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Can the Diagnostic Accuracy of Bone Scintigraphy be Maintained with Half the Scanning Time?

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Abstract:

Purpose: We aim to show that the acquisition time of a conventional bone scan can be reduced by one-half without loss of the diagnostic value of the scan.

Materials and Methods: Fifty adult patients (37 male and 13 female, mean age 62.5, SD 8.7 years) were enrolled. Patients were injected with 25–30 mCi (925-1110 MBq) 99mTc MDP IV. The Standard Protocol whole body planar images were acquired first [scan speed = 10 cm/min, acquisition time around 20 minutes] and were followed immediately by the Half-Time Protocol whole body planar images [scan speed = 20 cm/min; acquisition time around 10 minutes]. Both images were interpreted by two nuclear medicine physicians. Each reviewer, when reviewing the Standard Protocol images, was "self-blinded" to the result they had obtained when reviewing the Half-Time images, and vice-versa. This self-blinding was accomplished by allowing a minimum of two weeks to elapse between the two interpretations. We used the κ-coefficient to compare the agreement between the Standard-Protocol results and the Half-Time results.

Results: There was no difference in clinically significant diagnostic information for Half -Time and Standard Protocol. The diagnostic quality of Half-Time and the Standard Protocol images were not significantly different ($0.86 < \kappa < 1.0$).

Conclusion: Our data suggest that if we reduce the 99mTc MDP dose by half and keep the acquisition time at its standard value we gain the benefits of reduced dose without loss of diagnostic value of the scan.

Key words: Image wisely, Half time acquisition, 99mTcMDP bone scan

Background & Objectives

Medical imaging is the major source of the radiation dose to human populations (*1*). In medical imaging, the dose delivered by the injected radiopharmaceuticals used in Nuclear Medicine is second only to the dose given by computed tomography. Many of the radiopharmaceutical dose recommendations were formulated in 1970s and early 80s, and although there has been a significant improvement in gamma camera technology since then, many of those recommended radiopharmaceutical doses have remained unchanged. With the increase in use of medical imaging with ionizing radiation, the dose delivered to the human population has been increasing, and there is a concerted effort to reduce this radiation burden. For example, in nuclear cardiology, the initial attempt to reduce radiation dose for myocardial perfusion imaging was to use a protocol where the first image was a low- dose stress image (*2*), furthermore, the radiopharmaceutical dose has been reduced in the last 10 years by using advanced processing software such as Astonish (Philips, Milpitas, CA) (*3,4*). Radiation dose reduction has been possible also, with the use of solid state detectors such as Cadmium Zinc Telluride with better sensitivity (*5*).

As another example, the Society of Nuclear Medicine and Molecular Imaging (SNMMI) and other societies have taken the Image Wisely Initiative into practice (*1*). This has resulted in studies that demonstrate that a decreased dose of a radiopharmaceutical can result in a study with comparable diagnostic information. For example, technetium 99m (99mTc) mertiatide (MAG3) studies for renal function and obstruction assessment can be performed with a comparable diagnostic performance, by using a decreased dose of radiopharmaceutical (*6,7*). The Image Wisely Campaign was initially launched by The American College of Radiology and the Radiological Society of North America (*1)*.

Decreasing the injected dose of radiopharmaceuticals will not only decrease the radiation dose delivered to the patient but also will decrease the dose received by the technologist who performs the study. In times of Technetium shortage, which has been a recurrent problem in recent years, reducing the radiotracer dose may result in a greater patient throughput (*8*).

Technetium-99m-Methylene Diphosphonate (99mTc-MDP) planar bone scintigraphy is commonly used to evaluate malignant and benign conditions of the bone (*9, 10, 11*). Other bisphosphonate derived radiotracers are used in other continents, although MDP is the most widely used in the United States. In the United States the usual administered activity of 99mTc MDP dose for bone scintigraphy in adults is 500–1,110 MBq (~13–30 mCi) (*12*), in Europe the dose-range varies from 8 to 30 mCi (*11*). In markedly obese adults, the administered activity could be increased to 11–13 MBq/kg (300–350 μCi/kg) (*12*).

