Influence of Orthopedic Implant Structure on Adjacent Bone Density and on Stability

Fidèle Likibi, PhD, Gilles Chabot, MD, Michel Assad, PhD, and Charles-Hilaire Rivard, MD

Abstract

We evaluated the ability of a porous metallic interbody fusion implant made with porous nitinol (PNT) to achieve intervertebral fusion and the capacity of stabilization at the implantation site 3, 6, and 12 months after implantation. Sixteen sheep each received 1 PNT implant and 1 titanium (TiAlV) cage at intervertebral lumbar levels L2–L3 and L4–L5; 3 other sheep were used as untreated controls. The TiAlV cage was used as a control implant.

After animal sacrifice, computed tomography was used to study peri-implant bone mineral density (BMD), and histologic slices were used to evaluate implant osseointegration. BMD around PNT implants was close to physiological (control value) BMD, whereas BMD around TiAlV cages was usually higher (sclerosis) than physiological BMD. Histologic analysis showed better osseointegration with PNT implants than with TiAlV cages. Sclerosis might result from bone acting to stabilize implants in their implantation sites. Compared with PNT implants, TiAlV cages seemed to be unstable in their implantation sites. For PNT implants, osseointegration was successful, and surrounding BMD was close to physiologic BMD.

The intervertebral fusion technique using the artificial implant occupies an important place in the treatment of intervertebral disc pathologies.[1,2] This technique has become popular because of its ability to successfully bridge 2 adjacent vertebrae involving immobilization of the unstable degenerated disc area. The successful fusion allows maintenance of the load-bearing capacity of the spinal column and the disc height.[3] However, this technique has been associated with infection, neurologic complications, and implant migration.[4-6] Currently, several intervertebral fusion implant designs are available, and all are intended to improve the success of interbody fusion.[7,8] Most are at the preclinical stage of development or at the beginning of their feasibility studies.

Our group has developed a porous metallic implant made with porous nitinol (PNT) to aid interbody fusion. PNT has been used in maxillofacial and some orthopedic surgeries in Russia and China for approximately 15 years.[9-11]

PNT is a metallic biomaterial with good biocompatibility, high damping properties, a porous structure, and an elastic modulus close to that of the bone.[12-15] These features might encourage bone growth around and within the implant involving an efficient interbody bridge. Therefore, the PNT interbody fusion implant, which is still at its preclinical stage, might be a promising biomaterial for permanent bone implantation.

In the study reported here, we wanted to determine whether the full cylindrical porous implant could increase the interbody success rate over that achieved with the well-known traditional hollow cylindrical titanium (TiAlV) cage packed with autologous bone graft. We used computed tomography (CT) to measure bone mineral density (BMD) of tissue adjacent to the implant and used histologic slices to evaluate bone–implant bridging in order to assess the extent of the callus around each implant and to verify a possible correlation of movement rate, implant type, adjacent-tissue BMD changes, and implant osseointegration.

Materials and Methods

Animals and Surgical Procedures

Female sheep (1-2 years old) were given preanesthesia with ketamine (50 mg/mL, 0.12 mL/kg, 6 mg/kg; Ayest Laboratories, Guelph, Canada) by induction, and an equivalent injection of diazepam (5 mg/mL, 0.6 mg/kg; Sabex, Boucherville, Canada) was given intravenously with a 20-gauge catheter. The anesthesia was maintained by endotracheal intubation with halothane (1.0%-1.5% in O_2; MTC Pharmaceuticals, Cambridge, Canada). The animals were then laid out in decubitus, side right. The surgical technique consisted of a retroperitoneal approach

