Archives of the Balkan Medical Union
vol. 51, no. 2, pp. 190-198
June 2016

REVIEW

EVOLUTION TOWARD NEW BIOABSORBABLE MATERIAL FOR OSTEOSYNTHESIS IMPLANTS USED IN FOOT AND ANKLE SURGERY

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SUMMARY

Bioabsorbable osteosynthesis material is a new solution in the ankle and foot fracture surgery, being wide spread and in continuous expansion. Surgical fixation of these fractures requires small materials. Also, postoperative cast immobilization and mobilization without bearing limits the requirements for strength of materials. Thus, bioabsorbable polymers were optimal solution for a long period, in the form of pins, screws, plates made of poly-L-lactide, polyglycolide, polydioxanone or copolymers of polylactide and polyglycolide. In time, these materials have shown a number of complications, such as low strength, exudate and macrophage granuloma in the implant site. In order to eliminate these drawbacks, new bioabsorbable materials have been studied. These are made from magnesium, which is a natural element of the body. This paper evaluates the different Mg alloys, pointing out their advantages: high biocompatibility, high mechanical strength, density similar to that of bone. At the same time it evaluates the disadvantages of magnesium: increased rate of degradation emission of gas bubbles H+, rapid loss of initial mechanical strength. Several solutions have been proposed: combining with other compounds (alloys of Ca, Mn, Zn, rare earth as Y), grain refining and alloys coatings. These solutions have increased corrosion resistance up to coefficients sufficient to support callus formation, at the moment osteosynthesis material made from Mg alloys being marketed.
Key words: Bioabsorbable osteosynthesis material, Mg alloy, biocompatibility, mechanical strength, corrosion resistance

RÉSUMÉ

Evolution vers les nouveaux matériaux bio absorbable pour les implants d'ostéosynthèse utilisés dans la chirurgie du pied et de la cheville

Le matériel d'ostéosynthèse bio absorbable est une solution nouvelle dans la chirurgie de fracture de la cheville et du pied, étant largement répandue et en expansion continue. La fixation chirurgicale de ces fractures nécessite de petits matériaux. En outre, l'immobilisation postopératoire en plâtre et de la mobilisation sans roulement limite les exigences relatives à la résistance des matériaux. Ainsi, les polymères bio absorbables ont été une solution optimale pendant une longue période, sous forme de goupilles, des vis, des plaques de poly-L-lactide, du polyglycolide, du polydioxanone ou de copolymères de polylactide et de polyglycolide. Dans le temps, ces matériaux ont montré un certain nombre de complications, comme une faible résistance, de l'exsudat et granulome des macrophages dans le site de l'implant. Afin de remédier à ces inconvénients, de nouveaux matériaux bio absorbables ont été étudiés. Ils sont fabriqués à partir de magnésium, qui est un élément naturel du corps. Ce document évalue les différents alliages Mg, en soulignant leurs avantages: haute biocompatibilité, résistance mécanique élevée, densité similaire à celle de l'os. Dans le même temps il évalue aussi les inconvénients du magnésium: augmentation du taux de dégradation de l'émission de bulles de gaz H+, perte rapide de résistance mécanique initiale. Plusieurs solutions ont été proposées: la combinaison avec d'autres composés (alliages de Ca, Mn, Zn, terres rares Y), le raffinage du grain et des alliages de revêtements. Ces solutions ont une résistance accrue à la corrosion jusqu'aux coefficients suffisants pour soutenir la formation de cals, au moment où le matériau ostéosynthèse en alliages Mg est commercialisé.
Mots-clés: matériau bio absorbable d'ostéosynthèse, alliage Mg, biocompatibilité, résistance mécanique, résistance à la corrosion

INTRODUCTION

Ankle and foot fractures are common, occurring in all age groups, both elderly, with osteoporotic background, as well as young people due to sports or road accidents. The mechanism can be both directly by hitting with a blunt object or indirectly by falling or twisting. Of particular importance are malleolus fractures, tibial pillar or of the navicular, which directly affect the ankle joint. At the same time, other fractures, of the calca-

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neus and tarsal bones and those of metatarsals compromised the structural integrity of transverse and longitudinal arches of the foot. This frequently produces pesplanus with fore foot abduction and in that case the foot collapses when weight is borne in the foot, leading to biomechanical malfunction. To avoid these complications, it is necessary a good anatomical reduction and restoration of articular surfaces. This treatment can rarely be obtained by orthopedic treatment, requiring surgery. Osteosynthesis is performed using plates, screws and pins usually made of stainless steel.

Use of bioabsorbable osteosynthesis material is a new solution in the ankle and foot fracture surgery, being widespread and in continuous expansion. Surgical fixation of these fractures require small materials. Also, postoperative cast immobilization and mobilization without bearing limit the requirements for strength of materials.

The two major criteria of absorbable alloys are represented by biocompatibility and biofunctionality. Also they require physicochemical properties consistent with the physiology of the region, without toxicities when resorption occurs, bone adhesion and allowing bone cell proliferation, resorption by biodegradation and bone remodeling.

The main advantages of absorbable materials are

a) eliminating the need for a second intervention for ablation of osteosynthesis material, thus limiting patient stress, the possibility of postoperative infection and last but not least, cost reduction;
b) reducing the bone/implant contact stress effect;
c) transferring load gradually during resorption, toward the newly formed bone. Resorbable implant should allow load capacity transfer gradually to the bone in the same time with resorption, decreasing the risk of fracture after surgery, as in the case of metal one.

