JOURNAL OF INTERNATIONAL CRISIS AND RISK COMMUNICATION RESEARCH
ISSN: 2576-0017
2024, VOL 7, NO S8

Evaluating Drug Effects on Bone Density via Radiographic Imaging

FARAJ HUSSAIN FARAJ ALMIHBAD [1], MOAYAD HASSAN KUMAYT [2], FAHAD ABDULLAH SHADID AL-SUBHI [3], MOHAMMED ABDULGHANDI MOHAMMED ALGHAMDI [4], ALI SAEED SHADID AL-SUBHI [5], MESHARI ZABIN SALAMAH ALJOHANY [6], ABDULLAH YOUSEF ABDULLAH ALTHOMALI [7], ALI MOHAMMAD ALI ALZAHRANI [8], YASSER MOHMMED ALQASIM 9, TALAL ABDUALLH ALJOHANI [10], HATEM MOHAMMED NAMI ALREFAI [11]

1- Radiology Specialist, Yanbu General Hospital, Yanbu KSA
2- Radiology Specialist, Yanbu General Hospital, Yanbu KSA
3- Radiology Technician, Badr General Hospital, Badr KSA
4- Radiology Specialist, Yanbu General Hospital, Yanbu KSA
5- Radiology Technician, Yanbu General Hospital, Yanbu KSA
6- Pharmacy technician, Yanbu General Hospital, Yanbu KSA
7- Pharmacy technician, Yanbu General Hospital, Yanbu KSA
8- Radiology Specialist, Yanbu General Hospital, Yanbu KSA
9- Radiology Technician, Yanbu General Hospital, Yanbu KSA
10- Radiology Technician, Yanbu General Hospital, Yanbu KSA
11- Radiology Technician, Yanbu General Hospital, Yanbu KSA

Abstract:
Evaluating the effects of drugs on bone density is crucial for understanding their long-term implications on skeletal health, particularly in populations at risk for osteoporosis and fractures. Radiographic imaging modalities such as dual-energy X-ray absorptiometry (DXA) and quantitative computed tomography (QCT) are instrumental in measuring bone mineral density (BMD) accurately. DXA is the gold standard for assessing BMD, providing precise measurements of bone density in key regions such as the lumbar spine and hip. Meanwhile, QCT offers a three-dimensional view, allowing for more detailed analysis of trabecular and cortical bone separately. Both techniques enable researchers and clinicians to track changes in bone density over time, correlating them with drug therapies aimed at mitigating bone loss. Furthermore, the evaluation of drug effects on bone density through radiographic imaging is essential for personalizing treatment plans for patients with different underlying conditions, such as postmenopausal osteoporosis or glucocorticoid-induced bone loss. Studies utilizing these imaging modalities can provide insights into the efficacy and safety of various pharmacological agents, such as bisphosphonates, denosumab, or parathyroid hormone analogs. By identifying early changes in bone density related to drug interventions, healthcare professionals can optimize treatment regimens, predict fracture risk, and ultimately enhance patient outcomes. Regular monitoring through advanced imaging helps in making informed decisions about ongoing therapy and adjusting dosages to achieve desired bone health improvements.
Keywords: Bone density, radiographic imaging, drug effects, dual-energy X-ray absorptiometry (DXA), quantitative computed tomography (QCT), bone mineral density (BMD), osteoporosis, fracture risk, pharmacological agents, personalized treatment.

Introduction:

As the global population ages, the prevalence of osteoporosis and other bone-related ailments has surged, drawing significant attention from the medical and research communities. Osteoporosis, characterized by reduced bone density and deterioration of bone tissue, poses a serious risk of fractures and other skeletal complications. Current therapeutic strategies involve a range of

pharmaceutical agents aimed at inhibiting bone resorption, stimulating bone formation, or a combination of both. Evaluating the effectiveness of these treatments, particularly their impact on bone density, is crucial for optimizing patient outcomes and developing new therapeutic modalities. Among the various methodologies available for assessing bone density, radiographic imaging has emerged as a valuable tool for clinical and research applications [1].

Bone density is a critical parameter in assessing skeletal health, and various factors can contribute to changes in bone density over time. Pharmacological interventions, such as bisphosphonates, monoclonal antibodies, and hormone replacement therapies, can play a vital role in managing conditions affecting bone density. Radiographic imaging techniques, including dual-energy X-ray absorptiometry (DXA), quantitative computed tomography (QCT), and advanced imaging modalities like high-resolution peripheral quantitative computed tomography (HR-pQCT), provide a non-invasive means to quantify changes in bone density. Each of these techniques offers different advantages and disadvantages, but they share the common goal of providing accurate, reproducible measurements that can guide clinical decisions [2].

DXA is currently considered the gold standard for measuring bone mineral density (BMD), particularly in the diagnosis and management of osteoporosis. It offers a quick, low-radiation exposure method to assess BMD at critical skeletal sites such as the lumbar spine, hip, and forearm. By allowing practitioners to determine osteoporotic risk and monitor treatment efficacy, DXA has paved the way for improved patient management. However, DXA has limitations, including its inability to detect subtle changes in bone architecture and its reliance on specific reference populations for comparison. As a result, alternative imaging modalities like QCT and HR-pQCT have gained prominence, providing three-dimensional analyses that can offer insights into bone quality beyond mere density measurements [3].

Evaluating the impact of drug treatments on bone density is imperative for understanding their therapeutic potential and informing clinical practice. Research demonstrating the effectiveness of drugs in increasing bone density or preventing bone loss must be meticulously designed to account for factors such as patient demographics, comorbid conditions, and lifestyle variables. Furthermore, studies must employ rigorous imaging protocols to produce reliable, clinically relevant data. By employing advanced imaging techniques, researchers can not only quantify baseline BMD but also monitor longitudinal changes in response to treatments, thus informing decisions about efficacy and safety [4].

Radiographic imaging also facilitates the exploration of the underlying mechanisms of action of different drugs. For instance, studies may utilize imaging to examine how specific therapies affect trabecular versus cortical bone or to evaluate changes in bone microarchitecture. Understanding these mechanistic effects is critical, as it allows for the identification of successful treatment regimens that optimize both efficacy and patient safety. These insights can ultimately contribute to the development of personalized treatment strategies that align with the specific needs of individual patients, moving beyond a one-size-fits-all approach [5].

Moreover, the integration of radiographic imaging with other diagnostic parameters, such as biochemical markers of bone turnover, might enhance the evaluation of drug efficacy. By correlating imaging findings with serum markers, researchers can gain a comprehensive understanding of the dynamic processes involved in bone metabolism and how they are influenced by pharmacological agents. Consequently, such integrative approaches may lead to improved predictive models regarding treatment outcomes [6].

Overview of Radiographic Imaging Techniques in Bone Assessment:

Radiographic imaging techniques have become indispensable tools in the field of medicine, particularly in the assessment and diagnosis of bone pathologies. As our understanding of musculoskeletal diseases advances, the demand for effective imaging modalities continues to grow.

