J Mater Sci: Mater Med (2016) 27:80
DOI 10.1007/s10856-016-5690-9

BIOCOMPATIBILITY STUDIES

Original Research

Biological characterization of a new silicon based coating developed for dental implants

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Received: 17 September 2015 / Accepted: 17 February 2016 / Published online: 2 March 2016

Abstract Taking into account the influence of Si in osteoblast cell proliferation, a series of sol–gel derived silicon based coating was prepared by controlling the process parameters and varying the different Si-alkoxide precursors molar rate in order to obtain materials able to release Si compounds. For this purpose, methyltrimethoxysilane (MTMOS) and tetraethyl orthosilicate (TEOS) were hydrolysed together and the sol obtained was used to dip-coat the different substrates. The silicon release ability of the coatings was tested finding that it was dependent on the TEOS precursor content, reaching a Si amount value around ninefolds higher for coatings with TEOS than for the pure MTMOS material. To test the effect of this released Si, the in vitro performance of developed coatings was tested with human adipose mesenchymal stem cells finding a significantly higher proliferation and mineralization on the coating with the higher TEOS content. For in vivo evaluation of the biocompatibility, coated implants were placed in the tibia of the rabbit and a histological analysis was performed. The evaluation of parameters such as the bone marrow state, the presence of giant cells and the fibrous capsule proved the biocompatibility of the developed coatings. Furthermore, coated implants seemed to produce a qualitatively higher osteoblastic activity and a higher number of bone spicules than the control (uncoated commercial SLA titanium dental implant).

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1 Introduction

In the last decades, the number of procedures of insertion of dental implants has increased continuously worldwide, reaching about a million implantations per year in the U.S. [1]. Titanium and its alloys have been widely used to manufacture dental implants due to their many advantages over other materials [2]. In spite of its good properties, such as the biocompatibility, it is relatively inert due to the spontaneously formed oxide layer on its surface, so it cannot directly bind to the bone and therefore the osseointegration via this oxide layer may result a relatively long process [3]. For that reason, many surface modification methods have been investigated to modify their surface in order to fabricate implants with a higher bone-to-implant contact (BIC) ratio, enhance cell-implant interaction and promote a faster healing, the osseointegration and the longevity of the implant [4–7].

There are three main ways of modifying titanium implant surfaces which are morphological, physicochemical and biochemical, but until now no one has implied a reasonable improvement in the osseointegration of the implant [8]. The morphological methods are applied to create rough surfaces, known to enhance the cell response and improve the biomechanical fixation, where the more common techniques are titanium plasma-spraying, grit-blasting, acid-etching and anodization. However, they present some drawbacks which make their use limited, as the release of harmful titanium particles to adjacent areas [9, 10], the impossibility of removing alumina particles from the implant when cleaning the surface after the

blasting [11], the reduction of the mechanical properties of titanium after the treatment [12] and the difficulty of controlling all the parameters of a complex process [5], respectively. In the case of physicochemical modification, plasma-spraying coating method is the only one that has been used in clinical practice to obtain a hydroxyapatite layer on the surface of the implant [5]. Nevertheless, there is a concern about the use of this type of treatments because they are associated with clinical problems due to the weakness of the HA coating and adhesive failure [13]. The last trends in the research for a suitable implant surface are focussed on biochemical modifications, based on developing implants with a layer of adsorbed peptides. This technique seems to be one of the most promising, but passively bound biomolecules could be easily removed from the implant during the process of surgical implantation and their release kinetic is difficult to be controlled [14]. There is also a lack of in vivo trial to prove the performance of these materials placed into the bone.

Therefore, there is a real need on continuing the research on developing new modification treatments for titanium dental implants. In this context, on the one hand, sol–gel technology was selected in this work because among other benefits over other techniques, coatings with high adhesion strength to the substrate can be obtained in substrates with complex shapes [15, 16], what may promise to be a successful technology. On the other hand, silicon precursors were chosen due to their known ability to confer bioactivity on the material through the silanol groups on the surface [17], and to stimulate the osteoblast-like cell activity [18] and bone mineralization [19] due to the dissolution products of the silica network.

Owing to these properties we contemplate the possibility of the application of these coatings to Ti dental implants in order to use their ability to release Silicon compounds with proved osteoinductive properties [18, 19]. In this part of the work we aim to test the in vitro and in vivo performance of these coating, which were previously synthesised and characterised [20], focussing on the biological response to confirm their biocompatibility. A broad outline of the osseointegration of the sol–gel coating compared to commercial titanium dental implants will be also shown.

