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Regional distribution of spine and hip QCT BMD responses after one year of once-monthly ibandronate in postmenopausal osteoporosis ☆

Klaus Engelke [a,*], Thomas Fuerst [b], Gorana Dasic [c], Richard Y. Davies [d], Harry K. Genant [b,e]

[a] Institute of Medical Physics, University of Erlangen, Germany, and Synarc Inc, Hamburg, Germany
[b] Synarc Inc, San Francisco, CA, USA
[c] Formerly of GlaxoSmithKline R&D, King of Prussia, PA, USA
[d] GlaxoSmithKline R&D, King of Prussia, PA, USA
[e] University of California, San Francisco, CA, USA

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ABSTRACT

In the published placebo-controlled Ibandronate Quality (IQ) study, 12 months of once-monthly oral ibandronate increased femoral and vertebral integral and trabecular bone mineral density (BMD) measured by quantitative computed tomography (QCT). Ibandronate showed significant improvements versus placebo in finite element analysis of femoral and vertebral strength. This post hoc analysis examined QCT BMD changes in novel superior and inferior vertebral volumes of interest (VOIs) and femoral and vertebral subcortical, extended cortical, and extended trabecular VOIs. Ninety-three postmenopausal women (BMD_a T-scores ≤ -2.0 at lumbar spine, total hip, or femoral neck) received ibandronate 150 mg/month ($n=47$) or placebo ($n=46$) for 12 months. QCT with Medical Imaging Analysis Framework (MIAF)-Spine and MIAF-Femur used automated segmentation and coordinate system-based identification of integral, cortical, subcortical, and trabecular VOIs and combinations (extended cortical = cortical + subcortical; extended trabecular = trabecular + subcortical). Between-group differences in mean percentage changes from baseline were determined by treatment- and center-adjusted analysis of variance. *P* values were post hoc, exploratory, descriptive, and unadjusted for multiple comparisons. Ibandronate increased vertebral superior and inferior trabecular and extended cortical midsection BMD (4.9%, $p=0.032$; 4.6%, $p=0.055$; 3.9%, $p=0.014$, respectively) versus placebo. Femoral BMD treatment differences (ibandronate versus placebo) were significant in total hip (extended trabecular 4.0%, $p=0.005$; extended cortical 1.5%, $p=0.047$; subcortical 3.7%, $p=0.009$), trochanter (extended trabecular 5.2%, $p=0.007$; extended cortical 2.4%, $p=0.01$), and extended trabecular femoral neck (4.0%, $p=0.02$). Monthly oral ibandronate for 12 months improved QCT BMD versus placebo in the vertebral periphery, subcortical total hip, and all femoral extended trabecular regions.

Introduction

Bone mineral density (BMD) is central to the diagnosis of osteoporosis and the follow-up of treated patients. Areal BMD (BMD_a) measured by dual energy X-ray absorptiometry (DXA) has been a primary or secondary endpoint in almost all interventional osteoporosis trials. However, the adequacy of DXA as a monitoring method for pharmaceutical therapy has been questioned, as BMD_a changes under treatment do not fully explain the observed fracture reduction of currently approved therapies [1]. Small BMD_a changes may have large effects on fracture risk in patients with already low baseline BMD_a. Additional limitations accrue from the projectional nature of DXA. Vertebral posterior elements contribute unknown proportions of cortical bone to BMD_a measured in the standard posteroanterior projection of the spine. Vertebral degeneration or deformity [2–4], aortic calcifications [5,6] or unrecognized vertebral fractures also can contribute spurious BMD_a increases in elderly subjects; additionally, bone size changes parallel to the axis of projection (i.e., changes in bone depth) may leave physical BMD in g/cm^3 unchanged but increase apparent BMD_a [7–10]. Hence surrogate measurements of osteoporosis treatment efficacy complementary to DXA are needed [11].

In contrast to DXA, quantitative computed tomography (QCT) assesses cortical and trabecular bone separately and measures true 3-dimensional (3D) BMD in g/cm^3 [12]. For example, QCT responses to parathyroid hormone and alendronate separately or together in

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* Corresponding author. Institute of Medical Physics, University of Erlangen, Henkestr. 91, D-91052 Erlangen, Germany. Fax: +49 9131 8522824.
E-mail address: klaus.engelke@imp.uni-erlangen.de (K. Engelke).

