QCT PRO™

Bone Mineral Densitometry Software
Report Content and Interpretation Module

Version 5.1 – Revision 20130102

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QCT PRO BMD Applications

QCT PRO is a modular software application that can be customized via the installation of numerous application modules intended to support a variety of clinical needs and configurations. The QCT PRO family of application modules includes modules for estimating bone mineral density (BMD) in the spine and in the proximal femur. This guide describes operational characteristics of these BMD modules, their intended use, and relevant safety information.

The information provided in this guide covers the following QCT PRO application modules:

- 3D Spine
- 2D Spine
- CTXA Hip
- QA

Any combination of these application modules may be installed on a particular system.

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General Safety Precautions

Warning: United States Federal Law restricts this device to the sale, distribution, and use by or on the order of a physician.

The QCT PRO BMD application modules are intended for use as an accessory to a CT scanner. The QCT PRO documentation contains information regarding the installation of QCT PRO and optional BMD modules for use with your CT scanner, including instructions for verifying compatibility with your CT scanner, and directions for calibrating and monitoring the performance of your installed system. These instructions should be followed to assure the safe and effective use of these products.

The QCT PRO BMD application modules are intended for use with CT calibration phantoms that provide a calibration reference relative to aqueous K_2HPO_4.

Warning: the alternate use of different calibration phantoms in serial patient studies should be avoided.

While the QCT PRO BMD application modules do not deliver or control the delivery of ionizing radiation to a patient, these modules are used to analyze CT images that are derived as the result of delivery of ionizing radiation to a patient through a CT scanner. The CT scanner manufacturer's guidelines for the safe use of the CT scanner should be adhered to at all times.

Each QCT PRO BMD application module includes a user's guide containing operational instructions specific to each BMD application module. These instructions include guidelines for estimating appropriate patient exposure when acquiring CT image data intended for analysis within a specific BMD application module. Adherence to these guidelines will often result in the use of an exposure below that which might be used for studies intended for radiologic interpretation in the same anatomical region, thereby reducing patient exposure to ionizing radiation. Adherence to these guidelines will also reduce the risk associated with having to repeat a study due to the acquisition of data not suitable for analysis within a specific BMD application module.

Warning: There may be practical patient-size limits for QCT PRO BMD studies. Such limits depend on anatomical site and CT model, and will typically be limited by either scan field-of-view (SFOV) or x-ray tube output of your CT scanner. See BMD module-specific documentation for further information.

Warning: When the user selects a reference database and uses the software to plot population bone mineral versus age, the user does so at their own risk.

Note: Addenda to the QCT PRO documentation, including the QCT PRO BMD application modules may be included with the device documentation. Please review any such addenda for up-to-date information regarding the installation and use of QCT PRO and the QCT PRO BMD application modules.

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Indications for Use

Intended Use

Warning: United States Federal Law restricts this device to the sale, distribution, and use by or on the order of a physician.

The QCT PRO BMD application modules are intended to provide estimates of bone mineral content (BMC) and/or bone mineral density (BMD) at central anatomical sites as defined below:

The *3D Spine* application module is intended to provide BMD estimates, expressed in grams/cm^3 of equivalent K_2HPO_4 density, for trabecular bone within any combination of one to three vertebral bodies in the spine in the range of T11 to L4, as medically necessary as determined by a physician.

The *2D Spine* application module is intended to provide BMD estimates, expressed in grams/cm^3 of equivalent K_2HPO_4 density, for trabecular bone within any combination of vertebral bodies in the spine in the range of T11 to L4, as medically necessary as determined by a physician.

The *CTXA Hip* application module is intended to provide estimates of bone mineral content (BMC), expressed in grams of equivalent K_2HPO_4 mass, and bone mineral density (BMD), expressed in grams/cm^2 of equivalent K_2HPO_4 density, within the proximal femur as medically necessary as determined by a physician.

Common applications of each of the QCT PRO BMD application modules include the detection of low bone mass conditions, and monitoring bone loss or gain over time as might result from response to a specific treatment regimen or from natural aging processes. Specific indications and contraindications for use are provided in the following sections.

Indications for Use

Clinical indications for central BMD estimates include:

- Conditions where low estrogen levels in women may increase bone resorption, including spontaneous menopause at any age, ovariectomy, secondary amenorrhea from hyperprolactinemia, excessive exercise or nutritional deficiency, or use of GnRH agonists for endometriosis or other medical indications.
- Conditions where the diagnosis of osteopenia is suggested by other means, such as x-ray.
- Conditions known to induce bone loss, such as prolonged immobilization, alcoholism, intestinal malabsorption, or treatment with calcium-wasting diuretics.
- Conditions where bone loss may be induced by treatment with or high endogenous levels of corticosteroids.
- Patients with primary hyperparathyroidism in whom surgery is being considered, to determine if there is low BMD.
- Monitoring the effectiveness of therapy for preventing bone loss for the above conditions. At the present time, there is no evidence that serial BMD measurements need to be made in women receiving adequate estrogen therapy.
- Other conditions deemed appropriate as determined by a physician.

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Clinical conditions where central BMD estimates may be useful, but in which care must be taken in interpretation of the results:

- Patients with chronic renal disease, especially those undergoing maintenance hemodialysis.
- Patients recently started on high-dose corticosteroid therapy.
- For the *3D Spine* and *2D Spine* modules, patients with severe lumbar scoliosis, where there may be significant regional variation in BMD within the vertebral body.
- For the *3D Spine* and *2D Spine* modules, patients with severe vertebral osteophytes, where there may be significant regional variation in BMD within the vertebral body.
- For the *CTXA Hip* module, patients with severe osteoporosis in which thinning of the proximal femur cortex may cause difficulties in the analysis.

Contraindications for Use

Clinical conditions where BMD estimates should not be used:

- Patients who have recently had another radiological procedure that includes the introduction of high density contrast material (barium, iodine, thorotrast, thorium) or radio-opaque catheters and tubes.
- Patients who are pregnant or may be pregnant.

Patient Conditions That May Affect Results

The following are examples of conditions that may influence the accuracy and/or precision of BMC and/or BMD estimates derived with the QCT PRO BMD application modules. It is recommended that the presence of such conditions be clearly noted in the patient report.

- Recent introduction into a patient of contrast materials, such as barium, iodine, thorotrast or thorium.
- External objects, such as clothing fasteners, jewelry, ECG leads or ostomy devices.
- Internal objects, such as Harrington rods, bone implants, surgical staples or other foreign bodies.

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QCT PRO Quality Assurance

The QCT PRO Quality Assurance (QA) module is an integral part of any QCT PRO installation. QCT PRO QA studies help verify the operational integrity of your QCT system, and provide information to other QCT PRO application modules, including the QCT PRO BMD application modules, about the operating characteristics of your CT scanner and how those characteristics may change with time. Operational instructions for the QA module are provided in the QA Application Module user's guide.