2 Materials and methods

2.1 Materials

The coatings were synthesised using the sol–gel process from the methyl-trimethoxysilane (MTMOS, Sigma-Aldrich), and tetraethyl-orthosilicate (TEOS, Sigma-Aldrich) precursors. Coatings with different MTMOS:TEOS (M:T) molar ratios were prepared: 10:0 (MTMOS); 9:1 (9M:1T); 8:2 (8M:2T); 7:3 (7M:3T). To ensure a miscible solution of the silane precursors, 2-propanol (Sigma–Aldrich) was used as a solvent, in a volume ratio of alcohol:precursor 1:1. A stoichiometric amount of water acidified with HNO_3 (pH 1) was added as the catalyst of the reaction. Once the sol was obtained, it was deposited over glass coverslips (18 mm diameter) for silicon release test and in vitro assays, obtaining a film thickness of about 3 μm. For in vivo evaluation dental implants (3.75 mm diameter by 8 mm length) were coated. Then, coatings were dried at 100 °C for MTMOS and at 80 °C for MTMOS:TEOS hybrids for 2 h in the oven.

Glass coverslips were cleaned in an ethanol bath, ultrasonicated for 5 min at a power of 30 w using a Sonoplus HD 3200, rinsed in distilled water, soaked in ethanol and, finally, dried at 150 °C. Afterwards, to improve the wettability, the glass dishes were activated by an Argon plasma treatment (200 sccm) for 30 s (PLASMA-ELECTRONIC PICCOLO, 50 Pa, 300 W).

Titanium implants were used as purchased without any further purification. They were already supplied decontaminated and sterilized by gamma radiation.

2.2 Silicon release test

In order to determine the degree of silicon release, inductively coupled plasma mass spectrometry (ICP-MS) was used. The equipment that was used is an Agilent 7700 Series ICP-MS.

For the fulfilment of this test, glass coverslips were coated by the process of drop-casting. The test was carried out by sinking the coated discs into 50 mL of water mili Q (ultrapure water type I with a resistivity at 25 °C of 18.2 MΩ cm), in an oven at 37 °C during 5 weeks. Aliquots of 500 μL were taken at 1, 2, 3, and 5 test weeks. After the extraction of each aliquot, the volume was replaced with 500 μL of water mili-Q. The test was carried out with three replicas for each time point.

2.3 In vitro tests: assays with MSCs

The biocompatibility and the capability of the coatings to promote the osteogenic differentiation were in vitro tested with human adipose tissue-derived mesenchymal stem cells (AMSCs). To perform the cell culture onto the samples, the sol–gel coatings were deposited on glass coverslips as substrate and they were sterilized by 30 min exposure to UV in a tissue culture cabin. All samples were preconditioned overnight dipping in Dulbecco's Modified Eagle's Medium (DMEM-Glutamax) (Gibco) to ensure protein adsorption.

To perform cell adhesion and proliferation assays about 12500 cells/cm^2 were seeded onto the sample surfaces and incubated up to 14 days at 37 °C in 5 % CO_2/air

atmosphere. Proliferation of cells was measured by analyzing the mitochondrial activity using a colorimetric cell proliferation test kit (MTT, Roche) at different culture times, 0, 7, and 14 days. The absorbance was measured with a Multiskan Ascent plate reader at $\lambda = 550$ nm. The experiments were performed in triplicate.

In order to analyse the ability of coatings to induce the osteogenic differentiation of AMSCs, the calcium deposits formed by cells in an osteogenic culture medium were measured using Alizarin Red S staining. To perform the assay, about 2000 cell/cm^2 were seeded onto the surface and incubated in DMEM-Glutamax containing 10 % FBS during 7 days at 37 °C in 5 % CO_2/air atmosphere. After this period of time, the differentiation was induced by changing the medium to an Osteoblast Differentiation Medium (Gibco) and incubating the samples up to 14 days, changing the medium every 72–96 h. Finally, the calcium deposits were quantified using a 2 % Alizarin Red (Sigma-Aldrich) staining solution at pH 4.1–4.3. The absorbance was measured with a Multiskan Ascent plate reader at $\lambda = 570$ nm. The experiments were performed in triplicate.

2.4 In vivo implantation

With the purpose of evaluating the histological response of the selected coatings, dental implants were surgically placed in the tibia of New Zealand rabbits (*Oryctolagus cuniculus*). This implantation model in rabbit tibia is widely described in bibliography for osseointegration of dental implants [21–24]. All these studies were accomplished in accordance to protocols of Ethical Committee in University of Murcia (Spain) and European guidelines and the legal conditions laid in R. D. 223/1988 of March 14th and the Order of October 13rd, 1988 of the Spanish Government law about the protection of animals used for experimentation and other scientific purposes.

