INTRODUCTION

For years, mechanical stabilization has played a fundamental role in the successful management of foot and ankle trauma and elective surgeries. However, a multitude of risk factors have been shown to cause impaired osseous healing and delayed soft tissue regeneration, resulting in poor clinical outcomes in certain patient populations. In an effort to address this concern, research over the past decade has led to the exploration of numerous growth factors, namely platelet-rich plasma (PRP), bone morphogenetic proteins (BMPs), and recombinant human platelet-derived growth factor (rhPDGF), which may serve as potential biologic adjuncts to conventional therapy by promoting bone and soft-tissue healing.

PLATELET-RICH PLASMA

Platelet rich plasma (PRP) is a bioactive component derived from autologous blood that contains a concentrated volume of platelets, typically a 5-fold increase (~1,000,000/µl) above physiological levels. When activated, platelets within the concentrate release a number of growth factors that have been shown to set the stage for healing and regeneration of musculoskeletal tissues. These growth factors include platelet-derived growth factor (PDGF), transforming growth factor (TGF), insulin-like growth factor (IGF), vascular endothelial growth factor (VEGF), and epidermal growth factor (EGF). Their role(s) in the various stages of osseous and soft-tissue healing, including hematoma formation, chemotaxis of inflammatory cells, proliferation and differentiation of mesenchymal cells, remodeling, angiogenesis, and extracellular matrix formation, have been well-described (Gandhi, Bibbo et al. 2005; Alsousou, Thompson et al. 2009).

Several PRP preparation systems are currently available (Dohan Ehrenfest, Rasmusson et al. 2009). While no accepted standard for the preparation of PRP exists, the basic process consists of a two-step centrifugation of autologous, anticoagulated blood to first obtain plasma, followed by isolation of a platelet-rich concentrate (Foster, Puskas et al. 2009). Additionally, some investigators choose to activate PRP with thrombin in an effort to provide an immediate high-dose delivery of the various growth factors to the site of application. Each preparation system delivers varying final platelet and growth factor concentrations (Dohan Ehrenfest, Rasmusson et al. 2009).

PRP was first clinically applied in oral and maxillofacial surgery in the 1990s, where initial studies provided support for its use as an osteoconductive agent (Tayapongsak, O’Brien et al. 1994; Marx, Carlson et al. 1998). In plastic surgery and other surgical subspecialties, applications for the use of PRP were in the realm of hemostasis and wound healing to improve postoperative prognosis with respect to infection, blood loss, and pain (DelRossi, Cernaianu et al. 1990; Eppley, Pietrzak et al. 2006). Over the past decade, orthopaedic surgeons have used PRP as a bioadjuvant to improve bone healing in spinal fusion, fracture repair, and limb lengthening procedures (Lowery, Kulkarni et al. 1999; Dallari, Savarino et al. 2007; Kitoh, Kitakoji et al. 2007; Kitoh, Kitakoji et al. 2007). More recently, the utility of PRP in sports medicine as a safe bioadjuvant to accelerate tendinous healing has been shown (Hall, Band et al. 2009; Mishra, Woodall et al. 2009). However, only limited data are currently available that definitively describes the role of the clinical application of PRP in foot and ankle surgery. Several investigators have proposed that PRP can serve as a safe adjunct, when applied locally; especially in high-risk patients who demonstrate risk factors for impaired bone healing.

Review of Literature: Bibbo and colleagues (Bibbo, Bono et al. 2005) published the first evidence-based study demonstrating the use of PRP in high-risk patients undergoing elective foot and ankle surgery. In this prospective observational study, 62 high-risk patients (encompassing 123 operative procedures) were followed for a period of 6 months after receiving PRP applied locally to the surgical site. At least 1 risk factor for poor or delayed osseous healing (as listed in TABLE) was identified in all patients. Patients demonstrated various pathologies involving the hindfoot, forefoot, or ankle for which they underwent...
operative fixation, as appropriately determined by the surgeon. Additionally, some patients received bone graft in combination with PRP if it was required to fill a bony defect or in order to correct alignment (e.g. lateral column lengthening). Evaluation for radiographic union was performed every 2 weeks. The clinical outcomes and complications associated with the local application of PRP were assessed. Overall, a 94% union rate was achieved at a mean of 41 days. The mean time to union for patients treated with PRP alone was 40 days, versus 45 days for patients that received bone graft in combination with PRP. The investigators concluded that the adjunctive use of PRP is an important tool in high-risk elective foot and ankle surgery with or without the use of bone graft, resulting in an acceptable time to union with low risk for complications. However, due to the varying pathologies, inconsistent surgical technique, and absence of a control group, the efficacy of the local application of PRP cannot be directly determined from this study.

