



Available online at
ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com/en



Review

Trabecular Bone Score: Where are we now?



Valérie Bousson^{a,*,b}, Catherine Bergot^b, Bruno Sutter^c, Thierry Thomas^d,
 Sauveur Bendavid^e, Claude-Laurent Benhamou^f, Hubert Blain^g, Michel Brazier^h,
 Véronique Breuilⁱ, Karine Briot^j, Roland Chapurlat^k, Laure Chapuis^l,
 Martine Cohen Solal^m, Patrice Fardelloneⁿ, Jean-Marc Feron^o, Jean-Bernard Gouvain^p,
 Michel Laroche^q, Erick Legrand^r, Eric Lespessailles^f, Agnès Linglart^s, Christian Marcelli^t,
 Christian Roux^j, Jean-Claude Souberbielle^u, Florence Tremollières^v, Georges Weryha^w,
 Bernard Cortet^x, Groupe de Recherche et d'Information sur les Ostéoporoses (GRIO)

^a Radiologie ostéo-articulaire, université Paris VII–Denis-Diderot, Sorbonne Paris Cité, hôpital Lariboisière, AP–HP, 2, rue Ambroise-Paré, 75010 Paris, France

^b B2OA, CNRS UMR 7052, 10, avenue de Verdun, 75010 Paris, France

^c Unité de médecine nucléaire, institut Calot, groupe HOPALE, 62608 Berck/Mer cedex, France

^d Inserm U1059, service de rhumatologie, CHU de Saint-Étienne, 42055 Saint-Étienne cedex 2, France

^e Médecine générale, 75014 Paris, France

^f EA4708 I3MTO, university of Orleans, 45100 Orleans, France

^g Pôle de gériatrie, centre Antonin-Balmes, CHU de Montpellier, 34295 Montpellier, France

^h Laboratoire de biologie endocrinienne et ostéo-articulaire, CHU d'Amiens, 80054 Amiens, France

ⁱ Service de rhumatologie, université Nice Sophia-Antipolis, CHU de Nice-1, 06200 Nice, France

^j Service de rhumatologie, université Paris-Descartes, hôpital Cochin, 75014 Paris, France

^k Inserm U 403, service de rhumatologie, hôpital Edouard-Herriot, 69003 Lyon, France

^l Service de rhumatologie, 35500 Vitry, France

^m Inserm U606, université Paris-Diderot Paris 7, hôpital Lariboisière, 75010 Paris, France

ⁿ Inserm ERI 12, service de rhumatologie, CHU d'Amiens, 80054 Amiens cedex 2, France

^o Service de chirurgie orthopédique, hôpital Saint-Antoine, 75012 Paris, France

^p Centre de médecine gériatrique, CHR d'Orléans, 45032 Orléans, France

^q Centre de rhumatologie, CHU Purpan, 31059 Toulouse, France

^r Service de rhumatologie, CHU d'Angers, 49933 Angers cedex 09, France

^s Service d'endocrinologie–diabétologie pédiatrique, 94270 Le Kremlin-Bicêtre, France

^t Service de rhumatologie, hôpital Côte-de-Nacre, 14033 Caen cedex 09, France

^u Inserm U845, Laboratoire d'explorations fonctionnelles, hôpital Necker–Enfants-Malades, 75015 Paris, France

^v Centre de ménopause, hôpital Paule-de-Viguier, 31000 Toulouse, France

^w Service d'endocrinologie, CHU de Nancy, 54511 Vandœuvre-lès-Nancy, France

^x Service de rhumatologie, hôpital Roger-Salengro, 59037 Lille cedex, France

ARTICLE INFO

Article history:

Accepted 4 February 2015

Available online 24 April 2015

Keywords:

Osteoporosis

Fragility fracture

Densitometry

Bone mineral density

Trabecular Bone Score

ABSTRACT

The Trabecular Bone Score is a rather new index obtained at the lumbar spine at the same time as a real bone mineral density. It was developed to reflect bone microarchitecture. It was proposed to be easily used in everyday practice as a surrogate of bone strength. Our aim was to review 1. technical points such as correlations between Trabecular Bone Score and bone microarchitectural parameters, Trabecular Bone Score and bone strength, the effects of dual-energy X-ray absorptiometry image spatial resolution, age, macroarchitecture, body mass index, and osteoarthritis, on Trabecular Bone Score, and 2. evidences to use Trabecular Bone Score for separating individuals with fragility fractures from controls, predicting fragility fractures, and for longitudinally monitoring changes related to treatments. Correlations between Trabecular Bone Score and bone microarchitectural parameters vary widely across bone sites, microarchitectural parameters, and study designs. In vivo, the Trabecular Bone Score explains little of the variance

* Corresponding author at: Radiologie ostéo-articulaire, université Paris VII–Denis-Diderot, Sorbonne Paris Cité, hôpital Lariboisière, AP–HP, 2, rue Ambroise-Paré, 75010 Paris, France. Tel.: +33 1 49 95 61 80; fax: +33 1 49 95 86 99.