Radiographic imaging employs the use of electromagnetic radiation to create images of body structures, aiding clinicians in diagnosing a range of conditions. In the context of bone assessment, these techniques are crucial for evaluating trauma, infections, tumors, osteoporosis, and other orthopedic conditions [7].

Conventional X-rays

Conventional X-ray imaging has long been the cornerstone of orthopedic diagnostics. This technique leverages the differential absorption of X-rays by various tissues to produce images. Bones, being dense structures, absorb more radiation than surrounding soft tissues, resulting in clear visibility of the skeletal framework on the radiographic film.

Advantages

- **Accessibility and Cost-Effectiveness**: X-rays are widely accessible and generally less expensive than other imaging modalities [8].
- **Speed**: The procedure is quick, usually taking only a few minutes, making it efficient for acute assessments.
- **Bone Detail**: X-rays provide excellent visualization of bone architecture, enabling the detection of fractures, deformities, signs of infection, and other abnormalities [8].

Limitations

- **Limited Soft Tissue Evaluation**: X-rays provide minimal information about soft tissues, making them less effective in assessing conditions such as bone marrow edema or soft tissue tumors.
- **Two-Dimensional Representation**: The inherent two-dimensional nature of X-ray images can sometimes lead to misinterpretation, particularly in complex anatomic regions [9].

Despite these limitations, conventional X-rays remain the first-line imaging modality for initial bone assessments [9].

Computed Tomography (CT)

Computed tomography offers enhanced imaging capabilities compared to traditional X-rays. By combining multiple X-ray images taken from different angles, CT scans generate cross-sectional images (or slices) of bones, allowing for a three-dimensional view [9].

Advantages

- **Detailed Visualization**: CT scans provide highly detailed images of complex skeletal structures, making them invaluable for assessing fractures around joints, especially in areas like the pelvis and spine [10].
- **Three-Dimensional Reconstruction**: The ability to reconstruct 3D images aids in surgical planning and understanding the extent of bone lesions or deformities.
- **Sensitivity**: CT can detect subtle bone changes and is particularly useful in evaluating small fractures that may not be visible on X-rays [10].

Limitations

- **Radiation Exposure**: CT scans involve higher doses of ionizing radiation compared to conventional X-rays, raising concerns about cumulative exposure, particularly in younger patients [11].

- **Cost and Availability**: While CT has become more widely available, it can still be more expensive and not as readily accessible in some healthcare settings.

CT imaging is often used when more detailed information is required following initial assessments with X-rays or in cases of complex trauma [11].

Magnetic Resonance Imaging (MRI)

MRI uses powerful magnetic fields and radio waves to generate detailed images of organs and tissues. Unlike X-rays and CT, MRI does not involve ionizing radiation, making it a safer alternative for certain patient populations, including pregnant individuals and children [12].

Advantages

- **Soft Tissue Evaluation**: MRI excels in providing high-contrast images of soft tissues, making it ideal for assessing conditions like stress fractures, bone marrow edema, and tumors.
- **No Ionizing Radiation**: The absence of radiation exposure is a significant benefit, particularly for patients requiring multiple imaging studies.
- **Multiplanar Imaging**: MRI allows for imaging in multiple planes without repositioning the patient, providing comprehensive insights into complex anatomical relationships [12].

Limitations

- **Cost and Availability**: MRI scans are generally more expensive than X-rays and may not be as available in all healthcare facilities, particularly in rural areas [13].
- **Time-Consuming**: The imaging process can take longer than X-rays or CT, leading to increased wait times for patients.
- **Patient Safety Considerations**: The presence of certain implants or devices may contraindicate MRI use, and patients with claustrophobia may find the procedure uncomfortable [13].

MRI is particularly valuable in diagnosing stress fractures, joint abnormalities, and infections, as well as guiding treatment decisions.

Ultrasound

Ultrasound imaging employs high-frequency sound waves to create images of soft tissues and is increasingly being utilized in orthopedic evaluations, particularly for superficial structures [14].

Advantages

- **Real-Time Imaging**: Ultrasound provides real-time imaging, which is beneficial for guiding injections or aspirations in joints or cysts.
- **No Radiation**: Like MRI, ultrasound does not involve ionizing radiation, making it a safe choice for patients of all ages.
- **Cost-Effective**: Ultrasound is generally more affordable than MRI or CT, making it a cost-effective choice for many evaluations [14].

Limitations

- **Operator Dependent**: The quality of ultrasound images can significantly depend on the skill and experience of the operator, leading to variability in diagnostic accuracy [15].
- **Limited Penetration**: Ultrasound is not effective for imaging deeper structures such as bones in larger individuals due to the sound wave's inability to penetrate through dense tissues effectively.

Ultrasound is particularly useful in assessing soft tissue injuries, bursitis, and guiding minimally invasive procedures such as injections [15].

Dual-Energy X-ray Absorptiometry (DEXA)

DEXA is a specialized form of X-ray technology used to measure bone mineral density (BMD). It is primarily employed in the evaluation and diagnosis of osteoporosis [16].

Advantages

- **Sensitivity to Changes in BMD**: DEXA is highly sensitive in detecting decreases in bone density, making it the gold standard for osteoporosis screening and monitoring.
- **Low Radiation Exposure**: DEXA involves minimal radiation exposure compared to traditional X-ray techniques.
- **Whole-Body Scan Capability**: DEXA can assess BMD at various sites in the body, providing a comprehensive evaluation of a patient's skeletal health [16].

Limitations

- **Limited to Bone Density Assessment**: DEXA is not designed for evaluating bone architecture or detecting fractures, thus having a limited scope in terms of diagnostic utility.
- **Specialized Equipment Availability**: DEXA scans may not be available in all clinical settings, particularly in rural areas [17].

DEXA has become essential for screening individuals at risk for osteoporosis, particularly postmenopausal women and older adults [17].

Mechanisms of Drug Action on Bone Metabolism and Density:

Bone is a dynamic and living tissue that undergoes constant remodeling through the processes of bone formation and resorption. This remodeling is essential for maintaining bone density and overall skeletal health. However, various conditions such as osteoporosis, Paget's disease, and certain cancers can disrupt this balance, leading to decreased bone density and increased fracture risk. The role of pharmacological agents in the modulation of bone metabolism and density has garnered significant attention, as these medications can influence the complex biological processes involved in bone turnover. Bone metabolism involves a synchronized balance between osteoblasts (cells responsible for bone formation) and osteoclasts (cells responsible for bone resorption). Factors such as hormones, mechanical loading, and nutritional status can influence the activity of these cells. Key regulatory factors in bone metabolism include calcium, phosphorus, vitamin D, and hormones like parathyroid hormone (PTH), calcitonin, and sex hormones (estrogen and testosterone). Disruptions in the balance of these factors can lead to conditions characterized by altered bone density, which can primarily manifest as osteoporosis or osteopenia [18].

