Non-invasive, objective determination of pain using pressure platform gait analysis:

The effect of post-operative analgesic protocol and surgical method on limb function in

cats following onychectomy

by

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#### ABSTRACT

Our first objective was to perform pressure platform gait analysis on 26 adult cats that had or had not undergone bilateral forelimb onychectomy to determine peak vertical force (PVF) and vertical impulse (VI). The PVF and VI were collected from all limbs of each cat with a 2-m long pressure platform walkway. No significant difference was found for PVF and VI between cats that had or had not had onychectomy. Results suggest that bilateral forelimb onychectomy did not result in altered vertical forces measured more than 6 months after surgery in cats.

Our second objective was to perform pressure-platform gait analysis on 27 adult cats to document the analgesic effects of topical administration of bupivacaine, IM administration of butorphanol, and transdermal fentanyl following onychectomy. Peak vertical force (PVF) and vertical impulse (VI) data were collected before and 1, 2, 3, and 12 days after unilateral (left forelimb) onychectomy. Two days after surgery, cats treated with bupivacaine had significantly lower PVF than did cats in the other groups. Results suggest that limb function following onychectomy is significantly better in cats treated with fentanyl transdermally or butorphanol IM than in cats treated with bupivacaine topically. Regardless of the analgesic regimen, limb function was still significantly reduced 12 days after surgery, suggesting that long-term analgesic treatment should be considered for cats undergoing onychectomy.

Our third objective was to compare the level of post-operative limb function and discomfort in cats after scalpel and laser onychectomy as measured by pressure platform gait analysis on 20 healthy adult cats. Peak vertical force (PVF) and vertical impulse (VI) data were collected as described for the second objective. Cats in the laser group had significantly higher ground reaction forces (GRFs) on days 1 and 2 and significantly higher PVF ratio on day 12 when compared to cats in the scalpel group. Results suggest that cats have improved limb function following onychectomy when performed with a  $CO_2$  laser as compared to with a scalpel.

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### CHAPTER 1. LITERATURE REVIEW AND RESEARCH PLAN Introduction

Pain has been defined by the International Association for the Study of Pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage" and recently " the inability to communicate in no way negates the possibility that an individual is experiencing pain and is in need of appropriate pain relieving treatment." Most will agree that pain is inappropriately or inadequately approached as a result of difficulty or inability in accurate assessment of the animal's degree or perception of pain.

Nociception is the term that is used to describe the physiologic process that leads to perception of pain in any species. Specifically, a noxious stimulus is detected by specialized free nerve endings at the level of the skin, muscle, bone, joint, and viscera. This signal is converted into an electrical signal or action potential and is then transmitted to the dorsal horn of the spinal cord where the signal is either amplified or suppressed. The signal is then conveyed or projected via nerve tracts to the brain, where the signal is received, integrated, processed, and recognized. The thalamus serves as a central integration point for pain perception and response, however, numerous aspects are involved and communicate via interneurons for a coordinated response to the painful stimulus. In veterinary medicine, nociception and the perception of pain are important, but the role of the veterinarian encompasses the associated suffering and related behaviors that occur as a result of pain.

It is widely accepted that feline onychectomy is a painful procedure<sup>1,2</sup> for which many attempts to reduce patient pain have been approached through development of improved post-operative analgesic regimens and surgical techniques (laser onychectomy, tendonectomy). However, defining the most effective protocols have been limited by the inability to objectively compare analgesic regimens or surgical techniques. More importantly, numerous reports of complications have been reported<sup>1, 3</sup> as a result of persistent and untreated pain following feline onychectomy.

Specifically, these reports discuss the specific physiologic responses that induce detrimental complications via the neuroendocrine response to pain. In a study conducted by Lascelles et al, of a large group of small animal surgeons were surveyed to determine that only 22% of these clinicians administer post-operative analgesics to their patients<sup>4</sup>. Even more surprisingly, canine patients represent the majority of the patients administered post-operative analgesics according to several reports<sup>4,5</sup>.

In particular, opioids such as fentanyl citrate and butorphanol have been proven to be safe and efficacious analgesics in cats<sup>6,7</sup>. Fentanyl citrate is classified as a pure agonist which binds to one or more receptors to exert therapeutic effect. Butorphanol is classified as an agonist-antagonist and exerts effect at the level of kappa and mu receptors. There is currently much debate over whether the effects of Butorphanol are maximal at kappa and minimal at mu receptors<sup>8</sup>. Specifically, Butorphanol has been shown to be a more efficacious analgesic than medetomidine in cats that have undergone ovariohysterectomy<sup>9,10</sup>. Transdermal fentanyl patches have not been found to cause many common complications (lethargy, respiratory depression, excitement, or dysphoria)<sup>7,11</sup> and has been found to be an effective, well-tolerated method for delivery of analgesia in cats<sup>11</sup>.

Local anesthetics such as Bupivacaine have also been employed in post-operative analgesic regimes for onychectomy. Specifically, Bupivacaine is considered a long acting, potent, anesthetic that is effective following intrapleural or intra-articular administration in dogs and is recommended for use in cats<sup>12-14</sup>. However, the efficacy of bupivacaine following onychectomy in cats has been questioned<sup>15</sup>.

Three major surgical techniques have been described for feline onychectomy and include: scalpel excision, guillotine-style shearing, and carbon dioxide ( $CO_2$ ) laser excision<sup>16,17</sup>. One of the major incentives towards development of the laser onychectomy is the suggestion that it decreases the amount of post operative pain and is associated with a lower rate of complications.<sup>16-18</sup> Although

there are numerous claims in the veterinary literature as to the ability of the CO<sub>2</sub> laser to reduce post operative pain when compared to other forms of onychectomy, these reports appear largely anecdotal.<sup>17,18</sup> In a study conducted by Rocha et al., several incisions made by cautery, scalpel, and CO2 laser in rat skin demonstrated no significant difference in the number of intact peripheral nerve structures in the proximity of the incisions. In addition, the results of this study also demonstrated no significant difference in the number of intact peripheral nerve structures between rats that had or had not undergone skin incision<sup>19</sup>. In addition, CO2 laser excision has been associated with a lower rate of complications, specifically with respect to application of tourniquets and bandages. Improper tourniquet application has been documented to result in neurapraxia of the radial nerve, tissue ischemia and muscle damage; bandages have also been associated with occurrence of tissue necrosis<sup>1,20,21</sup>.

Historically, pain has been quantified through the use of visual analog scales, numerical rating scales, and physiologic indices in the evaluation of analgesic regimens as well as surgical procedures. However, the results of these studies are quite variable and do not correlate well with objective data<sup>22,23,24,25</sup> Specifically, visual analog scales (VAS) and numerical rating scales (NRS) have been used in human hospitals for the evaluation of patient pain based on where they choose the level of the pain they are experiencing, (one end of the scale is labeled as "no pain or a "③" and the other end of the scale is labeled "most pain possible" or "③"). Unfortunately, veterinary patients are unable to choose a level and their behavior must be evaluated by veterinary personnel to determine whether an adequate level of analgesia is being provided. Through assigning specific behaviors such as vocalization, depression, excessive movement within the cage, or aggression to a numerical value, the degree of pain in these patients can be subjectively evaluated. However, these behavioral characteristics can be difficult to differentiate from effects of analgesia. Also, considerable interobserver variability has been well documented (Holton). In addition, these behaviors may not

always be demonstrated by exhausted or obtunded patients post-surgically. These behavior changes may also be less apparent in feline patients as compared to canine patients and may be significantly underestimated<sup>2,14,26,27</sup> Nevertheless, analgesics should always be administered to any patient undergoing a procedure that could potentially cause pain, and the inability of animals to communicate should not be interpreted as a lack of pain.

Numerous physiologic indices such as heart rate, blood pressure, pupil size, blood catecholamines, serum glucose, B-endorphins, and cortisol levels have been used for pain evaluation. Physiologic measurements such as plasma cortisol and B-endorphin concentrations were not significantly different between control and cats that underwent surgery<sup>22</sup>. Unfortunately, the results of these objective methods correlate poorly with the subjective pain evaluations<sup>14,22,23,24,25,28</sup>, namely due to the inability to remove stress as an influential factor for many of these indices.

Most will agree that lameness, or the inability or lack of desire to use a limb, can occur as a result of malunions or variation in limb length, lameness often occurs with painful conditions of the joints<sup>29</sup>. Specifically, the function of a joint is to serve as a load bearing transfer point between long bones, promoting smooth movement and ambulation. In other words, bones provide axes of rotation and levers about which muscles generate movements. Lameness may also be considered as a mechanism to avoid stimulation of nociception. Force platform gait analysis has been considered as one of the most accurate and precise tools for the evaluation of limb function in dogs. However, traditional force platform gait analysis cannot be used to evaluate feline patients due to their short stride length. Recently, pressure platform gait analysis has been found to be equally as precise and accurate as the force platform when comparing ground reaction forces of clinically normal greyhounds<sup>30</sup>. Pressure platform gait analysis is also advantageous as it permits collection of data from sequential foot falls for multivariate statistical analyses.

#### **Research Plan**

The specific aims of this project include: determination if limb function can be measured in cats using pressure platform gait analysis, determination of effect of analgesic regime and surgical technique on limb function and pain following onychectomy in cats. In order to determine the effect of analgesic regime, cats will be treated with topical bupivacaine, a transdermal fentanyl patch, or intramuscular butorphanol and evaluated before surgery, at 1, 2, 3, and 12 days after surgery. To determine the effect of surgical technique, pressure platform gait analysis will be used to measure limb function after laser and scalpel onychectomy through evaluating patients before surgery, at 1, 2, 3, and 12 days after surgery, at 1, 2, 3, and 12 days after surgery, at 1, 2, 3, and 12 days after surgery.

It was hypothesized that gait analysis could be successfully performed in cats, the distribution of vertical forces in the fore- and hind limbs of cats would be similar to that reported in the dog, and that vertical forces between intact and declawed cats would be similar. We also hypothesized that postoperative limb function, as reflected in PVF and VI, would be better in cats treated with fentanyl than in cats treated with bupivacaine or butorphanol because of a longer duration of analgesia. In addition, we hypothesized that there would be no significant difference in the level of discomfort, as measured by pressure platform gait analysis, between cats undergoing scalpel or laser onychectomy.

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# CHAPTER 2. USE OF PRESSURE PLATFORM GAIT ANALYSIS IN CATS WITH AND WITHOUT BILATERAL ONYCHECTOMY

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#### Abstract

<u>Objective</u>: To determine peak vertical force (PVF) and vertical impulse (VI) in cats that had or had not undergone bilateral forelimb onychectomy.

Animals: 26 healthy adult cats.

<u>Procedure</u>: Onychectomized cats (n=13) had undergone surgery more than 6 months prior to the study. The PVF and VI were collected from all limbs of each cat with a 2-m long pressure platform walkway. Cats were allowed to walk at a comfortable velocity and acceleration was restricted to  $\pm 0.5$  m/s<sup>2</sup>. Five valid trials were recorded for each cat with all trials collected in a single 1-hour session. All forces were normalized to and expressed as a percentage of the cat's body weight. <u>Results</u>: Gait data were successfully collected in all cats studied. No significant difference was found for PVF and VI between cats that had or had not had onychectomy. Limb loads were greater in front limbs than hind limbs for all trials. Mean PVF and VI in the front limb were 56.41% and 18.85%, respectively. Mean PVF and VI in the rear limb were 49% and 15% of body weight, respectively.