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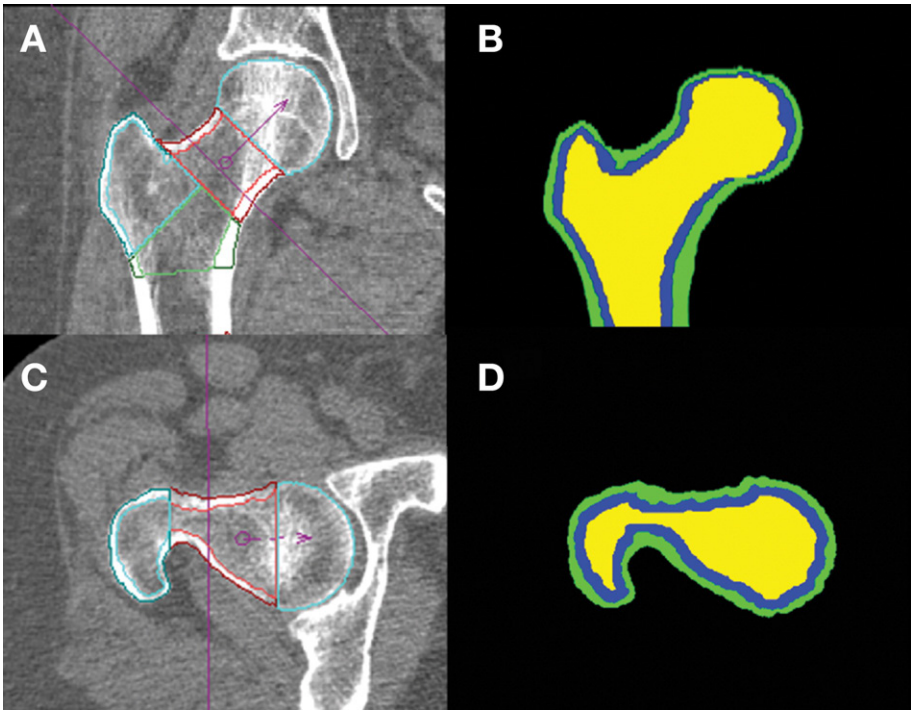

Fig. 1. Femoral QCT VOIs. A and B: coronal view, C and D: axial view. A and C: CT images with segmentation results; the periosteal and endosteal surfaces, visualized as contours, define the cortical compartments (trochanter, deep blue periosteal surface; femoral neck, deep red periosteal surface; endosteal surfaces are shown in lighter shades). Peeling the endosteal surface by 1.5 mm towards the inside of the bone defines the corresponding trabecular VOI. B and D: schematic view of the cortical (green), subcortical (blue), and trabecular (yellow) VOIs. For clarity the subcortical VOI is not visualized on the CT images shown on the left side.

the Parathyroid Hormone and Alendronate Study (PaTH) [13] reflected predominantly trabecular BMD increases in the femur and lumbar spine; alendronate alone increased cortical volume and bone mineral content, although not cortical BMD. In the Ibandronate Quality (IQ) study [14], once-monthly oral ibandronate for 12 months induced femoral and vertebral integral and trabecular BMD gains.

In the spine, traditional single-slice-based QCT VOIs include the elliptical trabecular VOI in the anterior portion of the vertebra, and the osteo VOI, a region shaped like the PacMan character that extends

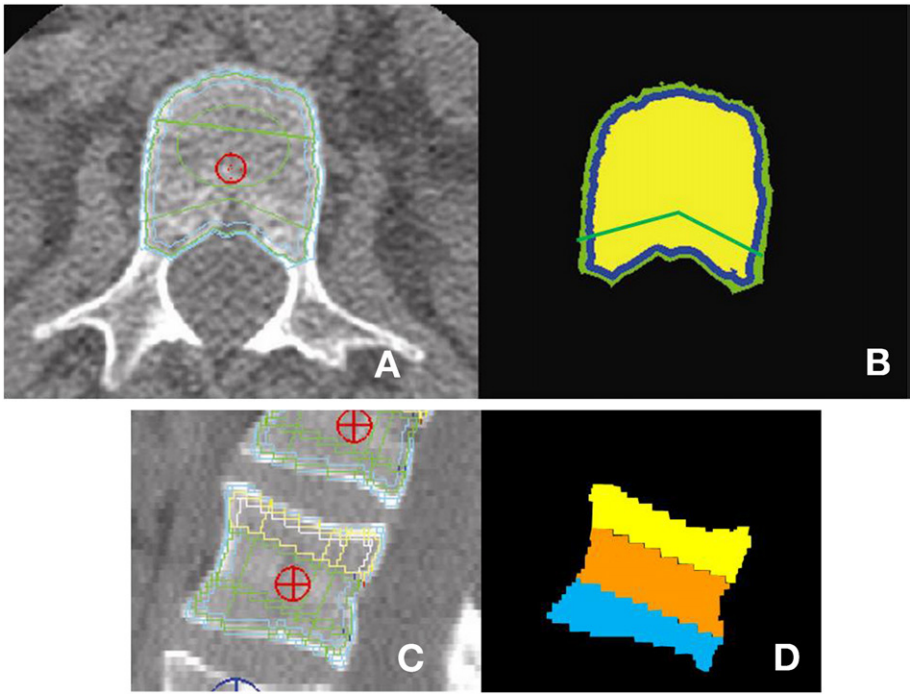

Fig. 2. Lumbar vertebral QCT VOIs. A and B: Axial view; the total vertebral body is separated into cortical (green), subcortical (blue), and trabecular (yellow) VOIs. The integral VOI is the sum of these three VOIs, schematically shown in (B). The subcortical VOI is peeled from the inner surface of the cortical VOI by 1.5 mm. The "osteo VOI," used in trabecular and cortical analyses, omits the posterior vertebral structures. The border is also shown in (B). C and D: coronal view. The integral superior (yellow), midsection (orange), and inferior (blue) VOIs are schematically shown in (D).