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Australasian Association of Nuclear Medicine Specialists

Trabecular Bone Score in the Assessment and Management of Osteoporosis in Australia: A Position Statement from ANZBMS August 2025

Summary

Osteoporosis is characterised by both reduced bone mass (bone quantity) and compromised bone microarchitecture (bone quality), leading to increased bone fragility and susceptibility to low-trauma fracture(s). While dual-energy X-ray absorptiometry (DXA)-derived bone mineral density (BMD) remains central to diagnosis and risk stratification, many individuals who sustain fragility fractures have BMD values above the diagnostic threshold for osteoporosis. Trabecular bone score (TBS) is a validated, complementary indirect index of bone microarchitecture derived from the textural analysis of lumbar spine DXA images. As an independent predictor of fracture risk, TBS provides additional insight into lumbar spine vertebral microarchitecture, enhancing fracture risk assessment and informing clinical decision-making when used alongside BMD and clinical risk factor tools such as FRAX.

Key Positions:

1. Osteoporosis reflects both low bone mass and disrupted bone microarchitecture. Within the limitations of tissue thickness TBS provides a validated index of bone microarchitecture, derived from standard lumbar spine DXA images.
2. TBS is an independent predictor of fracture risk and adds value beyond BMD alone and/or most common clinical risk factors, therefore should be used where available.
3. TBS should not be used alone, but it supports clinical assessment by identifying patients at increased fracture risk, particularly those with osteopenia or those with osteoporosis who may be at very high risk of fracture.
4. FRAX estimates can be improved with TBS adjustment, which may reclassify fracture risk in individuals near treatment thresholds.
5. TBS may be particularly useful in individuals with secondary causes of osteoporosis, including those with glucocorticoid therapy, chronic kidney disease, or endocrine disorders.
6. TBS may respond to therapy with bisphosphonates (BP), but generally the response is more one of preservation and is less marked than the changes observed with BMD.
7. TBS will respond to therapy with denosumab although generally the response is less marked than the changes observed with BMD. TBS in conjunction with BMD may be useful for monitoring response to densoumab therapy.
8. TBS will respond to therapy with anabolic agents to a greater extent than with antiresorptives and is useful in monitoring response to therapy in conjunction with BMD. In treatment decision-making, the presence of both low TBS and low BMD may help identify patients who could benefit from initiating anabolic therapy.
9. TBS is less affected by degenerative spinal changes than BMD. TBS does require a miniumum of two vertebrae for calculation.
10. TBS requires no additional scan time or radiation and can be integrated into standard lumbar DXA scans.

Background

Osteoporosis is characterised by both reduced bone mass (bone quantity) and deterioration in bone microarchitecture (bone quality), which result in increased bone fragility and fracture risk. Clinically, osteoporosis is diagnosed after a minimal trauma fracture (MTF) in individuals over 50 or based on a bone mineral density (BMD), a T-score of -2.5 or lower, measured by dual-energy X-ray absorptiometry (DXA). Quantitative Computed Tomography (QCT) may also be used to measure comparable proximal femoral T-scores, albeit with higher radiation dose than DXA. BMD categories based on T-scores were defined by a WHO Study Group and are widely used in clinical practice: normal (T-score ≥ –1.0), osteopenia (T-score between –1.0 and –2.5), and osteoporosis (T-score ≤ –2.5) (Peck et al., WHO Consensus Development Conference, 1993).

Although BMD is a key component of osteoporosis assessment, it does not fully capture other components of bone strength, including bone microarchitecture, which is also an independent determinant of fracture risk. Multiple large cohort studies have shown that more than half of low-trauma fractures occur in individuals with BMD in the osteopenic or normal range (Schuit et al., 2004; Siris et al., 2004; Tremollieres et al., 2010; Hillier et al., 2011). These studies underscore the need for complementary tools that provide additional skeletal information beyond BMD.

Despite the availability of effective treatments which significantly reduce mortality and subsequent fracture risk, around 70–85% of patients presenting with minimal trauma fractures do not receive adequate osteoporosis assessment or appropriate therapeutic intervention (Kanis et al., 2014; Naik-Panvelkar et al., 2020; Fuggle et al., 2021, Bell et al 2022). Data from Australian primary care further reveals that fewer than one in three such patients are prescribed anti-osteoporosis medications, highlighting the widespread underdiagnosis and undertreatment of this high-risk population (Nguyen et al., 2004; Teede et al., 2007).

Fracture-related morbidity includes pain, reduced mobility, loss of function, and diminished quality of life. Many patients, particularly after hip fractures, lose the ability to live independently, and long-term morbidity persists for most symptomatic osteoporotic fractures. Mortality following osteoporotic fractures significantly increases, especially in those aged over 60. The mortality rate within one year after hip fracture can be up to three-fold higher compared to age-matched individuals without fractures, and up to two-fold higher following other major fractures, such as pelvic and vertebral fractures (Bliuc et al., 2009; Norring-Agerskov et al., 2013).

