Clinical assessment of repeated propofol-associated anesthesia in cats

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Objective—To assess the effects of repeated episodes of propofol-associated anesthesia on quality of recovery from anesthesia, clinical status, and erythrocyte physiology in cats.

Design—Original study.

Animals—37 cats undergoing short-duration anesthesia for radiotherapy.

Procedures—Twice daily on 5 consecutive days, 13 cats with squamous cell carcinoma of the nasal planum (group 1) underwent anesthesia: first via administration of propofol or a midazolam combination and then via administration of ketamine and midazolam each day (latter data were not analyzed). During a 19-day period, 24 cats with vaccine-associated sarcoma (group 2) were anesthetized 12 times with propofol or a midazolam-propofol combination. Anesthesia was maintained with propofol in both groups. Hematologic analysis was performed before, during, and on completion of radiotherapy; changes in Hct and hemoglobin concentration between groups were compared.

Results—Mean duration of anesthesia was 8.1 minutes (range, 5 to 20 minutes); no adverse events were detected during recovery. Total dose of propofol administered did not differ between groups 1 (6.34 mg/kg [2.88 mg/lb]) and 2 (4.71 mg/kg [2.14 mg/lb]). Midazolam administration decreased the propofol dose by 26%. Overall decreases from baseline in Hct and hemoglobin concentration were not significantly different between the 2 groups, nor clinically important; however, compared with baseline, values in group 2 were significantly lower after 6 and 12 anesthetic episodes for both protocols. Heinz bodies were identified in low numbers in both groups during radiotherapy.

Conclusions and Clinical Relevance—Results indicated that repeated propofol-associated short-duration anesthesia does not lead to clinically relevant hematologic changes in cats undergoing short-duration radiotherapy. (J Am Vet Med Assoc 2007;231:1347–1353)

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Propofol (2,6 di-isopropyl-phenol) is an anesthetic drug that is commercially available as an emulsion for IV administration and has properties that make it attractive for use in animals that require medical or minor surgical procedures on consecutive days. For many species, propofol is associated with smooth and rapid onset of action that facilitates easy titration to the desired anesthetic plane, short duration of activity, lack of systemic accumulation, and rapid recovery without unwanted excitatory effects even following prolonged continuous infusion or repeated bolus administration.1 In felids, the safety of prolonged continuous infusion of propofol for maintenance of anesthesia and of repetitive administration of propofol is of current concern.2,3 Andress et al2 reported adverse effects on the quality of recovery from anesthesia, clinical status, and erythrocyte physiology when propofol was administered on consecutive days to induce anesthesia in domestic cats. The possibility of prolonged recovery from propofol-associated anesthesia in this species has also been reported.3 In contrast, no adverse clinical or hematologic effects were detected in cats that received propofol as a single induction dose on 3 consecutive days.4

Compared with other species, hemoglobin in cats has higher concentrations of oxidizable sulphydryl groups; thus, feline RBCs are particularly susceptible to oxidative injury.5,6 This oxidative damage is manifested most commonly as Heinz body formation and less commonly as methemoglobinemia.7 In cats, increased formation of Heinz bodies in erythrocytes, accompanied by clinical illness, has been attributed to phenolic oxidative injury induced by propofol administered on consecutive days.2

Hematologic and physiologic effects of repetitive propofol administration have been investigated2,5-7 in an experimental setting in healthy cats but not, to the authors’ knowledge, in a clinical setting. Cats with neoplastic disease require repeated anesthetic episodes (frequently on consecutive days) for radiation therapy of short duration; a total IV anesthetic protocol incorporating propofol remains a convenient option for management of these cats. The use of propofol in such a setting would clearly be precluded by evidence of

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ABBREVIATION

CRP Corrected reticulocyte percentage

From the Sections of Diagnostic Imaging and Radiation Oncology, Vetsuisse Faculty (Rohrer Bley, Russ-Melzer, Buchholz, Poirier, Kaser-Hotz) and Biostatistics, ISPM (Roos), University of Zurich, CH-8006 Zurich, Switzerland; and the Section of Anesthesiology, Department of Clinical Studies, Saint George’s University Veterinary School, Grenada, West Indies (Price).

