Fertility in adult bitches previously treated with a 4.7mg subcutaneous deslorelin implant

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Content

The absence of fertility problems in male dogs after a single treatment with deslorelin acetate (Suprelorin®) is well acknowledged, but reports on deslorelin application in the bitch and information concerning fertility after implantation however are limited. In this retrospective study, data concerning induced and spontaneous oestruses of 39 bitches from 17 breeds treated with deslorelin acetate implants (4.7mg Suprelorin®, Virbac, France) were retrieved to assess post-treatment fertility (determination of ovulation, pregnancy rate and litter size). Animals were grouped according to treatment characteristics: group 1 (Gr1) - females submitted to oestrus induction, presenting natural oestruses thereafter (n=19); group 2 (Gr2) - females re-implanted with 4.7mg deslorelin acetate to re-induce oestrus, showing subsequent spontaneous post implant oestruses (n=7); group 3 (Gr3) - females submitted to a 4.7mg deslorelin acetate implant for oestrus suppression, evaluated at subsequent spontaneous post-implant oestruses (n=13). Comparison of fertility traits between induced and post-treatment spontaneous oestruses in Gr1 and Gr2 (short-treatments), or between spontaneous oestruses after long-treatment schedules (Gr 3) showed a slightly better performance in the spontaneous compared to induced cycles: ovulation rate post-treatment was 97.1%, 94.1% and 94.4% and post-treatment pregnancy rate was 91.2%, 88.9% and 84,6% for groups 1, 2 and 3, respectively. Nevertheless, fertility in induced and post-treatment oestruses was considered normal. Moreover, the individual litter size did not differed within the group between induced and spontaneous cycles. From these findings, we concluded that treatment with 4.7mg deslorelin implants did not compromise the female dog fertility in subsequent oestruses.

Keywords: canine, estrus induction, GnRH agonist, deslorelin, fertility

41 **Introduction**

42 The search for a practical and successful method of oestrus control (induction or
43 suppression) in the bitch has been a frequent research topic in the past 25 years (Thun et al.
44 1977; Wright 1980; Shille et al. 1989; Kutzler 2005; De Gier et al. 2008; Kutzler et al.
45 2009). In the last decade, there has been an upsurge of publications describing the use of
46 slow gonadotropin-releasing hormone (GnRH) agonist releasing implants in several
47 species (Johnson et al. 2002; Padula and MacMillan 2005), predominantly in dogs
48 (Volkmann et al. 2006; Kutzler et al. 2009; Fontaine et al. 2011). The findings concerning
49 oestrus induction and subsequent ovulation rate have been encouraging (Fontaine et al.
50 2011).

51

52 The use of a slow release GnRH implant, containing 4.7mg of deslorelin acetate
53 (Suprelorin®, Virbac, France) in adult bitches has been described (Fontaine et al. 2011;
54 Walter et al. 2011). Deslorelin implants act by suppressing the pituitary-gonadal axis
55 (Trigg et al. 2001) in a dual phase mechanism: the implant initially stimulates the pituitary
56 axis (flare-up effect), releasing both follicle-stimulating hormone (FSH) and luteinizing
57 hormone (LH) and subsequently activates a complex network of transduction pathways
58 resulting in a down-regulation of the GnRH receptors through the inhibition of mRNA
59 coding for the β-subunits of the gonadotropins LH and FSH (Navarro and Schober 2012).
60 For suppression of oestrus in bitches, the duration of efficacy varies greatly, ranging from
61 2.1 months (Maenhoudt et al. 2014) to 27 months (Trigg et al. 2001; Sung et al. 2006).
62 The initial flare-up effect, in which oestrus is first induced before being prevented, is a
63 major disadvantage when deslorelin acetate is used for oestrus suppression. To date, no
64 satisfactory method to prevent induction of oestrus after insertion of the implant has been
65 described in bitches, despite the suggestions that short-term progestin administration would

