Appropriate Use Criteria for Bone Scintigraphy in Prostate and Breast Cancer: Summary and Excerpts

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From the Newsline editor: Appropriate use criteria (AUC) are statements that contain indications describing when and how often an intervention should be performed under the optimal combination of scientific evidence, clinical judgment, and patient values while avoiding unnecessary provisions of services. SNMMI is a qualified provider-led entity under the Medicare Appropriate Use Criteria program for advanced diagnostic imaging, allowing referring physicians to use SNMMI AUC to fulfill the requirements of the 2014 Protecting Access to Medicare Act. SNMMI follows a balanced multidisciplinary approach to guidance development by including various stakeholders in the development process. For background and a detailed explanation of this development process, see http://www.snmmi.org/ClinicalPractice/content.aspx?ItemNumber=15665. The complete text of the AUC is available at www.snmmi.org/auc.

EXECUTIVE SUMMARY

Nuclear medicine imaging studies are essential to the diagnosis and management of many diseases, including neoplastic disease (*1*). Modern imaging studies allow noninvasive examination of anatomic and physiologic processes that often change patient management and improve outcomes. The ready availability and high sensitivity of medical imaging in conjunction with concerns about missed diagnoses has, at times, resulted in inappropriate use of the technology. This has resulted in an unnecessary financial burden on the health-care system and in some cases unnecessary exposure to ionizing radiation (*1–5*). Inconsistent use of specific imaging procedures for similar clinical scenarios has prompted a push for consensus documents outlining the most appropriate and cost-effective use of these imaging procedures. It is hoped that this expert guidance will help make the use of bone scintigraphy more consistent and improve healthcare outcomes for the intended patient population while minimizing unnecessary imaging costs.

The purpose of this document is to describe the appropriate use of bone scintigraphy in patients with prostate and breast cancer, the two most common diagnoses for which bone scintigraphy is ordered in the adult population. It is hoped that through these recommendations, bone scintigraphy will be used to benefit patients with prostate and breast cancer in the most cost-effective manner.

Representatives from the Society of Nuclear Medicine and Molecular Imaging (SNMMI), the European Association of Nuclear Medicine (EANM), and the American Society of Clinical Oncology (ASCO) assembled as an autonomous workgroup to develop the following appropriate use criteria (AUC). This process was performed in accordance with the Protecting Access to Medicare Act of 2014. This legislation requires that all referring physicians consult AUC using a clinical decision support mechanism before ordering any advanced diagnostic imaging services. Such services are defined as diagnostic MRI, CT, nuclear medicine procedures (including PET), and others as specified by the secretary of Health and Human Services in consultation with physician specialty organizations and other stakeholders (*6*). The AUC in this paper are intended to aid referring medical practitioners in the appropriate use of bone scintigraphy for the more common scenarios encountered in patients with prostate and breast cancer.

INTRODUCTION

The following document describes the appropriate use of nuclear medicine bone scintigraphy in patients with breast and prostate cancer. The authors have tried to cover the most common clinical scenarios for bone scintigraphy in patients with these two common malignancies. However, the reader is reminded that a patient may present with variations of the scenarios covered here, or with signs or symptoms not described, for which bone scintigraphy may still be indicated. This document is presented to assist health-care practitioners considering bone scintigraphy for patients with breast and prostate cancer; however, each patient is unique, as is each patient's clinical presentation, and therefore this document cannot replace clinical judgement. Bone scintigraphy can also be used for a variety of other conditions, both malignant and benign, for which assessment of osteoblastic activity is important for patient management. These other scenarios are beyond the scope of this document.

Bone scintigraphy is distinguished from conventional radiographic studies by its ability to assess the entire body at a comparatively low financial cost. Bone-seeking agents such as ^{99m}Tc-methylene diphosphonate (MDP) (*7*), ^{99m}Tc-hydroxy-MDP (*8*), and ^{18}F-NaF (*9*) are incorporated into the hydroxyapatite matrix of the bone in proportion to

osteoblastic activity. The location of neoplastic disease that has metastasized to bone and caused an increase in osteoblastic activity, such as occurs with most types of breast and prostate cancer, can be discerned from surrounding normal bone osteoblastic activity.

Bone scintigraphy is one of the highest-volume procedures in nuclear medicine imaging facilities. In 2014, approximately 407,000 bone scintigraphy studies were performed on Medicare patients for all indications (*10*). Although bone scintigraphy can be performed on patients with both benign and neoplastic disease, most bone scintigraphy studies are performed for oncologic indications. Of these, patients with breast cancer and prostate cancer make up most of the bone scintigraphy subjects.

