied to the dried wound site (synovium and bony cutting edges of femur and tibia); thereafter, the wound was closed in layers. The subcutaneous tissues of the patients randomized to receive PG were also sprayed with 10 mL of PPP

Peerbooms JC et alActa Orthopaedica 2009; 80 (5): 557–562

	PG group	Control group	95% CI	p-value
Wound closure)	n = 32	n = 41		
Second day postoperatively	0	0		–
Third day postoperatively	7	6	7% (–11% to 25%)	0.5
Fourth day postoperatively	7	13	–9% (–30% to 10%)	0.4
Wound closure	n = 36	n = 46		
2 weeks postoperatively	4	16	–24% (–41% to 7%)	0.02
Drop in Hb, mean (SD)	n = 50	n = 52		
mmol/L	–1.58 (0.63)	–1.75 (0.58)	0.16 (–0.07 to 0.4)	0.2
Pain at rest, median (range)	n = 50	n = 52		
At inclusion	3 (1–5)	3 (1–5)		0.8
6 weeks	2 (1–5)	2 (1–5)		0.08
3 months	2 (1–5)	2 (1–5)		0.8
Pain during walking, median (range)	n = 50	n = 52		
At inclusion	4 (1–5)	4 (1–5)		0.4
6 weeks	2 (1–5)	2 (1–5)		0.07
3 months	2 (1–5)	2 (1–5)		0.9
Use of pain medication, median (range)	n = 50	n = 52		
At inclusion	2 (1–5)	2 (1–5)		0.5
6 weeks	2 (1–5)	2 (1–5)		0.9
3 months	2 (1–5)	2 (1–5)		0.1
WOMAC score, mean (range)	n = 50	n = 52		
At inclusion	45 (8–76)	44 (14–74)		
6 weeks	26 (3–76)	24 (0–65)	0 (–8 to 8)	0.7
3 months	25 (0–76)	21 (0–66)	–3 (–6 to 1)	0.4
ROM, mean (SD)	n = 32	n = 36		
Second day postoperatively	53 (14)	50 (17)		
Third day postoperatively	68 (13)	65 (16)		
Fourth day postoperatively	72 (13)	73 (14)		0.7
ROM, mean (SD)	n = 34	n = 45		
2 weeks postoperatively	91 (13)	89 (13)		
6 weeks postoperatively	99 (11)	100 (13)		
3 months postoperatively	102 (12)	101 (12)		0.9

Autologous platelet gel in total knee arthroplasty: a prospective randomized study

Wieger G. Horstmann · Robert Slappendel · Gijs G. van Hellemondt · Ate W. Wymenga · Nigel Jack · Peter A. M. Everts

Knee Surg Sports Traumatol Arthrosc 2011;19:115–121

- Postop Hb drop on the first postop day not different.
- Haematomas larger in controls at 5th postop day (P = 0.03);
- Trend towards more wound healing disturbances in the control group (4/20 pts vs 0/20);
- Less pain at rest in the APG group, significantly less on the 3rd postoperative day, (P = 0.04).
- Pain scores during exercise not statistically different.
- Range of motion of the knee was similar preoperatively and on the 3rd and the fifth postoperative day in both groups.
- **Total hospital stay was 1.3 days shorter in the PG group.**

SPINE Volume 30, Number 9, pp E243–E246

Platelet Gel (AGF) Fails to Increase Fusion Rates in Instrumented Posterolateral Fusions

Leah Yacat Carreon, MD,* Steven D. Glassman, MD,* Yoram Anekstein, MD,† and Rolando M. Puno, MD*

- Retrospective cohort study.
- Treated group: 76 consecutive pts who underwent instrumented posterolateral lumbar fusion **with autologous iliac crest bone graft** mixed with **autologous growth factor** (AGF).
- Control group: 76 pts randomly selected from pts who underwent instrumented posterolateral lumbar fusion **with autologous bone graft alone**.