In attempts to follow current optimal practices of of patient centered care by reducing the radiation dose in routine nuclear medicine studies, our study aims to prospectively evaluate the diagnostic value of half-time bone scans compared with standard dose scans. We used a full dose scan using half the normal acquisition time, obtained after the standard full acquisition scan time. This stratagem allowed us to obtain the clinical value of the standard protocol scan and at the same time obtain the half-time scan for comparison of diagnostic value without the need to get scans on different days and without increase in the radiation dose to the subjects.

Methods

This was an IRB approved prospective study. Adult patients scheduled to receive an MDP bone scan, who were over the age of 18 years, and who gave written consent, participated in this research study from May 2016 to December 2017. Fifty patients (37 male and 13 female, mean age 62.5,

SD 8.7 years) were enrolled; their findings prior to this study were as follows: 47 had a malignancy (32 prostate cancer, 9 breast cancer, 1 thyroid cancer, 2 rectal cancer, 2 lung cancer, 1 esophageal cancer) and 3 had benign bone lesions (2 Paget's and 1 benign spinal lesion on MRI). Body mass index (BMI) of the patients enrolled was in the range of 17.5 to 43.2 with a mean BMI of 28.2 and SD of 7.9.

Patients were injected with 25–30 mCi 99mTc MDP (925-1110 MBq) intravenously, which is the standard of practice for adults in the United States (*12).* Images were acquired after approximately 180-240 minutes post injection. The Standard Protocol whole body planar images were acquired first [scan speed = 10 cm/min, acquisition time = approximately 20 minutes] and were followed immediately by the Half-Time Protocol total body planar images [scan speed = 20 cm/min; acquisition time = approximately 10 minutes]. Philips gamma cameras (Philips Bright View and Precedence) with Low-Energy High-Resolution collimators were used.

Standard Protocol and Half-Time images were independently interpreted by two experienced nuclear medicine physicians (Reviewer A and Reviewer B), who were blinded to the results of the other reviewer. The image interpretation was subjective as well as objective. Reviewer A has more than 30 years of experience and reviewer B has 10 years of experience. Each reviewer, when reviewing the Standard Protocol images, was "self-blinded" to the result they had obtained when reviewing the Half-Time images, and vice-versa. This self-blinding was accomplished by allowing a sufficient amount of time (a minimum of two weeks) to elapse between the two interpretations. The order in which the Standard Protocol and Half-Time images were interpreted was random. The time of injection to time-to-imaging was recorded for all patients in both protocols.

After the above analysis, one reviewer then looked at the Standard Protocol and Half-Time images side by side in order to assess whether there were any artifacts, noise, patient motion or change in positioning between the two studies.

The reviewers used the following objective scoring scale for each Standard Protocol and Half-Time study identified lesion: 1- intensity hotter than background; 2- moderate intensity; 3- intensity similar to bladder or kidney; 4- photopenic. In addition, the following lesion characterizations were used: D (degenerative); M (metastases); C (contamination); P (primary bone tumor); O (Other). In order to minimize bias, clinical information, results of the prior bone scans, or reports from other imaging modalities, were not made available to the reviewers while interpreting for this research study. The usual artifacts such as urine contamination, minor dose infiltration or photpenic artifacts due to prosthesis did not pose problems for both experienced readers.

Results

Figure 1 shows images for a subject with negative findings, where comparison is made between the Standard Protocol and Half-Time Protocol anterior images [Fig. 1A and Fig.1B] respectively, and the Stand Protocol and Half-Time Protocol posterior images [Fig. 1C and Fig.1D] respectively. Figure 2 shows the same comparison images for a subject showing extensive metastases [Fig. 2A and Fig.2B] respectively, and the Stand Protocol and Half-Time Protocol posterior images [Fig. 2C and Fig.2D] respectively.

