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Bone-specific alkaline phosphatase as a marker of bone formation: Clinical and imaging correlates

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Abstract

Bone-specific alkaline phosphatase (BSAP) is a biochemical marker of bone formation, reflecting osteoblast function and bone turnover. Unlike bone mass and structure measurements using dual-energy X-ray absorptiometry or high-resolution peripheral quantitative computed tomography, BSAP does not directly measure bone mass or microarchitecture but provides dynamic information on bone metabolism. BSAP has high specificity for bone formation with low biological variability and consistent levels across many clinical conditions, making it a reliable biochemical indicator of bone turnover, especially early response to anabolic treatment and in high-turnover bone conditions. Biologically, BSAP is synthesized by osteoblasts and is important in matrix maturation and mineralisation. In clinical practice, BSAP increases with anabolic treatment, often before changes in bone density, and is thus a predictor of early treatment response. Low levels of BSAP are found in conditions with delayed fracture healing, such as hypophosphatasia, and high levels are found in high-turnover conditions such as Paget's disease. BSAP also has a role in conditions such as chronic kidney disease, where it can discriminate between states of bone turnover. However, its use is hampered by variability between laboratories, the absence of reference ranges, and the lack of normative data in different populations. Novel methods combining BSAP with innovative imaging techniques have the potential to improve personalised diagnosis, but need further research. This review highlights the potential of BSAP as an adjunct biomarker in use in early diagnosis, monitoring therapeutic intervention and overall assessment of bone metabolism for clinical decision making in metabolic bone diseases in conjunction with imaging.

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Key Words: Bone-specific alkaline phosphatase; Osteoblast; Wnt/β-catenin; Skeletal metabolism; Bone formation

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Core Tip: Bone-specific alkaline phosphatase (BSAP) is a good indicator of osteoblastic bone formation, released by osteoblasts as the matrix matures and becomes mineralized. In contrast to imaging, BSAP reflects metabolic activity, increasing early with anabolic therapies and helping to differentiate bone disorders, including Paget's disease, hypophosphatasia and chronic kidney disease-related bone disease. However, due to the difficulties in standardization and in having norm values, BSAP's combination with imaging and artificial intelligence models holds the promise of a more accurate and personalized approach to skeletal health.

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INTRODUCTION

Bone is a living tissue that is constantly being remodelled by the activities of osteoblasts and osteoclasts. The former is involved in the formation of new bone matrix, and the latter is involved in the removal of old and damaged bone[1]. This process is called bone remodeling and is essential to bone's mineral balance and strength. Osteocytes, a type of bone cell, sense when the bone is under stress or damaged and regulate the action of the osteoblasts and osteoclasts.

While imaging techniques can measure bone mass and structure, biochemical markers can give insight into bone metabolism and turnover dynamics[2]. The markers may be generally divided into bone resorption markers [for example, C-terminal telopeptide (CTX) and tartate-resistant acid phosphatase 5b, indicative of osteoclast activity) and markers of bone formation (such as osteocalcin, procollagen type 1 n-terminal propeptide (P1NP), and bone-specific alkaline phosphatase (BSAP), which reflect osteoblast activity). These markers are useful to analyse bone metabolic disorders, monitor treatment effectiveness, and fracture risk[3-6]. There are however

some differences in specificity, biological variability and clinical applicability which could restrict the reliability of these markers in some conditions.

BSAP is an isoenzyme, mainly secreted by osteoblasts, which is a key factor in the bone formation process. Early studies used total alkaline phosphatase (ALP) as a marker of bone formation, but it lacks tissue specificity and is produced by other tissue types including the liver. To discover that BSAP is a bone-specific isoenzyme greatly enhanced the specificity of biochemical assessment of bone formation. The amount of BSAP reflects the amount of new bone turnover by the active osteoblasts[7]. Biological variability and stability under clinical conditions is lower for BSAP than for other markers of bone formation like osteocalcin and P1NP[8]. Osteocalcin is biologically highly variable, and P1NP is sensitive, but it may depend on systemic factors and assay variability. This review, therefore, is intended to critically discuss the biological background, clinical uses, and diagnostic value of BSAP, especially its superiority over other markers of bone formation and its role in conjunction with imaging methods in the diagnosis of bone metabolism (Figure 1).

