*J Vet Intern Med* 2011;25:1084–1088

# Comparison of a Continuous Glucose Monitoring System with a Portable Blood Glucose Meter to Determine Insulin Dose in Cats with Diabetes Mellitus

S. Dietiker-Moretti, C. Müller, N. Sieber-Ruckstuhl, F. Tschuor, M. Osto, M. Franchini, M. Ackermann, T.A. Lutz, C.E. Reusch, and E. Zini

**Background:** The continuous glucose monitoring system (CGMS) Guardian REAL-Time® allows the generation of very detailed glucose profiles in cats. The performance of CGMS to generate short-term glucose profiles to evaluate treatment response has not been yet evaluated in diabetic cats.

**Hypothesis:** Analysis of glucose profiles generated using the CGMS produces insulin dose recommendations that differ from those of profiles generated using the portable blood glucose meter (PBGM) in diabetic cats.

**Animals:** Thirteen client-owned diabetic cats.

**Methods:** Prospective, observational study. Simultaneous glucose profiles were generated over an 8-10 hour period using the CGMS, blood glucose concentration was measured every 2 hours with the PBGM. Profiles were submitted to three internal medicine specialists who used them to determine the insulin dose. Differences between insulin doses deduced from paired profiles were compared. Percentages of nadirs recorded with the CGMS that were lower, higher, or equal to those derived with the PBGM were calculated.

**Results:** Twenty-one paired glucose profiles were obtained. There was no difference of insulin doses based on CGMS and PBGM profiles (median 0 U; range: −1 to +0.5). Treatment decisions did not differ among investigators. Compared with the observed PBGM nadir, the CGMS nadir was lower, higher, or equal in 17, 2, and 2 of 21 cases, respectively.

**Conclusions and Clinical Importance:** Adjustments in insulin dose based on glucose profiles generated with the CGMS are similar to those based on the PBGM. The common occurrence of lower nadirs recorded with the CGMS suggests that this device detects hypoglycemic periods that are not identified with the PBGM.

**Key words:** Feline; Glucose profile; Hyperglycemia; Insulin treatment.

Diabetes mellitus is one of the most common endocrine diseases of cats and its incidence is increasing because of an increase in predisposing factors such as obesity and physical inactivity.[1–3] The mainstay of treatment of feline diabetes is insulin, generally combined with a high-protein, low-carbohydrate diet.[4] Assessing insulin requirement is a critical aspect of monitoring in diabetic cats because the dose may vary over time. For instance, an increase in the dose of insulin may be required in cats that develop concurrent disease, or discontinuation of insulin administration is advised when treatment results in clinical remission of diabetes mellitus. The history and results of a physical examination, serum fructosamine concentration, and blood glucose profiles are required for monitoring the response to insulin.

**Abbreviations:**

| | |
|---|---|
| CGMS | continuous glucose monitoring system |
| PBGM | portable blood glucose meter |
| U | unit(s) insulin |

Blood glucose profiles can be generated in a hospital, or at home by cat owners, in which case they are evaluated later by a veterinarian.[5–7] Blood glucose profiles are usually made by measuring the blood glucose concentration every 1-2 hours over an 8- to 10-hour period using a portable blood glucose meter (PBGM). To obtain better glycemic control, continuous glucose monitoring systems (CGMS) were developed for human diabetics and later evaluated for use in animals.[8–10] CGMS measure glucose in the subcutaneous interstitial fluid every few seconds, thus allowing the generation of more detailed glucose profiles.

Recently, a CGMS[a] of a new generation, which allows glucose readings every 5 minutes and instantaneous visualization of the recorded data on a separate screen, was successfully validated for use in cats. This instrument provided measurements in real-time and yielded clinically accurate and reproducible results.[11] In another report, the same CGMS allowed identification of an episode of hypoglycemia in a diabetic cat that had received an inappropriately high insulin dose.[12]

It is not reported whether treatment decisions based on glucose profiles obtained with a CGMS differ from those derived using a PBGM in cats. Therefore, the aim of the present study was to compare insulin doses recommended by internal medicine specialists based on

*From the Clinic for Small Animal Internal Medicine, Vetsuisse Faculty (Dietiker-Moretti, Müller, Sieber-Ruckstuhl, Tschuor, Reusch, Zini), Institute of Veterinary Physiology, Vetsuisse Faculty (Osto, Lutz), Institute of Virology, Vetsuisse Faculty (Franchini, Ackermann), University of Zurich, Zurich, Switzerland; Istituto Veterinario di Novara, Novara, Italy (Zini); and Department of Veterinary Clinical Sciences, University of Padua, Legnaro, Italy (Zini).*

