

A randomized controlled trial of the efficacy of autologous platelet therapy for the treatment of osteoarthritis in dogs

Maria A. Fahie, DVM, DACVS; Girolamo A. Ortolano, PhD; Vincent Guercio, BS; Jeffrey A. Schaffer, DVM; Gary Johnston, DVM, DACVR; Jennifer Au, DVM, DACVS; Bianca A. Hettlich, Dr med vet, DACVS; Tom Phillips, DVM, PhD; Matthew J. Allen, Vet MB, PhD; Alicia L. Bertone, DVM, PhD, DACVS

Objective—To determine efficacy of a single intra-articular injection of an autologous platelet concentrate for treatment of osteoarthritis in dogs.

Design—Randomized, controlled, 2-center clinical trial.

Animals—20 client-owned dogs with osteoarthritis involving a single joint.

Procedures—Dogs were randomly assigned to a treatment or control group. In all dogs, severity of lameness and pain was scored by owners with the Hudson visual analog scale and the University of Pennsylvania Canine Brief Pain Inventory, respectively, and peak vertical force (PVF) was determined with a force platform. Dogs in the treatment group were then sedated, and a blood sample (55 mL) was obtained. Platelets were recovered by means of a point-of-use filter and injected intra-articularly within 30 minutes. Control dogs were sedated and given an intra-articular injection of saline (0.9% NaCl) solution. Assessments were repeated 12 weeks after injection of platelets or saline solution.

Results—Dogs weighed between 18.3 and 63.9 kg (40.3 and 140.6 lb) and ranged from 1.5 to 8 years old. For control dogs, lameness scores, pain scores, and PVF at week 12 were not significantly different from pretreatment values. In contrast, for dogs that received platelet injections, lameness scores (55% decrease in median score), pain scores (53% decrease in median score), and PVF (12% increase in mean PVF) were significantly improved after 12 weeks, compared with pretreatment values.

Conclusions and Clinical Relevance—Results suggested that a single intra-articular injection of autologous platelets resulted in significant improvements at 12 weeks in dogs with osteoarthritis involving a single joint. (*J Am Vet Med Assoc* 2013;243:1291–1297)

Lameness secondary to osteoarthritis is one of the most common clinical problems in dogs, with the stifle and elbow joints most commonly affected.¹ Although estimates of the prevalence of osteoarthritis in dogs vary,^{2,3a} the need for better treatments is indisputable.

Intra-articular injection of autologous platelets holds promise as a potential treatment for osteoarthritis in dogs. Growth factors present in platelets reportedly can enhance regenerative processes in osteoarthritic joints,⁴ elaboration of growth factors (including platelet-derived growth factors, vascular endothelial growth

ABBREVIATIONS

CBPI	Canine Brief Pain Inventory
HVAS	Hudson visual analog scale
PVF	Peak vertical force

factor, transforming growth factor- β , basic fibroblast growth factor, and platelet factor-4) from the α granules of platelets can directly promote healing,^{5,6} and growth factors may recruit stem cells to the site of application, facilitating tissue repair.^{7–9} Additionally, intra-articular administration of autologous platelet concentrates derived from whole blood has been reported to be efficacious in human patients with osteoarthritis, as judged by subjective rating scale measurements.^{10,11}

The purpose of the study reported here was to determine the efficacy of a single intra-articular injection of an autologous platelet concentrate for the treatment of osteoarthritis in dogs. Specifically, we wanted to determine whether there would be significant changes in severity of lameness or pain (as determined with the HVAS and University of Pennsylvania CBPI, respectively) or weight bearing (as determined by measurement of PVF) 12 weeks after a single intra-articular injection of autologous platelet concentrate in dogs with osteoarthritis involving a single joint.

From the Department of Small Animal Surgery, College of Veterinary Medicine, Western University of Health Sciences, Pomona, CA 91766 (Fahie, Johnston, Phillips); the Medical Group, Life Sciences Division, Pall Corp, 25 Harbor Park Dr, Port Washington, NY 11050 (Ortolano, Guercio, Schaffer); and the Comparative Orthopaedic Research Laboratory, College of Veterinary Medicine, The Ohio State University, Columbus, OH 43210 (Au, Hettlich, Allen, Bertone).

Supported in part by the Pall Corp.

Presented in abstract form at the 39th Annual Congress of the Veterinary Orthopedic Society, Crested Butte, Colo, March 2012; and at the American College of Veterinary Surgeons Annual Symposium, National Harbor, Md, October 2012.

The authors thank Dr. Akikazu Ishihara for data compilation; Nicole Stingle for study coordination; Dr. Marc Togneri, Dr. David Clark, and Kimberly Holt for study participation; and Dr. Michael P. Kowaleski for serving as a scientific advisor.

Address correspondence to Dr. Bertone (alicia.bertone@cvm.osu.edu).

Materials and Methods

Study design—The study was conducted as a randomized, controlled, 2-center clinical trial. The study design followed published guidelines^{12,13} and was approved by the Institutional Animal Care and Use Committees of the Western University of Health Sciences and The Ohio State University. All dogs used in the study were client owned, and all owners signed a consent form prior to study enrollment.