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adverse clinical or hematologic effects or by recovery from anesthesia that was prolonged or associated with complications. The purpose of the study reported here was to assess the effects of repeated episodes of propofol-associated anesthesia (performed according to a protocol that allowed short-duration radiotherapy to be completed) on quality of recovery from anesthesia, clinical status, and erythrocyte physiology in cats. The intent was to gain information to guide development of appropriate anesthetic protocols for other minor medical and surgical procedures in this species.

Materials and Methods

Cats—Thirty-seven client-owned cats (18 neutered females, 17 neutered males, and 2 sexually intact males) of various breeds admitted to the Section of Diagnostic Imaging and Radiation Oncology, Vetsuisse Faculty, University of Zurich, Switzerland for radiotherapy of squamous cell carcinoma of the nasal planum (13 cats [group 1]) or vaccine-associated sarcoma (24 cats [group 2]) were included in this study. In 18 of the 24 cats in group 2, radiotherapy was instituted within 30 days of surgical excision of the primary tumor. Because propofol is licensed for induction and maintenance of anesthesia in cats at the doses used in the study and is routinely used at licensed doses in the university clinic, ethical approval of the study was not required at our institution. Clinical practice at the university includes assessment of hematologic values (particularly Hct and hemoglobin concentration) in cats during repeated anesthesias for radiotherapy or other radiation protocols, and informed consent specifically for these assessments was not obtained from owners. No additional blood samples were collected for preparation of blood smears.

Thoracic radiography, computed tomography, and palpation of regional lymph nodes or cytologic examination of lymph node samples were performed when considered necessary to achieve complete tumor staging (data not analyzed). Before radiation therapy began, a jugular venous blood sample was collected from each cat for hematologic (CBC and blood smear examination) and serum biochemical analyses. For monitoring purposes, baseline measurements of heart rate, respiratory rate, and mucous membrane color and hydration were made prior to each treatment. A 20-gauge catheter was placed in a cephalic vein and changed at least twice weekly. Food was withheld from the cats for at least 6 hours before anesthesia, and access to water was not allowed for 30 minutes before induction of anesthesia.

In group 1, cats were anesthetized twice daily on 5 consecutive days. For the first period of radiation treatment (administered in the morning) on any given day, anesthesia was induced by use of either propofol (administered IV) as the sole induction agent or by use of midazolam (0.2 mg/kg [0.09 mg/lb], IV) followed by administration of propofol to effect. Each cat was randomly assigned to 1 particular anesthetic protocol and thus received either propofol alone (n = 6) or midazolam-propofol combination (7) on each of 5 consecutive days. For either protocol, IV bolus administration of propofol was used to maintain the desired plane of anesthesia. For the second period of radiation treatment (administered in the afternoon) on any given day, anesthesia was induced by use of midazolam (0.2 mg/kg, IV) followed by ketamine (6 to 8 mg/kg [2.7 to 3.6 mg/lb], IV) and maintained with bolus IV injections of ketamine (1 to 2 mg/kg, to effect). The mean induction dose of ketamine was 8.2 mg/kg (3.7 mg/lb; range, 6.0 to 10.6 mg/kg [2.7 to 4.8 mg/lb]). Data from the second anesthetic episode each day were not used in the study.

In treatment group 2, cats were anesthetized once daily on 4 days of each week (Monday, Tuesday, Thursday, and Friday) during a 19-day period (12 anesthetic episodes/cat). These cats were randomly assigned to receive either propofol administered IV as the sole anesthetic agent (n = 13) or midazolam (0.2 mg/kg) administered IV followed by administration of propofol to effect (11). For either protocol, IV bolus administration of propofol was used to maintain the desired plane of anesthesia. In both groups 1 and 2, each cat was assigned to 1 particular propofol protocol and received either propofol alone or midazolam-propofol combination for all anesthetic episodes.

Propofol was administered as repeated boluses to effect to maintain a plane of anesthesia sufficient to allow radiotherapy to be performed by use of a linear accelerator with applicable electron beams. The target plane of light to moderate anesthesia was evaluated and maintained according to criteria similar to those described by Matthews et al (ie, no movement, palpebral reflexes present or barely absent, and corneal reflex present). The cats were not intubated and breathed spontaneously during the procedure. Supplementary oxygen was administered via a face mask with a flow rate of 2 L/min. During anesthesia, heart rate was measured via auscultation; respiratory rate was assessed via observation of thoracic excursions, and oxyhemoglobin saturation was monitored by use of a pulse oximeter with a probe attached to a peripheral site (tongue or a toe). These variables were assessed for monitoring purposes only.