*Corresponding author: E. Zini, Clinic for Small Animal Internal Medicine, Vetsuisse Faculty, University of Zurich, Winterthurerstrasse 260, 8057 Zurich, Switzerland; e-mail: ezini@vetclinics.uzh.ch.*

*Submitted December 23, 2010; Revised May 14, 2011; Accepted July 5, 2011.*



*10.1111/j.1939-1676.2011.00778.x*

the blinded assessment of paired glucose profiles generated with a new-generation CGMS and a reference PBGM in diabetic cats.

## Materials and Methods

### Diabetic Cats

Fourteen client-owned diabetic cats were hospitalized to generate simultaneous paired 8–10 hour glucose profiles using a CGMS and a PBGM during a follow-up examination at the Clinic for Small Animal Internal Medicine, University of Zurich, Switzerland. The cats had been treated with insulin glargine[b] for a median of 4 weeks (range 0–26 weeks) before blood glucose profiles included in the study were generated. All cats were treated with insulin twice daily before the examination. Informed consent was obtained from the owners. The cats consisted of 9 neutered males, 1 intact male and 4 spayed females, and there were 10 European shorthair, 1 European-longhair, 1 Norwegian Forest, 1 Birman, and 1 Ragdoll cat. Median age was 12 years (range: 8–15 years). All the cats had been diagnosed with diabetes mellitus at our clinic, based on clinical signs, including polyuria, polydipsia, polyphagia and weight loss, and laboratory tests, including hyperglycemia, increased serum fructosamine concentration and glucosuria.

### Continuous Glucose Monitoring System

The Guardian REAL-Time®,[a] CGMS consists of a disposable sensor, a transmitter, and a pager-sized monitor. The sensor is able to measure the glucose concentration in the interstitial fluid via an enzymatic reaction that generates a small electrical current. This signal is subsequently converted to a glucose concentration (mg/dL). The transmitter sends the data to the monitor where they are displayed in real-time. Measurements are made every 10 seconds and displayed on the monitor as 5-minute means. It should be noted that the monitor displays glucose concentrations from 40 to 400 mg/dL; concentrations outside this range are correctly recorded by the CGMS but need to be downloaded to be visualized.[11]

After starting the sensor, the CGMS needs a 2-hour period of initialization. Glucose values are not provided until the system is ready for calibration. For calibration, the cat's current glucose concentration is measured with a PBGM and entered into the device as a reference value. The CGMS needs to be further calibrated within 6 hours of initial calibration and then every 12 hours. Only values between 40 and 400 mg/dL can be used for calibration. If the blood glucose concentration is outside this range, calibration needs to be postponed until the concentration has returned to within the range.

In accordance with a previous study,[11] the CGMS sensor was placed in the subcutaneous tissue of the lateral chest wall, at the 6th or 7th intercostal space, and about halfway between the vertebral column and sternum. A small area of skin in this region was clipped and disinfected with an alcohol solution.[c] After the skin was dry, the sensor was inserted under the skin through a disposable hypodermic needle and fixed to the patient with tape. The transmitter was connected to the sensor and a soft bandage was placed around the chest to protect the device.

### Portable Blood Glucose Meter

The PBGM AlphaTRAK®,[d] specifically designed for dogs and cats, was used to obtain a 2nd glucose profile. This device was previously shown to provide precise and accurate measurements in cats[13] and is routinely employed in our clinic to measure capillary blood glucose concentrations in cats. The working range of the device is 20–500 mg/dL.

### Generation of Glucose Profiles

All the cats received insulin glargine[b] and were fed at home before admission to the clinic, in the morning. A baseline capillary blood glucose concentration was determined using the PBGM and blood collected via ear puncture before examination and manipulation of the patient. After physical examination, venous blood samples were collected for hematological and biochemical analyses. Additional analyses were carried out when indicated.

The CGMS sensor was then placed and fixed to the animal as described above, and the monitor was secured to the cage door. Cats were housed individually in a cage from shortly after admission to late afternoon. They had free access to water but food was not provided. The CGMS was calibrated twice; once before the start of measurements and again 6 hours later. Glucose readings with the CGMS were first available 2 hours after 1st calibration. After the baseline measurement, glucose concentrations were measured every 2 hours with the PBGM. Immediately after the last glucose measurement with the PBGM, the CGMS was turned off.

