Comparison of hydroxyapatite-coated and uncoated pins for transfixation casting in horses

Timothy B. Lescun, BVSc, MS; Debra K. Baird, DVM, PhD; Laurinda J. Oliver, BVSc, MS; Stephen B. Adams, DVM, MS; Jan F. Hawkins, DVM; George E. Moore, DVM, PhD

Objective—To determine the extent to which a hydroxyapatite coating promotes pin stability in the third metacarpal bone during transfixation casting in horses.

Animals—14 adult horses.

Procedures—7 horses each were assigned to either an uncoated or hydroxyapatite-coated pin group. Three transcortical pins were placed in the third metacarpal bone of each horse and incorporated into a cast for 8 weeks. Insertion and extraction torque were measured, and torque reduction was calculated. Radiography was performed at 0, 4, and 8 weeks. Lameness evaluation was performed at 2, 4, 6, and 8 weeks. Bacteriologic culture of pins and pin holes was performed at pin removal.

Results—All horses used casts without major complication throughout the study. Insertion torque was higher in uncoated pins. There was no effect of group on extraction torque. Hydroxyapatite-coated pins had lower torque reduction. Five of 15 hydroxyapatite-coated pins maintained or increased stability, whereas all uncoated pins loosened. Pin hole radiolucency, lameness grades, and positive bacteriologic culture rates were not different between groups.

Conclusions and Clinical Relevance—Hydroxyapatite coating increased pin stability within the third metacarpal bone of horses during 8 weeks of transfixation casting but did not improve pin performance on clinical assessments. Clinical use of hydroxyapatite-coated transfixation pins may result in greater pin stability; however, further research is necessary to improve the consistency of pin osteointegration and elucidate whether clinical benefits will ultimately result from this approach in horses. (*Am J Vet Res* 2012;73:724–734)

Transfixation casting, a modified form of external skeletal fixation, has been used to treat distal limb fractures in horses, including open and comminuted fractures.[1–3] Horses treated with transfixation casting typically bear considerable weight on the affected limb as long as the construct remains stable.[3] A key limitation is that transfixation pins, similar to external fixation pins, invariably loosen over time because of osteoclastic bone resorption and fibrous tissue deposition at the BPI.[4] This occurs more rapidly in the presence of high bending loads,[3–5] such as those encountered with the weight of an adult horse. A study[1] of fractures treated with transfixation casting revealed that premature pin loosening occurred in 68% of cases, and approximately one-third of cases had pin loosening within 30 days after casting. Pin hole osteolysis and cortical ring sequestrum formation at the pin hole result in pin hole enlargement and may increase the risk of catastrophic fracture through the pin hole.[3,6,7] The high rate of premature pin loosening and the occurrence of serious pin-associated complications such as pin hole fracture are presently the primary limitations of transfixation casting in horses, restricting its use as a reliable method for treatment of distal limb fractures.

Abbreviation

BPI	Bone-pin interface

The weakness of both transfixation casting in horses and traditional external skeletal fixation used in other species, including humans, is the BPI.[8–10] Bone resorption and pin loosening result from mechanical and thermal damage to bone tissue during pin insertion as well as cyclic loading of pins and pin hole infection.[5,11] Both pin loosening and infection contribute to patient morbidity through loss of construct stability, pain, increased risk of catastrophic bone failure through an enlarged pin hole, and an eventual requirement for ad-

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From the Department of Veterinary Clinical Sciences, College of Veterinary Medicine, Purdue University, West Lafayette, IN 47907.
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Address correspondence to Dr. Lescun (tlescun@purdue.edu).

ditional surgery to replace pins, debride infected pin holes, or reconfigure fracture fixation. Premature pin loosening could be eliminated by enhancing pin stability within the bone. In addition, BPI stresses may be reduced in the case of a rigidly bonded (ie, osteointegrated) BPI, compared with a pin with a loose BPI,[12] potentially reducing the risk of pin hole fracture.

A variety of strategies have been developed to prevent implant loosening.[9,13–15] Among these, hydroxyapatite has been used as an external fixation pin coating to promote osteointegration and prevent pin loosening. Osteointegration occurs when bone at the BPI adheres directly to the coating surface, creating stability.[9,16,17] Hydroxyapatite coatings result in increased pin stability in humans and increase the extraction torque required to remove external fixation pins.[9,16,17] Reduced pin hole infection rates have also been found when hydroxyapatite-coated pins are used in human fracture patients.[16,18] To our knowledge, hydroxyapatite-coated external fixation pins have not been evaluated in horses.

A feasibility study[19] conducted on cadaveric equine third metacarpal bones compared temperature and insertion torque of 6.3-mm large animal transfixation pins prepared with 2 hydroxyapatite coatings. Pins with a solution-precipitated a biomimetic hydroxyapatite coating (thickness, approx 5 µm) performed similarly to uncoated stainless steel pins; this pin coating method was deemed suitable to evaluate in vivo without modifying standard transfixation pin drills and taps. Therefore, the purpose of the study reported here was to compare the same solution-precipitated biomimetic hydroxyapatite–coated pins with uncoated transfixation pins used in vivo in horses. Specifically, our objective was to determine whether the hydroxyapatite pin coating would enhance stability of pins in the third metacarpal bone of adult horses during an 8-week period of transfixation casting and to compare the clinical performance of horses in the hydroxyapatite-coated pin group with that of horses in the uncoated transfixation pin group. Our first hypothesis was that hydroxyapatite coating of transfixation pins would improve pin stability, as assessed with pin torque measurements, under full weight-bearing conditions, relative to uncoated pins during an 8-week period. We also hypothesized that the clinical features of lameness, radiolucency around the pin, and positive bacteriologic culture rate for pins and pin holes would be lower for horses in the hydroxyapatite coating group as a result of pin osteointegration, compared with results for the uncoated pin group, during an 8-week period of transfixation casting.

