Proximal tibial fractures are grossly heterogeneous lesions associated with many complications and their prognosis is related to articular comminution with severity of collapse and degree of articular step-off, as well as to osteoporosis, soft tissue envelope and patient’s comorbidities [1, 2].

The disadvantages of classic Open Reduction and Internal Fixation (ORIF) with laterally placed plates (skin necrosis, nonunions and infections) [3-5], prompted the introduction of biological techniques with Minimally Invasive Plate Osteosynthesis/MIPO using classic plates [6, 7] or the ideal locking plates with monoaxial angular stability [8, 9]. The last acquisition in angular stability type Less Invasive Stabilization System – proximal lateral tibia/LISS-PLT [8, 9]. The last acquisition in angular stability fixation techniques and design was Locked Compression Plate/LCP with combi-holes and the new Polyaxial Locking Plates that allow screw angulation according to the pattern of comminuted fracture [10, 11].

One of the biggest challenges of the tibial plateau fractures is the successful management of the metaphyseal bone defects which are associated with massive comminution, osteoporosis and reduction techniques. [12-14].

Autografts are still considered the golden standard in treatment of bone defects, even if the literature reports difficulties in graft harvesting and graft availability [13]. The allograft usage involves the infection risk (viral or bacterial) and high costs, while it requires a bone bank with all facilities [15].

For over a century, scientists are trying to discover or synthesize inorganic products that could be used as bone substitutes; these products must provide long lasting bone biocompatibility and must provide bone healing abilities. These bone substitutes must solve the autograft and allograft disadvantages [16-18].

Bone grafting materials are those implants that promotes bone healing by one of the following actions: osteogenesis, osteoinduction and osteoconduction [19-22].

A material is osteogenous when it contains living cells, able to form bone tissue (for example, autografts of living bone). An osteoinductive material is a biological stimulus which induces local differentiation of mesenchymal cells from the soft parts in osteoblasts and osteocytes (for example, bone morphogenetic proteins/BMP). An osteoconductive material allows the apposition of a new bone on its surface, acting mainly as a support for the bone tissue (for example, hydroxyapatite, tricalcium phosphate) [19, 23].

Autografts or cancellous autogenous bone grafts, as well as the vascularized cortical ones, can be osteogenous (since they contain living bone cells), osteoinductive (due to the protein matrix), and osteoconductive (due to the mineral bone matrix). These properties also describe the ideal bone substitute. [24] Osseointegration is a term used to describe the biological interaction between the grafted material (graft/implant) and the host in the process of bone healing [15].

Osteoconductive materials became more important especially in bone pathology while they are used as bone substitutes. These substances have a composition similar to the bone mineral matrix and are biocompatible. Their main function is of bone tissue support; allowing bone apposition on their surface; thus, they are used mainly for treating the bone defects [25]. More recently, they are used as a vehicle for osteoinductive substances, augmenting bone formation [28].

While initially, only coral hydroxyapatite, calcium phosphate (Plaster-of-Paris) and then bioactive glasses (bioviroceramics) were used as bone substitutes,
nowadays we are using phosphocalcic cements and osteoconductive ceramic materials [29, 30].

Phosphocalcic cements (CPC) consist in one or more calcium phosphates (CaP) soluble in aqueous solutions. Many experimental and clinical studies have used phosphocalcic cements [31, 32].

In the past 80 years, the ceramic materials (phosphocalcic products) were intensively investigated and used in bone repair [33]. The most important property of the phosphocalcic compounds is the water solubility, so as a compound is more resorbable as it is water soluble (e.g. β-TCP) when a compound is less soluble in water and in the bone matrix, it will be less or hard to be resorbed (e.g. HA). The most used compounds in the medical field are represented by the tricalcium phosphates (β-TCP), hydroxyapatite (HA) [34] and biphasic tricalcium phosphates (BCP, a mixture of β-TCP and HA in a variety of ratios) [25].

