Recovery of grizzly and American black bears from xylazine, zolazepam, and tiletamine

Thomas G. Radandt

US Fish and Wildlife Service, Room 309 Main Hall, University of Montana, Missoula, MT 59812, USA

Abstract: Field workers handling bears continually strive to improve their field methods and reduce risks to animals during capture. Zolazepam–tiletamine (ZT) is the standard anesthesia currently used in bear captures, but has a prolonged recovery because there is no antagonist. Researchers are increasingly using xylazine, zolazepam, and tiletamine (XZT) in combination as an improvement to ZT alone. Because xylazine provides excellent analgesic qualities and can be antagonized, XZT has the potential for effective anesthesia and faster recovery time for bears. I assessed recovery times and considered physiological parameters to assess the quality of anesthesia of grizzly (Ursus arctos) and American black (U. americanus) bears anesthetized with XZT, for which the xylazine portion was antagonized by yohimbine (XZT/Y). I compared these recovery times with unpublished recovery time data on bears anesthetized with ZT only. My XZT/Y samples came from research projects in western Montana, northern Idaho, and southeast British Columbia; bears anesthetized with ZT only came from Alberta, Canada, and the Greater Yellowstone Project of Montana, Wyoming, and Idaho, USA. Bears administered the XZT/Y protocol recovered from anesthesia 1.61 (95% CI = 1.28–2.01) times faster than bears anesthetized with ZT combinations. Bears administered XZT/Y at dosage rates presented here received adequate anesthesia for humane handling as indicated by the physiological parameters monitored.

Key words: American black bear, anesthesia, grizzly bear, recovery time, Rocky Mountains, tiletamine, Ursus americanus, Ursus arctos, xylazine, zolazepam

Field workers handling anesthetized bears desire an agent that is inexpensive and quickly absorbed; has small induction volume, a large therapeutic index, and minimal side effects; yields minimal exposure risks to humans; provides quality anesthesia; and reversible (Franzmann 1982). To date, no one drug meets all these criteria. A combination of ketamine–xylazine has been used since 1979 (Addison and Kolenosky 1979) but has disadvantages: it requires large dosage volumes, allows a brief time to safely handle the bear, and can result in potential spontaneous recovery (Garshelis et al. 1987, Hellgren and Vaughn 1989, White et al. 1996). Stewart et al. (1980) first reported on the use of zolazepam–tiletamine (ZT) to anesthetize bears, and this combination has become the standard for bear handling (Taylor et al. 1989, Gibeau and Paquett 1991, White et al. 1996, Ryan et al. 2009). ZT is characterized by a wide safety margin, rapid absorption, and predictable recovery. The disadvantages of ZT are a prolonged, rough recovery, and no available antagonist (Caulkett and Cattet 1997). In a comparison of the xylazine–zolazepam–tiletamine (XZT) combination with zolazepam–tiletamine (ZT), Cattet et al. (2003b) found XZT to be effective for grizzly bears as an anesthetic agent with a wide therapeutic index and excellent analgesic qualities, and particularly useful for painful procedures such as tooth extraction. Cattet and colleagues also found a tendency for hyperthermia at ambient temperatures >25°C and slightly reduced blood oxygen concentrations. These conditions can be managed by temperature monitoring and cooling procedures, when appropriate, and with the administration of supplemental oxygen. Cattet et al. (2003b) further reported that reversal of the xylazine portion of XYT with yohimbine yielded highly variable results, but did not quantify differences in recovery times between the two drug regimes.

I compared anesthesia recovery times of grizzly and black bears administered XZT/Y to those

1Thomas_radandt@fws.gov
administered ZT. I used dosage rates developed as part of this project.

Study areas
I anesthetized bears in 3 conterminous study areas (Fig. 1) within 6200 km² of the Purcell Mountains, 2004–08, in southern British Columbia, Canada, northwestern Montana, (Kasworm et al. 2006) and in northeastern Idaho, USA (Lewis et al. 2007). These study areas are in or adjacent to the Cabinet–Yaak grizzly bear recovery zone (US Fish and Wildlife Service 1993). I also used unpublished data (1998–2002) from The East Slopes Project (ESP) in Alberta, Canada, and the Interagency Grizzly Bear Study Team (IGBST) of the Yellowstone Ecosystem. The ESP study area covered approximately 41,000 km² within the central Canadian Rocky Mountains of western Alberta, Canada (Gibeau et al. 2001). The IGBST study area was 23,833 km² and included Yellowstone and Grand Teton National Parks, portions of 6 adjacent national forests, and state and private lands within Montana, Wyoming, and Idaho, USA (Schwartz et al. 2006).