Materials and Methods

Study design—Hydroxyapatite-coated and uncoated transcortical pins, incorporated into a cast applied to the distal aspect of the limb, were compared in vivo during an 8-week period. Institutional Animal Care and Use Committee approval was obtained for all animal procedures. Fourteen geldings, from 4 to 10 years of age, were determined to be healthy and free of lameness and radiographic abnormalities of the forelimbs distal to the carpus. All horses were Quarter Horse–type breeds (7 Quarter Horses, 4 Paint Horses, 2 Quarter Horse crosses, and 1 Appaloosa). Horses weighed from 336 to 573 kg (mean ± SD, 429 ± 69 kg) at the time of inclusion in the study. Seven horses were randomly assigned to each group. Three pins of the same type (either hydroxyapatite coated or uncoated) were placed in each horse for transfixation casting. The right limb was used in all horses to ensure consistent pin placement, casting technique, anesthetic recovery procedures, and videographic analysis of lameness between horses. Each horse was housed in a box stall for the duration of the study. Insertion torque was measured at pin insertion, and extraction torque was measured at the end of the 8-week casting period. Radiographic images of the metacarpus, including the metacarpophalangeal joint, were obtained prior to pin placement, immediately after surgery, and 4 and 8 weeks following transfixation cast placement. Lameness and cast evaluations were performed daily throughout the study. A lameness evaluation was also performed at weeks 2, 4, 6, and 8 by personnel without knowledge of group assignments using videographic recordings of each horse standing and at a walk in a straight line immediately outside the stall. Aerobic microbiological cultures were performed for all pins and pin holes at the conclusion of the study. Histologic examination of the pins from 2 predetermined, randomly assigned horses of each group was performed.

Pin preparation—Twenty-one centrally threaded, positive profile large animal transfixation pins[a] were coated with a biomimetic hydroxyapatite coating[20,b] applied to the pins over a 90-mm-length area; the coating was centered on the threaded portion of the pin. Grit blasting of the stainless steel surface was performed to enhance coating adhesion in the hydroxyapatite-coated pins. Coated pins were sterilized with irradiation prior to implantation. Twenty-one stainless steel pins, identical to those submitted for coating, were used as uncoated control pins.

Surgical preparation—The hooves of each horse were trimmed prior to surgery. An IV jugular catheter was placed aseptically, and each horse was premedicated with gentamicin sulfate (6.6 mg/kg, IV), potassium penicillin (22,000 U/kg, IV), and phenylbutazone (2.2 mg/kg, IV). The right limb was clipped circumferentially from the carpus to the foot and cleaned of gross contamination with a 4% chlorhexidine gluconate solution prior to entering the surgical suite. Horses were sedated for general anesthesia with xylazine hydrochloride (1.1 mg/kg, IV), butorphanol tartrate (0.02 mg/kg, IV), and 5% guaifenesin solution (IV) to effect. Ketamine hydrochloride (2.2 mg/kg, IV) and diazepam (0.06 mg/kg, IV) were used for anesthetic induction, and general anesthesia was maintained with isoflurane in oxygen via a semiclosed circle rebreathing system. Routine anesthetic monitoring and patient support were used throughout the procedures.

Surgical procedures—Following induction of general anesthesia, horses were placed in left lateral recumbency. The surgical site was aseptically prepared. A 1-cm stab incision was made with a No. 15 scalpel blade through the skin, subcutaneous tissue, and periosteum down to the bone surface at locations measured

1, 3.5, and 6 cm proximal to the palpable prominence of the physeal scar on the distal lateral aspect of the third metacarpal bone. A drill guide was used to protect skin and soft tissues during drilling. Irrigation with sterile saline (0.9% NaCl) solution was maintained for all placement procedures at a constant flow rate of 150 mL/min with a fluid pump delivery system. All pin holes were drilled through the bone in a lateral to medial direction with a 6.2-mm drill bit[c] and tapped with an 8.0-mm tap.[d] The drill bit and tap were withdrawn from the bone and cleaned 3 to 4 times during the process to minimize heat generation and bone debris accumulation within the pin hole. All drilling, tapping, and pin placement procedures were performed with a battery-powered drill.[e] Pins were placed perpendicular to the long axis of the bone in a lateral to medial direction with up to 30° divergence from the frontal plane between pins.[21] Pin locations in the third metacarpal bone were designated 1, 2, and 3 in proximal to distal direction (**Figure 1**). At surgery, a pin was placed at location 3 first and directed in the frontal plane. Next, a pin was placed at location 2 in a dorsolateral to palmaromedial direction by approximately 15°. Finally, a pin was placed at location 1 in a palmarolateral to dorsomedial direction with a similar degree of deviation from the frontal plane (**Figure 2**). The same placement procedures were performed for all horses. The end-insertion torque of each pin was measured by means of a digital torque wrench[f] with a chuck adaptor,[g] as previously described.[19] Torque measurements were performed by turning the pin 180° in 1 movement and recording the peak torque value.

Pins were cut 3 to 4 cm from the skin, leaving enough pin exposed to be incorporated into the cast. The skin incisions were covered with a sterile dressing. A compressible foam pad[h] (thickness, 2.5 cm) was placed on the bottom of the foot prior to casting (Figure 2) to ensure that the digit was at least partially unloaded and that pins were loaded during weight bearing. A layer of polyurethane-impregnated foam padding[i] was applied from the coronary band to the proximal metacarpus. A half-limb cast was applied with fiberglass casting tape[j] from the proximal extent of the third metacarpal bone, incorporating each pin and the foot.[8] The ends of each pin and the ground surface of the cast were coated in nonsterile polymethylmethacrylate for protection. Horses were allowed to recover from anesthesia in a padded recovery stall, with the use of tail ropes and manual assistance as necessary.

Postoperative treatment and monitoring—Following recovery from anesthesia, horses were returned to their stall, and an elevated boot was placed on the opposite limb. The boot was a commercially available horse boot[k] with a 2.5-cm wooden block attached to its base for elevation. Gentamicin sulfate (6.6 mg/kg, IV, q 24 h), procaine penicillin (22,000 U/kg, IM, q 12 h), and phenylbutazone (2.2 mg/kg, IV, q 12 h) were administered for the first 3 days after surgery. A complete physical examination was performed daily on each horse, monitoring specifically for lameness, cast failure or cracking, swelling above the cast, purulent drainage at pin sites, and other drainage through the cast.

Radiographic evaluation—Lateromedial and dorsopalmar digital radiographs of the left and right metacarpus of each horse were obtained prior to inclusion in the study, immediately following pin placement, and 4 and 8 weeks after surgery. Radiographs were evaluated by a board-certified veterinary radiologist unaware of treatment group and time of radiographic evaluation. Radiographically visible bone damage such as acute periosteal cortical fracture,[22] radiolucency associated with the pin holes, and periosteal and endosteal new bone formation were specifically assessed. Other notable radiographic abnormalities were recorded. Width of cortical radiolucency was measured and expressed as a percentage of the total cortical width for both lateral and medial cortices from the dorsopalmar radiographic view[22] (Figure 1). The mean of the lateral and medial cortical measurements was used for statistical analysis. In addition, measurement of the height of radiolucency proximal and distal to the pin surface was made at 3 locations across each pin: the center of the lateral cortex, midpoint of the bone, and center of the medial cortex. The mean value of these 6 measurements was used for statistical analysis and was designated as the height of

