

Effects of a magnesium adhesive cement on bone stability and healing following a metatarsal osteotomy in horses

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Objective—To compare biodegradable magnesium phosphate cement (Mg-cement), calcium phosphate cement (Ca-cement), and no cement on bone repair, biocompatibility, and bone adhesive characteristics in vivo in horses.

Animals—8 clinically normal adult horses.

Procedures—Triangular fragments (1-cm-long arms) were created by Y-shaped osteotomy of the second and fourth metatarsal bones (MTII and MTIV, respectively). Fragments were replaced in pairs to compare Mg-cement (MTII, n = 8; MTIV, 8) with Ca-cement (MTIV, 8) or with no cement (MTII, 8). Clinical and radiographic evaluations were performed for 7 weeks, at which time osteotomy sites were harvested for computed tomographic measurement of bone density and callus amount, 3-point mechanical testing, and histologic evaluation of healing pattern and biodegradation.

Results—All horses tolerated the procedure without clinical problems. Radiographically, Mg-cement secured fragments significantly closer to parent bone, compared with Ca-cement or no treatment. Callus amount and bone remodeling and healing were significantly greater with Mg-cement, compared with Ca-cement or no cement. Biomechanical testing results and callus density among treatments were not significantly different. Significantly greater woven bone was observed adjacent to the Mg-cement without foreign body reaction, compared with Ca-cement or no cement. The Mg-cement was not fully degraded and was still adherent to the fragment.

Conclusions and Clinical Relevance—Both bone cements were biocompatible in horses, and Mg-cement may assist fracture repair by osteogenesis and fragment stabilization. Further studies are warranted on other applications and to define degradation characteristics. (*Am J Vet Res* 2007;68:370–378)

Treatment of fractures in horses is still challenging despite substantial improvements in osteosynthesis in horses.¹ Fractures that do not heal or have delayed healing are problematic and afflict horses undergoing fracture repair.¹ In horses, fractures can be a substantial cause of morbidity caused by complexity and extensive soft tissue damage.² Optimal fracture healing restores the original bone integrity and strength and is accomplished by an active interaction between osteocytes, osteoclasts, and osteoblasts that is well regulated by biological signals^{3,a}; these signals are dependent on sufficient vascularization and mechanical loading at the fracture site.⁴ Delayed bone healing is associated with traumatic accidents,³ infection,^{3,4} and concomitant dis-

ABBREVIATIONS

MTII	Second metatarsal bone
MTIV	Fourth metatarsal bone
Mg-cement	Magnesium phosphate cement
Ca-cement	Calcium phosphate cement

ease^{5,6} that may alter the local environment. Horses are prone to delayed or nonunion healing of their inherently dense brittle bones because many fractures are high-energy injuries and frequently associated with comminution and extensive soft tissue damage. Further complicating factors are the low osseous blood supply and the necessity for immediate loading after treatment.

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Although surgical fracture repair is well established in fracture management,⁷⁻⁹ many types of bone injuries exceed the natural capacity for bone healing. Existing repair methods yield imperfect or slow healing in many fractures.

Historically, human and veterinary surgeons used bone grafts exclusively for augmentation of fracture repair, bone replacement, or substantial bone loss in fracture sites.¹⁰⁻¹⁴ In human medicine, bone grafting has become the second most common transplantation procedure, with 2.2 million/y worldwide.^{15,16} These grafts enhanced bone healing by their osteogenic, osteoinductive, and osteoconductive capacity and provide mechanical support.^{17,18} However, donor site morbidity and limited availability¹⁹ initiated the search for appropriate alternatives and led to the development of biocompatible bone fillers and cements.²⁰⁻³¹ In the past decade, the clinical application of bone fillers and cements as bone substitutes in trauma and orthopedic surgery became established, and their use has increased exponentially.³²⁻³⁹ Particularly, calcium phosphate compounds, including tricalcium phosphate,^{40,41} tricalcium sulfate,^{42,43} and hydroxyapatite,^{33,44-48} have been intensively investigated over the last few decades. Calcium phosphate and tricalcium sulfate bone fillers and cements are considered to be highly biocompatible,⁴⁹ osteoconductive, and biodegradable.⁴¹ Several products in different formulations are commercially available, including blocks,⁴⁵ granules,⁴⁵ and self-setting injectable pastes.^{27,29,32,34,50-52} Further, injectable calcium-based pastes are currently being investigated as delivery vehicles for proteins into fractures.⁵³ However, their slow absorption rate and nonadhesive qualities do not offer any advantage to bone healing other than to serve as a carrier for other materials that may promote bone formation and to provide a scaffold for bony ingrowth. Biomechanically, available cements have sufficient strength under compression, but are weak under tension.^{50,54}

The desire of surgeons for alternatives to simplify the procedures of restoration and avoid follow-up surgeries to remove mechanical devices has resulted in development of a variety of synthetic (epoxide, polyurethane, and cyanoacrylate) and biological (fibrin) bone adhesives.^{55,56} Focus is currently placed on the development of adhesives based on peptides,⁵⁷ oligo- and polylactates,^{58,59} and alkylene bis(dilactoyl)-methacrylate.⁶⁰ However, despite intensive efforts, a clinically applicable bone glue is not available.⁵³ The application has consistently failed as a result of incompatibility between material and the biological and biomechanical conditions within the body system.^{55,56,61}

