The Modified Maquet Procedure (MMP) in Dogs: Technical Development and Initial Clinical Experience

Malcolm Graham Ness, DECVS, BVetMed, CertSAO, DFRCVS

ABSTRACT

The literature about tibial tuberosity advancement surgery in dogs and humans informed the development of a version of the operation using a wedge-shaped implant of titanium foam. Computer-assisted drawing and stereolithography was used to create instruments and implants that were evaluated by cadaver surgery. A trial, involving 26 client-owned dogs with lameness due to cranial cruciate ligament failure, was started. Follow-up was done by clinical and radiographic examination after 4 wk and clinical examination again 6–11 mo after surgery. The titanium foam implant maintained tibial tuberosity advancement easily and effectively. The same major complication occurred in 2 of the first 6 cases before, a slightly modified technique was used to treat 20 dogs without complication. At mid-term follow-up (6–11 mo), 20/26 dogs (77%) had returned to full function, two dogs (7.7%) had acceptable function, two dogs (7.7%) could not be evaluated due to recent contra lateral modified Maquet procedure surgery, and two (7.7%) dogs had died for reasons unrelated to the study. This is the first clinical report of the use of titanium foam in veterinary orthopaedics. Modified Maquet procedure appears to be an effective treatment for lameness due to failure of the cranial cruciate ligament in dogs. (J Am Anim Hosp Assoc 2016; 52:242–250. DOI 10.5326/JAAHA-MS-6304)

Introduction

Advancement of the tibial tuberosity in humans was first described by Maquet in the early 1960s and reported some years later in the English language medical literature.1 Loss of cartilage between the patella and femur in the human knee is a cause of significant pain and the aim of Maquet’s osteotomy was to alleviate that pain by reducing patello-femoral contact pressure. Subsequently, several published reviews concluded that, while the Maquet osteotomy was effective, complications associated with fixation failure were a problem and it was noted that the procedure had an unforeseen biomechanical effect: the redirected pull of the quadriceps muscles reduced the femoro-tibial shear force.2,3,4 Tibial tuberosity advancement (TTA) in dogs is thought to impart functional stability to the stifle during motion by reducing the femoro-tibial shear force and what was an unforeseen biomechanical consequence of the Maquet osteotomy in humans has become the primary aim of TTA in dogs.

The treatment of cranial cruciate ligament (CCL) failure in dogs using a tibial osteotomy to change stifle mechanics became common during the 1990s.5 Tibial plateau levelling osteotomy (TPLO), first described by Slocum and Devine (1983), was the first of the mechanics-altering osteotomy procedures to be widely used. More recently, TTA operations similar to Maquet’s procedure in humans have been described for use in dogs.6–8

Although TTA is widely used, the theory underpinning TTA procedures in dogs remains controversial and the methods proposed for presurgical planning have been shown to be unreliable. By review of the evolution of tibial tuberosity advancement procedures in human and veterinary surgery, it was hoped that some of the limitations of TTA in dogs could be...
identified and addressed. While TTA has been shown to be effective at resolving the lameness caused by CCL failure in dogs, the surgery is time-consuming and complex. Hoffmann et al. (2006) reported a surgical time of 125 ± 37 minutes while Proot and Corr (2013) evaluated the learning curve and reported that a surgeon needed experience of more than 50 TTA procedures before the major complication rate fell below 10%. Others have reported complication rates of 25–59% and, while most were minor, complications requiring revision surgery have been reported in 4.6–14% of dogs after TTA.

To date, approximately 500 cases of TTA have been reported in several case series, but none of these published accounts includes a description of the method, or methods, used to estimate the required amount of tibial tuberosity advancement in sufficient detail to allow its replication. It seems that a 135° extended stifle lateral radiograph including the femur and tibia has been used consistently. However, producing a radiograph with a stifle in lateral radiograph including the femur and tibia has been used variable. Commonly used methods are remarkably inconsistent and controversial, and recently published evidence suggests that the most technically flawed, their theoretical underpinning remains controversial, and frequently published evidence suggests that the most commonly used methods are remarkably inconsistent and variable.