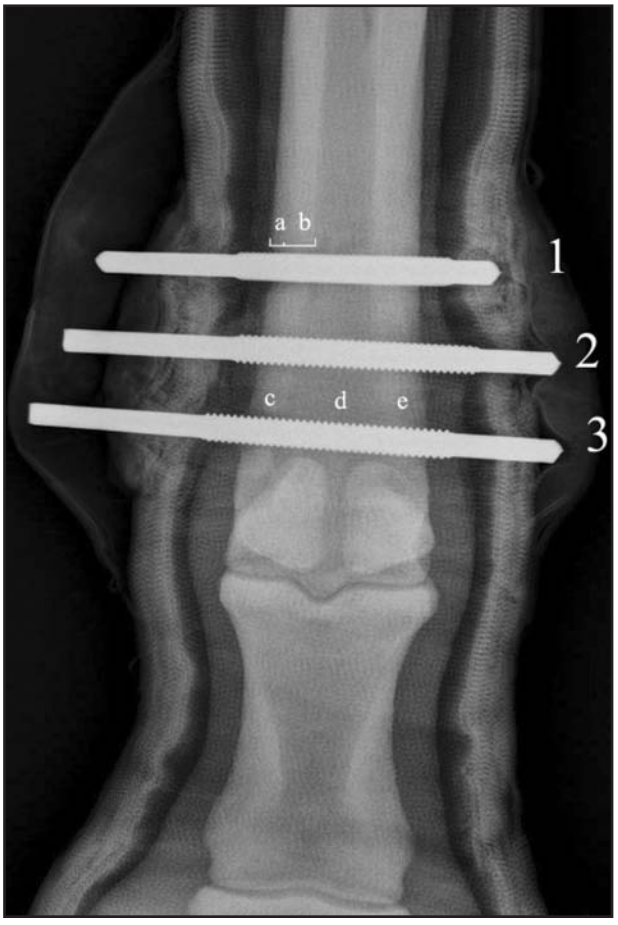

Figure 1—Dorsopalmar radiographic view of the distal portion of the limb of a horse with a transfixation pin cast in place. Pin locations are in the distal third metacarpal bone and designated 1, 2, and 3 from proximal to distal. a = Area where radiolucency is present adjacent to the pin within the cortex. b = Area where no radiolucency is present adjacent to the pin within the cortex. c, d, and e = Locations where measurement of the height of proximal (or distal) radiolucency was made on each pin. The width of cortical radiolucency was determined from radiographs as a/(a + b).

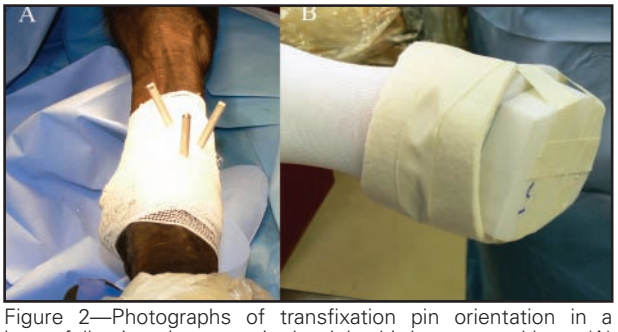

Figure 2—Photographs of transfixation pin orientation in a horse following placement in the right third metacarpal bone (A) and foam pad positioning under the foot prior to half-limb cast application (B).

radiolucency for each pin. Radiographic measurements were corrected for magnification with the transfixation pin diameter for calibration with a commercial digital radiographic software package.[l]

Lameness evaluation—Two separate methods of lameness evaluation were performed: a daily grading by individuals who were aware of group assignments and a videographic analysis performed every 2 weeks throughout the study by individuals who were unaware of group assignments. Daily grades on a scale from 0 to 4 were determined inside the stall on the basis of the following predetermined criteria: grade 0 = horse willing to move about the stall, not visibly lame, and readily allows the opposite forefoot to be lifted; grade 1 = horse willing to move about the stall, has occasional (< 50% of the time) lameness, and readily allows the opposite forefoot to be lifted; grade 2 = horse has some reluctance to move about the stall and consistent lameness (> 50% of the time) and resists having the opposite forefoot lifted; grade 3 = horse reluctant to move about the stall, has consistent moderate lameness, and will not permit lifting of the opposite forefoot; and grade 4 = horse unwilling to move, has severe or non–weight-bearing lameness at a walk, and will not permit lifting of the opposite forefoot.

Lameness evaluations were performed from videographs of each horse both standing and walking outside the stall. The videographs were evaluated by 2 observers unaware of group assignments and experienced in evaluating clinical orthopedic patients for signs of pain and lameness. Lameness associated with the casted limb was graded as mild (grade 1), moderate (grade 2), or severe (grade 3). Half grades were applied by both observers during the evaluation process, and ultimately, a grade based on a scale from 0 to 6 (original grades doubled for statistical convenience) was compared between groups, with 0 = a horse with no lameness in the casted limb and 6 = a horse with severe or non–weight-bearing lameness in the casted limb.

Necropsy—Horses were euthanized with an overdose of pentobarbital sodium (39 g, IV) and phenytoin sodium (5 g, IV) 8 weeks following transfixation cast placement. A complete necropsy evaluation was performed on each horse, including examination of the viscera, head, neck, and all 4 limbs. The cast limb was disarticulated at the carpus, and the cast was removed, leaving the pins in place. Extraction torque measurements were made in an identical manner to the insertion torque measurements, with peak torque recorded following a 180° rotation of the pin. Extraction torque measurements were made in 5 horses from each group. Limbs were held firmly in a vise and stabilized by an assistant to perform the measurements. Following torque measurements, the pin segments exiting the medial cortex were cut adjacent to the skin and the limb was aseptically prepared from the metacarpophalangeal joint to the proximal third metacarpal bone. Pins were removed from the lateral side of the limb. Aerobic microbiological sampling of the pins and pin holes was performed with sterile swabs and samples submitted for routine bacteriologic culture and susceptibility testing.