In 2005, Barrow and Pomeroy (Barrow and Pomeroy 2005), and later, Coetzee and colleagues (Coetzee, Pomeroy et al. 2005), demonstrated that PRP reduced the time to union in ankle syndesmotic fusions in total ankle replacement (TAR), which is a critical "next step" required before patients can proceed with advanced weight bearing status and the overall success of the Agility® TAR (Depuy, Inc, Warsaw, IN).

Barrow and Pomeroy (Barrow and Pomeroy 2005) investigated the effect of PRP-augmented bone grafting on syndesmotic fusion rates in 20 consecutive patients undergoing Agility TAR for post-traumatic arthritis, rheumatoid arthritis, or osteoarthritis. Prior to surgery, at least 6 months of conservative management (i.e. bracing) was attempted. The operative technique for the Agility TAR as described by Alvine was employed with some modifications (Alvine 2002). Symphony PCS autologous platelet concentrate (Depuy Corp, Warsaw, Indiana) was sprayed on the bone surfaces of the syndesmosis, the cut surfaces of the distal tibia and talus, and over the porous coating of the ankle prosthesis. PRP was also mixed with local autograft derived from resected bone, which was packed in the distal tibiofibular joint after insertion of the TAR components. The investigators reported successful fusion of the syndesmosis in all 20 cases within 6 months; 85% at 2 months, 95% at 3 months, and 100% at 6 months. This was compared to previously reported distal tibiofibular joint fusion rates of 62-82% at 6 months (Pyevich, Saltzman et al. 1998; Saltzman and Alvine 2002).

Similarly, in a preliminary study by Coetzee and colleagues (Coetzee, Pomeroy et al. 2005), PRP was used to promote syndesmotic fusion in patients undergoing TAR. The investigators compared fusion rates in 66 patients using PRP augmented bone grafting versus 114 patients as historical controls with non-PRP augmented bone grafting of the ankle syndesmosis performed during TAR. The operative technique was similar to that used by Barrow and Pomeroy (Barrow and Pomeroy 2005). Patients were followed to assess radiographic union, which was evaluated by standard ankle radiographs or with computed tomography (CT) scans if there was questionable radiographic evidence of a syndesmotic fusion. The results of this study showed statistically significant improvement in 8- and 12-week fusion rates from 61.4% and 73.6% respectively, in historical controls (n=114), to 76% and 93.9% respectively, in patients with PRP-augmented bone grafting (n=66). Additionally, a significant reduction in delayed unions and nonunions at 6 months with the addition of PRP was observed.

Dallari and colleagues (Dallari, Savarino et al. 2007) demonstrated that the supplementation of locally implanted allograft bone chips with bone marrow aspirate containing pluripotential stromal cells, in combination with PRP significantly enhanced healing rates in patients undergoing tibial osteotomy. This concept was further explored by Pinzur (Pinzur 2009); who studied the effects of PRP and bone marrow aspirate in high-risk patients with Charcot arthropathy of the foot. In this prospective case series, 44 diabetic patients (46 feet) at high risk (immunodeficient, morbidly obese, osteomyelitis at deformity site, or demonstrating multiple diabetic co-morbidities) for unfavorable clinical results with conventional surgery underwent surgical correction for their deformity. A static external fixator was applied to maintain postoperative surgical correction. Prior to wound closure, freshly-prepared PRP and bone marrow aspirate were injected locally into the fusion site. After partial weight-bearing for 8 weeks, the external fixator was removed, and a total contact cast was placed for 4 to 6 weeks. Serial radiographs were obtained to evaluate osseous healing. In spite of having risk factors for delayed or impaired bone healing, 91.3% (n=46) of all fusion sites showed radiographic evidence of osseous union at 16 weeks after surgery.
and clinically acceptable results were also observed, as evident by patients’ ability to ambulate using commercially available therapeutic footwear.

**BONE MORPHOGENETIC PROTEINS**

Bone morphogenetic proteins are the key modulators of osteoprogenitor and mesenchymal cells during osseous healing. With more than 20 BMPs identified so far, all but BMP-1, belong to the Transforming Growth Factor beta super family of proteins and have regulatory effects in the differentiation and proliferation of cartilage and bone-forming cells from pleuripotent mesenchymal stem cells during the process of bone healing(Reddi 1994).