The total volume of propofol administered and the duration of anesthesia (from induction until the end of radiotherapy) were recorded. Recovery from anesthesia (ie, time from cessation of propofol administration to complete recovery from anesthesia) was evaluated subjectively for each cat after each anesthetic episode.

Collection of hematologic data—Baseline jugular venous blood samples were collected prior to radiotherapy (time [T] 0). Midtherapy (T1) samples were collected after the third morning anesthetic episode involving propofol in group 1 (day 3) or after the sixth anesthetic episode in group 2 (day 9). Samples were collected at the end of radiotherapy (T2), which occurred on day 5 (after the fifth morning anesthetic episode involving propofol) for group 1 and on day 19 (after the 12th anesthetic episode) for group 2. When possible, another blood sample was collected at a clinical examination performed 3 weeks after radiation treatment (T3); this occurred a median of 30 days after T0 for group 1 and 40.5 days after T0 for group 2. Hematologic data were collected from all cats prior to and during treatment, in 35 of the 37 cats at the end of radiotherapy, and in 13 of the 37 cats at an examination 3 weeks after radiation treatment. The undesired loss of hematologic data was a result of incomplete written orders to the laboratory.
For each blood sample, Hct, hemoglobin concentration, WBC count, mean corpuscular volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration were determined by use of an automated analyzer. Heinz bodies were identified via examination of blood smears stained with supravital new methylene blue, and the total number of Heinz bodies in each smear was classified as none, few, intermediate, or many. The blood smears were assessed by laboratory technicians who were unaware of the group allocation or anesthesia protocol of each cat. A reticulocyte count (calculated as percentage of reticulocytes per 1,000 RBCs) was performed on the same blood smears. To correct for coexistent anemia, the CRP was determined to estimate the reticulocyte percentage if the cat were not anemic. The CRP was calculated according to an equation as follows:

\[
\text{CRP} = \left(\frac{\text{cat's Hct}}{\text{mean Hct for species}}\right)^7
\]

The mean Hct for the species was 36%. Wintrobe's erythrocyte indices (mean corpuscular volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration) were used to characterize erythrocytes in peripheral blood and detect regenerative anemia when a reticulocyte count was unavailable.

### Statistical analysis

Data are presented as mean ± SD unless otherwise specified. A 2-sample t test was applied to compare propofol doses and durations of anesthesia among the anesthesia groups. Baseline variables (T0 data) were described. Data were plotted graphically, and the Kolmogorov-Smirnov test was applied. No signs of violation of the approximate normality assumption (\(P > 0.4\)) were found.

### Differences between the relevant baseline T0 value and Hct at T1, hemoglobin concentration at T1, Hct at T2, and hemoglobin concentration at T2 were computed, and a 1-sample t test was used to describe the decreases in the hematologic variables. The analysis was applied to the differences at T1 and T2 for each of the groups separately. A 2-sample t test was applied to assess differences in the Hct and hemoglobin concentration changes between groups 1 and 2; at the various time points, only \(P < 0.025\) were considered to be significant (according to Bonferroni correction). Statistical analyses were performed by use of computer software; for all remaining analyses, a value of \(P < 0.05\) considered significant unless otherwise specified.

### Results

**Cats**—At the time of diagnosis, mean weight of the cats was 4.9 kg (10.78 lb; range, 3.5 to 7.9 kg [7.7 to 17.38 lb]); mean age was 9.5 years (range, 3.0 to 15.0 years). None of the cats had clinical evidence of metastasis, and none had notable systemic disease other than the diagnosed neoplasia.

**Anesthesia protocols**—For groups 1 and 2, the total dose of propofol or midazolam-propofol combination administered for induction and maintenance of anesthesia and mean duration of anesthesia (8.1 minutes; range, 5 to 20 minutes) did not differ significantly (Table 1). Nineteen cats (6 in group 1 and 13 in group 2) were anesthetized with propofol alone; 18 cats (7 in group 1 and 11 in group 2) were anesthetized with the midazolam-propofol combination. Among cats that received propofol as the sole anesthetic agent in both groups, the mean dose of propofol per time administered during an anesthetic episode was 0.80 ± 0.18 mg/kg/min (0.36 ± 0.08 mg/lb/min) and the mean total volume was 6.34 ± 1.19 mg/kg (2.88 ± 0.54 mg/lb). Among cats that received the midazolam-propofol combination for induction of anesthesia, the mean dose of propofol administered during the procedure was significantly less with 0.61 ± 0.17 mg/kg/min (0.28 ± 0.08 mg/lb/min; \(P = 0.003\)) and the mean total volume of propofol administered was 4.71 ± 1.0 mg/kg (2.14 ± 0.45 mg/lb; \(P = 0.001\)). The mean dose of midazolam administered during induction was 0.2 mg/kg (range, 0.17 to 0.25 mg/kg [0.08 to 0.11 mg/lb]). In both radiation treatment groups, administration of midazolam before propofol decreased the total volume of propofol required to induce and maintain anesthesia by 26%.

