

ΟΤΙ ΝΕΟΤΕΡΟ ΑΠΟ ΤΗΝ ΑΠΕΙΚΟΝΙΣΗ ΤΟΥ ΣΚΕΛΕΤΟΥ

ΚΩΝ/ΝΟΣ ΔΙΟΝ. ΣΤΑΘΟΠΟΥΛΟΣ M.D., Ph.D
ΟΡΘΟΠΑΙΔΙΚΟΣ ΧΕΙΡΟΥΡΓΟΣ
ΕΠΙΣΤΗΜΟΝΙΚΟΣ ΣΥΝΕΡΓΑΤΗΣ ΙΑΤΡΙΚΗΣ ΣΧΟΛΗΣ ΕΚΠΑ
ΠΜΣ “ΜΕΤΑΒΟΛΙΚΑ ΝΟΣΗΜΑΤΑ ΟΣΤΩΝ”



ΜΕΤΑΒΟΛΙΚΑ ΝΟΣΗΜΑΤΑ ΤΩΝ ΟΣΤΩΝ
Βιβλιογραφική Ενημέρωση

Επιστημονικό Πρόγραμμα

2^η ΗΜΕΡΑ | Σάββατο 18 Μαρτίου 2023

DXA: ΤΙ ΔΕΝ ΜΕΤΡΑΕΙ?

<i>Factor</i>	<i>Variable</i>	<i>Method*</i>
Bulk	BMC	DXA, (p)QCT, ashing
Morphology		
Dimensions	Cortical wall thickness (mean and direction specific)	(p)QCT, μ -CT, MRI
	Cortical cross-sectional area	(p)QCT, μ -CT, MRI
	Total cross-sectional area	(p)QCT, μ -CT, MRI
	Diameters (max, min, other direction)	(p)QCT, MRI, (caliper)
	Trabecular cross-sectional area, marrow area	(p)QCT, μ -CT
	Axial length of whole bone/anatomic structures	Caliper, tape measure, radiograph, DXA, QCT, MRI
Geometry	Cross-sectional moment of inertia (max, min, other direction)	(p)QCT, μ -CT, MRI
	Eccentricity (shape of bone cross-section)	(p)QCT, MRI
	Center of mass (location)	(p)QCT, MRI
	Angle between distinct anatomic structures, curvature	Radiograph, DXA, QCT, MRI
Texture		
	Cortical porosity (cortical apparent density)	μ -CT, SR- μ -CT [(p)QCT]
	Trabecular apparent density (-BV/TV)	(p)QCT, μ -CT, HR-MRI, histomorphometry
	Trabecular architecture and (micro)structure	μ -CT, HR-MRI, histomorphometry
	Mineralization	μ -CT, qBSE
	(Micro)damage	Confocal microscopy, histomorphometry

* Not an exhaustive list. Evaluation of the given variable is mainly based on manual, semiautomatic analysis of the scan (image) data of measured bone projection, cross-section or volume.

SR, synchrotron radiation; MRI, magnetic resonance imaging; HR, high resolution; qBSE, quantitative backscattered electron imaging.

ΠΟΣΟΤΙΚΗ ΑΞΟΝΙΚΗ ΤΟΜΟΓΡΑΦΙΑ

- ΣΠΟΝΔΥΛΙΚΗ ΣΤΗΛΗ (QCT)
- ΙΣΧΙΟ (QCT)
- ΠΕΡΙΦΕΡΙΚΗ ΠΟΣΟΤΙΚΗ ΑΞΟΝΙΚΗ ΤΟΜΟΓΡΑΦΙΑ (pQCT) : ΚΕΡΚΙΔΑ, ΚΝΗΜΗ
- ΠΕΡΙΦΕΡΙΚΗ ΠΟΣΟΤΙΚΗ ΑΞΟΝΙΚΗ ΤΟΜΟΓΡΑΦΙΑ ΥΨΗΛΗΣ ΕΥΚΡΙΝΕΙΑΣ (High Resolution pQCT): ΚΕΡΚΙΔΑ, ΚΝΗΜΗ

Position Statement

Clinical Use of Quantitative Computed Tomography and Peripheral Quantitative Computed Tomography in the Management of Osteoporosis in Adults: The 2007 ISCD Official Positions

*Klaus Engelke,^{*1,2,a} Judith E. Adams,^{3,b} Gabriele Ambrecht,^{4,b} Peter Augat,^{5,b} Cesar E. Bogado,^{6,b} Mary L. Bouxsein,^{7,b} Dieter Felsenberg,^{8,b} Masako Ito,^{9,b} Sven Prevrhal,^{10,b} Didier B. Hans,^{11,c} and E. Michael Lewiecki^{12,c}*

- ΤΡΙΣΔΙΑΣΤΑΤΗ ΤΕΧΝΙΚΗ
- ΔΙΑΚΡΙΣΗ ΣΠΟΓΓΩΔΟΥΣ-ΦΛΟΙΩΔΟΥΣ ΟΣΤΟΥ
- ΟΓΚΟΜΕΤΡΙΚΗ ΟΣΤΙΚΗ ΠΥΚΝΟΤΗΤΑ
- ΠΛΗΡΟΦΟΡΙΕΣ ΓΕΩΜΕΤΡΙΑΣ
- ΠΛΗΡΟΦΟΡΙΕΣ (ΜΙΚΡΟ)ΑΡΧΙΤΕΚΤΟΝΙΚΗΣ ΣΠΟΓΓΩΔΟΥΣ ΚΑΙ ΦΛΟΙΩΔΟΥΣ
- ΥΨΗΛΗ ΑΚΤΙΝΟΒΟΛΙΑ ΣΤΟΝ ΑΞΟΝΙΚΟ ΣΚΕΛΕΤΟ (ΣΣ, ΙΣΧΙΟ) vs ΠΟΛΥ ΧΑΜΗΛΗ ΑΚΤΙΝΟΒΟΛΙΑ ΣΤΟΝ ΠΕΡΙΦΕΡΙΚΟ ΣΚΕΛΕΤΟ (ΚΕΡΚΙΔΑ, ΚΝΗΜΗ)

High Resolution pQCT



~ 80 μm^3 voxel size

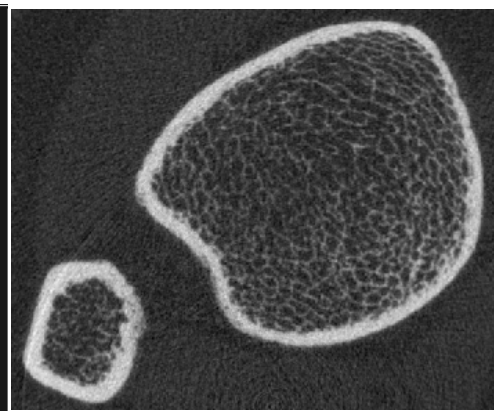
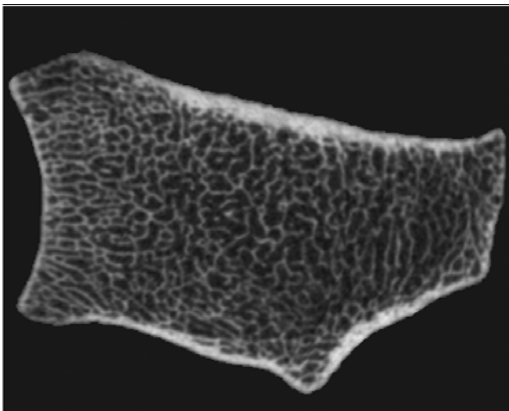
~ 3 min scan time, < 4 μSv

Distal radius and tibia only

Reproducibility:

density: 0.7 - 1.5% *

μ -architecture: 1.5 - 4.4% *



ΟΓΚΟΜΕΤΡΙΚΗ ΟΣΤΙΚΗ ΠΥΚΝΟΤΗΤΑ-ΜΙΚΡΟΑΡΧΙΤΕΚΤΟΝΙΚΗ ΣΠΟΓΓΩΔΟΥΣ/ΦΛΟΙΩΔΟΥΣ

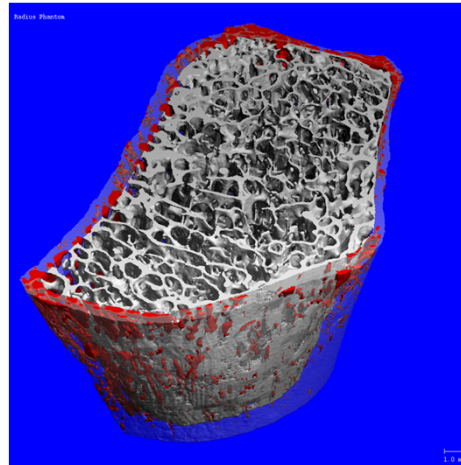
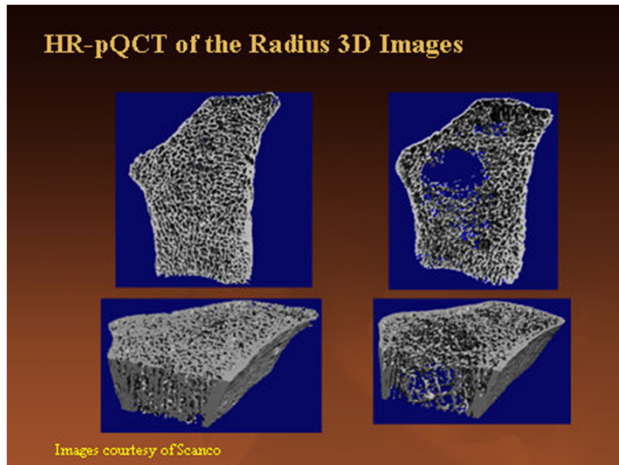
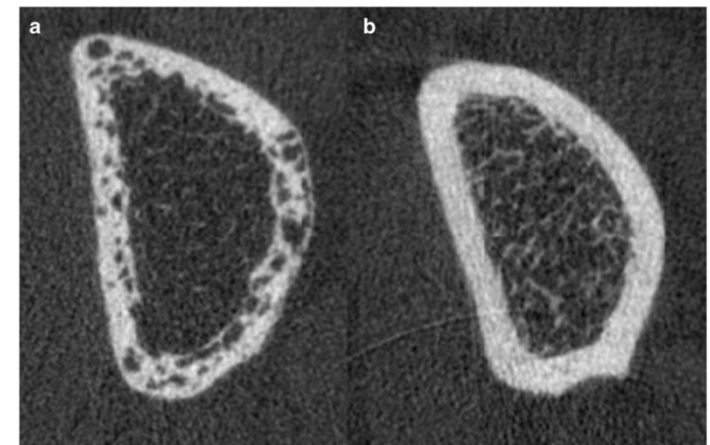
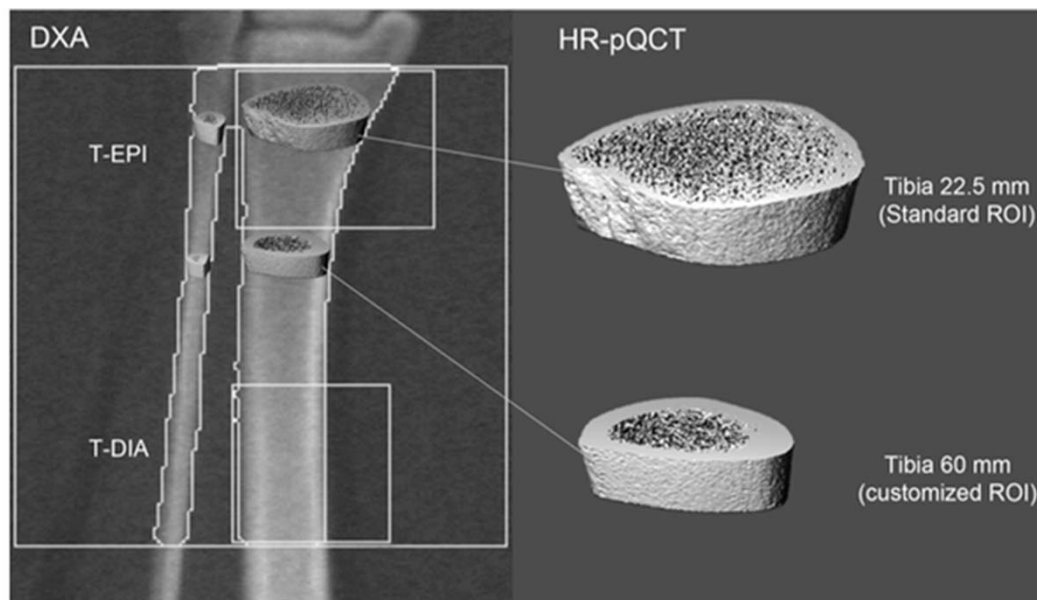


Fig. 2 3D render of HR-pQCT data (82 μm voxel size; in vivo) acquired from a 9.02-mm segment of human distal radius. The cortical shell has been segmented as has the internal cortical porosity (the trabecular envelop has been virtually removed)

- In vivo : HR-pQCT



ΟΤΙ ΝΕΟΤΕΡΟ ΑΠΟ ΤΗΝ ΑΠΕΙΚΟΝΙΣΗ ΤΟΥ ΣΚΕΛΕΤΟΥ

2/2022-2/2023

- ΟΣΤΕΟΠΟΡΩΣΗ
- ΣΑΚΧΑΡΩΔΗΣ ΔΙΑΒΗΤΗΣ **ΚΑΙ** ΟΣΤΑ
- ΒΑΡΙΑΤΡΙΚΗ ΚΑΙ ΟΣΤΑ
- ΥΠΟΚΛΙΝΙΚΟΣ ΥΠΟΘΥΡΕΟΕΙΔΙΣΜΟΣ ΚΑΙ ΟΣΤΑ
- ΜΕΣΟΓΕΙΑΚΗ ΑΝΑΙΜΙΑ ΚΑΙ ΟΣΤΑ

Effect of Denosumab Compared With Risedronate on Bone Strength in Patients Initiating or Continuing Glucocorticoid Treatment

Piet Geusens,^{1,2} Melissa SAM Bevers,^{3,4,5} Bert van Rietbergen,^{5,6} Osvaldo D Messina,⁷ Eric Lespessailles,⁸ Beatriz Oliveri,⁹ Roland Chapurlat,¹⁰ Klaus Engelke,^{11,12} Arkadi Chines,¹³ Shuang Huang,¹³ Kenneth G Saag,¹⁴ and Joop P van den Bergh^{1,2,3,4}

Table 1. Baseline Characteristics

	GC-initiating		GC-continuing	
	Risedronate (N = 24)	Denosumab (N = 32)	Risedronate (N = 30)	Denosumab (N = 24)
Female sex	15 (62.5)	19 (59.4)	28 (93.3)	19 (79.2)
Premenopause	0 (0.0)	1 (5.3)	0 (0.0)	1 (5.3)
Postmenopause	15 (100.0)	18 (94.7)	28 (100.0)	18 (94.7)
Age (years)	66.0 ± 13.1	68.5 ± 9.8	64.2 ± 8.8	63.6 ± 9.8
Race				
White	24 (100.0)	32 (100.0)	30 (100.0)	23 (95.8)
Asian	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Black or African American	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.2)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Baseline daily GC dose (mg) ^a	18.91 ± 9.91	21.41 ± 15.68	10.32 ± 6.52	11.33 ± 4.95
Duration of prior GC use				
<12 months	24 (100.0)	32 (100.0)	4 (13.3)	4 (16.7)
≥12 months	0 (0.0)	0 (0.0)	26 (86.7)	20 (83.3)
BMD T-score (DXA)				
Lumbar spine	-0.77 ± 1.83 ^b	-0.98 ± 1.95	-2.60 ± 1.08	-1.64 ± 1.80
Total hip	-0.77 ± 0.79	-1.15 ± 0.97 ^b	-1.73 ± 0.86	-1.62 ± 0.85

GC = glucocorticoid; BMD = bone mineral density; DXA = dual-energy X-ray absorptiometry.

