

THE PROCESS OF POROUS TANTALUM IMPLANTS OSSEOUS INTEGRATION A REVIEW

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ABSTRACT

Porous tantalum is a biomaterial that was recently introduced in orthopaedics in order to overcome problems of the past related to implant loosening. Its use has led to very good results, especially in difficult cases where severe bone defect is present, as it is found to have osteoconductive and possibly, osteoinductive properties. So, it is of great interest to shed light to the mechanisms through which this material leads to new bone formation after being implanted. For this reason, a review of the current literature was undertaken. Porous tantalum is, biologically, relatively inert, meaning that its bonding capacity to the bone is restricted. In order to overcome this obstacle, it undergoes thermal processing in alkaline environment. This process leads to extensive hydroxyapatite formation on its surface and thus, to better integration of porous tantalum implants. Apart from this, new bone tissue formation occurs inside the pores of porous tantalum after its implantation and this new bone retains the characteristics of normal bone, i.e., bone remodeling and Haversian systems formation. This finding is enhanced by the observation that porous tantalum is an appropriate substrate for osteoblast adherence, proliferation and differentiation. Furthermore, the finding that osteoblasts derived from old women (>60 years old) and cultivated on porous tantalum may grow faster than osteoblasts taken from younger women (<45 years old) and cultivated on other substrates, can partially explain porous tantalum good performance in cases of patients with severe bone defects. In conclusion, porous tantalum chemical and mechanical properties are those that, probably, define the already noticed good performance of this material. However, further research is needed to totally clarify the mechanisms through which they contribute to that.

Keywords: Porous Tantalum, Osseous Integration, Bone Ingrowth, Osteoconductive, Osteoblast, Scaffold

1. INTRODUCTION

Porous tantalum is a relatively new biomaterial in orthopaedics, used in domains such as hip and knee arthroplasty, hip osteonecrosis surgery and spine surgery. It consists of a carbon scaffold on which pure tantalum is deposited. Porous tantalum possesses some unique mechanical properties, mainly due to its high porosity. It has a low modulus of elasticity, close to that of subchondral and cancellous bone, leading to better load transfer and minimized stress shielding phenomenon. Its coefficient of friction is among the highest when talking about biomaterials, allowing for sufficient primary stabilization of implants, even

without screw fixation. These parameters are thought to contribute to the good and sometimes excellent, clinical results achieved with the use of porous tantalum. However, it is more interesting and probably, of even greater importance, to assess the processes taking place at the bone-porous tantalum interface, in terms of hydroxyapatite and bone tissue formation, not only on the surface, but also inside the biomaterial. Furthermore, it is equally important to examine the role of porous tantalum as a substrate for osteoblast proliferation and differentiation, as the procedure of porous tantalum integration takes place through new bone tissue formation and osteoblasts are the key cells for this process.

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1.1. Porous Tantalum Thermal Processing in Alkaline Environment

Porous tantalum is biologically relatively inert (Levine *et al.*, 2006), which means that its bonding capacity to the bone is restricted. This kind of biologic activity is necessary when talking about a metal, in order to achieve an enhanced attachment to the surrounding soft tissues and also, to the underlying bone-especially when bone defect is present. For this reason, the development of biologically active tantalum is of great importance. Previous studies testing the formation of biologically active ceramics concluded that the most crucial point in order to achieve bone integration of the implants- is the formation of a biologically active hydroxyapatite layer on their surface after being implanted (Kotani *et al.*, 1991). This can be achieved by hydroxyapatite plasma-spraying (Kitsugi *et al.*, 1996). When this procedure takes place, the temperature of the hydroxyapatite powder may reach the value of 10000°C, which leads to its partial melting and degradation. This results to the formation of a coating of different structure, if compared to hydroxyapatite. As a consequence, this coating may detach from the underlying bone (Geesink *et al.*, 1995). In order to overcome these difficulties, a different procedure is needed for the formation of hydroxyapatite coating. This is achieved through the use of porous tantalum implants that have undergone thermal processing in an alkaline environment.