BMPs interact with specific receptors on the cell surface, referred to as bone morphogenetic protein receptors (BMPRs) which are heteromeric complexes of type 1 and type 2 serine/threonine kinase receptors. Binding of BMPs to the receptor complex results in the phosphorylation of intracellular SMAD proteins which then translocates to the nucleus, where they regulate transcription(Shi and Massague 2003). SMAD proteins are a family of proteins that are involved in the translocation of signals from TGF-beta receptors; bone morphogenetic protein receptors; and other surface receptors to the cell nucleus.

BMPs induce new bone formation by way of endochondral ossification and in high concentration can even form new bone by intramembranous ossification(Wozney 1993). Several BMPs, like BMP 2, 4 and 7 are shown to have prominent roles in bone formation(Lieberman, Daluiski et al. 2002). BMP-4 mRNA is reported to be up-regulated at the fracture site as early as 12 hours and BMP-2 and BMP-4 protein concentrations have been shown to be elevated as early as 2 days following fracture(Nakase, Nomura et al. 1994; Bostrom, Lane et al. 1995; Yoshimura, Nomura et al. 2001). Further, BMP 2 and 4 drive osteoprogenitor cells to mature into osteoblasts(Onishi, Ishidou et al. 1998). Finally, BMP 3a, 4 and 7 show increased concentration in the osteogenic phase when bone maturation commences(Bostrom, Lane et al. 1995; Ishidou, Kitajima et al. 1995; Cho, Gerstenfeld et al. 2002). As the precursor cells mature and callus remodels, BMP 2 expression decreases(Bostrom and Asnis 1998).

Genetic engineering techniques have enabled production of growth factors, like recombinant human bone morphogenetic proteins (rhBMPs) for both experimental and clinical uses. Currently, only rhBMP-2 and rhBMP-7 are commercially available, after having been approved by FDA for clinical use in open tibia fracture and posterior lumbar fusion and as humanitarian device exemption for failed treated tibia non-unions, respectively(Axelrad and Einhorn 2009)**.

**Review of Literature**

Clinical studies have recently reported on the successful use of rhBMP-2 in complex ankle and hindfoot arthrodesis. In a prospective study, Bibbo and Haskell(Bibbo 2007) utilized rhBMP-2 (Infuse) in complex ankle and hindfoot fusions. In 45 procedures, the authors reported the mean time of union of 10 weeks (range 4-30 weeks) and wound issues in only 2 patients. In a more recent follow-up of their original series, Bibbo and colleagues(Bibbo, Patel et al. 2009)* retrospectively analyzed the use of rhBMP-2 in a total of 112 high-risk ankle and hindfoot fusions in 69 patients. These patients were categorized as high-risk based upon risk-factors for poor bone healing including diabetes mellitus, high-energy injury, and immunosuppression. Overall, 108 of 112 fusion sites underwent union in these high-risk patients with a mean time of union of 11 weeks, with no significant difference in union-rates seen amongst the different sites of fusion. Wound complications were seen in only 3 patients, which were successfully treated with local wound care and antibiotics.

**PLATELET-DERIVED GROWTH FACTOR**

Platelet-derived growth factor (PDGF) is a family of growth factors released from platelets and macrophages in response to tissue injury that form a series of disulfide-linked dimers including PDGF-AA, AB, BB, CC, and DD(Alvarez, Kantarjian et al. 2006). PDGF has been shown to promote the synthesis and release of several other growth factors, and to stimulate various mesenchymal-derived cells to further enhance DNA synthesis, augment collagen deposition, and increase synthesis of extracellular matrix(Hollinger, Hart et al. 2008)**. PDGF-BB is the most potent among the prevalent circulating isoforms. As a consequence of these biologic properties, the therapeutic potential of recombinant human PDGF-BB
(rhPDGF-BB) has been a focus of recent interest in orthopaedic surgery, among other surgical subspecialties. Although its utility in the clinical arena has not been well-described in orthopaedic literature, several recent scientific studies highlight the future potential of rhPDGF-BB in foot and ankle surgery.