E-mail address: valerie.bousson@lrp.aphp.fr (V. Bousson).

in trabecular microarchitectural parameters. We emphasize that it is a texture parameter. The Trabecular Bone Score is reduced in patients with fragility fracture. Several retrospective and prospective studies have shown its discriminative ability regarding the fracture risk. When combining the areal Bone mineral Density and Trabecular Bone Score, the Trabecular Bone Score remains a predictor of fracture but not the areal Bone Mineral Density. However in prospective studies, the best predictor of fracture remains hip areal bone mineral density. Due to the lack of evidence, we recommend not to use Trabecular Bone Score for following patients treated by anti-osteoporotic drugs.

© 2015 Société française de rhumatologie. Published by Elsevier Masson SAS. All rights reserved.

1. Introduction

Areal bone mineral density (aBMD) measurement using dual-energy X-ray absorptiometry (DXA) fails to fully capture the fragility fracture risk. The Trabecular Bone Score (TBS) was developed to reflect bone microarchitecture. It analyses local gray-scale variations in 2D projection images. The method was initially described on 2D projection images of 3D micro-computed tomography (μ CT) images [1], and subsequently adapted for DXA images. TBS and aBMD are computed in the same region of interest of the lumbar spine (LS) but successively and via different methods. A high TBS value is thought to reflect a trabecular microarchitecture associated with good mechanical strength. A low TBS value, in contrast, may indicate poor-quality microarchitecture. The TBS is currently easily used in everyday practice as a surrogate of bone strength.

On behalf of GRIO, we published in 2011 a review on the TBS [2]. Since this, the United States Food and Drug Administration approved TBS, and numerous studies have been published, encouraging us to update our work. In the first part of the manuscript, we further focused on the question: what evidence do we have today that TBS reflects microarchitecture and perhaps bone strength? Also, we analyzed the influence of spatial resolution, demographic factors (age and body mass index), and osteoarthritis, on TBS, and finally correlations between TBS and aBMD. Much of the first part is accessible as [Appendix A \(S1, S2 and S3; see the supplementary material associated with this article online\)](#). The second part focused on the interest of TBS in clinical practice.

2. What evidence do we have today that Trabecular Bone Score computed from dual-energy X-ray absorptiometry images reflects bone microarchitecture and perhaps bone strength?

2.1. Correlation between the Trabecular Bone Score computed from raw dual-energy X-ray absorptiometry images and microarchitectural parameters on one hand, and bone strength on the other hand, ex vivo and in vivo

Results from ex vivo studies are provided in [2] as well as in Text S1 [3–5].

There are few in vivo studies establishing correlations between TBS and microarchitectural parameters. In a study from Silva et al. [6], 71 pre- and 44 postmenopausal women were investigated using DXA, QDR 4500A, Hologic (aBMD at lumbar spine [LS], total hip [TH], femoral neck [FN], one-third radius, and LS TBS), QCT of the spine and hip (L1-L2 vertebral body cross sectional area [CSA], trabecular vBMD at mid-vertebra, FN minimal CSA, integral, trabecular [Tb] and cortical [Ct] vBMD at the FN and TH), and HRpQCT at the radius and tibia (total vBMD, Ct.vBMD, Ct.Th, Tb.vBMD, BV/TV, Tb.N, Tb.Th, Tb.Sp). TBS correlated with all QCT indices of vBMD, with the strongest association at LS trabecular vBMD ($r=0.664$; $P<0.001$). TBS correlated with an estimate of cortical thickness at the FN and TH ($r=0.54$; $P<0.001$ for both), but not with bone size

(CSA). The strength of the association between FN integral vBMD and TBS was even greater than the association between FN integral vBMD and LS aBMD (0.651 vs 0.508, value comparison $P=0.01$). Correlations between TBS and HRpQCT indices of vBMD at radius and tibia were weaker than those observed with QCT (at the radius $r=0.22$; 0.23; 0.34 for total vBMD; cortical vBMD; trabecular vBMD respectively. At the tibia $r=0.34$; 0.52; 0.33 for total vBMD; cortical vBMD; trabecular vBMD respectively). Correlations between TBS and microstructural indices at radius and tibia ranged between 0.135 and 0.266 (absolute r values). For example, Tb.N at the radius and tibia explained 4% of the TBS variance, Tb.Sp 6%. In summary, this study indicates that TBS is correlated to vBMD but poorly to microarchitecture, perhaps due to measurements performed on different sites.