The broader epidemiological and economic burden of osteoporosis in Australia is significant. In 2023, an estimated 6.2 million Australians aged over 50 were living with osteoporosis or osteopenia (Mudiyanselage et al., 2024). The associated annual economic impact, including both direct and indirect healthcare costs, in 2023 was estimated at approximately AUD $4.84 billion (Mudiyanselage et al., 2024).

Given these challenges, there is increasing recognition of the need to enhance the identification of individuals at risk of fracture. One promising approach involves improving fracture risk prediction through the incorporation of bone quality measures. Trabecular bone score (TBS) is a grey-level textural variation index derived from lumbar spine DXA images that provides an indirect assessment of bone microarchitecture. TBS correlates with key microstructural features of trabecular bone, including trabecular thickness, number, separation, connectivity density, and the structure model index (Pothuaud et al., 2008; Pothuaud et al., 2009; Hans et al., 2011; Silva et al., 2013; Winzenrieth et al., 2013; Muschitz et al., 2015; Ramalho et al., 2018; Gama et al., 2024). TBS has also been shown to predict fracture risk independently of BMD and established clinical risk factors (Shevroja et al., 2023). In 2012, TBS was cleared by the U.S. Food and Drug Administration to support osteoporosis treatment decision- making alongside BMD. In 2022, TBS was assigned four Category I CPT codes in the United States, reflecting formal reimbursement and integration into clinical workflows.

Although TBS has seen widespread international adoption (Shevroja et al., 2023), no national guidelines currently exist in Australia regarding the clinical application of TBS.

This position statement, developed by Australian and New Zealand Bone and Mineral Society (ANZBMS), provides the first Australian position statement for the clinical use of TBS. It aims to provide evidence-informed guidance to support consistent and appropriate use of TBS in clinical practice, address knowledge gaps, and discuss the role of TBS in fracture risk assessment, treatment decision-making, and therapy monitoring relevant to the Australian healthcare setting.

Purpose and Scope

This position statement is not intended to replace current clinical guidelines, but rather to support enhanced risk stratification and patient management with TBS. It is intended primarily for endocrinologists, radiologists, nuclear medicine physicians, and other specialists involved in osteoporosis care. It is also of relevance to general practitioners and medical practitioners in other disciplines, such as geriatric medicine, who regularly manage patients at risk of fracture. The document focuses on the clinical application of TBS in the assessment of osteoporosis (Section A), its response to therapy (Section B), and practical implementation (Section C).

Methods

The evidence-based review and recommendations addressing the utility of TBS in standard clinical practice were formulated based on the clinical evidence-based guidelines (CEG) development process protocol which involves a qualitative synthesis of statements and recommendations based on the existing scientific evidence and clinical experience.

Core Team

The ANZBMS Clinical Imaging Committee (CIC) consists of six experts with recognised experience in osteoporosis diagnosis and management. All members have at least 11 years of experience, in the field of osteoporosis and its management and practice in the Australian Health System, and active participation in scientific research or teaching on osteoporosis. The core team all provided input into the development of the statement.

Literature review

To acquire proper evidence-based background knowledge for consideration, a literature search was carried out using PubMed/ MEDLINE, Embase, and Cochrane databases. Clinical studies were included from January 2011 to April 2025 inclusive. Following the data extraction and review of the published recommendations, the experts of the CIC provided a comprehensive list of propositions for the use of TBS in clinical practice based on the available research evidence and their own clinical expertise. Additional relevant studies were retrieved by reviewing the reference lists of studies identified with the database search strategies that met the inclusion criteria.

Study selection

Relevant studies were selected by applying inclusion and exclusion criteria to the literature retrieved with the search strategies.
Inclusion criteria

Articles included were systematic reviews, randomized controlled trials (RCTs), uncontrolled trials, observational studies including cohort, case control, and cross-sectional studies.

Exclusion criteria

Editorials, commentaries, conference abstracts and nonevidence-based narrative/personal reviews, and manuscripts lacking English version were excluded.

The position statement developed by the Clinical Imaging Committee of the ANZBMS was presented to the ANZBMS Council for review by expert members of the Society and additional authors with expertise in this field. All potential conflicts of interests of participating authors were declared prior to approval of the manuscript (Appendix).