These materials are biocompatible and osteoconductive ceramics representing synthetic scaffolds which provide structural support for cells and newly formed tissue [26]; these scaffolds act as extracellular matrix for natural process of tissue regeneration [25, 27]. In the same time, the rate of degradation for scaffolds must be comparable with osseous apposition [35].

One of the main disadvantages of biphasic tricalcium phosphate ceramics is their fragility with low fracture resistance which limits their use in cases with high strength; these macroporous ceramics are weaker in bending or torsion comparing to compression [36, 37]. This is the reason for increasing the mechanical strength using osteosynthesis implants [15, 38].

Atlantik® biphasic tricalcium phosphate substitute

Atlantik® (MedicalBiomat, France) is ceramic bone substitute [39] representing a mixture of 70% Hydroxyapatite \([\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2]\) and 30% beta-tricalcium phosphate \([\text{Ca}_3(\text{PO}_4)_2]\).

This ceramic bone substitute (table 1) is produced in various geometric blocks (70% total porosity, partially interconnected by 300-600 µm pores) as well as in granular form with a granule diameter of 0.5 mm, 1 mm, 2 mm and 4 mm (70% total porosity, with a minimum pore size 300-600 µm and maximum size 2500-5000 µm). The granular form of Atlantik® must be used in areas with no or low mechanical stress while the blocks will be used in regions with maximal compression stress of 10 MPa. [39]

While a pore size larger than 100 µm is necessary, the optimal interconnection size is still debatable. However, the increasing of porosity content or size strongly decreases the mechanical properties [25, 37, 40].

Exponential functions are used to assess the strength-porosity dependence of ceramics [37]:

\[ \sigma_R = \sigma_0 \exp(\beta \rho) \]

Where \( \sigma_R \) represent the strength for a volume fraction of pores \( \rho \), and \( \sigma_0 \) represent the strength of the material to porosity.

Observations of micro- and macropores were conducted with a scanning electron microscope (SEM). In figure 1 and figure 2 there are revealed the macroporosity and microporosity, respectively, for Atlantik® substitute with a porogen particle size 300-600 µm [37].

The aim of this retrospective study is to assess the use of a macroporous biphasic synthetic bone substitute Atlantik® (MedicalBiomat, France) combined with plate osteosynthesis for management of complex tibial plateau fractures, while exhibiting the biocompatibility, quality and extent of osseous healing.

| CHARACTERISTICS | BLOCKS | GRANULATES |
|----------------|--------|------------|
| CRYSTAL PHASES | HAP: Ca10(PO4)6(OH)2 = 70 + 5% | TCP: Ca3(PO4)2 = 30 + 5% |
| DIMENSIONS | \( \pm 0.5 \text{ mm (except specific shapes)} \) | 0.5 mm: 300-600 µm (1 mm: 600-1250 µm) |
| %POROSITY | 70 + 2% | \( \approx 70 \% \) |
| MACROPOROSITY | \( \approx 300-600 \mu\text{m} \) | \( \approx 20-1300 \mu\text{m} \) |
| COMPRESSION STRENGTH | 10 MPa | X |
| ENDOXINES | \( \leq 20 \text{ EU} \) |
Experimental part

Materials and methods

Our retrospective study was realized between April 2015 – December 2016 in Department of Orthopaedics of Universtary Sf. Spiridon Hospital Iasi and Vaslui County Hospital. A sample of 27 patients with acute tibial plateau fractures were evaluated, 12 males and 15 females with a mean age of 46.5 years (range 22-76 years). Leading causes of the fractures were high-energy traffic accidents and falls. The classification of fractures was realized according to Schatzker and we included 10 fractures type II, 4 fractures type IV, 8 fractures type V, 5 fractures type VI. The imagistic exam included in all cases radiographs of the knee and tibia as well as CT scans with 3D reconstruction for articular comminution and collapse.