Methods
All bears were captured using Aldrich foot snares or culvert traps (Jonkel 1993) following approved Animal Use Protocols (006-03-CSWB-040105-02, University of Montana, Missoula; 466410, University of Alberta, Edmonton; 2005–27, University of Idaho, Moscow; US Geological Survey, Biological Resources Division, Midcontinent Ecological Science Center). Weights of captured bears were estimated visually then quantified using a spring-scale while bears were anesthetized. The XZT combination was created following methods described by Cattet et al 2003b. Captured bears were darted with a Palmer Cap-Chur™ gun (Palmer Cap-Chur Inc., Powder River, Georgia, USA), Pneudart® rifle (Pneu-dart Inc., Williamsport, Pennsylvania, USA), or homemade pole syringe. I began by injecting bears the published dose of XZT for grizzly bears (6.7 mg/kg, Cattet et al. 2003b) and through experimentation increased it to 7.04 mg/kg (2.86 mg/kg xylazine, 4.18 mg/kg zolazepam/tiletamine) to achieve appropriate anesthesia (unpublished data). Also through experimentation, I developed a black bear dose by decreasing the grizzly bear dose until appropriate anesthesia was obtained. The final black bear dose was 5.28 mg/kg (2.2 mg/kg xylazine, 3.08 mg/kg zolazepam/tiletamine). I provided bears anesthetized with XZT supplemental oxygen at 3 L/hour via nasal canula. Bears were administered diazepam (Hospira, Inc., Lake Forest, Illinois, USA) at 0.22 mg/kg to smooth recovery of ZT, and yohimbine (Ben Venue Laboratories, Bedford, Ohio, USA) at 0.11 mg/kg, intramuscularly (IM), intravenously (IV), or half IM half IV, at least 60 minutes post induction. I administered atropine sulfate (Vet Tek Inc., Blue Springs, Missouri, USA) at 0.04 mg/kg if bradycardia (<45 bpm) was imminent.

I recorded respiration rate, oxygen saturation, heart rate (Nellcor N-20/P pulse oximeter, Nellcor Inc., Pleasanton, California, USA), and rectal temperature (continuous read thermometer, Radio Shack, Fort Worth, Texas, USA) at approximately 15-min intervals. I considered the ideal physiological parameters indicating a targeted surgical plane of anesthesia to be a respiration rate of 8–15 breaths/min (Wagner et al. 2003), a pulse rate of 60–90 beats/min (Jonkel 1993), oxygen saturation >80%, and temperature of 36.0–39.4°C (Kreeger 1997). During anesthesia, when parameters are within these ranges, bears should be close to homeostasis and in a satisfactory level of anesthesia. I defined recovery time as the period from injection until the bear stood on all 4 feet. Bears that required more >1 injection for induction were not included in the analysis (these
bears typically did not receive the entire dose from the first injection due to mechanical failure, making it difficult to measure how much drug it received). I used ANCOVA (STATg™, StataCorp, College Station, Texas, USA) to determine if grizzly and black bears within the XZT/Y regime recovered at different rates. The results from this analysis allowed me to pool the data from both species, and again using ANCOVA, quantify recovery time (the dependent variable) as a function of drug regime, age class (subadult ≤4 years old, adult >4 years old), sex (independent variables), and the discrepancy between my species-specific intended dose and the actual administered dose as a covariate. Minutes to recovery and covariate data were natural log-transformed prior to analysis.