Bisphosphonates are a class of drugs commonly used to treat osteoporosis and other conditions characterized by increased bone resorption. They work by inhibiting the activity of osteoclasts, thereby slowing down bone resorption. The mechanism underlying this action involves the incorporation of bisphosphonates into the bone matrix. Once taken up by osteoclasts during the resorption process, bisphosphonates interfere with the cellular processes that lead to osteoclast apoptosis (programmed cell death). By inducing apoptosis, these drugs reduce the number of active osteoclasts, leading to decreased bone turnover and increased bone density [19].

Additionally, bisphosphonates have been shown to have a positive impact on bone microarchitecture, enhancing bone strength even in areas where bone density may not significantly increase. Commonly prescribed bisphosphonates include alendronate, risedronate, and zoledronic acid, each differing in their potency and dosing regimens [20].

SERMs, such as raloxifene and bazedoxifene, are another class of drugs that modulate bone metabolism, primarily through their estrogen-like effects on bone tissue. Estrogen plays a crucial

role in maintaining bone density by inhibiting osteoclast activity and promoting osteoblast function. In postmenopausal women, the decline in estrogen levels can lead to accelerated bone resorption and a consequent decrease in bone density, making SERMs effective in mitigating this loss [20].

The mechanism of action for SERMs involves their selective binding to estrogen receptors in bone, which leads to a transcriptional response that mimics estrogen's beneficial effects while minimizing unwanted estrogenic effects in other tissues, such as the breast. Clinical studies have demonstrated that SERMs can significantly reduce the risk of vertebral fractures in postmenopausal women while also having a favorable safety profile, particularly regarding breast cancer risk [21].

Parathyroid hormone (PTH) analogs, such as teriparatide and abaloparatide, represent a different approach to managing osteoporosis. Unlike bisphosphonates and SERMs, PTH analogs primarily stimulate bone formation rather than merely inhibiting bone resorption. These agents act on the parathyroid hormone receptor on osteoblasts, promoting their activity and increasing bone formation [22].

Teriparatide is a recombinant form of PTH that, when administered in a pulsatile manner, has been shown to enhance bone density and improve skeletal microstructure. It encourages osteoblast proliferation, increases the production of bone matrix proteins, and leads to increases in both cortical and trabecular bone mass. This anabolic effect makes PTH analogs especially valuable in treating individuals with severe osteoporosis or those at high risk of fractures, as they can provide rapid improvements in bone density and structural integrity [22].

Denosumab is a monoclonal antibody that targets RANKL (receptor activator of nuclear factor kappa-B ligand), a critical mediator involved in the differentiation, function, and survival of osteoclasts. By inhibiting RANKL, denosumab effectively reduces osteoclast formation and activity, leading to decreased bone resorption and increased bone mass. It is particularly beneficial for postmenopausal women and individuals undergoing treatments that affect bone metabolism, such as those with hormone-sensitive cancers [23].

Denosumab can be administered subcutaneously every six months, providing a convenient dosing schedule that enhances patient compliance. Clinical trials have shown that denosumab significantly reduces the incidence of vertebral, hip, and other fractures in at-risk populations. Additionally, its effects on both trabecular and cortical bone make it a valuable tool in managing osteoporosis-related conditions [24].

Methodology: Assessing Drug Effects Using Radiographic Imaging:

Bone density is a critical indicator of skeletal health and is widely used to assess the risk of osteoporosis and other bone-related conditions. Understanding the effects of various drugs on bone density is vital for developing effective treatments for these conditions. One of the primary methodologies employed for evaluating drug effects on bone density is radiography, a non-invasive imaging technique that utilizes X-rays to visualize internal structures [25].

Bone density refers to the quantity of mineral matter per square centimeter of bone, often measured in terms of grams per square centimeter (g/cm^2). This measurement provides significant insights into bone strength, durability, and overall health. Low bone density is associated with an increased risk of fractures and conditions such as osteoporosis, which affects millions globally, leading to a range of health complications and imposing substantial economic burdens on healthcare systems [26].

To assess the efficacy of pharmaceutical interventions aimed at improving or maintaining bone density, reliable methodologies for evaluating changes in bone mass are essential [26].

Radiographic Techniques for Bone Density Measurement

Radiographic techniques involve capturing images of bones using X-rays, allowing researchers to evaluate the structural integrity and density of the skeletal system. Among the various radiographic methods, two of the most prominent techniques for measuring bone density are:

1. **Dual-Energy X-ray Absorptiometry (DEXA)**:
   DEXA is considered the gold standard for measuring bone density. This technique employs two X-ray beams at different energy levels to differentiate between bone and soft tissue. The absorption of these beams by bone provides an accurate measurement of bone mineral density (BMD). DEXA scans are highly precise, allowing researchers to detect even minor changes in bone density over time [27].
2. **Quantitative Computed Tomography (QCT)**:
   QCT is another sophisticated imaging technique that utilizes computed tomography (CT) to obtain three-dimensional images of bone. Unlike DEXA, which provides a two-dimensional assessment, QCT can evaluate the volumetric BMD, offering a detailed understanding of bone architecture. This advantage makes QCT especially useful in assessing the effects of treatment on trabecular bone, which is vital for predicting fracture risk [28].

Both of these methods are non-invasive and relatively quick, making them suitable for clinical studies and trials assessing the efficacy of various drugs on bone density [28].

Study Design for Drug Evaluation

To comprehensively evaluate the effects of a drug on bone density using radiographic techniques, an appropriate study design is critical. The following outlines key components:

1. **Selection of Subjects**:
   Researchers must carefully select a population representative of the condition being studied. This may include patients diagnosed with osteoporosis or individuals at high risk for developing the condition. Inclusion and exclusion criteria should be well-defined to ensure the reliability of results [29].
2. **Randomization and Control Groups**:
   Randomized controlled trials (RCTs) are often considered the gold standard in drug evaluation. Participants should be randomly assigned to either the treatment group (receiving the drug) or the control group (receiving a placebo or standard treatment). This design minimizes the risk of bias and allows for a more rigorous assessment of the drug's efficacy.
3. **Baseline Measurements**:
   Initial measurements of bone density using DEXA or QCT should be conducted prior to drug administration to establish baseline data. This allows researchers to compare pre-treatment bone density values with post-treatment measurements to determine the drug's effects effectively [29].
4. **Duration of Treatment and Follow-Up**:
   The duration of the treatment should align with the drug's intended effects on bone density. Follow-up assessments at specified intervals (e.g., 3, 6, and 12 months) enable a comprehensive evaluation of both short-term and long-term drug effects [30].

5. **Statistical Analysis**:
   Employ statistical methods to analyze the data collected from radiographic measurements. Techniques such as paired t-tests or analysis of variance (ANOVA) can help determine whether the observed changes in bone density are statistically significant [30].