Another in vivo study [7] tested correlations between TBS and microarchitectural parameters in 22 postmenopausal women with primary hyperparathyroidism (PHPT, mean age: 67 years). Correlations were observed between TBS and aBMD at the one-third and ultradistal radius ($r=0.43$ and 0.45; $P=0.047$ and 0.036), but not at the LS, TH, FN. TBS was significantly correlated with vBMD (HRpQCT) at the radius and tibia, cortical, trabecular and total (r ranged between 0.471 and 0.619), BV/TV, cortical thickness ($r=0.453$ at the radius and $r=0.515$ at the tibia), and whole bone stiffness. At the radius, TBS explained 25%, 21% and 10% of the variance in Tb.N, Tb.Sp and Tb.Th; at the tibia respectively 8.8%, 13.3%, and 0.3%. In addition, when body weight was included in the analyses, TBS was no longer correlated with HRpQCT indices, indicating interactions between TBS and weight. The authors also suggested a tendency for higher correlations between TBS and LS BMD when Hologic scanners were used in comparison with Lunar devices.

In summary, although TBS was proposed as a parameter reflecting bone microarchitecture, a critical point is that the correlations between TBS and bone microarchitectural parameters vary widely across bone sites, microarchitectural parameters, and study designs. In the only ex vivo published study [5], TBS explains 34% and 38% of the variance in trabecular BV/TV and SMI respectively. In vivo [6], some correlations are significant but even weaker. Based on these in vivo data, two questions remains without clear answer. Is the peripheral site for microarchitecture assessment a sufficient explanation for the weak correlations? Is there a confounding role for the interposition of soft tissues in the assessment of TBS? Concerning bone strength, TBS explains 41% of the variance in bone stiffness but does not explain a significant part of the variance in failure load [5].

2.2. Effects of image spatial resolution

The effects of image spatial resolution [8,9], age [10–17], macroarchitecture [5,6], body mass index [13,14], and osteoarthritis [10,17,18], on Trabecular Bone Score, and correlations between Trabecular Bone Score and Bone Mineral Density [1,7,16] are developed in Text S2.

3. What evidence do we have today that Trabecular Bone Score can be used for separating individuals with fragility fractures from controls, predicting fragility fractures, and for longitudinally monitoring changes related to treatments?

3.1. Studies of the fracture-discriminating ability of Trabecular Bone Score

Five retrospective cross-sectional studies [11,19–22] conclude that TBS is capable of separating individuals with fractures from controls, that the discriminative power of the TBS is similar to that of LS aBMD, and that, in some situations, combining the TBS and LS aBMD provides better discrimination than LS aBMD alone. The discriminative capability of TBS as compared with hip aBMD, that is a key point, has been less investigated.

The first cross-sectional study [19] was a retrospective case-control study of 200 women, of whom 45 had fractures (radiographic vertebral fractures, $n = 20$; hip fractures, $n = 5$; other, $n = 20$) and 155 did not. Controls were matched to cases for age and LS aBMD. aBMD and TBS were determined using a Hologic QDR 4500A machine, in the L2–L4 region, after exclusion of vertebrae with fractures or osteoarthritis. The TBS was significantly lower in the patients with fractures than in the controls (all fractures, $P = 0.0005$; vertebral fractures only, $P = 0.0004$). Concerning fracture discrimination, the TBS had an OR of 1.95 and an area under the ROC curve (AUC) of 0.685 for all fractures (45 fracture patients and 90 matched controls), and an OR of 2.66 and AUC of 0.776 for vertebral fractures only (20 fractured patients and 60 age and LS aBMD matched controls).

The second cross-sectional study [20] was a retrospective case-control evaluation of the TBS as a tool for identifying patients with osteopenia and fractures. Only vertebral fractures were considered. The 81 patients with fractures were compared to the 162 other patients. Vertebral fractures were identified on radiographs. aBMD and the TBS were determined at the L1–L4 spine after exclusion of vertebrae with fractures or osteoarthritis. After adjustment on body weight, the ORs were 1.63 for LS aBMD and 1.97 for the TBS, and the AUC values differed significantly with higher AUC with TBS than with aBMD ($P = 0.02$; AUC values after adjustment on body weight were not reported). When LS aBMD and weight-adjusted TBS were combined, the OR was 2.04 and the AUC (not reported) was significantly larger than for LS aBMD alone ($P = 0.005$).

The third cross-sectional study [21] was conducted in a population of postmenopausal women with aBMD T -scores < -1.0 . Forty-two patients with vertebral fractures were compared to 126 controls. After adjustment for body weight, the ORs were 2.48 for LS aBMD and 3.81 for the TBS. No significant difference was found between the AUCs for LS aBMD alone and for the TBS alone ($P = 0.140$). When LS aBMD and the TBS were used in combination (OR = 3.55), the AUC was significantly larger than with LS aBMD alone ($P = 0.006$).

