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Review Article

Bone Microarchitecture Quantification on High-Resolution Peripheral QCT in Pre-Menopausal Women

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ABSTRACT

Bone health depends not only on bone mineral density (BMD) but also on microarchitectural integrity, which strongly influences skeletal strength and fracture risk. Conventional dual-energy X-ray absorptiometry (DXA), while widely used, provides only areal BMD and lacks the ability to capture three-dimensional microarchitecture. This limitation is particularly important in premenopausal women, where fragility fractures may occur despite normal BMD values. High-resolution peripheral quantitative computed tomography (HR-pQCT) overcomes these shortcomings by enabling in vivo, three-dimensional assessment of trabecular and cortical compartments with high spatial resolution. The technique provides volumetric BMD, detailed microstructural parameters, and finite element analysis (FEA)-based estimates of mechanical competence.

This review synthesizes current evidence on the application of HR-pQCT in premenopausal women. Normative data demonstrate generally favourable trabecular and cortical profiles in this group, yet studies reveal that women with idiopathic osteoporosis or fragility fractures exhibit significant cortical thinning, increased porosity, and disrupted trabecular organization despite near-normal BMD. HR-pQCT has also provided insights into skeletal alterations in metabolic disorders, diabetes, amenorrhea, and endocrine diseases, underscoring its role in detecting early microstructural compromise. Moreover, FEA derived from HR-pQCT images offers functional estimates of stiffness and failure load, strengthening its predictive value for fracture risk.

Despite its clinical promise, HR-pQCT adoption is limited by cost, availability, and lack of standardized reference ranges for premenopausal women. Nonetheless, ongoing technological advances and longitudinal research are likely to establish HR-pQCT as an essential tool for early detection of skeletal fragility, monitoring treatment response, and guiding preventive strategies in young women.

Keyword: Bone Density, Bones pathology, Tomography, X-Ray Computed, Osteoporosis diagnosis, Perimenopause

INTRODUCTION

Overview of Bone Microarchitecture

Bone microarchitecture refers to the three-dimensional organization and structural arrangement of bone tissue components, including trabecular and cortical compartments. This microstructural organization is a critical determinant of skeletal health, influencing bone strength and resistance to fracture beyond what bone mass alone can explain. Bone strength results not solely from bone quantity, such as mineral density or mass but also from structural quality, including parameters like trabecular number, thickness, connectivity, and cortical porosity. These microarchitectural features collectively govern the capacity of bone to sustain mechanical loads without failure.

The distinction between bone mass and bone quality is pivotal in understanding bone strength. While traditional assessments have largely focused on bone mineral density (BMD), recent insights emphasize that bone quality, encompassing microarchitectural parameters, material properties, and turnover, plays an equally crucial role in fracture risk prediction. For example, conditions such as idiopathic osteoporosis in premenopausal women illustrate that individuals may sustain fractures despite having a relatively normal areal BMD, implicating microarchitectural deficits as a major contributor to skeletal fragility [1]. Similarly, body composition, particularly central adiposity, has been shown to correlate inversely with bone quality, highlighting that bone remodeling and microarchitecture are influenced by systemic factors beyond bone mass [2].

Conventional bone density measurements, predominantly dual-energy X-ray absorptiometry (DXA), provide areal BMD in two dimensions and have been instrumental in osteoporosis diagnosis. However, DXA captures limited information regarding bone geometry and lacks the capability to distinguish cortical from trabecular compartments or assess three-dimensional microarchitecture. The reductionist nature of DXA impedes its capacity to fully represent bone quality, which limits its predictive accuracy for fracture risk. This limitation is particularly evident in populations such as premenopausal women who may exhibit normal or near-normal BMD yet experience fragility fractures due to microarchitectural deterioration [3]. Accordingly, there is an urgent need for imaging modalities capable of in vivo, noninvasive, high-resolution analysis of bone microarchitecture to better characterize skeletal health.