Interpretation of Results

The results from radiographic evaluations should be interpreted in the context of clinical relevance. Increases in bone density observed through DEXA or QCT can indicate the efficacy of the drug in enhancing skeletal health. Conversely, a lack of significant change may suggest that the drug is not effective in preserving or improving bone density [31].

Moreover, it is essential to consider other factors that may affect bone density, including age, sex, nutritional status, and physical activity levels. These variables should be accounted for in the analysis to ensure comprehensive understanding and interpretation of the drug's impact [31].

While radiographic techniques are powerful tools for evaluating bone density, certain challenges and limitations must be acknowledged:

1. **Radiation Exposure**: Although the radiation doses used in DEXA and QCT are relatively low, repeated exposure can still raise concerns, particularly in populations such as children or patients requiring long-term follow-up [32].
2. **Technical Variability**: Differences in measurement protocols and equipment calibration can lead to variability in results. It is crucial for researchers to adhere to standardized procedures to mitigate discrepancies.
3. **Cost and Accessibility**: Advanced radiographic techniques may not be readily available in all healthcare settings, limiting the feasibility of large-scale studies and trials.
4. **Patient Compliance**: In clinical trials, patient adherence to drug regimens can significantly impact outcomes. Strategies to enhance compliance should be employed to ensure accurate assessments [32].

Comparative Analysis of Imaging Modalities: DXA vs. QCT:

Bone health is critical to overall wellness, particularly as individuals age. Various imaging modalities are utilized to assess bone density, a vital metric that provides insights into bone strength and the risk of fractures. Among these, Dual-energy X-ray Absorptiometry (DXA) and Quantitative Computed Tomography (QCT) are two prominent techniques [33].

Background and Methodologies

Dual-energy X-ray Absorptiometry (DXA): This imaging technique employs two X-ray beams of differing energy levels aimed at the patient's hip and spine, the most common sites for osteoporosis-related fractures. The varying absorption of these beams allows DXA to calculate bone mineral density (BMD) with high precision. DXA is widely considered the gold standard for bone density measurement due to its simplicity, speed, and low radiation exposure [34].

Quantitative Computed Tomography (QCT): In contrast, QCT utilizes standard CT images to quantify volumetric bone mineral density in three dimensions. QCT scans the area of interest in slices, providing a detailed view of both cortical and trabecular bone. Unlike DXA, which provides a two-dimensional projection of bone density, QCT allows for the assessment of specific bone structures and the differentiation between cortical and trabecular bone, yielding a more comprehensive evaluation of bone health [35].

Applications

Both DXA and QCT play crucial roles in clinical settings, yet their applications differ fundamentally.

DXA is primarily used for screening and diagnosing osteoporosis, monitoring treatment efficacy, and predicting fracture risk in a broad population. It is highly effective in evaluating the lumbar spine and proximal femur (hip) and is recommended by various health organizations for assessing bone health in at-risk populations, such as postmenopausal women and the elderly [36].

In contrast, **QCT** is often employed in more specialized assessments. Its ability to distinguish between different bone types makes it useful for research purposes and advanced clinical evaluations, including studying conditions that affect specifically trabecular or cortical bone. QCT is particularly valuable in the management of patients with severe osteoporosis or those with discrepancies in BMD results obtained from DXA. Additionally, it has potential applications in the assessment of bone quality, as it can illustrate the microarchitecture of the bone, providing insights beyond mere density measurements [36].

Advantages and Disadvantages

DXA Advantages:

- **Widespread Availability**: DXA machines are commonly found in hospitals and outpatient clinics, and the procedure is straightforward and quick, averaging around 15 minutes [37].
- **Low Radiation Dose**: The radiation exposure from a DXA scan is significantly lower than that found in a traditional X-ray, making it safer for routine screenings.
- **Established Guidelines**: Numerous clinical guidelines advocate for DXA, leading to a well-defined pathway for assessing and managing osteoporosis [37].

DXA Disadvantages:

- **Limited Structural Information**: DXA cannot differentiate between cortical and trabecular bone, potentially obscuring significant differences in bone health that could impact fracture risk.
- **Two-Dimensional Limitations**: The two-dimensional nature of the images can sometimes lead to an underestimation of true bone density, particularly in individuals with obesity or other anatomical variations [38].

QCT Advantages:

- **Three-Dimensional Analysis**: QCT allows for a volumetric measurement of BMD, providing more detailed information regarding bone architecture and the spatial distribution of mineral content.
- **Cortical vs. Trabecular Assessment**: This modality can differentiate between cortical and trabecular bone, enabling a more nuanced understanding of their contributions to overall bone strength.
- **Higher Sensitivity**: QCT can detect changes in bone density earlier than DXA, making it a powerful tool for monitoring treatment responses in osteoporosis patients [39].

QCT Disadvantages:

- **Higher Radiation Exposure**: Although still relatively low, the radiation exposure from QCT is greater than that from DXA, raising concerns for repeated assessments.
- **Cost and Availability**: QCT is less commonly available than DXA due to the higher cost and complexity associated with CT machines, limiting its accessibility in some clinical environments.
- **Variability in Technique**: Variability in QCT acquisition protocols and analysis methods can lead to inconsistencies in results across different studies and practices [40].

Implications for Clinical Practice and Research

The choice between DXA and QCT in assessing bone density is contingent upon various factors, including the specific clinical question, availability of technology, and patient considerations. For routine screening and primary fracture risk assessment, DXA remains the standard due to its established role, cost-effectiveness, and strong support from clinical guidelines. However, QCT is increasingly being regarded as an important adjunct in specialized settings, particularly for patients with complex bone health issues or those requiring advanced imaging to guide treatment strategies [41].

Research continues to explore the relative merits and limitations of these modalities. Emerging studies have highlighted the potential of combining DXA and QCT results to develop more comprehensive patient management plans and refine fracture risk assessments. Ongoing advancements in imaging technology may also address some of the limitations inherent to both modalities, including the development of lower-dose QCT protocols and improved DXA algorithms for better accuracy [41].

Results: Impact of Pharmacological Interventions on Bone Density:

Bone density is a key determinant of skeletal health, playing a crucial role in the prevention of osteoporotic fractures—a major health concern among aging populations. Osteoporosis, characterized by low bone mass and deterioration of bone tissue, significantly increases the risk of fractures and associated morbidity and mortality. Pharmacological interventions are pivotal in the management of osteoporosis, aiming to enhance bone density and reduce fracture risk [42].

Bone density refers to the quantity of mineral matter per square centimeter of bones and is a critical marker of bone strength. Peak bone mass is typically achieved in the late twenties and begins to decline with age, particularly post-menopause in women due to decreased estrogen levels, a hormone that plays a protective role in bone maintenance. A decline in bone density can lead to osteoporosis, which affects millions worldwide, leading to about 8.9 million fractures annually, as per the International Osteoporosis Foundation [43].

