ORIGINAL ARTICLE

Diagnostic sensitivity of Tc-99m HYNIC PSMA SPECT/CT in prostate carcinoma: A comparative analysis with Ga-68 PSMA PET/CT

Ismaheel O. Lawal1 | Alfred O. Ankrah1,2 | Neo P. Mokgoro1 | Mariza Vorster1 | Alex Maes1,3 | Mike M. Sathekge1

1 Department of Nuclear Medicine, University of Pretoria and Steve Biko Academic Hospital, Pretoria, South Africa
2 Department of Nuclear Medicine and Molecular Imaging, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands
3 Department of Nuclear Medicine, AZ Groeninge, Kortrijk, Belgium

Correspondence
Mike M. Sathekge, MD, PhD, Department of Nuclear Medicine, University of Pretoria and Steve Biko Academic Hospital, Private Bag X169, Pretoria 0001, South Africa.
Email: mike.sathekge@up.ac.za

Background: Emerging data from published studies are demonstrating the superiority of Ga-68 PSMA PET/CT imaging in prostate cancer. However, the low yield of the Ge-68/Ga-68 from which Gallium-68 is obtained and fewer installed PET/CT systems compared to the SPECT imaging systems may limit its availability. We, therefore, evaluated in a head-to-head comparison, the diagnostic sensitivity of Ga-68 PSMA PET/CT and Tc-99m HYNIC PSMA SPECT/CT in patients with prostate cancer.

Methods: A total of 14 patients with histologically confirmed prostate cancer were prospectively recruited to undergo Ga-68 PSMA PET/CT and Tc-99m HYNIC PSMA SPECT/CT. The mean age of patients was 67.21 ± 8.15 years and the median PSA level was 45.18 ng/mL (range = 1.51-687 ng/mL). SUVmax of all lesions and the size of lymph nodes with PSMA avidity on Ga-68 PSMA PET/CT were determined. Proportions of these lesions detected on Tc-99m HYNIC PSMA SPECT/CT read independent of PET/CT findings were determined.

Results: A total of 46 lesions were seen on Ga-68 PSMA PET/CT localized to the prostate (n = 10), lymph nodes (n = 24), and bones (n = 12). Of these, Tc-99m HYNIC PSMA SPECT/CT detected 36 lesions: Prostate = 10/10 (100%), lymph nodes = 15/24 (62.5%), and bones = 11/12 (91.7%) with an overall sensitivity of 78.3%. Lesions detected on Tc-99m HYNIC PSMA SPECT/CT were bigger in size (P < 0.001) and had higher SUVmax (P < 0.001) as measured on Ga-68 PSMA PET/CT compared to those lesions that were not detected. All lymph nodes greater than 10 mm in size were detected while only 28% of nodes less than 10 mm were detected by Tc-99m HYNIC PSMA SPECT/CT. In a univariate analysis, Lymph node size (P = 0.033) and the SUVmax of all lesions (P = 0.007) were significant predictors of lesion detection on Tc-99m HYNIC PSMA SPECT/CT.

Conclusion: Tc-99m HYNIC PSMA may be a useful in imaging of prostate cancer although with a lower sensitivity for lesion detection compared to Ga-68 PSMA PET/CT. Its use is recommended when Ga-68 PSMA is not readily available, in planning radio-guided surgery or the patient is being considered for radio-ligand therapy with Lu-177 PSMA. It performs poorly in detecting small-sized lesions hence its use is not recommended in patients with small volume disease.

Keywords
Tc-99m, PET/CT, prostate cancer, PSMA, SPECT/CT
1 | INTRODUCTION

Prostate cancer is a leading cause of cancer among men and the sixth cause of cancer death worldwide.1,2 In South Africa, it is only second to basal cell carcinoma of the skin as the commonest cancer type in men and is responsible for 13% of all cancer deaths among South African men.3 In the management of prostate cancer, imaging plays an important role in disease detection, initial staging, therapy response evaluation, and surveillance following initial curative radical prostatectomy or external beam radiotherapy.4