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THE BIOLOGY AND BIOCHEMISTRY OF BSAP IS SUMMARIZED

ALP is an enzyme that is present throughout the body, particularly in the liver, bile ducts and bones[9]. It is involved in dephosphorylation, a process which is necessary for metabolism and bone mineralization[10,11]. Four ALP isoenzymes exist in humans - placental, germ cell, intestinal and the tissue nonspecific isoform. Osteoblasts are the source of BSAP, which is found on the surface of osteoblasts, and this gives it specific properties for bone tissue[12].

Organic matrix of bone is synthesized by osteoblasts and is made up of mainly type I collagen and other proteins. They also produce BSAP, which they bind to their surface and to small matrix vesicles. Signaling pathways that regulate osteoblast activity and differentiation regulate this process. When mineralization is initiated, BSAP hydrolyzes pyrophosphate which is a key inhibitor of mineralization, into inorganic phosphate, providing more phosphate for mineral deposition in the collagenous matrix. It also

alters the proteins like osteopontin which aids the formation and stabilization of hydroxyapatite crystals, a critical process for bone strength and rigidity. Such processes take place in the context of bone remodeling, the balance between bone formation by osteoblasts and bone resorption by the osteoclasts. Factors that upregulate BSAP production include hormonal factors like parathyroid hormone and vitamin D, while other factors like fibroblast growth factor 23 limit phosphate availability leading to potential failure of mineralization[11].

Besides the biologic role, circulating BSAP levels are also dependent on the physiologic stage and the skeletal activity[12]. In adults, levels are generally low, but they tend to elevate during childhood, adolescence, after fractures, and following surgery[13]. In women, levels remain stable until menopause, then the rate of bone turnover increases, leading to higher ALP and BSAP levels compared to younger women. Liver disorders, some cancers, or very high turnover bone disorders can elevate the total ALP and make BSAP measurements less reliable. Unlike several other bone markers, BSAP remains relatively stable in chronic kidney disease, supporting its clinical utility in such conditions.

Other bone turnover markers include osteocalcin and procollagen type 1 propeptides [N-terminal propeptide of type I procollagen (PINP) and C-terminal propeptide of type I procollagen]. These markers provide a dynamic assessment of skeletal metabolism and reflect osteoblast and osteoclast activity more rapidly than changes in bone mineral density. PINP reflects type 1 collagen synthesis and demonstrates relatively low variability. Osteocalcin, produced from osteoblasts, has a short half-life, complex post-translational processing, and depends on vitamin K. Unlike PINP - which accumulates when kidneys fail - BSAP is not affected by kidney function, so it is more reliable for patients with kidney disease. For bone resorption, the main markers are serum CTX and N-terminal cross-linked telopeptide of type I collagen. CTX responds quickly to antiresorptive drugs and has a significant diurnal variation; thus, morning fasting samples are preferred. In contrast, BSAP demonstrates minimal circadian variation. Together, BSAP, PINP, and CTX provide complementary information on bone

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formation and resorption, and their selection depends on the clinical context and the specific aspect of bone turnover being assessed[14].

CLINICAL APPLICATIONS OF BSAP

Monitoring of therapeutic response

When bone-building anabolic drugs are prescribed, the key clinical question is whether the osteoblasts are effectively stimulated. BSAP, as a marker of osteoblast activity, plays a vital role in assessing this response. When osteoblasts are active, BSAP levels elevate; thus, BSAP tracks the effectiveness of anabolic osteoporosis treatments like teriparatide, abaloparatide, and romosozumab. An early rise in BSAP following treatment usually indicates that the therapy is effective and bone turnover is active[15]. For example, in a postmenopausal woman receiving teriparatide therapy, a rise in BSAP levels within the first 3 months may indicate an effective anabolic response even before measurable changes in bone mineral density are observed.

Monitoring response to teriparatide, abaloparatide, romosozumab - teriparatide, a recombinant human parathyroid hormone analogue administered as a daily injection, rapidly rises BSAP, with peak concentrations observed between one and twelve months, followed by a decline when the therapy is discontinued[16,17]. Abaloparatide, which acts on parathyroid hormone-related protein/peptide, also boosts BSAP, but not quite as much as Teriparatide. Romosozumab inhibits sclerostin, so it stimulates bone formation and slows down bone breakdown. An early and marked rise in bone formation markers is observed initially, followed by a gradual decline to baseline over subsequent months. This early surge in the levels of biomarkers corresponds to the rapid anabolic effects[18,19].

