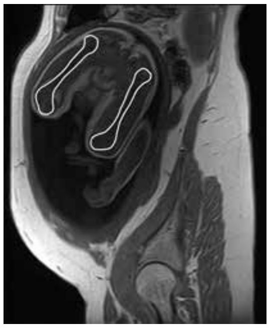

NORMAL DEVELOPMENT AND MATURATION OF BONE MARROW, ASSESSMENT BY MAGNETIC RESONANCE IMAGING

Desarrollo y maduración normal de la médula ósea, valoración por resonancia magnética

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Summary
Skeletal maturation occurs in an orderly and predictable manner. It can be documented by Magnetic Resonance Imaging even before histological changes occurs, so the importance of adequate knowledge and characterization must be stated.

Resumen
La maduración ósea ocurre de forma ordenada y predecible. Puede documentarse por medio de resonancia magnética incluso antes de que ocurran cambios histológicos, por lo cual es importante su adecuado conocimiento y caracterización.

Introduction
The development and maturation of the skeleton in kids is a dynamic process (1); the conversion of the bone marrow occurs in a predictable manner, orderly, symmetric and following a pattern. There are some physiological changes that can be documented through magnetic resonance imaging (MRI) and that must be differentiated from pathological processes.

Histology
Knowing the cellular composition of bone tissue is fundamental to understand the behaviour in magnetic resonance images:

In the periphery is the *compact* or *cortical bone*.

In the center is the spongy bone: It is constituted by trabecules that serve as an architectural support and for mineral deposit. In between the trabecules is the bone marrow (figure 1).

The bone marrow is a complex organ that contains multiple cells in the process of differentiation. In response to the stimulation from a diversity of hormones, cytokines and growth factors, the cells in bone marrow are susceptible of proliferation in the normal process of hematopoiesis.

Likewise, when stimulated with noxaes such as medicines, infections, radiation, toxins and nutritional deficit or neoplasias, the proliferation process can be supressed and enter into a pathological state.

Bone marrow composition
***Red bone marrow:** :* It is constituted by a 60% of hematopoietic cells and a 40% of adipocytes. Its chemical composition is of 40% fat, 40% water and 20% proteins. It is in charge of hematopoiesis and shows a rich vascularization.

***Medula* ósea *amarilla*:** : It is constituted almost in its totality by adipocytes (95%), and a 5% of hematopoietic cells. Its chemical composition is 80% fat, 15% water and 5% proteins. Its function is unknown. It is poorly vascularized in comparison to the red bone marrow (figure 2).

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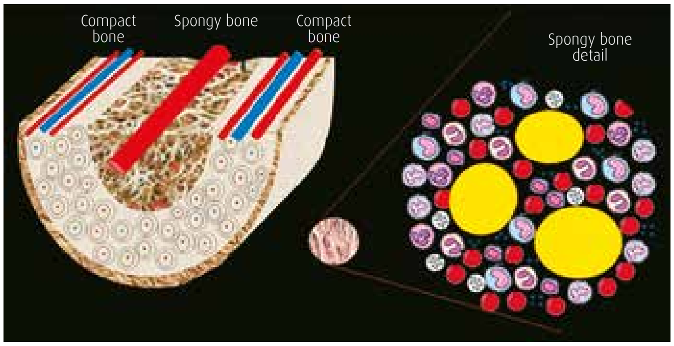

Figure 1. Transversal and longitudinal sections of a long bone that allows to observe bone structure details.