<u>Conclusions and Clinical Relevance:</u> Gait analysis was successfully performed in cats with a pressure platform walkway. The absence of differences in PVF and VI between the 2 groups of cats suggests that bilateral forelimb onychectomy did not result in altered vertical forces measured more than 6 months after surgery in cats.

#### Introduction

Approximately 14 million cats undergo onychectomy each year.<sup>1</sup> Although many receive medications for postoperative pain, defining the most effective protocol is limited by the inability to objectively compare analgesic regimes. Additionally, there are several onychectomy techniques. Claims have been made that onychectomy performed with a laser is less painful, compared with other surgical techniques.<sup>1,2</sup> In a recent study<sup>3</sup> that used a numerical rating system to estimate level of pain, it was reported that onychectomy with a laser technique resulted in less discomfort and fewer complications. That study, however, was limited by the subjective nature of the patient evaluations. Subjective evaluations often yield inconsistent results because of interobserver variation in interpretation of pain and because the observed behavior may not accurately portray the degree of pain. <sup>4, 5</sup> Unfortunately, there are no objective physiologic measurements that consistently determine the level of pain in dogs or cats. <sup>5, 6</sup>

An objective, reliable, noninvasive method for quantifying postoperative pain and limb function in cats after onychectomy would be beneficial. Force platform gait analysis is an accurate, precise, and objective tool for measuring limb function in dogs. <sup>7, 8</sup> Unfortunately, traditional force platform gait analysis is not conducive to evaluation of animals after surgery because of inconsistent stride length and is difficult in cats because of their short stride length. Pressure platform gait analysis does not have these limitations. Pressure platforms have been evaluated by numerous laboratories and are precise and accurate. <sup>9-12</sup> In addition, pressure platforms are a suitable alternative to a force platform for generating peak vertical force (PVF) and vertical impulse (VI) data in dogs. <sup>9</sup>

The purposes of the study reported here were to determine whether limb function could be measured in cats by use of pressure platform gait analysis, describe the vertical forces found in clinically normal cats, and compare those forces with those of cats that underwent onychectomy more than 6 months prior to the study. Our hypotheses were that pressure platform gait analysis

could be successfully performed in cats, the distribution of vertical forces in the fore- and hind limbs of cats would be similar to that reported in dogs, and vertical forces would be similar between cats that had and had not undergone onychectomy more than 6 months after surgery.

#### Materials and Methods

Healthy, client-owned, adult cats (n=13) that had not undergone onychectomy were recruited as controls for this study. In addition, cats (n=13) that had a successful outcome after bilateral forelimb onychectomy more than 6 months before this study were recruited. Prior to inclusion in the study, the owner of each cat signed an informed client consent form and each cat was determined to be clinically normal on the basis of owner history and physical examination results, with an emphasis on detecting orthopedic or neurologic abnormalities. The protocol for this study was approved by Iowa State University's Care of Animal Use Committee.

A 2-meter by 0.75-meter pressure measurement platform<sup>a</sup> was placed in the center of and level with a 10-m runway. The platform was linked to a dedicated computer<sup>b</sup> with specific software<sup>c</sup> designed for collection of gait analysis data. Prior to data acquisition, the walkway sensors were equilibrated and calibrated in accordance with manufacturer specifications.<sup>13</sup> Preceding data collection, each cat was weighed on an electronic scale<sup>d</sup> and allowed to acclimate itself to the runway area and the pressure platform.

Cats were allowed to walk across the pressure platform at a comfortable velocity. Data were collected from all limbs of each cat for consecutive footfalls. Five valid trials were recorded for each cat, and all trials were collected in a single 1-hour session. A valid trial consisted of the cat walking at a comfortable velocity and each of the 4 limbs fully contacting the walkway at least 2 consecutive times during the pass. A single observer evaluated each trial and determined if a trial was valid or not. Pressure distribution data (PVF and VI) were then collected from each footfall for each of the 5 valid trials. All forces were normalized to and expressed as a percentage of the cat's body weight.

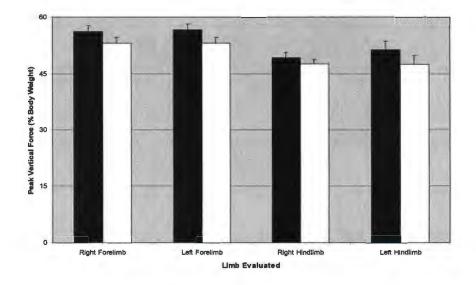
Summary statistics were calculated for all variables and repeated measures ANOVA was performed. <sup>14</sup> A *t* test was used to evaluate group differences in body weight, trial velocity and trial acceleration. Match-paired *t*-tests were used to compare the left forelimb (and hind limb) to the right forelimb (and hind limb) for PVF and VI to ensure that forelimbs (and hind limbs) were not significantly different. In addition, distribution of velocity was performed to determine whether regression analysis was needed. Regression analysis would be required if velocity was significantly different between groups. Regression analysis did not need to be performed. Significance for comparisons between limbs was set at p<0.05, and data were expressed as mean  $\pm$  SD. All analyses were performed by use of computer software<sup>e</sup>.

#### Results

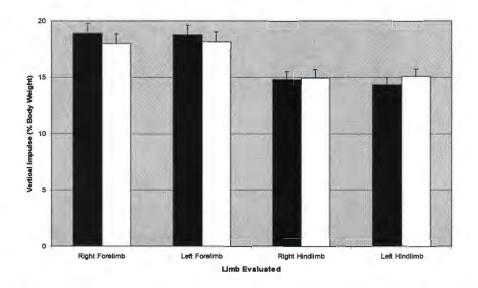
No significant difference was found between groups for sex, breed, or age. Cats in the control group had a mean body weight of  $4.70 \pm 0.38$  kg whereas cats in the onychectomy group had a mean body weight of  $5.31 \pm 0.38$  (p=0.27). Mean age of the cats in the control group was  $3.0 \pm 0.47$  years, and mean age of the cats in the onychectomy group was  $4.42 \pm 0.84$  years. Gait analysis was successfully performed in 13 of 13 cats in both groups. Although cats were allowed to establish their own gait velocity, there was no significant difference in mean gait velocity (p=0.45) or acceleration (p=0.41) between groups. In addition, there was no difference in the distribution of trial velocities between groups. Cats in the control group had mean velocity of  $0.69 \pm 0.029$  m/s, and cats in the onychectomy group had a mean velocity of  $0.66 \pm 0.029$  m/s.

No significant difference was found between the left and right forelimb for cats in the control (p=0.57) or onychectomy (p=0.99) group for PVF, and there was no difference between groups for PVF (p=0.66; **Figure 2.1**). Mean PVF for the forelimbs of cats in the control group was  $56.41 \pm 1.44\%$  of body weight, and mean PVF for the forelimbs of cats in the onychectomy group was  $53.04 \pm 1.44\%$ . Similarly, no significant difference was found between the forelimbs for cats in the control

or onychectomy group for VI (control, p=0.67; onychectomy, p=0.61) and no difference existed between groups for VI (p=0.50; **Figure 2.2**). Mean VI for the forelimbs of cats in the control group was  $18.85 \pm 0.85\%$  and mean VI for cats in the onychectomy group was  $18.09 \pm 0.84\%$ 



**Figure 2.1**—Mean ± SD peak vertical force in cats at a walk that either had (open bars) or had not (solid bars) undergone onychectomy.



**Figure 2.2**—Mean ± SD vertical impulse in cats at a walk that either had (open bars) or had not (solid bars) undergone onychectomy.

Limb loads were greater in the forelimbs than hind limbs for all trials. No significant difference was found between the left and right hind limbs for cats in the control (p=0.42) or onychectomy (p=0.89) group for PVF, and there was no difference between groups for PVF (p=0.42). Mean PVF for the hind limbs of cats in the control group was  $50.22 \pm 1.31\%$  and mean PVF for the hind limbs of cats in the onychectomy group was  $47.45 \pm 2.28\%$ . Similarly, no difference was found between the hind limbs for cats in the control (p=0.14)or onychectomy (p=0.72) groups for VI, and no difference existed between groups for VI (p=0.50). Mean VI for the hind limbs of cats in the control group was  $14.56 \pm 0.70\%$ , and mean VI for cats in the onychectomy group was  $15.01 \pm 0.66\%$ .

#### Discussion

In this study, we demonstrated that gait analysis could be successfully performed in cats. Computer generated gait analysis has proven to be beneficial in the evaluation of lameness in dogs and is commonly used to test a treatment effects of surgical procedures and pharmaceuticals. <sup>15, 16</sup> Similar situations that exist in the cat would benefit from objective evaluation of limb function. In several recent studies<sup>16-19</sup> on analgesic protocols used for onychectomy, only subjective evaluations were used to assign a pain score. However, if these subjective measurements were combined with an objective measure of a cat's willingness to use the operated limbs, better estimation of the amount of pain experienced by the cat would be possible.

We were also able to determine that when measured at least 6 months after onychectomy, vertical forces are similar between cats that have and have not had onychectomy. Because we failed to reject the null hypothesis, we need to address the probability of a type II error. As an example, we determined the statistical power for forelimb VI between groups, which is arguably the single most important variable reported. With 13 cats in each group, the power is 59%. In effect, there is a 41% chance that there is a type II error. However it is important to note that the probability of a statistical error does not change the difference between the means of each group. In this example, the

difference between the means is quite small (control, 18.85; onychectomy 18.09) and consistent with our finding of no significant difference between groups, so we believe that the difference between means is also not likely to be clinically important.

In the cats in the onychectomy group, onychectomy was performed by either scalpel or laser excision. Although there was an equal distribution in the frequency that either procedure was performed, we made no attempt to discriminate differences between those procedures. In addition, for the purposes of future studies that use this gait analysis method in cats, cats with or without previous onychectomy can be grouped; a successful outcome after previous onychectomy may not need to be considered as an additional variable.

Finally, the distribution of vertical forces at a walk between the fore- and hind limbs in cats is similar to that in dogs. In a recent study, mean PVF for the forelimb of Greyhounds was 58.11% and mean PVF of the hind limb was 42.05% of body weight.<sup>9</sup> Similarly, vertical forces in the forelimbs of our control cats were greater than that in the hind limbs. However, if we consider the mean PVF reported here (forelimb = 56.41%; hind limb = 50.22%) it is apparent that the disparity between fore- and hind limb forces in cats is much less. However, the importance of this species difference is not known.

Gait analysis in small dogs and cats with a traditional force platform <sup>7,8</sup> is difficult because of their short stride length and the manner in which force platforms and their associated software collect and process the data. The pressure platform allows for the collection of vertical force data in these small animals. Although collecting gait data from some cats required a bit of encouragement and investigator patience, we were able to collect satisfactory data from every cat. The system has reported limitations<sup>9</sup>; however, it functions as an acceptable alternative to force platform gait analysis and provides investigators with an objective method for measuring limb function in cats.

#### Footnotes

- a. Tekscan Inc., South Boston, MA.
- b. Latitude CPx personal laptop, Dell Computer Corporation, Round Rock, TX.
- c. I-scan v4.20, South Boston, MA.
- d. Vet-50 electronic scale, Detecto-Cardinal Scale, Webb City, MO.
- e. SAS Institute, Cary, NC.

