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Research Article

IMAGING TECHNIQUES FOR BONE MASS EVALUATION IN CHILDREN AND ADOLESCENTS: A COMPREHENSIVE REVIEW OF CURRENT METHODS AND CLINICAL IMPLICATIONS

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ABSTRACT

The assessment of bone health in children and adolescents is essential for early detection of low bone mass and the prevention of future skeletal disorders. This review explores various imaging methods used to evaluate bone mass in pediatric populations, emphasizing the advantages, limitations, and potential clinical applications of each technique. Dual-energy X-ray absorptiometry (DXA) remains the gold standard for bone mineral density (BMD) assessment across all age groups due to its reliability and extensive research support. However, DXA has limitations in pediatric populations, particularly in accounting for growth-related changes in bone size and structure, and the lack of robust pediatric reference curves. Other imaging modalities, such as quantitative computed tomography (QCT), peripheral QCT (pQCT), high-resolution pQCT (HR-pQCT), bone quantitative ultrasound (QUS), magnetic resonance imaging (MRI), and automated radiogrammetry, offer additional insights into bone strength, structure, and quality. However, these methods are still under evaluation for routine clinical use in children and adolescents, and each presents unique challenges, including accessibility, standardization, and the need for more comprehensive reference data. The review underscores the importance of integrating local reference curves and considering skeletal growth when interpreting bone mass results in pediatric patients. While DXA remains the primary tool for diagnosing low bone mass, particularly in children at risk of primary or secondary bone diseases, further research is needed to optimize and validate the use of alternative imaging methods in clinical practice.

Keywords: - Bone mass evaluation, Pediatric bone health, Dual-energy X-ray absorptiometry (DXA), Quantitative computed tomography (QCT), Peripheral quantitative computed tomography (pQCT).

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INTRODUCTION

The study of bone health in children and adolescents has gained increasing attention in recent years due to the critical importance of establishing strong skeletal foundations during early life. Identifying individuals with low bone mass during childhood and adolescence is considered a key strategy in preventing future skeletal disorders. Early identification allows for the implementation of preventive and therapeutic measures that promote healthy bone growth, which is essential for reducing the risk of osteoporosis and fractures later in life. Several studies have emphasized the importance of early intervention in bone health, highlighting the need for accurate and reliable methods to assess bone mass in younger populations [1–8].

However, the most appropriate technique for evaluating bone mass in children and adolescents remains a subject of considerable debate within the medical community [9–12].

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Unlike adults, where bone mass assessment methods are more established and standardized, pediatric populations present unique challenges. These challenges stem from the dynamic nature of skeletal growth and development, which can complicate the interpretation of bone density and mass measurements. Moreover, the availability of suitable methods for clinical practice is often limited, leading to findings that may raise more questions than provide answers. The need to consider additional factors, such as the cost of the assessment and the potential risks associated with ionizing radiation, further complicates the situation, especially when the tests are conducted for preventive purposes.

Among the various methods available for assessing bone mineral density (BMD) and bone mineral content (BMC), dual-energy X-ray absorptiometry (DXA) is the most commonly used technique and is considered the gold standard across all age groups, including children [13]. DXA's widespread use can be attributed to its reliability and the extensive body of research supporting its application. However, DXA is not without limitations, particularly in pediatric populations where growth-related changes in bone size and structure must be carefully accounted for to avoid misinterpretation of the results.

In addition to DXA, several other imaging techniques have been developed to provide a more comprehensive assessment of bone health in children and adolescents. These include central quantitative computed tomography (central QCT), peripheral QCT (pQCT), high-resolution pQCT (HR-pQCT), bone quantitative ultrasound (QUS), magnetic resonance imaging (MRI), and automated radiogrammetry [14–16]. Each of these methods offers distinct advantages in terms of providing detailed information about bone strength, including aspects such as bone size, geometry, microarchitecture, and overall bone quality. However, the utility of these methods in clinical practice is still under evaluation, and their roles are not yet fully defined.

The assessment of bone mass in children and adolescents is further complicated by the need to consider skeletal growth during the interpretation of test results. Unlike adults, whose bone mass remains relatively stable, children and adolescents experience continuous changes in bone structure and density as they grow. This makes the evaluation of bone health in this age group more complex and necessitates a nuanced understanding of the factors that influence bone development. In response to these challenges, the International Society for Clinical Densitometry (ISCD) has reviewed and updated guidelines for the performance and interpretation of DXA in children and adolescents. The goal of these guidelines is to enhance the accuracy and reliability of bone mass assessments in pediatric populations [9, 18–21].

