Investigation of physical activity using accelerometry in dogs receiving chemotherapy.

Summary

Objectives

To perform a preliminary study to assess whether single-agent palliative or adjuvant chemotherapy has an impact on objectively measured physical activity (PA) in dogs.

Methods

Fifteen dogs with neoplasia (treatment group (TG)) wore ActiGraph^{TM} accelerometers for five day periods; before, during and after receiving single-agent, adjuvant or palliative chemotherapy. Mean 5-day volume of PA and time spent in 3 different intensities of PA (sedentary, light-moderate and vigorous) before, during and after receiving chemotherapy were compared to a group of fifteen healthy dogs (control group (CG)). Results were also compared within the treatment group across time.

Results

Prior to chemotherapy, TG dogs tended to be less active than CG dogs. Treatment group dogs were slightly more active at restaging than they were prior to treatment but had similar activity levels to CG dogs. Marked effects of chemotherapy on PA were not found. Physical activity was slightly lower in TG dogs during chemotherapy when compared to CG dogs but when PA of TG dogs was compared before and during chemotherapy, a slight increase in PA was seen. Additionally, little change in the mean 5-day volume of PA was seen between TG dogs on chemotherapy and at restaging. However, a mild decline in the time spent sedentary and increase in time spent in light-moderate activity was seen at restaging.

Clinical Significance

Single-agent, adjuvant or palliative chemotherapy, measured objectively had minimal impact upon PA or in dogs with neoplasia.

Keywords

Cancer, Chemotherapy, Dog, Accelerometer, Quality of life

Introduction

Veterinary chemotherapy is a growing field and patients are often either treated to ameliorate clinical signs (in the case of unresectable or disseminated disease, so called palliative intent treatment) or to prolong survival in those with micro-metastatic disease following surgery or radiation therapy (adjuvant chemotherapy). Traditionally, outcomes of veterinary chemotherapy studies have concentrated on drug tolerability, adverse events (primarily effects on the haemopoietic and gastrointestinal systems), tumour response and survival parameters (for example median survival times, disease free intervals or time to tumour progression) (Mellanby and others 2003, Ehrhart and others 2013). In both humans and animals it has been suggested that the measure of outcomes of cancer trials, particularly those investigating palliative and adjuvant chemotherapy protocols, should also include measures of patient quality of life (QOL) (Spitzer and others 1981, Gunnars and others 2001, Sprangers 2002). Acceptable QOL during cancer treatment is important to both pet owners (Mellanby and others 2003) and veterinarians (Yeates and Main 2009). The risk of prolonging or inducing suffering, or of reducing QOL is often cited by owners as a reason for electing euthanasia rather than treatment (Slater and others 1996). Therefore, a better understanding of the effects of treatments on QOL would help with informed decision making. In patients

receiving palliative or adjuvant treatment, patient QOL is affected not only by the treatment itself but also by residual disease. The goals of treatment are thus to achieve a balance between an anti-tumour response and increased patient longevity whilst avoiding deleterious effects on patient QOL.

Quality of life is multifactorial and includes a range of physical and behavioural parameters. It is difficult to define and the concept likely varies between different people (McMillan 2000, Gunnars and others 2001). One symptom included in QOL questionnaires in people with cancer is fatigue (Aaronson and others 1983, the WHOQOL Group 1998, Carrison and Hamrin 1996). Fatigue, an extreme form of tiredness, is one of the most commonly reported side-effects of chemotherapy (Skerman and others 2012, Backman and others 2014). It is multifactorial and is thought to result in a reduction in physical activity (PA) (Vermaete and others 2014). Studies in humans using accelerometers to objectively measure PA have shown that it is reduced in patients on chemotherapy (Tan and others 2013, Vermaete and others 2014).

In veterinary medicine, assessment of QOL in oncology patients has been largely subjective, often using owner questionnaires either to ask them to quantify their pet's QOL or to ask about specific determinants of QOL such as demeanor, appetite, pain and mobility (Fox and others 2000, Malik and others 2001, Mellanby and others 2003, Tzannes and others 2008, Bowles and others 2010, Lynch and others 2011, Iliopoulou and others 2013). It is not possible in veterinary studies to determine whether the patient feels fatigued and therefore PA levels have been subjectively assessed by asking questions about the patients' mobility, tiredness, lethargy and play activity (Bowles and others 2010, Iliopoulou and others 2013, Rivera and others 2013). The inclusion of questions regarding PA confirms the importance of

its evaluation in QOL assessment but using this methodology; it is difficult to quantify changes in PA and the results may be biased by client preconceptions of chemotherapy. Comparison between clients is also difficult as the perception of PA likely varies between different people. In addition, questionnaires are often completed retrospectively, sometimes months after the administration of chemotherapy (Mellanby and others 2003, Tzannes and others 2008, Bowles and others 2010). The detection of diminished activity during cancer treatment may be even more relevant in veterinary patients, where the incapacitation that accompanies treatment in some people would simply not be acceptable in our patients.