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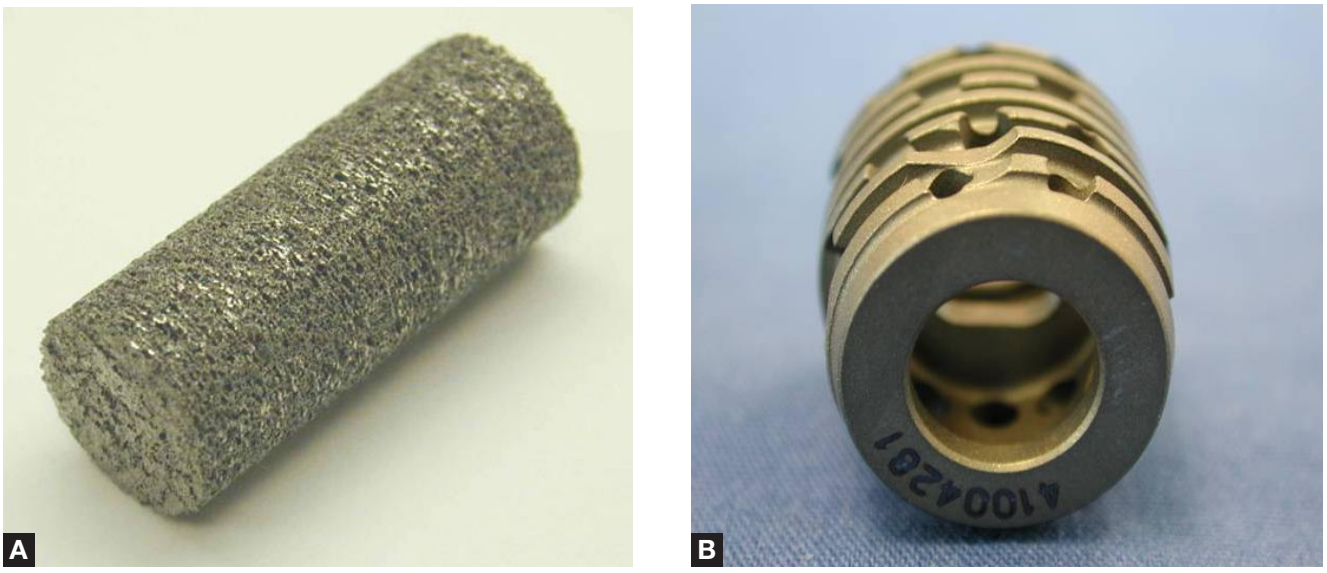

Figure 1. (A) Porous nitinol implant. Image courtesy of Biorthex, Inc. (B) Titanium cage. Image courtesy of Sulzer Spine Tech.

to the left side of the lumbar area. A longitudinal incision of 10 to 15 cm was made along the left side at the level of the transverse apophyses, and blood loss was controlled with electrocoagulation. The external abdominal muscles were detached from the points of the transverse apophyses, thus making it possible to expose the psoas muscle. After a partial discectomy, a PNT intervertebral fusion implant (Figure 1A: Actipore™, ϕ, 11×20 mm; pores, 230 ± 130 µm; porosity, 65% ± 5%; elastic modulus, 1.13 GPa; Biorthex, Montreal, Canada) and a TiAlV intervertebral fusion implant (Figure 1B: TiAlV, BAK™, ϕ, 11×20 mm; elastic modulus, 110 GPa; Sulzer Spine Tech, Minneapolis, Minn) were inserted in each of 16 sheep at alternate intervertebral lumbar levels L2–L3 and L4–L5 using slightly modified posterior lumbar interbody fusion (PLIF) instrumentation.[16,17] The TiAlV cage, which is not porous, required an osseous autograft harvested from the iliac crest. Postsurgical positioning control of the implants in the lumbar spine was carried out with (TV) the 2-dimensional radiologic view. However, the difference between the stability of 2 implants after implantation and at the postsurgical follow-up has not been demonstrated with the radiologic view. No mechanical tests were done to test the pullout forces.

Pentobarbital 0.1 mg/kg (Euthanyl; MTC Pharmaceuticals) and a 20-gauge needle were used to sacrifice the 16 sheep 3 months (n = 6), 6 months (n = 6), and 12 months (n = 4) after implantation. One untreated control sheep (no implants, no surgery) was sacrificed at each implantation period.