66 be helpful (Corrada et al. 2006). Conversely, this flare-up effect has been successfully
67 applied to induce oestrus in dogs (Kutzler et al. 2009; Fontaine et al. 2011). Induction of
68 oestrus has been achieved in a large number of cases, shortly after implantation, regardless
69 of the stage of the cycle (Walter et al 2011, Fontaine et al. 2011). However, ovulation rate
70 may higher when females are in late anoestrus (van Haaften et. al 1994, Wolf et al., 2012).
71 Therefore, depending on the time the implant is left in place, it can be used for either
72 oestrus induction (implant removed shortly after insertion) or suppression (implant left in
73 place until inhibition of pituitary gonadotropins occur).
74
75 In order to optimize fertility in bitches, protocols for oestrus induction using a 4.7mg
76 deslorelin acetate implant the female should be clinically examined to verify the late
77 anoestrus (van Haaften et al 1994, Verstegen et al. 1999) and to discard an ovarian of
78 uterine pathology.
79
80 Several side effects have been reported following the insertion of a 4.7mg deslorelin
81 implant in bitches, including persistent oestrus probably due to ovarian cysts (Arlt et al.
82 2011), induced lactation, metropathies and miscellaneous problems such as vomiting,
83 cystitis and allergic reactions (Palm and Reichler 2012), which occur with variable
84 incidence.
85
86 The inhibition by GnRH agonists has been reported to be fully reversible on
87 discontinuation of the drug (Trigg et al. 2001). Reversibility of the effects of GnRH agonist
88 implants and its safety is a major issue when considering temporary contraception and the
89 female breeding is foreseen. Typically, most male dogs treated with an implant regain
90 fertility within a 12-month period (Trigg et al. 2006). In the bitch, Trigg and collaborators

91 (2001) described 6/9 (66.7%) pregnant females in the first spontaneous oestrus after
92 treatment with deslorelin acetate implant. However, there are no reports describing the
93 putative negative effects of the number of deslorelin treatments, on the post-treatment
94 fertility or on the litter size.
95
96 Data on the subsequent fertility in bitches after a single deslorelin implant is still scarce. As
97 pregnancy rate and prolificity (number of puppies/litter) is an important fertility trait in
98 purebred dogs intended for further breeding, we were interested in the female capacity to
99 ovulate and sustain pregnancy in subsequent oestrus periods after a total 4.7mg deslorelin
100 implant. Our study, retrospectively looked at 1) the reversibility of the effects of the
101 implant after short and long-term treatments (respectively following induction or
102 postponement of oestrus); 2) the fertility of treated bitches at subsequent induced and
103 spontaneous oestrus following treatment with subcutaneous implantation of 4.7mg
104 deslorelin acetate, which took into account ovulation and pregnancy rates, along with litter
105 size; and 3) comparison of the effects of single or multiple deslorelin 4.7mg implants on
106 the fertility of post-treatment spontaneous oestruses.
107
108 **Materials and methods**
109 This study used data from the clinical records of 39 bitches from 17 different breeds, with
110 ages ranging between 1 and 9 years (see Table 1 and 2) seen in consultation at CERCA
111 between 2008 and 2014. Inclusion criteria for selection of the clinical selection were the
112 existence of, at least, one treatment with slow releasing GnRH agonist implants, containing
113 4.7mg of deslorelin acetate (Suprelorin®, Virbac, France); the records of the breed and age
114 of the animals; and the existence of reproductive information concerning breeding in
115 induced or spontaneous oestruses, including data regarding ovulation, breeding timing,