**Recovery from anesthesia**—Although the interval between discontinuation of propofol final administration and recovery and maintenance of sternal recumbency was not measured, there appeared to be no marked increase in the time taken to achieve full recovery associated with repeated anesthetic episodes. There was interindividual variation in the time taken to achieve full recovery, but individual cats typically had the same pattern of behaviour during recovery with repeated anesthetic episodes. All cats stretched intermittently during the recovery period, and a few cats sneezed and breathed deeply throughout the recovery phase. One cat in group 1 vocalized during the recovery period.

### Table 1—Mean ± SD total dose of propofol and duration of anesthesia in 13 cats with squamous cell carcinoma of the nasal planum (group 1) and 24 cats with vaccine-associated sarcoma (group 2) that underwent repeated anesthetic episodes induced with propofol alone or a midazolam-propofol combination and maintained with propofol for radiation treatments.

<table>
<thead>
<tr>
<th>Group</th>
<th>Anesthetic protocol*</th>
<th>Total dose of propofol (mg/kg)</th>
<th>Duration of anesthesia (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Propofol (n = 6)</td>
<td>6.38 ± 1.42</td>
<td>8.1 ± 1.57</td>
</tr>
<tr>
<td></td>
<td>Midazolam-propofol</td>
<td>5.08 ± 1.57</td>
<td>8.2 ± 1.35</td>
</tr>
<tr>
<td></td>
<td>(n = 7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Propofol (n = 13)</td>
<td>6.32 ± 1.40</td>
<td>8.03 ± 1.22</td>
</tr>
<tr>
<td></td>
<td>Midazolam-propofol</td>
<td>4.46 ± 0.70</td>
<td>8.36 ± 1.06</td>
</tr>
<tr>
<td></td>
<td>(n = 11)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*In group 1, cats were anesthetized twice daily on 5 consecutive days. For the first period of radiation treatment (administered in the morning) on any given day, anesthesia was induced and maintained by use of either propofol (administered IV) as the sole induction agent or midazolam (0.2 mg/kg, IV) followed by administration of propofol to effect. For the second period of radiation treatment (administered in the afternoon) on any given day, anesthesia was induced by use of midazolam (0.2 mg/kg, IV) followed by ketamine (6 to 8 mg/kg, IV) and maintained with bolus IV injections of ketamine (1 to 2 mg/kg, to effect). These data were not analyzed. In group 2, cats were anesthetized once daily on 4 days of each week (Monday, Tuesday, Thursday, and Friday) for 3 weeks (12 anesthetic episodes/cat during a 19-day period). These cats were randomly assigned to receive either propofol administered IV as the sole anesthetic agent or midazolam (0.2 mg/kg) administered IV followed by administration of propofol to effect. In both groups, propofol was administered as repeated boluses to effect to maintain a plane of anesthesia sufficient to allow radiotherapy to be performed; each cat was assigned to 1 particular protocol and received either propofol alone or midazolam-propofol combination for all anesthetic episodes. To convert kilograms to pounds, multiply by 2.2.
rubbed their faces transiently. No cat included in the study was anorexic or developed signs of malaise at any time following anesthesia; thus, the full complement of repeated anesthetic episodes was performed in all cats.

Hematologic data—Before radiotherapy, mean Hct and hemoglobin concentrations in both radiation treatment groups were within laboratory reference limits (reference range for Hct, 33% to 45%; reference range for hemoglobin concentration, 11.3 to 15.5 g/dL; Table 2). The baseline hemoglobin concentrations of cats in both groups that were subsequently anesthetized with the midazolam-propofol combination was significantly (P = 0.014) lower than the values of cats that were subsequently anesthetized with propofol alone, although there was no significant difference in baseline Hct between the 2 protocols. No differences in Hct and hemoglobin concentration were detected between groups 1 and 2 at any time point, indicating that previous excision of the primary tumor (group 2) did not have an effect on these hematologic variables.