SECTION A: ASSESSMENT OF OSTEOPOROSIS

While BMD remains the gold standard for diagnosing osteoporosis, there are other aspects of bone quality that contribute independently to bone strength (Choksi et al., 2018). Consequently, a proportion of individuals who experience major osteoporotic (MOF) and hip fractures can have BMD values within the osteopenic, or normal range (Schuit et al., 2004; Siris et al., 2004; Tremollieres et al., 2010; Hillier et al., 2011; Bandaru et al., 2020; Binkley et al., 2020; Kadri et al., 2023). In postmenopausal women and older men, followed over 7 to 13 years, between 56% and 79% of fractures occurred in those with BMD in the osteopenic or normal range (Schuit et al., 2004; Tremollieres et al., 2010; Hillier et al., 2011). In a registry-based cohort study of postmenopausal women aged ≥ 50 years, 10% of women with prevalent or incident fractures had normal BMD. When TBS was included in the assessment, this proportion was reduced to 5%, indicating improved identification of individuals with compromised bone quality (Binkley et al., 2020). Similarly, a retrospective study within a Fracture Liaison Service (FLS) cohort found that 8% of patients with fractures had normal spine and hip BMD. Of these, 52% had low bone mass as assessed by computed tomography-derived Hounsfield units, and 42% showed degraded or partially degraded trabecular microarchitecture based on TBS (Bandaru et al., 2020). Adjunctive measures have potential for enhancing risk stratification by identifying deficits in bone quality that may not captured by BMD alone.

TBS and fracture risk assessment in primary osteoporosis

Multiple, prospective, population cohort studies have consistently shown that lower TBS is independently associated with an increased risk of major osteoporotic, vertebral, and hip fractures. This evidence has been appraised and summarised in international positions (Harvey et al., 2015; Shevroja et al., 2023), and includes population studies, involving men and women aged 40 years and older, with cohort sizes up to 45,185 individuals and follow-up durations extending to 10 years (Table 1; Hans et al., 2011; Boutroy et al., 2013; Briot et al., 2013; Iki et al., 2014; Leslie et al., 2014; Iki et al., 2015; McCloskey et al., 2016; Popp et al., 2016; Schousboe et al., 2016; Martineau et al., 2017; Su et al., 2017a; Su et al., 2017b; Schousboe et al., 2017; Leslie et al., 2018; Martineau et al., 2018; Kuzma et al., 2018; Tamaki et al., 2019; Shevroja et al., 2019; Shevroja et al., 2022). These studies demonstrate an enhanced fracture risk assessment when adding TBS to either BMD alone, or with the Fracture Risk Assessment Tool (FRAX) (Harvey et al., 2015; Shevroja et al., 2023).

The FRAX-adjustment for TBS derives from an individual-level, international meta-analysis of fourteen prospective cohort studies, which demonstrated that TBS significantly predicts incident fracture independently of FRAX (McCloskey et al., 2016). In this meta-analysis, adjusting FRAX scores to include TBS resulted in clinically meaningful improvements in fracture risk prediction across diverse populations, irrespective of sex or ethnicity (McCloskey et al., 2016). Subsequent prospective studies in women and men have reported that TBS with FRAX enhances the prediction of any osteoporotic fracture, hip fracture, and vertebral fracture, compared to using FRAX alone (Table 1). For example, in men, the MrOS cohort study with a follow-up of almost nine years, demonstrated TBS was a significant predictor of incident MOF and hip fracture, independently of FRAX scores, BMD and prevalent radiographic vertebral fracture (Schousboe et al.,

2016). Each standard deviation reduction in TBS was associated with a 27% higher risk of MOF and a 20% higher risk of hip fracture.

The earliest population cohort study of TBS and fracture risk included 29,407 postmenopausal women (mean age 65.4 y) from the Canadian Manitoba Bone Density Programme (Hans et al., 2011), examining TBS as a complementary measure to BMD. Over a mean follow-up of five years, 1,668 women sustained a major osteoporotic fracture, including 439 vertebral and 293 hip fractures. TBS and lumbar spine BMD were each independently associated with fracture risk. Combining both parameters resulted in significantly improved predictive accuracy compared to either alone. While lumbar spine and total hip BMD were strongly correlated ($r = 0.72$), lumbar spine BMD and TBS showed only a weak correlation ($r = 0.32$), confirming that TBS provides complementary information on bone properties that are distinct from BMD. Similar findings have been reported in other studies (Leib et al., 2014, Di Gregario et al., 2015). Receiver Operating Characteristic (ROC) analysis in the Manitoba study, showed that the combination of total hip BMD and lumbar spine TBS provided the highest predictive accuracy for vertebral and hip fractures, with Area Under the Curve (AUC) values of 0.73 (95% CI: 0.71–0.75) and 0.82 (95% CI: 0.79–0.84), respectively. Furthermore, inclusion of TBS significantly improved AUC values ($p < 0.001$) when added to femoral neck, total hip, and lumbar spine BMD. Fracture incidence also increased progressively across TBS tertiles (normal to degraded) regardless of BMD category, indicating the incremental clinical value of TBS for fracture risk stratification (Hans et al., 2011).