Time course of BSAP changes after therapy - the time duration for the response varies among the anabolic agents. Romosozumab produces a significant rise within days to one month of therapy, while teriparatide and abaloparatide require nearly 3 months to produce a significant elevation of BSAP. With teriparatide, the elevated levels persist

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for several months, while with romosozumab, it declines approximately after a period of 6 months[20,21].

Predicting bone mineral density gains - an early rise in BSAP levels is a sign of an increased rate of formation of new bone and improved bone mineral density. As the biochemical changes precede the measurable changes by imaging techniques, it is an indication that increased BSAP is associated with long-term bone mineral density gains. A mild increase is suggestive of partial anabolic response, while a significant elevation is suggestive of a stronger therapeutic effect[22]. Compared to other bone formation markers such as PINP and osteocalcin, BSAP demonstrates greater specificity for osteoblastic activity and improved stability across clinical conditions. When used alongside CTX, it provides a more comprehensive assessment of bone turnover.

Assessment of bone turnover and fracture healing

Fracture healing is a dynamic process involving stages of inflammation, repair, and remodeling. Clinically, in patients with long bone fractures, a rise in BSAP levels during 3-6 weeks reflects active callus formation, whereas persistently low levels may indicate delayed healing. Immediately after the injury, hematoma formation occurs, and an inflammatory reaction sets in to clear the debris and initiate tissue repair. This is followed by the formation of a soft callus, which stabilizes the fracture site. The osteoblasts synthesize new bone matrix, which converts the soft callus into mineralized hard callus[23,24].

BSAP changes during fracture healing - the levels of BSAP do not rise immediately following a fracture. During the stage of inflammation, the concentration tends to remain at the baseline. Approximately 3-6 weeks post-injury, the levels begin to rise, reflecting increased osteoblast activity during the stage of callus formation and mineralization. Peak levels are observed most commonly between 6 weeks and 12 weeks, corresponding to active bone deposition. As the remodeling phase regresses, the bone formation declines, and BSAP levels return toward baseline[20,25].

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Link to callus formation and remodeling - as it is known that elevated BSAP corresponds to callus formation and mineralization, elevated levels of BSAP correspond to new bone formation and mineralization, supporting the structural stabilization and remodeling at the fracture site[26-28].

BSAP in delayed union or non-union - in cases of delayed union or non-union of the fracture, BSAP levels may not increase or may even decline. Persistently low levels beyond 6-8 weeks indicate impaired osteoblastic activity and insufficient callus formation. Declining BSAP levels may suggest non-union. However, it should be correlated with other clinical diagnostic methods and imaging studies to provide an accurate diagnosis[29].

Participate in metabolic bone disorders

Bone is a living tissue which is continually being built up and broken down to to preserve structural integrity, mineral homeostasis. If this balance is upset, different metabolic bone diseases may arise. BSAP helps in identifying and evaluating osteoporosis, Paget's, osteomalacia, and renal osteodystrophy[30-32]. Osteoporosis - osteoporosis is the most common metabolic bone disorder. It is low bone mass and a loss of normal bone structure, which make Weakens bones and increases their risk of breaking. It typically occurs due to an an imbalance between the processes of bone formation and bone resorption. From diagnostic point of view, BSAP levels can be elevated or normal in postmenopausal women and older adults. This varies, depending on the rate of bone turnover.

BSAP is one of the important indicators of high turnover osteoporosis and is helpful in distinguishing high turnover and low turn over states. This serves as an early biochemical signal which can help in risk stratification and guidance of individualized therapeutic decisions. When interpreted alongside resorptive markers such as CTX, BSAP provides a more comprehensive assessment of bone remodeling dynamics[33,34]. For prognosis and treatment monitoring, elevated BSAP levels indicate enhanced osteoblastic activity and improved bone mineral density[35]. If BSAP levels remain low

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persistently, it often indicates low bone turnover or weak response to treatment. On the other hand, if BSAP levels rise too high, it might indicate overtreatment or temporary remodeling of bone[36].