Bioabsorbable polymers implants review

Bioabsorbable polymers were optimal solution for a long period, in the form of pins, screws, rods, plates, staples or suture anchors.

Ideal polymer characteristics are: the absence of toxic, inflammatory reactions, metabolized by the body after fulfilling purpose without leftover residue, easy processing, extended shelf life, easy to sterilize.

This ostheosynthesis materials were most often made of poly-L-lactide, polyglycolide, polydioxanone or copolymers. But there is a large scale of materials such as: LPLA Poly(L-lactide), DLPLA Poly(DL-lactide), LDLPLA Poly(DL-lactide-co-L-lactide), LPLA-HA Poly(L-lactide) with hydroxylapatite, PGA Poly(glycolide), PGA-TMC Poly(glycolide-co-trimethylene carbonate) or polyglyconate, PDO Poly(dioxanone), LPLG Poly(L-lactide-co-glycolide), DLPLG Poly(DL-lactide-co-glycolide)s of polylactide and polyglycolide.

The table 1 shows the main products currently used.

Examples of biodegradable implants used in foot & ankle surgery are showed in the figures 1, 2, 4.

Biodegradable semi-crystalline polymers are used to manufacture load bearing implants. The crystallinity of the implant is dependent upon the exact material used, and the crystallinity can affect the biocompatibility of the implant.

Resorption of polymers and copolymers presented above is achieved by enzymatic hydrolysis reaction. Many factors affect the degradation of the polymer and the resulting reaction of the body to the polymer including implant material, implant geometry, site of implantation, and method of sterilization.

With the wide spread use of polymers also began to highlight their disadvantages. The main disadvantages are represented by low mechanical resistance, adverse tissue reactions

Table 1 - Main bioabsorbable polimers products currently used

Manufacturer	Product	Material	Use
Arthrex	Bio Tenodesis Screw; Bio-Trans Fix; Bi-Cortical Bio-Post; Tissue Button	LPLA	Fracture fixation, suture anchor
	Bio-Corkscrew; Tissue Tak II; Bio-FASTak; Bio-Anchor	LDLPLA	Rotator cuff repair, SLAP and Bankart repair, suture anchor
Biomet, Arthrotek	Bio-Phase Suture Anchor; Reunite Screws, Pins, Plates; Gentle Threads	LPLG	Fracture fixation, arthrodesis
Bionx, Linvatec	SmartPin	LPLG	Fracture fixation
	Smartscrew ACL; Duet Suture, Anchor; BioCuff;	DLPLA	Fracture fixation, ACL repair
DePuy, Mitek, Ethicon, J&J	Orthosorb Pins	PDO	Fracture fixation
	PDS/PGA staple PDO coated)	PGA	Scaffold fixation, grafting
	Panaloc RC; BioRoc EZ; Phantom screws	LPLA	Rotator cuff repair, suture anchor
Smith &Nephew	Biologically Quiet Screw	DLPLG	ACL reconstruction
Stryker, Howmedica, Osteonics, Surgical Dynamics	SD Sorbanchors, Staples, EZ Tac	LPLG	Suture anchor, meniscus repair, rotator cuff repair
Zimmer	Bio-Statak	LPLA	Suture anchor
Inion	FreedomScrew/Plate FreedomPin	LPLA, DLPLA and TMC	Fracture fixation

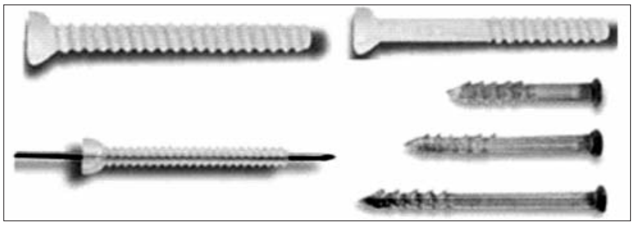

Figure 1 - Bionx Smart Pin

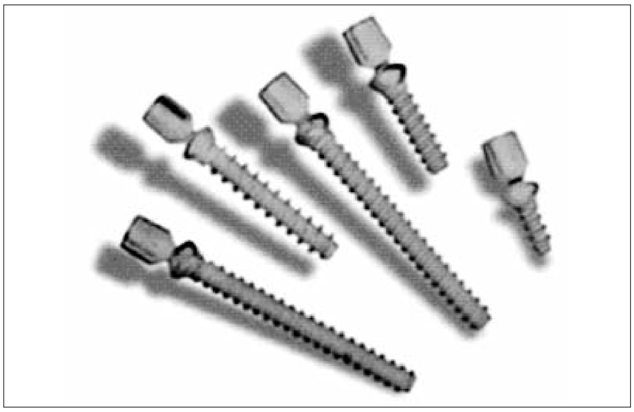

Figure 2 - Biomet Reunite Screws

(foreign body), and the increased cost, but the latter is still balanced by eliminating costs for ablation.

In terms of strength, tests revealed the following data for resistance to bending/traction forces: DL-PLA (lactic acid polymer enantiomers DL) 1.9Gpa, Elongation3-10%; PGA-TMC (glycolic acid polymers, trimethylene carbonates) 2.4 GPa. For stainless steel implant values were - 210 GPa, while normal values for bone are about 10-20 GPa.

