2 Bone Mineral Analysis

The Bone Mineral Analysis (BMA) application is designed to measure a patient’s bone density, helping the physician assess the patient's risk of osteoporosis. Osteoporosis is characterized by low bone mass and structural deterioration of bone tissue. The BMA application uses the patient's own muscle and fat tissues as internal references, instead of using an external phantom. This helps reduce reproducibility errors when later studies are used to track the patient’s bone density changes over time.

NOTICE

Before continuing, refer to the “Instructions for Use” that came with your scanner.

NOTICE

BMA results should not be used as the sole basis for clinical diagnosis.

The BMA application can process subsequent studies of the patient to determine the trending of the patient’s bone density. However, the same scan parameters must be used on subsequent exams to maintain accuracy.

NOTICE

There are two situations under which the bone density program might be applied to analyzing a patient's spine CT image: either the imaging was performed as (1) a dedicated bone mineral density (BMD) study or (2) as an adjunct to a lumbar spine procedure. The images used in the BMD calculations should be targeted so that the lumbar spine is centered and the retrospinal muscle and fat are included in the images.

CAUTION

Ensure proper selection of suitable vertebrae. In the case of follow-up examinations, previous studies have to be reviewed and the same vertebrae and ROIs (position and size) should be selected for scanning.

The CT values of the muscle and fat ROIs should be as close as possible to the respective values in the preceding measurements.

Please refer to the user documentation that came with the scanner (from which the images derived) for more information about scanning protocols, etc., before beginning the Bone Mineral Density (BMD) analysis.

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WARNING

When loading images into the application, all images which contain 16 bit data are converted into 12 bit images. (Therefore, when the rescale intercept equals -1000, Hounsfield Unit values above 3095 are displayed as 3095, and when the rescale intercept equals -1024, Hounsfield Unit values above 3071 are displayed as 3071.)

Load Multiple Studies in Application

To load multiple studies in the application:

1. Use the **Ctrl** key when selecting studies from the Directory list.
2. Select the application from the Applications menu.
3. Confirm the studies are from the same patient.

NOTICE

Depending on your Portal configuration, this application may not be available.

Indications for Use

The Bone Mineral Analysis (BMA) application is designed to measure bone density in one or multiple time points, helping to assess risk of osteoporosis and compare patient's to several reference populations.

The application supports users with the measurement of Bone Mineral Density (BMD) in one or multiple time points using an internal (phantom-less) calibration method on non-contrast CT imaging.

CAUTION

The use of contrast CT images may bias the results.

Guidelines for Defining Osteoporosis

The Bone Mineral Density Results table displays the list of measured vertebrae, the vertebral average BMD score and indicates the QCT Trabecular Spine BMD range with its equivalent WHO diagnostic category.

Bone Mineral Density Results				
Date	Measured Vertebrae	Average BMD (mg/cm³)	QCT Trabecular Spine BMD ...	Equivalent WHO diagnostic cate...
12 Nov 2007	T12, L1	151.7(mg/cm³)	BMD>120mg/cm³	Normal

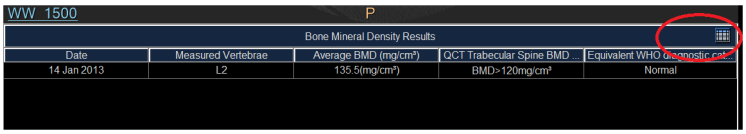
According to the average Spine BMD range of the measured vertebrae, the equivalent WHO diagnostic category is automatically displayed.

BMD Range	Equivalent WHO diagnostic Category
BMD >120 mg/cm^3	Normal
80 mg/cm^3 ≤ BMD ≤120 mg/cm^3	Osteopenia
BMD <80 mg/cm^3	Osteoporosis

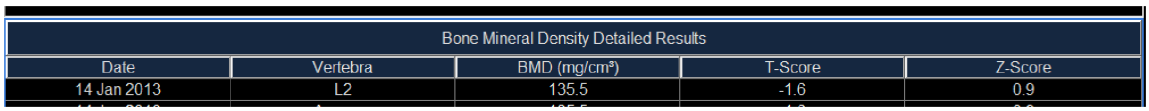
Tab. 1: Guidelines for Bone Mineral Density Results Analysis

(Reference: CR–SPR–SSR Practice parameter for the performance of Quantitative Computed Tomography (QCT) bone densitometry. Revised 2013, Resolution 32.)

If further analysis pertaining to bone density measurements and the average BMD color graph is required, the Bone Mineral Density Detailed Results table is accessible both from the Control Panel or through the BMD results table.



The detailed Results obtained from a BMD study include a Bone Mineral Density (BMD) score and a T-score and a Z-score for each body vertebra measured.