Given the increasing indications for bone mass investigation during childhood and adolescence, it is crucial to critically evaluate the strengths and limitations of each available imaging method. This review aims to summarize the particularities, advantages, and disadvantages of various techniques for assessing bone health in younger populations. By discussing the current literature and highlighting key findings, the review seeks to provide a better understanding of the roles these methods can play in clinical practice. Additionally, it aims to stimulate further research and development to improve the applicability and standardization of bone health assessments in children and adolescents.

MATERIALS AND METHODS

This review focuses on the clinical evaluation of bone mass in children and adolescents up to 20 years of age, analyzing a range of imaging methods used for this purpose. The publications considered for this review were sourced from literature published in the last decade, specifically between 2006 and 2016. Both English and Portuguese language studies were included to provide a comprehensive overview. The literature search was conducted using two primary databases: the Regional Library of Medicine (BIREME) and PubMed.

To ensure the relevance and depth of the review, a strategic combination of keywords was employed in the search process. The keywords included "bone density," "osteoporosis/diagnosis," "densitometry," "tomography," "ultrasonography," "magnetic resonance imaging," and "radiogrammetry." These terms were used in various combinations, but always in conjunction with either "bone density" or "osteoporosis/diagnosis" to maintain the focus on bone mass evaluation. The search strategy was designed to capture a broad spectrum of studies, including both original research articles and review papers that specifically addressed the characteristics and effectiveness of different imaging methods for assessing bone mass in the specified age groups.

In addition to the primary studies published within the 2006–2016 timeframe, certain earlier publications were also included in the review. These earlier studies were deemed relevant for providing foundational knowledge or for contributing significant insights into the methods used for bone mass assessment. The inclusion of these older studies allowed for a more complete understanding of the evolution of imaging techniques and their application in pediatric and adolescent populations.

The selection of articles was based on their relevance to the topic, focusing on studies that provided detailed information on the characteristics, advantages, and limitations of various imaging methods used to evaluate bone mass in children and adolescents. The methods examined included dual-energy X-ray

absorptiometry (DXA), quantitative computed tomography (QCT), peripheral QCT (pQCT), high-resolution pQCT (HR-pQCT), bone quantitative ultrasound (QUS), magnetic resonance imaging (MRI), and automated radiogrammetry. These methods were analyzed to determine their applicability, reliability, and potential for use in clinical practice, with particular attention given to their suitability for the pediatric population.

By integrating findings from a wide range of studies, this review aims to provide a comprehensive overview of the current state of imaging methods used in the clinical evaluation of bone mass in children and adolescents, while also identifying areas where further research and development are needed.

RESULTS

The evaluation of bone mass in childhood and adolescence can be conducted using various imaging methods. These include dual-energy X-ray absorptiometry (DXA), central quantitative computed tomography (central QCT), peripheral QCT (pQCT), high-resolution pQCT (HR-pQCT), quantitative ultrasound (QUS), magnetic resonance imaging (MRI), and automated radiogrammetry. Each of these methods offers unique advantages and challenges, particularly in pediatric populations, where the assessment of bone health is complicated by ongoing growth and development.

Dual-Energy X-ray Absorptiometry (DXA)

DXA is widely regarded as the gold standard for measuring bone mineral density (BMD) and bone mineral content (BMC) across all age groups, including children and adolescents. Its popularity stems from several advantages, including the widespread availability of DXA scanners, the speed of the scanning process, and the method's precision. However, DXA presents several limitations when applied to pediatric populations:

1. **Lack of Robust Reference Databases:** Particularly for younger children, there is a scarcity of comprehensive reference databases, making it difficult to accurately interpret results.
2. **Limited Clinical Outcomes:** The correlation between DXA measurements and significant clinical outcomes in children is not well-established.
3. **Inaccuracies Due to Growth:** Changes in body size and composition during growth can lead to inaccuracies and artifacts in DXA measurements [12].

