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UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 8-K

CURRENT REPORT
PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

Date of report (date of earliest event reported):
May 17, 2005

Aastrom Biosciences, Inc.

(Exact name of registrant as specified in its charter)

Michigan	**0-22025**	**94-3096597**
(State or other jurisdiction of incorporation)	(Commission File No.)	(I.R.S. Employer Identification No.)

24 Frank Lloyd Wright Drive
P.O. Box 376
Ann Arbor, Michigan 48106
(Address of principal executive offices)

Registrant's telephone number, including area code:
(734) 930-5555

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

o Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

o Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

o Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

o Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

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Item 8.01 Other Events.

(b) On May 17, 2005, Aastrom Biosciences, Inc. published a report providing the results from its feasibility clinical trial in Barcelona, Spain to evaluate the use of Tissue Repair Cells (TRCs) for the treatment of severe long bone non-union fractures. This report, which provides the details of the clinical study, including information on each patient treatment and the results obtained, is attached hereto as Exhibit 99.1.

Item 9.01 Financial Statements and Exhibits.

(c) Exhibits.

Exhibit No.	Description
99.1	Report on Barcelona feasibility clinical trial

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: May 17, 2005

AASTROM BIOSCIENCES, INC.

By: /s/ Alan M. Wright
Alan M. Wright
Senior Vice President, Administrative and
Financial Operations, CFO

EXHIBIT 99.1

Cultured, enriched, autologous bone marrow cell graft for refractory nonunion fracture healing

Clinical Feasibility Study: The Use Of Cultured Enriched Autologous Bone Marrow Cells To Treat Refractory Atrophic And Hypotrophic Nonunion Fractures.

L Orozco[1], L Rodriguez[2], C Torrico[2], J Douville[3], JM Hock[3], RD Armstrong[3],J.Garcia, C Solano[1]. Institut de Terapia Regenerativa Tisular (Clinica Teknon)[1] and Unitat de Terapia Cellular (Centre de Transfusio I Banc de Teixits)[2] Barcelona, Spain; Aastrom Biosciences, Inc, Ann Arbor, MI[3].

Keywords: (fractures, ununited); (stem cells); (bone marrow stromal cells); (fracture healing)

Acknowledgements: this trial was supported by Institut de Terapia Regenerativa Tisular (Clinica Teknon), and Unitat de Terapia Cellular (Centre de Transfusio i Banc de Teixits) at Hospital Duran i Reynalds, Barcelona, Spain, and Aastrom Biosciences Inc, Ann Arbor, MI. We thank Joan Garcia, Director of the Unitat de Terapia Cellular (Centre de Transfusio i Banc de Teixits) for providing support to prepare and characterize TRCs.

Cultured, enriched, autologous bone marrow cell graft for refractory nonunion fracture healing

Abstract

Background: Autologous iliac crest bone grafts successfully stimulate bone healing, although their use is limited by tissue availability and the risk of complications at the harvest site. We tested the feasibility of using an autologous bone marrow cell product, expanded *ex vivo* by a proprietary automated, single pass perfusion process to enrich for adult stem cells, progenitors and stromal cells of mesenchymal, endothelial and myeloid lineages (Aastrom Tissue Repair Cells, TRCs), as a bone graft substitute. In prior clinical trials in more than 160 cancer patients, TRCs were used for bone marrow transplantation, and safely and effectively engrafted. We report data for a prospective, consecutive case series of 6 procedures in 5 patients, using TRCs in combination with internal fixation and ß-tricalcium phosphate matrix (ßTCP, Calcibon Granules, Biomet Merck), to restore healing competency to chronic, refractory atrophic and hypotrophic nonunion fractures of long bones.

Method: Twelve days prior to surgery, 7-30 ml bone marrow aspirate was inoculated into the automated AastromReplicell System to culture TRCs. At surgery, fracture sites of 3 tibiae, 2 humeri and 1 clavicle, which had failed to heal in the previous 6-28 months, were debrided, decorticated, and stabilized with new titanium fixation. Then, TRCs were mixed with ßTCP matrix, gelled with autologous platelet-poor, fibrin-enriched plasma to enhance ease of handling, and placed around the fractured bone, within the intramedullary canal, and along periosteal surfaces. Lateral and anterior-posterior radiographs were taken to monitor bone regeneration.

Results: TRCs in matrix were viable, and available in large numbers. Radiographic callus formation occurred in 5/6 patients between 6-24 weeks (mean 11 weeks), and was stable in 5/6 patients by 10 - -24 weeks. Clinically, healing was uneventful, and inflammation and swelling were absent at the surgical site post-operatively. No adverse events related to the use of cells or matrix. A cutaneous infection in one patient, unrelated to cell therapy, healed with antibiotics. Patients recovered some range of motion and were load-bearing on their healed bone within 3-6 months.

Conclusion: Five of 6 patients with atrophic or hypotrophic bone fractures regenerated bone when engrafted with autologous TRCs in a synthetic matrix. Because cells were collected by percutaneous injection, we avoided invasive bone collection and its associated adverse events. This feasibility trial suggests that Aastrom TRCs derived from autologous bone marrow, may offer an alternative to conventional autografts when there is a need for viable cells in large numbers to restore healing competency to non-union fractures.