All patients were operated with reconstruction of the proximal tibia fracture, augmentation of the bone defect with Atlantik® bone substitute in granular form and osteosynthesis with supportive plate (fig. 3, fig. 4).

![Image](http://www.revistadechimie.ro REV.CHIM.(Bucharest) • 70 • No.1 • 2019)

**Fig. 3 (A-V)** Fracture of the lateral tibial plateau type II Schatzker. Plate and bone substitute. (A, B) preoperative X-rays; (C-H) CT exam; (I, J) intraoperative fluoroscopic image with excellent reduction of the articular surface, filling the bone defect with Atlantik® bone substitute, osteosynthesis with 2 Kirschner wires and a locked plate; (K, L) X-ray control at 1 month; (M, N) X-ray control at 3 months (radiologic evidence of decreasing granular aspect of bone substitute); (O, P) X-ray control at 12 months; (Q) intraoperative aspect after plate removal with cortical window and osseointegration of the bone substitute; (R, S) wounds aspect after plate removal with MIPO incisions and plate position; (T-V) aspect and design of a LCP-PLT plate with limited contact.

Results and discussions

The anatomical reconstruction of the articular surface was recorded with postoperative and follow-up X-rays for 20 patients, while in 7 patients we found minimal secondary displacement (less than 2 mm) due to fracture comminution and osteoporosis.

An uneventful union was present after an average 2.8 months (limits 2-4 months). The radiological aspects as well as the osseointegration of the bone substitute were recorded using 3 important aspects: the zone between ceramic and surrounding bone, the radiological density of the ceramic and ceramic biodegradation [15]. Postoperative X-ray showed radiolucent zones between the implanted ceramic and receiving tissue. Over time, the radiolucent aspect disappeared and new bone developed on the ceramics, due to osteoconductive properties [41]. The mean interval for disappearance of radiological gap was 15 weeks, while the granularity disappeared at 5.5 months with apparent increasing in radiographic density and homogenization.

In the present series, we observed no reactions to ceramic implant, such as wound problems with excessive postoperative drainage, dermattis, allergic reactions or infections; no obvious evidence of ceramic biodegradation was detected even after 2 years post implantation. At the most recent follow-up, 6 patients developed secondary mild osteoarthritis signs but there were well tolerated in most of the cases. The mean Range of Motion (ROM) was 118° (range 10° -130°) while the final result was graded with the Neer Score (mean value 85 points, range 70-100 points); we have found 19 excellent and 8 satisfactory results.

Three patients with skin injuries were operated with temporary bridging external fixator while the conversion to a plate fixation and augmentation with bone substitute was realized after 7, 10 and 14 days respectively.

For all patients we have used a lateral curved incision with disinsertion of the anterior tibial muscle 1-2 cm from the tibial ridge for minimally invasive insertion of the plate. Reposition of the articular collapse was realized through a metaphyseal lateral cortical window using a special curved instrument and fluoroscopic control.

The bone defect was augmented with Atlantik® bone substitute according to the triad of osteoconduction [13,15]: a. direct apposition of the implant with the surrounding bone; b. viability of the surrounding bone; c. augmentation of the interface between surrounding bone and substitute by internal fixation with plates (we have used classic plates in 10 cases and locked plates in 17 cases).

The patients were immobilized with a fixed orthosis for 2-3 weeks; they started walking without weight-bearing until 6-8 weeks (according to the radiographic results) and rehabilitation after removal of the orthosis. Total weight-bearing was allowed at 10-12 weeks post-operatively. The clinical and radiographic follow-up for all patients was recorded for a minimum period of 12 months (average 18,5 months, range 12-28 months). We recorded the quality of articular reconstruction as well as the stability of the construct, the time to fracture healing, the osseointegration of the bone substitute [26], the functional results and rehabilitation according to Neer Score.
comminution and osteoporosis represents a great challenge in clinical practice [12,38,44].