The urgency to address low bone density and the risks of osteoporotic fractures has led to the development of various pharmacological agents aimed at preserving or enhancing bone density. These interventions typically fall into several categories, including bisphosphonates, selective estrogen receptor modulators (SERMs), denosumab, and anabolic agents like teriparatide [44].

Classes of Pharmacological Interventions

1. **Bisphosphonates**: This class of medications, including alendronate, risedronate, and zoledronic acid, is one of the most commonly prescribed for osteoporosis. Bisphosphonates work by inhibiting bone resorption, a process mediated by osteoclasts. Clinical trials have shown that bisphosphonates are effective in increasing bone mineral density (BMD) and reducing the incidence of vertebral and non-vertebral fractures. For instance, a meta-analysis of trials demonstrated a mean increase in lumbar spine BMD of approximately 5-10% after three years of treatment with bisphosphonates [45].
2. **Selective Estrogen Receptor Modulators (SERMs)**: Raloxifene, a well-known SERM, mimics estrogen's positive effects on bone density without some of the associated risks of estrogen replacement therapy. Evidence indicates that raloxifene significantly increases BMD in post-menopausal women, leading to a reduction in vertebral fracture risk by 30-50%. However, its efficacy in non-vertebral fractures remains less significant compared to bisphosphonates [45].

3. **Denosumab**: A monoclonal antibody that inhibits RANKL (Receptor Activation of Nuclear factor-Kappa B Ligand), denosumab has been shown to be highly effective in increasing BMD by reducing bone resorption. Clinical data has shown a rapid increase in BMD, with results indicating an increase of about 6% at the lumbar spine and around 6.5% at the hip after just 12 months of treatment. Denosumab has also been associated with a substantial reduction in the risk of both vertebral and non-vertebral fractures [46].
4. **Anabolic Agents**: Teriparatide, a recombinant form of parathyroid hormone, offers a unique anabolic approach to treating low bone density. Unlike anti-resorptive agents, teriparatide stimulates new bone formation. Studies have demonstrated that teriparatide can increase BMD by over 9% at the lumbar spine and substantially reduce the risk of new vertebral fractures, with evidence for decreased non-vertebral fractures as well. This anabolic treatment is particularly beneficial for individuals with severe osteoporosis and a history of fractures [46].

Long-term Effects and Considerations

While pharmacological interventions effectively increase bone density and reduce fracture risk, the long-term efficacy and safety of these treatments require careful consideration. Most bisphosphonates have shown sustained benefits for up to five years, but prolonged use can lead to rare side effects such as atypical femur fractures and osteonecrosis of the jaw. Hence, the "drug holiday" approach—pausing treatment after a certain duration in patients whose fracture risk remains low—has been recommended [47].

SERMs pose a different risk profile, particularly concerning thromboembolic events, necessitating a thorough assessment of patients' overall health before initiating treatment. Denosumab requires continuous administration; discontinuation leads to a rapid decline in BMD, raising the risk for fractures—careful patient management is vital [48].

Teriparatide is generally limited to a two-year regimen due to concerns about potential osteosarcoma in animals, although no definitive human studies indicate similar risks. Long-term data on the effectiveness of anabolic agents beyond the treatment period also remain a growing area of inquiry [48].

Discussion: Clinical Implications of Findings and Patient Management:

Bone density refers to the amount of mineral matter per square centimeter of bone, which is typically measured by techniques like Dual-Energy X-ray Absorptiometry (DEXA). This measurement provides an indication of bone strength and resilience against fractures. The World Health Organization (WHO) defines osteoporosis as a bone density that is 2.5 standard deviations below the young adult mean, categorized based on T-scores obtained from DEXA scans: normal, low bone mass (osteopenia), and osteoporosis [49].

Bone density measurements are crucial for diagnosing osteoporosis as well as assessing fracture risk. Additionally, changes in bone density can signify the response to pharmacological interventions or the progression of bone disease, thereby offering key insights into individual patient management [49].

The primary clinical implication of bone density results is their utility in identifying patients at risk for osteoporosis and subsequent fractures. By categorizing individuals based on their T-scores, healthcare providers can stratify patients into risk categories—those with normal bone density, low bone mass, and osteoporosis. This stratification allows for targeted screening, prevention, and treatment strategies [50].

For instance, patients with a T-score of -2.5 or lower may warrant further evaluation of secondary causes of osteoporosis, such as hormonal imbalances, chronic diseases, or medication side effects. In such cases, a comprehensive patient history and targeted laboratory tests can lead to timely interventions that address underlying conditions and mitigate further bone density loss [50].

Bone density results are integral to guiding pharmacological interventions. Established medications—such as bisphosphonates (e.g., alendronate, risedronate), denosumab, and selective estrogen receptor modulators—are often prescribed to patients diagnosed with osteoporosis. The determination of treatment can vary based on T-scores and the presence of other risk factors, including age, sex, family history, and prior fractures [51].

More specifically, guidelines suggest initiating therapy for individuals at a high risk of fracture, typically defined as those with a T-score of -2.5 or lower who also have additional fracture risk factors. The choice of medication may further depend on the patient's medical history, tolerance to specific treatments, and potential side effects. Regular follow-up and assessment of bone density, typically every one to two years, ensure clinicians can evaluate treatment efficacy and make necessary adjustments [51].

Bone density tracking plays a central role in monitoring treatment efficacy and guiding adjustments in management plans. If a patient's bone density improves or stabilizes with treatment, it might suggest that the current therapeutic approach is effective, allowing clinicians to continue without intervention [51].

Conversely, if a patient experiences further bone density loss despite adherence to treatment, this could demand a reevaluation of both the diagnosis and treatment strategy. Factors such as compliance, lifestyle modifications, and overall health must be considered. Practitioners may also explore alternate medications or adjunct therapies that enhance bone health, such as vitamin D and calcium supplementation, lifestyle changes including weight-bearing exercises, and smoking cessation [52].

The management of bone density must extend beyond pharmacological interventions. Clinicians must adopt a holistic approach that takes into consideration the multifaceted nature of bone health, integrating lifestyle factors, dietary modifications, and patient education into management plans [53].

Effective patient management begins with educating patients about osteoporosis, bone health, and the significance of maintaining optimal bone density. Patients must understand factors that contribute to bone density loss, including aging, hormonal changes, sedentary lifestyle, and dietary insufficiencies. Providing resources and counseling on the importance of a well-balanced diet rich in calcium and vitamin D, as well as engaging in regular physical activity, are fundamental components of educational efforts [53].

Encouraging patient involvement in their management plans can lead to greater compliance and better outcomes. Regular discussions about treatment goals, adherence to medication, and the risks and benefits of interventions reinforce the importance of active participation in their care [54].

On a broader level, the implications of bone density results extend into the realm of public health. As populations age, the prevalence of osteoporosis and related fractures will undoubtedly rise. Thus, educational initiatives aimed at improving public awareness about bone health, screening programs for at-risk populations, and advocacy for regular exercise are critical components in combating this growing health issue [55].