Another critical consideration is the use of ionizing radiation in DXA, albeit at low levels. This is a particular concern in children, especially those under 4 or 5 years of age, who may have difficulty remaining still during the procedure without sedation. Additionally, DXA provides a measure of areal bone mineral density (aBMD), a two-dimensional measure that does not accurately reflect true volumetric bone density. The aBMD measurement (g/cm^2) is derived from the bone mass (BMC) per bone area, but it does not account for the third dimension—depth—since this cannot be directly measured due to the orientation of the X-ray beam [22].

The growth of children's bones introduces another layer of complexity, as the increase in bone volume often outpaces the increase in bone area. This discrepancy can lead to the underestimation of bone density in smaller children and the overestimation in larger ones [23, 24]. Studies have shown that while aBMD increases with age, volumetric bone mineral density (vBMD), measured by computed tomography, remains relatively stable until puberty [27, 28]. This suggests that aBMD, as measured by DXA, may not provide an accurate comparison across children with varying heights and bone sizes. For instance, research by Wren et al. found that DXA identified three times more children with low BMD compared to tomography, particularly in those with chronic disease and short stature, where DXA may underestimate BMD [29].

Several approaches have been proposed to adjust densitometric measurements in children, taking into account factors such as bone size, height, bone age, pubertal stage, and lean body mass [23, 30–35]. However, there is no consensus on the best method for making these adjustments, and the corrections introduce significant complexity into studies [33]. Mathematical models have been developed to estimate vBMD from DXA measurements, assuming specific bone shapes (e.g., cylindrical or cuboid), although the validity of these assumptions remains debated [23, 36].

Despite its limitations, DXA remains a valuable tool in pediatric bone health assessment. For example, the study of BMC is favored for its reproducibility, reliability, and accuracy. BMC measurements by DXA have shown strong correlations with BMC assessed by QCT ($r = 0.94$) [33]. Moreover, BMC and bone area adjusted for height are closely related to bone strength parameters measured by pQCT [34].

However, DXA cannot differentiate between cortical and trabecular bone aBMD, as it provides an aggregate measure of the bone beneath the periosteal envelope. Nonetheless, DXA is useful for screening asymptomatic vertebral fractures in high-risk populations, such as those on long-term glucocorticoid therapy, with newer software improving image quality and reducing radiation exposure compared to conventional radiography [19].

In 2013, the International Society for Clinical Densitometry (ISCD) provided updated guidelines for DXA use in children and adolescents:

1. **Recommended Sites:** The lumbar spine (LS) and total body (TB) are recommended sites for densitometric evaluation, with the head excluded in small children. The hip is not a preferred site due to variability in skeletal development [19].
2. **Z Scores:** Densitometric variables should be expressed as standard deviations (Z scores) rather than T scores, as used in adults, to indicate differences from the average value of the healthy population of the same age and gender [19].
3. **Low BMC or BMD:** Diagnosed when the Z score is less than or equal to −2 standard deviations (SD) for age, gender, ethnicity, and/or body size [19].
4. **Osteoporosis Diagnosis:** Should not be based solely on DXA results without clinical evidence of bone fragility. If the Z score is ≤−2 SD but there is no fracture history, the term "low bone mineral content or low bone mineral density for age" should be used [20].
5. **Fracture History:** A significant fracture history includes two or more long bone fractures before age 10, three or more long bone fractures up to age 19, or one or more vertebral compression fractures, with the latter indicating osteoporosis regardless of DXA results [20].
6. **Adjustments:** In children with growth disorders, adjustments should be made to BMC and aBMD to prevent misinterpretations, using estimated vBMD or Z scores adjusted for height [19].
7. **Follow-up Scans:** Should be conducted with a minimum interval of 6–12 months [19].

Despite being the most studied and widely available method, DXA's application in pediatric populations remains limited by high costs and the use of ionizing radiation, which precludes its widespread use in preventive studies for children and adolescents.

Quantitative Computed Tomography (QCT)

QCT refers to the analysis of computed tomography (CT) images using specialized software to derive quantitative bone parameters. QCT offers significant advantages over DXA, as it provides three-dimensional measurements of bone. This method can assess true volumetric BMD (vBMD) in g/cm³, independent of bone size. Additionally, QCT evaluates bone structure and geometry—both crucial determinants of bone strength—and can separately analyze cortical and trabecular bone [15, 37].