Among 528 patients selected from a French Fracture Liaison Service (FLS) [22], 362 patients were studied with aBMD and vertebral fracture assessment (VFA) using DXA (QDR 4500A Hologic device). Prevalence of vertebral fracture was 36.7%. Performance of TBS was similar to LS aBMD and hip aBMD for the identification of patients with vertebral fracture. In the population with aBMD in the non-osteoporotic range ($n = 173$), AUC of TBS for the discrimination of vertebral fracture was higher than the AUC of LS aBMD (0.671 vs 0.541, $P = 0.035$) but not of hip aBMD (0.670 vs 0.585, $P = 0.264$). Combination of TBS and LS aBMD was superior to LS aBMD alone but with borderline significance ($P = 0.043$). There was a negative correlation between TBS and spinal deformity index (SDI) ($r = -0.31$; $P < 0.0001$). To summarize, in a study not specifically dedicated to TBS, TBS was lower in elderly patients with a

recent fragility fracture evidenced by VFA than in non-fractured subjects.

A fifth cross-sectional study [11] evaluated the ability of LS TBS to discriminate subjects with hip fracture (the four previous studies dealt with vertebral fractures). The study population consisted of 83 patients with a femoral neck fracture and 108 control subjects. Significantly lower lumbar spine and hip aBMD and TBS values were found in women who had experienced a hip fracture ($P < 0.0001$). Correlation between LS-aBMD and spine TBS was moderate ($r = 0.41$, $P < 0.05$). LS-BMD and TBS independently discriminated fractures equally well (OR = 2.21 and 2.05, respectively) but remained less performant than aBMD at neck or at total femur (OR = 5.86 and 6.06, respectively). After adjusting for age, LS-aBMD and TBS remained significant for hip fracture discrimination (OR = 1.94 and 1.71, respectively). TBS and LS-BMD combination (OR = 2.39) improved fracture risk prediction by 25%. Nevertheless, hip aBMD remained the best discriminator of hip fracture.

3.2. Studies of Trabecular Bone Score as a predictor of fragility fractures

Three studies [15,16,23,24] reported similar capabilities of LS TBS and aBMD to predict fragility fractures.

3.2.1. Manitoba Cohort [23]

The objective of this study published in 2011 [23], was to prospectively compare TBS and LS aBMD as tools for predicting fragility fractures (Prodigy, GE-Lunar). The study used the Manitoba cohort (29,407 women aged 50 years or older). Sixteen hundred and sixty-eight women (5.67%) experienced a major osteoporotic fracture as defined in the FRAX tool. For a given LS aBMD range (normal or osteopenic or osteoporotic), the annual number of incident fractures was higher in the lowest TBS tertile. LS aBMD and TBS were weakly correlated ($r = 0.32$, P value not provided). Results were similar for predicting hip fractures or any of the four fracture types considered. For the four fracture types together, vertebral fractures only, and hip fractures only, the predictive ability of vertebral or femoral aBMD was significantly improved by combination with the TBS ($P < 0.0001$ or $P = 0.006$).

The results of the Manitoba study indicate that not only aBMD, but also TBS can predict the occurrence of major fractures with and without multiple adjustments. The strength of the association for assessing the risk of fracture was similar for TBS and LS aBMD. However aBMD both at the total hip and FN was a better predictor of a major fracture than TBS and than aBMD at the spine. Combining aBMD and TBS significantly increased the prediction of a major fracture suggesting that TBS and aBMD do not provide the same information. Unfortunately the authors did not study the usefulness of combining aBMD at the hip and at the spine for predicting major fractures. Also women with the lowest values of aBMD (osteoporosis according to the WHO classification) and the lowest values of TBS (lower tertile) had a 6-fold increased risk of fracture (major fracture) compared to women with the highest aBMD values (normal aBMD according to the WHO classification) and the highest TBS values (higher tertile of TBS).

3.2.2. OFELY Cohort [15,16]

A lumbar spine and a hip DXA examination (QDR 4500A, Hologic, USA) was done at baseline in 2000–2001. At baseline, women with incident fractures were significantly older (70 ± 9 years vs. 65 ± 8 years), were more prone to have a personal history of fracture (30% vs 14%, $P = 0.001$), had significantly lower values for LS aBMD and TH aBMD (respectively T -score, -1.9 ± 1.2 vs. -1.4 ± 1.3 and -1.3 ± 0.9 vs. 0.7 ± 0.9 , $P < 0.001$ for both), and lower values of TBS (1.237 ± 0.098 vs. 1.284 ± 0.105 , $P < 0.001$) than women without fractures.

Considering the WHO classification scheme, 38% of the patients with incident fractures had osteoporosis ($n = 36/123$; fracture rate, 29%), 47% had osteopenia ($n = 44/280$, fracture rate, 16%), and 15% had normal aBMD values ($n = 14/161$, fracture rate, 9%) at baseline. Among patients with fractures and osteopenia, 39% were in the lowest TBS tertile ($n = 17/89$, fracture rate, 19.3%), and 61% of patients with fractures and osteopenia were in the middle or highest TBS tertile.

