H. 知的財産権の出願・登録情況

１．特許取得：なし

２．実用新案登録：なし

３．その他：なし

# Ⅲ．研究成果の刊行に関する一覧表

| 著者・発表者氏名 | タイトル名 | 書籍・雑誌名 | ページ | 出版年 |
|---|---|---|---|---|
| Daisuke Y, Hiroyuki S, Atsushi H, Yasumoto M, Yoshihito S, Takao S | Estimation of appendicular muscle mass and fat mass by near infrared spectroscopy in older persons | Geriatrics and Gerontology International | 12(4): 652-658 | 2012 |
| Tetsuro H, Naoki I, Hiroshi S, Yoshihito S, Yasumoto M, Marie T, Yasuhito T, Atsushi H | High prevalence of sarcopenia and reduced leg muscle mass in Japanese patients immediately after a hip fracture | Geriatr Gerontol Int | | In press |
| Yasumoto M, Marie T, Atsushi H, Fujiko A, Hiroshi S | Divergent significance of bone mineral density changes in aging depending on sites and sex revealed through separate analyses of bone mineral content and area | J Osteoporosis | 1-6 | 2012 |
| Keizo S, Naoto E, Atsushi H, Takenori S, Kazuyo T, Kiyoshi K, et al | Why not use your own body weight to prevent falls? A randomized, controlled trial of balance therapy to prevent falls and fractures for elderly people who can stand on one leg for ≤15 s | J Orthop Sci | 18(1): 110-120 | 2013 |
| 原田敦 | 巻頭言 ー運動器障害は虚弱における身体的脆弱性にどこまで関与しているのかー | CLINICAL CALCIUM | 22(4): 11-12 | 2012 |
| 原田敦 | 転倒・骨折患者にみられる虚弱(Frailty) | CLINICAL CALCIUM | 22(4): 27-33 | 2012 |
| 原田敦 | 骨粗鬆症・骨折の合併症とQOL 1.大腿骨近位部骨折 骨粗鬆症診療ハンドブック改訂5版 | 医薬ジャーナル社 | 182-192 | 2012 |
| 原田敦 | 転倒リスクの評価と転倒予防 | CLINICAL CALCIUM | 22(6): 68-72 | 2012 |
| 原田敦 | 第Ⅱ章 運動器の評価 2.ロコモの疑いの人の診察法 3)主な疾患の診断と保存治療 大腿骨近位部骨折 | ロコモティブ・シンドローム | 183-191 | 2012 |
| 原田敦 | 骨粗鬆症性椎体骨折に対する我が国での医療行為 | 整形外科最小侵襲手術ジャーナル | 64: 15-18 | 2012 |
| 原田敦 | ロコモティブシンドロームの原因疾患と治療 大腿骨近位部骨折 | 臨床と研究 | 11: 31-34 | 2012 |
| 竹村真里枝、原田敦 | 高齢者の骨折 | Journal of Clinical Rehabilitation | 21(12): 1168-1176 | 2012 |

| | | | | |
|---|---|---|---|---|
| 原田敦、秋下雅弘、江頭正人、金憲経、金信敬、神崎恒一、重本和宏、島田裕之、下方浩史、鈴木隆雄、橋本有弘、細井孝之 | 特別報告　サルコペニア：定義と診断に関する欧州関連学会のコンセンサス―高齢者のサルコペニアに関する欧州ワーキンググループの報告―の監訳とQ&A | 日本老年医学会雑誌 | 49(6)：788-805 | 2012 |
| 原田敦他 | 高齢者医療の今－運動器不安定の最新の知見－ 高齢者のサルコペニア | 第14回日本医学会公開フォーラム DVD | | 2012 |
| 松井康素、原田敦 | 特集　老化と生体運動機能 Review　関節の老化 | CLINICAL CALCIUM | 23(1)：15-22 | 2013 |
| 原田敦 | 特集　サルコペニア－筋研究の最前線－ サルコペニアの定義や診断基準 | Bone Joint Nerve | 3(1)：9-13 | 2013 |
| 斎藤充、原田敦、村木重之、重本和宏 | 特集　サルコペニア―筋研究の最前線―　座談会 サルコペニア－筋研究の最前線－ | Bone Joint Nerve | 3(1)：139-149 | 2013 |
| Furuya T, Hosoi T, et al | Prevalence of and factors associated with vitamin D deficiency in 4,793 Japanese patientswith rheumatoid arthritis | Clinical Rheumatology | Vol.20 | 2012 |
| Orimo H, Hosoi T, et al | Japanese 2011 Guidelines for prevention and treatment of osteoporosis-executive summary | Arch Osteoporos | 7(1-2)：3-20 | 2012 |
| Furuya T, Hosoi T, et al | Risk factors associated with the occurrence of hip fracture in Japanese patients with rheumatoid arthritis:a prospective observational cohort study | Osteoporosis | | In press |
| Koudu Y, Hosoi T, et al | Association of CYP19 Gene Polymorphism with Vertebral Fractures in Japanese Postmenopausal | Biochmical Genetics | 50(5-6)：389-396 | 2012 |
| 細井孝之、黒田龍彦、中村利孝、白木正孝、太田博明、原田敦、森聖二郎、大橋靖雄、折茂肇 | 全国的データベースを用いた骨粗鬆症性骨折の予防と治療に関する研究 | Osteoporosis Japan | 20(4)：661-668 | 2012 |
| 細井孝之 | 骨粗鬆症講座　Q&A　ガイドラインの改訂 | O.li.v.e.－骨代謝と生活習慣病の連関 | 20-25 | 2012 |
| 細井孝之 | 特集　骨粗鬆症の薬物療法の新戦略アレンドロネート | 関節外科　基礎と臨床 | 48-52 | 2012 |
| 細井孝之 | 19　骨粗鬆症 | M.P.実地医家のための臨床検査のすすめかた・評価のしかた | 252-256 | 2012 |
| 細井孝之 | 骨粗鬆症 | 青淵 | 14-16 | 2012 |
| 細井孝之 | 骨粗鬆症の予防と治療ガイドライン 2011年版 | Ortho community 2012 | 11-12 | 2012 |
| 細井孝之 | 臨床　骨折リスク評価ツール「FRAX®」の日本人への応用 | ORTHO-VIEWS | 6-7 | 2012 |

| | | | | |
|---|---|---|---|---|
| 細井孝之 | 特集　骨粗鬆症診療に関する新しい展開　骨粗鬆症治療における薬物治療介入のポイント（2011年改訂版ガイドラインの考え方） | 内分泌・糖尿病・代謝内科 | 410-414 | 2012 |
| 細井孝之 | 5.特集　骨粗鬆症治療薬のBreakthrough-ガイドライン2011年版を踏まえて-骨折リスク評価の実際とFRAX® | MEDICINAL | 43-48 | 2012 |
| 細井孝之 | 特集：知っておきたい最新骨粗鬆症診療マニュアル<br>骨折危険因子から | Orthopaedics | 25-30 | 2012 |
| 細井孝之 | マンスリーレクチャー 老年内科　標榜をめざして | 週刊　日本医事新報 | 41-45 | 2012 |
| 細井孝之 | 骨粗鬆症の治療―新たな薬物治療開始基準 | CLINICIAN 運動器の10年 | 38-43 | 2012 |
| 細井孝之 | 特集：骨密度測定の再考 MD法（最新の＋DIPシステムについて） | 骨粗鬆症治療 | 14-18 | 2012 |
| 細井孝之 | 特集：「骨粗鬆症の予防と治療ガイドライン2011年版」を踏まえた今後の骨粗鬆症治療 | 骨粗鬆症治療 | 10-14 | 2012 |
| 細井孝之 | 特集：変わる骨粗鬆症治療－内科医が知っておきたい最新トピックから基本的知識まで－ | Mebio | 41-46 | 2012 |
| 細井孝之 | 特集「骨粗鬆症の予防と治療ガイドライン2011」をめぐって | CLINICIAL　CALCIUM | 73-79 | 2012 |
| 細井孝之 | シリーズ　よく使う日常治療薬の正しい使い方 | レジデントノート | 1927-1930 | 2012 |
| 細井孝之 | 骨折リスクに基づいた骨粗鬆症の診断と対策の実際 | M.P.骨粗鬆症の実地診療 | 1886-1890 | 2012 |
| 細井孝之 | ロコモティブシンドロームの予防と骨粗鬆症 | 日本未病システム学会 | 74-78 | 2012 |
| 細井孝之 | 診断基準の改定に向けて-骨粗鬆症診療の新たな展開をめざして- | Osteoporosis Japan | 629-32 | 2012 |
| 細井孝之 | Ⅱ.運動器の評価　2．ロコモの疑いの人の診察法 | ロコモティブシンドローム | 167-175 | 2012 |
| 細井孝之 | Ⅱ.病態・疾患別のガイドライン<br>代謝性骨疾患１（骨粗鬆症）<br>骨粗鬆症の評価・治療指針 | 運動器診療　最新ガイドライン | 182-187 | 2012 |
| 細井孝之 | 高齢者に多い疾患に対する薬の使い方1）骨粗鬆症（Q13～Q16） | 高齢者の薬よろずお助け　Q&A100 | 39-50 | 2012 |
| 細井孝之 | 第4章　ロコモティブシンドロームと遺伝子多型性 | ロコモティブシンドロームと栄養 | 55-64 | 2012 |
| 細井孝之 | Ⅵ　骨粗鬆症の治療<br>２．骨粗鬆症の治療薬<br>６）その他（カルシトニン、ビタミンK、イプリフラボン） | 骨粗鬆症診療ハンドブック 改訂5版 | 320-330 | 2012 |