**Review of Literature**

Hollinger and colleagues (Hollinger, Onikepe et al. 2008) used a tibial osteotomy model to study the effect of locally delivered rhPDGF-BB (in 20mM sodium acetate buffer or acetate buffer alone) in combination with β-tricalcium phosphate (β-TCP) and collagen matrix in geriatric, osteoporotic ovariectomized female rats. Mechanical testing at 5 weeks demonstrated no statistical difference in torsional strength of fractured tibiae treated with rhPDGF-BB versus the non-fractured contralateral tibiae, while non-rhPDGF-BB treated groups showed significant reduction in torsional strength. Histological analysis at the same timepoint indicated accelerated callus formation in the rhPDGF-BB treated group. Al-Zube and colleagues (Al-Zube, Breitbart et al. 2009)* demonstrated similar results with the use of rhPDGF with β-TCP and collagen matrix in a femur fracture model using diabetic BB Wistar rats. Upon local application at the fracture site, rhPDGF-BB was shown to increase cellular proliferation at Day 4, enhance biomechanical callus properties (i.e. torsional strength) at Week 8, and increase bony bridging as evident on histomorphometric analysis at Week 12 post-fracture, in a dose-dependent manner. The investigators (Hollinger, Onikepe et al. 2008; Al-Zube, Breitbart et al. 2009) concluded that rhPDGF-BB significantly enhanced bone healing in their osteoporotic and diabetic animal models, respectively, and may prove beneficial in orthopaedic applications for patients at risk for impaired osseous healing.

**Summary for Growth Factor**

Despite ongoing advances in orthopaedics, reconstructive surgery of the foot and ankle continues to be a challenging endeavor. This is especially true when operating on high-risk patients with compromised musculoskeletal-healing ability, for which PRP, BMPs, and rhPDGF-BB may contribute significantly to achieve more favorable clinical outcomes, reduce complication rates, and improve patient satisfaction. While there is ample scientific research that demonstrates the potential role of the described bioadjuvants on bone and soft tissue healing, further clinical investigation by way of prospective randomized studies is needed to establish safety, determine efficacy, and define ideal patient populations that can benefit from the use of these orthobiologics. Only then can their routine application in foot and ankle surgical interventions be considered and widely accepted.

**BIOPHYSICAL STIMULATION**

Several options are currently available for clinicians to promote the healing of fractures and accelerate the rate of union in elective arthrodesis, including the utility of biophysical stimulators, namely low intensity pulsed ultrasonography (LIPUS) and electrical bone stimulation devices such as pulsed electromagnetic field (PEMF) and direct current (DC). A Canadian survey of 450 trauma surgeons, with a response rate 60%, found that 45% of surgeons reported using bone stimulators to manage tibial fractures, with their use evenly divided between LIPUS and PEMF therapy (Busse, Morton et al. 2008). We plan to review the specific literature of the use of LIPUS and PEMF in the field of foot and ankle, with a focus in DM patients.

**Low-intensity Pulsed Ultrasonography**

The Food and Drug Administration approved the use of LIPUS for acceleration of healing of conservatively managed fresh fracture healing in 1994, and for treatment of established nonunions in 2000 (Rubin, Bolander et al. 2001). In vitro and animal experimental studies suggests that beneficial effects of LIPUS on bone healing may include a positive impact on signal transduction, gene expression, blood flow, and tissue modeling and remodeling (Khan and Laurencin 2008).

Based on the clinical data, LIPUS reduces time to healing (approximately 40%) in non-operatively managed radius and tibial fractures by a mean of 32 days (154 v 122 days) (Cook, Ryaby et al. 1997). Heckman and colleagues (Heckman, Ryaby et al. 1994), and later Kristiansen and colleagues (Kristiansen, Ryaby et al. 1997), studied the influence of LIPUS on the healing rate of acute tibial shaft and distal radius fractures, respectively. Both showed a significant reduction in time to union, and neither of the studies
reported any complications from the ultrasound. Cook and colleagues (Cook, Ryaby et al. 1997) further evaluated the data from Heckman and showed a reduction in the number of delayed unions with the use of ultrasound bone stimulation despite smoking. One economic analysis estimated savings of $13,259 per fracture (Heckman and Sarasohn-Kahn 1997). This economic analysis considered both direct and indirect costs; however, data for this model were based on a case series of 60 patients and an ultrasound registry, using radiographic healing as a surrogate for functional recovery.