Histologic processing and evaluation—Two horses from each group were used for histologic examination of the BPI. An approximately 4-cm section of bone, containing each pin in the center, was harvested by making transverse cuts with a bone saw through the third metacarpal bone and placed in 70% ethanol. Each bone-pin section was cut by means of a histologic bone band saw[m] with a diamond grit cutting band through the long axis of the pin, separating the pin and bone into dorsal and palmar halves. Medial, lateral, proximal, and distal orientations were marked on each specimen. Specimens were dehydrated through a series of dilutions of ethanol of increasing concentration in an enclosed automatic tissue processor, placed in 4 sequential changes of a light polymerizing resin,[n] and polymerized in a polymerizing unit.[o] Each embedded specimen was then surface ground to expose the pin and both cortices. A slide was polymerized to the specimen surface, the specimen was attached to a slide cutting device,[p] and a section was cut. Slides were ground to a final thickness of approximately 50 µm on a slide grinder[q] and surface etched to permit penetration of stain. Toluidine blue stain was used for qualitative evaluation of the BPI. Slides were examined with a microscope,[r] and images were digitized with digital image capture equipment connected to a personal computer by a commercial software program.[s]

Statistical analysis—Sample size calculations for the study were performed on the basis of estimates of insertion torque and variability for hydroxyapatite-coated and uncoated pins from a previous cadaveric study[19] in equine third metacarpal bones and data for extraction torque and variability following implantation of hydroxyapatite-coated external fixation pins in other species.[9,16,23] On the basis of these estimates, a sample size of 5 horses/group was used to detect a 50% difference in extraction torque between groups with a type I error rate of 0.05 and a power of 80%. Torque reduction was defined as the difference between insertion and extraction torque for each pin, with a positive value representing a pin that loosened during the 8-week study period (extraction torque lower than insertion torque) and a negative value representing a pin that tightened during the study period (extraction torque higher than insertion torque). Insertion and extraction torque, torque reduction, percentage cortical radiolucency, height of radiolucency, and masked lameness scores were compared between groups via mixed-

model analysis with statistical software,[t] with horse as a random variable. Data were assessed for normality by examining conditional and marginal residual plots. When necessary, data were transformed via a natural log transformation to improve data normality and satisfy model assumptions. Multiple comparisons were made with the Tukey method on the difference of least squares means. Positive bacteriologic culture rates for pins and proportions of unmasked daily lameness grades were compared between groups with a χ^2 test. Values of $P < 0.05$ were considered significant for all comparisons.

Results

Clinical observations—All surgical procedures were performed without incident. Mean ± SD weight of the horses in the uncoated pin group was 436 ± 69 kg, which was not significantly different from the weight of horses in the hydroxyapatite-coated pin group (422 ± 73 kg). Following surgery, all horses used the casted limb without major complications throughout the study. Horses appeared most comfortable on the casted limb for the first 2 weeks. Mean daily lameness grades increased in both groups between 2 and 4 weeks and then remained consistent for the remainder of the study (**Figure 3**). One horse in the hydroxyapatite-coated pin group developed a crack in the cast in the interphalangeal (pastern) region. Swelling above the cast and increased lameness necessitated replacement of the cast on day 28, which was performed with the horse standing and under heavy sedation. A cast sore with associated cellulitis was present on the medial aspect of the pastern. The cast sore was treated by cleaning the wound and placing protective padding around the area prior to cast replacement. A 7-day course of trimethoprim-sulfamethoxazole treatment (30 mg/kg, PO, q 12 h) was also administered. The horse tolerated the replacement cast well, and lameness decreased steadily during the following week. No other complications necessitated cast replacement in any horse.

Mild or moderate swelling was observed proximal to the cast in 5 of 7 horses of the hydroxyapatite-coated pin group. The swelling observed did not necessitate cast replacement and was first noticed between days 15 and 21 in 4 of the horses. The swelling resolved completely between days 24 and 36 in 3 of the horses and did not completely resolve in 2 of the horses but gradually improved. None of the horses in the uncoated pin group were observed to have swelling proximal to the cast during the 8-week study period.

No drainage through the cast was observed at any location in either group. Three broken pins were observed on radiographs or at necropsy in each group. In all but 1 horse, this occurred at pin location 1 and pins remained in their original position. Broken pins were not accompanied by increased signs of lameness and were incidentally found in each case.

Pin torque measurements—Pin torque measurements were summarized (**Table 1**). Overall, uncoated pins had higher insertion torque than did hydroxyapatite-coated pins ($P < 0.001$). An effect of group and pin location and an interaction effect between group and pin location were found for pin insertion torque ($P = 0.01$). Specifically, uncoated pins had a higher insertion torque than did hydroxyapatite-coated pins at location 3 ($P < 0.001$). Within the uncoated pin group, insertion torque was significantly lower at location 1, compared with that at locations 2 and 3. There was no effect of pin location on the insertion torque of hydroxyapatite-coated pins.

There was no effect of group on pin extraction torque ($P = 0.44$). An effect of pin location and an interaction effect between group and pin location were found for extraction torque. Overall, pins at location 3 had a significantly higher extraction torque than did pins at locations 1 and 2. Within the uncoated pin group, pins at location 1 had lower extraction torque than did pins at location 3 ($P = 0.02$). Extraction torque was not different among pin locations within the hydroxyapatite-coated pin group.

There was an effect of group on torque reduction, with hydroxyapatite-coated pins having less torque reduction during the 8-week period, compared with uncoated pins ($P = 0.03$). There was neither an effect of pin location nor an interaction effect between group and pin location found for torque reduction. Overall, 5 of 15 pins in the hydroxyapatite-coated pin group had either consistent or increased stability within the bone (up to an 8-fold increase in 1 pin), whereas all uncoated pins had decreased stability within the bone. The hy-

Table 1—Mean ± SD values for insertion torque, extraction torque, and torque reduction for uncoated and hydroxyapatite-coated pins placed in third metacarpal bones for an 8-week period of transfixation casting in horses.

Pin location	Group	Insertion torque (Nm)	Extraction torque (Nm)	Torque reduction (Nm)
1	Uncoated	0.53 ± 0.27[a]	0.22 ± 0.18[a]	0.32 ± 0.18
	Hydroxyapatite-coated	0.55 ± 0.59	0.86 ± 1.29	–0.21 ± 1.45
2	Uncoated	1.63 ± 0.81[b]	0.49 ± 0.41[a,b]	1.15 ± 0.80
	Hydroxyapatite-coated	0.58 ± 0.16	0.21 ± 0.17	0.31 ± 0.25
3	Uncoated	3.70 ± 3.30[A,b]	1.50 ± 0.83[b]	2.77 ± 3.68
	Hydroxyapatite-coated	0.41 ± 0.08[B]	0.95 ± 1.26	–0.57 ± 1.28

Pin locations 1, 2, and 3 correspond to proximal, middle, and distal pins in the third metacarpal bone, respectively. Negative values for mean torque reduction represent an increase in stability of the pins at that location.

[a,b]For each category, values with a different superscript letter are significantly ($P \leq 0.05$) different within groups and between pin locations. [A,B]For each category, values with a different superscript letter are significantly ($P \leq 0.05$) different between groups and within pin locations.