Data are reported as n (%) or mean ± standard deviation.

^aDose in prednisone equivalents.

^bAssessed in N-1 individuals.

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Table 2. Baseline Characteristics of HR-pQCT Measurements in Patients Initiating Glucocorticoid Therapy (GC-I) or on Long-Term Therapy (GC-C) at the Distal Radius and Tibia

	GC-initiating		GC-continuing	
	Risedronate (N = 24) n = 24	Denosumab (N = 32) n = 29	Risedronate (N = 30) n = 21	Denosumab (N = 24) n = 20
Distal radius				
μFE				
Stiffness (kN/mm)	77.8 ± 28.6 ^a	75.3 ± 33.4 ^b	49.7 ± 9.81 ^e	59.6 ± 23.1 ^f
FL (kN)	3.94 ± 1.40 ^a	3.78 ± 1.64 ^b	2.51 ± 0.50 ^e	2.98 ± 1.17 ^f
Total bone				
Total volume (mm ³)	2842.5 ± 639.1 ^c	3060.5 ± 822.7	2538.6 ± 447.2 ^g	2603.6 ± 658.4
Tt.BMD (mg HA/cm ³)	279.2 ± 75.8	267.5 ± 69.5	213.5 ± 54.3	236.0 ± 70.0
Cortical bone				
Cortical volume (mm ³)	522.5 ± 148.9 ^c	535.8 ± 162.7	416.3 ± 71.4 ^g	458.5 ± 98.3
Ct.BMD (mg HA/cm ³)	792.1 ± 69.4	790.7 ± 77.3	787.4 ± 48.4	777.5 ± 104.8
Ct.Th (mm)	0.68 ± 0.23	0.67 ± 0.24	0.53 ± 0.13	0.58 ± 0.23
Ct.Po (%)	2.55 ± 1.12 ^c	2.75 ± 1.24	2.67 ± 1.10 ^g	2.83 ± 1.34 ^h
Trabecular bone				
Tb.BMD (mg HA/cm ³)	149.1 ± 49.7	140.0 ± 46.8	95.2 ± 42.9	106.6 ± 50.3
Tb.BV/TV (-)	0.12 ± 0.04	0.12 ± 0.04	0.08 ± 0.04	0.09 ± 0.04
Tb.N (mm ⁻³)	1.78 ± 0.37	1.71 ± 0.39	1.36 ± 0.44	1.44 ± 0.47
Tb.Th (mm)	0.07 ± 0.01	0.07 ± 0.01	0.06 ± 0.01	0.06 ± 0.01
Tb.Sp (mm)	0.52 ± 0.15	0.56 ± 0.21	0.79 ± 0.40	0.72 ± 0.30

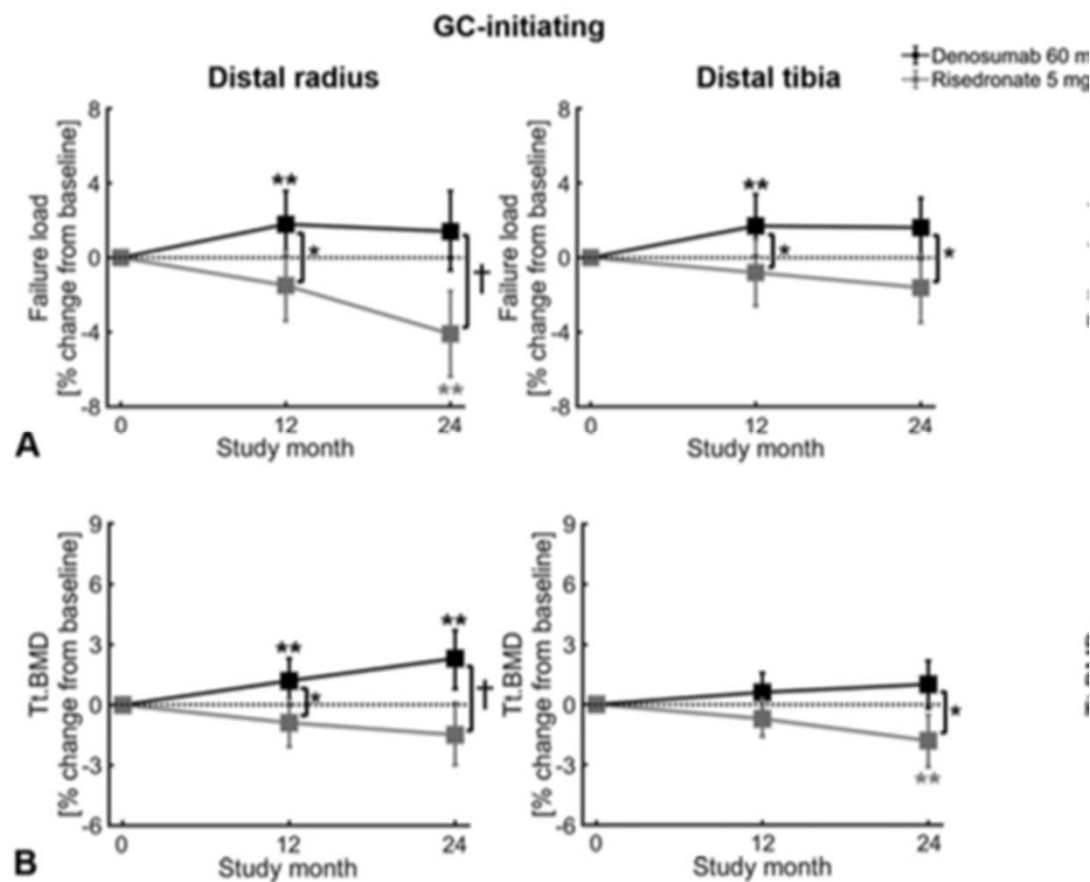
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	GC-initiating		GC-continuing	
	Risedronate (N = 24)	Denosumab (N = 32)	Risedronate (N = 30)	Denosumab (N = 24)
Distal tibia	n = 24	n = 29	n = 24	n = 21
μ FE				
Stiffness (kN/mm)	197.8 \pm 56.3 ^d	194.4 \pm 65.5 ^b	134.4 \pm 27.6 ^h	155.9 \pm 37.8 ^e
FL (kN)	9.99 \pm 2.76 ^d	9.85 \pm 3.20 ^b	6.90 \pm 1.44 ^h	7.95 \pm 1.83 ^e
Total bone				
Total volume (mm ³)	6866.2 \pm 1096.0 ^a	6963.0 \pm 1315.9	6462.9 \pm 1013.9	6345.7 \pm 911.2
Tt.BMD (mg HA/cm ³)	259.5 \pm 69.7	261.7 \pm 55.3	192.8 \pm 41.0	232.2 \pm 53.4
Cortical bone				
Cortical volume (mm ³)	1048.5 \pm 319.8 ^a	1085.5 \pm 347.2	803.1 \pm 140.5	925.5 \pm 140.4
Ct.BMD (mg HA/cm ³)	805.3 \pm 61.6	795.1 \pm 60.9	793.5 \pm 61.2	800.2 \pm 88.2
Ct.Th (mm)	1.03 \pm 0.37	1.04 \pm 0.35	0.73 \pm 0.14	0.89 \pm 0.27
Ct.Po (%)	7.16 \pm 1.75 ^a	7.43 \pm 2.12	7.40 \pm 3.18	7.60 \pm 2.88
Trabecular bone				
Tb.BMD (mg HA/cm ³)	151.3 \pm 42.2	155.1 \pm 32.3	106.3 \pm 41.4	127.6 \pm 45.8
Tb.BV/TV (-)	0.13 \pm 0.04	0.13 \pm 0.03	0.09 \pm 0.03	0.11 \pm 0.04
Tb.N (mm ⁻¹)	1.72 \pm 0.38	1.81 \pm 0.31	1.44 \pm 0.40	1.63 \pm 0.46
Tb.Th (mm)	0.07 \pm 0.01	0.07 \pm 0.01	0.06 \pm 0.01	0.07 \pm 0.01
Tb.Sp (mm)	0.53 \pm 0.13	0.50 \pm 0.10	0.68 \pm 0.19	0.62 \pm 0.32