There is some indication that magnesium-based implants may promote bone formation, and magnesium-based alloys are being studied as orthopedic biomaterials.^{62-64,b} Use of magnesium as the principal component of a bone filler and cement may also be less prone to other complications associated with a calcium-based biomaterial, such as the activation of clotting.^c Recently, a magnesium-based biomaterial formulation had an increased adherence to bone, tendon, and stainless-steel implants, compared with similar calcium-based bone fillers or no cement.^{c,d}

The purpose of the study reported here was to evaluate a novel biodegradable, magnesium-based in-

jectable bone filler for biocompatibility and effectiveness in promoting bone healing following a metatarsal osteotomy in horses. We hypothesized that direct, in situ delivery of a magnesium-based bone filler, appropriately administered to a surgically created metatarsal fracture, would adhere bone fragments to the parent bone and support healing of the fracture in an accelerated and clinically safe manner.

Materials and Methods

Animals—Eight clinically normal female adult horses of various breeds (median age, 9.6 years; range, 6 to 17 years) were included in the study. Horses were considered healthy on the basis of physical examination findings and CBC determination and were sound at the walk and trot with no palpable or radiographic abnormalities of the metatarsal bones. Each horse was housed in an individual box stall (5.7 × 5.7 m) 5 days prior to surgery until termination of the study at 7 weeks. The institutional laboratory animal care and use committee approved the study protocol.

Experimental design and procedure—Horses (n = 8), hind limbs (2 limbs/horse), and MTII or MTIV (4 metatarsal bones/horse) were assigned in a nested paired design to receive Y-shaped osteotomies in which triangular fragments with 1-cm-long arms were created for a total of 32 metatarsal bones (Figure 1). One MTII and MTIV of each horse (16 total metatarsal bones) were assigned Mg-cement treatment consisting of monopotassium phosphate (54%), magnesium oxide (33%), tricalcium phosphate (9%), and C₁₂H₂₂O₁₁ (4%).^c The contralateral metatarsal bone was treated with either Ca-cement^f (8 MTIV) or received no treatment (8 MTII; served as untreated control).

Triangular fragments of MTII and MTIV were created on the plantar surface under general anesthesia at day 0 (Figure 1). Horses received antimicrobials (procaine penicillin, 22,000 IU/kg, IM; gentamicin sulfate, 6.6 mg/kg, IV) and analgesics (phenylbutazone, 4.4 mg/kg, IV) 30 minutes prior to anesthesia. Horses were sedated with xylazine hydrochloride (1.1 mg/kg, IV), induced with ketamine hydrochloride (2.2 mg/kg, IV), and maintained in dorsal recumbency under anesthesia by use of isoflurane (1% to 4%) vaporized in oxygen in a semiclosed system. The surgical site was aseptically prepared, and the metatarsal bones were approached through small 2-cm-long incisions made over the plantar palpable surface of the metatarsal bone 10 cm distal to the palpable head of MTIV and MTII. A curved spatula was placed under MTII or MTIV to protect adjacent bones, and a nitrogen-driven oscillating bone saw^g was used to create a triangular fragment (90° angle with 1-cm-long arms) by performing Y-shaped osteotomies. The bone saw removed a 1-mm-wide piece of bone. Incisions were flushed liberally with saline (0.9% NaCl) solution to remove bone dust, and the cut bone surfaces were blotted dry. Subsequently, the triangular piece of bone was press fit for 5 minutes back into the parent defect according to assignment. Metatarsi assigned to receive cement formulations, which were mixed according to recommendations of the manufacturer, and 1 mL of the cement was placed onto the cut bone sur-

face prior to replacing the triangular piece of bone. A routine closure of the incision was performed with 2-0 polyglactin 910 suture in a simple continuous suture pattern, followed by closure of the skin with a simple interrupted suture pattern with 2-0 nonabsorbable monofilament polypropylene suture; sterile bandages were applied, and horses recovered from anesthesia. After surgery, sterile bandages were maintained for 2 weeks and changed every other day. Administration of phenylbutazone (4.4 mg/kg, PO, q 24 h) and procaine penicillin (22,000 IU/kg, IM, q 12 h) was maintained for 3 days. Horses were housed separately in box stalls (5.7 × 5.7 m) and clinically evaluated twice daily until specimen harvesting at 7 weeks. Horses had ad libitum access to hay and water.

Clinical evaluation—Physical examinations were performed before (baseline) and after surgery twice daily until termination of the study. Variables included rectal temperature, heart rate, respiratory rate, gastrointestinal sounds, and digital pulses. After surgery, lameness evaluation at a walk (0 = no lameness; 1 = lame), inspection of the incision line (0 = no drainage; 1 = drainage), and measurement of the circumference (cm) of the metatarsal area to evaluate swelling were performed weekly. The same observers (MW and ALB) who were blinded to the treatment groups made all evaluations. Horses were euthanized at 7 weeks after

surgery by IV administration of an overdose of pentobarbital.^h Metatarsi were immediately harvested and frozen until further processing.