The main complication of polymers is represented by foreign body reaction. Foreign body reaction timing is related to the final stage of degradation. The phagocytic reaction of the resulting product will lead to some changes in the peri-implant soft tissues, like: exudate, cyst, sinus, or in the bone: cyst and peri-implant osteolysis.

Bostman estimated that, in case of PGA and PLA use, the time until occurrence of adverse tissue reactions was 11 weeks and 4.3 years respectively, following surgery. Their incidence was between 4.8% and 61% (1). Histopathological examination of tissue damage revealed sterile nonspecific inflammatory changes, anti foreign body polynucleic cells, intra and extra cellular polymeric residues, osteolytic lesions, edema. Clinically this expresses itself through pain, hyperemia and local hyperthermia, fistulas and limited functionality.

As for PGA, LPLG implants, multiple studies (Bostman 2000, Tuompo 2001) report the occurrence of an accumulation of fluid, sinus formation, osteolysis, with an incidence between 3% and 60% in case of wrist fractures. The timing until foreign body response ranged from 1 to 6 month post surgery (2).

In case of PGA-TMC implant use, fluid accumulation, cyst formation and synovitis complications were reported. The complications rates ranged from 2 to 30% and the

Figure 3 - Artrex biotrasfix

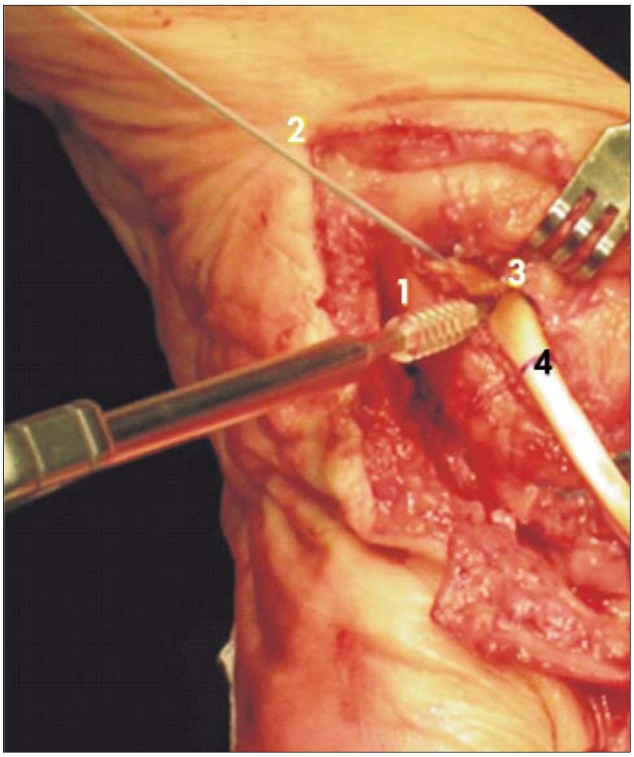

Figure 4 - Artrex Biotenodesis

timing of reaction ranged from 2 weeks to 6 months after surgery (Beneditte, Burkard, Bach) (3, 4).

In case of LD-LPLA use, Cummings (2003) (5) reported their clinical outcomes for rotator cuff repair using metal suture anchors versus bioabsorbable screws. The bioabsorbable group had a higher pain score after 3 months and lower shoulder function scores after 1 year. Three of nine patients (33%) subsequently underwent a revision surgery. This revealed a focal foreign body giant cell reaction to the absorbable material.

For DLPLA implants, complications included the cartilage lesions, when meniscal anchors were used (Ellerman 2002) (6). The total incidence of complications ranged from 1 to 47% and the timing of reactions ranged from 2 weeks to 1 year. The LPLA take the longest to degrade in vivo, and any adverse reaction cannot be expected to occur within the first 3 years of implantation. These complications have arisen as late as 9,5 years after the implantation and all have occurred more than 1 year after the implantation. The reported complications are swelling, cyst, sinus, fluid accumulation, foreign body reaction. Histological examination demonstrated needle like particles of LPLA, fibrous tissue and macrophages with foreign body giant cells.

Thus, on average, foreign body reaction occurs, at 3 months after surgery (7). Biological response is due either to the accumulation of acidic degradation byproducts or in response to polymer particles. The risk factors for the inflammatory foreign body response are the presence of quinone dye, implant site with low vascularity, an implant with a large surface area. (2) However, these reports clearly indicate that reaction to bioresorbable implants, occurs to same degree to most of the currently available materials.

Other complications mentioned in the literature are related to the low mechanical strength of materials, this could cause rupture of the implant and secondary displacement of the fracture. Also, there were concerns about the risk of infection, local exudates formation representing a culture medium for bacteria. In practice, there were not statistically significant differences compared to metallic materials, in their case infection risk increasing due to ablation operation.

Thus, their main drawbacks, degradation by hydrolysis compounds that may be toxic (monomers), or may give adverse inflammatory reaction (additives / catalysts), persistent degradation compounds that induce foreign body response, absorption of water and biomolecules in adjacent tissues, that can induce exudate appearance and their low mechanical strength, have led to the need to develop new bioresorbable materials. The solution can be represented by bioresorbable magnesium alloys.