Data are emerging to show the superiority of gallium-68 labeled prostate specific membrane antigen imaging with combined positron emission tomography and computed tomography (Ga-68 PSMA PET/CT) over other molecular imaging modalities as well as morphologic imaging with computed tomography (CT) or magnetic resonance imaging (MRI).5–7 Prostate specific membrane antigen (PSMA) is a trans-membrane glycoprotein that is overexpressed on prostate cancer cells.8 It’s level of expression increases with increasing tumor aggressiveness.9 Gallium-68 (Ga-68) is obtained from a long-lived Germanium-68/Gallium-68 generator (Ge-68/Ga-68 generator) and provides about 6 month supply of Ga-68. Ga-68 PSMA is labeled in-house in the nuclear medicine laboratory hence a reliable supply of the radiopharmaceutical is ensured. The 68 min half-life of Ga-68 is attractive in that patients are exposed to a relatively lower radiation dose.

Despite the success reported with the use of Ga-68 PSMA PET/CT imaging in prostate carcinoma, there exist challenges in meeting the high demand for this imaging modality in patient care. The amount of Ga-68 obtainable from the Ge-68/Ga-68 generator in a single elution is only sufficient to synthesize tracer for one or two patients. This limits the number of patients that can be imaged in a single day. There are fewer PET cameras installed worldwide than most other imaging machines which also limit the utility of this modality in daily clinical practice.

These challenges with Ga-68 PSMA PET/CT have stimulated interest in Technetium-99m-labeled PSMA with HYNIC used as a linker molecule. Technetium 99m (Tc-99m) is obtainable from a Molybdenum-99 generator capable of producing large activity sufficient to prepare radiotracer for a multitude of patients every day. When Technetium-99m HYNIC PSMA is used as the radiopharmaceutical, imaging is done with a gamma camera. There are more gamma cameras installed worldwide than there are PET cameras.10

The synthesis and biodistribution of Tc-99m HYNIC PSMA in animals and humans have been reported.11,12 Few studies have reported promising results with the use of Tc-99m-labeled PSMA ligand SPECT/CT imaging in patients with prostate carcinoma.13 To our knowledge, no study has reported a comparison of the diagnostic sensitivity of Tc-99m HYNIC PSMA SPECT/CT with that of Ga-68 PSMA PET/CT which is currently the gold standard molecular imaging technique in the management of prostate cancer.

The aim of this study was, therefore, to determine the sensitivity of Tc-99m HYNIC PSMA SPECT/CT for lesions expressing the PSMA glycoprotein detected on Ga-68 PSMA PET/CT imaging in patients with prostate carcinoma.

2 | MATERIALS AND METHODS

2.1 | Patients

Patients with histologically confirmed prostate carcinoma were prospectively recruited to undergo Ga-68 PSMA PET/CT and Tc-99m HYNIC PSMA SPECT/CT. A total of 14 patients were included in this study. Patients underwent the two scans in no particular order. Both scans were acquired within a median time interval of 4 days (range = 1-13 days). Demographic and clinicopathologic characteristic were determined in each patient and recorded.

The mean age of 14 men included in this study was 67.21 ± 8.15 years (median age = 68 years, range = 50-81 years). The median PSA level of the patients was 45.18 ng/mL (range = 1.51-687 ng/mL). A total of seven patients had imaging done for the initial staging of their disease. Seven patients had been treated before imaging: bilateral orchidectomy (n = 3), radical prostatectomy (n = 2), and radical prostatectomy followed by pelvic radiotherapy for recurrence (n = 1) and androgen deprivation therapy with Zoladex (n = 1). Table 1 shows the demographic and the clinicopathologic characteristics of the patients.

In addition to Ga-68 PSMA PET/CT and Tc-99m HYNIC PSMA SPECT/CT, nine patients had bone scan imaging with Tc-99m MDP. Bone scan was done in each patient within 2 weeks of the PSMA-based scans. Bone scan was acquired 3 h post intravenous administration of 30mCi Tc-99m MDP. Whole-body images, static oblique images of the head and chest as well as SPECT imaging of the thoraco-lumbar spine were acquired.