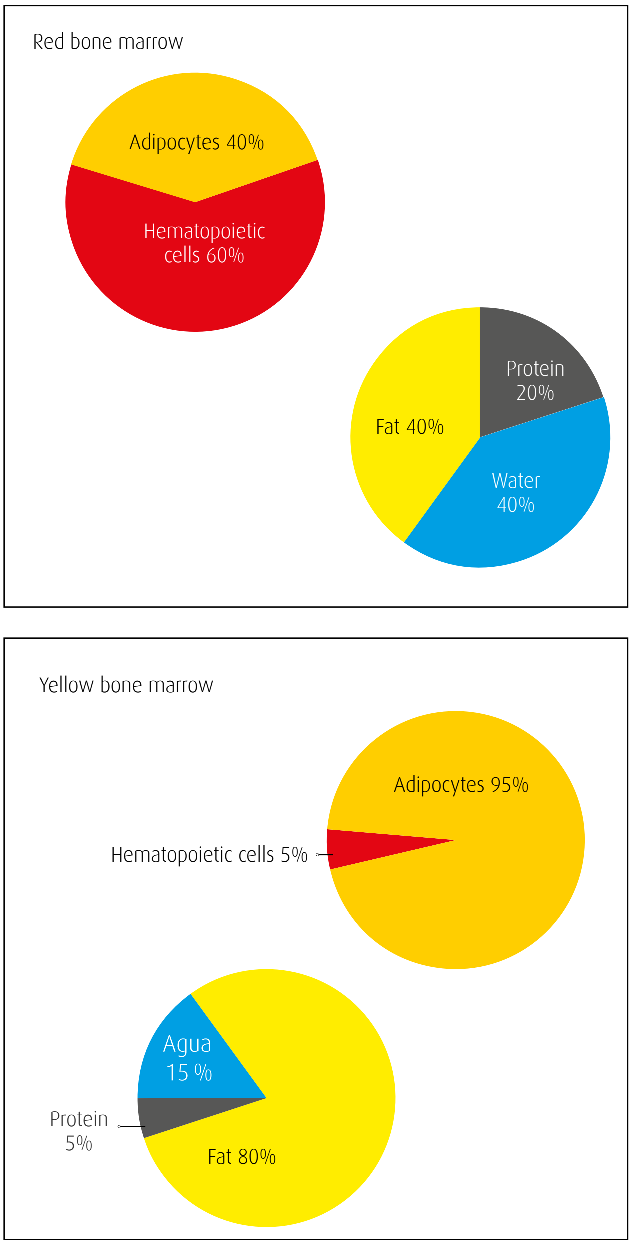

Figure 2. Red and yellow bone marrow composition.

Magnetic Behaviour

The normal magnetic behaviour, both for yellow and red bone marrow, must be recognized in an appropriate way in order to be in capacity of recognizing physiological and pathological processes (2).

To illustrate what the magnetic behaviour of the bone marrow is, an obstetric MRI can be taken as example, where the bone marrow of the foetus (mostly red bone marrow) can be compared to that of its mother (mostly fat) (figure 3).

In sequences with T2 information, the red bone marrow also presents a minor signal than the fatty marrow, but the difference between fatty marrow and hematopoietic marrow is less striking that in sequences with T1 information (figure 4).

The fatty marrow presents a high signal in the majority of sequences, so it can be annulled through fat suppression sequences. In sequences with T1 information, the fatty marrow presents an analogous signal to the subcutaneous fat (figure 5). Due to the high sensitivity of the MRI for the detection of differences in the bone marrow composition, the fatty component can be localized earlier with this technic when compared to histological studies (figure 6).

Since approximately three decades ago, studies have been performed taking into account the chemical displacement in phase and out of phase in echo gradient magnetic resonances sequences in order to evaluate the bone marrow. It is based on the chemical composition of the bone marrow - fat, water and cells, supported by stromes -, which proves a loss of the signal when out of phase as compared to images in phase when there are similar marrow fat and water, which cancel each other out. This allows determining if there are pathological processes, such as tumours, where the fatty bone marrow has been replaced, since the fat/water proportion is lost and there is no loss of signal in the images out of phase (3).

Marrow conversion

Foetal age - New born

In the foetal age, the diaphysis and metaphysis of the long bones have low signal in sequences with T1 information because red bone marrow is predominant, while the epiphysis, which contains abundant cartilage, shows an intermediate signal in sequences with T1 information (figure 7a). As soon as the epiphysis starts to ossify, the fatty narrow signal appears which is evident in the ossification centers as areas with a high signal in sequences with T1 information (figure 7b). There is also a high signal that is characteristic of the epiphysis, phalanges and metatarsals given their high water content (figures 8 and 9).

1 to 10 years of age

Near the end of the first year of life the marrow conversion begins in the phalanges of the hands and feet, which is complete around the first year. Additionally, at this age starts the conversion in femoral diaphysis and, subsequently in the remaining long bones (figures 10 and 11).

At 10 years of age, the fatty bone marrow occupies most of the diaphyseal regions of the superior and inferior extremities and the skull, while the red bone marrow persists in the metaphysis. This is evident in the MRO as a relatively high signal in the diaphysis with an intermediate to low signal in the metaphysis in sequences with T1 information.