SPINE Volume 30, Number 9, pp E243–E246

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Leah Yacat Carreon, MD,* Steven D. Glassman, MD,* Yoram Anekstein, MD,† and Rolando M. Puno, MD*

- **Platelet gel:**

  30 ml of AGF were obtained from 500mL of whole blood collected preoperatively using an autotransfusion device. **Data on Plt concentration not reported.**

- **Results:**

  In both groups, mean age was 50 years, and 24% were smokers. The nonunion rate was 25% in the AGF group and 17% in the control group. **This difference was not statistically significant (*P* 0.18).**

Clin J Sport Med 2011;21:37–45

Platelet-Rich Plasma Treatment for Ligament and Tendon Injuries

Justin Paoloni, MBBS, PhD, Robert J. De Vos, MD,† Bruce Hamilton, MBChB,*‡*

TABLE 2. Human Clinical Trials on PRP in Ligament and Tendon Injuries, Description of the Type of Study, Level of Evidence Results, and Relevant Comments

Authors	Diagnosis	Design	Results	Comments	Level Evider
Nin et al[21]	Ligament injury: ACL bone-patellar tendon-bone allograft	Prospective randomized controlled trial (n = 50 each group) ☹	No difference inflammation, MRI, or clinical evaluation	RCT with appropriate statistical power, with 2-year follow-up, single PRP application, possible type 2 error ☺	1b
Silva and Sampaio[22]	ACL hamstring allograft	Prospective randomized controlled trial (N = 10 each group) ☹	No difference in MRI evaluation	Small RCT with 3-month follow-up only, single and multiple PRP application groups, possible type 2 error ☺	1b
Ventura et al[23]	ACL hamstring allograft	Prospective randomized controlled trial (n = 10 each group) ☹	No difference in clinical evaluation or functional scores. Increased ACL density on computed tomographic scan in PRP group, similar to density of posterior cruciate ligament	Small RCT with 6-month follow-up only, single PRP application, possible type 2 error. Computed tomographic scan is not commonly used to assess ACL ☺	1b
Sanchez et al[31]	Acute tendon injury: Achilles tendon rupture	Case–control study (n = 6; control n = 6) ☺	Significant improvement in earlier ankle range of motion, earlier return to gentle running and earlier return to sports, smaller cross-sectional tendon area on ultrasound	Case–control study with small numbers and 12-month follow-up (but only 6 months reported), single PRP application at surgery with fibrin scaffold ☹	3b
Schepull et al[32]	Achilles tendon rupture	Prospective randomized controlled trial (n = 16 PRP; n = 14 control group) ☹	No difference in functional measures (Achilles Tendon Total Rupture Score)	RCT with 12-month follow-up. Platelet-rich plasma–implanted bead application in depots proximal and distal to rupture ☺	1b
de Vos et al[36]	Chronic Tendon Injury; Achilles tendinopathy	Prospective randomized controlled trial (N = 27 each group) ☹	No difference in pain scores or functional measures (VISA-A)	RCT with appropriate statistical power but with only 6-month follow-up. Single PRP application in multiple depots under ultrasound guidance compared with saline injection. Saline injection into tendon is not commonly performed ☺	1b

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Platelet-Rich Plasma Treatment for Ligament and Tendon Injuries

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Gaweda et al[44]	Achilles tendinopathy	Case series (N = 15)	Significant improvement in functional measures (VISA-A and AOFAS)	Case series only with 18-month follow-up, single or repeated ultrasound guided PRP injections and rehabilitation	4
Kon et al[38]	Patellar tendinopathy	Case series (N = 20)	Significant improvement in quality of life scores (EQ-VAS and SF-36) and function (Tegner score)	Case series only with 6-month follow-up, 3 PRP injections into depots at intervals of 15 days, no guidance, quality of life scores	4
Mishra and Pavelko[40]	Elbow tendinopathy (wrist extensor tendinopathy or wrist flexor tendinopathy)	Case–control study (n = 15; control n = 5)	Significant improvement in pain (VAS) and function (modified Mayo score)	Case–control study with 24-month follow-up, single PRP application, no guidance. Different diagnoses (medial and lateral elbow tendinosis). Only 2 controls after 8 weeks and not followed after this, 1 control asymptomatic	4
Peerbooms et al[41]	Elbow tendinopathy (wrist extensor tendinopathy)	Prospective randomized controlled trial (n = 51 PRP group; n = 49 corticosteroid injection group)	Significant improvement in "successful outcomes" of decrease 15% in pain (VAS) and function (DASH scores)	RCT with appropriate statistical power but with 12-month follow-up only, single PRP application compared with single corticosteroid injection, unexplained crossover interventions, and unusual statistical analysis	1b
Filardo et al[39]	Patellar tendinopathy	Prospective randomized controlled trial (n = 15 PRP; n = 16 control group)	No significant improvement in PRP group with pain (VAS) and function (Tegner score)	Small RCT with 6-month follow-up only, 3 PRP injections, compared with exercise only group, possible type 2 error	1b
Randelli et al[43]	Complete rotator cuff tear	Case series (N = 14)	Significant improvement in pain (VAS) and function (UCLA and Constant scores)	Case series with 24-month follow-up, single PRP application at surgery. Joint-specific scores	4