Limited studies currently exist regarding the efficacy of LIPUS in fracture healing in animals with experimental diabetes (Gebauer, Lin et al. 2002). Specific studies on the effect of LIPUS on elective fusion in diabetics do not exist but one may extrapolate from the current literature studying LIPUS upon elective foot and ankle fusions. In a 12-month prospective study, Coughlin and colleagues (Coughlin, Smith et al. 2008) evaluated the healing rate and clinical results of patients undergoing primary subtalar arthrodeses with adjuvant LIPUS. Fifteen consecutive patients participated in the study, obtaining routine radiographs, CT scans, and clinical outcomes. The clinical and radiographic data were compared to a similar cohort of patients previously reported on that had not received ultrasound bone stimulation. Results of the patients who received ultrasound bone stimulation showed a statistically significant faster healing rate on plain radiographs at 9 weeks ($p = 0.034$) and CT scan at 12 weeks ($p = 0.017$). A 100% fusion rate was noted. The American Orthopaedic Foot and Ankle Society (AOFAS) ankle and hindfoot score was also improved at 12 months postoperatively, a finding that was statistically significant ($p = 0.026$). Coughlin’s study (Coughlin, Smith et al. 2008) is unique in being the first paper to prospectively evaluate ultrasound bone stimulation in primary hindfoot arthrodesis patients. While these patient did not have DM (actually an exclusion criteria), the faster rate of healing demonstrates its potential role in the high risk arthrodesis patient.

**Electrical Bone Stimulation**

With respect to foot and ankle surgery in high-risk patients, two techniques of electrical bone stimulation have been well-described: pulsed electromagnetic field (PEMF) and direct current (DC).

PEMF devices use pulses of exogenous electrical potentials in the form of an electromagnetic field applied locally to the area of interest (fracture and/or nonunion site) to accelerate osseous healing. PEMF devices are worn directly on the skin or a cast, and are therefore a noninvasive method of augmenting bone healing in the management of patients at high risk for delayed union or nonunion, including diabetics. Long periods of use, ranging from 3 to 10 hours a day depending on the system, are recommended, whereas application below the recommended minimal period of 3 hours per day has been shown to significantly reduce the efficacy electrical bone stimulation with respect to union (Garland, Moses et al. 1991). Hence, patient noncompliance is a potential issue.

DC devices are internally applied with a subcutaneously placed battery unit that houses the anode, and an attached titanium cathode wire electrode placed into the fracture/fusion site. While the electrical current can be delivered at maximal intensity for constant stimulation at the operative site, and patient compliance is rarely an issue, DC devices have their own disadvantages, namely local irritation or pain at the site of hardware implantation, and the potential need for a secondary procedure for hardware removal in case of infection (Figure 12).

Several studies (Donley and Ward 2002; Dhawan, Conti et al. 2004; Lau, Stamatis et al. 2007) have demonstrated the beneficial effect of electrostimulation in the treatment of primary hindfoot fusions, while only one prospective study (Dhawan, Conti et al. 2004) has described the clinical application of PEMF in primary foot and ankle arthrodesis. Dhawan and colleagues (Donley and Ward 2002) performed a clinical trial consisting of 64 patients (144 joints) undergoing elective triple or subtalar arthrodesis (primary and revision) randomized into two groups (with and without postoperative PEMF). The study excluded patients considered to be at high risk for impaired bone healing, specifically those with rheumatoid arthritis, diabetes or corticosteroid use. Blinded radiographic analysis was performed to assess fusion. The mean time to union for the PEMF group was 12.9 weeks for primary subtalar fusions (100% unions), 12.2 weeks for talonavicular fusions, and 13.1 weeks for calcaneocuboid fusions, while the corresponding fusions in non-PEMF control group demonstrated an average time to union of 14.5 weeks, 17.6 weeks, and 17.7 weeks, respectively. While determining time-to-union by assessing standard radiographs is not a reliable method for quantifying this endpoint (Coughlin, Smith et al. 2008) and no sham PEMF units for
controls were used, this randomized prospective study showed a statistically significant reduction in time required for union in both the talonavicular and calcaneocuboid fusion groups treated with PEMF, and a trend towards faster union in the subtalar arthrodesis group. Interestingly, patients who had PEMF treatment for multiple joint arthrodeses showed a tendency for the remaining joints to fuse quicker when one of the joints fused rapidly.

Donley and colleagues (Donley and Ward 2002) conducted a case series to assess the outcome of DC device implantation and subsequent electrical bone stimulation in 13 patients with primary hindfoot or ankle fusions (six tibio-talo-calcaneal, three ankle, two subtalar, and two tibiocalcaneal arthrodeses). All patients enrolled in this study demonstrated at least two risk factors for nonunion, including a history of nonunion, smoking, and osteonecrosis of the talus. Postoperative follow-up at one year showed successful fusion in 12 of 13 patients (92%). Clinically, postoperative pain and modified AOFAS scores at one-year showed significant improvement when compared to preoperative scores. Complications were superficial infections requiring local wound care in 4 patients, and 8 patients reported the subcutaneous battery pack to be bothersome, 4 of which underwent surgical removal.