Using data collected from owners, reductions in PA have been reported in some dogs following treatment with single-agent carboplatin, doxorubicin, epirubicin and mitoxantrone, all of which are drugs used in palliative or adjuvant settings (Ogilvie and others 1991, Lucroy and others 1998, Bowles and others 2010, Marrington and others 2012). It however unknown to what extent reductions in PA actually occur in patients receiving these chemotherapy agents and objective measurements of PA in veterinary patients receiving chemotherapy has not been attempted.

Accelerometers are motion sensors that provide real-time monitoring of the frequency, duration and intensity of PA in free-living individuals. They have been used extensively in adults and children, both with and without cancer, to objectively measure PA (Corder and others 2008, Reilly and others 2008, deVries and others 2009, Tan and others 2013, Vermaete and others 2014, Lowe and others 2014). Accelerometers have been validated for the measurement of habitual PA in dogs (Yam and others 2011). They have the advantage of giving a quantitative measure of PA whilst being portable, lightweight and non-invasive.

The aims of this preliminary study were to objectively measure PA in dogs using accelerometers, before, during and after receiving palliative intent or adjuvant single-agent chemotherapy, and to compare PA in the chemotherapy treatment group to that of a control group of healthy dogs. In so doing, we hope to better understand the extent to which a reduction in PA truly occurs in these patients.

Materials and Methods

In this prospective study, all dogs presented to a veterinary teaching hospital from March 2012 to October 2013 and suspected of having a malignant tumour were considered for inclusion. Dogs eligible for the treatment group (TG) were subsequently excluded if histopathology was not consistent with malignant neoplasia, they did not receive single-agent chemotherapy, they were inconsistently treated with other drugs (including non-steroidal anti-inflammatory drugs, opioids and corticosteroids) or modalities (including radiotherapy) throughout their chemotherapy or they had significant co-morbidities that could independently affect activity levels (such as cardiac disease, osteoarthritis, endocrine or metabolic disorders). Co-morbidities were excluded on the basis of the history, physical examination and staging results. Any additional tests were performed on a case-by-case basis at the clinician's discretion.

The final TG therefore consisted of dogs that had malignant neoplasms, had undergone full staging (complete blood count (CBC), blood biochemistry panel, thoracic radiography or computed tomography and abdominal ultrasound examination) and received single-agent chemotherapy (carboplatin, doxorubicin, epirubicin or mitoxantrone). For each TG dog, a control dog matched as closely as possible for sex, age, weight, body condition score (BCS) and breed was included in a control group (CG). Control dogs were client-owned healthy

individuals that were taking part in a concurrent study (Morrison and others 2013a, Morrison and others 2013b, Morrison and others 2014).

Chemotherapy was administered via the standard hospital protocol, in brief; CBCs were performed immediately prior to chemotherapy administration and treatments were delayed if neutrophil counts were $<3 \times 10^9$ L^{-1}. Carboplatin was administered at 300 mg/m^2 q3 weeks, doxorubicin and epirubicin at 30 mg/m^2 q3 weeks and mitoxantrone at 5.5 mg/m^2 q3 weeks for a total of four to six treatments. Chemotherapy was administered through an intravenous catheter in a saline infusion over 20 minutes. Cases were discharged on the day of treatment. Supportive medications (for example anti-emetics) were administered according to standard protocols or when adverse events were experienced. Dogs receiving analgesic drugs or nutraceutical joint supplements were only included if they remained on the same drug and dose throughout the study.

Physical activity was measured using GT3-X and GT3-X+ accelerometers (ActiGraph™) attached to the dog's collar, as previously described (figure 1) (Yam and others 2011). Accelerometers were placed for a minimum of 5 consecutive 24-hour periods. For the TG dogs, accelerometers were first placed at initial presentation or postoperatively. When placed postoperatively this had to be at least 7 days, and as long as possible, following surgery but no less than 5 days prior to chemotherapy administration. After this, accelerometers were removed by owners and returned by post for the data to be downloaded. All owners completed a diary detailing any problems associated with the accelerometer placement (e.g. collar removal or loss during the measurement period). Accelerometers were again placed when patients returned for their first (C1), third (C3) and fifth (C5) doses of chemotherapy and were set to start recording from midnight on the day of chemotherapy administration.