Concretely, the rabbits were kept under 12-h span darkness-light cyclic conditions; room temperature was set at 20.5 ± 0.5 °C and room relative humidity ranged between 45 and 65 %. The animals were individually caged and fed with a standard diet and filtered water ad libitum.

Dental implants were supplied by Ilerimplant SL (Spain). The implants were internal connection made with titanium grade IV, trademark GMI® dental implants, 3.75 mm diameter by 8 mm length Frontier model, with ADS® (Advanced Doubled-Grip Surface) surface treatment, a combination of white corundum micro-bubble treatment and acid etching with nitric acid and sulphuric acid solution. A total amount of 40 of these implants were used, 20 uncoated as control and 20 coated as test samples. Both, control sample and test sample were implanted at the same conditions and their results were compared.

The total number of rabbits used was 20, with weights between 2000 and 3000 g, aged near the physeal closure, which is indicative of an adequate bone volume. The implantation periods of the experimental model were at 1, 2, 4, and 8 weeks. These periods were chosen because a time in between 4 and 6 weeks is adequate for the complete osseointegration of titanium implants on animal models [25]. Thus, five rabbits were used for each experimental period. Implants were inserted in both left and right proximal tibiae, each animal having a total of two implants, one control sample and one test sample. Animals were sedated (chlorpromazine hydrochloride) and prepared for surgery, and then they were anesthetized (ketamine chlorhydrate). On the implantation place in the proximal tibia a coetaneous incision was made. Periosteum was removed and osteotomy was made by low revolution micromotor and drills of successive diameters of 2, 2.8, and 3.2 mm, with continuous irrigation. Implants were put by press-fit and surgical wound was sutured by planes, washed with saline solution and covered with plastic spray dressing (Nobecutan®, Inibsa Laboratories, Barcelona, Spain).

After each implantation period, the animal was euthanized with carbon monoxide inhalation, to retrieve the screws in order to study their surrounding tissues.

2.5 Processing of samples

Samples for histological examination were processed following the methodology described by Peris et al. [26]. Briefly, the samples were embedded in methyl methacrylate and 25–30 μm thick sections were obtained using EXAKT® technique (EXAKT Technologies, Inc., Oklahoma, USA). For optical microscopy examination, all the sections were stained using Gomori Trichrome solution.

2.6 Biocompatibility analysis

The biocompatibility of a material can be defined as the biological acceptance of it once is placed in the organism [27]. This can be examined by looking at different parameters. In this case, in order to evaluate tissue response after the implantation of the coated and uncoated implants, certain parameters were considered such as the condition of the bone marrow, the presence of foreign bogy giant, the development of the fibrous capsule and the response of bone tissue.

Histological samples were analyzed by light microscope in order to establish qualitatively the level of damage induced for the coating presence in the adjacent tissues in comparison with the control (uncoated implant) [28]. For the analysis of the bone marrow status, the architecture of adipose tissue was studied, as well as the balance between adipocytes and the rest of cellular components of the bone

marrow parenchyma. The frequency of giant cells in reaction with a foreign body in contact with the coating surface, in the case of tests samples, or in contact with the implant surface, in the case of control, was studied. The formation of a fibrous capsule around the coated and uncoated implants was studied, also the evolution of it along the time after the implantation, comparing quantitatively the thickness change with time. The response of bone tissue was evaluated by observation of the new bone formation around the implants; the observation of osteoblast lines secreting osteoid, the formation of new spicules and their maturation in bone trabeculae.

2.7 Statistical analysis

For results analysis, mean and standard deviation values were calculated using the 1-way ANOVA statistical technique, using SPSS 17. The error protection method used in this research was the Tukey HSD method and the confidence limit used was 95 %.

3 Results

3.1 Silicon release test

Figure 1 shows the silicon release from the four different coatings. The incorporation of TEOS to the hybrid formulation had a drastic effect on the matrix dissolution kinetic, making the coating more soluble and in consequence increasing the Si delivery. As expected, the kinetic of Si release was very sensible to TEOS addition, showing an initial "burst" silicon release that increased until the second week of the test, reaching values ninefold higher than the pure MTMOS coating. However, there was not a trend in the release kinetic of 9M:1T, 8M:2T and 7M:3T coatings, all of them reached similar values at the end point of this experiments, 8 ppm for 8M:2T and 10 ppm for 9M:1T and 7M:3T, not significant differences were found between them. MTMOS coating released around only 1 ppm in 5 weeks.

