The Effects of Implant Composition on Extensor Tenosynovitis in a Canine Distal Radius Fracture Model

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Purpose: Dorsal plating of distal radius fractures with titanium plates has resulted in clinically observed tenosynovitis and tendon rupture. The goal of this study was to investigate whether titanium-based implants result in more extensor tendon inflammation than matched stainless-steel implants in a canine fracture model.

Methods: An osteotomy was created in the distal radius of 18 beagles and fixed with 2.7-mm 4-hole plates composed of commercially pure titanium, titanium alloy (Ti-Al6-V4), or 316L stainless steel. Animals were killed at an average of 4 months. Tendon gliding was assessed by applying a force at the extensor musculotendinous junction and noting gliding. Histologic grading (mild, moderate, severe) was based on cellular hypertrophy, hyperplasia, and leukocytic infiltration.

Results: Tendons glided freely in 100% stainless-steel specimens, 75% of titanium alloy, and 43% of commercially pure titanium groups. A severe inflammatory reaction was identified in 60% of the titanium alloy (Ti-A16-V4) group, 57% of the pure titanium group, and 0% of the stainless-steel group.

Conclusions: Dorsal plating of the canine radius with commercially pure titanium or titanium alloy implants produced a greater inflammatory peritendinous response than matched stainless-steel implants. (J Hand Surg 2005;30A:300–307. Copyright © 2005 by the American Society for Surgery of the Hand.)

Key words: Π plate, distal radius fractures, titanium metallosis.

Comminuted fractures of the distal radius with dorsal angulation are difficult to stabilize and resultant malalignment can result in major disability. Dorsal plating to restore articular congruity is an accepted clinical technique. Newer low-profile and more anatomically correct designs such as the π plate (Synthes Ltd., Paoli, PA) have been introduced to allow rigid fixed-angle reconstitution of the distal radius.[1] The versatility of the implant, which has a periarticular segment and metaphyseal segments, has expanded the indications for open reduction and internal fixation of highly comminuted fractures. Re-

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ports of dorsal wrist pain, aggressive tenosynovitis, and extensor tendon rupture after the use of the titanium distal radius π plate are becoming more widespread.[2–5] Low-profile double plating of the intermediate and lateral columns of the radius with 2.0 titanium plates also have resulted in reports of extensor tenosynovitis and rupture when plates were cut.[6] Milder forms of synovitis, sometimes requiring plate removal, have been reported with the use of dorsally placed stainless-steel implants[7,8]; however, to our knowledge there have only been 2 reports of extensor tendon ruptures.[9,10] The clinically observed differences in the volume and extent of complications between stainless steel and titanium implants is a clinically relevant phenomenon.

The corrosion behavior of titanium-based implants is considerably different from that of stainless steel implants. Titanium metallosis, or regional metallic contamination of surrounding tissues, has been described previously in the orthopedic literature after the use of titanium implants for reconstruction.[1,11–22] Histologic findings have included aggressive inflammatory reactions in soft tissue,[23–25] skin,[12] and muscle[26] around titanium-based implants. Titanium corrosion can propagate these aggressive inflammatory reactions; however, its relative contribution to development and progression of synovitis, tendon rupture, capsular contracture, and loss of joint mobility seen with the use of titanium-based dorsal plating is unknown.

Our hypothesis is that corrosion resulting from titanium-based plates promotes a more aggressive tenosynovitis than stainless steel, independent of plate design. To test this hypothesis a distal radius fracture model in the beagle was created to simulate the *in vivo* conditions after dorsal plating for fractures in the human wrist. Similar to the orientation in the human wrist the canine abductor pollicis longus tendon crosses the extensor carpi radialis tendon at the distal radius.[27] Gross and histologic charcteristics of the tendon adjacent to plates of different metallurgic composition were used as an assessment of tissue reaction to a particular metal. Extensor tendon complexes from the contralateral limb were used as controls.

Materials and Methods

Eighteen skeletally mature female beagles were quarantined for at least 1 week and then taken to surgery. The Institutional Animal Care and Use Committee approved the protocol at our institution. Seven animals were assigned to the titanium implant group, 5 to the titanium alloy group, and 6 to the stainless-steel group (this disparity was based on implant availability). Preoperative radiographs were taken to ensure skeletal maturity of the distal radius and normal anatomy.

