



Planar ^{99m}Tc -PSMA Imaging of Prostate Cancer in a Low-Resource Setting: A Series Report

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Abstract

Objective Technetium-99m labeled prostate-specific membrane antigen (PSMA) single-photon emission computed tomography/computed tomography (SPECT/CT) is a suitable alternative to prostate-specific membrane antigen-positron emission tomography (PSMA-PET) imaging. However, the availability of SPECT/CT in many developing countries is limited.

Materials and Methods To evaluate the utility of planar ^{99m}Tc -PSMA in the absence of SPECT/CT, we compared planar ^{99m}Tc -PSMA and routine bone scan imaging in low-, intermediate-, and high-risk prostate cancer in five patients with histologically confirmed prostate cancer who had both scans within a period of less than 4 days. The mean age of patients was 66.8 ± 5.24 , and the median prostate-specific antigen level was 175 ng/mL (range: 0–778 ng/mL).

Results Planar ^{99m}Tc -PSMA scan provided no additional benefit over bone scans in the low-risk prostate cancer cases. In the cases with intermediate-risk prostate cancers, planar ^{99m}Tc -PSMA indicated complete and partial response to treatment in oligometastatic and widespread metastatic disease, respectively. In one patient with high-risk prostate cancer, planar ^{99m}Tc -PSMA detected additional skeletal lesions that were not seen on bone scan.

Conclusion In the absence of SPECT/CT, planar ^{99m}Tc -PSMA was useful for confirming extent of disease in treated intermediate- and high-risk prostate cancer. It showed little value in low-risk prostate cancer, especially when bone scan is normal. It was particularly useful for treatment response assessment in oligometastatic disease, and its utility should be further explored.

Keywords

- planar ^{99m}Tc HYNIC PSMA
- bone scan
- equivocal scans
- SPECT

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Introduction

Prostate-specific membrane antigen positron emission tomography (PSMA-PET) is recommended for the evaluation of rising prostate-specific antigen (PSA) levels in treated localized prostate cancer, and initial evaluation of untreated high-risk prostate cancer.¹ It is well established that PSMA PET imaging detects metastatic prostate cancer that is missed by conventional imaging.^{1,2} Where PSMA-PET is not available, technetium-99m labeled PSMA with single-photon emission computed tomography and X-ray computed tomography (SPECT/CT) is a suitable alternative.³ The relative lower cost and ubiquitous utility of SPECT scanners have led to proposals that it is ideal for low-resource settings where nuclear medicine is still developing.⁴ As such, ^{99m}Tc -PSMA promises to fill the gap created by lack of access to PET imaging in low-resource settings.^{3,5} ^{99m}Tc -PSMA-SPECT continues to be of interest, especially its potential advantages over bone scanning.^{5,6} However, since the first clinical reports of ^{99m}Tc -PSMA imaging for prostate cancer,⁷ its application to clinical practice continues to be surpassed by PSMA-PET studies.^{1,3,5} The deficiency of ^{99m}Tc -PSMA SPECT/CT imaging centers around its poor identification of smaller lesions and the limited proposals for patient selection.^{2,3,6,8} Additionally, SPECT/CT is not readily available in many low-resource settings, especially in developing African countries.⁹ Thus, planar bone scanning is the current standard of care for the evaluation of skeletal metastases, despite its well-recognized limitations.¹⁰

To determine if planar ^{99m}Tc -PSMA imaging successfully provides improved staging over planar technetium-99m labeled -methyl-diphosphonate (^{99m}Tc -MDP) bone scans, we compared both scans in five cases of prostate cancer with different risk stratifications.

Methods

Ethical statement: The human research ethics committee of our institution approved this study, ethics number UI/EC/20/0198, and waived the need for participant's consent due to the retrospective design of this study.

Patients: Five consecutive patients with histologically confirmed prostate cancer who had both ^{99m}Tc -PSMA scans and ^{99m}Tc -MDP within 72 hours were evaluated. Patients were classified using the prostate cancer clinical states comprising the dynamic transition model described by Scher et al.¹¹ Data on age, baseline serum PSA, initial Gleason score, serum testosterone levels, and indication for scanning, history of previous trauma or concomitant cancers were obtained by a single examiner (OAT).