In accordance to this, an effort was made to form hydroxyapatite coating on porous tantalum surface. Through trials, it was observed that hydroxyapatite- like coating can be formed on amorphous tantalite hydrogel surface when it is prepared in a 0.2-0.5 M NaOH solution (Miyazaki *et al.*, 2000; 2002). This layer gets stabilized after thermal treatment at 300°C and becomes a stable layer of amorphous tantalum salt (Kato *et al.*, 2000; Kokubo, 2004). When impregnated to SBF (Simulated Body Fluid) - consisting of an acellular fluid with ion concentration similar to that of human serum- the substrate that has undergone treatment in an alkaline environment shows hydroxyapatite formation within one week (Kokubo *et al.*, 1990; Kim *et al.*, 1996). By the time sites of hydroxyapatite formation appear, they begin to absorb calcium and phosphate ions from the surrounding fluid, they grow spontaneously and they lead to the formation of chemical bonding between the bone and the implant. Titanium seems to have the same property, as hydroxyapatite layer may form on its surface in SBF environment. To the contrary, this is not the case for stainless steel and Cr- Co alloys (Kim *et al.*, 1996).

In another trial (Kato *et al.*, 2000), the bond between the bone and tantalum plates that had been thermally treated in alkaline environment was examined, in terms of mechanical and histological properties. The findings were compared to the findings of tantalum plates that had not undergone such treatment. In the first case, a bond between the plates and the bone could be detected within 16 weeks, whereas no such bond could be identified in the case of non-treated plates. Histologically, also, it could be seen that, again in the first case, there was direct contact between the plate and the bone. To the contrary, in the second case, fibrous tissue had developed in this interface.

The different reaction of the bone against pretreated porous tantalum, compared to non-pretreated, was explained later (Miyazaki *et al.*, 2002), in terms of biochemistry. In this study, it was found that amorphous sodium tantalate forms on pretreated plates' surface and pretreatment through the already presented way is a prerequisite for this formation to happen. The formation of amorphous sodium tantalate rapidly leads to the formation of Ta-OH groups on its surface, through the exchange of Na⁺ ions to H₃O⁺ ions. It should be mentioned that the pretreatment of porous tantalum in a more alkaline environment (5.0 M NaOH) did not lead to hydroxyapatite formation on its surface, as the formation of Ta-OH groups could not be achieved, due to the high Na⁺ concentrations that slowed down the already presented cation exchange (Miyazaki *et al.*, 2000). The presence of Ta-OH groups is of great importance, as they interconnect to Ca⁺⁺ ions and subsequently, form a type of calcium tantalate, which reacts to phosphate anions that are present at the SBF environment. Finally, larger amounts of calcium and phosphate ions are absorbed, leading to hydroxyapatite formation (Miyazaki *et al.*, 2002). Hydroxyapatite cores form at first, leading to the accumulation of calcium and phosphate and ending to the formation of a hydroxyapatite layer. This has also been shown in earlier studies (Ohtsuki *et al.*, 1992). Apart from Ta-OH groups, it is known that Si-OH and Ti-OH groups also induce the formation of hydroxyapatite, through their transformation to calcium silicate and calcium titanate respectively (Takadama *et al.*, 2000; Nishiquchi *et al.*, 2001). It has been noticed in the past that these groups are negatively charged in SBF environment (Parks, 1965; Li *et al.*, 1994; Kosmulski, 1997). It is probably the negative charge that leads to the selective calcium absorption and subsequently, to hydroxyapatite formation.