Bone grafting (autografts, allografts and synthetic substitutes) is an important treatment for bone defects while successful incorporation of grafted biomaterial into bone defects requires the ability and performance of material to promote new bone formation and provide a scaffold for osteogenesis [25,45]. While the autograft techniques have limited resources and the allograft used is restricted due to the spreading of infectious disease, developing the ideal substitute is an actual trend in orthopaedics [15, 24]. The characteristic of an ideal artificial bone material include safety, biocompatibility, excellent biodegradability, ideal porosity, good mechanical properties, osteogenesis, osteoinduction and osteoconductuion [24, 46]. Every bone substitute has strengths and weaknesses and no one has demonstrated all the mentioned requirements. Pore diameter and the porosity, which are connected, are important physical parameters for scaffolds since they allow adequate space for cell migration and expansion [25, 47].

A minimum pore size of 100 µm is considered optimal for bone ingrowth, while the pore size more than 200 µm allows the development of mature osteon [25, 48]. Biphasic calcium phosphate (BCP) bone substitutes (HA-β-TCP in a variety of ratios) are considered the most promising alternative to autologous bone graft [37].

In the last years there were investigated a lot of chemical and physical characteristics with important effects in functionality in vivo and in vitro: porosity, grain size and roughness [28, 49]. These studies demonstrated that BCP are biocompatible, bioactive and osteoconductive [41]. The treatment of the most difficult fractures of tibial plateau by plates osteosynthesis was improved with the use of bone substitutes [12-14].

In our institution, until 2015, we have used for bone defects 2 types of macroporous BCP: Ceraform® (Teknimed, France - a mixture 65% HA, 35% β-TCP) and Eurocer® (FH Orthopedics, France - a mixture 55% HA, 45% β-TCP): we exhibited the efficacy of this ceramics, with a fast and good quality osseointegration, while the osteosynthesis was used in most of the cases. [15].

In the present investigation with Atlantik®, bone substitute, we found that grafted ceramic was well incorporated into surrounding host bone; the radiolucent gaps disappeared after a mean time of 15 weeks and these radiological changes represent direct bone apposition to the ceramic implant, due to the osteoconduction [41].

The difficulties of developing new bone substitutes using a single material, prompted the research for preparing composites biomaterials for repairing bone defects [24]. A new biomedical composite with a good similarity to a human bone, a porous nano-hydroxyapatite/polyamide 66 (n-HA/PA66) has been developed in the last years [24, 50].

Calcium phosphate-crystals became ideal drug delivery systems, minimizing the effective dose of the drugs and the side effects. A lot of studies presented the outstanding surface interaction properties of ceramics, which make them appropriate candidates for transporting antibiotics, hormones, bone morphogenetic proteins, vitamins, and oncological drugs [28].

Conclusions

The successful treatment of bone defects in complex tibial plateau fractures is difficult. Ceramic BCP (a mixture of HA and β-TCP in a variety of ratios) are considered the most promising alternative to autologous bone graft.

The retrospective study on 27 collapse tibial plateau fractures demonstrated that biphasic ceramic biomaterial Atlantik®, combined with supportive plate osteosynthesis, is an effective synthetic bone substitute due to a fast healing and good quality osseointegration with no mechanical failures or inflammatory reactions.