3.2 In vitro tests

3.2.1 Mesenchymal stem cells (AMSC) proliferation test

Figure 2 displays the proliferation plot of the AMSCs on the MTMOS coating and the MTMOS:TEOS coatings series at different periods of time, 1, 7, and 14 days of culture. The MTMOS coating shows low proliferation in the entire test time, having a slight but continuous cell number increase until 7 days, which decreases slightly at the end of the test. We cannot say that the addition of 10 and 20 % of TEOS, coatings 9M:1T and 8M:2T, improves the cell proliferation with regards to the MTMOS coating. The 9M:1T coating shows values which are only higher than MTMOS at the beginning of the test, and in the case of 8M:2T material, values slightly higher than those of MTMOS are achieved only at 14 days of testing. However, when adding 30 % of TEOS, coating 7M:3T, a significant improvement is produced with respect to the MTMOS coating. Thus, 7M:3T coating shows the best initial proliferation, in spite of a slight decrease at the first day. Finally, cell proliferation undergoes a huge increase until the day 7, which continues increasing until the end of the test. The 7M:3T coating is the material that promotes the fastest proliferation, giving a value of absorbance fivefold higher than the other materials ($P < 0.05$).

A possible reason of the decrease in proliferation observed at 1 day test in the TEOS containing coatings could be the degradation of such coatings that hinder the initial cell adhesion step [20].

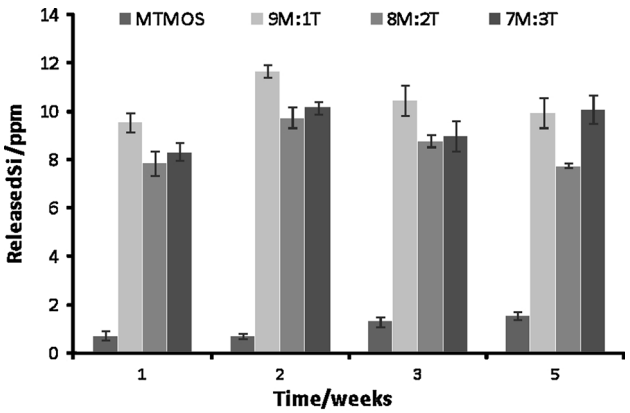

Fig. 1 Cumulative silicon release from MTMOS, 9M:1T, 8M:2T, 7M:3T coatings in an aqueous medium at 37 °C up to 5 weeks

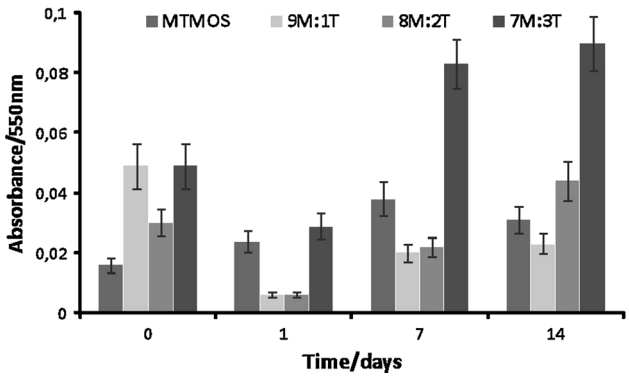

Fig. 2 Proliferation of AMSCs seeded onto the MTMOS, 9M:1T, 8M:2T y 7M:3T coatings up to 14 days

3.2.2 Mesenchymal stem cells (AMSC) differentiation and mineralisation test

Figure 3 shows the quantification of the calcium deposits formed by the AMSCs on the different coatings referred to the MTMOS coating, in order to be able to determine the influence on mineralisation of the incorporation of different percentages of TEOS to the base coating.

The results show that all the coatings exceed the calcium deposits values obtained for the MTMOS coating. Furthermore, the formation of calcium deposits increases from 7 to 14 days after the cell seeding for all the coatings.

At day 7, the 9M:1T coating registered an absorbance relative to the MTMOS coating of 104 %, the 8M:2T of 131 % and 7M:3T of 184 %. At day 14, the absorbance of all the coatings with TEOS exceed significantly ($P < 0.05$) the value of the base coating. Moreover, the 7M:3T coating even doubled the value.

3.3 Biocompatibility analysis

At the sight of the previous results, the 7M:3T coating was selected as the best candidate for the purpose of this research, to be tested in vivo. Thus, the observation of the biocompatibility of the selected coating, i.e.: 7M:3T, in comparison to the implants without coating from the in vivo test, was based on a comparative study of parameters during the implantation time like the bone marrow condition (3.3.1.), the presence of giant cells (3.3.2.), the development of the fibrous capsule and its evolution in time (3.3.3.) and the formation of new bone (3.3.4.).