The use of autologous platelet gel to treat difficult-to-heal wounds: a pilot study (Mazzucco L et al, Transfusion, 2004)

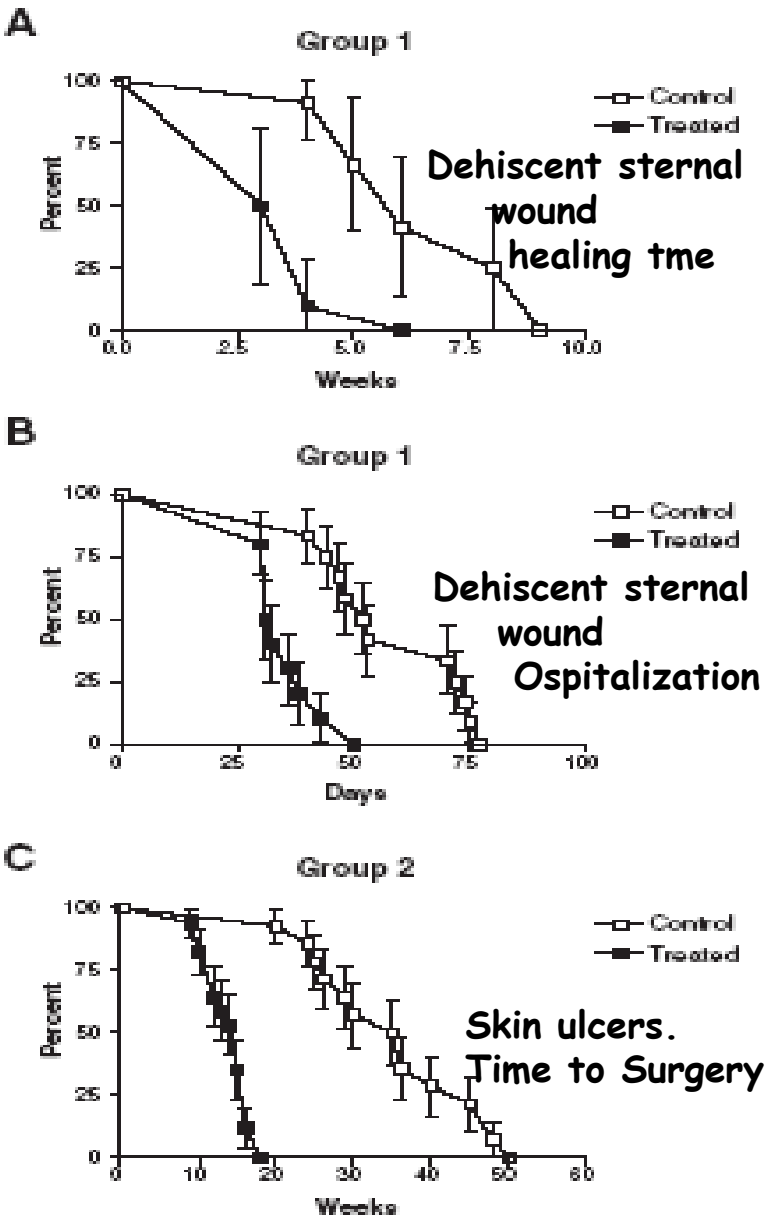


Fig. 1. Clinical endpoints: treated versus control group. Kaplan-Meier plots. (A) Group 1 (dehiscent sternal wounds): complete (100%) healing time (wks). (B) Group 1 (dehiscent sternal wounds): hospitalization time required to achieve complete healing (days). (C) Group 2 (Necrotic skin ulcers): time required to have surgery.