High-Resolution Peripheral Quantitative Computed Tomography (HR-pQCT) Technology

High-resolution peripheral quantitative computed tomography (HR-pQCT) represents a significant technological advancement in bone imaging. Developed in the early 2000s, HR-pQCT utilizes a cone-beam CT scanner with high spatial resolution (nominal voxel size approximately 82 microns in the first-generation devices) to image peripheral skeletal sites such as the distal radius and tibia. This modality enables three-dimensional visualization of bone microstructure with differentiation between cortical and trabecular compartments [4]. HR-pQCT technology was pioneered to overcome the limitations of planar radiographic methods like DXA and even central quantitative computed tomography (QCT), offering a low-radiation, non-invasive assessment alternative capable of volumetric BMD measurement and microarchitectural quantification in vivo [5].

The advantages of HR-pQCT are multifold. Unlike DXA, it provides volumetric BMD it measures true volumetric density independent of bone size. Moreover, it captures intricate microstructural features such as trabecular number, thickness, separation, connectivity density, and cortical porosity, which are essential parameters influencing mechanical bone competence. The high resolution and three-dimensional nature of HR-pQCT afford detailed evaluation of bone geometry and microarchitecture, facilitating more precise assessments of bone strength. Furthermore, HR-pQCT also enables application of finite element analysis (FEA) on reconstructed images to estimate biomechanical properties, such as stiffness and failure load, providing functional insights into fracture risk [4], [6].

The distal radius and tibia have been the primary imaging sites for HR-pQCT, given their mixed composition of cortical and trabecular bone, accessibility, and clinical relevance as common fracture locations. The relevance of peripheral skeletal assessment is enhanced by evidence that microarchitectural properties at these sites correlate significantly with those at central sites like the spine and hip [7]. Hence, HR-pQCT evaluations at the radius and tibia serve as representative measures for overall skeletal health and fracture susceptibility.

Focus on Premenopausal Women

Premenopausal women exhibit distinct bone characteristics compared to their postmenopausal counterparts. The premenopausal skeleton is typified by a more favorable bone microarchitecture, with thicker cortices, higher trabecular number, and lower porosity. This population generally maintains higher estrogen levels that actively preserve bone mass and quality. However, some premenopausal women suffer fractures that cannot be explained by conventional DXA-derived BMD alone, suggesting that microarchitectural integrity plays a pivotal role in skeletal fragility in this group [7].

Understanding bone microarchitecture in premenopausal women is essential for early fracture prevention strategies. Identifying structural deficits before menopause, when bone loss accelerates due to hormonal changes, offers an opportunity for interventions that may mitigate long-term fracture risk [8]. However, research on bone microarchitecture quantification in premenopausal women remains sparse relative to extensive studies in postmenopausal populations. Challenges include relatively lower fracture incidence, variability in hormonal status, and limited normative data, which all contribute to the complexity of interpreting HR-pQCT findings in this group [9]. Consequently, dedicated investigations focusing on microarchitectural assessment in premenopausal women are critical to fill current knowledge gaps.

METHODOLOGY

A narrative review approach was adopted. Relevant studies were identified through PubMed, Scopus, and Web of Science using the terms “HR-pQCT,” “bone microarchitecture,” “cortical porosity,” “trabecular bone,” “finite element analysis,” and “premenopausal women.” Only English-language human studies published up to June 2025 were included. Eligible articles focused on HR-pQCT-based assessment of trabecular and cortical bone parameters, volumetric BMD, and finite element analysis in premenopausal women. Data were extracted on imaging protocols, segmentation methods, microarchitectural indices, and clinical applications. Findings were synthesized to summarize methodological aspects, normative values, alterations in fracture-prone individuals, and clinical implications.

Bone Microarchitecture Parameters Assessed by HR-pQCT

Trabecular Bone Metrics

The trabecular compartment, characterized by a network of interconnected plates and rods, provides structural support and absorbs mechanical loads. HR-pQCT allows precise quantification of key trabecular parameters: trabecular number (Tb. N), trabecular thickness (Tb. Th), and trabecular separation (Tb. Sp). Trabecular number refers to the number of trabeculae per unit length, thickness denotes the average thickness of trabeculae, and separation reflects the average distance between trabeculae. These parameters collectively reflect the integrity and connectivity of the trabecular network, which influences bone resilience.