### Assessment of Glucose Profiles

Three clinicians with board certification in small animal internal medicine (CM, NSR, and CER) assessed the profiles generated using the 2 measuring devices and based on the results, recommended insulin dosages for the diabetic cats. Each clinician evaluated the glucose profiles independently, without knowledge of the insulin dose chosen by the others. The 21 paired profiles were split and randomly numbered, with different numbers for PBGM and CGMS profiles; with this method, examiners were blinded to which CGMS profile was paired with the respective PBGM profile. To evaluate PBGM profiles all measurements were made accessible, including the 1st glucose value obtained after admission at the clinic. To evaluate CGMS profiles there was a delay of 2 hours due to the initialization period. The following information was available for each profile for determining the insulin dose: amount of insulin administered before the blood glucose profile, whether the cat received 1 or 2 insulin injections per day, and body weight ($\leq$4 kg, or >4 kg). Body weight was reported because in our clinic, diabetic cats >4 kg initially receive an additional 0.5–1 U of insulin per treatment. Other information, including history (eg, improvement of clinical signs), physical examination (in particular, whether body weight had increased or decreased), and serum fructosamine concentrations, were deliberately omitted to further minimize bias and ascertain that the recommended insulin dose was mainly based on the glucose profiles.

In our clinic, we define 3 concentration ranges for the glucose nadir; the ideal range is between 90 and 160 mg/dL. When the nadir is below 90 mg/dL (low range), the insulin dose is reduced by 0.5–1 U per injection. When the nadir is above 160 mg/dL (high range), the insulin dose is increased by 0.5–1 U per injection. The 3 investigators used this criterion during analysis of blood glucose profiles.

### Statistical Analysis

A commercial software[e] was used for statistical analysis. The glucose nadir, peak, and mean were recorded for each CGMS and corresponding PBGM profile, and the median and range of the differences among the nadirs, peaks, and means of the paired

profiles were calculated (CGMS values subtract to PBGM value). The percentages of CGMS and PBGM nadirs below 90 mg/dL, above 160 mg/dL, and between 90 and 160 mg/dL were also determined.

For each investigator, the differences between the insulin doses deduced from the paired glucose profiles were calculated, which was followed by calculating the median and range of these differences. The Wilcoxon matched pairs test was used to analyze differences between treatment decisions that were based on the corresponding glucose profile. Finally, the proportions of insulin doses deduced from the CGMS profiles that were lower, higher, and equal to the insulin doses deduced from the PBGM profiles were calculated.

To analyze interobserver agreement on treatment recommendations, insulin doses were compared for CGMS and PBGM profiles separately among investigators using the Friedman test, followed by Dunn's multiple comparisons test. Significance was set at $P < .05$.

## Results

A total of 21 paired CGMS and PBGM profiles from 13 diabetic cats were available for analysis. One pair of glucose profiles was generated in 8 cats, 2 pairs of profiles in 3 cats, 3 pairs of profiles in 1 cat, and 4 pairs of profiles in 1 other cat. In 1 cat, paired glucose profiles could not be obtained because the sensor of the CGMS failed to read the interstitial fluid glucose concentrations. In all other cases, calibration of the CGMS was straight-forward because glucose concentrations measured in the capillary blood with the PBGM were between 40 and 400 mg/dL. Representative paired glucose profiles from 2 diabetic cats are shown in Figure 1.

The median difference between glucose nadirs of the paired glucose profiles was −25.2 mg/dL (range −124.2 to +10.8). Compared with the PBGM profile, the nadir of the CGMS profile was lower, equal, or higher in 17 (81%), 2 (9.5%), and 2 (9.5%) profile pairs, respectively. Of the 19 pairs of glucose profiles in which the nadirs differed, the lowest glucose concentration was <90 mg/dL measured with the CGMS and between 90 and 160 mg/dL measured with the PBGM in 4 cases, and between 90 and 160 mg/dL measured with the CGMS and >160 mg/dL measured with the PBGM in 1 case. In the remaining 14 cases, paired nadirs were in the same range of glucose concentration (either <90 mg/dL, between 90 and 160 mg/dL, or >160 mg/dL). In 16 out of 21 cases, the CGMS nadir occurred within 2 hours from that of the PBGM; in 5 cases, the PBGM nadir anticipated that of the CGMS of 3.5–4.5 hours.