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## CHAPTER 3. EFFECT OF POSTOPERATIVE ANALGESIC PROTOCOL ON LIMB FUNCTION FOLLOWING ONYCHECTOMY IN CATS

A paper published in *The Journal of the American Veterinary Medical Association* Cory W. Romans, Wanda J. Gordon, Duane A. Robinson, Richard Evans,

Michael G. Conzemius

#### **Interpretive Summary**

Pressure-platform gait analysis was performed on 27 adult cats to document the analgesic effects of topical administration of bupivacaine, IM administration of butorphanol, and transdermal administration of fentanyl following onychectomy. Peak vertical force (PVF) and vertical impulse (VI) data were collected before and 1, 2, 3, and 12 days after unilateral (left forelimb) onychectomy.

Two days after surgery, cats treated with bupivacaine had significantly lower PVF than did cats in the other groups. The ratio of left forelimb PVF to PVF of the other 3 limbs was significantly lower in cats treated with bupivacaine than in cats treated with fentanyl, but not in cats treated with butorphanol. Vertical impulse was not significantly different between groups on any day. Values for PVF, VI, and the PVF ratio increased progressively following surgery. However, for all 3 groups, values were still significantly decreased, compared with baseline values, 12 days after surgery. Results suggest that limb function following onychectomy is significantly better in cats treated with fentanyl transdermally or butorphanol IM than in cats treated with bupivacaine topically. Regardless of the analgesic regimen, limb function was still significantly reduced 12 days after surgery, suggesting that long-term analgesic treatment should be considered for cats undergoing onychectomy.

#### Abstract

<u>Objective</u>: To evaluate the analgesic effects of topical administration of topical administration of bupivacaine, IM administration of butorphanol, and transdermal administration of fentanyl in cats undergoing onychectomy.

Design: Prospective study.

Animals: 27 healthy adult cats.

<u>Procedure:</u> Cats were randomly assigned to 1 of 3 treatment groups, and unilateral (left forefoot) onychectomy was performed. Gait analysis was performed before and 1, 2, 3, and 12 days after surgery. All forces were expressed as a percentage of the cat's body weight.

<u>Results:</u> On day 2, peak vertical force (PVF) was significantly decreased in cats treated with bupivacaine, compared with cats treated with butorphanol or fentanyl. The ratio of left forelimb PVF to PVF of the other 3 limbs was significantly lower on day 2 in cats treated with bupivacaine than in cats treated with fentanyl. No significant differences in vertical impulse (VI) were found between groups on any day. Values for PVF, VI, and the PVF ratio increased progressively following surgery. However, for all 3 groups, values were still significantly decreased, compared with baseline values, 12 days after surgery.

<u>Conclusions and Clinical Relevance</u>: Results suggest that limb function following onychectomy, is significantly better in cats treated with fentanyl transdermally or butorphanol IM than in cats treated with bupivacaine topically. Regardless of the analgesic regimen, limb function was still significantly reduced 12 days after surgery, suggesting that long-term analgesic treatment should be considered for cats undergoing onychectomy. Irrigation of the surgical incisions with bupivacaine prior to wound closure cannot be recommended as the sole method for providing postoperative analgesia in cats undergoing onychectomy.

#### Introduction

Onychectomy is a painful procedure in cats,<sup>1,2</sup> and can result in complications if the pain associated with onychectomy is not treated.<sup>3</sup> Unfortunately, cats typically receive analgesic medications for postoperative pain less often than do dogs.<sup>4,5</sup> This disparity could in part be explained by concerns about possible adverse effects in cats following administration of opioid analgesics or by difficulties in recognizing pain in this species.<sup>2,5-9</sup> Nevertheless, analgesics should always be administered to any patient undergoing a procedure that could potentially cause pain,<sup>7</sup> and the inability of animals to communicate should not be interpreted as a lack of pain.

Two major types of analgesics have been used in cats undergoing onychectomy: opioids and local anesthetics. In particular, opioids such as fentanyl citrate and butorphanol have been proven to be safe and effective analgesics in cats.<sup>10-12</sup> Butorphanol, for instance, has been shown to be a more efficacious analgesic than medetomidine in cats that have undergone ovariohysterectomy,<sup>13,14</sup> and transdermal administration of fentanyl has been shown to be an effective, noninvasive, well-tolerated method for delivery of analgesia in cats.<sup>15</sup> In addition, use of transdermal fentanyl patches in cats has not been found to cause lethargy, respiratory depression, excitement, or dysphoria,<sup>11,15</sup> and transdermal fentanyl patches can provide pain relief similar to that associated with butorphanol.<sup>16</sup>

Bupivacaine is a long-acting local anesthetic that has been shown to provide safe and effective analgesia following intrapleural or intra-articular administration in dogs and has been recommended for use in cats.<sup>17-19</sup> However, its effectiveness as an analgesic following onychectomy in cats has been questioned.<sup>20</sup>

Various subjective and objective methods have been used to evaluate the effectiveness of analgesic regimens, but such methods often are unreliable in defining the degree of pain.<sup>6,20,21</sup> Recently, a pressure-platform gait analysis system has been found to be an effective, objective method for evaluating limb function in cats.<sup>22</sup> This system generates values for **peak vertical force** 

(PVF) and vertical impulse (VI) that are comparable to those obtained with traditional force platform gait analysis systems.<sup>23</sup> Peak vertical force is the maximum load applied to the platform during gait analysis and can be used to identify subtle lameness that may be undetectable by physical examination.<sup>24</sup> Vertical impulse is the sum of all vertical loads applied to the platform during the stance phase of gait. Together, PVF and VI have been found to be the most useful measures for evaluating abnormal gaits in animals.<sup>24</sup>

The purpose of the study reported here was to use pressure-platform gait analysis to evaluate the analgesic effects of topical administration of bupivacaine, IM administration of butorphanol, and transdermal administration of fentanyl in cats undergoing onychectomy. We hypothesized that postoperative limb function, as reflected in PVF and VI, would be better in cats treated with fentanyl than in cats treated with bupivacaine or butorphanol because of a longer duration of analgesia.

#### **Materials and Methods**

<u>Cats:</u> Twenty-seven healthy, client- or shelter-owned, adult cats that were scheduled to undergo elective onychectomy were used in the study. Cats were included only if they were > 4 months but < 3 years old, had not received any analgesic or sedative medications within 24 hours prior to examination, and did not have any signs of orthopedic or neurologic disease during an initial physical examination. Informed consent was obtained from owners of cats included in the study. The experimental protocol was approved by the University Committee on Animal Care at Iowa State University.

Experimental protocol: Prior to surgery, cats were randomly assigned to 1 of 3 groups (bupivacaine group, 10 cats; butorphanol group, 9 cats; and fentanyl group, 8 cats). For cats in the fentanyl group, a 25 μg transdermal fentanyl patch<sup>a</sup> was applied to the skin between the scapulae 12 hours before surgery, as described.<sup>11,16</sup> Briefly, hair was clipped from an area large enough to allow a 1-cm margin around the patch, and tape was applied to the skin to remove hair clippings. The patch was applied

and held in place for 2 to 3 minutes to ensure maximum adherence. The site was then covered with a bandage.<sup>b</sup> All patches were removed 72 hours after initial application.

Anesthesia was induced with a mixture of ketamine (10 mg/kg [4.5 mg/lb], IM), acepromazine (0.1 mg/kg [0.045 mg/lb], IM), and atropine (0.4 mg/kg [0.18 mg/lb], IM) and maintained with isoflurane delivered with oxygen via a mask. Elastic bandage material<sup>c</sup> was applied as a tourniquet to the left forelimb, cats were placed in lateral recumbency, and the left front paw was aseptically prepared for surgery. Onychectomy was performed by means of disarticulation with a scalpel. Digital incisions were closed with a single interrupted suture of 4-0 chromic gut, and a bandage was applied to the paw. Cats were then allowed to recover from anesthesia. All surgeries were performed by a single individual (MGC).

For cats in the bupivacaine group, a total of 1 mL of 0.75% bupivacaine<sup>d</sup> was used to irrigate the digital incisions prior to closure, as described.<sup>21</sup> For cats in the butorphanol group, butorphanol<sup>e</sup> (0.4 mg/kg, IM) was administered before administration of isoflurane was discontinued and every 4 hours for the first 24 hours after surgery, as described.<sup>19</sup>

For all cats in the study, an accepted subjective pain scoring system<sup>10,16</sup> was used to determine whether rescue analgesia was required. Cats that required rescue analgesia were removed from the study.

<u>Gait analysis:</u> Pressure-platform gait analysis was performed before and 1, 2, 3, and 12 days after surgery. For gait analysis the day after surgery, the bandage was removed from the left forefoot within 1 hour of gait analysis.

A 2 X 0.75-m pressure measurement walkway<sup>f</sup> mounted in the center of and level with a 10m runway was used for gait analysis. Output from the walkway was linked to a dedicated computer<sup>g</sup> with software<sup>h</sup> designed for collection of gait analysis data. Prior to data acquisition, the walkway sensors were equilibrated and calibrated in accordance with manufacturer's specifications. Before each session, cats were weighed on an electronic scale<sup>i</sup> and allowed to acclimate to the runway area and the pressure platform.

Cats were allowed to walk across the pressure platform at a comfortable velocity. Five valid trials were collected for each cat at each session. A trial was considered valid if the cat walked along the runway at a comfortable velocity and each of the 4 limbs fully contacted the pressure measurement walkway at least 2 consecutive times during the pass. Pressure distribution data (PVF and VI) were determined for each footfall for each of the 5 valid trials, and mean values were calculated. Values were then expressed as a percentage of body weight.

Following gait analysis on day 12, the study ended, and onychectomy was performed on the right forefoot.

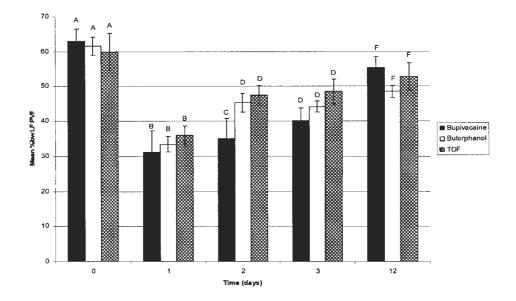
<u>Statistical analyses:</u> Student *t* tests were used to compare age, velocity, and acceleration between groups. Cross-sectional analysis was used to compare PVF, VI, and PVF ratio ratio of left forelimb PVF to PVF of the other 3 limbs) among groups while controlling for baseline (day 0) and day 12 values through analysis of covariance. This method was chosen because each day was a repeated measure. It was necessary to control for day 0 and day 12 values because drug effects were not present on these days. When a significant group effect was identified, the Tukey honest significant difference method was used to determine specific group differences. Overall significance for all comparisons was set at P < 0.05. The effect of time within treatment group was assessed by use of paired *t* tests. All analyses were performed with standard software.<sup>j</sup>

#### Results

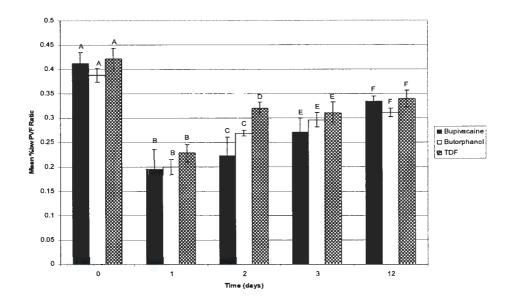
One cat in the bupivacaine group was removed from the study a few hours after surgery when it was considered to have severe pain on the basis of a visual observation of its behavior and rescue analgesia was administered. Thus, gait analysis data were available for 9 cats in the butorphanol group, 9 cats in the bupivacaine group, and 8 cats in the fentanyl group.