Summary of Performance Measures for the Bone Mineral Analysis Application

Non-contrast CT

Accuracy against phantom-based methodologies		Intra-operator variability/ Reproducibility	Publication
Bias, Precision, Range	Correlation		
Absolute difference of 3.3 mg/cm^3 (CI: -0.2-6.9 mg/ cm3, Min/Max: −63 to 118) and a relative difference of 5.1% (CI: 2.2%-8.1%).	Not Available	Intra operator variability was (5.8%) compared to the phantom-based (0.8%), inter operator variability was (5.8%) for the phantom-less method compared to the phantom-based (1.8%).	Therkilden et al.[2]
The mean HU (± SD) of reference values for fat for the internal and phantom references were -91.5 (±7.0) and -90.9 (±7.8), respectively. For muscle, the mean HU (± SD) for the internal and phantom references were 59.2 (±6.2) and 60.0 (±7.2), respectively.	The intra-class correlation coefficients for fat and muscle were 0.90 and 0.84 respectively.	Not Available	Boomsma et al.[3]
Bias was 3.9% ± 1.4.	r = 0.987, P < .001.	Not Available	Budoff et al. [4]
Bias of -0.9mg/cm^3.	Not Available	The analysis of cross-sectional inter observer and of longitudinal variability yielded precision values of 3.1mg/cm(3) (CV %=4.0) and 4.2mg/cm(3) (CV%=5.3) for fat and muscle, respectively.	Mueller et al.[1]

Tab. 2: Non-contrast CT

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Contrast Enhanced CT

Accuracy against phantom-based methodologies		Arterial phase vs. Venous Phase	Intra-operator variability/ Reproducibility	Publication
Bias	**Conversion Formula**			
Contrast scans were associated with a significantly higher Bone Mineral Density (BMD) compared with un-enhanced scans (un-enhanced computed tomography: 97.8 mg/cc; arterial CECT: 106.3 mg/cc, portalvenous CECT: 106.3 mg/cc).	Un-enhanced BMD= 0.89×arterialBMD+ 3,74mg/cc(r2 = 0.94) and Unenhanced BMD = 0.88×venousBMD+ 4,56mg/cc(r2 = 0.93).	No significant difference of PLvBMD between data acquisition in arterial and portal venous phases (increase of 8.6% each, standard deviation ratio 37.7%-38.3%).	In Bland-Altman analysis, there was no evidence of a relevant reader-related bias or an increase in standard deviation of PLvBMD measurements in contrast-enhanced scans compared with un-enhanced scans.	Abdullayev et al.[7]
A significant difference ($p < 0.001$) was found between BMD values on un-enhanced and contrast-enhanced CT scans.	unenhanced BMD = -2.287 + 0.964 * [arterial BMD value] and -4.517 + 0.978 * [venous BMD value].	The mean BMD value in the unenhanced MDCT scans was 79.76 mg/cm³ (SD 31.20), in the arterial phase it was 85.09 mg/cm³ (SD 31.61), and in the venous phase it was 86.18 mg/cm³ (SD 31.30). There was no significant difference between BMD values in the arterial and venous phases ($p = 0.228$).	The intrarater agreement of BMD measurements was calculated with an intraclass correlation (ICC) of 0.984 and the interobserver reliability was calculated with an ICC of 0.991.	Toelly et al.[5]
All average BMD estimates derived from contrast-enhanced scans differed significantly from BMD (all $P < 0.005$) and led to notable systemic BMD biases (mean difference at least > 6.0 mg/mL).	All regression fits revealed a consistent linear dependency (R range, 0.861-0.963).	Overall accuracy and goodness of fit tended to decrease from AR to PV contrast phase.	Not Available	Kaesmacher et al. [6]

