

## The Use of Whole-Body MR Imaging in Children with HMO, an Extended Case Study in Two Patients

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### Abstract

**Background:** Patients with hereditary multiple osteochondromas (HMO) undergo frequent radiographs to evaluate the growth of their osteochondromas. The conventional radiographic images clearly show the growth of the bony part of the osteochondromas and the growth direction of the long bones. The radiographs do not show the cartilage cap on top of the osteochondroma nor do they show the surrounding soft tissue or the cartilage of the nearby epiphysis. Alongside these disadvantages taking frequent radiographs carries the potential risk of inducing malignant degeneration through ionizing radiation. In this study we investigated the use of whole-body MR imaging as a screening tool to follow patients with HMO.

**Findings:** Two HMO affected children underwent two whole-body MR imaging scans in one-year time to identify the osteochondromas and to evaluate their growth. The MR images were compared to regular follow-up radiographs of these patients. All radiographically detectable osteochondromas were visible on the whole-body MR images. At least one osteochondroma was clearly seen on the whole-body MR images before detection was possible on the radiographs. The proton density sequence with fat suppression proved to be the best sequence to visualize osteochondromas.

**Conclusion:** Whole-body MR imaging is an effective follow-up tool for patients with hereditary multiple osteochondromas.

**Keywords:** Whole-body MRI; HMO; HME; Osteochondroma

### Introduction

Hereditary multiple osteochondromas or exostosis (HMO or HME) is an autosomal dominant inherited disease caused by mutated exostosin genes. HMO is characterized by the outward growth of cartilage-capped bone tumours called osteochondromas. The osteochondromas grow on the external surface of bones and contain a bone marrow cavity continuous with the normal bone cavity [1,2]. They often occur at the metaphysis of the long bones but are also found on the spine, scapulae, the ribs and the pelvis. The osteochondromas develop in the first decade of life and continue to grow until the patient reaches skeletal maturity. Most osteochondromas are symptomless but patients can suffer from pain and discomfort of the osteochondromas giving pressure on the overlying structures such as tendons, ligaments, nerves and even on the spinal cord. HMO can further lead to growth disturbances including Madelung's deformity (40-60%), unequal limb length (10-50%), joint deformity (2-55%) and a disproportionally short stature (37-45%) [3-6].

In patients diagnosed with HMO multiple conventional radiographs are taken for follow up. The radiographs give clear information about the bones and the ossified osteochondromas. Furthermore, growth deformations of the long bones can be detected. In adults regular follow-up every (other) year is advocated [7]. In fast growing children every six-month radiographs are taken to evaluate the growth

deformities and to determine the need for early intervention. For example early resection of the osteochondromas in the forearm can prevent forearm deformity and early hemi-epiphyseal stapling can prevent ankle deformities. Since growth deformities and joint dislocations in children with multiple hereditary osteochondromas can cause significant disability; early treatment of the deformity may prevent or decrease later deterioration of function. The aim of treatment is surgical resection of the masses and the prevention of deformities [8-10].

Next to the deformities osteochondromas can cause pain. Pressure of the osteochondroma on the surrounding soft tissues can be painful. The top of the osteochondroma, the cartilage cap, is not ossified and therefore cannot be seen on the radiographs. These soft tissues are not seen on radiographs but are clearly visible on MR images. MR images can also provide information about the cartilage of the nearby epiphysis and thus about the potential growth deformation.

Whole-body MR imaging (Wb MRI) is a non-invasive screening technique that acquires images of the entire body. Patients with HMO in regular follow up [7] may need a high number of radiographs (estimated 10-20 radiographs per year in a fast growing child) and thereby receive a significant dose of ionizing radiation with the potential risk of inducing malignant degeneration of the cartilage cap of the osteochondroma. Because of the visibility of the top and of the tissues surrounding the osteochondromas and the visibility of the epiphysis of the long bones, and at the same time the lack of radiation,

Wb MRI is a promising imaging modality for serial imaging surveillance in the paediatric age group.

The advantages of MR imaging over radiographic follow up are known, but up until now it was difficult to scan the whole body in a reasonable scanning time. To make a whole body scan every body part had to be scanned separately and sometimes in different coils. Since modern MRI technology provides MRI systems with high-density coil elements with flexible switching possibilities, multiple receiver channels and automatic table movements, Wb MRI has become clinically available. The use of Wb MRI in the paediatric population for oncologic applications has become more established in recent literature [11-17]. The role for Wb MRI in other multisystem disease processes still has to be investigated. As mentioned by Lenk in 2004 the Wb MRI has a potential application in the regular screening of children with HMO as alternative for screening with radiographs [18].