The types of CT scanners used in bone densitometry include whole-body general-purpose CT scanners, as well as dedicated peripheral QCT (pQCT) and high-resolution pQCT (HR-pQCT) scanners. Central QCT is applied to the spine and proximal femur using general-purpose CT scanners, while pQCT is used for appendicular skeletal sites, such as the arms or legs. HR-pQCT allows for detailed quantification of trabecular and cortical architecture [37].

Central QCT

Central QCT, particularly of the spine, is often used in research settings to measure vBMD in the trabecular compartment of vertebral bodies. Trabecular bone is more metabolically active than cortical bone, making it more responsive to changes over time, disease progression, and treatment interventions. Modern machines offer rapid scan times, and the supine positioning on a full-length table may be more comfortable for children, particularly those with physical disabilities (e.g., cerebral palsy, Duchenne muscular dystrophy). However, the main disadvantage of central QCT is the high radiation dose required, rendering it unsuitable for routine use in pediatric populations [38]. There is an urgent need to develop pediatric-specific protocols that minimize radiation exposure while maintaining diagnostic accuracy [37].

Peripheral Quantitative Computed Tomography (pQCT)

Peripheral quantitative computed tomography (pQCT) offers a three-dimensional analysis of appendicular bones, primarily focusing on the radius and tibia. One of the main advantages of pQCT is its ability to use lower doses of radiation compared to central QCT, making it a more suitable option for pediatric populations. pQCT enables detailed evaluation of both cortical and trabecular volumetric bone mineral density (vBMD), as well as geometric parameters derived from cross-sectional images, such as total area, cortical area, cortical thickness, and periosteal and endosteal circumferences. Additionally, pQCT can assess cross-sectional muscle area, which is often reported and can be used to calculate an index of bone strength [39].

Despite its advantages, pQCT faces unique challenges when applied to children. The smaller and thinner cortical bones in children are more susceptible to partial volume effects, which occur due to the resolution of the imaging system (voxel size) and the small size of the bones being measured. Voxels near the bone edges may include both bone and soft tissue, resulting in a lower density value than voxels that only capture bone tissue. This issue is more pronounced in smaller bones, leading to an underestimation of cortical vBMD [40]. Moreover, the presence of the epiphyseal plate and the variation in metaphysis size due to growth complicate consistent measurements at the same location in longitudinal studies. Although pQCT generates three-dimensional vBMD measurements that are not affected by body size, the interpretation of cortical geometry and muscle area, which are size-dependent, remains complex, particularly in children with advanced or delayed growth.

Furthermore, pQCT has not been standardized, and reference databases are lacking, limiting its routine clinical use to specialized centers with the necessary expertise [37].

High-Resolution pQCT (HR-pQCT)

High-resolution peripheral quantitative computed tomography (HR-pQCT) is a recently introduced imaging modality that provides a detailed three-dimensional assessment of bone microarchitecture and vBMD in the cortical and trabecular compartments of the distal radius and tibia. HR-pQCT offers a level of accuracy previously unattainable with relatively low radiation doses. This technique shows promise as a research tool for examining changes in bone architecture during skeletal maturation. HR-pQCT provides numerous outcome measures, some of which are analogous to histomorphometric parameters, including trabecular number (Tb.N), trabecular thickness (Tb.Th), trabecular separation (Tb.Sp), cortical thickness (Ct.Th), cortical porosity (Ct.Po), bone volume/total volume (BV/TV), and cortical, trabecular, and total bone area. Proper patient positioning is crucial to ensure accuracy and reproducibility in HR-pQCT scans. Due to its high resolution and relatively long scan times (approximately 3 minutes), the limb must be securely fixed, and the scanning environment must be quiet to minimize movement artifacts [42].

Bone Quantitative Ultrasonography (QUS)

Bone quantitative ultrasonography (QUS) has garnered recent interest as it offers a non-invasive and radiation-free method to evaluate bone tissue. QUS assesses not only bone mineral density but also bone quality, including characteristics such as connectivity, elasticity, and architecture. As a result, QUS provides a more comprehensive measure of bone strength. The method is safe, easy to use, cost-effective, and portable, making it particularly appealing for use in children and adolescents [14, 44]. The high reproducibility and short time required for measurements further enhance its potential for primary prevention studies in younger populations.