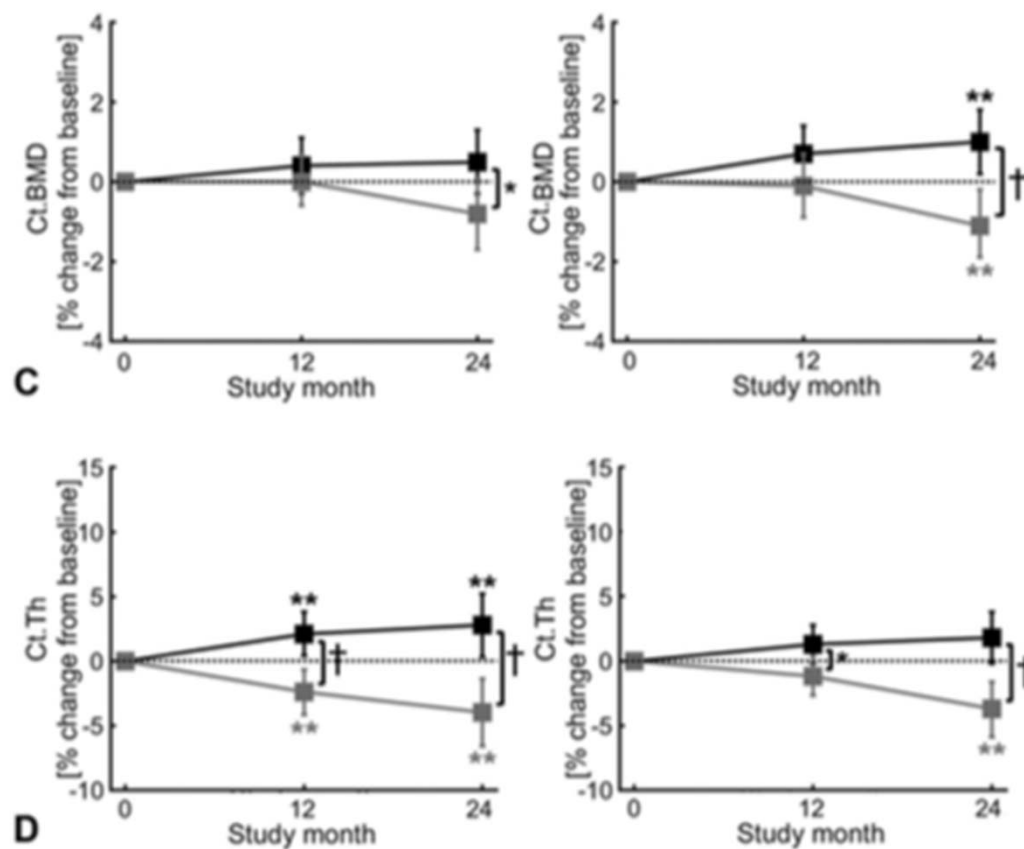
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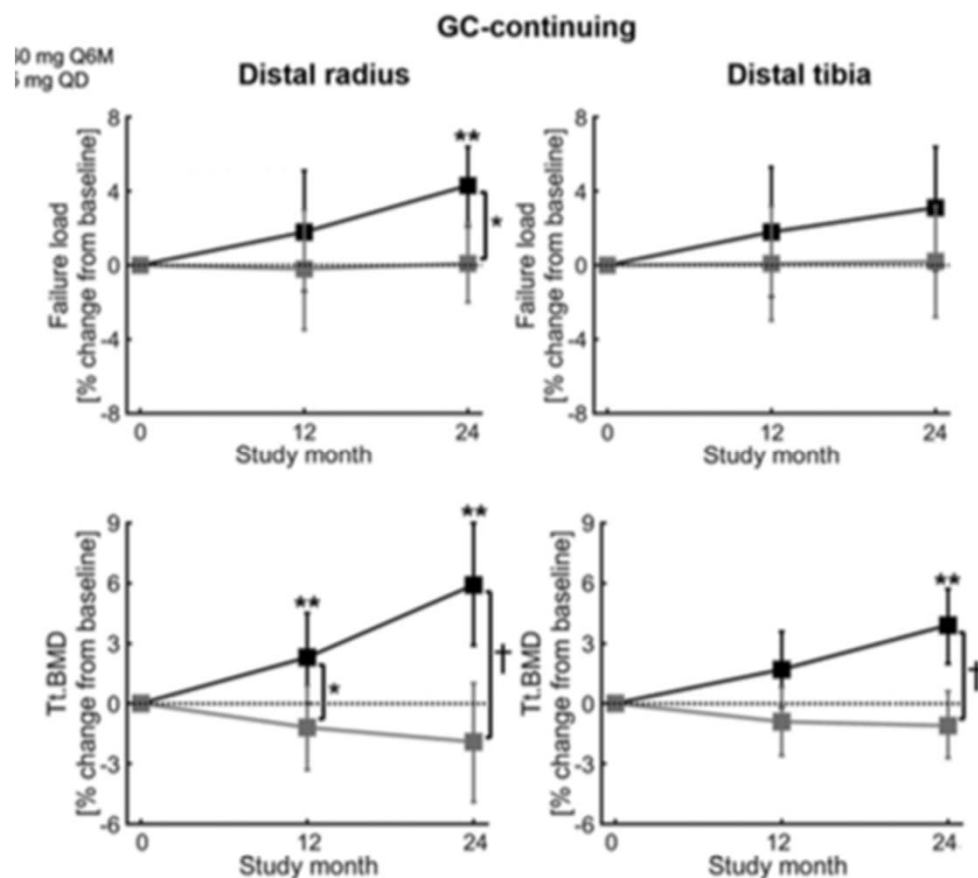
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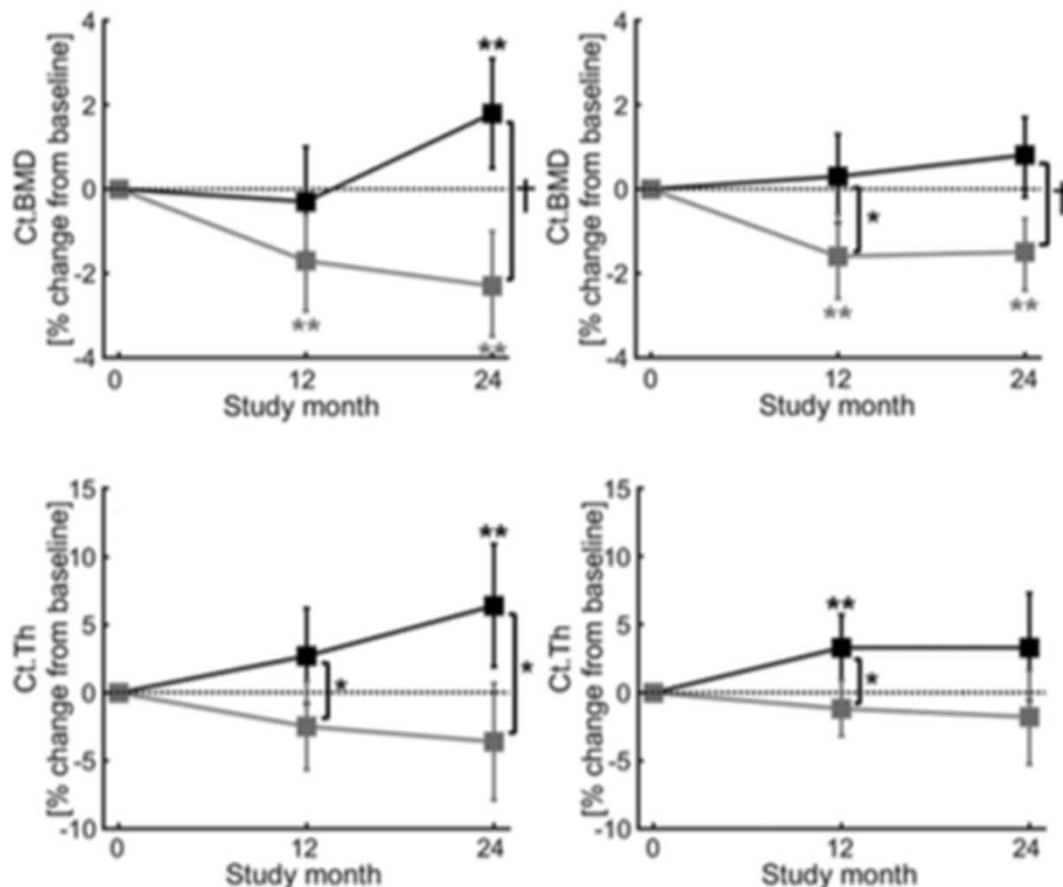
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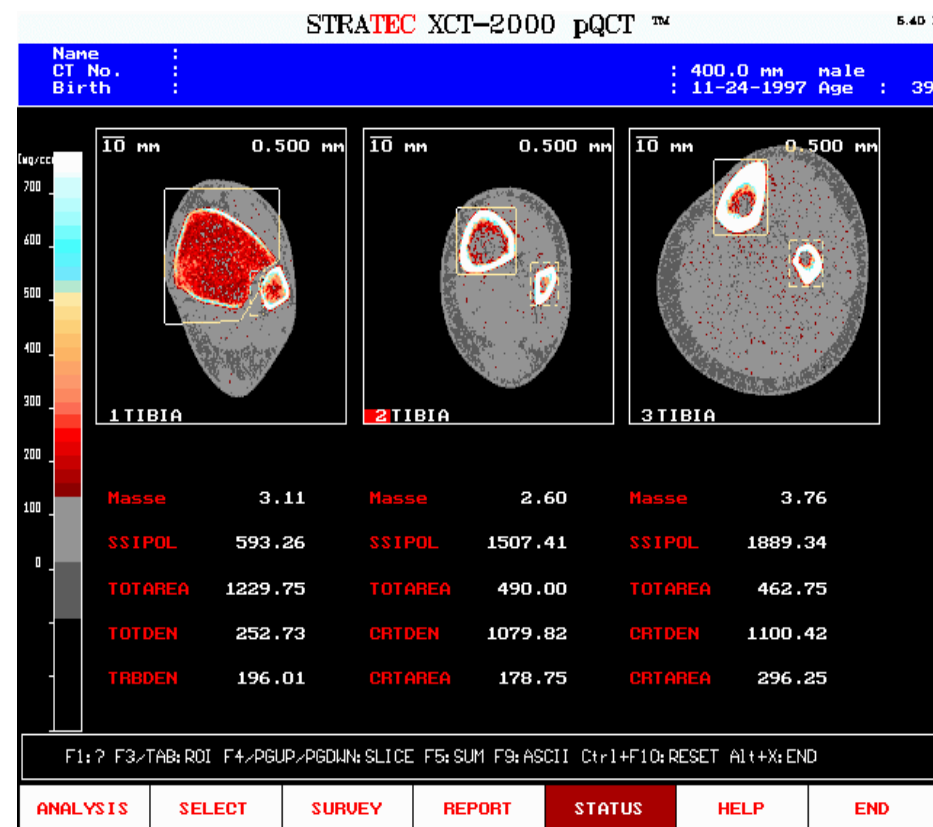
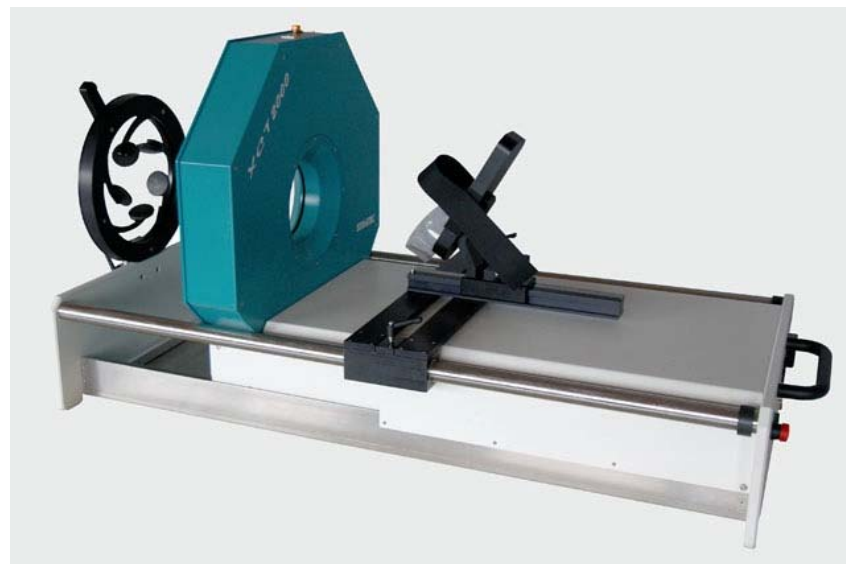
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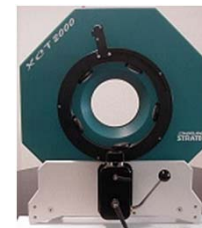
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Greater pQCT Calf Muscle Density Is Associated with Lower Fracture Risk, Independent of FRAX, Falls and BMD: A Meta-Analysis in the Osteoporotic Fractures in Men (MrOS) Study

Nicholas C. Harvey,^{1,2} Eric Orwoll,³ Jane A. Cauley,⁴ Timothy Kwok,⁵ Magnus K. Karlsson,⁶ Björn E. Rosengren,⁶ Eva Ribom,⁷ Peggy M. Cawthon,^{8,9} Kristine Ensrud,^{10,11} Enwu Liu,¹² Faidra Laskou,¹ Kate A. Ward,¹ Elaine M. Dennison,¹ Cyrus Cooper,^{1,2,13} John A. Kanis,^{12,14} Liesbeth Vandenput,^{12,15} Mattias Lorentzon,^{12,15} Claes Ohlsson,¹⁵ Dan Mellström,¹⁵ Helena Johansson,^{12,15} and Eugene McCloskey^{14,16}





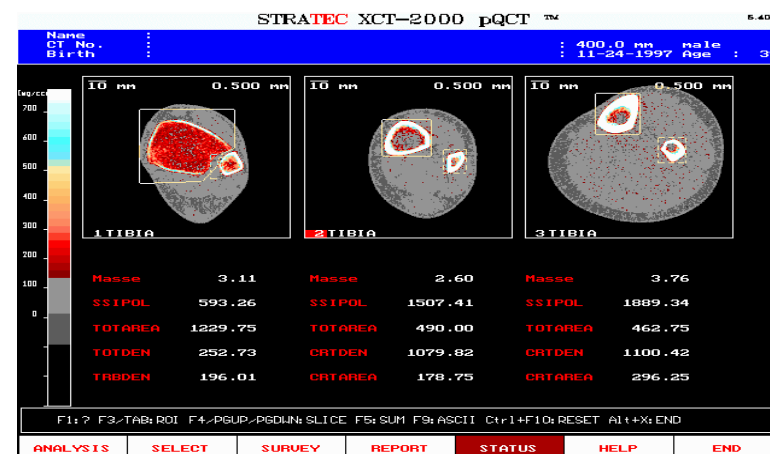
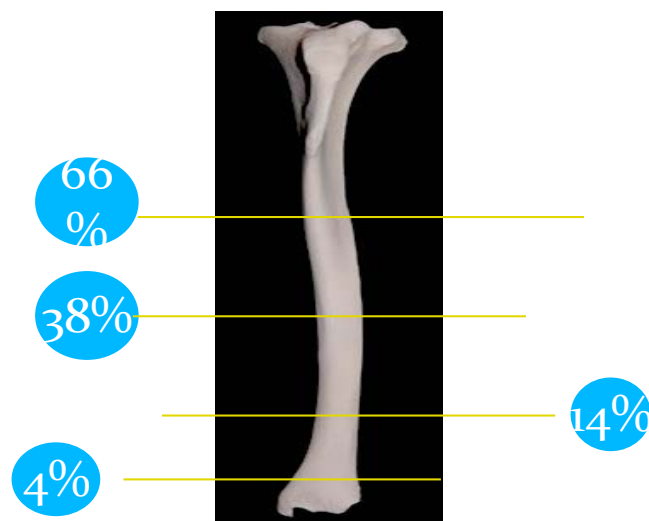
ΠΕΡΙΦΕΡΙΚΗ ΠΟΣΟΤΙΚΗ ΑΞΟΝΙΚΗ ΤΟΜΟΓΡΑΦΙΑ (pQCT)

ΣΕ ΚΑΘΕ ΤΟΜΗ ΕΞΕΤΑΖΟΥΜΕ:

- AREA MM² (TOTAL AREA, TRABECULAR AREA, SUBCORTICAL AREA, CORTICAL AREA)
- MINERAL CONTENT, MG/CM (TOTAL CONTENT, TRABECULAR CONTENT, SUBCORTICAL CONTENT, CORTICAL CONTENT)
- BMD, MG/CM³ (TOTAL DENSITY, TRABECULAR DENSITY, SUBCORTICAL DENSITY, CORTICAL DENSITY)
- PERIOSTEAL / ENDOSTEAL CIRCUMFERENCE, MM² (PERI-C, ENDO-C)
- CORTICAL THICKNESS, MM

MUSCLE AREAS: 66% (BONE TO MUSCLE RATIO) AND OR 38%

MUSCLE DENSITY (STRATEC XCT 3000)