Radiography—Oblique radiographic views (dorso-medial-plantarolateral and dorsolateral-plantaromedial oblique views)ⁱ of the metatarsal bones were taken at weeks -1, 0, 1, 2, 4, 6, and 7. Radiographs were measured for fracture gap (mm), bone callus width (dorsoplantar, mm), and length (proximodistal, mm) and scored by 2 investigators (MW and ALB) who had no knowledge of time or treatment. Scores (0 = none to 4 = most) were assigned for bone remodeling and bone healing. Bone remodeling was defined as the amount of bone irregularity on the surface of the osteotomy site and fragment and the amount of decrease in the distinction of interface between parent bone and fragment. Bone healing was defined as the amount of bone at the osteotomy site, overall stable appearance of the fragment, bony bridging around the fragment, and bone filling of the fracture gap.

Quantitative computed tomographic evaluation—Quantitative computed tomography^j of the distal portions of the limbs was performed at 1-cm intervals for identification of soft tissue abnormalities. Subsequently, metatarsal bones were cleaned of soft tissue and scanned in sagittal sections at 1-mm-thick slices from medial to lateral and from 1 cm proximal to 1 cm distal to the callus to determine area and density of mineralized callus. Quantitative computed tomography is a reliable, noninvasive method for estimating bone mineral density and bone material properties.⁶⁵⁻⁶⁷ The central sagittal slice of the metatarsal scans that transected the fragment was selected as the region of interest and traced for quantitation of bone density and size of the fracture gap, bone fragment, and bone callus. For density measurements, each slice was standardized for x-ray attenuation differences by use of potassium phosphate standards. Therefore, Hounsfield unit density values were converted to dipotassium phosphate-equivalent density values.⁶⁵⁻⁶⁷

Biomechanical testing—Ends of metatarsal bones were secured and tested quasistatically to failure in 3-point bending (1.5 mm/s) by use of a servohydraulic materials testing system (Figure 2).^k Bones were positioned in the jig to ensure equivalent bending for right and left bones. Peak load to failure (N) and cross-sectional diameter (mm²) were recorded, and calculations were made for peak stress to failure (N/mm²).

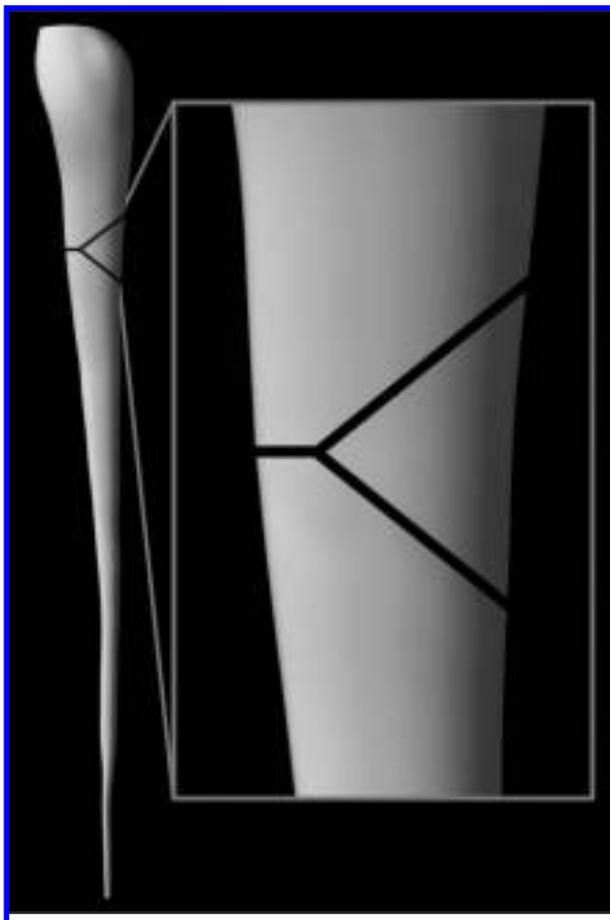


Figure 1—Illustration of a Y-shaped osteotomy performed on the plantar aspect of equine MTII and MTIV, resulting in a triangular wedge of separated bone that mimics a comminuted fracture.

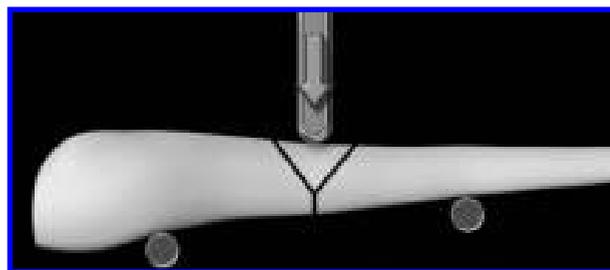


Figure 2—Illustration of biomechanical testing of an equine MTII and MTIV in 3-point bending. Peak load to failure (N) and area at the site of failure (mm²) were recorded. Peak stress to failure (N/mm²) was calculated.