QUS operates on the principle that the transmission speed and amplitude of an ultrasound signal are influenced by the physical properties of the medium through which it travels. As the ultrasound wave propagates through bone tissue, changes in its shape, intensity, and speed reflect the characteristics of the bone [45, 46]. Although QUS has shown potential clinical applications across various bone-related diseases [44, 47–53], it remains underutilized and requires further study.

Several QUS devices are available, each assessing different peripheral skeletal sites and providing specific ultrasonographic parameters. The most common devices consist of two transducers—a transmitter and a receiver—placed on opposite sides of the bone, with the distance between them varying based on bone and soft tissue thickness. At sites such as the heel and phalanges, the ultrasound wave generated by the transmitter crosses the bone and is received by the second transducer [14]. However, soft tissue, such as subcutaneous fat or edema, can affect the velocity and attenuation of the signal, which may introduce variability in measurements. Multisite devices, which evaluate the radius and tibia, combine the transmitter and receiver into a single probe positioned on one side of the bone. These devices measure the ultrasound velocity along the cortical bone longitudinally [14].

The most validated QUS technique, calcaneal QUS, predominantly assesses trabecular bone and has been recognized by the International Society for Clinical Densitometry (ISCD) as a method for screening low bone mass in postmenopausal women and men over 65 years of age. According to the ISCD, calcaneal QUS, in combination with clinical risk factors, can help identify individuals at very low fracture risk, for whom further diagnostic evaluation may not be necessary [54].

QUS devices provide two main variables: speed of sound (SoS), expressed in meters per second (m/s), and broadband ultrasound attenuation (BUA), expressed in decibels per megahertz (dB/MHz). SoS is calculated as the ratio of the distance traveled by the ultrasound signal to the time taken for the signal to travel that distance. In children, SoS has been found to be a more accurate measure than BUA, similar to findings in adults [55]. However, foot placement can affect the accuracy of BUA measurements, which may limit its use in longitudinal studies [56].

A more recent QUS technique, phalangeal QUS, has shown great accuracy and reproducibility in assessing bone mineral status in children. This method examines the distal end of the diaphysis of the proximal phalanges of the 2nd to 5th fingers on the non-dominant hand, using two transducers (an emitter and a receiver) positioned on either side of the bone. This anatomical region contains approximately 60% cortical bone, in addition to trabecular bone and a small amount of surrounding soft tissue, providing a reliable measure of bone health in pediatric populations [14].

Phalangeal Quantitative Ultrasound (QUS)

Phalangeal quantitative ultrasound (QUS) has gained attention for its ability to assess bone health in children and adolescents. It provides two key parameters: amplitude-dependent speed of sound (AD-SoS) and bone transmission time (BTT). These measurements are automatically calculated by the device from an average of 96 acquisitions across four fingers, making the results consistent and not reliant on the operator [58].

Amplitude-Dependent Speed of Sound (AD-SoS):

AD-SoS, expressed in meters per second (m/s), represents the speed at which sound waves travel through bone. The device calculates this by measuring the width of the finger, including soft tissue, and dividing it by the time taken for the sound wave to travel from the transmitter to the receiver. The calculation is dependent on the amplitude of the signal, making it distinct from the standard speed of sound measurement [58, 59].

Bone Transmission Time (BTT):

BTT, expressed in microseconds, measures the time it takes for the sound wave to travel through bone, independent of soft tissue interference. It is calculated by comparing the time taken for the signal to peak in bone tissue versus when only soft tissue is present. This makes BTT a more specific indicator of bone properties, especially useful in cases where soft tissue might confound other measurements [58]. BTT is primarily calculated for the second to fourth phalanges, with soft tissue measurements taken from the base of the thumb to the index finger [58].

Both AD-SoS and BTT have shown high correlation, indicating they provide similar information about bone health [58]. Clinical studies suggest that these parameters reflect cortical mass, porosity, and geometric features such as cortical thickness and area [57, 60, 61].

Multisite QUS Devices:

Multisite QUS devices measure the speed of sound along the cortex of the mid-shaft tibia and the distal third of the radius. The speed of sound in these measurements is influenced by several bone characteristics, including cortical thickness, density, microstructure, and elasticity. However, this dependency diminishes when cortical thickness exceeds 4 mm [63].