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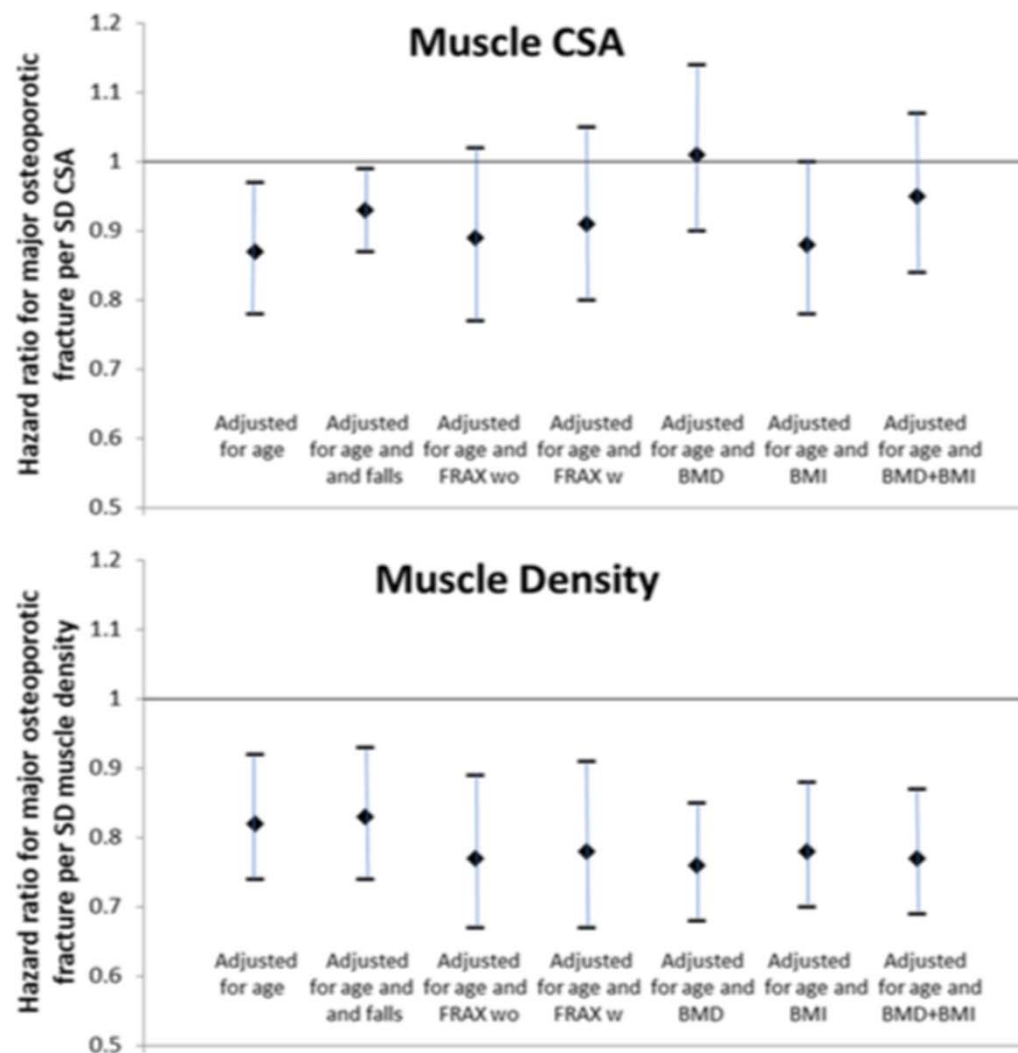
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Table 1. Baseline Characteristics and Fracture Outcomes of Study Participants by Country

Characteristic	Hong Kong	Sweden	US
<i>n</i>	1662	1521	991
Person-years (total)	13541.8	8057.5	7777.5
Age (years), mean (range)	73.9 (66.0–94.0)	79.5 (73.1–87.7)	77.0 (69.0–93.0)
BMI, mean ± SD	23.4 ± 3.1	26.2 ± 3.3	27.8 ± 3.7
Previous fracture (%)	15.2	37.1	29.6 (<i>n</i> = 989)
Family history hip fracture, <i>n</i> (%)	1382 (5.1)	1000 (13.5)	785 (13.4)
Smoker (%)	9.8	7.8 (<i>n</i> = 1517)	2.9
Glucocorticoids (%)	0.2	1.4 (<i>n</i> = 1518)	2.3
Rheumatoid arthritis (%)	1.0	1.7 (<i>n</i> = 1507)	5.7
Excess alcohol (%)	18.8	2.2 (<i>n</i> = 1497)	7.5 (<i>n</i> = 600)
BMD FN T-score, mean ± SD	−1.41 ± 0.91	−0.92 ± 1.02	−0.53 ± 1.06
Previous fall (%)	17.3	13.2	23.2
Muscle cross-sectional area (cm ²), mean ± SD	35.4 ± 7.0	38.9 ± 7.4	75.5 ± 11.8
Muscle density (mg/cm ³), mean ± SD	77.0 ± 3.6	69.6 ± 3.7	70.5 ± 4.6
FRAX MOF without BMD, mean ± SD	7.9 ± 3.4 (<i>n</i> = 1382)	15.7 ± 6.7 (<i>n</i> = 976)	10.6 ± 5.0 (<i>n</i> = 478)
FRAX hip without BMD, mean ± SD	4.3 ± 3.0 (<i>n</i> = 1382)	9.6 ± 6.4 (<i>n</i> = 976)	4.8 ± 4.2 (<i>n</i> = 478)
FRAX MOF with BMD, mean ± SD	7.2 ± 3.7 (<i>n</i> = 1382)	11.8 ± 6.7 (<i>n</i> = 976)	8.2 ± 4.3 (<i>n</i> = 478)
FRAX hip with BMD, mean ± SD	3.5 ± 3.1 (<i>n</i> = 1382)	6.2 ± 6.2 (<i>n</i> = 976)	2.8 ± 3.2 (<i>n</i> = 478)
FU (years), mean ± SD	8.1 ± 2.3	5.3 ± 2.0	7.8 ± 2.2
Any fx, <i>n</i> (%)	161 (9.7)	238 (15.6)	137 (13.8)
Osteoporotic fx, <i>n</i> (%)	125 (7.5)	206 (13.5)	103 (10.4)
MOF fx, <i>n</i> (%)	94 (5.7)	180 (11.8)	68 (6.9)
Hip fx, <i>n</i> (%)	47 (2.8)	78 (5.1)	31 (3.1)

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Table 2. Associations between Muscle Cross-Sectional Area and Incident Fracture (US, Hong Kong, and Sweden)

	Adjusted for	Any fx	Ost fx	MOF	Hip fx
Muscle cross-sectional area	Base: Age and follow-up time	0.88 (0.80, 0.96)	0.87 (0.79, 0.97)	0.87 (0.78, 0.97)	0.84 (0.72, 1.00)
	Base + FN BMD <i>T</i> -score	0.98 (0.90, 1.08)	0.99 (0.89, 1.10)	1.01 (0.90, 1.14)	1.04 (0.88, 1.24)
	Base + FRAX MOF wo	0.88 (0.79, 0.99)	0.85 (0.75, 0.96)	0.89 (0.77, 1.02)	0.83 (0.69, 1.01)
	Base + FRAX MOF w	0.90 (0.81, 1.01)	0.87 (0.77, 0.98)	0.91 (0.80, 1.05)	0.87 (0.71, 1.05)
	Base + prior falls	0.88 (0.80, 0.97)	0.87 (0.79, 0.96)	0.93 (0.87, 0.99)	0.85 (0.72, 1.00)
	Base + BMI	0.88 (0.79, 0.97)	0.87 (0.78, 0.98)	0.88 (0.78, 1.00)	0.88 (0.74, 1.06)
	Base + FN BMD <i>T</i> -score and BMI	0.92 (0.84, 1.02)	0.93 (0.83, 1.03)	0.95 (0.84, 1.07)	0.97 (0.81, 1.16)
	Base + muscle density	0.87 (0.80, 0.95)	0.87 (0.78, 0.96)	0.87 (0.78, 0.97)	0.84 (0.72, 0.99)

Values are gradient of risk (GR) (95% CI). Models are presented adjusted for age and FU time alone and then additionally for either prior falls, FRAX MOF probability without BMD (FRAX MOF wo), FRAX MOF probability with BMD (FRAX MOF w), BMI, FN BMD *T* score or muscle density. *N* = 4174 except for +FRAX with and without BMD (*n* = 2836).

BMI = body mass index; FN = femoral neck; FU = follow-up; Fx = fracture; MOF = major osteoporotic fracture; Ost = osteoporotic; w = with; wo = without.

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Discussion

We have demonstrated, consistent with our previous findings with DXA appendicular lean mass, that in this large population of older men across three countries, calf muscle CSA, assessed by pQCT, is only modestly predictive of incident fracture and this relationship is no longer apparent after adjustment for fn BMD. In contrast, calf muscle density, again assessed by pQCT, remained predictive of fracture outcomes after adjustment for fn BMD, and independently of adjustment for FRAX probability, prior falls, and BMI.

Table 3. Associations Between Muscle Density and Incident Fracture (US, Hong Kong and Sweden)

	Adjusted for	Any fx	Ost fx	MOF	Hip fx
Muscle density	Base: Age and follow-up time	0.85 (0.78, 0.93)	0.82 (0.74, 0.90)	0.82 (0.74, 0.92)	0.78 (0.66, 0.91)
	Base + FN BMD T-score	0.80 (0.73, 0.87)	0.76 (0.69, 0.84)	0.76 (0.68, 0.85)	0.69 (0.59, 0.82)
	Base + FRAX MOF wo	0.79 (0.71, 0.88)	0.78 (0.69, 0.88)	0.77 (0.67, 0.89)	0.73 (0.60, 0.89)
	Base + FRAX MOF w	0.81 (0.72, 0.90)	0.79 (0.70, 0.89)	0.78 (0.67, 0.91)	0.74 (0.61, 0.90)
	Base + prior falls	0.86 (0.78, 0.94)	0.82 (0.75, 0.91)	0.83 (0.74, 0.93)	0.78 (0.66, 0.92)
	Base + BMI	0.82 (0.74, 0.90)	0.78 (0.70, 0.87)	0.78 (0.70, 0.88)	0.72 (0.61, 0.86)
	Base + FN BMD T-score and BMI	0.81 (0.74, 0.89)	0.77 (0.70, 0.86)	0.77 (0.69, 0.87)	0.71 (0.60, 0.84)
	Base + cross sectional area	0.85 (0.77, 0.93)	0.81 (0.74, 0.90)	0.82 (0.73, 0.92)	0.77 (0.65, 0.91)

Values are gradient of risk (GR) (95% CI). Models are presented adjusted for age and FU time alone and then additionally for either prior falls, FRAX MOF probability without BMD (FRAX MOF wo), FRAX MOF probability with BMD (FRAX MOF w), BMI, FN BMD T-score or muscle cross-sectional area. $N = 4174$ except for +FRAX with and without BMD ($n = 2836$).

BMI = body mass index; Fx = fracture; FN = femoral neck; FU = follow-up; MOF = major osteoporotic fracture; Ost = osteoporotic; w = with; wo = without.

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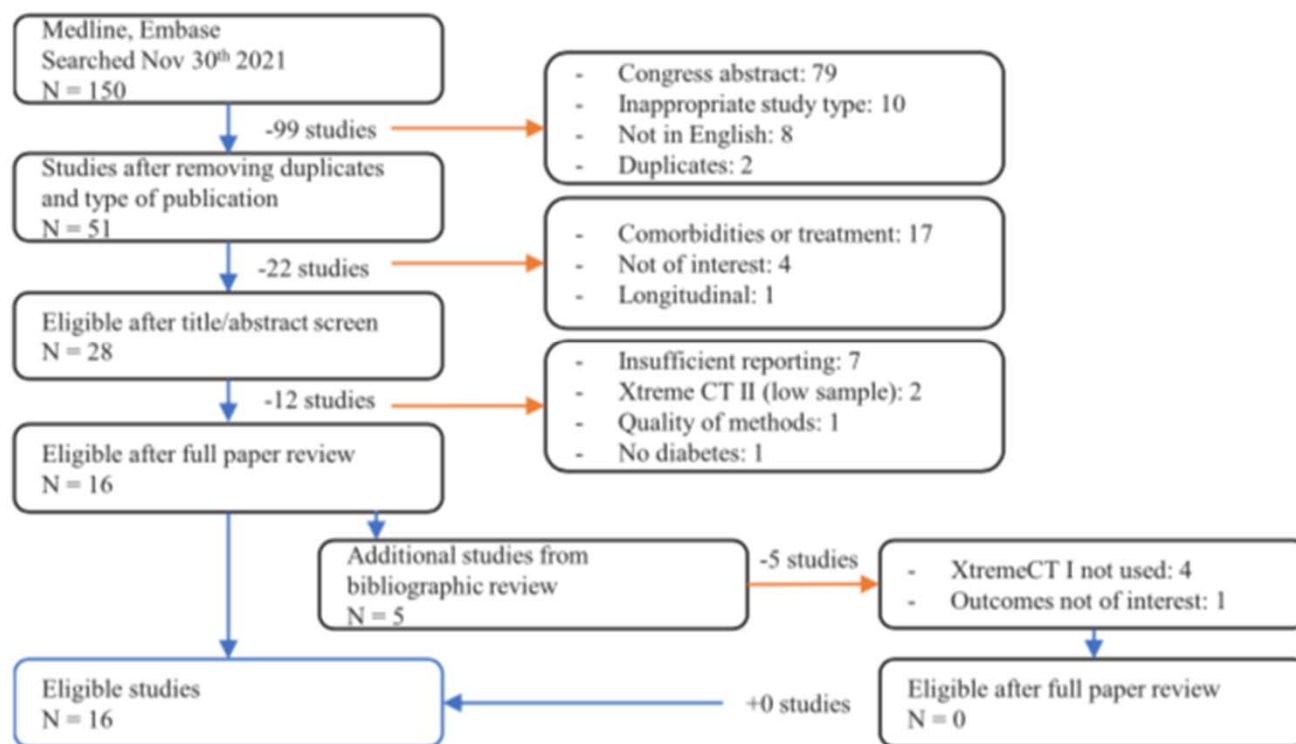
Although the majority of sarcopenia definitions that incorporate an estimate of muscle mass using **DXA appendicular lean mass (ALM)**, our results have implications for the use of **CT muscle measures**, which can be accommodated in the most recent guidelines from the **European Working Group on Sarcopenia in Older people**.⁽³¹⁾ Consistent with our findings in MrOS, where the predictive capacity for fracture of sarcopenia definitions incorporating DXA ALM was attenuated by adjustment for femoral neck BMD,⁽³²⁾ **the present results suggest that a similar situation would arise using pQCT muscle CSA**. Overall then, there seems little evidential support for the use of DXA or pQCT muscle mass/area measures in the assessment of sarcopenia⁽²⁸⁾; **muscle density might offer some extra predictive value, but of course would need to be balanced against the lack of pQCT scanners in most clinical departments and the high radiation dose associated with the standard CT body scanner**. An alternative strategy, particularly with the advent of machine learning image analysis, might be **opportunistic use of images obtained through routine body CT scanning**, as is being undertaken for detection of vertebral fractures.⁽³³⁾ **Creatine dilution** has shown some promise, and data supporting its predictive value for fracture independent of BMD



Meta-analysis of Diabetes Mellitus-Associated Differences in Bone Structure Assessed by High-Resolution Peripheral Quantitative Computed Tomography

Matthias Walle¹ · Danielle E. Whittier¹ · Morten Frost² · Ralph Müller¹ · Caitlyn J. Collins^{1,3}

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Table 1 Primary HR-pQCT parameters included in the meta-analysis