Radiopharmaceutical preparation: Kits were labeled in-house by two trained radiopharmacists under aseptic technique in accordance with conditions and practices to prevent harm to the participants and following the manufacturer's instructions.¹² A digital dry block heater (Capintec, United States) was used for the heating stage of the PSMA kit labeling and tracer was injected within 15 minutes of prepa-

ration. The quality of ^{99m}Tc -PSMA labeling was observed visually on the images. No quality control was done on the final products prior to injection due to low-resource setting of the study.

Imaging: Images were acquired on a single-head (E. Cam, Siemens gmbh) or a SPECT/CT (Mediso, Hungary) gamma camera using a low energy all-purpose or low energy high-resolution collimator, respectively. No adverse events were recorded during and after injection for all images. Although a SPECT/CT camera was available at the study site, the functionality was limited to planar acquisition due to equipment downtime.

Bone scanning was performed with ^{99m}Tc -MDP. The mean (standard deviation [SD]) activity injected intravenously was 22.175 (2.487)mCi, (range: 17.21–26.7 mCi) followed by whole body planar imaging after 3 hours and imaging in accordance with international guidelines.

^{99m}Tc -PSMA imaging was performed using HYNIC iPSMA kits (*Instituto Nacional De Investigaciones Nucleares, La Marquesa Ocoyoacac, Mexico*). The mean (SD) activity injected intravenously was 22.225 (12.32) mCi of ^{99m}Tc -PSMA (range: 16.7–25.9 mCi) followed by imaging at 30 minutes, 1 hour, and 2 hours as described previously.¹²

Results

► **Table 1** summarizes the characteristics of the cases.

^{99m}Tc -PSMA and ^{99m}Tc -MDP scans were congruent in the two patients with untreated low-risk prostate cancer. The first was a newly diagnosed patient who complained of low back pain in whom both scans were reported as being normal. The second had a recent rise in serum PSA levels and both MDP (► **Fig. 1A**) and PSMA (► **Fig. 1B**) scans showed abnormal increased uptake in the mandible with a corresponding history of a recent toothache. On the other hand, in the two cases of treated intermediate-risk prostate cancer, planar ^{99m}Tc -PSMA indicated complete (► **Fig. 2A** and **B**) and partial response (► **Fig. 3A** and **B**) to treatment in oligometastatic and widespread metastatic disease, respectively. Also in the single case of treated high-risk prostate cancer, planar ^{99m}Tc -PSMA detected additional skeletal lesions that were not seen on bone scan (► **Fig. 4A** and **B**). Expectedly, abnormal visceral uptake suggestive of metastatic involvement of the lymph nodes was noted.

Discussion

The superiority of ^{99m}Tc -PSMA SPECT/CT over SPECT/CT bone scanning has been established.⁵ However, the potential utility of planar ^{99m}Tc -PSMA was of interest in this study as modern SPECT/CT gamma cameras are expensive and beyond the reach of many developing countries.⁹ In this report, ^{99m}Tc -PSMA and bone scans were congruent in untreated low-risk prostate cancer. Thus, planar ^{99m}Tc -PSMA may not provide additional information over routine bone scans in the evaluation of untreated low-risk prostate cancer. We demonstrated abnormal and potentially benign uptake on ^{99m}Tc -PSMA as a limitation of PSMA imaging. The normal biorouting of PSMA and

Table 1 Characteristics of patients

Patients	Case 1	Case 2	Case 3	Case 4	Case 5
Age (y) at time of scan	63	62	79	65	71
Clinical state	Hormone-resistant metastatic prostate cancer	Newly diagnosed, hormone-sensitive non-metastatic prostate cancer	Nonmetastatic hormone sensitive prostate cancer	Hormone-resistant metastatic prostate cancer	Hormone-resistant metastatic prostate cancer
Initial PSA at diagnosis (ng/mL)	5.9	7	4.6	12	46.6
Initial Gleason Score at diagnosis	5 + 4	3 + 3	3 + 3	3 + 4	3 + 4
PSA at time of scan (ng/mL)	778	7	36	< 0.1	230
Year of prostate cancer diagnosis	2016	2019	2011	2016	2013
Year of PSMA scan	2019	2019	2020	2020	2020
Treatment history	TURP Orchidectomy Abiraterone Dialysis	Bicalutamide	TURP, watchful waiting	Bicalutamide Orchidectomy Goserelin External beam radiotherapy	Abiraterone Chemotherapy External beam radiotherapy
Measured activity of ^{99m} Tc-MDP injection (mCi)	17.21	21.1	22.2	26.7	22.2
Number of skeletal lesions suggestive of metastases on ^{99m} Tc-MDP bone scan	1	0	0	1	> 48
Number of skeletal lesions that were equivocal on ^{99m} Tc-MDP bone scan	2	0	1	0	0
Measured activity of ^{99m} Tc-PSMA injection (mCi)	25	25.9	16.7	23.6	22.1
Number of abnormal skeletal lesions suggestive of metastases on PSMA scan	6	0	0	0	< 30
Number of skeletal lesions that were equivocal on ^{99m} Tc-PSMA	0	0	1	0	0
Presence of abnormal viscera uptake suggestive of metastases	Yes	No	No	No	No
Impact on treatment	Palliative care	Watchful waiting	Watchful waiting	Downstage	None