### Results
I anesthetized 122 bears with XZT, of which 21 were observed to full recovery. During 1998–2002, 20 bears were anesthetized with ZT and observed to full recovery by ESP and IGBST research personnel (Table 1). There was no difference between recovery times of grizzly and black bears administered XZT/Y ($F = 1.94; 1, 18$ df; $P = 0.18$), thus data from both species of bears were pooled for the test between drug regimes. The discrepancy between the intended and administered dose was a significant predictor of recovery time within the XZT/Y treatment ($F = 4.57; 1, 18$ df; $P = 0.05$), as was drug regime ($F = 18.13; 1, 38$ df; $P = 0.0001$). Discrepancy between intended and administered dose was also significant in the ANCOVA model of recovery times, with drug regimes as the main effect ($F = 8.18; 1, 38$ df; $P = 0.0068$). The geometric mean of the recovery time of bears administered ZT (197.7 min) was 1.61 times (95% CI = 1.28–2.01) longer than that of bears administered XZT/Y (123.0 min; Table 2). The confidence interval does not overlap 1.0, indicating a significant reduction in recovery time with XZT/Y.

Bears administered XZT/Y showed physical characteristics within the acceptable range of each measured parameter. Bears administered XZT/Y had a mean heart rate of 78.5 beats/min (Fig. 2a), mean respiration of 16.3 breaths/min (Fig. 2b), mean oxygen saturation of 88.0% (Fig. 2c), and mean rectal temperature of 38.0°C (Fig. 2d). These results suggest that bears were provided adequate anesthesia for humane handling under the doses administered. Two XZT bears required atropine during the course of anesthesia. I observed no spontaneous recoveries. Behavioral phases of recovery were similar to those described by Taylor et al. (1989). One adult male grizzly bear displayed minor convulsions for approximately 2 min, 122 min post injection.

### Discussion
Bears administered XZT/Y recovered faster from anesthesia than bears administered ZT, making them less vulnerable to inter- and intraspecific predation, human disturbance, or complications from anesthesia. The advantage of the XZT/Y regime likely stems from the lower amount of total ZT administered. Combining xylazine with ZT reduces the ZT necessary to reach a safe level of anesthesia. When xylazine is antagonized by yohimbine, the lower ZT dose allows for faster recovery. Recovery times may be further reduced by using atipamezole, a more aggressive

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### Table 1. Mean dose of xylazine–zolazepam–tiletamine (XZT) and zolazepam–tiletamine (ZT) delivered to grizzly and American black bears captured in the central Rocky Mountains, 1998–2008. All bears were observed to full recovery.

<table>
<thead>
<tr>
<th>Species</th>
<th>XZT n</th>
<th>Dose mg/kg</th>
<th>ZT n</th>
<th>Dose mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grizzly</td>
<td>7</td>
<td>10.17</td>
<td>19</td>
<td>8.55</td>
</tr>
<tr>
<td>Black</td>
<td>14</td>
<td>5.92</td>
<td>1</td>
<td>4.78</td>
</tr>
</tbody>
</table>

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### Table 2. Adjusted mean recovery time (min) from induction injection, for grizzly and American black bears administered xylazine–zolazepam–tiletamine–yohimbine (XZT/Y) or zolazepam–tiletamine (ZT) in the Rocky Mountains, 1998–2008.

<table>
<thead>
<tr>
<th>Drug regime</th>
<th>Species (n)</th>
<th>Sex (n)</th>
<th>Adjusted $\bar{x}$ (min)</th>
<th>SE (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>XZT</td>
<td>grizzly (7)</td>
<td>M (4), F (3)</td>
<td>123.0</td>
<td>(9.44, 10.22)</td>
</tr>
<tr>
<td></td>
<td>black (14)</td>
<td>M (9), F (5)</td>
<td>197.7</td>
<td>(15.25, 16.52)</td>
</tr>
<tr>
<td>ZT</td>
<td>grizzly (19)</td>
<td>M (13), F (6)</td>
<td>123.0</td>
<td>(9.44, 10.22)</td>
</tr>
<tr>
<td></td>
<td>black (1)</td>
<td>M (1), F (0)</td>
<td>197.7</td>
<td>(15.25, 16.52)</td>
</tr>
</tbody>
</table>
alpha₂ antagonist, to antagonize xylazine (Jalanka and Roeken 1990). I did not test atipamezole.

Taylor et al. (1989) found that grizzly bears immobilized with ZT (7–9 mg/kg) stood on all 4 legs 85–160 min after handling, with a mean heart rate of 99 bpm (n = 77). White et al. (1996) found a mean recovery time for ZT black bears of 150.5 min (SD = 84, n = 27) at 5.4 mg/kg. These bears had a mean heart rate of a relatively high 101 bpm (n = 10), suggesting that they may not have been in a surgical plane of anesthesia. Cattet et al. (2003b) found that grizzly bears anesthetized with XZT had a slower heart rate than bears anesthetized with ZT. Xylazine has been shown to induce bradycardia in some species (Klein and Klide 1989).