Paget's disease - in Paget's disease of bone, the process of bone remodeling is highly dysregulated with accelerated and disorganised cycles of bone formation and resorption. During the active phase of the disease, the BSAP levels are elevated around 10-25 times the upper limit of the normal range, indicating excessive osteoblastic activity secondary to excessive turnover. BSAP is preferred over total ALP because it is specific to the bones and its levels decline with appropriate treatment with bisphosphonates[37,38].

Osteomalacia - osteomalacia is another condition, where bones do not mineralize properly, often due to low vitamin D, phosphate imbalance, or renal dysfunction. BSAP levels tend to be high in these patients, reflecting enhanced osteoblast activity and bone matrix synthesis, which is not properly mineralized. When high BSAP levels are present alongside low vitamin D, calcium, and phosphate, the diagnosis is more suggestive of osteomalacia than osteoporosis, as in osteoporosis, mineralisation is generally preserved despite reduced bone mass[39].

Renal osteodystrophy - renal osteodystrophy encompasses a spectrum of skeletal abnormalities associated with chronic kidney disease and may present with both high and low bone turnover. In secondary parathyroidism, elevated human parathyroid hormone stimulates bone turnover, resulting in increased BSAP. Conversely, in dynamic bone diseases, BSAP levels are decreased as bone formation is suppressed[40-42]. In patients with chronic kidney disease, BSAP can help differentiate low-turnover adynamic bone disease from high-turnover states, aiding clinical decision-making.

Applications in special populations

In children, bone is in a continuous state of growth and remodeling, characterised by rapid modelling, elongation, and structural adaptation. Naturally, bone turnover markers like BSAP are higher in the pediatric population than in adults[43]. But in some

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childhood bone diseases, BSAP may deviate from the reference range, providing an important diagnostic insight. Interpretation of BSAP levels in pediatric populations requires age-specific reference ranges due to physiologically elevated bone turnover.

In rickets, the BSAP levels increase drastically, even reaching ten to twenty times the normal upper limit for age. This reflects the heightened osteoblastic activity in response to defective mineralization, making it a highly sensitive biochemical marker for diagnosis and treatment monitoring[44]. On the contrary, in rare genetic conditions like hypophosphatasia[45], mutations in the *ALPL* gene result in abnormally low levels of BSAP. In other disorders, like osteogenesis imperfecta, the BSAP levels can be normal or high, depending on the rate of bone turnover and extent of disease at a given time (Table 1).

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IMAGING CORRELATES OF BSAP

Though conventional imaging techniques such as X-rays, dual-energy X-ray absorptiometry (DXA), and computed tomography scans provide information about the bone density and structure, they cannot directly reflect the biological processes of bone remodeling. BSAP is a marker of osteoblastic activity that indicates the rate of new bone formation. When biochemical and imaging results are interpreted together, a more detailed analysis of bone health can be made[46]. Imaging modalities primarily provide structural information, whereas BSAP reflects the underlying metabolic activity, thereby allowing simultaneous assessment of bone quantity and turnover.

Correlation of BSAP levels with DXA, quantitative computed tomography, and high-resolution peripheral quantitative computed tomography findings

The standard diagnostic tool for the assessment of bone mineral density and diagnosis of osteoporosis is DXA. It quantifies bone mineral density but does not measure the turnover rates. In contrast, BSAP reflects the rate of bone turnover as a marker of osteoblastic activity. In cases of osteoporosis, initially, elevated BSAP levels with low bone mineral density (BMD) are suggestive of rapid bone turnover and bone loss. When

anabolic therapy is initiated, the levels of BSAP are elevated even before any changes can be detected in DXA, while when antiresorptive drugs are initiated, BSAP levels fall even before the BMD starts to recover. Thus, BSAP acts as an early indicator of therapeutic response. The difference in time is indicative of biochemical changes in BSAP often precede structural changes detected by imaging, making it particularly useful for early evaluation of effectiveness of treatment. Quantitative computed tomography (QCT) and high resolution peripheral quantitative computed tomography (HR-pQCT) allow for 3D evaluation of bone structure, such as trabecular thickness, spacing, and thickness of the cortex[47]. The linkage between BSAP and these scans is a subject of research shows that older persons with high BSAP have lower BMD and higher porosity.