53 patients enrolled
- 22 had dehiscent sternal wounds (10 treated and 12 controls)
- 31 had skin necrotic ulcers (17 treated and 14 controls)

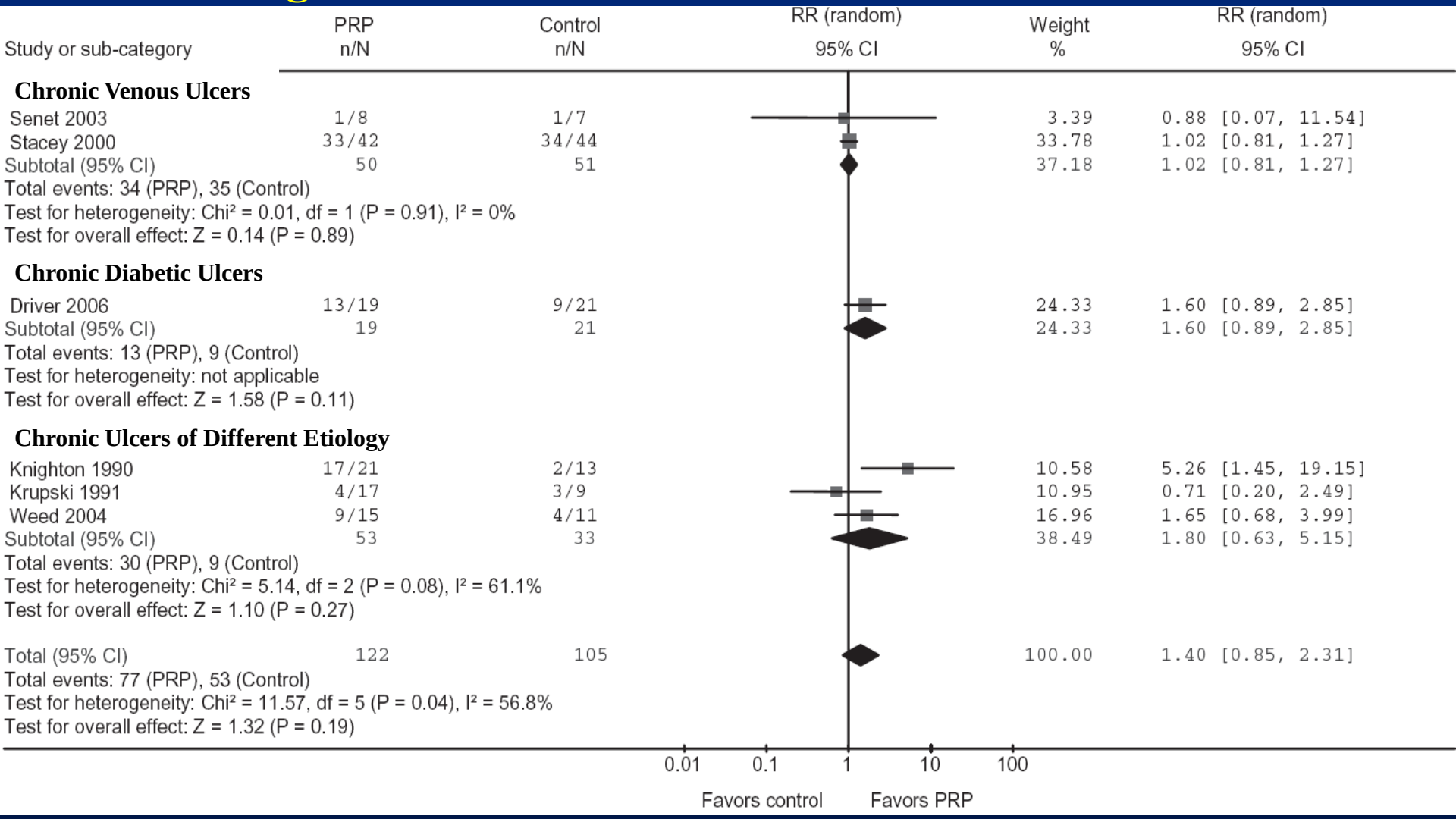
Compared with patients under conventional treatment, patients with dehiscent sternal wounds (Group 1) treated with PLT gel achieved 100-percent healing in nearly half the time (median, 3.5 vs. 6.0 wks; $p = 0.0002$). The difference in hospital stay between treated and control groups was substantial (median, 31.5 vs. 52.5 days; $p < 0.0001$). During the follow-up, neither recurrence nor complication occurred.

In patients with necrotic skin ulcers (Group 2) treated with PLT gel, the time required to have surgery was significantly shorter (median, 15.0 vs. 35.5 wks; $p < 0.0001$). Local recurrence did not occur in patients after surgery.

