

## Research report

# Effect of cervical sympathetic ganglionectomy on facial nerve reconstruction using polyglycolic acid-collagen tubes



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## ABSTRACT

A polyglycolic acid-collagen (PGA-c) tube was used as an artificial nerve guide during facial nerve reconstruction performed in a canine model of stellate ganglion block (SGB). The model was generated using a cervical sympathetic ganglionectomy. We evaluated the effects of blood flow on nerve regeneration.

First, we resected the left cervical sympathetic ganglion in beagles ( $n = 6$ ). We assessed buccal mucosal blood flow and nasal skin temperatures once per week for 12 weeks and Horner's sign 2, 4, and 6 months after resection. We compared these values to those measured prior to resection. Blood flow was increased for 6–11 weeks, but sympathetic control remained blocked after 6 months.

Second, we divided beagles into 3 groups: resection models (negative control), from which 7 mm of the left facial nerve buccal branch was resected ( $n = 5$ ); reconstruction models, which underwent nerve reconstruction using PGA-c tubes ( $n = 6$ ); and SGB + reconstruction models, which underwent a left cervical sympathetic ganglionectomy immediately after reconstruction ( $n = 6$ ). The right side of the face served as control ( $n = 17$ ). Nerve regeneration was significantly greater in the SGB + reconstruction model dogs than in the reconstruction model dogs, as measured by both electrophysiological and morphological analyses at postoperative week 12. In particular, motor nerve conduction velocity was increased approximately 2-fold ( $p = 0.018$ ). We were able to generate an SGB model with long-term increased blood flow facilitated by the promotion of facial nerve regeneration by PGA-c tubes.

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## 1. Introduction

When peripheral nerves are damaged, their axons undergo Wallerian degeneration and regression. Subsequently, Schwann cells surrounding the peripheral axons divide and proliferate, facilitating nerve regeneration by forming the so-called Bungner's band, which induces the extension of elongated side buds from the proximal severed stump (Raivich and Makwana, 2007). However, extension from the proximal stump to the distal stump is difficult if the distance from the injury or defect is large or if the regenerative process is impeded by the interposition of connective scar tissue. Cases of incomplete nerve regeneration, such as neuromas, can lead to permanent paralysis, pathological synkinesis, and dysreflexia (Kerrebijn and Freeman, 1998; Glaus et al., 2011). At present,

autogenous nerve transplant is considered the gold standard treatment (Lundborg et al., 2004) in cases where direct suture of the nerve cannot be performed. However, the thickness and length of the nerve to be collected is limited by the pain and paralysis that will occur at the donor site (Gerth et al., 2015). Nerve guide tubes using various artificial materials have been used to overcome these problems. These tubes can be used instead of autogenous nerve transplantation (Gaudin et al., 2016). The polyglycolic acid-collagen (PGA-c) tube is a nerve-guiding tube lined with collagen sponge contained in a lumen knitted with a bioabsorbable PGA fiber and covered with collagen on the surface (Nakamura et al., 2004). The collagen filling consists of atelocollagen extracted from the skins of enzyme-treated pigs treated to remove antigenic telopeptides. This allows for bioresorbability and ensures that the material is suitable for nerve regeneration using thermal crosslinking. When this tube is connected to the nerve stump, it prevents invasion of fibrous tissue and incorporates germinated nerve fibers into the periphery. Consequently, although neural regeneration is promoted both functionally and histologically (Nakamura et al., 2004; Yoshitani et al., 2007; Suzuki et al., 2009; Yamanaka et al.,

Abbreviations: PGA-c tube, polyglycolic acid-collagen tube; SGB, stellate ganglion block; MCV, motor nerve conduction velocity; TEM, transmission electron microscope.

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2014), a long period is necessary for recovery (Inada et al., 2004, 2005, 2007; Seo et al., 2008, 2016).

Yoshitani et al. (2007) compared dogs that had undergone phrenic nerve reconstruction using PGA-c tubes sheathed in a perivascular fat pad with dogs that had undergone nerve reconstruction using an unsheathed PGA-c tube. They reported better recovery of motor function in the fat pad-sheathed nerve group (Yoshitani et al., 2007). This suggests that blood flow in the reconstructed area is important during motor nerve regeneration when using PGA-c tubes.

The stellate ganglion block (SGB), which blocks the cervical sympathetic ganglion via once or twice daily administration of local anesthetic, increases blood flow in the head, neck, and upper limbs (Boas, 1998). As such, if SGB is used during facial nerve reconstruction with a PGA-c tube, it may lead to an increase in blood flow around the reconstruction site and promote nerve regeneration. However, a few studies have reported the application of SGB in nerve regeneration therapy (Hanamatsu et al., 2002). The SGB effect is a function of the duration of action of the local anesthetic used (Abdi and Yang, 2005; Terakawa et al., 2007; Gulcu et al., 2009). Therefore, frequent anesthesia is required to increase long-term blood flow. However, blocking the cervical sympathetic ganglia of an animal is technically difficult. Therefore, after resecting the cervical sympathetic ganglion in dogs, we used SGB to induce long-term increases in cervical blood flow. We prepared a canine model of SGB exhibiting long-term increased blood flow and assessed the effects of SGB on the restoration of canine facial nerves during treatment with a PGA-c tube.