Mean  $\pm$  SE ages of cats in the bupivacaine, butorphanol, and fentanyl groups were  $16.6 \pm 4.2$ months,  $12.9 \pm 2.8$  months, and  $30.6 \pm 9.1$  months, respectively. There were no significant differences in age between groups, and age was not significantly associated with PVF. Mean  $\pm$  SD velocities during gait analysis for cats in the bupivacaine, butorphanol, and fentanyl groups were 0.76  $\pm 0.09$  m/s,  $0.76 \pm 0.08$  m/s, and  $0.81 \pm 0.06$  m/s, respectively. There were no significant differences in velocity or acceleration between groups.

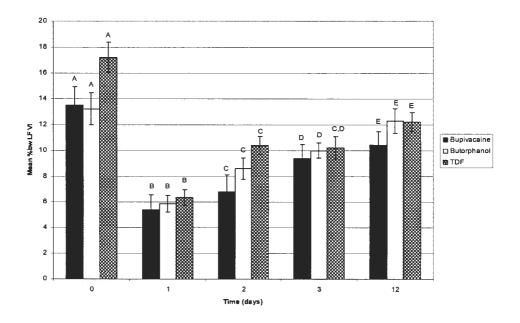
On day 2, PVF was significantly (P < 0.01) lower for cats in the bupivacaine group than for cats in the other 2 groups (Figure 3.1).



**Figure 3.1**—Mean peak vertical force (PVF) of the left forelimb, expressed as a percentage of body weight, in cats that underwent unilateral onychectomy and received bupivacaine topically (n=9), butorphanol IM (9), or fentanyl transdermally (TDF; 8) for postoperative analgesia. Error bars represent SEM. Columns with different letters were significantly (P < 0.05) different.



**Figure 3.2**—Mean of the ratio of the left forelimb PVF to the PVF of the remaining 3 limbs for cats that underwent unilateral onychectomy and received bupivacaine topically (n=9), butorphanol IM (9), or fentanyl transdermally (8) for postoperative analgesia. See Figure 3.1 for key.



**Figure 3.3**—Mean vertical impulse (VI) of the left forelimb in cats that underwent unilateral onychectomy and received bupivacaine topically (n=9), butorphanol IM (9), or fentanyl transdermally (8) for postoperative analgesia. See figure 3.1 for key.

Significant differences among groups were not found on days 1, 3, and 12, although the P value for day 1 was close to the established value for significance (P = 0.054). Similarly, the ratio of left forelimb PVF to PVF of the other 3 limbs (ie, the PVF ratio) was significantly (P = 0.015) lower on day 2 in cats treated with bupivacaine than in cats treated with fentanyl, but was not significantly different from the value for cats treated with butorphanol (Figure 3.2). There were no significant differences in VI among groups on any day (Figure 3.3).

In all 3 groups, PVF, VI, and the PVF ratio were significantly decreased the day after surgery, compared with baseline values. Values increased progressively during the subsequent days. However, for all 3 groups, PVF, VI, and the PVF ratio were still significantly decreased, compared with baseline values, 12 days after surgery.

#### Discussion

In a strict sense, inclusion of a control group of cats in the present study that did not receive any analgesics may have been considered advantageous, but was not considered because previous research has indicated that this procedure is painful and that cats should be treated with analgesics postoperatively.<sup>25</sup> We found that IM administration of butorphanol and transdermal administration of fentanyl provided similar degrees of analgesia, but that topical administration of bupivacaine was less effective. This most likely reflects the duration of action of bupivacaine (ie, 3 to 10 hours<sup>3</sup>) and the fact that it was administered only once (ie, just prior to closure of the digital incisions). We elected to evaluate the analgesic effects of topical bupivacaine administration because it was our opinion that this procedure is used in clinical veterinary practice. Although our results may have been different if bupivacaine had been infiltrated in the area, rather than administered topically, topical and infiltrative administration of local anesthetics have been found to be equally effective in providing analgesia following total ear canal ablation in dogs.<sup>26</sup>

Our findings are supported by a report<sup>3</sup> that the duration of action of bupivacaine is between 3 and 10 hours. In contrast, a previous study<sup>18</sup> suggested that bupivacaine may provide 24 hours of analgesia in dogs. In that study, however, bupivacaine was administered intra-articularly following surgery for rupture of the cranial cruciate ligament, and the intra-articular route of administration may have affected the duration of action or availability of the drug. The shorter apparent duration of action for bupivacaine in the present study may also be attributable, in part, to loss of some of the drug from the incision during suture closure or dilution with blood, either of which could have decreased the effectiveness of the drug.<sup>21</sup> It has also been suggested that injection of bupivacaine may itself cause some mild discomfort<sup>17,21</sup> that could possibly persist for several hours or days. However, the authors are not aware of any information documenting this phenomenon in cats.

In the present study, transdermal administration of fentanyl and IM administration of butorphanol resulted in similar degrees of analgesia, in that results of gait analyses were not significantly different between these groups during the 12 days after surgery. These findings are consistent with the results of previous reports<sup>10,16</sup> on the analgesic efficacy of fentanyl and butorphanol in cats. Although we found these treatment regimens to provide similar degrees of analgesia in this clinical situation, different results could occur in a different clinical situation or species. Different species have different degrees of skin permeability to fentanyl owing to differences in diffusion and thickness of the stratum corneum.<sup>11</sup> Fentanyl is a highly lipophilic narcotic that selectively diffuses to lipid-rich tissues, such as the stratum corneum of the epidermis.<sup>15</sup> The stratum corneum of haired skin in cats varies from 3 to 20 µm thick, which may suspend diffusion of the drug.<sup>27</sup> Individual cats that are treated with transdermal fentanyl patches had these species differences as well as individual variations in plasma fentanyl concentrations over a 48-hour period. In cats, plasma fentanyl concentration has been reported to range from 0.3 to 7 ng/mL during the 48-hours after application of a transdermal fentanyl patch to the lateral aspect of the thorax.<sup>16</sup> When a

transdermal fentanyl patch was applied in the dorsal cervical region of a group of cats, plasma fentanyl concentration ranged from 0.50 to 6.38 ng/mL 12 hours after patch application.<sup>11</sup>

Following patch removal in dogs, plasma fentanyl concentration rapidly decreases, with a reported half-life of 1.39 hours<sup>11,28</sup>; however, plasma concentration in cats decreases at a much slower rate after patch removal.<sup>11</sup> One possible explanation for the greater half-life of fentanyl in cats is the presence of a cutaneous depot of fentanyl beneath the patch; this phenomenon has been observed in humans.<sup>11</sup> Information on the plasma concentration of fentanyl associated with effective analgesia in cats with superficial or orthopedic pain would be of value in defining the most effective analgesic protocol following onychectomy.

Results of the present study indicate that IM administration of butorphanol is a reasonable analgesic regimen for cats undergoing onychectomy. It has been documented previously that cats that receive butorphanol IV have lower subjective lameness scores the day after discharge, compared with cats given a placebo (saline [0.9% NaCl] solution),<sup>19</sup> but perioperative IM administration of butorphanol at doses ranging from 0.05 to 0.4 mg/kg (0.023 to 0.18 mg/lb) has also been associated with adequate analgesia.<sup>13</sup> In the present study, butorphanol was administered before administration of isoflurane was discontinued, which may have contributed to its efficacy.

In previous studies<sup>16,19,20,29,30</sup> of the effectiveness of various analgesic regimens and surgical techniques, onychectomy was performed bilaterally. However, this may complicate evaluations, as both forelimbs would be expected to be painful following surgery. We suggest that unilateral onychectomy allows for a better evaluation of limb function and degree of pain, as it provides the animal the choice to use the limb on which surgery was performed or to ambulate only with the 3 remaining limbs. Although all cats consistently used the left forelimb by 2 days after surgery, some cats had clinical evidence of non-weight-bearing lameness during gait analyses after surgery. We did not include an evaluation of patient behavior as an indicator of pain in the present study because the

interpretation of cat behavior seems to be wrought with subjectivity. In addition, we did not collect other objective parameters of pain (eg, heart rate and serum cortisol concentration) because we were more concerned with the long-term effects of the procedure (ie, 1 through 12 days after surgery) than with the immediate postoperative effects (ie, the first 24 hours after surgery).

The gait analysis system in the present study measured limb function, not strictly limb pain, and it is possible that a cat could have had normal limb function but still be in pain. However, this was not apparent, in that PVF, VI, and the PVF ratio were all less than baseline values at all times after surgery in all cats. It is also possible that factors other than pain (eg, incisional inflammation, early infection, tendonitis, and suture reactivity) could have contributed to the decrease in limb function. However, we are not aware of a better method for evaluating pain in cats 1 to 12 days after limb surgery and believe that our method was at least as good a method of evaluating limb pain as any method that has been described. In addition, ground reaction forces have commonly been used as a measure of limb pain in dogs with osteoarthritis.

Although cats were permitted to walk across the pressure platform at a comfortable pace, no significant differences in velocity or acceleration were detected between groups on any day. In addition, we were able to collect satisfactory gait data for every cat. Despite its limitations, the pressure-platform gait analysis system is considered an acceptable alternative to force platform gait analysis systems and can be regarded as an acceptable objective method for evaluating limb function in cats.<sup>23</sup>

On the basis of results of the present study, topical administration of bupivacaine cannot be recommended as a method for obtaining postoperative analgesia in cats undergoing onychectomy. Limb function, as reflected in PVF and the PVF ratio, was significantly better in cats treated with fentanyl transdermally or butorphanol IM than in cats treated with bupivacaine topically. Although a previous study<sup>22</sup> revealed that ground reaction forces recorded 6 months after surgery in cats that had

undergone onychectomy were similar to forces in cats that had not undergone surgery, limb function in cats in the present study was still significantly decreased 12 days after surgery. Thus, providing analgesia for the duration of this period should be strongly considered.

#### Footnotes

- a. Duragesic, Janssen Pharmaceutical Products, Titusville, NJ.
- b. Expandover, Kendall Company, Mansfield, Mass.
- c. Vetrap, 3M Animal Care Products, St. Paul, Minn.
- d. Marcaine, Abbott Labs, North Chicago, Ill.
- e. Torbugesic, Fort Dodge Animal Health, Fort Dodge, Iowa.
- f. Tekscan Inc, South Boston, Mass.
- g. Latitude CPx personal laptop, Dell Computer Corporation, Round Rock, Tex.
- h. I-scan v 4.20, South Boston, Mass.
- i. Vet-50 electronic scale, Detecto-Cardinal Scale, Webb City, Mo.
- j. JMP v 5.1.1, SAS Institute, Cary, NC.

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# CHAPTER 4. EVALUATION OF PAIN AND LIMB FUNCTION FOLLOWING CO2 LASER OR SCALPEL EXCISION FOR ONYCHECTOMY

A paper submitted to the Journal of the American Veterinary Medical Association

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# Abstract

<u>Objective</u>: To compare the level of post-operative limb function and discomfort in cats after scalpel and laser onvchectomy as measured by pressure platform gait analysis.

Design: Randomized, prospective study.

Animals: 20 healthy adult cats.

<u>Procedure:</u> Cats were randomly assigned to the laser or scalpel onychectomy group. A unilateral left forelimb onychectomy was performed. Pressure platform gait analysis was performed prior to and 1, 2, 3 and 12 days after onychectomy. Peak vertical force (PVF), vertical impulse (VI) and the ratio of the PVF of the left forelimb to the sum of the remaining limbs (PVF ratio) were used as outcome measures.

