American College of Radiology
ACR Appropriateness Criteria®
Osteoporosis and Bone Mineral Density

Variant 1: **Osteoporosis screening or initial imaging of clinically suspected low bone mineral density.**

Procedure	Appropriateness Category	Relative Radiation Level
DXA lumbar spine and hip(s)	Usually Appropriate	☢
DXA distal forearm	May Be Appropriate	☢
QCT lumbar spine and hip	May Be Appropriate	☢☢☢
QUS calcaneus	Usually Not Appropriate	O
SXA distal forearm	Usually Not Appropriate	☢
TBS lumbar spine	Usually Not Appropriate	☢
Radiography appendicular skeleton	Usually Not Appropriate	☢☢
Radiography axial skeleton	Usually Not Appropriate	Varies

Variant 2: **Follow-up imaging of patients demonstrated to have risk for fracture or surveillance of established low bone mineral density.**

Procedure	Appropriateness Category	Relative Radiation Level
DXA lumbar spine and hip(s)	Usually Appropriate	☢
DXA distal forearm	May Be Appropriate	☢
TBS lumbar spine	May Be Appropriate	☢
QCT lumbar spine and hip(s)	May Be Appropriate	☢☢☢
QUS calcaneus	Usually Not Appropriate	O
DXA VFA	Usually Not Appropriate	☢
SXA distal forearm	Usually Not Appropriate	☢

Variant 3: **Follow-up imaging. Patients with T-scores less than −1.0 (by DXA) and one or more of the following: 1) Females equal to or greater than 70 years of age or males equal to or greater than 80 years of age; 2) Historical height loss greater than 4 cm (greater than 1.5 inches); 3) Self-reported but undocumented prior vertebral fracture; 4) Glucocorticoid therapy equivalent to equal to or greater than 5 mg of prednisone or equivalent per day for equal to or greater than 3 months.**

Procedure	Appropriateness Category	Relative Radiation Level
DXA lumbar spine and hip(s)	Usually Appropriate	☢
DXA VFA	Usually Appropriate	☢
DXA distal forearm	May Be Appropriate	☢
Radiography axial skeleton	May Be Appropriate	Varies
QCT lumbar spine and hip	May Be Appropriate	☢☢☢
QUS calcaneus	Usually Not Appropriate	O
SXA distal forearm	Usually Not Appropriate	☢
TBS lumbar spine	Usually Not Appropriate	☢
Radiography appendicular skeleton	Usually Not Appropriate	☢☢

Variant 4: **Initial imaging for premenopausal females or males less than 50 years of age. Individual with risk factors that could alter bone mineral density.**

Procedure	Appropriateness Category	Relative Radiation Level
DXA lumbar spine and hip(s)	Usually Appropriate	☢
DXA distal forearm	May Be Appropriate	☢
QUS calcaneus	Usually Not Appropriate	O
SXA distal forearm	Usually Not Appropriate	☢
TBS lumbar spine	Usually Not Appropriate	☢
Radiography appendicular skeleton	Usually Not Appropriate	☢☢
Radiography axial skeleton	Usually Not Appropriate	Varies
QCT lumbar spine and hip	Usually Not Appropriate	☢☢☢

Variant 5: **Premenopausal females with risk factors. Males less than 50 years of age with risk factors. Follow-up to low bone mineral density.**

Procedure	Appropriateness Category	Relative Radiation Level
DXA lumbar spine and hip(s)	Usually Appropriate	☢
DXA distal forearm	May Be Appropriate	☢
QCT lumbar spine and hip	May Be Appropriate	☢☢☢
QUS calcaneus	Usually Not Appropriate	O
SXA distal forearm	Usually Not Appropriate	☢
TBS lumbar spine	Usually Not Appropriate	☢

Variant 6: **Males and females greater than or equal to 50 years of age. Suspected osteoporosis. Advanced degenerative changes of the spine with or without scoliosis, or other conditions that may spuriously elevate BMD. Initial imaging.**

Procedure	Appropriateness Category	Relative Radiation Level
DXA distal forearm	Usually Appropriate	☢
DXA lumbar spine and hip(s)	Usually Appropriate	☢
QCT lumbar spine and hip	Usually Appropriate	☢☢☢
QUS calcaneus	Usually Not Appropriate	O
SXA distal forearm	Usually Not Appropriate	☢
Radiography appendicular skeleton	Usually Not Appropriate	☢☢
Radiography axial skeleton	Usually Not Appropriate	Varies

OSTEOPOROSIS AND BONE MINERAL DENSITY

Expert Panel on Musculoskeletal Imaging: Joseph S. Yu, MD[a]; Nidhi G. Krishna, MD[b]; Michael G. Fox, MD, MBA[c]; Donna G. Blankenbaker, MD[d]; Matthew A. Frick, MD[e]; Shari T. Jawetz, MD[f]; Guibin Li, MD[g]; Charles Reitman, MD[h]; Nicholas Said, MD, MBA[i]; J. Derek Stensby, MD[j]; Naveen Subhas, MD, MPH[k]; Mark Tulchinsky, MD, MD[l]; Eric A. Walker, MD, MHA[m]; Francesca D. Beaman, MD.[n]