Inclusion criteria—Twenty client-owned dogs examined at the Western University of Health Sciences (n = 10) or The Ohio State University (10) because of osteoarthritis involving a single joint were enrolled in the study. Dogs were eligible for inclusion in the study if they were otherwise healthy, weighed > 11 kg (24.2 lb), were between 1.5 and 10 years of age, had clinical evidence of unilateral lameness with the cause localized to a single joint, did not have any palpable laxity of that joint when examined with the dog awake, and had radiographic evidence of osteoarthritis involving the joint (ie, radiographic evidence of osteophytes and an irregular or narrowed joint space without complete loss of the joint space). In addition, dogs were enrolled in the study only if they had not had any surgical interventions involving the affected joint in the preceding 6 months, had not received any injections of polysulfated glycosaminoglycans in the preceding 4 months, and had not received any intra-articular or systemic injections of glucocorticoids in the preceding 1 month. Dogs that were being treated with NSAIDs PO were eligible for enrollment in the study, provided that oral administration of NSAIDs was discontinued at least 1 week prior to study enrollment and for the duration of the study. In addition, owners were asked to not give their dogs any nutritional supplements (eg, glucosamine, chondroitin sulfate, and omega-3 fatty acids) for the duration of the study.

Study protocol—At the time of study enrollment (week 0), dogs were randomly assigned to a treatment or control group with the aid of a random number table. Radiographs of the affected joint were obtained, and scores for lameness severity and pain severity were assigned by owners of the participating dogs with the HVAS¹⁴ and the University of Pennsylvania CBPI,^{15–17,b} respectively. In addition, for dogs evaluated at The Ohio State University, force platform analysis was performed to measure PVE.

After these initial evaluations were completed, dogs in the treatment group were sedated with dexmedetomidine (4 µg/kg [1.8 µg/lb], IM) and a blood sample was obtained. Platelets were recovered by means of a point-of-use filter and injected intra-articularly within 30 minutes. Control dogs were sedated and given an intra-articular injection of saline (0.9% NaCl) solution. Assessments were repeated 12 weeks after injection of platelets or saline solution. Group assignment was then unmasked, and owners of dogs that had received saline solution were given the option of having their dogs receive an injection of autologous platelets.

The study was conducted in a blinded manner. Owners and attending veterinarians were unaware of group allocation until after lameness and pain scores

were assigned by the owners at week 12, and veterinarians who performed the intra-articular injections were not involved in patient assessments. Radiographs were collected and scored at the conclusion of the study by a single board-certified radiologist (GJ) who was unaware of group allocation. Force plate analyses were performed by staff at The Ohio State University who were unaware of the study protocol or group allocation.

Preparation and administration of autologous platelets—Autologous platelet concentrates were prepared with a commercially available, point-of-use, platelet filtration system^c in accordance with the manufacturer's directions. In brief, after dogs were sedated, a jugular vein blood sample (55 mL) was collected and mixed with 5 mL of acid-citrate-dextrose-A anticoagulant. Clamps isolating the platelet filter from the top and bottom blood collection bags of the filtration system were closed, 9 mL of injection-grade sterile water was added to the top blood collection bag, and the anticoagulated blood sample was then slowly injected into the top bag. Contents of the top bag were thoroughly mixed by inverting the bag during addition of the blood sample and by rocking the bag at least 10 times after addition of the blood sample was completed. The clamps isolating the platelet filter from the top and bottom blood collection bags were then opened, and blood was allowed to flow by gravity alone from the top bag through the filter and into the bottom bag, causing the platelets and leukocytes to be selectively sequestered on the surface of the filter. The clamps were then closed, and platelets were recovered by discarding the top and bottom blood collection bags and flushing hypertonic saline (2% NaCl) solution (8 mL) into the bottom port, through the filter, and into an empty syringe attached to the top port. Aseptic technique was used for all steps that involved preparing the platelet concentrates; processing of each blood sample to obtain a platelet concentrate required 5 to 15 minutes.

For administration of the platelet concentrate, arthrocentesis was performed and synovial fluid was withdrawn to confirm the needle was positioned within the joint space. With the needle maintained in place, the syringe used to aspirate synovial fluid from the joint was then removed and replaced with the syringe containing the platelet concentrate. Platelet concentrate was injected until sufficient resistance to push back the syringe plunger was reached.

Administration of saline solution—Dogs in the control group were sedated, and arthrocentesis was performed as described for dogs in the treatment group. Synovial fluid was withdrawn to confirm the needle was positioned within the joint space, and the syringe used to aspirate synovial fluid from the joint was then removed and replaced with a syringe containing saline solution. Saline solution was injected until sufficient resistance to push back the syringe plunger was reached.

Analysis of platelet concentrates—Following preparation of each platelet concentrate, a sample (0.5 mL) of the concentrate was added to a tube containing EDTA and submitted, along with a blood sample (1 mL) from the dog, for determination of Hct, platelet count, and WBC count. All blood samples were sent to 1 of 2 independent contract laboratories for processing.^{d,e}

Radiographic evaluation—Radiographs of the affected joints obtained at weeks 0 and 12 were examined by a board-certified radiologist (GJ) blinded to treatment group assignment, who assigned scores for severity of osteoarthritic changes on the basis of a standardized system.^{18,19} Briefly, joints were assessed for evidence of increased synovial fluid volume displacing the infrapatellar fat pad cranially (stifle joints only), periarticular osteophyte formation along the sites of synovial attachment, enthesiophyte formation at points of insertion of tendons or ligaments, narrowing of the joint space, subchondral bone sclerosis, remodeling of the subchondral bone, mineralization of intra-articular and periarticular soft tissues, and subchondral cysts. Osteoarthritis was then scored as mild (1), moderate (2), moderate to severe (2 to 3), or severe (3).