Table 2—Mean ± SD values for percentage width of cortical radiolucency and height of radiolucency at 0, 4, and 8 weeks following transfixation casting for uncoated and hydroxyapatite-coated pins placed in third metacarpal bones in horses.

Pin location	Group	Width of cortical radiolucency (%)			Height of radiolucency (mm)		
		Week 0	Week 4	Week 8	Week 0	Week 4	Week 8
1	Uncoated	29 ± 12[a]	41 ± 20[a]	54 ± 26[b]	0 ± 0[a]	1.6 ± 0.5[b]	1.9 ± 0.4[b]
	Hydroxyapatite-coated	31 ± 10[a]	48 ± 27[b]	83 ± 31[c]	0 ± 0[a]	2.8 ± 1.9[b]	3.7 ± 2.0[c]
2	Uncoated	29 ± 13[a]	35 ± 16[a]	55 ± 11[b]	0 ± 0[a]	1.5 ± 0.5[b]	1.7 ± 0.4[b]
	Hydroxyapatite-coated	24 ± 12[a]	46 ± 33[b]	70 ± 31[c]	0 ± 0[a]	1.9 ± 1.4[b]	2.8 ± 1.4[c]
3	Uncoated	16 ± 9[a]	17 ± 8[a]	34 ± 15[b]	0 ± 0[a]	1.0 ± 1.1[b]	1.2 ± 0.7[b]
	Hydroxyapatite-coated	6 ± 7[a]	34 ± 34[b]	60 ± 35[c]	0 ± 0[a]	1.5 ± 1.5[b]	2.2 ± 2.3[c]

[a–c]For each category, values with a different superscript letter are significantly ($P \leq 0.05$) different within groups and pin locations and between time points.
See Table 1 for remainder of key.

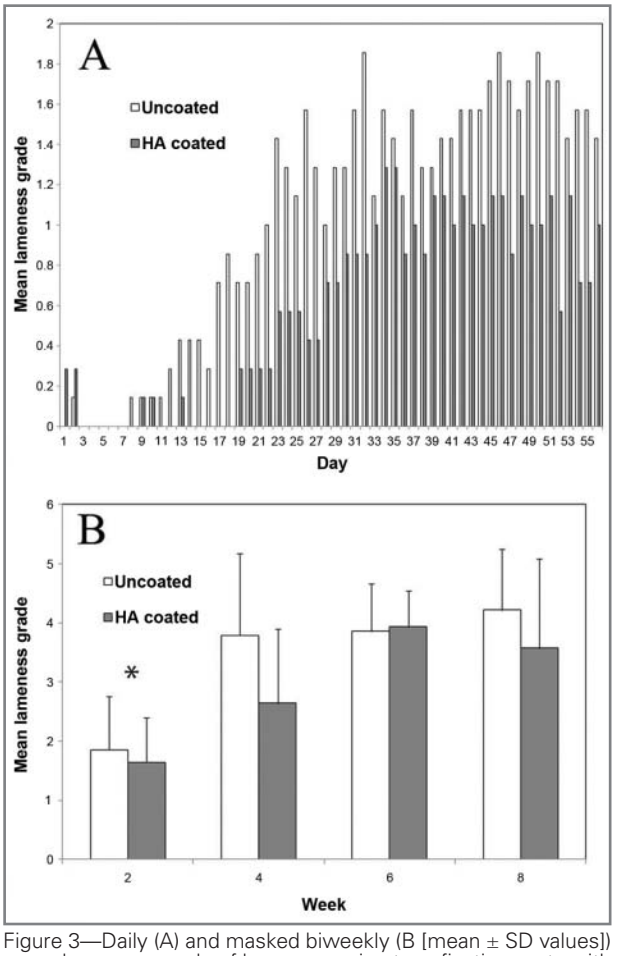

Figure 3—Daily (A) and masked biweekly (B [mean ± SD values]) mean lameness grade of horses wearing transfixation casts with hydroxyapatite (HA)-coated or uncoated pins during an 8-week period. *Significantly ($P < 0.05$) lower masked mean lameness grades for both groups, compared with all other time points.

droxyapatite coating was observed to be intact on the pins following removal from the bone.

Radiographic evaluation—No major complications of transfixation casting were seen on the radiographs. Periosteal and endosteal responses of various degrees were observed consistently in all horses and were associated with each pin location. Osteopenia of the bones distal to the transfixation pins was observed most consistently in the proximal sesamoid bones but was also observed in the proximal phalanx and the distal aspect of the third metacarpal bone. The degree of osteopenia ranged from mild to severe. A radiographic diagnosis of pin hole infection, with greater than expected irregular radiolucency of bone associated with the pins, was made in 4 horses, including 3 in the hydroxyapatite-coated pin group and 1 in the uncoated pin group.

Radiographic measurements made for each pin location at weeks 0, 4, and 8 were summarized (**Table 2**). There was no effect of group on the observed percentage cortical radiolucency ($P = 0.19$) or height of radiolucency ($P = 0.15$) associated with transfixation pins. There was an effect of pin location and time on the percentage of cortical radiolucency and height of radiolucency associated with transfixation pins ($P < 0.001$). There was also an interaction effect observed between group and time for percentage cortical radiolucency and height of radiolucency associated with transfixation pins ($P = 0.04$). Less radiolucency was observed at pin location 3, compared with locations 1 and 2, in terms of both cortical width and height ($P < 0.05$). Greater width of cortical radiolucency was observed at week 8, compared with weeks 0 and 4, and at week 4, compared with week 0 ($P < 0.001$). The hydroxyapatite-coated pin group had an increase in the percentage of cortical radiolucency between weeks 0 and 4 and between weeks 4 and 8, whereas uncoated pins had an increase in the percentage of cortical radiolucency only between weeks 4 and 8 ($P = 0.03$). Overall, the height of radiolucency was greater at week 8, compared with weeks 4 and 0 ($P < 0.001$). Within groups, height of radiolucency was different between weeks 4 and 8 for the hydroxyapatite-coated pin group ($P < 0.001$) but not for the uncoated pin group.