Introduction

Treatment of nonunion, delayed union and malunion fractures of long bones remains challenging. Good surgical techniques and stable immobilization favor healing, but the voids in bone that result from corrective surgery require bone grafting to stimulate healing (12;25). Typically, iliac crest autografts are used, and were successful in up to 90% of 402 anterior lumbar spine fusion cases in a prospective, controlled, randomized, single blind study (4). However, the bone volume that can be harvested from iliac crest is limited; the cells within the autograft degrade rapidly (5), and there is some risk of morbidity at the site of graft harvest that results from an invasive surgical technique (24;25). We report the use of a new autologous cell therapy in which a small volume of iliac marrow aspirate may be expanded ex vivo under controlled, automated single-pass perfusion culture conditions over a period of 12 days, to generate a large amount of viable mesenchymal and hematopoietic stem and progenitor cells (Tissue Repair Cells, TRCs) appropriate for use in bone grafting.

The proprietary culture process for the *ex vivo* production of bone marrow cells (AastromReplicell® System, Aastrom Biosciences, Inc, Ann Arbor, Mi) consists of an automated, computer-controlled perfusion of tissue culture medium (6;15;16), that mimics conditions found within human tissues. The cell composition of the original bone marrow aspirate is generally retained, while the frequency distribution of cell subsets shifts. The process enriches the production of adult stem cells, as well as early and late progenitor cells of mesenchymal, endothelial, and myeloid lineages (15). Lymphoid and erythroid cell lineages decrease (15). In addition, TRCs collectively synthesize a wide variety of cytokines, chemokines, and growth factors to provide a microenvironment that supports growth and maintenance of adult multi-lineage adult stem and progenitor cells (6;15;16); (14;26). In-house experiments have shown that these cells will mineralize and exhibit properties of osteoblasts when culture conditions are adjusted to favor induction of osteoblasts; under culture conditions that favor induction of endothelial cells, vascular tubes will form in vitro. Based on this collective data, we hypothesized that if fractured bones that had previously failed to heal, were stabilized and immobilized by fixation, TRCs, which have the potential to form bone and blood vessels, would increase the probability of healing.

TRCs have been previously used to substitute for bone marrow transplants in clinical trials of cancer patients on chemotherapy to help restore hematopoiesis. In 163 patients treated, there

were no adverse events related to cell therapy; allergic reactions in four patients were not cell-dependent as all patients successfully received the full complement of cells.

The clinical bone forming capability of TRCs was suggested by the treatment of a patient with hypophosphatasia (Whyte, et.al.). The eight-month-old female was born with an infantile form of hypophosphatasia, a genetic skeletal bone disease. The child received a single intravenous infusion of TRCs, derived from a matched sibling donor bone marrow, which was followed by a significant, prolonged, clinical and radiographic improvement of skeletal bone within a very short time. The authors concluded that long-term engraftment of the bone-forming cells in Aastrom TRCs resulted in the amelioration of the child's skeletal disease.

Because these early trials demonstrated clinical safety of TRCs, a feasibility trial was initiated to evaluate the ability of TRCs to restore healing competency to severe non-union type fractures that had failed to respond to conventional standard of care treatment.

Materials and Methods

Approval for a small Phase 1/2 study to study the use of TRCs in recalcitrant, chronic atrophic and hypotrophic nonunion long bone fractures was obtained from the Ethics Committee of Clinical Investigations del Consorci Sanitari Integral, Hospital de l'Hospitalet, Barcelona, Spain. In a consecutive case series (Table 1) of 6 procedures in 5 patients with nonunion fractures, present for 6-28 months, autologous bone marrow cells, processed *ex vivo* in the automated Aastrom Replicell System, were mixed with a synthetic matrix of beta-tricalcium phosphate (22;23) (Calcibon Granules, 2-4mm in size with 100-550µm pores, Biomet Merck) and used instead of iliac crest bone autograft to promote healing. Because of the nature of their fractures and their failed response to prior standard of care treatment approaches, all patients were considered to have poor prognosis for healing.

TRC preparation and Surgical Grafting Procedure

Twelve days prior to orthopedic surgery, bone marrow was aspirated from the posterior iliac crest, with the patient under conscious sedation and local anesthesia**.** Bone marrow cells from 7 to 30ml aliquot of the marrow aspirate, were isolated by density gradient centrifugation and inoculated into the AastromReplicell System for culture in Iscove's Modified Dulbecco's Media, supplemented with 10% fetal bovine serum, 10% horse serum, hydrocortisone ($5x10^{-6}M$), gentamicin sulfate (5 µg/ml), L-glutamine (4 mM), vancomycin (20 µg/ml), PIXY321 [5 ng/ml], erythropoietin [Epo 0.1 U/ml], Flt3-L [25 ng/ml] . The cells were cultured for 12 days at 37° C,

using single pass perfusion conditions previously established to allow production of a cultured bone marrow cell product that contained multi-lineage stem and progenitor cells. To confirm there were non-detectable levels of bacterial and fungal contaminants and endotoxins, culture medium was sampled at 48 hours prior to harvest. The cells were harvested on Day 12, using trypsin and EDTA, and thoroughly and repeatedly washed to reduce media components by 4-log fold. We confirmed that exogenous growth factors and other reagents added during culture, were below detectable limits, using a sensitive ELISA assays (R&D Systems, Minneapolis, MN and Immunex Research Corporation, Seattle, WA). Flow cytometry, cell viability, and clonogenic assays were performed to confirm composition and viability of the cell mixture. The final cell product was suspended in Normosol and 0.5 % human serum albumin, and transported in a sterile bag to the surgical suite.