Abbreviations: PSA, prostate-specific antigen; ^{99m}Tc-PSMA, technetium ^{99m}Tc-labeled prostate-specific membrane antigen; ^{99m}Tc-MDP, technetium ^{99m}Tc-labeled methyl-diphosphonate.

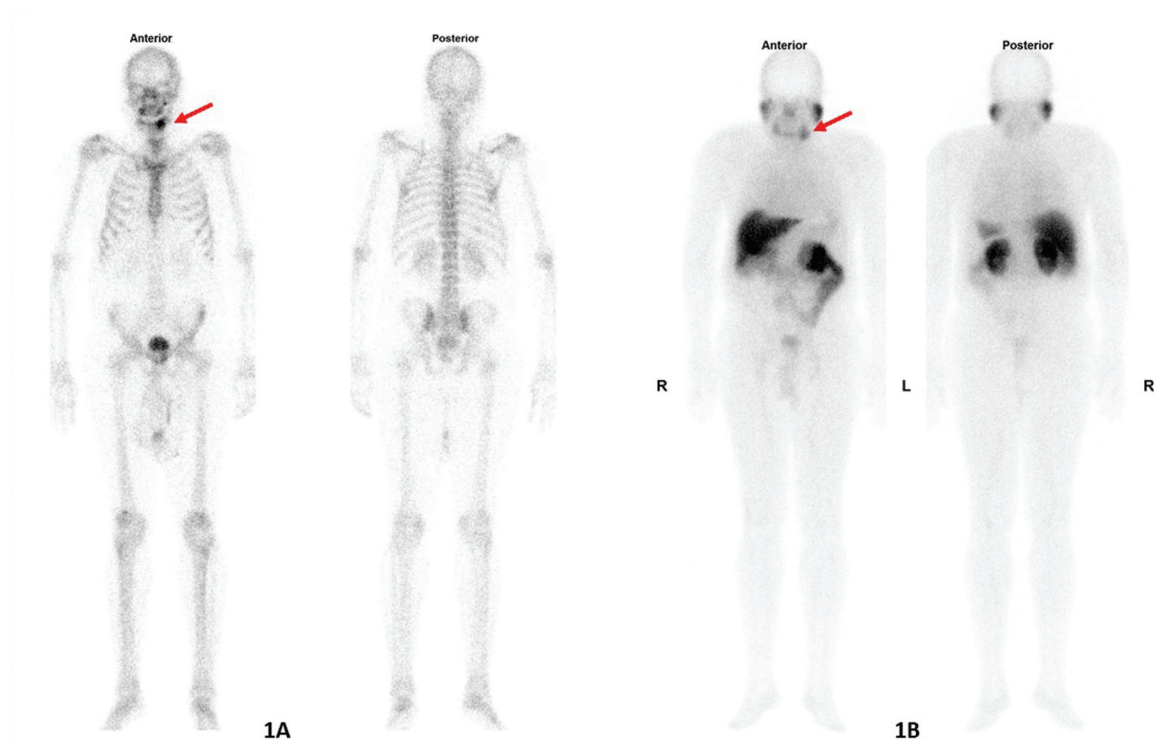


Fig. 1 A 79-year-old patient with untreated low-risk prostate cancer of 11 years duration. Planar bone scan (A) shows focal area of increased uptake in the mandible. Planar technetium-99m labeled prostate-specific membrane antigen scan (B) showed uptake in the same region. Red arrows indicate congruent uptake.