Increased risk of fracture due to low bone density (cortical bone) on QCT. When started on anabolic HR-pQCT demonstrates improvement in trabecular number and BSAP rises early cortical thickness[48]. These results show a correlation between high BSAP and correlation of biochemical activity with structural changes in bone microarchitecture remodeling. These patterns are useful in distinguishing in patients with CKD between high and low bone turnover[49].

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BSAP and bone microarchitecture

Bone microarchitecture (namely trabecular internal network) is important for the integrity of bone. The mineralization of the bone sponge and the formation of a strong cortical shell are important to the strength of the bone regardless of the bone mineral density. Even when the DXA values are within the normal range, minute microarchitectural deterioration can increase the risk of fracture. This explains why patients with normal BMD may still experience fractures, as BSAP reflects ongoing remodeling that may compromise bone quality. Persistently elevated BSAP indicates excessive remodeling, which disrupts the trabecular connectivity and increases porosity. HR-pQCT can detect these microarchitectural changes; however, sustained elevation of BSAP is indicative of high bone turnover. A transient rise in BSAP levels

may be associated with moderate aerobic exercise, which suggests that short-term elevations reflecting adaptive remodeling may be beneficial when accompanied by improvements in bone architecture[50].

Integration of biochemical and imaging markers in clinical decision making

The integration of biochemical and imaging markers enhances clinical decision-making. For example, low DXA-derived bone mineral density with normal BSAP may indicate low-turnover bone loss, as seen in ageing. In contrast, low bone mineral density with elevated BSAP indicates high-turnover conditions, such as in postmenopausal states. Despite the presence of normal bone mineral density values in conditions such as Paget's disease of bone and osteomalacia, BSAP levels remain elevated. Thus, combining BSAP with imaging studies can help differentiate between structural bone loss and changes in bone turnover, increasing the accuracy of diagnosis and This will help facilitate more informed therapeutic decisions.

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METHODOLOGICAL CONSIDERATIONS

While BSAP is a great bone formation marker and osteoblast function, more than just numbers are needed for accurate interpretation. Analytical methodology, biological variability, and patient-specific factors like age, renal function and In order to accurately interpret, comorbidities should be taken into account.

Assay types and standardization issues

Although the measurement of BSAP requires only a single blood sample, testing methodologies vary across laboratories. Earlier, techniques such as electrophoresis and heat inactivation were used to differentiate BSAP from hepatic ALP. In recent years, immunoassays, such as enzyme-linked immunosorbent assay, immunoradiometric assays, and electrochemiluminescence immunoassays, have been used to target the bone-specific isoform. Automated immunoassays employing monoclonal antibodies are increasingly used for improved sensitivity and specificity[51-53].

Biological variability and confounding factors

BSAP reflects the current osteoblastic activity but is influenced by physiological and pathological factors. Intra-individual variability exists as the BSAP levels fluctuate with factors such as age, growth spurts, fracture healing, liver disease, and certain medications. ALP levels may be elevated in liver disease due to hepatic isoforms, which can act as a confounding factor[54]. In addition, medications such as antiresorptive agents and anabolic therapies can significantly alter BSAP levels, which should be considered when interpreting results. BSAP exhibits only minimal diurnal variation, and its levels remain relatively unaffected by intake of food, menstrual cycle, and routine physical activity. Transient elevations may be present in acute skeletal injury. These confounding factors highlight the importance of interpreting BSAP levels in conjunction with clinical context and other diagnostic findings.

Interpretation in the context of renal function, age, sex, and comorbidities

Since the excretion of BSAP is not *via* the renal route, it remains a reliable marker in patients with chronic kidney disease, unlike other biomarkers that are renally excreted and accumulate in cases of renal failure[55]. Children and adolescents generally have higher levels of BSAP due to growth spurts, while postmenopausal women often exhibit elevated BSAP levels due to an increased rate of bone turnover. Other co-existing factors and comorbidities, including liver disorders or genetic conditions such as hypophosphatasia, should also be considered as they may influence the results and complicate result interpretation[42,56]. However, standardized normative reference ranges for BSAP across different age groups, sexes, and ethnic populations remain limited, which may affect its interpretation across diverse clinical settings. Furthermore, variations in BSAP levels across age, sex, and ethnicity highlight the need for population-specific reference ranges to improve diagnostic accuracy.

