Article published online: 2024-07-03

Activity Levels in Seven Cats with Osteoarthritis Monitored by GPS Tracker Following Frunevetmab Injection

Ashley M. Power[1] Lindsay L. St. Germaine[1]

[1] Department of Surgery, Veterinary Specialists and Emergency Services, Rochester, New York, United States

VCOT Open 2024;7:e97–e102.

Address for correspondence Ashley M. Power, MA, VMD, Department of Surgery, VCA Veterinary Referral & Emergency Center, Westbury, NY 11590, United States (e-mail: ashleypowervmd@gmail.com).

Abstract

Objective The goal of the current pilot study was to use a commercially available accelerometer (Tractive GPS Tracker for Cats) in a setting evaluating the activity level of cats exhibiting different forms of osteoarthritis in their natural habitat before and after treatment with frunevetmab, using each individual cat as its own control. We hypothesized that treatment with frunevetmab would be associated with increased activity level.

Methods Activity data, measured as minutes of active time per day via accelerometer worn on a collar, were obtained from seven employee-owned cats with radiographically confirmed evidence of osteoarthritis. Cats were randomly assigned to two different protocols in which treatment and no treatment (control) were reversed; that is, undergoing the control period prior to treatment with frunevetmab ("standard" control) versus first assessed without treatment (control period) followed by frunevetmab treatment after minimum 30-day washout period ("inverse" control period).

Results Activity time, on average, was 30 minutes longer per day for frunevetmab versus control ($p = 0.007$).

Conclusions Based on measurements obtained with piloted use of the Tractive, the activity level in osteoarthritic cats appeared greater when treated with frunevetmab compared to self-control without frunevetmab treatment (either pretreatment or following washout period). The small sample size here does warrant caution in interpreting results for a broader population.

Keywords
- arthritis
- chronic pain
- monoclonal antibody
- frunevetmab
- feline

Introduction

Osteoarthritis (degenerative joint disease) has a high prevalence among domestic cats, with anywhere from 64 to 90% having radiographic evidence, and 45% exhibiting clinical signs of discomfort and/or decreased mobility.[1,2] Historically, feline osteoarthritis has been underdiagnosed and undertreated.[3] Growing recognition of this disease has become evident as practitioners seek effective long-term treatment options to improve comfort and quality of life for arthritic cats. While nonsteroidal anti-inflammatory drugs can be effective, they carry risk of kidney damage, precluding use in the many aging cats with concurrent chronic kidney disease.[4] Other drugs such as gabapentin,[5] tramadol,[6–8] and amantadine[9] have shown varied success in previous studies, however, can cause stress for cats that are not amenable to receiving indefinite daily oral medication.

received
November 26, 2023
accepted after revision
May 29, 2024

DOI https://doi.org/10.1055/s-0044-1788038.
ISSN 2625-2325.

Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

Nerve growth factor (NGF) has been identified as a therapeutic target for treating osteoarthritis. NGF is pronociceptive, and can trigger peripheral sensitization as well as potentiate inflammatory responses.[10,11] Use of anti-NGF monoclonal antibodies has been investigated in companion animals.[12] A feline anti-NGF monoclonal antibody (frunevetmab) was demonstrated to exhibit an acceptable safety and efficacy profile in a feline model of chronic pain.[13] Frunevetmab is administered as a once-monthly injection and has been approved by the Food and Drug Administration for use in cats with osteoarthritis (Solensia, Zoetis Animal Health, Parsippany, New Jersey, United States).[14]

A preliminary proof-of-concept study[15] and a multi-site pilot field study[16] have further demonstrated efficacy of frunevetmab in treating chronic pain associated with osteoarthritis in client-owned cats. Outcome assessments incorporated both subjective factors, including clinical metrology assessments completed by owners (client-specific outcome measures and feline musculoskeletal pain index [FMPI]) and physical examination findings, as well as objective factors, including accelerometry data gathered via activity monitor.[15,16]

