# Response evaluation of bone metastasis in prostate cancer: Preliminary comparison of computerized bone scan index versus standardized clinical criteria

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## Abstract

**Objective:** The correlation between the computer-assisted bone scan index (BSI) responses versus clinical response classification if bone metastases in prostate cancer patients are not clear. We compared changes in BSI with Prostate Cancer Working Group-3 (PCWG3) and MD Anderson (MDA) criteria. **Materials and Methods:** Fifty-six consecutive patients with at least two bone scans (BS) within 12 months were included, who had BS before and after treatment with the same anticancer agent. **Results:** Progressive disease (PD) by PCWG3 criteria was seen in 28% of the cases (median BSI increased by 1.69 units) versus non-PD in 72% (BSI change -0.13). MD Anderson showed PD in 34% (BSI increase 0.49), 45% stable disease (BSI change 0.00), and 20% partial responses (BSI decrease 1.44). Absolute BSI changes differed significantly among response categories by PCWG3 and MDA criteria (both $P<0.0001$). Response classification using dichotomized BSI data ($>0/\leq 0$ and $>0.3/\leq 0.3$ BSI units) showed a significant correlation with PCWG3 and MDA criteria (all $P<0.001$). Absolute BSI changes and dichotomized BSI correlated to prostate-specific antigen responses (both $P<0.001$) but not to clinical responses. **Conclusion:** Absolute changes in BSI and BSI response classification correlated significantly with standardized clinical response criteria for the assessment of treatment responses of skeletal metastases in prostate cancer

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## Introduction

Prostate cancer is a common cancer and represents the second most common cause of cancer-related death among men [1]. Bone metastases are a serious complication of cancer in general [2] and prostate cancer in particular with skeletal involvement being observed in more than 85% of patients who die from prostate cancer [3]. Imaging plays a vital role in the detection and monitoring of bone metastases in prostate cancer, and bone scintigraphy (BS) remains the recommended imaging modality [4-6]. Standardized criteria for the assessment of bone responses have been proposed, including the Prostate Cancer Working Group-3 (PCWG3) [7] and MD Anderson (MDA) criteria [8]. The PCWG criteria are clinically validated in terms the prediction of overall survival in several trials [9]; these response criteria are standard of care in clinical trials in metastatic prostate cancer.

Computer-assisted analysis of bone scintigraphy, and calculation of a total skeletal tumor burden, bone scan index (BSI), may be valuable in the assessment of treatment response of bone metastases [10, 11]. Several studies have documented BSI to possess crucial clinical information regarding prognosis, risk classification, and prediction of treatment response [12]. However, there is sparse head-to-head comparative analysis of response assessment by BSI and PCWG [13], and, to the best of our knowledge, no comparison of BSI with MD Anderson criteria.

It may be that computer-assisted analysis can replace subjective response assessment of bone scans by PCWG3 and MDA criteria based on objectivity, high test-retest agreement, scan reads per time unit as well as improved predictive values. The main aim of this preliminary study was to evaluate the treatment responses of skeletal metastases by BSI versus PCWG3 and MDA criteria.

## Materials and Methods

### Patients

Consecutive prostate cancer patients referred for BS over a five year period were retrospectively identified as previously described[14]. In short, eligibility criteria were as follows: 1) A diagnosis of prostate cancer, 2) at least 12 weeks of treatment with androgen deprivation therapy (ADT), next-generation hormonal therapy (NGH, e.g., abiraterone or enzalutamide), or chemotherapy (first-line with docetaxel or second-line with cabazitaxel), and 3) a pair of BS; one imaging at baseline and one during ongoing treatment within 12 months of treatment with the same agent. The baseline bone scintigraphy had to be performed within a window of 12 weeks before and 2 week after initiation of therapy. This time window excluded any treatment-induced flare reactions to interfere with the reading [15-17]. Patients could provide more than one set of BS, provided that sequential treatments fulfilled the criteria listed above. There were no requirements for prior radical prostatectomy.

