Supplementary Appendix

NHANES 2005-2010 Hip Re-Analysis Study

Comparison of femur BMD using Discovery 12.4 versus Apex 4.0 analysis software

I. Background

This appendix summarizes results of a method comparison study performed to assess the effect of changing from Hologic DXA scan analysis software Discovery 12.4 (used in NHANES 2005-2010) to Apex 4.0 (used in NHANES 2013-2014) on femur bone mineral density (BMD) data collected in these NHANES survey cycles. Differences in DXA scan results for the same individuals have been noted previously when different DXA scan analysis software versions were used(1). Since secular trends in femur skeletal status of the population will involve comparing data from NHANES 2005-2010 with NHANES 2013-14, it is important to assess the impact of the software change that occurred between these NHANES survey cycles.

II. Methods

600 femur scans for respondents age 40 years and older from NHANES 2005-2010 that were originally analyzed with Discovery 12.4 were randomly selected and provided to the Bone and Breast Group at the University of California San Francisco (UCSF) for re-analysis with Apex 4.0 software. This UCSF group has provided quality control oversight of DXA measurements collected in NHANES since 1999. The age range for the Hip Re-analysis Sample was restricted to 40+ because femur scans were not performed on respondents < age 40 in NHANES 2013-14.

The sample was selected by stratifying respondents age 40+ with valid femur scans by decile of femur neck BMD within each survey year. Ten individuals per femur neck BMD decile were selected from each survey year (n=100 per year), resulting in a total of 600 respondents from the 6 survey years between NHANES 2005-2010.

Data analysis:

Mean BMD (age 40+, n=600) and prevalence with osteoporosis or low bone mass (age 50+, n=438) at five femur regions of interest (ROI) were calculated using both the original Discovery and re-analyzed Apex BMD values using SAS 12.1. The WHO diagnostic criteria and NHANES III femur reference data were used to define osteoporosis and low bone mass (2,3). Mean differences between Apex and Discovery BMD values at the five femur ROI were calculated and plotted by BMD decile.

Regression models to predict Apex values from Discovery values were also developed using the Hip Re-Analysis Sample data. Two modeling approaches were used: ordinary least squares (OLS) regression and Deming regression. OLS regression, which assumes there is no error in the dependent variable, was performed with SAS 12.1. Deming regression, which allows for error in both dependent and independent variables, was performed with the MCR routine in the R statistical package. Models were run before and after performing a natural log transformation of the BMD values. Models were evaluated for fit using mean square error and/or R2 values.

III. Results:

Supplementary Table 1 summarizes mean BMD, mean BMD difference, and percent difference between Discovery and Apex values for the five femur ROI. Mean femur neck BMD did not differ between the two software versions (p=0.25), with mean femur neck BMD based on Apex only being -0.14% lower than Discovery. However, mean Apex BMD was significantly lower than mean Discovery BMD for the other 4 ROI. The largest difference was noted for the trochanter, where the mean based on Apex was approximately 2% lower than the mean based on Discovery. Mean Apex BMD for the total femur, intertrochanter, and Ward’s triangle were ~0.2-0.9% lower than mean Discovery BMD.

Mean BMD difference is plotted by BMD decile for the femur neck, trochanter, and total femur in Supplementary Figures 1-3. Results for the intertrochanter and Ward’s triangle are not shown because there was no significant trend in mean BMD difference by BMD decile and these femur ROI are not typically used in epidemiological or clinical studies. There was no significant trend in the mean BMD difference across the BMD distribution at the femur neck (Supplementary Fig 1), and the mean differences were small (< 0.01 g/cm2). However mean BMD difference at the trochanter (Supplementary Fig 2) and total femur (Supplementary Fig 3) each showed a significant, positive trend across the BMD distribution, with the difference reaching 0.036 g/cm2 in the highest decile of trochanter BMD and 0.16 g/cm2 in the highest decile of total femur BMD.

Supplementary Table 2 compares prevalence of osteoporosis and low bone mass based on observed Discovery and observed Apex BMD values in 438 respondents from the Hip Re-Analysis sample who were age 50 years and older. Differences in the osteoporosis estimates between Discovery and Apex were small (-0.4 to +0.9 percentage points) and 95% confidence intervals (CI’s) for the estimates based on the two software versions overlapped almost completely, which suggests that none differed significantly. Differences in the low bone mass estimates were slightly larger (-0.3 to 2.3 percentage points) but 95% CI’s for the low bone mass estimates based on Apex versus Discovery also overlapped almost completely, which suggests that none differed significantly.

The OLS and Deming regression models developed to predict Apex BMD from Discovery BMD values had similar R2 values, ranging from 0.97-0.98 for the femur neck, 0.94-0.95 for the trochanter, and 0.99 for the total femur. Models using log transformed BMD values had slightly larger mean square errors than models using untransformed values, so only the prediction equations based on untransformed BMD values were used in subsequent analyses to assess the impact of the software change on observed trends in BMD. Prediction equations developed from the untransformed models are shown in Supplementary Table 3.

IV. Summary and conclusions:

There were significant differences in mean BMD between Discovery 12.4 and Apex 4.0 at four of the five femur ROI, but the software version had little effect on prevalence of low values at these four femur ROI. This is likely due to the fact that the software differences were either small overall (femur neck, intertrochanter) or were minimal in the lower end of the BMD distributions, and only tended to became more pronounced for BMD values above the midpoint of the BMD distribution (trochanter, total femur).