Histologic preparation and evaluation—After mechanical testing, metatarsal bones were harvested 30 mm proximal and distal to the surgical site and longitudinally halved. Specimens were fixed in 70% ethanol, dehydrated in graded concentrations of alcohol, and embedded undecalcified in polymethylmethacrylate. Undecalcified bone blocks were sectioned^l (10 μ m thickness) in the longitudinal sagittal plane, stained with Masson trichrome stain, and evaluated by 3 investigators (MW, ALB, and SEW) who were blinded to the treatment group. The osteotomy area was evaluated for tissue type in the fracture gap and adjacent to the fragment, the presence or absence of Ca-cement or Mg-cement, and the location of cement.

Sections were scored by the same 3 investigators (0 = none to 4 = most) for inflammation in the healing tissue, amount of new bone in the fracture gap, and osteoclastic osteolysis of the fragment. Histologic evidence of inflammation was defined as the presence of neutrophilic, giant, or mononuclear cells in the fracture gap or in the tissue adjacent to cement or fragment.

Statistical analysis—A 2-factor ANOVA (factor 1 = treatment; factor 2 = time) with a least significant difference post hoc test was used to analyze serial objective

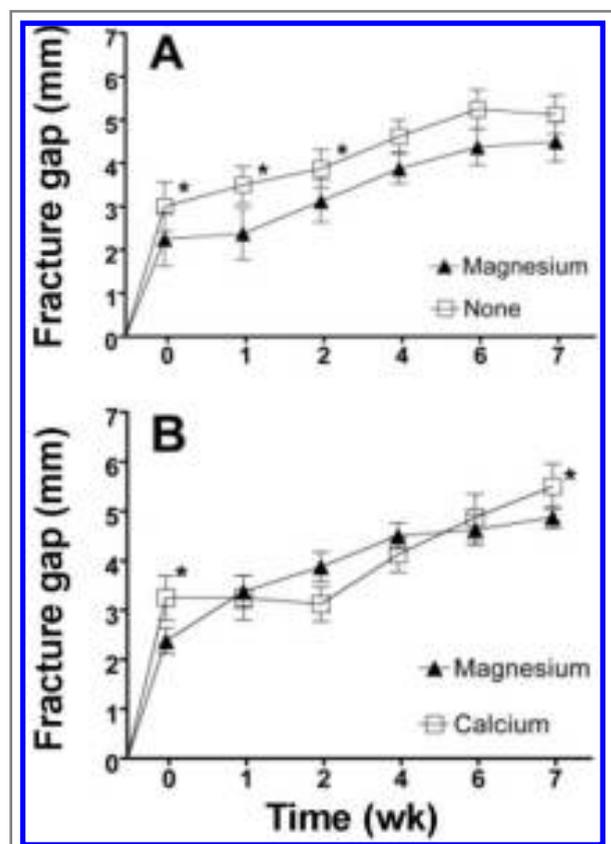


Figure 3—Fracture gap over time in horses with metatarsal osteotomy sites treated with Mg-cement, compared with no treatment (A) and Ca-cement (B). Fracture gap, as measured from radiographs, significantly ($P < 0.05$) increased with time for all treatment groups. *Significantly ($P < 0.05$) closer secured fragment to parent bone in the Mg-cement treatment group, compared with the no-treatment or Ca-cement treatment group, at indicated times.

data (fragment migration and callus formation) from the Mg-cement group and compared with data from the Ca-cement group or no-treatment group.^m Single objective data obtained after termination of the study, such as 3-point bend testing, quantitative computed tomography measurements, and histologic evaluation results, were analyzed by use of a paired t test.ⁿ Scored data (bone remodeling and healing) were expressed as median and range values and analyzed by use of the Mann-Whitney U rank test. Differences were considered significant at $P < 0.05$.

Results

Clinical evaluation—Eight horses successfully had triangular metatarsal osteotomies and completed the 7-week study. Horses were not lame at any time point following surgery as estimated by lameness score (median, 0; range, 0). Physical examination variables remained within reference ranges throughout the study. Incisions healed primarily without swelling or drainage (median, 0; range, 0), and no difference was found between treatments.