Activity monitors that have been evaluated in the current literature include the Actical (Respironics, Mini Mitter Division, Bend, Oregon, United States),[17,18] PetPace (PetPace LLC, Burlington, Massachusetts, United States),[19,20] and PlusCycle (JARMeC, Kanagawa, Japan).[21] The Actical has been validated in the dog[17] and has been shown to correlate well with computer-analyzed video movement data in the cat[18]; however, the latter study noted that there was variability between subjects, and so the authors advised that future accelerometer-based studies in cats should use each cat as its own control.[18] The PetPace, while demonstrated to correlate well with data from the validated Actical, has only been evaluated in dogs.[19,20] The PlusCycle demonstrated strong correlations with Actical data in cats,[21] however, is only commercially available in Japan at this time.

The Tractive GPS Tracker for Cats (Tractive Inc, Seattle, Washington, United States) has not been previously evaluated in clinical studies. It offers a simplified user interface whereby a pet owner can easily view and understand their pet's activity data. Compared to the PetPace, the Tractive is offered at a more reasonable retail price ($49.99 vs. $299.99, plus subscription fees, at the time of this writing) and is also lower profile (35 g device that can be affixed to pet's usual collar vs. 60 g standalone collar). Size and comfort of the activity monitor is an important consideration in tolerating wear, particularly for feline patients; indeed, previous work has shown that a more cumbersome harness-type fixation of an activity monitor was associated with decreased activity level in cats over an acclimation period.[18]

While clinical metrology assessments such as the FMPI have been refined and shortened to encourage responsiveness, consistent owner evaluation of their cats at home remains a major impediment in assessing pain and activity level.[21] Therefore, the Tractive, a relatively small, inexpensive activity monitor with simplified data output, shows promise as a tool to objectively evaluate feline activity levels at home with improved owner responsiveness.

The goal of the current study was to pilot use of the Tractive activity monitor in a clinical study evaluating the activity level of cats when treated with frunevetmab. The study was designed to be a simple, objective, single-outcome, paired analysis, using each individual cat as its own self-control. We hypothesized that treatment with frunevetmab would be associated with increased activity level compared to control.

Materials and Methods

Study Population

Employee-owned cats with suspected osteoarthritis were recruited for enrollment via email listserv and flyers placed in the hospital. Owner informed consent was obtained. Animal ethics approval was not obtained as frunevetmab injection was administered per its labeled use. Cats were eligible for inclusion if they (1) had radiographically documented evidence of osteoarthritis in at least one joint, (2) tolerated wearing of the activity monitor on a neck collar, and (3) were not currently receiving analgesics, anti-inflammatory medication, or supplements to treat osteoarthritis.

Treatment Categories

Cats were randomized via coin-toss to undergo the control period either prior to treatment with frunevetmab ("standard" control, cats A, B, C, D), or after frunevetmab treatment following minimum 30-day washout period ("inverse" control, cats E, F, G; washout periods, 49 days, 35 days, and 68 days, respectively). The inverse control period was utilized in an effort to minimize variation in acclimation period for monitor wear . Each cat was administered a 7 mg subcutaneous injection of frunevetmab (Solensia 7 mg/mL solution in a single-use 1 mL vial, Zoetis Animal Health, Parsippany, New Jersey, United States)[13] on "day 0" of the treatment period.

Activity Data Collection

Owners were instructed to secure a GPS-based accelerometer (Tractive GPS Tracker for Cats, Tractive Inc., Seattle, Washington, United States) to the cat's collar. For the experimental period, activity data were gathered beginning no sooner than "day 1" following treatment. For the standard control period, activity data were gathered immediately; for the inverse control period, activity data were gathered following a minimum 30-day washout period after treatment with frunevetmab. This washout period was justified on the basis of: (1) previous work demonstrating an average plasma half-life of 9 days (range: 7–15 days) following a 2 mg/kg subcutaneous injection of felinized anti-NGF monocloncal antibody,[13] and (2) manufacturer label claim recommending monthly administration of frunevetmab for therapeutic efficacy,[14] citing previous multisite pilot field study.[16]