116 pregnancy diagnosis and litter size. The retrospective information collected from
117 individual clinical records, in the university hospital database, included breed and age, aim
118 of the treatment (oestrus induction or suppression) and fertility data (confirmation of
119 ovulation, post-treatment pregnancy and litter size) in subsequent induced or spontaneous
120 post implant oestruses.
121 The mean age at the insertion of the first 4.7mg deslorelin implant was not significantly
122 different among groups (Table 1). Breeds represented in each group are summarized in
123 Table 2.
124
125 ***Treatment protocols***
126 All medical procedures were performed with the approval of the owners and in accordance
127 with the Ethics Committee of the Alfort Veterinary School.
128 All the animals used in the present study had been treated with 4.7mg deslorelin
129 subcutaneous implants, targeting oestrus induction (26/39; short-term treatment) or oestrus
130 suppression (13/39; long-term treatment).
131 Only females in anoestrus (vaginal swab proved the absence of oestrogen impregnation,
132 the progesterone levels were below 1ng/mL, and on ultrasound examination, the ovaries
133 showed absence of follicles or corpora lutea) and without ultrasound signs of ovarian cysts
134 or uterine disease were treated with 4.7mg deslorelin implant.
135 For the study, animals were grouped as follows (Figure 1):
136 Group 1 (Gr1) – Females submitted to one short treatment for oestrus induction, having
137 been mated at the induced and at two or more subsequent spontaneous post-treatment
138 oestruses (19/39).

139 Group 2 (Gr2) – Females submitted to multiple (between 2 and 4) successive short
140 treatments for oestrus induction (7/39); for some of these bitches, data existed regarding
141 two or more subsequent spontaneous post-treatment oestruses (3/7).
142 Group 3 (Gr3) – Females submitted to one long-term treatment for oestrus suppression,
143 which were bred in one or more spontaneous oestruses post-treatment (13/39).
144
145 In deslorelin short-term treatments, for estrus induction, the implant was left in place until
146 the day of ovulation (12.4 ± 2.9 days). Ovulation day was estimated based on progesterone
147 assays and ultrasound examination; the later was also used confirm ovulation. In long-term
148 treatments, for oestrus postponement, the implant was not removed (Figure 1).
149
150 In all groups, litter size was evaluated for bitches achieving parturition, except for 10/13
151 females in Gr3, which were ovariohysterectomized (OVH) at mid pregnancy, after being
152 bred at the first spontaneous post implant oestrus. In these animals, the number of embryos
153 was recorded.
154
155 ***Breeding management***
156 The breeding soundness evaluation was performed prior to the implantation procedure, and
157 the females considered apt to reproduction. The females in all the groups were bred after
158 identification of ovulation day (ovulation day = 0). Briefly, progesterone levels of 5 – 6
159 ng/mL were considered as indicative of day of ovulation; occurrence of ovulation was
160 estimated on the ultrasound changes of follicle appearance (change in intra-follicular
161 echoic pattern) on the day of ovulation, as described by Fontaine and colleagues (2011).
162 Breeding was achieved using natural mating or artificial insemination with fresh semen,

after semen assessment, according to the owner selection, twice, on post-ovulatory days 1 and 2.

Statistical analysis:

From the animals in every group, the retrieved data on reproductive traits was organised as representing fertility in the induced oestrus or fertility in spontaneous oestrus occurring after short- or long-term treatments with deslorelin implants. For each group and situation (induced *vs.* spontaneous oestruses), the parameters analysed included the number of subsequent oestruses, the occurrence of ovulation, the pregnancy rate and the litter size in each cycle.

Statistical analyses were performed using SAS 9.4 software. Student's t-test or one-way ANOVA were used for testing the differences between groups for quantitative variables. A two-way ANOVA was used to test the effects of group and animal frame on litter size. Qualitative variables were compared between groups using χ^2 test or Fisher's exact test. All tests used were two-sided with $\alpha = 0.05$. Data are presented as mean ± standard deviation (SD). The fertility parameters were analysed for each group in general (named as overall fertility traits), and independently for the total of induced and spontaneous post-treatment oestruses in each group.