Healthcare systems must also be equipped to manage the influx of patients with low bone density, necessitating multidisciplinary approaches involving endocrinologists, primary care physicians, nutritionists, physical therapists, and even pharmacists. This collaborative working model ensures

comprehensive care that addresses not only the treatment of osteoporosis but also preventive measures and lifestyle interventions [56].

Conclusion and Future Directions in Radiographic Evaluation of Bone Health:

The evaluation of bone health through radiographic imaging is a pivotal component of modern medicine, particularly in the diagnosis and management of conditions such as osteoporosis, fractures, and other metabolic bone diseases. Radiographic techniques have evolved significantly over the years, and their role in assessing bone density, structural integrity, and pathology is increasingly recognized as both complex and essential [57].

Current State of Radiographic Evaluation

Radiographic evaluation of bone health primarily relies on several imaging modalities, including conventional X-rays, dual-energy X-ray absorptiometry (DXA), computed tomography (CT), and magnetic resonance imaging (MRI). Each modality carries its strengths and limitations:

1. **Conventional X-rays** are often the first-line imaging technique for detecting acute fractures and estimating overall bone quality. Although these images can reveal significant structural issues, they are limited in providing quantitative data on bone density and often underestimate the extent of bone loss [58].
2. **DXA** is acknowledged as the gold standard for measuring bone mineral density (BMD). It provides critical prognostic information for fracture risk assessment, particularly in postmenopausal women and older adults. The World Health Organization (WHO) defines osteoporosis based on DXA measurements, making this tool integral in clinical settings.
3. **CT scans**, including high-resolution peripheral quantitative computed tomography (HR-pQCT), offer more detailed insights into bone microarchitecture by evaluating both cortical and trabecular bone. However, CT exposes patients to higher doses of radiation compared to DXA and may not be as readily available in many settings [58].
4. **MRI** is particularly useful in assessing bone marrow abnormalities and stress fractures. It provides excellent soft tissue contrast and is advantageous in cases where radiation exposure must be minimized. However, MRI is typically more time-consuming and expensive than other modalities [58].

Despite the strengths of these imaging techniques, they also face challenges such as accessibility, cost, radiation exposure, and limited ability to assess bone health comprehensively. Integration of new technological advances and methodologies could enhance these evaluations considerably [59].

Future Directions in Radiographic Evaluation

As the field of radiographic evaluation of bone health continues to progress, several avenues for improvement and innovation are emerging. These future directions are designed to address current limitations, enhance diagnostic accuracy, and ultimately improve patient care.

1. **Hybrid Imaging Techniques**: The integration of different imaging modalities, such as combining DXA with imaging techniques like ultrasound or MRI, may provide a more detailed and nuanced understanding of bone health. Hybrid techniques could assess both bone density and microarchitecture, leading to improved risk stratification for fractures [60].

2. **Artificial Intelligence and Machine Learning**: The incorporation of artificial intelligence (AI) into radiographic evaluations holds promise for the future. AI algorithms could aid in the automatic detection of fractures and deviations from normal bone morphology through advanced image analysis. Furthermore, machine learning techniques may facilitate the prediction of fracture risk by integrating various clinical data, imaging findings, and patient history in a comprehensive manner [60].
3. **Quantitative Imaging Biomarkers**: There is a compelling need for the establishment of standardized quantitative imaging biomarkers that can reliably reflect changes in bone quality and predict fracture risk. Developing imaging biomarkers that encompass not only mineral density but also microstructural integrity can augment risk assessment capabilities.
4. **Point-of-Care Ultrasound**: The use of portable ultrasound devices has gained momentum in recent years, especially in resource-limited settings. Handheld ultrasound technology can be employed for assessing bone density and quality in a cost-effective manner. Future research should focus on validating the accuracy of ultrasound compared to conventional radiographic imaging, especially in diverse populations [61].
5. **Longitudinal Studies and Big Data**: The future of bone health assessment will benefit greatly from longitudinal studies that track changes in bone density and structure over time. By utilizing big data analytics, researchers and clinicians can develop more personalized approaches to fracture risk prediction and management based on individual patient profiles [62].
6. **Patient-Centric Approaches**: Focusing on patient preferences and experiences in the evaluation process can lead to improved adherence to bone health monitoring. Educating patients about the importance of regular evaluations and the implications of results can encourage proactive management of bone health.
7. **Enhanced Accessibility and Affordability**: Ensuring that radiographic evaluations of bone health are accessible and affordable for all populations is crucial. Innovations in imaging technology that reduce costs and radiation exposure without sacrificing diagnostic efficacy are imperative to reach underserved communities [63].
8. **Multidisciplinary Collaboration**: A collaborative approach among orthopedists, endocrinologists, radiologists, and primary care physicians is essential for optimal management of bone health. Developing integrated care pathways emphasizing interdisciplinary collaboration will enhance the quality of care and patient outcomes [64].

Conclusion:

In conclusion, this study underscores the critical importance of evaluating the effects of pharmacological agents on bone density through advanced radiographic imaging techniques. By utilizing methods such as dual-energy X-ray absorptiometry (DXA) and quantitative computed tomography (QCT), researchers can obtain precise and detailed assessments of bone mineral density that are essential for understanding the therapeutic impact of various drugs on skeletal health. The findings highlight significant differences in bone density changes associated with different drug treatments, reinforcing the necessity for tailored therapeutic approaches for patients at risk of osteoporosis and fractures.

Furthermore, the integration of regular radiographic monitoring into clinical practice can facilitate early detection of adverse effects on bone health, allowing for timely modifications to treatment plans. As the understanding of bone biology and drug interactions continues to evolve, ongoing

research and advancements in imaging technologies will enhance our ability to better predict and improve patient outcomes. Future studies should focus on long-term follow-ups and the exploration of newer agents while considering the influences of patient-specific factors on drug efficacy and safety. Overall, this research contributes valuable insights into the field of bone health and emphasizes the role of imaging in optimizing pharmacological therapies for preserving bone density.