The final accelerometer was placed a minimum of 1 month after the final dose of chemotherapy when dogs returned for restaging. Control group dogs had accelerometers placed on one occasion.

The accelerometer measured and recorded time-varying accelerations ranging in magnitude from approximately 0.05 to 2.5*g* (GT3-X) and +/- 6*g* (GT3-X+) in 3 axes. There is excellent agreement between these two models meaning that they can be used interchangeably within the same study (Robusto and Trost 2012). The accelerometer output was digitised by a 12-bit analog to digital converter at a rate of 30 times per second (30 Hz). Once digitised, the signal passed through a filter that band limited the accelerometer to the frequency range of 0.25 to 2.5 Hz to eliminate any acceleration noise outside the normal activity frequency bandwidth. Each sample was summed over a 15 second time interval (epoch).

Actilife v6.6.2 software (ActiGraph™) was used to download the data. This software also calculated the integrated output (Vector Magnitude) which is the magnitude of the resulting vector that forms when combining the sampled acceleration from all 3 axes (ActiGraph™ 2013). The raw data files were imported to a Microsoft Office Excel 2007 (Microsoft) spreadsheet. Outputs were analysed from the integrated output and data was expressed in counts per minute (cpm) by summing the counts from 4 epochs. Figure 2 shows a graph of the PA (calculated from the integrated output) for a dog over a 24 hour period.

The mean daily volume of PA per minute (cpm) and the mean 5-day volume of PA per minute (cpm) were calculated for each dog at each timepoint. The amount of time (minutes/day) spent in 3 different intensities of activity (sedentary, light-moderate and

vigorous) was calculated for each day and and a daily mean calculated for each 5 day period. The three levels of activity were defined as follows (from Yam and others 2011):

1) Sedentary behaviour - no movement of the trunk, includes time spent sleeping
2) Light to moderate intensity PA - slow to moderate translocation of the trunk, with the dog on a lead
3) Vigorous intensity PA - rapid translocation of the trunk whilst running (usually outdoors) off a lead.

Each minute was categorised as spent in sedentary behaviour, light-moderate intensity or vigorous intensity PA using cut points based on a "calibration" study derived from data obtained in a previous validation of the ActiGraph™ accelerometers (Yam and others 2011, Morrison and others 2013a).

Data was also recorded on signalment, staging results, surgical treatment, tumour type, chemotherapy administered, concurrent medications, concurrent physiotherapy or hydrotherapy, adverse events, and outcome of TG dogs.

Data were tested for normality using the Anderson-Darling test. As data was not normally distributed, median and interquartile ranges (IQR) were calculated. The median of the mean 5-day volume of PA per minute and medians of the mean daily time (minutes/day) spent at each intensity of PA for the 5 day periods were calculated for the CG. To compare the PA of the treatment dogs and control dogs pre-treatment, after chemotherapy and after restaging, box and whisker plots of the mean 5-day volume of PA per minute were drawn. The medians of the mean daily time (minutes/day) spent at each intensity of PA for the 5 day periods were calculated for each time point for the treatment dogs and their paired control dogs. To examine the effect of chemotherapy on the TG dogs, the difference in the mean 5-day volume

of PA per minute and the difference in mean daily time (minutes/day) spent at each intensity of PA for each 5 day period at different time points was calculated for each dog. Results were then graphed or median differences were calculated. Dogs were only included if they had data available from both time points. Finally, to determine changes in TG dogs over the 5 days following each chemotherapy dose, box and whisker plots of the mean daily volume of PA per minute were drawn and the median time spent each day at each intensity of PA were calculated. Analyses were carried out and graphs drawn using Minitab 16.1.1 (Minitab Inc.) and Microsoft Office Excel 2007 (Microsoft).

Informed consent was given by all dog owners and the study was approved by the relevant Ethics and Welfare Committee.

Results

Twenty five dogs were recruited to the TG, however 2 dogs were ultimately diagnosed with non-neoplastic diseases, 4 dogs were not treated with chemotherapy and 2 dogs were intermittently treated with other drugs or radiotherapy. Of the remaining 17 dogs, 2 were excluded due to corrupt accelerometer data.

The TG and CG dog descriptive characteristics are shown in Table 1. Matching for breed between the TG and CG dogs was not possible.