The median difference between glucose peaks of paired profiles was −45 mg/dL (range −307.8 to +91.8); the median difference between glucose means of paired profiles was −28.4 mg/dL (range −160.2 to +19.5).

There was no significant overall difference between the insulin doses deduced from the CGMS and PBGM profiles (p for examiner 1 = 0.22; p for examiner 2 = 0.13; p for examiner 3 = 0.12); the median difference between the doses was 0 U per injection and ranged from −1 to +0.5. Of the 21 pairs of corresponding glucose profiles, the three investigators deduced doses that differed from each other in 7 (33.3%), 4 (19.0%), and 8 (38.1%) pairs of glucose profiles, respectively. The dose deduced from the CGMS was lower than the dose deduced from the PBGM in five of the seven cases of investigator 1, in four of the four cases of investigator 2, and in six of the eight cases of investigator 3. There were no significant differences among investigators with respect to recommended insulin doses within profiles generated by the CGMS or within profiles generated by the PBGM.

## Discussion

Insulin dose adjustments after evaluation of glucose profiles generated by CGMS did not significantly differ from those obtained by the standard method PBGM. A study period of 8–10 hours was chosen to closely mimic the clinical setting, where a CGMS might be used during a 1-day hospitalization, similarly to glucose profiles generated with the PBGM.

Because a CGMS measures glucose concentration more frequently, we hypothesized that 8–10 hour glucose profiles generated using the CGMS lead to insulin dose recommendations that differ from profiles generated using a PBGM. However, the overall treatment recommendations based on CGMS and PBGM profiles did not differ significantly, and the median recommended insulin doses differed by 0 U with a maximal divergence of −1 to +0.5. This suggests that treatment decisions based on CGMS profiles are generally similar to those obtained using PBGM profiles.

There was disagreement between the two insulin doses deduced from the two corresponding glucose profiles in 19 (30.2%) of the 63 treatment recommendations made by the three blinded investigators; in 15 of these, the dose deduced from the CGMS profile was lower than the dose deduced from the PBGM profile. A likely reason for this was that the CGMS provided glucose concentrations every 5 minutes and thus more detailed glucose profiles. This allowed the detection of nadirs that may not have been identified in glucose profiles generated by a PBGM, in which blood glucose concentration was determined every 2 hours. Because the nadir is crucial for determining the most appropriate insulin dose,[7] detection of lower nadirs with the CGMS may explain the differences in these dosage recommendations. Two of the corresponding nadirs were numerically identical and the remaining 19 differed; in 17 of the latter, the nadir of the CGMS profile was lower. Furthermore, in five of the 19 cases, the two corresponding nadirs were in different blood glucose ranges (high/ideal ranges in one case and ideal/low ranges in four), which highlights the potential for erroneous treatment decisions, particularly when relying on the PBGM (yielded higher nadirs). In one case, the difference between nadirs was particularly pronounced (ie, −124.2 mg/dL). The reason for this finding is unclear and may be due to dysfunction of the CGMS sensor or, possibly, to a very rapid change in blood glucose concentration leading to a delay in