To enhance precision, some QUS devices offer additional variables, such as the stiffness index (SI), quantitative ultrasound index (QUI), and ultrasound bone profile index (UBPI). SI and QUI are derived from both speed of sound and broadband ultrasound attenuation (BUA), providing a percentage-based score. UBPI, used in phalangeal QUS, quantifies sound wave transmission characteristics, with values ranging from zero to one—the higher the index, the lower the fracture risk. UBPI is thought to reflect bone quality, including elasticity and microarchitecture, and its values remain stable across age groups [53]. However, further validation is needed to establish the clinical usefulness of these variables in children [14].

Challenges in Interpretation:

Ultrasonographic and densitometric measurements are correlated with height, necessitating careful interpretation, particularly in pediatric populations. This correlation likely arises because QUS variables reflect not only bone density but also other indicators of bone resistance, such as geometry, which adapts to biomechanical forces during growth [51]. For instance, bone size can significantly impact ultrasonographic parameters, particularly in the heel [67]. However, phalangeal QUS appears to be less influenced by finger width, with only 6% of AD-SoS values affected by this factor [68].

Soft tissue thickness at measurement sites, such as the heel, phalanges, tibia, and radius, can also influence QUS variables, leading to potential underestimations. Phalangeal QUS devices address this issue by using BTT to correct for soft tissue effects, making it a more accurate measure of bone mineral status, particularly in obese individuals [14]. Higher absolute values of ultrasonographic variables, such as SoS, BUA, AD-SoS, and BTT, are indicative of better bone mineral status within an age group.

Some pediatric reference curves have been developed, allowing bone measurements to be expressed as Z-scores adjusted for age, height, and pubertal stage, depending on the QUS device used. Similar to DXA interpretation in children, a Z-score below -2 SD indicates low bone mineral status or bone health impairment relative to the anthropometric variable considered [14].

Comparative Studies:

QUS measurements at the heel, phalanges, and radius have been found to be comparable to DXA in identifying postmenopausal women with vertebral fractures [75–78]. In children, calcaneal QUS has been shown to identify those with a history of low-impact fractures with sensitivity similar to that of DXA [49]. Similar results were observed in studies measuring AD-SoS in the phalanges and BMD in the lumbar spine using DXA [79]. Additionally, phalangeal QUS has been effective in distinguishing fractured from non-fractured children, particularly those with bone fragility [80]. Calcaneal QUS may predict bone fragility independently of BMD, and combining QUS with DXA data can improve fracture prediction [81, 82].

Correlation between QUS and other methods like DXA and pQCT varies. For instance, a weak but significant correlation ($r = 0.22$; $p < 0.05$) has been found between SoS in the heel and vBMD in the radius, measured by pQCT [64]. Moderate correlations have also been observed between AD-SoS and forearm BMD measured by DXA in children with genetic diseases ($r = 0.66$; $p < 0.000001$) [84]. Recent studies in Brazilian children with congenital adrenal hyperplasia have also demonstrated significant correlations between phalangeal QUS parameters and DXA measurements of the lumbar

spine and total body (correlations ranging from 0.59 to 0.72; $p < 0.001$) [86].

However, discrepancies between DXA, QUS, and pQCT results do not necessarily indicate methodological errors. Since these methods assess different properties of bone tissue, they may not be interchangeable or identify the same patients [10]. Some authors suggest that QUS provides complementary information to DXA, such as insights into trabecular connectivity (measured by BUA) or bone density (reflected by SoS) [53, 81]. The use of different reference data for each method may also contribute to inconsistencies. Further research is needed to better understand the correlation and agreement between these bone mass evaluation methods.

Limitations of QUS:

One limitation of QUS is its inability to separately analyze bone mass, density, and geometry, instead providing an integral estimation of bone mineral status [15]. The interpretation of QUS variables can also be challenging, and more studies are needed to clarify the determinants of each variable. Additionally, pediatric reference curves are scarce, particularly for various ethnic groups. A recent study involving over a thousand healthy Brazilian children and adolescents (aged 6-17 years) addressed this gap, but more data are needed [73, 90].

The availability of different QUS devices complicates the comparison of results across studies, and the International Society for Clinical Densitometry (ISCD) has noted that this variability hinders the method's validation in clinical practice. Consequently, the ISCD recommends that QUS should not yet be used for diagnosing low bone mass in children and adolescents [18]. Standardization of QUS devices and further research are required to establish its role in clinical practice.