Bioresorbable magnesium alloys review

Magnesium was first described and used as a biodegradable metallic implant (ligature wire for bleeding vessels) by Edward C. Huse in 1878 (8). Magnesium has several important properties. It is safe and biocompatible, being present in large amounts in human body. This cation is involved in many metabolic reactions and biological mechanisms. It is indispensable to adenosine-5 triphosphate metabolism and for the function of more than 300 enzymes. Thus, the implant is dissolved in the body without inducing toxicities and foreign body reactions. Also Mg is osteoconductive, promoting the formation of new bone by stimulating the adhesion of osteoblastic cells, leading to a hard callous at fracture site. Also, Mg based implants, shows superior mechanical properties compared to polymers. The Mg alloy posses a density of 1,7 – 2,0 g/cm^3, that is close to that of the natural bones (1,8 – 2,1 g/cm^3) (9). In the same time the elastic modulus of Mg alloys is approximately 45 GPa, closer to that of the natural bone (10 -40 GPa). These provides to the Mg alloys the potential to avoid stress shielding effect, that can be induced by other metallic orthopaedic implants (Ti, Co-Cr alloy). All of that leads to the idea that Mg based alloys can be used as light weight degradable, load bearing implants.The main drawback, however, is represented by the rapid biodegradation of Mg. It shows an increased rate of corrosion in the body, at a physiological pH of 7.4 to 7.6. Rapid corrosion will lead to loss of mechanical capabilities before completion of the callus formation. The bending strength can decrease in a first stage of erosion from 652 MPa to 390 Mpa (10).

The corrosion of magnesium in solutions proceeds by following reactions.

$$Mg \rightarrow Mg^{2+} + 2e^- \;/\; 2H_2O + 2\,e^- \rightarrow H2 + 2\,OH^- \;/$$
$$Mg^{2+} + 2OH^- \rightarrow Mg\,(OH)_2$$

According to the above reactions, $Mg(OH)_2$ is formed on the surface of the magnesium sample. Chlorine ions from the human body will interact with magnesium implant. Chloride ion is known to be detrimental to corrosion resistance of magnesium. When the concentration of chloride in the environment exceeds 30 mmol / L, the chloride ions will transform $Mg(OH)_2$ into more soluble $MgCl_2$. A lot of investigations have proven that high chloride concentration will accelerate the transform reaction of $Mg(OH)_2$ to $MgCl_2$ and promote the dissolution of magnesium alloy. (11).

To test the biocompatibility and corrosion rate of Mg and its alloys, a series of in vivo (mice, rabbits) and in vitro tests, are carried out. Currently used artificial biological fluids for in vitro tests, are SBF (simulated body fluid), Hank solution, artificial plasma.

Due to high hydrogen evolution rate and to the high hemolysis rate (25% - 57%) (12) and as well to the rapid corrosion, although pure Mg induces formation of new bone, it is not a proper material for orthopaedic implants.

Table 2 - In vivo and in vitro tests

In vitro tests	**In vivo tests**
Immersion tests (weight gain, weight loss, corrosion rate)	Surgical procedure
Electrochemical tests (tafel polarization, EIS)	Radiographic evaluation
Volume change test	Fluorescent observation
Hydrogen evolution test	Routine pathological examination
pH change test	Immunohistochemistry
Cell culture (attachment, morphology, proliferation,	
cytocompatibility, and alkaline phosphatase activity)	Microstructural study by using SEM, EDS, XPS, and XRD
Bioactivity tests (SEM-EDX, XRD, AAS)	Analysis of the magnesium ion concentration in blood of implanted samples

According to ISO 10993-5:2009, a reduction of cell viability more than 30% it is considered a cytotoxic effect. To eliminate these deficiencies, purifying and alloying can be a solution for getting Mg based biomaterials with proper properties. In studies conducted by Song and Ren (11) they noticed that Magnesium purifying process, lowers its corrosion rate. The most harmful impurities are Fe, Cu, Ni, with a tolerance limit of 170 X 10-6 1000 X 10-6 and 5 X 10-6. These limits are influenced by the manufactured method. Thus, the corrosion behavior of Mg is directly influenced by the content ratio of impurities, such as Fe/Mn ratio rather than their content values. Thus, in order to improve the rate of corrosion of alloys, they must be obtained only from as pure component as possible. Even values of the impurities less than 0.2 wt% may result in a marked acceleration of the rate of corrosion. In the same time, an efficient method to enhance the corrosion rezistance of Mg alloys, is represented by grain refinement through hot rolling or forging. Moreover, combining with other elements, will improve implants qualities

Alloying elements, play an important role for biodegradable Mg alloys. The main requested qualities, are improving the mechanical properties, the rate of biodegradation and biocompatibility of the alloy. Thus the elements released from the implant must not be toxic for the human tissues. The most common biodegradable magnesium alloys are shown in the table 3 (9):

The major influence of alloying elements on the corrosion rate of Mg alloys is presented in a study by Kirkland (13). In the same time it shows that It is possible to produce magnesium alloys of customized biodegradation rates-based on corrosion specific. The mass loss can vary over a range of 3 orders of magnitude, showing that some alloys can dissolve at a very high rate, being to rapid for the purposes of orthopaedic implants. The mass loss was converted to a penetration in mm/yr, fig. 5.