Before treatment, 1 of the 37 cats was anemic (Hct = 26%). On the basis of a low reticulocyte count, anemia in this cat was defined as nonregenerative. This cat had nasal squamous cell carcinoma, and hemorrhage may have occurred prior to the start of radiation treatment. At the midpoint of therapy (T1), CRP was measured in 17 cats (mean, 0.18%; range, 0% to 0.69%) and values were within reference range (0% to 1.0%) in all cats. At the end of radiotherapy (T2), CRP was measured in 13 cats (mean, 0.13%; range, 0% to 0.43%) and values were within reference range in all cats.

Comparison of hematologic variables before (T0) and during (T1) radiotherapy—Compared with the mean baseline value, Hct decreased by 7.17 ± 10.94% at T1 in group 1 cats anesthetized with propofol only (Table 2). In group 1 cats receiving the midazolam-propofol combination, the mean difference in Hct values at T1 and T0 was lower than the baseline T0 value by 2.29 ± 6.08%. However, these differences between the anesthesia protocols for group 1 were not significant (P = 0.33). Also in group 1, the decreases in hemoglobin concentration at T1, compared with the value at T0, in the cats anesthetized with propofol only and those anesthetized with the midazolam-propofol combination did not differ significantly (P = 0.17).

After 6 anesthetic episodes during a 9-day period (T1), mean Hct had decreased significantly from baseline by 8.85 ± 6.94% (P = 0.001) in group 2 cats that received propofol only and by 5.18 ± 6.12% (P = 0.02) in group 2 cats that received the midazolam-propofol combination. However, these decreases were not significantly (P = 0.17) different between the 2 anesthetic protocols. Compared with baseline values, mean hemoglobin concentration at T1 was significantly lower in group 2 cats anesthetized with propofol only (value decreased by 2.73 ± 2.18 g/dL; P < 0.001) and those anesthetized with the midazolam-propofol combination (value decreased by 1.48 ± 1.74 g/dL; P = 0.018). These decreases were not significantly (P = 0.15) different between the 2 anesthetic protocols.

Comparison of hematologic variables before (T0) and at the end (T2) of radiotherapy—Compared with baseline values, neither anesthetic protocol resulted in significant changes in mean Hct and hemoglobin concentration at T2 (Table 2). After 12 anesthetic episodes during a 19-day period (T2), mean Hct had decreased significantly from baseline by 9.0 ± 6.18% (P < 0.001) in group 2 cats that received propofol only and by 6.55 ± 7.02% (P = 0.01) in group 2 cats that received the midazolam-propofol combination. Compared with baseline values, mean hemoglobin concentration at T2 was significantly lower in group 2 cats anesthetized with propofol only (value decreased by 2.78 ± 2.01 g/dL; P = 0.001) and those anesthetized with the midazolam-propofol combination (value decreased by 1.9 ± 2.33 g/dL; P = 0.02). The decreases in Hct and hemoglobin concentration were not significantly (P = 0.35 and P = 0.40, respectively) different between the 2 anesthetic protocols.

Table 2—Mean ± SD values of Hct, hemoglobin (Hb) concentration, and CRP determined at various time points in 13 cats with squamous cell carcinoma of the nasal planum (group 1) and 24 cats with vaccine-associated sarcoma (group 2) that underwent repeated anesthetic episodes induced with propofol alone or a midazolam-propofol combination and maintained with propofol for radiation treatments. Assessments were performed before (T0), during (midpoint; T1), and at the end (T2) of radiotherapy, as well as at 3 weeks after completion of radiotherapy (T3). Values in parentheses represent the number of cats.