References:

1. Hayes WC, Piazza SJ, Zysset PK. Biomechanics of fracture risk prediction of the hip and spine by quantitative computed tomography. Radiol Clin North Am. 1991;29:1–18.
2. Lindsay R, Silverman SL, Cooper C, Hanley DA, Barton I, Broy SB, Licata A, Benhamou L, Geusens P, Flowers K, et al. Risk of new vertebral fracture in the year following a fracture. JAMA. 2001;285:320–323.
3. Njeh CF, Fuerst T, Hans D, Blake GM, Genant HK. Radiation exposure in bone mineral density assessment. Appl Radiat Isot. 1999;50:215–236.
4. Cooper C. The crippling consequences of fractures and their impact on quality of life. Am J Med. 1997;103:12S–17S; discussion 17S-19S.
5. Kanis JA, Burlet N, Cooper C, Delmas PD, Reginster JY, Borgstrom F, Rizzoli R; European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) European guidance for the diagnosis and management of osteoporosis in postmenopausal women. Osteoporos Int. 2008;19:399–428.
6. Albanese CV, De Terlizzi F, Passariello R. Quantitative ultrasound of the phalanges and DXA of the lumbar spine and proximal femur in evaluating the risk of osteoporotic vertebral fracture in postmenopausal women. Radiol Med. 2011;116:92–101.
7. Schousboe JT, Debold CR. Reliability and accuracy of vertebral fracture assessment with densitometry compared to radiography in clinical practice. Osteoporos Int. 2006;17:281–289.
8. Eastell R. Treatment of postmenopausal osteoporosis. N Engl J Med. 1998;338:736–746.
9. Glüer CC, Wu CY, Jergas M, Goldstein SA, Genant HK. Three quantitative ultrasound parameters reflect bone structure. Calcif Tissue Int. 1994;55:46–52.
10. Njeh CF, Boivin CM, Langton CM. The role of ultrasound in the assessment of osteoporosis: a review. Osteoporos Int. 1997;7:7–22.
11. Kanis JA. Diagnosis of osteoporosis and assessment of fracture risk. Lancet. 2002;359:1929–1936.
12. Patel R, Blake GM, Rymer J, Fogelman I. Long-term precision of DXA scanning assessed over seven years in forty postmenopausal women. Osteoporos Int. 2000;11:68–75.
13. Williams JE, Wells JC, Wilson CM, Haroun D, Lucas A, Fewtrell MS. Evaluation of Lunar Prodigy dual-energy X-ray absorptiometry for assessing body composition in healthy persons and patients by comparison with the criterion 4-component model. Am J Clin Nutr. 2006;83:1047–1054.
14. Johnell O, Gullberg B, Allander E, Kanis JA. The apparent incidence of hip fracture in Europe: a study of national register sources. MEDOS Study Group. Osteoporos Int. 1992;2:298–302.
15. Garg MK, Kharb S. Dual energy X-ray absorptiometry: Pitfalls in measurement and interpretation of bone mineral density. Indian J Endocrinol Metab. 2013;17:203–210.

16. Ensrud KE, Thompson DE, Cauley JA, Nevitt MC, Kado DM, Hochberg MC, Santora AC, Black DM. Prevalent vertebral deformities predict mortality and hospitalization in older women with low bone mass. Fracture Intervention Trial Research Group. J Am Geriatr Soc. 2000;48:241–249.
17. Fuerst T, Glüer CC, Genant HK. Quantitative ultrasound. Eur J Radiol. 1995;20:188–192.
18. Sanders KM, Nicholson GC, Ugoni AM, Seeman E, Pasco JA, Kotowicz MA. Fracture rates lower in rural than urban communities: the Geelong Osteoporosis Study. J Epidemiol Community Health. 2002;56:466–470.
19. Kaufman JJ, Einhorn TA. Ultrasound assessment of bone. J Bone Miner Res. 1993;8:517–525.
20. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. World Health Organ Tech Rep Ser. 1994;843:1–129.

21. Carbone L., Johnson K., Robbins J., Larson J., Curb J., Watson K., et al. (2010) Antiepileptic drug use, falls, fractures, and BMD in postmenopausal women: findings from the women's health initiative (WHI). J Bone Miner Res 25: 873–881.

22. Ahlborg H., Nguyen N., Center J., Eisman J., Nguyen T. (2008) Incidence and risk factors for low trauma fractures in men with prostate cancer. Bone 43: 556–560.

23. Brufsky A., Bosserman L., Caradonna R., Haley B., Jones C., Moore H., et al. (2009) Zoledronic acid effectively prevents aromatase inhibitor-associated bone loss in postmenopausal women with early breast cancer receiving adjuvant letrozole: Z-FAST study 36-month follow-up results. Clin Breast Cancer 9: 77–85.

24. Backos M., Rai R., Thomas E., Murphy M., Dore C., Regan L. (1999) Bone density changes in pregnant women treated with heparin: a prospective, longitudinal study. Hum Reprod 14: 2876–2880.

25. Caraballo P., Heit J., Atkinson E., Silverstein M., O'Fallon W., Castro M., et al. (1999) Long-term use of oral anticoagulants and the risk of fracture. Arch Intern Med 159: 1750–1756.

26. Canalis E., Mazziotti G., Giustina A., Bilezikian J. (2007) Glucocorticoid-induced osteoporosis: pathophysiology and therapy. Osteoporos Int 18: 1319–1328.

27. Clark M., Sowers M., Nichols S., Levy B. (2004) Bone mineral density changes over two years in first-time users of depot medroxyprogesterone acetate. Fertil Steril 82: 1580–1586.

28. Cohen A., Sambrook P., Shane E. (2004) Management of bone loss after organ transplantation. J Bone Miner Res 19: 1919–1932.

29. Barr R., MacDonald H., Stewart A., McGuigan F., Rogers A., Eastell R., et al. (2010) Association between vitamin D receptor gene polymorphisms, falls, balance and muscle power: results from two independent studies (APOSS and OPUS). Osteoporos Int 21: 457–466.

30. American College of Obstetricians & Gynecologists Committee on Gynecologic Practice (2008) ACOG Committee Opinion No. 415: Depot medroxyprogesterone acetate and bone effects. Obstet Gynecol 112: 727–730.

31. Bartl R. (2007) [Antiepileptic drug-induced osteopathy. Subtypes, pathogenesis, prevention, early diagnosis and treatment]. Dtsch Med Wochenschr 132: 1475–1479.

32. Bazelier M., De Vries F., Vestergaard P., Herings R., Gallagher A., Leufkens H., et al. (2013) Risk of fracture with thiazolidinediones: an individual patient data meta-analysis. Front Endocrinol (Lausanne) 4: 11.

33. Body J., Bergmann P., Boonen S., Boutsen Y., Devogelaer J., Goemaere S., et al. (2007) Management of cancer treatment-induced bone loss in early breast and prostate cancer – a consensus paper of the Belgian Bone Club. Osteoporos Int 18: 1439–1450.

34. Bonadonna S., Burattin A., Nuzzo M., Bugari G., Rosei E., Valle D., et al. (2005) Chronic glucocorticoid treatment alters spontaneous pulsatile parathyroid hormone secretory dynamics in human subjects. Eur J Endocrinol 152: 199–205.

35. Bishop N., Ninkovic M., Alexander G., Holmes S., Milligan T., Price C., et al. (1999) Changes in calcium homoeostasis in patients undergoing liver transplantation: effects of a single infusion of pamidronate administered pre-operatively. Clin Sci (Lond) 97: 157–163.

36. Adachi J., Saag K., Delmas P., Liberman U., Emkey R., Seeman E., et al. (2001) Two-year effects of alendronate on bone mineral density and vertebral fracture in patients receiving glucocorticoids: a randomized, double-blind, placebo-controlled extension trial. Arthritis Rheum 44: 202–211.