As we had mentioned before,some of the most used and researched alloys are those of Mg-Ca, which are composed of two elements naturally present in the human body. The solubility of Ca in Mg is 1.34 wt% (11).

Microstructure of Mg-Ca alloys consists of a Mg primary phase and eutectic phase, a lamella structure, composed of Mg2Ca phases. To obtain improved mechanical properties and corrosion resistance, it is possible to turn MgCa2 phase into smaller particles (grain size refinement) by hot rolling or hot extrusion. However, in case of Mg-5wt%Ca, at immersion of the alloy in Hank's solution,

Table 3 - Alloying elements

Family	Alloys	Alloying elements
Pure Mg	Mg	
Mg-Ca	Mg-xCa (x = 1, 2, 3, ...)	xCa
Mg-Zn-Ca	Mg-1Zn-1Ca	1Zn / 1Ca
Mg-Zn	Mg-xZn (x = 1, 3, 6, 10)	xZn
Mg-Zn-Mn	Mg-1Zn-1Mn	1Zn / 1Mn
Mg-Mn	Mg-1Mn	1Mn
RE containing		
magnesium alloy	WE43	4Y / 3RE
	Mg-8Y	8Y

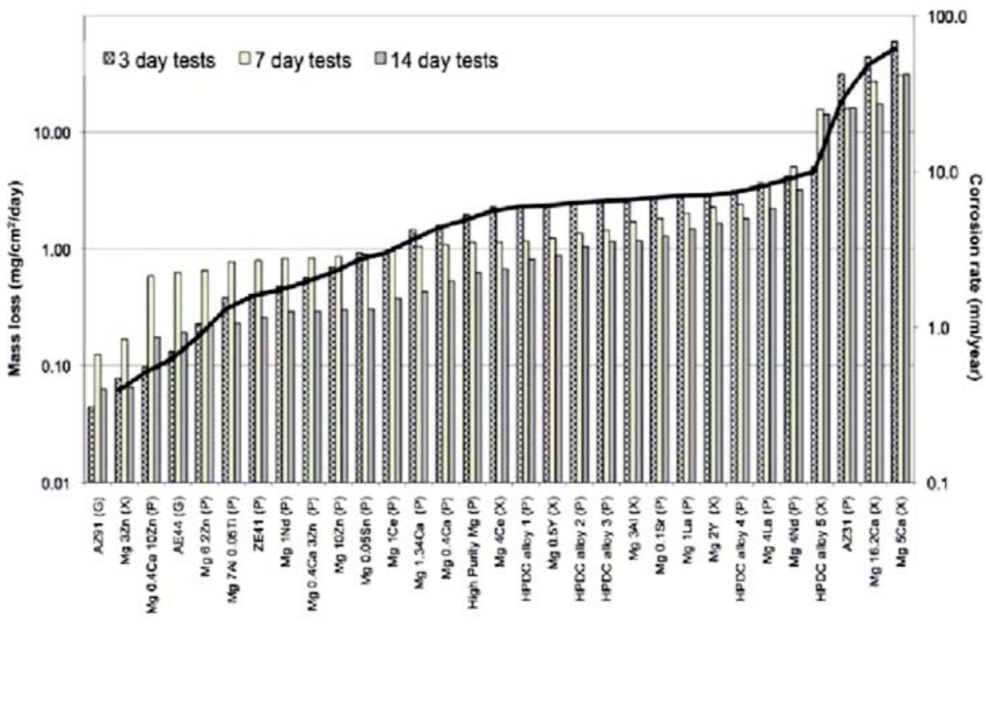

Figure 5 (13) – alloy general corrosion mode; P – pitting corrosion mode; X – extremely localized corrosion severe, immediately corrosion is observed. This is due to the formation of a galvanic circuit, due to electrochemical potential difference between Mg and $MgCa_2$ phase. Corrosion is uneven, leading to disintegration of the alloy and to the mechanical properties loss. Improvement of the corrosion rate was observed when lower concentrations of Ca were used to obtain Mg-Ca alloys. Ca values of 0.8 to 2 Wt% led to marked extension of time in which the implant loses its mechanical properties.

Another option in order to block galvanic circuit was Zn addition to the Mg-Ca alloy. Corrosion decreased proportionally with Zn concentration increase. Thus, in a concentration of more than 0.5 wt% Zn, there was no corrosion process observed after 300 hours of immersion. In this case, the process was uniform, surface corrosion one, eliminating the abrupt disintegration of Mg-Ca alloys (10). For a concentration of 1 wt% Zn, after 408 hours of immersion, there was noticed the persistence of smooth corrosion surfaces, maintained after an slight initial corrosion process. Also, as for Ca-Mg alloys, the corrosion rate decreases with grain size decrease. In the case of pure magnesium grain size was 25 μm, and in the case of Mg 5 wt% Ca 1 wt% Zn was 10 μm (10). Also, an alloy made by Sun, Mg4Zn 0,2Ca has showed great mechanical integrity after 30 days of immersion in SBF solution. The values of ultimate tensile strength, the elongation and the elastic modulus were 220 Mpa, 160 Mpa, 8,5% and 40 Gpa, still enough for bone fixing (11).