Fracture prediction was similar for LS aBMD and TBS (ORs for each 1.0 SD change, 1.6 and 1.7, respectively). LS aBMD and TBS correlated significantly with age ($r = -0.17$ and $r = -0.49$, respectively; $P < 0.001$) and with each other, with 39% of the TBS variance being explained by the LS aBMD ($r = 0.63$, $P < 0.001$). After adjustment on age and presence of a prevalent fracture, adding TBS to aBMD did not significantly improve the prediction of incident fracture.

In summary, the results of the OFELY study indicate that not only aBMD, but also TBS can predict the occurrence of fragility fractures with and without multiple adjustments. When combining LS aBMD and TBS, TBS remains a predictor of fracture but not LS aBMD. TBS seems to be particularly relevant for women without osteoporosis according to the WHO classification. Indeed using a threshold of 1.209 for TBS, non osteoporotic women with low TBS had an incidence of fracture more than twice higher compared to non osteoporotic women with high TBS values. Finally, multivariate analysis showed that among three parameters: LS aBMD, TBS and TH aBMD, the sole significant predictor of fracture was TH aBMD. A striking result was that, among osteopenic patients with fractures, 39% were in the lowest TBS tertile, suggesting that the TBS may indicate bone fragility in more than one-third of patients with aBMD *T*-scores between -1.0 and -2.5 . However after adjustment for age and the number of prevalent fractures, the TBS failed to significantly improve fragility fracture prediction over aBMD alone conversely to what was observed in the Manitoba study [23].

3.2.3. OPUS cohort [24]

The objective of this study conducted in the multicenter prospective OPUS cohort was to consider whether TBS improves the prediction of incident fractures in postmenopausal women compared with the measurement of aBMD alone. Subject with incident clinical osteoporotic fracture (or incident vertebral fracture), were older, reported more frequently a history of low trauma fracture and had more prevalent radiographic vertebral fractures and significantly lower baseline LS aBMD, FN aBMD and TBS than patients without incident clinical osteoporotic fracture (or incident vertebral fracture). For the prediction of incident clinical osteoporotic fracture, performance of TBS was significantly better than LS aBMD ($P = 0.007$) but similar to FN aBMD ($P = 0.215$) or TH aBMD ($P = 0.08$) or combination of TBS and aBMD (LS, FN or TH). For the prediction of radiographic vertebral fracture, performance of the combination of TBS and LS aBMD was significantly better ($P = 0.046$) than that of LS aBMD alone but similar to FN aBMD and TH aBMD. In the 672 non-osteoporotic women at baseline, TBS and aBMD had similar performance for incident clinical fracture but only aBMD (not TBS) predicted incident radiographic fracture.

3.3. Changes in the Trabecular Bone Score related to diseases or treatments associated with bone loss

3.3.1. Clinical factors associated with Trabecular Bone Score [14]

This study [14] was conducted in the Manitoba cohort (same population as in [23]). The aim of the study was to identify clinical factors that are associated with baseline LS TBS. There was a negative correlation between TBS and age, height, weight, and BMI (r ranged from -0.10 to -0.31 , $P < 0.05$). A positive correlation was seen between LS TBS and LS aBMD ($r = 0.33$) and LS TBS and

FN aBMD ($r = 0.27$). Multiple linear and logistic regressions (lowest vs highest tertile of TBS) were used to define the sensitivity of TBS to other risk factors associated with osteoporosis. Only a small component of the TBS measurement (7–11%) could be explained by aBMD measurements. In multiple linear and logistic regression models, reduced LS TBS was associated with recent glucocorticoid use, prior major fracture, rheumatoid arthritis, chronic obstructive pulmonary diseases (COPD), high alcohol intake, and higher BMI. In contrast, recent osteoporosis therapy was associated with a significantly lower likelihood of reduced TBS. Similar findings were seen after adjustment for LS or FN aBMD. The conclusion of this study is that LS TBS is strongly associated with many of the known risk factors of osteoporotic fractures that are incorporated into the FRAX tool.

3.3.2. Diabetes [25]

A retrospective cohort study included 2356 patients with a diagnosed diabetes, among the 29,407 women from the Manitoba cohort clinical registry. Diabetes (type 1 and type 2) was associated with higher aBMD at all sites but lower LS TBS in unadjusted as well as adjusted models (all $P < 0.001$). Major osteoporotic fractures were identified in 175 women (7.4%) with and 1493 (5.5%) without diabetes ($P < 0.001$). TBS was an aBMD-independent predictor of fracture in patients with diabetes (adjusted hazard ratio 1.27) and without diabetes (hazard ratio 1.31). TBS values were lower and aBMD higher in diabetic patients. TBS better predicted occurrence of fracture than aBMD. The BMI represents a confounding factor in this robust study because three quarters of diabetic patients had a metabolic syndrome with increased abdominal fat that has been reported to lower TBS values.

3.3.3. Primary hyperparathyroidism [7,26,27]

TBS has been also assessed in small cohorts of patients with primary hyperparathyroidism [7,26,27] (Text S3). Whereas aBMD at the lumbar spine is not different for patients with and without vertebral fracture, TBS is lower in the former compared with the latter after multiple adjustments.