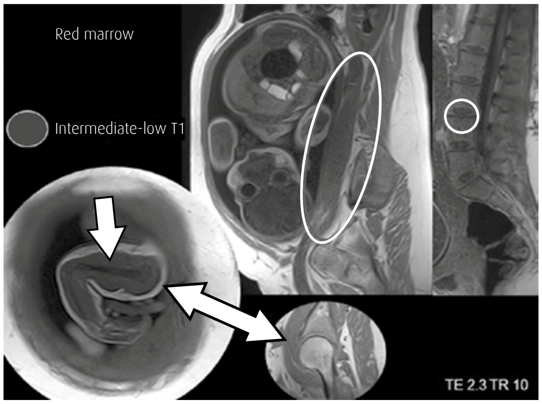

Figure 3. Sequences with T1 information: Magnification, foetus arm, shows a low to intermediate signal. Even though the red bone marrow contains some fat, it high cellular content results in a relatively low signal when compared with fatty bone marrow (of the mother`s femoral head), but generally higher than the signal of the muscle or the intervertebral discs (ellipses).

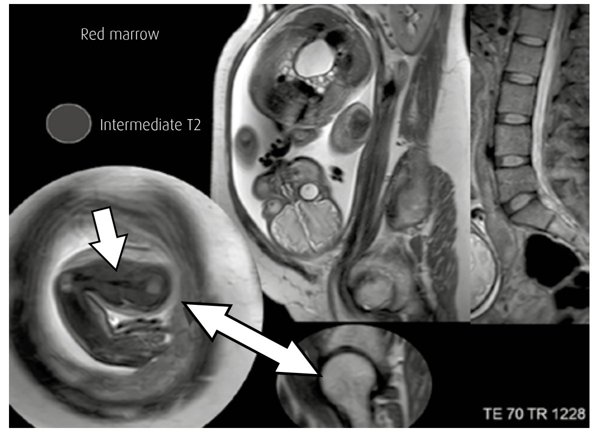

Figure 4. Obstetric MRI sequences with T2 information. The single arrow indicates the intermediate signal of the red bone marrow of the foetus in sequences with T2 information. The double arrow compares it with the adult femoral head bone marrow, which is yellow, so its signal is high.