Information regarding the interpretation of QCT PRO QA reports is presented in this section. QA reports provide qualitative and quantitative summaries of the current and past performance your CT scanner as used with QCT PRO. In most cases the information contained in QA reports is primarily of interests to technologists or other persons involved with the daily operation of QCT PRO and QCT PRO application modules. However, the QA report also provides information that might be of use to a clinician in some circumstances.

QA Reports

QA studies are acquired under idealized circumstances relative to patient studies. Phantoms used for QA studies have known attenuation properties and consistent geometries. This simplifies the interpretation of QA study results, and allows inferences to be made regarding the operational capabilities of your QCT PRO system when used with patients. Because of the idealized circumstances associated with QA studies, it is generally best to interpret inferences regarding the capabilities of your system with patients as "best case" scenarios. That is, all things neglected or missing from QA studies, such as patient motion, will only make things worse.

QA reports provide information relevant to several operational issues associated with QCT PRO when used with your CT scanner, and CT calibration and QA phantoms. First, QA studies are used to derive calibration factors that are used by QCT PRO BMD application modules to normalize derived results for variations in operational characteristics of CT scanners. Normalization of derived BMD results is intended to compensate for variations in the operational characteristics of your CT scanner and phantoms relative to the performance of the equipment used to acquire measurements from a reference population. Comparing patient-specific BMD measurements to a reference population measurement is a common method used by clinicians when interpreting patient BMD measurements. Second, QA studies provide an estimate of the precision with which a hypothetical QCT BMD measurement can be made with your system. The precision estimate shown on QA reports applies only to the hypothetical scenario, and this scenario is probably different than the one used for patient studies analyzed with a QCT PRO BMD application module. However, precision estimates for the hypothetical case provide a basis for comparing the relative capabilities of different systems and it provides a mechanism for estimating patient-specific exposure requirements on different CT scanners. And third, QA studies are used to monitor the performance on your system (including CT scanner and phantoms). Performance changes may be indicative of problems that should be rectified prior to using or continuing to use your QCT PRO system for patient studies.

Information regarding the content and interpretation of information provided on QCT PRO QA reports follows.

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Scanner Information

QA results are indexed in the QCT PRO QA database table by CT scanner. CT scanners are identified by their make, model and ID as reported in CT image file headers. These identifiers are shown on QA reports.

Technique

The following QA study-specific technique parameters are shown on QA reports:

- KVp
- Table Height
- Scanned Field of View (SFOV)
- Exposure (mAs)
- Slice Thickness

Of the above parameters, the first three are considered important for calibration purposes and are used to index the QA information in the QA database table. Thus, if a QCT PRO BMD application module requests QA information for calibration purposes, it does so by requesting information for a particular scanner when used at particular kVp, table height (±5mm) and SFOV settings. Exposure is important when applying QA study results to estimating patient exposure requirements for a particular type of QCT PRO application module study. Slice thickness is reported for informational purposes only.

Some CT scanners do not include all of the technique parameters listed above in their file headers, so the values displayed may not reflect the actual technique used. In such cases, QCT PRO cannot verify that consistent parameters were used between QA studies used for calibration purposes and patient studies. QCT PRO application modules may still be used in these situations, but the burden of verifying consistent technique falls to a greater extent on the technologist acquiring the CT study data.

Qualitative Results

Six qualitative tests are performed during a QA study analysis. The QA report summarizes the result of each of these tests. Typically the status of all six tests should be reported as "OK".

If the status of a test is not reported as "OK", it will be reported as "CHECK". If a test status is reported as "CHECK", then possible causes for this status should be sought if this status is abnormal for your system. If it has been determined that a status of "CHECK" for a particular test is normal for your system, then a "CHECK" status should be ignored for the associated test. This situation is not common, but may occur, especially with some older CT scanners.

The six qualitative checks are summarized below:

A minimum of 4 QA images should be included to ensure an accurate QA analysis. More images improve the sensitivity of the QA checks. The recommended number of images in a QA study is 7-10. This number of images appears to provide good sensitivity, while not requiring excessive time or data handling efforts.

If any of the QA images produce results that are statistically inconsistent with the other measurements in a QA data set, then the QA report will show a status of "CHECK" for the "Absence of Outliers in QA Data" test. A status of "CHECK" often indicates the presence of excessive streaking or shading or other abnormal image characteristics in one or more images acquired in a QA data set. A "CHECK" status

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may also occur if a QA axial image extends just beyond the edge of the QA phantom. Issues such as contrast agent on the patient table or improper phantom positioning can cause unwanted image artifacts. Problematic images should be excluded from the QA analysis.

QCT PRO BMD application modules use a Field Uniformity Correction (FUC) value to normalize patient results. The precision of the FUC value is estimated during the analysis of a QA data set. If the precision is worse than 1%, then this test will be flagged as "CHECK". This normally will not occur with a good-quality set of QA images. Image quality problems or insufficient mAs are common causes for out-of-spec FUC precision estimates, as are conditions mentioned previously that may lead to outliers.

The precision of the slope and intercept of the CT calibration phantom data is calculated from a QA data set. If the precision of these parameters leads to a precision worse than 1.5 mg/cm^3 at a BMD value of 100 mg/cc for the hypothetical measurement case, then the status of this test is flagged as "CHECK". Image quality problems or inappropriate mAs are common causes for out-of-spec CT calibration parameters. Using a higher kVp setting (e.g., 120-140 kVp relative to 80-100 kVp) may alleviate calibration precision issues on some CT scanners.

The precision of a hypothetical ROI measurement due to variations in pixel values within the ROI is estimated from QA data sets. If this value is worse than 1.5 mg/cm^3, then this test status is set to "CHECK". Image quality problems or inappropriate mAs are common causes for out-of-spec ROI precision estimates. Using a higher kVp setting (e.g., 120-140 kVp relative to 80-100 kVp) may alleviate measurement precision issues on some CT scanners.

The theoretical limiting precision for a hypothetical ROI measurement, taking into account precision loss due to system calibration factors, CT calibration phantom data fits (slope and intercept), and ROI noise at a BMD of 100 mg/cm3 is calculated based on QA study data. If this value is worse than 3 mg/cm3, then the status of this test is set to "CHECK." A "CHECK" status for this test is generally accompanied by a "CHECK" condition with one or more of the precision checks documented above. A theoretical limiting precision greater than 3 mg/cm^3 for the overall hypothetical BMD measurement may indicate that your QCT PRO system (including CT scanner) will deliver poorer precision results than might be achieved on other CT systems. This condition is uncommon, but has been seen on some older CT scanners with relatively unstable, low output, x-ray tubes. While QCT PRO BMD application modules may still be used under these circumstances, the relatively poorer precision is likely to compromise the sensitivity of patient results.

Quantitative Results

The quantitative information that forms the basis for the qualitative checks discussed above is shown on QA reports. The quantitative results presented are described below.