| | | | | |
|---|---|---|---|---|
| 細井孝之 | 4.骨粗鬆症　4.1　骨粗鬆症の概念と分類 | 高齢者用食品の開発と展望 | 23-28 | 2012 |
| 細井孝之 | A.骨粗鬆症の評価と指針　1.「骨粗鬆症の予防と治療ガイドライン2011年版」の概要とおもな改訂点 | 新しい骨粗鬆症治療 | 2-4 | 2012 |
| 細井孝之 | 第13章　骨・運動器疾患 | 標準理学療法学・作業療法学 | 146-158 | 2012 |
| Kozakai R, Ando F, Kim HY, Rantanen T, Shimokata H | Regular exercise history as a predictor of exercise in old age among community-dwelling Japanese older people | J Phys Fitness Sports Med | 1: 1-8 | 2012 |
| 安藤富士子、今井具子、加藤友紀、大塚礼、松井康素、竹村真里枝、下方浩史 | 血清カロテノイドと2年後の骨粗鬆症／骨量減少発症リスクに及ぼす影響 | 日本未病システム学会雑誌 | 18: 89-92 | 2012 |
| 下方浩史、安藤富士子 | 日常生活機能と骨格筋量、筋力との関連 | 日老会誌 | 49: 195-198 | 2012 |
| 下方浩史、安藤富士子 | 疫学研究からのサルコペニアとそのリスクー特に栄養との関連 | 日老会誌 | 49: 721-725 | 2012 |
| 幸篤武、安藤富士子、下方浩史 | サルコペニア、虚弱の疫学ー日本人データから | Bone Joint Nerve | 3(1): 67-74 | 2013 |
| 下方浩史、安藤富士子 | 検査基準値の考え方ー医学における正常と異常ー | 日老会誌 | | 印刷中 |
| 下方浩史、安藤富士子 | 健康長寿社会を築く長期縦断疫学研究 | 日本未病システム学会雑誌 | | 印刷中 |
| 大塚礼、下方浩史、安藤富士子 | 高齢者の栄養に関する疫学研究 | Geriatric Medicine | | 印刷中 |
| 松井康素、竹村真里枝、原田敦、安藤富士子、下方浩史 | 地域在住中高齢者の膝関節変形と膝伸展筋力との関連 | Osteoporosis Japan | | 印刷中 |
| 橋本有弘 | 骨格筋幹細胞-最新基礎知見を踏まえて- | Bone Joint Nerve | 3(1): 21-26 | 2013 |
| Kojima T, Akishita M, Nakamura T, Nomura K, Ogawa S, Iijima K, Eto M, Ouchi Y | Polypharmacy as a risk for fall occurrence in geriatric outpatients | Geriatr Gerontol Int | 12: 425-430 | 2012 |
| Kojima T, Akishita M, Kameyama Y, Yamaguchi K, Yamamoto H, Eto M, Ouchi Y | Factors associated with prolonged hospital stay in a geriatric ward of a university hospital in Japan | J Am Geriatr Soc | 60: 1190-1191 | 2012 |
| Mori S, Kishi M, Kubo S, Akiyoshi T, Yamada S, Miyazaki T, Konishi T, Maruyama N, Shigemoto K | 3,4-diaminopyridine improves neuromuscular transmission in a MuSKantibodies-induced mouse model of myasthenia gravis | Journal of Neuroimmunology | 245: 75-78 | 2012 |
| Mori S, Shigemoto K | Mechanisms associated with the pathogenicity of antibodies against muscle-specific kinase in myasthenia gravis | Autoimmunity Revies | | In press |

| | | | | |
|---|---|---|---|---|
| 福永大地、久保幸穂、森秀一、宮崎剛、樋上賀一、重本和宏 | 老齢マウスの筋線維タイプ特異的な筋萎縮の病態解明 | 基礎老化研究 | 36: 47-49 | 2012 |
| 重本和宏、福永大地、森秀一 | 筋肉と神経-最新基礎知見を踏まえて | Bone Joint Nerve | 3(1): 27-31 | 2013 |
| Kim H | Behavioral Treatment for Geriatric Syndrome | Geriatrics | 85-104 | 2012 |
| Kim MJ, Kim H | Accuracy of segmental multi-frequency bioelectrical impedance analysis for assessing whole-body and appendicular fat mass and lean soft tissue mass in frail women aged 75 years and older | European Journal of Clinical Nutrition | 1-7 | 2013 |
| 金憲経 | I. 転倒リスク評価－歩行速度－, －環境因子－ ; III. 転倒予防－運動－ | 高齢者の転倒予防ガイドライン | 17-19, 38-42, 119-122 | 2012 |
| 大久保善郎、金憲経 | III. 介護予防編 6. 転倒予防に向けたエクササイズ | エクササイズ科学 | 245-256 | 2012 |
| 金憲経 | 複合介入 | サルコペニアーその成因と運動・栄養－ | 140-146 | 2013 |
| 田中千晶、藤原佳典、安永正史、桜井良太、齋藤京子、金憲経、深谷太郎、他6人 | 複合健康増進プログラムが地域在住高齢者の日常的な身体活動量へ与える影響－無作為化比較試験による検討－ | 日本老年医学会雑誌 | 49: 372-374 | 2012 |
| 金憲経 | 地域在住高齢女性におけるサルコペニアとロコモティブシンドローム | Japanese Journal of Rehabilitation Medicine | 49(9): 596-599 | 2012 |
| 鈴木隆雄、金憲経 | サルコペニアと骨粗鬆症 | Medical Rehabilitation | 150: 12-18 | 2012 |
| 金憲経 | 地域在住高齢者におけるサルコペニア予防のための包括的介入 | 日本未病システム学会雑誌 | 18: 66-73 | 2012 |
| 金憲経 | 虚弱・サルコペニアへの介入研究 | 日本老年医学会雑誌 | 49: 726-730 | 2012 |
| 金憲経 | 筋肉への運動や栄養による介入—現状と今後と展望— | Bone Joint Nerve | 3(1): 89-95 | 2013 |
| 金憲経 | 身体活動の指導からみた高齢者支援—老年症候群の早期予防のための支援— | 大阪体育学研究 | 51: 41-46 | 2013 |
| 金憲経 | 老化防止・介護予防に効果的な運動—とくにサルコペニア予防の観点から | Aging & Health | 64: 20-23 | 2013 |
| Shimada H | Glucose uptake during exercise in skeletal muscles evaluated by positron emission tomography | Positron Emission Tomography - Current Clinical and Research Aspects | 319-336 | 2012 |

| | | | | |
|---|---|---|---|---|
| Yoshimatsu T, Yoshida D, Shimada H, Komatsu T, Harada A, Suzuki T | The relation between near-infrared spectroscopy, and subcutaneous fat and muscle thickness measured by ultrasonography in Japanese community-dwelling elderly | Geriatr Gerontol Int | | In press |
| Hashidate H, Shimada H, Shiomi T, Shibata M, Sawada K, Sasamoto N | Measuring indoor life-space mobility at home in frail older adults with difficulty to perform outdoor activities | J Geriatr Phys Ther | | In press |
| 島田裕之 | Part-6 その他の介入法: 運動 | 栄養・運動で予防するサルコペニア | 134-139 | 2013 |
| 大矢敏久、内山靖、島田裕之、 牧迫飛雄馬、 土井剛彦、 吉田大輔、 上村一貴、 鈴木隆雄 | 手段的日常生活活動の自立した地域在住高齢者における転倒恐怖感に関連する要因の検討 | 日本老年医学会雑誌 | 49(4): 457-462 | 2012 |
| 橋立博幸、島田裕之、 潮見泰藏、 笹本憲男 | 高齢者における筋力増強運動を含む機能的トレーニングが生活機能に及ぼす影響 | 理学療法科学 | 39(3): 159-166 | 2012 |
| 水本淳、島田裕之、 井平光、 野村知広、 古名丈人、 鈴川芽久美 | ステップエルゴメーターのアイソキネティック運動におけるピークパワーと筋活動特性との関連 | 理学療法科学 | 27(4): 411-415 | 2012 |
| 島田裕之、吉田大輔 | サルコペニア診断のための筋量、筋力の評価法 | Bone Joint Nerve | 3(1): 61-66 | 2013 |
| Atsushi A, Koichi K, et al and the Japanese Elderly Diabetes Intervention Trial Study Group | Long-term multiple risk factor interventions in Japanese elderly diabetic patients: The Japanese Elderly Diabetes Intervention Trial-study design, baseline characteristics and effects of intervention | Geriatr Gerontol Int | 12: 7-17 | 2012 |
| Atsushi A, Koichi K, et al and the Japanese Elderly Intervention Trial Research Group | Non-high-density lipoprotein cholesterol: an important predictor of stroke and diabetes-related mortality in Japanese elderly diabetic patients | Geriatr Gerontol Int | 12: 18-28 | 2012 |
| Kenji T, Kumiko N, Sayaka K, Yukiko Y, Ayako M, Akiko I, Masahiro A, Koichi K | New dorsiflexion measure device:A simple method to assess fall risks in the elderly | Geriatr Gerontol Int | 12(3): 563-564 | 2012 |
| Nagai K, Akishita M, Shibata S, Kobayashi Y, Yamada Y, Kimura S, Machida A, Toba K, Kozaki K | Relationship between testosterone and cognitive function in elderly men with dementia | J Am Geriatr Soc | 60(6): 1188-9 | 2012 |
| Akishita M, Ishii S, Kojima T, Kozaki K, Kuzuya M, Arai H, Arai H, Eto M, et al | Priorities of healthcare outcomes for the elderly | J Am Med Dir Assoc | | In press |

# Ⅳ. 研究成果の刊行物・別刷

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ORIGINAL ARTICLE: EPIDEMIOLOGY, CLINICAL PRACTICE AND HEALTH

# Estimation of appendicular muscle mass and fat mass by near infrared spectroscopy in older persons

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**Aim:** Near infrared spectroscopy has been reported to have a high reliability and accuracy in assessing the percentage of body fat. However, whether muscle mass can be accurately estimated using this method has not been established. This study examined whether a near infrared spectroscopy method could estimate appendicular muscle mass and fat mass, with dual-energy X-ray absorptiometry as the standard method for comparison.

