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1 **Inter- and intra-observer reliability of quantitative sensory testing performed with the Small**  
2 **animal ALGometer (SMALGO) to evaluate pain associated with feline gingivostomatitis**

3

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21

22 **Abstract**

23

24 **Objectives** To evaluate the inter-observer and the intra-observer reliability of quantitative sensory  
25 testing performed with the SMALGO (SMall animal ALGOmeter) in healthy cats and in cats with  
26 chronic gingivo-stomatitis (CGS), and to evaluate the SMALGO as a tool to detect and quantify  
27 pain in cats with CGS.

28 **Methods** Thirty cats of a private shelter were included in this study, and assigned to one of two  
29 groups: group C (healthy cats; n = 15) and group CGS (cats with chronic gingivo-stomatitis; n =  
30 15). In all cats the mechanical thresholds were measured with the SMALGO, with the sensor tip  
31 applied on the superior lip above the canine root, by two independent investigators (A,  
32 experienced, and B, unexperienced), on two different occasions (day 1 and day 2) with a 24 hour-  
33 interval. A CGS scale was used in the diseased cats to assess the severity of the condition. For the  
34 reliability analysis, the intra-class correlation coefficients (ICC) were calculated. Other statistical  
35 tests used were Pearson correlation coefficient and paired T-test.

36 **Results** The inter-observer and intra-observer levels of agreement were fair (ICC = 0.50) and good,  
37 respectively (ICC = 0.73 for investigator A and ICC = 0.60 for investigator B). However, the  
38 thresholds measured in healthy cats ( $169 \pm 59$  g) did not differ from those obtained from diseased  
39 cats ( $156 \pm 82$  g;  $P = 0.35$ ). There was no correlation between the scores of the CGS scale and the  
40 thresholds measured in diseased cats (Pearson correlation coefficient = 0.047;  $P = 0.87$ ).

41 **Conclusions and relevance** Quantitative sensory testing performed with the SMALGO in cats are  
42 repeatable and reliable regardless the expertise of the investigator. However, the findings of this  
43 study suggest that the mechanical thresholds measured with the SMALGO may not be a valuable  
44 indicator of pain in cats with CGS.

45 **Introduction**

46

47 The feline chronic gingivo-stomatitis (CGS) is a severe inflammatory disease of the oral cavity  
48 that can affect cats of every age. It differentiates from gingivitis in the fact that inflammation  
49 extends not only to the mucogingival junction, but also to the oral mucosa.<sup>1</sup>

50 The condition may involve different areas such as gingiva, alveolar mucosa, fauces, pharynx,  
51 tongue, palate and labio-buccal and caudal oral mucosa.<sup>2</sup> It is characterised by pain, swollen,  
52 ulcerated or bleeding gums, hypersalivation, halitosis, anorexia, dysphagia, weight loss and  
53 enlarged submandibular lymph nodes, and it can severely affect the quality of life of the affected  
54 cats, as well as their behaviour.<sup>3,4</sup> The prevalence of the disease is high, accounting for the 0.7 -  
55 12% of the cats in the United States.<sup>1</sup> Although the exact ethiology of FCGS is still unknown, it is  
56 widely recognised that many factors, namely environmental factors, dental disease, various  
57 bacterial and viral infections, immune response and stress, contribute to its development.<sup>3-5</sup>

58 Cats with CGS are very likely to experience pain. Unfortunately, pain can easily go  
59 underdiagnosed in feline patients, and quantifying pain in cats can be extraordinarily challenging  
60 even for the most experienced veterinarian.<sup>6,7</sup> The scales currently available to evaluate pain in  
61 cats have been developed to assess acute surgical pain, and may not be adequate to evaluate  
62 chronic, non-surgical conditions.<sup>8,9</sup> Therefore, there is a need for valid and reliable methods to  
63 detect and measure chronic pain in cats.