But apart from porous tantalum implants that have been treated in alkaline environment in order to induce hydroxyapatite formation on their surface after their implantation, it is equally interesting to assess the osseointegration of porous tantalum implants that are already covered by hydroxyapatite. In such a trial (Barrere *et al.*, 2003a), porous tantalum cylinders were used. On their surface, Bone-like Carbonated Apatite (BCA) was formed, after being treated in a SBF environment. The thickness of BCA was 30 μm . These cylinders were then implanted in sheep's femoral bones and were removed after 6, 12 or 24 weeks. In all cases, the BCA covered implants outperformed the non-covered ones in terms of bone integration. The bone showed an accelerated biologic response to the BCA covered implants, underlining the biologically active and osteoconductive nature of BCA coating. This study concluded that BCA covered porous tantalum implants lead to a faster and superior development of bone tissue when compared to non-covered ones. This results to a more stable fixation of the implant to the bone, something favorable in the case of implants that undergo weight-bearing.

A more recent study (Barrere *et al.*, 2003b), again from the same center, examined the use of Octa-Calcium Phosphate (OCP) as a coating of porous tantalum implants. The findings of this study showed that OCP has a greater potential in terms of bone integration in comparison to BCA. Apart from that, the most impressive finding was that OCP might possess osteoinductive properties when covering porous surfaces, as it was found that it induced bone formation even when the implants were placed intramuscularly. This fact could be explained if considering OCP's rough surface, its slower resorption rate compared to BCA and probably, the presence of Bone Morphogenetic Proteins (BMPs) inside calcium phosphate crystals (Yuan, 2001; Ripamonti, 1996; Yuan *et al.*, 1998). Further amelioration of calcium phosphate coatings may lead to an even better microscopic structure and an even slower resorption rate, allowing a more successful *in vivo* osseointegration of porous tantalum implants.

1.2. Bone Tissue Formation

As it has been found in the past (Bobyne *et al.*, 1980), concerning bone formation on Cr-Co alloy implants and its mechanical properties, the ideal pore diameter is 50-400 μm . When tested, these implants had a maximum strength of 17MPa, 8 weeks after their implantation. The same investigator, in following studies, assessed the bone

formation inside structures of porous tantalum. Porous tantalum cylinders (Bobyne *et al.*, 1999a) and acetabular implants (Bobyne *et al.*, 1999b) were used. The findings were highly supportive for the use of porous tantalum.

In the case of the first study, porous tantalum cylinders with a size of 5x10 mm were used. They were implanted to dog bones, crossing both bone cortices. Implants porosity was 75-80% and pore diameter was 430 and 650 μm . Cylinders with 430 μm pore diameter were assessed at week 4, 16 and 52 postoperatively, whereas cylinders with 650 μm were examined at week 2, 3, 4, 16 and 52. The samples were histologically examined. Also, mechanical testing was performed at week 4 and 16 in the case of implants with 430 μm pore diameter. Bone tissue formation inside the implants is shown at **Table 1**. At week 4, bone tissue occupied 52.9% of pore volume of the implants with 650 μm pore diameter. The same value for implants with 430 μm pore diameter was 41.5%. The difference between the two groups was considered as statistically significant. This difference remained statistically significant at week 16, as the values were 69.2 and 63.1% respectively. To the contrary, at week 52, the difference was again statistically significant, but this time in favor of the group of the implants with a smaller pore size, as the values were 79.7% for this group and 70.6% for the other one. However, the practical and clinical significance of these differences is doubtful. The extensive bone formation in both groups is the most important finding and this should be kept in mind. So, if we consider the superior mechanical properties of porous tantalum with a smaller pore diameter, than this form of porous tantalum is, probably, more appropriate to use in the construction of implants.

The pattern of bone tissue formation inside the pores of porous tantalum was clarified through examination of specimens under electron microscopy. At week 2, bone was formed mainly at the drilling site and intramedullary. Although bone ingrowth was limited, there was bone formation close to porous tantalum trabeculae. At week 3, bone ingrowth could be detected, whereas, at week 4, bone tissue formation throughout the whole implant was a common finding. Finally, at week 16 and week 52, bone ingrowth was really dense and that was also the point for the bone-implant interface. Another interesting finding was the formation of Haversian systems and the activation of the procedure of bone remodeling inside the pores.