An alternative approach to TBS has been developed with the most recent TBS software providing adjustment of BMD T-scores based on TBS. This is currently supported for women aged ≥50 years and, in a forthcoming update, will extend to women aged ≥ 40 years. This approach is based on a study from the Manitoba cohort (n = 45,185 aged 40 years and over; 3,925 MOF), that examined the risk of MOF and hip fractures using Cox regression models (Leslie et al., 2018). Over the study period, 8.7% of women experienced at least one MOF, and 2.3% had a hip fracture. Each standard deviation decrease in TBS was associated with a 26%, 25%, and 22% higher risk of MOF after adjusting for lumbar spine, femoral neck, and total hip BMD, respectively, and results which remained significant after controlling for age and BMI. Risk-equivalent TBS adjustments were applied to derive TBS-adjusted BMD T-scores for each site. These adjusted scores improved fracture prediction and showed strong agreement with FRAX-adjusted for TBS outputs when using the adjusted femoral neck T-score as the BMD input (Leslie et al., 2018). The Australian Pharmaceutical Benefits Advisory Committee (PBAC) and the Medical Services Advisory Committee (MSAC) do not currently have a position on the use of TBS adjusted T-scores.

Fracture risk reclassification

TBS adjustment can improve fracture risk stratification in postmenopausal women, particularly among those near clinical treatment thresholds. In a study of 34,316 postmenopausal women (mean age 63.5 years) followed over 8.7 years, the impact of incorporating TBS into FRAX was evaluated using treatment intervention thresholds from three widely used clinical guidelines: the Bone Health and Osteoporosis Foundation, Osteoporosis Canada, and the UK National Osteoporosis Guideline Group (Martineau et al., 2017). Across all guideline thresholds, the TBS-adjustment demonstrated a significant improvement in fracture risk classification, and most reclassification occurred in women with osteopenic BMD T-scores. An age-related interaction was also observed, with greater reclassification among women under 65 years ($p < 0.001$). As seen in other studies, the greatest clinical impact was for women close to the intervention threshold, with reclassification rates ranging from 9% to 18%. Findings from the Geelong Osteoporosis Study also support the utility of TBS in individuals with intermediate fracture risk. In this population-based cohort of 1,576 men and women, approximately 25% of those classified as osteopenic by BMD had degraded TBS (Anderson et al., 2019). Furthermore, the OPUS study, compared 6-year fracture risk predictions derived from TBS-based versus BMD-based models in 998 French postmenopausal women. Among those who subsequently experienced a fracture, 55% were correctly reclassified into a higher risk category using the TBS model, primarily from low to moderate risk (Briot et al., 2013). These results indicate the complementary

value of TBS in individuals who may not otherwise be considered for treatment based on BMD alone.

Beyond reclassification, TBS may also aid in identifying patients at '*very high or imminent'* fracture risk. Evidence from the Manitoba cohort and other studies indicates that individuals with both osteoporosis by BMD and degraded TBS have a substantially elevated incident fracture risk (Hans et al., 2011, Boutroy et al., 2013, Briot et al., Popp et al., 2016). In the SEMOF cohort study, the highest fracture incidence was observed in women with osteoporosis and degraded TBS (70 fractures per 1,000

patient-years) compared to women with osteoporosis and normal TBS (40 fractures per 1,000 patient-years). This near doubling of fracture risk within the same BMD category supports the added prognostic value of TBS and its use in identifying patients at very high or imminent fracture risk who may warrant early intervention with anabolic therapy.

TBS and fracture risk assessment in secondary causes of osteoporosis

Secondary causes of osteoporosis refers to bone fragility resulting from underlying medical conditions or treatments that adversely affect bone metabolism, including endocrine disorders, chronic inflammatory diseases, renal or hepatic dysfunction, and medications such as glucocorticoids or aromatase inhibitors. The Australian guidelines recommend that individuals over 50 years with conditions or therapies known to increase fracture risk should undergo BMD testing and formal fracture risk assessment (Wong et al., 2025). However, it is also recognized that BMD may underestimate skeletal fragility in many of these conditions, particularly as bone quality, rather than bone mass, may be disproportionately compromised.

