

# Osseous integration in porous tantalum implants

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## ABSTRACT

Porous tantalum is a biomaterial that was recently introduced in orthopedics in order to overcome problems related to implant loosening. It is found to have osteoconductive, and possibly, osteoinductive properties hence useful in difficult cases with severe bone defects. So, it is of great interest to shed light on the mechanisms through which this material leads to new bone formation, after being implanted. Porous tantalum is biologically relatively inert, with restricted bonding capacity to the bone is restricted. In order to overcome this obstacle, it undergoes thermal processing in an 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 the porous tantalum after its implantation and this new bone retains the characteristics of the normal bone, that is, 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's good performance in cases of patients with severe bone defects. In conclusion, porous tantalum's 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.

**Key words:** Bone ingrowth, osseous integration, osteoblast, osteoconductive, porous tantalum, scaffold

## INTRODUCTION

Porous tantalum is a relatively new biomaterial in orthopedics, used in domains such as hip and knee arthroplasty, hip osteonecrosis surgery, and spine surgery.<sup>1</sup> It consists of a carbon scaffold on which pure tantalum is deposited.<sup>2,3</sup> Porous tantalum possesses some unique mechanical properties,<sup>4,6</sup> 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 a minimized stress shielding phenomenon.<sup>7,8</sup> Its coefficient of friction is among the highest when talking about biomaterials,<sup>9</sup> 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. The existing knowledge on these, not well-elucidated processes, is presented here.

## POROUS TANTALUM THERMAL PROCESSING IN ALKALINE ENVIRONMENT

Porous tantalum is biologically relatively inert,<sup>6</sup> which means that its bonding capacity to the bone is restricted. This kind of biological 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

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– is the formation of a biologically active hydroxyapatite layer on their surface, after being implanted.<sup>10</sup> This can be achieved by hydroxyapatite plasma-spraying.<sup>11</sup> 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 in the formation of a coating of a different structure, if compared to hydroxyapatite. As a consequence, this coating may detach from the underlying bone.<sup>12</sup> 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 a hydroxyapatite coating on porous tantalum surface. Through trials, it was observed that hydroxyapatite like coating can be formed on an amorphous tantalite hydrogel surface when it is prepared in a 0.2–0.5 M NaOH solution.<sup>4,13</sup> This layer gets stabilized after thermal treatment at 300°C and becomes a stable layer of amorphous tantalum salt.<sup>14,15</sup> 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.<sup>16,17</sup> 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 the hydroxyapatite layer may form on its surface in the SBF environment. On the contrary, this is not the case with stainless steel and Cr–Co alloys.<sup>17</sup>

In another trial,<sup>16</sup> 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 with the findings of the 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 a direct contact between the plate and the bone. On the contrary, in the second case, fibrous tissue had developed on this interface.

The different reaction of the bone against pretreated porous tantalum, compared to nonpretreated, is explained later,<sup>15</sup> in terms of biochemistry. In this study, it was found that amorphous sodium tantalate forms on the pretreated plates' surface, and pretreatment in the already presented manner 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<sup>+</sup> ions and H<sub>3</sub>O<sup>+</sup> ions. It must 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<sup>+</sup> concentrations, which slowed down the already presented cation exchange.<sup>12</sup> The presence of Ta-OH groups is of great importance, as they interconnect with the Ca<sup>++</sup> ions, and subsequently, form a type of calcium tantalate, which reacts with the phosphate anions that are present at the SBF environment. Finally, larger amounts of calcium and phosphate ions are absorbed, leading to hydroxyapatite formation.<sup>4</sup> Hydroxyapatite cores form at first, leading to the accumulation of calcium and phosphate and ending in the formation of a hydroxyapatite layer. This has also been shown in earlier studies.<sup>18</sup> 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.<sup>19,20</sup> It has been noticed in the past that these groups are negatively charged in the SBF environment.<sup>21-23</sup> It is probably the negative charge that leads to selective calcium absorption, and subsequently, to hydroxyapatite formation.