Magnetic Resonance Imaging (MRI)

Magnetic Resonance Imaging (MRI) offers a volumetric assessment of bone similar to Quantitative Computed Tomography (QCT), but with the significant advantage of not utilizing ionizing radiation [91]. MRI can be used to study both the central and appendicular skeleton, providing detailed information about bones and muscles across multiple anatomical planes without requiring patient repositioning [8]. While full-body MRI for bone structure quantification is limited due to accessibility issues, dedicated peripheral MRI (pMRI) units have been developed. In adults, pMRI has been used to analyze trabecular and cortical bone microstructure in areas such as the distal radius, distal tibia, calcaneus, and proximal femur, achieving resolutions of 200 μm or higher [92].

However, MRI's application in pediatric populations presents several challenges. The technique is difficult to standardize, is not widely accessible, and has been infrequently used in children. Additionally, MRI accuracy is still being optimized for bone structure assessment. Other limitations include the noise generated by the equipment during scanning and the extended scan times, which can range from 20 to 30 minutes depending on the imaging sequence used. These factors make it challenging to keep children still for the duration of the scan, increasing the potential for motion artifacts. The long horizontal gantry of the MRI scanner can also be distressing for claustrophobic individuals, and the overall environment of the scanner room is often not child-friendly. Furthermore, parents cannot accompany their children during the scan, which may exacerbate anxiety in young patients.

To date, MRI has primarily been used within research protocols, and its applicability in routine clinical practice remains to be fully evaluated [8].

Automated Radiogrammetry

Radiogrammetry is one of the oldest methods for the quantitative assessment of the skeleton and involves the analysis of a radiograph of the nondominant hand [93]. Measurements of metacarpal dimensions are used to calculate various indices, such as metacarpal bone mass, providing insights into skeletal health.

Automated radiogrammetry is a longstanding method for quantitative skeletal assessment, particularly of the nondominant hand. This technique involves measuring metacarpal dimensions, including cortical thickness, and calculating the pediatric bone index using the three middle metacarpals. The pediatric bone index is determined through a formula incorporating the average values for transverse cortical area (A), bone width (W), and bone length (L): pediatric bone index = A/(W^1.33 * L^0.33) [94]. Radiogrammetry is particularly sensitive to cortical bone changes, such as periosteal apposition and endosteal resorption, making it a valuable tool for tracking bone changes during growth and aging [8]. Although widely available and relatively low-cost, early radiogrammetry was limited in clinical and research applications due to poor precision when using manual calipers. However, advancements in computer-aided analysis have significantly improved its precision by automating the identification of regions of interest [93]. Automated radiogrammetry has shown promise in adults as a predictor of bone fragility [95] and has been used in children to identify those at increased fracture risk [97], study normal bone growth and development [98], and assess differences between patient groups and healthy children [99]. It has also been incorporated into the BoneXpert system, which combines automated radiogrammetry with bone age assessment [99]. Despite

these advances, radiogrammetry remains primarily a research tool [8].

Table 2 summarizes the advantages, disadvantages, and potential clinical indications of various bone mass evaluation methods for children and adolescents. Significant methodological variation exists, and further progress is needed before these techniques become viable for routine clinical use. Tomographic methods (central QCT, pQCT, and HR-pQCT) and MRI, despite their advantage in assessing true bone mineral density, are not yet available for widespread clinical application [18]. Central QCT is particularly problematic due to its high radiation dose. The absence of radiation and technical simplicity make QUS a promising option for evaluating bone health in children and adolescents, especially those considered "healthy" or those with chronic conditions that may affect the skeleton [14, 73]. However, additional studies are required to standardize the technique and define parameters that will allow QUS to be used for diagnosing low bone mass and monitoring affected children. Automated radiogrammetry shows potential for identifying individuals who may benefit from a comprehensive bone assessment, but the clinical value of its measurements still needs to be established [95]. A common limitation across all methods, including DXA, is the lack of sufficient pediatric reference data, necessitating caution when interpreting results. Ideally, comparisons should be made using local reference data. In this age group, a diagnosis of osteoporosis should only be made if there is clinical evidence of bone fragility, as unlike in adults, no strong correlation has been established between any bone measure and future fracture risk.