The right forelimb and paw of each animal was shaved and prepped with antibiotic soap and draped from the midforearm to the paw. The animals were anesthetized with thiopental 15 mg/kg intravenously, intubated, and maintained on isoflurane 1.5% to 2.5%. Antibiotics were administered perioperatively. A dorsal approach through a combination of sharp and blunt dissections was used to expose the distal radius. The plane between the abductor pollicis longus (APL) and the extensor carpi radialis brevis (ECRB) and extensor carpi radialis longus (ECRL) was dissected. Care was taken to locate the medial branch of the radial nerve, branches of the radial artery, and the cephalic vein. The ECRB, ECRL, and the APL were retracted laterally and elevated to expose the distal radius. An osteotomy was created by using an oscillating saw 2 cm proximal to the radiocarpal joint. The fracture was reduced and a 2.7-mm 4-hole dynamic compression plate (stainless steel, titanium alloy [Ti-A16-V4] or pure titanium) was secured to the distal radius beneath the intersection of the 2 wrist and thumb extensors (Fig. 1). We used standard, clinically available, small-fragment plates; all were polished implants and complied with American Society for Testing and Materials standards and Food and Drug Administration guidelines for human implants. The implants were of equivalent size and profile but not exactly identical in size based on variability between manufacturers. There were no manipulations to the implants such as cutting or bending. All screws were well seated within the plate. After closure of the fascial layers and skin, soft dressings were applied. Postoperative radiographs were taken to confirm satisfactory alignment and internal fixation placement (Fig. 2). Epidural morphine 0.1 mg/kg was administered for postoperative pain. The animals were allowed to weight bear as tolerated in their cages immediately after surgery and were exercised daily. The dogs were followed-up for a minimum of 12 weeks before death with intravenous pentobarbital. All animals were killed by 16 weeks.

After euthanasia the forelimb was dissected free from the upper limb. Radiographs of the operated limb were taken to document bony union and hardware stability. The forelimb was skinned and the musculature of the dorsal forelimb was inspected. A 2–0 suture was passed through the substance of the ECRB and ECRL myotendinous junction. Passive

Figure 1. Insertion of plate underneath extensor tendons.

wrist extension was attempted by applying a single continuous manual load through the suture. Gliding of the wrist extensor tendons over the implant was assessed by using a binary grading system of either normal or restricted gliding.

The extensor tendons of the forelimb adjacent to the plate were dissected from the experimental and control limbs. Tendon specimens included the ECRB, ECRL, and their associated tendon sheaths. A second specimen included the extensor digitorum, extensor pollicis longus, and extensor indices proprius tendons, which are contained in the same sheath. Each sample was prepared and stained with hematoxylin-eosin. Approximately 5 longitudinal slices were acquired from each sample; sections were examined with light microscopy by an orthopedic surgical pathologist (M.P.).

A 3-level grading system was developed in conjuction with an experienced orthopedic patologist to assess peritendinious inflammation. Histologic markers used included fibroblastic hypertrophy, fibroblastic hyperplasia, and infiltration by inflammatory cells at ×100 and ×400 magnification. The specimens were graded blindly and placed in rank order of increasing severity of inflammation and fibrosis. The resulting analysis allowed differentiation into 3 categories: (1) mild, (2) moderate, or (3) severe inflammation (Table 1). Representative examples of these categories can be seen at ×100 magnification in Figure 3 and corresponding ×400 magnification in Figure 4.

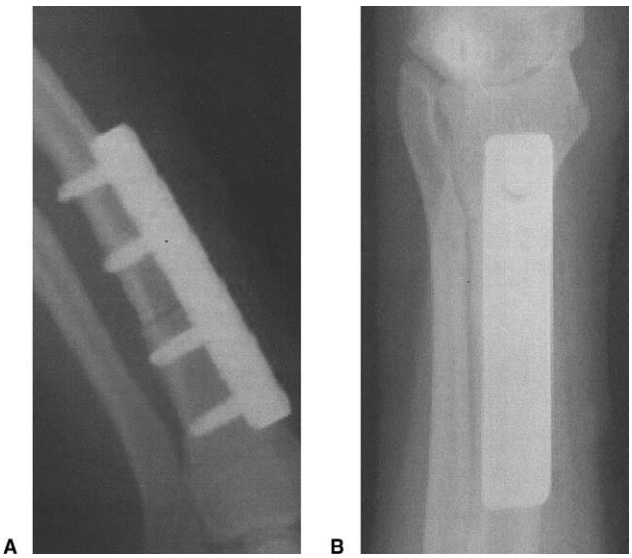

Figure 2. (A) Lateral postreduction radiograph. (B) Anteroposterior post reduction radiograph.