The Tractive monitor contains a GPS module as well as an accelerometer. The built-in SIM card connects to cellular data networks via LTE/4G technology, which transmits positional data for the inbuilt GPS module to calculate location via

satellite. The "LIVE Tracking Mode" provides location updates to the system every 2 to 3 seconds. The accelerometer outputs data on the user interface as active minutes per day (the number of minutes the cat is was moving, vs. at rest/stationary). Data are transmitted wirelessly to a smartphone-based application where it can be reviewed.[22] For this study, data were transmitted directly to the investigators.

A minimum of 7 complete days (24 hours) of activity data were obtained for each cat in each treatment category (control, experimental). The monitor required charging approximately every 48 hours, during which time it would need to be removed from the cat. Due to necessary charging cycles, as well as owner compliance (e.g., forgot to replace monitor on cat's collar for several days following charging period), days following treatment were not consecutive. Days that did not include a full 24 hours of data were not included in analysis. Activity measurements were obtained over a range of 17 days (►**Table 1**). All cats were indoor-only and maintained in their usual home environment for the entirety of each period in the study. Homes varied from single-level apartment flats to multi-story homes. Owners were instructed not to restrict, confine, or otherwise alter the cat's usual access within the home.

Statistical Analysis

Two data sets with measures of activity were initially evaluated. The first data set contained seven measurements of each patient for each treatment category (control, experimental), numbering those days 1–7. The second data set also contained seven measurements of each patient for each treatment category (control, experimental); however, in this set, measurements were numbered as the actual day that activity was measured over the 17 days of observation. There were missing data, and the model failed to converge when all 17 days were included. The model successfully converged when only actual days 1–8 were included. Mixed-models analysis of variance (treatment category and time fixed, cat random) was performed and revealed no effect of day ($p = 0.94$ and $p = 0.64$) or interaction of day*treatment category ($p = 0.74$ and $p = 0.55$), respectively, in the two analyses. Normality of the errors was confirmed by means of histogram and normal probability plot.

Therefore, we considered the seven measurements obtained over the study period of each patient for each treatment category (control, experimental) as random repetitions, and obtained the mean of these values. A Shapiro–Wilk test was performed and confirmed that the differences in activity were normally distributed ($p = 0.38$). A paired *t*-test was then performed to compare frunevetmab versus control. Data were reported as mean and standard deviation. $p = 0.05$ was considered significant.

Results

Seven cats were eligible for study inclusion. There were four castrated males and three spayed females. The mean age was 10.71 years (range: 7–15 years). The mean weight was 5.48 kg (range: 3.0–9.5 kg). Average dose of frunevetmab administered was 1.5 mg/kg (range: 0.7–2.3 mg/kg). Breeds represented included domestic short hair (4), domestic medium hair (1), domestic long hair (1), and Norwegian forest cat (1). Physical examination was performed on all cats prior to initiation of the study and was reactive upon manipulation of the affected joint(s).

Individual cat descriptions were as follows:

- Cat A: 13-year-old male neutered Norwegian forest cat, body weight 6.75 kg, two joints affected (bilateral elbows).
- Cat B: 8-year-old female spayed domestic long hair, body weight 5.5 kg, two joints affected (bilateral coxofemoral joints).
- Cat C: 8-year-old male castrated domestic short hair, body weight 3.36 kg, one joint affected (right elbow).
- Cat D: 15-year-old female spayed domestic short hair, body weight 3.18 kg, one joint affected (left elbow).
- Cat E: 7-year-old male castrated domestic short hair, body weight 7.04 kg, four joints affected (bilateral coxofemoral joints, bilateral stifles).
- Cat F: 15-year-old female spayed domestic medium hair, body weight 3.0 kg, four joints affected (bilateral coxofemoral joints, bilateral stifles).
- Cat G: 7-year-old male castrated domestic short hair, body weight 9.5 kg, multiple joints affected of the spine (lumbar vertebrae).