Results:

The records covered data from 97 oestruses (respectively 53, 26 and 18 oestruses in Gr1, Gr2 and Gr3) and a total of 71 pregnancies (Table 3). When considering the total of oestruses, no significant differences were found on the overall ovulation rate between groups (respectively 92.5% (49/53), 92.3% (24/26) and 94.4% (17/18) in Gr1, Gr2 and Gr3). Likewise, the overall pregnancy rate was similar between groups (72% (38/53), 77%

188 - 20/26 and 72% (13/18) in Gr1, Gr2 and Gr3, respectively), if no distinction between
189 induced or spontaneous oestruses is considered. Overall, the average litter size was 5.21 ±
190 2.97.
191
192 In total, 36 records represented induced oestruses (19 in Gr1 and 17 in Gr2 females) and 61
193 records concerned spontaneous oestruses (34 in Gr1, 9 in Gr2 and 18 in Gr3).. In general,
194 ovulation occurred in 88.9% (32/36) of the induced oestruses and in 95.1% (58/61) of the
195 spontaneous post implant oestruses, the difference being not significant. Pregnancy rate did
196 not differ between induced and spontaneous post implant oestruses (p=0.05), although
197 tendency towards statistical significance was observed; it was 52.8% (19/36) in induced
198 oestruses and 85.2% (52/61) in spontaneous post implant oestruses. Non-ovulatory
199 situations encompassed ovarian cysts (in one Argentinian Dogo, for an induced oestrus)
200 and anovulation. The latter occurred both in induced (n=3, in Gr1, being two in Boxer
201 females and one in an English Bulldog) and spontaneous oestrus (n=3; these were found in
202 a 4 year old White Swiss Shepherd in Gr1, in a 4 year old German Shepherd, in Gr2; and
203 in a 6.1 year old Estrela Mountain Dog, in Gr3).
204
205 Information on previous interoestrous intervals for animals in this study was not recorded
206 in the individual clinical file. Nevertheless, table 4 summarises the intervals (in months)
207 between breeding records and therefore for the length of the period between the induced
208 and the first spontaneous oestrus for animals in Gr1, the intervals between sequential
209 induced oestrus and the intervals from the last implant-induced and the first spontaneous
210 oestrus for bitches in Gr2, as well as the intervals between Insertion of implant and first
211 spontaneous oestrus and between post-treatments spontaneous oestrus for animals in Gr3.
212 No differences were found within groups, or between groups for these parameters.

213

214 In Gr1, the information covered oestruses induced with 4.7mg deslorelin implants (n=19)
215 and spontaneous oestruses (n=34) (Tables 3 and 5), where the number of surveyed
216 oestruses per animal ranged from 1 to 4 (1.79 in average). Overall, the ovulation in this
217 group occurred in 92.4% (49/53) of the oestruses surveyed. The ovulation was more
218 frequent ($p<0.05$) in spontaneous (97.1%; 33/34) than in induced oestruses (84.2%; 16/19).
219 The pregnancy rates were also higher ($p\leq0.001$) in spontaneous (91.2%; 30/34) compared
220 to induced oestruses (36.8%; 7/19) (Table 3). The overall litter size was 5.51 ± 3.54
221 puppies (n=38) in this group (Table 5). Prolificity was similar between induced and
222 spontaneous post implant oestruses (respectively, 4.43±3.87 *vs.* 5.61±3.53 puppies).

223

224 In Gr2, data was gathered from a total of 17 successive induced oestruses (Tables 3 and 5)
225 and from nine spontaneous oestruses in a limited number of animals (n=4). The number of
226 successive induced oestruses surveyed ranged from 1 to 4, with a mean number of 2.43.
227 The overall ovulation rate for Gr2 was 92.3% (24/26). Ovulation did not differ either
228 between induced (94.1%; 16/17) and spontaneous oestruses (88.9%; 8/9), or between
229 multiple induced oestruses. Pregnancy rate did not differ between induced and spontaneous
230 oestruses (70.6%, 12/17 *vs.* 88.9%, 8/9, respectively; Table 3/4) or between multiple
231 induced oestruses (Table 3). The overall litter size was 5.10±1.89 in this group. It was
232 significantly higher in induced than in spontaneous oestruses (respectively, 5.83±1.58 *vs.*
233 4.00±1.85) ($p<0.05$), but a tendency towards statistical significance was found among
234 induced oestruses ($p= 0.054$) (Table 5).