Summary of Literature Review

Introduction/Background

Osteoporosis is a systemic skeletal condition characterized by reduced bone density and deterioration of osseous tissue that leads to bone fragility and increased susceptibility to fracture [1]. Bone strength is a product of bone mineral density (BMD), a quantifiable property, and the integrity of trabecular microarchitecture. Currently, the consensus approach to screening and monitoring osteoporosis in the population is measurement of BMD, which is an effective way to identify patients who are at risk for fracture. An estimated 10.2 million adults in the United States >50 years of age have osteoporosis; however, the aging of the population is projected to increase this number by >30% by 2030, even though most experts agree that osteoporosis is generally underdiagnosed [2,3]. Approximately one-half of women and nearly one-third of men >50 years of age will sustain an osteoporotic fracture [4]. The yearly number of fractures is projected to increase from 1.9 million in 2018 to over 3.2 million fractures by 2040, with direct medical costs increasing from $48.8 billion to $81.5 billion during the same time range [5,6]. When indirect societal costs are also considered, the total projected cost could exceed $95 billion by 2040 [6].

Osteoporotic fractures are associated with subsequent fractures and premature mortality. In patients who have sustained a fracture, 10% will have another within 1 year, 18% within 2 years, and 31% within 5 years [7]. The first-year mortality rate is 20%, but there is also a 3- to 4-fold increased risk of mortality in the subsequent 5 years following any fragility fracture [8]. It is highest after sustaining a hip fracture, where there is a 1-year mortality of 24% in women and 38% in men [9]. Fragility fractures are also associated with a decrease in quality of life, diminished physical function, and reduced independence [10]. Given the proven efficacy of pharmacologic therapy, the role of imaging to appropriately identify and monitor high-risk individuals is critical in substantially reducing osteoporosis-associated morbidity and mortality.

Special Imaging Considerations

Dual-energy X-ray absorptiometry (DXA) is the mainstay of bone densitometry to screen for osteopenia and osteoporosis. Because this modality relies on precision, it is essential for patients to be scanned on the same DXA machine because differences in vendor technologies prohibit a direct comparison unless cross calibration has been performed [11,12].

CT is a cross-sectional-based X-ray technology that uses tomographic technique coupled with computer processing to generate a cross-sectional image. CT has a higher sensitivity to subtle differences in electron densities than radiography and therefore creates an image with markedly improved contrast.

Quantitative CT (QCT) is performed on a standard clinical scanner and is highly accurate in determining tissue density within a region of interest. Scanning sites for QCT include the lumbar spine and hip. Several studies have assessed using conventional CT scans for measurement of bone density by establishing threshold Hounsfield unit levels that are diagnostic for osteopenia and osteoporosis, but this concept remains an opportunistic use of CT and not a screening tool [13-15]. High-resolution peripheral QCT uses the same technology in a smaller dedicated machine and focuses on the distal radius and tibia. Currently, peripheral QCT studies are not approved for diagnosis

[a]The Ohio State University Wexner Medical Center, Columbus, Ohio. [b]Research Author, Ohio State University, Columbus, Ohio. [c]Panel Chair, Mayo Clinic Arizona, Phoenix, Arizona. [d]University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin. [e]Mayo Clinic, Rochester, Minnesota. [f]Hospital for Special Surgery, New York, New York. [g]The Ohio State University Wexner Medical Center, Columbus, Ohio, Primary care physician. [h]Medical University of South Carolina, Charleston, South Carolina; North American Spine Society. [i]Duke University Medical Center, Durham, North Carolina. [j]University of Missouri Health Care, Columbia, Missouri. [k]Cleveland Clinic, Cleveland, Ohio. [l]Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania, Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania; Commission on Nuclear Medicine and Molecular Imaging. [m]Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania and Uniformed Services University of the Health Sciences, Bethesda, Maryland. [n]Specialty Chair, University of Kentucky, Lexington, Kentucky.

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of osteoporosis, although it has research applications in determining alterations in the bone architecture. It should be noted that peripheral QCT is commonly performed in children [16].

Initial Imaging Definition

Initial imaging is defined as imaging at the beginning of the care episode for the medical condition defined by the variant. More than one procedure can be considered usually appropriate in the initial imaging evaluation when:

- There are procedures that are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care)

OR

- There are complementary procedures (ie, more than one procedure is ordered as a set or simultaneously where each procedure provides unique clinical information to effectively manage the patient's care).

Discussion of Imaging Modalities by Variant

Variant 1: Osteoporosis screening or initial imaging of clinically suspected low bone mineral density.

The indications for BMD testing according to the International Society for Clinical Densitometry (ISCD) are [17]:

1. All women ≥65 years of age and men ≥70 years of age (asymptomatic screening)
2. Women <65 years of age who have additional risk for osteoporosis, based on medical history and other findings. Additional risk factors for osteoporosis include:
   a. Estrogen deficiency
   b. A history of maternal hip fracture that occurred after the age of 50 years
   c. Low body mass (<127 lb or 57.6 kg)
   d. History of amenorrhea (>1 year before 42 years of age)
3. Women <65 years of age or men <70 years of age who have additional risk factors, including:
   a. Current use of cigarettes
   b. Loss of height, thoracic kyphosis
4. Individuals with bone mass osteopenia or fragility fractures on imaging studies such as radiographs, CT, or MRI
5. Individuals ≥50 years of age who develop a wrist, hip, spine, or proximal humerus fracture with minimal or no trauma, excluding pathologic fractures
6. Individuals of any age who develop 1 or more insufficiency fractures
7. Individuals being considered for pharmacologic therapy for osteoporosis
8. Individuals being assessed for the effectiveness of osteoporosis drug therapy

DXA

DXA is recommended for osteoporosis screening or initial imaging of clinically suspected low BMD. It is a clinically proven method of measuring BMD in the lumbar spine, proximal femur, forearm, and whole body. BMD measurements derived from DXA has been shown to accurately predict fracture risk [18,19]. Epidemiological studies have demonstrated that BMD correlates to population fracture risk and amount of force necessary to fracture bone [20,21].