All TG dogs had solid tumours; 3 anal sac adenocarcinomas, 2 malignant melanomas, 3 appendicular osteosarcomas, 3 haemangiosarcomas, one splenic sarcoma, one soft tissue sarcoma, one mammary carcinoma and one nasal adenocarcinoma. Fourteen dogs (93%) were staged to the local site only and one dog had local lymph node involvement. None of the

dogs had distant metastases at the time of diagnosis. Fourteen dogs had surgery to de-bulk gross disease before entering the study. The dog with a nasal tumour did not have surgery. Of these 14 dogs, 9 (60%) had accelerometers placed prior to chemotherapy and therefore had baseline data collected. Eight of these had surgery and this included two limb amputations, one splenectomy, two anal sac resections for stage I anal sac adenocarcinoma, one debulking of a maxillary malignant melanoma, one enucleation due to intraocular melanoma and one soft tissue sarcoma resection (medial thigh). All dogs recovered uneventfully from surgery. The first accelerometer was placed a median of 13 days later (range: 7 to 44 days) by which time, 6/9 dogs had had their sutures removed.

Over the course of the study, 9 TG dogs (60%) received carboplatin, 3 dogs received doxorubicin, 1 dog epirubicin and 2 dogs a combination of epirubicin and doxorubicin. Fifteen dogs had one or more chemotherapy doses, 14 dogs had 3 or more chemotherapy doses and 6 dogs had 5 or more chemotherapy doses (figure 3). Five dogs (33%) received concurrent medication throughout the data collection period (meloxicam (3 dogs), prednisolone (1 dog) and tramadol (1 dog)). One dog received concurrent joint supplementation throughout the data collection period with a glucosamine and methylsulfonylmethane combination nutraceutical. The same dog received weekly hydrotherapy which was performed the day prior to chemotherapy administration which was not during accelerometer placement.

Collars were not removed overnight, however some owners did remove accelerometers for short periods of time and results were adjusted to account for this. Specifically there were 8 problems (out of 49 accelerometer placements) recorded by owners in the activity diaries.

These resulted in exclusion of the whole accelerometer episode from analysis in one case, an exclusion of one day of data in one case and no action in six cases.

Physical activity measured over 5 days in the CG

The median of the mean 5-day volume of PA for all 15 dogs in the CG was 482 cpm (IQR: 275). A median of the mean of 1268 minutes/day (21.1 hours/day) (IQR: 88 minutes/day) was spent in sedentary behaviour, 154 minutes/day (2.6 hours/day) (IQR: 76 minutes/day) in light-moderate activity and 6 minutes/day (0.1 hours/day) (IQR: 10 minutes/day) in vigorous activity.

Physical activity measured over 5 days at different accelerometer placement time points for TG dogs versus CG dogs

Figure 4 shows box and whisker plots for the mean 5-day volume of PA (cpm) at each accelerometer time point for the TG dogs and their paired CG dogs. Table 2 shows the median of the mean daily time spent at each intensity of PA (minutes/day).

Changes in PA in TG dogs measured over 5 days at different accelerometer placement time points

Figure 5 is a box and whisker plot of the median change in mean 5-day volume of PA (cpm) for TG dogs between the different accelerometer placement time points. Table 3 shows the differences between the mean daily time spent at each intensity of PA for TG dogs at different accelerometer placement time points.

Daily PA in TG dogs on each of the 5 days following chemotherapy

Figure 6 shows the median of the mean daily volume of PA (cpm) for the TG dogs on each of the 5 days following chemotherapy for doses 1, 3 and 5. Table 4 shows the median time spent

at different activity intensity levels (minutes/day) for the TG dogs on each of the 5 days following chemotherapy for doses 1, 3 and 5.

Discussion

The aim of this study was to objectively measure PA in dogs before, during and after receiving chemotherapy as an objective measure of QOL. This was successfully achieved in 15/17 dogs that fulfilled the inclusion criteria.

Prior to chemotherapy, TG dogs had a slightly lower mean 5-day volume of PA (figure 4A) and tended to spend more time sedentary and slightly less time in light-moderate intensity activity (table 2), compared to the CG dogs. This may have occurred as TG dogs were not healthy and were either presumed to have micrometastatic disease (gross metastases were ruled out on initial staging) or had gross disease (one case only), both of which could have affected their PA. Additionally, 8/9 TG dogs had had tumour resection surgery a median of 13 days before accelerometer placement and either the surgery itself or post-surgical exercise restriction ("lead walks" only until suture removal) could have affected their PA. To reduce the effect of surgery on PA, post-operative accelerometer placement was delayed for as long as possible; however given that the optimal time for chemotherapy administration is when there is minimal residual disease, the time between surgery and the first dose of chemotherapy is often short. Surgery is likely to have had the greatest effect on the 3 dogs in this group that had had limb surgery and the effect of post-surgical exercise restriction was only likely to be relevant in the 3 patients that had accelerometers placed before suture removal.