235

236 Gr3 represented females that had been submitted to one long-treatment with a 4.7mg
237 deslorelin implant to prevent oestruses. We collected the results of pregnancy rate in the

238 first spontaneous oestrus in 13 females, and for the subsequent spontaneous oestruses with
239 breeding in only 2 females (average of 2.67 oestruses surveyed) (Tables 3 and 5). In
240 overall, ovulation in spontaneous oestruses occurred in 94.4% (17/18) of the cases. The
241 pregnancy rate in this group reached 72.2% (13/18). However pregnancy rates were
242 estimated in this group using data from females that whelped at term pregnancy (n=3) and
243 from females submitted to ovariohysterectomy at mid pregnancy (n=10). For those two
244 situations, pregnancy rates were respectively 100% (3/3) and 80% (8/10) (Table 3). No
245 differences were observed between the first and subsequent spontaneous oestruses after
246 one long-term treatment. The overall litter size in this group (Table 5) was 4.54±2.57
247 puppies; it was 4.6±3.78 puppies for females reaching term and 4.5±1.85 foetuses in
248 females ovariohysterectomized at mid-pregnancy.
249
250 In general, the length of treatments with 4.7mg deslorelin implant (short *vs.* long
251 treatments) did not affect the subsequent fertility of the bitches in respect to ovulation,
252 overall pregnancy rate, pregnancy rate at the first spontaneous oestrus post-treatment or
253 litter size. Litter size after induced oestruses (Table 5) did not differ between females in
254 Gr1 and Gr2 (4.43 ± 3.87 *vs.* 5.67 ± 1.15 and 5.33 ± 1.63 puppies, respectively for the Gr1
255 and the first and second induced oestruses in Gr2), even when dog frame was tested in
256 combination.
257
258 **Discussion**
259 This is the first study with detailed data regarding the fertility of the bitch (determination
260 of ovulation, pregnancy rate and litter size), after the use of a 4.7mg deslorelin implant for
261 oestrus induction or postponement that has examined single or multiple sequential
262 implantations. Furthermore, this study surveyed a larger number of females than previous

263 studies and allowed the comparison of fertility data between the deslorelin-induced oestrus
264 and subsequent spontaneous oestrus cycles.
265
266 In the present study, overall ovulation rates at induced oestruses (88.9%) were higher than
267 those reported earlier by Fontaine (Fontaine et al. 2011) for 25/32 bitches (78.1%) with a
268 single short treatment. In addition, we found no differences in the ovulation rate for
269 induced oestruses between groups with one or multiple treatments. Furthermore, animals
270 submitted to one induction treatment (Gr1) showed a slightly lower incidence of
271 anovulation (15.8%) compared with the incidence of anovulation (18.7%) in previous
272 studies (Volkmann et al. 2006; Fontaine et al. 2011; von Heimendahl and Miller 2012),
273 whereas in animals submitted to multiple treatments for oestrus induction (Gr2) the
274 anovulation incidence was rather lower (5.9%). A possible explanation for the lower
275 anovulation incidence may relate to the insertion of the implant in late anoestrus for most
276 females in groups 1 and 2. Fontaine (Fontaine et al. 2011) showed that higher ovulation
277 rates occur when bitches are induced in late anoestrus (87.5%) rather than early anoestrus
278 (62.5%). In our study, anovulation was seldom observed in subsequent spontaneous
279 oestruses. The one exception was a female from Gr2 – anovulation occurred after an
280 interoestrus interval of 8 months at her first spontaneous oestrus after two consecutive
281 deslorelin implant treatments.
282
283 Although a tendency was observed (p=0.054), pregnancy rate was not significantly
284 different between induced (52.8%) and spontaneous post implant oestruses (85.2%). In our
285 study, pregnancy rate obtained in induced oestruses with deslorelin acetate agree with the
286 results of Walter et al (Walter et al. 2011), in Beagle bitches, and Fontaine (Fontaine et al.
287 2011) in a multi-breed study. The design of our study did not allow us to determine the

