THE EFFECTS OF BOTULINUM TOXIN, TYPE A ON MUSCLE DURING DISTRACTION OSTEOGENESIS

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Introduction
Distraction osteogenesis is a surgical procedure used to lengthen a bone, and the process often induces complications in the surrounding soft tissues1-2. One of the more debilitating complications encountered during tibial elongation is contracture about the ankle3-5. Botulinum toxin, type A (BTX-A) administration has been used to help ankle contractures caused by other pathologies, and experiments were conducted to explore its efficacy in treating distraction induced contracture.

Methods
All procedures were performed following protocol approval by the Institutional Animal Care and Use Committee. Following surgical fixation and osteotomy, the tibias of 15 New Zealand White rabbits were lengthened with a distraction rate and final elongation selected to generate the complications reported during limb lengthening. 1.5 mm/day and ~20%, respectively. The animals undergoing distraction were divided into three treatment groups. The first group received saline injections; the second group received BTX-A injections into the tibialis anterior (TA) muscle; and the third group received botulinum injections into the gastrocnemius muscle (GA). For model validation, sham and injection-only treatments were performed on an additional 13 animals. Animals were evaluated for range of motion and muscle strength (torque production) at the start and conclusion of the experiments. Each experiment lasted eight weeks after which the animals were sacrificed. Their muscles and tendons were measured in situ and then harvested. Muscles were flash frozen, sectioned, and stained for vimentin to identify fibrotic activity.

Results
Limb lengthening adversely affected the TA, but not the GA muscle. In the TA muscles of saline controls, torque production was reduced by 68% (Figure 1). In the BTX-A treated groups, those animals receiving injections into the TA showed greater weakness, with torque deficits of 94%. Conversely, animals receiving toxin injections into the GA showed torque reductions of 59%, which was a 9% improvement over distraction alone.

Distraction alone caused a loss in range of motion from 150° to 57° (Figure 2). The greatest loss was in dorsiflexion with the animals no longer able to reach 90°, with 0° measured from the tibia. Injection of BTX-A improved this range: when injected into the GA muscle, dorsiflexion was increased by 15° to a total range of 75°; when injected into the TA, plantarflexion was increased by 22°, resulting in a total range of 85°. Dorsiflexion increases were not due to increased muscle length, but rather correlated well to increases in the Achilles tendon (Figure 1).

Additional connective tissue was not limited to the tendon increases but was pervasive throughout the muscle. Vimentin staining demonstrated that distraction increased fibrotic activity. When the TA muscles were injected with BTX-A, this fibrosis increased (Figure 3); when the antagonist GA muscles were injected, fibrosis decreased in the TA but increased in the GA (Figures 3 and 4).

Discussion
Botulinum toxin injection helped preserve range of motion and muscle function of the opposing un-injected muscle. It resulted in less fibrosis in the opposing muscle, and enabled increased Achilles tendon elongation. Despite these improvements, however, the effects on the injected muscle include weakness and increased fibrosis throughout the entire length of the muscle. Therefore despite the apparent benefits to the un-injected agonist muscle, the potential for fibrosis in the BTX-A injected antagonist requires additional scrutiny.

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References