Table1: Characteristics of the main QUS methods available in the market to evaluate the child (adapted from Baroncelli) [14]

Skeletal site of measurement	**Bone region of interest**	**Bone components at region of interest**	**Pathway of ultrasound transmission inside the bone**	**Main parameters obtained**	**Related CV, %**
Heel	Midcalcaneus	Trabecular bone (>90%) with thin cortical shell	Transverse	SoS BUA SI and QUI	0.2–3.9 2.7–7.0 1.9–2.7
Proximal phalanges (fingers II–V) of the hand	Distal end of diaphysis below the condyles	Cortical bone (-60%) Trabecular bone (-40%) Small medullary canal	Transverse	AD-SoS BTT UPBI	0.3–0.9 1.0–3.5 2.85
Radius	Distal third	Cortical bone (>95%)	Axial	SoS	0.4–0.9
Tibia	Midshaft	Cortical bone (-100%)	Axial	SoS	0.3–1.0

Table 2: Advantages, disadvantages and possible indications in clinical practice of the imaging methods for bone mass evaluation in children and adolescents.

Methods	Advantages	Disadvantages	Possible indications in clinical practice
DXA	Widely available in tertiary Centers Most used, known and studied method (gold-standard) Short analysis time Good accuracy	Radiation is used, albeit in small doses: 6.7–31 µSv (with a multiple X-ray beam) Demands that the child remain Still Bidimensional measure, providing only an estimate of bone mineral density Lack of robust pediatric reference curves High cost	Children and adolescents (0–19 years) with primary chronic bone disease or at risk of secondary bone disease (if an intervention to reduce fracture risk is potentially beneficial and DXA results can influence the management) [9] In children under 3 years, only lumbar spine DXA should be performed (no RV and positioning difficulties in total body DXA in this age group) [18] Vertebral fracture analyses in selected patients No indication for preventive studies
Central QCT	Measures cortical and trabecular volumetric bone mineral density	High dose radiation is used (50–100 µSv), which prevents routine use in children Non-portable machine, lack of accessibility and lack of RV High cost	No indication to date [18]

pQCT	Measures cortical and trabecular volumetric bone mineral density Use minimal dose of radiation (<2 µSv) Portable and less expensive machine	Difficult to correct positioning in children Cortical vBMD may be underestimated due to partial volume effects Not clinically available and lack of RV	No indication to date, except in some local centers with appropriate expertise [18]
HR-pQCT	Measures cortical and trabecular volumetric bone mineral density Use minimal dose of radiation (<2 µSv) Provides measures of microarchitecture Portable and less expensive machine	Difficult to correct positioning in children Not clinically available and lack of RV	No indication to date
QUS	Portable and practical device for use in primary care Measures are obtained quickly and easily No radiation is used Reduced cost High reproducibility Quantitative and qualitative bone evaluation	Less available, known and studied Uncertainty about what each variable does reflect. It does not assess bone mass, density and geometry separately Scarce reference curves There are several types of devices available, making it difficult to compare studies It cannot be done if there is history of previous fracture or deformity at the measurement site	Good perspective for use in primary prevention actions in 0–19 years individuals [14] There is no formal indication yet (from ISCD) for confirmation of low bone mass, monitoring and evaluation of response to treatment of this condition [18]
MRI	Measures cortical and trabecular volumetric bone mineral density No radiation is used Provides measures of microarchitecture	Difficult to correct positioning in children Long scan times High potential for motion artifact Lack of accessibility and lack of RV High cost	No indication to date
Automated radiogram metry	High precision Low dose of ionizing radiation Low cost Good potential to be widely available Can be used in primary care environments	Clinical value of measures still needs to be established Limited reference values	No indication to date

CONCLUSION

The reviewed studies indicate that, despite the advent of new imaging technologies, DXA remains the gold standard for confirming a diagnosis of low bone mass across all age groups. It is particularly useful for evaluating children and adolescents (ages 0–19) who have primary chronic bone diseases or are at risk of secondary bone conditions. However, accurate interpretation of DXA results requires a thorough understanding of its specific characteristics and limitations. In pediatric populations, the complexities introduced by skeletal growth must always be considered, as they add layers of difficulty to the evaluation process.

For an accurate assessment, normal bone values should ideally be established by accounting for not only age, gender, and ethnicity but also stature and pubertal stage. Having appropriate local reference curves is crucial to ensure that these patients are properly evaluated in clinical settings. This approach helps mitigate the challenges posed by growth variations and ensures that the DXA results are interpreted in a way that reflects the true bone health of the patient.

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