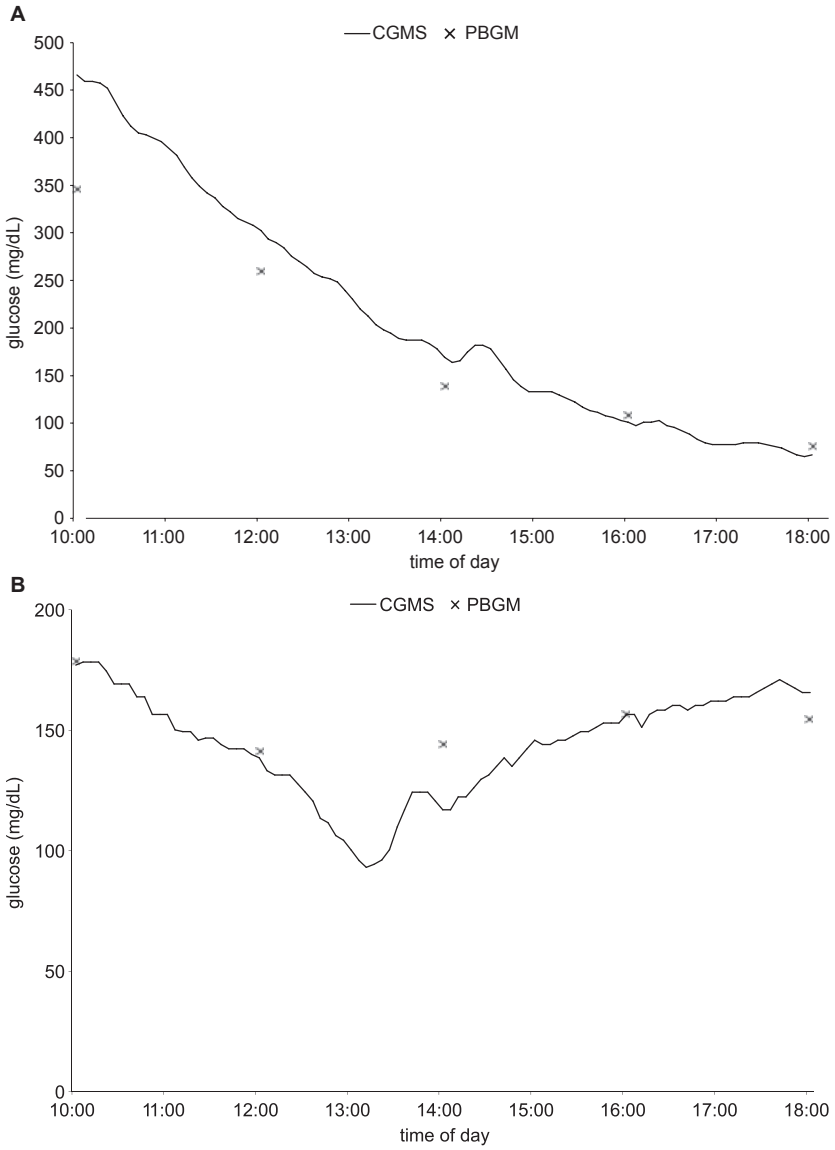


**Fig 1.** Paired CGMS and PGBM glucose profiles in diabetic cats. **A.** This cat received 1.5 U insulin glargine[b] twice daily at home. Nadirs recorded with the 2 devices are similar. **B.** This cat received 0.5 U insulin glargine[b] twice daily at home. The CGMS nadir is near to 90 mg/dL, whereas the PBGM nadir is approximately 140 mg/dL.

interstitial glucose fluid equilibration.[11] The latter may also have been responsible for the marked differences observed in one case for the glucose peak (ie, −307.8 mg/dL) and for the mean glucose concentration (ie, −160.2 mg/dL). In a previous study,[11] the time delay between a rapid rise in blood glucose and interstitial glucose concentrations measured with a CGMS was 11.4 minutes. It is assumed that a rise in glucose concentrations after rapid blood glucose fluctuations would be read by the CGMS approximately 11 min after the PBGM.

In 16 cases paired nadirs occurred within 2 hours. However, in five cases the delay between PBGM and CGMS nadirs was of 3.5–4.5 hours; of note, in all five cases the PBGM nadir anticipated that of the CGMS. By examining CGMS profiles (data not shown) it was possible to observe that after insulin administration glucose concentrations dropped slowly and with some fluctuations in each case. Fluctuations might have been responsible for the apparently longer delay between nadirs.

Overall treatment recommendations did not differ among the three investigators with regard to CGMS or PBGM profiles, which suggested that the criteria used to assess the glucose profiles were reliable. In dogs, Davison et al,[14] evaluated the difference between treatment recommendation made by two examiners, using an earlier generation of CGMS together with a PBGM used as reference. Recommendations were equal in 12 out of 20 cases, leading the authors to conclude that the CGMS can be safely employed for clinical use in dogs with diabetes mellitus.

A major advantage of using the CGMS to generate glucose profiles during follow-up examinations is

reduced restraint and handling of patients.[11] In particular, glucose concentrations are more reliably and easily monitored with a CGMS in frightened or aggressive cats. With regard to technical limitations encountered in this study, it is worth noting that in 1 cat, a CGMS profile could not be obtained because of sensor failure. Technical problems such as sensor failure or calibration errors may constitute drawbacks of using a CGMS for generating glucose profiles over an 8- to 10-hour period.[11] Of note, measurements obtained over 8–10 hours, although sufficient to generate glucose profiles in cats receiving insulin twice daily, may not be enough to evaluate treatment response and thus to give recommendations about insulin dose in cats previously treated with insulin once daily, especially if the insulin dose is administered in the evening.

