

Healing of induced osteochondral injury in goat's knee, by application of a recombinant amelogenin protein.

Introduction

Cartilage injuries represent a major cause of disability. Current cartilage repair techniques often result in the formation of biomechanically inferior fibrous tissue. Previously, we have shown that application of a recombinant human amelogenin protein to a rat knee osteochondral injury (OCI) induced significant healing of the structure and composition of the tissues. This study aimed to evaluate the effect of an amelogenin-based product, Remelix[®] (Prudentix Ltd), on the healing of an induced OCI in a goat knee.

Design & Methods

The experimental protocol was approved by the ethical committee of the Hebrew University. A reproducible large OCI was created in the medial femoral condyle of both hind legs in 12 female goats. The right legs were treated with 0.25 or 0.5 mg/ml Remelix[®] (a proprietary composition of amelogenin dissolved in a Poloxamer (PX) 407-based carrier), while the left legs with PX carrier or saline alone. The degree of healing was evaluated six months post-treatment by MRI scans, clinical evaluation, histological and immunohistochemical staining.

Results

Significantly better healing was observed after treatment with 0.5mg/ml Remelix[®], showing shallower OCIs mostly covered with thick arranged hyaline cartilage expressing the hyaline cartilage components proteoglycans and type II collagen. The healing of the subchondral bone, which supports and nourishes the cartilage, was also better. Treatment with 0.25mg/ml Remelix[®] also resulted in shallower OCIs. However, these OCIs were covered by a thinner cartilage layer mixed with hyaline cartilage and fibrocartilage. On the other hand, minimal healing was detected after treatment with the carrier alone or with saline, where large OCIs were observed, showing minimal staining for the hyaline cartilage components.

Discussion

In this study, we showed that the amelogenin-based product Remelix[®] induced significant healing of injured articular cartilage and subchondral bone in a large animal goat model. Additionally, treatment with Remelix[®] prevented the deterioration of destructive post-traumatic osteoarthritis, known to occasionally occur in patients with cartilage injuries.

Clinical Relevance

Based on these results, a clinical study of treating human knee and ankle osteochondral defects or injuries, with this medical composition is currently on-going at Hadassah Medical Center.

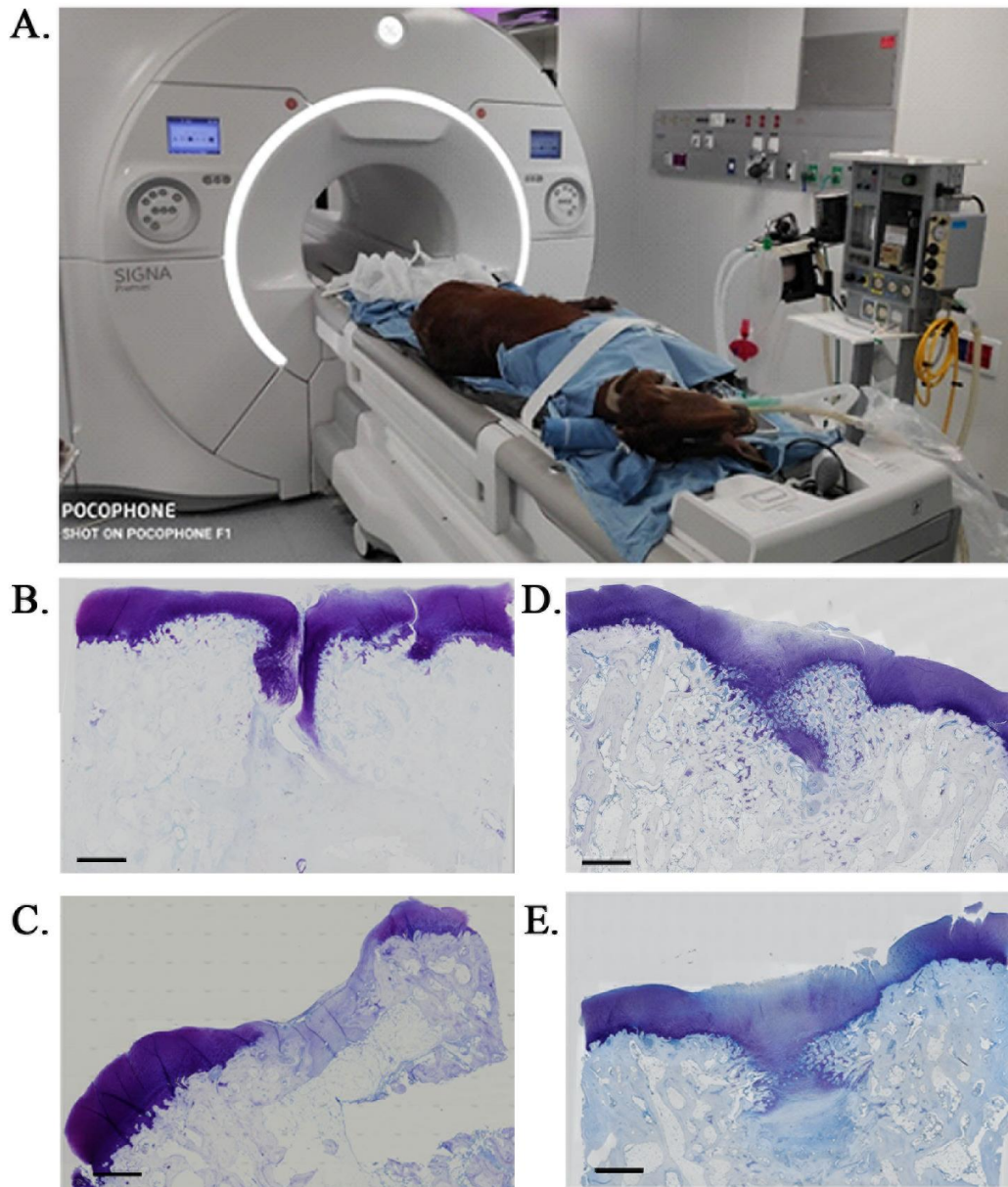


Figure 1: (A) MRI scan of goat knees, 5.5 months after surgery. The MRI scans were performed at the MRI center at Hadassah Ein-Kerem Medical Center. (B-E) Histological analyses of the OCI 6 months after OCI creation. Toluidine blue staining was performed. (B) 0.5ml/mg rAmelX in PX carrier; (C) PX; (D) 0.25ml/mg rAmelX in PX carrier; (E) Saline.