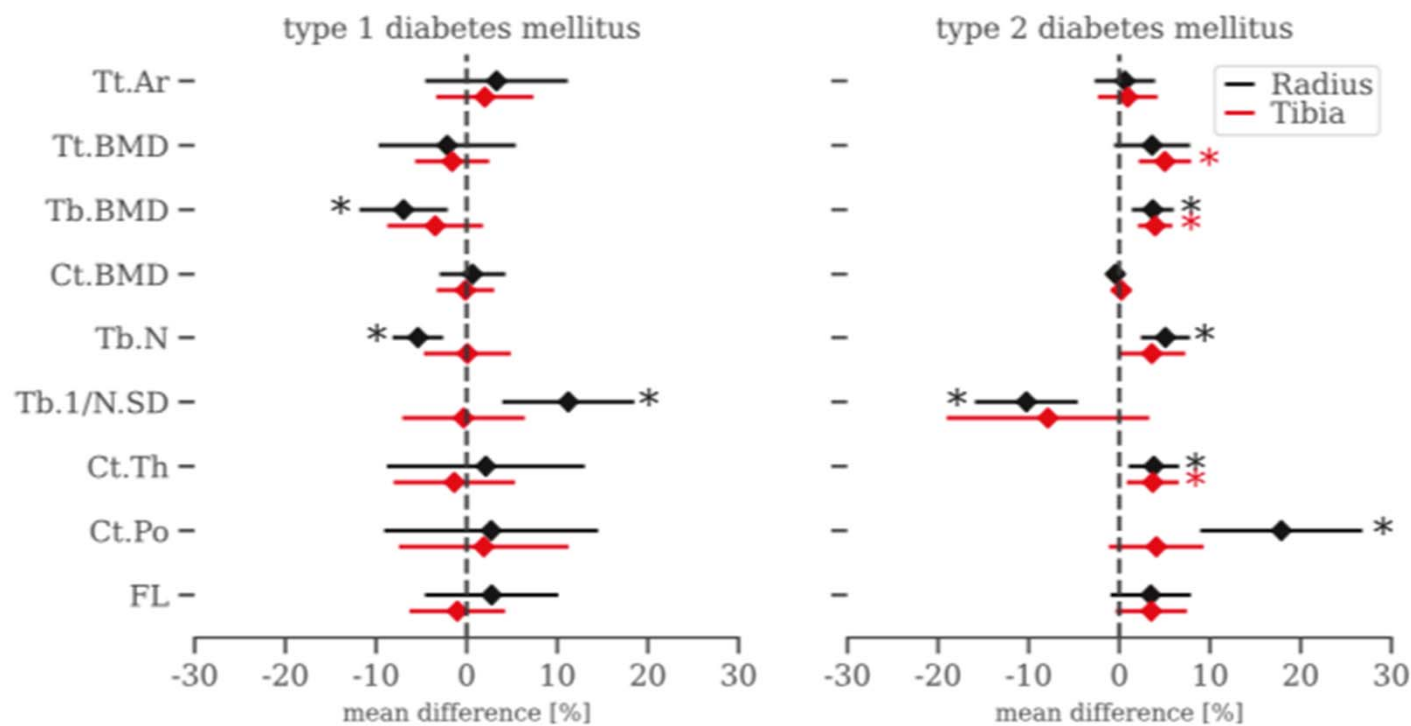
Parameter (abbreviation)	Description	Units
Areal (Ar) bone measures		
Total (Tt.Ar)	Total bone area	mm ²
Volumetric bone mineral density (BMD) measures		
Total (Tt.BMD)	Total volumetric density	mg HA/cm ³
Cortical (Ct.BMD)	Cortical volumetric density	mg HA/cm ³
Trabecular (Tb.BMD)	Trabecular volumetric density	mg HA/cm ³
Cortical (Ct.) measures		
Cortical thickness (Ct.Th)	Mean cortical thickness, calculated directly	mm
Cortical porosity (Ct.Po)	Cortical porosity, calculated using a density-based method [33]	%
Trabecular (Tb.) measures		
Trabecular number (Tb.N)	Mean number of trabeculae per unit length	mm ⁻¹
Inhomogeneity of trabecular network (Tb. I/N.SD)	Deviation of the distance between trabeculae	mm
Finite element analysis (FEA) measures		
Failure Load (FL)	Estimated maximum load using the Pistoia criterion [34]	N



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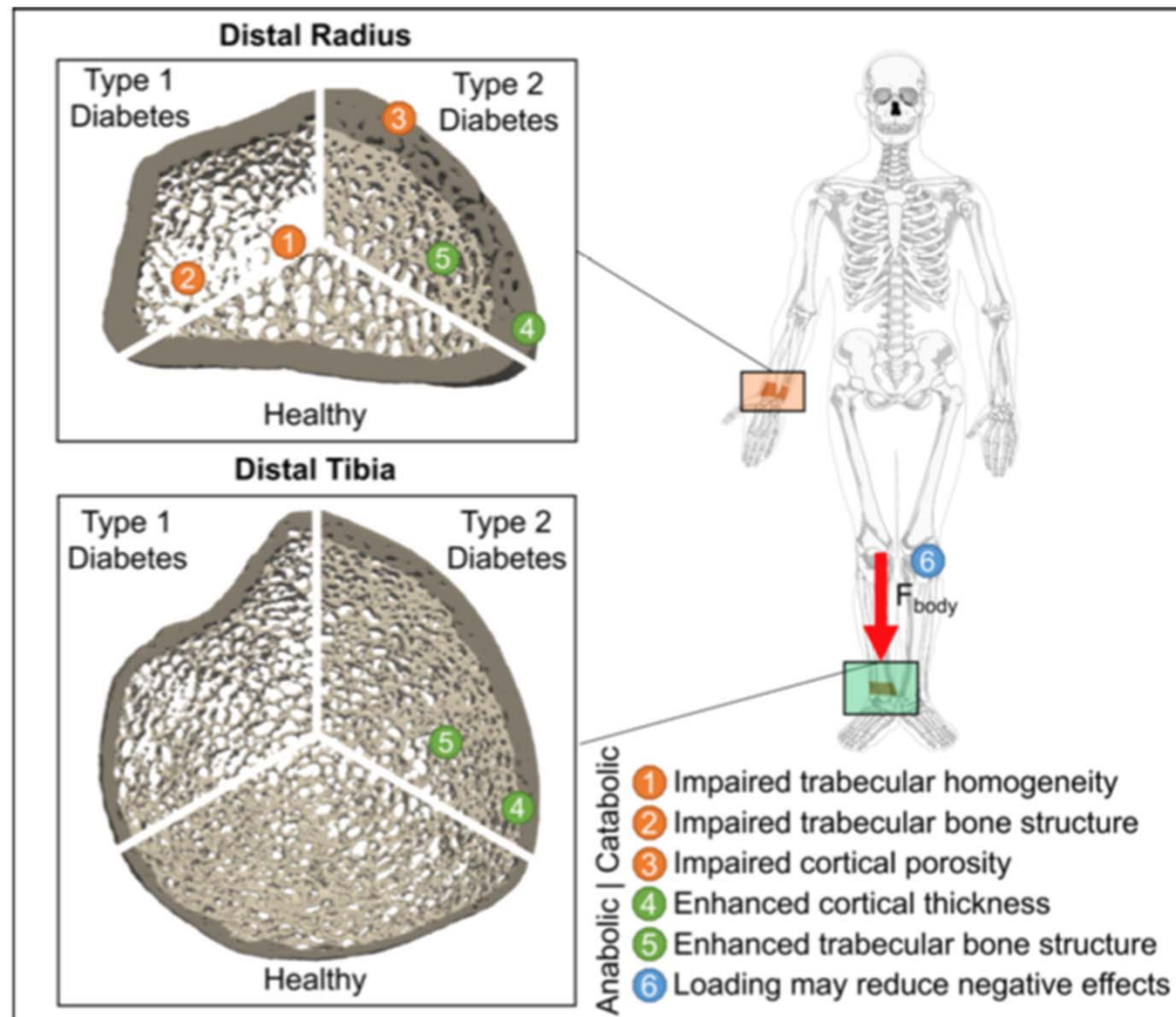




Meta-analysis of Diabetes Mellitus-Associated Differences in Bone Structure Assessed by High-Resolution Peripheral Quantitative Computed Tomography

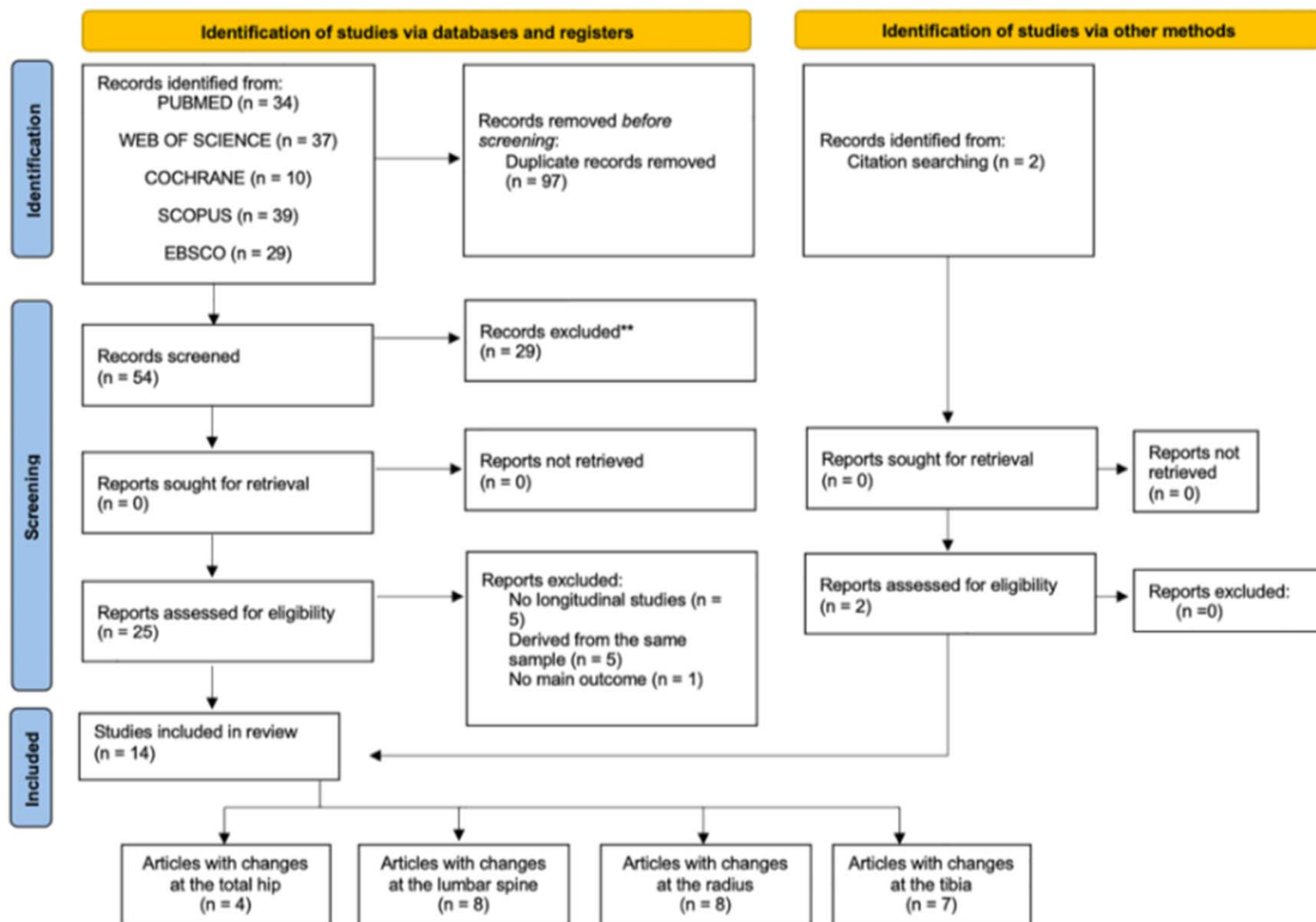
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Changes in volumetric bone mineral density and bone quality after Roux-en-Y gastric bypass: A meta-analysis with meta-regression

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TABLE 1 Characteristics of the included studies