**Methods:** A total of 20 orthopedic inpatients (mean age 73.2 ± 6.8 years) were recruited for this study. Their body composition was assessed using near infrared spectroscopy and dual-energy X-ray absorptiometry. Appendicular muscle mass and fat mass were estimated from height, weight and optical densities.

**Results:** The optical densities for the upper arm (biceps, triceps) and forearm (flexor carpi radialis) were significantly correlated with appendicular muscle mass ($r = 0.534$ to 0.623) or fat mass ($r = -0.483$ to $-0.827$). Estimated appendicular muscle mass and fat mass explained 89% and 80% of the variance in the dual-energy X-ray absorptiometry-derived muscle mass and fat mass estimates using height, weight and optical density values of the proximal flexor carpi radialis.

**Conclusions:** Near infrared spectroscopy is a useful method to assess not only fat mass, but also muscle mass in older adults. **Geriatr Gerontol Int 2012; 12: 652–658.**

**Keywords:** aged, body composition, body fat, sarcopenia, skeletal muscles.

## Introduction

Age-related loss of muscle mass (so-called sarcopenia) can lead to functional decline in older persons.[1–5] Two published Health, Aging and Body Composition reports showed that sarcopenia, as determined by computed tomography (CT) in the mid-thigh, was a weak to modest predictor of loss of physical function over the following 2 to 3 years.[6,7] Furthermore, one study reported that older sarcopenic patients were twice as likely to contract infection during a hospital stay compared with older patients with a normal muscle mass.[8] This suggested that sarcopenic individuals might have decreased immunity, which might provide a mechanistic link between sarcopenia and mortality risk. In addition, reduced arm muscle area was reported to be an independent predictor of long-term mortality in community-dwelling older adults.[9] According to the

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New Mexico Elder Health Survey, the prevalence of sarcopenia increased from 13 to 24% in persons aged under 70 years to >50% in persons aged over 80 years.[1] To achieve successful aging, it is important to preserve muscle mass to maintain function.

Recently, some researchers reported that sarcopenic patients who were obese were at particularly high risk of functional impairment and physical disability.[10–13] The condition was termed sarcopenic obesity, and it was suggested that approximately 15% of those with sarcopenia were also obese.[10] This suggests that it is necessary to assess not only muscle mass, but also fat mass accurately in the elderly.

There are various methods for measurement of body composition. Total body and regional skeletal muscle mass can now be accurately quantified using imaging methods, including CT and magnetic resonance imaging (MRI).[14] However, CT and MRI are costly methods and access to the equipment can be limited. Dual-energy X-ray absorptiometry (DXA) has been widely used in clinical practice, not only for osteoporosis screening and diagnosis, but also for assessment of body composition, such as skeletal muscle mass and fat mass. DXA is less expensive and less invasive compared with MRI and CT. Previous studies have shown good correlations between DXA-derived lean soft tissue mass and skeletal muscle mass in the lower limb region when CT and MRI were used as the standards for comparison.[15,16] However, DXA methods take more time, although whole-body scanning by this method exposes the patient to minimal radiation.

Bioelectrical impedance analysis (BIA) is a non-invasive, portable, quick and inexpensive method for measuring body composition.[17] Previous studies have shown that there is a strong correlation between BIA resistance and skeletal muscle measurements in the arms[18] and legs.[19] In addition, one report suggested that BIA could provide rapid and accurate estimates of whole body skeletal muscle mass in adults.[20] There are some disadvantages with the BIA method. First, fat tissue also holds water, although the proportion is small.[21] Second, the volume of muscle derived by BIA might overestimate the actual volume. Third, there are a large proportion of older adults who have a changed distribution of body water, such as edema. One report showed that the expansion of extracellular water relative to intracellular water and to regional lean volume masks actual muscle cell atrophy during aging.[22] This suggested that it might be difficult to accurately assess body composition in older adults.

Another development that might have potential for use in older adults is near infrared spectroscopy (NIRS). NIRS is also a non-invasive, simple and rapid method of assessing the percentage of body fat. There are some reports that the NIRS method has a high reliability and accuracy in determination of the percentage of body fat.[23–25] In contrast, it has not been established whether muscle mass can be estimated accurately by NIRS.

The present study investigated whether a NIRS method could provide an accurate estimate of appendicular muscle mass (AMM) and appendicular fat mass (AFM) using DXA as the standard method for comparison.

## Methods

### *Participants*

A total of 20 orthopedic patients who were admitted to the National Hospital for Geriatric Medicine and who were aged 60 years or older were recruited for the present study. Patients with dementia or who had major laterality of muscle mass in the arms and legs, or who had surgery just before the study were excluded. All participants had their height (to the nearest 0.1 cm) and weight (to the nearest 0.1 kg) measured after admission. The details of the study were explained in advance and written consent was obtained from each participant. In addition, the present study was approved by the ethics committee of the National Center for Geriatrics and Gerontology.

### *Measurement of body composition*

Whole and regional body composition was measured using DXA (Lunar DPX, Madison, WI, USA). This system provided the mass of lean soft tissue, fat and bone mineral for both the whole body and specific regions. Appendages were isolated from the trunk and head by using a DXA regional computer-generated default line. AMM or AFM was derived as the sum of the fat-free soft tissues or fat tissue of the arms and legs. A previous study reported that total body skeletal muscle mass can be accurately predicted from DXA-estimated appendicular lean soft tissue mass.[26,27]

### *NIRS*

The NIRS measurements were carried out with the Fitness Analyzer BFT-3000 (Kett Electrical Laboratory, Tokyo, Japan, Fig. 1), the Japanese version of the Futrex 5000 (Futrex, Gaithersburg, MD, USA; 1988), which has potential for estimating body composition.[22,28] This device uses optical densities (OD) at two wavelengths (OD1 = 937 nm, OD2 = 947 nm) measured at each site. The NIRS instrument was tested immediately before taking measurements on each patients by using an optical standard, which was provided with the instrument and situated in a flexible light shield, to ensure that its performance was consistent throughout the study.

OD values were obtained at six sites: distal biceps (5 cm from the olecranon), distal triceps (5 cm from the

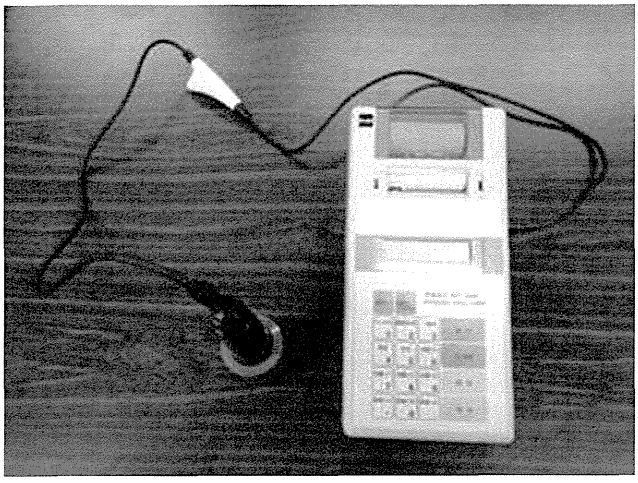

**Figure 1** The near infrared spectroscopy instrument (Fitness Analyzer BFT-3000).

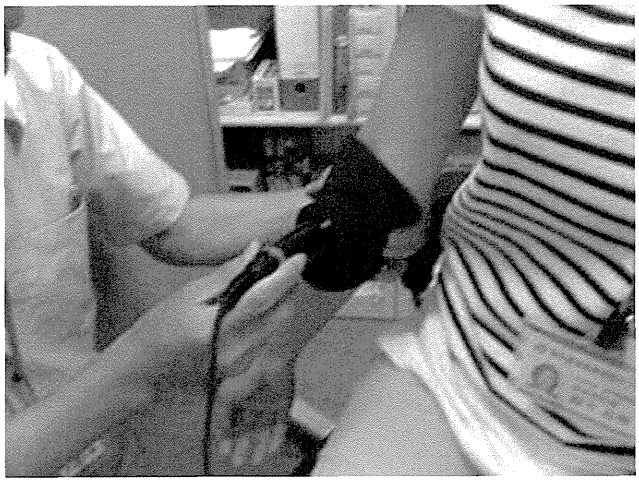

**Figure 2** Method of measurement.

olecranon), proximal flexor carpi radialis (5 cm from the olecranon), distal quadriceps (5 cm from the upper edge of patella), proximal tibialis anterior (5 cm from the caput fibulae) and proximal calf (5 cm from the caput fibulae). The reliability was confirmed by test–retest. The test–retest reproducibility was excellent (intraclass correlation coefficient = 0.95–0.97, $P < 0.01$). Patients were required to maintain a seated position, with their arms relaxed at their sides (Fig. 2). NIRS measurements were carried out by a single trained physical therapist, and completed within a few minutes.

### *Statistical analysis*

Pearson's correlation coefficient was used to determine the relationship between AMM or AFM and each OD value. Equations for estimation of AMM and AFM were developed with the use of multiple linear regression analysis. Potential explanatory variables included OD value, height and weight. DXA-measured AMM and AFM were set as the objective variable. The coefficient of determination ($R^2$) values were used to quantify the accuracy of model fit. The mean difference between DXA-measured AMM (AFM) and estimated AMM (AFM) was tested using the paired Student's *t*-test. Statistical analyses were carried out using PASW Statistics 18 for Windows (SPSS, Chicago, IL, USA) and the significance level was less than 5%.