64 Quantitative sensory testing (QTS) is a semi-quantitative method to assess dysfunctions of  
65 the sensory system, and the use of mechanical thresholds has been described in cats,<sup>10-15</sup> also to  
66 evaluate chronic pain.<sup>15</sup> Various pressure algometers have been designed for use in animals within  
67 the last two decades, of which two were specific for cats.<sup>11,12</sup>

68 The SMall animal ALGOmeter (SMALGO, Bioseb, France) is a pressure-based algometer  
69 designed for measuring allodynia and hyperalgesia in laboratory rodents.<sup>16</sup> The device has also  
70 been also used to evaluate chronic and neuropathic pain in small animals,<sup>17</sup> and to perform QTS  
71 in dogs with osteoarthritis.<sup>18</sup> The first reports in small-sized companion animals seem to suggest  
72 that the SMALGO may be a useful tool to measure various types of pain in clinical feline patients.<sup>14</sup>

73 If the measurement of mechanical thresholds with the SMALGO could be proven to be an  
74 effective tool for the assessment of CGS-associated pain, this finding may potentially represent a  
75 step forward in the recognition and management of feline chronic pain.

76 The primary objectives of this study were therefore the following:

- 77 • To evaluate the inter-observer and intra-observer reliability of QST performed with  
78 SMALGO in healthy cats and in cats with CGS;
- 79 • To determine whether the SMALGO would be a useful tool to differentiate, on the basis  
80 of the mechanical sensory thresholds, between healthy cats and cats with CGS.

81 A secondary objective of this study was to determine whether there was any association  
82 between the mechanical thresholds measured with the SMALGO and the scores of a CGS scale,  
83 developed by the authors based on previous publications,<sup>19,20</sup> to evaluate the severity of the clinical  
84 condition in cats.

85 We hypothesized that the SMALGO would provide reliable and repeatable measurements of  
86 the sensory thresholds, regardless the level of expertise of the investigator, and that the thresholds  
87 measured in cats with CGS would be lower than those obtained from healthy cats.

88

## 89 **Materials and methods**

90

91 **Ethical approval**

92 The study was conducted with permission of the Clinical Research Ethical Review Board of the  
93 Royal Veterinary College (license number: URN 2017 1709-3). A written informed consent was  
94 obtained by the owner of the cat shelter prior to commencing the trial.

95

96 **Animals and determination of sample size**

97 Thirty rescued cats of a private cat shelter (Associazione di Promozione Sociale Amici di Poldo,  
98 Udine, Italy) were enrolled in this study.

99 Based on medical history and physical examination, performed by the veterinarian in charge  
100 for routine medical procedures in the shelter, the cats were assigned to one of two groups: group  
101 CGS (cats with chronic gingivo-stomatitis) and group C (control: healthy cats). Each group was  
102 composed of 15 subjects. Exclusion criteria were presence of other systemic disease or condition  
103 other than CGS potentially associated with pain, recent admission to the shelter that would have  
104 resulted in limited medical history, administration of analgesics or other medication that could  
105 potentially have influenced the assessments, and fractious behaviour. All the cats included in the  
106 study were comfortable with the human presence and were used to be handled.

107 The sample size was based on a calculation performed with a program available on line  
108 (<https://www.stat.ubc.ca>), with the following setting of variables: mean mechanical thresholds of  
109 cats of group CGS = 100 g; mean mechanical thresholds of cats of group C = 150 g (50% more of  
110 diseased cats); SD = 50 g;  $\alpha$  value = 0.05; power = 0.80. This resulted in a minimal number of cats  
111 to be included in the trial equal to 13, similarly as reported in previous studies that evaluated the  
112 use of QST in dogs with osteoarthritis, in which the sample size was calculated based on pilot  
113 data.<sup>18</sup>

114

### 115 **Diagnosis of chronic gingivo-stomatitis**

116 Beside the physical examination and a detailed revision of the medical history, a scale developed  
117 by the authors was used to discriminate between healthy and diseased cats, to confirm group  
118 assignment and to quantify the severity of the clinical condition (CGS scale; Table 1). This scale  
119 was derived from two previously published scoring systems, adjusted to match the specific  
120 research setting and melded together: the “Feline Chronic Gingivo-Stomatitis Veterinary  
121 Surgeon’s Questionnaire” and the scale developed by Lommer to evaluate the degree of buccal  
122 inflammation in cats with chronic stomatitis.<sup>19,20</sup> Some descriptors of both scales that were  
123 considered by the investigators unfeasible in the non-sedated cats, for example the stomatitis index  
124 that is part of the original scale from Lommer, were excluded. The total score of the CGS scale  
125 used in the current study ranged from 0 to 24. One of the investigators (HM) completed the scale  
126 with the help of the shelter volunteers, who fed and handled the cats routinely.