<table>
<thead>
<tr>
<th>Group</th>
<th>Anesthetic protocol*</th>
<th>Hct (%)</th>
<th>Hb concentration (g/dL)</th>
<th>CRP (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>T0</td>
<td>T1</td>
<td>T2</td>
</tr>
<tr>
<td>1</td>
<td>Propofol (n = 6)</td>
<td>34.7 ± 8.8 (6)</td>
<td>27.5 ± 3.3 (6)</td>
<td>31.2 ± 4.2 (6)</td>
</tr>
<tr>
<td></td>
<td>Midazolam-propofol (n = 7)</td>
<td>33.4 ± 4.4 (7)</td>
<td>31.1 ± 3.6 (7)</td>
<td>31.7 ± 4.3 (7)</td>
</tr>
<tr>
<td>2</td>
<td>Propofol (n = 13)</td>
<td>37.5 ± 4.9 (13)</td>
<td>28.7 ± 4.1 (13)</td>
<td>28.5 ± 2.9 (13)</td>
</tr>
<tr>
<td></td>
<td>Midazolam-propofol (n = 11)</td>
<td>3.3 ± 4.4 (11)</td>
<td>28.1 ± 5.6 (11)</td>
<td>26.7 ± 5.4 (11)</td>
</tr>
</tbody>
</table>

T0 = Before radiotherapy in both groups 1 and 2; T1 = After 3 morning anesthetic episodes involving propofol (3 days) in group 1 and after 6 anesthetic episodes (9 days) in group 2; T2 = After 5 morning anesthetic episodes involving propofol (5 days) in group 1 and after 12 anesthetic episodes (19 days) in group 2; T3 = Median of 30 days after T0 in group 1 and 40.5 days after T0 in group 2. Reference range for Hct, 33% to 45%. Reference range for Hb, 11.3 to 15.5 g/dL. CRP = Reticulocyte percentage × (cat’s Hct/mean Hct for species); reference range, 0% to 1.0%.

See Table 1 for remainder of key.
Heinz body count—Because markedly low or absent reticulocyte counts were detected and Heinz bodies in routine blood smears were not evident prior to radiation treatment, a Heinz body count was not available at T0. The presence of Heinz bodies was evaluated in blood smears from 17 cats at T1 and 18 cats at T2. At T1 and T2, Heinz bodies were detected in some cats in each anesthetic protocol subgroup in groups 1 and 2 (Table 3). When present, the extent of Heinz body formation was classified as mild to moderate at T1 and as mild to severe at T2.

Discussion

There are many potential anesthetic options for repeated procedure-associated anesthesia of domestic cats, including protocols that are based on induction and maintenance of anesthesia with agents administered via inhalation or IV (eg, propofol, ketamine, thiopentone, etomidate, and alphaxalone). Although propofol has properties that make it attractive as an agent for repeated short-duration anesthesia for procedures such as radiotherapy, we were concerned about previously reported adverse effects associated with repeated administration of high doses of propofol in cats.2-4 Because of the potential for adverse effects, a decision was made that the cats in group 1 requiring anesthesia twice daily for 5 consecutive days would undergo 1 anesthetic episode involving propofol (alone or in combination with midazolam) and 1 anesthetic episode with midazolam and ketamine each day. The adverse behavioral effects commonly observed during recovery from short-duration midazolam-ketamine anesthesia were considered to be less disadvantageous than the potential adverse effects of progressively more delayed recoveries and development of clinical illness that have been previously reported2 following repetitive anesthesia involving high doses of propofol.

Midazolam-ketamine combinations are commonly used for repeated anesthetic episodes in pediatric human patients and in laboratory animals.8-11 Although midazolam and ketamine is a well-characterized and popular combination for induction and short-term anesthesia in cats,12-13 undesirable behavioral effects during recovery including sedation, excitement, restlessness, vocalization, and difficulty in handling must be expected.14-15 The pharmacokinetic profile and clinical effects of repeated ketamine anesthesia in cats have not been determined; thus, in group 1 cats of the present study, we must recognize that the hematologic changes detected may have been at least partly attributable to repeated daily ketamine administration.

The total dose of propofol used in the cats of the present study to induce and maintain an anesthetic plane adequate for completion of radiotherapy was slightly lower than doses used in previous studies,2-4 in which propofol was also administered without preanesthetic medication. This finding is mostly attributable to the fact that, compared with those other investigations, the procedure used in the present study was of shorter duration. Prior administration of midazolam, however, resulted in a 26% reduction in the total dose of propofol required for completion of radiotherapy. Although detrimental effects of midazolam in cats have been reported,18 they were not evident in our study.