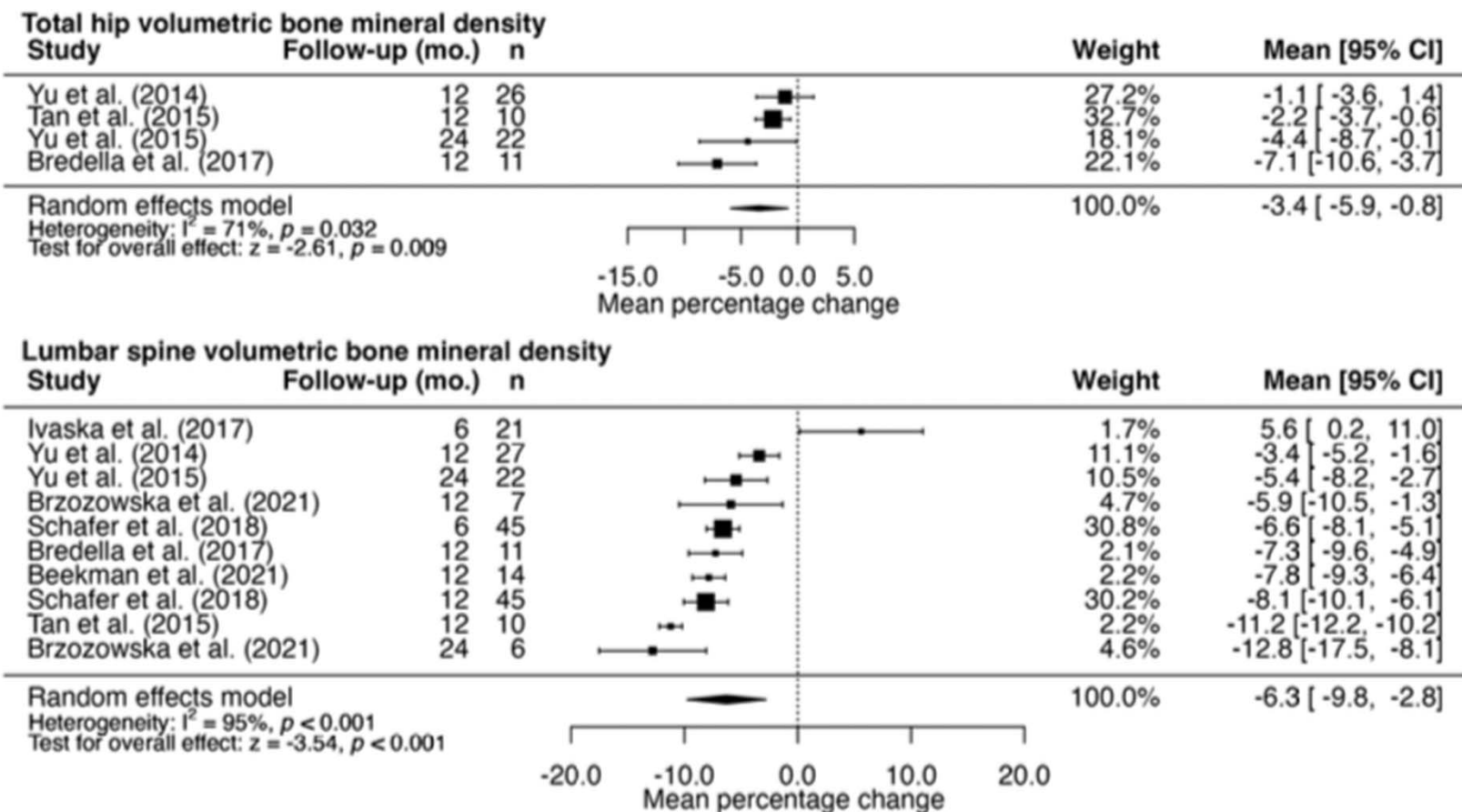
Author and year	Sample size (n%; %q; %postm)	Sample characteristics [mean ± SD or median (IQR)]		Post-RYGB drugs and supplements	Outcomes	Follow-up (months)	Quality
		Age (years)	Pre-RYGB-BMI (kg m ⁻²)				
Beekman et al. 2021 ⁴⁴	14; 100%q; 100%	58 ± 4	38 ± 4	Omeprazole and calcium carbonate/ cholecalciferol	QCT: LS	12	Good
Bredella et al. 2017 ³²	11; 90%q; NR	48.6 ± 8.9	44.1 ± 5.1	NR	QCT: TH, LS; DXA: TH, LS	12	Good
Brzozowska et al. 2021 ⁴⁵	7; 71%q; 60%	51.1 ± 7.6	42.3 ± 7.7	Vitamin D (25-OH > 75 nmol/L) and calcium (≥ 1000 mg/day)	QCT: LS; DXA: TH, LS, 1/3radius	12, 24	Good
Frederiksen et al. 2016 ⁴⁶	24; 58%q; 6.7%	41.2 ± 8.06	42.9 [38.7 to 47.0]	Daily intake of vitamin D (1920 IU) and calcium (800 mg)	HR-pQCT: 1/3radius, tibia; DXA: TH, LS	6, 12	Good
Hansen et al. 2020 ⁴⁷	17; 59%q; 5.9%	43 ± 9	42 ± 6	Daily intake of vitamin D3 (38 mg), calcium carbonate (1000–1200 mg) and multivitamin tablet	HR-pQCT: 1/3radius, tibia; DXA: TH, LS	24, 84	Fair
lvaska et al. 2017 ¹⁵	21; 91%q; NR	47.1 ± 9.9	48.5	Daily intake of vitamin D3 (20 µg), calcium (1000 mg) and multivitamin tablet (including 10 µg vitamin D3)	QCT: LS	6	Good
Krez et al. 2021 ²⁹	17; 100%q; 41%	43 ± 10	44 ± 5	Vitamin D (50,000 IU/week)	HR-pQCT: 1/3radius, tibia; DXA: TH, LS, 1/3 radius	12, 24, 36, 48	Good
Lindeman et al. 2018 ⁴⁸	21; 81%q; 44%	51.1 ± 14	45 ± 7	Daily intake of vitamin D (3000 IU) and calcium (1200–1500 mg)	QCT: LS; HR-pQCT: 1/3radius, tibia; DXA: TH, LS	24, 42, 60	Fair
Murai et al. 2019 ⁴⁹	24; 100%q; 19%	42.1 ± 8.2	48.5 ± 8.1	Daily intake of vitamin D3 (3000 IU), calcium (1200–1500 mg) and protein (≥ 60 g)	HR-pQCT: 1/3radius; DXA: TH, LS, 1/3radius	9	Fair
Schafer et al. 2018 ¹⁴	45; 79%q; 23%	46 ± 12	44 ± 7	Intake of vitamin 25OHD to maintain ≥ 30 ng/ mL and daily intake of calcium (1200 mg)	QCT: LS; HR-pQCT: 1/3radius, tibia; DXA: TH, LS, 1/3radius	6, 12	Good
Shanbhogue et al. 2017 ⁵⁰	23; 61%q; 4%	42.6 ± 7.8	42 [38 to 47]*	NR	HR-pQCT: 1/3radius, tibia; DXA: TH, LS	12, 24	Good
Tan et al. 2015 ⁵¹	10; 50%q; 0%	45.6 ± 9.1	36.7 ± 4.4	Daily intake of calcium (100 mg) and ergocalciferol (50,000 IU)	QCT: TH, LS; DXA: TH, LS	12	Good
Yu et al. 2014 ²²	26; 87%q; 33%	47 ± 14	45 ± 6	NR	QCT: TH, LS; DXA: TH, LS	12	Good
Yu et al. 2015 ²⁰	22; 87%q; 33%	47 ± 14	45 ± 6	Daily intake of vitamin D (3000 IU) and calcium (1200–1500 mg)	QCT: TH, LS; HR-pQCT: 1/3radius, tibia; DXA: TH, LS	12, 24	Fair

q, women; BMI, body mass index; DXA, dual-energy X-ray absorptiometry; HR-pQCT, high resolution peripheral QCT; LS, lumbar spine; NR = not reported; postm, postmenopausal; QCT, quantitative computed tomography; RYGB, Roux-en-Y-gastric bypass; TH, total hip.

*Range.

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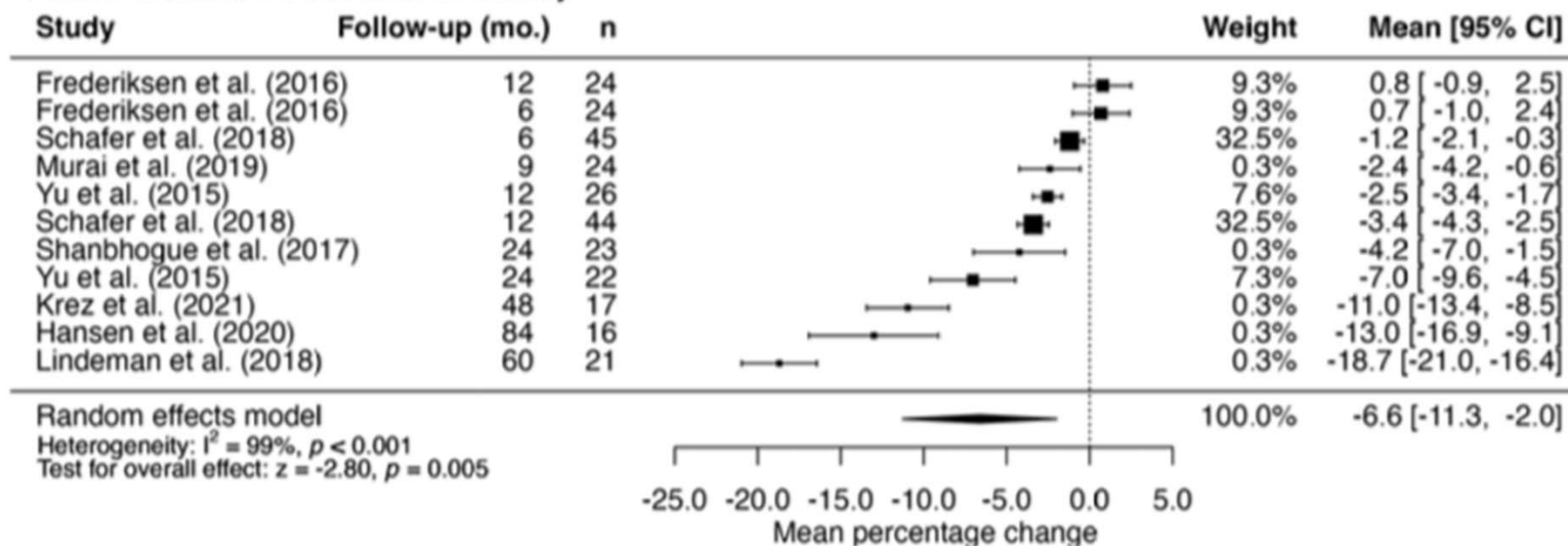
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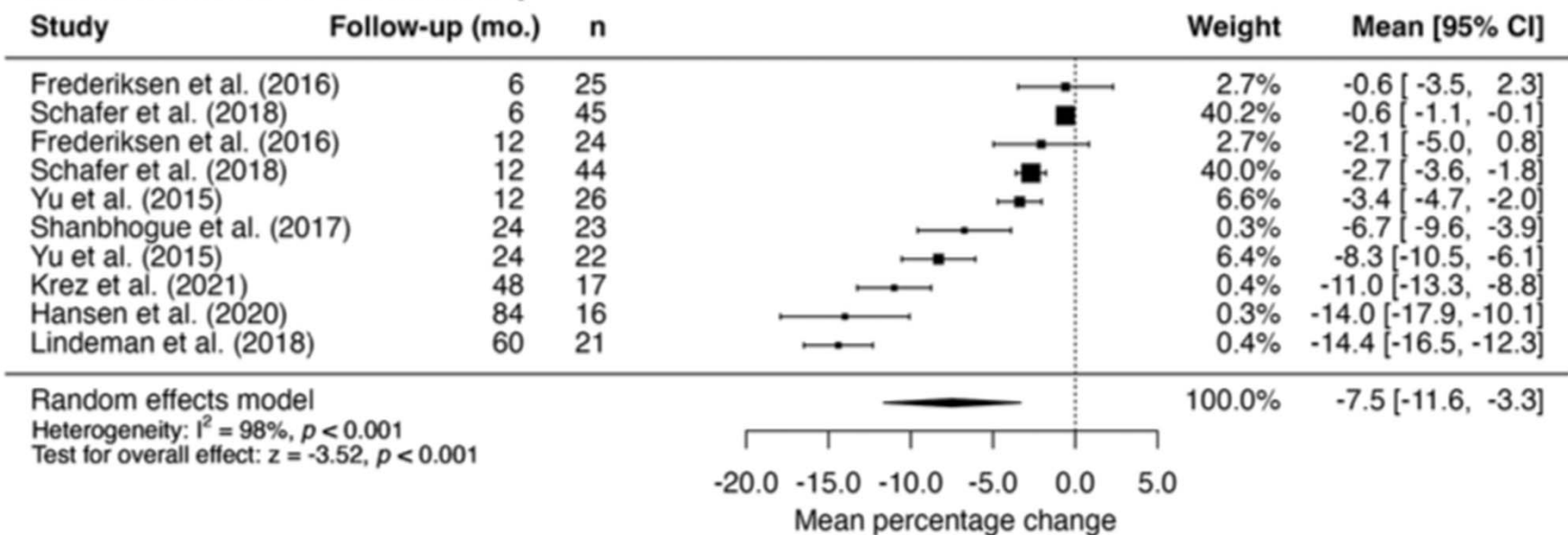
Radius volumetric bone mineral density



Changes in volumetric bone mineral density and bone quality after Roux-en-Y gastric bypass: A meta-analysis with meta-regression

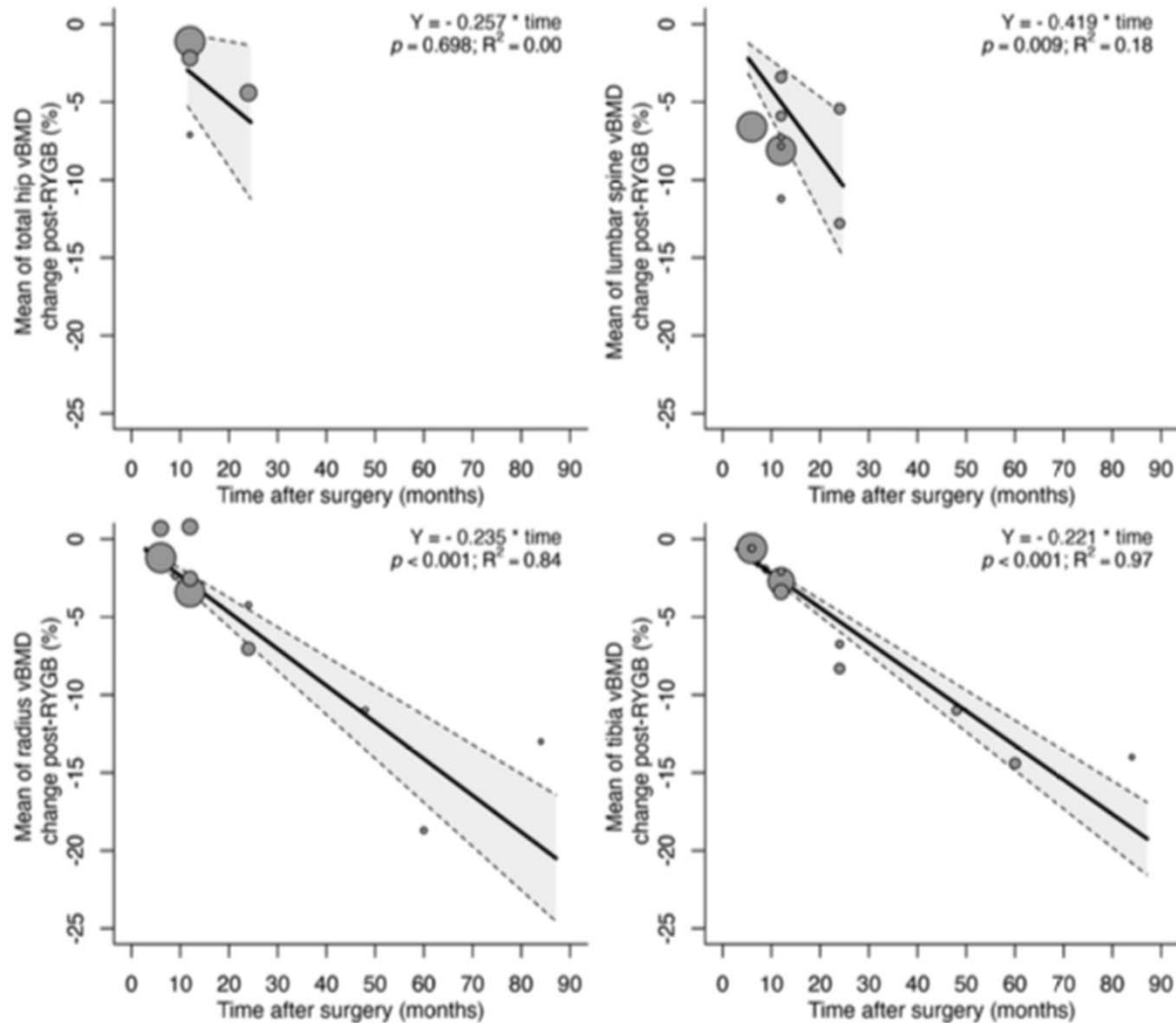
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Tibia volumetric bone mineral density