Table 1 Days on which activity data were collected

	Control period	Washout period	Control	Experimental (frunevetmab)
Cat A	Standard	–	Days 1, 2, 3, 4, 5, 6, 7	Days 1, 2, 4, 5, 6, 8, 9
Cat B	Standard	–	Days 1, 2, 3, 4, 6, 7, 12	Days 1, 3, 6, 7, 9, 12, 13, 17, 18, 22
Cat C	Standard	–	Days 1, 2, 3, 5, 6, 7, 13	Days 1, 2, 3, 4, 11, 12, 13
Cat D	Standard	–	Days 1, 2, 3, 4, 5, 6, 7	Days 5, 6, 11, 12, 13, 16, 17
Cat E	Inverse	49 days	Days 1, 2, 5, 6, 7, 8, 10	Days 3, 4, 5, 10, 13, 15, 17, 19, 20, 21
Cat F	Inverse	35 days	Days 1, 2, 3, 5, 6, 7, 8	Days 6, 7, 8, 9, 10, 11, 12, 13, 14, 16
Cat G	Inverse	68 days	Days 1, 2, 6, 7, 8, 12, 13	Days 1, 2, 3, 4, 5, 8, 9

Note: "Day 1" was defined as the first day the cat started wearing the monitor and that data were collected for the particular study period. For the experimental period, treatment was administered on "day 0."

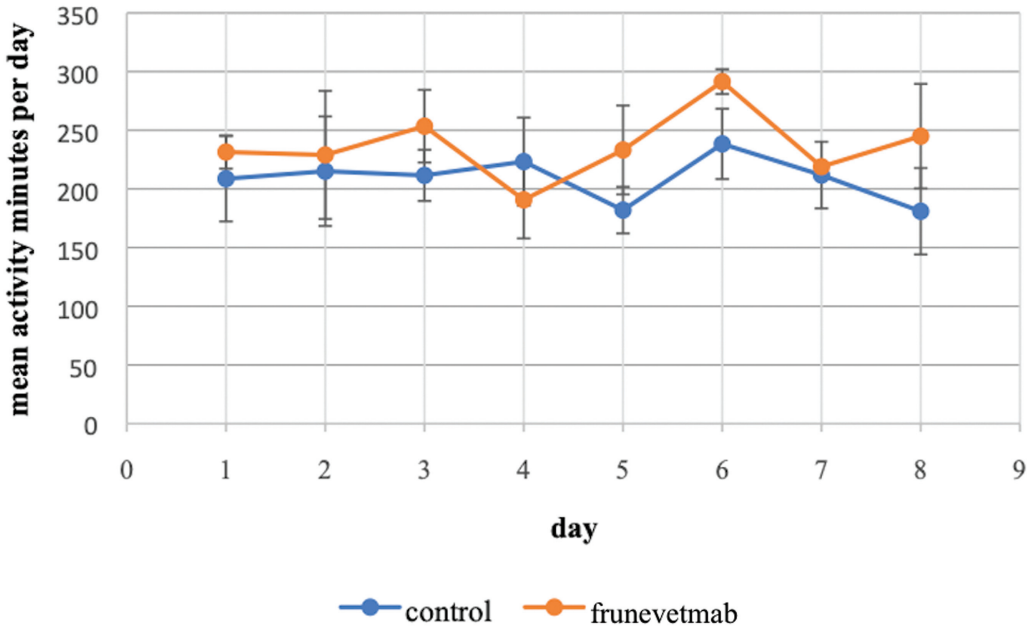

Fig. 1 Mean activity minutes per day for control and for frunevetmab plotted over day in treatment period (error bars represent standard error of the mean).