Although our aim was to compare the results of the Standard-Protocol with the Half-Time Protocol, we also checked the inter-observer variability between the two reviewers. We note that there was complete concordance between the two reviewers when using the Standard Protocol

images, that is, both reviewers found the same **21** patients to have metastatic lesions and the same **29** patients to be without metastatic lesions. When comparing results of Half-Time images between the two reviewers, the reviewers had different interpretations for only one patient in which reviewer A interpreted the foci to be degenerative and reviewer B did not mention the metastatic lesion. Except for this one lesion, all other lesions were identified by both reviewers in the Standard-Protocol and Half-Time study. There were a small number of discordant interpretations between the two reviewers in categorizing degenerative versus metastatic disease, however this discordance was similar in Standard-Protocol vs. Half-Time protocols.

We used the κ-coefficient *(13*) to compare the agreement between the Standard-Protocol results and the Half-Time results, for the same reviewer. That is, the Standard-Protocol and Half-Time protocol were treated as separate "reviewers." The comparison used six categories:

D (= one or more degenerate lesions found); M (= one or more metastatic lesions found);

T (=trauma); D & M ; T & M; (none (=no lesion).

For example, for one patient, the Half-Time review found only degenerative lesions while the Standard protocol review found both degenerate and metastatic lesions , while for 6 patients, both the Standard-Protocol review and the Half-Time review found both degenerative and metastatic lesions. For reviewer A we obtain κ = **0.9390** ; the calculated standard deviation σ = **.0421**

The 95% confidence interval for is thus $0.86 < \kappa < 1.0$

Similar results obtained for reviewer B.

Discussion

Bone scintigraphy is one of the most common studies performed on a daily basis in Nuclear medicine departments with a high volume of oncologic patients. Although it is considered to have a modest radiation exposure to patients, its amount is not to be underestimated. Bone scintigraphy is also done in patients where a benign condition is being evaluated. For example osteomyelitis, stress fractures, Paget's disease, pain, fractures, suspected infection of prosthetics, among other (*11*).

Reducing radiation dose is important in all groups of patients including cancer and non-cancer patients. Efforts in radiation dose reduction have been more intense in the area of nuclear cardiology.

This prospective study consisting of 50 adult patients showed that there was no statistical difference in diagnostic information between the scans obtained for half time and standard acquisition.

Factors such as poor renal function, poor hydration, and infiltration of the dose, large body habitus and patient motion and can affect the quality of bone scintigraphy images. Renal function, poor hydration and infiltrated dose will have the same effect both on the half time or standard acquisition protocol.

A large body habitus can increase attenuation to photons and adversely affect the quality of the scan. BMI assessment is a good indicator of body habitus and the patient population we studied had a wide range of BMI. There were no differences in quality and accuracy between the Standard and Half-Time studies in the BMI range of this study**.**

There were no incidents of large infiltration of the injected dose in our study. However, the side-by-side comparison of the Standard and Half-Time images, carried out after the separate readings, showed one patient with head and pelvis motion between the two scans; this was the one patient for which the Half-Time protocol found only degenerative lesions but the Standard Protocol found both degenerative and metastatic lesions.

Some limitations of this study are that it used a relatively small number (50) of only adult subjects, all from a single institution, and that it employed gamma cameras from a single vendor (Philips). The particulars of our patient population also led to some biases. Prostate cancer metastases are typically osteoblastic and show increased tracer concentration, while multiple myeloma, renal and thyroid disease usually demonstrate osteolytic lesions and avascular necrosis of the bone which present as photopenic defects on bone scintigraphy images. Since the majority of the patients in this study had prostate cancer, there were more instances of areas with intense focal areas of uptake and very few with photopenic regions, and thus our study could not satisfactorily test the detection rates of osteolytic lesions presenting as photopenic lesions. Finally, we note that the time-to-imaging from the time of injection was 2 hours and 30 minutes for Standard Protocol images and 2 hours 55 minutes for the Half-Time images. Although this 25 minute difference would not be expected to cause a significant change in the bio-distribution of the isotope, an ideal research study might have had the Half-Time images taken first for 25 of the 50 our patients. However, since the Standard Protocol images were part of the standard clinical protocol for these patients, good clinical practices required that we obtain them first.