Results

There were no cases of wound dehiscence, infection, or gait disturbance after union. All fractures healed clinically and radiographically. All plates were well fixed with no evidence of plate breakage or screw loosening.

Tendons glided freely in all of the control limbs. Complete tendon gliding was seen in all animals implanted with a stainless-steel dynamic compression plate. After exclusion of the animal with iatrogenic tendon laceration in the titanium-alloy group, 3 of 4 specimens exhibited free gliding. In the pure titanium group only 3 of 7 glided freely (Fig. 5). Restricted gliding was associated with observed fibrosis and scarring with adhesion of the tendons to the implant (Fig. 6).

After removal of blinding the following results were obtained. The control tendons had no inflammation. In

Table 1. Criteria Used for Histologic Analysis

Mild inflammation	From a normal histologic appearance of tendon to mild fibroblastic hyperplasia and hypertrophy with no inflammatory cells
Moderate inflammation	Villous hypertrophy, hyperplasia, granulation tissue, thickening of the aereolar tissue, and focal lymphocytosis
Severe inflammation	Severe villous hypertrophy and hyperplasia, granulomas, cartilaginous metaplasia, diffuse infiltration by inflammatory cells: lymphocytic proliferation, neutrophils, macrophages, and plasma cells

the stainless-steel group 4 specimens were classified with minimal inflammation whereas 2 specimens displayed moderate inflammation. The titanium-alloy group consisted of 2 specimens with moderate inflammation and 3 specimens with severe inflammation. In the titanium group 3 specimens had moderate inflammation and 4 specimens had severe inflammation (Table 2).

During one of the surgeries (titanium-alloy implant) the ECRL tendon was severed unintentionally; the tendon ends were re-approximated and sutured. The animal was able to weight bear as tolerated and when analyzed histologically was similar to the other titanium-alloy specimens. The data regarding gliding for this animal was excluded.

Discussion

The titanium distal radius π plate was designed to allow for intercompartment placement with less dissection and its low profile was purported to be kinder to the overlying tendons. Initial clinical trials reported a 23% rate of tendonitis explained by the more radial extension of this implant.[1] Ring et al recommend the use of a retinacular flap to protect the dorsal compartment tendons from direct contact with the implant.[1] Chiang et al,[28] however, showed that a retinacular flap did not alleviate dorsal wrist pain; 9 of 20 patients required plate removal for dorsal wrist pain. There have been several reports of extensor tendon rupture[2,5,29] with the use of the π plate and Lowry et al[3] reported rupture of the extensor digitorum communis to the third digit 7 months after π plate fixation despite a lack of plate failure or prominent screws. They concluded that tendons gliding over a titanium implant may incur a cellular reaction to metal that results in tenosynovitis and tendon rup-