The mean minutes of activity per day were obtained for each patient in each treatment category (control, frunevetmab) (►**Fig. 1**; ►**Table 2**). Mean activity minutes per day were significantly greater for frunevetmab (242.1) compared to control (209.9) ($p = 0.007$) (►**Table 3**).

Discussion

The present pilot study suggests that this group of osteoarthritic cats demonstrated increased activity levels following frunevetmab treatment, compared to self-control, when measured via a GPS-based accelerometry device (Tractive). The self-control study design was selected due to perceived wide variability in activity level between individual cats, as well as differences in home environment (e.g., studio apartment vs. multi-story home). Therefore, we surmised that the most representative means to evaluate a change in activity level with treatment would be to compare the individual to itself, rather than to another control population that may encompass a wider range of variables. Indeed, previous work by Lascelles and others noted the importance of utilizing each cat as its own self-control to minimize such variations

Table 2 Mean activity minutes per day for each cat in each treatment category

	Mean activity minutes per day		% increase in activity minutes	Frunevetmab dose (mg/kg)
	Control	Experimental (frunevetmab)		
Cat A	242.6	281.4	16.0%	1.0
Cat B	284.4	289.4	1.8%	1.3
Cat C	182.9	205.0	12.1%	2.1
Cat D	218.0	258.6	18.6%	2.2
Cat E	246.9	254.0	2.9%	1.0
Cat F	106.9	161.0	50.6%	2.3
Cat G	187.9	245.3	30.5%	0.7

Table 3 Descriptive statistics for paired *t*-test ($p = 0.007$)

	n	Mean activity minutes per day	Standard deviation
Control	7	209.9	57.6
Experimental (frunevetmab)	7	242.1	45.0

and thereby obtain more clinically meaningful outcome assessments.[18]

While multiple schemes have been validated for subjective evaluation of acute or postoperative pain in cats,[23–25] and for evaluation of chronic pain in dogs,[26–28] currently there is not a validated method to assess chronic pain in cats. Although ongoing refinements have been made to the FMPI, owner responsiveness at this point is poor and often zero.[29] Our goal with this study was an attempt to objectively assess activity level in osteoarthritic cats treated with frunevetmab via a means which encourages owner compliance and thereby improves clinical assessment of therapeutic impact. To be fair, this method assumes that "mobility" or "activity" represents "comfort," which may not necessarily correlate perfectly. Additionally, the data available on the user interface do not provide speed/velocity information, and so we could not elucidate details as to how robust or vigorous the activity was (e.g., running/jumping vs. walking)—just that the cat was moving versus stationary. However, considering current limitations in owner-based clinical metrology scales and even subjectivity in clinical examination, it seems reasonable to extrapolate activity data as at least in large part representative of comfort level. This precedent has been established in the veterinary literature for a number of years; Lascelles and others previously showed that accelerometer-based activity data correlate well with computer-detected video movement in cats, serving as an accurate surrogate for mobility and, by extension, effect of pain-relieving therapies.[18]

A limitation of this study is the use of an as of yet unvalidated activity monitor (Tractive). However, this device represents potential to easily assess feline activity level at home via a modality that may engage owners more consistently than a clinical metrology scale. As it were, the scope of this study was focused on a means of convenient, user-friendly activity monitoring at home that could be adaptable to client use. We did not seek to precisely replicate previous feline accelerometry data obtained in a formal research setting. With Tractive, owners can view their cat's activity clearly on a user-friendly interface, with simple, objective data output. Involving and empowering owners in such a way is instrumental in optimizing clinical treatment plans. Looking toward the future of feline pain management and assessment, we propose that refinement of objective in-home assessments will not only lead to more reliable data acquisition, but will also help solve the issue of poor owner compliance.

