

MINIMALLY INVASIVE CLEFT PALATE REPAIR USING INJECTABLE HYDROGELS

436

C. Martínez-Álvarez, B. González-Meli, B. Berenguer, I. Paradas-Lara, Y. López-Gordillo and E. Martínez-Sanz

Facultad de Odontología. Universidad Complutense de Madrid, Spain

In cleft palate (CP) patients, traditional palatoplasty seems to impair mid-facial growth due to the extensive mucoperiosteal flaps. In this study we aimed to develop a novel flapless procedure for cleft palate repair by injecting a BMP-2 containing hydrogel: the injection/adhesion technique.*

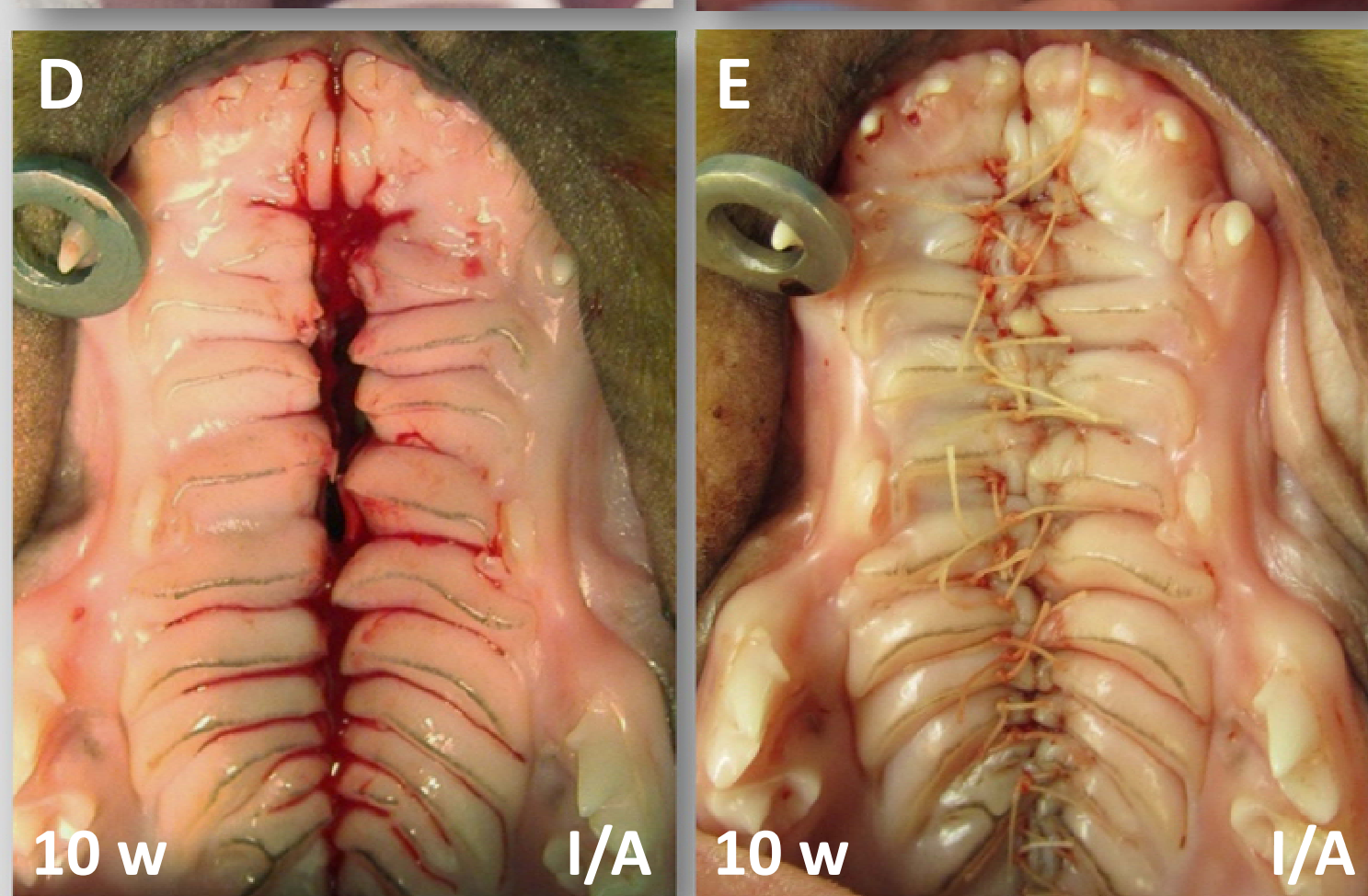
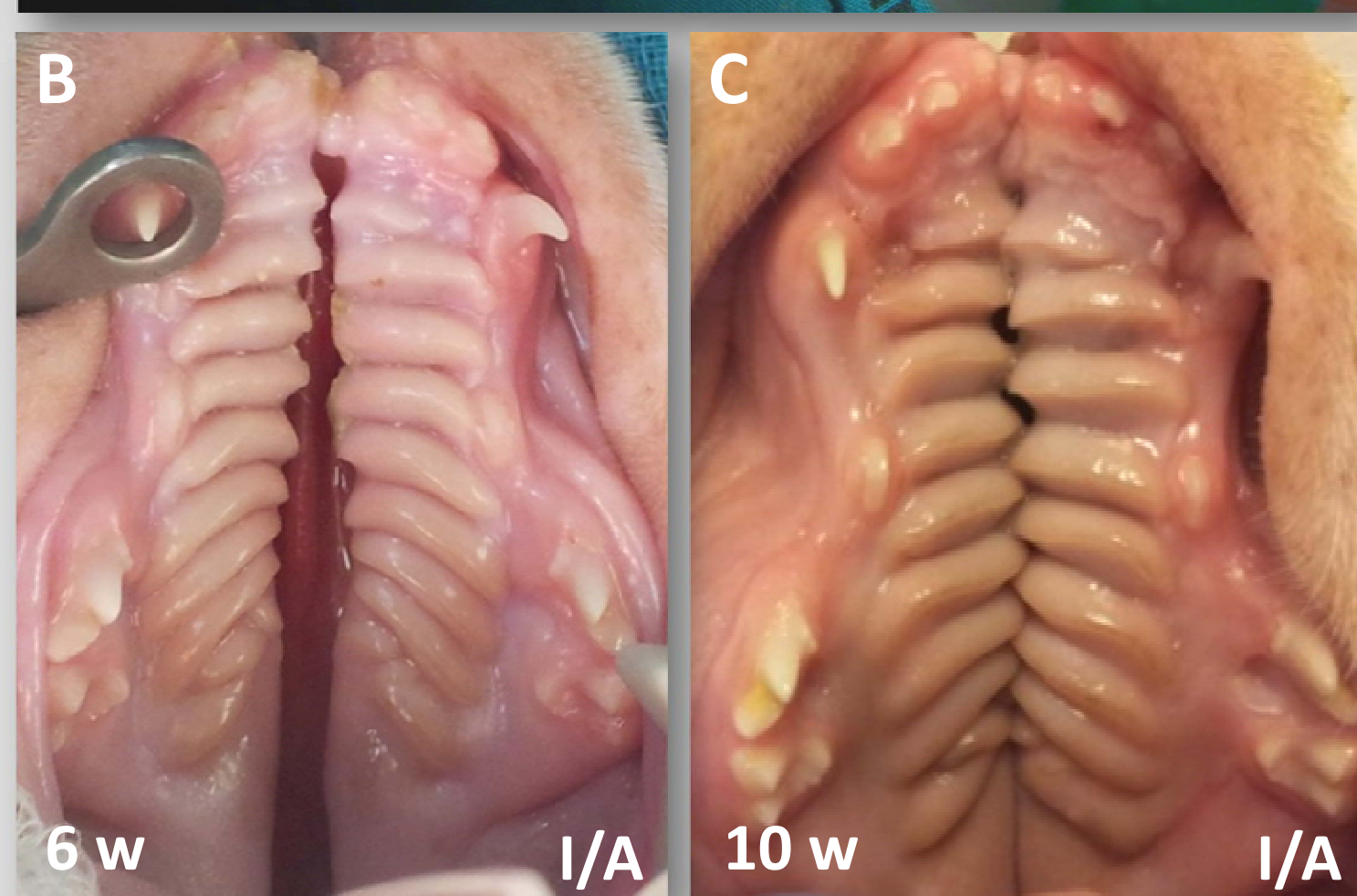
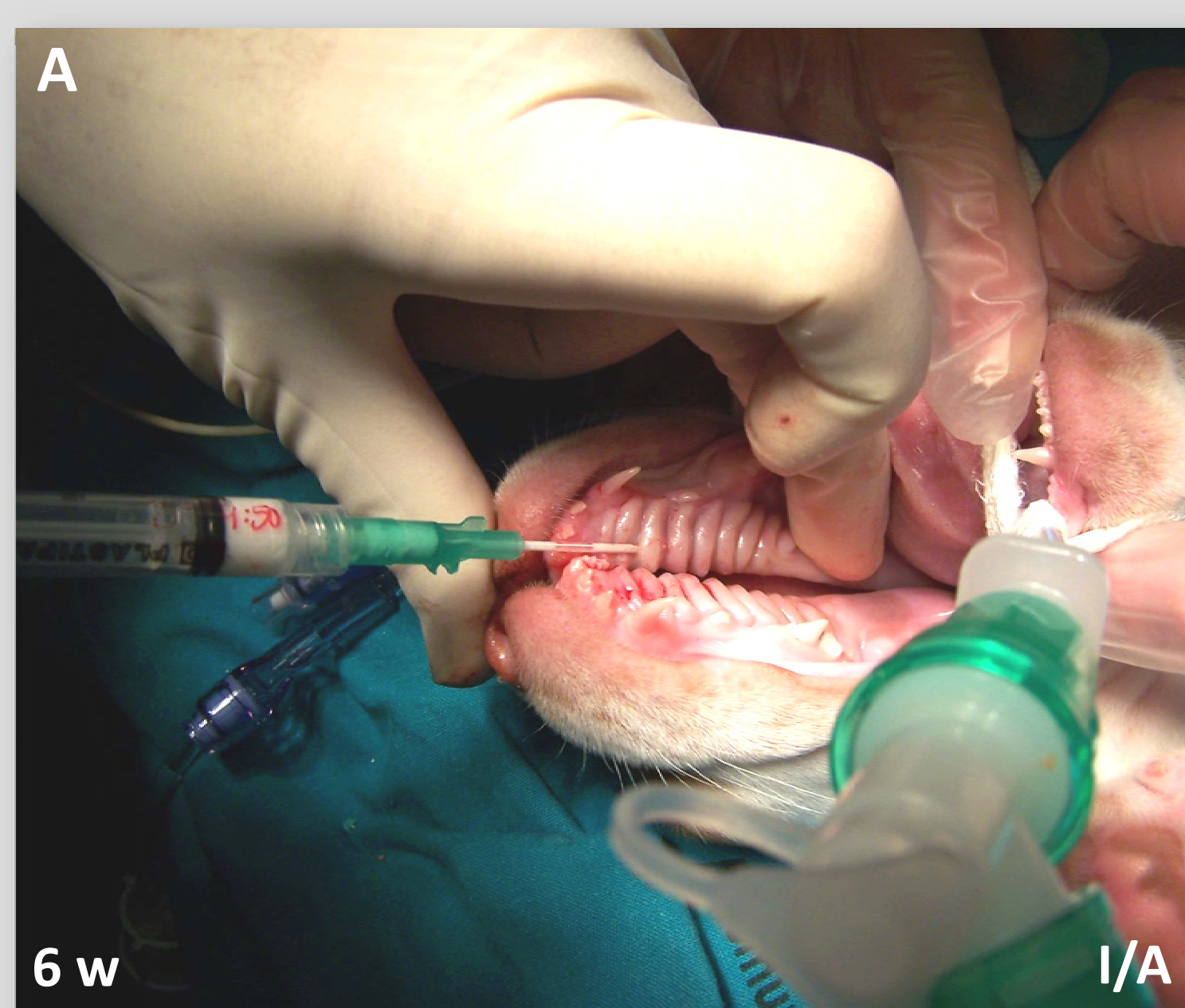
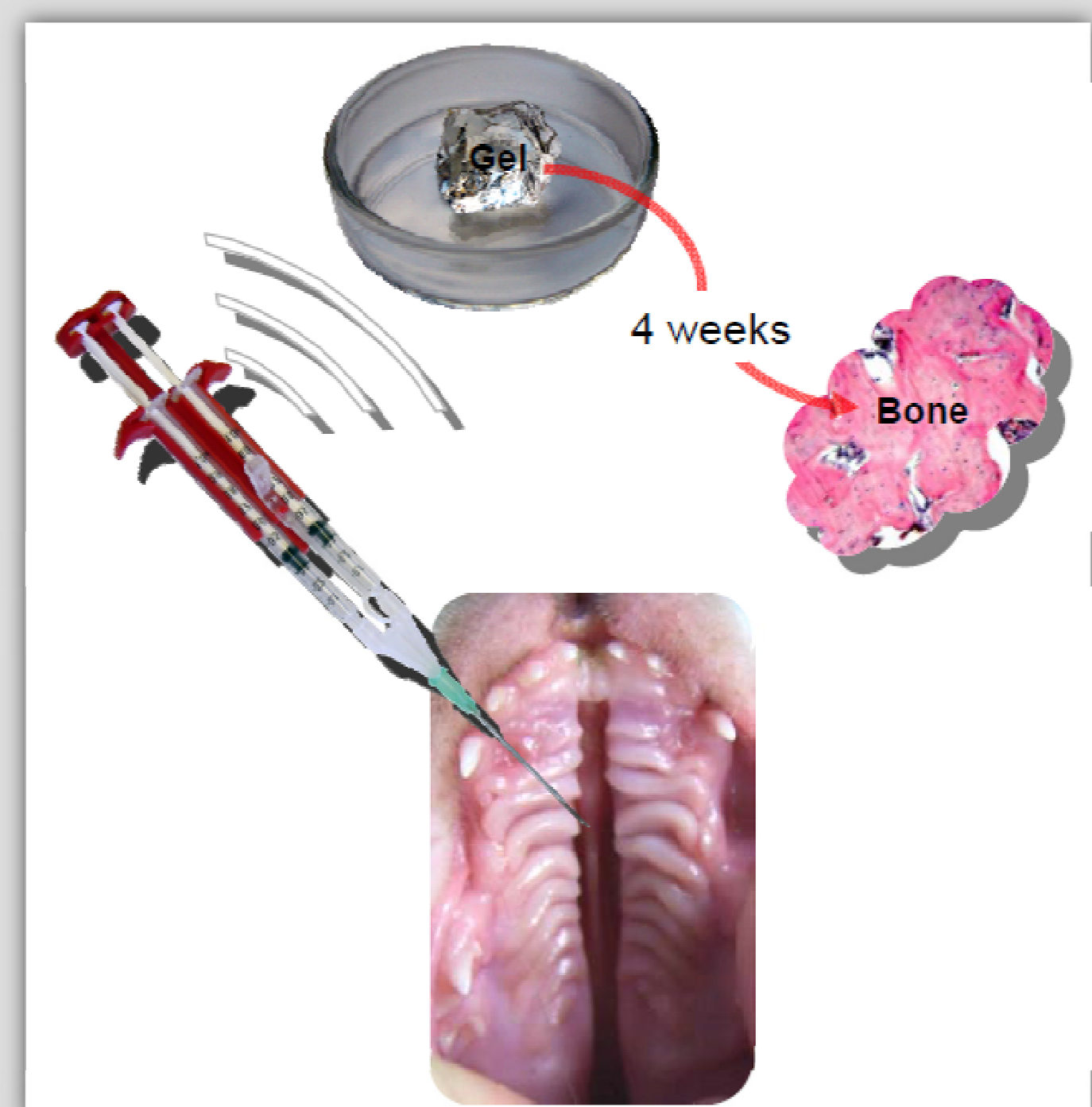