The successful use of a porous tantalum implant in TTA in humans has been reported. However, the manufacture of porous tantalum involves a complex and costly electrochemical process so it is likely that such implants will remain too expensive for routine use in veterinary orthopaedic surgery. Unalloyed, chemically pure titanium is known to be biocompatible and an appropriate material from which to form orthopaedic implants. Porous titanium foams have been developed recently and these materials have obvious potential for use in orthopaedic surgery. A significant body of research has established the optimum pore size to promote bone ingrowth and because the manufacturing process allows control of pore size, percentage porosity, material density, and stiffness, the titanium foam implant can be manufactured to optimize the structural properties as well as the potential for bone ingrowth. Two features of a bone-ingrowth biomaterial are important: pore size and material stiffness (Young’s Modulus). With regard to pore size, it is generally accepted that the optimum pore size for bony ingrowth is in the range of 50–800 μm. The titanium foam wedge implant used in this case series has a mean pore size of 500 μm with 80% of all pores within the optimum size range of 50–800 μm. With regard to Young’s Modulus, it is well known that excessively stiff orthopedic implants can cause stress protection leading to bone atrophy or failure of bone ingrowth. The Young’s Modulus of commonly used implant materials, for example stainless steel and solid titanium alloys, are in the region of 120 GPa and 100 GPa, respectively, while the values for cortical and cancellous bone are approximately 20 GPa and 15 GPa, respectively. The Young’s Modulus of the titanium foam used in this case series was in the range 5–8 GPa. It was recognized that a wedge shaped implant formed from titanium foam could be used in TTA surgery in dogs, filling the bone void created behind the advanced tibial tuberosity and offering early structural support and a suitable environment for bone healing by osteoconduction.

Limitations of conventional TTA surgery include its complexity and the imprecise, unreliable surgical planning methods. The aims of this project included developing a simple, cost-effective method of tibial tuberosity advancement for dogs and establishing a theoretically sound, precise, reliable, and reproducible means of presurgical planning. Strategies included critical review of relevant literature documenting the evolution of tibial tuberosity advancement in human and veterinary surgery as well as the investigation of potentially useful new biomaterials. The purpose of this paper is to report the early development and initial clinical evaluation of a modified Maquet procedure (MMP) to treat the lameness caused by failure of the CCL in dogs.

**Materials and Methods**

**Design and Development Phase**

An instrumented tibial tuberosity osteotomy made through a limited surgical approach to the proximal tibia was proposed. With the distal bone bridge intact, the tibial tuberosity would be reflected cranially and a titanium foam wedge placed to fill the void and fixed using a pin and tension band wire. Sketches of the proposed surgery were used to guide computer-aided design drawings of the wedges, a saw-guide, and other instrumentation. The “fit” and size of the wedges and instruments was estimated using three-dimensional reconstructions of computed tomography images of the stifles of three dogs of breeds commonly treated with surgery for CCL failure: one boxer, one Labrador retriever, and one rottweiller.
This work led to the adoption of a series of wedges 40.0 mm long, 15.0 mm wide, and with a variable thickness, 6.0 mm, 7.5 mm, 9.0 mm, 10.5 mm, 12.0 mm, 13.5 mm, and 15.0 mm, depending upon the required amount of tibial tuberosity advancement.

A method for estimating the desired amount of tibial tuberosity advancement, based exclusively on a tibial radiograph, was developed. A lateral radiograph of the stifle was obtained using the method described by Caylor and others (2001). A calibration marker was included in the radiograph to permit correction for magnification artifact during the templating procedure.

Figure 2 shows a radiograph with measuring drawing. The tibial plateau (A–B) and the tibial long axis (C–D) were drawn as described by Caylor and others (2001). A calibration marker was included in the radiograph to permit correction for magnification artifact during the templating procedure.