FUC (Field Uniformity Correction)

The FUC value is the factor used by QCT PRO BMD application modules to normalize patient measurements for reference data comparisons. Raw bone mass measurements are multiplied by an FUC value to compensate for scanner and phantom performance variations. The mean and standard deviation of the estimated FUC value is reported. The FUC value is commonly in the range of 0.98 to 1.05; although, slightly larger or smaller values have been seen and are normal.

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QCT Calibration

CT image pixel values are converted to bone mass estimates in QCT PRO BMD application modules by means of a QCT calibration line characterized by three parameters: slope, intercept, and correlation coefficient (R). The mean values are given for each of these parameters, along with the standard deviation of the slope and intercept measures. The intercept will typically have a value between about 990 and 1030, while the slope is commonly between about 1.25 and 1.75. However, values outside these ranges may be observed under normal conditions. The value of R is generally negative, indicating that if a new calibration measurement was made, then it is more likely that the slope and intercept will change in opposite directions (e.g., if the slope is greater in the second measurement than in the first measurement, then it is more likely that the intercept will be less in the second measurement than in the first measurement. Note, R is NOT the correlation coefficient between the known and estimated mineral content of the calibration phantom ROIs. This latter correlation coefficient is usually greater than 0.99.

Precision Estimates

Estimates of the theoretical limiting precision for hypothetical BMD measurements at 50, 100, and 200 mg/cm^3 are given in the table, along with estimates of the relative contributions of precision loss due to uncertainties in the FUC value, the QCT calibration line, and noise in ROIs. In general, these estimates are not direct measurements of precision that you will obtain using a particular QCT PRO BMD application module with patient data. However, these measurements do provide insight into the relative contributions of basic sources of error that limit precision of patient measurements. Inspection of the relative contributions can also help isolate possible problems with your CT calibration phantom, QA phantom or incompatibilities with the QCT PRO software.

Serial Monitor Results

Two types of QA studies are defined: "Characterization" and "Monitor" studies. These two types of QA studies are essentially identical except for their interpretation and subsequent usage. These differences are described below.

FUC values returned to QCT PRO BMD application modules are obtained from the most recent QA characterization study using the same critical technique parameters as were used for a particular patient study. As indicated previously, the critical parameters are CT scanner, kVp, table height and SFOV. QA characterization studies are intended to be performed when first installing a QCT PRO system, when any significant upgrade of your overall system components is made (e.g., new x-ray tube or new phantoms or a new CT scanner), or when the operational performance of your overall system has changed significantly since your last QA characterization study. In most cases, events leading to the need for a new QA characterization study will be infrequent. Only providing FUC values to QCT PRO BMD application modules based on results from QA characterization studies reduces the impact of FUC value fluctuations on the precision of patient-specific BMD estimates by holding the FUC value constant in time intervals between QA characterization studies.

FUC values obtained from QA "monitor" studies are used to detect significant changes in the operational performance of your overall system. Weekly QA monitor studies are recommended, as opposed to as-needed QA characterization studies. Routine QA monitor studies provide evidence of the operational integrity of your QCT PRO BMD system, including phantoms and CT scanner, as well as indications of significant performance shifts that can be used to determine the need for a new QA characterization study.

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Results of serial QA study comparisons are summarized following the quantitative results. These results give an indication of how your QCT system is performing over time. The mean FUC value from the most recent "characterization" study is shown along with the standard deviation of this measurement, and the date of the characterization exam. A table of monitor study results done at various times is also given shown in the form of mean BMD and the standard deviation for the "spine" region of the QA phantom for each monitor study shown. The nominal BMD value should be 200 mg/cm^3, but normal imprecision in the measurement technique will lead to scatter in the measured values. The results are also shown in a graphical form that includes "95% confidence interval" error bars and a "95% confidence interval" band that represents the 95% confidence interval for the retrieved characterization study. Qualitatively, if a monitor measurement, including its associated error bar, falls completely outside of the 95% confidence interval for the retrieved characterization study, then there is a very good chance that the performance of your QCT PRO BMD system has changed significantly (in a statistical sense) since the last characterization. Monitor measurements that fall outside of a quantitatively estimated 95% confidence interval are flagged on the report.

The use of a 95% confidence interval for serial comparison test implies that, on average, 1 out of 20 QA monitor studies will by chance fail this test. When you see a monitor point fall outside the 95% confidence interval, it is advised that you repeat the QA study to see if the second QA study also fails this test. The probability of observing two sequential failures with no (true) significant performance change (i.e., a false positive) is about 1 in 400.

Two common scenarios resulting in QA results falling outside the 95% confidence interval include: (1) a sudden shift in the performance of the scanner, where the QA results have been stable but all of a sudden fall outside the limits, and (2) a slow drift, where the serial QA results will show a slow trend upwards or downwards within the yellow band, eventually falling outside the limits. The former case tends to be indicative of a sudden change in the CT scanner characteristics as might occur with some CT scanner software upgrades or with the installation of a new x-ray tube. The latter case of a slow performance drift is commonly seen with normal x-ray tube aging. Assuming no technical reasons can be found for excluding a QA result based on problems with acquired QA image data, and assuming the operation of the system is stable as evidenced by repeated QA studies giving similar results, then a new QA characterization study should be performed prior to new patient studies to derive a new FUC value to be used in normalizing subsequent patient results.

QA Summary

The QA summary provides a very quick synopsis of the result of the QA study. The possible summary conditions are "PASS", "FAIL" and "EQUIVOCAL".

"PASS" means that none of the QA tests performed gave a result indicative that some problem might exist or that some condition should be verified prior to using your QCT PRO system for patient studies. This is the typical QA summary result.

"FAIL" implies one of two things: (1) a condition was detected that should be addressed prior to performing additional patient studies, or (2) insufficient data was available to complete all of the QA tests. The former case typically either indicates the presence of a technical problem with your phantoms, CT scanner or QA data acquisition that should be resolved, or that a new characterization study should be performed because the CT scanner performance has drifted significantly since it was last characterized via QA. The latter case results from having too few images to accurately perform all of the statistical tests used in the analysis of QA data. This problem is easily resolved by acquiring a new set of QA images with a minimum of 4 good images.

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"EQUIVOCAL" results when any of the conditions for the current exam results in a status of "CHECK" rather than "OK". It is possible that your QCT system will perform in such a way that the QA summary is normally "EQUIVOCAL". This is not common, but may occur with some older CT scanners. If your QCT system normally returns a QA summary of "OK", then a summary of "EQUIVOCAL" may indicate the presence of an abnormal condition that might impact the accuracy and/or precision of patient results.

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QCT PRO Bone Densitometry Modules

Application modules for estimating bone mineral density (BMD) in the hip and in the spine are currently available. BMD estimates for the hip and spine are recognized by numerous bodies within the medical field as providing the most accurate and precise measurements for detecting low bone mass conditions, such as osteopenia or osteoporosis, and for tracking bone mass changes over time.

