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Developmental changes in condylar bone and their mechanical consequences

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SUMMARY AND CONCLUSIONS

The research work presented in this thesis was directed at examining the effects of the developmental changes in bone of the porcine mandibular on its micromechanical properties. As the events of normal early postnatal growth and development of bone from the porcine mandibular condyle are largely unknown, the first aim of the project was to describe and quantify the developmental changes of microstructure and composition of porcine condylar bone. This was followed by the investigation of the effects of these developmental changes on the micromechanical properties of condylar bone. The period of condylar development under investigation reached a maximum at 100 weeks of age, which is considered equivalent to 30 years of age in humans.

Chapter 2 of this thesis describes the development of microarchitecture and tissue mineral density (TMD) including its distribution, as it was analyzed in cancellous compartment of condylar bone. It was found that, corresponding to the course of porcine general and mandibular growth, most of the microarchitectural parameters studied change during the first postnatal months and stabilize thereafter during development. A relatively low mean TMD was revealed, and large local differences in TMD were found to exist within single bone trabeculae. These intratrabecular differences in TMD became more pronounced during development, which was caused by a higher rise of mineralization degree within the trabecular cores compared with the surfaces. It was concluded that growth and development of the porcine mandibular condyle largely takes place before the age of 40 weeks which is thought to be the end of adolescence. The relatively low

mineralization degrees as observed in this study suggest that the porcine mandibular condyle has a high rate of bone turnover which tends to decrease during later development.

In the study reported in **chapter 3**, the developmental changes of TMD, collagen content, and the number of the most abundant mature collagen cross-links in cancellous and cortical condylar bone were assessed. It was hypothesized on the basis of the results of the study described in **chapter 2**, that the number of mature collagen cross-links increases with tissue maturation after the age of 40 weeks. This hypothesis was disproved because the most prominent changes in TMD and the number of mature collagen cross-links (Pen, HP, and LP) were detected before the age of 40 weeks.

The second part of the thesis deals with the effects of the above compositional changes on the micromechanical properties of porcine condylar bone. In **chapter 4**, stiffness of cancellous and cortical bone tissue was assessed in three directions and correlated with the number of Pen, HP, and LP cross-links. It was found that 51% of variance in bone tissue stiffness was explained by the mean TMD. After correction for the mean TMD, the collagen cross-links studied did not significantly increase the explained variance in the mean bone tissue stiffness. These data suggest that the contribution of collagen cross-links to stiffness of bone tissue is rather limited.

In **chapter 5**, TMD and bone tissue stiffness were examined locally at 5 points over the width of single trabeculae. The measurements exhibited considerable local differences in TMD and bone tissue stiffness. It was found that 55% of the variance in the mean bone tissue stiffness was explained by the mean TMD, whereas only 7% of the

variance in all individual stiffness measurements was explained by the local TMD values. These data suggest, in contrast to previously held contentions, that the local mineralization degree is not a decisive determinant of the local bone tissue stiffness.

The aim of the work reported in **chapter 6** was to explore the role of collagen in the micromechanical properties of porcine cancellous condylar bone. The number of Pen cross-links was experimentally increased *in vitro* by means of ribose incubation, followed by an assessment of bone tissue stiffness. It was hypothesized that a higher number of Pen cross-links would lead to higher bone tissue stiffness, and that the latter would be more prominent in superficially demineralized bone compared with non-demineralized bone. It was found that ribose treatment caused an up to 300-fold increase in the number of cross-links compared to controls. This increase in Pen cross-links, however, did not affect bone tissue stiffness. Data from this experimental study suggest that collagen cross-links play no significant role in bone stiffness.

Chapter 7 reviews the information available from fundamental research on basic bone mechanics, describes growth and development of the human mandibular condyle, and discusses the correlation between structural and biomechanical properties of bone in general and of the mandibular condyle in particular, and puts this knowledge in a clinical perspective. Results of the work presented in this thesis are discussed in this chapter. It was concluded that the mandibular condyle is highly adaptive to changing mechanical conditions, and that further research is required to provide detailed understanding of exact microstructural and biomechanical mechanisms of physiological adaptation and pathological derangement of the mandibular condyle.

Results reported in this thesis add up to the following conclusions:

- the substantial mineral heterogeneity, low TMD, and low number of mature cross-links suggest that the porcine mandibular condyle has a high bone turnover rate;
- the porcine mandibular condyle likely has a high rate of bone remodeling, which appears to remain high after adolescence;
- mechanical properties of the mandibular condyle improve during adolescence and are optimal during adulthood;
- the local mineralization degree might not be a decisive determinant of the local bone tissue stiffness as was believed hitherto;
- the heterogeneity in mineralization degree is of importance when correlating mineralization degree with bone mechanical properties;
- the role of bone collagen and its cross-links in the mechanical properties of bone might not be as large as suggested in literature;
- data presented in this thesis are in accordance with the current idea that collagen influences toughness and tensile strength of bone, but not its compressive mechanical properties;
- the mandibular condyle is highly reactive to changes in its mechanical environment.