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Using computer-aided design files and stereolithography, prototype plastic instruments and wedges were produced. These were used on a series of cadaver stifles to develop a surgical technique. A skin incision approximately 8 cm long was made over the medial aspect of the proximal tibia, through fascia and periosteum, to the bone. Peripheral dissection was avoided. A short incision was made just behind the distal attachment of the straight patellar ligament to accommodate the long proximal locating pin of the saw guide (Figure 1). With the long proximal pin in contact with the cranial, proximal tibia, and the distal locating pin of the osteotomy guide held against the cranial cortex of the distal tibial tuberosity, a 3.5 mm hole was made into the tibia through the appropriate hole in the saw guide. Throughout this part of the surgery, the limb was positioned exactly as it was for radiography and both the saw guide and the drill were kept perpendicular to the operating table. The 3.5 mm drill bit was left in situ, effectively fixing the saw guide in position (Figure 2). A guided osteotomy was made through the tibial tuberosity avoiding any further distal or lateral soft tissue dissection (Figure 3). Prior to its removal, this same guide was used to position a 1.5 mm drill hole to accommodate a tension band wire (Figure 1). The 3.5 mm drill and the guide were removed and the short length of bone remaining between the end of the osteotomy and the 3.5 mm drill hole was identified. This was cut using the oscillating saw taking care to avoid extending the osteotomy beyond the 3.5 mm hole. Gentle traction allowed reflection of the tibial tuberosity and insertion of a wedge.
An instrument attached to the wedge accommodated a drill guide that was used to make a 1.5 mm hole through the tibial tuberosity coincident with the hole in the implant and a 1.6 mm Kirschner wire was advanced through the tibial tuberosity and the implant and into the caudal cortex of the tibia. Further distal soft tissue dissection was avoided while a length of 0.8 mm orthopaedic wire was formed into a figure-of-eight tension band around the Kirschner wire and through the 1.5 mm tibial diaphyseal hole.

Following evaluation of the instrumentation and validation of the surgical technique on cadavers, a set of prototype instruments was manufactured from 316LVM surgical stainless steel. Prototype titanium foam wedges were manufactured in three sizes: 40.0 mm x 15.0 mm x 7.5 mm, 40.0 mm x 15.0 mm x 9.0 mm, and 40.0 mm x 15.0 mm x 12.0 mm.

Clinical Trial—Original Technique
A clinical trial involving 20 client owned dogs was planned. Suitable patients were those presented with lameness due to failure of the CCL that would otherwise have been treated by TPLO. Following receipt of informed consent for surgical treatment by TPLO, the owners were offered the possibility of treatment by MMP. Following further discussion specifically about MMP and its novelty, additional informed consent was obtained from owners. No incentives, financial or otherwise, were offered or given to owners considering MMP.

Surgery was performed as previously described for the cadaver stifles, but with several additions. A single intramuscular injection of antibiotic was given just before first skin incision (clavulanate potentiated amoxicillin 12.5 mg/kg) and wound closure was done by simple continuous suturing of the fascia and subcutis using 3 m glycolide-dioxanone followed by a single, continuous skin suture (simple continuous or Ford interlocking pattern) using 2 m monofilament nylon 2 m.

FIGURE 3 Prototype instruments were manufactured and tested on cadavers. This cadaver surgery image is analogous to the illustration in Figure 2 and shows the tibial tuberosity saw guide in position on the tibia. A long pin at the proximal end of the guide is passed caudal to the straight patella ligament and a second pin abuts the cranial tibial cortex. The guide is fixed with a 3.5 mm drill placed into the cranial tibial diaphysis.

Clinical Trial—Modified Technique
Remarkably, similar tibial diaphyseal fractures occurred within 2 wk of surgery in two of the first six dogs operated upon (Figure 4). The surgical technique was modified such that the 1.5 mm hole made to receive the tension band wire was repositioned approximately 10 mm distal to the center of the 3.5 mm drill hole (Figure 5). A further 20 dogs were treated using this single modification of the protocol.

Results
There were 12 Labrador retrievers, 6 mixed-breed dogs, 2 boxers, 2 Bernese mountain dogs, 1 bearded collie, 1 English springer spaniel, 1 German shorthaired pointer, and 1 rottweiler. Patient age
at the time of surgery was 5.87 ± 2.83 years (mean ± standard
deviation) (range 1.5–11 yr) and weight was 33.96 ± 6.53 kg (mean
± standard deviation) (range 21–44 kg). Sixteen dogs received a 9.0
mm wedge, seven dogs received a 12.0 mm wedge, and three dogs
received a 7.5 mm wedge.

Six dogs were treated using the original surgical technique and
20 were treated using the modified technique. At the 4 wk follow-
up examination, the function was judged acceptable in 24/26 (92%)
dogs and unacceptable in 2/26 (8%) dogs—almost identical
proximal tibial diaphyseal fractures occurred in these two dogs
and that was the cause of the unacceptable function. One fracture
was managed conservatively while the other was treated by open
reduction and fixation using a single, medially applied bone plate
and screws (Figure 4). The same minor complication was found in
4/26 (15%) dogs—a cranial displacement of the distal end of the
tibial tuberosity that was evident radiographically, but not detected
on clinical examination. The maximum displacement between the
distal end of the wedge and the caudal surface of the tibial
tuberosity was measured and found to be between 3 and 8 mm. In
each of these four dogs, the proximal end of the tibial tuberosity
remained in contact with the wedge, which was not displaced, and
there was no discernable loss of advancement. There were no
catastrophic complications.