Alloys biocompatibility was evaluated by in vitro cytotoxicity assays, indicating that Mg1Ca, does not induce toxicity to L929 cells (11). Cytotoxicity can be defined as the degree in which the material used as a subject is destructive to the exposed cells. Cytotoxicity can be assessed by direct or indirect tests. In a direct test the cells from the culture are in direct contact with one sample of Mg alloy. In indirect tests, the Mg alloy is inserted in a extraction solution, and this extract replaces the medium of cell culture in different concentrations.

Magnesium cell adhesion properties are tested in vitro, by observing hydroxyapatite crystal deposition of composite surface after suspension in SBF (simulated body fluid). In the same time tests are performed by suspension of osteoblasts in culture: it counts the number of osteoblasts per unit area (1 mm^2), lowering it through the process of cell adhesion to biomaterial.The effects of Mg-3Nd-0.2Zn-0.4Zr (weight %, JDBM) alloy on osteoblastic cell function involving cell adhesion, cell proliferation, and mineralization were investigated using scanning electron microscopy (SEM), MTT assay and ambramycin staining, in a study conducted by Wang (14). He concluded that the JDBM alloy has excellent bioactivity, improving the cell function of osteoblastic cells seeded on it.

In case of in vivo tests on rats and rabbits, it was observed that Mg 1Ca alloy pins gradually degraded within 90 days and new bone was formed (15). As-Extruded Mg-0,8Ca alloy implanted into rabbit tibiae for 6 month maintained more than half of the initial volume (10). Still, in case of Mg Ca As Cast implanted in rats, there were radiological and clinical signs of gas bubbles, formed

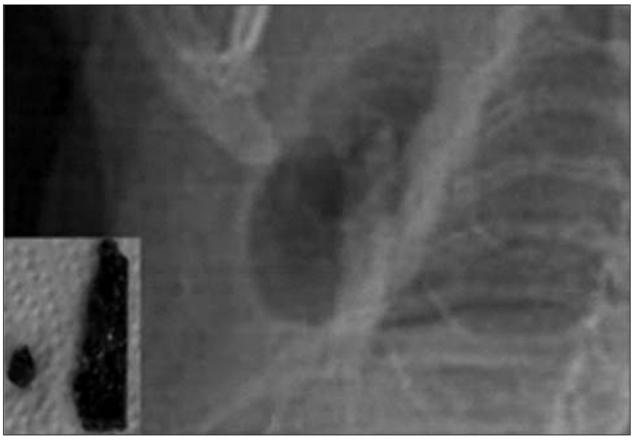

Figure 6a (10) - Cast Mg-5 wt%Ca

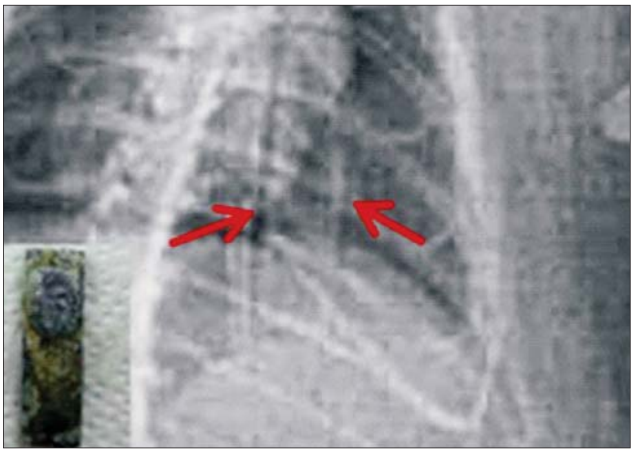

Figure 6b (10) - Extruded Mg-5 wt%Ca-1 wt%Zn

in the first week fig. 6a. The rats implanted with extruded Mg-Ca-Zn plates showed no visible gas bubbles, clinically and radiographically after 12 weeks, fig. 6b.

Histologic analysis performed for Mg 5 wt%Ca 1wt% Zn, screw implanted in a rabbit femur for a period of 24 weeks showed bone remodeling and new bone formation without significant bubble formation, and no foreign body response in the tissue surrounding the implant. Also, the screw was not degraded to the point were it loses the mechanical properties, fig 7.

In the case of Mg-Zn alloys, Mg-6Zn is the most investigated. Exhibits good biocompatibility in vitro: cytotoxicity to L 929 cells was found to be Grade 0-1 and the hemolysis rate 3,4% (16). In vivo tests, performed on rabbit femur, have showed a degradation rate of 2,32 mm/yr and new bone formed arround the implant (11).

Extensively studied and with satisfactory properties, are Mg-RE alloys (Rare Earth). Rare earths are used to improve corrosion resistance and to strengthen the material. The most used are Ytrium RE (Y), Gadolinium (Gd). WE43 alloy containing Y, shows good mechanical properties and corrosion resistance. The addition of Y into Mg alloys increases the solubility of the matrix due to its high solubility in Mg (8,0wt%). In this way, it's slowing down the corrosion rate. The cytotoxic effects are still incompletely