Figure 1. (A) Hyaluronic acid-based hydrogel injection into the cleft palate margins in a 6 weeks old dog. (B) Palate of a dog taken before the gel injection at week 6 and (C) four weeks after the gel injection. Notice the separation of the cleft palate margins in (B) and their augmentation and the almost total contact between them in the midline in (C). (D) Cleft palate margins refreshed in an injected dog at the age of 10 weeks. (E) Closure of the cleft by using U-sutures.

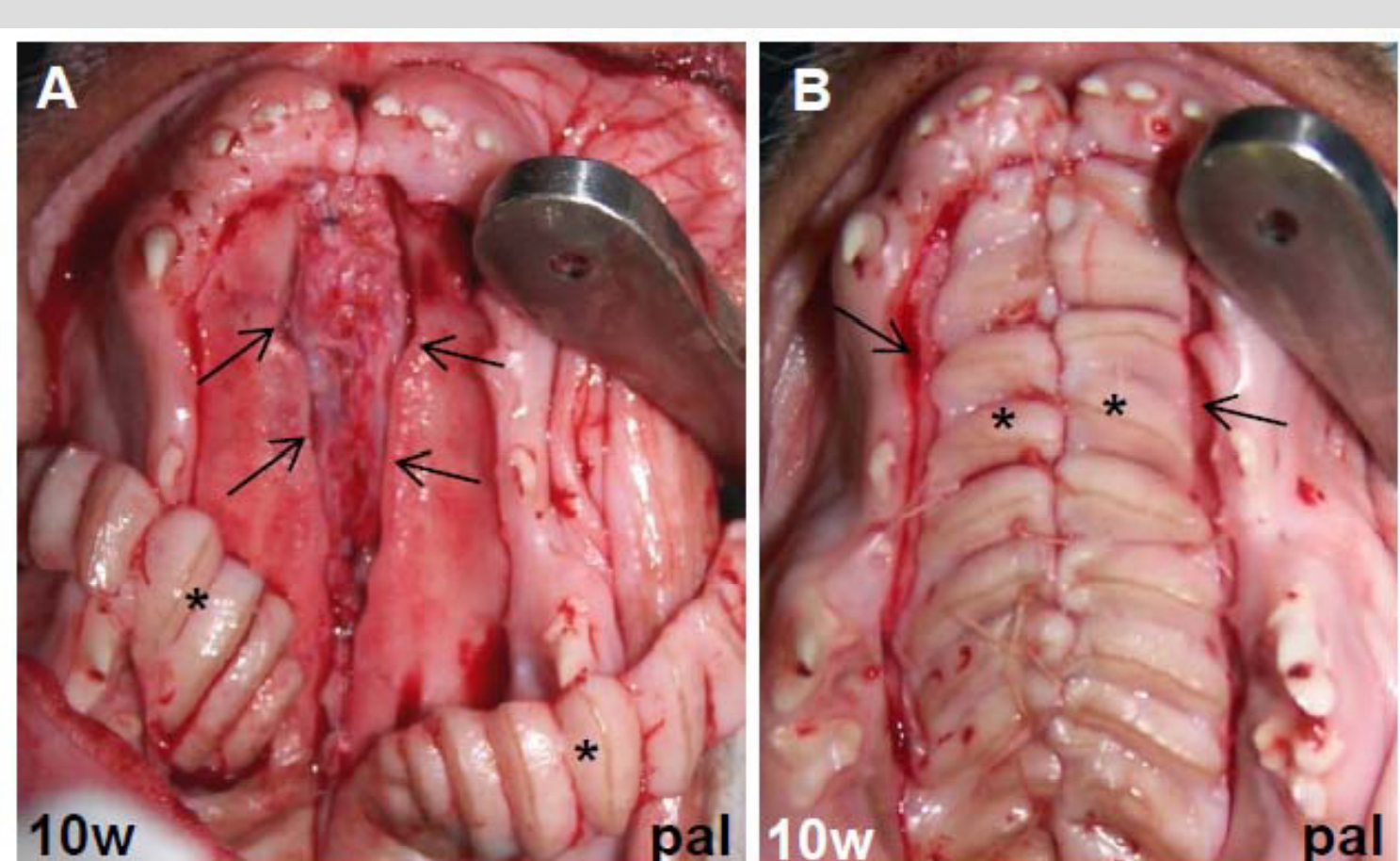


Figure 2. (A) Flaps (asterisks) obtained in a dog operated by flap palatoplasty at week 10. Notice the cleft of the palatal bones (arrows). (B) After having sutured the nasal mucosal flaps, the oral flaps (asterisks) are sutured in the midline. Observe the antero-lateral area uncovered by mucosa (arrows).

We used the Old Spanish Pointer dog breed, which develops CP in 15-20% of the offspring. Twenty pups were included in 4 groups. A: normal palate controls (n=5), B: cleft palate controls (untreated) (n=4), C: cleft palate individuals repaired with 2-flap palatoplasty (n=6) and D: cleft palate individuals repaired with the injection/adhesion technique (n=5) as the novel experimental approach. The technique consisted in the injection of a hyaluronan based hydrogel (Termira, Sweden), containing BMP-2 and nanosized hydroxyapatite, in the CP medial edges of pups aged 6 weeks, followed by the removal of the overlying mucosa and suture of the medial edges of pups aged 10 weeks. Traditional 2-flap palatoplasty was performed in the individuals of group C. Occlusal photographs and CT scans were obtained at weeks 5, 8, 20 and 30. The two treatment options were compared in terms of results of repaired tissues, difficulty, duration, and complications.