A systematic review of the literature for this AUC revealed that strong evidence for this commonly used diagnostic imaging procedure is incomplete. Several factors may be behind the lack of randomized controlled trials supporting bone scintigraphy in breast and prostate cancer.

First, bone scintigraphy was developed more than 40 y ago. At that time, there were few alternatives for the detection of bony metastases, and the development of this unique and sensitive imaging modality was such an obvious improvement in the staging of metastatic prostate and breast disease that the technology was quickly adopted without randomized, controlled trials. Also at that time, randomized controlled trials looking at patient outcomes were not as common as were trials looking at diagnostic accuracy. Second, the widespread use of bone scintigraphy for staging breast and prostate cancer for so many years has meant that it has become a standard-of-care diagnostic study for staging these types of cancer; thus, there has been little call for expensive, long-term studies demonstrating the importance of a test that is already widely accepted.

Recent refinement of the diagnosis and staging of prostate cancer, along with development of new technologies such as MRI, CT, and ultrasound, have caused referring physicians to reexamine the need for bone

TABLE 1
Clinical Scenarios for Prostate Cancer

Scenario no.	Description	Appropriateness	Score
1	Initial staging for asymptomatic patient with normal alkaline phosphatase level, PSA $<$ 10, and Gleason score $\leq$ 6	Rarely appropriate	2
2	Initial staging for asymptomatic patient with elevated alkaline phosphatase level, PSA $<$ 10, and Gleason score $\leq$ 6	May be appropriate	4
3	Initial staging for asymptomatic patient with PSA = 10–20 or Gleason score = 7	May be appropriate	6
4	Initial staging for asymptomatic patient with PSA $\geq$ 20 or Gleason score $\geq$ 8 or $\geq$T3 prostate cancer	Appropriate	8
5	Initial staging for asymptomatic patient with PSA $<$ 10, Gleason score $\leq$ 6, and T2 prostate cancer	Rarely appropriate	3
6	Initial staging for asymptomatic patient with PSA $\geq$ 10, Gleason score $\leq$ 6, and T2 prostate cancer	May be appropriate	6
7	Initial staging for asymptomatic patient with PSA $<$ 10, Gleason score = 7, and T2 prostate cancer	May be appropriate	6
8	Initial staging for asymptomatic patient with PSA $\geq$ 10, Gleason score = 7, and T2 prostate cancer	Appropriate	8
9	Initial staging for symptomatic patient with normal alkaline phosphatase level, PSA $<$ 10, and Gleason score $\leq$ 6	Appropriate	8
10	Initial staging for symptomatic patient with elevated alkaline phosphatase level, PSA $<$ 10, and Gleason score $\leq$ 6	Appropriate	8
11	Evaluation of patient (at any clinical stage) presenting with new pathologic fracture	Appropriate	9
12	Initial staging for patient with bone pain	Appropriate	8
13	Restaging for asymptomatic patient when change in treatment is planned	Appropriate	7
14	Restaging for patient with bone pain when change in treatment is planned	Appropriate	8
15	Restaging for patient with bone pain	Appropriate	8
16	In patient with remote history of prostate cancer who has undergone imaging for another clinical reason, evaluation of incidental findings equivocal for osseous metastatic disease	Appropriate	7
17	Evaluation of patient before radionuclide bone therapy	Appropriate	9

PSA levels are in ng/mL.

scintigraphy in neoplastic disease (*11–14*). In addition, the rising cost of health care and the inconsistencies in the use of bone scintigraphy have encouraged third-party payers to push the medical community to reevaluate the importance of many advanced imaging technologies, including bone scintigraphy.

The rapid advancement of imaging technology has meant that long-term outcome trials are impractical, with results often obsolete by the time the investigation is completed (*15*). Therefore, the Centers for Medicare and Medicaid Services has recognized that expert opinion is often needed in the absence of evidence-based outcome literature. Without published outcome data, the authors of this document have relied on expert opinion from nuclear medicine specialists in the United States and Europe and from the referring oncology community. It is felt that by combining multispecialty expert opinion with the existing literature, the most accurate assessment possible can be made for the clinical utility of bone scintigraphy.

The lack of published evidence for the use of bone scintigraphy in specific clinical scenarios has not yet had a dramatic effect on relative reimbursement for this important test; however, as new regulations take effect requiring referring physicians to consult clinical decision support tools before ordering bone scintigraphy, access to this important technology may become severely limited unless AUC are written for inclusion of this test as an option in clinical decision support tools.