## Imaging procedure

Planar whole-body BS was obtained accordance with institutional procedures and guidelines from the European Association of Nuclear Medicine [18]. The images were acquired at least two hours after intravenous tracer injection of 750-1000MBq of technetium-99m-labelled hydroxymethylene diphosphonate ($^{99m}$Tc-HMDP). All BS were performed using Symbia dual-head gamma camera with multi-purpose, low-energy, high-resolution collimators (Symbia T16, Siemens Medical Solutions, Erlangen, Germany). The scan speed was 24cm/min with 30% alpha blending. Any additional single-photon emission computed tomography (SPECT) data were was not included in the analysis in this study.

## Imaging evaluation

Imaging evaluation was performed by a panel of five board-certified nuclear medicine physicians as described previously [14]. Any discrepancy between the readers was resolved by consensus. The readers conducted response evaluation on each scan according to: 1) The PCWG criteria as progressive disease (PD) vs. non-progressive disease (non-PD) based on the appearance of two or more, confirmed skeletal lesions, and 2) according to the MDA criteria [8] as PD, stable disease (SD), partial response (PR), and complete response. The MDA criteria have unique criteria for classification of outcome for X-ray, computed tomography (CT), magnetic resonance imaging (MRI), and BS. The outcome is based on visual classification. With MDA criteria for BS, PD can be declared based on a new lesion or increased activity in existing lesions. The initial classification by PCWG criteria was done by PCWG2 criteria, but since the PCWG2 and PCGW3 criteria for BS are very similar, data was reported data as PCWG3 criteria [7]. There was no requirement for confirmation of PD by PCWG criteria in this study. The PCWG criteria were made for use in CRCP, but in the absence of well-established criteria for the assessment of disease progression in metastatic, hormone-sensitive PCa, we applied PCWG criteria to compare findings with the automatic software analysis.

## Bone scan index

Bone scan index values were calculated automatically using the computer-assisted software EXINI® BoneBSI version 2.1.2 (EXINI Diagnostics AB, Lund, Sweden). Original uncompressed imaging files in Digital Imaging and Communications in Medicine format were imported into the software, and the analysis of anterior and posterior images was made with a balanced sensitivity setting [19]. Whenever the software program misclassified a benign, physiological, or artificial uptake (e.g. urinary tract, urostomy, injection site) as malignant, manual correction was undertaken. The change in BSI from baseline to follow-up was defined as ΔBSI. In addition to quantitative changes, changes in BSI were categorized as increased, unchanged, or decreased by cut-off values 0.0 BSI units as well as ΔBSI numerical greater than 0.3 units, which has been proposed as a consistent and reliable BSI-change [20, 21].

## Biochemical evaluation

The biochemical response in each patient case was evaluated by prostate-specific antigen (PSA) measurements from baseline to follow-up bone scintigraphy. Patients were classified according to PCWG criteria: 1) PSA progression (≥ 25% increase and ≥2ng/mL above the nadir after therapy start), 2) PSA drifters (initial response with ≥50% decline followed by progression with ≥25% increase and ≥2ng/mL above the nadir), 3) stable PSA (<25% increase or <50% decline), and 4) PSA response (≥50% decline from baseline measured twice three to four weeks apart). The time intervals between PSA measurements varied among patients due to treatment type, individual baseline PSA, and PSA dynamics (doubling time and/or velocity) at the discretion of the treating physician.

## Clinical response

The clinical response was evaluated based on available information such as performance status as reported by the treating physician. In the absence of an exact performance score, the cumulated signs and symptoms of cancer, e.g. tumor-related symptoms, pain, weight loss, and fatigue were used to classify the performance score if possible. The patients' medical files were independently reviewed by two readers; any discrepancy among readers for the classification of performance score was solved by consensus. The patients were classified as having: 1) clinical progression, 2) stable disease, 3) clinical improvement or 4) clinical response that could not be assessed.