Lameness—Horses in the hydroxyapatite-coated pin group were assigned a daily grade of 0 more often than were horses in the uncoated pin group. Conversely, horses in the uncoated pin group were assigned a daily grade of 2 more often than were horses in the hydroxyapatite-coated pin group ($P = 0.03$). Mean daily lameness grades during the course of the study were plotted (**Figure 3**). Only 1 horse was given a daily grade of 3, and no horses were given a grade of 4. The horse with the grade 3 lameness had the cast replaced, and

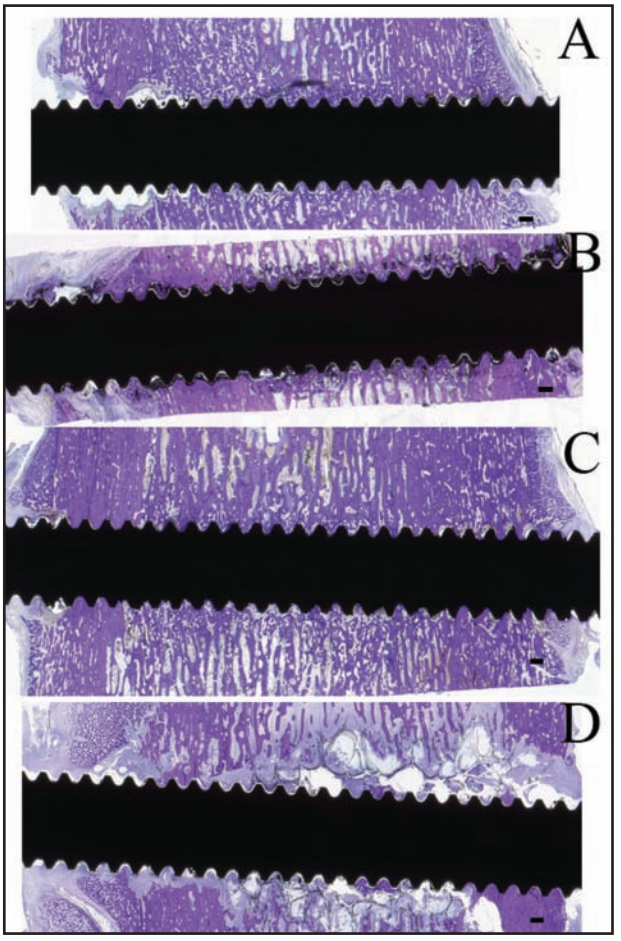

Figure 4—Photomicrographs of histologic sections of 6.3-mm transfixation pins within right third metacarpal bones of 4 horses used for in vivo evaluation of hydroxyapatite-coated and uncoated pins. Proximal is to the top, and lateral is to the left. All sections are through the frontal plane of middle pins in the third metacarpal bone. A and B—Histologic sections of uncoated pins. Notice a thin layer of fibrous tissue (light or no staining) between the BPIs and direct bone-pin contact in several locations. C and D—Histologic sections of hydroxyapatite-coated pins. Notice consistent bone-pin contact across section C, with only discrete areas of fibrous tissue associated with occasional threads. Notice the substantial bone lysis in section D, consistent with a pin hole infection that occurred in this horse. Toluidine blue stain; bar = 1 mm.

a cast sore and localized cellulitis were subsequently treated as previously described.

There was no difference between groups for lameness grades assigned by observers unaware of group assignments ($P = 0.25$). There was an effect of time on lameness grade, with horses having lower lameness grades at week 2, compared with results at weeks 4, 6, and 8 ($P < 0.001$). Mean lameness grades assigned by those observers were plotted and followed a pattern similar to the daily lameness grades assigned during the 8-week study period (Figure 3).

Bacteriologic culture of pins and pin holes—The positive bacteriologic culture rate for pins and pin holes was not different between groups. The overall positive bacteriologic culture rate for hydroxyapatite-coated pins and pin holes was 83% (25/30) and for uncoated pins and pin holes was 87% (26/30).

Necropsy findings—There were no major abnormalities found at gross necropsy other than those associated with the casted limbs. Axillary lymph nodes were enlarged in the casted limb of all horses, compared with the opposite limb. For 2 horses in the hydroxyapatite-coated pin group, the axillary lymph nodes were 3 to 4 times as large as those of the opposite limb. In one of these horses, a small draining sinus was found near the top of the cast associated with a subcutaneous tract from the proximal pin location. Joints of the distal aspect at the limb had a reduced range of motion in all horses following removal of the transfixation pin cast. Synovial congestion, serosanguinous synovial fluid, and cartilage thinning were consistent gross observations in the metacarpophalangeal and proximal and distal interphalangeal joints of all horses. There was a partial thickness cast sore present at the dorsal proximal region of the rim of the cast in a horse from the hydroxyapatite-coated pin group. The cast sore in 1 horse was healing well at the time of necropsy. No other cast sores were present in any horse. Some degree of skin loss and the formation of granulation tissue around the pins at the skin surface were present in all horses.

Histologic evaluation—The range of histologic findings observed in a section that included a pin at location 2 from each of the 4 horses used for histologic evaluation was determined (**Figure 4**). Qualitative histologic analysis revealed formation of fibrous tissue at the BPI of uncoated pins, although bone-pin contact was still present in some areas of the uncoated pin surfaces. One of the horses from the hydroxyapatite-coated pin group assigned to undergo histologic evaluation had evidence of gross infection around the proximal pin at necropsy and complete histologic absence of bone-pin contact. The other 2 pins from the same horse had variable amounts of bone lysis associated with the pin hole and obvious histologic evidence of pin hole infection. The other horse from the hydroxyapatite-coated pin group assigned to undergo histologic evaluation had consistent bone-pin contact across the pin; however, discrete locations on some pin thread surfaces contained fibrous tissue rather than bone.

Discussion

Results of the present study indicated that hydroxyapatite-coated pins had significantly less reduction of torque, compared with uncoated pins, following 8 weeks of transfixation casting in horses. Uncoated pins consistently loosened during the 8-week casting period, and histologic examination predominantly revealed the formation of fibrous tissue at the BPI. These results supported our first hypothesis that hydroxyapatite coating improves pin stability within the equine third metacarpal bone under full weight-bearing conditions, compared with uncoated pins, during an 8-week period. Results also indicated that lameness, radiolucency surrounding the pins, and positive bacteriologic culture rate for pins and pin holes observed during transfixation pin casting were similar between the hydroxyapatite-coated and uncoated pin groups. These findings led us to reject our second hypothesis and conclude that the clinical performance of hydroxyapatite-

coated pins was no better than that of uncoated pins during the 8-week casting period.