Assessment of lameness and pain—At weeks 0 and 12, scores for severity of lameness and pain were assigned by owners of the participating dogs using the HVAS¹⁴ and CBPI,^{15–17,b} respectively. Because the standard CBPI uses lower numbers to represent less severe pain (0 = no pain; 10 = worst pain), whereas the standard HVAS uses higher numbers to represent less severe lameness, we elected to change the HVAS questionnaire by inverting the scale, so that 0 represented no lameness and 10 represented non-weight-bearing lameness, to make it less confusing for owners to complete both questionnaires at the same time.

Measurement of PVF—For dogs evaluated at The Ohio State University, force platform analysis was performed at weeks 0 and 12 with a computer-assisted kinetic analysis system.^f The system included a 2 × 1-foot force plate mounted in a 1 × 5-m runway. The force plate and runway surface were covered with a mat to prevent dogs from slipping and to avoid recognition of the plate. Dogs were led over the force plate at a trot until 5 valid repetitions were recorded for the osteoarthritic limb, where a valid measurement was defined as passage by the dog over the force plate during which the paw of the limb of interest fully contacted the surface of the plate and the gait velocity was within the range of 1.3 to 2.1 m/s. Before data collection, all dogs were allowed to warmup by walking and trotting them 5 to 10 times through the examination runway to accustom the dog to the environment and ensure that the dog would trot calmly along the runway at a constant speed. Gait velocity was measured by means of 2 photoelectric switches that were connected to the computer analysis system. Force-versus-time curves generated by the computer analysis system were used to compute PVF; values for PVF were expressed as a percentage of body weight.

Data analysis—Data were assessed for normality with the Shapiro-Wilk test, and parametric (repeated-measures ANOVA for analysis of PVF at weeks 0 and 12 and paired *t* tests for comparison of platelet count, WBC count, and Hct in blood vs platelet concentrates) and nonparametric (Wilcoxon matched pairs test for analysis of owner-assigned HVAS and CBPI scores at weeks 0 and 12) methods of data analysis were used. For HVAS score, CBPI score, and PVF, the percentage change before (week 0) versus after (week 12) treatment was calculated for each group.

For the 10 dogs evaluated at The Ohio State University, repeated-measures ANOVA with factors for treatment (platelet concentrate vs saline solution), time (week 0 vs week 12), and repetition number (1 through 5) was used to

analyze PVF data. Repetition number was not a significant factor in the analysis. For the significant factor of treatment within time, posttest comparisons were performed with a mixed procedures statistical model for continuous outcome variables. Variables were considered nested within dog, with dog treated as a random variable and the distribution of data assessed by use of a subset of normality.

For each individual dog, the mean, median, and range of gait velocities for the 5 valid measurements obtained at weeks 0 and 12 were calculated and analyzed by means of repeated-measures ANOVA. For all dogs, gait velocity at week 0 was compared with gait velocity at week 12, and at weeks 0 and 12, mean gait velocity for dogs that received the platelet concentrate was compared with mean gait velocity for dogs that received saline solution.

All analyses were performed with standard software^{g,h}; values of *P* < 0.05 were considered significant.

Results

Patients—The 20 dogs used in the study included 2 Rottweilers, 8 retrievers, and 10 other dogs representing a variety of medium to large breeds. Body weight ranged from 18.3 to 63.9 kg (40.3 to 140.6 lb; mean, 38.7 kg [85.1 lb]), and age ranged from 1 to 8 years (mean, 4.3 years).

Affected joints included the stifle joint (*n* = 13), elbow joint (5), tarsal joint (1), and shoulder joint (1). Thirteen dogs had a left forelimb or hind limb joint affected, and 7 had a right forelimb or hind limb joint affected.

No adverse effects associated with injection of platelet concentrate or saline solution were reported. One of the control dogs with stifle joint osteoarthritis evaluated at the Western University of Health Sciences was removed from the study at week 4 because of an acute onset of non-weight-bearing lameness and palpable joint laxity presumed to be attributable to progression of cranial cruciate ligament disease warranting surgical management. This was considered to be unassociated with injection of saline solution 4 weeks earlier.

Owners of the remaining 9 control dogs that completed the study were offered the chance to have their dogs receive an injection of autologous platelets, and all accepted.

Radiographic osteoarthritis scores—At week 0, 9 dogs had mild osteoarthritis (radiographic grade 1), 2 had moderate osteoarthritis (radiographic grade 2), 6 had moderate to severe osteoarthritis (radiographic grade 2 to 3), and 3 had severe osteoarthritis (radiographic grade 3). For all dogs, radiographic scores assigned at week 12 were the same as the scores assigned at week 0.