In a routine DXA study, 2 sites (the lumbar spine and hip) are reported. In the spine, a frontal projection measures up to 4 vertebral bodies from L1 to L4, and in the hip, a frontal projection measures 2 regions: the femoral neck and total hip [17]. In the event of a falsely elevated BMD of the lumbar spine caused by fracture, facet joint osteoarthritis, or spondylosis, up to 2 vertebral levels may be excluded from analysis. However, if exclusion of more than 2 vertebral body levels is necessary, then the second hip can be scanned as a substitute for the spine [22]. Alternatively, the distal one-third radius of the nondominant arm may be used as a third site in situations in which only one hip is available. Otherwise, the distal one-third radius is used primarily in patients with hyperparathyroidism. Primary hyperparathyroidism preferentially decreases mineralization at cortical-rich sites such as the hip and mid radius, in contrast to the predominantly cancellous bone of the lumbar spine [22].

The accuracy and reproducibility of DXA has led to the establishment of standards for the diagnosis of osteoporosis set forth by the World Health Organization (WHO), with endorsement by the National Osteoporosis Foundation (NOF) and the American Association of Clinical Endocrinologists [23,24]. Fracture risk is determined when BMD as measured by DXA is compared with a gender-matched asymptomatic reference population. Diagnosis is based on T-scores, the number of SDs that the patient's BMD is above or below the mean in a reference population, which varies with gender and race. The Z-score represents the number of standard deviations above or below the mean of age-matched controls. Z-scores are used to detect secondary causes of osteoporosis.

The WHO defines normal BMD as a T-score ≥−1.0. Low bone mass or osteopenia is defined as T-score between −1.0 and −2.5, whereas T-scores ≤−2.5 indicate osteoporosis [25]. An osteoporotic fracture supersedes any DXA measurement, so that patients who are in the osteopenic range who have a fragility fracture should be upgraded to the diagnosis of osteoporosis [1]. The NOF recommends pharmacologic treatment for all postmenopausal women and men >50 years of age with a T-score ≤−2.5 [26]. In patients with low bone mass, a fracture risk assessment tool, most commonly FRAX, is used. The FRAX tool factors include hip BMD, age, sex, height, weight, family history of hip fracture, smoking, steroid use >3 months, rheumatoid arthritis, and alcohol use [27]. The FRAX algorithm is country specific and intended for use in previously untreated postmenopausal women and men 40 to 90 years of age. The NOF recommends treatment in patients with a 10-year probability of a hip fracture ≥3% or a 10-year probability of a major osteoporosis-related fracture ≥20% based on FRAX [28].

Although DXA is an accurate screening tool, it remains underused. According to 2 recent reports, only 6.7% of patients underwent evaluation with DXA 6 months after sustaining a fragility fracture in 1 study, and only 8% of patients on long-term glucocorticoid therapy had follow-up DXAs [29,30]. Underutilization may lead to under-treatment in approximately 70% of these patients, and patients who are not adequately treated are at increased risk of incurring additional fractures in their lifetime [7,29].

QCT

QCT also provides volumetric BMD (vBMD), and both the trabecular and cortical bone compartments can be assessed [31,32]. QCT can be performed on a vast majority of commercially available CT scanners, provided they include densitometry analysis software and a calibration phantom. When interpreting QCT vBMD results, it is important to recognize 2 important differences to DXA. Z- and T-scores can be calculated from the vBMD, but the T-scores do not apply to the WHO definition of osteoporosis or osteopenia [31]. The exclusive application of the WHO classification is inherent to projectional BMD [25]. The ACR QCT cutoff values for low bone mass or osteopenia are 80 to 120 mg/mL and <80 mg/mL for osteoporosis [12]. Another major difference between QCT and DXA is related to monitoring. Spine BMD values measured by QCT demonstrate higher rates of bone loss with advancing age, principally because of the exclusive measurement of cancellous bone. The rate of change in cancellous bone is significantly greater than that of cortical bone. By contrast, the projectional properties of DXA summate the cortically predominant end plates and posterior elements with the cancellous vertebral body measurements, thereby decreasing their rate of change over time [31].

Projectional QCT of the hip is a technique that simulates DXA-type images from QCT. It provides a calculated measurement of areal BMD in the hip. Because the postprocessed areal BMD is comparable to DXA, the WHO classification definition of osteoporosis as a T-score ≤−2.5 is applicable to this CT technique [33].