PROSTATE CANCER

Introduction

Adequate and appropriate staging is of paramount importance in decision making for initial and subsequent treatment of prostate cancer. Overuse of imaging in patients with a low probability of having metastases results in unnecessary additional expense, not only for bone scintigraphy but for studies such as CT and MRI. At the same time, underuse of imaging studies such as bone scintigraphy in high-risk patients results in misdiagnosis and the resultant morbidity from ineffective local therapies (*5*). Bone scans are used to stage and determine the appropriate therapy for early disease or whether the therapy needs to be changed in advanced disease. A change in therapy is contemplated on the basis of changes in the patient's symptoms, changes in prostate-specific antigen (PSA) doubling time, rapid rises in serum PSA level, and a new appearance of or change in visceral metastases (*16*). The purpose of this section of the AUC is to evaluate the appropriate use of bone scintigraphy in patients with prostate cancer both at

TABLE 2
Clinical Scenarios for Breast Cancer

Scenario no.	Description	Appropriateness	Score
1	Evaluation of patient with prior ^{18}F-FDG PET/CT study showing avid bone lesions	Rarely appropriate	2
2	Evaluation of patient with prior ^{18}F-FDG PET/CT study showing nonavid bone lesions	May be appropriate	4
3	Evaluation of patient with prior ^{18}F-FDG PET/CT study showing no bone lesions	Rarely appropriate	2
4	Initial staging for asymptomatic patient with elevated alkaline phosphatase level and clinical stage I or II breast cancer	Appropriate	7
5	Initial staging for symptomatic patient	Appropriate	8
6	Initial staging for patient with clinical stage IV breast cancer	Appropriate	8
7	Initial staging for patient with clinical stage III breast cancer	Appropriate	8
8	Initial staging for patient with clinical stage 0 breast cancer	Rarely appropriate	2
9	Restaging for asymptomatic patient with change in treatment plan	Appropriate	7
10	Restaging for patient with new bone pain	Appropriate	8
11	Restaging for asymptomatic patient with increase in alkaline phosphatase level	Appropriate	8
12	Restaging for suspicion of nonosseous recurrence	Appropriate	7
13	Evaluation of patient (at any clinical stage) presenting with new pathologic fracture	Appropriate	9
14	Evaluation of patient before radionuclide bone therapy	Appropriate	9
15	In patient with remote history of breast cancer who has undergone imaging for another clinical reason, evaluation of incidental findings equivocal for osseous metastatic disease	Appropriate	7
16	Routine surveillance in patient with history of breast cancer and no prior evidence of bone metastasis	Rarely appropriate	1

initial diagnosis and during the subsequent course of their disease.

Summary of Recommendations

Clinical scenarios for the use of bone scintigraphy and final AUC scores in prostate cancer are presented in Table 1. Bone scintigraphy is usually appropriate for initial staging in patients with intermediate-risk disease (stage T2, PSA level $>$ 10 ng/mL, or Gleason score $\geq$ 7); for initial evaluation of patients with high-risk disease (stage T3, PSA level $>$ 20 ng/mL, or Gleason score $>$ 8); for evaluation of patients with symptoms referable to the bones regardless of stage or risk; for evaluation of patients in whom a change in treatment is anticipated; for evaluation of patients presenting with a pathologic fracture; and for evaluation of patients who are to undergo radium or other radionuclide bone therapy.

Bone scintigraphy is usually not appropriate for initial staging in patients with a low risk of metastatic disease (PSA level $<$ 10 ng/mL, Gleason score $<$ 6, and no other clinical signs or symptoms of disease).

BREAST CANCER

Introduction

Like prostate cancer, breast cancer does not require bone scintigraphy in all patients at the time of diagnosis. Breast neoplastic disease discovered at an early stage is unlikely to metastasize to bone; therefore, unless there are signs or symptoms suggesting metastasis in early-stage disease, bone imaging is not necessary (*17*). If bone scintigraphy is felt necessary, imaging of pregnant patients requires special consideration. Recommendations for the appropriate use of bone scintigraphy in breast cancer are described in this section.

Summary of Recommendations

Clinical scenarios for the use of bone scintigraphy and final AUC scores in breast cancer are presented in Table 2. Bone scintigraphy is appropriate for initial staging in patients with node-positive disease; for patients at any stage or risk who have symptoms referable to the bones; and for patients who are to undergo bone-directed radionuclide therapy.

Bone scintigraphy is usually appropriate for breast cancer patients who present with a pathologic fracture, require a change in treatment plan, or are suspected of having nonosseous or osseous disease progression.

Bone scintigraphy is usually not appropriate for initial staging in patients with low-risk disease (clinical stage 0 or I) and no other clinical signs or symptoms of disease.

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