Table 1. Bone ingrowth in porous tantalum cylinders in relation to the time of examination and the value of pore diameter (Bobyne *et al.*, 1999a, modified)

(week)	Bone ingrowth		Confidence interval	
	Time diameter	430 μ m pore diameter	650 μ m pore (CI) 95%	P value
2	-	13.3 (n = 24) (95% CI 10.8 - 15.8)	-	-
3	-	23.0 (n = 24) (95% CI 20.0 - 26.0)	-	-
4	41.5 (n = 12) (95% CI 37.3 - 45.8)	52.9 (n = 23) (95% CI 50.4 - 55.4)	6.9 - 15.9	0.00003
16	63.1 (n = 18) (95% CI 58.2 - 68.0)	69.2 (n = 24) (95% CI 67.0 - 71.5)	1.5 - 10.8	0.01
52	79.7 (n = 24) (95% CI 76.9 ω 82.5)	70.6 (n = 23) (95% CI 68.3 ω 73.0)	-12.9 ω -5.4	0.000008

Mechanical testing revealed that, at week 4, the shear strength of the implant was, at least, 18.5MPa. This is considered as a high value, compared to the shear strength obtained after 4 weeks of implantation for other porous materials. For example, at week 4, the shear strength of Cr-Co alloy was 9.3 MPa in a study under the same investigator (Bobyne *et al.*, 1980), whereas in other studies it varies from 1.2-13.1MPa (Camron *et al.*, 1976). Porous tantalum superior results could better be explained if we consider its higher porosity. Porous tantalum has a porosity of 75-80%, whereas fiber mesh coating has a porosity of 40-50% and porous beads coating just 30-35%. This means that there is more space inside the implant for bone tissue to form, leading to more favorable mechanical properties of the implant in terms of strength and of the time needed to achieve this strength after the implantation. The fast bone ingrowth seems to have major clinical importance, as it accelerates the procedure of implant's stabilization, thus allowing earlier full weight-bearing after surgery with the use of porous tantalum implants.

The same investigator studied, also, the patterns of bone ingrowth inside implants that underwent loading (Bobyne *et al.*, 1999b). He studied a canine model, where he implanted acetabular monoblock prosthesis and observed them for 6 months. The bone-implant interface underwent radiological, histological and electron microscopy examination. The implant's fixation was found to be stable in all cases. In all cases bone ingrowth was observed. Bone ingrowth varied from 0.2-2 mm which is the maximum of space left for bone ingrowth, as the rest of the implant is occupied by polyethylene. These results are comparable to the ones of studies examining titanium fiber mesh (Pidhorz *et al.*, 1993). Bone ingrowth was more intense and deeper at the periphery of the implant, probably because of the elliptical shape of the implant and the load concentration at the area. In average, 16.8% of the pores were occupied by bone tissue. The same value for the periphery of the implant was 25.1%. These findings are comparable to those of older studies (Jasty *et al.*, 1993), which studied the bone penetration inside prosthesis with a titanium

fiber mesh coating or with a Cr-Co alloy porous beads coating. The values for these structures were 21.5 and 13.4% respectively. Apart from that, porous tantalum value is very close to cancellous bone density, which is 17.7%. So the combination of porous tantalum high porosity with the good bone ingrowth that it shows is probably the reason for its superior mechanical strength.

Another serious finding was the filling of the gaps that were initially observed in some cases- as a result of inadequate reaming- between the implant and the acetabulum. The gaps were filled by new bone formation. This has been observed after the implantation of monoblock acetabular prosthesis in humans too (Macheras *et al.*, 2006). It has been also observed in some cases of prosthesis with a titanium fiber mesh coating (Jasty *et al.*, 1993), but to a lesser extend.

Potentially clinically significant was also the observation that fibrous tissue had formed inside the pores in areas that were not occupied by bone. This tissue might serve as a mechanical barrier that blocks debris from moving to the bone- implant interface.

What needs to be further clarified is the factor that plays the key role and leads to this extensive bone ingrowth inside porous tantalum implants. *In vitro* and *in vivo* studies have shown that bone formation is enhanced at the presence of rough, sandblasting- type, surfaces (Brunette, 1988; Goldberg *et al.*, 1995; Hacking *et al.*, 1999; Kieswetter *et al.*, 1996a). As it is known, porous tantalum surface presents such a pattern and leads to extensive bone formation. So, probably, the role of its rough surface should be considered too.