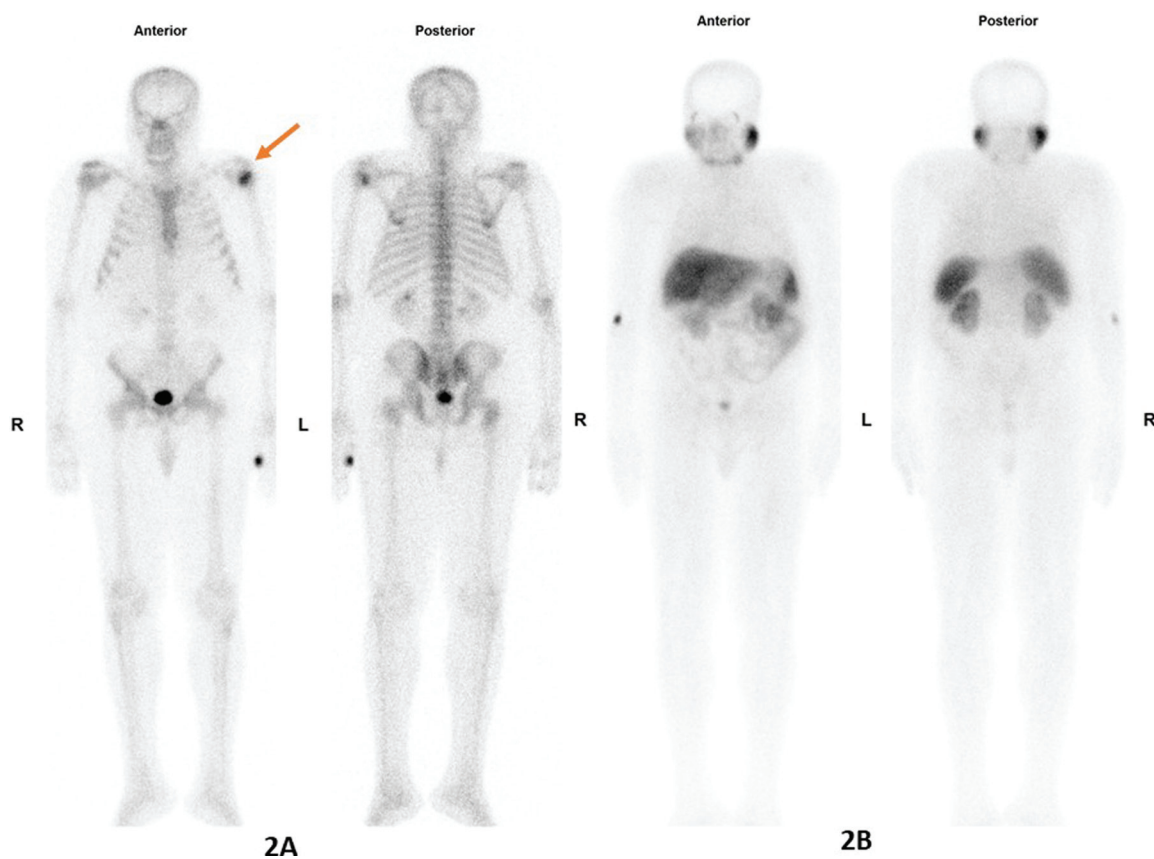


Fig. 2 A 65-year-old man with treated metastatic castrate-resistant prostate cancer who had external beam radiotherapy to the right humerus. Planar bone scan (A) showed abnormal uptake in the left humerus (red arrow). Planar technetium-99m-labeled prostate-specific membrane antigen scan (B) was normal.