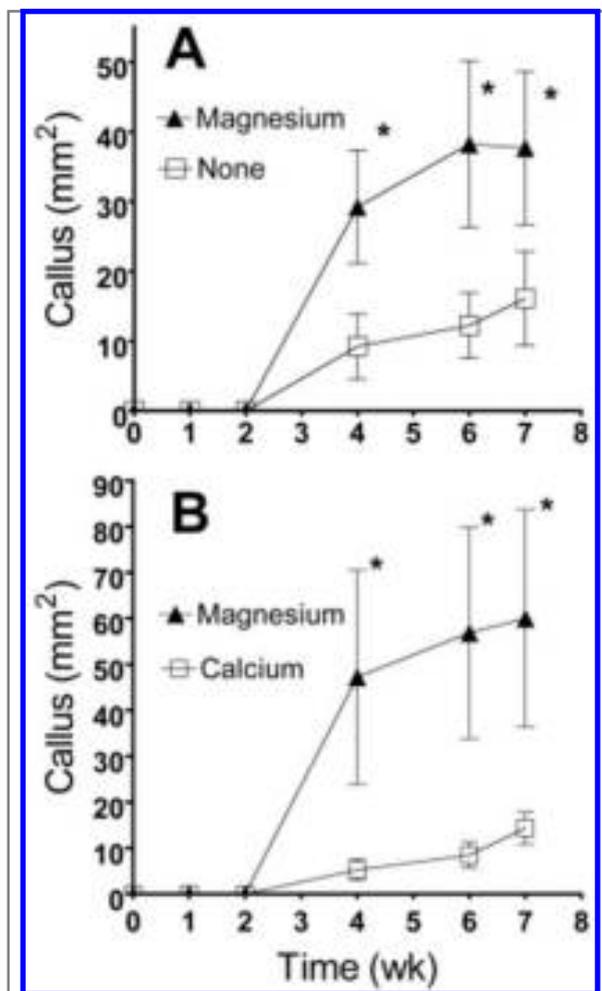


Figure 4—Bone callus formation over time in horses with metatarsal osteotomy sites treated with Mg-cement, compared with no treatment (A) and Ca-cement (B), as measured from radiographs. *Significantly ($P < 0.05$) greater bone callus formation in the Mg-cement treatment group, compared with the no-treatment or Ca-cement treatment group, at indicated times.

Radiographic evaluation—The Mg-cement secured the fragment significantly closer to the parent fragment bed than either no treatment ($P = 0.004$) or the Ca-cement ($P = 0.029$). Post hoc test results revealed this effect to be significant in the no-treatment group immediately after surgery at week 0 ($P = 0.029$) and at weeks 1 ($P < 0.001$) and 2 ($P = 0.001$), and the Mg-cement-treated fragment remained closer to the parent bone at all subsequent time points (Figure 3). In the Mg-cement group, the bone fragment was significantly closer to the parent bone immediately after surgery at week 0 ($P = 0.003$) and at week 7 ($P = 0.027$). New bone callus was significantly greater in the Mg-cement group than in the Ca-cement group ($P = 0.002$) and no-treatment group ($P = 0.006$). Significant formation of bone occurred by 4 weeks and persisted through 7 weeks in the Mg-cement group (Figure 4). Radiodense material was identified in the fracture gap between the fragment and

parent bone in the Mg-cement group more frequently and for greater duration, compared with the Ca-cement group. Bone remodeling score was greater in the Mg-cement group than in the no-treatment group ($P = 0.010$) or Ca-cement group ($P = 0.041$), except for week 2 (Figure 5). Bone healing score was significantly greater in the Mg-cement group, compared with the no-treatment group ($P = 0.024$), at all time points and at weeks 4, 6, and 7, compared with the Ca-cement group ($P = 0.005$; Table 1).

Quantitative computed tomography and biomechanical testing—On quantitative computed tomography, no abnormal mineralization was observed in the adjacent soft tissue, specifically in the suspensory ligament, tendons, or surrounding skin. Amount of bony callus was greater in the Mg-cement group, compared with the no-treatment group ($P = 0.014$) and Ca-cement group ($P = 0.024$). No difference was found in fragment or callus density or fragment size among treatments (Table 2). During biomechanical testing, peak load to failure and stress were not different among treatments (Table 3).

Qualitative histologic evaluation—Magnesium-based material was detectable in a greater number of metatarsal bones (94%) than was calcium-based material (25%; $P < 0.001$). Tissue type adjacent to the fragments, material, and parent bone was either mature fibrous tissue or bone (Figure 6). Inflammatory cells or granulomatous response (influx of giant cells) was not evident in any of the treatments. A greater amount of new bone was scored within the fracture gap in the Mg-cement group, compared with the

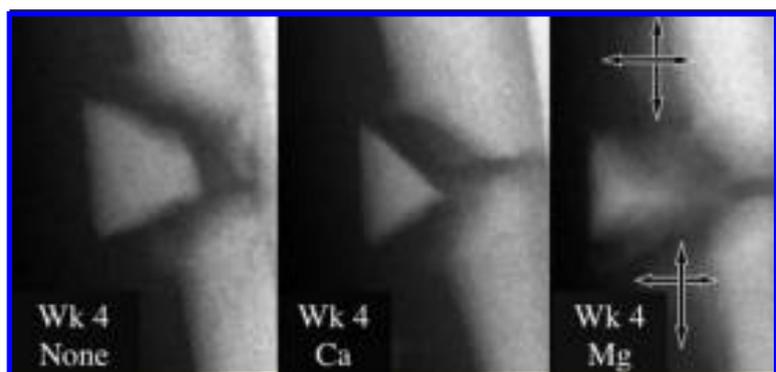


Figure 5—Representative radiographic images of 4-week-old metatarsal osteotomy sites in horses. Notice the greater bone callus (arrows indicating length and width of new bone), bone remodeling activity, and healing with Mg-cement treatment, compared with no cement treatment or Ca-cement treatment. None = No cement treatment. Ca = Ca-cement treatment. Mg = Mg-cement treatment.