<u>Glucocorticoid-induced and cortisol excess:</u>

Both exogenous glucocorticoid therapy and endogenous cortisol excess are recognised causes of secondary osteoporosis. Longitudinal glucocorticoid treatment studies report significant reductions in TBS, with annual declines ranging from –3% to –10% (Chuang et al., 2017, Corrado et al., 2021, Rymuza et al., 2022). The largest reported TBS reduction (–10%) was observed in men and women with rheumatoid arthritis receiving high-dose glucocorticoids (compared to -1.7% in those receiving lower dose), suggesting a dose-dependent effect (Corrado et al., 2021). In cross-sectional studies of patients treated with glucocorticoids, degraded TBS has more frequently been observed than low BMD, amongst those with recent fractures (Belaya et al., 2015; Florez et al., 2020; Lee et al., 2021; Nowakowska-Plaza et al., 2021). In endogenous glucocorticoid excess, such as Cushing's syndrome, similar patterns are observed. In one study, 84% of patients with vertebral fractures had degraded or partially degraded TBS values, compared to only 41% with low BMD (Belaya et al., 2015). More recently, a longitudinal study by Tan et al. (2024) evaluated changes in TBS and BMD before and after successful treatment of Cushing's disease. Both metrics improved significantly, with TBS increasing by 8.2% and BMD by 3.9% post-treatment. Notably, the TBS improvements were independent of baseline BMI, and lower baseline TBS predicted greater recovery following cortisol normalisation.

<u>Aromatase inhibitors:</u>

Aromatase inhibitors are first-line adjuvant therapies for reducing recurrence in postmenopausal women with hormone receptor–positive breast cancer. By inhibiting the peripheral conversion of androgens to estrogen, these agents suppress circulating estrogen levels. However, this mechanism contributes to accelerated bone turnover, resulting in net bone loss and increased risk of fragility fractures. Studies have examined the effect of aromatase inhibitor therapy on TBS in postmenopausal or early postmenopausal women receiving treatment for breast cancer, demonstrating decreases in TBS, uncorrelated with changes in BMD (Pedrazzoni et al., 2014, Hong et al., 2017, Mariotti et al., 2017, Tsang et al., 2018).

Chronic kidney disease:

Chronic kidney disease (CKD) is characterized by complex alterations in bone turnover, mineralisation, and microarchitecture. These changes often lead to fracture risk underestimation when using BMD or FRAX alone. A recent systematic review and meta-analysis (Bioletto et al. 2024) evaluated 22 studies (n = 2,675 CKD patients) and confirmed a consistent reduction in TBS across all stages of CKD, including non-dialysis patients, those on maintenance dialysis, and kidney transplant recipients. TBS was significantly lower in CKD patients compared to matched non-CKD controls (mean difference:
−0.057 to −0.106, all $p < 0.01$). Importantly, TBS predicted fracture risk in non-dialysis patients (HR per SD decrease = 1.45, 95% CI 1.05–2.00), although significance was attenuated after full FRAX adjustment (HR = 1.26, 95% CI 0.88–1.80). In dialysis patients, the pooled data showed that those with vertebral fractures had significantly lower TBS than controls with no previous fracture (mean difference
−0.070, $p < 0.01$). In kidney transplant recipients, TBS was shown to be an independent predictor of incident fractures, after adjusting for FRAX with BMD (HR per SD decrease = 1.55, 95% CI 1.06– 2.27) (Naylor et al., 2014). Additionally, TBS was shown to correlate with histomorphometric indices and HR-pQCT parameters, validating its relevance to trabecular bone microstructure (Luckman et al., 2017, Ramalho et al., 2018).

Rheumatological and autoimmune diseases:

Chronic inflammatory conditions are associated with increased skeletal fragility, which may not be captured by BMD alone, especially at the lumbar spine where structural changes and degenerative changes may confound interpretation. Numerous studies have investigated TBS in populations with rheumatoid arthritis, axial spondyloarthritis, ankylosing spondylitis, polymyalgia rheumatica, systemic lupus erythematosus, and systemic sclerosis (Kim et al., 2016, Choi et al., 2017, Kang et al., 2018, Lai et al., 2020, Richards et al., 2020, Lee et al., 2023). In these studies, TBS has been shown to be significantly associated with prevalent vertebral or major osteoporotic fractures, independently of BMD. In ankylosing spondylitis, degraded TBS was more common in fracture cases despite no difference in lumbar spine BMD (Killinger et al., 2021), which is often elevated due to syndesmophytes (Kaya et al., 2009, Shuhart et al., 2024). Notably, in postmenopausal women with rheumatoid arthritis, TBS outperformed lumbar spine BMD in discriminating vertebral fractures (AUC 0.683 vs. 0.482), and FRAX-adjusted for TBS further improved fracture risk prediction (Lee et al., 2023). A recent study by Silva et al. (2024) involving 265 women with long-standing RA provides additional support for the clinical value of TBS in this population. In this cross-sectional analysis, the prevalence of vertebral and non-vertebral fractures was 30.6% and 17.4%, respectively. In multivariable models, lower TBS was independently associated with vertebral fractures (OR = 1.6, 95% CI 1.09–2.36, $p = 0.017$), while disease activity indices were not significant predictors. In contrast, non-vertebral fractures were more strongly associated with low appendicular muscle mass and other functional parameters.