<u>Results:</u> Cats in the laser onychectomy group had significantly higher ground reaction forces (GRFs) on days 1 and 2 and significantly higher PVF ratio on day 12 when compared to cats in the scalpel group. Similarly, significant differences were found with respect to the change in GRFs on days 1 and 2 and with the PVF ratio on day 12 when compared to day 0. No cats required rescue analgesia during the course of the study. One cat in the laser group became depressed and reluctant to walk on Day 2 post-operatively, was found to have cardiac insufficiency and was euthanized. <u>Conclusions and Clinical Relevance:</u> Cats have improved limb function following onychectomy when performed with a  $CO_2$  laser as compared to with a scalpel. This improved limb function implies that, on average, cats are less painful following laser onychectomy during the first 48 hours after surgery.

#### Introduction

It is accepted that onychectomy in the cat is a painful procedure and attempts have been made to address this not only with pharmacologic remedies but also in developing different surgical techniques (i.e. laser onychectomy, tendonectomy). In fact, recent evidence would suggest that in the early postoperative period cats that have unilateral onychectomy performed are more reluctant to use their operated leg because of pain than dogs recovering from surgery for a torn cranial cruciate ligament and medial meniscus.<sup>1,2</sup> This can be drawn from the fact that dogs had a smaller decrease in PVF 24-hrs after knee surgery than did cats after onychectomy. It has also been demonstrated that 12 days after unilateral onychectomy in the cat, ground reaction forces have not returned to pre-operative levels.<sup>1</sup> However, long term, this lameness does resolve.<sup>3</sup>

An important component of evaluating a pharmaceutical or surgical technique with regards to quality of analgesia in veterinary medicine is patient assessment. The use of pain scales is widely accepted in human medicine and has been used for the evaluation of pain in the cat.<sup>4-10</sup> Some of the pitfalls of using pain scales in veterinary medicine are that the patient cannot verbally communicate thus an observer is required to estimate the level of pain and it has been reported that the evaluation process is subjective and dependent upon observer experience.<sup>5,9</sup> Several studies have attempted to use weight bearing, behavioral responses (i.e. vocalization, posture), lameness or response to palpation of the feet as an indication of pain.<sup>5-7,9,11-13</sup> Nonetheless, with the exception of studies where they used a palpometer to squeeze the paw<sup>7</sup> and where a thermal threshold device was used to assess antinociception<sup>14,15</sup> these assessments have some degree of subjectivity. In addition, the use of physiologic values (i.e. heart rate, respiratory rate, temperature and appetite), βendorphin levels and serum cortisol levels, although objective, have yielded inconsistent results in cats<sup>5,9,16,17</sup>, and have been reported to correlate poorly with behavioral measures of pain in dogs.<sup>13,18</sup> Pressure platform gait analysis, similar to force platform gait analysis, is an objective, accurate

means of assessing normal and pathologic changes in gait and has recently been utilized in assessing limb function and pain in both canine and feline populations.<sup>1-3,19,20,a,b</sup>

Three major surgical techniques have been described for feline onychectomy: scalpel excision, guillotine-style shearing, and carbon dioxide (CO<sub>2</sub>) laser excision.<sup>8,21,22-24,c</sup> One of the major incentives towards development of the laser onychectomy is the suggestion that it decreases the amount of post operative pain and is associated with a lower rate of complications.<sup>8,23,25-28,c</sup> Although there are numerous claims in the veterinary literature as to the ability of the CO<sub>2</sub> laser to reduce post operative pain when compared to other forms of onychectomy, these reports appear largely anecdotal.<sup>23,25</sup>

The objective of this prospective study was to compare the level of post-operative discomfort and limb function in cats after scalpel and laser onychectomy as determined using pressure platform gait analysis. Our hypothesis was that there would be no significant difference in the level of discomfort between cats undergoing scalpel or laser onychectomy.

## **Materials and Methods**

<u>Cats:</u> Healthy, adult cats (n=20) that were scheduled for elective onychectomy were recruited based on the following inclusion criteria: between 6 and 24-months of age, no analgesic or sedative medications within 24 hours of presentation, no orthopedic or neurologic disease present on preoperative physical examination, and informed owner consent for patient participation. The institutional Committee on Animal Care approved the experimental protocol for this study. <u>Experimental protocol:</u> Pre-operatively, cats were randomly assigned to one of two groups: scalpel onychectomy (n=10) or CO<sub>2</sub> laser onychectomy (n=10). A mixture of ketamine hydrochloride (10mg/kg [4.5mg/lb], IM), acepromazine maleate (0.1mg/kg [0.045mg/lb], IM), and atropine sulfate (0.4mg/kg [0.18mg/lb], IM) were injected intramuscularly fifteen minutes before induction of anesthesia. Anesthesia was induced and maintained using isoflurane in oxygen delivered via a mask. A tourniquet wrap was used only in cats designated for scalpel onychectomy. Vetrap<sup>d</sup> was applied to the left forelimb, starting at the paw and extending proximally to just below the elbow. The wrap was then cut distally and rolled proximally to provide a surgical field that exposed only the phalanges.

Cats were placed in right lateral recumbency and the left front paw was prepared for surgery using traditional aseptic technique, except that the fur was not clipped. For both scalpel and CO<sub>2</sub> laser methods, the claw was grasped with a hemostat and the 3<sup>rd</sup> phalanx of each digit on the left front paw was amputated by incising over the ungula crest followed by dissection between the second and third phalanx, disarticulation of the distal interphalangeal joint, and incision of the deep digital flexor tendon. An experienced surgeon (MGC) performed the scalpel onychectomy. Each digital incision was closed with a single, simple interrupted suture of 4-0 chromic gut and a bandage was placed on the operated limb. The bandage was removed 12-15 hours after surgery and at least 1 hour before gait analysis. Another surgeon (WJG) experienced in laser onychectomy using a CO<sub>2</sub> laser<sup>e</sup> performed onychectomy with a 0.3-mm steel laser tip on a 6 watt continuous power setting. A new 3-mm tip was used after every 2 paws to avoid excessive charring of the tissue. Simple interrupted sutures of 4-0 chromic gut were placed but a bandage was not applied in the laser onychectomy group. Cats were then placed in individual cages for recovery. All cats were treated with intramuscular butorphanol tartrate<sup>f</sup> (0.4 mg/kg [0.18mg/lb] IM) prior to discontinuation of anesthesia and every four hours for the first 24 hours following surgery.<sup>1,5-7,9,14-17</sup>

A previously reported subjective assessment system of pain<sup>1,5,29</sup> was used to determine whether rescue analgesia and removal from the study was necessary. Similarly, cats were monitored during surgery and post-operatively for the amount of hemorrhage and any other complications that occurred. As the observer was not blinded to which procedure had been

performed, subjective evaluation of gait or patient behavior was not included as part of the comparison between groups.

<u>Gait analysis</u>: Pressure platform gait analysis was performed 1 day before (referred to as Day 0) and 1, 2, 3 and 12 days after surgery. A 2-meter by 0.75 meter pressure measurement walkway (TS)<sup>g</sup> was placed in the center of and level with a 4-meter runway. The TS walkway was linked to a dedicated computer<sup>h</sup> with specific software<sup>i</sup> designed for collection of gait analysis data. Prior to data acquisition, the walkway sensors were equilibrated and calibrated in accordance with manufacturer specifications. Preceding data collection, each cat was weighed on an electronic scale<sup>j</sup> and allowed to acclimate itself to the runway area and the pressure platform.

Cats were allowed to walk across the pressure platform at a comfortable velocity. The first five valid trials were recorded and saved for data evaluation. A valid trial consisted of the cat walking at a comfortable velocity with each of the four limbs fully contacting the walkway at least two consecutive times during the pass. Pressure distribution data (peak vertical force (PVF) and vertical impulse (VI)) were then determined from each footfall for each of the five valid trials. The PVF ratio, which was defined as the ratio of PVF of the left front to the sum of the three remaining limbs, was also calculated. Ground reaction forces (GRFs) were expressed as a percent of bodyweight.

Statistical analysis: All analyses were performed with standard software.<sup>k</sup> Summary statistics are presented as mean ± standard deviation (SD). A linear regression analysis was used to evaluate the relationship between the overall mean PVF of the left forelimb and age of the cats. Students' t-test was used to compare age, velocity and acceleration on each study day; and weight on Day 0 and 12 between the laser and scalpel groups. PVF and VI for the left forelimb and the ratio of the left forelimb PVF to the remaining 3 limbs' PVF were compared using matched pairs t-tests. For these analyses group effect was determined using Day 0 as a baseline for all outcome measures.

The data was further evaluated by calculating the mean percent change in PVF, VI and PVF ratio on Days 1, 2, 3 and 12 from Day 0 for each cat using the following formula:

## mean GRF Day X - mean GRF Day 0 x 100%

#### mean GRF Day 0

where the GRF is the PVF, VI or PVF ratio and Day X is day 1, 2, 3 or 12. The result for each cat was then used to calculate the mean values for each of the laser and scalpel groups. Using this formula, a negative value represents a GRF that is less than the Day 0 value and likewise a positive value represents a GRF that is greater than the Day 0 value. This data is presented as mean percent change  $\pm$  standard error (SE). Students' t-test was used to compare the percent change in PVF, VI and PVF between the laser and scalpel groups on Days 1, 2, 3 and 12. Overall significance for all comparisons was set a p<0.05.

# Results

Twenty cats were enrolled in the study, 10 in each of the laser and scalpel groups. One cat in the laser group became depressed and reluctant to walk on Day 2 post-operatively. Physical examination revealed signs consistent with pulmonary edema and cardiac insufficiency. The cat was euthanized and necropsy confirmed the presence of pulmonary edema with left ventricular dilation. Data from this cat was not used in the final analyses. No cats required rescue analgesia during the course of the study. No additional complications were noted during the study period.

There were 10 males and 9 females (laser group: 3 males and 6 females; scalpel group: 7 males and 3 females). Mean  $\pm$  SE age of cats in the laser and scalpel groups were 20.0  $\pm$  2.83 months and 15.2  $\pm$  3.44 months, respectively. Age was not significantly different between the groups and was not significantly associated with the PVF or VI. Mean velocities for cats in the laser and scalpel groups were 0.74  $\pm$  0.18 m/s and 0.76  $\pm$  0.27 m/s, respectively. Mean acceleration for cats in the laser and scalpel groups were 0.08  $\pm$  0.18 m/s<sup>2</sup> and 0.06  $\pm$  0.20 m/s<sup>2</sup>, respectively.

There were no significant differences in velocity or acceleration between groups. Mean body weight for cats in the laser and scalpel groups were  $3.53 \pm 0.53$  kg  $(7.77 \pm 1.17 \text{ lb})$  and  $3.27 \pm 0.50$  kg  $(7.19 \pm 1.10 \text{ lb})$  on Day 0; and  $3.54 \pm 0.61$  kg  $(7.79 \pm 1.34 \text{ lb})$  and  $3.33 \pm 0.54$  kg  $(7.32 \pm 1.19 \text{ lb})$  on Day 12, respectively. There were no significant difference in body weight between groups nor was the change over time significant.

