Use of Dual-energy X-ray Absorptiometry Region-Free Analysis (DXA-RFA) to Resolve Bone Remodeling around Non-Standard Prosthesis Designs

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Introduction: Total hip arthroplasty (THA) causes a change in the local mechanical environment of the proximal femur, resulting in strain-adaptive bone remodeling. Dual energy x-ray absorptiometry (DXA) is the gold standard method for measuring bone remodeling events around joint prostheses. However, current analysis approaches using this method are limited by their reliance on a region of interest (ROI) approach that precludes direct comparisons between differing implant geometries or in non-standard implant designs such as metaphyseal fitting implants, and is insufficiently sensitive to resolve remodeling events at local level. We have developed and validated a high-spatial resolution tool, termed DXA-Region-Free Analysis (DXA-RFA) that sheds these limitations by quantitating bone mineral density (BMD) at the individual pixel-level (1). Here we compared DXA-RFA quantitation of focal bone remodeling events around a stemless, hydroxyapatite (HA) coated femoral prosthesis (Silent Hip, DePuy Ltd, Leeds, UK) with BMD quantitated using a conventional ROI-based approach.

Methods: The analyzed DXA scans were collected as part of a single-center, prospective cohort study of 18 patients undergoing primary THA using the Silent Hip. Patients underwent a DXA scan of the operated hip using an Hologic QDR4500A densitometer (Hologic, Bedford, MA) in metal-removal mode at post-operative baseline within 10 days of surgery, and at months 3, 6, 12, and 24 thereafter. DXA scan analysis using conventional ROI approach: A 5 ROI analysis model was applied, similar to that used in previous studies, and adapted for the shorter length of the Silent Hip. Average BMD change was calculated for each region at all follow-up time points and significance was calculated by paired t-test. The precision of this method, expressed as the coefficient of variation (CV\%) between 2 independent observers was 0.3, 1.0, 0.5, 1.6, and 4.3 for ROIs 1 to 5, respectively, and similar to that described by Albanese et al (1.9 to 3.4\%) (2). DXA scan analysis using high-resolution DXA-RFA: DXA scan analysis using DXA-RFA was performed as previously described (1). Heat-maps were generated to show the baseline post-operative BMD distribution at pixel-level and the change in BMD at each time-point. The P-value of that change versus baseline was also shown and calculated using a paired t-test. The median pixel-level accuracy error of the method following calibration is within 1.9\% (interquartile range -7.2 to 3.5\%). The median pixel-level precision in clinical application, expressed as CV\%, is 1.4\% (IQR 1.2 to 1.6) (1).

Results: A regional pattern of BMD change was observed using the conventional analysis approach (Figure 1). ROI3, placed distal to the tip of the prosthesis, showed no change in BMD at any time-point, and an increase in BMD of 6\% (P<0.05) in ROI 4 was identified at 24 months. Falls in BMD were measured in ROIs 1, 2, and 5 (P<0.05), with greatest loss in region 5 (20\%, P<0.001). In contrast,
quantitation using DXA-RFA showed pixel-level BMD distribution consistent with the macro-architecture of the proximal femur, with high bone mass in anatomic cortical areas below the metaphysis, and lower mass in cancellous bone areas of the metaphysis and trochanters. Postoperatively BMD change was found in discrete, focal areas that were not resolved by the conventional ROI model (Figure 2). A focal layer of increased BMD was found at the prosthesis-bone interface (30-40%, P<0.001) that was also not resolved using conventional DXA analysis. The 20% bone loss observed in ROI5 with conventional DXA was resolved to a focal area adjacent to the cut surface of the infero-medial femoral neck (up to -40%, P<0.0001).
Discussion: The ability to resolve remodeling events without the limitations of ROI-based approaches represents a technological advance in this imaging field. This computational solution to the challenges of tracking remodeling events at the individual pixel-level allows visualization of remodeling events at a resolution that is not possible using conventional ROI-based approaches. Our finding that remodeling events occurred in small but spatially discrete ‘quanta’ is consistent with the biology of bone remodeling that is known to occur in discrete multicellular bone remodeling units. The observation of large focal changes in BMD at the implant-bone interface suggests that high-resolution analysis approaches may allow visualization of remodeling events at the osseointegration interface. DXA-RFA may provide a novel, low radiation, non-invasive tool to detect the effects of prosthesis surface modifications on bone remodeling at the prosthesis-bone interface in clinical trials.

Significance: DXA-RFA is a novel tool for high-resolution quantitation of local bone remodeling events after THA, and sheds the limitations of ROI based approaches. Further studies will determine the sensitivity of this tool to facilitate the non-invasive study of prosthesis design, surface coatings, and biological or pharmacological intervention on the local bone environment after joint replacement.

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