## Statistical analysis

Data were described by a median with a total range. Chi-square tests (with Yates correction) were used to analyze categorical data. Differences in numerical ΔBSI among response criteria categories were analyzed using Mann-Whitney tests for two groups and one-way, unpaired, non-parametric analysis of variance tests for more than two categories using GraphPad Prism version 9 (GraphPad Software Inc., CA, US).

## Ethical approval and consent

This retrospective quality assessment study did not require ethical approval or informed consent in accordance with national legislation. The study was approved by the Danish

Data Protection Agency in the North Denmark Region, which provided a waiver for informed consent for access to information in medical files.

## Results

### Patients

Fifty-six patients fulfilled the eligibility criteria, of which six patients had two different treatments with related BS and were included twice, while one patient was included three times with three different treatments. Thus, the final study population included in the analysis consisted of 64 BS cases. The patients were predominantly high-risk patients, and most patients had bone metastases at study entry (Table 1). Most patients were treated with ADT or chemotherapy. No patients received chemotherapy for hormone-sensitive prostate cancer or radium-223 therapy. The baseline bone scintigraphy was performed median 7 days before initiation of treatment. Follow-up bone scintigraphy was conducted between 12 to 48 weeks (median 26 weeks) after start with ADT and 12 to 28 weeks (median 18 weeks) for treatment with NGH and chemotherapy. No patients underwent radical prostatectomy as their primary therapy.

***Table 1.*** *Demographics and baseline information for the patients and cases (bone scan pairs).*

| | |
|---|---|
| Number of patients | 56 |
| Number of patient cases | 64 |
| Mean age, years (range) | 70 (53-89) |
| Clinical tumor stage at diagnosis (patients) | |
| T1 | 4 (7.1%) |
| T2 | 12 (21.4%) |
| T3 | 36 (64.3%) |
| T4 | 4 (7.1%) |
| Gleason score at diagnosis (patients) | |
| ≤6 | 0 (0.0%) |
| 7 (3+4) | 3 (5.4%) |
| 7 (4+3) | 4 (7.1%) |
| 8 | 9 (16.1%) |
| 9 | 33 (58.9%) |
| 10 | 3 (5.4%) |
| Unknown | 4 (7.1%) |
| PSA at baseline (cases) | |
| Median, ng/mL | 235.0 |
| Range, ng/mL | 4.3-9708 |
| Disease stage at baseline (cases) | |
| Hormone sensitive | 8 (12.5%) |
| Metastatic hormone sensitive | 19 (29.7%) |
| CRPC | 1 (1.6%) |
| Metastatic CRPC | 36 (56.3%) |
| Treatment (cases) | |
| ADT | 26 (40.6%) |
| NGH before chemotherapy | 3 (4.7%) |
| NGH after chemotherapy | 8 (12.5%) |
| Chemotherapy | 27 (42.2%) |
| Time from baseline to follow-up (cases) | |
| 3-6 months | 48 (75.0%) |
| 6-9 months | 11 (17.2%) |
| 9-12 months | 5 (7.8%) |

*ADT = androgen deprivation therapy; BS = bone scintigraphy; CRPC = castration-resistant prostate cancer; NGH = next-generation hormonal therapy; PSA = prostate-specific antigen.*

### BSI compared to PCWG3 criteria

Progressive disease by PCWG criteria was reported in 18 cases (28%) compared to non-PD in 46 cases (72%). A comparison of quantitative BSI changes values versus PCWG3 dichotomous outcome indicated an increase in BSI in cases categorized as PD, and a decline in non-PD cases (Figure 1). In cases with PD, median ΔBSI increased by 1.69 units (Table 2). Among the 18 cases with PD, most cases showed any numerical increase as well as at least >0.3 BSI unit increase (Table 2). In PCWG non-PD cases, ΔBSI decreased by a median of 0.13 units (Table 2). Overall, numerical BSI values differed significantly among cases classified as PD vs. non-PD (P< 0.0001). Using a BSI value of >0.0 units for significant change, 34 of 46 non-PD cases did not show any increase in BSI (with BSI units >0.3, the number was 42). Twelve patients had a significant increase in BSI using the 0.0 unit as cut-off (four cases using BSI >0.3) but were not classified with PD by PCWG3. Response categorization by dichotomized ΔBSI responses (i.e., any BSI increase versus no increase or decrease) versus PCWG3 responses (PD vs. non-PD) showed a significant difference between the two methods (P=0.0003). Using a BSI 3 cut-off >0.3, the P-value was <0.00001).