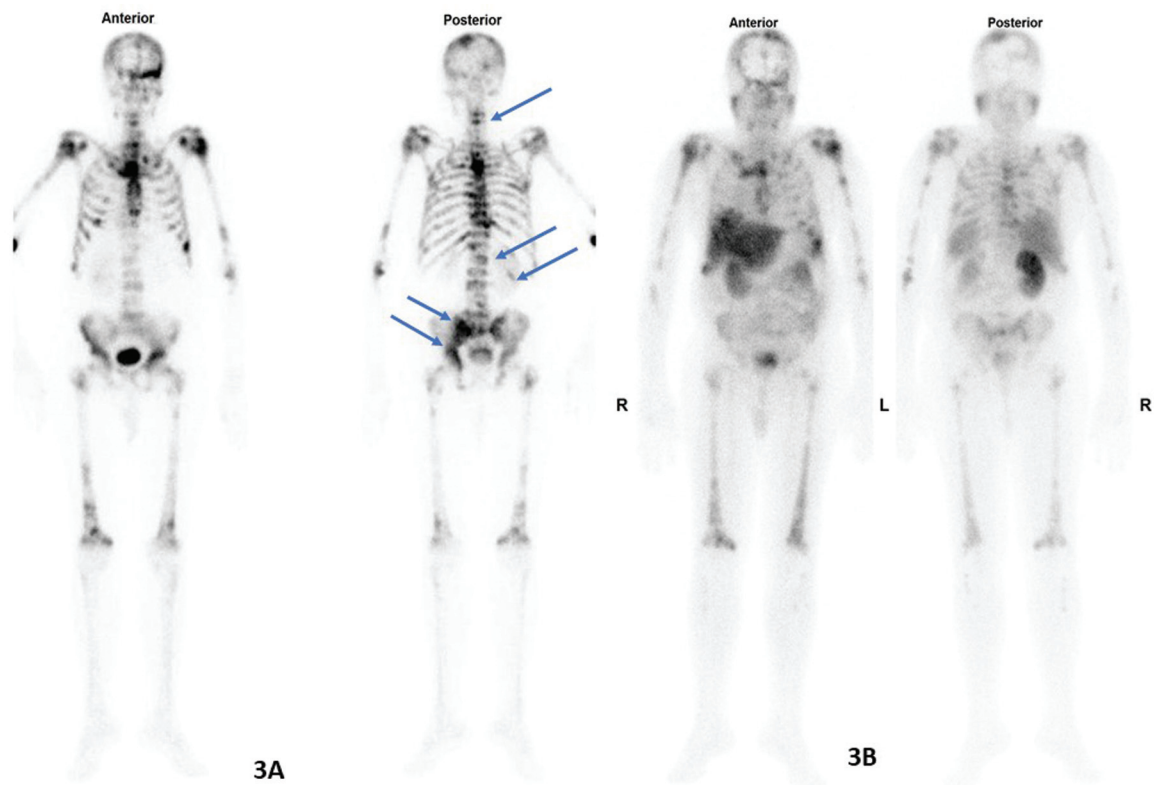


Fig. 3 A 69-year-old man with treated metastatic castrate-resistant prostate cancer who had a bone scan to monitor treatment response (A). Blue arrows indicate abnormal areas of increased uptake on bone scan that are not visualized on technetium-99m-labeled prostate-specific membrane antigen scan (B).

