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Tanck, E.; Hannink, G.; Ruimerman, R; Buma, P.; Driessen, L.; Burger, E.H.; Huiskes, H.W.J.

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TRABECULAR MERGING INTO CORTICAL BONE UNDER THE GROWTH PLATE DURING GROWTH IS REGULATED BY MECHANICAL LOAD TRANSFER

+++Tanck, E; +Hannink, G; **Ruimerman, R; +Buma, P; +Driessen, L; +++Burger, EH; +++Huiskes R
+Orthopaedic Research Lab, University Medical Center Nijmegen, The Netherlands

Introduction: During growth, a small long bone develops into a mature one, adapted to mechanical forces. Longitudinal growth occurs because the growth plate produces new trabeculae, later resorbed or merged into the cortical shell. Initially, the cortex consists of plexiform bone, later remodelled into lamellar bone. Seen in a longitudinal spatial-temporal context, this process implies transition of trabecular metaphyseal sections into diaphyseal ones. Hence, the cortex below the growth plate emerges from trabeculae, which gradually densify towards the diaphysis. We hypothesize that the development is governed by mechanical stimuli. We also hypothesize that trabecular and cortical bone share the same regulatory mechanisms for adaptation to mechanical loads. To test these hypotheses, we monitored the complicated 3D development of the tibial cortex in growing pigs, using micro-computer tomography (µCT). We then tested if regulation mechanisms for trabecular bone adaptation can also explain cortical bone development.

Methods: Tibiae from 6, 23 and 230 week pigs (skeletally mature at 100 weeks) from a farm were studied. Specimens were sawn from the posterior cortex at three levels: just below the growth plate (GP), at one-third of tibial length (metaphyseal (M) level), and at one-half of tibial length (diaphyseal (D) level). They were scanned using µCT20 (Scanco) with a resolution of 12 µm. Afterwards they were prepared for histology.

To analyze if regulation mechanisms for trabecular bone adaptation could explain cortical bone development, the tendency of cortical bone development was simulated using our mechanical stimulation theory, which could explain bone modeling and remodeling of trabecular bone [1]. The theory assumes local dynamic loading variables (SED-rate) to activate osteocytes in the bone matrix to transfer osteoblastic formation stimuli to trabecular surfaces, through the canalicular network. The stimulus received at the surface depends on osteocyte density, mechano-sensitivity and signal decay by distance. Bone is formed at trabecular surfaces, where and while the stimulus exceeds a threshold value. Concurrently, osteoclasts are assumed to resorb bone that is (micro)damaged, the sites of which are determined at random per iteration. Coupling between osteoclastic and osteoblastic activities in remodeling is governed implicitly by the mechanics through SED concentrations around resorption cavities. This scheme was implemented in a 3D Finite Element Analysis for a section of cortical bone. This was loaded in longitudinal direction with a distributed load that increased from 0 MPa endosteally to 80 MPa periosteally (fig 1A).

Results: At 6 weeks, at GP level, the cortex consisted of trabecular bone (fig 1B). At M level, a cortex was present, but could hardly be separated from trabecular bone (fig 1C). At D level, a cortex was clearly present (fig 1D, 2AB); the endosteal surface was irregular due to trabecular merging into the cortex, and osteoclast resorption. Circumferential plexiform plates, interconnected by radially oriented bone rods, were present periosteally. The pores in the cortical bone, mainly longitudinally oriented, could be visualized (fig 2C). They represented soft tissue. Bone around the pores was plexiform; no osteons were present.

At 23 weeks, at GP level, the situation was similar to 6 weeks. At M and D levels, the endosteal surface had smoothened, but the circumferential plates were still present periosteally. In the center of the cortex, the plates had filled with plexiform bone. Osteons were only present endosteally.

At 230 weeks, a porous cortex was present at GP level, in which trabeculae merged. The inner and outer cortical surfaces at M and D levels were smooth, consisting of circumferential lamellar bone. Osteons were present throughout the cortex.

The computer simulation model showed the tendency of cortical bone development (fig 1E-G). At increment (inc) 0, the initial homogeneous distribution of bone had developed into trabecular bone, a situation comparable with 6 and 23 weeks at GP level. At inc 40, the structure corresponded with 6 weeks at M level, and at inc 80, the structure corresponded with 6 weeks at D level and with 230 weeks at GP level.

Discussion: Not only trabecular fusion with the cortex could be visualized with µCT, but also the distribution and orientation of pores within the cortex. In little time, pigs increase their weight enormously. To withstand the increasing force, it is efficient to form bone located far from the bone axis. The periosteal apposition plates illustrate this at 6 and 23 weeks of age. Another advantage of bone plates is that bone mass can be increased relatively fast as osteoblasts can form bone at both sides of the plates. The cortical structure changed significantly during growth. From the growth plate towards the diaphysis, the pores of the trabecular structure gradually filled in, so density increased and a cortex developed. Hence, cortex emerged from trabecular bone, suggesting that the regulation mechanisms of trabecular and cortical bone are similar. This was confirmed by the results of the computer simulation model, largely predicting this morphological development, using the same bone regulation theory that worked for trabecular bone [1]. Only the smooth surface at the endosteal side was not predicted, probably due to the short longitudinal size of the FE model.

We conclude that merging of metaphyseal trabeculae under the growth plate into cortex is likely to be governed by mechanical stimuli. Further, diaphyseal cortex development of growing long bones can be explained as a form of trabecular bone adaptation, without need of different regulation mechanisms for cortical and trabecular bone.

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++Dept Oral Cell Biology, ACTA-VU, Amsterdam, The Netherlands.

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