## Results

The characteristics of the patients are shown in Table 1. Mean age was 73.2 ± 6.8 years (range 62–84 years) and 70% were female. The subjects were diagnosed with the following: spinal canal stenosis ($n = 11$), disc herniation ($n = 1$), spinal tumor ($n = 2$), knee osteoarthritis ($n = 2$), compression fracture ($n = 1$), femoral neck fracture ($n = 1$) and others ($n = 2$).

The correlation coefficients between AMM or AFM and each OD value are listed in Table 2. AMM was significantly correlated with OD values at the distal triceps (OD1: $r = 0.623$; OD2: $r = 0.534$). AFM was significantly correlated with OD values at the distal biceps (OD1 $r = -0.570$; OD2 $r = -0.551$), distal triceps (OD1 $r = -0.483$; OD2 $r = -0.494$) and proximal flexor carpi radialis (OD1 $r = -0.827$; OD2 $r = -0.821$). In the correlation analysis between muscle mass or fat mass and the OD value, correlation coefficients were mostly higher with OD1 than with OD2. Thus, OD1 was used as the representative value of NIRS data for the estimation equation.

The results from linear regression analyses for the multivariate models are presented in Table 3. The multiple regression equations incorporated height, weight and OD1. Using anthropometric data (height and weight) as the explanatory variables, the $R^2$ value of AMM and AFM were 0.81 (standard error of the estimate [SEE] = 1.67 kg) and 0.50 (SEE = 1.77 kg), respectively (model 1). When OD1 was added to the explanatory variables, the $R^2$ values of AMM and AFM ranged from 0.85 to 0.89, and 0.58 to 0.80, respectively (models 2–5). The highest $R^2$ values of AMM and AFM were 0.89 (SEE = 1.33 kg) and 0.80 (SEE = 1.16 kg), respectively, when OD1 at the proximal flexor carpi radialis was added to the explanatory variables. For separate estimation equations (upper and lower limb), the accuracy of model fit was slightly less (muscle mass $R^2 = 0.82$–$0.87$, fat mass $R^2 = 0.53$–$0.55$). There were no significant differences between DXA-measured AMM and estimated AMM (mean difference 0.01, 95% confidence interval −0.56 to 0.58), or between DXA-measured AFM and estimated AFM (mean difference −0.25, 95% confidence interval −0.75 to 0.25).

**Table 1** Physical characteristics of the study participants

| Variables | All subjects ($n = 20$) | Men ($n = 6$) | Women ($n = 14$) |
|---|---|---|---|
| Age (years) | 73.2 ± 6.8 | 67.8 ± 8.1 | 75.5 ± 4.9 |
| Height (cm) | 153.2 ± 9.5 | 166.1 ± 3.2 | 147.8 ± 4.3 |
| Weight (kg) | 53.9 ± 10.3 | 64.3 ± 6.8 | 49.4 ± 8.2 |
| BMI (kg/m$^2$) | 22.8 ± 2.9 | 23.3 ± 2.1 | 22.6 ± 3.2 |
| AMM (kg) | 15.7 ± 3.7 | 20.5 ± 1.2 | 13.6 ± 2.0 |
| AFM (kg) | 4.8 ± 2.4 | 4.1 ± 2.2 | 5.1 ± 2.4 |
| Diagnosis *n* (%) | | | |
| Spinal canal stenosis | 11 (55%) | | |
| Disc herniation | 1 (5%) | | |
| Spinal tumor | 2 (10%) | | |
| Knee osteoarthritis | 2 (10%) | | |
| Compression fracture | 1 (5%) | | |
| Femoral neck fracture | 1 (5%) | | |
| Others | 2 (10%) | | |

Values are mean ± standard deviation or *n* (%).
AFM, dual-energy X-ray absorptiometry-derived appendicular fat mass; AMM, dual-energy X-ray absorptiometry-derived appendicular muscle mass; BMI, body mass index.

**Table 2** Correlation coefficients between limb muscle mass or fat mass and each optical densities value

| | Biceps | | Triceps | | Flexor carpi radialis | |
|---|---|---|---|---|---|---|
| | OD1 | OD2 | OD1 | OD2 | OD1 | OD2 |
| Upper limb muscle mass | | | | | | |
| Four limbs | 0.369 | 0.350 | 0.623** | 0.534* | 0.343 | 0.324 |
| Upper limb | 0.292 | 0.286 | 0.572** | 0.462* | 0.279 | 0.267 |
| Upper limb fat mass | | | | | | |
| Four limbs | −0.570** | −0.551* | −0.483* | −0.494* | −0.827** | −0.821** |
| Upper limb | −0.423 | −0.394 | −0.403 | −0.411 | −0.723** | −0.705** |
| | Quadriceps | | Tibialis anterior | | Calf | |
| | OD1 | OD2 | OD1 | OD2 | OD1 | OD2 |
| Lower limb muscle mass | | | | | | |
| Four limbs | 0.332 | 0.190 | 0.139 | 0.118 | 0.297 | 0.327 |
| Lower limb | 0.383 | 0.248 | 0.138 | 0.125 | 0.346 | 0.373 |
| Lower limb fat mass | | | | | | |
| Four limbs | −0.348 | −0.220 | −0.421 | −0.388 | −0.426 | −0.443 |
| Lower limb | −0.333 | −0.218 | −0.434 | −0.401 | −0.458* | −0.472* |

*$P < 0.05$; **$P < 0.01$. Optical density (OD)1 = 937 nm, OD2 = 947 nm.

## Discussion

Recently, Sanada *et al.* reported prediction models for skeletal muscle index using body mass index (BMI) in Japanese adults.[29] The results showed that the $R^2$ values for the skeletal muscle index were 0.56 in men and 0.45 in women. Similarly, Gallagher *et al.* reported that height and weight accounted for 64% and 67% of the total variance of the appendicular skeletal muscle mass in African-American and Caucasian women, respectively, and 63% and 39% of the total variance in African-American and Caucasian men, respectively.[30] These results showed the difficulty in estimating the AMM accurately using only anthropometric measurements, and the need for an objective method for accurate measurement of body composition.

To address this problem, we investigated whether AMM and AFM could be estimated by a combination of height, weight and NIRS data (OD values). The present results showed that OD1 of the proximal flexor carpi

**Table 3** Regression equation for estimating appendicular muscle mass and fat mass

| Model | Equation | $R^2$ | SEE |
|---|---|---|---|
| Appendicular muscle mass | | | |
| 1 | $y = 0.23 \times$ (height) + $0.13 \times$ (weight) − 26.35 | 0.81 | 1.67 |
| 2 | $y = 0.17 \times$ (height) + $0.17 \times$ (weight) + $8.45 \times$ [OD1 [biceps]) − 28.97 | 0.89 | 1.34 |
| 3 | $y = 0.13 \times$ (height) + $0.18 \times$ (weight) + $10.49 \times$ (OD1 [triceps]) − 23.19 | 0.85 | 1.55 |
| 4 | $y = 0.10 \times$ (height) + $0.24 \times$ (weight) + $7.82 \times$ (OD1 [flexor carpi radialis]) − 21.42 | 0.89 | 1.33 |
| 5 | $y = 0.20 \times$ (height) + $0.15 \times$ (weight) + $6.12 \times$ (OD1 [calf]) − 29.44 | 0.85 | 1.57 |
| Appendicular fat mass | | | |
| 1 | $y = -0.22 \times$ (height) + $0.25 \times$ (weight) + 25.39 | 0.50 | 1.77 |
| 2 | $y = -0.17 \times$ (height) + $0.21 \times$ (weight) − $7.89 \times$ (OD1 [biceps]) + 27.84 | 0.65 | 1.52 |
| 3 | $y = -0.10 \times$ (height) + $0.20 \times$ (weight) − $12.11 \times$ (OD1 [triceps]) + 21.73 | 0.61 | 1.60 |
| 4 | $y = -0.06 \times$ (height) + $0.12 \times$ (weight) − $10.01 \times$ (OD1 [flexor carpi radialis]) + 19.08 | 0.80 | 1.16 |
| 5 | $y = -0.19 \times$ (height) + $0.23 \times$ (weight) − $6.55 \times$ (OD1 [calf]) + 28.70 | 0.58 | 1.66 |

$R^2$, coefficient of determination; SEE, standard error of the estimate.

radialis, in association with anthropometric data, can provide accurate estimates of both AMM and AFM in older adults, although the NIRS data alone did not reflect muscle mass except at the distal triceps. Furthermore, compared with the estimation equation that included only anthropometric data, the estimation equation that included both anthropometric and NIRS data had a higher coefficient of determination.

In the present study, the NIRS data were obtained at six sites to determine the best location for estimating AMM and AFM. As a result, OD values measured at the distal triceps and proximal flexor carpi radialis showed a good correlation coefficient with limb muscle mass and fat mass, respectively. Yasukawa *et al.* reported that the NIRS data (OD values) measured by BFT-2000 (old model of BFT-3000) had higher correlations with percentage fat at the thinner adipose sites than thicker adipose sites,[31] and similar results were observed by Futrex 5000 in another report.[25] Inconsistent strengths of the association of OD values with total body fat at the various sites might simply be a result of differences in the depth of penetration of the infrared radiation. These results suggested that it might be preferable to carry out measurements at sites where there is little subcutaneous fat, such as the flexor carpi radialis.

There are several reports of NIRS being a valid method to assess the percentage of fat or fat mass. For example, Sawai *et al.* reported that the correlation coefficient between percentage body fat as predicted by the NIRS method and as predicted by the hydrostatic weighing technique was 0.88 ($P < 0.001$, SEE = 3.2).[24] Fuller *et al.* also suggested that NIRS methods using Futrex 5000 have the potential to replace skinfold thickness (SFT) for estimation of body composition.[25] The BFT-3000 used in the present study was developed for Japanese patients, and the principle of measurement was the same as for Futrex 5000. Our findings that NIRS data could accurately reflect fat mass are consistent with a previous study.[25] These results suggest that NIRS is a valid method for the estimation of AFM.