Table 1—Mean (range) healing scores* of metatarsal osteotomy sites over time in 8 horses.

Treatment pair	Time after osteotomy (wk)				
	1	2	4	6	7
Mg-cement	1.12 (0.5–2.0)†	2.12 (1.5–3.0)†	2.56 (1.5–4.0)†	2.37 (1.0–4.0)†	2.62 (1.0–4.0)†
No cement	0.25 (0.0–1.5)	0.56 (0–1.0)	0.93 (0–2.0)	0.93 (0–1.5)	1.62 (0–4.0)
Mg-cement	0.81 (0.0–1.5)	1.37 (0–2.5)	1.17 (0.5–4.0)†	2.18 (1.0–4.0)†	2.0 (1.0–3.5)†
Ca-cement	0.43 (0.0–1.0)	0.75 (0–1.5)	0.87 (0–2.0)	0.68 (0–2.0)	0.5 (0–2.0)

*Healing scores: 0 = no healing to 4 = most. †Significantly ($P < 0.05$) greater in Mg-cement treatment, compared with contralateral metatarsal bone with no cement treatment or Ca-cement treatment.

Table 2—Mean \pm SD quantitative computed tomography measurements obtained for metatarsal osteotomy sites in 8 horses at week 7 after the procedure.

Treatment pair	Measurement			
	Fragment size (mm ²)	Fragment density (PPED)	Callus area (mm ²)	Callus density (PPED)
Mg-cement	18.25 \pm 19.19	1,061.70 \pm 166.53	8.50 \pm 8.50*	528.73 \pm 230.67
No cement	13.00 \pm 10.05	966.79 \pm 176.05	2.37 \pm 1.9	457.00 \pm 311.45
Mg-cement	18.75 \pm 8.63	1,107.70 \pm 108.15	9.62 \pm 12.88*	584.37 \pm 96.97
Ca-cement	19.00 \pm 11.04	1,049.30 \pm 138.56	5.12 \pm 4.05	528.99 \pm 125.67

*Significantly ($P < 0.05$) greater value for Mg-cement treatment, compared with contralateral metatarsal bone with no cement treatment or Ca-cement treatment.
PPED = Dipotassium phosphate–equivalent densities.

no-treatment group ($P = 0.003$) or Ca-cement group ($P = 0.006$). New woven bone, without evidence of necrosis, was evident directly adjacent to the magnesium-based material, firmly bonded to the fragment, and integrated in the parent bone. Calcium-based material when observed was integrated in the parent bone callus. Osteoclastic bone resorption was greater in the no-treatment group, compared with the Mg-cement group ($P = 0.022$).

Table 3—Mean \pm SD biomechanical failure measurements obtained for metatarsal osteotomy sites in 8 horses at week 7 after the procedure.

Treatment pair	Measurement	
	Peak load to failure (N)	Peak stress to failure (N/mm ²)
Mg-cement	174.39 \pm 107.86	1.124 \pm 0.6467
No cement	220.26 \pm 118.21	1.356 \pm 0.2948
P value	0.200	0.200
Mg-cement	394.47 \pm 162.92	1.774 \pm 0.4952
Ca-cement	330.30 \pm 261.80	1.500 \pm 0.8879
P value	0.240	0.240

Discussion

To our knowledge, our study is the first in which this novel biodegradable magnesium-based injectable bone filler was used to assist fracture repair in vivo. Our study compared this magnesium-based material with a biodegradable calcium phosphate material that is commercially available and has similar appearance as well as handling and hardening characteristics. Our clinical and histologic data indicate that the magnesium-based material does not result in any adverse reactions within the bone repair site or adjacent soft tissue. Neither calcium- nor magnesium-based material incited an excessive inflammatory reaction and the body did not wall off the materials, which were reported in an earlier study⁶⁸ on calcium phosphate.

In the Mg-cement group, mature woven bone or fibrous tissue was the anticipated tissue type in the early phase of bone healing and was more abundant, although not excessive, and in close proximity to or within the cement material. Consistently, the magnesium-based material persisted and remained at the site for ≥ 7 weeks. The calcium-based material was less fre-