During surgery, TRCs were mixed with the synthetic ß-tricalcium phosphate matrix, and excess fluid volume was removed using filtration and low-grade vacuum (Figure 1). Next, 10% by volume of autologous platelet-poor, fibrin enriched plasma was added. At the time of grafting, calcium chloride was added to gel the plasma, thus entrapping cells and matrix for ease of handling. A small sample of gelled “bone cell graft” was resected, and cultured ex vivo to confirm that cells adhered to matrix granules. Ex vivo culture resulted in mixed cell morphology, and enrichment for osteogenic, alkaline phosphatase positive cells, which formed mineralized nodules within 1-2 weeks of culture.

After wound debridement, placement of new internal fixation, and preparation of the graft bed, gelled cells in matrix were placed around the bones, along the periosteum and within bone marrow. The surgery was completed using conventional procedures; patients monitored by clinical observations and anterior-posterior and lateral radiographs at 0, 3-4, 6-7, 10-12, 14.5-18, and 20-24 weeks post-operatively. The surgeons evaluated both the clinical data and radiographs. In addition, a 3rd party radiologist in the US evaluated the radiographs for evidence of bone bridging, disappearance of the fracture line and callus formation. There were no treatment-associated adverse reactions reported at the time of surgery or post-operatively, and no documented narcotic analgesia was requested *after* discharge from the hospital. A cutaneous infection in one patient, unrelated to cell therapy, healed with antibiotics.

Radiographic callus formation occurred in 5/6 patients by a median of 8 weeks (minimum 6 weeks, maximum 24 weeks), and was stable by a median of 24 weeks (minimum 10 weeks,

maximum 24 weeks). An unexpected observation was that inflammation and edema characteristically associated with bone grafting in bone fractures, were reduced or absent at the surgical site post-operatively in all patients. There were no safety concerns.

Case 1.

A 47 year-old man weighing 71kg, suffered a metaphyseal fracture of the distal tibia (Muller Class 42-C3) and transversal transyndesmal fracture of the distal fibula in a work-related accident. He had been treated 3 days later by internal fixation using double plates in the original surgery. Failure of bones to heal over 10 months was attributed to poor vascularity in the fracture fragments and associated soft tissue. He presented with hypotrophic pseudoarthrosis, broken plates and deviated bones (Table 1, Fig 3). At surgery, periosteum was present; the wound was debrided, bones decorticated and bone fragments realigned. Old fixation was removed and replaced with a titanium low contact plate combined with the Aastrom TRC autologous bone marrow cell graft. Radiographic callus formation and some loss of fracture line were observed at 6 weeks, stable callus formation at 14.5 weeks; healing was judged present in 7 week radiographs. The patient received physiotherapy, and recovered range of motion in the injured leg by 3 weeks. His joint was stable and he was weight-bearing by 6 weeks. He is unemployed.

Case 2

A 38 year-old female, weighing 60kg, suffered a diaphyseal fracture of the distal humerus (Muller Class 12-C) in a domestic accident. She had been immediately treated using internal fixation with a low contact plate. The bone failed to heal, and she was retreated 7 months later with an allograft and replacement fixation. This had failed to heal by 8.7 months; failure was attributed to the poor vascularity in the fracture fragments and associated soft tissues. This patient presented with severe atrophic pseudoarthrosis, broken plates and severe deviation of the bones (Table 1, Figure 4). At surgery, periosteum was lacking; the wound was debrided, and the bone fragments realigned. Old fixation was partially removed, replaced with a titanium, low contact plate, and combined with the Aastrom TRC autologous bone marrow cell graft. Some loss of fracture plane, indicative of early healing, was observed in the 8 week radiographs. Radiographic callus formation was observed at 16 weeks, and stable callus formation at 24 weeks, resulting in conclusion of securely united bone. The patient received physiotherapy and recovered range of motion at 12 weeks and was weight bearing at 16 weeks. She had returned to work by 24 weeks post-operatively.