Indications for utilization of QCT as a screening modality are the same as DXA. However, in the setting of screening or initial imaging, QCT is regarded as a secondary tool to DXA. QCT may be considered as a primary imaging modality in certain conditions. Cases in which QCT is considered superior to DXA include extremes in height (very tall and very small patients), patients with obesity (BMI >35 kg/m^2), patients with severe degenerative spine disease, and when an increased sensitivity to small changes in trabecular bone density is desired (parathyroid hormone and glucocorticoid treatment monitoring) [34]. It was recently reported that opportunistic QCTs of the lumbar spine was more predictive of spine fractures in neurological and oncologic patients than reference DXA scans, but there were only 84 patients in this study [35].

QUS

There is insufficient evidence to support the current use of quantitative ultrasound (QUS) as a screening tool in patients suspected of having osteoporosis or low BMD. Dense structural complexity demonstrates increased attenuation, whereas osteoporotic bone demonstrates lower velocities. The limitations of QUS are a lack of precision and sensitivity [36]. Dedicated QUS scanners are available for the calcaneus, phalanx, and tibia. However, the heel represents the only validated site for the clinical use of QUS. QUS does not measure BMD, and therefore, the WHO

classification system cannot be used and a diagnosis of osteoporosis cannot be made. Discordance between QUS and central DXA is not infrequent [37]. A recent meta-analysis conducted to assess the role of QUS in inflammatory rheumatic diseases came to the conclusion that the current literature does not support the substitution of QUS for DXA in the diagnosis and monitoring of osteoporosis in rheumatic diseases [38].

Radiography Appendicular Skeleton

There is insufficient evidence to support the current use of radiography as a screening tool in patients suspected of having osteoporosis or low BMD. Radiography is a projectional X-ray-based technology that is widely used in current medical practice for rapid image acquisition for an extensive number of indications. Radiography use differences in electron density to generate contrast between different tissues, including bone. Although there are several standards used to identify demineralized bone on radiographs, radiography has a substantially lower sensitivity to bone loss than DXA. Osteopenia is not a reliable finding until 30% to 40% of the bone has been lost [39]. Patients who have radiographic evidence of osteopenia and/or fragility fractures should be referred to DXA for further characterization.

Radiography Axial Skeleton

There is insufficient evidence to support the current use of radiography as a screening tool in patients suspected of having osteoporosis or low BMD. Reportedly, patients with a low second metacarpal index may have a higher risk for developing hip fractures [40]. A recent study using artificial intelligence to segment metacarpal morphometry has shown potential as a screening tool with a sensitivity of 82.4% and specificity of 95.7% and a pipeline accuracy of nearly 94% [41]. Patients who have radiographic evidence of demineralization and/or fragility fractures should be referred to DXA for further characterization.

SXA

There is insufficient evidence to support the current use of single X-ray (SXA) in patients suspected of having osteoporosis or low BMD. SXA is a projectional X-ray-based technology that used one X-ray tube as a photon source and was shown to precisely measure BMD at the forearm. It is no longer widely used in current practice and has been supplanted by DXA.

TBS

Although DXA provides an accurate evaluation of BMD, it is not always an accurate predictor of fracture risk because there is considerable overlap between BMD values in individuals with and without fractures. Trabecular bone score (TBS) is an independent predictor of fracture risk because TBS values quantify bone microarchitecture, a determinant of bone strength [42]. This analytical tool performs textural analysis on 2-D lumbar spine DXA images and captures information by measuring grey-level variations from one pixel to adjacent pixels, providing 3-D bone characteristics such as trabecular number, trabecular separation, and the connectivity density [43]. There is evidence that TBS can differentiate between two 3-D microarchitectures that exhibit identical BMD measurements bone quality rather than bone quantity as measured by DXA, QCT, and ultrasound. Elevated values of TBS correlate with fracture resistance, whereas porous osteoporotic bone depict lower values than normal bone [44]. The advantages of TBS are that it can be assessed retrospectively from previously obtained DXA scans providing longitudinal data, and it is not impacted by the presence of overlying calcifications or degenerative changes in the spine [45].

In the setting of screening or initial imaging, TBS is regarded as an adjunct tool to DXA. However, TBS should not be used alone in clinical practice either to screen for osteoporosis or for treatment decisions [17]. TBS may be useful in certain populations. TBS when used in conjunction with BMD, clinical risk factors, and/or FRAX consistently enhances their accuracy [46-50]. Significantly reduced TBSs are associated with fragility fractures in secondary osteoporosis. In these patients, TBS has been found to have a substantially higher association with fracture risk than BMD [51,52]. TBSs in patients with type 2 diabetes, chronic renal disease, glucocorticoid therapy, rheumatoid arthritis, and hyperparathyroidism have demonstrated increased fracture risk, even in the setting of normal BMD [47,53].

Variant 2: Follow-up imaging of patients demonstrated to have risk for fracture or surveillance of established low bone mineral density.

Follow-up imaging is recommended in patients who have increased risk for fracture, been previously diagnosed with osteopenia or osteoporosis, or initiated treatment for osteoporosis. Additionally, as outlined in Variant 3, vertebral fracture assessment (VFA) may be considered in patients with documented spine fractures or if they have

been diagnosed with osteopenia and meet certain age criteria, have experienced height loss or undocumented vertebral fractures (VFs), or have a history of use of glucocorticoid medication for >3 months.