References

1. Fan B, Lewiecki EM, Sherman M, et al. Improved precision with Hologic Apex software. Osteoporosis International. 2008;19(11):1597-602.

2. Kanis JA, Melton LJ, Christiansen C, Johnston CC, Khaltaev N. The diagnosis of osteoporosis. Journal of Bone and Mineral Research. 1994;9(8):1137-41.

3. Looker AC, Wahner HW, Dunn WL, et al. Updated data on proximal femur bone mineral levels of US adults. Osteoporos Int. 1998;8(5):468-89.

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| Supplementary Table 1.  |  |  |
| Mean BMD difference (g/cm2) between Discovery and Apex values at five femur regions of interest,NHANES 2005-2010 Hip Re-Analysis Study sample, Adults age 40+ (n=600)  |
|  | Mean BMD (g/cm2) | Mean BMD difference | Percent  |
|   | Discovery | Apex | (g/cm2) | *p, mean diff=0* | difference |
|  |  |  |  |  |  |
| Femur neck | 0.797 | 0.796 | -0.0011 | *0.25* | -0.14 |
|  |  |  |  |  |  |
| Total Femur | 0.943 | 0.937 | -0.0061 | *<0.001* | -0.65 |
|  |  |  |  |  |  |
| Trochanter | 0.711 | 0.696 | -0.0156 | *<0.001* | -2.24 |
|  |  |  |  |  |  |
| Intertrochanter | 1.118 | 1.116 | -0.0018 | *0.05* | -0.16 |
|  |  |  |  |  |  |
| Ward's triangle | 0.605 | 0.599 | -0.0055 | *<0.001* | -0.92 |
| Data are unweighted |
| Mean BMD difference =BMD by Apex - BMD by Discovery.  |
| Note: Apex BMD values were rounded to 3 decimal places |  |  |

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| Supplementary Table 2.  |  |  |  |  |  |
| Prevalence of osteoporosis and low bone mass at 4 femur ROI based on Discovery or Apex BMD values:  |
| NHANES 2005-10 Hip Re-analysis Sample, Adults age 50+ (n=438)  |   |   |
|  Femur Region | Osteoporosis (%) | Low Bone Mass (%) |
|  of Interest | Discovery | Apex | Difference | Discovery | Apex | Difference |
|  |  |  |   |  |  |  |
| Femur neck | 5.3 | 6.2 | 0.9 | 38.6 | 39 | 0.4 |
|  95% CI | 3.2, 7.3 | 3.9, 8.4 |   | 34.0, 43.2 | 34.5, 43.6 |  |
|  |  |  |   |  |  |  |
| Total Femur | 2.7 | 2.3 | -0.4 | 27.4 | 28.3 | 0.9 |
|  95% CI | 1.2, 4.3 | 0.9, 3.7 |   | 23.2, 31.6 | 24.1, 32.5 |  |
|  |  |  |   |  |  |  |
| Trochanter | 3.2 | 3.7 | 0.5 | 28.5 | 30.8 | 2.3 |
|  95% CI | 1.5, 4.8 | 1.9, 5.4 |   | 24.3, 32.8 | 26.5, 35.2 |  |
|  |  |  |   |  |  |  |
| Intertrochanter | 2.3 | 2.1 | -0.2 | 23.1 | 22.8 | -0.3 |
|  95% CI | 0.9, 3.7 | 0.7, 3.4 |   | 19.1, 27.0 | 18.9, 26.8 |   |
| Data are unweighted  |  |  |  |  |  |

Supplementary Table 3

Equations to predict Apex BMD values from Discovery BMD values for three femur regions of interest

NHANES 2005-2010 Hip Re-analysis Study, Adults age 40+.

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| 1. Femur neck BMD equations:Predicted Apex FNBMD\_OLS = -**0.00176** + **1.00086**\*FNBMD;Predicted Apex FNBMD\_DEMING = -**0.01195** + **1.01365**\*FNBMD;2. Total femur BMD equations:Predicted Apex TOTBMD\_OLS = **0.03232** + **0.95923**\*TOTBMD;Predicted Apex TOTBMD\_DEMING = **0.02705** + **0.96481**\*TOTBMD;3. Trochanter BMD equations:Predicted Apex TROCHBMD\_OLS = **0.06193** + **0.89106**\*TROCHBMD;Predicted Apex TROCHBMD\_DEMING = **0.04658** + **0.91263**\*TROCHBMD; |

FNBMD=femur neck BMD

TOTBMD= total femur BMD

TROCHBMD=trochanter BMD

OLS=Ordinary Least Squares regression result

DEMING=Deming regression result

Supplemental Figure Legends

Supplemental Figure 1. Mean femur neck bone mineral density (BMD) difference by BMD decile

Note: BMD difference = BMD by Discovery – BMD by Apex software

N= 600 scans from NHANES 2005-2010 Hip Re-analysis project

Supplemental Figure 2. Mean trochanter bone mineral density (BMD) difference by BMD decile

Note: BMD difference = BMD by Discovery – BMD by Apex software

N= 600 scans from NHANES 2005-2010 Hip Re-analysis project

Supplemental Figure 3. Mean total femur bone mineral density (BMD) difference by BMD decile

Note: BMD difference = BMD by Discovery – BMD by Apex software

N= 600 scans from NHANES 2005-2010 Hip Re-analysis project