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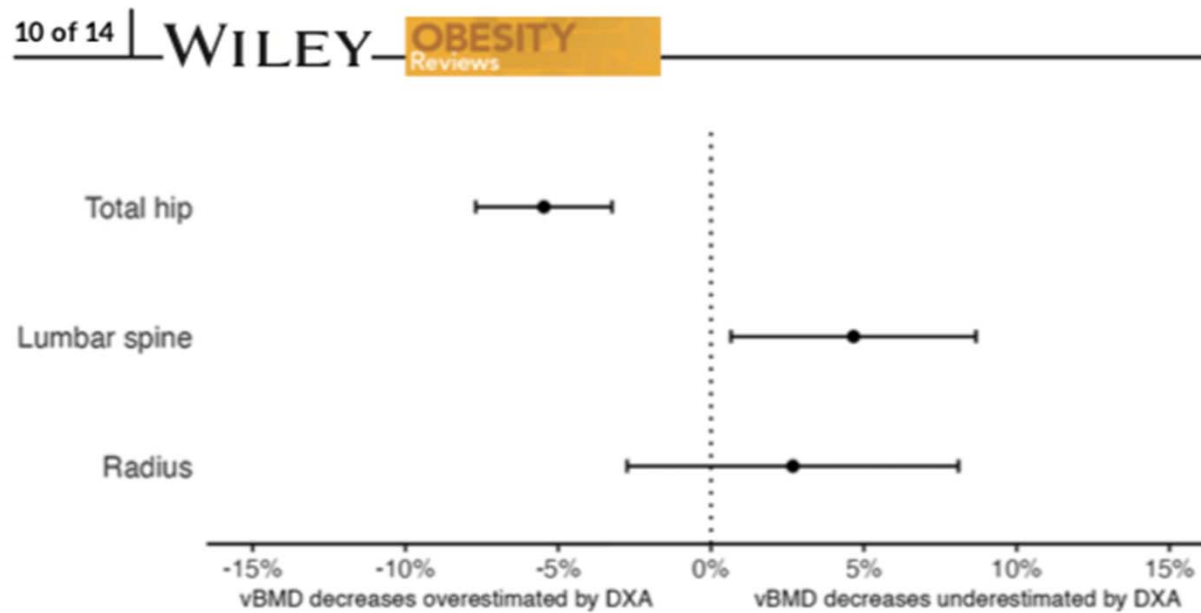


FIGURE 6 Differences between BMD assessment techniques (DXA versus QCT and HR-pQCT)

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5 | CONCLUSION

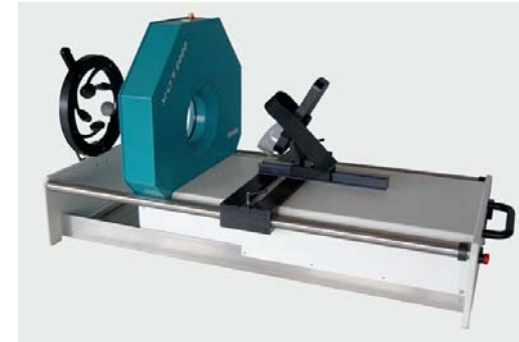
The main findings of this systematic review and meta-analysis with meta-regression indicate that, after RYGB, there is a significant vBMD loss at the TH, LS, radius, and tibia. Importantly, there was an estimated annual vBMD loss of 5.0% at the LS, 2.8% at the radius, and 2.7% at the tibia during the assessed follow-up time after RYGB. Bone quality is also negatively affected by RYGB as shown by the deterioration of almost all cortical and trabecular bone parameters assessed at the radius and tibia. We also sought to determine the differences in aBMD assessed by DXA and vBMD assessed by QCT or HR-pQCT in these patients. With QCT and HR-pQCT as a reference, DXA significantly underestimated LS and overestimated TH post-BS BMD losses.



Full Length Article

Bone geometry in older adults with subclinical hypothyroidism upon levothyroxine therapy: A nested study within a randomized placebo controlled trial

Annina Elisabeth Büchi^{a,b}, Martin Feller^{a,b}, Seraina Netzer^{a,b}, Manuel R. Blum^{a,b}, Elena Gonzalez Rodriguez^c, Tinh-Hai Collet^d, Cinzia Del Giovane^b, Diana van Heemst^e, Terry Quinn^f, Patricia M. Kearney^g, Rudi G.J. Westendorp^h, Jacobijn Gussekloo^{f,i}, Simon P. Mooijaart^e, Didier Hans^c, Douglas C. Bauer^{j,k,l}, Nicolas Rodondi^{a,b}, Daniel Aeberli^{m,*}



- Community-dwelling individuals aged ≥ 65 years with persistent SHypo were included, as detailed before [20].
- In short, persistent SHypo was diagnosed by elevated TSH levels (≥ 4.6 and ≤ 19.9 mIU/L) at two measurements at least 3 months apart, and FT4 levels within the assay reference range.
- Exclusion criteria were prior use of LT4, antithyroid, amiodarone or lithium treatment within 12 months before enrollment, thyroid surgery or radio-iodine, severe acute comorbidities, dementia, terminal illness or galactose intolerance [20].
- For this study, we included participants from Bern, Switzerland, of the TRUST trial who had pQCT measurements at baseline and follow-up at 1 or 2 years. The pQCT measurements were started later after funding of this nested study

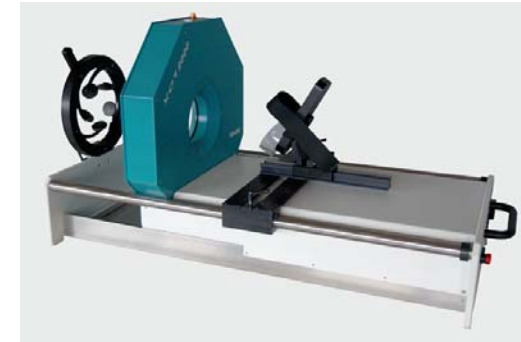
- Participants were randomized 1:1 to placebo or LT4, with stratification according to country, sex and starting dose of LT4 using randomly permuted blocks.
- Treatment started with 50 μg daily (25 μg in individuals < 50 kg body weight or with known coronary heart disease) of LT4 or the corresponding placebo.
- The dose was titrated according to target TSH levels ≥ 0.4 and < 4.6 mIU/L in the LT4 arm, and a computerized mock titration was used in the placebo arm to ensure blinding.
- The intervention resulted in a significant reduction in TSH levels after 6–8 weeks and after 12 months ($p < 0.001$), resulting in normalization in the levothyroxine group (mean 3.63 mIU/l, SD 2.11 mIU/l) compared to placebo (5.48 mIU/l, SD 2.48 mIU/l) at 12 months.
- The average dose of levothyroxine at 1 year was 50 μg



Full Length Article

Bone geometry in older adults with subclinical hypothyroidism upon levothyroxine therapy: A nested study within a randomized placebo controlled trial

Annina Elisabeth Büchi^{a,b}, Martin Feller^{a,b}, Seraina Netzer^{a,b}, Manuel R. Blum^{a,b}, Elena Gonzalez Rodriguez^c, Tinh-Hai Collet^d, Cinzia Del Giovane^b, Diana van Heemst^e, Terry Quinn^f, Patricia M. Kearney^g, Rudi G.J. Westendorp^h, Jacobijn Gussekloo^{f,i}, Simon P. Mooijaart^e, Didier Hans^c, Douglas C. Bauer^{j,k,l}, Nicolas Rodondi^{a,b}, Daniel Aeberli^{m,*}

**Table 1**

Baseline characteristics of included participants, by treatment group.

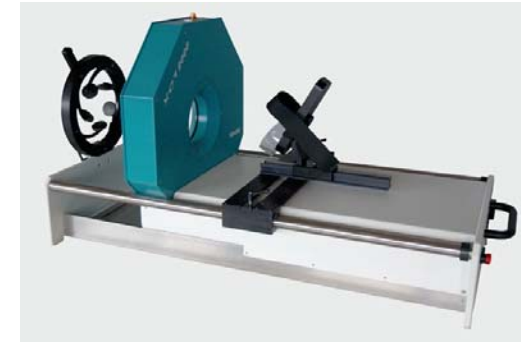
	Placebo	Levothyroxine
Sample size	48	50
Female	19 (39.6)	26 (52.0)
Age (years)	74.0 ± 5.8	74.1 ± 4.9
Weight (kg)	76.5 ± 15.8	75.9 ± 15.2
Height (cm)	166.8 ± 8.1	166.4 ± 9.7
BMI (kg/m ²)	27.4 ± 4.8	27.4 ± 5.0
Current smoking	6 (12.5)	2 (4.0)
Excess alcohol consumption	2 (4.2)	2 (4.0)
TSH (mIU/L)		
Baseline	6.1 ± 1.5	6.3 ± 2.0
Median (IQR)	5.5 (5.2–6.8)	5.7 (5.1–6.8)
Range	4.6–11.8	4.6–16.8
Free T4 (pmol/L)	14.3 ± 1.7	14.0 ± 2.1
Osteoporosis history	6 (12.0)	6 (12.0)
Diabetes history	5 (10.0)	6 (12.0)
Calcium supplemented	1 (2.0)	2 (4.0)
Vitamin D treatment	6 (12.0)	11 (22.0)
Bone affecting medication		
Anti-osteoporotic or HRT	1 (2.0)	0 (0.0)
HCTZ	0 (0.0)	0 (0.0)
Systemic GC	0 (0.0)	0 (0.0)
Potentially deleterious	5 (10.0)	1 (2.0)
Forearm muscle CSA (cm ²)	3325 ± 934	2982 ± 841
Lower leg muscle CSA (cm ²)	7189 ± 1480	6555 ± 1322



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Baseline, follow-up and yearly change in pQCT measurements by groups.

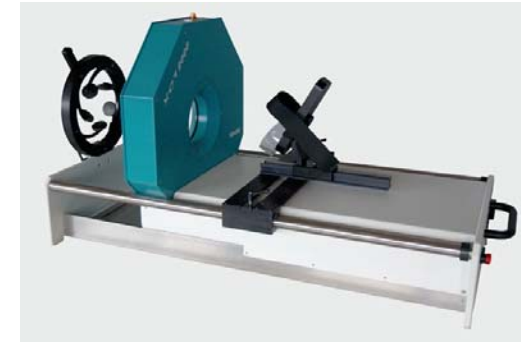
	Placebo Mean (SD) (n = 48)	LT4 Mean (SD) (n = 50)	Adjusted between-group difference (95% CI)	p-Value
Radius at 4% (epiphysis)				
BMC				
Baseline (g/cm)	1.4 (0.4)	1.2 (0.4)		
Follow-up (g/cm)	1.4 (0.4)	1.2 (0.4)		
Yearly change (%)	-0.2 (2.3)	-0.5 (2.5)	0.2 (-4.3; 3.8)	0.91
Total CSA				
Baseline (g/cm)	400.2 (80.9)	378.9 (80.2)		
Follow-up (g/cm)	403.5 (78.9)	380.1 (80.2)		
Yearly change (%)	0.5 (4.2)	0.3 (4.8)	2.3 (-5.4; 10.0)	0.56
Total BMD				
Baseline (g/cm)	341.4 (61.5)	324.9 (69.7)		
Follow-up (g/cm)	339.4 (66.1)	322.5 (69.3)		
Yearly change (%)	-0.6 (3.2)	-0.7 (3.8)	2.5 (-8.4; 3.5)	0.41
Trabecular BMD				
Baseline (g/cm)	201.7 (43.2)	189.1 (55.8)		
Follow-up (g/cm)	202.6 (42.6)	189.1 (55.5)		
Yearly change (%)	0.4 (2.7)	-0.1 (3.1)	2.7 (-2.2; 7.6)	0.28
Radius at 66% (diaphysis)				
BMC				
Baseline (mm ²)	1.0 (0.3)	1.0 (0.3)		
Follow-up (mm ²)	1.1 (0.3)	1.0 (0.3)		
Yearly change (%)	-0.6 (1.6)	-0.9 (2.1)	0.1 (-3.1; 3.2)	0.97
Total CSA				
Baseline (mm ²)	160.3 (36.0)	159.2 (41.1)		
Follow-up (mm ²)	160.2 (35.8)	159.6 (41.8)		
Yearly change (%)	-0.0 (2.4)	0.2 (3.2)	-2.1 (-1.7; 5.9)	0.27
Cortical CSA				
Baseline (mg/cm ³)	82.6 (22.1)	76.5 (23.2)		
Follow-up (mg/cm ³)	81.9 (22.1)	75.8 (24.0)		
Yearly change (%)	-1.0 (2.4)	-1.2 (3.8)	2.5 (-6.6; 1.7)	0.24
Cortical BMD				
Baseline (mg/cm ³)	1102.4 (56.0)	1097.5 (60.8)		
Follow-up (mg/cm ³)	1102.8 (55.5)	1093.6 (59.9)		
Yearly change (%)	0.0 (0.7)	-0.3 (1.1)	1.4 (-0.1; 2.9)	0.06
Cortical thickness				
Baseline (mm)	3.8 (0.7)	3.8 (0.7)		
Follow-up (mm)	2.2 (0.5)	2.0 (0.6)		
Yearly change (%)	-1.2 (2.5)	-1.3 (3.7)	4.2 (-9.4; 1.1)	0.12