127

### 128 **Measurements**

129 The measurements were carried out in an area of the shelter the cats were familiar with, and were  
130 they normally spent most of their time, free to roam. An acclimatisation period of 15 minutes was  
131 allowed before the beginning of the trial so that the cats could get used to the presence of the  
132 investigators. Additionally, one of the volunteers of the shelter with whom the cats were very  
133 familiar was present during each measurement, in order to try to minimize the stress related to  
134 handling.

135 During the acclimatisation, the SMALGO was prepared and checked for accuracy as  
136 follows: the sensitive probe was equipped with the 3 mm tip and the unit selected (g). Thereafter,

137 the control unit was zeroed and the key “max” pressed, to enable the algometer to store the  
138 maximum force value recorded during the measurement.

139 During the measurements, the cats were allowed to choose the most comfortable position for  
140 them (either sitting or standing), and were minimally restrained in order to minimise the stress.  
141 The sensor tip of the SMALGO was applied on the right superior lip, at a level right above the  
142 canine root, of each cat, with a steady increasing force until a positive behavioural response was  
143 elicited; at that point, the sensor tip was removed and the last force measured was recorded as  
144 threshold. In this study vocalization, head withdrawal/turning, hissing or growling, attempt to  
145 escape and/or aggression/attempt to bite were defined as positive behavioural responses. In each  
146 cat, the measurements were carried out by two investigators with different level of expertise in  
147 pain assessment: a resident in Veterinary Anaesthesia and Analgesia (investigator A: HM) and a  
148 medicine student with no previous experience in pain evaluation in animals (investigator B: SP).

149 For each cat, the investigator who started the measurements was chosen randomly by  
150 flipping a coin. Each investigator obtained three threshold values from every cat included in the  
151 study; a minimal interval of 30 seconds was allowed between subsequent measurements carried  
152 out by the same investigator, in order to avoid temporal summation.<sup>21</sup> The means of the three  
153 measured values were used for statistical analysis. One hour-break was allowed before the second  
154 investigator could commence the measurements in the same cat. The entire trial was repeated after  
155 24 hours, with an inverted order of the investigators compared to the previous day.

156

157 **Statistical analysis**



158 Data were analysed with commercially available software (IBM SPSS Statistics 24, IBM  
159 Corporation, NY, USA; and SigmaPlot 10 and SigmaStat 3.5, SYSTAT Software Inc, CA, USA).  
160 P values < 0.05 were considered statistically significant.

161 Data distribution was analysed with the Shapiro-Wilk test. Paired t-test was used to assess  
162 normality of the data.

163 The intra-observer and the inter-observer reliability were assessed by calculating the intra-  
164 class correlation coefficient (ICC), with a two-way mixed Cronbach's Alpha model and 95%  
165 confidence intervals (CI; upper and lower bounds); the type of agreement selected was absolute  
166 agreement. The level of agreement (both inter- and intra- observer) was scored as follows: ICC <  
167 0.40= poor; ICC between 0.40 and 0.59= fair; ICC between 0.60 and 0.74= good; and ICC between  
168 0.75 and 1= excellent.<sup>22</sup>

169 A paired-T test was used to compare the thresholds measured in the two groups of cats  
170 (healthy versus diseased). The Pearson Correlation Coefficient was calculated to identify any  
171 correlation between the mechanical sensory thresholds measured with the SMALGO and the  
172 scores of the CGS scale.

173

## 174 **Results**

175 Data are presented as either means and SD or medians and ranges [max-min], depending on data  
176 distribution.

177 Thirty cats, of which 14 were spayed females and 16 neutered males, completed the trial.  
178 Their estimated age ranged from 1 to 18 years old and their body weight was 4 [3-5] kg. Of the 15  
179 cats with CGS, 6 were FELV and FIV positive.