Other reports (by Futrex 5000) showed that NIRS might have little or no advantage over SFT in determining body composition.[32,33] One of the reasons for this controversy is that the degree of obesity differs in each patient. Elia *et al.* concluded that NIRS might underestimate body fat in very obese patients.[32] In the present study, the mean BMI of the patients was $23.3 \pm 2.1$ kg/m$^2$ in men and $22.6 \pm 3.2$ kg/m$^2$ in women, and there was no patient whose BMI was over 30 kg/m$^2$. Previous studies of older Japanese patients also reported a BMI ranging from 19.9 to 23.3 kg/m$^2$.[21,22] These results imply that NIRS data might be less affected by subcutaneous fat in older Japanese patients, and that NIRS is a valid method to assess their percentage fat and fat mass.

In contrast, NIRS data were not correlated significantly with whole and regional muscle mass except in the distal triceps. It is possible that quantitative assessment of skeletal muscle mass might be difficult using only NIRS data, because near infrared light might not reach the deeper muscle layer. However, when bodyweight is divided into fat mass and fat-free mass, skeletal muscle constitutes the largest fraction of appendicular fat-free mass. Previous investigators also proposed several models for predicting skeletal muscle mass with DXA. Lean body mass consists mostly of skeletal muscle. If we obtain an accurate bodyweight and the fat mass, the lean body weight (i.e. skeletal muscle mass) can be calculated automatically. The results in the present study suggest that AMM might be estimated indirectly by using NIRS data and bodyweight.

The present study is limited by the small sample size and orthopedic patients who were mostly women. The estimation equations of AMM and AFM developed in

the present study might have high specificity. In addition, we did not confirm the validity of these estimation equations. Thus, further studies are required to check the validity of these equations in other older adults (cross-validity) and longitudinally monitored populations (predictive validity) in the future. Furthermore, these equations will be developed for each sex using larger samples. Finally, to our knowledge, it is unclear whether the OD value (wavelength 937–947 nm) is influenced by blood flow and oxygen saturation. In the previous study, investigators did not mention this point. However, all patients were maintained in a resting position before and during the measurement in the present study. We think that the influence of blood flow and oxygen saturation is not likely to be marked, but this should be considered in a future study.

In conclusion, NIRS data can provide reliable and accurate estimates of AMM and AFM in older adults with the use of anthropometric data (height and weight). The estimation equations of AMM and AFM suggest the possibility that NIRS is a convenient method to assess body composition and to screen sarcopenic (or sarcopenic-obesity) patients. For further adjustment of this equation, it might be expected that sarcopenia or sarcopenic-obesity patients can be screened easily.

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## Disclosure statement

The authors have no financial disclosures or other conflicts of interest to report.

## References

1 Baumgartner RN, Koehler KM, Gallagher D *et al.* Epidemiology of sarcopenia among the elderly in New Mexico. *Am J Epidemiol* 1998; **147**: 755–763.
2 Janssen I, Heymsfield SB, Ross R. Low relative skeletal muscle mass (sarcopenia) in older persons is associated with functional impairment and physical disability. *J Am Geriatr Soc* 2002; **50**: 889–896.
3 Janssen I, Baumgartner RN, Ross R, Rosenberg IH, Roubenoff R. Skeletal muscle cutpoints associated with elevated physical disability risk in older men and women. *Am J Epidemiol* 2004; **159**: 413–421.
4 Janssen I. Influence of sarcopenia on the development of physical disability: the Cardiovascular Health Study. *J Am Geriatr Soc* 2006; **54**: 56–62.
5 Janssen I. Evolution of sarcopenia research. *Appl Physiol Nutr Metab* 2010; **35**: 707–712.
6 Visser M, Goodpaster BH, Kritchevsky SB *et al.* Muscle mass, muscle strength, and muscle fat infiltration as predictors of incident mobility limitations in well-functioning older persons. *J Gerontol A Biol Sci Med Sci* 2005; **60**: 324–333.
7 Goodpaster BH, Park SW, Harris TB *et al.* The loss of skeletal muscle strength, mass, and quality in older adults: the health, aging and body composition study. *J Gerontol A Biol Sci Med Sci* 2006; **61**: 1059–1064.
8 Cosquéric G, Sebag A, Ducolombier C, Thomas C, Piette F, Weill-Engerer S. Sarcopenia is predictive of nosocomial infection in care of the elderly. *Br J Nutr* 2006; **96**: 895–901.
9 Miller MD, Crotty M, Giles LC *et al.* Corrected arm muscle area: an independent predictor of long-term mortality in community-dwelling older adults? *J Am Geriatr Soc* 2002; **50**: 1272–1277.
10 Baumgartner RN. Body composition in healthy aging. *Ann N Y Acad Sci* 2000; **904**: 437–448.
11 Morley JE, Baumgartner RN, Roubenoff R, Mayer J, Nair KS. Sarcopenia. *J Lab Clin Med* 2001; **137**: 231–243.
12 Baumgartner RN, Wayne SJ, Waters DL, Janssen I, Gallagher D, Morley JE. Sarcopenic obesity predicts instrumental activities of daily living disability in the elderly. *Obes Res* 2004; **12**: 1995–2004.
13 Rolland Y, Lauwers-Cances V, Cristini C *et al.* Difficulties with physical function associated with obesity, sarcopenia, and sarcopenic-obesity in community-dwelling elderly women: the EPIDOS (EPIDemiologie de l'OSteoporose) Study. *Am J Clin Nutr* 2009; **89**: 1895–1900.
14 Lee RC, Wang ZM, Heymsfield SB. Skeletal muscle mass and aging: regional and whole-body measurement methods. *Can J Appl Physiol* 2001; **26**: 102–122.
15 Visser M, Fuerst T, Lang T, Salamone L, Harris TB. Validity of fan-beam dual-energy X-ray absorptiometry for measuring fat-free mass and leg muscle mass. Health, Aging, and Body Composition Study – Dual-Energy X-ray Absorptiometry and Body Composition Working Group. *J Appl Physiol* 1999; **87**: 1513–1520.
16 Shih R, Wang Z, Heo M, Wang W, Heymsfield SB. Lower limb skeletal muscle mass: development of dual-energy X-ray absorptiometry prediction model. *J Appl Physiol* 2000; **89**: 1380–1386.
17 Tanimoto Y, Watanabe M, Higuchi Y, Hirota C, Kono K. Evaluation of the best indicator of muscle mass in community-dwelling elderly persons. *Nippon Ronen Igakkai Zasshi* 2008; **45**: 213–219.
18 Miyatani M, Kanehisa H, Fukunaga T. Validity of bioelectrical impedance and ultrasonographic methods for estimating the muscle volume of the upper arm. *Eur J Appl Physiol* 2000; **82**: 391–396.
19 Miyatani M, Kanehisa H, Masuo Y, Ito M, Fukunaga T. Validity of estimating limb muscle volume by bioelectrical impedance. *J Appl Physiol* 2001; **91**: 386–394.
20 Janssen I, Heymsfield SB, Baumgartner RN, Ross R. Estimation of skeletal muscle mass by bioelectrical impedance analysis. *J Appl Physiol* 2000; **89**: 465–471.
21 Yamada Y, Kimura M, Nakamura E, Masuo Y, Oda S. Limb muscle mass decrease with aging in Japanese men and women aged 15–97 yr. *Jpn J Phys Fitness Sports Med* 2007; **56**: 461–472. (In Japanese.)
22 Yamada Y, Schoeller DA, Nakamura E, Morimoto T, Kimura M, Oda S. Extracellular water may mask actual muscle atrophy during aging. *J Gerontol A Biol Sci Med Sci* 2010; **65**: 510–516.

23 Conway JM, Norris KH, Bodwell CE. A new approach for the estimation of body composition: infrared interactance. *Am J Clin Nutr* 1984; **40**: 1123–1130.
24 Sawai S, Shirayama M, Mutoh Y, Miyashita M. Estimation of body fat by near infrared spectroscopic technique. *Jpn J Phys Fitness Sports Med* 1990; **39**: 155–163. (In Japanese.)
25 Fuller NJ, Dewit O, Wells JC. The potential of near infrared interactance for predicting body composition in children. *Eur J Clin Nutr* 2001; **55**: 967–972.
26 Kim J, Wang Z, Heymsfield SB, Baumgartner RN, Gallagher D. Total-body skeletal muscle mass: estimation by a new dual-energy X-ray absorptiometry method. *Am J Clin Nutr* 2002; **76**: 378–383.
27 Chen Z, Wang Z, Lohman T *et al.* Dual-energy X-ray absorptiometry is a valid tool for assessing skeletal muscle mass in older women. *J Nutr* 2007; **137**: 2775–2780.
28 Kalantar-Zadeh K, Dunne E, Nixon K *et al.* Near infra-red interactance for nutritional assessment of dialysis patients. *Nephrol Dial Transplant* 1999; **14**: 169–175.
29 Sanada K, Miyachi M, Yamamoto K *et al.* Prediction models of sarcopenia in Japanese adult men and women. *Jpn J Phys Fitness Sports Med* 2010; **59**: 291–302. (In Japanese.)
30 Gallagher D, Visser M, De Meersman RE *et al.* Appendicular skeletal muscle mass: effects of age, gender, and ethnicity. *J Appl Physiol* 1997; **83**: 229–239.
31 Yasukawa M, Horvath SM, Oishi K, Kimura M, Williams R, Maeshima T. Total body fat estimations by near-infrared interactance, A-mode ultrasound, and underwater weighing. *Appl Human Sci* 1995; **14**: 183–189.
32 Elia M, Parkinson SA, Diaz E. Evaluation of near infra-red interactance as a method for predicting body composition. *Eur J Clin Nutr* 1990; **44**: 113–121.
33 Brooke-Wavell K, Jones PR, Norgan NG, Hardman AE. Evaluation of near infra-red interactance for assessment of subcutaneous and total body fat. *Eur J Clin Nutr* 1995; **49**: 57–65.