Pascoe et al2 used propofol doses of 7.4 to 7.8 mg/kg (3.36 to 3.55 mg/lb) for induction of anesthesia in cats, similar to doses reported in earlier studies2-4 involving cats that were not premedicated. In 1 study in healthy cats,2 6 mg of propofol/kg was administered IV followed by an infusion of 0.2 to 0.3 mg of propofol/kg/min (0.09 to 0.14 mg/lb/min) for 30 minutes, providing a total dose of 15 mg of propofol/kg (6.8 mg/lb) for each 30-minute period of anesthesia. In another study involving 10 cats,4 a single bolus dose of 10 mg of propofol/kg was administered IV during a 70-second period and provided 6 to 8 minutes of anesthesia before first movements occurred.

The reason for the reduced dose requirements of cats for propofol when it was administered alone in the present study is unclear. The end point of light anesthesia is fairly subjective and could account for this difference in dose. Induction and maintenance doses of propofol were sufficient to allow short-duration radiotherapy to be completed in cats that remained lightly anesthetized and breathed spontaneously throughout the procedure without development of postinduction apnea. Because the cats were closely monitored during radiotherapy, supplementary oxygen was administered to each cat via a face mask, and oxyhemoglobin saturation was maintained > 95% for the duration of all anesthetic procedures in all animals, endotracheal intubation was not considered necessary. However, propofol administration used in our study involved an induction dose followed by IV boluses as needed and should not be used as a guideline for constant-rate infusions.

Clearly, in theory, the reduction in propofol requirements among domestic cats following prior administration of midazolam can be advantageous in this species, especially with the reduced risk of adverse effects associated with multiple injections of propofol, which is often associated with increased frequency of postoperative complications.

Table 3—Distribution of Heinz body formation (number of cats) in blood smears from cats that underwent repeated anesthetic episodes induced with propofol alone or a midazolam-propofol combination and maintained with propofol for series of radiation treatments determined at the midpoint (T1; n = 17) and end (T2; 18) of radiotherapy.

<table>
<thead>
<tr>
<th>Group</th>
<th>Anesthetic protocol*</th>
<th>No. of cats</th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>No. of cats</th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
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<td>1</td>
<td>Propofol</td>
<td>3</td>
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<td>0</td>
<td>0</td>
<td>6</td>
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<td>4</td>
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<tr>
<td></td>
<td>Midazolam-propofol</td>
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<td>5</td>
<td>2</td>
<td>2</td>
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</tr>
<tr>
<td>2</td>
<td>Propofol</td>
<td>6</td>
<td>0</td>
<td>6</td>
<td>0</td>
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<td>5</td>
<td>0</td>
<td>1</td>
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</tr>
<tr>
<td></td>
<td>Midazolam-propofol</td>
<td>6</td>
<td>1</td>
<td>3</td>
<td>2</td>
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<td>2</td>
<td>0</td>
<td>1</td>
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<td>0</td>
</tr>
</tbody>
</table>

*See Table 1 for key.
in which impaired metabolism of propofol and concerns about subsequent inhibition of cytochrome P450 enzyme function are of concern. However, potential interactions at the metabolic level among the cats in the present study can not be ruled out. Further reduction in propofol dose requirements and subsequent decreased risk of adverse effects following repeated propofol anesthetic episodes could be achieved by administration of preanesthetic medication selected from the wide range of sedative drugs that have been characterized in cats, including acepromazine and opioids.17,18

Among the cats in the present study, the interval between final administration of propofol and attainment of sternal recumbency was not recorded, but interindividual variation in the time taken to achieve full recovery was evident. The uneventful recoveries from anesthesia and absence of adverse effects in the study cats contrast with findings of another investigation2 of repeated daily propofol anesthesia in 6 cats; 5 of those 6 cats were withdrawn from that study because of development of generalized malaise, anorexia, and diarrhea. Similarly, no adverse effects were detected in cats anesthetized by use of a single bolus of 10 mg of propofol/kg daily for 3 days.4 The absence of adverse clinical effects of repeated daily propofol anesthesia in the cats of the present study may be attributed principally to the markedly lower total dose of propofol administered.

Although all cats in the present study had neoplastic disease and 18 of 24 cats in group 2 had undergone surgery within 30 days before commencement of radiotherapy, no concurrent disease was evident in any cat, with the exception of 1 cat with anemia. Although the prevalence of infectious diseases among cats in Switzerland is low, FeLV or FIV seronegativity was not confirmed in the cat with anemia; infection with either virus was not excluded as a differential diagnosis and neither was anemia of chronic disease.