Osteointegration has been defined clinically as the stability and ankylosis of an implant within the bone and experimentally as the microscopic contact between the bone and the implant surface.[13] Insertion torque, extraction torque, and the difference between the 2 measurements (ie, torque reduction) have been used to quantitatively assess osteointegration of external fixation pins with and without hydroxyapatite coatings in previous clinical studies.[9,16,17,24] Insertion torque is the rotational force required to advance a threaded implant following engagement of both cortices by the threads.[5] It reflects the friction present between the implant and bone at the time of insertion. Extraction torque is the force necessary to break the attachment of bone to a threaded implant surface during removal.[25] Considering the results of a preliminary study,[19] which evaluated pin insertion at the mid-diaphyseal location of the third metacarpal bone, we did not anticipate pin insertion torque to be different between the 2 groups in the present study. However, distal pin locations had higher insertion torque among uncoated pins and insertion torque of hydroxyapatite-coated pins did not differ with location. Higher insertion torque results in delayed pin loosening.[24] Considering that insertion torque was significantly different between groups for pins at location 3, the only meaningful overall comparison of pin stability between groups was torque reduction, which was calculated for individual pins by means of insertion and extraction torque values. Although the torque reduction results indicated that osteointegration of a hydroxyapatite-coated transcortical pin is possible in horses, histologic examination findings supporting these results were available from only 1 horse because of development of pin hole infections in the second horse that was used for examination of the BPI. We believe that the increase in torque required to remove hydroxyapatite-coated pins following 8 weeks of transfixation casting is best explained by osteointegration, despite the lack of histologic confirmation from multiple horses. In support of this, a moderate yet significant correlation has been found between extraction torque and histologic bone to implant contact in a study[26] assessing screw anchorage. In addition, several experimental studies[27–30] have documented histologic evidence of bone-implant contact on hydroxyapatite-coated external fixation pins in conjunction with enhanced or maintained pin stability over time, without specifically determining a statistical correlation. These studies also reveal that the formation of fibrous tissue at the BPI is accompanied by a reduction in pin stability. We believe that osteointegration is the only logical explanation for the extraction torque measurements that were equivalent to or higher than insertion torque for individual pins following 8 weeks of transfixation casting in the hydroxyapatite-coated pin group. In addition, we believe the mean reduction in torque of 60%, 71%, and 75% for pins at locations 1, 2, and 3, respectively, was attributable to the formation of predominantly fibrous tissue at the BPI of uncoated pins.

A recent review[31] of randomized controlled trials that involved the use of hydroxyapatite-coated external fixator pins in humans noted that less pin loosening occurred, compared with results when uncoated pins were used; however, there was insufficient evidence of an overall clinical benefit for patients when hydroxyapatite-coated pins were used. In the present study, in the hydroxyapatite-coated pin group, either pin stability increased or pins failed to maintain stability (ie, an all-or-nothing effect), with 5 of 15 pins having increased (up to 8-fold) or equivalent extraction torque, compared with their insertion torque 8 weeks earlier. We believe that the lack of difference in clinical variables observed between groups was primarily because of this all-or-nothing effect, with enhanced stability of a small number of pins being overshadowed by a larger number of hydroxyapatite-coated pins failing to maintain stability. Future research on this topic needs to focus on the potential causes of this inconsistent response. We believe that strategies need to be developed to address the 2 likely causes of BPI breakdown in horses: pin hole infections and thermal bone damage during hole drilling and pin insertion.

Although the positive bacteriologic culture rate for pin holes was similar between groups, several findings suggested that infections had a greater effect on the hydroxyapatite-coated pin group. Five of 7 horses in the hydroxyapatite-coated pin group had swelling develop proximal to the cast, 4 of which developed swelling during the first 3 weeks of the casting period. The swelling resolved in 3 horses but persisted, albeit with improvement, in 2 horses. None of the horses in the uncoated-pin group had swelling proximal to the cast. The 2 horses with the most prominent axillary lymph node enlargement detected at necropsy were from the hydroxyapatite-coated pin group, and 1 of these horses developed a subcutaneous draining tract proximal to the most proximal pin. In addition, 3 horses in the hydroxyapatite-coated pin group were suspected of having a pin hole infection on the basis of findings from radiographic assessments (severe irregular osteolysis), compared with results for 1 horse in the uncoated pin group. Although none of these findings alone was conclusive, considering these findings together, we propose that the hydroxyapatite coating may have played an important role in the higher number of clinically important pin hole infections.

We speculate that the hydroxyapatite coating may have promoted dermal adherence to the pin[32–34] during the first 2 weeks following pin placement, subsequently trapping bacteria subcutaneously at the BPI. The result of this lack of normal drainage at the junction of the skin and the pin may have exacerbated the development of pin hole infection in these horses. The presence of a subcutaneous draining tract in 1 horse and swelling proximal to the cast in 5 horses of the hydroxyapatite-coated pin group would be consistent with this reasoning. Although hydroxyapatite coatings have been used to encourage adherence of the dermis in some orthopedic applications,[32,33] placing pins beneath a cast is a unique application for a hydroxyapatite coating and may not provide the postoperative wound environment necessary to avoid ascending infection. Surface treatments other than hydroxyapatite have been used to reduce bacterial colonization of percutaneous ortho-

pedic implants, with results for hydroxyapatite coating similar to those for stainless steel in terms of microbial culture and biofilm formation.[32] Pin coatings or surface treatments that promote osteointegration and reduce bacterial colonization may result in improved consistency of transfixation pin osteointegration in horses.

A second potential contributing factor in the development of clinically important pin hole infections and early increases in radiolucency around the pin hole in the hydroxyapatite-coated pin group was thermal damage to the BPI at the time of hole drilling and pin insertion. Drilling and tapping procedures were consistent for all pins, so any thermal damage created during this stage should have been similar between groups. However, it is unclear why the insertion torque of the hydroxyapatite-coated pins did not change with pin location, whereas the uncoated pins had higher insertion torque when placed further distal in the limb. We speculate the hydroxyapatite coating may have increased the abrasiveness of the surface, similar to the action of an abrasive grain bonded to a substrate found in coated abrasives (ie, a sandpaper effect), resulting in greater thermal damage to the bone from friction during pin insertion, compared with the uncoated pins. Increased friction and wearing of the bone surface by the hydroxyapatite-coated pins during insertion could have widened the thread forms. Wider thread forms could ultimately result in lower static friction at the end of insertion when the insertion torque measurements were made. This effect was not detected in a cadaver study[19] that assessed insertion characteristics of the same hydroxyapatite coating used in the study reported here. However, only a mid-diaphyseal location was tested in the cadaver specimens,[19] whereas in the study reported here, the difference in insertion torque between hydroxyapatite-coated and uncoated pins was most profound at the most distal pin location in the metaphyseal region. It is possible that this effect is more important at pin locations where cancellous bone predominates because the trabecular spaces provide a location for any bone particles removed during pin insertion to lodge away from the BPI and not affect the static friction present at the end of insertion. Nonetheless, greater thermal damage to bone may have resulted from the presence of the hydroxyapatite coating and subsequently contributed to both progression of pin hole infections and earlier development of radiolucency around the pins.