### BSI compared to MD Anderson criteria

When using the MDA criteria, PD occurred in 22 cases (34%), SD in 29 cases (45%), and PR in 13 cases (20%). No patients achieved a complete response. ΔBSI increased in most cases with PD; whereas those with a PR showed decreasing BSI values (Figure 2, Table 3). Patients with SD had mixed responses by ΔBSI. Among the 22 patients with PD by MDA criteria, 17 patients showed an increase in ΔBSI (of whom 14 had BSI change >0.3), and five showed decreased ΔBSI. Among the 13 patients with a PR, 12 patients showed reduced ΔBSI (11 had a decline >0.3 units), and one patient showed an increase. There was a significant association of numerical ΔBSI across the response categories (P<0.0001). A 3x2 Chi-square analysis with the three MDA categories and dichotomized BSI response criteria (cut-off 0.0 units) as explained above showed a significant association (P<0.0001)(BSI >0.3; P=0.000174) (since Chi-square does not work with empty fields, 0 vs. 13 cases with PR was replaced with 1 vs. 14). Two illustrative examples are shown in Figure 3.

***Table 2.*** *Changes in BSI categorized by PCWG2 response criteria (progression vs. non-progression).*

| Treatment | PD (n=18) | Non-PD (n=46) |
|---|---|---|
| All treatments (n=64) | | |
| ΔBSI median, units | 1.69 (31.3%) | -0.13 (-15.5%) |
| ΔBSI range, units | -0.98–11.61 | -11.71–3.54 |
| ΔBSI (cut off 0 units) | | |
| >0 | 15 | 12 |
| =0 | 0 | 7 |
| <0 | 3 | 27 |
| ΔBSI (cut off 0.3 units) | | |
| >0.3 | 15 | 4 |
| -0.3 to 0.3 | 2 | 20 |
| <-0.3 | 1 | 22 |
| ADT (n=26) | | |
| ΔBSI median, units | 1.31 (30.1%) | 0.00 (0.0%) |
| ΔBSI range, units | -0.98–5.76 | -7.41–0.08 |
| NGH (n=11) | | |
| BSI median, units | 1.73 (49.2%) | 0.04 (8.3%) |
| BSI range, units | -0.02–11.61 | -11.45–3.54 |
| Chemotherapy (n=27) | | |
| ΔBSI median, units | 2.17 (28.6%) | -0.73 (-30.2%) |
| ΔBSI range, units | 0.45–3.43 | -11.71–0.67 |

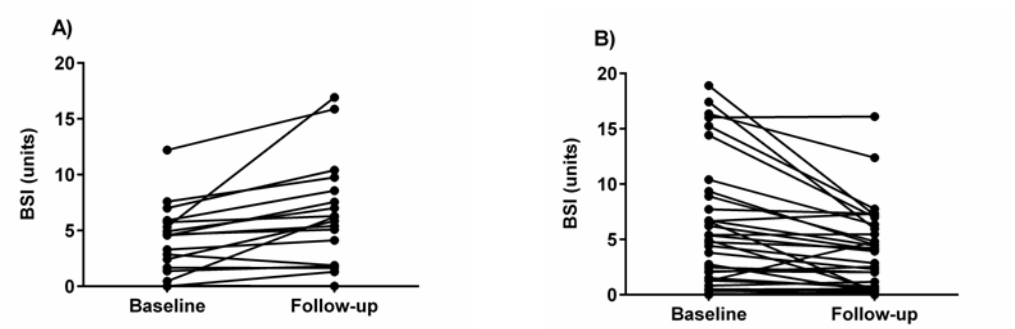


**Figure 1.** Changes in bone scan index (BSI) from baseline to follow-up among 18 individual cases classified as having progressive disease (PD) (A) by Prostate Cancer Working Group criteria versus 46 cases of non-PD (B). Changes in BSI differed significantly among PD and non-PD cases (P<0.0001).