Case 3

A 45 year-old man, weighing 76kg, suffered open, diaphyseal fractures of both distal tibiae (Muller Class 42-C3) in a work related accident. Treatment had used external fixation. Failure of the left and right tibia to heal after 11.8 and 13.6 months respectively, was attributed to inadequate immobilization. The patient presented with normotrophic fractures with synovial involvement and severe deviation in both tibiae (Table 1). Each tibia was treated in a separate operation. Periosteum was present in both tibiae. The wounds were debrided, bone surfaces were decorticated and bone fragments were realigned, creating large bone voids. The size of the voids was large enough that a conventional iliac bone autograft would not have provided enough fill tissue. Treatment consisted of removal of fixation, replacement with titanium, low contact plate, combined with the Aastrom TRC autologous bone marrow cell graft. The right tibia was treated in the same manner. The patient exhibited a local, mild, cutaneous infection associated with the right tibia wound, 1 month post-operatively, which resolved satisfactorily with antibiotics, and was not considered relevant to the cell therapy. Stable callus formation and disappearance of the fracture line were reported in the posterior aspect of the left tibia at 24 weeks. The patient received physiotherapy, and was weight bearing at 20 weeks in the left tibia and 18 weeks in the right tibia. The patient is unemployed.

Case 4

A 28 year old man, weighing 75kg, suffered a Class 3 open, transverse fracture of the humerus shaft (Muller Class 12-C) in a traffic accident. This was originally treated with external fixation; when it failed to heal after 12 months, the nonunion fracture was re-treated with internal fixation. Failure of the reoperated bone to heal by 5.8 months was attributed to poor vascularity in the bone fragments and associated soft tissues. The patient presented with atrophic pseudoarthrosis with severe deviation of the bone (Table 1). At surgery, periosteum was present; old fixation was removed, the wound debrided, bone surfaces decorticated and bone fragments realigned. Fixation was with a titanium, low contact plate, combined with the ex vivo cultured autologous bone marrow cell graft. At 24 weeks, the fracture line had disappeared from the anterior one fourth of the transverse shaft dimension, and bone alignment was improved and anatomic. There was still no radiographic evidence of callus or bony union at 30 weeks. The patient received physiotherapy and recovered range of motion and weight bearing by 4 weeks. Based on radiographs, this patient was judged to have a fibrous union on anterior surfaces, but no radiographic evidence of bony union of the humerus at 24 weeks; no further

change was seen at 30 weeks. Despite this, he exhibited a stable joint clinically, and returned to employment by 12 weeks post-operatively.

Case 5

A 64 year-old man, weighing 62kg, suffered an oblique fracture of the left clavicle (Muller Class 91.2-C), resulting in bone displacement, in a domestic accident. The bone was immobilized using a sling, and failed to heal by 7 months. Failure was attributed to a combination of inadequate immobilization and poor vascularity of the bone fragments. He presented with atrophic pseudoarthrosis with no contact between bone fragments (Table 1, Figure 5). At surgery, periosteum was lacking; the wound was debrided and bone fragments realigned, exposing large bone voids. Treatment consisted of internal titanium fixation using a reconstruction plate, combined with the Aastrom TRC autologous bone marrow cell graft. Radiographic callus formation was observed at 6 weeks, and stable callus formation at 24 weeks. The patient is retired.

Discussion

We report the first use of autologous bone marrow cells, expanded *ex vivo* using a specialized process to enrich for a mixed population of mesenchymal and hematopoietic stem and progenitor cells, to treat recalcitrant atrophic and hypotrophic nonunion fractures in humans at high risk for nonunion. The surgeons' clinical and radiographic assessment assumed healing in all 5 patients and 6 sites. A third party evaluation of the radiographs confirmed that 5/6 of the fracture sites exhibited stable callus and bony healing. All patients recovered range of motion to varying degrees, and were weight-bearing at the time this report was submitted. The frequency of these outcomes is within the range that could be anticipated with autologous iliac crest cancellous bone autografts, and is unlikely to have occurred by chance alone. Considering 5 of 6 TRC-grafted bones healed, and the published 50-80% success rates for iliac crest autografts, our dataset reveals a 83% success rate, with a 95% confidence interval ranging from 35.9% to 99.6%.

The risk of morbidity at the site of iliac crest bone graft harvest was avoided by using percutaneous marrow aspiration in the posterior iliac crest, and extracting only small volume aliquots. The limitations of insufficient autologous bone graft to fill the bone voids was also avoided by using cell grafts containing abundant viable cells, representing a mix of mesenchymal stem cells, progenitors and mature cells of the mesenchymal, endothelial and

myeloid lineages, as characterized by flow cytometry. Successful healing of nonunion fractures depends on insertion of stable fixation, availability of cells and a supportive host environment.

There has long been an interest in using bone marrow cells to replace autologous iliac crest bone grafts, because these cells are known to home to sites of injury, differentiate into the required cell lineages and induce host cell induction via cytokines, chemokines and growth factors, please see reviews (1;21;27). One osteogenic cell alternative to autograft was fresh autologous bone marrow aspirated from the iliac crest (8-10). A single surgeon, single site prospective study, in which autologous bone marrow was applied directly to the fracture site, or given as percutaneous injections, reported bone healing of complex, open tibial fractures and nonunion fractures (8-10). An alternative strategy uses aspirated bone marrow cells, which are cultured, passed through demineralized bone allograft which selects for osteogenic precursor cells, but reduces the overall cell number (19;20). Although both these approaches are viable alternatives to iliac crest autografts, the problems of limited cell quantity persist. An alternate approach that enriches specifically for “mesenchymal stem cells” (MSCs) has shown success as allogeneic cell grafting in a number of animal models of critical bone defects (1;3). Bone marrow cells were cultured after removing non-adherent cells, to increase cell number by ex vivo proliferation, thereby enriching for “mesenchymal stem cells” and excluding many of the other cell types found in bone marrow (MSCs) (2;27). Aastrom-sponsored studies demonstrated that MSCs and TRCs from the same donor induce an equivalent quantity of ectopic bone when cells are placed in a ceramic matrix under the skin of immunodeficient mice(11).

