In this thesis the natural development and growth of osteochondromas is addressed to increase the understanding of the disease Hereditary Multiple Osteochondroma (HMO). The three subjects described are origin and development, structure and clinical visualisation. Osteochondromas are defined as cartilage-capped bony outgrowths on the surface of long bones containing a marrow cavity that is continuous with that of its underlying host bone\(^1\,^2\). They are usually localized near the metaphysis of bones that develop by endochondral ossification\(^3\,^4\). In theory every bone element that is formed by endochondral bone formation is thought to be susceptible for osteochondroma formation.

In this thesis the first study into the bone structure of human osteochondromas is described (chapter five). By using Micro-Ct imaging \textit{in vitro}, the structure of the bone morphology was visualized. It showed a difference between bone morphology of children and the morphology of the osteochondromas. The bone structure of osteochondromas showed thicker and wider spaced trabeculae. This wider spacing could possibly explain the osteoporotic-like \textit{in vivo} structure and might also explain the tendency of osteochondromas to easily fracture. These observations might lead the way in future studies, directed toward the use of the HR-pQCT (XtremeCT) for imaging the bone structure of osteochondromas \textit{in vivo}. With the HR-pQCT we might be able to visualize the difference in bone formation of the host bone and the adjacent osteochondroma. Which might give a hint on why some osteochondromas subsist and others disappear, possibly giving a clue on how to intervene in an early stage.

For a better understanding of the natural growth of HMO patients, two radiological studies were conducted. Both studies (chapters three and four) showed that growth of osteochondromas is linked to general skeletal growth of individuals. Chapter four further shows a discrepancy, especially in adolescent boys, between the skeletal and the calendar age. This observation is of relevance to patients with HMO because leg length discrepancy and axial deviation are common in HMO\(^5\,^6\). These deformities can be treated operatively to guide the patient’s growth\(^7\).
kind of surgical intervention it is of utmost importance to know the remainder of growth, to calculate the best possible moment to intervene in order to correct the deformity at best. The presented findings show that the prediction models for normal growth in children do not apply to children with HMO. This implies that for timing of surgery in children with HMO, it is essential to use individual growth curves of each individual patient to predict their growth and not the broadly used general growth predictors of normal children. Regular bone age tests, height and bone-length measurements are therefore advised in children with HMO.

To follow the skeletal growth and bone deformity formation in HMO patients in current practice, subsequent radiographs are used. The results presented in chapter seven show an alternative with the use of Whole body MRI. Using the Whole body MRI to subsequently follow growth in HMO patients has clear advantages: less radiation is needed, soft tissues can be visualized and costs can be reduced. Subsequent radiographs of all involved bones in severe HMO outweigh the costs of Whole body MRI. The proton density SPIR setting showed the best visibility of osteochondromas in Whole body MRI, the cartilage cap clearly visible and was even more intensely visible than articular cartilage. Therefore this setting is advised for Whole body MR imaging in children with HMO. In future, with the right setting and scanning protocol and shorter scanning time, Whole body MRI screening can replace conventional radiological monitoring in the future.

Deformities in HMO develop slowly over time. Therefore the presently used conventional radiographs can be used in a clinically more informative manner by projecting the radiographs in a time lapse (chapter eight). In this way the changes over time in the development of osteochondromas and their surrounding anatomical structures become more evident and may be clinically more easily interpretable. Knowledge about these growth changes may aid in the search for early interventions in osteochondroma formation and in the possible interventions in order to prevent deformities of the host bone or surrounding tissues.

Increased understanding of osteochondroma growth patterns and host bone development may help in the search of early diagnosis and early treatment of
osteochondromas. This might make minimal or non-invasive treatment possible in the future. Treatment opportunities like for instance cryosurgery or laser treatment in an early stage of the development of the cartage cap could be thought of. Furthermore the work in this thesis may contribute to the development of universal follow-up protocols on how to follow growth in HMO patients, aiding clinicians and patients in foreseeing deformity formation and planning the timing of surgical treatment.

REFERENCES