3.3.1 Bone marrow condition

Figure 4a.1–a.4 shows the bone marrow in contact with an uncoated titanium implant for 1, 2, 4, and 8 weeks, while the row below (Fig. 4b.1–b.4) correspond to 7M:3T coating at the same times.

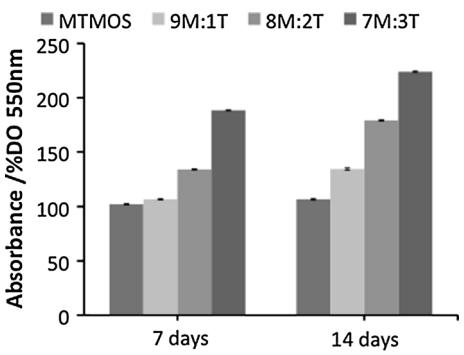

Fig. 3 Quantification of mineralization by analyzing calcium-rich deposits produced by the AMSCs cultured on the 9M:1T, 8M:2T and 7M:3T coatings

The behaviour of the bone marrow and its evolution for control and the coating is very similar. There is a good initial state in the bone marrow for both cases (control and 7M:3T) after 1 week of implantation. A worsening is observed after 2 weeks of implantation for both samples showing a decrease of the cellular charge, an increase of the adipose cells and a loss of their architecture. After 4 weeks, a minimum recovery of the bone marrow condition was observed. Moreover, after 8 weeks of implantation (Fig. 4a.4, b.4), there is a clear improvement of the bone marrow state, almost arriving to the initial situation.

3.3.2 Giant cells

Although some foreign body reaction cells in contact either with titanium (Fig. 4c.1, c.2) or 7M:3T coating were observed (Fig. 4d.1) at different times, the number of giant cells was the expected for a normal foreign body response. Thus, such body reaction did not impact the biocompatibility of the implant.

3.3.3 Fibrous capsule

In contact with the bone marrow zone, both the control (Fig. 4e.1–e.4) and 7M:3T coating (Fig. 4f.1–f.4) induced the formation of a fibrous capsule around them. First, at 1 week after implantation, the capsule was wide and lax. After 2 weeks, fibrous capsule aspect did not change notably. However, as time passed, the tissue of the capsule showed different behaviours depending on the dental implant area. It became thinner and denser in contact with the bone marrow zones, while disappeared in osteogenesis areas for control and 7M:3T.

3.3.4 New bone formation

The response of the bone tissue to the titanium and coating was similar. Figure 5 shows the process of new bone formation in the case of the control (a. series) and in the case of 7M:3T coating (b. series). After the first week of implantation protein deposits could be observed together with a presence of osteoblasts (Fig. 5a.1, b.1), that indicates the formation of new spicules in this period. Spicules continued growing and maturing during the 2 weeks period (Fig. 5a.2, b.2). So, after 4 weeks well-structured trabeculae could be observed (Fig. 5a.3, b.3), achieving the implants osseointegration after 8 weeks (Fig. 5a.4, b.4).

In spite of both behaviours were very similar, some differences between control and coating were observed. At 1 week, osteoblasts forming osteoid were observed with more frequency in the case of 7M:3T coating samples (Fig. 5b.5, b.6), forming at 2 weeks more spicules and a more robust trabeculae at 4 weeks, as can be observed when