DXA

Follow-up DXA scanning is important for monitoring patients who have low BMD, either for progression or therapeutic response, and in those with normal BMD who have increased fracture risk and/or diminishing bone mass. The measurement of hip BMD continues to be the most reliable way of evaluating hip fracture risk, whereas imaging of the spine is optimal for monitoring treatment response. It is essential for patients to be scanned on the same DXA machine because differences in vendor technologies prohibit a direct comparison unless cross calibration has been performed [54]. Obtaining a quality BMD measurement every time underscores its importance because it is the BMD values, not T-scores, that are compared between scans [55]. BMD measurements do not need to be repeated routinely in patients with osteopenia unless the baseline T-score is <−2.0 or risk factors develop [56].

When a nontreated patient has a statistically significant decrease in BMD on follow-up DXA, therapy initiation may be considered in the setting of confirmed primary osteoporosis or when there is clinical correlation identifying potential secondary causes of osteoporosis [57]. Serial BMD testing combined with clinical risk factors, bone turnover markers, and other factors such as height loss and TBS may also be used to determine whether treatment should be initiated. Patients receiving treatment who demonstrate decreasing BMD on follow-up scans may require an adjustment in their pharmacotherapy regimen [24].

In the majority of patients, the time interval for monitoring is based on the change rate of bone mineralization, which is typically about 2 years; however, it is preferable for this interval to be shorter (1 to <2 years) after therapy has been initiated [23]. Patients who are at high risk for a more rapid decline of bone mass, such as those receiving glucocorticoid therapy, also require shorter intervals between imaging; 1-year intervals after initiation or change of therapy is appropriate with progressively longer intervals once therapeutic effect is established [58]. Scan intervals <1 year are discouraged [24]. Serial BMD testing is encouraged in individuals after cessation of pharmacologic therapy for osteoporosis as well.

Forearm BMD measurements should be performed under the following circumstances; when the hip and/or spine cannot be measured or interpreted, in patients with primary and secondary hyperparathyroidism, and in patients who exceed the weight limit for the DXA table. In older patients with chronic kidney disease, the percentage of patients with osteopenia and osteoporosis has been shown to increase with chronic kidney disease progression; the decrease in BMD predominantly affects the hip and not the spine [59]. According to the Third International Workshop on Hyperparathyroidism, patients with hyperparathyroidism with T-scores ≤−2.5 at any of the 3 routinely measured sites should be scanned every 1 to 2 years as well as undergo a parathyroidectomy [60].

DXA VFA

In this setting, use of VFA is not supported. This differs from variant 3 in which VFA may be considered in patients with documented spine fractures or if they have been diagnosed with osteopenia and meet certain age criteria, have experienced height loss or undocumented VFs, or have a history of use of glucocorticoid medication for >3 months [17].

QCT

QCT is regarded as a secondary or adjunct tool to DXA. QCT may be useful in unique populations in which there is a need for added precision. QCT demonstrates excellent precision and reproducibility to changes and can be used for the monitoring of BMD in untreated and treated patients provided that there is routine calibration [22]. QCT is more sensitive to change than DXA because it detects mineralization in the cancellous bone, the portion of bone most sensitive to rapid changes, as well as at the cortex, such as newly formed bone in the cortical and subcortical compartments [61-63]. Femoral neck and total hip T-scores calculated from follow-up projectional QCT data are equivalent to corresponding DXA T-scores for monitoring of osteoporosis in accordance to the WHO criteria, and can be used longitudinally [22].

QUS

There is insufficient evidence to the support the routine use of QUS for monitoring of untreated and treated patients.

SXA

There is insufficient evidence to the support the routine use of SXA for monitoring of untreated and treated patients.

TBS
TBS is regarded as an adjunct tool to DXA. TBS may be useful in a small population where there is a need to look at marginal changes beyond BMD. TBS may be of benefit stratifying risk in individuals with relatively normal or osteopenic BMD values because most fractures occur in this subset of nonosteoporotic patients. Multiple studies have shown associations of TBS with fractures in postmenopausal women as well as a few fractures in men [64-68].

TBS is potentially useful for monitoring anabolic therapy, but its role in monitoring antiresorptive therapy is unclear [69-72]. There are data to indicate that in follow-up, smaller changes are more evident in TBS than in BMD, especially in patients with degenerative disease of the spine. In a clinical scenario in which there is discordance between the spine and hip BMD, TBS may provide additional information of the patient's fracture risk. In patients with a normal BMD but a low TBS and multiple fractures, changes in TBS may influence therapeutic management [73].

Variant 3: Follow-up imaging. Patients with T-scores less than −1.0 (by DXA) and one or more of the following: 1) Females equal to or greater than 70 years of age or males equal to or greater than 80 years of age; 2) Historical height loss greater than 4 cm (greater than 1.5 inches); 3) Self-reported but undocumented prior vertebral fracture; 4) Glucocorticoid therapy equivalent to equal to or greater than 5 mg of prednisone or equivalent per day for equal to or greater than 3 months.

VF are the most common osteoporotic fracture, particularly in postmenopausal women. The majority of these fractures are clinically silent, meaning that they do not elicit sufficient pain to warrant clinical evaluation or imaging [74]. Patients who sustain a VF have a high predilection for developing a subsequent VF; therefore, detection is a strong predictor of high fracture risk independent of BMD [75,76]. Numerous modalities are available for diagnosing suspected fractures in the spine.