LIMITATIONS AND FUTURE DIRECTIONS OF BSAP

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Although BSAP is a useful measure of bone formation, it is only an one of the elements of the overall framework for comprehensive evaluation of bone health. There are several limitations and gaps in knowledge that need to be overcome before it can be has become a routine clinical tool that is standardized.

Gaps in current evidence

Incomplete standardization - a universally standardized method for measuring BSAP has not yet been established, despite many years of progress. This is because laboratories use different assay methods, reference ranges, and calibration standards, and thus the interlaboratory BSAP results vary by as much as 15%-20%, which affects the clinical interpretation[57].

Limited data on certain groups - most BSAP research focuses on older adults and postmenopausal women. Thus, significant gaps remain in men with hypogonadism and osteoporosis, the pediatric and adolescent population, individuals with diverse ethnic backgrounds whose baseline levels may vary, and patients with chronic systemic diseases. These gaps limit the generalizability of BSAP interpretation across diverse populations.

Uncertain predictive thresholds - although an early rise in BSAP is associated with improvement in bone density and fracture healing, precise predictive thresholds have not been defined. BSAP levels are affected by various factors such as age, therapeutic modality, and baseline status. This limits the use of BSAP as a standalone predictive biomarker for clinical decision-making.

Need for longitudinal and interventional studies.

Long-term monitoring - prospective long-term longitudinal studies are needed to correlate BSAP with imaging modalities such as DXA, QCT, and HR-pQCT for obtaining detailed clinical outcomes. Intervention-based trials - though it is known that levels of BSAP elevate with anabolic therapies and decline with antiresorptive agents, evidence on whether treatment adjustments based on BSAP levels improve clinical

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outcomes remains limited. Therefore, randomized clinical trials are required to evaluate this.

Potential for BSAP in artificial intelligence-driven bone health and precision medicine

BSAP as a digital biomarker - BSAP may be incorporated into data-driven predictive models integrating biochemical, imaging, and clinical data to enhance assessment of bone health[58]. Personalization of therapy - such integrative approaches may support personalized treatment strategies by identifying patients at higher risk of fracture or altered bone turnover; however, these applications require further validation before clinical implementation, particularly in predicting fracture healing and identifying high-risk individuals. Implementation challenges - the integration of BSAP into data-driven platforms requires standardized data collection, assay harmonization, and robust validation. Secure and interoperable data systems are essential to integrate biochemical, imaging, and clinical information while ensuring patient privacy. Further, transparent interpretation of models and representation of diverse groups are essential for fair and consistent implementation.

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CONCLUSION

BSAP is an important biochemical marker of bone formation and is more specific of osteoblastic activity than many other biochemical markers. It offers useful information on skeletal remodelling, and can sometimes find changes before they are identified by bone mineral density scans. It is also a recent study that confirms its utility as a dynamic and early marker of bone turnover and treatment response. In osteoporosis, the levels of BSAP may be a marker of early disease activity, and during the healing of fractures, BSAP levels are initially elevated and then decreased as the fracture progresses. BSAP is useful in disorders like Paget's disease or renal osteodystrophy, to determine if the bone is being formed excessively, or not formed at all, or if the bone is being formed in a dysregulated manner. In conjunction with imaging techniques such as dual-energy X ray absorptiometry and when used along with markers such as PINP and CTX, BSAP

provides comprehensive monitoring. Further validation is needed for the use of emerging integrative approaches, incorporating biochemical markers, imaging and clinical data, to further increase its clinical utility. An integrative approach allows early therapeutic intervention, personalized treatment strategies and better overall management of skeletal disorders. In addition, there will be a need for interdisciplinary cooperation between biochemists, radiologists and clinicians to maximize the use of this in clinical practice.