Significant correlations exist between trabecular microarchitecture and bone strength, independent of areal BMD. For example, decreased trabecular number and thickness or increased separation have been associated with increased bone fragility. These changes translate to a less robust, more fragile trabecular matrix, impacting load distribution and predisposing to fractures [7]. The OFELY study, a large prospective cohort observing postmenopausal women, has shown that lower trabecular density and connectivity parameters independently predict incident fractures, underscoring the clinical significance of these trabecular features [10].

In premenopausal women, microarchitectural deterioration of trabecular bone has been observed in those with fractures, highlighting the importance of these parameters in risk stratification. Comparisons between fracture cases and controls reveal lower trabecular thickness and number, accompanied by increased trabecular separation, which may not be evident through DXA alone [9]. Moreover, in young athletic populations with menstrual disturbances, compromised trabecular morphology has been implicated in increased fracture risk reflecting compromised microarchitectural integrity [11]. These findings emphasize the crucial role of trabecular metrics assessed by HR-pQCT in understanding fracture susceptibility in premenopausal women.

Cortical Bone Metrics

Cortical bone, constituting the dense outer shell of bones, plays a fundamental role in resisting bending and torsional forces. HR-pQCT allows evaluation of cortical parameters including cortical thickness (Ct. Th), cortical porosity (Ct. Po), and cross-sectional area (CSA). Cortical thickness reflects the size of the cortical shell, whereas porosity represents the presence of microscopic pores within the cortical matrix that reduce its mechanical competency. Cross-sectional area captures the overall size and geometric distribution of cortical bone, influencing biomechanical strength.

Cortical bone properties contribute substantially to overall bone stiffness and strength. Increased cortical porosity leads to weakening of the cortical shell, reducing its load-bearing capacity and thus negatively influencing bone stiffness. Studies have demonstrated that cortical porosity and reduced cortical thickness are associated with elevated fracture risk, rendering these parameters vital biomarkers for skeletal health [12], [13]. Particularly in the context of premenopausal fractures, cortical microstructural deterioration has been reported. Women with idiopathic osteoporosis or fragility fractures, despite normal or low-normal BMD, show profound cortical thinning and increased porosity at peripheral sites, potentially underpinning their skeletal fragility [8].

Therefore, detailed cortical assessments using HR-pQCT enable a more nuanced understanding of fragility mechanisms and complement trabecular evaluations to provide a comprehensive microarchitectural profile relevant to fracture risk.

Mechanical Properties and Stiffness Estimation

Beyond direct morphometric assessments, HR-pQCT images serve as inputs for finite element analysis (FEA), a computational modelling technique to estimate the mechanical competence of bone. FEA utilizes reconstructed three-dimensional bone geometry and volumetric density data to simulate bone response under loading conditions, predicting stiffness, failure load, and other mechanical properties noninvasively.

Finite element-derived stiffness correlates strongly with actual bone strength measured in vitro and enhances fracture risk discrimination beyond BMD or microarchitectural metrics alone [7]. The functional assessment provides a surrogate biomechanical marker reflecting the cumulative effect of bone mass, geometry, and microarchitecture. This capacity is particularly valuable in premenopausal women, where standard density measurements may not reveal underlying structural deficits. Studies applying FEA in this population have identified significant reductions in stiffness concomitant with microarchitectural deterioration, reinforcing the association between biomechanical compromise and fractures [4].

The predictive value of stiffness parameters for fractures has been substantiated in prospective cohorts, demonstrating that lower FEA-estimated bone stiffness is linked to increased fragility fracture risk independent of BMD [10]. Hence, mechanical properties derived from HR-pQCT through FEA constitute a powerful adjunct in assessing bone strength and guiding clinical decisions.