A major limitation of this study is the small sample size. Nonetheless, statistical analysis indicated that this was an adequately powered study for the number of data points per patient being used as its own self-control. Due to the short battery life of the activity monitor, and, occasionally, owner compliance with charging, data acquisition typically took multiple weeks to capture 7 full days' worth of activity. The timeline was further prolonged by the 30-day washout period in the inverse control treatment category. This limited the number of cats for which we could obtain complete data during the time period of the study. Certainly, future studies incorporating a larger population of cats are warranted to corroborate these results.

An important future direction from this pilot study with the Tractive is to compare data output to a more extensively studied device such as the Actical, as previously done in cats with the Plus Cycle. Indeed, further studies are warranted on the Actical itself to definitively validate its use in cats. The information gleaned from the Tractive in this study is but a starting point in exploring the means of assessing feline activity level, and, by proxy, pain management, in the home environment.

In conclusion, this population of osteoarthritic cats exhibited an increase in activity level following frunevetmab treatment compared to self-control. This information was obtained via piloted clinical use of the Tractive device, which, while unvalidated, is user-friendly and could encourage owner engagement in future studies. This introductory work corroborates findings in previous literature demonstrating clinical benefit of frunevetmab,[15,16] and suggests an alternative and potentially desirable method of assessing feline activity levels and pain management.

Authors' Contribution

Both authors contributed to study conception, study design, acquisition of data, data analysis and interpretation, drafting and revising of the manuscript, and approval of the submitted manuscript.

Funding

No external funding was provided.

Conflict of Interest

None declared.

Acknowledgements

The authors thank Joseph G. Hauptman, MS, DVM, DACVS for performing statistical analysis and interpretation.

References

1 Lascelles BD, Henry JB III, Brown J, et al. Cross-sectional study of the prevalence of radiographic degenerative joint disease in domesticated cats. Vet Surg 2010;39(05):535–544
2 Slingerland LI, Hazewinkel HA, Meij BP, Picavet P, Voorhout G. Cross-sectional study of the prevalence and clinical features of osteoarthritis in 100 cats. Vet J 2011;187(03):304–309
3 Bennett D, Zainal Ariffin SM, Johnston P. Osteoarthritis in the cat: 1. how common is it and how easy to recognise? J Feline Med Surg 2012;14(01):65–75
4 Marino CL, Lascelles BD, Vaden SL, Gruen ME, Marks SL. Prevalence and classification of chronic kidney disease in cats randomly selected from four age groups and in cats recruited for degenerative joint disease studies. J Feline Med Surg 2014;16(06):465–472
5 Guedes AGP, Meadows JM, Pypendop BH, Johnson EG, Zaffarano B. Assessment of the effects of gabapentin on activity levels and owner-perceived mobility impairment and quality of life in osteoarthritic geriatric cats. J Am Vet Med Assoc 2018;253(05):579–585
6 Guedes AGP, Meadows JM, Pypendop BH, Johnson EG. Evaluation of tramadol for treatment of osteoarthritis in geriatric cats. J Am Vet Med Assoc 2018;252(05):565–571
7 Monteiro BP, Klinck MP, Moreau M, et al. Analgesic efficacy of an oral transmucosal spray formulation of meloxicam alone or in combination with tramadol in cats with naturally occurring osteoarthritis. Vet Anaesth Analg 2016;43(06):643–651