When the activity of the TG dogs at restage was compared to the CG dogs, no obvious differences in PA were seen (figure 4E, table 2). Furthermore, when the PA of TG dogs before chemotherapy was compared to that at restaging, a slight increase in total volume of PA was seen (figure 5) with a slight reduction in sedentary behaviour and increase in light-moderate intensity activity (table 3). These findings suggest that some factor was reducing PA in the TG dogs before chemotherapy, however these effects were only very small and a large variation was seen between TG and CG dogs.

The effect of chemotherapy on PA in our patients was not marked. Slightly lower mean 5-day volumes of PA (figure B-D) and greater amounts of time spent sedentary rather than in light-moderate intensity activity (table 2) were seen in TG dogs after all chemotherapy doses when compared to CG dogs, but there was considerable overlap. Conversely, when TG dogs were compared to themselves, there was a slight increase in the mean 5-day volume of PA from before chemotherapy to after chemotherapy doses 1 and 3 (but not 5) (figure 5). This effect was quite marked in some dogs. Likewise, there was a slight decrease in the amount of time spent sedentary and a corresponding increase in the time spent in light-moderate intensity activity from before chemotherapy to after doses 1 and 3 (table 3). The opposite was seen after dose 5. The apparent contradiction between the results when TG dogs were compared to CG dogs and when TG dogs were compared to themselves may be because of ongoing effects of the tumour itself or of surgery which would affect the former but not the latter.

Similarly, little effect of chemotherapy on PA was seen in the 5 days immediately after treatment (figure 6, table 4). If anything, there was a slight reduction in the time spent sedentary and corresponding increase in time spent at light-moderate intensity activity on day 3 post-chemotherapy.

When the PA of TG dogs was compared during chemotherapy to the restage time point (figure 5, table 3), the mean 5-day volume of PA was relatively unchanged and only a very mild decline in time spent sedentary and increase in time spent in light-moderate intensity activity was seen. This either suggests that the chemotherapy was not having a major effect on PA or that the negative effects of chemotherapy are offset by the negative effects of the residual tumour at the restage time point.

The relative lack of an effect of chemotherapy on PA is somewhat at odds with the information in both the human and veterinary literature. In people, fatigue is one of the most commonly reported symptoms during palliative and adjuvant chemotherapy (Skerman and others 2011, Backman and others 2014), however it is a subjective feeling and may not necessarily translate into a decline in PA. In the only two studies using accelerometry to measure PA in people on chemotherapy (Tan and others 2013, Vermaete and others 2014), a reduction in PA was seen. These were, however, studies of patients treated with multi-agent, curative-intent protocols for acute leukaemias and lymphomas which may be more likely to have negative effects on PA than the palliative/adjuvant single-agent protocols used in this study.

In dogs, chemotherapy has frequently been reported to cause lethargy (Lucroy and others 1998, Mellanby and others 2003, Bowles and others 2010, Marrington and others 2012, Rivera and others 2013), however these studies all rely on owner reporting, in some cases months after the treatment took place (Mellanby and others 2003, Bowles and others 2010). This methodology may introduce bias as some owners may expect their dogs to be lethargic because of preconceptions about chemotherapy or they may under or overestimate their pet's

activity levels due to difficulties recalling and reporting this type of information accurately (Durante and Ainsworth 1996, Kriska and others 1997, Sirard and Pate 2001). This study, by contrast, used an objective measure of PA which eliminates many of these problems.

It is a concern that if the effects of chemotherapy on PA (and therefore QOL) are over-exaggerated this could lead to the misinformation of owners. As the risk of reducing QOL is often cited by owners as a reason for electing euthanasia rather than treatment (Slater and others 1996) this could incorrectly deter owners from electing to treat their pets. It should be remembered, however that the numbers in this study are small and therefore effects on PA could have been missed. Additionally, QOL is multifactorial and only one aspect was studied, therefore comments cannot be made on QOL as a whole.

It was not possible, in this study, to perform meaningful statistical analyses due to the small sample size. Post-hoc power calculations were performed which suggested large numbers of dogs would be needed in each group to detect a meaningful difference in PA. This suggests future studies would need to involve multiple centres and a longer period of data collection. The power of this study was further reduced because we did not succeed in placing accelerometers on all TG dogs at all time points (particularly the pre-chemotherapy time point).