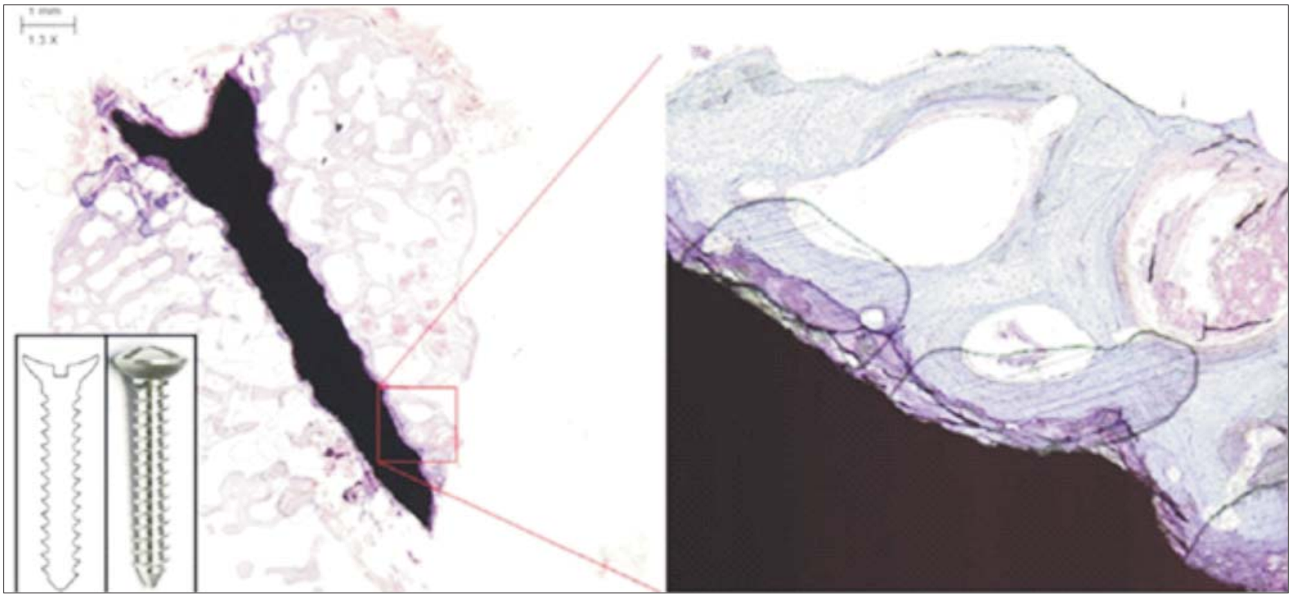

Figure 7 (10) - Histological analysis of extruded Mg-5 wt%Ca-1 wt%Zn alloy screw

known, RE quantities released from alloy, must be carefully controlled.

Corrosion resistance enhancement

As mentioned before, a good way to improve the corrosion rate is represented by grain refinement. Alloys treated by hot rolling (HR) showed a low rate of corrosion at immersion in Hank's solution compared to those treated by squeeze cast (SC) or equal channel angular pressing (ECAP). H. Wang demonstrated that in case of AZ31 alloy, the initial rate of degradation in Hank's solution for SC samples, was 2.08, and after 20 days of it decreased to 0.87. In what concerns, HR and ECAP samples, initial degradation rates were 1.33, 1.49 respectively. At the end of 20 days of immersion, both of these materials had a ratio of 0.74, fig. 8. The reduced corrosion rate of AZ31 by HR treatment must be associated with the grain refinement effect, but a further reduction of the grain size by ECAP method did not influenced the corrosion rate (17).

Thus, enhancement of corrosion resistance for HR alloys is induced by grain refinement effect. Grain refinement obtained by hot rolling, lead to an enhancement of corrosion rezistance and in the same time to a significant enhancement of fatigue life and endurance limits of the Mg alloys.

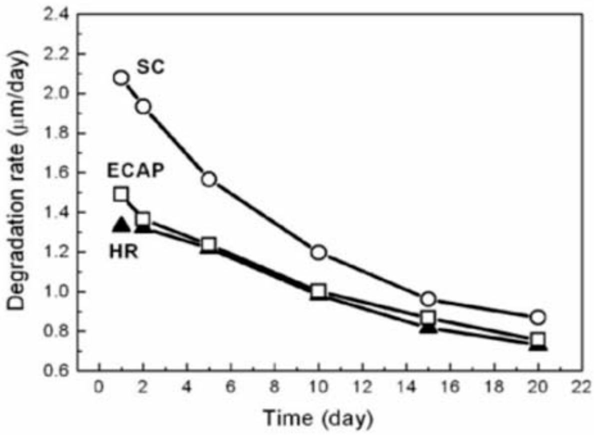

Figure 8 (16) - Degradation rate of SC, HR, and ECAP samples in Hank's solution

Table 4 - Alloy cytotoxicity

Materials	Type	Cell line	Culture time (d)	Cell viability (%)
Pure Mg	As-cast	L929	4	65.7
	As-cast	NIH3T3	7	90.6
Mg-1Ca	As-cast	L929	4	81.8
Mg-3Ca	As-cast	L929	4	55
	RS30	L929	4	100
Mg-6Zn	As-extruded	L929	4	100
Mg-1Zn-1Ca	As-cast	L929	7	75
Mg-2Zn-1Ca	As-cast	L929	7	70
Mg-3Zn-1Ca	As-cast	L929	7	72

A good control of biodegradation rate of Mg alloy is also provided by coating procedures. Coating should enable biodegradation at a desired rate, offering a limited barrier function. Coating can be devided in two large classes: conversion coatings and deposited coatings.