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Tibia at 4% (epiphysis)

BMC

Baseline (g/cm)	3.5 (0.8)	3.4 (0.9)		
Follow-up (g/cm)	3.5 (0.8)	3.3 (0.9)		
Yearly change (%)	-0.2 (1.7)	-0.9 (1.9)	0.0 (-3.1; 3.0)	0.99

Total CSA

Baseline (g/cm)	1210.5 (221.6)	1204.3 (170.5)		
Follow-up (g/cm)	1201.9 (175.6)	1203.9 (222.3)		
Yearly change (%)	-0.4 (2.8)	-0.5 (2.2)	1.1 (-3.2; 5.4)	0.62

Total BMD

Baseline (g/cm)	292.0 (53.8)	276.7 (49.2)		
Follow-up (g/cm)	293.0 (55.0)	275.7 (49.9)		
Yearly change (%)	0.3 (2.1)	-0.3 (1.6)	1.1 (-4.3; 2.0)	0.47

Trabecular BMD

Baseline (g/cm)	221.7 (41.6)	213.0 (44.2)		
Follow-up (g/cm)	221.8 (40.7)	211.8 (45.3)		
Yearly change (%)	0.0 (2.1)	-0.6 (1.8)	0.6 (-2.7; 3.9)	0.74

Tibia at 66% (diaphysis)

BMC

Baseline (mm ²)	4.0 (0.8)	3.9 (0.8)		
Follow-up (mm ²)	4.0 (0.8)	3.9 (0.8)		
Yearly change (%)	-0.3 (0.8)	-0.6 (0.9)	0.2 (-1.2; 1.6)	0.79

Total CSA

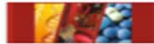
Baseline (mm ²)	672.0 (140.5)	659.9 (125.2)		
Follow-up (mm ²)	671.2 (140.8)	660.7 (127.7)		
Yearly change (%)	-0.1 (1.6)	0.0 (1.1)	-0.3 (-2.0; 2.6)	0.80

Cortical CSA

Baseline (mg/cm ³)	300.8 (57.8)	296.4 (62.2)		
Follow-up (mg/cm ³)	299.2 (58.8)	293.4 (62.6)		
Yearly change (%)	-0.5 (1.3)	-0.9 (1.6)	1.3 (-3.8; 1.1)	0.29

Cortical BMD

Baseline (mg/cm ³)	1088.0 (37.1)	1094.2 (36.2)		
Follow-up (mg/cm ³)	1087.8 (38.4)	1092.7 (36.0)		
Yearly change (%)	-0.0 (0.6)	-0.1 (0.5)	0.1 (-0.8; 1.0)	0.82



The role of opportunistic quantitative computed tomography in the evaluation of bone disease and risk of fracture in thalassemia major

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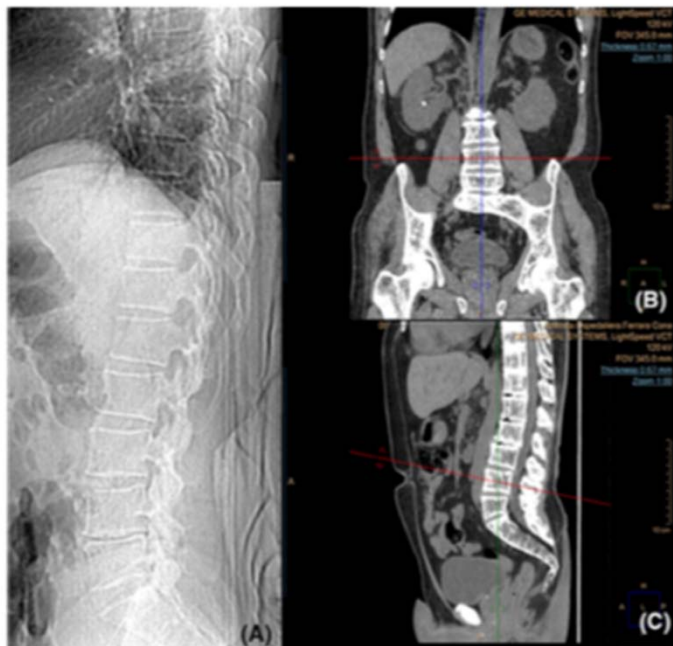


FIGURE 1 Lateral scout view is shown in (A); axes used in phantom-less QCT to detect the middle of vertebral body for BMD assessment are visible in the coronal plane (B) and sagittal plane (C), respectively

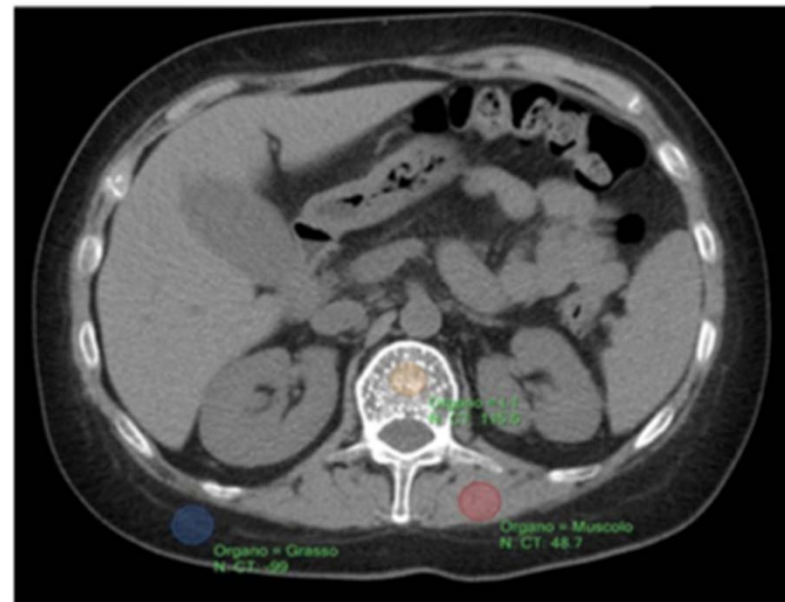


FIGURE 2 Axial CT scan in a patient with Thalassemia major. ROIs for vertebral body (orange circle), paraspinal muscle (red circle) and subcutaneous fat (blue circle) are shown with their respective CT numbers (in Hounsfield Units, HU)



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3 | RESULTS

We included 43 consecutive patients with β -thalassemia major (mean age \pm SD: 42.6 \pm 8.8 years, range 23–66 years). Among them, 28 were males (mean age \pm SD: 44 \pm 9; range, 23–66 years), and 15 females (mean age \pm SD: 40 \pm 8; range, 28–65 years). We analyzed 53 DXA and CT scans performed on the study population.

Comparison between DXA and QCT-derived T- and Z-scores.

In the study cohort, T- and Z-scores are reported in Table 1.

After comparison of lumbar spine T_{DXA} with T_{QCT} , we found that QCT values were significantly higher (i.e., less negative) than those determined by DXA ($p = .002$) (Diagram S1).

TABLE 1 T-score and Z-score by DXA and QCT, expressed as medians with first and third quartiles

Parameter	Method	Median	Quartiles
Lumbar T-score	DXA	-2.90	-4.00/-2.00
	QCT	-2.30	-3.25/-1.05
Lumbar Z-score	DXA	-2.60	-3.80/-1.75
	QCT	-1.30	-2.65/-0.25
Femoral T-score	DXA	-2.60	-3.20/-1.55
Femoral Z-score	DXA	-2.30	-2.85/-1.25



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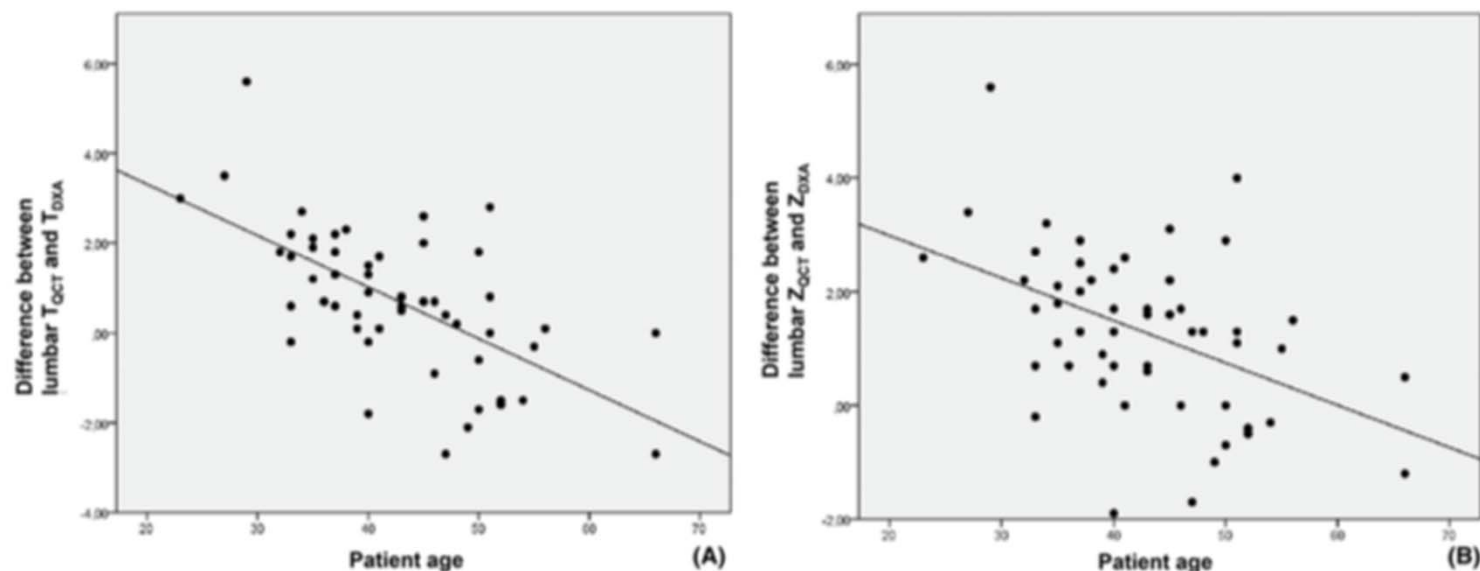


FIGURE 3 (A) Comparison between patient age (x-axis) and the difference between T_{QCT} and T_{DXA} at lumbar spine (y-axis) of the 53 DXA and QCT scans performed on the study population. The regression line, which represents the trend line, going down from top left to bottom right, suggests a negative correlation ($r = -0,626$). (B) Comparison between patient age (x-axis) and the difference between Z_{QCT} and Z_{DXA} at lumbar spine (y-axis) of the 53 DXA and QCT scans performed on the study population. The regression line, which represents the trend line, going down from top left to bottom right, suggests a negative correlation ($r = -0,454$)

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The comparison between lumbar T_{DXA} and T_{QCT} , using, for both parameters, the ISCD classification into normal, osteopenic and osteoporotic categories (Table S2), showed the following:

- Six patients were categorized with normal BMD_{DXA} . Of these, four showed normal BMD_{QCT} , and two had osteoporotic BMD_{QCT} ($p < .001$);
- 14 patients were classified with osteopenic BMD_{DXA} . Of these, seven had osteopenic BMD_{QCT} , whereas five had normal BMD_{QCT} and two had osteoporotic BMD_{QCT} ($p < .001$);
- The 33 patients were categorized with osteoporotic BMD_{DXA} . Of these, 22 had osteoporotic BMD_{QCT} , while 2 had normal BMD_{QCT} and 9 had osteopenic BMD_{QCT} ($p < .001$).

TABLE 2 Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the best predictive variables for risk of fracture

Parameter	Total fractures			
	Sensitivity	Specificity	PPV	NPV
ACR classification	100%	80%	68%	100%
Femoral DXA T-score	100%	77%	65%	100%
Lumbar QCT T-score	100%	23%	62%	100%

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Prediction of risk of fracture.

In the study population (43 patients):

- The 12 patients had radiographic vertebral fractures (five at baseline, five during follow-up, and two at both baseline and follow-up). Among them, using the semiquantitative method by Genant, in nine patients vertebral fractures were classified as mild, in two patients as moderate and in one patient as severe;
- Five patients had rib fractures;
- One patient had a lower extremity (feet and ankles) fracture;
- No patients had femoral or upper limb fractures.



TABLE 3 Z-scores and T-scores obtained by DXA and QCT, in patients with and without fractures, reported as medians with quartiles

Parameter	Technique	Fracture	Median	Quartiles	p value
Z-score	Femoral DXA	Without	-1.50	-2.22/-0.95	<.001
		With	-2.90	-3.40/-2.40	
Z-score	Lumbar DXA	Without	-2.15	-3.00/-1.05	.016
		With	-3.00	-4.10/-2.60	
Z-score	Lumbar QCT	Without	-0.95	-1.37/0.40	<.001
		With	-2.70	-3.35/-2.10	
T-score	Femoral DXA	Without	-1.85	-2.45/-1.07	<.001
		With	-3.20	-3.70/-2.70	
T-score	Lumbar DXA	Without	-2.30	-3.17/-1.57	.017
		With	-3.10	-4.20/-2.70	
T-score	Lumbar QCT	Without	-1.70	-2.60/0.32	<.001
		With	-3.30	-4.30/-2.75	



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5 | CONCLUSIONS

In a population of thalassaemic patients, DXA provides more negative measures than those determined by phantom-less QCT, and therefore a more pathological classification of bone mineralization. However, it seems that QCT may evaluate osteopathy better than DXA in these specific settings, since volumetric BMD would seem to have a stronger predictive role for fracture risk than DXA scans. We believe that, in the future, QCT could play a major role in conditions where interest is focused on trabecular bone deterioration, such as in β -thalassemia. Findings from this study could suggest the use of opportunistic phantom-less QCT, derived from routine abdominal CT scans, as an integrative tool in clinical practice, to obtain a comprehensive radiological evaluation of thalassaemic osteopathy using simple PACS measurement tools and a modest amount of time.

ΕΥΧΑΡΙΣΤΩ!

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