INSTRUCTIONS FOR CROSS-CALIBRATING DXA SCANNERS

When Should Cross-Calibration Be Used And What Are Its Limitations?

Cross-calibration is used to make the BMD values measured with a new scanner match as closely as possible the values measured with a reference scanner. Most often this occurs in the context of research studies, though it may also arise when clinicians change or upgrade their scanners and wish to have new measurements match the old. There are two major limitations on cross-calibration. First, no phantoms have yet been developed which can adequately mimic the patterns of bone and tissue density variation found in vivo. It is therefore necessary to acquire in vivo measurements of patients using both the reference and new scanners. The resources required for this may be prohibitive in some clinical settings. The second limitation is that, while it can greatly reduce any systematic differences in average BMD measurements between scanners, differences in measured values for individual patients may occur. If it is necessary to cross-calibrate, these instructions describe how to best utilize the Excel Cross-Calibration Workbook to minimize the difference in results.

Make Sure Each Densitometer Is In Good Working Order

Often a cross-calibration is applied to a new densitometer replacing an older device. It is necessary to assure both systems are operating within manufacturer's specifications before acquiring patient results used in the cross-calibration application. Examine quality assurance tests to determine proper operation. Perform phantom scans, if available, and confirm results are within expected limits. Consult the manufacturer's service organization to assure each system is operating properly and generating valid results.

Selection And Measurement Of Study Subjects

The worksheets allow room for data from 50 subjects, and a minimum of 30 subjects is recommended. Subjects for the studies should have as wide a range of BMD values as possible. This usually requires measuring young adults in addition to the older patients normally requiring measurement. Be sure that the operator(s) of both scanners understand and have practiced the proper procedures for positioning and scanning subjects. The measurements of each subject do not have to be made on the same day, but the time interval between measurements should be short enough that no significant changes in bone density are expected.

For each subject, scan each region (spine and/or femur) to be cross-calibrated on both scanners. The scans should show no gross deformities (e.g. osteophytes, crushed vertebrae, pins or other artifacts) in the region-of-interest (ROI). If the Lunar OneScan mode (where the legs are not elevated) is used to acquire with one scanner but not the other (where the legs are elevated), there will be differences in spine BMD which will require an extra step in the analysis (see Known Difference in ROI Values).

Analyze each of the scans using the standard procedures for each scanner. Be aware that some ROIs may be positioned differently by the software from different manufacturers. Manually adjusting the ROI boundaries to be identical for each scanner will give the best correspondence between BMD values, but may not be the best choice if you wish to rely on the automated analysis of the calibrated scanner. In that case it may be better to leave the software defined boundaries in place unless gross errors exist.

Check the software defined ROIs, bone edges, and bone and tissue point-typing to make certain these are correct. Make printouts showing the ROI placement, particularly if you will not have access to both scanners throughout the cross-calibration study.

Analyzing The Measurements Using The Excel Workbook

The workbook uses macros for some calculations. The macro security level must be set to medium or low In before opening the workbook in order for these macros to operate. To set the macro security level, select Tools Macro Security from the Excel tool bar and click medium or low on the Security Level tab. If you set the level to low, you will have no protection from potentially unsafe macros . If you set the security level to medium, you will see a message box reporting that there are macros when you open the workbook file. Click the Enable Macros button to make the macros operational .

The workbook has pages for cross-calibrating values for the L1-L4 and L2-L4 AP spine and femur neck, trochanter, and total ROIs. These are the ROIs most often used for clinical assessment. The same type of BMD must be entered in the workbook for both scanners – e.g. both are Lunar-equivalent, sBMD, etc.

Data Conversion

When calibrating GE Lunar scanners to those of a different manufacturer, the usual procedure is to convert the BMD values of measurements made with the non-Lunar scanner to Lunar-equivalent values using published conversion factors for spine[1] and femur[2]. For Hologic and Norland scanners, this is done using the Lunar-Equivalent Values Calculator to the right of the data form on each worksheet. Enter the BMD values into appropriate column and click the “Reference “ button above it to transfer the converted values to the Reference scanner data column.

An additional step is required for GE Lunar spine values measured using the OneScan mode. Because spine BMDs measured with the legs not elevated (as in OneScan), are slightly higher than those measured with the legs elevated, it is necessary to adjust the OneScan values when calibrating against other scan modes (see Known Difference in ROI Values). In the worksheet, enter the OneScan spine BMDs into first column of the Lunar OneScan Adjustment calculator, located to the right of the Lunar-Equivalent Values Calculator. Typically the OneScan measurements will be made with the New scanner, in which case the “New” button is clicked to transfer the adjusted values to the New scanner data column.

Data Entry

Most of the worksheet is protected, but information can be entered near the “Dataset:” and below the statistical test results section. Enter your facility name, as well as the models of the Reference and New scanners, in the regions provided on the worksheet.

Cross-calibration is used to make the BMD values measured with the scanner being calibrated (New) match as closely as possible the values measured with the reference scanner. Often, the reference scanner is one used previously at a center while the calibrated scanner is a new one. Values measured with the reference scanner are entered into the “Reference” column and values measured with the scanner to be calibrated are entered into the “New” column. As described in the previous section, data from Hologic and Norland scanners, as well as Lunar spine values measured with OneScan mode compared with values from other modes or manufacturers, can be automatically entered from the corresponding calculator.