These alternatives differ significantly from the autologous expanded and enriched TRC bone cell graft reported here. Alternatives are limited by either the number of cells, the functionality of the cells, or by the lack of variety of cells due to selection process employed. TRCs contain stem cells capable of developing into hematopoietic, mesenchyman or vascular tissues, and contain a population of stromal cells that are actively producing various natural tissue and stem cell regeneration growth factors (Koller et.al., 1993 and 1995). The mix of cells is likely important as osteoblasts provide a niche microenvironment for hematopoietic stem cells (7;28;29), and osteoclasts and their progenitors (18). Most recently, BMP2, a potent bone growth factor, has been used as an alternative therapy for complex open tibial fractures treated by intramedullary nail and reaming (13). BMP2 may not activate all the mechanisms activated by cell therapy. A rat study that used BMP2 alone, or in combination with fresh bone marrow

cells, to heal a critical size defect, found BMP2 and fresh bone marrow cells to be biologically synergistic, consistent with complementary rather than overlapping mechanisms of action (17).

It may be possible to optimize the TRC and matrix mix for surgical use by modifying the physical properties of the matrix. The surgical approach used in this study mixed the Aastrom TRCs with a synthetic matrix of ß-TCP granules, 2-4mm in size, with 100-550 µm pores. The size of the matrix particles, along with the concurrent use of autologous platelet-poor, fibrin enriched plasma gel, limited the ability of the surgeons to pack graft into bone voids. Because the distance a bone cell can travel through a void is limited, it is important to eliminate spaces between the grafted cells and fractured bone surfaces. Smaller granules and more pliable cell/matrix formulations may improve the ability of surgeons to pack cells within their matrix scaffolding into fracture gaps, so that bone healing is consistently initiated earlier on more surfaces. Aastrom has other clinical trials in progress that are evaluating this type of delivery approach for nonunion fractures.

In conclusion, this feasibility trial suggests the Aastrom TRC autologous bone marrow cell grafts may provide an alternative to conventional cancellous bone autografts, when there is a need for viable cells in large numbers to restore healing competency to nonunion fractures.

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Table 1. Patient demographics at time of acceptance into the clinical trial

Case	Age years	Gender	Body weight Kg	Bone	Cause of injury	Muller Class fracture	Time since initial trauma months	Time since last surgery months	Prior stabilization	Diagnosis & Recorded Reason For Failure of fracture to heal
1	47	M	71	Distal tibia diaphysis	Work-accident	42-C3	12	10	Internal fixation with double plate on medial and anterior of tibia	• Hypotrophic pseudoarthrosis • Broken plates • 12º deviation
2	38	F	60	Distal humerus diaphysis	Domestic accident	12-C	12	0 9	1. Internal fixation with posterior plate 2. Internal fixation with plate + autograft	• Atrophic pseudoarthrosis • Broken plates • Severe deviation
3Left	45	M	76	Left tibia diaphysis	Work accident	42-C3	11	11	External fixation and multiple splints	• Normotrophic with synovial involvement • Severe 20º deviation
3Right				Right tibia diaphysis	Work accident	42-C3	11	12	External fixation and multiple splints	• Normotrophic with synovial involvement • Severe 20º deviation
4	28	M	75	Humerus shaft	Motor vehicle accident	12-C	13	12	External fixation	• Atrophic pseudoarthrosis • Severe deviation
5	64	F	62	Clavicle diaphysis	Domestic accident	91.2-C	19	19	Immobilization	• Atrophic pseudoarthrosis • No contact between bone fragments