Methodological Considerations in HR-pQCT Imaging

Scan Acquisition and Standardization Protocols

HR-pQCT imaging requires meticulous attention to scan acquisition protocols to ensure reproducibility and validity. Anatomical landmarks used to position scans at the distal radius and tibia follow standardized conventions. For the distal radius, the reference line is generally positioned at the proximal margin of the radial endplate, with the scan volume extending distally by a fixed distance (usually around 9 mm). The distal tibia scan protocol uses the tibial plafond as a landmark. Accurate and reproducible positioning relative to these landmarks is critical because small spatial shifts can significantly influence measured microarchitectural parameters due to regional heterogeneity within the bone [3].

Despite these guidelines, challenges exist in ensuring scan reproducibility. Minor variations in limb positioning or reference point identification can cause misalignment, leading to measurement variability. Variations in metaphyseal morphology between individuals further complicate acquisition consistency. The literature reports that offset as little as 1 mm in scan positioning can alter microarchitecture measurements by up to 38%, highlighting the necessity for stringent standardization and operator training [3]. To address these issues, consensus guidelines have been developed to standardize HR-pQCT image acquisition and interpretation, emphasizing quality control, consistent patient positioning, and use of automated software to reduce operator-dependent variability [14].

Image Processing and Segmentation Techniques

Once acquired, HR-pQCT images undergo processing to segment cortical and trabecular compartments for quantitative analysis. Segmentation algorithms may be manual, semi-automated, or fully automated, with increasing reliance on automated methods to improve efficiency and reproducibility. Cortical segmentation is particularly challenging due to the thinness and porosity variability of the cortical shell at peripheral sites. Accurate cortical-trabecular separation is essential for reliable parameter extraction [15].

Thresholding strategies employed to delineate bone tissue from marrow and soft tissues vary, encompassing global and local adaptive threshold methods. Local adaptive thresholding techniques account for image inhomogeneity and enhance trabecular segmentation accuracy compared to fixed global thresholds, which may misclassify voxels in regions of varying mineralization [15]. Beyond morphology, advanced image texture analyses and clustering algorithms have been developed using three-dimensional texture features to classify trabecular microarchitecture into distinct phenotypes, offering refined characterization of microstructural classes that may relate to fracture susceptibility [16]. These novel approaches show promise for enhancing sensitivity to subtle microarchitectural alterations and warrant further validation.

Precision, Accuracy, and Validation

The accuracy of HR-pQCT microarchitectural parameters has been validated against gold-standard methods such as micro-computed tomography (micro-CT) and histomorphometric analyses. Studies comparing HR-pQCT to micro-CT of cadaveric distal radius specimens have demonstrated strong correlations for key cortical ($r^2 > 0.80$ for cortical thickness) and trabecular parameters, confirming the validity of HR-pQCT in assessing bone microstructure in vivo [12].

Reproducibility has been established with coefficients of variation (CV) for microarchitectural variables generally below 5%, although precision varies by parameter and compartment. For example, trabecular metrics typically exhibit higher reproducibility than cortical porosity or thickness measurements due to the latter's sensitivity to partial volume effects and segmentation errors [14]. Nonetheless, observed inter- and intra-individual variability, partly attributable to intrinsic anatomical differences and scan positioning, impose limitations on measurement stability.

Spatial resolution of current HR-pQCT (approx. 82 microns) is insufficient to resolve the finest microstructural elements such as thin trabeculae or cortical pores below this size, leading to partial volume effects. These resolution constraints affect direct measurement of true microarchitecture but are partially mitigated by advanced image processing algorithms and calibration against histologic standards [3]. Despite limitations, HR-pQCT remains an invaluable tool for in vivo bone microarchitecture assessment with acceptable accuracy and precision.

Bone Microarchitecture in Healthy Premenopausal Women

Baseline Reference Values and Variability

Establishing normative data for bone microarchitecture parameters in healthy premenopausal women is essential to contextualize deviations associated with disease or fracture risk. Studies employing HR-pQCT have characterized typical trabecular and cortical values stratified by age and ethnicity, revealing ranges of trabecular number, thickness, separation, cortical thickness, and porosity. For example, correlations between peripheral site microarchitecture and central skeletal sites reinforce the representativeness of radius and tibia measurements [7].