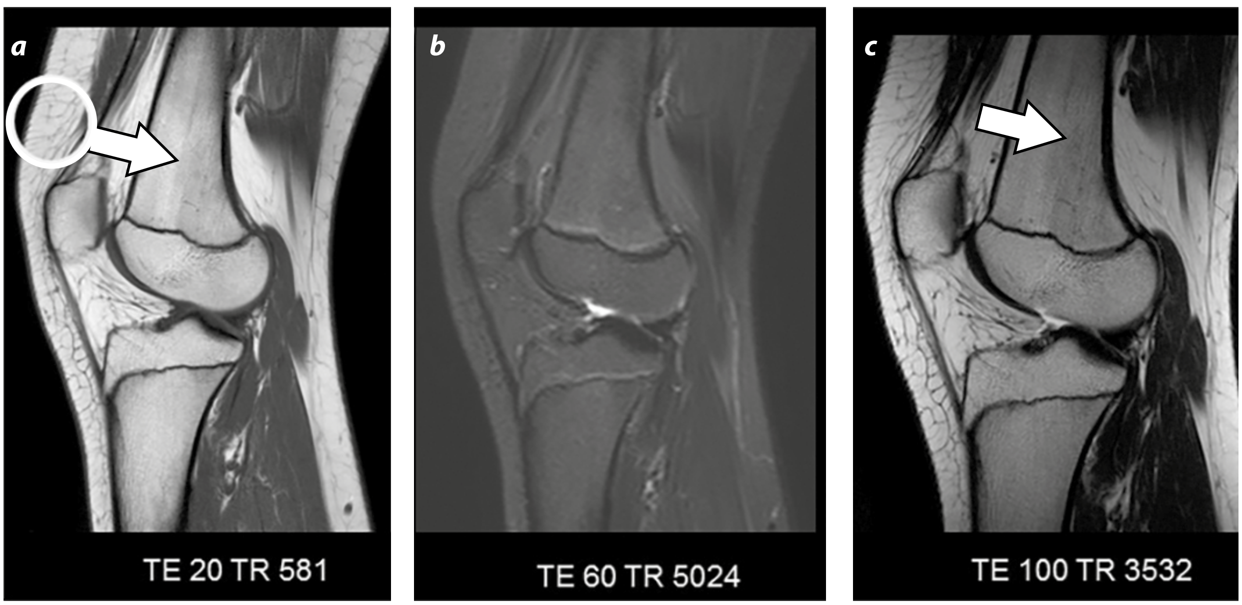

Figure 5. a) MRI with T1 information. (b) STIR. (c) Fast Spin Echo with T2 information. 14 year old girl. In sequences with T1 information, the fatty marrow presents a signal analogous to that of the subcutaneous fat (circle and arrow) and its signal is annulled using fat suppression sequences (middle MRI).

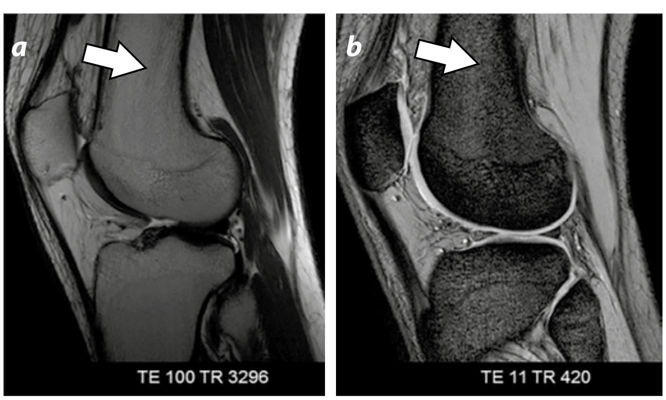

Figure 6. a) Fatty bone marrow example, that shows an intermediate to high signal in Fast Spin Echo with T2 information. b) In an echo gradient sequence, the signal varies according to the amount of marrow trabecules.

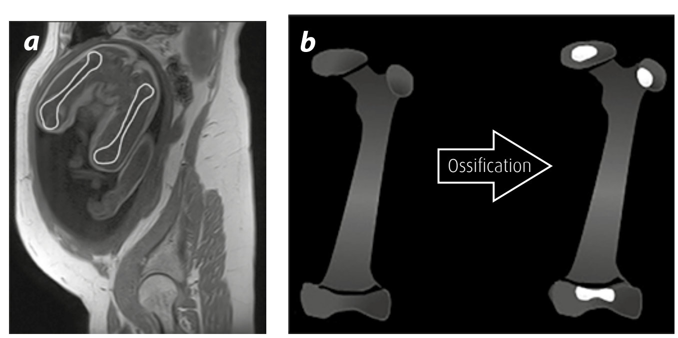

Figure 7. a) In foetuses, the bones have a low signal in sequences with T1 information due to the red bone marrow signal. b) Later on, during childhood, the ossification centers show a high signal in sequences with T1 information.

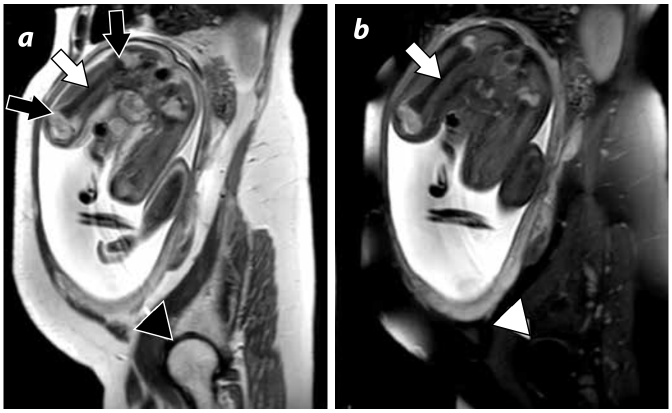

Figure 8. Obstetric MRI with T2 information without saturation (a) and with fat saturation (b). In the foetus, red bone marrow prevails in its femurs (white arrow), which show an intermediate to low signal. The epiphysis that are not yet ossified show a high signal given the presence of cartilage with abundant amounts of water (black arrows). If the mother's femoral heads are compared, where yellow bone marrow prevails, signal suppression can be observed in sequences with T2 information with fat saturation (head of white arrow).