180 The mechanical sensory thresholds were normally distributed when each set of  
181 measurements was analysed separately; however, data distribution was not normal when all the  
182 values were pulled together. The score of the CGS obtained from the diseased cats was 7 [3-12].

183 The inter-observer reliability was fair (ICC = 0.50), whereas the intra-observer reliability  
184 was good for both investigators A (HM; ICC = 0.73) and B (SP; ICC = 0.60). The details of  
185 reliability analysis are presented in Table 2. Data pertaining to sensory thresholds measured by the  
186 two investigators on day 1 and day 2 are shown in Figure 1.

187 There was no statistically significant difference between the thresholds measured in the cats  
188 with chronic gingivo-stomatitis ( $156 \pm 82$  g) and those measured in healthy cats ( $169 \pm 59$  g;  $P =$   
189  $0.35$ ; Figure 2). There was no statistically significant correlation between the scores of the CGS  
190 scale and the mechanical thresholds measured with the SMALGO in the group of cats with CGS  
191 (Pearson Correlation coefficient:  $0.047$ ;  $P = 0.87$ ).

192

## 193 **Discussion**

194 The main finding of this study is that the SMALGO is a reliable tool to measure mechanical  
195 thresholds in cats, regardless the expertise of the investigator and the repetition of the  
196 measurements. However, as demonstrated by a lack of difference in thresholds between healthy  
197 and diseased cats, the quantitative sensory testing performed with the SMALGO failed to detect  
198 and quantify pain in cats with chronic gingivo-stomatitis.

199 There may be various reasons for this outcome. The number of animals used in this study  
200 may be too small, the application site of the sensor tip may not be the most appropriate to detect  
201 chronic pain associated to gingivo-stomatitis, the mechanical thresholds may not increase in cats

202 with gingivo-stomatitis or, alternatively, the SMALGO may not be sensitive enough to  
203 differentiate between buccal pain and normal sensory response.

204 The sample size was determined based on the assumption that healthy cats would reasonably  
205 have thresholds of about 100 g, and that in cats with gingivo-stomatitis this value may increase by  
206 approximately 50%. The data obtained from the study cats suggest that such difference in  
207 thresholds may be much smaller than expected, as indicated by the very similar threshold values  
208 recorded in the two groups of cats. This suggests that a larger sample size may be needed to  
209 differentiate between healthy cats and cats with gingivo-stomatitis by means of quantitative  
210 sensory testing.

211 Regarding the application site for the sensor probe, this could also carry the risk for bias. A  
212 previous study that investigated the use of algometers other than the SMALGO in healthy cats  
213 concluded that the sensor probe applied at the mouth carries the potential for results  
214 misinterpretation, as a result of discomfort of the cats, when the device is applied near the head  
215 and can therefore be directly seen, or when the whiskers are mechanically stimulated.<sup>13</sup> Applying  
216 the sensor probe directly over the buccal mucosa, on the other hand, was found by the investigators  
217 unfeasible in untrained cats.

218 It is also possible that the SMALGO, whilst this study proved its reliability, repeatability and  
219 simplicity to use even for investigators with no previous experience in pain assessment, is not a  
220 sensitive enough instrument to detect a difference in thresholds between cats with normal and  
221 diseased buccal mucosa.

222 One interesting finding of this study is that the mechanical sensory thresholds not only were  
223 useless to discriminate between healthy and diseased cats, but also failed to serve as a measure of  
224 the severity of the disease, as demonstrated by their lack of correlation with the score of the CGS

225 scale. The CGS scale was used by the authors to quantify the severity of the gingivo-stomatitis.  
226 With the attempt to obtain a more comprehensive evaluation of the clinical condition, two different  
227 published scoring systems were melded together to obtain one single scale, used in the current  
228 study to quantify the severity of the CGS in the diseased cats.<sup>19,20</sup> The modified version implied  
229 the exclusion of a number of questions regarding certain details, such as specific location of the  
230 lesions within the oropharynx, which would have been impossible to answer without sedating the  
231 cats. The scale used in the current study, however, is not validated and might not be a sensitive  
232 instrument to quantify the severity of feline CGS.