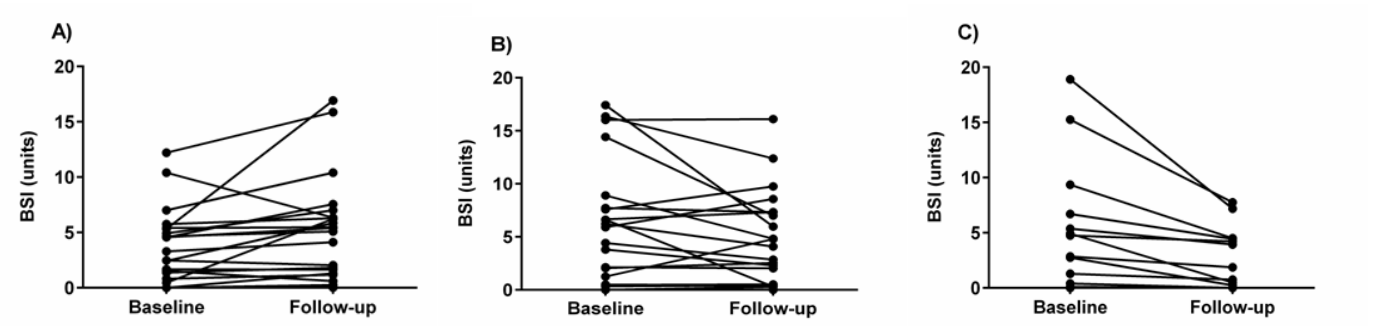


**Figure 2.** Changes in BSI from baseline to follow-up among 22 cases with PD by MD Anderson criteria (A), 29 cases with stable disease (B), and 13 cases with a partial response (C). Changes in BSI differed significantly among these three categories (P<0.0001).

***Table 3.*** *Changes in BSI categorized by MDA response criteria (progression vs. stable disease vs- partial response).*

| Treatment | PD (n=22) | SD (n=29) | PR (n=13) |
|---|---|---|---|
| All treatments (n=64) | | | |
| ΔBSI median, units | 0.49 (23.9%) | 0.00 (0.0%) | -1.44 (-96.9%) |
| ΔBSI range, units | -4.07–11.61 | -11.45–3.54 | -11.71–0.03 |
| ΔBSI (cut off 0 units) | | | |
| >0 | 17 | 9 | 1 |
| =0 | 0 | 7 | 0 |
| <0 | 5 | 13 | 12 |
| ΔBSI (cut off 0.3 units) | | | |
| >0.3 | 14 | 5 | 0 |
| -0.3 to 0.3 | 5 | 15 | 2 |
| <-0.3 | 3 | 9 | 11 |
| ADT (n=26) | | | |
| ΔBSI median, units | 1.31 (29.6%) | 0.00 (0.0%) | -0.76 (-62.1%) |
| ΔBSI range, units | -0.02–5.76 | -7.41–0.08 | -2.51–0.03 |
| NGH (n=11) | | | |
| BSI median, units | 0.45 (24.6%) | 0.08 (16.1%) | – |
| BSI range, units | -0.43–11.61 | -11.45–3.54 | – |
| Chemotherapy (n=27) | | | |
| ΔBSI median, units | 0.31 (14.4%) | -0.05 (-2.2%) | -2.26 (-100.0%) |
| ΔBSI range, units | -4.07–3.43 | -3.95–2.66 | -11.71–(-0.11) |