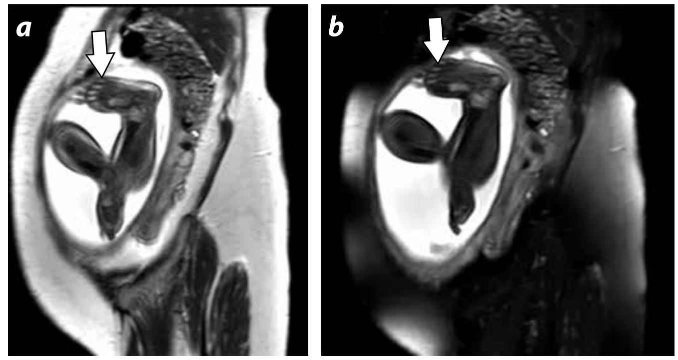

Figure 9. The phalanges and metatarsals contain abundant cartilage, for which their signal is high in sequences with T2 information (a) and its signal intensity does not vary in a significant way in sequences with fat suppression (b).

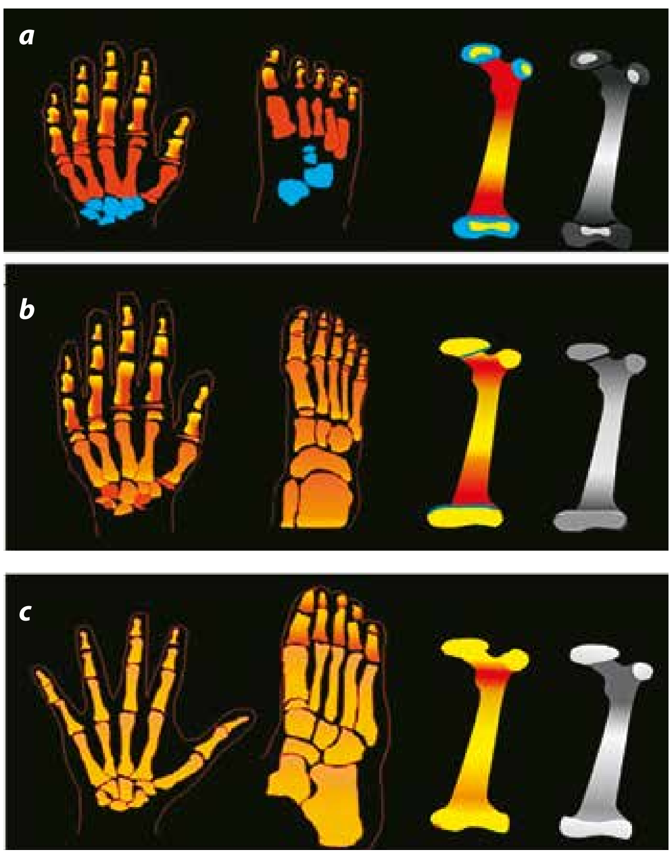

Figure 10. Schemes representing the behaviour of the bone marrow in the hands, feet and femur of children between 1 and 10 years of age. b) Schemes representing the behaviour of the bone marrow in the hands, feet and femur in people between 10 and 25 years of age. c) Schemes representing the behaviour of the bone marrow in the hands, feet and femur in people above 25 years of age. The images to the right represent the MRI with T1 information.

Additional factors to consider

There are differences in the bone marrow maturation according to sex. It is earlier in girls (figure 12).

When comparing MRI of patients of the same sex and same age, differences can be found. It is because of this that interpretation of the studies must be made in an individual manner (figure 13).

Furthermore, the technical factors should be taken into consideration when interpreting a given study (figure 14). It is fundamental to establish the correct parameters in the protocols in order to achieve an adequate acquisition of the images and, in a similar fashion, correctly recognizing each one of the sequences so as to not interpret erroneously lesions that are not. For example, a STIR sequence where the red bone marrow can have a high intensity must not be confused with a T1 potentiated sequences with gadolinium where some lesions can be highlighted and in both cases the signal is high.

Finalizing the 1 to 10 years of age phase, a complete ossification of the centers is observed, though the physis remain open (figure 15).

The conversion in the axial skeleton occurs a bit after. In the first decade, red bone marrow persists in the spinal column, the thorax and the pelvis (1). Marrow conversion is present posteriorly with a less predictable patter than in the appendicular skeleton (4, 5) (figures 16 a, b and c).