1.3. Osteoblast Differentiation and Functionality

What has been already presented is the bone ingrowth inside porous tantalum. This is a common finding among many studies. What has not been studied that much and is of great interest, is the presence of osteoblasts inside the pores and furthermore, their potential for differentiation and their functionality.

When the first such study was conducted (Findlay *et al.*, 2004), the surface of solid tantalum was compared to a

surface of tantalum disposed through the CVD method- the method used in the fabrication of porous tantalum. These surfaces were also compared to the surfaces of the most common orthopedic metals and to the surface of Tissue Culture Plastic (TCP). This study concluded that tantalum is a suitable substrate for the proliferation and differentiation of osteoblasts. This fact is supported by the findings concerning the primary adhesion of osteoblasts to tantalum and their morphology after their adhesion. These findings do not differ from those of TCP, which is a benchmark in *in vivo* osteoblast study. Apart from that, the proliferation rate of the cells on tantalum surface was comparable to those observed for the other substrates. Expression of genes related to osteoblast function was also at the same levels for all substrates. What was studied is the expression of transcription factor CBFA1, of the extracellular proteins COL-1 and OCN, of the cytokines IL-11, TNF- α and RANKL and of OPG. No statistically significant difference was found at the expression of these genes among the different substrates. The mineralization rate was found to be faster in the cases of solid and CVD tantalum, but the difference was not considered as statistically significant.

What is different in this study, compared to previous studies, is that the surface morphology of the substrates did not affect the function of osteoblasts. This could be partly expected, as, with the exception of CVD tantalum, all the surfaces were relatively smooth. As it has been already noticed, previous *in vivo* studies (Kieswetter *et al.*, 1996b; Bigerelle *et al.*, 2002; Keller, 1998; Schwartz *et al.*, 2001) have shown that osteoblasts get more activated when they grow on rough surfaces. Probably, this could be explained if we keep in mind the borderline roughness of CVD tantalum surface, which means that it might not affect the proliferation and functionality of osteoblasts.

It should be mentioned, though, that this study examined the proliferation and functionality of osteoblasts on surfaces. In a following study (Welldon *et al.*, 2008), the same investigators examined the same parameters for the osteoblasts, but, this time, in three dimensions. Concerning porous tantalum, the presence of osteoblasts could be detected everywhere inside the pores, independently of the depth of the area examined. At day 3, already, the cells seemed to adhere to trabeculae surface, after a few mitosis rounds. The mitotic process continued and reached a peak by day 14 and day 21.

What was further examined is the degree of osteoblasts' differentiation. The expression of STRO-1 and alkaline phosphatase was measured, given that the expression of STRO-1 gets lower as the procedure of osteoblasts maturation progresses, whereas the expression of alkaline phosphatase gets higher (Gronthos *et al.*, 1999).

It was concluded that the differentiation of osteoblasts inside the pores of porous tantalum took place faster, in comparison to other substrates and this could be seen even by day 14. This means that, probably, the presence of porous tantalum promotes osteoblasts differentiation.

One more finding enhancing the idea that the differentiation of osteoblasts is accelerated when they grow on a porous tantalum surface, was the level of expression of genes associated to the function of osteoblasts. At day 14, collagen type 1 (COL-1) and Bone Sialoprotein (BSP-1) gene expression was lower for osteoblasts cultivated on porous tantalum, compared to other substrates. The reduced expression of both genes reflects the reduction occurring during the procedure of osteoblasts differentiation (Stein and Lian, 1996), first for COL-1 and then for BSP-1, ending to the loss of expression of both of them by the time of maturation of osteoblasts (Aubin *et al.*, 1995).