Twenty-four dogs were presented for mid-term follow-up at
6–11 mo after surgery. Two dogs (7.7%) had died from causes
unrelated to the surgery, one road traffic accident and one
metastatic hemangiosarcoma. Full function was recorded in 20/26
(77%) dogs and acceptable function was recorded in 2/26 dogs
(7.7%). Two dogs, 2/26 (7.7%), could not be properly evaluated
because they were recovering from similar surgery to the other
stifle.

Discussion

MMP is the first veterinary clinical use of titanium foam. Titanium
has been widely used both in human and veterinary orthopaedics
mainly because of its osteoconductivity and excellent

![FIGURE 4](image-url) (A) Lateral radiograph showing a proximal tibial
diaphyseal fracture that occurred nine days after modified Maquet
procedure surgery; the fibula is intact and the wedge remains well
positioned. Two of six dogs treated using the initial technique
featuring a proximal tension wire hole suffered fractures, which
occurred without external trauma as the dogs rose from a squatting
position. The fracture morphology was similar in both cases with the
fracture line linking the 3.5 mm drill hole and spiralling proximally
through the 1.5 mm towards the exit point of the Kirschner wire in the
caudal cortex. (B) Eight wk, lateral follow-up radiograph of the
proximal tibial diaphyseal fracture shown in A. There is good bone
union following only conservative management, comprising limited
exercise and pain control.
biocompatibility when compared with other commonly used implant materials, for example 316LVM surgical stainless steel. The work of Fernandez-Fairen and others (2010) showed that Tantalum was a good bone-graft substitute in human tibial tuberosity advancement and the experience of the 26 MMP cases reported in this paper demonstrates similarly that titanium foam is effective at filling the bone void created when performing tibial tuberosity advancement in dogs. Typically, radiographic follow-up of veterinary fracture studies is made between 8 and 12 wk after surgery. In this series, radiographic follow-up was made after only 4 wk and this was informed by earlier work on dogs that showed deep growth of bone into the titanium foam material implanted in experimental dogs. Typically, radiographic follow-up of veterinary fracture studies is made between 8 and 12 wk after surgery. In this series, radiographic follow-up was made after only 4 wk and this was informed by earlier work on dogs that showed deep growth of bone into the titanium foam material implanted in experimental dogs. There was no clinical evidence of implant movement or other complication beyond this 4 wk radiographic review, but longer term studies, including projects involving postmortem implant recovery, are needed to confirm that titanium foam, when implanted in clinical patients, behaves exactly as predicted by the preclinical experimental animal studies. However, the short-term follow-up in these cases revealed clinical and radiographic signs consistent with the lack of inflammation, early bone ingrowth, and stability reported following experimental implantation of titanium foam.

Although this series of 26 dogs demonstrates that MMP is an effective method of achieving tibial tuberosity advancement in dogs, further work is needed to evaluate the long-term outcomes and to establish the range and rate of complications associated with the procedure. However, the incidence of complications was comparable with other TTA techniques. The impact of the two major complications was not onerous insofar as the tibial fractures were resolved without difficulty and without compromising the functional outcome. The four minor complications were not associated with clinical signs.

The original intention had been to rely upon existing TTA theory and established surgical planning methods to determine the amount of tibial tuberosity advancement required. However, that was not possible because, at that time, the techniques previously used had not been reported in the peer-reviewed literature in enough detail to allow their replication. Establishing the amount of tibial tuberosity advancement required has been considered an important part of TTA surgery. Abolition of the femoro-tibial shear force has been suggested to occur, in the loaded stifle joint, at a "crossover point," which is said to coincide with a patellar tendon angle of 90° to the tibial plateau. Although this suggestion appears to underpin the concept of TTA surgery and its presurgical planning in dogs, it derives largely from a two-dimensional mathematical model of the human knee, a model that has not been replicated in dogs. Similarly, its validity has been undermined to some extent by the findings of Apelt et al. (2007) who found that while the femoro-tibial shear force was abolished by tibial tuberosity advancement, the amount advancement needed varied considerably between the 10 cadaver limbs they studied: it was not predictably coincident with a patellar angle of 90°. Furthermore, a detailed, three-dimensional mathematical model of the canine stifle has been developed, described, and validated to a limited extent by data comparison and that work indicates that the caudal cruciate ligament is not loaded at any point during the stance phase suggesting that a biomechanically relevant "crossover" point might not exist in dogs casting some doubt upon the validity of the notional ninety-degrees end-point for TTA surgery. In relation to the biomechanical consequences of Maquet’s original osteotomy on the human knee, Besette and Hunter (1988) observed that the operation created a caudally, (posteriorly) directed vector femoro-tibial shear force due to the redirection of quadriceps pull and it is possible that the clinical benefit seen with TTA in the dog also arises simply from the