10 to 25 years of age

From the 10 to 25 years of age, the fatty marrow signal is predominant in the extremities, though there is residual red bone marrow en the metaphysis of the femur and humerus. This is evident in the MRI as a higher signal in the diaphysis in sequences with T1 information. (5, 6) (Figures 10 b, 17, 18 and 19).

Above 25 years of age

At 25 years of age the adult bone marrow pattern is achieved. In MRI, signal for red bone marrow in the axial skeleton, the sternum, the ribs, the femur and the proximal humerus is observed. The epiphysis are separated from the diaphysis by a low signal band en sequences with T1 information corresponding to growth cartilage, though a fine residual line persists when it closes (5) (figure 10 c).

Figure 11. In this coronal sections of MRI with proton density sequences, STIR and with T2 information, it can be observed how after ending the second year of life, the ossification center made of yellow bone marrow occupies most of the epiphysis (white arrow) and the physis still remain open (black arrow).

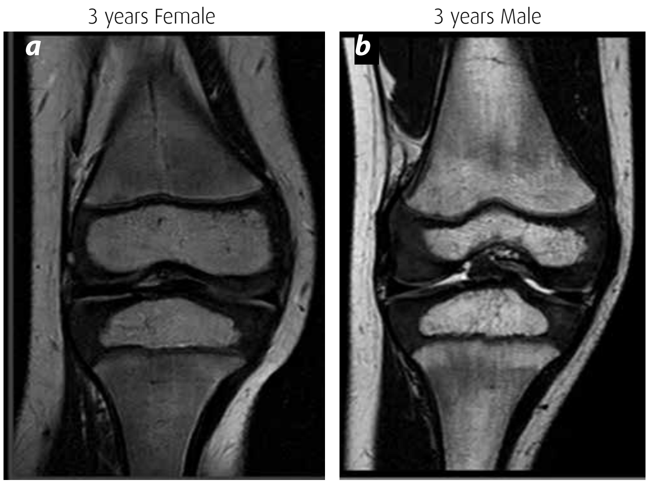

Figure 12. MRI with T2 information. Coronal sections in two patients of the same age, which shows that bone maturation in girls is quicker during the first decade of life.

Figure 13. MRI in sagittal sections: a) Echo gradient with T2 information and c) TSE with T2 information. MRI in coronal sections: b) with T1 information and STIR. d) TSE DP and STIR. Images of two boys of 4 years of age, the first with a normal knee (a and b) and the second (c and d) with a Salter Harris type II fracture in the distal metaphysis of the femur (arrow). Significant differences in the bone maturation of these two patients can be observed.

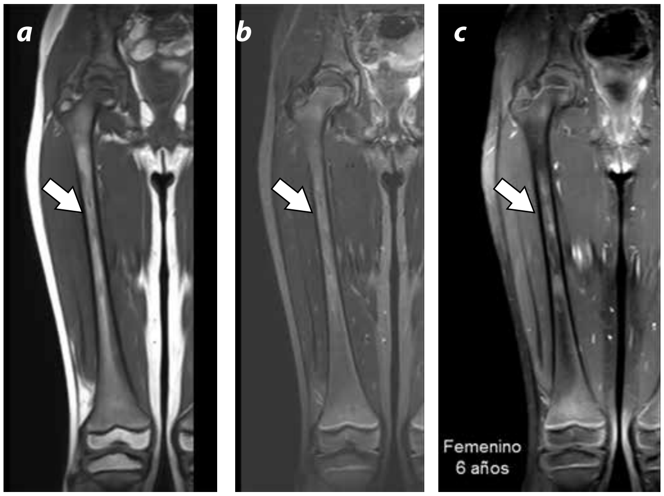

Figure 14. Femur MRI of a healthy 6-year-old girl, where there is an apparent heterogeneity in the intensity of the signal of the bone marrow of the diaphysis (arrow). It could be confused with a pathology if the adequate acquisition of the images which could be conditioned to technical factors to be corrected, are not considered.