Platelet count, WBC count, and Hct—Fourteen paired blood and platelet concentrate samples were submitted for determination of platelet count, WBC count, and Hct (10 paired samples obtained from treatment group dogs and an additional 4 paired samples obtained from control group dogs that received injections of autologous platelets after the conclusion of the study). Platelet count for the platelet concentrates (mean ± SD, 739,000 ± 365,000 platelets/μL) was significantly (*P* < 0.001) higher than platelet count for the blood samples (240,000 ± 82,000 platelets/μL), representing a 3.0-fold (SD, 1.1) increase in platelet count. Similarly, WBC count for the platelet concentrates (15,100 ± 7,800 WBCs/μL) was significantly (*P* < 0.001)

higher than WBC count for the blood samples ($7,900 \pm 2,000$ WBCs/ μ L), representing a 1.8-fold (SD, 0.6) increase in WBC count. In contrast, Hct for the platelet concentrates ($27.1 \pm 7.0\%$) was significantly ($P < 0.001$) lower than Hct for the blood samples ($45.2 \pm 5.6\%$).

Owner-assigned lameness and pain scores—For the control dogs ($n = 9$), HVAS scores assigned at week

12 (median, 3.5; interquartile [25th to 75th percentile] range, 1.8 to 5.5) were not significantly ($P = 0.932$) different from scores assigned at week 0 (median, 3.0; interquartile range, 2.0 to 5.5; **Figure 1**). In contrast, for dogs that received the platelet concentrate ($n = 10$), HVAS scores assigned at week 12 (median, 2.3; interquartile range, 1.0 to 3.0) were significantly ($P = 0.009$) improved, compared with scores assigned at week 0 (median, 5.0; interquartile range, 2.8 to 5.6), representing a 55% improvement in median score.

Similarly, CBPI scores assigned at week 12 for the control dogs ($n = 9$; median, 3.0; interquartile range, 2.0 to 6.0) were not significantly ($P = 0.725$) different from scores assigned at week 0 (median, 3.0; interquartile range, 2.5 to 5.8), whereas for dogs that received the platelet concentrate ($n = 10$), scores assigned at week 12 (median, 1.8; interquartile range, 1.0 to 3.0) were significantly ($P = 0.014$) improved, compared with scores assigned at week 0 (median, 3.8; interquartile range, 2.4 to 7.0), representing a 53% improvement in median score.

When component scores used to calculate owner-assigned HVAS and CBPI scores were examined, scores for all components of the HVAS and CBPI were not significantly different between week 0 and week 12 for control dogs (**Table 1**). For dogs that received the platelet concentrate, scores for all components of the HVAS except activity, playfulness, exer-

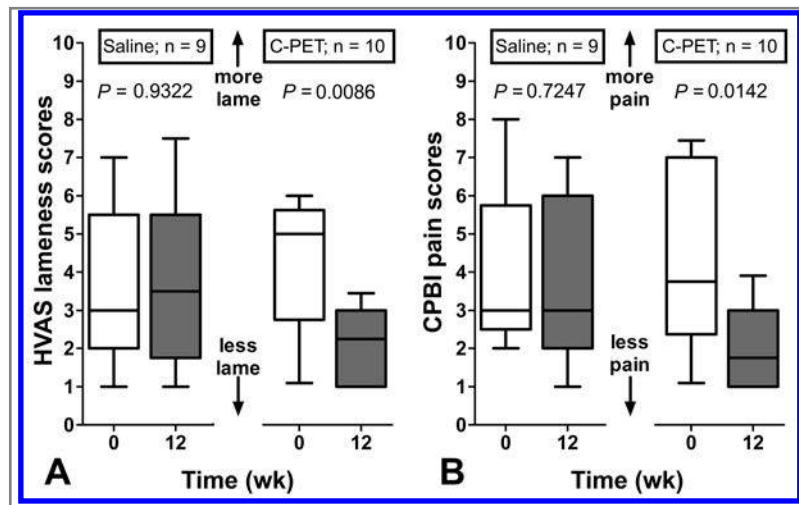


Figure 1—Box-and-whisker plots of owner-assigned scores for severity of lameness (A; HVAS scores) and pain (B; University of Pennsylvania CBPI scores) for 19 dogs with osteoarthritis involving a single joint that received a single injection of autologous platelets (C-PET; $n = 10$) or saline (0.9% NaCl) solution (saline; 9). Scores were assigned immediately prior to treatment (wk 0) and again 12 weeks later (wk 12). For each box plot, the box represents the interquartile (25th to 75th percentile) range, the horizontal line represents the median, and the whiskers represent the 10th to 90th percentiles.

Table 1—Owner-assigned scores for components of the HVAS and University of Pennsylvania CBPI in a study involving 19 dogs with osteoarthritis involving a single joint that received a single injection of autologous platelets (platelet therapy; $n = 10$) or saline (0.9% NaCl) solution (9); scores were assigned immediately prior to treatment (week 0) and again 12 weeks later (week 12).