DXA
Follow-up DXA is supported for monitoring patients who have low BMD and VF risk factors [56].

DXA VFA
In their 2019 guidelines, the ISCD recommended that densitometric spine imaging, or VFA, be considered for the listed indications in this variant [17]. VFA is a feature of DXA scanners in which a lateral thoracic and lumbar spine image from T5 to L5 is provided for the purpose of detecting vertebral body deformities; most VFs occur between the T7 and L4 levels [77]. This procedure is complementary to DXA; the image is obtained during the DXA session and represents a point-of-care service. A semiquantitative visual method used for diagnosis characterizes the morphology based on shape (wedge, concave, or crush) and location (anterior, posterior, and/or middle) and the total number of involved vertebrae [78,79]. In general, grade 2 fractures (moderate or 26%-40% reduction) and grade 3 fractures (severe or >40% reduction) are more predictive of future fractures than grade 1 fractures (mild or 20%-25% reduction), which have a greater overlap with nonfracture deformities [80]. A solitary, asymptomatic grade 1 fracture is likely to be minimal to no clinical significance, whereas a grade 3 fracture is an important predictor of fracture risk not only in the spine but also in nonvertebral sites [81].

It is estimated that two-thirds of radiographically evident VFs are not recognized clinically and are incidentally detected [82]. Numerous epidemiologic studies have provided the incidence and prevalence of VFs in different populations [83-85]. The risk for developing a VF rises substantially in women after >70 years of age and in men >80 years of age [86-88]. In patients with chronic exposure to glucocorticoid medication, the prevalence of VF is >50% in those >70 years of age, approximately 17% in patients treated for autoimmune disease, and 22% in patients with Crohn disease [89-91]. The incidence is 2 to 2.5 times higher in women than in men [77].

The utility of VFA is identifying patients who would not otherwise qualify for treatment under the guidelines of the NOF, which are based solely on BMD measurements. Multiple studies have demonstrated populations of patients who were reclassified because of detection of VFs [92-95]. A study in the Netherlands demonstrated that 60% of patients with a fracture on VFA were in the nonosteoporotic range, and of these, 74% were previously unknown to have fractures [92]. In another recent study of postmenopausal women, 17.2% of patients had their diagnosis upgraded to severe osteoporosis owing to VFs diagnosed on VFA [96]. A meta-analysis based on VFA-detected VFs reported that among women who had prevalent VFs, up to 43% had low BMD (osteopenia), and up to 32% had normal bone density [76]. Detection of unknown VFs influences initiating therapy in asymptomatic patients as well as guides therapeutic decisions in treated patients whose BMD may have remained stable or shown improvement on DXA [97].

QCT
QCT is regarded as a secondary or adjunct tool to DXA. It may be considered as a primary modality in cases in which there is severe degenerative disease of the spine or significant scoliosis (see Variant 6) and when it is desirable to have higher spatial resolution to optimize bone detail.

QUS
There is insufficient evidence to support the use of QUS to image the spine.

Radiography Appendicular Skeleton
There is insufficient evidence to support the use of appendicular radiography to image the spine.

Radiography Axial Skeleton
Lateral radiographs of the spine may be considered when VFA is not diagnostic or when images cannot be adequately derived. Additionally, radiographs of the spine may be considered as an alternative to VFA in patients who have low BMD and risk factors for developing VFs [17]. The benefit of radiography over VFA is superior spatial resolution. The sharp delineation of the end plates and cortical margins affirms confident detection of subtle Genant grade 1 fractures [98]. When reporting the severity of a vertebral body defect, the semiquantitative methodology by Genant should be used [78].

SXA
There is insufficient evidence to support the use of SXA to image the spine.

TBS
TBS is regarded as an adjunct tool to DXA. TBS may be useful in a small population in which there is a need to look at marginal changes beyond BMD. TBS enhances FRAX in patients whose BMD level lies close to the intervention threshold and may provide data that facilitates treatment decisions, but TBS should not be used by itself in monitoring patients with VF risk factors [47].

Variant 4: Initial imaging for premenopausal females or males less than 50 years of age. Individual with risk factors that could alter bone mineral density.

1. Individuals with medical conditions that could alter BMD, such as:
   a. Chronic renal failure
   b. Rheumatoid arthritis and other inflammatory arthritides
   c. Eating disorders, including anorexia nervosa and bulimia
   d. Organ transplantation
   e. Prolonged immobilization
   f. Conditions associated with secondary osteoporosis, such as gastrointestinal malabsorption or malnutrition, sprue, osteomalacia, vitamin D deficiency, endometriosis, acromegaly, chronic alcoholism or established cirrhosis, and multiple myeloma
   g. Individuals who have had gastric bypass for obesity. The accuracy of DXA in these patients might be affected by obesity
   h. Individuals with an endocrine disorder known to adversely affect BMD (eg, hyperparathyroidism, hyperthyroidism, or Cushing syndrome)
2. Individuals receiving (or expected to receive) glucocorticoid therapy for >3 months
3. Hypogonadal men >18 years of age and men with surgically or chemotherapeutically induced castration
4. Individuals beginning or receiving long-term therapy with medications known to adversely affect BMD (eg, anticonvulsant drugs, androgen deprivation therapy, aromatase inhibitor therapy, or chronic heparin).