Hormonal and biochemical factors modulate bone microarchitecture in this population. Serum insulin-like growth factor I (IGF-I) levels exhibit positive associations with trabecular thickness and negative correlations with trabecular number in younger adults, signifying hormonal influence on remodeling dynamics and microstructural shaping [17]. Furthermore, adiposity, particularly central fat accumulation, negatively impacts bone quality by associating with inferior trabecular volume, increased cortical porosity, and reduced bone formation, conveying the complex interplay between body composition and skeletal health [2].

Sex and Ethnic Differences

Microarchitectural features differ between sexes, with men displaying unique patterns compared to women, potentially driven by hormonal milieu and mechanical loading differences. For instance, men tend to have larger and denser bones with distinct trabecular and cortical geometries compared to women, which translates into varied fracture risk profiles [17]. Ethnic variability is also evident, as studies report that premenopausal Asian women possess similar or superior microarchitecture to their Caucasian counterparts despite lower areal BMD, underlying racial differences in skeletal fragility profiles [3].

These variations arise from a nexus of genetic and environmental influences. Genetic predispositions regulate peak bone mass attainment and microarchitecture, while environmental factors such as nutrition, physical activity, and lifestyle modify bone remodelling processes [7]. Understanding these differences is vital for developing ethnic- and sex-specific reference standards and for precise fracture risk assessment.

Age-Related Changes Pre-Menopause

Contrary to the pronounced bone loss observed post menopause, premenopausal women experience relatively stable microarchitecture through early and mid-adulthood. Nonetheless, subtle declines in trabecular and cortical parameters can commence in the third and fourth decades, potentially impairing peak bone mass acquisition and predisposing to future fragility [7]. Such changes include reductions in trabecular number and cortical thickness alongside increases in cortical porosity.

Endogenous hormonal fluctuations, particularly in estrogen and growth hormone axes, are implicated in modulating bone microarchitecture during this period. Declining IGF-I levels with age have been linked to trabecular thinning and loss of connectivity, emphasizing the need to integrate biochemical markers when interpreting age influences on bone quality [17]. These early microstructural changes may signal the initial phases of skeletal aging and warrant monitoring for preventive interventions.

Bone Microarchitecture Alterations in Premenopausal Women with Fracture

Microarchitectural Deterioration Associated with Fractures

Premenopausal women presenting with fragility fractures exhibit marked microarchitectural deficits detectable by HR-pQCT, despite often having normal or near-normal aBMD by DXA. Studies document reductions in trabecular total density, thickness, and number, along with increased trabecular separation and heterogeneity, signifying disruption of the trabecular framework [9]. Cortical abnormalities, including increased porosity and reduced thickness, have been reported, which compromise the mechanical integrity of the cortical shell and precipitate fracture susceptibility [12].

Finite element analyses underscore the functional impact of these structural changes, revealing significant reductions in estimated bone stiffness and failure load at fracture sites compared with controls [18]. This functional deficit is more pronounced than would be anticipated solely from aBMD, affirming the role of microarchitectural deterioration in fracture pathophysiology in this demographic.

Idiopathic Osteoporosis in Premenopausal Women

Idiopathic osteoporosis (IOP) defines a condition characterized by unexplained low bone mass and increased fracture risk in otherwise healthy premenopausal women. HR-pQCT investigations into IOP cohorts have revealed distinct microarchitectural abnormalities, including decreased trabecular thickness and number and increased cortical porosity, differentiating IOP cases from both normal controls and low BMD non-fracturing individuals [8]. Notably, bone size may be preserved or reduced variably, but microstructural disruption is a consistent finding.

These microarchitectural deficits correspond with lower FEA-estimated stiffness, reinforcing the concept of functional impairment underlying fracture risk in idiopathic osteoporosis beyond measured bone mass. Clinically, HR-pQCT provides critical diagnostic insights in this population, guiding management decisions where traditional BMD assessments are insufficient [8].