<table>
<thead>
<tr>
<th>No.</th>
<th>Age</th>
<th>PSA level</th>
<th>Gleason score</th>
<th>Prior treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>68</td>
<td>66.90</td>
<td>5 (2 + 3)</td>
<td>Radical prostatectomy</td>
</tr>
<tr>
<td>2</td>
<td>67</td>
<td>9.27</td>
<td>8 (4 + 4)</td>
<td>Orchidectomy</td>
</tr>
<tr>
<td>3</td>
<td>78</td>
<td>14.01</td>
<td>6 (3 + 3)</td>
<td>Orchidectomy</td>
</tr>
<tr>
<td>4</td>
<td>50</td>
<td>687.00</td>
<td>8 (4 + 4)</td>
<td>None</td>
</tr>
<tr>
<td>5</td>
<td>69</td>
<td>68.98</td>
<td>9 (4 + 5)</td>
<td>None</td>
</tr>
<tr>
<td>6</td>
<td>58</td>
<td>7.70</td>
<td>9 (5 + 4)</td>
<td>None</td>
</tr>
<tr>
<td>7</td>
<td>72</td>
<td>369.00</td>
<td>8 (4 + 4)</td>
<td>None</td>
</tr>
<tr>
<td>8</td>
<td>81</td>
<td>215.00</td>
<td>6 (3 + 3)</td>
<td>Orchidectomy</td>
</tr>
<tr>
<td>9</td>
<td>61</td>
<td>1.51</td>
<td>5 (3 + 2)</td>
<td>Radical prostatectomy</td>
</tr>
<tr>
<td>10</td>
<td>62</td>
<td>11.46</td>
<td>6 (3 + 3)</td>
<td>ADT-ZOLADEX</td>
</tr>
<tr>
<td>11</td>
<td>63</td>
<td>23.46</td>
<td>9 (4 + 5)</td>
<td>Radical prostatectomy</td>
</tr>
<tr>
<td>12</td>
<td>75</td>
<td>80.60</td>
<td>9 (5 + 4)</td>
<td>None</td>
</tr>
<tr>
<td>13</td>
<td>68</td>
<td>74.16</td>
<td>9 (5 + 4)</td>
<td>None</td>
</tr>
<tr>
<td>14</td>
<td>69</td>
<td>11.95</td>
<td>8 (4 + 4)</td>
<td>None</td>
</tr>
</tbody>
</table>

ADT, androgen deprivation therapy; PSA, prostate specific antigen.
2.2 Synthesis of the tracers

DKFZ-PSMA-11 was obtained from ABX advanced biochemical compounds (Biomedizinische Forschungsreagenzien GmbH, Radeberg, Germany). Ga-68 was obtained from a Ge-68/Ga-68 generator (iThemba LABS, Somerset West, South Africa). Synthesis of Ga-68 DKFZ-PSMA-11 was done in-house as we have previously reported.14 Radiochemical purity was above 98% in all syntheses administered to patients for imaging.

Kit for the preparation of Tc-99m HYNIC-iPSMA was obtained from the Instituto Nacional De Investigaciones Nucleares (La Marquesa Ocoyoacac, Mexico). The kit was formulated in accordance with the manufacturer’s instruction as contained in the packet insert. Briefly, 1 mL of 0.2M phosphate buffer with a pH = 7 was added to the vial containing freeze dried formulation of the pharmaceutical mixture. This was stirred for 10 s. Tc-99m Sodium pertechnetate 30mCi was added to the solution and stirred vigorously for 20 s. The reaction mixture was heated in a water bath at 95°C for 10 min. The prepared radiotracer was injected into patient within 1 h of preparation.

2.3 Imaging

Ga-68 PSMA PET/CT imaging was acquired on a Biograph 40 Truepoint PET/CT scanner (Siemens Medical Solution, IL). No special patient preparation was observed. Ga-68 PSMA (44-120MBq) was injected intravenously. Whole-body (vertex to mid-thigh) CT imaging was commenced at 60 min post tracer injection. CT parameters were adjusted for patients’ weight (120 KeV, 40-150mAs) with a section width of 5 mm and pitch of 0.8. Vertex to mid-thigh PET imaging was acquired in 3D mode at 4 min per bed position after CT imaging. Computed tomography data were used for attenuation correction. Image reconstruction was done with ordered subset expectation maximization iterative reconstruction algorithm (4 iterations, 8 subsets). A Gaussian filter was applied at 5.0 mm at FWHM.