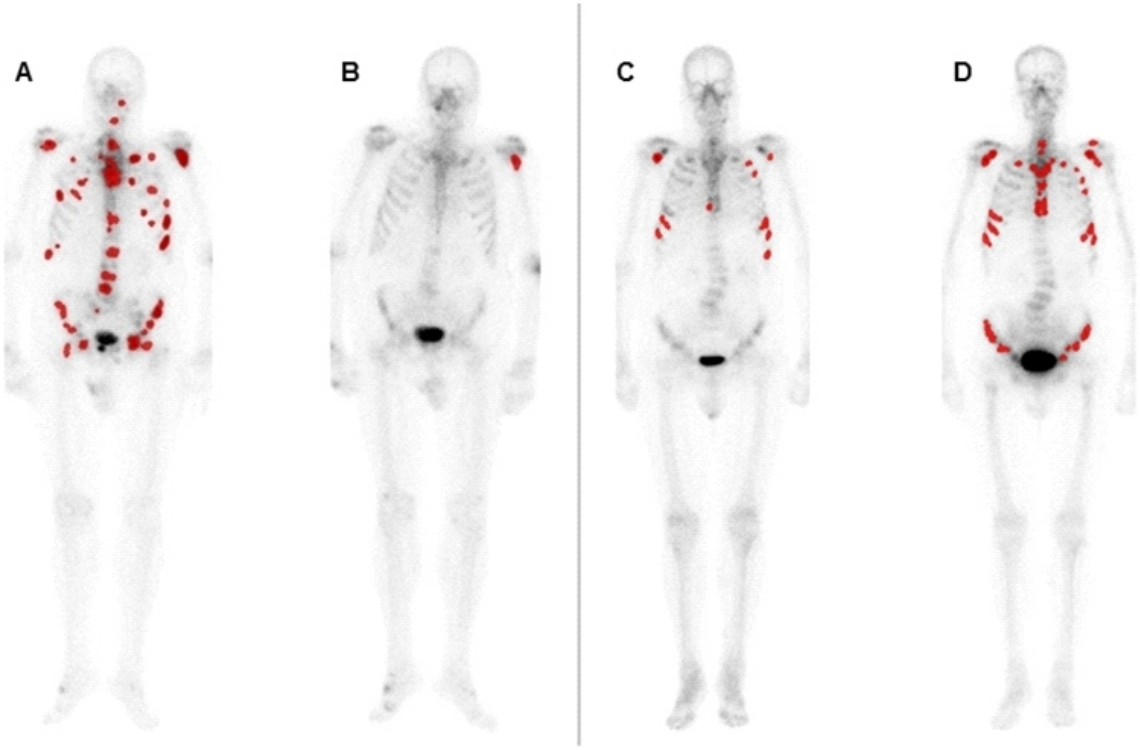


**Figure 3.** Two illustrative patient cases (all images are anterior projections of planar bone scans). A 77-year-old man with metastatic, hormone-sensitive prostate cancer received androgen deprivation therapy. BSI decreased from 6.63 units at baseline (A) to 0.31 units at follow-up at 6 months (B). This case was classified as non-PD by PCWG criteria and SD by MD Anderson criteria. The patient had PSA response (92ng/mL at baseline and 8.8 ng/mL at follow-up), and the clinical condition was evaluated as stable disease. A 71-year-old man with metastatic, castration-resistant prostate cancer received next-generation hormonal therapy (C). BSI increased from 1.35 units at baseline to 4.79 units follow-up at 4 months (D). The patient had non-PD according to the PCWG criteria and SD by MD Anderson criteria, although visual assessment suggested a malignant superscan. Prostate-specific antigenincreased from 11 to 29ng/mL, while the clinical response was classified as stable disease.