QCT PRO BMD application modules use quantitative computed tomography (QCT) techniques to derive BMD estimates from CT images. QCT techniques for estimating BMD were developed in the 1970s[1]. The outstanding performance characteristics of QCT have been documented in numerous academic publications since its development. Studies have repeatedly and consistently demonstrated that the QCT BMD methodology provides BMD measurement accuracy and precision meeting or exceeding the capabilities of alternative methods, such as dual energy x-ray absorptiometry (DXA), for estimating BMD in the hip and/or spine[2,3].

The QCT PRO BMD application modules simplify the routine clinical utilization of QCT BMD measurement techniques by automating and otherwise shielding the user from many technical aspects associated with deriving BMD estimates from CT data, and searching for indications of conditions that might lead to degraded measurement quality.

QCT PRO Spine Bone Density Reports

QCT PRO spine BMD reports include basic examination results, comparisons, if prior data is available, to previous QCT PRO spine BMD exams, and comparisons of examination results to young normal and age-matched reference populations when such information is available. This information is intended to be used by the patient's referring physician or other medical care provider for two purposes: diagnosis of low bone density and monitoring the bone density of a patient with time.

QCT PRO spine BMD modules ship with reference data for both males and females obtained from studies performed at the University of California—San Francisco (UCSF). QCT PRO supports the installation of user-defined reference data so that reference data from other studies may be used at the user's discretion. It is the responsibility of the interpreting physician to determine the applicability of any set of reference data when interpreting patient results.

The following sections provide descriptions of the UCSF spine reference data and the contents of QCT PRO spine BMD reports.

UCSF Reference Data

WARNING: *When the user selects a reference database and uses the software to plot population bone mineral versus age, the user does so at their own risk.*

The US (UCSF) Normal Database for Females and Males

The original UCSF database for normal QCT BMD versus age was published by researchers at the University of California[4], and this database has been updated for use in QCT PRO by incorporating more recent published data from the same research groups[5,6]. Pediatric data using the same calibration phantom have also been incorporated[7,8]. Approximately 800 females and 300 males are included in these databases.

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All these data were acquired using General Electric CT scanners (Models 7800, 8800, and 9800) and the UCSF-design K_2HPO_4 liquid CT Mineral Calibration Phantom. Data were acquired at either 80 kVp or 140 kVp. The data at 140 kVp were normalized to 80 kVp using the relationship BMD(80)=0.94*BMD(140)+10.7[9]. At a young normal BMD, this normalization is less than 1 mg/cm^3, and at an osteoporotic level it is less than 4 mg/cm^3. QCT PRO BMD software does not normalize patient BMD values by kVp because the effect is very small when using the K_2HPO_4 calibration phantom.

The definition of a "normal" subject for the purposes of inclusion in this database is:

Age: 1–80 years; US Caucasian or Asian ethnicity; ambulatory; no history of disease or medication use known to affect bone metabolism (diabetes, severe arthritis, hyperthyroidism, hyperparathyroidism, Crohn's disease, intestinal malabsorption, clinical obesity, kidney stones, history of amenorrhea or prolonged immobilization, chronic alcohol or drug abuse; use of corticosteroids, thiazide diuretics, or other medications known to affect bone). Women who have gone through a normal menopause and are taking hormone, calcium or vitamin D therapy, unless under 40 years old, are included. Men or women with a history or current use of fluoride or bisphosphonates are excluded. Pediatric inpatients admitted within the prior 3 days for head trauma only are included; no other hospital patients have been included.

Clinical Report Content

Patient Information

The top-left section of the BMD spine report shows pertinent patient information. Of particular note is the "Comments" line. Usage of the "Comments" line will vary and is at the discretion of the site performing the QCT spine exam. This field is generally intended to be completed by the technologist performing the study, and may include information about why the study was done and/or observations noted during the exam. For example, the presence of osteophytes or aortic calcification might be noted during data analysis. Such structures will tend to increase DXA-derived spine BMD estimates relative to QCT spine BMD estimates that exclude such structures, so this information might be helpful when comparing a QCT spine measurement to a past or future DXA spine measurement. Abnormally high densities in a single vertebra might also be noted, and can signify a vertebra that is about to compress, even though it does not appear compressed on the CT lateral localizer. Any vertebrae noted to be compressed on the CT localizer might also be identified.

Analysis Results

The patient's results for individual vertebrae and the average trabecular bone mineral density are given at the top of this section. The BMD results are given in terms of mg/cm^3 of equivalent aqueous potassium phosphate (K_2HPO_4) density. T-scores and Z-scores are also reported based on the average BMD in comparison to the selected, gender-matched, reference data (UCSF by default). The T-score is reported as the number of standard deviations (SD) above or below the expected BMD at age 30 for the selected reference population. The Z-score is the number of SD the patient BMD value is above or below the mean value for the selected reference population at the same age as the patient. The expected age-matched BMD and SD from the selected reference data are shown on the report in the row labeled "Age Matched Normal". A Z-score will not be calculated if the selected reference data does not include data for the patient's age. The equations defining T-score and Z-score are shown below

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$$T-Score=\frac{BMD_{Patient}-BMD_{Age30}}{SD_{Age30}}$$

$$Z-Score=\frac{BMD_{Patient}-BMD_{AgeMatched}}{SD_{AgeMatched}}$$

Comparison with Previous Examinations

If the patient has been in for previous QCT BMD exams, the date, average BMD and BMD change relative to the most recent BMD exam will be shown on the report for each previous exam. In addition, an estimate of the average BMD change per year will be shown. Serial comparisons are based only on vertebrae in common across the serial exams, and the vertebrae used for the serial comparisons are shown on the report. It is necessary to consult reports from previous examinations for data, if any, regarding vertebrae not used in the serial comparisons.

Graphical Presentation of Patient Results

Patient results are shown graphically on the QCT reports as described below.

The patient BMD measurements are shown graphically on a chart that also illustrates the gender-matched reference data selected for the study. The reference data is shown as average BMD as a function of age, and optionally includes bands illustrating the area within 1 and 2 standard deviations of the average. A band is also included on the graph that shows the level of an empirically-determined "fracture threshold" level above which vertebral deformities were not seen in the clinical population[5]. This level is approximately at a T-score of –2.5 for both women and men.

If available, gender and age matched fracture prevalence data is shown. Fracture prevalence data is currently available with the UCSF reference data for females in the age range of 41-60 and 61-80. The fracture prevalence data is presented as a bar graph, with each bar representing the percentage of patients seen, as a function of BMD range, during the collection of reference data that presented indications of vertebral deformity or fracture at that time[5]. The bar with the BMD range containing the patient's measurement is highlighted.

Serial exam information is presented graphically as average BMD as a function of date of examination. The patient serial exam information plotted is the same as that tabulated on the exam report. The serial graph also shows 90% and 95% confidence intervals that may be used to judge the significance of the difference between a pair of BMD measurements. Confidence intervals are based on the estimated precision of the BMD measurements for the site. A conservative precision estimate of 3.0 mg/cm^3 is used by default for sites that do not wish to make measurements to estimate their site-specific technique precision. The precision used for confidence interval estimation is shown on the report.