Tab. 3: Contrast Enhanced CT

1. Mueller, D. K. et al. Phantom-less QCT BMD system as screening tool for osteoporosis without additional radiation. Eur. J. Radiol. 79, 375–381 (2011).
2. Therkildsen, J. et al. Vertebral Bone Mineral Density Measured by Quantitative Computed Tomography With and Without a Calibration Phantom: A Comparison Between 2 Different Software Solutions. J. Clin. Densitom. 21, 367–374 (2018).
3. Boomsma, M. F. et al. Use of internal references for assessing CT density measurements of the pelvis as replacement for use of an external phantom. Skeletal Radiol. 44, 1597–1602 (2015).
4. Budoff, M. J. et al. Diagnostic Performance of 64-Multidetector Row Coronary Computed Tomographic Angiography for Evaluation of Coronary Artery Stenosis in Individuals Without Known Coronary Artery Disease. Results From the Prospective Multicenter ACCURACY (Assessment by Coro. J. Am. Coll. Cardiol. 52, 1724–1732 (2008).
5. Toelly, A. et al. Influence of Contrast Media on Bone Mineral Density (BMD) Measurements from Routine Contrast-Enhanced MDCT Datasets using a Phantom-less BMD Measurement Tool. RoFo Fortschritte auf dem Gebiet der Rontgenstrahlen und der Bildgeb. Verfahren 189, 537–543 (2017).
6. Kaesmacher, J., Liebl, H., Baum, T. & Kirschke, J. S. Bone mineral density estimations from routine multidetector computed tomography: A comparative study of contrast and calibration effects. J. Comput. Assist. Tomogr. 41, 217–223 (2017).
7. Abdullayev, N. et al. Effects of Contrast Enhancement on In-Body Calibrated Phantomless Bone Mineral Density Measurements in Computed Tomography. J. Clin. Densitom. 21, 360–366 (2018).

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Process Follow-up Studies

To ensure accurate reproducibility for BMD trend analysis evaluations, use the same scan parameters on all subsequent exams.

1. From the Directory, select the patient's original study, and all follow-up studies, along with the results file saved from the original study.
2. Load the studies into the Bone Mineral Density analysis application.
3. Starting with the Define stage, follow the same procedure for follow-up studies as described for original studies.
   - The new Results stage displays the information from all the studies. The trend lines and rate of change calculations are expressed as the rate of bone change in mg/cm^3/year.

     Rate Of Change = [(BMD value for first date – BMD value for last date)] / (number of days between first date and last date) * 365
   - The results will be saved into the newer study.

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BMAP Trend Graph

This graph displays if you are doing a comparison when subsequent studies are loaded for trend analysis calculations. It shows the change in BMD value and the rate of change. Results are presented in both graph and table form, and indicate the rate of bone change in mg/cm^3/year.

Define Work Stage

The default display in the Define work stage opens with a main axial image and coronal and sagittal reference images. The BMD histogram graphs are blank until ROIs are placed.

Key Images

Save groups of images that can be reviewed in any system supporting the defined standard. See **Instructions for Use** > **Directory** > **Key Image Notes** for more information.

Mark Locations

Draw locations/ROIs (regions of interest) in specific bone, muscle, and fat locations on patient images. The BMD application will generate histograms of each ROI's Hounsfield values, then (in the section "Results Work Stage"), determine the patient's bone density from the data.

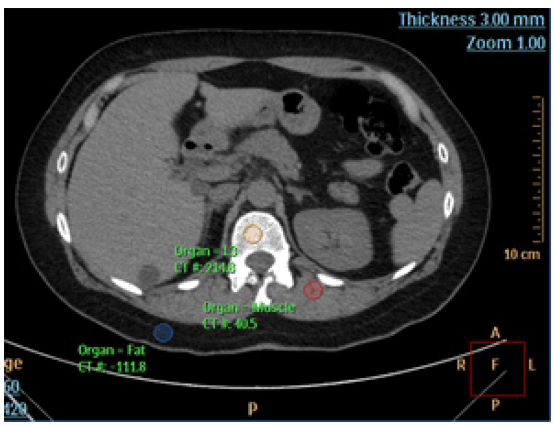
Draw ROIs in at Least 3 Different Vertebral Bodies

To ensure accurate results, you must draw the ROIs on at least 3 different vertebral bodies. The recommended vertebral bodies are L1 through L4. You can use T12 or L5 if pathology exists in other vertebral bodies.

Draw ROIs in Sets of Three

The ROIs must be drawn on at least three images of vertebral bodies, in sets of three (3):

- **Vertebral ROI.** Placed in the central portion of the trabecular bone.
- **A Muscle ROI.** Placed in retrospinal muscle.
- **A Tissue ROI.** Placed in fat tissue.



Place ROIs

On each of at least three vertebral bodies, you will draw an ROI on a vertebral body and label it. After you label the ROI, the application automatically draws two more ROIs for muscle and fat. They are placed in unspecific locations. You must move and re-shape them to accurately include only the desired tissue.

1. Scroll through the images.
2. Find the mid-portion of the first desired vertebral body (L1 for example). You can angle the image to the vertebral body if necessary.
3. Activate the desired ROI shape (circle, ellipse, or spline) using the “Mark bone & locate muscle/fat” function.
4. Click near the anterior portion of the vertebral body and drag the ROI to include only the Trabecular Bone.

NOTICE

When drawing an ROI, avoid any pathology, nerves, or blood vessels that are in the body of the vertebra. If there is no optimal location to place the ROI, go to the next vertebral body.