Tc-99m HYNIC PSMA imaging was done on an Infinia Hawkeye dual head hybrid scanner (GE Healthcare, Milwaukee, WI). Whole-body planar imaging was acquired 3 h post tracer injection. This was followed by SPECT/CT imaging of the abdomino-pelvic region.

2.4 Image processing and interpretation

The reconstructed PET/CT images were displayed on a dedicated workstation equipped with a syngo software (Siemens Medical Solutions, IL). Maximum standardized uptake value (SUVmax), a measure of lesion avidity for the tracer, was determined for all tracer-avid lesions and recorded. The longest diameter of all tracer-avid lymph nodes were measured and recorded.

The planar and the reconstructed SPECT/CT images of Tc-99m HYNIC PSMA were viewed on a Xeleris workstation (GE Healthcare). Areas of abnormal tracer uptake consistent with PSMA expressing lesions were determined and recorded.

Image analysis and interpretation were done by two nuclear physicians independently. Images were presented randomly to the interpreters who were blinded to the clinical history of the patient and findings on the other PSMA study. Areas of disagreement were resolved by consensus. When consensus could not be reached, a third interpreter resolved the disagreement.

2.5 Statistical analysis

Statistical analysis was carried out using IBM SPSS Statistics 21.0 (IBM Corp., Armonk, NY). The statistical significance level was set at a P-Value of <0.05. Chi square test was used to determine if there was statistically significant difference in the lesion detection rates between Ga-68 PSMA PET/CT and Tc-99m HYNIC PSMA. The same test was used to determine if the size of a nodal lesion was significant in predicting lesion detection on Tc-99m HYNIC PSMA SPECT/CT. A comparison was made using Mann-Whitney U-test between lesion seen on Tc-99m HYNIC PSMA and those not seen. A univariate analysis was done to test if any of SUVmax of lesions, size of lymph node or PSA level was a significant predictor of lesion detection on Tc-99m HYNIC PSMA SPECT/CT scan.

3 RESULTS

A total of 46 PSMA expressing lesions were seen in 14 patients imaged with Ga-68 PSMA PET/CT. These lesions were localized to the prostate (n = 10), lymph node (n = 24), and bone (n = 12). No extra-prostatic visceral lesion was seen. In the 14 patients, tracer uptake on the Ga-68 PSMA PET/CT study was localized to: the prostate only (n = 4), the prostate and lymph nodes (n = 4), the prostate and bones (n = 2), the prostate, lymph nodes and bones (n = 2), bony only (n = 1), and lymph nodes only (n = 1). Tc-99m HYNIC PSMA SPECT/CT detected 78.3% of lesions (36/46) seen on Ga-68 PSMA PET/CT. No new lesion was seen on the Tc-99m HYNIC PSMA study that was not visualized on the Ga-68 PSMA PET/CT study. Figure 1 shows the performance of Tc-99m HYNIC PSMA SPECT/CT in lesion detection in the patients. Table 2 shows the distribution of lesions detected by both studies.

![FIGURE 1](image-url)
TABLE 2 Comparison in lesion detection rates between Ga-68 PSMA PET/CT and Tc-99m HYNIC PSMA SPECT/CT

<table>
<thead>
<tr>
<th>Lesion detected by Ga-68 PSMA</th>
<th>Tc-99m HYNIC PSMA SPECT/CT</th>
<th>n (%)</th>
<th>n (%)</th>
<th>N (100.0%)</th>
<th>( \chi^2 )</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td></td>
<td>0 (0.0)</td>
<td>10 (100.0)</td>
<td>10</td>
<td>4.888(^Y)</td>
<td>0.087</td>
</tr>
<tr>
<td>Node</td>
<td></td>
<td>9 (37.5)</td>
<td>15 (62.5)</td>
<td>24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone</td>
<td></td>
<td>1 (8.3)</td>
<td>11 (91.7)</td>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>10 (21.7)</td>
<td>36 (78.3)</td>
<td>46</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\( \chi^2 \), Chi square; Y: yates corrected chi square.