233         One considerable limitation of this study is that cats with different stages and degree of CGS  
234 were recruited. This implies that the population was poorly standardised with respect to the  
235 severity of the clinical condition and, presumably, to the degree of pain and discomfort perceived  
236 by the cats varied between subjects. To complicate this picture, pain assessment in cats has always  
237 been considered extraordinarily challenging,<sup>6</sup> and feline gingivo-stomatitis is a chronic condition  
238 subject to re-acutisation episodes, whose associated pain is likely to be complex, with both chronic  
239 and acute components.<sup>3,4</sup>

240         Quantitative sensory testing in non-verbal patients has an important intrinsic limitation.  
241 Although the idea to quantify and measure pain is fascinating, this semi-quantitative method still  
242 relies on a subjective evaluation of the investigator, who is in charge to classify the behavioural  
243 responses to mechanical stimulation as either “positive” or “negative”. The cat may, indeed, turn  
244 its head because distracted by the surrounding environment or as an attempt to escape a painful  
245 stimulus. As a result, the force values recorded as threshold may be affected by procedural  
246 variabilities as well as by the level of attention of the cats.

247

248 **Conclusions**

249 Quantitative sensory testing performed with the SMALGO failed to detect any differences in  
250 mechanical thresholds between healthy cats and cats with chronic gingivo-stomatitis. Although  
251 the SMALGO provided reliable and repeatable measurements regardless the level of expertise of  
252 the investigator, its use cannot be recommended to evaluate pain associated to feline CGS.

253

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257 of the cat shelter and all the cats enrolled in this study.

258

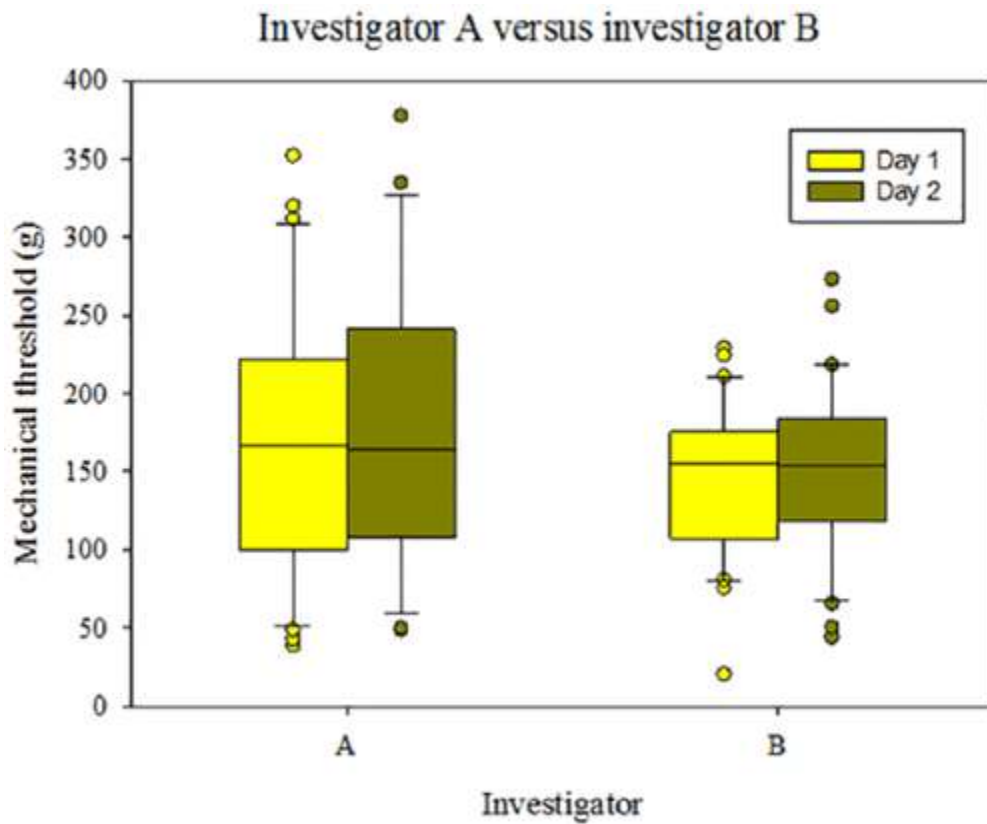
259 **Conflict of interest** The authors declared no potential conflict of interest with respect to the  
260 research, authorship, and/or publication of this article.