Hematocrit values at the midpoint of radiotherapy (T1) were lower than baseline values in each anesthetic protocol subgroup in groups 1 and 2, but the differences were not significant, reflecting wide interindividual variation. The values did not decrease further between the midpoint and end of radiotherapy. Although the decreases in Hct were not cumulative over days and were not associated with a critical degree of anemia in any individual cat, the Hct values (and, in association, hemoglobin concentrations) at the end of radiotherapy were decreased relative to baseline values in all 4 anesthetic protocol subgroups. There was considerable interindividual variation in the change in Hct associated with repeated propofol anesthesia; it is possible that the magnitude and direction of the change would have become significant if a larger number of cats had been included in the study. A power analysis for the 1-sided unpaired and 2 sample t tests (for T1 minus T0 hemato- locyte values) with α of 5% and power of 80% revealed that inclusion of 7 cats receiving the midazolam-propofol combination and 12 cats receiving propofol alone in group 1 would have been needed to detect a difference of 10% in Hct changes between the 2 groups.

Although no significant changes in RBC variables relative to baseline values were detected in 6 healthy cats that received repeated daily administrations of propofol for as many as 7 days, Hct and total protein has been reported3 to decrease during propofol infusion in dogs and cats, possibly as a result of propofol-induced splenic sequestration of erythrocytes or changes in peripheral circulation. The apparent decrease in Hct during the initial phase of repeated daily propofol anesthesia detected in the cats of the present study warrants further investigation.

Among the cats from both anesthetic groups 1 and 2 in which RBC Heinz body counts were evaluated, most had a mild to moderate Heinz body count in the examined blood smears at the midpoint and end of radiotherapy, regardless of anesthetic protocol. In healthy cats, a significant daily increase in the percentage of Heinz bodies following the third day of propofol anesthesia was detected in parallel with development of clinical illness.2 In another study,4 there was an unspecified increase in Heinz body formation in 6 of 10 cats that were administered 10 mg of propofol/kg (4.5 mg/lb) on each of 3 consecutive days, but the significance of that change was not analyzed.

The relationship between propofol administration, Heinz body formation, and clinical disease in cats remains unproven. The incidence of Heinz bodies in clinically normal cats ranges from 0% to 96%19; this relatively high proportion has been attributed to ultrastructural properties of the nonsinusoidal feline spleen, which make it unable to remove nondeformable erythrocytes containing Heinz bodies from the circulation.3 Although increases in Heinz body formation following propofol administration may be the result of oxidative erythrocyte damage induced by propofol, important antioxidant properties have been attributed to propofol in humans, rats, and pigs, including protection of cerebral glutamate clearance mechanisms from oxidative damage, enhanced tissue antioxidant activity, and protection of RBCs against oxidative stress.20-24

On the basis of the results of the present study, propofol appears to be a clinically useful and effective anesthetic agent for repeated daily anesthetic episodes of short duration in cats. Propofol administered at the doses and dosing interval used in our study provided anesthesia that was adequate for completion of short-duration radiation treatments and was not associated with adverse effects in any cat included in the study. Preanesthetic medication with an appropriate neuroleptic combination and prior administration of midazolam allowed a significant reduction in the total dose of propofol required to induce and maintain anesthesia. Despite the lack of significance, the apparent decreases in Hct and hemoglobin concentration over the study period promote the recommendation of routine hematologic monitoring of cats that are anesthetized repeatedly with propofol for procedures of short duration.

References

a. Propofol 1%, Fresenius, Stans, Switzerland.
b. Dormicum, 5 mg/mL, Roche AG, Basel, Switzerland.
c. Dymaray LA20, ABB/VARIAN, Baden, Switzerland.
d. Vet/Ox SSI 4402, San Diego Instruments, San Diego, Calif.
e. Abbott Cell-Dyn 3500, Abbott, Baar, Switzerland.

Correction: Survival rate and short-term fertility rate associated with the use of fetotomy for the resolution of dystocia in mares: 72 cases (1991–2005)

In the report “Survival rate and short-term fertility rate associated with the use of fetotomy for the resolution of dystocia in mares: 72 cases (1991–2005)” (J Am Vet Med Assoc 2007; 230;1502–1505), the dosage for detomidine chloridrate in the third line in the first full paragraph in the right-hand column on page 1503 is incorrect. The correct dosage for detomidine is 0.008 µg/kg (0.0036 µg/lb), IV.