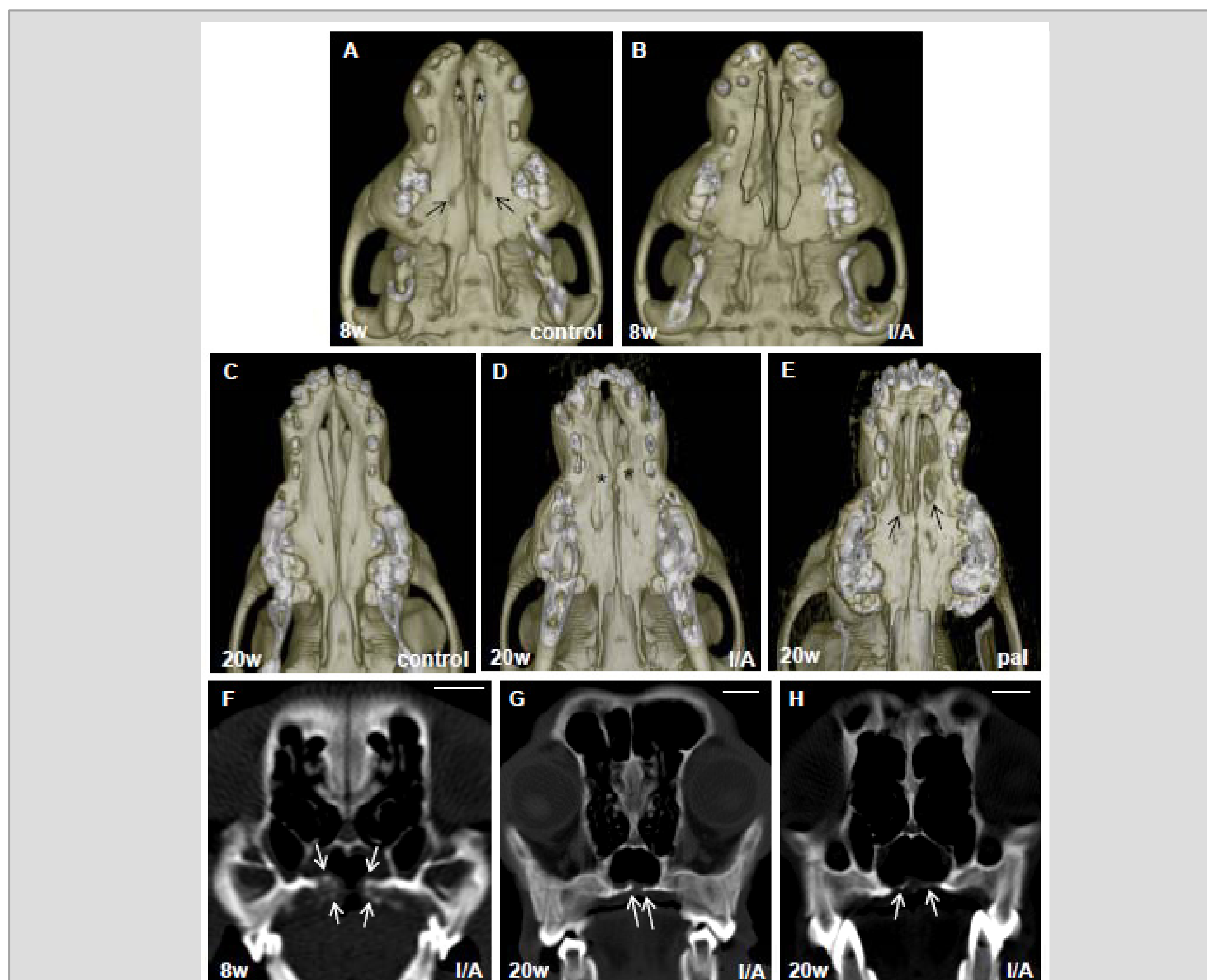


Figure 3. (A-E) 3D reconstructions of the palatal bones of cleft dogs at the age of 8 wk (A), (B), and 20 wk (C-E). (A), (C) correspond to control dogs, (B), (D) correspond to dogs operated with the injection/adhesion technique, and the dog in (E) was treated with 2-flap palatoplasty. (A), (B) Notice the nasal bones visualized through the cleft (asterisks in A) and the palatine foramina (arrows in A) in the control dog, which are not seen in the injected one at the same age (B). New bone is present at the oral and medial palatal surfaces in the injected dog (surrounded area in B). (C-E) Areas of extra-bone appear at the margins of the palatal bones in the injected dogs (asterisks in D), which are not observed in the control (C), reducing the cleft size. In the 2-flap palatoplasty treated dogs, bone defects are observed (arrows in E). (F)-(H) CT scans from a cleft dog treated with the injection/adhesion technique at 8 wk (F) and 20 wk (G, H). Notice that 2 wk after the gel injection, new bone is observed at the cleft palate margins (arrows in F), which is more clearly visible in some areas three months later (arrows in G) and faint in some other areas (arrows in H). Bar: 1 cm.