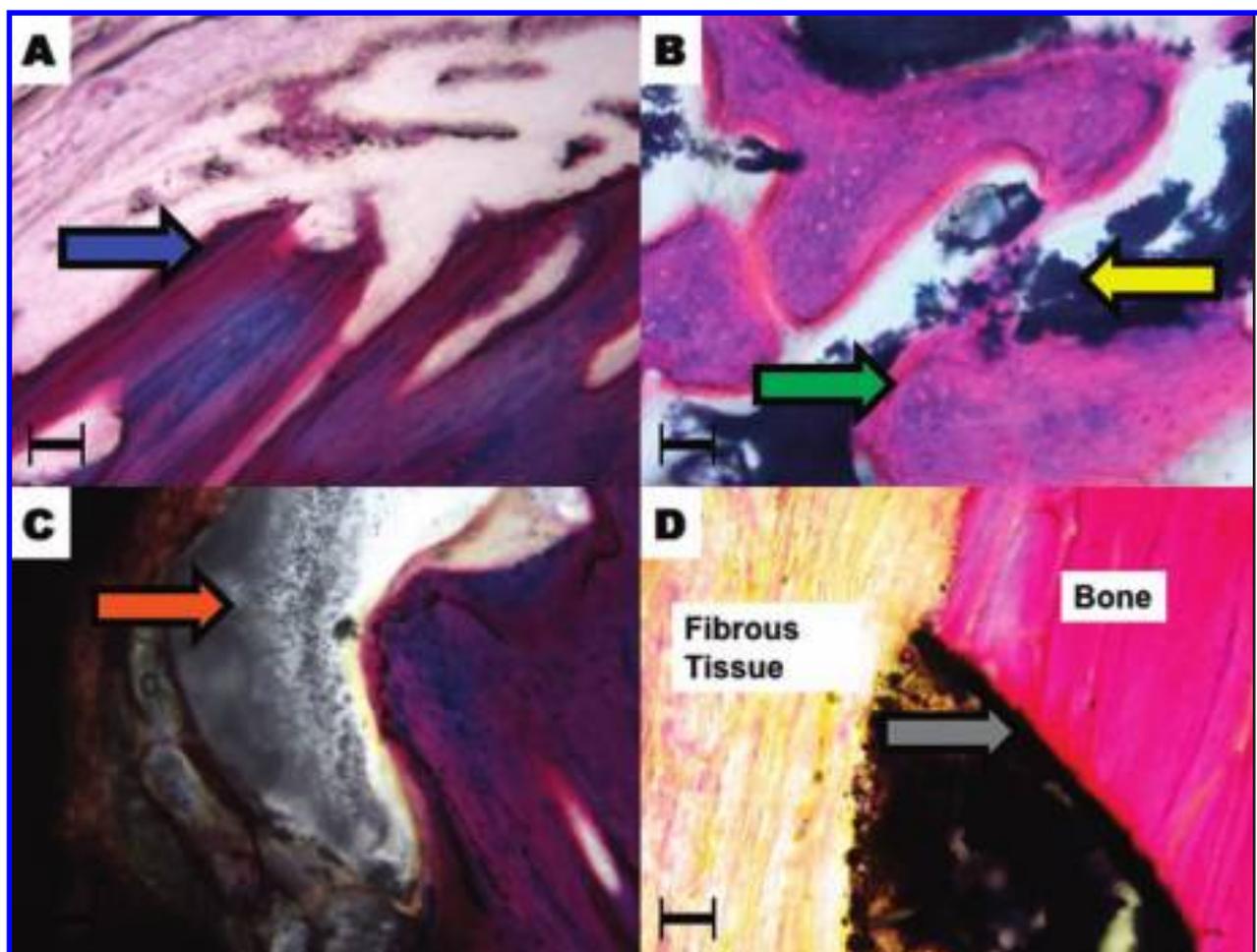


Figure 6—Photomicrographs of sections of fracture gaps in horses at week 7 after metatarsal osteotomy. Notice the osteotomy site (blue arrow) with no cement (A), new woven bone (green arrow) directly adjacent to Mg-cement (yellow arrow; B), new woven bone directly adjacent to Ca-cement (orange arrow; C), and Mg-cement directly bonded (gray arrow) to the bone fragment (D). The direct attachment of the Mg-cement to the bone fragment is apparent at 7 weeks. Adjacent fibrous tissue and bone is without evidence of granulomatous foreign body reaction, osteolysis, or sequestration suggesting in vivo biocompatibility. Masson trichrome stain; bars = 100 μ m.

quently evident grossly or histologically (2 specimens). Calcium-based material most likely migrated from the site or was, contrary to results of an earlier study,⁴¹ absorbed by 7 weeks. Published data suggest an absorption time of ≥ 24 weeks for calcium phosphate materials.⁴¹ Studies over a longer time frame would need to be conducted to evaluate degradation. Results of a study^o on different magnesium-based formulations revealed an 18-week degradation time for pin implantation in guinea pigs. In general, it is anticipated that magnesium-based materials will degrade more rapidly than corresponding calcium phosphate materials, which typically take 6 months.⁴¹ The study^p of bone healing following a metatarsal osteotomy provides an effective means to quantify bone production in weight-bearing horses. A study⁶⁹ on similar metatarsal fracture gaps has been performed in horses. The ability to isolate this bone radiographically permits reliable serial assessment of healing, and quantitative computed tomography permits verification of uniformity of fractures and fracture location. Evaluation of our data confirmed creation of equally sized fragments (on the basis of lack of a significant difference in computed tomography measurements of fragment size) and supported a standardized surgical technique. Our sample size was sufficient to identify differences, and the ability to use each horse as its own control animal decreased variability among treatments and increased statistical power.