This preliminary study showed that it was possible to use accelerometers in clinical patients receiving chemotherapy to collect objective, contemporaneous data on PA. This methodology could therefore be used in future studies looking at the QOL of patients on chemotherapy possibly in combination with questionnaires. In this setting, it might also be interesting to compare results to a control group of patients in which treatment was declined. This would

provide information on the effect of surgery and the tumour itself, variables which could not be isolated in this study. Combining accelerometry with other methods of assessing QOL would also allow relationships between these methods to be investigated. The routine use of accelerometers in outcome studies of veterinary patients receiving palliative and adjuvant chemotherapy protocols, where it is suggested that measuring QOL is particularly important (Spitzer and others 1981, Gunnars and others 2001, Sprangers 2002), should be considered. The inclusion of more homogeneous groups of patients (with regards to tumour type and drug administered) would allow additional conclusions to be drawn. Objective measurement of PA may be particularly relevant in studies of drugs like the tyrosine kinase inhibitors which are known to have a direct effect on the musculoskeletal system (London and others, 2009). As accelerometry was well tolerated and contemporaneous, it could also be used in individual clinical patients to provide objective information on patient QOL that could help owners and clinicians decide whether to make changes or discontinue a protocol.

In conclusion, we have shown that the concept of measuring PA using accelerometry in canine oncological patients is valid and our results support the use of single-agent adjuvant chemotherapy in dogs given that marked changes in PA were not seen during treatment.

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CONFLICT OF INTERESTS

None of the authors of this article has a financial or personal relationship with other people or organisations that could inappropriately influence or bias the content of the paper.

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FIGURE LEGENDS

Figure 1: Dog wearing ActiGraph™ accelerometer attached to collar.

Figure 2: Counts recorded for each minute of a 24 hour day for a dog wearing an accelerometer. The y-axis is divided into sections to show the cut points for the different physical activity intensity levels. PA = physical activity.

Figure 3: Flow diagram demonstrating TG dogs throughout the study (number of dogs, number of dogs with accelerometers fitted). [a] 8 of these dogs had surgery prior to accelerometer placement (median time from surgery to accelerometer placement was 13 days), [b] the median time to restage for all dogs was 33 days.

Figure 4: Box and whisker plots for the mean 5-day volume of physical activity (counts per minute [cpm]) at each accelerometer time point for the treatment group dogs and their paired control dogs. The n-value is the number of dogs in each group. The lower and upper boundaries of the box represent the first and third quartiles of the data respectively and the line within the box represents the median. The whiskers represent the complete range of the data. Outliers (*) are observations that are at least 1.5 times the interquartile range from the edge of the box.

Figure 5: Box and whisker plot of the change in mean 5-day volume of physical activity (counts per minute [cpm]) for treatment group dogs between the different time points listed on the y-axis. Values below zero represent an increase in the mean 5-day volume of physical activity whereas values above the line represent a decrease in the mean 5-day volume of physical activity. Dogs were only included in each group if data was available from both time points. Pre = pre-chemotherapy, C1 = after 1st chemotherapy, C3 = after 3rd chemotherapy, C5 = after 5th chemotherapy. The n-value is the number of dogs in each group. The lower and upper boundaries of the box represent the first and third quartiles of the data respectively and the line within the box represents the median. The whiskers represent the complete range of the data. Outliers (*) are observations that are at least 1.5 times the interquartile range from the edge of the box.

Figure 6: Box and whisker plots of the mean daily volume of physical activity (counts per minute [cpm]) for the treatment group dogs on each of the 5 days following chemotherapy doses 1, 3 and 5. The n-value is the number of dogs in each group. *Only dogs with all 5 days of data were included. The lower and upper boundaries of the box represent the first and third quartiles of the data respectively and the line within the box represents the median.

TABLE LEGENDS

Table 1: Descriptive characteristics of the dogs in the treatment and control groups.

Table 2: Mean daily time spent at each intensity of physical activity (minutes per day) at each accelerometer time point for the treatment group dogs and their paired control dogs.

601 Table 3: Difference between the mean daily time spent at each intensity of physical activity
602 by the treatment group dogs at different accelerometer time points.
603
604 Table 4: Time spent at different activity intensity levels (minutes per day) for the treatment
605 group dogs on each of the 5 days following chemotherapy doses 1, 3 and 5.
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