Parathyroid and thyroid disorders:

Studies have examined TBS in individuals with primary hyperparathyroidism, hypoparathyroidism, or thyroid dysfunction, demonstrating lower TBS in fracture cases compared to non-fractured individuals, even where BMD does not differ (Grigorie et al., 2015, Sakane et al., 2019, Jones et al., 2022, Saha et al., 2022, Vendrami et al., 2022). TBS demonstrated the highest predictive accuracy for low-trauma fractures in Australian patients with primary hyperparathyroidism (AUC 0.706) (Jones et al., 2022). In patients with postsurgical hypoparathyroidism, degraded TBS was more common than low BMD in those with fractures (Saha et al., 2022). Further, in patients with asymptomatic primary hyperparathyroidism, over 30% had degraded TBS, which was strongly associated with prior fractures (34.2% vs. 8.3% in those with degraded TBS, $p < 0.001$) (Bisceglia et al., 2025).

Other causes of secondary osteoporosis:

A recent meta-analysis of TBS in Type 2 diabetes mellitus reported (T2DM) reported that adversely affects TBS, despite BMD on average being increased. The evidence that increased fracture risk in T2DM is related to lower TBS requires further validation.
Systematic Review and Meta-AnalysisStudies in smaller cohorts with conditions such as HIV infection, liver cirrhosis, chronic obstructive pulmonary disease, acromegaly, and thalassemia also suggest that TBS is associated with vertebral fracture risk independently of BMD (Ciullini et al., 2018, Watanabe et al., 2018, Kužma et al., 2019, Teawtrakul et al., 2020, Ogiso et al., 2022). In addition, a prospective study examined the clinical impact of TBS in patients attending a specialist outpatient unit, with a high prevalence and wide range of secondary causes of osteoporosis (Al-Hashimi et al. 2022). TBS influenced treatment decisions in approximately 40% of patients being considered for anti-osteoporosis therapy. Furthermore, TBS identified degraded bone microarchitecture in 21–25.5% of patients who had non-osteoporotic BMD, suggesting diagnostic value, particularly in conditions associated with impaired bone quality despite preserved bone density.

SECTION B: TBS RESPONSE TO THERAPY

The effective management of osteoporosis involves a combination of lifestyle modifications, pharmacologic treatments, and regular monitoring to ensure optimal bone health and reduce fracture risk. TBS potentially may complement BMD in assessing treatment response. As with BMD, monitoring the effect of treatment on TBS requires the knowledge of the least significant change (LSC) based on center-specific precision errors. TBS precision errors are comparable to those of BMD, ranging from 0.8 to 2.1%CV, with the equivalent LSC ranging from 2.2 to 5.8%CV, and averaging 3.8%CV (Hans et al., 2011, Breban et al., 2012, Briot et al., 2013, Dufour et al., 2013, Iki et al., 2015, Krueger et al., 2015, Popp et al., 2016, Choi et al., 2017, Messina et al., 2019, Kang et al., 2018, Guan et al., 2021, Kang et al., 2022, Sandeep et al., 2022). The corresponding LSC unit change in TBS has been reported to be 0.05, based on a precision of 1.4% CV (Shevroja et al., 2023).

Pharmacologic treatments differ in their mechanisms of action, and it is therefore expected that their effects on bone density and quality, as measured by BMD and TBS, are not equivalent. Antiresorptive agents, such as bisphosphonates, menopausal hormone therapy (MHT), selective estrogen receptor modulators (SERMs), and denosumab, suppress osteoclast activity and reduce bone turnover, thereby preserving trabecular microarchitecture (Baron et al., 2011). Across multiple studies of 12 to 49 months, including those in women with type 2 diabetes, these therapies have been associated with maintenance or small increases in TBS (Table 2; Di Gregorio et al., 2015, Shin et al., 2017, Sooragonda et al., 2019, Kim et al., 2022, Kang et al., 2022). Denosumab, a more potent antiresorptive, has shown consistent and slightly greater TBS gains (up to 1.8% per year), over treatment durations ranging from 20 months to 10 years, albeit significantly less than BMD (Hans et al., 2022, 2023). Longitudinal studies confirm that TBS improvements with denosumab are sustained up to 10 years, with associated reductions in fracture rates and a decline in the prevalence of degraded TBS over time. Importantly, individuals with the largest increases in TBS also had fewer new or worsening fractures (Hans et al., 2023).