### Subgroup analyses by treatment category

For each treatment regimen, the BSI values at baseline and at follow-up were compared to the PCWG3 criteria (Table 2) and MD Anderson criteria (Table 3). The numerical, as well as relative changes of BSI across response categories, varied notable across regimens and the response criteria method, likely reflecting heterogeneity among patients and small cohorts; thus, no further analyses were made across treatment regimens.

### BSI versus biochemical response

The biochemical responses showed five cases (8%) of PSA progression (median change ΔBSI 0.82 units, range -0.92 to 3.54), 22 cases (34%) were PSA drifters (ΔBSI 0.10, -11.45 to 11.61), 8 (13%) cases had stable PSA (ΔBSI 0.58, -4.44 to 3.00), and 29 (45%) cases had a PSA response (ΔBSI -0.14, -11.71 to 0.36). There was a significant difference in numerical ΔBSI among these PSA response categories (P=0.003) as well as significantly different in BSI response (dichotomized, cut-off 0.0 units) versus PSA responses (4x2 Chi-Square, P=0.0005) (BSI cut-off 0.3; P=0.000345).

### BSI versus clinical response

The clinical response could be established in 57 of 64 patient among which 13 patients (20%) had a progressive clinical disease (ΔBSI 0.07 units, range -11.71 to 11.61), 32 patient (50%) had stable disease (ΔBSI 0.00, -11.45 to 3.54), and 12 patients (19%) had clinical improvement (ΔBSI 0.03, -7.51 to 3.67). There were no differences in absolute ΔBSI values between clinical responses (P=0.68), nor any significant differences across clinical response categories (BSI 0.0 cut-off, P=0.48; BSI 0.3 cut-off, P=0.30).

## Discussion

This preliminary study aimed to compare treatment responses in prostate cancer patients receiving systemic anticancer treatment as assessed by BSI, calculated automatically by dedicated software, and clinical response classification according to PCWG3 and MDA criteria by a panel of blinded, expert readers. The results showed that absolute changes in BSI were significantly related to PCWG3 and MDA response classifications. In addition, the dichotomized rating of BSI response was significantly associated with PCWG3 and MD Anderson responses as well as PCWG3-based PSA responses. To the best of our knowledge, this is the first report comparing absolute BSI changes and categorical BSI responses with major clinical response systems for skeletal metastases in prostate cancer treated with a wide variation of anticancer regimens. The findings indicate opportunities for automatic calculation of treatment responses in clinical trials and daily clinical practice.

Bone scan index is a continuous numeric variable from an automated, computer-assisted analysis of planar bone scans. This imaging marker has been documented to be highly reproducible in the calculation of the extent of metastatic bone involvement [22-24]. A recent meta-analysis summarized the existing knowledge of the prognostic and predictive information [12]. Many studies indicated a significant prognostic and predictive value of BSI. Some studies identified treatment-induced changes in BSI as a predictor of radiological progression-free survival and overall survival to chemotherapy, androgen deprivation therapy and next-generation hormonal therapy [21, 25-29] but no radium-223 therapy [30, 31]. No studies have so far compared BSI with MDA criteria, and only one study has assessed BSI with PCWG2 [13].

The conversion of quantitative changes of BSI into categorical responses for comparison with clinical response criteria can be done in several ways. We used cut-off values of 0.0 as well as an absolute change in ΔBSI greater than 0.3 units to classify responders from non-responders. A dichotomous classification makes sense in comparison to the dichotomous PCWG3 classification. Our findings indicated that cut-off values of 0.0 and 0.3 showed response classifications by BSI, which were significantly related to PCWGs categories. Haupt et al. (2017) compared responses by BSI and PCWG2 among 49 patients with metastatic prostate cancer using changes in BSI of 5% and 10% from baseline [13]. However, progression was found among 49% and 43% of the patients, respectively, significantly higher than the 27% seen with visual PCWG criteria. A 25% change in BSI from baseline resulted in comparable response rates (28% vs 27%). These findings indicated some variation across studies in terms of the BSI cut-off value. Our findings are broadly in line with several studies that have shown thatsome change in BSI change (>0.3 BSI units) is a consistent and reliable change of BSI [20, 21]. We compared 0.3 with 0.0 as cut-off and found quite similar results, indicating that minor changes in BSI should not be regarded as clinical significant changes in skeletal status. The stringent and concise PCWG3 criteria are recommended in clinical trials [7] and have been applied as a validated and standardized model in phase 3 trials [32, 33]. Large trials are required to document the optimal BSI cut-off limit, both in terms of comparison to standard clinical response criteria and the predictive value to anticancer therapy, in terms of clinically relevant outcomes, e.g., overall survival. Such values may depend on the skeletal status at study entry, e.g., lesion numbers and malignant superscan [20], and the treatment type (radium-223 vs. other regimens).