Risk Factors and Predictive Microarchitectural Markers

Identification of specific microarchitectural predictors of fracture risk in premenopausal women is an emerging area of research. Parameters such as trabecular heterogeneity, network connectivity, and cortical porosity serve as crucial discriminators independent of aBMD measurements. For instance, trabecular network heterogeneity and separation variability are significantly associated with fracture occurrence and may improve risk stratification models [19]. Cortical deterioration, particularly elevated porosity, has been implicated in premenopausal fragility fractures, emphasizing the need for comprehensive cortical assessment [13]. These microarchitectural markers can be incorporated into predictive algorithms to enhance early detection of at-risk individuals, facilitating timely interventions.

Clinical Applications of HR-pQCT in Premenopausal Women

Diagnostic Improvements over DXA

While DXA remains the clinical standard for osteoporosis diagnosis, it falls short in detecting microarchitectural deterioration and cortical porosity changes that predispose to fractures, especially in premenopausal women. HR-pQCT adds diagnostic value by revealing bone quality impairments invisible on DXA scans. Its ability to provide volumetric bone density and detailed microstructural parameters enhances fracture risk stratification accuracy [7].

Clinical case studies have demonstrated instances where HR-pQCT identified deterioration in trabecular and cortical compartments among premenopausal fracture patients with normal DXA results, highlighting its potential role in resolving diagnostic uncertainty [9]. This improved sensitivity supports the integration of HR-pQCT in specialized clinical scenarios.

Monitoring Disease Progression and Treatment Response

HR-pQCT offers utility in longitudinal assessment of bone microarchitecture changes, supporting monitoring of disease progression and therapeutic efficacy. Serial imaging facilitates evaluation of remodelling dynamics and mechanoregulation within the bone microenvironment [20]. Moreover, alterations in cortical thickness, porosity, and trabecular architecture can be tracked to gauge responses to anti-osteoporotic treatments or interventions targeting bone remodelling pathways [4].

Emerging applications include the use of HR-pQCT in detecting subtle changes in bone quality earlier than traditional methods, potentially allowing clinicians to optimize treatment timing and strategies [21].

Integrating HR-pQCT into Clinical Practice

Despite its promise, clinical integration of HR-pQCT faces barriers including high cost, limited availability, and the need for specialized operator expertise. Nonetheless, it is increasingly recommended for evaluating secondary osteoporosis, rare metabolic bone diseases, and atypical fracture presentations in premenopausal women [20]. Development of standardized protocols and user-friendly software will facilitate broader adoption.

Looking forward, HR-pQCT has the potential to play a pivotal role in personalized medicine approaches by refining individual fracture risk assessments and guiding targeted interventions [7].

HR-pQCT in Special Populations of Premenopausal Women

Premenopausal Women with Diabetes and Metabolic Disorders

Diabetes mellitus, both type 1 and type 2, imposes detrimental effects on bone microarchitecture irrespective of BMD levels. HR-pQCT studies reveal increased cortical porosity and reduced trabecular density among diabetic premenopausal women, which likely contribute to impaired bone strength and elevated fracture risk [22]. Glycaemic control impacts these microarchitectural features, highlighting the complex metabolic influences on skeletal integrity [13].

Fracture risk assessment is particularly challenging in diabetic populations due to the paradox of normal or increased BMD despite greater fragility. HR-pQCT offers a valuable tool to detect microstructural compromise and assist in clinical management [22].

Athletes and Amenorrhoeics Women

Premenopausal athletes with amenorrhea present with compromised microarchitecture relative to eumenorrheic and non-athletic peers. HR-pQCT studies demonstrate lower trabecular density, disrupted cortical parameters, and altered bone geometry in these individuals, reflecting the combined adverse effects of hypoestrogenism and energy deficiency on bone health [11].

These microarchitectural anomalies align with increased fracture rates in amenorrhoeic athletes, underscoring the clinical relevance of HR-pQCT in this population and emphasizing the importance of monitoring menstrual status as part of bone health evaluation [23].

Women with Primary Hyperparathyroidism and Other Endocrine Disorders

Primary hyperparathyroidism (PHPT) exerts catabolic effects on bone, leading to cortical thinning, increased porosity, and trabecular deterioration. HR-pQCT assessments demonstrate that women with PHPT have decreased volumetric densities and altered microarchitecture at the distal radius and tibia, with plate-like trabecular structures particularly affected [24]. Post-parathyroidectomy improvements in bone geometry and microarchitecture have also been documented [25].