In contrast, anabolic therapies such as PTH analogues and romosozumab stimulate bone formation, with romosozumab also inhibiting bone resorption. These agents have been associated with early and greater increases in TBS compared to the changes seen with antiresorptive drugs alone (Jiang et al., 2003). In RCTs comparing abaloparatide and teriparatide, TBS increased rapidly over 6 months, with greater gains in the abaloparatide group (Bilezikian et al., 2018). In the ACTIVE and ACTIV Extend trials, almost 50% of women had a TBS gain which exceeded LSC, and those with greater TBS improvements experienced fewer vertebral fractures (Cosman et al., 2023). Romosozumab has demonstrated TBS increases of 2.5% to 7.5% within 6 to 12 months in a range of populations, including postmenopausal women with osteoporosis,

premenopausal women with low bone mass, individuals with type 2 diabetes, and patients with osteogenesis imperfecta. These gains were paralleled by rapid BMD increases and a substantial shift from degraded to normal TBS categories (Jeong et al., 2021; Kusakabe et al., 2024; Ferrari et al., 2025; Lee et al., 2025; McClung et al., 2025).

Evidence supports the use of sequential treatment, starting with anabolic agents followed by antiresorptives, for patients at high or very high fracture risk (Curtis et al., 2022). In the DATA-Switch trial, women who began treatment with teriparatide and transitioned to denosumab achieved greater TBS gains than those treated in the reverse order (Tsai et al., 2017). Similarly, the ARCH trial showed that TBS improvements with romosozumab were maintained during subsequent alendronate therapy (5.2% gain at 36 months), whereas alendronate alone produced smaller changes (McClung et al., 2025).

The treatment-related changes in TBS from multiple clinical trials, align with expected response concerning the drug mechanism of action and bone remodelling dynamics. TBS, as a complementary metric to BMD, may be useful for monitoring treatment effects in patients receiving anabolic agents, in high-turnover states, or where early response assessment is needed. Incorporating TBS into longitudinal treatment monitoring potentially may improve therapeutic adjustments and enhance fracture risk management.

SECTION C: TECHNICAL AND CLINICAL CONSIDERATIONS

The use of TBS software requires a license separate to the DXA license. This remains a limiting factor in Australia where the majority of DXA scanners do not have a TBS licence (June 2025).

TBS software versioning and tissue thickness adjustment

TBS can be influenced by soft tissue thickness surrounding the spine, which affects X-ray attenuation and quality of image texture. Recognising this, earlier versions of TBS software (TBS version 3) incorporated a correction based on body mass index (BMI) as a practical surrogate for soft tissue thickness. This approach has enabled broad clinical use of TBS, with validated interpretation across a defined BMI range (typically 15–37 kg/m²), but relies on the accurate manual input of height and body mass by the DXA technician. The limitation of TBS to patients with a BMI less than 37, in TBS version 3, is a limiting factor in the utility of the software in obese patients at increased fracture risk (e.g. Type 2 Diabetes).

Recent advances in the software incorporates tissue thickness adjustment of TBS (Osteo Advanced - version 4) applies a direct adjustment of TBS for soft tissue thickness, obtained from the DXA images, avoiding errors inherent in the use of BMI. This approach supports accurate TBS assessment across a wider range of body sizes, using a validated soft tissue thickness range of 7–30 cm, which may be useful in populations where BMI alone may not fully reflect individual body composition (Gatineau et al., 2025). In very obese individuals however, with tissue thickness exceeding 30cm, the new software (Osteo Advanced - version 4) is not validated. In subjects exceeding the BMI or tissue thickness recommended limits, the current TBS software will not provide a result. Older versions of the software issued a warning but did provide a TBS estimate, potentially causing confusion. Monitoring response to therapy is preferentially achieved using DXA BMD. However, change in TBS estimate may influence interpretation. The change in TBS software from version 3 to version 4 potentially may impact on interpretation of long-term change in TBS.

Vertebral artefacts

TBS requires no additional radiation exposure or patient burden, as the measurement is acquired during the same lumbar spine scan as used for BMD. This makes TBS a practical adjunct to routine DXA- based osteoporosis assessment. Degenerative changes at the lumbar spine, such as osteophytes, disc space narrowing, and vascular calcifications, are known to artificially elevate lumbar spine BMD, potentially confounding fracture risk assessment. In contrast, TBS has been shown to be less influenced by these

artefacts. An Australian population-based study from the Geelong Osteoporosis Study involving 728 men aged 40–90 years demonstrated that the impact of degenerative spinal changes on BMD was more than threefold higher than on TBS (partial r^2 = 0.257 vs. 0.076), with a significant interaction between age, measurement method, and presence of artefacts (Anderson et al., 2018). Further evidence (Juweid et al., 2023) evaluated the influence of vertebral degenerative change on TBS and FRAX-adjusted for TBS estimates. Although minor statistical differences were observed, the absolute differences in fracture risk prediction were small (e.g., 0.12% for major osteoporotic fracture and 0.04% for hip fracture).

The effect of lumbar spine vertebral fractures on TBS was also assessed in a study from the Manitoba BMD Registry (Leslie et al., 2024). Although vertebrae with fractures showed slightly elevated TBS values, the overall effect of excluding fractured vertebra from L1–L4 TBS was modest, with a mean change of -1.0%, and -1.7% for grade 3 fractures. In clinical practice, however the recommendation is to exclude vertebral fractures from the ROI used to calculate TBS.