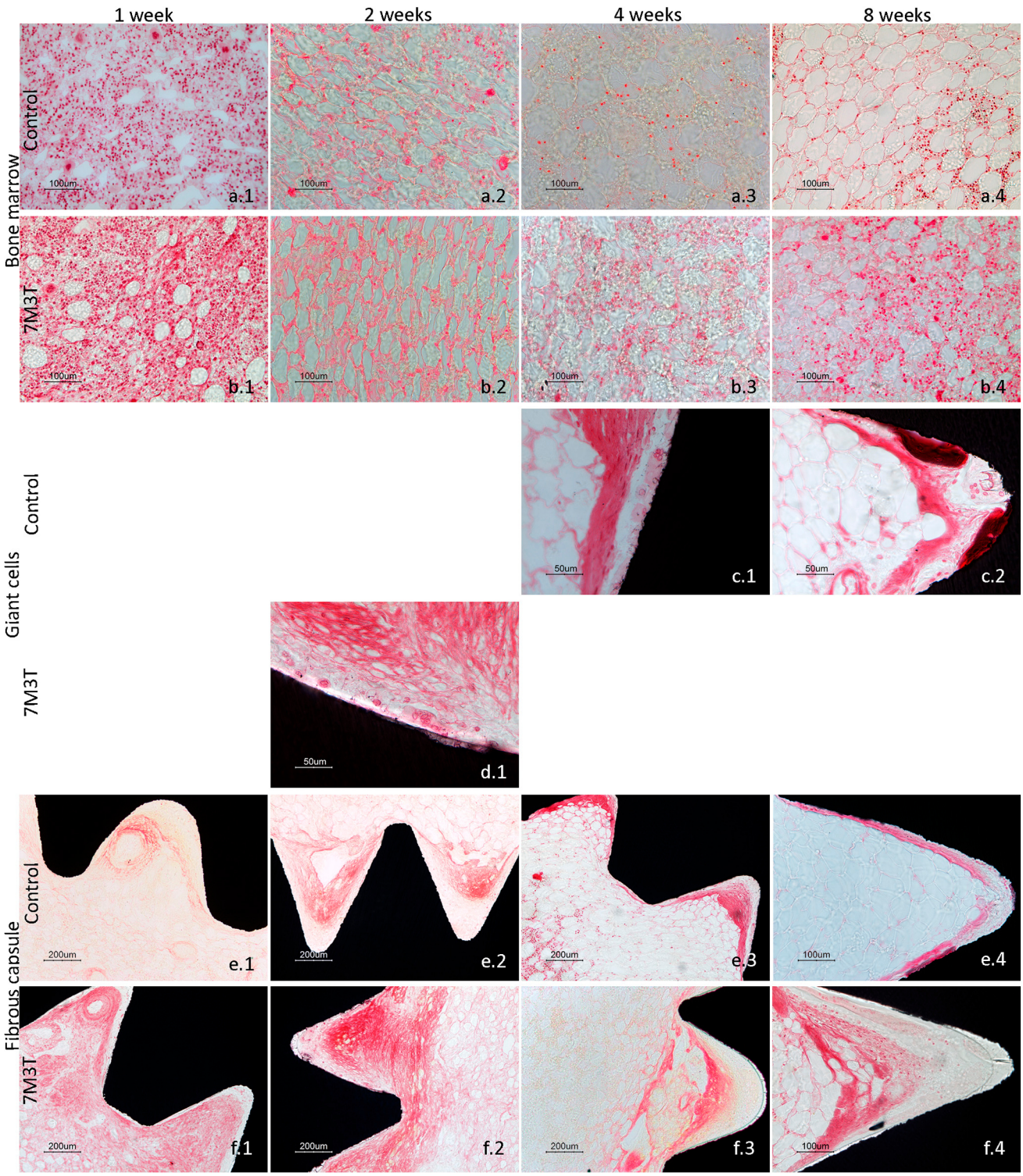

Fig. 4 Biocompatibility analysis after 1, 2, 4, and 8 weeks of implantation: bone marrow state after implantation of control (**a.1**–**a.4**) and 7M:3T coating (**b.1**, **b.2**) samples; Presence of giant cells in control (**c.1**, **c.2**) and 7M:3T coating (**d.1**) samples; Presence of fibrous capsule and its evolution in time for control (**e.1**–**e.4**) and 7M:3T coating (**f.1**–**f.4**) samples

comparing images 5.a.2 and 5.a.3 of control with images 5.b.2 and 5.b.3 of coating. At 4 weeks of implantation, the sol–gel coating did not degrade at all and the direct bone contact with the implant surface cannot still be seen (Fig. 5b.3). However, after 8 weeks of implantation the coating disappeared even at the bottom of the valleys