3.3.4. Glucocorticoids [28,29]

In a retrospective study of 136 Caucasian women aged 45 to 80 years on glucocorticoid therapy and 136 age-matched control women [28], the subgroup on treatment for at least one year (5, 10, or 15 mg/day prednisone-equivalent) had significantly 4% lower TBS values compared to age-matched individuals not taking glucocorticoids, while there was no difference in BMD. The TBS decreased with decreasing BMD and varied according to the type and number of fractures. Indeed the TBS difference was -3.4% in patients without fractures, -6.2% in those with grade 2 or higher vertebral fractures, -4.6% in those with at least one peripheral fracture, and -7.8% in those with two or more peripheral fractures.

In another retrospective study of 140 women aged 55.9 ± 14 years with rheumatoid arthritis (mean duration, 15.2 ± 2 years) [29] (the mean TBS was significantly lower in the 94 patients taking glucocorticoids [1.19 ± 0.11] compared to the 46 other patients [$P = 0.03$]). In this population, no significant differences were found for aBMD values or vertebral fracture prevalence. Although not significantly different, the vertebral fracture prevalence was 23.9% in the non-glucocorticoid-treated group versus 13.0% in the glucocorticoid-treated group. These results are difficult to interpret due to a recruitment bias in the study population, with a higher vertebral fracture prevalence in the non-glucocorticoid-treated group. The findings are puzzling, as the TBS was lower in the group taking glucocorticoids but was not lower in the group with the highest vertebral fracture prevalence.

3.3.5. Effects of anti-resorptive agents [30,31]

The objective of the study by Krieg et al. [30] was to assess the sensitivity of TBS as compared to LS aBMD to detect change over time in the Manitoba cohort both for treated and untreated women. Results were presented as mean annualized change both for TBS and aBMD.

The final sample comprised 1,684 women: 534 treated (86% were on bisphosphonates) and 1,150 untreated. At baseline, treated women were older (66.1 ± 8.0 years vs. 62.2 ± 7.9 years, $P < 0.001$). Both baseline LS aBMD *T*-score and TBS were lower in treated women ($P < 0.001$). Also, the proportion of women with prior history of major fracture was higher in treated women compared with untreated women (15.4% vs. 10.4%, $P = 0.009$). Treated subjects exhibited a significant mean increase in LS aBMD: $+1.86\%/year$ ($P < 0.002$). The increase in TBS was also significant: $+0.20\%/year$, (< 0.001), but was substantially lower than for LS aBMD. The least significant change (LSC) was more frequently achieved for LS aBMD than for TBS for both untreated and treated patients. The correlation between the change in lumbar spine TBS and LS aBMD was low albeit significant in both untreated ($r = 0.11$, $P < 0.001$) and treated subgroups of women ($r = 0.18$, $P < 0.001$).

To summarize, TBS and LS aBMD changes were quite comparable for untreated women. For women treated by anti-resorptive agents, the annualized increase of both LS aBMD and TBS were significant. Nevertheless, for treated women, the mean annualized increase in LS aBMD ($+1.86\%$) was substantially higher than the mean annualized increase of TBS ($+0.2\%$). At the individual level, the number of untreated women below the LSC (significant decrease) was higher for LS aBMD than for TBS: 24% vs. 18% ($P = 0.0003$). The number of treated women above the LSC (significant increase) was greatly higher for LS aBMD than for TBS: 54% vs. 12%, $P < 0.0001$. Anyway, further research delineating the value of TBS as an index of treatment-related anti-fracture effect is clearly warranted.

A second study aimed at comparing the effects of yearly intravenous zoledronate (ZOL) versus placebo (PLB) on TBS and LS aBMD in postmenopausal women with osteoporosis [31]. Vertebral fractures and degenerative changes were excluded from analyses. At baseline both groups were similar in terms of age, height, weight, BMI, TBS. LS aBMD was lower ($P = 0.01$) in ZOL group than in PLB group. In the PLB group, 19% of patients were below LSC for LS aBMD, 26% for TBS. In the ZOL group, 96% of patients showed an increase above LSC for LS aBMD, 35% for TBS. Over three years, there was a weak correlation ($r = 0.20$) between LS aBMD and TBS but no correlation between the change in TBS and LS aBMD at any time. It was concluded that the subset of patients was not large enough for establishing the predictive value of TBS alone or in combination with LS aBMD with regard to fracture risk.

Finally, no study has been conducted to evaluate the responsiveness of TBS to bone forming agents.

4. Conclusion

The TBS meets the need for a noninvasive method for assessing bone microarchitecture, a key determinant of bone strength. It is a quantitative value that is reproducible and easy to handle. It is a texture parameter. It does not measure the trabecular microarchitecture. The way by which TBS reflects microarchitecture *in vivo* is still questionable.