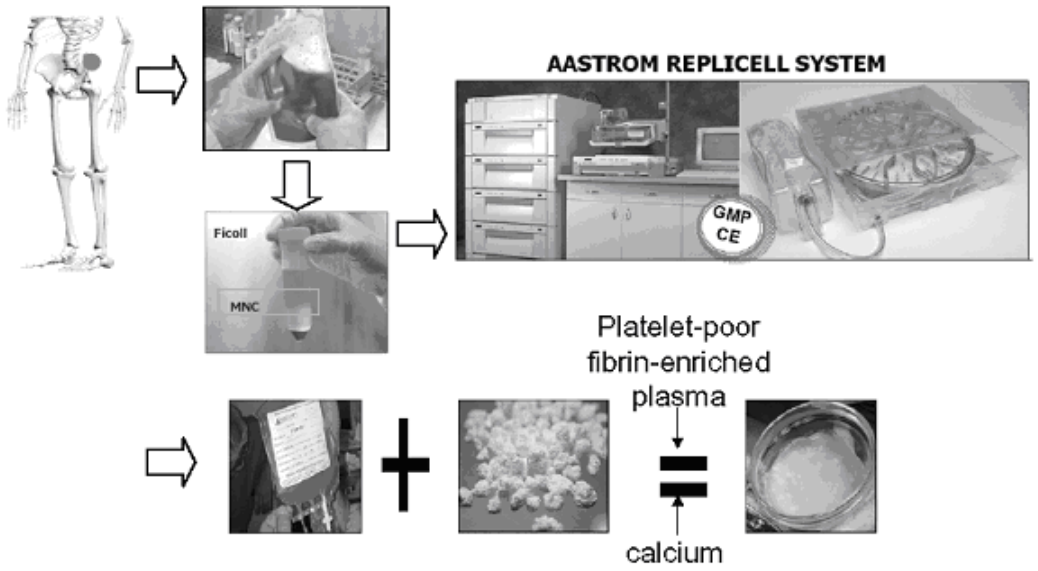

Figure 1. Cartoon to show preparation of Tissue Repair Cells (TRCs). Small marrow aspirate is removed from the posterior iliac crest, and harvested for density centrifugation. Bone marrow cells are removed and inoculated into the cassette, which is inserted into the manufacturing incubator for culture under single pass perfusion for 12 days. The cells in the cassette, Tissue Repair Cells, TRCs, are removed after trypsinization, added to the beta-TCP matrix and mixed with platelet-poor fibrin-enriched plasma. When needed in surgery, the bone cell “graft” is gelled with calcium chloride, and placed between bone fragments, within the exposed bone marrow, and along periosteal surfaces.

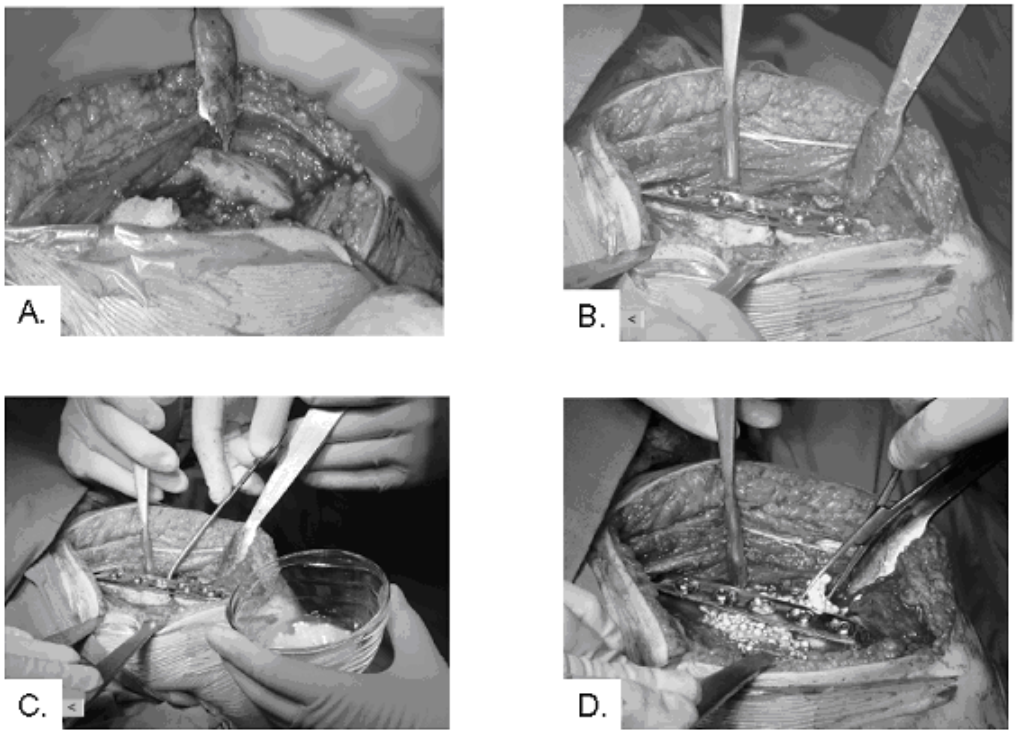

Figure 2. Surgical series to show (A) displaced bone fragments in on-union fracture; (B) internal fixation in place to immobilize and stabilize bone fragments; (C) gelled TRCs and synthetic matrix graft ready to place in fracture area; (D) placement of gelled TRCs and synthetic matrix granules into fracture site.