8 Monteiro BP, Klinck MP, Moreau M, et al. Analgesic efficacy of tramadol in cats with naturally occurring osteoarthritis. PLoS One 2017;12(04):e0175565
9 Shipley H, Flynn K, Tucker L, et al. Owner evaluation of quality of life and mobility in osteoarthritic cats treated with amantadine or placebo. J Feline Med Surg 2021;23(06):568–574
10 Mantyh PW, Koltzenburg M, Mendell LM, Tive L, Shelton DL. Antagonism of nerve growth factor-TrkA signaling and the relief of pain. Anesthesiology 2011;115(01):189–204
11 Bannwarth B, Kostine M. Targeting nerve growth factor (NGF) for pain management: what does the future hold for NGF antagonists? Drugs 2014;74(06):619–626
12 Enomoto M, Mantyh PW, Murrell J, Innes JF, Lascelles BDX. Anti-nerve growth factor monoclonal antibodies for the control of pain in dogs and cats. Vet Rec 2019;184(01):23
13 Gearing DP, Huebner M, Virtue ER, et al. In vitro and in vivo characterization of a fully felinized therapeutic anti-nerve growth factor monoclonal antibody for the treatment of pain in cats. J Vet Intern Med 2016;30(04):1129–1137
14 Solensia product label. Released by Zoetis Inc. August, 2021. Accessed 18 June 2024 at: https://www.zoetisus.com/products/cats/solensia
15 Gruen ME, Thomson AE, Griffith EH, Paradise H, Gearing DP, Lascelles BD. A feline-specific anti-nerve growth factor antibody improves mobility in cats with degenerative joint disease-associated pain: a pilot proof of concept study. J Vet Intern Med 2016;30(04):1138–1148
16 Gruen ME, Myers JAE, Lascelles BDX. Efficacy and safety of an anti-nerve growth factor antibody (frunevetmab) for the treatment of degenerative joint disease-associated chronic pain in cats: a multisite pilot field study. Front Vet Sci 2021;8:610028
17 Hansen BD, Lascelles BDX, Keene BW, Adams AK, Thomson AE. Evaluation of an accelerometer for at-home monitoring of spontaneous activity in dogs. Am J Vet Res 2007;68(05):468–475
18 Lascelles BD, Hansen BD, Thomson A, Pierce CC, Boland E, Smith ES. Evaluation of a digitally integrated accelerometer-based activity monitor for the measurement of activity in cats. Vet Anaesth Analg 2008;35(02):173–183
19 Belda B, Enomoto M, Case BC, Lascelles BDX. Initial evaluation of PetPace activity monitor. Vet J 2018;237:63–68
20 Rowlison de Ortiz A, Belda B, Hash J, Enomoto M, Robertson J, Lascelles BDX. Initial exploration of the discriminatory ability of the PetPace collar to detect differences in activity and physiological variables between healthy and osteoarthritic dogs. Front Pain Res (Lausanne) 2022;3:949877
21 Yamazaki A, Edamura K, Tanegashima K, et al. Utility of a novel activity monitor assessing physical activities and sleep quality in cats. PLoS One 2020;15(07):e0236795
22 Tractive. Accessed 6 February 2024 at: tractive.com.
23 Brondani JT, Mama KR, Luna SP, et al. Validation of the English version of the UNESP-Botucatu multidimensional composite pain scale for assessing postoperative pain in cats. BMC Vet Res 2013;9:143
24 Reid J, Scott EM, Calvo G, Nolan AM. Definitive Glasgow acute pain scale for cats: validation and intervention level. Vet Rec 2017;180(18):449
25 Evangelista MC, Watanabe R, Leung VSY, et al. Facial expressions of pain in cats: the development and validation of a Feline Grimace Scale. Sci Rep 2019;9(01):19128
26 Wiseman ML, Nolan AM, Reid J, Scott EM. Preliminary study on owner-reported behaviour changes associated with chronic pain in dogs. Vet Rec 2001;149(14):423–424
27 Wiseman-Orr ML, Nolan AM, Reid J, Scott EM. Development of a questionnaire to measure the effects of chronic pain on health-related quality of life in dogs. Am J Vet Res 2004;65(08):1077–1084
28 Brown DC, Boston RC, Coyne JC, Farrar JT. Development and psychometric testing of an instrument designed to measure chronic pain in dogs with osteoarthritis. Am J Vet Res 2007;68(06):631–637
29 Enomoto M, Lascelles BDX, Robertson JB, Gruen ME. Refinement of the Feline Musculoskeletal Pain Index (FMPI) and development of the short-form FMPI. J Feline Med Surg 2022;24(02):142–151

Erratum: An erratum has been published for this article (DOI: 10.1055/s-0044-1788641).