Variable	Saline solution			Platelet therapy		
	Week 0	Week 12	P value	Week 0	Week 12	P value
HVAS						
Overall	3 (2–4)	3.5 (3–5)	0.798	3.5 (2–5.75)	1 (1–3)	0.020
Mood	2 (1–4)	2 (1–3.25)	0.890	2 (1–3.75)	1 (1–2)	0.057
Attitude	2 (1–4)	1.5 (1–3.25)	1.000	2 (1–3)	1 (1–2)	0.053
Comfort	2 (2–5)	2.5 (1–3.25)	0.832	3 (2.25–4.5)	2 (1–2.75)	0.034
Activity	9 (8–9)	8 (5–9)	0.170	3 (1.75–5)	3 (2–3)	0.850
Playfulness	2 (1–3)	2 (1–5)	0.443	3 (1–3.25)	2 (2–3)	1.000
Exercise	3 (3–4)	3 (3–4)	0.498	5 (3–6)	4 (3–5)	0.892
Arising stiff	7 (5–8)	6.5 (5–8)	1.000	8 (5–8)	4 (2–5)	0.036
Bedding stiff	7 (5–8)	6 (5–8)	0.598	5 (4–7)	3 (2–3)	0.023
Walking comfort	8 (5–8)	6 (3–9)	0.622	7 (5–9)	4 (2–5)	0.114
Turning comfort	4 (2–5)	5 (1–6)	0.932	5 (3–6)	2 (1–3)	0.034
CBPI						
Worst pain	7 (4–8)	4 (3–8)	0.551	5.5 (3.5–7)	2.5 (1.25–4)	0.009
Least pain	2 (2–3)	2 (1–4)	0.784	2.5 (1.25–4)	1 (1–2.75)	0.034
Typical pain	4 (3–6)	3 (2–6)	0.410	4 (2–7)	2 (1–3)	0.014
Pain now	2.5 (2–4.5)	3 (2–5)	0.667	3 (2–7)	1.5 (1–2)	0.035
General activity	3 (2–3)	3 (2–4)	0.824	5 (2–6)	2 (1–3)	0.029
Enjoys life	3 (2–3)	2 (1–3)	0.105	4 (2–6)	2 (1–2)	0.042
Can rise	6 (3–7)	5 (3–6)	0.280	8 (4–8)	3 (2–3)	0.014
Can walk	3 (3–4)	3 (2–4)	0.951	3 (3–7)	2 (1–3)	0.058
Can run	4 (3–5)	3 (2–5)	0.798	4 (3–8)	3 (2–3)	0.022
Can climb	2 (2–8)	4 (2–7)	0.930	3 (3–8)	3 (1–3)	0.058

Data are given as median (interquartile range). For all components of both scoring systems, possible scores range from 1 to 10, with lower scores indicating less lameness or pain.

cise, and walking comfort and for all components of the CBPI were significantly different between week 0 and week 12.

PVF—For the control dogs ($n = 5$), PVF (expressed as a percentage of body weight) at week 12 (mean \pm SE, $70.55 \pm 5.72\%$) was not significantly ($P = 0.694$) different from PVF at week 0 ($69.04 \pm 5.27\%$). In contrast, for the dogs that received the platelet concentrate ($n = 5$), PVF at week 12 ($71.69 \pm 4.15\%$) was significantly ($P = 0.012$) improved, compared with PVF at week 0 ($64.13 \pm 4.08\%$), representing a 12% increase in mean PVF. Mean change in PVF (ie, week 12 value minus week 0 value) was not significantly ($P = 0.508$) different from 0 (mean \pm SE, $-2.0 \pm 2.7\%$) for the control dogs, but was significantly ($P = 0.019$) different from 0 for dogs that received the platelet concentrate ($17.3 \pm 6.0\%$).

For all dogs, gait velocity ranged from 1.4 to 1.8 m/s (overall mean, 1.7 m/s), and gait velocity was not significantly ($P = 0.57$) different between control dogs and dogs that received the platelet concentrate. Mean absolute difference in gait velocity between week 0 and week 12 was 0.08 m/s (median, 0.08 m/s; range, 0.01 to 0.18 m/s). For both groups, gait velocity at week 0 was not significantly ($P = 0.33$ for control dogs and 0.59 for dogs that received the platelet concentrate) different from gait velocity at week 12.

The 5 control dogs evaluated at The Ohio State University that received an injection of autologous platelets at the end of the study all underwent force plate analysis immediately prior to injection of platelets and again 12 weeks later. In these dogs, mean \pm SE PVF increased from $70.55 \pm 6.80\%$ immediately prior to the platelet injection to $79.65 \pm 1.74\%$ 12 weeks later.

Discussion

Results of the present study suggested that in dogs with osteoarthritis involving a single joint, administration of a single intra-articular injection of autologous platelets resulted in significant improvements 12 weeks later, as determined by subjective (ie, owner-assigned scores for severity of pain and lameness) and objective (ie, PVF) measures. To our knowledge, the present study is the first to show subjectively and objectively that intra-articular platelet therapy can relieve pain in osteoarthritic dogs for up to 3 months, and our data support the use of platelet therapy as an alternative treatment option.

Options for the treatment of osteoarthritis in dogs range considerably,²⁰ with authors of a relatively recent systematic review²¹ concluding that for many of the more widely accepted alternatives, there is adequate evidence of efficacy, but that many studies fail to provide sufficient data to draw definite conclusions. Although studies continue to emerge in support of various treatment options such as weight control,²² NSAIDs,²³ and nutraceuticals,²⁴ there appears to be few, short of joint replacement surgery, that can offer a cure. The present study was designed to overcome some of the limitations of other work by including an objective measure of lameness severity, PVF, which is a measure of weight bearing, as well as the more popular and easily ap-

plied subjective measures of lameness (HVAS) and pain (CBPI) severity, which reflect an observer's opinion, over time, of the dog's behavior.