Mean PVF, VI and PVF ratio for all time periods are presented in Table 1 and Figures 4.1-4.3. On Day 1 and 2, the cats that had undergone laser onychectomy had a significantly higher PVF (Day 1: p<0.01, Day 2: p=0.04); VI (Day 1: p=0.01, Day 2: p=0.01); and PVF ratio (Day 1: p<0.01, Day 2: p<0.01) compared to the cats in the scalpel group.

		r	
		Laser	Scalpel
Day 0	PVF	52.00 ± 15.09	60.75 ± 12.92
	VI	$12.71 \pm 3.71$	$13.30 \pm 4.63$
	PVF Ratio	0.38 ± 0.09	$0.39 \pm 0.07$
Day l	PVF*	$45.76 \pm 12.81$	34.81 ± 9.70
	VI*	9.74 ± 2.97	6.31 ± 2.81
	PVF Ratio*	$0.34 \pm 0.08$	0.21 ± 0.07
Day 2	PVF*	46.87 ± 9.44	45.26 ± 11.24
	VI*	11.96 ± 3.12	8.98 ± 3.43
	PVF Ratio*	$0.37 \pm 0.07$	$0.27 \pm 0.06$
Day 3	PVF	40.65 ± 5.96	44.49 ± 8.53
	VI	$10.90 \pm 3.09$	$10.04 \pm 2.96$
	PVF Ratio	$0.32 \pm 0.05$	$0.29\pm0.06$
Day 12	PVF	45.83 ± 6.74	48.71 ± 9.18
	VI	$13.98 \pm 3.46$	$12.18 \pm 3.83$
	PVF Ratio*	$0.35 \pm 0.06$	0.31 ± 0.05

**Table 4.1**—Ground reaction forces as measured on days 0, 1, 2, 3 and 12. Data is presented as mean  $\pm$  standard deviation. PVF= peak vertical force. VI= vertical impulse. PVF ratio= the ratio of PVF of the left front to the sum of the three remaining limbs. A \* denotes a statistically significant difference.

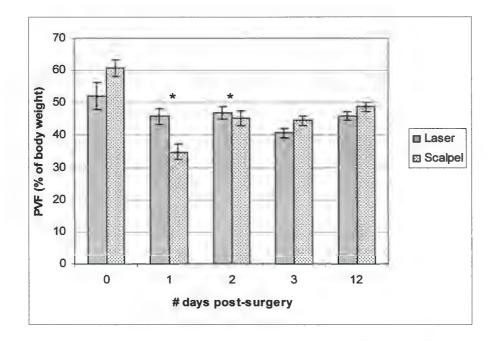


Figure 4.1—PVF expressed as % of body weight on days 0, 1, 2, 3 and 12 Data is presented as mean  $PVF \pm$  standard error. PVF= peak vertical force. A \* denotes a statistically significant difference.

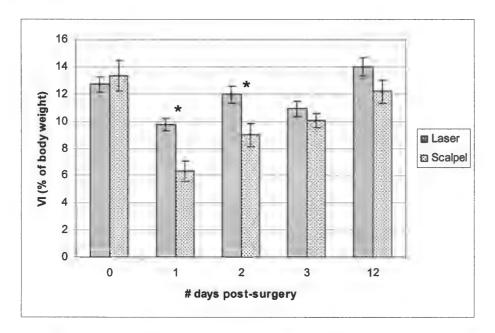
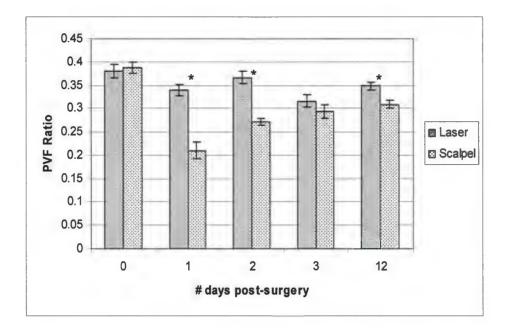


Figure 4.2—VI as % of body weight on days 0, 1, 2, 3 and 12. Data is presented as mean VI  $\pm$  standard error. VI= vertical impulse. A \* denotes a statistically significant difference.



**Figure 4.3**—PVF ratio on days 0, 1, 2, 3 and 12. Data is presented as mean PVF ratio ± standard error. PVF ratio= the ratio of PVF of the left front to the sum of the three remaining limbs. A \* denotes a statistically significant difference.

No significant differences were found between groups with respect to Day 3 ground reaction forces (PVF: p=0.36, VI: p=0.21 and PVF ratio: p=0.36). On Day 12 cats in the laser group had a significantly higher PVF ratio (p=0.04), but other ground reaction forces were not different between groups (PVF: p=0.18, VI: p=0.14).

Mean percent change in PVF, VI and PVF ratio for Days 1, 2, 3 and 12 compared to Day 0 are presented in Table 2. With the exception of the VI on Day 12; PVF, VI and PVF ratio were all less than Day 0 values on Days 1, 2, 3 and 12 for both the laser and scalpel groups. On Day 1 and 2, the cats undergoing scalpel onychectomy had a significantly greater decrease in PVF (Day 1: p<0.01, Day 2: p=0.02); VI (Day 1: p<0.01, Day 2: p=0.01); and PVF ratio (Day 1: p<0.01, Day 2: p=0.01) compared to the cats in the laser group. There were no significant differences in the change in PVF (p=0.34), VI (p=0.29) or PVF ratio (p=0.31) on Day 3 between groups. On Day 12,

a significant difference was found between groups with respect to the change in PVF ratio (p=0.02) but not for PVF (p=0.11) or VI (p=0.16).

	% change	Laser	Scalpel
Day 1	PVF*	-8.47 ± 7.8	$-41.89 \pm 4.8$
	VI*	$-21.80 \pm 5.6$	$-51.02 \pm 5.9$
	PVF Ratio*	$-9.25 \pm 5.8$	$-45.56 \pm 4.4$
Day 2	PVF*	$-7.84 \pm 4.2$	$-24.47 \pm 4.9$
	VI*	$-5.21 \pm 4.3$	$-30.17 \pm 7.0$
	PVF Ratio*	$-3.16 \pm 3.9$	$-29.32 \pm 2.3$
Day 3	PVF	$-18.94 \pm 5.3$	$-25.53 \pm 4.3$
	VI	$-13.01 \pm 5.8$	$-21.58 \pm 5.4$
	PVF Ratio	$-15.49 \pm 5.8$	$-23.43 \pm 4.8$
Day 12	PVF	$-9.13 \pm 5.0$	$-19.01 \pm 3.1$
	VI	$12.13 \pm 8.2$	$-4.27 \pm 7.6$
	PVF Ratio*	$-7.64 \pm 3.7$	$-19.68 \pm 3.0$

**Table 2**—Percent change in PVF, VI and PVF ratio on days 1, 2, 3 and 12 compared to day 0. Data is presented as mean percent change ± standard error. PVF= peak vertical force. VI= vertical impulse. PVF ratio= the ratio of PVF of the left front to the sum of the three remaining limbs. A \* denotes a statistically significant difference.

## Discussion

Onychectomy is a common, sometimes controversial, elective procedure performed in cats in North America.<sup>3,7,30</sup> In recent years the debate over this practice has lead to changes in perceptions about this procedure in both owners and veterinarians. On one hand some advocate tendonectomy as an alternative<sup>24,31-33</sup>, while others suggest the use of a carbon dioxide laser results in less discomfort and complications.<sup>8,23,25-28,c</sup>

One study found that although the laser onychectomy may decrease the postoperative stress and level of pain, as determined via serial blood cortisol concentrations, behavioral changes and urine cortisol:creatinine ratio, it may also increase the number of complications in the immediate post-operative period.<sup>c</sup> In another study, subjective assessments and scoring of pain, lameness and swelling were used to compare laser versus scalpel onychectomy. Their conclusion was that although laser onychectomy resulted in less discomfort and complication scores in the immediate post-operative period, the difference did not appear to be clinically important.<sup>8</sup> In our study, on Days 1 and 2 after surgery cats in the laser surgery group had significantly higher PVF, VI and PVF ratio when compared cats in the scalpel group. These results would indicate that, in the immediate post-operative period, cats in the laser surgery group were less lame and arguably experiencing less limb pain than cats in the scalpel group. Day 3 post-operatively, there was no significant difference between the groups and on Day 12 no difference was found with respect to PVF and VI, but there was a difference between the groups with respect to PVF ratio.

When the data was evaluated by examining the change in ground reaction forces compared to Day 0, we found similar results. Over the entire study period, the laser group of cats had a mean PVF, VI and PVF ratio that were closer to the Day 0 values than did the scalpel group. However, the difference was only statistically significant for all three parameters on Day 1 and 2 and for PVF ratio on Day 12. Also of interest was the finding that on Day 12 the mean VI for the laser group of cats was greater than the mean value on Day 0. Given that statistical significance was not achieved with respect to the Day 12 change in VI, this is likely due to normal variation. Overall these findings do not support our hypothesis and instead, suggest that when performed with a carbon dioxide laser, onychectomy is less painful than when performed with a scalpel, which is in agreement with previous studies.<sup>8,c</sup>

Plasma cortisol concentrations are considered by many to be a good, objective indication of pain in both dogs and cats.<sup>5,16,17</sup> However, cortisol can be affected by parameters other than pain resulting in inconsistencies with these measurements.<sup>5,7,9,13,16,17</sup> Plasma cortisol concentration

remains an impractical and invasive means of assessing pain that is often limited to use in research settings. The use of a pressure platform gait analysis is relatively new in veterinary medicine and has been advocated for subjects that are not amenable to force platform gait analysis because of size or short stride length.<sup>2,3,19,a,b</sup> The pressure platform has been validated as an alternative to the force platform for measuring peak vertical force and vertical impulse in the dog<sup>19,a</sup> and has been used to suggest that onychectomy itself does not alter forelimb vertical impulses when compared to unoperated cats.<sup>3</sup> This system has also been used to evaluate clinically normal cats<sup>b</sup>, the efficacy of perioperative analgesia in dogs<sup>2</sup> and post-operative analgesia in cats.<sup>1</sup> This pressure platform system is appealing because it allows an objective assessment of vertical forces (PVF and VI) which, together, are the most commonly used kinetic parameters to assess normal and pathologic changes in gait. Although the ground reaction forces could be affected by other factors, the measurement of PVF and VI are widely accepted as an assessment of limb function and discomfort. In our study the unilateral onychectomy as well as the use of the pressure platform system gave us the opportunity to obtain a more accurate assessment of limb pain. Unlike the subjective pain assessment, where an observer assigns a pain score, the cat determined the amount of weight they applied to the operated limb. With this in mind, a unilateral onychectomy was essential as it provided a normal, unoperated forelimb to which weight could be transferred. Overall, we agree with Horstman et al in that pressure platform gait analysis is not necessarily a 100% reliable indication of pain.<sup>2</sup> However, we are not aware of a better method of objectively evaluating limb pain in cats in the perioperative period.