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Figures and Tables

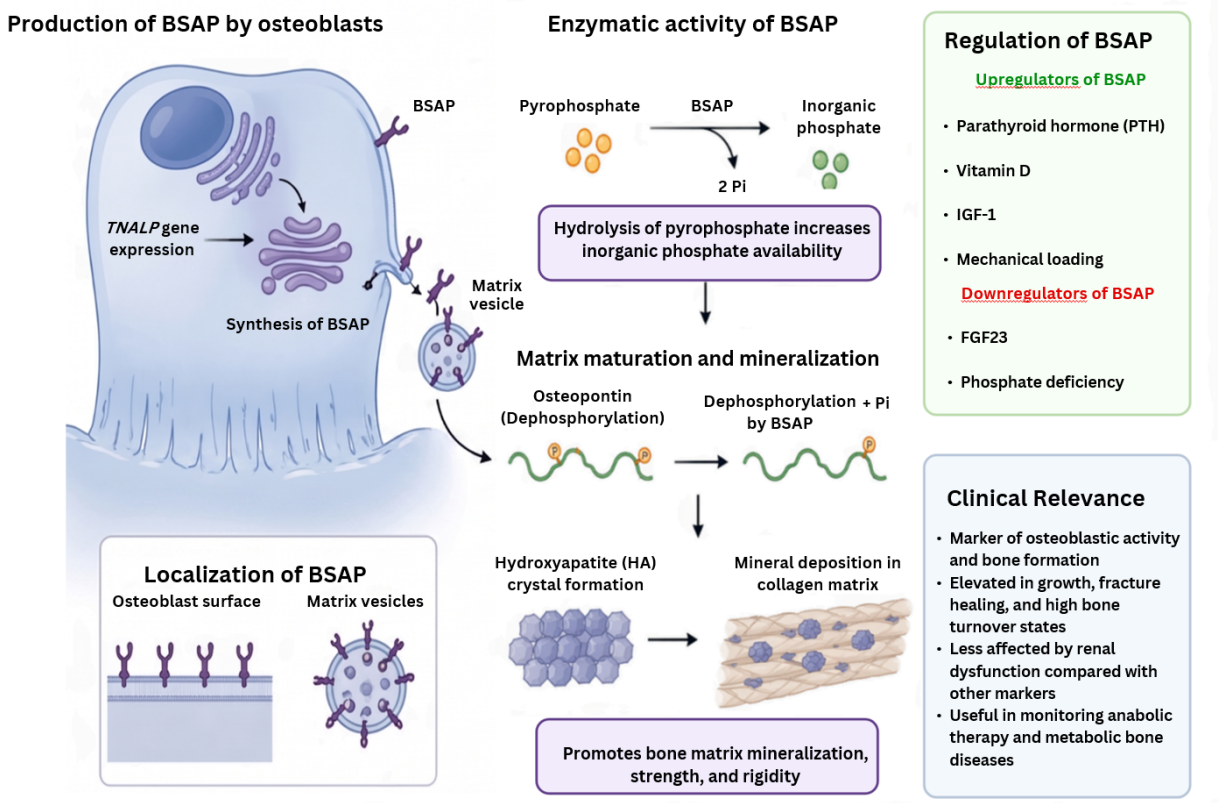


Figure 1 Biological role of bone-specific alkaline phosphatase in bone formation. BSAP: Bone specific alkaline phosphatase; TNALP: Tissue non-specific alkaline phosphatase; PTH: Parathormone; IGF-1: Insulin-like growth factor-1; FGF23: Fibroblast growth factor-23; HA: Hyaluronic acid.

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Table 1 Clinical applications of bone-specific alkaline phosphatase

Clinical scenario	BSAP pattern	Clinical interpretation	Utility
Anabolic therapy	↑ Early rise	Increased osteoblast activity	Early response marker
Antiresorptive therapy	↓ Decrease	Reduced bone turnover	Monitor treatment
Fracture healing	↑ Peak at 6-12 weeks	Callus formation	Assess healing
Osteoporosis	↑ Or normal	High *vs* low turnover	Guide therapy
Paget's disease	↑↑ Markedly elevated	Excess bone formation	Diagnosis and monitoring
Osteomalacia	↑	Defective mineralization	Diagnostic support
CKD bone disease	↑ or ↓	Turnover differentiation	Clinical decision-making

BSAP: Bone specific alkaline phosphatase; CKD: Chronic kidney disease.

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