Tracer avidity by a lesion measured by SUVmax on Ga-68 PSMA PET/CT is a significant predictor of detection of the same lesion on Tc-99m HYNIC PSMA SPECT/CT (\( P = 0.001 \)). Almost all lesions (19/20) with SUVmax greater than 20 were detected on the SPECT/CT study. This contrast to only 28.6% of lesions with SUVmax less than 10 seen on the SPECT/CT. Table 3 shows the distribution of lesion detection rate of Tc-99m HYNIC PSMA by SUVmax of the same lesion on Ga-68 PSMA PET/CT scan.

Table 4 shows how lymph node size measured on Ga-68 PSMA PET/CT influenced detection of the same lymph node on the Tc-99m HYNIC PSMA study. There is a statistically significant positive correlation between nodal size and detection rate (\( P = 0.002 \)). All lymph nodes that were not detected were less than 10 mm in their widest diameter with only 2/11 of these sub-centimeter nodes seen on Tc-99m HYNIC PSMA (Fig. 2). All PSMA expressing lymph nodes greater 10 mm in size were clearly visualized.

A Mann-Whitney U-test done to compare the SUVmax and the size of lymph nodes between lesions detected and those not detected confirmed that lesions detected have significantly higher SUVmax than lesions not detected (\( P < 0.001 \)). Similarly, lymph nodes that were detected had significantly higher diameter than those not detected (\( P < 0.001 \)) (Table 5). In a univariate analysis to determine significant predictors of lesion detection by Tc-99m HYNIC PSMA SPECT/CT, nodal size and the SUVmax were strong predictors of lesion detection (Table 6). The effect of PSA level in predicting lesion detection rate on Tc-99m HYNIC PSMA, however, did not reach a statistically significant level.

Among nine patients that had additional evaluation with a bone scan, skeletal metastasis was seen in two patients. No skeletal metastasis was seen in seven patients. These seven patients had only soft tissue on their PSMA-based scans (Fig. 3).

4 | DISCUSSION

Emerging data are demonstrating the superiority of Ga-68 PSMA PET/CT in prostate cancer management. The different scenarios in which this functional imaging technique has outperformed other imaging modalities include detection of site of recurrence in biochemical failure and disease staging for treatment planning.\(^{15-17}\) Ga-68 PSMA PET/CT imaging has shown promise in areas where morphologic imaging with CT and MRI have demonstrated deficiencies especially in post treatment evaluation of disease recurrence in the prostate bed as well as in the evaluation of metastasis in normal-sized lymph nodes.\(^{7,18}\) In this study, we undertook a head-to-head comparison of Ga-68 PSMA PET/CT and Tc-99m HYNIC PSMA SPECT/CT for PSMA-expressing lesions in patients with carcinoma of the prostate. We found a sensitivity of 78.3% for Tc-99m HYNIC PSMA in detecting PSMA-avid lesions demonstrated on Ga-68 PSMA PET/CT (Fig. 1). Reinfelder et al evaluated another Tc-99m PSMA-based agent and found a lesion detection rate of 70% in patients with biochemical recurrence. In this study, the gold standards for confirmation were histological evaluation and findings on other imaging modalities.\(^{13}\) In another study,\(^{19}\) 13 patients with biochemical recurrence were initially evaluated with Ga-68 PSMA PET/CT. This was followed by injection of Tc-99m PSMA on the day of surgery for metastectomy. Intra-operative gamma probe was used to localize Tc-99m PSMA-avid lymph node metastases. A sensitivity of 85% was found for Tc-99m PSMA in localizing sites of metastasis using intra-operative gamma
FIGURE 2  Images of an 81-year-old male with prostate carcinoma, Gleason 6, PSA = 215 ng/mL (patient number 8). Previous treatment was bilateral orchidectomy. (A) Ga-68 PSMA PET/CT showed uptake in the prostate, right axillary node and 2 sub-centimeter pelvic nodes. (B) Tc-99m HYNIC PSMA SPECT/CT identified lesion in the prostate and right axillary node. The small pelvic nodes were not detected.