Although the results of these investigations (Donley and Ward 2002; Dhawan, Conti et al. 2004; Lau, Stamatis et al. 2007) show a positive influence of electrical bone stimulation on the fusion rates in foot and ankle primary arthrodeses, and are therefore promising, insufficient evidence exist to support the routine use of PEMF or DC devices in primary arthrodesis. Additionally, the use of invasive DC devices with its concomitant risks over PEMF devices for primary arthrodesis is not supported by sufficient clinical data.

Because foot and ankle arthrodesis procedures pose a high nonunion risk, considerable interest has been generated regarding the application of electrostimulation to revision arthrodeses. However, only one case series by Saltzman and colleagues (Saltzman, Lightfoot et al. 2004) has described the effect of PEMF on revision arthrodesis. In this retrospective study, 19 patients who developed nonunion after primary foot and ankle arthrodeses were treated with PEMF, immobilization, and limited weight-bearing. Only 5 of the 19 patients went on to achieve union, while 9 of the remaining 14 underwent revision surgery yielding similar fusion rates (2 of 9). Patients' risk factors included smoking (5 patients) and previous non unions (8 patients). The authors hypothesized that the lower rate of success of PEMF for revision arthrodesis of the foot and ankle, when compared to its application on long bones (de Haas, Watson et al. 1980; Heckman, Ingram et al. 1981; Bassett, Mitchell et al. 1982; Sharrard 1990; Holmes 1994), may be attributable to mechanical difficulties in orienting the coils around the foot and ankle.

Contrary to Saltzman’s results, Midis and Conti (Midis and Conti 2002) reported a case series of 10 consecutive patients with aseptic nonunions of the ankle requiring revision arthrodesis, supplemented with DC bone stimulation. Radiographic evidence showed that acceptable clinical alignment and solid fusion was achieved in all 10 patients at a mean of 12.8 weeks after revision surgery. Additionally, clinical examination through a modified AOFAS ankle/hindfoot scoring system showed 70% good to excellent results.

In view of the limited number of clinical studies and their associated findings, which demonstrate inconsistent outcomes, it is difficult to justify the utility of electrical bone stimulation on foot and ankle revision arthrodeses. Furthermore, contrary to the previous indications, limited data exist to support the use of DC devices over PEMF devices for revision arthrodesis.

Nonunion and delayed union occur frequently in certain high-risk foot and ankle fractures, such as tibial (shaft and pilon) and metaphyseal-diaphyseal fifth metatarsal fractures. In an effort to prevent these potential complications, some orthopaedic surgeons have used electrical bone stimulation upon fresh fractures. However, there is no peer-reviewed literature at this time that demonstrates the beneficial effect of the utility of electrical bone stimulation upon fresh fracture healing. Therefore, prospective, randomized controlled studies are required before routine clinical use can be considered in this scenario.

**BONE MARROW ASPIRATION**

The concept of osteogenic capacity of bone marrow aspiration is not novel (Burwell 1964; Burwell 1966; Beresford 1989) and has been exploited by several to reinforce the osteogenic properties of bone allograft by the augmentation of the graft with bone marrow (Burwell 1985; Boehm and Muschler 1999) and its use in several tibia non union clinical series (Connolly, Guse et al. 1989; Hernigou, Poignard et al. 2005).
Hernigou et al (Hernigou, Poignard et al. 2005) recently evaluated the number and concentration of progenitor cells in bone marrow concentrate for the treatment of tibia non-union, the callus volume after transplantation of concentrated bone marrow, and clinical union rate. First, aspiration contained an average of 612+134 progenitors/cm³ before concentration and at average of 2579+1121 progenitors/cm³ after concentration. The bone marrow that had been injected into non-union contained >1500 progenitors/cm³ and averaged total of 59,962 +17,431 progenitors. Osseous union was obtained in 53 of 60 patients. The concentration(634+187 progenitor/cm³) and the total number (17,324+6834) of progenitor injected into the non-union site of seven patients in whom non-union was not obtained were both significantly lower (p=0.0001 and p<0.01, respectively) than those in patients who achieved union. The surgical technique of percutaneous autologous bone marrow grafting appears to be effective but its efficacy appears to be related to the number of progenitor in the graft and the number of progenitors available in bone marrow aspirated from the iliac crest graft appear to be less than optimal in absence of concentration.