Interpreting QCT PRO Spine Studies

This section presents information about various factors that should be considered when interpreting QCT PRO spine BMD measurements, as well as general guidelines for using these BMD estimates as part of the diagnosis of low bone-mass conditions and for monitoring the evolution of such conditions.

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CT Calibration Reference Standard

QCT PRO reports BMD estimates in terms of equivalent aqueous K_2HPO_4 density. K_2HPO_4 has almost identical x-ray absorption properties as calcium hydroxyapatite/amorphous calcium phosphate[10]. In addition, aqueous K_2HPO_4 has been shown to provide a more accurate representation of the composition of the trabecular bone mixture (bone mineral, collagen, marrow) than hydroxyapatite/plastic solid mixtures which have also been used as calibration standards[11].

QCT Methodologies and Selection of Vertebrae for Analysis

Normally, two to four vertebrae are scanned and the values averaged for QCT spine BMD estimates. Four vertebrae are commonly scanned when using the conventional "single-slice" QCT method. This method involves gantry angulation and the acquisition of a single, thick CT slice through each of a set of vertebrae. Two or three vertebrae are more commonly scanned when using the 3D QCT method. This method involves no gantry angulation, and the acquisition of a multiple, evenly spaced, narrow CT images through a set of vertebrae for subsequent 3D analysis. Measurement precision using four vertebrae and the conventional QCT method is comparable to measurement precision using two vertebrae and the 3D QCT method. QCT PRO includes software modules for supporting both of these QCT methods.

QCT spine BMD exams are usually made using multiple vertebrae from T11 to L4. Ideally, a set of contiguous vertebrae will be used. T12 to L3 are typically used with the conventional QCT method, while L1 and L2 are commonly used with the 3D method. Notations as to why an atypical set of vertebrae were scanned for a particular patient may be helpful when interpreting an exam.

Generally, BMD of adjacent vertebrae are comparable, with a slow decrease in BMD values going cephalad to caudad in the spine[12]. If the value for one vertebra is significantly higher or lower than adjacent vertebrae, the images should be evaluated to make sure a partially compressed vertebra, bone island or hemangioma is not present. If an anomaly is present, results from the affected vertebra(e) should be excluded from the BMD analysis.

QCT T-Scores

The T-score computed by QCT PRO is referenced to age 30. For DXA, the T-score is defined as the number of standard deviations away from "peak bone mass." However, peak bone mass as measured by QCT (or by iliac crest bone biopsy Trabecular Bone Volume) occurs at an earlier age than as measured by other techniques such as DXA, SPA/SXA or radiogrammetry. The physiologic reason for this is that trabecular bone, being high turnover bone, "matures" more rapidly than the cortical bone of the radius or the mixed cortical/trabecular bone measured by DXA in the spine or hip. The peak bone mass as measured by QCT actually occurs immediately after puberty[8], but then drops slightly by age 25-30,while BMD measured by DXA or SPA increases to about age 30 as the compact bone formed in adolescence continues to mineralize to its adult density.

As a general rule, the T-score of an older patient as measured by QCT will be lower (more negative) than the T-score measured by DXA. This is due to two factors. First, the range of QCT values is larger than for DXA values, when compared to young normals. QCT BMD measures trabecular bone only, and trabecular BMDs extend from about 240 mg/cm^3 to 0 mg/cm^3. There are in fact patients with no trabecular bone left in the spine. Both trabecular and cortical bone are measured with DXA. DXA spinal BMD values typically range from 1.4 gm/cm^2 to 0.5 gm/cm^2. Because patients lose trabecular bone earlier, and at a faster rate than cortical bone, QCT T-scores tend to be less than DXA T-scores. The second factor has to do with extraosseous mineral in the older population. QCT measurements are not

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influenced by osteophytes, ligamentous calcification or aortic calcification, but these mineralizations can falsely elevate spinal BMD measurements by DXA[13].

Diagnosis of Osteoporosis

Osteoporosis is a condition characterized by low bone mass, microarchitectural deterioration of bone leading to bone fragility, and consequent susceptibility to fracture. Various operational definitions of osteoporosis have been proposed and used based on T-scores derived from BMD measurements. Guidelines for the diagnosis and treatment of osteoporosis have been published and are periodically reviewed by several professional organizations, including the National Osteoporosis Foundation, the International Osteoporosis Foundation, the International Society for Clinical Densitometry, and an international committee of the World Health Organization[14-17]. The diagnosis and treatment of osteoporosis remains an active ground for new research.

Because of the dynamic nature of our knowledge of osteoporosis, QCT PRO does not provide a diagnosis or other type of patient classification or labeling on QCT spine BMD reports. Interpretation of QCT spine BMD results is the responsibility of a physician, and may involve consideration of factors outside the context of a BMD measurement.

The information in the following paragraphs is intended to provide basic information regarding the diagnosis of osteoporosis from T-scores. This information is provided because of the common clinical usage of this approach today, and to provide the reader with some insight regarding how the interpretation of QCT-derived T-scores may differ from DXA-derived T-scores. Note that the current (2003) position of the International Osteoporosis Foundation/National Osteoporosis Foundation/World Health Organization committee on osteoporosis is that a T-score of -2.5 or lower should be used to make a diagnosis of osteoporosis ONLY for measurements of the proximal femur, and that T-scores derived from BMD measurements at any other site in the body, including the spine, should not be used in this way[15].

The following definitions are frequently used in the diagnosis of osteoporosis from T-scores:

Osteoporosis: T-Score of –2.5 or lower

Osteopenia: T-Score between –1 and –2.5

Normal: T-Score greater than –1

As noted previously, QCT spine BMD measurements tend to result in lower T-scores than DXA spine BMD measurements due to the fact that QCT measures only trabecular bone. This implies that using the same T-score threshold for defining osteoporosis with QCT spine measurements as is used for DXA measurements is likely to result in a diagnosis of osteoporosis via QCT measurement before, up to ten years according to some studies, the same diagnosis would be made via DXA. Some researchers have advocated using a lower T-score threshold for the diagnosis of osteoporosis via QCT to better enforce concordance on the timing of the diagnosis for osteoporosis with QCT and DXA. A T-score threshold of –3.5 for the diagnosis of osteoporosis by QCT spine BMD has been proposed by several researchers[18]. However, use of such a threshold is an opinion expressed by researchers but not endorsed by any of the international organizations.

Patient Monitoring

Various clinical guidelines call for monitoring of BMD in a patient in several clinical situations. As with the diagnosis of osteoporosis, the reader is referred to publications from medical organizations for

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guidelines regarding current clinical practice. Representative examples of the application of patient BMD monitoring are provided below.