Although the results of this and other studies<sup>8,c</sup> demonstrate that an onychectomy performed with a  $CO_2$  laser is less painful than those performed with a scalpel, the mechanism responsible for the difference remains to be elucidated. This phenomenon is not unique to veterinary medicine as the use of  $CO_2$  laser for surgical procedures of the head and neck in humans

appears to result in less post-operative pain when compared to procedures with a scalpel or electrocautery.<sup>34</sup> In one study, transection of the tibial branch of the rat sciatic nerve with a CO<sub>2</sub> laser resulted in a significant decrease in the retrograde transport of horseradish peroxidase when compared to a scalpel group.<sup>34</sup> Although these results may support the theory that a decrease in post-operative pain with laser onychectomy is the result of a decreased initiation of action potential at the transected nerve ending<sup>28</sup>, the clinical significance in an onychectomy remains unclear. Similarly, to the authors' knowledge, there are no published reports that demonstrate these changes in the nerve endings of cats. In another study, incisions made in the dorsal surface of a rat tongue with cautery, a scalpel and CO<sub>2</sub> laser in both continuous and pulsed modes were compared immunocytochemically to normal, unoperated tissue. There was no significant difference in the total number of intact nerves adjacent to the incisions and only the cautery group was significantly different than the unoperated and scalpel groups. Based on this, the authors concluded that it was unlikely that the destruction of peripheral nerves was the mechanism of analgesia following CO<sub>2</sub> laser surgery.<sup>35</sup> Regardless of the pathophysiology, the analgesic effects of the CO<sub>2</sub> laser remain controversial and further investigation into the mechanism of decreased discomfort is warranted.

The tissue interaction of a given laser depends on the composition of the target tissue. The amount of hemoglobin, proteins, melanin and, most importantly, water are key in the tissue heating process associated with lasers that emit energy in the infrared wavelengths.<sup>25,35-38</sup> The CO<sub>2</sub> laser is ideally suited for use in small animal soft tissue surgery as the wavelength of the light emitted is in the far infrared region and is highly absorbed by water with minimal thermal damage to surrounding tissues.<sup>8,23,25,36,38,39</sup> The precision of a CO<sub>2</sub> laser is attributed to the fact that approximately 98% of the lasers energy is absorbed within 0.01mm of the target tissue.<sup>38</sup> The resultant effects are vaporization of the tissue and apparent sealing of blood vessels and lymphatics.<sup>8,36,37,39,40,41</sup> The clinical effects of which are decreased intra- and post-operative

hemorrhage and post-operative swelling. In this study, it was the impression of the surgeon that, the use of the  $CO_2$  laser resulted in less hemorrhage, especially given the fact that a tourniquet was not used in the laser group. Although it would have been ideal to measure the amount of hemorrhage objectively, we feel that our observations support the claim that  $CO_2$  lasers result in less intra-operative hemorrhage. Similarly, comparison of the laser group to a scalpel group without a tourniquet would have been ideal. However, this was not possible due to concerns for excessive hemorrhage and associated complications.

Other reported advantages of the CO<sub>2</sub> laser onychectomy include the fact that neither a tourniquet nor bandage was required. Complications associated with each of these have been reported and can be significant. Improper tourniquet application can result in neurapraxia of the radial nerve, tissue ischemia and muscle damage and bandages have been associated with tissue necrosis.<sup>21,22,30</sup> Although other studies that have compared laser and scalpel onychectomy used a tourniquet in both groups<sup>8,c</sup> we chose not to use a tourniquet or bandage in the laser group because it was our goal to more accurately emulate the routine clinical procedure. Other complications, such as claw regrowth, chronic draining tracts, persistent lameness and incomplete healing<sup>22,30</sup>, have been reported in the long term but were not addressed in our study. To the authors' knowledge there are no reports evaluating the long term complications associated with laser onychectomy and this is an area that warrants further study.

As with all studies, this one does have some limitations. Although, it would have been ideal to have the same surgeon perform the surgery for both groups of cats, we do not feel that this adversely affects our data. Both surgeons had considerable experience with their respective procedure, thus we feel the difference in groups due to surgical technique would be small if present at all. The inclusion of a control group that was anesthetized, had a tourniquet placed and were bandaged without surgery would have added to the overall results. However, Lapham et al

included such a group and found that, when using behavioral changes, the CO<sub>2</sub> onychectomy group had less negative behavioral changes and smaller percent increases in percent serum and urine cortisol values.<sup>c</sup> Given these findings, the lack of a similar control group does not affect our results. Similarly, some may argue that the use of the tourniquet in the scalpel cats may have contributed to morbidity. However, another study in which a tourniquet was used in both the scalpel and laser group found that, one day post-operatively, the laser group had significantly lower discomfort scores.<sup>8</sup> With these results in mind we would suggest that, although the tourniquet has the potential to result in increased morbidity, with proper application the likelihood is not clinically significant. Several studies that have assessed pain in cats have used combinations of objective and subjective observations.<sup>5-9,16,17,c</sup> In our study we did not compare subjective evaluations for two reasons. First, the observer was not blinded to treatment group and second, subjective variables have been shown to be unreliable. Instead we choose to use subjective variables only as a means of deciding if rescue analgesia was required.

Regardless of the underlying mechanism, cats with an onychectomy performed using the  $CO_2$  laser were less lame and therefore less painful 24 to 48 hours after surgery than those performed with a scalpel.

# Footnotes

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## **CHAPTER 5. GENERAL CONCLUSIONS**

# **General Discussion**

Although cats were permitted to walk across the pressure platform at a comfortable pace in each of these studies, no significant differences in velocity or acceleration were detected between groups on any day. Although collecting gait data from some cats required a bit of encouragement and investigator patience, we were able to collect satisfactory data from every cat. Despite its reported limitations, the pressure platform gait analysis system functions as an acceptable alternative to force platform gait analysis and provides investigators with an objective method for measuring limb function in cats.<sup>1</sup>

The gait analysis system used in each of these studies measured limb function, not strictly limb pain, and it is possible that a cat could have had normal limb function but still be in pain. However, this was not apparent, in that PVF, VI, and the PVF ratio were all less than baseline values at all times after surgery in all cats. It is also possible that factors other than pain (eg, incisional inflammation, early infection, tendonitis, and suture reactivity) could have contributed to the decrease in limb function. However, we are not aware of a better method for evaluating pain in cats 1 to 12 days after limb surgery and believe that our method was at least as good a method of evaluating limb pain as any method that has been described. In addition, ground reaction forces have commonly been used as a measure of limb pain in dogs with osteoarthritis.

#### Introductory gait study:

In the introductory study, we demonstrated that gait analysis could be successfully performed in cats. Pressure platform gait analysis functions as an acceptable alternative to force platform gait analysis and provides investigators with an objective method for measuring limb function in cats. In several recent studies<sup>2-5</sup> on analgesic protocols used for onychectomy, only subjective evaluations were used to assign a pain score. However, if these subjective measurements were combined with an

objective measure of a cat's willingness to use the operated limbs, better estimation of the amount of pain experienced by the cat would be possible.

We also determined that when measured at least 6 months after onychectomy, vertical forces are similar between cats that have and have not had onychectomy. Because we failed to reject the null hypothesis, we need to address the probability of a type II error. However it is important to note that the probability of a statistical error does not change the difference between the means of each group. On evaluation of VI measurements between groups, the difference between the means is quite small and consistent with our finding of no significant difference between groups, so we believe that the difference between means is also not likely to be clinically important.

In the cats in the onychectomy group, onychectomy was performed by either scalpel or laser excision. Although there was an equal distribution in the frequency that either procedure was performed, we made no attempt to discriminate differences between those procedures. In addition, for the purposes of future studies that use this gait analysis method in cats, cats with or without previous onychectomy can be grouped; a successful outcome after previous onychectomy may not need to be considered as an additional variable.

Finally, the distribution of vertical forces at a walk between the fore- and hind limbs in cats is similar to that in dogs. In a recent study, mean PVF for the forelimb of Greyhounds was 58.11% and mean PVF of the hind limb was 42.05% of body weight.<sup>1</sup> Similarly, vertical forces in the forelimbs of our control cats were greater than that in the hind limbs. However, if we consider the mean PVF reported here (forelimb = 56.41%; hind limb = 50.22%) it is apparent that the disparity between fore- and hind limb forces in cats is much less. However, the importance of this species difference is not known.

## Postoperative Analgesia objective:

In the postoperative analgesia objective, our results indicated that IM administration of butorphanol

and transdermal administration of fentanyl provided similar degrees of analgesia, but that topical administration of bupivacaine was less effective. This most likely reflects the duration of action of bupivacaine (ie, 3 to 10 hours<sup>6</sup>) and the fact that it was administered only once (ie, just prior to closure of the digital incisions). We elected to evaluate the analgesic effects of topical bupivacaine administration because it was our opinion that this procedure is used in clinical veterinary practice. Although our results may have been different if bupivacaine had been infiltrated in the area, rather than administered topically, topical and infiltrative administration of local anesthetics have been found to be equally effective in providing analgesia following total ear canal ablation in dogs.<sup>7</sup>

Our findings are supported by a report<sup>6</sup> that the duration of action of bupivacaine is between 3 and 10 hours. In contrast, a previous study<sup>8</sup> suggested that bupivacaine may provide 24 hours of analgesia in dogs. In that study, however, bupivacaine was administered intra-articularly following surgery for rupture of the cranial cruciate ligament, and the intra-articular route of administration may have affected the duration of action or availability of the drug. The shorter apparent duration of action for bupivacaine in the present study may also be attributable, in part, to loss of some of the drug from the incision during suture closure or dilution with blood, either of which could have decreased the effectiveness of the drug.<sup>9</sup> It has also been suggested that injection of bupivacaine may itself cause some mild discomfort<sup>9,10</sup> that could possibly persist for several hours or days. However, the authors are not aware of any information documenting this phenomenon in cats.

In the present study, transdermal administration of fentanyl and IM administration of butorphanol resulted in similar degrees of analgesia, in that results of gait analyses were not significantly different between these groups during the 12 days after surgery. These findings are consistent with the results of previous reports<sup>11,12</sup> on the analgesic efficacy of fentanyl and butorphanol in cats. Although we found these treatment regimens to provide similar degrees of analgesia in this clinical situation, different results could occur in a different clinical situation or

species. Different species have different degrees of skin permeability to fentanyl owing to differences in diffusion and thickness of the stratum corneum.<sup>13</sup> Fentanyl is a highly lipophilic narcotic that selectively diffuses to lipid-rich tissues, such as the stratum corneum of the epidermis.<sup>14</sup> The stratum corneum of haired skin in cats varies from 3 to 20 µm thick, which may suspend diffusion of the drug.<sup>15</sup> Individual cats that are treated with transdermal fentanyl patches had these species differences as well as individual variations in plasma fentanyl concentrations over a 48-hour period. In cats, plasma fentanyl concentration has been reported to range from 0.3 to 7 ng/mL during the 48hours after application of a transdermal fentanyl patch to the lateral aspect of the thorax.<sup>12</sup> When a transdermal fentanyl patch was applied in the dorsal cervical region of a group of cats, plasma fentanyl concentration ranged from 0.50 to 6.38 ng/mL 12 hours after patch application.<sup>13</sup>

Results of the present study indicate that IM administration of butorphanol is a reasonable analgesic regimen for cats undergoing onychectomy. It has been documented previously that cats that receive butorphanol IV have lower subjective lameness scores the day after discharge, compared with cats given a placebo (saline [0.9% NaCl] solution),<sup>16</sup> but perioperative IM administration of butorphanol at doses ranging from 0.05 to 0.4 mg/kg (0.023 to 0.18 mg/lb) has also been associated with adequate analgesia.<sup>17</sup> In the present study, butorphanol was administered before administration of isoflurane was discontinued, which may have contributed to its efficacy.