Efficacy and safety of the use of autologous plasma rich in platelets for tissue regeneration: a systematic review

Martinez-Zapata et al. Transfusion 2009; 49: 44-56

Autologous PRP in Chronic Skin Ulcers. Results in RCT



Report/studies demonstrating efficacy of platelet gel for healing chronic wounds

- Hom D, Maisel R. Angiogenic growth factors: Their effects and potential in soft tissue wound healing. Ann Otol Rhinol Laryngol 1992; 101 (4): 349- 54.
- Wang H, Wan H, Yang T, et al. Acceleration of skin graft healing by growth factor. Burns 1996; 22 (1): 10-4.
- Powell D, Chang E, Farrior E. Recovery from deep plane rhytidectomy following unilateral wound treatment with autologous platelet gel. Arch Facial Plast Surg 2001; 3 (4): 245-50.
- Crovetti G, Martinelli G, Issi M, et al. Platelet gel for healing cutaneous chronic wounds. Transfus Apheresis Sci 2004; 30: 145-51.
- Bernuzzi G, Tardito S, Bussolati O, et al. Platelet gel in the treatment of cutaneous ulcers: the experience of the Immunoematology and Transfusion Centre of Parma. Blood Transfus 2010; 8: 237-47

Allogenic platelet gel in the treatment of pressure sores: a pilot study.

Scevola S, Nicoletti G, Brenta F, Isernia P, Maestri M, Faga A.

Int Wound J 2010; 7:184–190

- 13 Pts affected by spinal cord injury with 16 pressure sores. The ulcer considered the experimental unit of the study irrespective of the number of ulcers per patient.
- Each ulcer randomised to be treated either with PG or with current best practice approach to chronic wounds dressing protocol.
- 15 ulcers out of 16 improved clinically. **No statistically significant difference in volume reduction between the two groups**,
- Statistically significant difference in the onset time of granulation tissue proliferation (**in the wounds treated with platelet gel the healing process was triggered earlier**).

Platelet gel for treatment of mucocutaneous lesions related to graft-versus-host disease after allogeneic hematopoietic stem cell transplant

TRANSFUSION 2010;50:501-506.

Alessandra Picardi, Alessandro Lanti, Laura Cudillo, Raffaella Cerretti, Teresa Dentamaro, Gottardo De Angelis, Angelo Ferraro, Ambra Di Veroli, Gaspare Adorno, and William Arcese for the Rome Transplant Network

RESULTS: After the second PLT gel application, the pain disappeared in all cases and the granulation tissue was observed in the four patients with Grade II lesions. After a median of eight PLT gel applications (range, 4-10), five of six patients showed a complete response, while one patient with a partial response died early from multiorgan failure. No side effects were documented.

Report/studies demonstrating efficacy of platelet gel for reducing pain in surgical wounds

- Englert SJ et al Autologous Platelet Gel Application During Cardiovascular Surgery: Effect on Wound healing. , JECT 2005; 37: 148-52
- Gardner M, Demetraktopoulos D, Klepchick P, Mooar P. The efficacy of autologous platelet gel in pain control and blood loss in total knee arthroplasty. An analysis of haemoglobin, narcotic requirement and range of motion. Int Orthop 2007; 31 (3): 309-13.

Gel di piastrine

Efficacia terapeutica

Seppure gli studi randomizzati e controllati siano pochi ed il numero di pazienti in essi inseriti è spesso limitato, i risultati di questi studi, seppur non univoci, uniti alla ampia esperienza raccolta e descritta in studi osservazionali sembra dimostrare l'efficacia clinica del gel di piastrine nell'accelerare i processi riparativi in vari ambiti clinici

ISBT Science Series (2009) 4, 136–142

ORIGINAL PAPER

4A-S25-02

Blood-derived biomaterials: fibrin sealant, platelet gel and platelet fibrin glue

T. Burnouf,[1] C.-Y. Su,[2] M. Radosevich,[1] H. Goubran[3] & M. El-Ekiaby[4]

[57–59]. Moreover, it is important to carry out further investigations aiming at designing improved standardized PG biomaterials and at developing clinical techniques optimizing the physiological benefits of the cytokines. A drawback of PG are the variables often prevailing in its preparation and use, affecting its reproducibility and possibly explaining the inconsistency in clinical outcomes [56,60,61].