288 differences for the results obtained between induced and spontaneous post implant
289 oestruses. The differences could be due to several factors, some of them unavailable in the
290 clinical files. Possible contributing factors might include individual sensitivity to GnRH
291 agonist effects (Concannon et al. 2006); the age and parity of the female at each service;
292 the type of service and the fertility of the male dog selected by the owner; the moment of
293 anoestrus at the insertion of the implant; or the existence of metropathies. The present
294 study does not allow clarifying the existence of breed influences on either the fertility at
295 induced oestrus or the post-treatment fertility. The analysis of the intervals between
296 consecutive records for each female showed that in Gr1 and Gr2 some females were bred
297 shortly after pregnancy. A lower pregnancy rate was recorded after the first spontaneous
298 oestrus post-treatment, and was probably due to two females that were over 6 years of age.
299 Litter size did not differ among females in the three groups. In general, in the present study
300 the litter size was rather small. Although, litter size was quite constant for individual
301 females, therefore suggesting that other factors might be influencing: the differences in
302 female's fertility related to age or uterine status, or the differences between breeds and
303 frames (Borge et al. 2011) represented in each group. Genetic influences on litter size in
304 dogs have been acknowledged as an interaction between the breed and the age (Borge et al.
305 2011). Nevertheless, the litter size did not differ significantly between the induced and the
306 subsequent spontaneous post implant oestrus, suggesting that deslorelin treatment had no
307 effect on the post-treatment litter size in treated bitches.
308
309 Comparison between induced and post-treatment spontaneous oestruses showed that
310 deslorelin treatment did not seem to affect pregnancy rate, whether it was used in short
311 (induction) or long (postponement) treatments, or in single or multiple consecutive
312 treatments. The fact that deslorelin acetate controls the canine oestrus cycle by interfering

313 with the hypothalamic-hypophyseal system modulating gonadal function (Navarro and
314 Schober 2012), and not the uterus or the ovary itself, might represent a favourable factor.
315 However, it is also possible that, at particular points of the canine oestrus cycle, deslorelin
316 treatment for oestrus induction may encounter a hypophyseal deficit in gonadotropins,
317 particularly of LH, that may impair the pre-ovulatory LH surge, therefore predisposing the
318 female to anovulation (Fontaine et al. 2011) or to the development of ovarian cysts (Arlt et
319 al. 2011). Still, the lack of experiments establishing the existence of differences in breed
320 sensitivity to deslorelin implants does not allow us to discard this possibility. The nature of
321 the present study does not allow the differentiation between an individual characteristic
322 and breed sensitivity in respect to the effects of anovulation in induced or spontaneous post
323 implant oestruses. This issue should be addressed in future studies.
324
325 **Conclusion**
326 The present study showed that ovulation and pregnancy rates, as well as litter size,
327 presented equal or better results in post-treatment spontaneous cycles compared to those of
328 induced oestruses. This suggests that the use of a 4.7mg deslorelin implant for a short
329 (oestrus induction) or long treatment (oestrus suppression) does not compromise fertility
330 after treatment.
331
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337