Computed Tomography

After animal sacrifice, spinal columns L1–L6 were removed and placed under CT scan (PQ 5000 CT scan, fourth-generation helicoidal with spiral acquisition; Philips Medical Systems, Eindhoven, Netherlands). Three vertebral slices

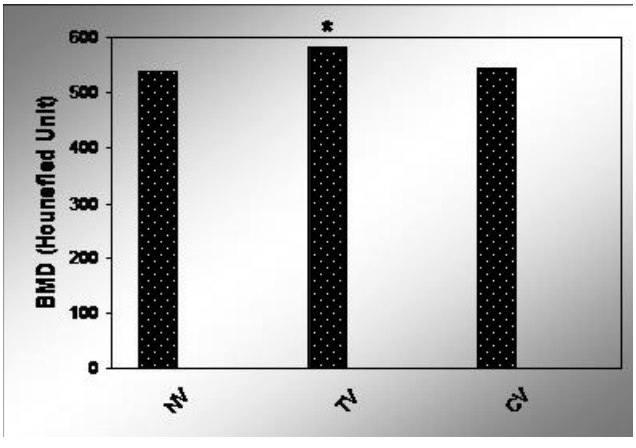

Figure 2. Bone mineral density around porous nitinol (NV) and titanium (TV) implants versus untreated control vertebrae (CV) over postsurgical recovery (12 months). *Statistically different from control vertebrae ($P \leq .01$, Student t test).

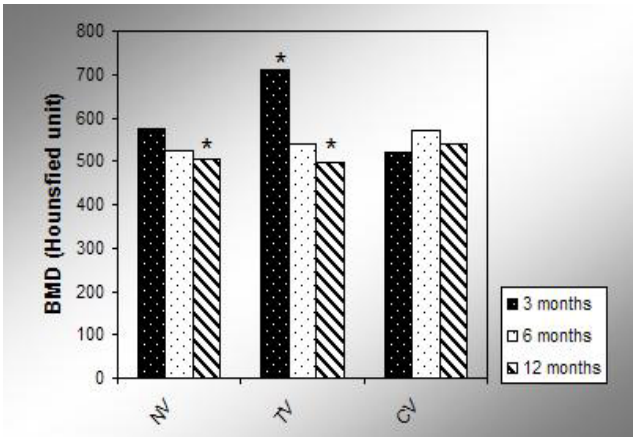

Figure 3. Bone mineral density around porous nitinol (NV) and titanium (TV) implants versus untreated control vertebrae (CV) 3, 6, and 12 months after implantation. *Statistically different from control vertebrae ($P \leq .05$, Student t test).