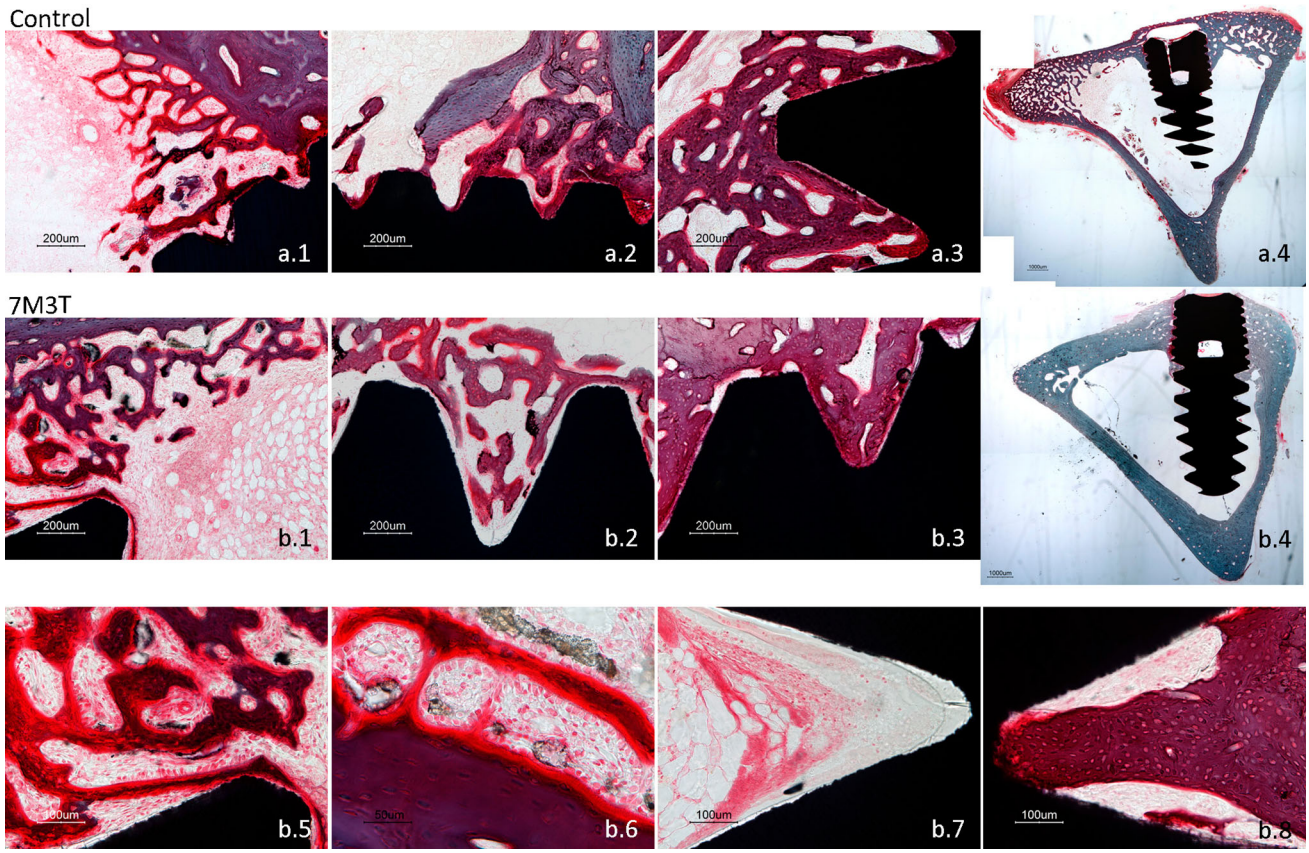

Fig. 5 New bone formation: bone spicules formation for control (**a** series) and 7M:3T coated samples (**b** series) after 1 (**a.1**, **b.1**) and 2 weeks of implantation (**a.2**, **b.2**); spicules form mature trabeculae after 4 weeks (**a.3**, **b.3**); osseointegration reached after 8 weeks of implantation (**a.4**, **b.4**); osteoblast detail forming osteoid in new bone spicules around the site of 7M:3T implantation after 1 week (**b.5**, **b.6**); complete degradation of 7M:3T coating after 8 weeks of implantation and bone in contact with the implant surface in the zone previously occupied by the coating (**b.7**, **b.8**)

between implant threads. The area previously occupied by the coating (Fig. 5b.7) at the bottom of the valley was filled with new bone after 8 weeks (Fig. 5b.8), allowing the direct contact between the new bone and the titanium implant. Fibrous tissue formed in some cases after implant insertion was transformed in new bone with time in every cases.

4 Discussion

As previously mentioned, the results of various studies have shown that silicon has a biological relevance in natural metabolic processes of bone due to its influence in:

- gene up regulation of osteoblastic cells inducing the formation of procollagen and mineralization [29].
- changing the signalling route OPG/RANKL, which is responsible for modelling the bone resorption, inhibiting the maturation and activation of the osteoclast [30].

Hence, silicon improves the osteoblasts activity [31], and the cellular proliferation and differentiation [32]. Other authors [18] proved that when silicon is dissolved as $Si(OH)_4$, it intervenes in the formation of bone tissue by activating the production of type I collagen. In addition, as it is known, the Si–OH groups confer bioactivity due to the fact that they react with the biologic fluid and induce the formation of the apatite layer [33]. Thus, the products of the degradation of the formulated coatings are presumed to be osteoinductive because they can participate in the nucleation of the apatite and in the first stages of the calcification, favouring collagen synthesis and the differentiation of the osteoblasts.

