

## **7 SUMMARY**

### **The Influence of Locally Applied Platelet-Derived Growth Factor-BB on Free Tendon Graft Remodeling After Anterior Cruciate Ligament Reconstruction**

Injury to the anterior cruciate ligament (ACL) is the most frequent trauma of the knee joint in humans. Due to its inability to heal spontaneously, surgical treatment of ACL injuries is constantly increasing. Although the positive influence of platelet-derived growth factor (PDGF) on wound healing has been proved, up to date there is no data of its influence on the healing of a free tendon graft. The objective of the study was to electron microscopically evaluate the effect of PDGF-BB on the structural transformation and recovery of a free tendon graft after ACL reconstruction in vivo.

In 48 sheep with skeletally mature hindlegs, the ACL was reconstructed using the superficial digital flexor tendon. The animals were divided into eight groups four of which served as control groups and four served as study groups. The grafts of the study groups received a local dose of 60  $\mu\text{g}$  of PDGF-BB. Two groups each were sacrificed 3, 6, 12 and 24 weeks postoperatively. Subsequently, electron microscopical evaluation of cross sections of midsubstance graft tissue samples was performed. Following standardized sample processing, six photomicrographs of randomly selected areas were taken and digitally analyzed at a magnification of 80,000. The following parameters were determined: total number of collagen fibrils/ $\mu\text{m}^2$ , fibril diameter, fibril area/ $\mu\text{m}^2$  and distribution of the different fibril diameters within the graft.

Ligaments and grafts are structurally and mechanically different. With regard to ultrastructure, only the fibril area/ $\mu\text{m}^2$  of the two tissues was significantly different, whereas all other parameters were similar. The flexor tendon used in this study presented a significantly higher failure load compared to the intact ACL. Based on these findings, also from an electron microscopical point of view, the digital flexor tendon is considered to be a suitable graft for ACL reconstruction.

Ultrastructurally, after reconstruction of the ACL, transformation of the flexor tendon graft took place primarily in the first 12 weeks postoperatively. Within the first six weeks, it was characterized by a large structural loss, decrease in number of fibrils, increase in fibril diameter and fibril area. Distribution of the different fibril diameters had shifted towards fibrils  $> 140$  nm.

This phase of degeneration was followed by a phase of regeneration, characterized by a significant increase in numbers of collagen fibrils, decrease in fibril diameter and fibril area, and absolute dominance of thin fibrils with a diameter of 20-60 nm.

In terms of PDGF application, the structural alterations of the graft after ACL reconstruction was similar in both groups, however, the graft had not reached the morphological features of a the native ACL.

The most striking difference between the control and study groups was the fact that the latter one underwent reconstruction three weeks earlier and presented a significantly higher number of collagen fibrils 12 weeks post surgically compared to the control groups. The differences between the study and control groups suggested a positive, albeit not very pronounced influence of PDGF on graft healing. Accompanying evaluations of the research group in terms of biomechanical and histological changes of the graft post surgically, confirmed the fundamental assertions of the own ultrastructural results.

In order to more accurately assess the potency of PDGF, its concentration and kinetics as well as its effectiveness alone or in combination with other growth factors on graft healing in vivo, further studies will have to be done. In conclusion it can be stated, however, that the local application of PDGF had a positive influence on graft healing and especially in the early postoperative healing phase, this growth factor provides opportunities, to enhance the structural and mechanical characteristics of a reconstructed ACL.