However, apart from the porous tantalum implants that have been treated in an alkaline environment 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,<sup>24</sup> porous tantalum cylinders are used. On their surface, bone-like carbonated apatite (BCA) forms after being treated in an SBF environment. The thickness of the BCA is 30 µm. These cylinders are then implanted in the sheep's femoral bones and are removed after 6, 12, or 24 weeks. In all cases, the BCA-covered implants have outperformed the non-covered ones, in terms of bone integration. The bone has shown an accelerated biological response to the BCA covered implants, underlining the biologically active and osteoconductive nature of the BCA coating. This study has concluded that BCA-covered porous tantalum implants lead to a faster and more superior development of bone tissue, when compared to the non-covered ones. This results in a more stable fixation of the implant to the bone, something favorable in the case of implants that undergo weightbearing.

A more recent study,<sup>25</sup> again from the same center, examined the use of octa-calcium phosphate (OCP) as a coating for porous tantalum implants. The findings of this study showed that OCP had 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 BMPs (Bone Morphogenetic Proteins) inside the calcium phosphate crystals.<sup>26-28</sup> Furthermore, the amelioration of calcium phosphate coatings might lead to an even better microscopic structure and an even slower resorption rate, allowing for a more successful *in vivo* osseointegration of porous tantalum implants.

## BONE TISSUE FORMATION

As it has been found in the past,<sup>29</sup> with regard to bone formation on Cr-Co alloy implants and its mechanical properties, the ideal pore diameter is 50–400  $\mu\text{m}$ . When tested, these implants had a maximum strength of 17 MPa, eight weeks after their implantation. The same investigator, in the following studies, assessed the bone formation inside the structures of porous tantalum. Porous tantalum cylinders<sup>2</sup> and acetabular implants<sup>30</sup> 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 5 × 10 mm were used. They were implanted to dog bones, crossing both bone cortices. Implant porosity was 75–80% and pore diameter was 430  $\mu\text{m}$  and 650  $\mu\text{m}$ . Cylinders with 430  $\mu\text{m}$  pore diameter were assessed at weeks 4, 16, and 52, postoperatively, whereas cylinders with 650  $\mu\text{m}$  were examined at weeks 2, 3, 4, 16, and 52. The samples were histologically examined. Also, mechanical testing was performed at weeks 4 and 16, in the case of implants with 430  $\mu\text{m}$  pore diameter. Bone tissue formation inside the implants is shown in Table 1. At week 4, bone tissue occupied 52.9% of the pore volume of the implants with 650  $\mu\text{m}$  pore diameter. The same value for implants with 430  $\mu\text{m}$  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.

On the contrary, at week 52, the difference was again statistically significant, but this time in favor of the group of 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 the porous tantalum was clarified through examination of the specimens under electron microscopy. At week 2, the bone was formed mainly at the drilling site and intramedullary. Although bone ingrowth was limited, there was bone formation close to the 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. Another interesting finding was the formation of the Haversian systems and the activation of the procedure of bone remodeling inside the pores.

Mechanical testing revealed that, at week 4, the shear strength of the implant was at least, 18.5 MPa. This was 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 the Cr-Co alloy was 9.3 MPa in a study under the same investigator,<sup>29</sup> whereas, in the other studies it varied from 1.2 MPa to 13.1 MPa.<sup>31</sup> Porous tantalum superior results could be better explained if we considered its higher porosity. Porous tantalum had a porosity of 75–80%, whereas, fiber-mesh coating had a porosity of 40–50%, and porous beads coating had just 30–35% porosity. This meant that there was more space inside the implant for bone tissues to form, leading to more favorable mechanical properties of the implant in terms of strength and of the time needed to

**Table 1: Bone ingrowth in porous tantalum cylinders in relation to the time of examination and the value of pore diameter**

Time (Weeks)	Bone ingrowth		Confidence interval (CI) 95%	P value
	430 $\mu\text{m}$ pore diameter	650 $\mu\text{m}$ pore diameter		
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 76.9-82.5)	70.6 (n = 23) (95% CI 68.3-73.0)	-12.9-5.4	0.000008

(Bobyn JD, 1999, modified)

achieve this strength, after the implantation. The fast bone ingrowth seemed to have major clinical importance, as it accelerated the procedure of the implant's stabilization, allowing full weightbearing earlier after surgery, with the use of porous tantalum implants.