Handling characteristics of both materials were good. Mixing was easily accomplished and hardening times were < 10 minutes for both materials. As anticipated with *in vivo* studies, control of bone-surface bleeding was often incomplete. It was immediately evident that the calcium-based material did not provide adhesion of the fragment to the site, but hardening provided some cementing of the fragment as a result of bone irregularities. It was observed that the hardened calcium-based material exposed to the surface could be flushed from the site by saline solution, so this was not performed. Magnesium-based material, once hardened, was not readily flushed from the site and immediately provided adhesion of the fragment to parent bone. Both materials hardened more slowly *in vivo* than in the mixing container. Our observations mimic a report⁷⁰ of clinical applications of Ca-cement in human medicine. Surgeons complain about poor injectability and intraoperative handling difficulties,⁷⁰ although few of the commercially available bone cements claim to be injectable.

In our study, radiographic and computed tomographic evaluation revealed better fragment anchoring and superior osseous integration, bone healing, and remodeling of the fracture site with the magnesium-based treatment. Radiographically, an increase in fracture gap formation occurred with time, even in the Mg-cement group that had a significantly smaller fracture gap. Histologically, this corresponded to separation within the substance of the magnesium-based material, not at the bonding sites with bone. Sufficient histologic evidence was available to determine that direct attachment of magnesium-based material to the fragment and the parent bone was still present.

Three-point bending testing of all metatarsi represented nonphysiologic loading; however, it is considered the most direct and accurate method to assess

the strength at osteotomy sites. The inability to detect significant biomechanical differences regardless of the treatment group may reflect incomplete healing at the osteotomy site because fracture lines were still present at the time of specimen harvesting. Additional studies on the effects of mechanical characteristics on the strength of magnesium-based material in torsion may assist in setting parameters for material failure and in determining appropriate *in vivo* uses. Biomechanical study of additional time points would be necessary to determine whether the greater and earlier bone callus translates to greater or earlier structural strength of the bone as expected. The greater fracture gap and separation in the calcium-based treatment are likely related to the lack of adhesion properties in these materials. Whereas the adhesive properties of magnesium-based material initially prevented fragment migration, ultimately, the bone fragment shifted as tissue (including bone) filled the defect. The increased bone remodeling and bone healing activity with osseous integration in the Mg-cement group support an osteogenic response related to the magnesium-based material. As a result of its functional roles and presence in the bone tissue, magnesium may have initiating effects on new bone formation.⁷¹⁻⁷³ Magnesium is essential in metabolism (cofactor for enzymes and stabilizes RNA and DNA), is naturally found in bone,⁶² and has osteoconductive bioactivity in implants (increased bone apposition and decreased time to form hard callus).^{62,64} Although a positive effect of magnesium has been seen on periosteal and endosteal bone formation and deposition of osseous callus has been observed, no effect on cancellous bone was reported in another study.⁶⁸

Bony callus was generally detectable radiographically at 4 weeks after surgery and was more prominent after Mg-cement application. Greater callus formation and fragment stability at the osteotomy site were determined for the Mg-cement group. On the basis of histologic evaluation, the increased distance between parent and fragment bone with time was likely caused by tissue growing into the fracture gap from the parent bone. Other potential explanations include breakdown in stability of the fragment; weight bearing and motion separating the bonding of the material, producing migration of the fragment; and the experiment terminating before complete bony union and callus maturation. It would be ideal and anticipated that greater bony callus would result in greater mechanical stability.⁷⁴ A longer-term study,⁷⁵ use of more standardized techniques (such as ulnar osteotomy in rabbits), or both may be necessary to determine that expected correlation. In concert, our data suggest that this Mg-cement may offer advantages *in vivo* over currently available Ca-cements. Novel *in vivo* properties that were identified in our study were the adherence to bone and osteogenesis. As with other available products, this Mg-cement was biocompatible in horses. Use of this product to support internal fixation, provide additional bonding of loose bone fragments in comminuted fractures, and provide a biodegradable biocompatible filler of bone void is supported by these data. Additional studies are warranted on other possible applications, including use as a delivery vehicle for bone graft, cell augmentation, growth

factor release, and antibiotic elution as well as serving as a biologic bonding material for implants to bone.

It is anticipated that the combination of adhesive bone cements, growth factors, and cells may provide the optimal formulation for acceleration of bone repair. These materials are expected to gain access to orthopedic trauma treatment in the near future and will provide an adjunct to the armamentarium of surgeons for bone repair.

Results of our study have revealed advantages of an *in vivo* application of a novel Mg-cement in horses with a metatarsal osteotomy, compared with a commercially available Ca-cement or no treatment. Both bone cements were biocompatible, demonstrated osseous integration, and thus were safe for use in equine bone repair. Greater fragment anchoring and bone healing and superior osteogenesis were observed in the Mg-cement group. Further studies are warranted on other applications and to define degradation characteristics. Use of this product to support internal fixation, provide additional bonding of loose bone fragments in comminuted fractures, and provide a biodegradable biocompatible filler of bone void is supported by the results of our study.

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