If a patient is diagnosed with low bone density, often they are treated and the bone density is measured again in 12-24 months. If the bone density is normal but the patient is at high risk of losing bone, such as women at menopause or asthma patients starting high-dose corticosteroids, repeat bone density measurements may be done yearly. Typical trabecular BMD losses measured by QCT are 8-10 mg/cm^3/yr in early menopausal women[19], 10-40 mg/cm^3/yr in women given GnRH treatment for endometriosis or after oophorectomy without estrogen replacement[20,21]. Bone gain after therapy depends on the patient and the therapy used, but is in the range 5-10 mg/cm^3/yr for estrogen, raloxifene or bisphosphonates, and significantly higher with parathyroid hormone or fluoride[22,23].

As a rule of thumb, a change in a pair of measurements of at least three times the measurement precision is likely to reflect a true, non-zero difference in the measurements at about the 95% confidence level. QCT BMD measurement precision of 3 mg/cm^3 or better is common. Measurement precisions of less than 1.0 mg/cm^3 have been reported for 3D QCT BMD measurements[18, 24]. Usage of an assumed measurement precision of 3.0 mg/cm^3 is recommended in the absence of site-specific clinical precision estimates. This implies that two BMD measurements must differ by at least 9 mg/cm^3 in order to conclude at the 95+% confidence level that such a difference is indicative of a true difference in BMD between the two measurements. A 9 mg/cm^3 BMD change in the context of the UCSF reference data implies a T-score difference of 0.4 or more between two measurements is likely indicative of a true BMD difference between two measurements.

Appropriate follow-up intervals for serial studies can be estimated given an estimate of the expected bone loss or gain for a patient, and a measured or assumed estimate of measurement precision for the site or sites providing BMD measurements. Yearly QCT BMD measurements have sufficient sensitivity for many clinical situations involving patient monitoring; although, aggressive therapy or expected rapid bone loss may indicate more frequent measurements.

CTXA Hip Bone Density Reports

CTXA Hip BMD reports include basic examination results, comparisons, if prior data is available, to previous CTXA hip BMD exams, and comparisons of examination results to young normal and age-matched reference populations when such information is available. This information is intended to be used by the patient's referring physician or other medical care provider for two purposes: diagnosis of low bone density and monitoring the bone density of a patient with time.

The CTXA Hip BMD module ships with reference data for females obtained from clinical studies sponsored by Mindways Software at a number of sites. QCT PRO supports the installation of user-defined reference data so that reference data from other studies may be used at the user's discretion. It is the responsibility of the interpreting physician to determine the applicability of any set of reference data when interpreting patient results.

The following sections provide descriptions of the CTXA Hip reference data and the contents of CTXA Hip BMD reports.

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CTXA Reference Data

WARNING: *When the user selects a reference database and uses the software to plot population bone mineral versus age, the user does so at their own risk.*

CTXA Hip reference data were derived from studies of approximately 300 US Caucasian females age 20-39 from sites distributed geographically across the US. Means and standard deviations for femoral neck, trochanter, intertrochanter and total hip regions of interest in the proximal femur are used as a reference against which to compare the patient's results. T-scores, % young normal mean, and Z-scores are calculated relative to these reference values.

Clinical Report Content

Patient Information

The top-left section of the CTXA Hip report shows pertinent patient information. Of particular note is the "Comments" line. Usage of the "Comments" line will vary and is at the discretion of the site performing the CTXA Hip exam. This field is generally intended to be completed by the technologist performing the study, and may include information about why the study was done and/or observations noted during the exam.

Analysis Results

Patient results for four ROIs commonly measured with DXA are reported on the CTXA clinical report. These regions are: (1) Femoral Neck, (2) Trochanter, (3) Intertrochanter, and (4) Total Hip. As with DXA, BMD measurements are reported in terms of bone mass per unit of bone projected area (i.e., area density). The BMD results are given in terms of g/cm^2 of equivalent aqueous potassium phosphate (K_2HPO_4) density. T-scores and percent BMD relative to the normal reference are reported for the all ROIs, and Z-scores are reported for the femoral neck and total hip ROIs. T-scores are reported as the number of standard deviations (SD) above or below the expected BMDs for the respective ROIs based on young normal reference measurements for the selected reference population. The Z-scores are the number of SD the patient BMD value is above or below the mean value for the respective ROIs for the selected reference population at the same age as the patient. The expected age-matched BMD and SD from the selected reference data are shown on the report under the "Reference Data" label. Z-scores will not be calculated if the selected reference data does not include data for the patient's age. The equations defining T-score, %Nrm, and Z-score are shown below

$$T-Score=\frac{BMD_{Patient}-BMD_{YoungNormal}}{SD_{YoungNormal}}$$

$$\%Nrm=100\times\frac{BMD_{Patient}}{BMD_{YoungNormal}}$$

$$Z-Score=\frac{BMD_{Patient}-BMD_{AgeMatched}}{SD_{AgeMatched}}$$

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Comparison with Previous Examinations

If the patient has been in for previous CTXA Hip exams, the date, average BMD for the femoral neck and total hip ROIs, and BMD change relative to the most recent BMD exam for the femoral neck and total hip ROIs will be shown on the report for each previous exam.

Graphical Presentation of Patient Results

Patient results are shown graphically on the CTXA Hip reports as described below.

The patient BMD measurements are shown graphically on a chart that also illustrates the reference data selected for the study. Two such graphs appear on the report. One graph presents femoral neck data and the other shows total hip data. Reference data is shown as average BMD as a function of age, and optionally includes bands illustrating the area within 1 and 2 standard deviations of the average. These graphs also include lines showing T-score thresholds of –1.0 and –2.5.

Serial exam information is presented graphically as average total hip BMD as a function of date of examination. The patient serial exam information plotted is the same as that tabulated on the exam report. The serial graph also shows 90% and 95% confidence intervals that may be used to judge the significance of the difference between a pair of BMD measurements. Confidence intervals are based on the estimated precision of the BMD measurements for the site. A precision estimate of 0.012 g/cm^2 is used by default for sites that do not wish to make measurements to estimate their site-specific technique precision. The precision used for confidence interval estimation is shown on the report.

Interpreting CTXA Hip Studies

This section presents information about various factors that should be considered when interpreting CTXA Hip BMD measurements, as well as general guidelines for using these BMD estimates as part of the diagnosis of low bone-mass conditions and for monitoring the evolution of such conditions.

CT Calibration Reference Standard

QCT PRO reports BMD estimates in terms of equivalent aqueous K_2HPO_4 density. K_2HPO_4 has almost identical x-ray absorption properties as calcium hydroxyapatite/amorphous calcium phosphate[10]. In addition, aqueous K_2HPO_4 has been shown to provide a more accurate representation of the composition of the trabecular bone mixture (bone mineral, collagen, marrow) than hydroxyapatite/plastic solid mixtures which have also been used as calibration standards[11].

QCT Methodology for CTXA

CTXA is intrinsically a 3D QCT technique. 3D QCT data sets are composed of a series of evenly spaced, without gantry angulation, axial CT images covering the anatomical region including the proximal femur. These data are used to construct a 3D representation of the scanned region within the CTXA software. CTXA Hip includes methods for isolating the hip from surrounding soft tissue in the acquired 3D data set. Identification of pixels within the hip involves consideration of local BMD and anatomy. BMD estimates are derived by referencing CT values in the data set to the CT calibration phantom scanned simultaneously with a patient.