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*Research Article*

# Divergent Significance of Bone Mineral Density Changes in Aging Depending on Sites and Sex Revealed through Separate Analyses of Bone Mineral Content and Area

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Bone mineral density (aBMD) is equivalent to bone mineral content (BMC) divided by area. We rechecked the significance of aBMD changes in aging by examining BMC and area separately. Subjects were 1167 community-dwelling Japanese men and women, aged 40–79 years. ABMDs of femoral neck and lumbar spine were assessed by DXA twice, at 6-year intervals. The change rates of BMC and area, as well as aBMD, were calculated and described separately by the age stratum and by sex. In the femoral neck region, aBMDs were significantly decreased in all age strata by an increase in area as well as BMC loss in the same pattern in both sexes. In the lumbar spine region, aBMDs decreased until the age of 60 in women, caused by the significant BMC decrease accompanying the small area change. Very differently in men, aBMDs increased after their 50s due to BMC increase, accompanied by an area increase. Separate analyses of BMC and area change revealed that the significance of aBMD changes in aging was very divergent among sites and between sexes. This may explain in part the dissociation of aBMD change and bone strength, suggesting that we should be more cautious when interpreting the meaning of aBMD change.

## 1. Introduction

Bone mineral density (aBMD) decreases with age [1] and it is the most significant and widely used index for the diagnosis of osteoporosis and for considering the effects of medication in its treatment [2]. When an aBMD decrease is found, the cause is usually considered to be a decrease in bone mineral content (BMC) in the region measured. ABMD is equivalent to BMC divided by an area. Since areal BMD depends both on bone mineral content and bone dimensions, it is difficult to interpret unambiguously [3]. Dimensional changes occur in long bone by aging [4–6], the shape of the bone, and conditions like osteophytes or vertebral fracture in lumbar spine [7–9] are well known. These can affect the measuring area of DXA examinations, and naturally their results. However, a longitudinal epidemiological DXA study on aging considering the effect of the area has not been carried out on a large scale, although there have been cross-sectional studies [10–17]. This study was performed in order to reconsider the significance of aBMD change and aging in different anatomical locations, by analyzing the longitudinal changes of both components of aBMD, namely, BMC and the area, and comparing the differences in sex. A large cohort for longitudinal studies of local inhabitants was used for this study.

## 2. Materials and Methods

*2.1. Subjects.* The subjects were selected among people who participated in both the 1st and 4th waves of the National Institute for Longevity Sciences Longitudinal Study

of Aging (NILS-LSA). Details of the NILS-LSA are presented elsewhere [18]. It is a biannual examination checking the physical and mental condition of ordinary Japanese people, so as to clarify the effect of aging. It is conducted by the National Center for Geriatrics and Gerontology (NCGG), in Japan. The National Institute for Longevity Sciences (NILS) is a research section of NCGG. The participants were chosen randomly from the residents of Obu city and Higashiura-cho, in Aichi prefecture, Japan. For this study, data from 1167 persons were analyzed ($59.2 \pm 10.9$, mean $\pm$ SD). Participants were 594 men and 573 women, whose ages ranged from 40 to 79 at the time of the 1st wave. The 1st and 4th waves were from November 1997 to April 2000, and June 2004 to July 2006, respectively.

*2.2. Measurements of Bone Mineral Density.* Areal bone mineral densities (aBMD) were measured using Hologic QDR4500, both at the 1st and 4th wave. Only one DXA scanner was used. Data on the right femoral neck (Figure 1) and the lumbar spine (L2–4) were used for the analysis. Coefficients of variance of the DXA instrument for aBMD were 1.3% (femoral neck), 1.0% (trochanter), and 0.9% (L2,1–4) [19]. ABMD is equivalent to BMC divided by an area, so the following formula was used for the theoretical calculation: aBMD ($g/cm^2$) = BMC (g)/Area ($cm^2$). Therefore, not only aBMD values but also those of BMC and the area measured were used for the analysis in the three different regions above. The annual change rates (CR) were calculated by the following formula. CR (%) = (the values in the 4th−the values in the 1st)/the values in the 1st $\times$ 100/6. The CRs of aBMD, BMC, and the area measured were calculated and described separately by the age stratum of 40s, 50s, 60s, and 70s and by sex. All who were 40 to 49 years at baseline belonged to the 40's age stratum, and so forth. Data are presented as the mean $\pm$ SD, including those in figures. The study protocol was approved by the Committee on Ethics of Human Research of the National Institute for Longevity Sciences. Written informed consent was obtained from each subject.

*2.3. Statistical Analyses.* The statistical analyses were made to test for significance of change (versus no change) in each subgroup defined by age decade and sex, using paired $t$-tests. Also, the trend analyses according to the increase of the age stratum were made for each subgroup using a general linear model procedure. Gender difference was checked for each subgroup. All analyses were conducted using SAS Ver. 8.2 (SAS Institute, Cary, NC, USA).

## 3. Results

Characteristics of subjects were shown in Table 1.

The change rates (CR) from the first to fourth what were expressed as an annual rate. Mean variation between the two DXA measurements was 6 years.

*3.1. Femoral Neck Region.* ABMDs significantly decreased in all age strata both in women ($-1.1 \pm 1.1\%$ in 40s, $-1.2 \pm 0.9\%$ in 50s, $-1.0 \pm 0.9\%$ in 60s, and $-0.8 \pm 1.1\%$ in 70s, all $P < 0.01$) and in men ($-0.4 \pm 0.8\%$ in 40s, $-0.5 \pm 0.7\%$ in 50s, $-0.6 \pm 0.9\%$ in 60s, and $-0.6 \pm 1.0\%$ in 70s, all $P < 0.01$) (Figures 2(a) and 2(b)). These declines were caused not merely by the decrease of BMC in most of the age strata (in women, $-0.7 \pm 1.4\%$ in 40s, $-0.8 \pm 1.2\%$ in 50s, and $-0.4 \pm 1.2\%$ in 60s, all $P < 0.01$, and in men, $-0.2 \pm 0.9\%$ in 50s and $-0.2 \pm 1.1\%$ in 70s, with $P < 0.01$ and $P < 0.05$, resp.), but also by the constant or significant increase of the area measured (in women, $0.4 \pm 1.1\%$ in 40s, $0.5 \pm 1.1\%$ in 50s, $0.6 \pm 1.2\%$ in 60s, and $0.5 \pm 1.5\%$ in 70s, all $P < 0.01$, and in men, $0.4 \pm 0.6\%$ in 40s, $0.3 \pm 0.8\%$ in 50s, $0.4 \pm 0.8\%$ in 60s, and in $0.4 \pm 0.8\%$ in 70s, all $P < 0.01$). This trend was the same in both sexes. The change rates (CR) of the aBMD and BMC, however, were different between women and men in their 40s, 50s, and 60s (Table 2). The CR became higher (in absolute value) only in women according to age in aBMD and BMC ($P$ trend = 0.0126 and 0.0027, resp.). As for the CR of the area, no significant trend according to age was observed in both sexes, and no sex difference was observed (Table 2).

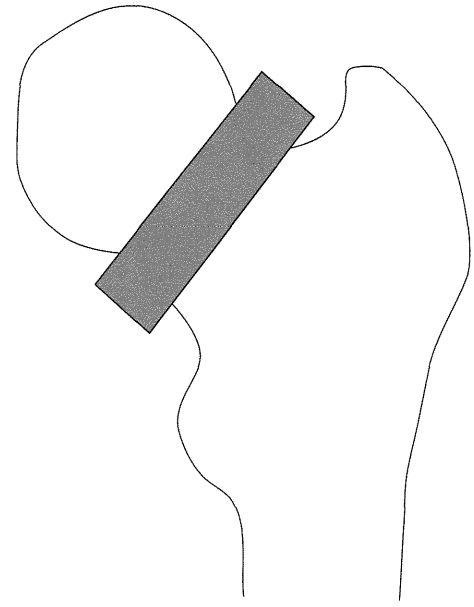

FIGURE 1: Femoral neck region of interest, derived from the Hologic QDR 4500 Operator's Manual.

*3.2. Lumbar Spine Region.* ABMDs significantly decreased in women in their 40s, 50s, and 60s ($-1.1 \pm 1.2\%$ in 40s, $-1.0 \pm 0.9\%$ in 50s, and $-0.2 \pm 1.1$ in 60s, with $P < 0.01$, $P < 0.01$ and $P < 0.05$, resp.) (Figure 3(a)). At earlier ages, these declines were caused by a significant decrease in BMC ($-1.2 \pm 1.5\%$ in 40s and $-1.2 \pm 1.2\%$ in 50s, both $P < 0.01$) accompanied by a small but significant decrease in the area. After their 60s, however, no further decrease in BMC occurred, and the small but significant increase of aBMD was caused by the significant increase in the area.