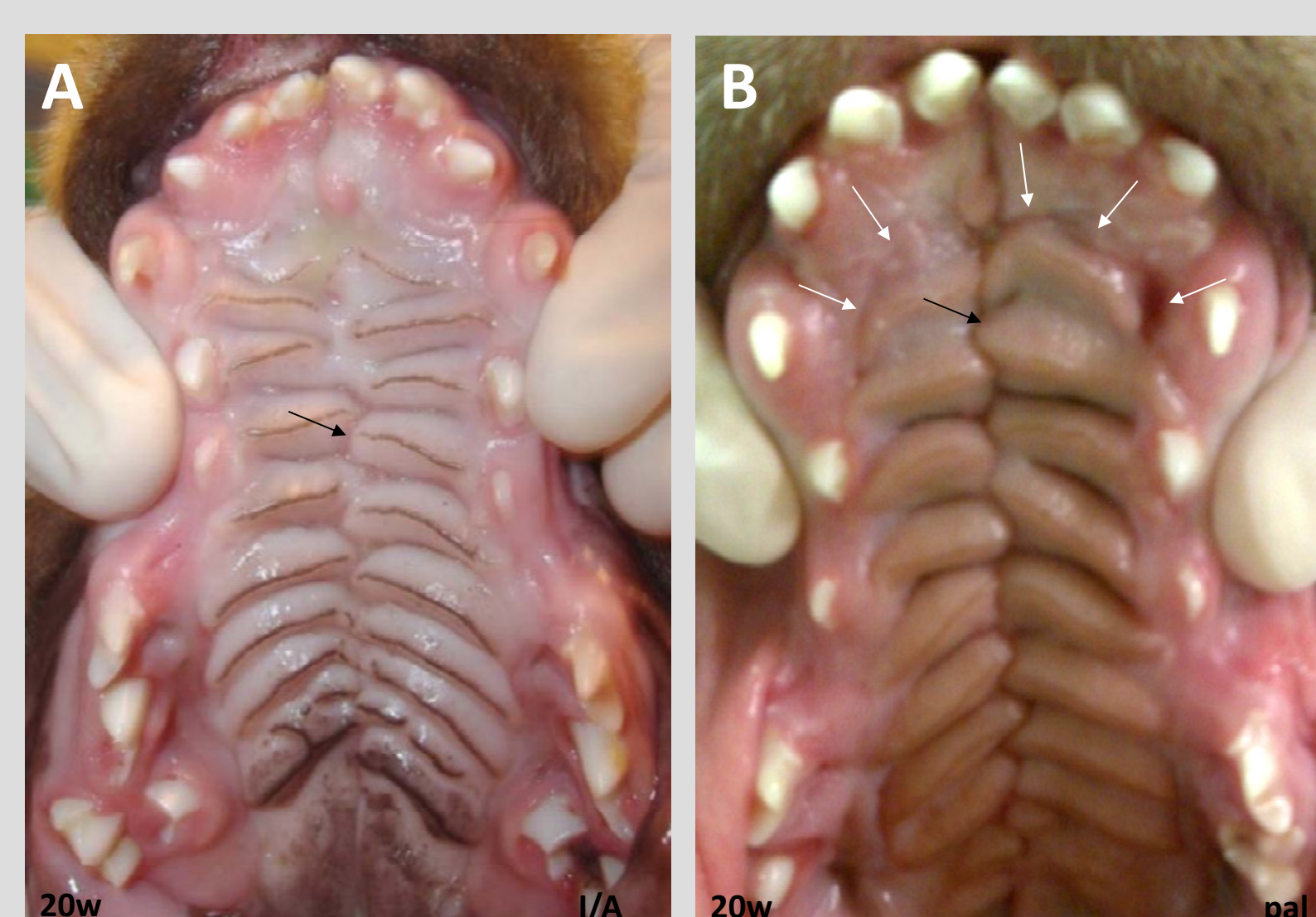


Figure 4. Palate from 20 weeks old dogs whose clefts were treated either with the injection/adhesion technique (A) or traditional palatoplasty (B). Observe a scar in the midline of both dogs (black arrows) and an antero-lateral scar only in the dog treated with palatoplasty (white arrows in B).