The same investigator also studied the patterns of bone ingrowth inside implants that underwent loading.<sup>30</sup> He studied a canine model, where he implanted an acetabular monoblock prosthesis and observed it for six 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. The bone ingrowth varied from 0.2 to 2 mm, which was the maximum amount of space left for bone ingrowth, as the rest of the implant was occupied by polyethylene.<sup>32</sup> These results were comparable to the ones from the studies examining the titanium fiber mesh.<sup>31</sup> The 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. On an 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 were comparable to those of the older studies,<sup>33</sup> which studied the bone penetration inside the 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, the porous tantalum value was very close to cancellous bone density, which was 17.7%. Therefore, a combination of porous tantalum high porosity with good bone ingrowth was probably the reason for its superior mechanical strength.

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

The extensive bone tissue formation inside the porous tantalum implants is confirmed by the findings in two cases,<sup>34,35</sup> wherein, a monoblock porous tantalum acetabular implant was removed, due to recurrent dislocations. In the first case,<sup>34</sup> the implant was removed two years after the first operation. When examined under electron microscopy, the bone tissue was found to penetrate deeply inside the implant, especially at its periphery. No fibrous tissue was detected. These findings were similar to those of the other mentioned case.<sup>35</sup> The only difference in the second case was the fact that bone tissue formation was found to be more extensive at the dome of the implant. An interesting finding in this case was that 90% of the volume of porous

tantalum pores was occupied by newly formed bone tissue, which was much higher compared to the results of the already mentioned experiment using a canine model.<sup>30</sup>

Another serious finding of this study<sup>30</sup> 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 was also observed in some cases of prosthesis with a titanium fiber mesh coating,<sup>33</sup> but to a lesser extent. Apart from this, similar results were obtained after the implantation of monoblock acetabular prosthesis in humans too.<sup>36-41</sup> In a big, prospective, multicentre study,<sup>37</sup> gaps of up to 5 mm were found to heal with new bone formation after 24 weeks. This was also the case in a majority of subchondral cysts. However, the elimination of the gaps could not be attributed to the new bone formation for sure, as migration of the implant could lead to the same result. Another study,<sup>38</sup> using the Ein-Bild-Roentgen Analyse (EBRA) program, proved that gap healing was not associated with acetabular cup migration. However, even though migration was not the case, the question remained as to whether the different radiographic appearances and the absence of gap occurred because of new bone formation, or because of the absorption of subchondral bone, due to stress-shielding, as stresses were concentrated to the well-fixed periphery of the elliptical implant.<sup>36</sup> New bone formation could definitely be confirmed only by a computed tomography (CT) scan of the area. However, a strong indication toward bone formation was the radiological finding of another clinical study.<sup>39</sup> In this study, not only was gap healing observed, but also the formation of trabeculae at the area that was previously occupied by the gap, was evident. Finally, apart from those interesting results of the use of porous tantalum in primary hip arthroplasty, equally good results were also achieved when it was used in cases of congenital high dislocation of the hip, in terms of the absence of serious migration and the absence of new radiolucent lines.<sup>40</sup>

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 in the presence of rough, sandblasting-type, surfaces.<sup>41-44</sup> As is known, a 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.