References

1. WADDELL JP, JOHNSTON DVC, NEIDRE A. Fractures of the tibial plateau: a review of ninety-five patients and comparison of treatment methods, J. Trauma, 1981; 21: 376–381.
2. BLOKKER CP, RORABECK CH, BOURNE RB. Tibial plateau fractures: an analysis of the results of treatment in 60 patients, Clin Orthop Relat Res., 1984; 182: 193–199.
3. YOUNG MJ, BARRACK RL. Complications of internal ûxation of tibial plateau fractures. Orthop Rev, 1994; 23: 149–154.
4. MILLS WJ, NORK SE. Open reduction and internal ûxation of high-energy tibial plateau fractures, Orthop Clin North Am, 2002; 33: 177-198.
5. ANISA EI, CIUENTU R, CANTEMIR A, ANTON N, DANIELESCU C, NEGRU R, BOGDANICI CM, VASILIUȚA C, GEORGESCU STO, SIRBU PD, CIUENTU BM, The Importance of Fluconazole in Treatment of Endogenous Endophthalmitis in Patients Prior Treated Using Negative Pressure Therapy for Wound Contamination with Methicillin-resistant Staphylococcus aureus, Rev. Chim. (Bucharest), 68, no. 7, 2017, p. 1598-1601.
6. KRETTEK C, GERICH F.T., MCLAU T.H. A minimally invasive medial approach for proximal tibia, Injury, 2001, vol. 32, suppl. 1, 4-13.
7. SIRBU P, MIHALAIRA G, GHIONIOU G, BRUARJ, ASAFTEI R. Minimally invasive plate osteosynthesis (MIPO) in proximal and distal fractures of the tibia, in Smrkolj VJ, (ed.) - 7th European Trauma Congress, Ljubljana (Slovenia), May 14-17, Ed. Medimond Italia, 2006, 349-354.
8. GOESLING T, FRENK A, APPENZELLER A, GARAPATI R, MARTI A, KRETTEK C, LISS PLT. Design, mechanical and biomechanical characteristics, Injury, Int. Care Injured, 2003, S-A 11-15.
9. SIRBU PD, E. CARATA, T. PETREUS, F. MUNTEANU, C. POPESCU, R. ASAFTEI AND P. BOTEZ. Minimally Invasive Surgery by Angular Stability Systems in Proximal Tibia Fractures – Biomechanical Characteristics and Preliminary Results, IFMBE Proceedings, International Conference on Advancements of Medicine and Health Care through Technology, 2009, 26, 413-416.
10. FRIGG R., FRENK A., HAAS N.P., REGAZZONI P.- The Locking Compression Plate System, Dialogue (AO International), 2001, 14, 1-8; 9.
11. HAUDEKEWYCH G, SEMS SA, HUEBNER D, HORWITZ D, LEVY B. Results of polyaxial locked-plate ûxation of periarticular fractures of the knee, . Surgical technique. J Bone Joint Surg Am., , 90 Suppl 2, 2008 Mar, 117-34.
12. BUCHOLZ RW, CARLTON A, HOLMES R. Interporous hydroxyapatite as a bone graft substitute in tibial plateau fractures. Clin Orthop Relat Res. 1989 Mar; (240):53-62.
13. NEWMAN JT, SMITH WR, ZIRAN BH, HASENOEHLER EA, STAHEL PF, MORGAN SJ. Efficacy of composite alloplast and demineralized bone matrix graft in treating tibial plateau fractures with bone loss., Orthopedics, 2008; Jul; 31(7):649.
14. KHOODADADYAN-KLOSTERMANN C, LIEBIG T, MELCHER I, RASCHKE M, HAAS NP. Osseous integration of hydroxyapatite grafts in metypseal bone defects of the proximal tibia (CT study), Acta Chir Orthop Traumatol Cech., 2002;69(3): 16-21.
15. SIRBU PD, T PETREUS, FL. MUNTEANU, M. PERTEA, S. LUNCA, P. POROCH, P BOTEZ. Clinical Experience with a Macroporous Synthetic Bone Substitue (Eurocer) in the Treatment of the Patients with Bone Defects. International Conference on Advancements of Medicine and Health Care through Technology IFMBE Proceedings, 2011, Volume 36, Part 5, 358-368.
16. VERNE E, BOSSETTI M, BROVARONE CV, MOISESCU C, LUPO F, SPRIANO S, CANNAS M., Fluorapatite glass-ceramic coatings on alumina: structural, mechanical and biological characterisation.; Biomaterials., 2002 Aug; 23(18): 3395-3403.