TABLE 5  Differences in SUV max and Lymph node size of lesions as they affect detection on Tc-99m HYNIC PSMA SPECT/CT

<table>
<thead>
<tr>
<th></th>
<th>Tc-99m HYNIC PSMA</th>
<th></th>
<th></th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Not detected</td>
<td>Detected</td>
<td>t/U</td>
<td></td>
</tr>
<tr>
<td>SUV max (mm)</td>
<td>Mean ± SD</td>
<td>5.78 ± 2.99</td>
<td>20.90 ± 12.27</td>
<td>-3.641 0.001*</td>
</tr>
<tr>
<td></td>
<td>Median (IQR)</td>
<td>4.80 (3.11-8.37)</td>
<td>21.09 (11.05-28.53)</td>
<td>29.000 &lt;0.001*</td>
</tr>
<tr>
<td></td>
<td>Lymph node size</td>
<td>Mean ± SD</td>
<td>1.00 ± 0.00</td>
<td>2.40 ± 0.74</td>
</tr>
<tr>
<td></td>
<td>Median (IQR)</td>
<td>1.00 (1.00-1.00)</td>
<td>3.00 (2.00-3.00)</td>
<td>7.000 &lt;0.001*</td>
</tr>
</tbody>
</table>

IQR: inter-quartile range; t: independent samples t-test; U: Mann-Whitney U-test; *P-value <0.05.
Unlike in our study, this study did not undertake SPECT/CT imaging for a head-to-head comparison with Ga-68 PSMA PET/CT.

SUVmax of all lesions and the size of lymph nodes demonstrating avidity for tracer on Ga-68 PSMA PET/CT were significant predictors for lesion detection on Tc-99m HYNIC PSMA. Whereas 29 of 30 lesions with SUVmax greater than 20 were visualized on Tc-99m HYNIC PSMA, only two of seven lesions with SUVmax less than 10 were similarly visualized. Only about half of lesions with SUVmax between 10 and 20 were seen on Tc-99 HYNIC PSMA SPECT/CT.

**TABLE 6** Determinants of lesion detection by Tc-99m HYNIC PSMA SPECT/CT (Univariate analysis)

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>OR (95%CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSA</td>
<td>0.051</td>
<td>1.053 (0.886-1.251)</td>
<td>0.559</td>
</tr>
<tr>
<td>SUV max</td>
<td>0.337</td>
<td>1.400 (1.097-1.787)</td>
<td>0.007*</td>
</tr>
<tr>
<td>Lymph node size</td>
<td>0.622</td>
<td>1.863 (1.051-3.304)</td>
<td>0.033*</td>
</tr>
</tbody>
</table>

REF: reference category; PSA: prostate specific antigen; SUVmax: maximum standardized uptake value; B: coefficient of logistic regression; 95%CI: 95% confidence interval; *P-value <0.05.

**FIGURE 3** Figure 3 are the images of a 50-year-old male newly diagnosed with prostate cancer with no treatment yet, Gleason = 8, PSA = 687 ng/mL. (A) Ga-68 PSMA PET/CT showed two large nodes with necrotic centers (left para-aortic node and left iliac node) and primary lesion within the prostate. (B) Tc-99m HYNIC PSMA also showed the primary prostate lesion and the two large nodes. (C) His bone scan was normal. 
radiotracers uptake has been reported in different non-prostatic carcinomas confirmed to be due to prostate cancer or its metastases in this study. In evaluating soft tissue metastasis, it is safe to suggest that Tc-99m HYNIC PSMA will complement bone scan alone as shown in the seven patients with negative bone scan but soft tissue disease on their PSMA-based scans. Bone scan alone may even be a more come site of distant metastases in prostate cancer. Bone scan has traditionally been the most commonly used nuclear medicine modality to evaluate for bone metastasis in patients with intermediate to high risk prostate cancer. Bone scan has an excellent sensitivity especially when combined with SPECT or SPECT/CT of the spine and pelvis—the commonest site of bone metastases. The specificity of bone scan is, however, modest. Though bone is a common site of metastasis (five of our patients had bone metastases), lymph node is equally or may even be a more come site of distant metastases in prostate cancer (seven of our patients had lymph node metastases). Bone scan alone will therefore under-estimate the extent of the disease when used alone as shown in the seven patients with negative bone scan but soft tissue metastases on the PSMA-based scans (Fig. 3). It is, therefore, safe to suggest that Tc-99m HYNIC PSMA will complement bone scan in evaluating soft tissue metastasis.