Fracture risk assessment

The Osteoporosis Management and Fracture Prevention guidelines for Australia recommend the calculation of absolute fracture risk using FRAX (Wong et al., 2025). Risk can be re-stratified with FRAX after DXA using BMD, and treatment may be indicated when BMD T-score is ≤-2.5 or, between
-1.5 and -2.5, and FRAX risk for MOF is ≥20% and/or hip fracture risk is ≥3% (Case-finding Recommendation 9 C). TBS complements BMD by providing an independent assessment of bone quality and is integrated into the FRAX algorithm as an optional adjustment. Incorporating TBS into FRAX can refine individualised risk estimates, particularly in individuals with osteopenic BMD (T- score between -1.5 and -2.5), where treatment decisions are sensitive to small differences in calculated risk. Multiple studies have demonstrated that FRAX-adjusted for TBS reclassifies fracture risk in a meaningful proportion of individuals near intervention thresholds, supporting its clinical value in cases where standard BMD-based FRAX may underestimate risk.

In addition to its integration with FRAX, there is potential for TBS to be incorporated into the Garvan Fracture Risk Calculator (https://www.garvan.org.au/research/bone-fracture-risk-calculator). This model, which already includes clinical risk factors and BMD, could be further refined by incorporating BMD T-score adjusted for TBS to improve the estimation of fracture risk, particularly in individuals whose risk may be underestimated by BMD alone.

Treatment decision-making

For individuals who meet treatment thresholds based on BMD and fracture risk (e.g. FRAX), current guidelines recommend initiating therapy with antiresorptive agents such as bisphosphonates, denosumab, or MHT, depending on age, sex, comorbidities, and patient preference (Wong et al., 2025). Among these, denosumab has demonstrated the most consistent and substantial improvements in TBS in addition to increasing BMD, especially with long-term use (McClung et al., 2017; Hans et al., 2022; Hans et al., 2023).

In individuals identified as being at very high fracture risk (and due to factors such as very low BMD T-scores, recent or multiple fractures, advanced age, glucocorticoid use, or comorbidities including type 2 diabetes), initial treatment with an anabolic agent (e.g. romosozumab, teriparatide, or abaloparatide) is now recommended (Wong et al., 2025). These therapies enhance both bone density and quality, with significant gains in TBS seen within the first 6–12 months of treatment (Bilezikian et al., 2018; Sandeep et al., 2022; Cosman et al., 2023; Hong et al., 2024; McClung et al., 2025; Ferrari et al., 2025). TBS can potentially improve selection of patients for anabolic therapy by identifying patients with bone quality deterioration that may not be captured by BMD alone. For example, patients with osteopenic BMD but degraded TBS, particularly those near or just below FRAX-based thresholds, may be reclassified into a higher risk category, making them eligible for pharmacologic treatment. In patients with osteoporosis by BMD, and low TBS, the

evidence demonstrates an elevated fracture risk (Hans et al., 2011, Boutroy et al., 2013, Popp et al., 2016, Shevroja et al., 2023), potentially warranting an anabolic-first approach.

In summary, where available, TBS integration into DXA assessments by improving fracture risk stratification, helps clinicians to select the most appropriate treatment, antiresorptive or anabolic, within current clinical guidelines, informed by both fracture probability and overall skeletal profile. (In Australia at present neither FRAX estimates, or TBS adjusted FRAX, are eligible criteria to access PBS listed therapies).

Conclusion

TBS is a validated adjunct to BMD and clinical risk factors that offers additional insight into bone quality. When used alongside BMD and clinical risk factors, TBS helps refine fracture risk assessment, particularly in individuals with osteopenia or secondary osteoporosis, where BMD alone may not fully reflect skeletal fragility. Incorporating FRAX-adjusted for TBS, improves risk stratification, especially in patients near intervention thresholds. TBS may also provide additional value in monitoring response to osteoporosis therapy, particularly with anabolic agents. This position statement aims to support consistent, evidence-informed use of TBS in Australia, with a focus on improving the clinical utility of DXA-based assessment and facilitating more informed management of patients at risk of fracture.

APPENDIX

Conflict of interest of members of ANZBMS Clinical Imaging Committee (CIC):

1. Assoc Prof Nicholas Pocock: Chairman.
   Director and owner DXA practices incorporating use of TBS.
2. Assoc Prof Christian Girgis.
   Director and owner DXA practices incorporating use of TBS
3. Mr Christopher Schultz
   Applications specialist for Getz Healthcare, a vendor of GE Healthcare DXA scanners and TBS.
4. Dr Angela Sheu. No conflicts
5. Dr Joseph Wong. No conflicts.
6. Dr Ali Ghasem-Zadeh. No conflicts

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