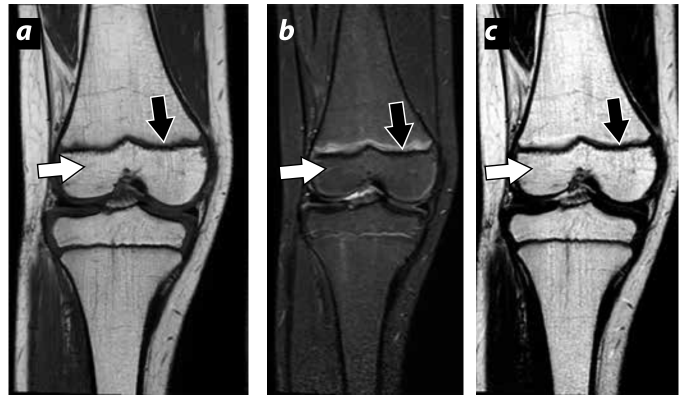

Figure 15. MRI, coronal sections, sequences with T1 information, STIR and with T2 information of an 8-year-old girl, where the ossification centers completely developed (white arrow) can be observed. The physis remain open (black arrow).

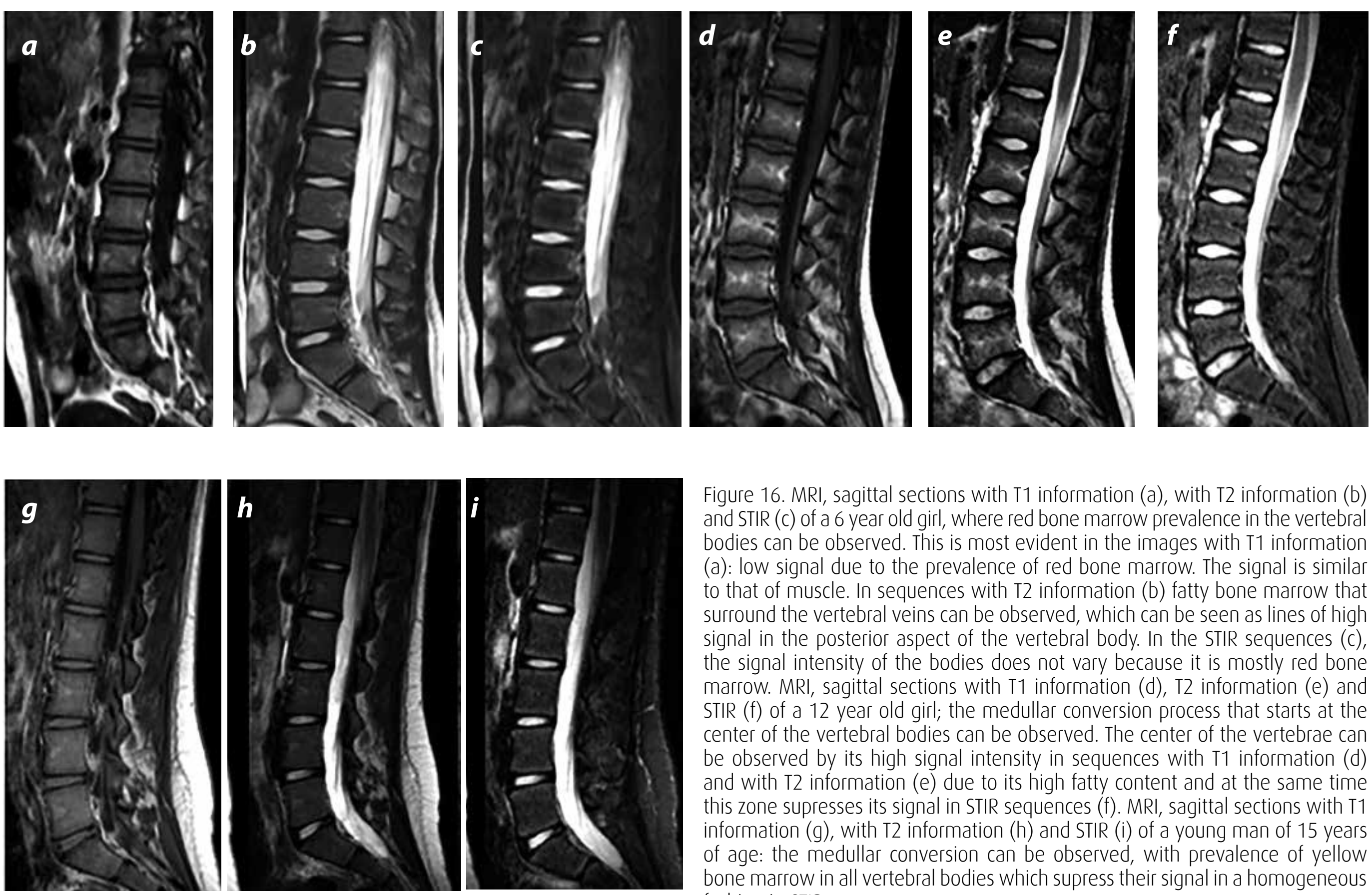

Figure 16. MRI, sagittal sections with T1 information (a), with T2 information (b) and STIR (c) of a 6 year old girl, where red bone marrow prevalence in the vertebral bodies can be observed. This is most evident in the images with T1 information (a): low signal due to the prevalence of red bone marrow. The signal is similar to that of muscle. In sequences with T2 information (b) fatty bone marrow that surround the vertebral veins can be observed, which can be seen as lines of high signal in the posterior aspect of the vertebral body. In the STIR sequences (c), the signal intensity of the bodies does not vary because it is mostly red bone marrow. MRI, sagittal sections with T1 information (d), T2 information (e) and STIR (f) of a 12 year old girl; the medullar conversion process that starts at the center of the vertebral bodies can be observed. The center of the vertebrae can be observed by its high signal intensity in sequences with T1 information (d) and with T2 information (e) due to its high fatty content and at the same time this zone supresses its signal in STIR sequences (f). MRI, sagittal sections with T1 information (g), with T2 information (h) and STIR (i) of a young man of 15 years of age: the medullar conversion can be observed, with prevalence of yellow bone marrow in all vertebral bodies which supress their signal in a homogeneous fashion in STIR sequences.