## 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,<sup>45</sup> the surface of the solid tantalum was compared to the surface of the 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 the 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 an *in vivo* osteoblast study. Apart from that, the proliferation rate of the cells on the tantalum surface is comparable to those observed on other substrates. Expression of genes related to osteoblast function is also at the same level for all substrates. What is studied is the expression of transcription factor CBFA1, of the extracellular proteins COL-1 and OCN, of the cytokines IL-11, TNF- $\alpha$ , and RANKL, and of OPG. No statistically significant difference has been found in the expression of these genes among the different substrates. The mineralization rate is found to be faster in the cases of solid and CVD tantalum, but the difference is not considered as statistically significant.

What is different in this study, compared to previous studies, is that the surface morphology of the substrates does not affect the function of the osteoblasts. This could be partly expected, as, with the exception of CVD tantalum, all the surfaces have been relatively smooth. As it has already been noticed, previous *in vivo* studies<sup>46-49</sup> have shown that osteoblasts get more activated when they grow on rough surfaces. Probably, this can be explained if we keep in mind the borderline roughness of the CVD tantalum surface, which means that it may not affect the proliferation and functionality of the osteoblasts.

It should be mentioned, however, that this study examined the proliferation and functionality of the osteoblasts on the surfaces. In a following study,<sup>50</sup> the same investigators examined the same parameters for the osteoblasts, but this time, in three dimensions. With regard to porous tantalum, the presence of osteoblasts could be detected everywhere inside the pores, independently of the depth of the area examined. On day 3, already, the cells seemed to adhere to the trabeculae surface, after a few mitosis rounds. The mitotic process continued and reached a peak by days 14 and day 21.

What was further examined was the degree of osteoblast differentiation. The expression of STRO-1 and alkaline

phosphatase was measured, given that the expression of STRO-1 became lower as the procedure of osteoblast maturation progressed, whereas, the expression of alkaline phosphatase became higher.<sup>51</sup> 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 probably meant that the presence of porous tantalum promoted osteoblast differentiation.

One more finding, enhancing the idea that the differentiation of osteoblasts was accelerated when they grew on a porous tantalum surface, was the level of expression of the genes associated with the function of osteoblasts. On 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 osteoblast differentiation,<sup>52</sup> first for *COL-1* and then for *BSP-1*, ending in the loss of expression of both of them by the time of maturation of the osteoblasts.<sup>53</sup>

Finally, it should be mentioned that in the same study,<sup>52</sup> the extension of *in vitro* mineralization of the substrates was examined. This was done at week six and the findings supported the idea that porous tantalum was, at least, as effective as the TCP in inducing mineralization. What could not be clarified was 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 were in accordance with the findings of a newer study.<sup>54</sup> In this study the morphology of osteoblasts was examined after being cultivated on different tantalum surfaces, with a different topography. It was found that, the deeper the cells of the substrate surface, the more elongated the osteoblasts got. In previous studies<sup>49,55-57</sup> it was shown that the more elongated the shape of the osteoblasts was getting, the more differentiated and more active these cells were. This meant that these substrates could serve as scaffolds, inducing bone formation inside their pores, no matter whether they were implanted to the bone or not. Thus, they could be used, not only as implants, but also as grafts.

## DIFFERENTIATION AND FUNCTIONALITY OF OSTEOBLASTS DERIVED FROM ELDERLY WOMEN

Orthopedic implants are widely used in osteoporotic patients and also in difficult cases of patients with insufficient bone stock. Good results have been achieved with the use of porous tantalum implants not only in osteoporotic patients, but also in cases of patients with poor bone stock,<sup>58</sup> such as patients suffering from femoral head osteonecrosis<sup>59</sup> and

patients who have undergone radiotherapy.<sup>60</sup> Therefore, 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 the porous tantalum.