Towards this end, the present research aimed to test, on the one hand, the hypothesis that sol–gel coatings influence the cell osteogenic differentiation by an in vitro biological assessment with AMSCs, and on the other hand, the performance of these coatings in comparison with commercial dental implants when they are placed in tibia bone, in order to test their biocompatibility and the local effect of silicon released.

In a previous research [20], we studied the hydrophilic/hydrophobic characteristics of the coatings, because this property influences on the foreign body response. The

obtained results confirmed that by adding TEOS, a higher hydrophilicity and an increasing coating degradability are achieved, observing that coatings with 30 % TEOS show a contact angle of 70° (this value is in the range of values considered optimum for protein and cell interaction [34, 35]), and degrade more rapidly than the others.

On the current research, the study of released silicon reveals a similar behaviour for the various MTMOS:TEOS coatings, where the incorporation of TEOS increases this release, which could influence the enhancement of the bone formation [36].

In vitro tests confirmed the importance of such chemical-physical characteristics of the coatings. Some research groups have reported that high amount of Si released may decrease the cell viability [37]. Gough et al. [38] set this limit in 8.2 mM Si released, from that concentration on, cell apoptosis occurred. Owing to the evolution of proliferation throughout the culture time, no one of the developed materials released cytotoxic amounts of Si to the medium. In this research an improvement in the cellular adhesion and consequently in the proliferation was obtained by addition of a 30 % TEOS to MTMOS.

Additionally, analysing the differentiation and mineralisation data, it is concluded that the osteogenic ability of the AMSCs increases with an augmentative TEOS content. Same behaviour was observed by Shirosaki et al. [8] when studying the differentiation of MG63 cells on different hybrid membranes containing TEOS. In that work, they concluded that Si ions might directly affect cell differentiation by improving the ALP activity. Therefore, in the case of the higher mineralization observed when the content of TEOS is 30 %, the main reason could be the effect of the silicon compounds released in the medium during the time of culture.

Consequently, taking into account all the previous results from the MTMOS:TEOS coating series, the 7M:3T coating was selected as the most adequate one to promote the osseointegration process, since in this coating is where the highest proliferation and differentiation of the AMSCs is observed.

The in vivo study allowed a more definitive observation of the silicon release effect. First, the results obtained with the coated and uncoated implants proved that both the coating material and the implant itself are biocompatible. We observe an expected evolution of the bone marrow after the implantation process. Thus, the bone marrow condition allowed assessing the foreign body response. At first, bone marrow appeared slightly altered as a consequence of the implantation in both cases, but it recovered a normal appearance as time progressed, either the coated implant or the uncoated one showed a normal behaviour. Moreover, the presence of giant cells in both cases, was the expected for a normal foreign body response. Nevertheless, slightly differences were observed from the new bone formation point of view. Figure 5 demonstrate that in spite of the big similarities between control and coated implants in the process of new bone formation, some differences merit special attention. On the coated surfaces, the number of osteoprogenitor cells that develop into well-aligned osteoblasts is very noticeable from the first days of the implantation. As the next step to form the osteoid is depending on the type I collagen, and the silicon participates in that process, we attribute the rapid formation of bone spicules to the presence of the polysiloxane coating. Furthermore, since when osteoblasts line up along the surface of the spicule they secrete more osteoid, the more rapid increase of the size of the trabeculae observed is attributed to the release of silicon too.

5 Conclusions

A sol–gel Si based coating with the ability of releasing silicon compounds to the medium has been developed. The release kinetic can be controlled by the TEOS addition to the composition. In vitro studies showed the biggest proliferation and mineralization for 7M:3T coating. In vivo studies of dental implants coated with 7M:3T material showed that the silicon released seems to improve the bone regeneration ability of the coating according to the earlier formation of new bone spicules. In addition, the studied foreign body response parameters such as the bone marrow state, the presence of giant cells and the evolution of the fibrous capsule, proved the biocompatibility of developed materials and their potential use in dental therapy.

Acknowledgments The authors wish to thank Dr. Vicente Ferrer from the University of Murcia for the surgery of the rabbits, and to Dr. Antonio López Bravo for his precious help in the histological study. The research Project has been supported by the Ministerio de Economía y Competitividad (Govern of Spain) and FEDER through Subprograma INNPACTO: BACDENT(IPT-2012-0218-090000), and University of the Basque Country (UFI 11/56; IT 611-13). The Basque Government awarded with a Grant to María Martínez.

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