338 **Conflict of interests:**

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342

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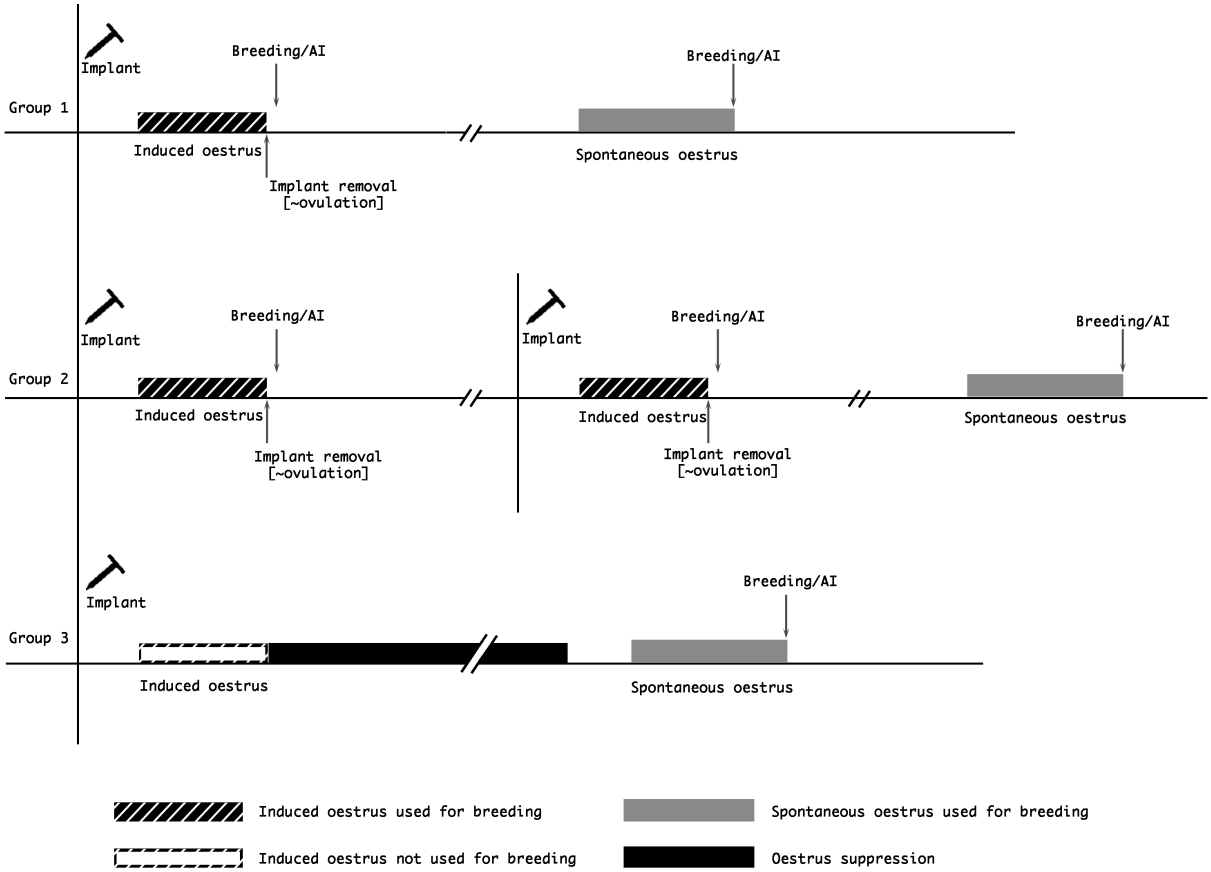
414

TABLES AND FIGURES

Figure 1 – Diagram of the study protocol (Gr1, Gr2 and Gr3)



420 Table 1 – Mean age, in years, at insertion of the first 4.7mg deslorelin implant in bitches of
421 group 1 (Gr1, one short-term treatment for oestrus induction), group 2 (Gr2, multiple short-
422 term treatments for oestrus induction) and group 3 (Gr3, one long-treatment to prevent
423 oestrus). *n* = number of bitches
424

Treatment groups	*n*	Average (y)	Min	Max	SD
Gr1	19	3.46	1.4	8.8	2.01
Gr2	7	2.69	1.5	5.5	1.44
Gr3	13	2.98	1.2	5.6	1.23
Total	39	3.26	1.2	8.8	1.69

425

426 Table 2 – Dog breeds represented in group 1 (Gr1, one short-term treatment for oestrus
427 induction), group 2 (Gr2, multiple short-term treatments for oestrus induction) and group 3
428 (Gr3, one long-treatment to prevent oestrus). *n* = number of bitches.