Such endocrine disorders intricately alter bone quality in premenopausal women, necessitating HR-pQCT-based evaluations for comprehensive skeletal assessment and therapeutic monitoring [24].

Limitations and Challenges in HR-pQCT Bone Microarchitecture Assessment

Technical and Instrumentation Constraints

HR-pQCT resolution (~82 μm) limits direct visualization of the smallest microstructural elements such as fine trabeculae and small cortical pores, causing partial volume effects that may underestimate porosity and trabecular thickness. These spatial limitations impose inherent constraints in measurement accuracy [3]. Additionally, segmentation algorithms and image processing pipelines vary across centers, introducing inconsistencies in quantitative outcomes [15]. Anatomical variability between individuals further complicates standardization of scan acquisition sites and interpretation [3].

Biological and Physiological Variability

Intra-individual variability arises from anatomical differences, physiological remodelling, and hormonal fluctuations, especially pertinent to premenopausal women with cyclical hormonal variations affecting bone turnover. Variability in body composition, such as adiposity, also influences image quality and bone parameter estimations [3]. These biological confounders necessitate careful methodological control and consideration when interpreting HR-pQCT data from diverse premenopausal populations [2].

Data Interpretation and Clinical Translation Issues

A major obstacle to broad clinical translation is the lack of standardized normative reference datasets specific for premenopausal women, limiting the interpretability of measurements [14]. Also, most existing studies are cross-sectional, with few longitudinal datasets establishing predictive thresholds linking microarchitecture to fracture outcomes in this demographic [3]. Integration of HR-pQCT parameters with established clinical risk scores remains undeveloped, constraining clinical utility [22].

Future Directions and Research Opportunities

Advancements in HR-pQCT Technology and Analysis

Next-generation HR-pQCT devices offer enhanced spatial resolution (down to ~61 μm voxel size) and faster scan speeds, improving image quality and patient throughput [20]. Emerging image analysis algorithms harness texture analysis and machine learning to classify trabecular patterns and detect early microarchitectural deterioration with increased sensitivity [16]. Integration of these advanced techniques with finite element modelling promises personalized bone strength estimations, facilitating precise risk stratification [4].

Longitudinal and Interventional Studies in Premenopausal Women

Prospective investigations linking microarchitectural changes to actual fracture outcomes in premenopausal women are urgently needed to validate predictive capabilities of HR-pQCT parameters [10]. Interventional studies evaluating pharmacological agents and lifestyle modifications through serial HR-pQCT imaging will elucidate effects on bone microarchitecture and functional strength [4]. Additionally, exploring hormonal and biochemical modulators across the lifespan can augment understanding of bone quality determinants in this group [17].

Clinical Implementation and Education

Development of comprehensive clinical guidelines and standardized protocols for HR-pQCT use in premenopausal populations is vital [14]. Training programs to enhance expertise among radiologists and clinicians in microarchitectural interpretation will facilitate broader adoption [20]. Reducing costs and improving access to HR-pQCT technology remain priorities to enable its widespread clinical application [20].

CONCLUSION

Current evidence underscores that bone microarchitecture, as assessed by HR-pQCT, provides critical information on bone quality beyond areal BMD in premenopausal women. Detailed evaluation of trabecular and cortical parameters reveals structural determinants integral to fracture risk identification. HR-pQCT combined with finite element analysis offers a functional assessment of bone strength that bridges morphology with biomechanics.

Despite demonstrated clinical potential, challenges remain in standardizing HR-pQCT protocols, establishing normative reference data, and validating longitudinal fracture risk predictions. Addressing these gaps through rigorous research is essential for integration into routine clinical practice.

Looking forward, HR-pQCT promises to transform personalized bone health care by guiding preventative and therapeutic strategies in young women, potentially mitigating lifelong fracture burden through early, targeted intervention [4]. The technique's enhanced sensitivity to microarchitectural deficits offers new horizons in the management of bone fragility beyond what conventional density measures can achieve, representing a paradigm shift in skeletal health assessment.

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