FIGURE 5 Lateral radiograph taken 4 wk after modified Maquet procedure surgery showing uncomplicated healing. Following the complication illustrated in Figure 4, the wire position was changed—the distal hole for the tension band wire was made somewhat distally to the end of the osteotomy to minimise the risk of creating linked stress-risers. The later twenty dogs of the series were treated using this modification and no more tibial diaphyseal fractures were seen.
more caudally redirected quadriceps pull and is not necessarily related to an extrapolation of the crossover point hypothesis.2 The dog after TTA will retain the potential to vary, separately, the magnitude of the quadriceps pull, and its hamstring antagonism. Consequently, there is potential for application of a variable femoro-tibial shear force that could stabilize the stifle joint, during motion, in response to proprioceptive and other neural input. There is a clear need for further detailed biomechanical research to better understand the function of the cruciate-deficient stifle and the impact of tibial tuberosity advancement. In the meantime, care must be taken to avoid the mistaken assumption that the reported favorable clinical outcomes necessarily validate the theoretical assumptions.

Notwithstanding the above, and recognizing that previously used methods have been associated with consistent clinical success, the presurgical planning technique used in this series was informed to a large extent by existing methods. A significant difference in the method used in this series was the reliance on tibial landmarks exclusively, thereby eliminating variations arising from the unpredictability arising from the use of a stifle radiograph.14,15 For example, drawing the line F–G (Figure 2) at 135° reflects the use of a 135° extended stifle radiograph; the line F–I reflects the notional end-point of a patellar angle perpendicular to the tibial plateau, and F–G was taken to represent the resultant direction of quadriceps pull. The distance H–J was assumed to be the difference between the “existing” and notional end-point of a ninety-degree patellar tendon angle and, therefore, similar to the required tibial tuberosity advancement. The length increase between J–H and F–M is a cosine ratio, which reflects the correction described by Echteparaborde et al. (2011).39 This novel radiographic method was employed without incident or need for modification. Inasmuch as a good, short-term clinical outcome was seen in most cases, and that none of the complications were attributed to over or under advancement of the tibial tuberosity, the method appears effective. Further study to determine inter and intra-observer variability using this radiographic method is in progress and additional investigation, perhaps involving in-vitro mechanical modeling, will be needed to fully evaluate and validate this estimating technique.

Before its use on patients, careful consideration was given to safety and ethical aspects of the surgery and an independent senior veterinary orthopaedic surgeon reviewed the proposed clinical trial. MMP is a modification of TTA, which is an already well-established veterinary surgical technique, and the use of chemically pure titanium as an implantable biomaterial is well established in both human and veterinary surgery so this work was considered to be a reasonable clinical treatment. Nevertheless, prior to use in veterinary patients, an independent, specialist veterinary histopathologist reviewed numerous sections of titanium foam implanted in bone that had been produced during earlier trials involving experimental animals (T. J. Whitbread, BSc, BVSc, MRCVS, Dip ECVP, oral communication, 2009).24,26,40 Additionally, titanium foam wedges were examined by electron microscopy and subject to analysis by energy-dispersive X-ray analysis, which confirmed that the implants were indeed formed from chemically pure titanium with no evidence of inclusion or contamination (E. A. Charles, BSc, PhD, FI Corr, CChem, MRSC, NACE International and Newcastle University, written communication, 2009).40,41,42