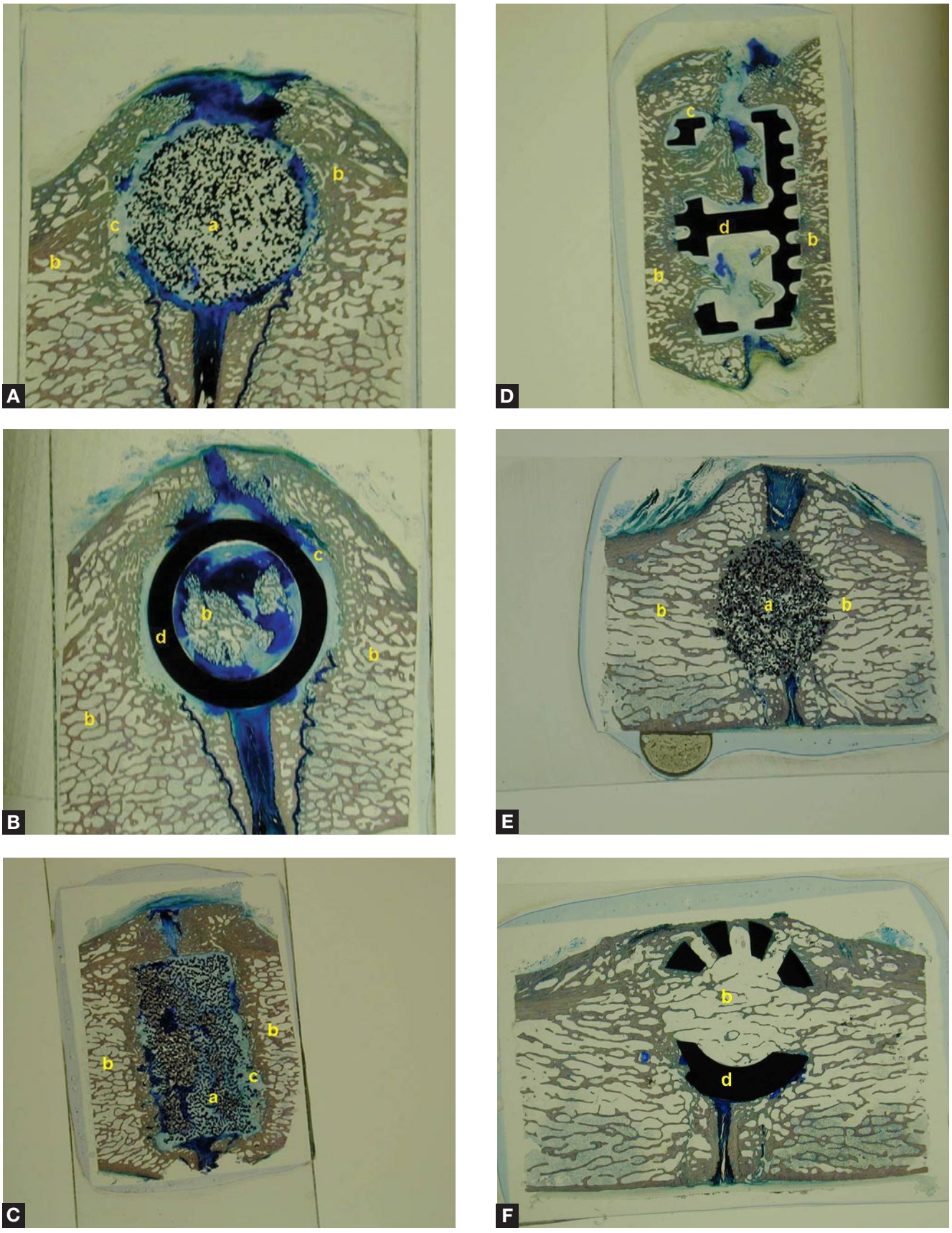

Figure 4. Results from macroscopic histologic analysis performed under digital camera (Nikon E950). (A) Porous nitinol (PNT) implant in fibrous capsule. (B) Titanium (TiAlV) cage in fibrous capsule. (C) PNT implant fused with mixed fibrous and bone tissue. (D) TiAlV cage fused with mixed fibrous and bone tissue. (E) PNT implant fused with 100% bone tissue. (F) TiAlV cage fused with 100% bone tissue. For Parts A-F: (a) PNT implant, (b) mineralized bone, (c) fibrous tissue, (d) TiAlV cage.

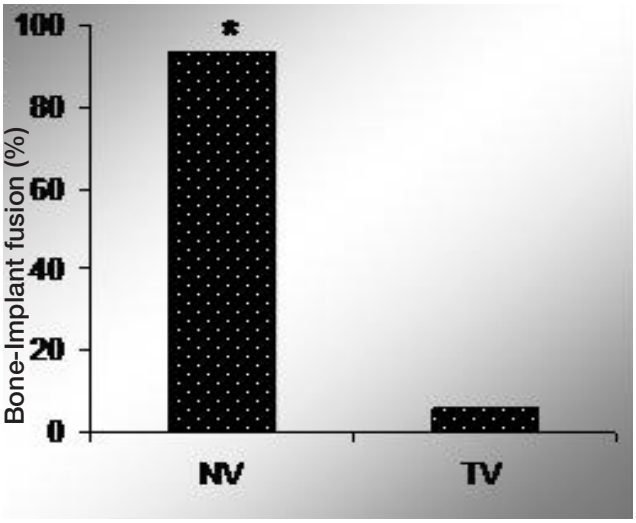

Figure 5. Bone–implant fusion over postsurgical recovery (12 months). *Statistically different from TiAlV-treated vertebrae ($P \leq .01$, χ^2 test). (NV = nitinol implant; TV = titanium implant)