Assessing the severity of lameness and pain associated with osteoarthritis is more challenging with canine patients than with human patients. The HVAS and CBPI have been evaluated in previous studies^{14–17,25,26,b} and are accepted subjective methods of assessing pain and lameness. Results of the present study suggested that some questions may be more revealing than others in assessing the effects of specific treatments. On the whole, however, the results indicated that clinical efficacy of platelet therapy should be evident to dog owners through observation of behavioral changes alone.

Force plate analysis is an established objective method to characterize gait kinetics in healthy^{27–29} and lame dogs³⁰ and to evaluate response to surgery³¹ or drug treatment³² in lame dogs. Although methods for evaluating gait kinetics continue to evolve,³³ we elected to focus on the most often cited response measure, PVF.^{34,35} In the present study, PVF was significantly increased at week 12 in dogs that received autologous platelets, and the magnitude of effect (12%) was comparable to that seen in studies²¹ of the efficacy of NSAIDs. Because PVF is dependent on gait velocity, with faster gait velocity associated with higher PVF, we examined our data to ensure that the increase in PVF seen at week 12 for dogs that received autologous platelets was not simply a result of a difference in gait velocity. For both groups of dogs in the present study, there was no significant difference in gait velocity between week 0 and week 12, and gait velocity was not significantly different between control dogs and dogs that received autologous platelets. Although dogs in the present study ranged widely with regard to body weight, breed, age, and limb affected, gait velocity during force plate analysis ranged from only 1.4 to 1.8 m/s. In addition, the absolute difference in velocity between week 0 and week 12 ranged from 0.01 to 0.18 m/s (mean, 0.08 m/s), which complies with the current recommendation that the variation in gait velocity be < 0.2 m/s when comparing multiple measurements of gait kinetics.³⁶ These findings suggest that differences in gait velocity alone cannot account for the significant increase in PVF seen in dogs that received autologous platelets.

In the present study, we elected to collect data on 5 valid repetitions each time gait analysis was performed. In a previous study³⁷ involving horses with experimentally induced forelimb synovitis, we found that order of repetition had a significant effect on PVF, with horses becoming less lame after 5 repetitions. For this reason, we elected to provide dogs a warmup period prior to gait analysis and collected data for 5 repetitions. In our analysis, we found that the order of the 5 repetitions did not have a significant effect on PVF. Even though gait analyses were performed by individuals who were blinded to treatment group allocation, we elected to exclude data collected from control dogs that subsequently received platelet therapy. Nevertheless, in these 5 dogs, we did see an increase in mean PVF 12 weeks after platelet injection, further supporting the benefit of platelet therapy in dogs with osteoarthritis.

The composition of the various platelet-rich products that are currently available is a subject of consider-

able research.³⁸ Four general types of such products are possible (leukocyte rich or poor and fibrin present or absent), and each may have more value in certain applications. For example, the presence of leukocytes could lead to deleterious effects, including inflammation,³⁹ in certain applications and to beneficial effects, such as infection-fighting capacity, in others.⁴⁰ In a study⁴¹ of rabbits, a WBC-rich platelet product elicited inflammation that was short-lived and did not alter the therapeutic effect of the platelet preparation 14 days after treatment. Also, topical use of a platelet gel containing leukocytes has been shown to reduce the severity of mediastinitis in human patients undergoing open heart surgery.⁴² The platelet concentrate in the present study would be classified as a WBC-enriched platelet product.

The platelet concentrates in the present study had a mean 3-fold increase in platelet count, compared with count for blood, and a mean 1.8-fold increase in WBC count. No adverse effects were reported, suggesting that inflammation that might have occurred as a result of the WBCs was not sufficient to have a clinical effect. Although the sample size was too small to determine whether WBCs in the platelet concentrates offered any measure of protection against iatrogenic joint infection, none of the joints in the present study became infected.

The specific mechanism of action of the platelet concentrate used in the present study is unknown. Platelet therapy may operate through direct delivery of platelet-derived growth factors, but these growth factors can also serve as chemoattractants for stem cells.^{43,44} Also, both growth factors and recruited cells may mediate local cell replication and differentiation and the release of additional growth factors.⁵⁻⁹

Minimally invasive methods for the treatment of osteoarthritis in dogs are appealing to both veterinarians and pet owners, particularly compared with surgical alternatives such as joint replacement. Subjectively, the filter-based device used to obtain the platelet concentrate in the present study was easy to use, and the entire procedure, from initial sedation to completion of the intra-articular injection, took about 30 minutes. Although the present study found significant effects at 12 weeks after treatment, further studies are needed to determine the optimal dose and the duration of effect.

- Lefebvre S, Associate Medical Advisor, Research, Banfield Applied Research and Knowledge (BARK) Team, Portland, Ore: Personal communication, 2012.
- Walton MB, Cowderoy E, Lascelles D, et al. Canine osteoarthritis: validation of the owner-administered clinical outcomes measurement tools LOAD, CBPI and HCPI (abstr), in *Proceedings*. 39th Annu Meet Vet Orthop Soc 2012;45.
- C-PET, Canine-Platelet Enhancement Therapy, Pall Corp, Port Washington, NY.
- Antech Inc, Rancho Cordova, Calif.
- Antech Inc, Medina, Ohio.
- Force plate and computer analysis system, Kistler Instrument Corp, Amherst, NY.
- Prism, version 5, GraphPad Inc, San Diego, Calif.
- SAS, version 9.2, SAS Institute Inc, Cary, NC.