Understanding The Results

The worksheets provide results for two statistical analyses, a paired t-test of the mean difference in values between the new and reference measurements and a regression of the new on the reference values. Both analyses assume normal distribution of errors, so outliers can invalidate the results. Check the Bland-Altman Comparison of Densitometers (top) graph for points which fall outside the red ± 2 S.D. lines. Some normal values may fall just outside the lines, particularly if there is a significant slope to the regression. The scans for points falling a distance outside of the lines should be checked to see if some cause for the difference can be determined. Check that the patient positioning is similar in both scans and that the ROI boundaries are correctly placed. If there is an ROI placement problem, it may be possible to reanalyze the scan(s) with boundaries properly placed. If reanalysis is impossible, it may be best to delete the values for that subject and, if possible, replace them with measurements of a new subject. If there are more than one or two outliers, it may be that proper technique is not being used with both scanners.

Regression Analysis

The most important statistic from the regression analysis is the probability that the slope is equal to 1, which is the third number listed below the heading. A probability value less than 0.05 means that there is a statistically significant slope, which will be indicated by the label next to the value. In that case, the cross-calibration should make use of the slope and intercept of the regression equation and the standard error of estimate (SEE) is an estimate of the precision error in comparing a measurement made with the new scanner with a measurement made with the reference scanner. If the slope is not significant, the regression values are irrelevant and the paired t-test values are used. The dashed blue calibration line in the Comparison of Densitometers (bottom) graph shows the regression line only if the slope is significant. At least 3 data points must be entered before the regression statistics are displayed.

Paired T-Test

This test is valid only if the slope is not statistically significant. The mean difference between the new and reference scanner values is labeled Δ. The most important statistic is p(t), the probability that Δ is equal to zero. If p(t) is less than 0.05, there is a statistically significant constant offset between values measured on the two scanners and calibration consists of a constant which is added to the BMD values. Note that the paired t-test is a more sensitive test for a constant offset in the absence of a slope than the test of whether the regression intercept is equal to zero. If both the slope and the offset are not statistically significant, there is no reason to cross-calibrate the scanners, since both are giving average values which are identical within the limits of the measurement precision.

The value for Δ is plotted as the solid blue "mean" line in the Bland-Altman Comparison of Densitometers (top) graph, and can be compared to the dotted "zero" line in the graph. If slope is not statistically significant but Δ is, the dashed "calibration" line in the Comparison of Densitometers (bottom) graph shows the constant offset. If neither offset nor slope is statistically significant, the graph does not show the calibration line. At least two data points must be entered before the paired t-test statistics will be displayed.

Conclusion and Calibration Equations

The conclusion statement summarizes the statistical test results. If either the slope or the offset is statistically significant, the conclusion statement also indicates whether the average difference between values measured with the two scanners exceeds 0.02 g/cm² anywhere within the range of values on the graph. The BMD ranges for each worksheet have been set to cover all the values normally encountered in clinical practice. We do not generally recommend applying cross-calibration when the mean difference is less than 0.02 g/cm², though the final decision is left up to the customer.

Calibration equations are displayed below the conclusion statement whenever either slope or intercept is statistically significant. The bottom equation is used to convert values measured with the new (calibrated) scanner to equivalency with the previous (reference) scanner and, in the case of a significant slope, is the mathematical inversion of the regression equation[3]. The top equation can be used to convert values measured with the previous (reference) scanner to equivalency with the new (calibrated) scanner.

At least 10 data points must be entered before the conclusion and calibration equations will be displayed.

Known Difference in ROI Values

There a situation where systematic differences in BMD values have been observed to occur. Spine measurements made using the Lunar OneScan mode (legs not elevated) have BMD values which average approximately 2% higher than Lunar BMD values and Hologic values (BMD adjusted to Lunar-equivalent values) where legs are elevated. The Lunar T score calculations compensate for these differences in BMD so that T scores with OneScan are comparable to those made with the legs elevated. These known differences should not be included in the cross-calibration equations, so the OneScan BMD Adjustment calculator in the spine ROI worksheets makes the same adjustment as the software to remove the difference before the calibration equations are calculated.

Using The Calibration Equations

The calibration equations provided by the worksheets can be used manually to convert values using calculators or spreadsheets. Scanners using GE Lunar enCORE software can be adjusted to apply the calibration to results reported by the instrument. Please note that only one calibration equation can be applied to each region, spine or femur, and not separate equations for each ROI (e.g. femur neck, total femur). Historically the femur neck was emphasized in clinical diagnosis, while the current trend is to place more emphasis on the total femur. If you would like to adjust your scanner to report cross-calibrated values, please contact your GE Lunar service representative for assistance.

[1] Genant H, Grampp S, Glüer C, Faulkner K, Jergas M, Engelke K, Hagiwara S, Van Kujik C. Universal standardization for duel X-ray absorptiometry: patient and cross-calibration results. J Bone Miner Res (1994) 10:1503-1514.

[2] Lu Y, Fuerst T, Hui S, Genant H. Standardization of bone mineral density at femoral neck, trochanter and Ward's triangle. Osteoporos Int (2001) 12:438-444.

[3] Standard regression, as is used in this workbook, is not transitive. I.e., switching the data columns will usually not give the same values as switching the regression equations. This is because the standard regression calculations assume all the measurement error is in the dependent (New) values. There are other regression approaches, such as Passing-Bablok and Deming regression, which do not make this assumption and are transitive. These alternatives require special software, but may deserve consideration in certain research situations.