The patterns of aBMD changes were much different in men. BMDs significantly increased in the 50s, 60s, and 70s ($0.3 \pm 0.8\%$, $0.5 \pm 1.5\%$, and $0.3 \pm 1.0\%$, all $P < 0.01$) due to

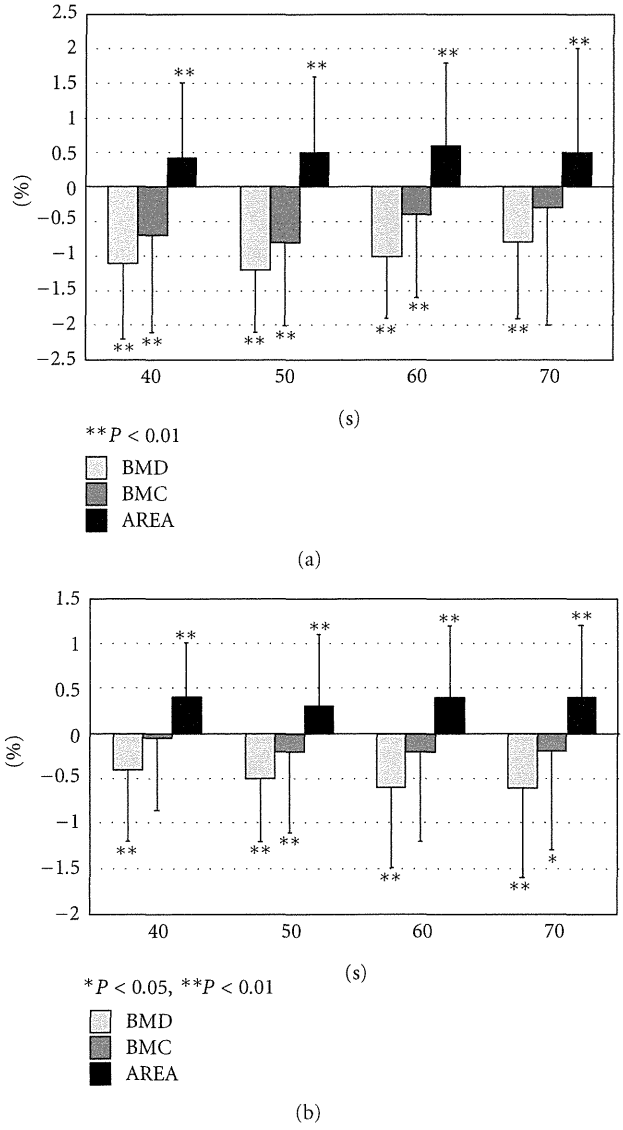


FIGURE 2: (a) Changes in the femoral neck region by age group in women. Results are the mean (±SD) CR of four different age strata. $^{**}P < 0.01$. (b) Changes in the femoral neck region by age group in men. Results are the mean (±SD) CR of four different age strata. $^{*}P < 0.05$, $^{**}P < 0.01$.

the significant increase of BMC (0.5 ± 1.0% in 50s, 1.0 ± 3.4% in 60s, and 0.4 ± 1.2% in 70s, all $P < 0.01$) (Figure 3(b)). The areas significantly increased in every age stratum (0.1 ± 0.5% in 40s, 0.2 ± 0.5% in 50s, 0.4 ± 1.2% in 60s, and 0.2 ± 0.6% in 70s, all $P < 0.01$). Since the increase of BMD occurred after the 50s, the rates of BMC increase surpassed those of the area. The change rates (CR) of the aBMD, BMC, and area were different between women and men in their 40s, 50s, and 60s (Table 2). And in women the CR increased according to age in aBMD, BMC, and area ($P$ trend <0 .0001, $P$ trend <0.0001, and $P$ trend = 0.0115, resp.). The CR increased in men according to age in aBMD and BMC ($P$ trend= 0.006 and $P$ trend = 0.027, resp.), but not in area (Table 2).

TABLE 1: Characteristics of subjects.

| | Women | Men |
|---|---|---|
| Age (years) | 56.5 ± 9.9 | 57.9 ± 9.9 |
| Height (cm) | | |
| All | 152.2 ± 5.7 ($n$ = 573) | 165.4 ± 5.9 ($n$ = 594) |
| 40s | 154.9 ± 5.0 ($n$ = 168) | 168.7 ± 5.5 ($n$ = 148) |
| 50s | 153.3 ± 4.8 ($n$ = 179) | 166.3 ± 5.7 ($n$ = 183) |
| 60s | 150.4 ± 5.6 ($n$ = 147) | 164.0 ± 4.7 ($n$ = 162) |
| 70s | 147.0 ± 5.0 ($n$ = 79) | 161.0 ± 5.2 ($n$ = 101) |
| Weight (kg) | | |
| All | 53.0 ± 8.0 ($n$ = 573) | 62.8 ± 8.5 ($n$ = 594) |
| 40s | 54.1 ± 8.0 ($n$ = 168) | 66.4 ± 8.8 ($n$ = 148) |
| 50s | 53.7 ± 7.4 ($n$ = 179) | 63.5 ± 8.1 ($n$ = 183) |
| 60s | 53.0 ± 8.0 ($n$ = 147) | 61.2 ± 7.8 ($n$ = 162) |
| 70s | 49.1 ± 7.9 ($n$ = 79) | 58.8 ± 7.5 ($n$ = 101) |
| BMI (kg/m$^2$) | | |
| All | 22.9 ± 3.2 ($n$ = 573) | 22.9 ± 2.6 ($n$ = 594) |
| 40s | 22.5 ± 3.3 ($n$ = 168) | 23.3 ± 2.6 ($n$ = 148) |
| 50s | 22.9 ± 3.2 ($n$ = 179) | 23.0 ± 2.5 ($n$ = 183) |
| 60s | 23.4 ± 3.1 ($n$ = 147) | 22.8 ± 2.7 ($n$ = 162) |
| 70s | 22.7 ± 3.1 ($n$ = 79) | 22.6 ± 2.5 ($n$ = 101) |
| BMD at 1st wave | | |
| Femoral neck (g/cm$^2$) | 0.7 ± 0.1 | 0.8 ± 0.1 |
| Trochanter (g/cm$^2$) | 0.6 ± 0.1 | 0.7 ± 0.1 |
| Lumbar spine (L2–4) (g/cm$^2$) | 0.9 ± 0.2 | 1.0 ± 0.2 |
| BMC at 1st wave | | |
| Femoral neck (g) | 3.2 ± 0.6 | 4.0 ± 0.7 |
| Trochanter (g) | 6.0 ± 1.3 | 8.7 ± 1.6 |
| Lumbar spine (L2–4) (g) | 38.1 ± 9.3 | 50.7 ± 10.0 |
| Area at 1st wave | | |
| Femoral neck (cm$^2$) | 4.6 ± 0.3 | 5.3 ± 0.3 |
| Trochanter (cm$^2$) | 10.2 ± 1.2 | 12.8 ± 1.4 |
| Lumbar spine (L2–4) (cm$^2$) | 42.3 ± 3.9 | 51.3 ± 4.5 |

Values are mean ± SD.

## 4. Discussion

ABMD is equivalent to BMC divided by an area, but when we encounter cases of BMD decline, we simply consider the decline of the BMC at the measured sites without

Table 2: $P$ trend according to age strata and $P$ value of sex difference analyses of subgroup.

| | | $P$ trend according to age strata | | Sex difference analysis | | | |
|---|---|---|---|---|---|---|---|
| | | women | men | 40s | 50s | 60s | 70s |
| Femoral neck | BMD | 0.0126 | 0.1682 | <0.0001 | <0.0001 | <0.0001 | 0.0982 |
| | BMC | 0.0027 | 0.2519 | <0.0001 | <0.0001 | 0.0298 | 0.7122 |
| | Area | 0.2084 | 0.9947 | 0.9436 | 0.0434 | 0.0987 | 0.2391 |
| Lumbar spine | BMD | <0.0001 | 0.006 | <0.0001 | <0.0001 | <0.0001 | 0.815 |
| | BMC | <0.0001 | 0.027 | <0.0001 | <0.0001 | <0.0001 | 0.4277 |
| | Area | 0.0115 | 0.3383 | <0.0001 | <0.0001 | 0.0052 | 0.0986 |

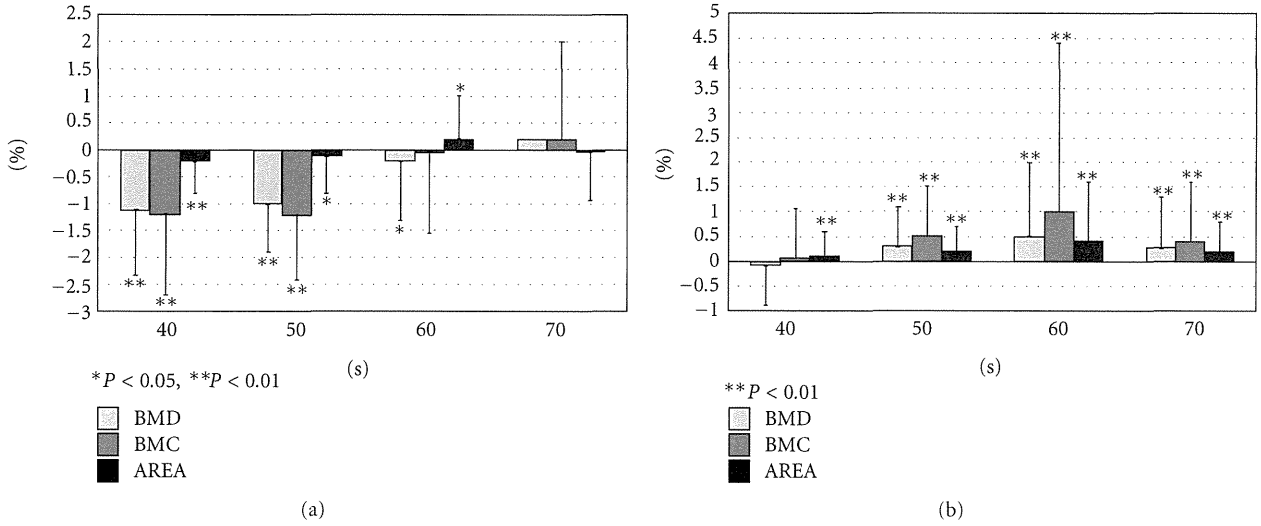


Figure 3: (a) Changes in the lumbar spine region by age group in women. Results are the mean (±SD) CR of four different age strata. $*P < 0.05$, $**P < 0.01$. (b) Changes in the lumbar spine region by age group in men. Results are the mean (±SD) CR of four different age strata. $**P < 0.01$.