Finally, it should be mentioned that, at the same study (Welldon *et al.*, 2008), the extension of *in vitro* mineralization of the substrates was examined. This was done at week 6 and the findings supported the idea that porous tantalum is, at least, the same effective as Tissue Culture Plastic (TCP) in inducing mineralization. What could not be clarified is the underlying reason that led to these results, as they could be the consequence of the fast proliferation of osteoblasts, or of their good functionality.

These findings are in accordance to the findings of a newer study (Justesen *et al.*, 2009). In this study the morphology of osteoblasts was examined after being cultivated on different tantalum surfaces, with different topography. It was found that, the deeper the cells of the substrate surface were, the more elongated osteoblasts got. In previous studies (Schwartz *et al.*, 2001; Dalby *et al.*, 2003; Rice *et al.*, 2003; Wojciak-Stothard *et al.*, 1996) it was shown that the more elongated the shape of osteoblasts is getting, the more differentiated and more active these cells are. This means that, these substrates can serve as scaffolds, inducing bone formation inside their pores, no matter if they are implanted to the bone or not. Thus, they can be used not only as implants, but also as grafts.

1.4. Differentiation and Functionality of Osteoblasts Derived from Elderly Women

Orthopaedic implants are widely used in osteoporotic patients and also in difficult cases of patients with insufficient bone stock. Good results have been achieved by the use of porous tantalum implants not only in osteoporotic patients, but also in cases of patients with poor bone stock (Nelson *et al.*, 2003), such as patients

suffering from femoral head osteonecrosis (Shuler *et al.*, 2007) and patients that have undergone radiotherapy (Rose *et al.*, 2006). So, it is of great interest to compare osteoblasts taken from elderly patients with osteoblasts from younger patients in terms of proliferation and retention of their functionality inside porous tantalum.

For this reason, a study was undertaken (Sagomyants *et al.*, 2011). Osteoblasts originating from young women (<45 years old) were compared to osteoblasts from elderly women (>60 years old). As a substrate for cell culture, porous tantalum, titanium fibre mesh and Tissue Culture Plastic (TCP) were used. A first finding of this study was the fact that the adherence, the new bone matrix formation, the mineralization and the rate of proliferation observed for the cells derived from old women were lower compared to the same parameters of the cells of young patients. These findings are in accordance to previous ones, including the observation that there is over expression of genes related to cellular apoptosis in elderly patients (Zhou *et al.*, 2008).

But, the most important finding of this study is the fact that porous tantalum induces new bone formation more extensively than titanium fiber mesh or tissue culture plastic, when talking about cultures of osteoblasts descending from elderly women. This could be mainly attributed to the fast cellular proliferation that takes place on the surface of porous tantalum. It is really interesting that osteoblast proliferation and new bone formation in cultures of cells derived from elderly women, when porous tantalum is present, is at least similar to that observed in cultures of cells from young women on the other substrates.

More specifically, the adherence of osteoblasts on porous tantalum was higher than that on the other substrates. This finding is in contrast to what has been already said (Welldon *et al.*, 2008). However, the different age and sex group of patients that donated the cells and the different culture environment used could explain this difference. Porous tantalum better performance could be explained in terms of differences in the surface topography of the examined materials. Apart from this, older studies (Kieswetter *et al.*, 1996a) have shown that osteoblast adherence depends not only on the microscopic texture of the surface of the material, but, also, on its physicochemical properties and on its surface energy. So, the rougher the surface is, the stronger the osteoblast adherence gets (Anselme *et al.*, 2005; Lincks *et al.*, 1998). This is, also, the fact for cellular proliferation. It seems that these processes are

mediated by specific integrins (Gronowicz *et al.*, 1996; Sinha *et al.*, 1996) and it is hypothesized that porous tantalum microstructure induces osteoblast adherence through the production of these integrins. Even more, porous tantalum microstructure is of especially irregular pattern. Such surfaces present with a higher surface energy, something that makes them friendlier to new bone formation (Kieswetter *et al.*, 1996b) and of course, the rougher the material is, the bigger its surface becomes, offering a wider area for the osteoblasts to adhere.