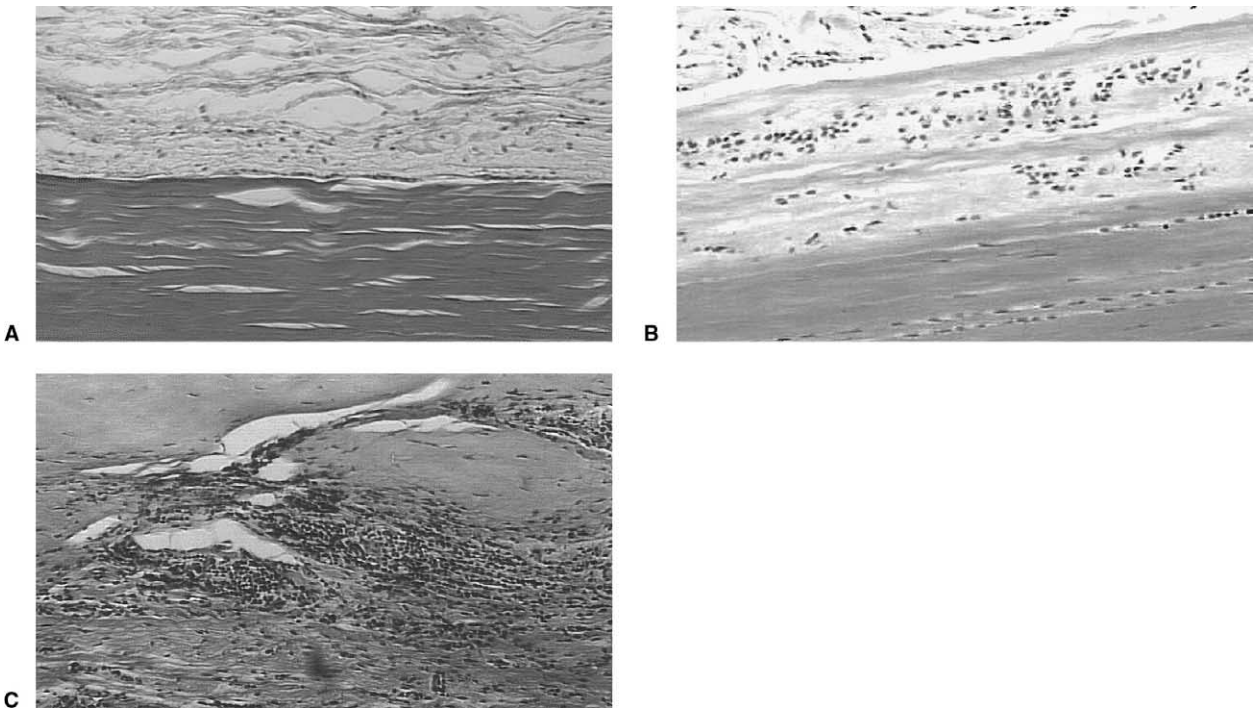

Figure 3. Representative histologic grading criteria at ×100 magnification: (A) mild, (B) moderate, and (C) severe.