My data suggest that bears administered XZT/Y at dosages presented here received adequate anesthesia for humane handling and recovered faster than bears administered ZT at previously published dosages. Physiological parameters were within ranges associated with a satisfactory level of anesthesia (Fig. 2). The XZT/Y bears showed adequate oxygen saturation. Elevated rectal temperatures in XZT/Y bears may be due to xylazine compromising an animal’s ability to thermoregulate (Klein and Klide 1989); however, the temperatures I measured were still lower than the published ZT temperatures (White et al. 1996, 39.3°C, SE = 0.37, n = 27; Stewart et al. 1980, 38.1°C SE = 0.1°C, n = 37). Cattet et al. (2003b) found higher rectal temperatures in bears anesthetized with XZT than in bears anesthetized with ZT. Although I did not test for analgesic quality of the XZT/Y combination, Cattet et al. (2003a) found that when physical stimulus was applied, heart rate and blood pressure rose for ZT bears but not in XZT/Y bears, suggesting that handling episodes involving painful procedures (pulling a tooth) should not be done under ZT. In
addition, Cattet et al. (2003b) reported that XZT was tolerated safely by grizzly bears at dose rates 2–3 times those administered here.

Wildlife anesthesia is complicated; one drug regime will not be applicable to all occasions. Recaptured bears need minimal anesthesia to be released; new study animals will require more anesthesia to process, while an injured animal will require more analgesia. The XZT/Y regime may be too complex for workers who do not often handle chemical agents (e.g., wildlife managers who handle only 1–2 animals/year) but may be more practical than a medetomidine–zolazepam–tiletamine (MZT) combination for researchers who handle many bears/year. Medetomidine has been combined with ZT to anaesthetize grizzly, black, polar (Ursus maritimus), and sun bears (Helarctos malayanus) (Cattet et al. 1997, Caulkett and Cattet 1997, Arnemo et al. 2001, Onuma 2003). Medetomidine is a stronger alpha2 agonist than xylazine; therefore, the side effects of this class may be more pronounced. Side effects may include a decrease in respiration and more potential for hyperthermia or spontaneous arousal (Klein and Klide 1989). Spontaneous arousal can develop into a dangerous situation for wildlife handlers, especially with grizzly bears. ZooPharm Inc. advises against administering medetomidine to animals that are in shock, severely debilitated, or stressed due to extreme heat, cold, or fatigue (ZooPharm 2009). Physically restrained bears often have one or more of these conditions (Cattet et al. 2008) and thus they may be more susceptible to complications from medetomidine. In addition, bears given MZT may be more prone to hyperthermia on hot days (Cattet et al. 1997). Onuma (2003) reported that 16 of 22 sun bears anesthetized with MZT vomited during induction, even though food was withheld for 17–20 hours before handling. In 122 handling events from 2004–08, I observed no XZT bears vomiting. Vomiting during induction can be dangerous as it may be associated with choking, blocked airways, or inhalation of vomitus.

The cost difference between MZT and XZT varies depending on location. MZT is approximately 68% more expensive than a XZT regime in North America (ZooPharm, Inc., Ft. Collins, Colorado, USA; MWI Veterinary Supply, Meridian, Idaho, USA). XZT is 25% more expensive than MZT in Norway (J. Arnemo, Norwegian School of Veterinary Science, Ås, Norway, personal communication, 2009). Patents have recently expired, making medetomidine more available in North America and Scandinavian countries. In some eastern European countries, medetomidine is difficult to obtain and xylazine is not available (D. Huber, University of Zagreb, Zagreb, Croatia, personal communication, 2009).

Ryan et al. (2009) considered ZT to be the best anesthetic drug currently available for black bears because they recover from it gradually and predictably. A gradual, predictable recovery is also particularly advantageous when working on grizzly bears. XZT/Y allows for faster recovery while still exhibiting ZT’s predictable recovery characteristics. Faster recovery reduces the amount of time a bear is vulnerable to anesthetic complications as well as interspecific and anthropogenic predation. This reduced mortality risk is critical, particularly when bears from small, threatened populations are being handled.

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**Literature cited**


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