The aim of this study was to qualitatively evaluate the use of the Wb MR imaging in HMO affected children. Therefore the regular conventional radiographs of two HMO affected children were compared to the Wb MRI findings during one year. The images in both methods were evaluated to see if all osteochondromas could be identified and to see if the possible deformity of the long bones was equally visible. Furthermore, we analysed the Wb MR images to verify if early detection of osteochondromas was possible.

## Patients and Methods

Two patients were included. Both patients were diagnosed with HMO. The evaluated imaging studies consisted of four consecutive whole-body MR imaging studies in the period from 2012 to 2014.

Patient one is a two-year-old boy who was seen at the orthopaedic outpatient clinic because of palpable swelling on the thorax and the scapulae. His mother was diagnosed with HMO. Conventional radiographs showed multiple osteochondromas of the pelvis, multiple ribs, the scapulae, and the long bones of the upper and lower extremities. His right ulna showed severe growth deformity and his right tibia minor growth deformity. Learning about the technique of Wb MRI and the possible use of the technique in patients with HMO [17,18] we considered this patient suited. At the age of three years we performed a Wb MRI. The first scan was performed without anaesthesia or sedatives. Mother asked for general anaesthesia for the second scan because her son had been anxious during the first scan. The second scan was done one year later under general anaesthesia.

The second patient was a seven-year-old boy known for several years with HMO. His father is also known with the disease. Both Wb MRI scans were done with a one-year interval without general anaesthesia.

In both patients every six months regular check-up was done in a fast growing period, with conventional radiographs and after one year the Wb MRI was repeated. The study was performed in accordance with the Declaration of Helsinki and was approved by the local ethics committee (MEC 08-4-028). Both the patients and their parents gave their informed consent prior to their inclusion.

## Imaging technique

MR imaging was performed with a 1.5 T MRI scanner (Ingenia; Philips Healthcare, Best, the Netherlands). Ingenia's Smart Selection automatically selects the coils and coil elements which contribute to the highest signal-to-noise ratio in any region or any length of the field

of view. As there is no consensus about which combination of MR sequences provides the highest diagnostic accuracy combined with reasonable time efficiency, at the beginning of the study a combination of sequences for screening for osteochondroma was chosen based on limited experience. The proposed imaging protocol consisted of a 1-mm-thick balanced Steady State Free Precession (bSSFP) sequence in the coronal plane (TR, 17 ms; TE, shortest ms; matrix, 432 × 432; FOV, 430 × 326 × 150 mm; 150 sections; acquisition time, 7 minutes), a 1-mm-thick 3D Volume Isotropic Turbo-Spin-Echo T1-weighted sequence in the coronal plane (TR, 350 ms; TE, 13 ms; matrix, 432 × 432; FOV, 430 × 322.5 × 150 mm; 150 sections; mean acquisition time, 6 minutes 25 seconds) and a 5-mm-thick multi-turbo spin-echo Proton-Density (PD)-weighted Spectral Saturation with Inversion Recovery (SPIR) sequence in the coronal plane (TR, 1800-4000 ms; TE, 20 ms; matrix, 512 × 512; FOV, 220 × 220 × 275 mm; 50 sections; mean acquisition time, 8 minutes 5 seconds).

## Imaging evaluation

The MR images were evaluated by experienced paediatric radiologists. The diagnosis of osteochondroma on Wb MRI was based on the presence of cartilage-capped osseous excrescence (sessile or pedunculated) with continuous cortex and marrow extending from underlying bone and pointing away from the epiphysis. The osseous excrescence had to be detectable on at least one of the different sequences of the Wb MRI protocol. The Wb MRI findings were correlated with radiographs. At the time we started performing Wb MRI studies no protocols were available, nor standard detection protocols for paediatric patients.

The visibility of the osteochondromas on the Wb MRI was compared to the visibility on the conventional radiographs. To detect growth deformations, the angle between the axis of the long bone and the epiphysis or articulation was calculated to determine the valgus and varus malalignment and ante- or recurvation.

## Results

In total 64 osteochondromas were found on the conventional radiographs of the long bones of the two patients. All osteochondromas that were detectable on conventional radiographs also could be identified on the Wb MR images. Even though one of the osteochondromas, situated on the left ulna of the first patient was very clear on the radiographic images, but hard to identify on MRI. This osteochondroma was located on the left distal ulna on the dorsal side. It is likely that this osteochondroma would have been missed if the first screening had been done by Wb MRI alone, however the visibility was better on the second scan.