DXA
The data providing imaging guidance in premenopausal women are few. The literature indicates that DXA remains the primary screening modality for evaluating bone mineralization in patients with these clinical scenarios [99]. Screening BMD should not be performed in premenopausal women. The 2 exceptions are young women with a history of fractures from minor trauma and those who have known causes of bone loss [100,101]. Chronic disease damage and low BMI are reported as risks factors for low BMD in premenopausal systemic lupus erythematosus patients, and early monitoring and/or treatment may prevent severe bone loss and future fractures [102]. In the 2017 American College of Rheumatology guidelines on glucocorticoid-induced osteoporosis, adults receiving

glucocorticoid therapy for >3 months and who have had a prior fracture or other risk factors should have their BMD evaluated every 2 to 3 years [103]. In organ transplant patients, owing to rapid bone loss in the first 6 to 12 months after transplantation, the same imaging guideline was proposed [103].

A baseline DXA should be considered in women age <40 years of age who experience premature menopause for any reason, especially when menopause was induced by chemotherapy. In untreated women undergoing initiation of an aromatase inhibitor, bone loss is most marked in the 12 to 24 months [104]. Men who undergo androgen deprivation therapy have substantially elevated risk of fracture. A baseline DXA study in men receiving androgen deprivation therapy should be considered after 6 months of therapy [105].

The WHO criteria for osteoporosis do not apply, and only Z-scores (not T-scores) should be reported [57]. The Z-score represents gender- and age-matched controls for the evaluation of secondary osteoporosis. Z-scores of ≤−2.0 are defined as "below the expected range for age," and Z-scores >−2.0 are "within the expected range for age" [106]. Z-scores should be population specific where adequate reference data exist, and the patient's self-reported ethnicity should be used in the calculation of the Z-scores. A diagnosis of osteoporosis cannot be made in men <50 years of age on the basis of BMD alone [17].

QCT
There is insufficient evidence to support the use of QCT as a screening study in this group of patients. A study using QCT in premenopausal women with idiopathic osteoporosis demonstrated good correlation between vBMD by QCT and areal BMD by DXA [107]. These results are consistent with 3-D bone imaging at the iliac crest, radius, and tibia in premenopausal idiopathic osteoporosis and suggest that the term osteoporosis may be appropriate in women with Z-scores <−2.0, whether or not there is a history of fracture [107]. An alternative study demonstrated a weak relationship between peripheral and central mechanical competence [108].

QUS
There is insufficient evidence to support the use of QUS as a screening study in this group of patients. The correlation between QUS parameters and DXA has been reported to be lower in premenopausal women than in postmenopausal women and not predictive of osteoporosis [109].

Radiography Appendicular Skeleton
There is insufficient evidence to support the use of radiography appendicular skeleton as a screening study in this group of patients.

Radiography Axial Skeleton
There is insufficient evidence to support the use of radiography axial skeleton as a screening study in this group of patients.

SXA
There is insufficient evidence to support the use of SXA as a screening study in this group of patients.

TBS
There is insufficient evidence to support the use of TBS as a screening study in this group of patients.

Variant 5: Premenopausal females with risk factors. Males less than 50 years of age with risk factors. Follow-up to low bone mineral density.

1. Individuals with medical conditions that could alter BMD, such as:
   a. Chronic renal failure
   b. Rheumatoid arthritis and other inflammatory arthritides
   c. Eating disorders, including anorexia nervosa and bulimia
   d. Organ transplantation
   e. Prolonged immobilization
   f. Conditions associated with secondary osteoporosis, such as gastrointestinal malabsorption or malnutrition, sprue, osteomalacia, vitamin D deficiency, endometriosis, acromegaly, chronic alcoholism or established cirrhosis, and multiple myeloma
   g. Individuals who have had gastric bypass for obesity. The accuracy of DXA in these patients might be affected by obesity

h. Individuals with an endocrine disorder known to adversely affect BMD (eg, hyperparathyroidism, hyperthyroidism, or Cushing syndrome)

2. Individuals receiving (or expected to receive) glucocorticoid therapy for >3 months
3. Hypogonadal men >18 years of age and men with surgically or chemotherapeutically induced castration
4. Individuals beginning or receiving long-term therapy with medications known to adversely affect BMD (eg, anticonvulsant drugs, androgen deprivation therapy, aromatase inhibitor therapy, or chronic heparin).

Follow-up for premenopausal women as well as for men 20 to <50 years of age is based on the underlying clinical conditions listed. Most expert groups recommend monitoring time interval of 1 to 2 years if there is a high risk for accelerated bone loss, but otherwise every 2 years if there are risk factors [24].

DXA
The literature indicates that DXA is the primary modality by which to monitor BMD in premenopausal women as well as adult men <50 years of age with risk factors [24]. The need for follow-up DXA is dictated by the clinical circumstance of the patients.

QCT
QCT is regarded as a secondary or adjunct tool to DXA. QCT may allow for monitoring BMD in premenopausal women and men between 20 to 50 years of age with risk factors. QCT demonstrates excellent precision and reproducibility to changes [31].