References

- Johnston SA. Osteoarthritis. Joint anatomy, physiology, and pathobiology. *Vet Clin North Am Small Anim Pract* 1997;27:699-723.
- Fox SM, Millis D. Osteoarthritis: the disease. In: *Multimodal management of canine osteoarthritis*. London: Manson Publishing Ltd, 2010;24-30.
- Veterinary Pet Insurance. Nation's largest pet insurer reveals most common causes of veterinary visits. Available at: press.petinsurance.com/pressroom/02222011Pet_Conditions_2010.aspx. Accessed Jun 15, 2012.
- Textor J. Autologous biologic treatment for equine musculoskeletal injuries: platelet-rich plasma and IL-1 receptor antagonist protein. *Vet Clin North Am Equine Pract* 2011;27:275-298.
- Fortier LA, Barker JU, Strauss EJ, et al. The role of growth factors in cartilage repair. *Clin Orthop Relat Res* 2011;469:2706-2715.
- Nguyen RT, Borg-Stein J, McInnis K. Applications of platelet-rich plasma in musculoskeletal and sports medicine: an evidence-based approach. *Phys Med Rehabil* 2011;3:226-250.
- Schmidt MB, Chen EH, Lynch SE. A review of the effects of insulin-like growth factor and platelet derived growth factor on in vivo cartilage healing and repair. *Osteoarthritis Cartilage* 2006;14:403-412.
- Kajikawa Y, Morihara T, Sakamoto H, et al. Platelet-rich plasma enhances the initial mobilization of circulation-derived cells for tendon healing. *J Cell Physiol* 2008;215:837-845.
- van den Dolder J, Mooren R, Vloon AP, et al. Platelet-rich plasma: quantification of growth factor levels and the effect on growth and differentiation of rat bone marrow cells. *Tissue Eng* 2006;12:3067-3073.
- Kon E, Mandelbaum B, Buda R, et al. Platelet-rich plasma intra-articular injection versus hyaluronic acid viscosupplementation as treatments for cartilage pathology: from early degeneration to osteoarthritis. *Arthroscopy* 2011;27:1490-1501.
- Filardo G, Kon E, Buda R, et al. Platelet-rich plasma intra-articular knee injections for the treatment of degenerative cartilage lesions and osteoarthritis. *Knee Surg Sports Traumatol Arthrosc* 2011;19:528-535.
- Cook JL, Evans R, Conzemius MG. Proposed definitions and criteria for reporting time frame, outcome and complications for clinical orthopedic studies in veterinary medicine. *Vet Surg* 2010;39:905-908.
- The CONSORT Group. The CONSORT Statement. Available at: www.consort-statement.org/consort-statement/overview0/. Accessed Jun 15, 2012.
- Hudson JT, Slater MR, Taylor L, et al. Assessing repeatability and validity of a visual analogue scale questionnaire for use in assessing pain and lameness in dogs. *Am J Vet Res* 2004;65:1634-1643.
- University of Pennsylvania School of Veterinary Medicine Veterinary Clinical Investigations Center. Canine Brief Pain Inventory. Available at: research.vet.upenn.edu/PennChart/AvailableTools/tabid/1969/Default.aspx. Accessed Jun 15, 2012.
- Brown DC, Boston RC, Coyne JC, et al. Ability of the canine brief pain inventory to detect response to treatment in dogs with osteoarthritis. *J Am Vet Med Assoc* 2008;233:1278-1283.
- Brown DC, Boston RC, Coyne JC, et al. Development and psychometric testing of an instrument designed to measure chronic pain in dogs with osteoarthritis. *Am J Vet Res* 2007;68:631-637.
- Allen GS. Radiographic signs of joint disease in dogs and cats. In: Thrall D, ed. *Textbook of veterinary diagnostic radiology*. 5th ed. St Louis: Saunders Elsevier, 2007;317-358.
- Innes JF, Costello M, Barr FJ, et al. Radiographic progression of osteoarthritis of the canine stifle joint: a prospective study. *Vet Radiol Ultrasound* 2004;45:143-148.
- Fox SM, Millis D. *Multimodal management of canine osteoarthritis*. London: Manson Publishing Ltd, 2010;96.
- Aragon CL, Hofmeister EH, Budsberg SC. Systematic review of clinical trials of treatments for osteoarthritis in dogs. *J Am Vet Med Assoc* 2007;230:514-521.
- Beraud R, Moreau M, Lussier B. Effect of exercise on kinetic gait analysis of dogs afflicted by osteoarthritis. *Vet Comp Orthop Traumatol* 2010;23:87-92.
- Kukanich B, Bidgood T, Knesl O. Clinical pharmacology of nonsteroidal anti-inflammatory drugs in dogs. *Vet Anaesth Analg* 2012;39:69-90.
- Vandeweerdt JM, Coisson C, Clegg P, et al. Systematic review of efficacy of nutraceuticals to alleviate clinical signs of osteoarthritis. *J Vet Intern Med* 2012;26:448-456.