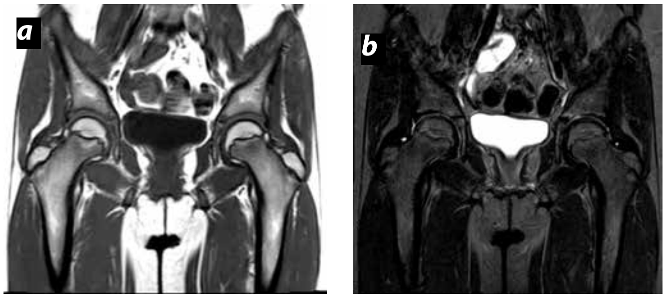

Figure 17. MRI of the pelvis of an 11-year-old girl. Scarce red bone marrow can be observed in the metaphysis of the femur in sequences with T1 information (a), along with adequate suppression of fatty bone marrow in STIR sequences (b).

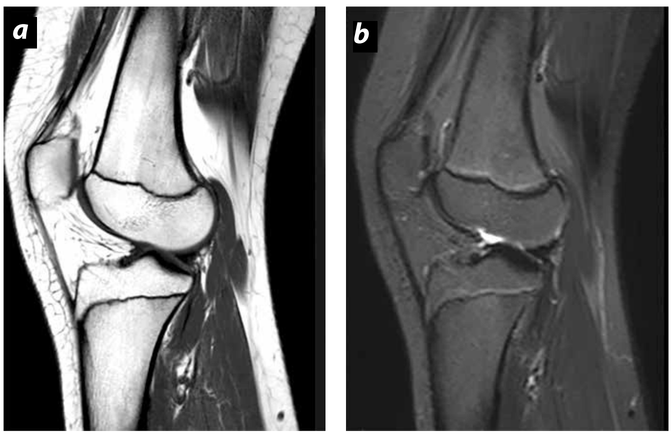

Figure 18. MRI of the knee in a 14 year old girl, sagittal sections, sequences with T1 information (a), STIR (b) and with T2 information (c). Prevalence of fatty bone marrow and its physis in a closing process can be observed.

Figure 19. MRI of the knee in a 20 year old man, sagittal sections in TSE proton density sequences (a) and sequences with T2 information (b). The clear prevalence of yellow bone marrow and the already closed physis can be observed.

Conclusions

Es fundamental reconocer el patrón normal de conversión medular It is fundamental to recognize the normal pattern of marrow conversion in paediatric age in a physiological way, in order to be capable of identifying pathologies in this population. In order to achieve this it is necessary to learn to differentiate the normal development processes for each sex and age, and also recognize the different MRI sequences and potential artefacts that can be generated, which allows in some cases to differentiate normal patients from the truly sick.

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