Apart from this, it is of great importance to mention the impact of porous tantalum on the proliferation rate of osteoblasts of both age groups (**Fig. 1**).

The proliferation rate that was observed on porous tantalum, for cells taken from young women, was 4 times higher compared to titanium fiber mesh and 12 times higher when compared to Tissue Culture Plastic (TCP). The findings for osteoblasts taken from old women were even more impressive, as the proliferation rate was 6 and 16 times higher respectively. These observations cannot be explained only in terms of increased adherence, as adherence is just 25-30% higher for porous tantalum compared to the other substrates. So it can be hypothesized that porous tantalum possesses inherent physicochemical properties that have an anabolic effect on osteoblast proliferation.

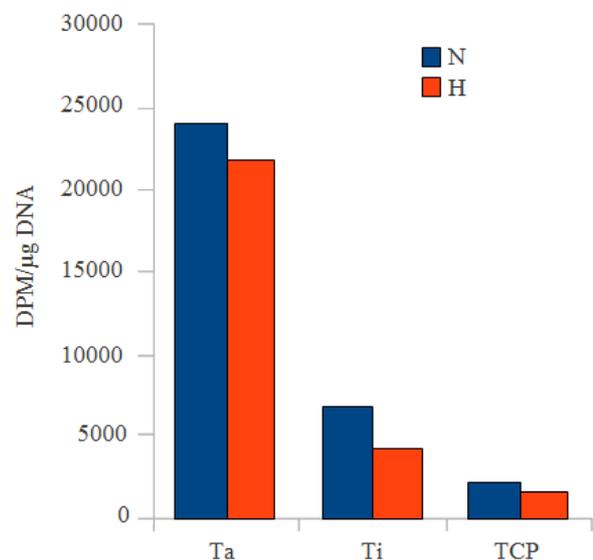


Fig. 1. Osteoblast proliferation rate in different materials cultures. (DPM: Disintegrations Per Minute). (Sagomyants *et al.*, 2011, modified)

It is also interesting that porous tantalum had a different impact on the mineralization rate of bone matrix, depending on the age group examined. Whereas no significant difference was observed at week 3 between porous tantalum and titanium fiber mesh in the cultures of cells of young women, the difference was really significant among the cultures of osteoblasts of elderly patients, in favor of porous tantalum. This is an evidence for porous tantalum impact on cellular differentiation. Apart from this, one more fact that can serve as evidence is the expression of certain genes. At the same study (Sagomyants *et al.*, 2011), it was found that alkaline phosphatase and osteocalcin gene expression on porous tantalum was at the same levels for both age groups. This was not the case for titanium fiber mesh, as the expression of these genes was higher among the cultures of cells from young women. Given the fact that these proteins are synthesized during osteoblast differentiation, it can be judged that osteoblasts present with a similar differentiation potential, no matter the age group examined, when growing on porous tantalum, which is not true for other materials, such as titanium fiber mesh.

2. CONCLUSION

Even though these findings are really encouraging, there is still the question on the way porous tantalum induces osteoblast adherence, proliferation and mineralization in general and more importantly, in cases of elderly women. In previous studies, it has been shown that topographic features of titanium and subsequently, osteoblast biologic response to titanium can be seriously modified through small changes in titanium chemical composition (Anselme *et al.*, 2005). On the other hand even though the findings of studies examining Tritanium (porous titanium with a porosity similar to that of porous tantalum) where encouraging, too, they were inferior to those observed with the use of porous tantalum (Frenkel *et al.*, 2004; Ramappa *et al.*, 2009). Consequently, it is speculated that both chemical and topographic porous tantalum properties contribute to the appearance of its special features. However, further research is required in order to shed light to the underlying mechanism that promotes this process, as porous tantalum is a really promising metal for the treatment of cases where bone defect is present.

2.1. Author's Contributions

All authors equally contributed in this work.

2.2. Ethics

This article is original and contains unpublished material. The corresponding author confirms that all of the other authors have read and approved the manuscript and no ethical issues involved.

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