The finding that insertion torque of hydroxyapatite-coated pins was significantly less than that of uncoated pins at the metaphyseal pin locations could be attributable to factors other than the sandpaper effect. Determinants of the insertion torque include the static coefficient of friction and the force present between (perpendicular or normal to) the bone and pin surfaces at the time of measurement.[35–38] Factors such as protein adsorption to the pin surface, lubrication, surface roughness, wear, and heating during pin insertion could each affect the coefficient of static friction between the pin and the bone. The biomimetic hydroxyapatite used in the present study added a thickness of approximately 10 to 16 μm to the pins.[19] This added thickness would result in greater friction for coated pins, compared with uncoated pins. To our knowledge, the coefficient of friction between hydroxyapatite and bone has not been determined, but if it were lower than the coefficient of friction between metal and bone, as has been found for an aluminum ceramic in a cadaver study[38] assessing hip implants, this may help explain the disparity of insertion torque measurements at the distal pin locations. However, this alone does not explain the finding that insertion torque was not different between groups at the proximal pin location (location 1).

Despite a higher proportion of grade 0 scores and a lower proportion of grade 2 scores assigned to the hydroxyapatite-coated pin group during daily assessments, the masked lameness evaluation revealed no difference between groups at 2, 4, 6, and 8 weeks following transfixation casting. A set of predetermined criteria was applied to minimize the subjectivity of the daily grading system; however, we cannot conclude that there was a definitive improvement in lameness in the hydroxyapatite-coated pin group, considering both methods of lameness assessment together. An objective assessment of limb use such as measurement of peak vertical force with a force plate would have reduced the potential bias and subjectivity inherent in the lameness grading approach; however, a force plate was not available for use in the present study. Masked videographic analysis was chosen to provide lameness evaluation of the 2 groups of horses at set time periods throughout the study by unbiased observers. Although videographic recordings were made consistently in the same location with similar videographic settings and timings for each horse, the lifting of the opposite foot and palpation of the cast during the daily assessments were not observed.

We believe that the methods described in the present study were clinically relevant and provided a meaningful test of the potential for hydroxyapatite coatings to be used for transfixation casting in horses. The use of a foam pad beneath the foot allowed for pins to be load bearing during the study without creating a fracture or performing an osteotomy in the horses. The development of mild to severe osteopenia, progression of pin loosening in all uncoated pin group horses within 8 weeks, and observation of 6 broken pins provided evidence that substantial, clinically relevant pin loading was achieved. In comparison, a clinical study[1] of transfixation casting for the treatment of distal limb fractures in horses found development of osteopenia distal to transfixation pins in 68% of cases, pin loosening in 68% of cases, and 3 broken pins in 29 treated adult horses. Although not typical clinically, an 8-week casting period without cast change in 13 of 14 horses also provided a test of the ability for hydroxyapatite-coated transfixation pins to osteointegrate. The study protocol included selected criteria by which a cast change would be performed during the 8-week period. However, only 1 horse met these criteria and required a cast change during the study. We routinely change transfixation pin casts within 3 to 4 weeks after placement in clinical cases,[1] and an alternative approach in the present study would have been to follow this practice rather than to extend casting for the full 8-week period.

A limitation of the present study was the lack of strong histologic evidence to support the torque and

clinical data. In designing the study, we anticipated that qualitative and quantitative histologic assessment of 6 pins/group would be available to support the clinical findings of the study and that bone-pin contact percentage would be compared between groups. Unfortunately, development of 3 pin hole infections in one of the horses in the hydroxyapatite-coated pin group resulted in an inability to make a legitimate comparison between groups regarding the histologic appearance of the BPI. Before beginning the study, horses were randomly determined to undergo histologic examination to avoid possible bias in their selection on the basis of known clinical data being collected. An alternative approach to the use of all 3 pins from the predetermined horses for histologic examination would have been to randomly allocate 1 pin/horse for histologic examination and the remaining 2 pins/horse for torque measurements. However, during the study design, pin locations were considered to be different within each horse on the basis of anatomic location and expected loading, so the horse was considered the experimental unit and a random variable for analysis, rather than the pins. Although the mixed-model statistical analysis could accommodate a random allocation of pins for histologic examination and the missing data points that would result from the assessment of torque measurements, it was considered more appropriate to attain complete data from the minimum number of horses required for appropriate statistical analysis of the torque measurements because torque was the primary outcome variable of interest. In addition, the rate of pin hole infection observed in the present study may have still resulted in a limitation to the histologic analysis, even with a random allocation approach of pins for histologic examination.

We conclude that the solution-precipitated biomimetic hydroxyapatite coating was able to improve pin stability, compared with uncoated pins, in horses during transfixation casting, albeit in an inconsistent or all-or-nothing manner. Future efforts should investigate methods to reduce the effect of thermal bone damage during hole drilling and pin placement and the development of pin hole infections associated with hydroxyapatite-coated pins to improve the consistency of osteointegration. At this time, hydroxyapatite pin coatings are not recommended for clinical use in horses because of the inconsistent results and lack of an observed clinical advantage.

a. Centerface LA transfixation pin, 1/4-inch shank, Imex Veterinary Inc, Longview, Tex.
b. Provided by DePuy, Warsaw, Ind.
c. 6.2-mm drill bit, Imex Veterinary Inc, Longview, Tex.
d. Part No. 2114T, Imex Veterinary Inc, Longview, Tex.
e. Large Battery Reamer/Drill, Synthes Inc, Paoli, Pa.
f. Electrotork Electronic Torque Wrench, Snap-On Inc, Kenosha, Wis.
g. Adapt-A-Drive, Milwaukee Electric Inc, Brookfield, Wis.
h. Plastazote foam pad, Technifab Products Inc, Avon, Ohio.
i. 3M Custom support foam, 3M Co, Saint Paul, Minn.
j. Dynacast Extra, BSN Medical Inc, Charlotte, NC.
k. Davis Horse Boot, Davis Manufacturing Co, Brandon, Wis.
l. eFilm Workstation, version 2.1, Merge Healthcare Inc, Milwaukee, Wis.
m. Exakt Macro Cutting Device, Exakt Technologies Inc, Oklahoma City, Okla.
n. Technovit 7200, Exakt Technologies Inc, Oklahoma City, Okla.
o. Histolux, Exakt Technologies Inc, Oklahoma City, Okla.
p. Exakt Macrocutting Device, Exakt Technologies Inc, Oklahoma City, Okla.
q. Exakt Microgrinde, Exakt Technologies Inc, Oklahoma City, Okla.
r. Nikon Optiphot-2, Nikon Inc, Melville, NY.
s. Stereo Investigator, MBF Bioscience Inc, Williston, Vt.
t. PROC MIXED, SAS, version 9.2 for Windows, SAS Institute Inc, Cary, NC.

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