5. Select the appropriate label from the “Select location” menu.
   - Fat and muscle ROIs automatically are drawn on the image. They are labeled and CT# values are displayed.
   - Histograms of the three ROIs are displayed at the display’s bottom.
   - The “mark bone & muscle fat” function becomes populated with a list of tissues when ROIs are drawn and labeled.
6. Move (by dragging) the fat and muscle ROIs to appropriate locations. If the ROI does not contain enough of the needed tissue, resulting in an invalid Hounsfield value, a caution sign appears in the list next to the label.
   - Vertebra ROI CT# should be above 15.
   - Muscle ROI CT# should be in the range of 40 – 120.
   - Fat ROI CT# should be in the range of -150 – 0.
7. If correction of the muscle or fat ROIs are needed, use the Editing ROIs procedure to adjust the ROIs to include only the desired tissue.
8. Repeat the above steps for each vertebral ROI that you place. You can scroll between images with Page Up and Page Down, or with Up Arrow and Down Arrow.

Optimize Histograms

Once the ROIs are placed the histograms is created. Make sure that the histogram displays an appropriate bell curve; this indicates good ROI placement. Once bone, muscle, and fat Histograms are defined, proceed to the Results stage using the navigation button next to the “Define” stage indicator.

1. Examine the histograms.
2. Make sure that the histogram displays an appropriate bell curve, which indicates good ROI placement.

3. If necessary, you can modify an ROI (and thus improve its corresponding Histogram), using the following techniques:
   - To move an ROI: Point the mouse into the ROI to activate it and drag the ROI to the desired location.
   - To resize an ROI: Point the mouse onto the ROI to activate it and drag a control point to resize or reshape the ROI.
   - To delete a Bone ROI: Point the mouse into a bone ROI to activate it. Right mouse click on the ROI, and select Delete. The Bone ROI and its corresponding fat and muscle ROIs are deleted. You cannot delete a fat or muscle ROI only.
4. If desired, you can move the ROI's on-screen label. Place the mouse over the label to make it active. Drag the label to the desired location.

Results Work Stage

In this work stage, review the patient's results and compare them to those of a normal (reference) population. You also can save the results for future use in trend analysis and send the results to a report.

Key Images

Save groups of images that can be reviewed in any system supporting the defined standard. See **Instructions for Use** > **Directory** > **Key Image Notes** for more information.

Results with Multiple Studies

When loading results with multiple studies, the Bone Results Table gives results for each vertebra which was marked on a study (only BMD results) per date.

NOTICE

Vertebra that were not marked on a specific date have the value of zero. Only vertebra marked on more than one study are marked.

The BMAP Trend Graph displays if you are doing a comparison when subsequent studies are loaded for trend analysis calculations. It shows the change in BMD value and the rate of change. Results are presented in both graph and table form, and indicate the rate of bone change in mg/cm^3 year.

Select Population Reference

You can compare the patient's bone mineral density to three reference populations. Two of the databases can be applied to male patients and all three to female patients.

- European - male or female

- Icelandic - female only
- University of California at San Francisco (UCSF) - male or female

WARNING

If the reference population is changed, all results are re-calculated. Verify the new values before continuing.

NOTICE

The European database is recommended because it fits a more general population model. It can be applied to both male and female patients, and to an age range from 20 to 80.

Bone Density Results Table and Graph

Results are presented in both graph and table forms. In the table form, each vertebral body measured includes a BMD, T-score, and Z-score value, as well as the date the BMD scan was acquired. Also included is an average BMD, T-score, and Z-Score.

The graph includes colored reference curves. These colored curves relate to the reference population database. The reference curves demonstrate the distribution of the mean population for the appropriate age and gender. The average BMD result (blue ball on graph) displays on top of the colored reference population curves. Standard deviation values are related to the following color codes:

T-score. Compares a given patient's BMD to the mean BMD of a young, healthy individual.

Z-score. Compares a patient's BMD to the average BMD value of other patients their own age and gender, displayed in units of standard deviation (SD).

Graph Colors

Green	1 to 2 SD above the average
Yellow	within ± 1 SD
Red	1 to 2 SD below the average

NOTICE

The active table may be added to the clipboard using **Ctrl + C** or by right-clicking on the table and selecting copy. The measurements may then be pasted into common document types, including plain text, Microsoft Word, and Microsoft Excel documents.

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Rate Calculation

NewM = BMD value from the most recent scan

PrevM = BMD value from the first scan

Diff = Time between scans (years)

The rate is calculated as follows:

$$Rate = \frac{NewM - PrevM}{Diff} \left[\frac{\frac{mg}{cc}}{Year}\right]$$