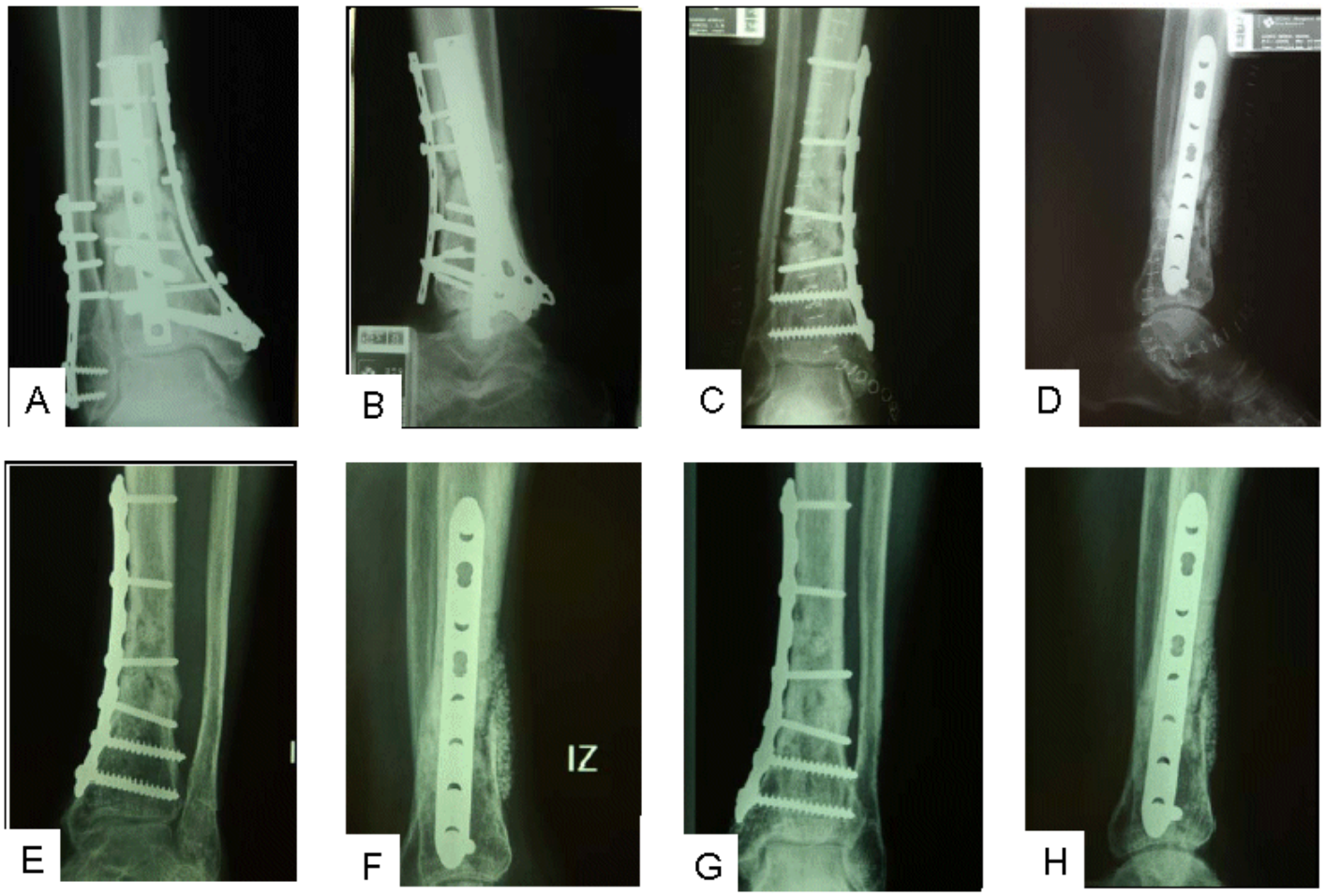

Figure 3. Case 1 with metaphyseal fracture of the distal tibia (Muller Class 42-C3) and transverse transyndesmal fracture of the distal fibula: radiographic series of anterior-posterior A, C, E, G) and lateral (B, D, F, H) views before surgery (A, B), and at 1 day (C, D), 3 months (E, F) and 6 months (G, H) after surgery. New internal fixation was inserted to stabilize and immobilize the bone fragments, and TRCs and synthetic beta-TCP granules were added as a gel with platelet-poor fibrin-enriched plasma. Patient was regarded as radiographically healed and clinically functional.