Another drawback of the CGMS for generating short-term profiles is the relatively long initialization period (2 hours), during which glucose readings are not provided by the instrument. This is particularly relevant when diabetic cats can be hospitalized for only a few hours during follow-up examination. Furthermore, calibration is only feasible when glucose concentrations are between 40 and 400 mg/dL. Values outside this range are inadequate for calibration, which means that CGMS recordings are delayed until the blood glucose concentration has returned to within the working range of the instrument. Although this did not occur in the present study, glucose values above 400 mg/dL occur frequently in diabetic cats with poor glycemic control. Finally, the few CGMS calibrations obtained for each glucose profile might have led to invalid assessment of insulin requirements in some cases. However, in the present investigation calibrations were performed as suggested by the manufacturer and as in previous CGMS studies in cats.[11,12]

In summary, insulin dose adjustments based on glucose profiles generated with the CGMS and PBGM are similar, suggesting that the former instrument is valuable for obtaining short-term glucose profiles in diabetic cats in a clinical setting. However, sensor failure and calibration delay may limit the usefulness of the CGMS. Better detection of nadirs with the CGMS may prove useful for improving adjustments in insulin dose in some diabetic cats. Further studies are needed to investigate whether long-term use of CGMS during follow-up examinations improves blood glucose control in diabetic cats.

## Footnotes

[a] Guardian REAL-Time continuous glucose monitoring system, Medtronic, Münchenbuchsee, Switzerland
[b] Lantus insulin, Sanofi Aventis, Geneva, Switzerland
[c] Sterilium, Bode AG, Münchenstein, Switzerland
[d] AlphaTRAK portable blood glucose meter, Abbot Animal Health, Maidenhead, UK
[e] GraphPad Prism 4.0, GraphPad, San Diego, CA

## References

1. Scarlett JM, Donoghue S, Saidla J, et al. Overweight cats: Prevalence and risk factors. Int J Obes Relat Metab Disord 1994;18:S22–S28.

2. Lederer R, Rand JS, Hughes IP, et al. Chronic or recurring medical problems, dental disease, repeated corticosteroid treatment, and lower physical activity are associated with diabetes in Burmese cats. J Vet Intern Med 2003;17:433.

3. Prahl A, Guptill L, Glickman NW, et al. Time trends and risk factors for diabetes mellitus in cats presented to veterinary teaching hospitals. J Feline Med Surg 2007;9:351–358.

4. Frank G, Anderson W, Pazak H, et al. Use of a high-protein diet in the management of feline diabetes mellitus. Vet Ther 2001;2:238–246.

5. Reusch CE, Kley S, Casella M. Home monitoring of the diabetic cat. J Feline Med Surg 2006;8:119–127.

6. Casella M, Hässig M, Reusch CE. Home-monitoring of blood glucose in cats with diabetes mellitus. Evaluation over a 4-month period. J Feline Med Surg 2005;7:163–171.

7. Kley S, Casella M, Reusch CE. Evaluation of long-term home monitoring of blood glucose concentration in cats with diabetes mellitus: 26 cases (1999–2002). J Am Vet Med Assoc 2004;225:261–266.

8. Ristic JM, Herrtage ME, Walti-Lauger SM, et al. Evaluation of a continuous glucose monitoring system for use in cats with diabetes mellitus. J Feline Med Surg 2005;7:153–162.

9. Wiedmeyer CE, DeClue AE. Continuous glucose monitoring in dogs and cats. J Vet Intern Med 2008;22:2–8.

10. Wiedmeyer CE, Johnson PJ, Cohn LA, et al. Evaluation of a continuous glucose monitoring system for use in dogs, cats, and horses. J Am Vet Med Assoc 2003;223:987–992.

11. Moretti S, Tschuor F, Osto M, et al. Evaluation of a novel real-time continuous glucose-monitoring system for use in cats. J Vet Intern Med 2010;24:120–126.

12. Moretti S, Zini E, Tschuor F, et al. First experiences with the continuous real-time glucose monitoring system (Guardian REAL-time CGMS) in a cat with diabetes mellitus. Schweiz Arch Tierheilkd 2009;151:448–451.

13. Zini E, Moretti S, Tschuor F, et al. Evaluation of a new portable glucose meter designed for the use in cats. Schweiz Arch Tierheilkd 2009;151:27–30.

14. Davison LJ, Slater LA, Herrtage ME, et al. Evaluation of a continuous glucose monitoring system in diabetic dogs. J Small Anim Pract 2003;44:435–442.