The 3D data set containing the hip isolated from surrounding soft tissue is used to generate a DXA-like bone projection image. This projection image is analyzed in a manner substantially the same as DXA-

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hip images are analyzed. In particular, BMD is measured in units of bone mass per projected area in four regions of interest: (1) femoral neck, (2) trochanter, (3) intertrochanter, and (4) total hip. Thus, from a user's perspective, CTXA Hip generates images substantially similar to DXA-hip images, the CTXA Hip images are analyzed in essentially the same manner as DXA-hip images, and the basic CTXA Hip exam results are intended to be interpreted in the same manner as DXA-hip exam results.

While CTXA Hip results share much in common with DXA-hip results, it should be remembered that CTXA Hip is a 3D QCT technique. Thus factors that influence DXA results in subtle ways may not influence CTXA Hip results in the same manner. For example, significant amounts of overlying fat may bias DXA measurements. Fat influences the dual-energy tissue decomposition method used by DXA to separate attenuation due to bone from that due to soft tissue. CTXA uses an anatomically-driven method to separate bone and soft tissue, and as such, is not influenced in the same manner as DXA by overlying fatty tissue.

The intrinsic 3D QCT character of CTXA also leads to the availability of information unattainable by 2D DXA methods. For example, CTXA Hip subclassifies bone as being either "cortical" bone or "trabecular" bone based on local, volumetric BMD and a simple threshold scheme for each bone pixel in the underlying 3D CTXA data. These measurements should be considered experimental since the clinical significance of these measurements has not yet been established. Experimental CTXA Hip measurements are not reported on the standard CTXA Hip clinical report. They are only reported on the CTXA Hip technical report.

CTXA Hip T-Scores

CTXA Hip T-scores are referenced to results obtained for a reference population covering the age range of 20 to 39 years. This reference is consistent with that used when interpreting DXA measurements in the context of NHANES reference data.

Diagnosis of Osteoporosis

Osteoporosis is a condition characterized by low bone mass, microarchitectural deterioration of bone leading to bone fragility, and consequent susceptibility to fracture. Various operational definitions of osteoporosis have been proposed and used based on T-scores derived from BMD measurements. Guidelines for the diagnosis and treatment of osteoporosis have been published and are periodically reviewed by several professional organizations, including the National Osteoporosis Foundation, the International Osteoporosis Foundation, the International Society for Clinical Densitometry, and an international committee of the World Health Organization. The diagnosis and treatment of osteoporosis remains an active ground for new research.

CTXA Hip exam results are intended to be interpreted in the same manner as DXA-hip exams. WHO criteria for interpreting DXA-hip exams are currently in clinical favor, and result in the classification of patients by reference to BMD measurements as follows:

Diagnosis	T-Score Range
Normal	T-Score > -1.0
Osteopenia	-2.5 T-Score -1.0
Osteoporosis	T-Score < -2.5

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The reference data graphs shown on CTXA Hip clinical reports include osteopenic and osteoporotic thresholds using WHO criteria.

While the WHO criteria provides a simple operational method for classifying patients, a more complete diagnosis and recommendation regarding therapeutic response may involve consideration of factors outside the context of a BMD measurement.

Patient Monitoring

Various clinical guidelines call for monitoring of BMD in a patient in several clinical situations. As with the diagnosis of osteoporosis, the reader is referred to publications from medical organizations for guidelines regarding current clinical practice. Representative examples of the application of patient BMD monitoring are provided below.

If a patient is diagnosed with low bone density, often they are treated and the bone density is measured again in 12-24 months. If the bone density is normal but the patient is at high risk of losing bone, such as women at menopause or asthma patients starting high-dose corticosteroids, repeat bone density measurements may be done yearly. Expected patient response and measurement precision should be considered when selecting a measurement interval for monitoring the efficacy of a particular treatment regimen.

As a rule of thumb, a change in a pair of measurements of at least three times the measurement precision is likely to reflect a true, non-zero difference in the measurements at about the 95% confidence level. By default, CTXA clinical reports are generated using an assumed measurement precision of 0.012 g/cm^2. This precision estimate is based on results derived from patient measurements. The estimated precision of CTXA Hip measurements based on phantom studies is 0.007 g/cm^2, or about 0.7% at a nominal density of 1 g/cm^2. Usage of an assumed measurement precision of 0.012 g/cm^2 is recommended in the absence of site-specific clinical precision estimates. This implies that two BMD measurements must differ by at least 0.036 g/cm^2 in order to conclude at the 95+% confidence level that such a difference is indicative of a true difference in BMD between the two measurements. A 0.036 g/cm^2 BMD change implies a T-score difference of 0.3 or more between two measurements is likely indicative of a true BMD difference between two measurements.

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Performance Specifications

Analysis Module	**2D-Spine**	**3D-Spine**	**CTXA-Hip**
Anatomical Region	Spine, T11-L4	Spine, T11-L4	Proximal Femur
BMD Regions of Interest	Vertebral Trabecular Bone	Vertebral Trabecular Bone	Femoral Neck Trochanter Intertrochanter Total Hip Wards- Triangle
BMD Calibration Standard	Aqueous K_2HPO_4 Mindways Model 3 Solid Phantom with aqueous K_2HPO_4 cross-calibration		
Units of Reported Densities	Equivalent K2HPO4 density mg/cm^3	Equivalent K2HPO4 density mg/cm^3	Equivalent K2HPO4 density g/cm^2 (area density) mg/cm^3 (volume density)
In Vitro BMD Precision	Up to 1%	Up to 1%	Area Density: 0.007 g/cm^2 (0.7% at nominal density of 1.0 g/cm^2) Volume Density: 1.4 mg/cm^3 (0.7% at nominal density of 200 mg/cm^3)
In Vivo BMD Precision	Up to 1%	Up to 1%	Femoral Neck 0.012 g/cm^2 (1.2% at nominal density of 1.0 g/cm^2) Total Hip 0.011 g/cm^2 (1.1% at nominal density of 1.0 g/cm^2)
Typical Radiation Dose	0.10 mSv	0.12 mSv	0.25mSv

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Alternative Reference Data Sets

While the QCT PRO spine and CTXA hip application modules are distributed with reference data, clinicians are not required to use or restricted to using the reference data distributed with these modules. A user may wish to use reference data not published or distributed by Mindways, including their own reference data. In all cases, it is ultimately the user's responsibility to determine the suitability of any reference data they use when interpreting a patient's BMD measurements. This section provides brief guidelines for the usage of alternative reference data sets with QCT PRO application modules.

