High Resolution Imaging of Periprosthetic Bone Remodeling Events Using Dual Energy X-ray Absorptiometry Region-Free Analysis (DXA-RFA)

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Disclosures:

Introduction: Periprosthetic bone loss following total hip arthroplasty (THA) is a risk factor for periprosthetic fracture and causes reconstruction challenges at revision surgery. Dual energy X-ray absorptiometry (DXA) is the gold standard method to quantitate bone loss after THA. A 2-dimensional image of the bone is acquired that contains data on the area and bone mineral density (BMD) of each pixel of the scan. At scan analysis the pixel-level BMD data is averaged to provide mean BMD values for predefined regions of interest (ROI) that are several square centimeters in area. This approach avoids the problem of tracking an individual pixel across serial scans and accommodates differences in anatomy between individuals when studying groups of patients. However, it reduces a BMD map containing several thousand information points to a small number of summary ROI datasets, and introduces a set of limitations. This data averaging greatly reduces the sensitivity of the method to quantitate and precisely localize periprosthetic remodeling events, limiting useful comparisons between DXA and predictive tools such as finite element modeling. DXA ROIs also lack standardization as different ROI constructs are required for different classes of prosthesis design and for different anatomic sites. Here we report the development and validation of a computational solution to DXA scan analysis that solves the challenges associated with individual pixel-tracking within an individual patient dataset and between patients for group-wise analyses. This solution, DXA-Region Free Analysis (DXA-RFA), resolves periprosthetic bone remodeling events at pixel-level and greatly enhances the sensitivity of DXA to local remodeling events. It also obviates the use of analysis ROIs, to better facilitate comparisons of remodeling events against in-silico models and in-vivo comparisons between prosthesis designs.

Methods: Tool development, precision, and accuracy studies: These studies were undertaken using a European Spine Phantom (ESP) consisting of 3 vertebrae and pairs of independently acquired DXA scans of the proximal femur taken on the same day after repositioning in 29 subjects. Prior to scan analysis, an identical copy of each scan was made to create 58 ‘identical’ pairs of scans in addition to the 29 ‘repositioning’ pairs. The precision of DXA-RFA was assessed using these pairs of scans and expressed as the coefficient of variation (CV%). DXA-RFA was implemented using Matlab software (MathWorks Inc, Cambridge, UK). We calculated the BMD of each pixel of a DXA scan using a semi-automated greyscale thresholding routine. Each femur was then approximated to a polygon using 62 points located in consistent anatomical locations throughout the given series. Subsequently, a master femur template was generated by Procrustes analysis and averaging of the shapes so as to represent the mean femoral shape across all scans to be analyzed. The individual scans were then morphed to fit this template using Thin-Plate Splines (TPS) warping, thus ensuring a common size and shape for every scan and a consistent positioning of each pixel within the femoral area across all scans.

Application of DXA-RFA to the study of longitudinal BMD change: Here we applied DXA-RFA to the evaluation of longitudinal BMD change within individuals and across groups. DXA acquisitions from a previous randomized clinical trial comparing BMD change around 2 cemented femoral prostheses of similar design geometry but made from metal alloys of different modulus of elasticity (stainless steel versus cobalt-chrome) were analyzed. Twenty-five subjects with hip osteoarthritis were randomized to receive either an Exeter Universal (Stryker, Newbury, UK) or Ultima-Total Polished Stem (‘Ultima-TPS’, DePuy-Synthes Ltd, Leeds, UK). BMD was measured post-operatively at baseline, 3 and 12 months follow-up.

Results: Accuracy and precision studies: Software calibration was performed against a standard BMD calibration phantom (ESP). The measured BMD by DXA-RFA was plotted against the known BMD of the ESP and a simple linear regression performed, to find the correct scaling factor for the software. Following calibration the ESP was re-analyzed. The maximum percentage difference between DXA-RFA and the known BMD of the ESP was 3.4%, similar to that of conventional Hologic software. Pixel by pixel precision was assessed first for identical scans and second for repositioned pairs of scans. For identical pairs of scans the median pixel-by-pixel CV was 0.23% (interquartile range (IQR) 0.16% to 0.35%). For repositioned scans the median CV was 1.37% (1.20% to 1.60%). Finally, precision was compared against that found when using the conventional 7 region of interest model, with the CV expressed for the net femur and for each region. The net CV after repositioning was 1.7% (range 2.9% to 3.7% between individual ROIs). This compared to a net CV of 1.6% (1.5% to 3.6%) using the traditional Gruen analysis approach.

The study of longitudinal BMD change: Images were produced to show the average BMD change at each pixel of the proximal femur for each prosthesis group and the difference between the groups at all of the follow-up time points. BMD change was shown as a percentage of the baseline BMD and P-value pixel maps were generated to show which pixels of the proximal femur showed significant BMD change over time and between the study groups (Figure 1). The general proximal to distal distribution...
of BMD change was consistent with that seen using conventional methods. However, the novel imaging demonstrated that periprosthetic BMD change also varies centrally to radially and occurs in discrete quanta, as areas of bone loss reside closely with areas of bone gain. The difference in material stiffness between the prostheses had little impact on the pattern of BMD change.

**Discussion:** DXA-RFA solves the problems of low sensitivity and limitations associated with ROI-based analysis of DXA information. Here we describe the development of this tool, and validate its accuracy, precision, and utility to analyze existing datasets. The ESP analysis data show the method has equivalent accuracy to conventional software. The low CV% of the identical scan analyses demonstrated that the use of a master template does not degrade scan precision and that the pixel registration process was effective. Next, the low CV% of the repositioned scans analysis demonstrated that this precision is preserved in the clinical setting and not affected by patient positioning variation between scans. Finally, comparison with the CV% of the Gruen ROI approach showed that this method has at least equivalent precision to traditional approaches. Next we demonstrated its clinical application to study bone remodeling events over time. Here we demonstrated that the software’s improved resolution allows identification of the exact areas where BMD change events occur. Our findings show that periprosthetic bone remodeling events occur in discrete quanta throughout the periprosthetic bone. Further, this data shows that positive and negative bone remodeling events can be geographically closely related and occur centrally to radially as well as proximal to distal, further highlighting the limitations of currently used ROI methodologies, and has implications for their continued use.

**Significance:** DXA-RFA allows the high-resolution measurement of bone modeling and remodeling events after THA. This tool can be applied to the non-invasive study of the effect of prosthesis design, surface coatings and biological interventions on prosthesis-bone biology.

**Acknowledgments:**

Reference:

ORS 2014 Annual Meeting
Poster No: 0958