For this reason, a study was undertaken.<sup>61</sup> 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 fiber 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 the previous ones, including the observation that there is overexpression of the genes related to cellular apoptosis in elderly patients.<sup>62</sup>

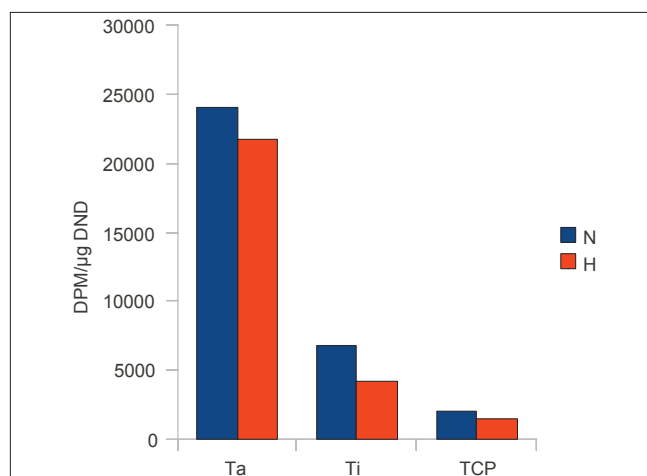
However, the most important finding of this study is the fact that porous tantalum induces new bone formation more extensively than titanium fiber mesh or tissue culture plastic, when talking about cultures of osteoblasts descending from elderly women. This could be mainly attributed to the fast cellular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

More specifically, the adherence of osteoblasts on porous tantalum was higher than that on the other substrates. This finding was in contrast to what was already stated.<sup>51</sup> However, the different age and sex group of patients who donated the cells and the different culture environment used, could explain this difference. Porous tantalum's better performance could be explained in terms of differences in the surface topography of the examined materials. Apart from this, older studies<sup>46</sup> 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 its surface energy. Therefore, the rougher the surface is, the stronger the osteoblast adherence gets.<sup>63,64</sup> This is also the fact for cellular proliferation. It seems that these processes are mediated by specific integrins<sup>65,66</sup> and it is hypothesized that a porous tantalum microstructure induces osteoblast adherence through the production of these integrins. Furthermore, a porous tantalum microstructure is of an especially irregular pattern. Such surfaces present

with a higher surface energy, something that makes them friendlier to new bone formation.<sup>46</sup> Furthermore, 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 [Figure 1]. The proliferation rate that was observed on porous tantalum for cells taken from young women, was four times higher compared to that from the titanium fiber mesh and 12 times higher when compared to that from the tissue culture plastic. The findings for osteoblasts taken from old women were even more impressive, as the proliferation rate was six 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. Thus, it can be hypothesized that porous tantalum possesses inherent physicochemical properties that have an anabolic effect on osteoblast proliferation.

It is also interesting that porous tantalum had a different impact on the mineralization rate of the bone matrix, depending on the age group examined. Although, no significant difference was observed at week 3 between porous tantalum and the titanium fiber mesh in the cultures of cells of young women, the difference was really significant among the cultures of the osteoblasts of elderly patients, in favor of porous tantalum. This is evidence for the impact of porous tantalum on cellular differentiation. Apart from this, one more fact that can serve as evidence is the expression of certain genes. In the same study,<sup>61</sup> 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



**Figure 1:** Bar diagram showing osteoblast proliferation rate in different materials cultures. N stands for women aged < 45 years old, whereas, H for women > 60 years old. DPM: disintegrations per minute. (Sagomyants KB, 2011, modified)

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 what the age group examined may be, when growing on porous tantalum, which is not true for other materials, such as titanium fiber mesh.

## CONCLUSION

The porous tantalum not only has osteoconductive properties, but in this domain, it also out performs the rest of the biomaterials used in orthopedics. 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 the previous studies, it has been shown that the topographic features of titanium, and subsequently, the osteoblast biological response to titanium can be seriously modified through small changes in the titanium chemical composition.<sup>63</sup> On the other hand, even though the findings of studies examining Tritanium (porous titanium with a porosity similar to that of porous tantalum) were also encouraging, they were inferior to those observed with the use of porous tantalum.<sup>67,68</sup> 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 on the underlying mechanism that promotes this process, and it is on these pathways that future studies should focus, as porous tantalum is a truly promising metal for the treatment of cases where bone defect is present.

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