QUS
There is insufficient evidence to support the use of QUS to monitor premenopausal women or adult men <50 years of age with risk factors.

SXA
There is insufficient evidence to support the use of SXA to monitor premenopausal women or adult men <50 years of age with risk factors.

TBS
There is insufficient evidence to support the use of TBS to monitor premenopausal women or adult men <50 years of age with risk factors.

Variant 6: Males and females greater than or equal to 50 years of age. Suspected osteoporosis. Advanced degenerative changes of the spine with or without scoliosis, or other conditions that may spuriously elevate BMD. Initial imaging.

DXA
DXA allows for screening patients with risk factors and advanced degenerative changes in the spine. In a routine DXA examination, both the lumbar spine and hip are scanned and measured. Owing to the projectional nature of DXA, spuriously elevated BMD values of the lumbar spine may be caused by spondylosis and degenerative facet osteoarthritis or dense overlying tissue. Reportedly, in examinations with falsely elevated measurements, the most common cause (>81%) is degenerative disease of the spine [110]. The ISCD recommends close inspection of the images and associated BMD values to monitor levels for exclusion. In patients with ankylosing spondylitis, a moderate correlation and fair agreement between the T-scores of hip and the lumbar spine has been reported, suggesting that DXA of the hip and the lumbar spine may both be useful for screening in patients with ankylosing spondylitis without fused spines [111].

In addition to degenerative changes in the spine, BMD measurements using DXA may also be spuriously elevated in patients with hemoglobinopathies who have an iron-overloaded liver and in patients with severe abdominal calcifications [112,113].

QCT
The literature indicates that QCT is ideally suited for the evaluation of the spine in the setting of advanced degeneration of the spine; it is preferred over DXA for monitoring under these conditions as well. Because it selectively samples only the cancellous portion of the vertebral body and excludes the end plates, cortices, and posterior elements, BMD using QCT is generally not negatively impacted by arthritis in the spine and has greater sensitivity to change than in DXA in this group of patients [32,114]. It also may provide adjunctive information in preoperative patients who may have diminished bone density [115].

QUS
There is insufficient evidence to support the use of QUS as a screening study for low BMD in patients with advanced degenerative changes in the spine.

Radiography Appendicular Skeleton
There is insufficient evidence to support the use of radiography appendicular skeleton as a screening study for low BMD in patients with advanced degenerative changes in the spine.

Radiography Axial Skeleton
There is insufficient evidence to support the use of radiography axial skeleton as a screening study for low BMD in patients with advanced degenerative changes in the spine.

SXA
There is insufficient evidence to support the use of SXA as a screening tool for low BMD in patients with advanced degenerative changes in the spine.

Summary of Recommendations

- **Variant 1**: DXA lumbar spine and hip(s) is usually appropriate for osteoporosis screening or initial imaging of clinically suspected low BMD.
- **Variant 2**: DXA lumbar spine and hip(s) is usually appropriate for the follow-up imaging of patients demonstrated to have risk for fracture or surveillance of established low BMD.
- **Variant 3**: DXA lumbar spine and hip(s) and DXA VFA is usually appropriate for the follow-up imaging of patients with T-scores less than −1.0 (by DXA) and one or more of the following: 1) Females equal to or greater than 70 years of age or males equal to or greater than 80 years of age; 2) Historical height loss greater than 4 cm (greater than 1.5 inches); 3) Self-reported but undocumented prior VF; 4) Glucocorticoid therapy equivalent to equal to or greater than 5 mg of prednisone or equivalent per day for equal to or greater than 3 months. VFA and DXA are complementary procedures that are performed concomitantly allowing point-of-care service at the same visit that one obtains a BMD measurement.
- **Variant 4**: DXA lumbar spine and hip(s) is usually appropriate for the initial imaging of patients with risk factors that could alter BMD including premenopausal females or males less than 50 years of age.
- **Variant 5**: DXA lumbar spine and hip(s) is usually appropriate for the imaging follow-up to low BMD of patients with risk factors including premenopausal females or males less than 50 years of age with risk factors.
- **Variant 6**: DXA distal forearm or DXA lumbar spine and hip(s) or QCT lumbar spine and hip is usually appropriate for the initial imaging of clinically suspected osteoporosis in patients with advanced degenerative changes of the spine with or without scoliosis, or other conditions that may spuriously elevate BMD. These procedures are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).

Supporting Documents

The evidence table, literature search, and appendix for this topic are available at https://acsearch.acr.org/list. The appendix includes the strength of evidence assessment and the final rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents go to www.acr.org/ac.

Appropriateness Category Names and Definitions

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, because of both organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared with those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® Radiation Dose Assessment Introduction document [116].

Relative Radiation Level Designations		
Relative Radiation Level*	**Adult Effective Dose Estimate Range**	**Pediatric Effective Dose Estimate Range**
O	0 mSv	0 mSv
☢	<0.1 mSv	<0.03 mSv
☢☢	0.1-1 mSv	0.03-0.3 mSv
☢☢☢	1-10 mSv	0.3-3 mSv
☢☢☢☢	10-30 mSv	3-10 mSv
☢☢☢☢☢	30-100 mSv	10-30 mSv
*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (eg, region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."		

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The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.