The size and precise location of at least 6 osteochondromas in the second patient, was much easier to evaluate on the Wb MR images. By using the Wb MR images it was possible to distinguish several osteochondromas that were located close to one another. These osteochondromas were located so close to one another that on the radiographs they projected like one big osteochondroma, but on the Wb MRI the osteochondromas were visible separately and located more ventral and more distal to each other instead of in continuity. Furthermore, in this patient it was possible to distinguish several osteochondromas from the normal bony outgrowth of the trochanter on the Wb MRI. On the conventional radiographs these osteochondromas at the proximal femur were easily mistaken for the major trochanter. Five osteochondromas were seen on the Wb MR

images but could not be identified on the conventional radiographs. This was due to their location of which no proper radiographic images were available. One osteochondroma in the first patient was visible on the Wb MRI before it became apparent on the conventional radiographs. It was situated on the right distal fibula near the tibia. It was visible on the first as well as on the second Wb MRI scan. On the first MRI scan only a small bump of osteochondromal cartilage was detectable (Figure 1).



**Figure 1:** Early detection of an osteochondroma. Figure 1A: Conventional radiograph of the distal tibia and fibula in AP view, showing no abnormalities. Figure 1B: Coronal fat-suppressed proton density weighted MR image of the distal tibia and fibula showing a cartilage bump, the onset of an osteochondroma, on the lateral site of the distal tibia and the medial site of the distal fibula.

Of all osteochondromas detected on the Wb MR images the cartilage cap could be clearly identified. In the same patient the diameter of the cartilage cap varied widely among the different osteochondromas and was not related to the volume of the bony outgrowth. The influence on the surrounding soft tissue structures of the osteochondroma was clearly visible, especially in the thoracic osteochondromas. No impingement or bursa formation was detected.

Measuring the angles between the axis of the long bone and the epiphysis or articulation to detect growths deformations, was equally possible on both the radiographs as well as on the Wb MR images. In both imaging techniques the articulation or epiphysis is shown along with the axis of the long bone, making it possible to detect axial deformities with both techniques. On top of the detection of the deformity, the Wb MR images showed the cartilage of the epiphyseal plate. No epiphyseal damage was seen even though a clear shortening of the right ulna was detected in the first patient, the two-year-old.

No signs of malignant degeneration of the osteochondromas were found.

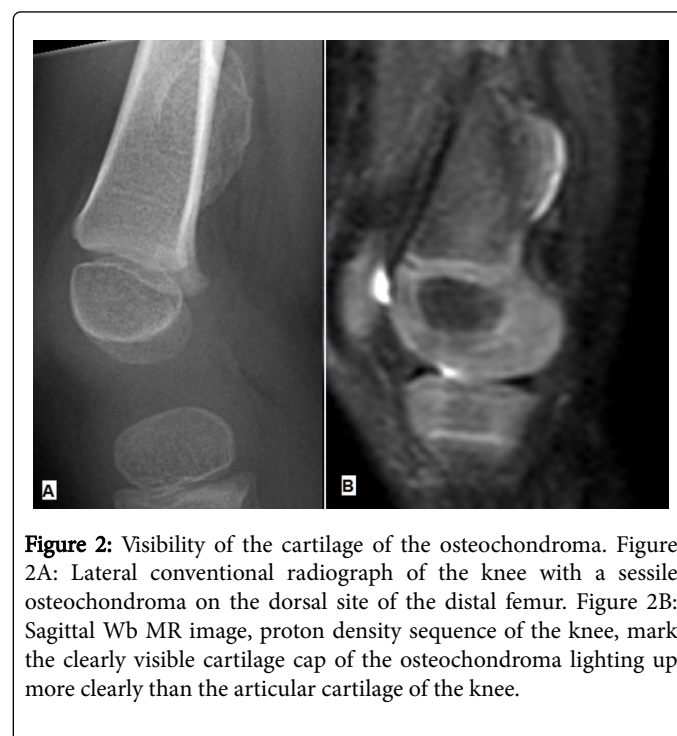
On average 20 conventional radiographs of the skeleton were taken per patient per year, respectively 18 in the first and 22 in the second patient. For this radiographic screening the estimated total radiation dose is 1.8 mSv per patient per year.

## Discussion

In this two patients case study Whole body MR images show more accurate detectability of the osteochondromas compared to conventional radiographs. Especially in the young children the osteochondromas are more cartilaginous and therefore better visualized on the MR images. These young children would probably benefit more from the Wb MRI as a screening device. This would also imply less ionizing radiation for screening purposes in the lifespan of these children. The number of radiographs taken in one year was on average 20, which approximately doubled their effective year dose from natural background radiation. Using the Wb MRI for screening purposes would sharply decrease their exposure to ionizing radiation.