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263 **Figure legends**

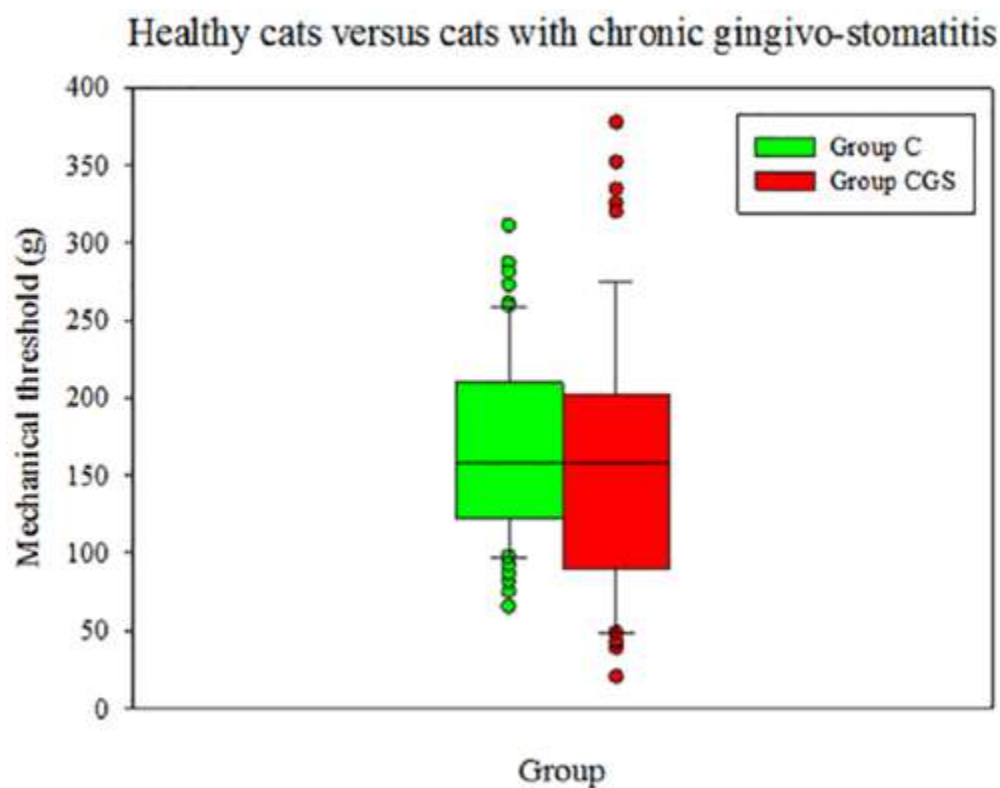
264 **Figure 1** Mechanical sensory thresholds (g) measured with the SMall Animal ALGometer by two  
265 independent investigators (investigator A and investigator B) in 30 cats of a shelter. Each  
266 investigator repeated the measurement twice, with 24 hour-interval between the two measuring  
267 sessions. The boxes represent the second and third quartiles, with the vertical line inside indicating  
268 the median value. The lower (25%) and upper (75%) quartiles are shown as horizontal lines either  
269 side of each box. The dots represent the outliers.



270

271

272 **Figure 2** Mechanical sensory thresholds (g) measured with the Small Animal ALGOmeter in 30  
273 cats of a shelter, of which 15 had Chronic gingivo-stomatitis (group CGS) and the remaining 15  
274 were healthy (group C; control). The boxes represent the second and third quartiles, with the  
275 vertical line inside indicating the median value. The lower (25%) and upper (75%) quartiles are  
276 shown as horizontal lines either side of each box. The dots represent the outliers.



277  
278

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