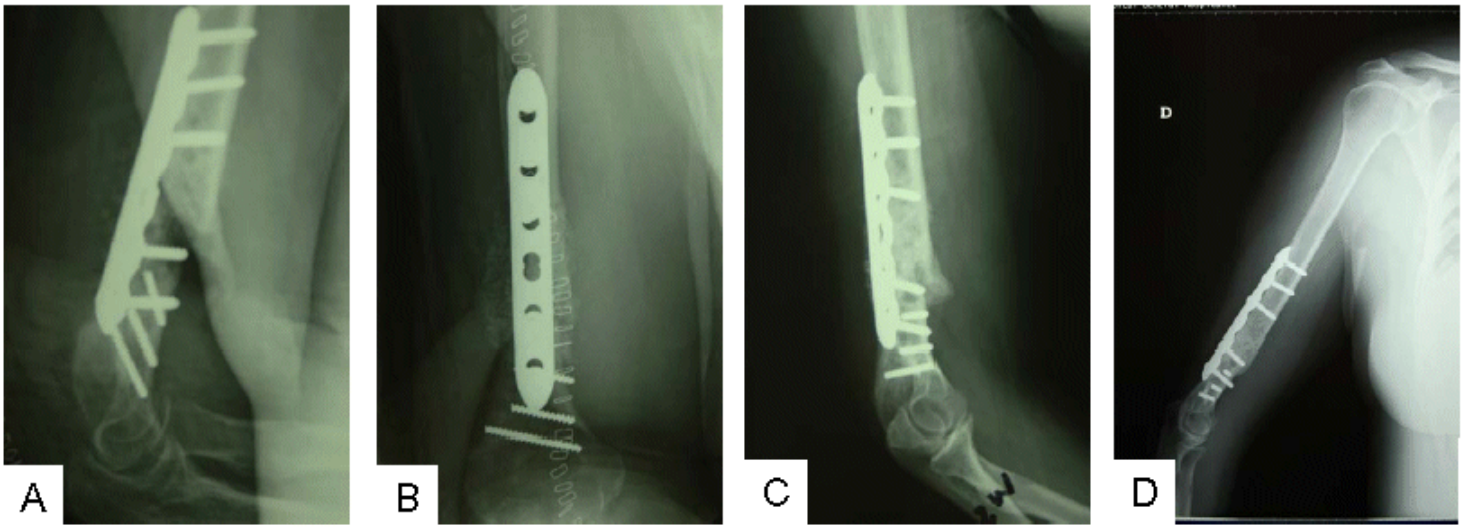

Figure 4. Case 2: diaphyseal fracture of the distal humerus (Muller Class 12-C). Radiograph series: anterior-posterior (A, C) and lateral (B, D) views of the humerus at 1 day (A, B), 3 months (C) and 12 months (D) after surgery. New internal fixation was inserted to stabilize and immobilize the bone fragments, and TRCs and synthetic beta-TCP granules were added as a gel with platelet-poor fibrin-enriched plasma. Patient was judged radiographically healed and clinically functional.

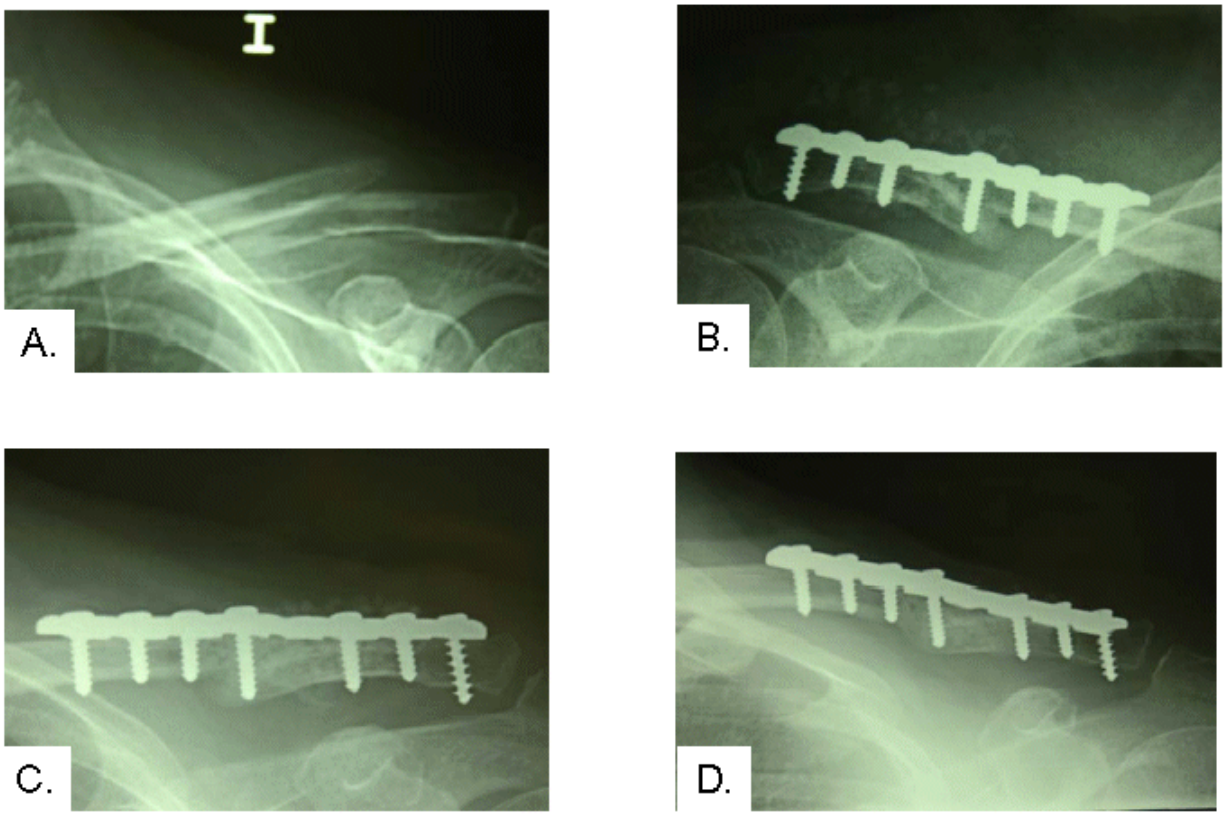

Figure 5. Case 3 presented with an oblique fracture of the left clavicle with displacement of bone fragments (Muller Class 91.2-C). Radiographic views prior to surgery (A), and at 1 day (B), 10 weeks (C) and 6 months (D) after surgery. Case was judged radiographically healed and clinically functional.