In previous studies<sup>12,16,18-20</sup> of the effectiveness of various analgesic regimens and surgical techniques, onychectomy was performed bilaterally. However, this may complicate evaluations, as both forelimbs would be expected to be painful following surgery. We suggest that unilateral onychectomy allows for a better evaluation of limb function and degree of pain, as it provides the animal the choice to use the limb on which surgery was performed or to ambulate only with the 3 remaining limbs. Although all cats consistently used the left forelimb by 2 days after surgery, some cats had clinical evidence of non-weight-bearing lameness during gait analyses after surgery. We did

not include an evaluation of patient behavior as an indicator of pain in the present study because the interpretation of cat behavior seems to be wrought with subjectivity. In addition, we did not collect other objective parameters of pain (eg, heart rate and serum cortisol concentration) because we were more concerned with the long-term effects of the procedure (ie, 1 through 12 days after surgery) than with the immediate postoperative effects (ie, the first 24 hours after surgery).

On the basis of results of the present study, topical administration of bupivacaine cannot be recommended as a method for obtaining postoperative analgesia in cats undergoing onychectomy. Limb function, as reflected in PVF and the PVF ratio, was significantly better in cats treated with fentanyl transdermally or butorphanol IM than in cats treated with bupivacaine topically. Although a previous study<sup>21</sup> revealed that ground reaction forces recorded 6 months after surgery in cats that had undergone onychectomy were similar to forces in cats that had not undergone surgery, limb function in cats in the present study was still significantly decreased 12 days after surgery. Thus, providing analgesia for the duration of this period should be strongly considered.

<u>Surgical technique objective:</u> In our study, on Days 1 and 2 after surgery cats in the laser surgery group had significantly higher PVF, VI and PVF ratio when compared cats in the scalpel group. These results would indicate that, in the immediate post-operative period, cats in the laser surgery group were less lame and arguably experiencing less limb pain than cats in the scalpel group. Day 3 post-operatively, there was no significant difference between the groups and on Day 12 no difference was found with respect to PVF and VI, but there was a difference between the groups with respect to PVF ratio.

When the data was evaluated by examining the change in ground reaction forces compared to Day 0, we found similar results. Over the entire study period, the laser group of cats had a mean PVF, VI and PVF ratio that were closer to the Day 0 values than did the scalpel group. However, the difference was only statistically significant for all three parameters on Day 1 and 2 and for PVF ratio on Day 12. Also of interest was the finding that on Day 12 the mean VI for the laser group of cats was greater than the mean value on Day 0. Given that statistical significance was not achieved with respect to the Day 12 change in VI, this is likely due to normal variation. Overall these findings do not support our hypothesis and instead, suggest that when performed with a carbon dioxide laser, onychectomy is less painful than when performed with a scalpel, which is in agreement with previous studies.<sup>22,23</sup>

One study found that although the laser onychectomy may decrease the postoperative stress and level of pain, as determined via serial blood cortisol concentrations, behavioral changes and urine cortisol:creatinine ratio, it may also increase the number of complications in the immediate post-operative period.<sup>c</sup> In another study, subjective assessments and scoring of pain, lameness and swelling were used to compare laser versus scalpel onychectomy. Their conclusion was that although laser onychectomy resulted in less discomfort and complication scores in the immediate post-operative period, the difference did not appear to be clinically important.<sup>22</sup>

Although the results of this and other studies<sup>22,23</sup> demonstrate that an onychectomy performed with a  $CO_2$  laser is less painful than those performed with a scalpel, the mechanism responsible for the difference remains to be elucidated. This phenomenon is not unique to veterinary medicine as the use of  $CO_2$  laser for surgical procedures of the head and neck in humans appears to result in less post-operative pain when compared to procedures with a scalpel or electrocautery.<sup>24</sup> In one study, transection of the tibial branch of the rat sciatic nerve with a  $CO_2$ laser resulted in a significant decrease in the retrograde transport of horseradish peroxidase when compared to a scalpel group.<sup>24</sup> Although these results may support the theory that a decrease in post-operative pain with laser onychectomy is the result of a decreased initiation of action potential at the transected nerve ending<sup>25</sup>, the clinical significance in an onychectomy remains unclear. Similarly, to the authors' knowledge, there are no published reports that demonstrate these changes in the nerve endings of cats. In another study, incisions made in the dorsal surface of a rat tongue with cautery, a scalpel and  $CO_2$  laser in both continuous and pulsed modes were compared immunocytochemically to normal, unoperated tissue. There was no significant difference in the total number of intact nerves adjacent to the incisions and only the cautery group was significantly different than the unoperated and scalpel groups. Based on this, the authors concluded that it was unlikely that the destruction of peripheral nerves was the mechanism of analgesia following  $CO_2$ laser surgery.<sup>26</sup> Regardless of the pathophysiology, the analgesic effects of the  $CO_2$  laser remain controversial and further investigation into the mechanism of decreased discomfort is warranted.

The tissue interaction of a given laser depends on the composition of the target tissue. The amount of hemoglobin, proteins, melanin and, most importantly, water are key in the tissue heating process associated with lasers that emit energy in the infrared wavelengths.<sup>26-30</sup> The CO<sub>2</sub> laser is ideally suited for use in small animal soft tissue surgery as the wavelength of the light emitted is in the far infrared region and is highly absorbed by water with minimal thermal damage to surrounding tissues.<sup>22,27-28,30-32</sup> The precision of a  $CO_2$  laser is attributed to the fact that approximately 98% of the lasers energy is absorbed within 0.01mm of the target tissue.<sup>30</sup> The resultant effects are vaporization of the tissue and apparent sealing of blood vessels and lymphatics.<sup>22,28-29,32,34,35</sup> The clinical effects of which are decreased intra- and post-operative hemorrhage and post-operative swelling. In this study, it was the impression of the surgeon that, the use of the CO<sub>2</sub> laser resulted in less hemorrhage, especially given the fact that a tourniquet was not used in the laser group. Although it would have been ideal to measure the amount of hemorrhage objectively, we feel that our observations support the claim that  $CO_2$  lasers result in less intra-operative hemorrhage. Similarly, comparison of the laser group to a scalpel group without a tourniquet would have been ideal. However, this was not possible due to concerns for excessive hemorrhage and associated complications.

Other reported advantages of the CO<sub>2</sub> laser onychectomy include the fact that neither a tourniquet nor bandage was required. Complications associated with each of these have been reported and can be significant. Improper tourniquet application can result in neurapraxia of the radial nerve, tissue ischemia and muscle damage and bandages have been associated with tissue necrosis.<sup>35-37</sup> Although other studies that have compared laser and scalpel onychectomy used a tourniquet in both groups<sup>22,23</sup> we chose not to use a tourniquet or bandage in the laser group because it was our goal to more accurately emulate the routine clinical procedure. Other complications, such as claw regrowth, chronic draining tracts, persistent lameness and incomplete healing<sup>36-37</sup>, have been reported in the long term but were not addressed in our study. To the authors' knowledge there are no reports evaluating the long term complications associated with laser onychectomy and this is an area that warrants further study.

As with all studies, this one does have some limitations. Although, it would have been ideal to have the same surgeon perform the surgery for both groups of cats, we do not feel that this adversely affects our data. Both surgeons had considerable experience with their respective procedure, thus we feel the difference in groups due to surgical technique would be small if present at all. The inclusion of a control group that was anesthetized, had a tourniquet placed and were bandaged without surgery would have added to the overall results. However, Lapham et al included such a group and found that, when using behavioral changes, the CO<sub>2</sub> onychectomy group had less negative behavioral changes and smaller percent increases in percent serum and urine cortisol values.<sup>23</sup> Given these findings, the lack of a similar control group does not affect our results. Similarly, some may argue that the use of the tourniquet in the scalpel cats may have contributed to morbidity. However, another study in which a tourniquet was used in both the scalpel and laser group found that, one day post-operatively, the laser group had significantly lower discomfort scores.<sup>22</sup> With these results in mind we would suggest that, although the tourniquet has

the potential to result in increased morbidity, with proper application the likelihood is not clinically significant. Several studies that have assessed pain in cats have used combinations of objective and subjective observations.<sup>22,38-44</sup> In our study we did not compare subjective evaluations for two reasons. First, the observer was not blinded to treatment group and second, subjective variables have been shown to be unreliable. Instead we choose to use subjective variables only as a means of deciding if rescue analgesia was required.

Regardless of the underlying mechanism, cats with an onychectomy performed using the  $CO_2$  laser were less lame and therefore less painful 24 to 48 hours after surgery than those performed with a scalpel.

# **Recommendations for Future Research**

With respect to the results obtained by these three studies, we can provide several recommendations as to the direction of future research. For additional research projects that employ this gait analysis method in cats, we suggest that cats with or without previous onychectomy can be grouped; a successful outcome after previous onychectomy may not need to be considered as an additional variable.

In light of the results obtained on evaluation of postoperative analgesics following feline onychectomy, the fentanyl patch represents a target for further research. Following patch removal in dogs, plasma fentanyl concentration rapidly decreases, with a reported half-life of 1.39 hours<sup>1,45</sup>; however, plasma concentration in cats decreases at a much slower rate after patch removal.<sup>13</sup> One possible explanation for the greater half-life of fentanyl in cats is the presence of a cutaneous depot of fentanyl beneath the patch; this phenomenon has been observed in humans.<sup>13</sup> Information on the plasma concentration of fentanyl associated with effective analgesia in cats with superficial or orthopedic pain would be of value in defining the most effective analgesic protocol following onychectomy. Specifically, defining how plasma concentration of fentanyl correlates with effective analgesia is imperative for appropriate usage and dosing of this drug in veterinary medicine.

In addition, our results also suggest that instillation of bupivacaine into onychectomy incisions is not recommended. Currently, it is not known whether bupivacaine administered into surgical incisions initiates any histopathologic changes within the tissues, contributing to discomfort following instillation into surgical inscisions, Furthermore, another avenue for research would encompass how various routes of administration of bupivacaine compare in the feline onychectomy setting.

On evaluation of surgical techniques for feline onychectomy, our results indicated that onychectomy with a  $CO_2$  laser contributes to statistically significant improvement of limb function as compared to onychectomy performed by scalpel excision. However, the mechanism behind the improved limb function, and possibly less postoperative pain, still remains to be elucidated. Specifically, we recommend further evaluation of histopathologic investigation of the nerve endings in cats as well as other species, and to repeat existing studies on peripheral nerve endings surrounding incisions made by various surgical instruments. In addition, improvement in understanding of the mechanism of decreased discomfort associated with laser surgery is warranted for improved understanding of this surgical tool.

Our study was limited to evaluation of scalpel and CO<sub>2</sub> onychectomy in cats using limb function as an objective measure of pain. We recommend that further studies be conducted using pressure platforms to objectively compare limb function between other surgical techniques for onychectomy or alternative procedures (guillotine, electrocautery; tenectomy) as well as for comparison for other orthopedic procedures. As our study design only encompassed a 12 day window into the postoperative period, evaluation of the long term effects (1 month, 3 months, 6 months.) following laser onychectomy on ground reaction forces in cats is warranted.

In order to completely establish the optimum technique for feline onychectomy, evaluation of wound closure methods is also a target for further research. Specifically evaluation of wound closure via suture or skin glue types, and histopathologic evaluation of feline skin reaction may be beneficial as an objective measurement for comparison.

Ultimately, these suggestions for future research could potentially shape the procedure of feline onychectomy to decrease postoperative pain, improve postoperative limb function, reduce the rate of complications, and improve recovery time for our veterinary patients.

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