25. Hjermstad MJ, Fayers PM, Haugen DF, et al. European Palliative Care Research Collaborative (EPCRC). Studies comparing numerical rating scales, verbal rating scales, and visual analogue scales for assessment of pain intensity in adults: a systematic literature review. *J Pain Symptom Manage* 2011;41:1073–1093.
26. Hielm-Björkman AK, Kapatkin AS, Rita HJ. Reliability and validity of a visual analogue scale used by owners to measure chronic pain attributable to osteoarthritis in their dogs. *Am J Vet Res* 2011;72:601–607.
27. Budsberg SC, Jevens DJ, Brown J, et al. Evaluation of limb symmetry indices, using ground reaction forces in healthy dogs. *Am J Vet Res* 1993;54:1569–1574.
28. DeCamp CE, Soutas-Little RW, Hauptman J, et al. Kinematic gait analysis of the trot in healthy Greyhounds. *Am J Vet Res* 1993;54:627–634.
29. Rumph PF, Lander JE, Kincaid SA, et al. Ground reaction force profiles from force platform gait analyses of clinically normal mesomorphic dogs at the trot. *Am J Vet Res* 1994;55:756–761.
30. Bennett RL, DeCamp CE, Flo GL, et al. Kinematic gait analysis in dogs with hip dysplasia. *Am J Vet Res* 1996;57:966–971.
31. Budsberg SC, Chambers JN, Lue SL, et al. Prospective evaluation of ground reaction forces in dogs undergoing unilateral total hip replacement. *Am J Vet Res* 1996;57:1781–1785.
32. Budsberg SC, Johnston SA, Schwarz PD, et al. Efficacy of etodolac for the treatment of osteoarthritis of the hip joints in dogs. *J Am Vet Med Assoc* 1999;214:206–210.
33. Al-Nadaf S, Torres BT, Budsberg SC. Comparison of two methods for analyzing kinetic gait data in dogs. *Am J Vet Res* 2012;73:189–193.
34. Budsberg SC, Torres BT, Zwijnenber RJ, et al. Effect of perzinfotel and a proprietary phospholipase A(2) inhibitor on kinetic gait and subjective lameness scores in dogs with sodium urate-induced synovitis. *Am J Vet Res* 2011;72:757–763.
35. Imhoff DJ, Gordon-Evans WJ, Evans RB, et al. Evaluation of S-adenosyl L-methionine in a double-blinded, randomized, placebo-controlled, clinical trial for treatment of presumptive osteoarthritis in the dog. *Vet Surg* 2011;40:228–232.
36. Oosterlinck M, Bosmans T, Gasthuys F, et al. Accuracy of pressure plate kinetic asymmetry indices and their correlation with visual gait assessments scores in lame and nonlame dogs. *Am J Vet Res* 2011;72:820–825.
37. Ishihara A, Bertone AL, Rajala-Schultz PJ. Association between subjective lameness grade and kinetic gait parameters in horses with experimentally induced forelimb lameness. *Am J Vet Res* 2005;66:1805–1815.
38. Dohan Ehrenfest DM, Bielecki T, Del Corso M, et al. Shedding light in the controversial terminology for platelet-rich products: platelet-rich plasma (PRP), platelet-rich fibrin (PRF), platelet-leukocyte gel (PLG), preparation rich in growth factors (PRGF), classification and commercialism. *J Biomed Mater Res A* 2010;95:1280–1282.
39. Boswell SG, Cole BJ, Sundman EA, et al. Platelet-rich plasma: a milieu of bioactive factors. *Arthroscopy* 2012;28:429–439.
40. Bielecki T, Dohan Ehrenfest DM, Everts PA, et al. The role of leukocytes from L-PRP/L-PRF in wound healing and immune defense: new perspectives. *Curr Pharm Biotechnol* 2012;13:1153–1162.
41. Dragoo JL, Braun HJ, Durham JL, et al. comparison of the acute inflammatory response of two commercial platelet-rich plasma systems in healthy rabbit tendons. *Am J Sports Med* 2012;40:1274–1281.
42. Trowbridge CC, Stammers AH, Woods E, et al. Use of platelet gel and its effects on infection in cardiac surgery. *J Extra Corpor Technol* 2005;37:381–386.
43. Forsberg-Nilsson K, Behar TN, Afrakhte M, et al. Platelet-derived growth factor induces chemotaxis of neuroepithelial stem cells. *J Neurosci Res* 1998;53:521–530.
44. Lee JM, Kim BS, Lee H, et al. In vivo tracking of mesenchymal stem cells using fluorescent nanoparticles in an osteochondral repair model. *Mol Ther* 2012;20:1434–1442.



Correction: Comparison of lateral fabellar suture and tibial plateau leveling osteotomy techniques for treatment of dogs with cranial cruciate ligament disease

In the report, “Comparison of lateral fabellar suture and tibial plateau leveling osteotomy techniques for treatment of dogs with cranial cruciate ligament disease,” (*J Am Vet Med Assoc* 2013;243:675–680), the following 2 sentences in the Results section are incorrect:

Six months after surgery, PVF values at a trot were not significantly ($P = 0.06$) different between groups. The percentage differences in mean PVF values between groups were 5% at a walk and 8% at trot at 6 months and 6% at a walk and 11% at a trot at 12 months ($P < 0.05$; Figures 1 and 2).

The sentences should have read as follows:

Six months after surgery, PVF values at a trot were significantly different between groups, but PVF values at a walk were not significantly ($P = 0.06$) different between groups at that time. The percentage differences in mean PVF values between groups were 5% at a walk and 8% at a trot at 6 months and 6% at a walk and 11% at a trot at 12 months (Figures 1 and 2).