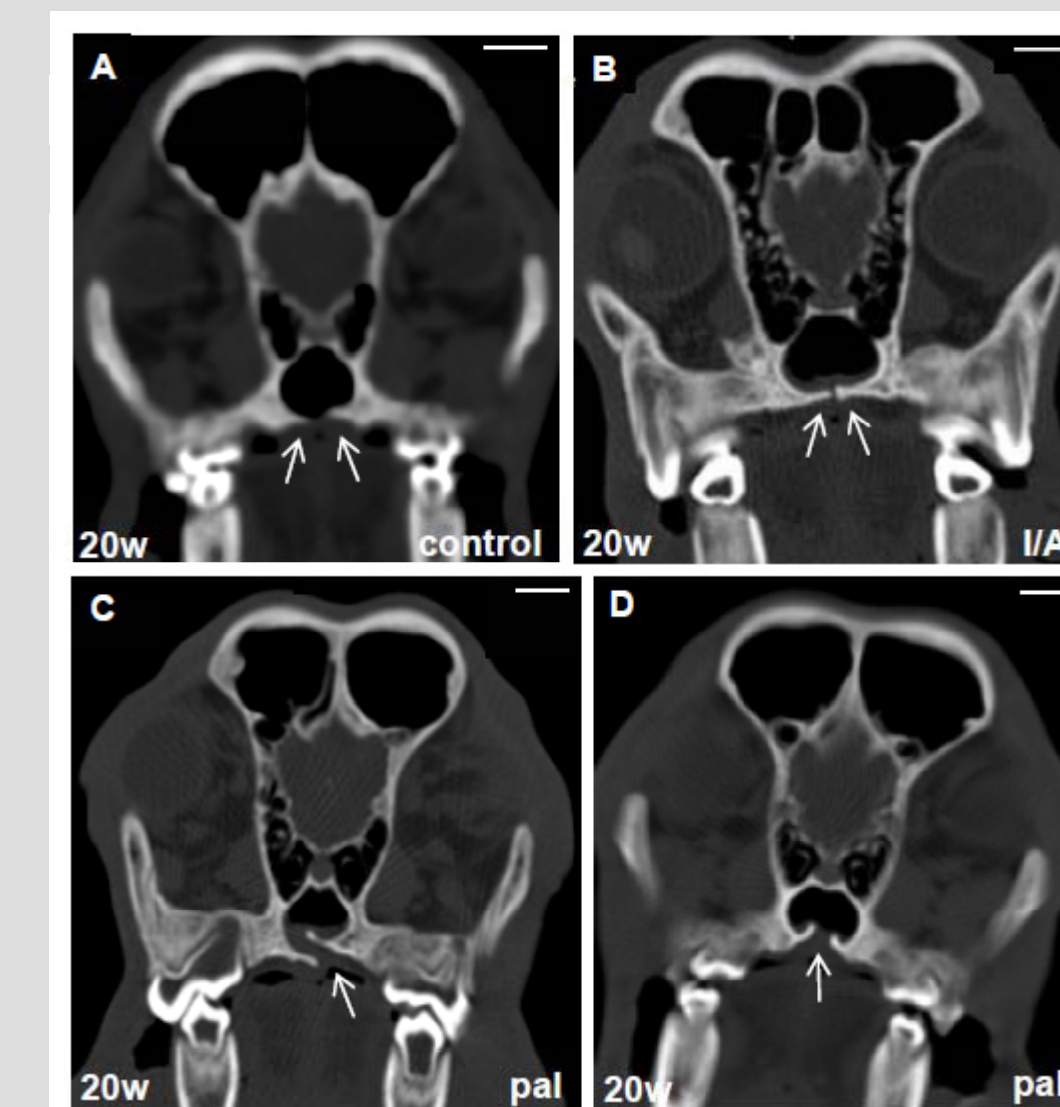


Figure 5. CT scans from 20 weeks old cleft dogs non-treated (A) or treated with the injection/adhesion technique (B) or with 2-flap palatoplasty (C, D). Notice the horizontal (arrows in A, B), approached (arrows in B), overlapped (arrow in D) and bent (arrow in D) disposition of the palatal bones in each case. Bar: 1 cm.

In the experimental group, four weeks after the hydrogel injection the cleft palate margins had reached the midline and engineered bone enlarged the palatal bones. Removal of the medial edge mucosa and suturing allowed complete closure of the cleft. Compared to traditional palatoplasty, the injection/adhesion technique was easier, and the post-surgical recovery was faster and better, although it required two sessions. Lateral scar and denuded bone were avoided with the experimental approach. The palatal bones did not show overlapping or bone defects in the experimental or untreated controls, as observed in the 2-flap palatoplasty group. No adverse effects were observed in the pups' palates, although small fistulas appeared in the first experimental pups.

We present herein a feasible minimally invasive technique for cleft palate repair upon injectable scaffolds in a dog model of congenital cleft palate: the injection/adhesion technique. Preliminary results suggest better maxillary growth. Therefore, this technique may represent an attractive clinical alternative to traditional palatoplasty for cleft palate patients.

* Martínez-Álvarez C, González-Meli B, Berenguer-Froehner B, Paradas-Lara I, López-Gordillo Y, Rodríguez-Bobada C, González P, Chamorro M, Arias P, Hilborn J, Casado-Gómez I, Martínez-Sanz E. "Injection and adhesion palatoplasty: a preliminary study in a canine model" *J Surg Res*, 2013. In press. doi:p11: S0022-4804(13)00207-2. 10.1016/j.jss.2013.03.009.