



# Is Nuclear Medicine Bone Scanning Necessary for Staging Gleason 7 Prostate Cancer, In the Asymptomatic Man with a PSA Less Than 20?

HR Patel<sup>1\*</sup>, C Barber<sup>2</sup>, J Virdi<sup>2</sup> and M Arya<sup>2</sup>

<sup>1</sup>Department of Urology, University Hospital North Norway, Norway

<sup>2</sup>Princess Alexandra Hospital NHS Trust, UK

## Introduction

Prostate Cancer (CaP) if localized on staging has good outcomes for cancer specific survival and long term functional outcomes in the modern era [1-4]. The EAU guidelines for prostate cancer staging confirm that Nuclear Medicine Bone Scanning (NMBS) is an established part of the staging process for CaP [5]. The likelihood of Bone Metastases (BM) at presentation rises with the PSA, and thus above a PSA of 20 there is no controversy about the use of a bone scanning, regardless of Gleason score [5]. Importantly, poorly differentiated cancers may not elaborate PSA which leads to a bone scan being indicated in Gleason 8,9 and 10 tumours even when the PSA is <20 ng/ml. Controversy lies with moderately differentiated tumours (3+4 or 4+3) when the PSA is <20 ng/ml, and this can lead to poor adherence to cancer network guidelines [6,7]. Currently, our CaP network guidelines stipulate that a NMBS should be performed for Gleason 7 CaP, even if the PSA <20. Thus, the aim of the current study is to assess the efficacy of NMBS in CaP Gleason 7, with a PSA <20.

## Methods

**Patient selection:** In accordance with the Declaration of Helsinki this clinical prospective observational study was carried out at a single hospital with CaP confirmed by prostate biopsy from 2014 to 2017. All new cases of CaP, with a PSA <20 and a Gleason score of 7 (3+4 and 4+3) undergoing a NMBS were assessed for Bone scan outcome.

**Data collection:** The PSA, Gleason Score, MRI staging, NMBS, further imaging, and where necessary clinical outcome were recorded.

**Nuclear medicine bone scan (NMBS):** Tc-99m Hydroxymethylenediphosphonate (650 MBq) was injected intravenously, and whole body scanning was performed 3 hours later. Planar images were obtained using a standard gamma camera, and reported by a qualified Radiologist.

**Confirmation of bone metastasis:** A Radiologist further evaluated NMBS with indeterminate Bone metastasis, before further imaging modalities were implemented.

**Guidelines for recommending a NMBS:** We examined our local guidelines within our CaP network and the European Association of Urology (EAU) guidelines [5]. According to our local guidelines any patient with a Gleason 7 prostate cancer, irrespective of the PSA, they must have a NMBS. The EAU guidelines state that a NMBS may not be indicated in asymptomatic patients with a well or moderately differentiated tumour if the serum PSA level is <20 ng/mL.

**Analysis:** We assessed the efficacy of bone scan use for staging moderately differentiated prostate cancer (Gleason 7) in patients with a PSA <20 ng/ml.

## Results

Two hundred and eighty six Bones scans were undertaken at our public hospital in the UK, on cases of newly diagnosed Gleason 7 prostate cancer. 58 cases had a PSA >20, therefore were removed from the group. The study group was further reduced when TNM staging was not complete; therefore the final study group consisted of 214 cases (Table 1).

Fifty eight of the 214 cases had initially reported Bone scans as indeterminate. After review, 9 were reported as normal, and 49 underwent further imaging (Table 2).

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### \*Correspondence:

HR Patel, Department of Urology,  
University Hospital North Norway,  
Tromsø, Norway,

E-mail: urology@hrhpatel.org

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**Table 1:** Newly diagnosed prostate cancer Grade, Stage and Nodal status demographic (n =214).

Cases with PSA <20		
Grade	Gleason 3+4	119
	Gleason 4+3	95
Stage	T1c to T2c	152
	T3a	53
	T3a	13
	T4	2
Nodal Status	N0	203
	N1	5

**Table 2:** Further imaging outcomes following initial indeterminate Bone scanning (n =49).

Imaging	N	Outcome
MRI spine	19	No metastases
CT chest	12	No metastases
SPECT - CT	10	No metastases
MRI Head	2	No metastases
Choline CT PET	1	No metastases
CT Pelvis	1	No metastases
MRI femur	1	No metastases
X ray femur	2	No metastases
CT Head	2	No metastases
X ray Lumbar spine	2	No metastases
CT foot	1	No metastases
CT Clavicle	1	No metastases
MRI foot	1	No metastases
PSMA CT PET	1	No metastases
CT guided bone biopsy	1	Myeloma

Three of the 49 cases (Table 2) undergoing further imaging having suspicious lesions on bone scan were reviewed: Case 1 has a solitary skull lesion on Bone scan, with the rest of the skeleton free of lesions. The patient was treated as “non-metastatic” and 3 years later, there is no evidence of prostate cancer progression; Case 2 has several bony lesions on CT Urogram for haematuria. Most were benign bone islands, but one lesion was predominantly lytic with subtle expansion and diagnosed as indeterminate. Neither a further MRI nor bone scan was diagnostic of metastases. A CT colon 2.5 years later showed no change in any of the skeletal observations; no new lesions, no change in size or character of the existing lesions and he remains well 3 years after presentation; Case 3 had an indeterminate rib lesion on bone scan. CT chest was also indeterminate. He died 2.25 years later of alcoholic liver disease, with no sign of prostate cancer progression.

Two of the 214 cases were reported as having Bone metastases on bone scan; however these were already diagnosed on MRI of pelvis. 1 of the 2 cases had concomitant Haematuria, therefore had a CT urogram which revealed the metastases were osteolytic in nature, and therefore had a CT guided biopsy which diagnosed co-existing Myeloma. The latter was unknown at the time of prostate cancer diagnosis.

Sixty eight cases of T3/T4 CaP and 5 Node positive cases had no metastases on NMBS.

The cost of 214 Bone scans and 49 further imaging tests was approximately £90,500.

## Discussion

Only 1 of 214 moderately differentiated CaP patients with a PSA <20 ng/ml had a NMBS positive outcome in our prospective series. These metastases were already diagnosed on MRI. Therefore, our study confirms NMBS in this specific group yields no useful information for treatment.

NMBS is time consuming for the patient who has already had multiple outpatient episodes, including the actual prostate biopsy procedure, an MRI, blood tests, possible clinical trials recruitment, and other interactions. NMBS therefore lengthens the “patient journey” which can lead to additional distress [8].

Indeterminate NMBS has occurred in 49 patients in the current series and subjected patients to further imaging and ionizing radiation. The latter has been shown to increase the risk of prostate cancer and possibly further progress the disease; hence our study confirmed the unnecessary exposure of patients with CaP to ionizing radiation risk [9].

In the current financial climate where austerity measure is in place within the National Health Service, our study clearly demonstrates clinical ineffectiveness, but also cost inefficiencies [10]. Our hospital spent at least an extra £30,000 per year, for unnecessarily imaging CaP patients due to a local CaP cancer guideline.

Importantly, the EAU guidelines are more reflective of our findings, but they do not categorically state the need to not perform NMBS in a patient who is asymptomatic, with moderately differentiated CaP and a PSA <20 ng/mL [5].

## Conclusion

Our study confirms that a patient who is asymptomatic, with moderately differentiated CaP and a PSA <20 ng/mL has no benefit in undergoing NMBS. We also confirm that this continued practice has an unacceptable cost burden to the health care provider, in our case the NHS (UK).

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