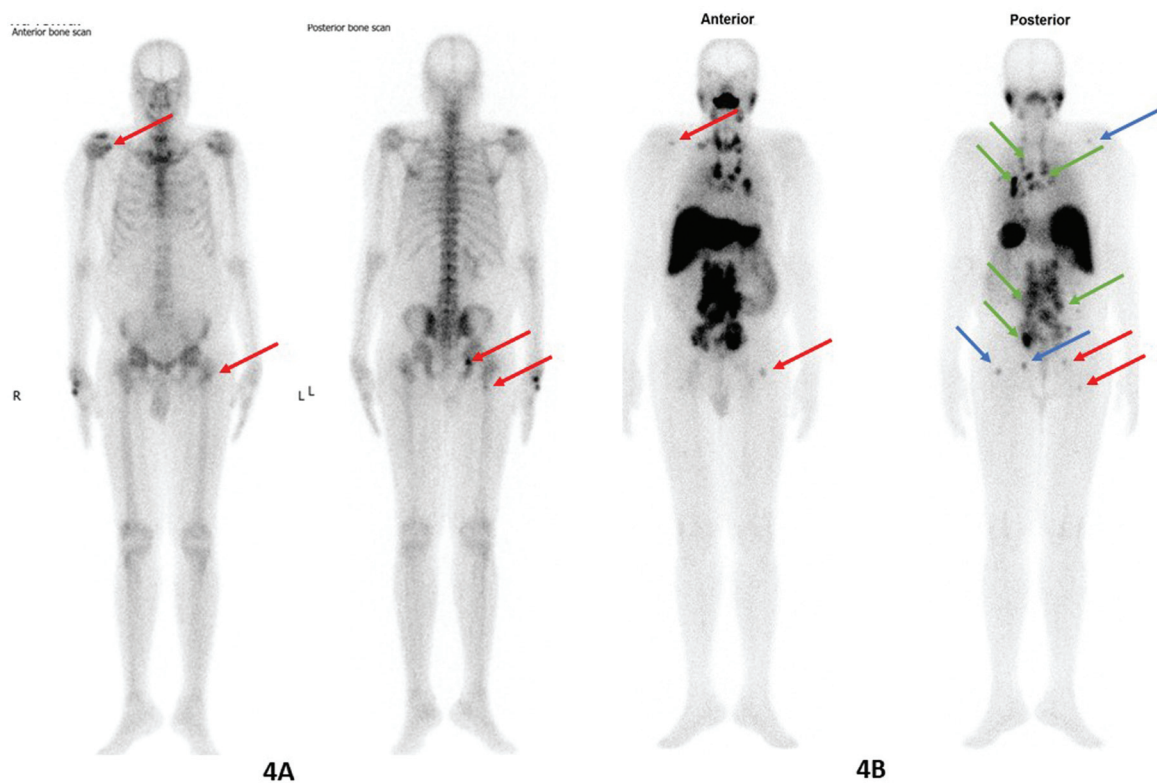


Fig. 4 A 63-year-old man with treated castrate-resistant prostate cancer who presented with elevated prostate-specific antigen of 778 ng/mL while on abiraterone. Bone scan showed radiological evidence of skeletal metastases (red arrows, A). Additional bone metastases (blue arrows, B) and previously unknown visceral metastases (green arrows) are seen on technetium-99m-labeled prostate-specific membrane antigen scan.

potential uptake in benign and malignant nonprostate tissues are known pitfalls for interpreting PSMA-PET scans.² In our case of congruent equivocal skeletal uptake in the mandible on both scans, SPECT/CT for localization may be of limited clinical value as solitary metastases to the mandible will be extremely rare.

While prior history of trauma, surgery or established degenerative bone disease could be a distinguishing factor for equivocal findings on bone scans, it is not particularly helpful with PSMA scans. Further imaging with SPECT or anatomical imaging (radiographs, CT, or magnetic resonance imaging) significantly confirms or excludes metastatic disease on bone scans.¹³ However, visceral PSMA uptake often leads to additional tests being ordered and results in highly variable outcomes.² Conclusively, the cost of evaluating equivocal skeletal uptake by PSMA-SPECT/CT is approximately 60% higher than bone scan SPECT/CT. Thus, the value of planar PSMA scanning for the evaluation of equivocal bone scans may be limited.

We propose that an advantage of planar ^{99m}Tc-PSMA may be to evaluate treatment response in oligometastatic prostate cancer. ^{99m}Tc-PSMA imaging confirmed complete radiological treatment response where bone scan was falsely positive. Among the known limitations of bone scans is the persistent uptake in healed/healing bone after treatment.^{5,6} Fewer skeletal lesions seen on planar ^{99m}Tc-PSMA scans in this study were associated with treatment, specifically external beam radiotherapy. This correlates with a study of late-stage patients with prostate cancer that reported the lower specificity of planar PSMA (86%) compared with bone scan (90%).⁵ Further exploration of the diagnostic impact of planar ^{99m}Tc-PSMA in oligometastatic disease is necessary to establish this indication.

Study limitations: Quality control to confirm the labeling efficiency of the tracer was not done in this study due to the low-resource setting. Although a SPECT/CT scanner was installed at the study site, the combination of lack of trained personnel and frequent downtime of the camera led to its underutilization for this study.

Conclusion

This study indicated the value of planar ^{99m}Tc-PSMA imaging for evaluating treated intermediate- and high-risk prostate cancer, particularly for treatment response evaluation of oligometastatic prostate cancer. We propose further studies on the diagnostic impact of ^{99m}Tc-PSMA in oligometastatic prostate cancer.

Authors' Contribution

OAT was involved in conceptualization, design, definition of intellectual content, clinical studies, data acquisition, data analysis, statistical analysis, manuscript preparation, and manuscript review. AAO was involved in literature search, clinical studies, data acquisition, data analysis, manuscript editing, and review. EUA was involved in literature search, clinical studies, data acquisition, manuscript editing, and

review. OAO was involved in designing, clinical studies, data acquisition, data analysis, manuscript preparation, and review. EOO was involved in designing, clinical studies, data acquisition, manuscript preparation, editing, and review. OAT has provided guarantee.

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None.

Conflict of Interest

None declared.

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