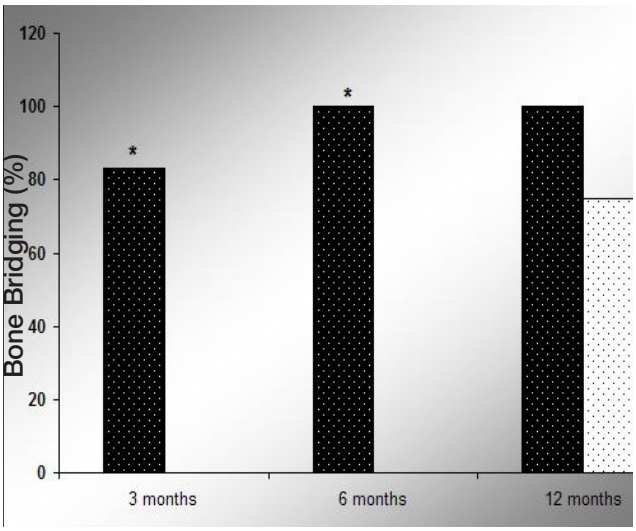

Figure 6. Bone–implant fusion 3, 6, and 12 months after surgery. *Statistically different from TiAlV-treated vertebrae ($P \leq .05$, Fisher exact test). At 12 months, the white column represents TiAlV cages and the black column represents PNT implants. The difference between the two is not statistically significant.

(2 mm thick, 2 mm between slices, images acquisition 120 mm, 130 KV, 30 mA, 1s, 512×512 pixels) were taken from the vertebrae adjacent to the implant. Data were obtained by measuring the mean BMD of the 1-cm^2 area at the center of the vertebral slice. To determine the BMD variation induced by the presence of implants, results were compared with data from vertebrae of untreated control sheep. Results were stratified by implant type and implantation period. Student *t* test was used to determine if there was any statistical difference between BMD of vertebrae adjacent to the implants. Then, the extent of this variation was compared with a BMD control. A standard and homogeneous control tube (Omnipack-300 in semiphysiologic medium; Nycomed, Melville, New York) was used as a calibration phantom and was positioned parallel to the spinal column to control the constancy of the acquisition parameters. Both materials were digitalized simultaneously using CT scan. Tube data were also obtained by measuring the mean density at the center of the tube slice.

Histology

After BMD measurement, lumbar levels were embedded in neutral formal (10%), rinsed, kept in ethanol 70%, and cleaned with xylene. Metal implant sections, including osseous and fibrous tissue, were obtained with a diamond saw (Exakt Technologies, Oklahoma City, Okla) to approximately 70 µm and stained with Stevenel blue (soft tissue) and Van Gieson picro-fuschsin (calcified bone tissue).[18,19] Macroscopic histological analysis was performed under a digital camera (Nikon E950). Statistical analyses were performed with χ^2 and Fisher exact tests.

Results

BMD changes in vertebrae adjacent to PNT implants and TiAlV cages were compared with those of untreated control vertebrae (CV) regardless of postsurgical implantation time (Figure 2). The difference in BMD between PNT-treated vertebrae (NV) and untreated CV was not statistically significant (NV, 540 HU; CV, 544 HU), but the difference between TiAlV-treated vertebrae (TV) and untreated CV was statistically significant (TV, 582 HU; CV, 544 HU; $P \leq .01$).

Figure 3 shows that, 3 months after implantation, periprosthetic BMD was significantly higher in TiAlV-treated sheep than in both PNT-treated sheep and untreated sheep ($P \leq .01$). At 6 months, there were no significant differences in BMD between treated and untreated vertebrae. After 12 months, BMD was significantly lower in both PNT- and TiAlV-treated sheep than in untreated sheep (NV vs CV, $P \leq .01$; TV vs CV, $P \leq .05$).

The variation in density obtained with the phantom control tube on successive scans was not statistically significant ($P = .8$, repeated analysis of variance). Therefore, there was no significant systematic error biasing our study results.

Histologic results (Figure 4) indicated that osseointegration was better in PNT implants (Figure 5) than in TiAlV cages and that, at 3 and 6 months, bone bridging was significantly better with PNT implants than with TiAlV cages (Figure 6).

Discussion

Successful osseointegration that leads to bone–implant fusion depends on several conditions being satisfied during peri-implantation bone healing. An implant that is not well tolerated by the body is at risk for irreversible destruction of the bone–implant interface and might have to be removed,[4,5] whereas an implant that is tolerated (is biocompatible) shows good adjacent osseous growth and effective bone–implant fusion.

Bone bridging reduces movement at the bone–implant interface. A callus forms to bridge the bone defect and

restore continuity of the bone. Callus tissue is weak during initial bone healing but subsequently ossifies to bridge bone fragments. Immobilization is needed to avoid movement at the trauma site and thereby ensure adequate bone healing. When there is movement at the implantation site, callus size and adjacent BMD increase considerably, until stability of the bone–implant interface is obtained.[20-23] Callus rigidity is thus a crucial aspect of bone healing. We can hypothesize that callus formation is a dynamic process in which movement at the trauma site determines the extent of the callus formation.