Conversion coatings are formed by specific reactions between the base materials and the environment, the metallic substrate surfaces being converted by chemical or electrochemical processes into an oxide layer. The produced layers are inorganic and show ceramic like characters. Deposited coating can be devided into metal, inorgarnic and organic based coatings.

There are many methods to coat or to modify the surface of Mg alloy, such as ion-beam assisted deposition, ion implantation, laser surface melting, heat-stearic acid treatment, but the most common methods used in medical implants are conversion one, bioceramic based coatings. By selecting a proper surface modification we can improve mechanical properties by reducing the biodegradation rate and inducing better bone-implant interfaces

Many coating methods have been developed but most studied are:

Calcium Phosphate (Ca-P) coating - has been succesfully applied in order to promote direct attachment of sorrounding bone tissue and to suppress release of corrosion products into human tissues. In vitro tests performed on Mg alloys, coated with Ca-P had showed that this provides the Mg alloy with a significanly improved surface cytocompatibility. In a study performed by Xu, the cell number on the surface of Ca-P coated Mg alloy, in a cell culture for 5 days, showed a significant increase at all time intervals. In the same time, there is no evident increase in the cell number at all time intervals ($p > 0,05$), for the naked Mg alloy (18). In vivo tests, showed that at 4 weeks after implantation, bone tissue deposition was observed around the implant, better than for simple Mg, showing that Ca-P coating significantly improves osteoconductivity and osteogenesis.

Hydroxyapatite (HA) coating - $Ca_{10}(PO_4)_6(OH)_2$, can improve the biocompatibility and bioactivity of an Mg alloy implant but due to poor mechanical strength can not improve the load bearing properties. The HA coating can be produced by electrochemical method (Jong) (19). In SBF solution Mg alloy suffers severe attack, due to the presence of Cl^-. In microscopic view , parts of flake like HA coating have been disolved in SBF, but the corrosion has not penetrate into the coating. Thus, the HA coating can reduce the biodegradation rate of Mg alloy in SBF solution, protecting it for a longer time.

Fluoridated hydroxiapatite (FHA) coating – $Ca_{10}(PO_4)_6(OH)_{2-2x}F_{2x}$ seems to be superior to HA coating. FHA has attracted attention due to its improved biological properties. It can provide low levels of fluoride, to act upon periimplant cells in order to improve the bone-like apatite formation. Thus, the fluoride ions induces the mineralization and crystalization of calcium phosphate in the bone formation process. In vitro results, have shown that FHA can provide better cell attachment, better protein absorption and higher corrosion resistance than HA itself. In cell cultures, FHA coated Mg alloy had a significant better stimulation effect to the HBMSC cells proliferation and differentiation. According to Li's molecular biological tests (20), FHA coatings can regulate the main osteogenic gens after 21 days of the cell culture.

Although coating is absolutely necessary to improve the corrosion resistance of Mg alloys, in many cases one coat layer is not enough to isolate alloy from the sorrounding environment, as long as it needed to. That's why the composites with 2-3 layers manufactured by different techniques may be an optimal solution.

Conclusions

Biodegradable orthopedic implants must meet two major criteria, biocompatibility and resistance to corrosion of sorrounding environment until the bone can sustain mechanical stresses. Thus, corrosion resistance is equally as important as the initial mechanical strength of the alloy, the degradation must be slow, to allow the bone healing to occur. In the case of orthopedic implants, this would require 3-4 months, to allow the formation of callus.

Polymer implants show low degradation rate, but low initial mechanical strength and adverse foreign body reaction induced by degradation products, are major drawbacks.

Mg alloys offer good biocompatibility, being comprised of natural elements present in the human body, and it produces no foreign body reactions when resorption occurs. In vitro studies, performed on cell lines show that Magnesium and its alloys have low cytotoxicity not affecting the viability and morphology of adjacent cells, also showing good adhesion of osteoblast cell. In vivo studies have shown that granulation tissue formed around the Mg alloy implant evolves to the formation of new bone tissue, that penetrates up to its surface providing a good oseointegration of Mg alloys implants. Stimulating the development of new bone perimplant will thus stimulate fracture consolidation. Also, it has good mechanical properties, initial strength being superior to the polymers and similar to that of the human bone.

The main disadvantages are rapid resorption, before callus formation, and the formation of gas bubbles. Reducing gas(H^+) emission can be obtained by both microstructural and electrochemical tailoring, obtained by addition of other elements (such as Zn). By mechanical properties, a Mg alloy implant should have a matching corrosion rate with tissue healing rate, in order to provide sufficient load bearing until bone healing appears. There are two major methods to improve the corrosion resistance of Mg alloy:

a) Tailoring the composition and microstructure, grain refinement and texture of the base material by alloying procedure and also through the development of optimized manufacturing methods (hot rolling) plus availability of suitable raw matherials

b) Surface treatement or form coating which produces ceramic or composite layers. Coating is mandatory in order to obtain an alloy with a satisfactory corrosion rate, HAF being an encouraging method.

Thus, Mg alloys that meet manufacturing requirements mentioned above, may be a viable solution for the manufacture of biodegradable orthopedic implants. In support of this idea comes that at this moment, it is used in orthopaedic surgery of the foot the first Mg alloy implant, (Mg-Y), which successfully passed all the preliminary tests, in vitro and in vivo.

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