Breed	Gr1 (n)	Gr2 (n)	Gr3 (n)	Total (n)
Argentinian Dogo	1	1	-	2
Boxer	2	-	-	2
Briard	2	-	-	2
Bull Terrier	1	-	-	1
Doberman	1	-	-	1
English Bulldog	1	1	-	2
German Shepherd	6	2	-	8
Rottweiler	1	-	-	1
Shetland	1	-	-	1
Weimaraner	1	-	-	1
White Swiss Shepherd	2	-	-	2
Australian Shepherd Mini	-	1	-	1
Cocker Spaniel	-	2	-	2
Beagle	-	-	10	10
Cane Corso	-	-	1	1
Estrela Mountain Dog	-	-	1	1
Malinese	-	-	1	1
Total	19	7	13	39

429

430

431 Table 3 – Summary of the prevalence of ovulation and pregnancy after induced and
432 spontaneous oestruses in females from group 1 (Gr1, one short-term treatment for oestrus
433 induction), group 2 (Gr2, multiple short-term treatments for oestrus induction) and group 3
434 (Gr3, one long-treatment to prevent oestrus). *n* = number of oestruses

Group	Type of oestrus		*n*	Ovulation		Pregnancy	
				Yes	No	Yes	No
Gr1	Induced (single)		19	16	3	7	12
	Spontaneous	1	19	18	1	16	3
		2	10	10	0	10	0
		>3	5	5	0	5	0
		Total	34	33	1	31	3
Gr2	Induced (multiple)	1	7	6	1*	3	4
		2	7	7	0	6	1
		>3	3	3	0	3	0
		Total	17	16	1*	12	5
	Spontaneous		9	8	1	8	1
Gr3	Spontaneous 1		13	13	0	11	2
	Spontaneous ≥2		5	4	1	2	3
Total			97	90	7	71	26

435 • - Ovarian cyst

436

Table 4 – Intervals in months (average ± SD [minimum : maximum] and number of oestrus intervals) between the last induced and the first spontaneous oestrus, the sequential induced oestruses, from the last implant insertion to the spontaneous oestrus used for breeding and between spontaneous oestruses.

Intervals (months) between	Gr1	Gr2	Gr3
(last) Induced and first spontaneous oestruses	11.58±5.04 [4 : 24] n=19	9.00±2.37 [7 : 12] n=4	-
Sequential induced oestruses	-	9.60±2.99 [5 : 12] n=10	-
Spontaneous oestruses	11.07±5.66 [2 : 20] n=15	9.40±4.28 [3 : 13] n=6	14.50±4.12 [14 : 20] n=4
Insertion of implant and first spontaneous oestrus	-	-	20.33±8.44 [10 : 30] n=12

Table 5 – Summary of data for litter size obtained at induced and spontaneous oestruses in females from group 1 (Gr1, one short-term treatment for oestrus induction), group 2 (Gr2, two or more short-term treatments for oestrus induction) and group 3 (Gr3, one long-treatment to postpone oestrus).

n = number of litters

Group	Oestrus		*n*	Mean	SD	Minimum	Median	Maximum
Gr1	Induced (single)		7	4.43	3.87	1.00	3.00	12.00
	Spontaneous	1	15	6.00	3.74	1.00	5.00	14.00
		2	10	6.20	3.68	1.00	6.50	12.00
		>3	5	4.20	2.17	1.00	4.00	7.00
		Total	31	5.61	3.53	1.00	5.00	14.00
Gr2	Induced (multiple)	1	3	5.67	1.15	5.00	5.00	7.00
		2	6	5.33	1.63	3.00	5.00	8.00
		>3	3	7.00	1.73	5.00	8.00	8.00
		Total	8	5.83	1.58	2.00	3.50	8.00
	Spontaneous		8	4.00	1.85	2.00	3.50	8.00
Gr3	Spontaneous 1		11	5.00	2.49	2.00	5.00	10.00
	Spontaneous ≥2		2	2.00	1.41	1.00	2.00	3.00