Not all lesions which demonstrate tracer avidity were histologically confirmed to be due to prostate cancer or its metastases in this study. This exercise would be necessary considering that PSMA-based radiotracers uptake has been reported in different non-prostatic malignancies as well as benign conditions resulting from PSMA expression in neovascularity.23–26 This was, however, not the purpose of this study. In this study, we aimed to evaluate the diagnostic sensitivity of Tc-99m HYNIC PSMA SPECT/CT for PSMA expressing lesions and compare it with the sensitivity of Ga-68 PSMA PET/CT scan which is currently the nuclear medicine imaging modality of choice in prostate cancer management. By this we believe our report will stimulate others to replicate this important venture and robust results may influence how functional imaging of prostate cancer is undertaken. We clearly demonstrate lower sensitivity for Tc-99m HYNIC PSMA SPECT/CT compared to Ga-68 PET/CT for lesions demonstrating PSMA glycoprotein expression in patients with prostate carcinoma.

imaging. All lymph nodes greater than 10 mm in their widest diameter were visualized irrespective of their SUVmax. This was in contrary to just 2 out of 11 lymph nodes less than 10 mm in diameter that were visualized (Fig. 2). The SPECT/CT system has a lower resolution and consequently lower ability to detect small-sized lesion compared to the PET/CT system. Rauschner et al compared the diagnostic sensitivity of Ga-68 PSMA PET/CT with that of In-111 PSMA I&T SPECT/CT and found lesion detection rate of 48.3%.20 The lesions detected on the SPECT/CT imaging in their study were slightly larger in size compared to the lesions not detected. The lower sensitivity reported in this study compared to our study is likely related to the use of Indium-111 (In-111) as the radionuclide. In-111 is expensive because of its production in a cyclotron and its long half live of 2.8 days is associated with high patient radiation dose. Due to radiation dose consideration, only 0.5mCi of In-111 is usually administered (compared to 30mCi for Tc-99m-based nuclides). This lower administered activity is associated with lesser photon flux and consequently lower sensitivity.

Bone scan imaging in nine of our study population was associated with a low yield with only two patients demonstrating skeletal metastases. The other seven patients were confirmed to have just soft tissue disease on their PSMA-based scans. Bone scan has traditionally been the most commonly used nuclear medicine modality to evaluate for bone metastasis in patients with intermediate to high risk prostate cancer. Bone scan has an excellent sensitivity especially when combined with SPECT or SPECT/CT of the spine and pelvis—the commonest site of bone metastases. The specificity of bone scan is, however, modest. Though bone is a common site of metastasis (five of our patients had bone metastases), lymph node is equally or may even be a more come site of distant metastases in prostate cancer (seven of our patients had lymph node metastases). Bone scan alone will therefore under-estimate the extent of the disease when used alone as shown in the seven patients with negative bone scan but soft tissue metastases on the PSMA-based scans (Fig. 3). It is, therefore, safe to suggest that Tc-99m HYNIC PSMA will complement bone scan in evaluating soft tissue metastasis.

The small population we studied is a significant limitation in this report. Similar results from another study with a larger population size will be required to support our findings.

5 | CONCLUSION

Tc-99m HYNIC PSMA SPECT/CT has a value in the management of patients with prostate cancer. Compared to Ga-68 PSMA PET/CT, its diagnostic sensitivity is lower. Lymph node size and tracer avidity are strong predictors of lesion detection rate on Tc-99m HYNIC SPECT/CT. Its use should be considered when Ga-68 PSMA PET/CT is not available or when PSMA expression in known lesions is being evaluated for such as when determining patient’s suitability for radioligand therapy with Lu-177 PSMA. Its sensitivity is sufficient for use in radio-guided surgery. It is not recommended in low volume disease such as in biochemical failure with low PSA levels.

ACKNOWLEDGMENT

NTP Radiopharmaceuticals SOC and Department of Nuclear Medicine at Steve Biko Academic hospital.

CONFLICTS OF INTEREST

No conflicts of interests.

REFERENCES


How to cite this article: Lawal IO, Ankrah AO, Mokgoro NP, Vorster M, Maes A, Sathekge MM. Diagnostic sensitivity of Tc-99m HYNIC PSMA SPECT/CT in prostate carcinoma: A comparative analysis with Ga-68 PSMA PET/CT. Prostate. 2017:1–8. https://doi.org/10.1002/pros.23379