incorporating the change of the area (or size), which may represent the change of the shape in the region. The present study demonstrated that in the femoral neck, the aBMD decline in aging occurs not only due to the decline of BMC, but also due to the increase in the area, for both men and women. In fact, the increase of the femoral neck area represents the physiological compensating effect of the weakened bone tolerance [4, 20–23], caused by BMC decline. This may be one of the reasons for the dissociation between the strength of the bone and aBMD values. The widening (or enlargement) of the femoral neck in elderly persons has been demonstrated by the hip structure analyses of DXA [10, 13–15], by computed tomography [23–26], or utilizing both [27, 28]. The annual change rates of aBMD in our study in the femoral neck region were around −1% in women (Figure 2(a)) and 0.5% in men (Figure 2(b)). This is almost equal to the level of the large population-based cohort in Hiroshima Japan, −1.14% in women, and −0.38% in men [29]. In the lumbar spine, however, a sexual difference was observed in the changes of aBMD and those of BMC or the area as well. The increase in BMC together with the area may be explained by the osteophyte formation found to be more marked in elderly men [7, 9]. This type of change, osteophyte formation, occurs also in women but later. The significant area increase in women may derive from the osteophyte formation in advanced age. The reason for the significant decrease in the areas in women in their 40s and 50s is unclear at the moment. More detailed studies, using CT scans, are warranted to elucidate the mechanism of the sex difference in the spinal region.

From this perspective, the meaning or significance of aBMD change should be diverse depending on the sites measured and gender. Moreover, the apparent decrease of aBMD may not simply represent the weakness of that measured region (e.g., in the femoral neck), since the greater diameter can make the cylindrical structure stronger [21].

The limitation of this study is that the measurements were carried out by the ordinary DXA method without using elaborate software like hip structure analysis or CT. DXA has an inherent inaccuracy [30–32]. If body composition or weight changed during the followup, it is possible that BMD is inaccurately measured, namely, it may be over- or underestimated. Also, the size measuring by DXA was not very accurate for volumetric analysis. But our method disclosed the differences among sites and between sexes, particularly in terms of longitudinal effect, which have been little investigated.

The strength of our study is its random selection of our samples from people in the local community with very little bias in the process. NILS-LSA is one of the few major epidemiological studies investigating the aging mechanism that is designed to select subjects in a completely random manner. The results of this study should therefore reveal characteristics of the entire Japanese population.

In summary, we investigated the meaning of aBMD changes in aging through separate analyses of BMC and area change. The results revealed that the significance of aBMD changes were very divergent among the sites measured, and between sexes. This may explain the dissociation of aBMD change and bone strength, which encourages one to be more cautious when interpreting the meaning of aBMD change.

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## References

[1] P. Steiger, S. R. Cummings, D. M. Black, N. E. Spencer, and H. K. Genant, "Age-related decrements in bone mineral density in women over 65," *Journal of Bone and Mineral Research*, vol. 7, no. 6, pp. 625–632, 1992.

[2] S. R. Cummings, D. Bates, and D. M. Black, "Clinical use of bone densitometry: scientific review," *Journal of the American Medical Association*, vol. 288, no. 15, pp. 1889–1897, 2002.

[3] H. Sievänen, "A physical model for dual-energy X-ray absorptiometry-derived bone mineral density," *Investigative Radiology*, vol. 35, no. 5, pp. 325–330, 2000.

[4] C. B. Ruff and W. C. Hayes, "Subperiosteal expansion and cortical remodeling of the human femur and tibia with aging," *Science*, vol. 217, no. 4563, pp. 945–948, 1982.

[5] R. P. Heaney, M. J. Barger-Lux, K. M. Davies, R. A. Ryan, M. L. Johnson, and G. Gong, "Bone dimensional change with age: interactions of genetic, hormonal, and body size variables," *Osteoporosis International*, vol. 7, no. 5, pp. 426–431, 1997.

[6] H. G. Ahlborg, O. Johnell, C. H. Turner, G. Rannevik, and M. K. Karlsson, "Bone loss and bone size after menopause," *New England Journal of Medicine*, vol. 349, no. 4, pp. 327–334, 2003.

[7] H. Kinoshita, T. Tamaki, T. Hashimoto, and F. Kasagi, "Factors influencing lumbar spine bone mineral density assessment by dual-energy X-ray absorptiometry: comparison with lumbar spinal radiogram," *Journal of Orthopaedic Science*, vol. 3, no. 1, pp. 3–9, 1998.

[8] A. Atalay, M. Kozakcioglu, R. Cubuk, N. Tasali, and S. Guney, "Degeneration of the lumbar spine and dual-energy X-ray absorptiometry measurements in patients without osteoporosis," *Clinical Imaging*, vol. 33, no. 5, pp. 374–378, 2009.

[9] Ö Karabulut, M. C. Tuncer, Z. Karabulut, A. Açlkgöz, E. S. Hatipoğlu, and Z. Akkuş, "Relationship between radiographic features and bone mineral density in elderly men," *Folia Morphologica*, vol. 69, no. 3, pp. 170–176, 2010.

[10] T. J. Beck, C. B. Ruff, W. W. Scott Jr., C. C. Plato, J. D. Tobin, and C. A. Quan, "Sex differences in geometry of the femoral neck with aging: a structural analysis of bone mineral data," *Calcified Tissue International*, vol. 50, no. 1, pp. 24–29, 1992.

[11] K. S. Tsai, W. C. Cheng, C. K. Chen et al., "Effect of bone area on spine density in Chinese men and women in Taiwan," *Bone*, vol. 21, no. 6, pp. 547–551, 1997.

[12] M. Peacock, G. Liu, M. Carey et al., "Bone mass and structure at the hip in men and women over the age of 60 years," *Osteoporosis International*, vol. 8, no. 3, pp. 231–239, 1998.

[13] T. J. Beck, A. C. Looker, C. B. Ruff, H. Sievanen, and H. W. Wahner, "Structural trends in the aging femoral neck and proximal shaft: analysis of the Third National Health and Nutrition Examination Survey dual-energy x-ray absorptiometry data," *Journal of Bone and Mineral Research*, vol. 15, no. 12, pp. 2297–2304, 2000.

[14] S. Kaptoge, N. Dalzell, N. Loveridge, T. J. Beck, K. T. Khaw, and J. Reeve, "Effects of gender, anthropometric variables, and aging on the evolution of hip strength in men and women aged over 65," *Bone*, vol. 32, no. 5, pp. 561–570, 2003.

[15] D. A. Nelson, J. M. Pettifor, D. A. Barondess, D. D. Cody, K. Uusi-Rasi, and T. J. Beck, "Comparison of cross-sectional geometry of the proximal femur in white and black women from Detroit and Johannesburg," *Journal of Bone and Mineral Research*, vol. 19, no. 4, pp. 560–565, 2004.

[16] X. F. Wang, Y. Duan, T. J. Beck, and E. Seeman, "Varying contributions of growth and ageing to racial and sex differences in femoral neck structure and strength in old age," *Bone*, vol. 36, no. 6, pp. 978–986, 2005.

[17] A. C. Looker, H. W. Wahner, W. L. Dunn et al., "Updated data on proximal femur bone mineral levels of US adults," *Osteoporosis International*, vol. 8, no. 5, pp. 468–489, 1998.

[18] H. Shimokata, F. Ando, and N. Niino, "A new comprehensive study on aging—the National Institute for Longevity Sciences, Longitudinal Study of Aging (NILS-LSA)," *Journal of Epidemiology*, vol. 10, no. 1, pp. S1–S9, 2000.

[19] Y. Yamada, F. Ando, N. Niino, and H. Shimokata, "Association of polymorphisms of interleukin-6, osteocalcin, and vitamin D receptor genes, alone or in combination, with bone mineral density in community-dwelling Japanese women and men," *Journal of Clinical Endocrinology and Metabolism*, vol. 88, no. 7, pp. 3372–3378, 2003.

[20] B. Martin, "Aging and strength of bone as a structural material," *Calcified Tissue International*, vol. 53, supplement 1, pp. S34–S39, 1993.

[21] E. Seeman, "Periosteal bone formation—a neglected determinant of bone strength," *New England Journal of Medicine*, vol. 349, no. 4, pp. 320–323, 2003.

[22] E. S. Orwoll, "Toward an expanded understanding of the role of the periosteum in skeletal health," *Journal of Bone and Mineral Research*, vol. 18, no. 6, pp. 949–954, 2003.

[23] C. R. Russo, F. Lauretani, E. Seeman et al., "Structural adaptations to bone loss in aging men and women," *Bone*, vol. 38, no. 1, pp. 112–118, 2006.

[24] T. F. Lang, J. H. Keyak, M. W. Heitz et al., "Volumetric quantitative computed tomography of the proximal femur: precision and relation to bone strength," *Bone*, vol. 21, no. 1, pp. 101–108, 1997.

[25] B. L. Riggs, L. J. Melton III, R. A. Robb et al., "Population-based study of age and sex differences in bone volumetric density, size, geometry, and structure at different skeletal sites," *Journal of Bone and Mineral Research*, vol. 19, no. 12, pp. 1945–1954, 2004.

[26] L. M. Marshall, T. F. Lang, L. C. Lambert, J. M. Zmuda, K. E. Ensrud, and E. S. Orwoll, "Dimensions and volumetric BMD of the proximal femur and their relation to age among older U.S. men," *Journal of Bone and Mineral Research*, vol. 21, no. 8, pp. 1197–1206, 2006.