## 2. Results

### 2.1. Changes in skin temperature

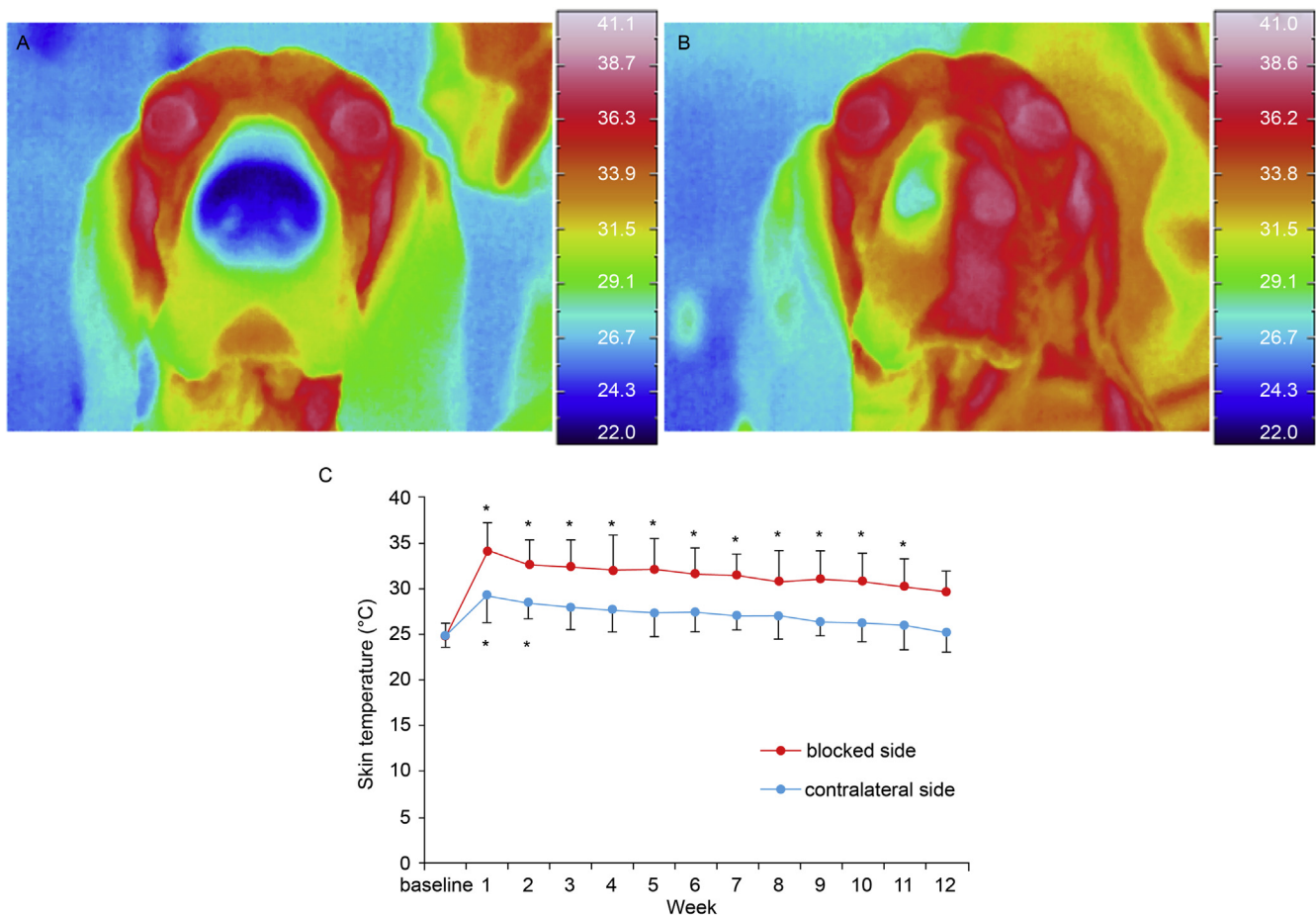
Although there was no difference between the left and right sides prior to the SGB (Fig. 1A), increased skin temperature on the cervical sympathetic ganglionectomy side (blocked side) was detected 1 week following the SGB (Fig. 1B). By week 11, the mean nasal skin temperature on the blocked side was significantly higher ( $p = 0.024$ ) than it had been before the SGB. The mean temperature was also significantly increased on the contralateral side until week 2 ( $p = 0.048$ ; Fig. 1C).

### 2.2. Changes in blood flow to the buccal mucosa

A significant increase in blood flow was observed 6 weeks following the SGB when compared to baseline ( $p = 0.042$ ; Fig. 2).

### 2.3. Changes in Horner's sign

Ptosis and miosis were observed on the blocked side in all dogs (Fig. 3). Changes in ptosis are described in Table 1(A), and changes in miosis are described in Table 1(B). Ptosis was observed until the fourth month following the SGB but was resolved after 6 months. Miosis was also observed 6 months following the SGB.



**Fig. 1.** Thermogram of a dog's face (A) before SGB and (B) 1 week after SGB. The color distribution represents changes in temperature (22 °C–41.1 °C). An increase in temperature on the blocked side (left side) was observed. (C) Changes in nasal skin temperature across the timeline of the SGB procedure. Asterisks represent statistical significance ( $p < 0.05$ ). Abbreviation: SGB, stellate ganglion block.

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