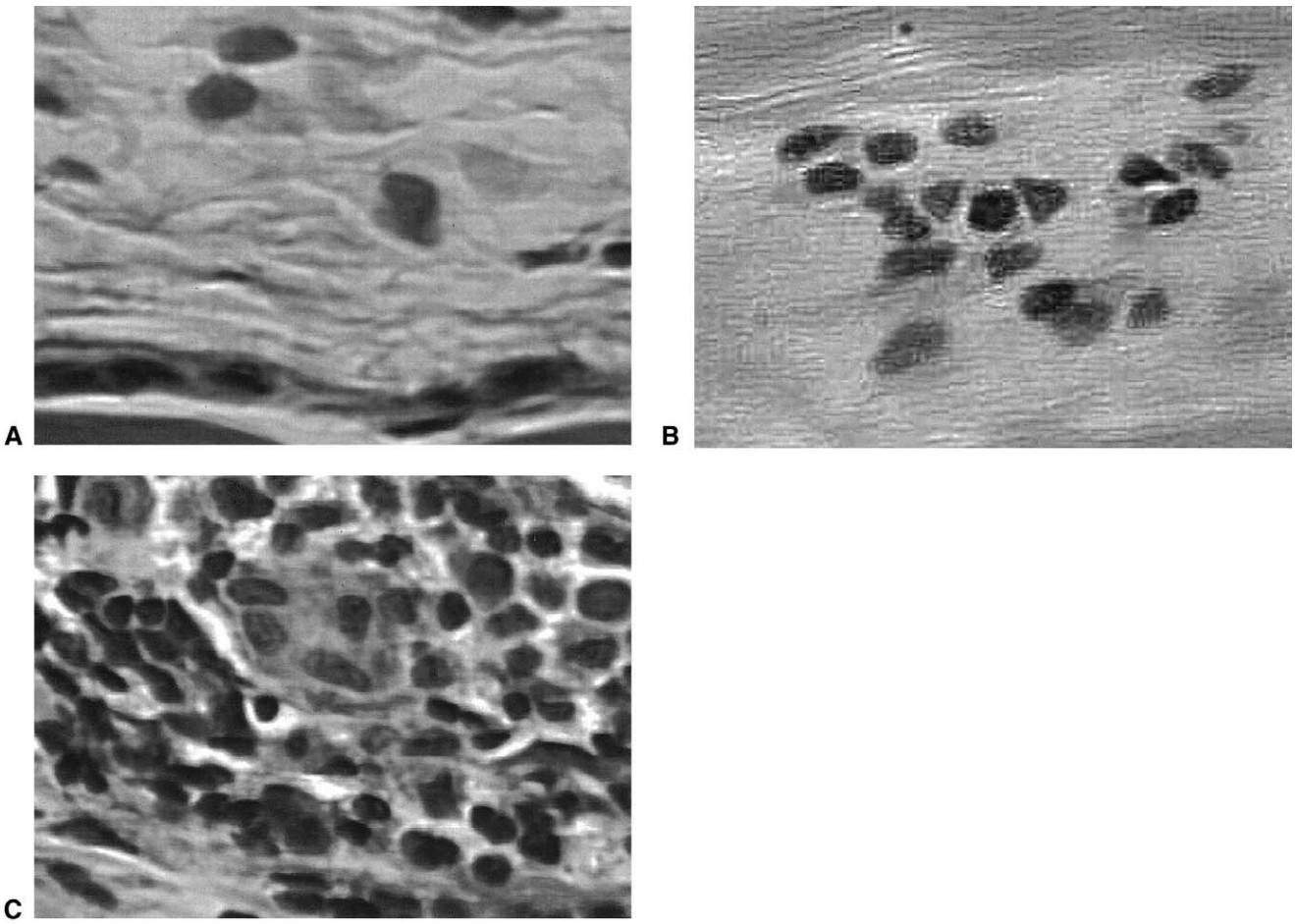

Figure 4. Representative histologic grading criteria at ×400 magnification: (A) mild, (B) moderate, and (C) severe.

ture in some cases. Hahnloser et al[4] reported 2 cases of tenosynovitis of the extensor pollicis longus of the 21 cases performed. A recent study[9] reported complications such as tendon tenosynovitis and rupture after plating with either stainless-steel or titanium π plates. Although not statistically significant complications requiring a second surgical procedure occurred in 67% when a titanium plate was used and in 38% when a stainless-steel plate was used.[9]

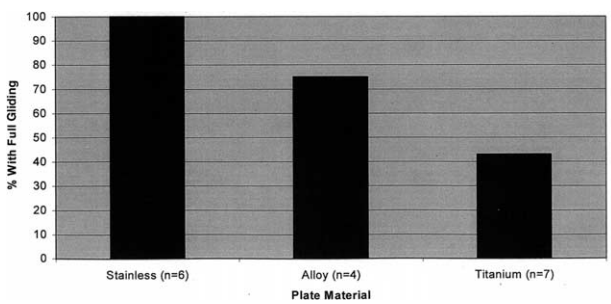

Figure 5. Results of gliding at the radiocarpal joint.

The benefits of using titanium and titanium-alloy implants include improved biomechanical properties and the ability of titanium to integrate with bone. Despite improvements in the wear characteristics of titanium implants they frequently have been found to be susceptible to abrasive wear and corrosion, resulting in the phenomenon of metallosis.[11,13–17,19,22,24] This black peri-implant staining was thought to be benign.[30] Early studies of soft tissue supported the notion of minimal adverse response in blackened tissue areas,[17,26,31,32] but numerous reports found a marked tissue reaction in peri-implant tissue.[21–25,33] Locally irritating metallic debris results in abundance of histiocytes and giant cells in peri-implant soft-tissue specimens.[11] Santavirta et al[21] noted a predominance of giant-cell granulomas forming as a result of phagocytosis of titanium particles in patients with loose acetabular components. Witt and Swann,[22] in a group of loose titanium alloy femoral stems, showed a fibroblastic reaction with