The problems that were encountered during the scanning and evaluation are described. The scanning time of the Wb MRI scans compared to obtaining the radiographs was longer. Besides the time the fact that the children had to lie still in a limited space was a disadvantage of the Wb MRI scan. Several scans were not suitable for evaluation due to motion artefacts. To reduce the motion artefacts and because of anxiety, the first patient needed to be anesthetized during the second scan. This makes the Wb MRI less attractive for serial imaging surveillance in children under the age of four.

The variable rotation angles of the position of fore example the forearm during scanning made it hard to compare the MR images to the conventional radiographs. This variation also made it difficult to compare the consecutive scans. A more standardized positioning during scanning could prevent this problem.



**Figure 2:** Visibility of the cartilage of the osteochondroma. Figure 2A: Lateral conventional radiograph of the knee with a sessile osteochondroma on the dorsal site of the distal femur. Figure 2B: Sagittal Wb MR image, proton density sequence of the knee, marking the clearly visible cartilage cap of the osteochondroma lighting up more clearly than the articular cartilage of the knee.

Since there is no standard scanning protocol the detectability of the osteochondroma itself was distinct among the different scan protocols. For example on the 3D TSE T1 and the bSSFP sequences, it was more difficult to distinguish the cartilage cap of the osteochondroma from the surrounding soft tissue. On the PD SPIR sequence the cartilage of the osteochondroma was more hyper intense compared to functional cartilage. Hypothetically this is due to the higher water concentration



in the osteochondromal cartilage caps compared to the functional cartilage, possibly due to the lack of pressure on the osteochondromal cartilage (Figure 2). Since the osteochondromas were best visualized on the PD SPIR sequence we would consider this sequence the most suitable sequence for screening purposes in HMO patients.

In this study we did not expect to find malignant degeneration because the patients were young, malignant transformation before the age of 20 is distinctly unusual [19]. In adult HMO patients the Wb MRI screening might be beneficial in this respect. So far bone-scintigraphy and FDG-PET scans have been applied for early detection of malignant transformation in adults [20-22].

Searching for newly formed osteochondromas the MR images showed one small new osteochondroma. It was found on the distal fibula and was not detectable on the conventional radiographs. No loose cartilage islands were detected. Douis et al. could not confirm the widely believed theory of an osteochondroma arising from misplaced cartilage in the metaphysis or an extension from the growth plate into the metaphysis, in a MRI study in 2012, nor could this case study confirm this hypothesis [23]. The imaging of very small osteochondromas however can potentially shed a light on the place of origin of the osteochondroma in the future and in the long run might lead to early treatment of the disease.

The costs of a Wb MRI are substantially higher than the costs of conventional radiographs, especially if general anesthesia has to be administered. For a standard Wb MRI the costs are about 400 euros compared to 50 euros for the conventional radiographs. No cost benefit analyses are available. Wuyts et al. suggested that monitoring of the size of osteochondromas in adults may aid in early identification of malignant degeneration, but they also found no cost/benefit analyses to support this routine [8].

In summary this case study shows that the use of Wb MRI is suitable as a screening tool for follow-up in HMO affected paediatric patients. Wb MRI showed accurate detectability of the osteochondromas, it reduces the exposure to ionising radiation and might lead to early detection of the osteochondromas. However it is more time consuming and at a higher cost than the conventional radiographic imaging follow-up, especially when general anaesthesia is needed. There is need for a standardized protocol of the Wb MRI settings for screening purpose. In this case study the PD SPIR sequence was found to be the most suited sequence, taken in coronal and sagittal plane and with the limb in a standardized position. For future studies we recommend the use of Wb MRI screening for children that have no need for anaesthesia during the scanning. With the use of the advised protocol the time needed for routine Wb MRI can be reduced.

## Conclusion

Whole-body MRI is an effective screening tool in the follow-up of patients with hereditary multiple osteochondromas. The osteochondromas can be accurately visualized. The PD SPIR sequence is the most suitable sequence for the detection of the osteochondromas and evaluation of their cartilage cap. The major disadvantage is the potential need for general anaesthesia to perform the scan in the very young age group.

## Competing Interest

The authors declare that they have no competing interests, no financial competing interest or non-financial competing interests.

## Authors Contribution

HS, MD and SR were responsible for the study design. HS, AW and LvR collected the patient data. MD and SR were responsible for the radiographic and MRI images. HS and MD coordinated the draft of the manuscript. All authors read, commented and approved the final manuscript.

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