While BSI is an objective computer-derived measure, PCWG3 responses depend on visual assessment of images, which is associated with some variation. In this study, a panel of experienced readers blindly reviewed the BS. In our experience, reading BS is generally a very reliable procedure [34], including the assessment of treatment responses of the presence of skeletal metastases in prostate cancer [14]. That study showed almost perfect agreement among readers for the assessment of responses by PCWG3 and notable more imperfect agreement with NDA criteria, also after reducing MDA from three to two categories (PD/non-PD). The added clinical value of BSI over visual PCWG3 response assessment awaits further clinical validation.

The BSI software also provides the feature for identifying individual metastasis-suspected lesions. A comparison of lesion numbers recorded by the software and PCWG3 criteria seems apparent but remains controversial. In a prior stu-

dy, a total of 130 prostate cancer patients with a valid reference standard of no bone metastasis at primary staging presented with a mean of 2 lesions (range 0 to 19) characterized as malignant by the software [35]. Kaboteh et al. (2013) used EXINI BoneBSI to calculate new lesions and BSI values in patients undergoing treatment with chemotherapy [23]. Bone scan index, but not the appearance of two new lesions, correlated with overall survival. It is currently premature to use individual lesion analysis with this software.

The requirement for manual correction of artifacts, e.g. urinary tract, urostomy, and injection sites, is a drawback with a fully automatic analysis of the skeleton for metastasis; manual adjustment has been reported to be required in nearly one in every five patients [35].

Comparisons of BSI with biochemical and clinical outcome were the secondary endpoints in this study. Several studies have investigated the relationship between BSI and PSA using different methods, but with inconclusive findings [12]. We showed significant associations of absolute BSI changes as well as BSI response categories across PSA response categories. These findings are in line with observations by Dennis et al. (2012), who described the correlation between BSI and PSA alterations at three and six months on treatment [36]. There was no correlation between ΔBSI and clinical responses. The expected sequence for progression (emerging skeletal metastases, PSA increase in peripheral blood, and eventually, clinical deterioration) implies that any such correlation was not evident within the observed period. The PCWG consortium considers symptoms and health-related quality of life independently from other outcome measures [7].

There are some limitations to this study, including the retrospective design, and the variability in the time from baseline to follow-up bone scintigraphy. However, the design reflected daily clinical practice. In addition, a small and uneven number of patients with different disease stages across treatment groups may have impaired the power of the statistical analyses. For these reasons, we did not perform a head-to-head comparison of the prediction of survival by BSI and PCWG3. However, the heterogeneous population allowed a preliminary analysis if there was any bias in the correlation between automatic and visual assessment of bone metastasis across treatment types. Such bias was not evident.

*In conclusion*, this preliminary study treatment-induced changes in BSI, expressed as absolute changes as dichotomous response criteria, to correlate significantly with the classification of responses by PCWG3 and MDA criteria during anticancer treatment. Although the automatic analysis of BSI with the use of computer-assisted software has potential as a simple and reliable method in response evaluation in prostate cancer patients, head-to-head comparative trials with PCWG3 criteria should reveal clinical utility and added clinical predictive value of the automatic analysis.

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