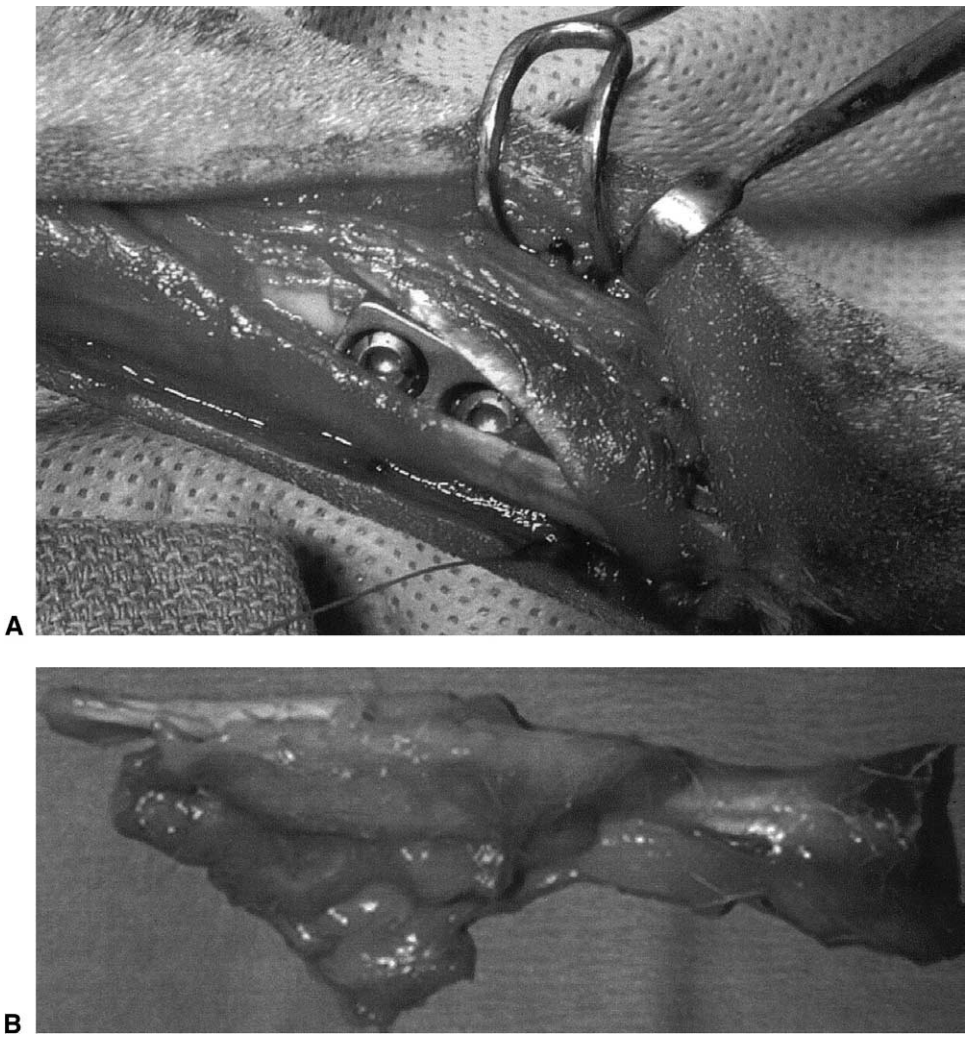

Figure 6. Scarring to the implant postmortem. (A) Before harvest and (B) after harvest.

abundant titanium extracellularly and intracellularly within histiocytes, and a foreign-body giant-cell reaction. Wang et al[33] described titanium debris and an activated macrophage cellular response in the soft tissue adjacent to pedicle screw fixation for spinal fusion.

Proliferation of histiocytic cells in response to titanium metallosis has been shown to lead to local osteolysis and contribute to the failure of total hip replacements as well as resorption of condylar bone in total elbow replacements.[11,13,14,22] Breen and Stoker[13] questioned whether a reactive response to a titanium knee prosthesis contributed to 3 ruptured extensor mechanisms.

Nasser et al[20] noted that in a series of titanium total joints, implantation for longer than 1 year resulted in discoloration indicative of metallosis, whereas after 2 years the synovium became hypertrophic and villiform.