The TBS discriminates and predicts fragility fracture independently from and as well as or better than LS aBMD. Therefore adding TBS to LS aBMD may improve fracture prediction especially when aBMD is in the normal or osteopenic range. Such an improvement was demonstrated in the Manitoba cohort but not in the OFELY cohort. In addition, while TBS is a relevant predictive parameter for fracture risk, most of the studies have shown that the best

predictor of fracture is aBMD at the hip or at the femoral neck. Finally adding TBS to hip aBMD has not been proved to improve fracture prediction.

Several studies have shown that TBS value below 1.2 is associated with an increased risk of fracture. However, there is no currently available study indicating that this threshold is relevant for beginning an anti-osteoporotic treatment. To the best of our knowledge, no society has edited recommendations integrating the TBS because it is not clear enough if TBS supplies additional information not provided by age, prevalent fractures, and glucocorticoid exposure. Nevertheless, the work is in progress with the integration of the TBS into the FRAX tool [32,33].

Finally, due to the lack of evidence, we recommend not to use TBS for following patients treated by bisphosphonates or other anti-osteoporotic drugs.

Disclosure of interest

S.B., C.B., H.B., V.Bo., M.B., V. Br., K.B., R.C., L.C., M.C., P.F., J.M.F., J.B.G., M.L., E.Leg., E.Les., A.L., C.M., C.R., J.C.S., B.S., T.T., F.T., and G.W. declare that they have no conflicts of interest concerning this article.

C.L.B. has been involved in several studies focused on bone texture analysis and description of the Hmean index, but stayed apart from the discussions of the GRIO concerning TBS.

B.C. has participated to one meeting organized by Medimaps during the ASBMR congress in 2013 at Minneapolis.

Appendix A. Supplementary data

Supplementary material (S1, S2, S3) associated with this article can be found at <http://www.sciencedirect.com> and <http://dx.doi.org/10.1016/j.jbspin.2015.02.005>.

References

- [1] Pothuaud L, Carceller P, Hans D. Correlations between grey-level variations in 2D projection images (TBS) and 3D microarchitecture: applications in the study of human trabecular bone microarchitecture. *Bone* 2008;42:775–87.
- [2] Bousson V, Bergot C, Sutter B, et al. Trabecular bone score (TBS): available knowledge, clinical relevance, and future prospects. *Osteoporos Int* 2012;23:1489–501.
- [3] Pothuaud L, Héraud A, Barthe N, et al. Validation of 2D/3D generic mathematical relationship between TBS as assessed by DXA, and BV/TV and TbTh as assessed by microcomputed tomography: an experimental study based on human cadaver vertebrae. Montreal Canada: ASBMR; 2008.
- [4] Pothuaud L, Héraud A, Carceller P, et al. TBS of the AP spine as assessed by DXA is correlated with 3D bone microarchitecture parameters: an experimental study based on human cadaver vertebrae. Barcelona, Espagne: ECTS; 2008.
- [5] Roux JP, Wegrzyn J, Boutroy S, et al. The predictive value of trabecular bone score (TBS) on whole lumbar vertebrae mechanics: an ex vivo study. *Osteoporos Int* 2013;24:2455–60.
- [6] Silva BC, Walker MD, Abraham A, et al. Trabecular bone score is associated with volumetric bone density and microarchitecture as assessed by central QCT and HRpQCT in Chinese American and white women. *J Clin Densitom* 2013;16:554–61.
- [7] Silva BC, Boutroy S, Zhang C, et al. Trabecular bone score (TBS)—a novel method to evaluate bone microarchitectural texture in patients with primary hyperparathyroidism. *J Clin Endocrinol Metab* 2013;98:1963–70.
- [8] Winzenrieth R, Piveteau T, Hans D. Evaluation des corrélations entre les paramètres de microarchitecture 3DmCT et TBS: effet de la résolution et corrélation avec les mesures TBS DXA. Paris, France: SFR; 2010.
- [9] Winzenrieth R, Michelet F, Hans D. Three-dimensional (3D) microarchitecture correlations with 2D projection image gray-level variations assessed by trabecular bone score using high-resolution computed tomographic acquisitions: effects of resolution and noise. *J Clin Densitom* 2013;16:287–96.
- [10] Dufour R, Winzenrieth R, Héraud A, et al. Generation and validation of a normative, age-specific reference curve for lumbar spine trabecular bone score (TBS) in French women. *Osteoporos Int* 2013;24:2837–46.
- [11] Del Rio LM, Winzenrieth R, Cormier C, et al. Is bone microarchitecture status of the lumbar spine assessed by TBS related to femoral neck fracture? A Spanish case-control study. *Osteoporos Int* 2013;24:991–8.
- [12] Lamy O, Metzger M, Krieg M-A, et al. [OsteoLaus: prediction of osteoporotic fractures by clinical risk factors and DXA, IVA and TBS]. *Rev Med Suisse* 2011;7:2130 [2132–4,2136].