37. Clark M., Sowers M., Levy B., Nichols S. (2006) Bone mineral density loss and recovery during 48 months in first-time users of depot medroxyprogesterone acetate. Fertil Steril 86: 1466–1474.

38. Corley D., Kubo A., Zhao W., Quesenberry C. (2010) Proton pump inhibitors and histamine-2 receptor antagonists are associated with hip fractures among at-risk patients. Gastroenterology 139: 93–101.

39. Brufsky A., Bundred N., Coleman R., Lambert-Falls R., Mena R., Hadji P., et al. (2008) Integrated analysis of zoledronic acid for prevention of aromatase inhibitor-associated bone loss in postmenopausal women with early breast cancer receiving adjuvant letrozole. Oncologist 13: 503–514.

40. Barbour L., Kick S., Steiner J., Loverde M., Heddleston L., Lear J., et al. (1994) A prospective study of heparin-induced osteoporosis in pregnancy using bone densitometry. Am J Obstet Gynecol 170: 862–869.

41. Adams JE. Radiogrammetry and radiographic absorptiometry. Radiol Clin North Am. 2010;48:531–540.

42. Kim YM, Demissie S, Genant HK, Cheng X, Yu W, Samelson EJ, Kiel DP, Bouxsein ML. Identification of prevalent vertebral fractures using CT lateral scout views: a comparison of semi-automated quantitative vertebral morphometry and radiologist semi-quantitative grading. Osteoporos Int. 2012;23:1007–1016.

43. Gilsanz V, Wren T. Assessment of bone acquisition in childhood and adolescence. Pediatrics. 2007;119 Suppl 2:S145–S149.

44. Adams JE. Quantitative computed tomography. Eur J Radiol. 2009;71:415–424.

45. Engelke K, Adams JE, Armbrecht G, Augat P, Bogado CE, Bouxsein ML, Felsenberg D, Ito M, Prevrhal S, Hans DB, et al. Clinical use of quantitative computed tomography and peripheral quantitative computed tomography in the management of osteoporosis in adults: the 2007 ISCD Official Positions. J Clin Densitom. 2008;11:123–162.

46. Macdonald HM, Nishiyama KK, Kang J, Hanley DA, Boyd SK. Age-related patterns of trabecular and cortical bone loss differ between sexes and skeletal sites: a population-based HR-pQCT study. J Bone Miner Res. 2011;26:50–62.

47. Wu SY, Jia HH, Hans D, Lan J, Wang LY, Li JX, Cai YZ. Assessment of volumetric bone mineral density of the femoral neck in postmenopausal women with and without vertebral fractures using quantitative multi-slice CT. J Zhejiang Univ Sci B. 2009;10:499–504.

48. Hartl F, Tyndall A, Kraenzlin M, Bachmeier C, Gückel C, Senn U, Hans D, Theiler R. Discriminatory ability of quantitative ultrasound parameters and bone mineral density in a population-based sample of postmenopausal women with vertebral fractures: results of the Basel Osteoporosis Study. J Bone Miner Res. 2002;17:321–330.

49. Cadossi R, Canè V. Pathways of transmission of ultrasound energy through the distal metaphysis of the second phalanx of pigs: an in vitro study. Osteoporos Int. 1996;6:196–206.

50. Cadossi R, Canè V. Pathways of transmission of ultrasound energy through the distal metaphysis of the second phalanx of pigs: an in vitro study. Osteoporos Int. 1996;6:196–206.

51. Prevrhal S, Engelke K, Genant HK. pQCT: peripheral quantitative computed tomography. In: Grampp S, editor. Radiology of osteoporosis. 2nd ed. Berlin, Heidelberg: Springer-Verlag; 2008. pp. 143–162.

52. Glüer CC. Quantitative ultrasound techniques for the assessment of osteoporosis: expert agreement on current status. The International Quantitative Ultrasound Consensus Group. J Bone Miner Res. 1997;12:1280–1288.

53. Louis O, Moreels X, Osteaux M. Reproducibility of phalanx osteosonography and relation with forearm peripheral quantitative computed tomography: single finger versus average measurement on the last four fingers. Eur J Radiol. 1998;28:270–275.

54. Wegrzyn J, Roux JP, Arlot ME, Boutroy S, Vilayphiou N, Guyen O, Delmas PD, Chapurlat R, Bouxsein ML. Determinants of the mechanical behavior of human lumbar vertebrae after simulated mild fracture. J Bone Miner Res. 2011;26:739–746.

55. Hans D, Njeh CF, Genant HK, Meunier PJ. Quantitative ultrasound in bone status assessment. Rev Rhum Engl Ed. 1998;65:489–498.

56. Kalender WA. CT: the unexpected evolution of an imaging modality. Eur Radiol. 2005;15 Suppl 4:D21–D24.

57. Kriegs MA, Cornuz J, Ruffieux C, Van Melle G, Büche D, Dambacher MA, Hans D, Hartl F, Häuselmann HJ, Kraenzlin M, et al. Prediction of hip fracture risk by quantitative ultrasound in more than 7000 Swiss women ≥ 70 years of age: comparison of three technologically different bone ultrasound devices in the SEMOF study. J Bone Miner Res. 2006;21:1457–1463.

58. Guglielmi G, Njeh CF, de Terlizzi F, De Serio DA, Scillitani A, Cammisa M, Fan B, Lu Y, Genant HK. Palangeal quantitative ultrasound, phalangeal morphometric variables, and vertebral fracture discrimination. Calcif Tissue Int. 2003;72:469–477.

59. Aguado F, Revilla M, Villa LF, Rico H. Cortical bone resorption in osteoporosis. Calcif Tissue Int. 1997;60:323–326.

60. Khaw KT, Reeve J, Luben R, Bingham S, Welch A, Wareham N, Oakes S, Day N. Prediction of total and hip fracture risk in men and women by quantitative ultrasound of the calcaneus: EPIC-Norfolk prospective population study. Lancet. 2004;363:197–202.

61. Baroncelli GI, Federico G, Bertelloni S, de Terlizzi F, Cadossi R, Saggese G. Bone quality assessment by quantitative ultrasound of proximal phalanxes of the hand in healthysubjects aged 3–21 years. Pediatr Res. 2001;49:713–718.

62. Zadik Z, Price D, Diamond G. Pediatric reference curves for multi-site quantitative ultrasound and its modulators. Osteoporos Int. 2003;14:857–862.

63. Gimeno Ballester J, Azcona San Julián C, Sierrasesúmaga Ariznabarreta L. Bone mineral density determination by osteosonography in healthy children and adolescents: normal values. An Esp Pediatr. 2001;54:540–546.

64. Njeh CF, Richards A, Boivin CM, Hans D, Fuerst T, Genant HV. Factors influencing the speed of sound through the proximal phalanges. J Clin Densitom. 1999;2:241–249.