Severe tenosynovitis and resulting disability noted with the use of titanium-based implants for distal radius fixation may be a result of this aggressive tissue response seen in other areas. Our study in a canine radius fracture model compared

Table 2. Results of Histologic Analysis for Stainless-Steel, Titanium-Alloy, and Pure Titanium Groups

Implant Material	Mild Inflammation	Moderate Inflammation	Severe Inflammation
Stainless steel (n = 6)	4	2	0
Titanium alloy (n = 5)	0	2	3
Pure titanium (n = 7)	0	3	4

the different tendon reactions to plates of different metallic composition. The implants internally fixed a metaphyseal distal radius fracture and were beneath the gliding extensor mechanism as in the clinical setting. Histologic examination of the tendon samples revealed significant differences between the 2 titanium-based groups and the stainless-steel group. All of the specimens in the titanium and titanium-alloy–based groups had a moderate to severe amount of intratendon inflammation. The commercially pure titanium implants displayed marked extratendinous synovial hypertrophy and villous hyperplasia. There also were inflammatory cells represented by lymphocytes, neutrophils, macrophages, and plasma cells infiltrating the tendon; in the most severe cases granulomas were observed. Cartilaginous metaplasia within synovial tissue also was seen occasionally within the titanium group. Our histologic observations are consistent with the observations in the literature that show histiocytic infiltration with villous hypertrophy of the synovium. The titanium alloy plate exhibited a similar, though slightly less severe, inflammatory picture as the pure titanium group. With the presumption that the inflammatory trigger is titanium, this result is not surprising because the alloy plate is 90% titanium. On the contrary no specimens in the stainless-steel group exhibited the degree of inflammation seen with the titanium-alloy and titanium group.

In our study there were no instances of hardware failure that could have contributed to the development of inflammation. We observed differences in tendon gliding between the subgroups. Four of 7 specimens displayed impaired gliding at the wrist joint in the titanium group as a result of the fibrosis. None of the forelimbs in the stainless group and 1 in the titanium-alloy group had evidence of impaired gliding. Gross examination consistently showed increased fibrosis over the titanium implant when compared with the tissue overlying the stainless-steel plates. When harvesting the tendons for histology the tendon bundles over the stainless plates were dissected easily whereas those overlying the titanium and alloy plates tenaciously adhered to the plate. The histologic observation of severe inflammation in the titanium group is consistent with fibrosis and concomitant loss of tendon mobility. Our results clearly show a markedly increased inflammatory response in the commercially pure titanium and alloy groups. Our histologic findings can explain the clinical complication of tendon ruptures seen with dorsal titanium plates. Disruption of the highly ordered architecture of the tendon substance by migratory cells and the resultant fibrotic reaction over time results in attenuation of tensile strength, thus predisposing to rupture. The data regarding surface roughness of these implants was not available from the manufacturers.

Previous reports examined soft tissue, skin, and muscle reaction around titanium orthopedic implants. This report examines the gross anatomy and histology of extensor tendons over fracture implants in an animal fracture model and compares the tissue reactivity related to metallurgy. Gross examination of the tendon sheath and soft tissue over the titanium implants revealed scar formation that likely resulted in impaired gliding at the radiocarpal joint. Histologically the study showed differences that could be stratified based on the degree of inflammation and metal, with pure titanium engendering the most cellular response including fibrobalastic invasion of the tendon ultrastructure. These results suggest that local tissue reaction to titanium metallosis may be the underlying cause of the complications seen with the use of the titanium-based π plate. Plate design is a factor in complications seen clinically as Rozental et al[9] recently reported a statistically significant increased rate of extensor tenosynovitis and rupture with the π plate compared with a low-profile plate regardless of plate composition. Notably the 2 tendon ruptures were in titanium plates (personal communication, D.J. Bozentka, January 2004). Herron et al[10] also reported a case of extensor tendon rupture with the use of a stainless-steel plate in a series of dorsal plating for intra-articular distal radius fractures. Lastly flexor pollicis longus rupture after volar fixation of distal radius fractures has been reported in association with steroid use[34] and inappropriate placement of the π plate on the volar surface of the radius.[35]

Complications after dorsal plating are likely multifactorial and the present study implies that they are not simply secondary to design or hardware loosening as has been suggested, but in part secondary to implant composition. We agree that dorsal plating with any implant can result in extensor tendon irritation and we designed this study specifically to evaluate the role of implant composition. Observations made in this study may have important clinical implications in the design and use of fracture implants.

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