In most cases, peri-implant BMD around PNT implants was found to be lower than around conventional TiAIV cages but not significantly different from general BMD in untreated control sheep vertebrae. These results indicate that bone healing was adequate with PNT implants and that BMD after PNT implantation probably resulted from normal bone healing (callus). As BMD around TiAIV cages was significantly higher than physiologic BMD, we hypothesized that a sclerosis and not a physiologic callus was involved. The sclerosis at the bone–implant periphery is usually considered a response of the body to potential micromovement at the bone–implant interface.[23]

In this study, we hypothesized that movement of TiAIV cages could account for their instability in their implantation sites. It is known that movement at the trauma level supports callus formation. Callus rigidity increases considerably (sclerosis) with trauma movement until stability of the bone–implant interface is obtained.[23] Instability of TiAIV cages in implantation sites and instability-associated complications (neurologic and vascular obstructions, dural complications, etc) have been reported.[24-27] Regardless of material used, lower BMD at 12 months is a normal consequence of traumatic ischemia involving lack of blood supply. Tissue that is not well supplied with blood can become deficient in nutrients and metabolites, experience cell death, and turn necrotic. Normal BMD is expected to be restored when the vascular network is completely reestablished, and nutrients and metabolites are correctly distributed.[28-31]

In the absence of biocompatibility, the bone–implant interface could be destroyed, the bone-healing mechanisms blocked, and callus formation impaired.[4,32] However, development of a sclerosis around the TiAIV cage indicates that the bone-healing mechanisms functioned relatively well in the presence of TiAIV, which besides being considered biocompatible is also a very corrosion-resistant metal.[33-36] The very high BMD (sclerosis) recorded around the TiAIV cages indicated that the intensity of movement in the implantation sites was stronger than with PNT implants. The sclerosis was therefore related to the instability of TiAIV cages at their implantation sites, as hypothesized.

Rigidity and porosity have probably had primary roles in the stability of both types of implants. The rigidity of PNT in compression (modulus of elasticity, 1.13 GPa), being close to that of bone (~15 GPa), probably favored good load-sharing at the bone–implant interface, with good and fast anchoring and consolidation between bone and implant.[37,38] The very high degree of rigidity of TiAIV in compression (modulus of elasticity, 110 GPa) compared with bone rigidity (~15 GPa) probably contributed to bad load-sharing at the bone–implant interface, with a delay in bone–implant anchoring and therefore instability of the couple. Furthermore, it is known that implants with a porous structure and rough surfaces are more osseointegrative than are implants with a nonporous structure and smooth surfaces.[39-41]

Histologic results showed that, in the majority of cases, osseointegration was better with PNT implants than with TiAIV cages. Time also seemed to affect osseointegration. At 3 and 6 months, BMD around TiAIV cages was very high, but bone bridging was significantly better with PNT implants. Then, at 12 months, when BMD was under control, osseointegration of TiAIV cages was good—indicating a correlation between BMD rate and implant osseointegration. The good-osseointegration phenomenon seems to occur while the BMD around an implant is close to or lower than physiologic BMD.

Conclusions

Our study results demonstrated a correlation of peri-implant BMD, implant type, and implant osseointegration. PNT implants were stabilized in their implantation sites probably because of their bone-like hardness, which allows good load-sharing at the bone–implant interface, and their porous structure, which allows bone adherence and dwelling. Compared with PNT implants, TiAIV cages have had difficulty stabilizing in their implantation sites, probably because of bone-adherence problems. Being smooth and harder than bone seemed to prevent or delay fusion of TiAIV cages with bone. Bone fusion may therefore be influenced by implant structure and shape.

Authors' Disclosure Statement

Michel Assad, PhD, wishes to note that he acquired a nonsignificant amount of shares of Biorthex, Inc., as part of a registered retirement savings plan. Charles-H. Rivard, MD, wishes to note that he is a paid consultant to Biorthex, Inc. Fidèle Likibi, PhD, and Gilles Chabot, MD, report no actual or potential conflict of interest in relation to this article.

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