- [13] Simonelli C, Leib E, Mossman N, et al. Creation of an age-adjusted, dual-energy X-ray absorptiometry-derived trabecular bone score curve for the lumbar spine in non-hispanic US white women. *J Clin Densitom* 2014;17:314–9.
- [14] Leslie WD, Krieg M-A, Hans D. Manitoba bone density program. Clinical factors associated with trabecular bone score. *J Clin Densitom* 2013;16:374–9.
- [15] Boutroy S, Hans D, Sornay-Rendu E, et al. Trabecular Bone Score helps classifying women at risk of fracture: a retrospective analysis of the OFELY Study. Toronto, ON, Canada: ASBMR; 2010.
- [16] Boutroy S, Hans D, Sornay-Rendu E, et al. Trabecular bone score improves fracture risk prediction in non-osteoporotic women: the OFELY study. *Osteoporos Int* 2013;24:77–85.
- [17] Kolta S, Briot K, Fechtenbaum J, et al. TBS result is not affected by lumbar spine osteoarthritis. *Osteoporos Int* 2014;25:1759–64.
- [18] Winzenrieth R, Dufour R, Popova Y, et al. Spine osteoarthritis has no effect on TBS assessment: a site matched study with BMD. Bucharest: International Society for Clinical Densitometry; 2010.
- [19] Pothuau L, Barthe N, Krieg M-A, et al. Evaluation of the potential use of trabecular bone score to complement bone mineral density in the diagnosis of osteoporosis: a preliminary spine BMD-matched, case-control study. *J Clin Densitom* 2009;12:170–6.
- [20] Winzenrieth R, Dufour R, Pothuau L, et al. A retrospective case-control study assessing the role of trabecular bone score in postmenopausal Caucasian women with osteopenia: analyzing the odds of vertebral fracture. *Calcif Tissue Int* 2010;86:104–9.
- [21] Rabier B, Héraud A, Grand-Lenoir C, et al. A multicentre, retrospective case-control study assessing the role of trabecular bone score (TBS) in menopausal Caucasian women with low areal bone mineral density (BMDa): analysing the odds of vertebral fracture. *Bone* 2010;46:176–81.
- [22] Nassar K, Paternotte S, Kolta S, et al. Added value of trabecular bone score over bone mineral density for identification of vertebral fractures in patients with areal bone mineral density in the non-osteoporotic range. *Osteoporos Int* 2014;25:243–9.
- [23] Hans D, Goertzen AL, Krieg M-A, et al. Bone microarchitecture assessed by TBS predicts osteoporotic fractures independent of bone density: the Manitoba study. *J Bone Miner Res* 2011;26:2762–9.
- [24] Briot K, Paternotte S, Kolta S, et al. Added value of trabecular bone score to bone mineral density for prediction of osteoporotic fractures in postmenopausal women: the OPUS study. *Bone* 2013;57:232–6.
- [25] Leslie WD, Aubry-Rozier B, Lamy O, et al. Manitoba Bone Density Program. TBS (trabecular bone score) and diabetes-related fracture risk. *J Clin Endocrinol Metab* 2013;98:602–9.
- [26] Romagnoli E, Cipriani C, Nofroni I, et al. “Trabecular Bone Score” (TBS): an indirect measure of bone micro-architecture in postmenopausal patients with primary hyperparathyroidism. *Bone* 2013;53:154–9.
- [27] Eller-Vainicher C, Filopanti M, Palmieri S, et al. Bone quality, as measured by trabecular bone score, in patients with primary hyperparathyroidism. *Eur J Endocrinol* 2013;169:155–62.
- [28] Colson F, Picard A, Rabier B, et al. Trabecular bone microarchitecture alteration in glucocorticoids treated women in clinical routine? Denver, CO, USA: ASBMR; 2009.
- [29] Bréban S, Briot K, Kolta S, et al. Identification of rheumatoid arthritis patients with vertebral fractures using bone mineral density and trabecular bone score. *J Clin Densitom* 2012;15:260–6.
- [30] Krieg MA, Aubry-Rozier B, Hans D, et al. Manitoba Bone Density Program. Effects of anti-resorptive agents on trabecular bone score (TBS) in older women. *Osteoporos Int* 2013;24:1073–8.
- [31] Popp AW, Guler S, Lamy O, et al. Effects of zoledronate versus placebo on spine bone mineral density and microarchitecture assessed by the trabecular bone score in postmenopausal women with osteoporosis: a three-year study. *J Bone Miner Res* 2013;28:449–54.
- [32] Leslie WD, Lix LM. Comparison between various fracture risk assessment tools. *Osteoporos Int* 2014;25:1–21.
- [33] Silva BC, Leslie WD, Resch H, et al. Trabecular bone score: a noninvasive analytical method based upon the DXA image. *J Bone Miner Res* 2014;29:518–30.