Tibial diaphyseal fractures occurred as a complication in two of the first six cases. The fractures occurred within 3 wk of surgery and without external trauma, apparently as the dog rose from squatting to urinate/defecate. The fracture morphology was remarkably similar between the two cases—a fracture line connected the two drill holes made at surgery (3.5 mm hole at the end of the osteotomy and the 1.5 mm hole accommodating the tension band wire) and spiraled proximally towards the exit point of the Kirschner wire on the caudal cortex of the tibia. The fibula remained intact. This fracture morphology is consistent with a torsional force applied relative to the long axis of the tibial diaphysis. With the paw planted firmly on the ground and the stifle flexed, the femur has the potential exert considerable torsional forces on the tibial diaphysis, which has been weakened by the drilling of holes. With the three drilled holes, lined-up and close together, acting as connected “stress-risers,” it is likely that this tibial torsional force caused these fractures. Subsequently, a more distally placed wire hole was used and the complication was not seen again. Longer term studies involving large numbers of patients will be needed to determine with confidence that this technical modification has resolved the problem.

In four dogs, a cranial displacement of the distal tibial tuberosity was discovered during the 4 wk radiographic examination. This complication was not detected on orthopaedic examination, neither was it associated with any additional lameness or discomfort. The existence of this complication prompted consideration of the use of larger (1.2 or 1.5 mm) wires and the use of a double wire technique. Further work is needed to investigate the effect of wire size and wiring technique on the incidence of this minor complication. The degree of cranial displacement of the distal tibial tuberosity was similar, modest, and, apparently, self-limiting in all four cases. The biomechanics of the stifle altered by TTA procedures are poorly understood and it is not certain whether the modest and, apparently, self-limiting extent of this cranial displacement is related to the preservation of distal soft tissues that is an integral part of the surgical technique, or
whether it is a genuinely biomechanically self-limiting displace-

In dogs, TTA surgery has involved the use of a titanium cage “spacer” with a complex plate and screw fixation. The original Maquet procedure used no implants and subsequent papers reviewing Maquet’s technique found that when others modified the technique by using implants, this was associated with increased rates of complication. This information influenced the decision to use a pin and wire fixation technique for this MMP in dogs. At the time, it was felt that leaving the osteotomy unsupported was inappropriate and that pin-and-wire was the least intrusive implant that was likely to be effective. Subsequent to this preliminary consideration, the work of Echteparaborde et al., in relation to the Modified Maquet Technique, has shown that an implant-free tibial osteotomy in dogs can be achieved, though the necessary osteotomy is relatively much longer than that proposed by Maquet.

Both TPLO and TTA are associated with significant risks of minor and major complication. Major complications were encountered in 2/26 (8%) of the cases in this short series and it seems that these 2 complications were related to a specific technical/design error associated with the original surgical technique. The incidence of complication associated with MMP cannot be inferred with any certainty from this small number of cases, but the data presented here suggest that complication rates are unlikely to be unduly high and, as such, MMP is worthy of further investigation.

While many surgeons consider stifle arthrotomy and meniscal inspection/surgery to be an essential part of the surgical management of the cruciate deficient stifle, this practice is not universal and it was not performed in these dogs. Functional CCL failure was diagnosed on the basis of clinical signs and history (including a positive cranial draw test) consistent with CCL failure as well as exclusion of other potential causes of pelvic limb lameness by clinical and radiographic examination. Lameness that might have been caused by late meniscal injury was not recognized in this short series, but that probably reflects nothing more than the relatively short follow-up period and the small number of dogs studied, and it would be a mistake to infer that MMP protects against lameness due to late meniscal injury. Further study is needed to define the incidence of lameness due to late meniscal injury following MMP surgery and, similarly, there is a need to determine precisely the benefit, or otherwise, of arthrotomy and meniscal surgery as an adjunct to MMP surgery in dogs.

Implant-associated infection was not encountered. Titanium is one of the most biocompatible of metals and the open pore structure of the foam provides free access for tissue fluids and vessels, which mitigates the risk of infection.

Conclusion

The results of this small, preliminary study suggest that MMP is an effective and relatively simple method of achieving TTA in the dog. This is the first clinical application of Titanium foam, and this study supports the use of this novel biomaterial in orthopaedic surgery.

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REFERENCES


FOOTNOTES

a Synulox; Pfizer Ltd, Kent, United Kingdom
b Biosyn; Covidien LLC, Mansfield, MA
c Monosof; Covidien LLC, Mansfield, MA
d Ethilon; Johnson and Johnson Medical Ltd, Wokingham, UK
e Metacam; Boehringer Ingleheim UK, Berkshire, United Kingdom

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