Guidelines for Developing a Normal Database

If the user wishes to establish their own normal database, the following guidelines should be used to ensure that the database accurately represents the normal population:

- The quality control and calibration procedures contained in this manual should be implemented rigorously.
- The variability for a QCT BMD value should be established for the user's site, after implementation of the quality control program and appropriate training of all individuals who are going to be doing the QCT BMD procedure. The variability should be determined taking into account:
- Short term variability of the system in vitro (scanning the QA phantom multiple times to determine machine variation under optimal conditions).
- Intraoperator variability for in vivo placement of the region of interest used for the BMD estimation.
- Interoperator variability for in vivo placement of the region of interest used for BMD estimation.
- A definition of "normal" for the reference population should be made, and adhered to rigorously when deciding if a subject should be included in the population. It is recommended that patients admitted to the hospital and having a CT scan for other purposes NOT be included in the definition of "normal."
- A reference database should include at least 50 subjects in each decade.

For a user-developed reference database, the site precision for the BMD estimate must be considered when comparing an individual patient's BMD value to the reference population.

Installing Alternative Reference Databases

Contact Mindways Software for assistance formatting and installing alterative reference data sets into the QCT PRO application module environment.

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Interpreting QCT Hip and Spine Reports

Proximal Femur BMD—WHO Criterion

Classification based on total hip or femoral neck T-score

- Interpret CTXA (QCT) Hip same as DXA Hip
- *Osteoporosis* (T-score < -2.5)
- *Osteopenia* (-2.5 ≤ T-score < -1.0)
- *Normal* (T-score ≥ -1.0)

Generally risk factors other than BMD should be taken into account in the diagnosis of osteoporosis or other low bone mass conditions.

Other Risk Factors

- Early menopause
- Long-term steroid use
- Family history
- Poor visual capacity
- Increase in body sway
- Low body weight (< 58 kg)
- Prior fracture after age 50
- Low gait speed
- Current cigarette smoking

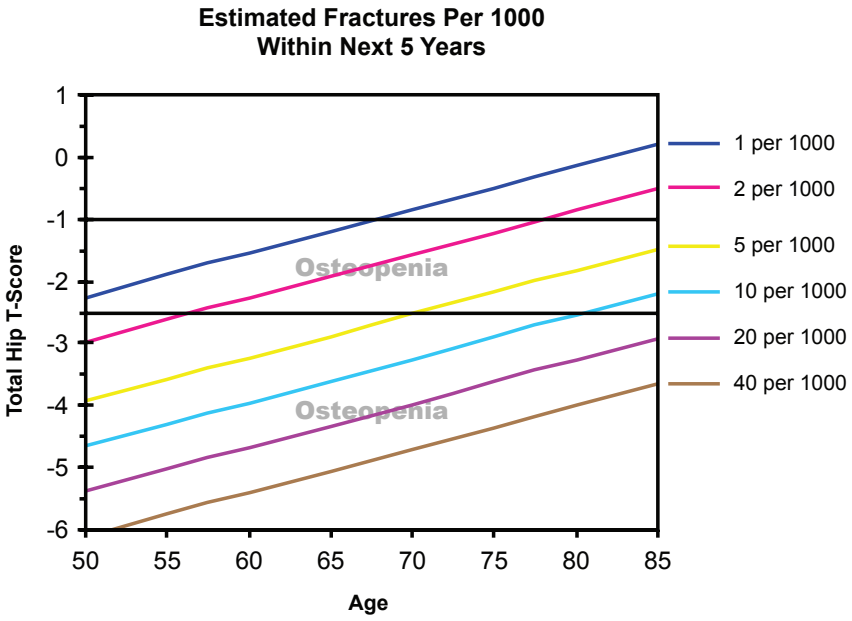
Patient Monitoring

For best sensitivity only compare:

- Measurements from the same device for a given patient
- BMD's directly (as opposed to T-scores)
- Results from the same anatomical site and ROI

Precision of CTXA Hip measurements:

- BMD precision 0.012 g/cm^2
- Change in BMD of 0.034 g/cm^2 significant at 95% confidence level



Spine BMD Who Criteria *Does Not Apply*

- QCT Spine BMD measures only trabecular bone
- QCT Spine does not measure extraosseous mineral
- Trabecular bone loss typically starts sooner than cortical bone loss
- Trabecular bone loss typically is faster than cortical bone loss
- T-score at the spine is typically less than the T-score at the hip

Incorrectly applying WHO osteoporosis criteria to the interpretation of QCT Spine T-scores results in overcalling osteoporosis relative to Hip BMD measurements.

Osteoporosis and Spine BMD

Use the following criteria results in patient classification that *approximately* matches hip-based classification:

- *Osteoporosis:* Spine BMD < 80 mg/cm^3
- *Osteopenia:* 80 mg/cm^3 <= Spine BMD < 120 mg/cm^3
- *Normal:* Spine BMD >= 120 mg/cm^3

Reporting based on BMD rather than T-score is recommended to reduce confusion and misapplication of WHO criteria.

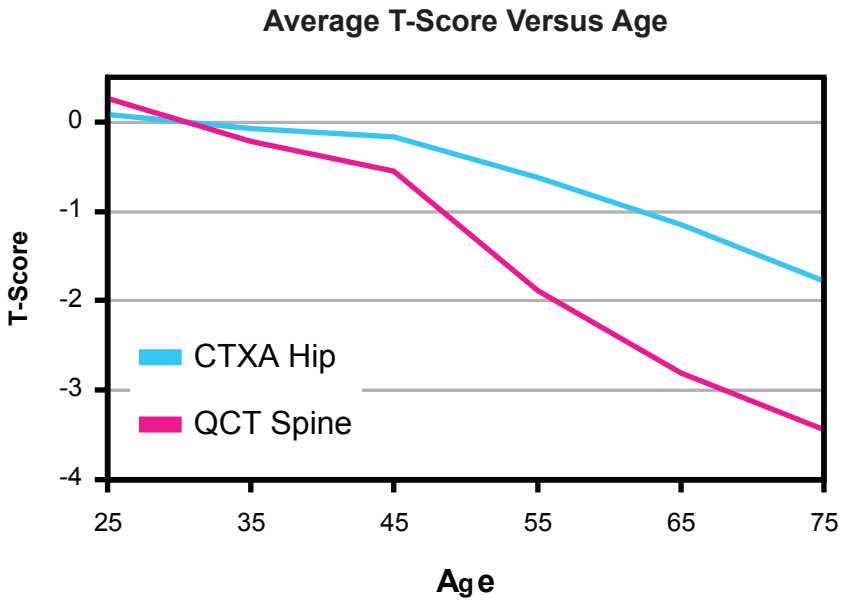
Patient Monitoring

For best sensitivity only compare:

- Measurements from the same device for a given patient
- BMD's directly (as opposed to T-scores)
- Results from the same anatomical site and ROI

Precision of QCT Spine measurements:

- BMD precision up to 1.0 mg/cm^3 for average BMD from two vertebra
- Change in BMD of 3.0 mg/cm^3 significant at about 95% confidence level
- Conservative estimated BMD precision of 3.0 mg/cm^3
- Conservative change in BMD of 8.5 mg/cm^3 significant at 95% confidence level



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