Conclusion:

We used our Half-Time image protocol, and compared their diagnostic accuracy with our Standard Protocol images which used the standard recommended radiation dose. We found that diagnostic quality of Half-Time and the Standard Protocol images were not significantly different ($0.86 < \kappa < 1.0$). Since the Half-Time images have on average half the counts as the Standard Protocol images, a reasonable assumption from these results, for our patient population, is that by reducing the original dose by half, but keeping the acquisition time at its standard value - which will also result in half the counts - will again result in a clinically useful image. A multi-center, multi-vendor camera study is needed to determine if our result would be true for other patient populations.

References

1. Brink JA. The art and science of medical guidelines: what we know and what we believe. *Radiology* 2010; **254**:20-1.
2. Bateman TM, Heller GV, McGhie AI, et al. Multicenter investigation comparing a highly efficient half-time stress-only attenuation correction approach against standard rest-stress Tc-99m SPECT imaging. *J Nucl Cardiol* 2009; **16**:726-35.
3. Slomka P, Germano G. Optimizing radiation dose and imaging time with conventional myocardial perfusion SPECT: Technical aspects. J Nucl Cardiol 2017; **24**:888-891.
4. Venero CV, Heller GV, Bateman TM, et al. A multicenter evaluation of a new post-processing method with depth-dependent collimator resolution applied to full-time and half-time acquisitions without and with simultaneously acquired attenuation correction. *J Nucl Cardiol* 2009; **16**:714-25.
5. Duvall WL, Sweeny JM, Croft LB, et al. Reduced stress dose with rapid acquisition CZT SPECT MPI in a non-obese clinical population: comparison to coronary angiography. *J Nucl Cardiol* 2012; **19:**19-27.
6. Taylor AT, Folks RD, Rahman A, et al. (99m)Tc-MAG3: Image Wisely. *Radiology* 2017; **284**:200-209.
7. Hsiao EM, Cao X, Zurakowski D, et al. Reduction in radiation dose in mercaptoacetyltriglycerine renography with enhanced planar processing. *Radiology 2011*; **261**:907-15.
8. Thomas GS, Maddahi J. The technetium shortage. *J Nucl Cardiol* 2010; **17**:993-8.
9. Sureka SK, Maheshwari R, Agnihotri S, et al. Predictors for progression of metastatic prostate cancer to castration-resistant prostate cancer in Indians. *Indian J Med Res* 2016; **143**:S68-S73.
10. Soloway MS, Hardeman SW, Hickey D, et al. Stratification of patients with metastatic prostate cancer based on extent of disease on initial bone scan. *Cancer* 1988; **61**:195-202.
11. Van den Wyngaert T, Strobel K, Kampen WU, et al. The EANM practice guidelines for bone scintigraphy. *Eur J Nucl Med Mol Imaging* 2016; **43**:1723-38.
12. Bartel TB, Kuruva M, Gnanasegaran G, et al. SNMMI Procedure Standard for Bone Scintigraphy 4.0. *J Nucl Med Technol* 2018; **46**:398-404.
13. Fleiss, JL. *Statistical Methods for Rates and Proportions.* 2nd ed. New York: John Wiley & Son; 1981, p.218

Figure 1.

Planar scintigraphic images of the skeleton of a patient being evaluated for prostate cancer metastasis. Planar anterior (A) and posterior (C) whole body images are obtained with the Standard Protocol. Planar anterior (B) and posterior (D) whole body images are obtained with the Half Time protocol. The bladder on image B is larger than on image A, which reflects the time lapse between the Standard and the Half-time acquisition. There were no findings suspicious for metastasis on this scan.

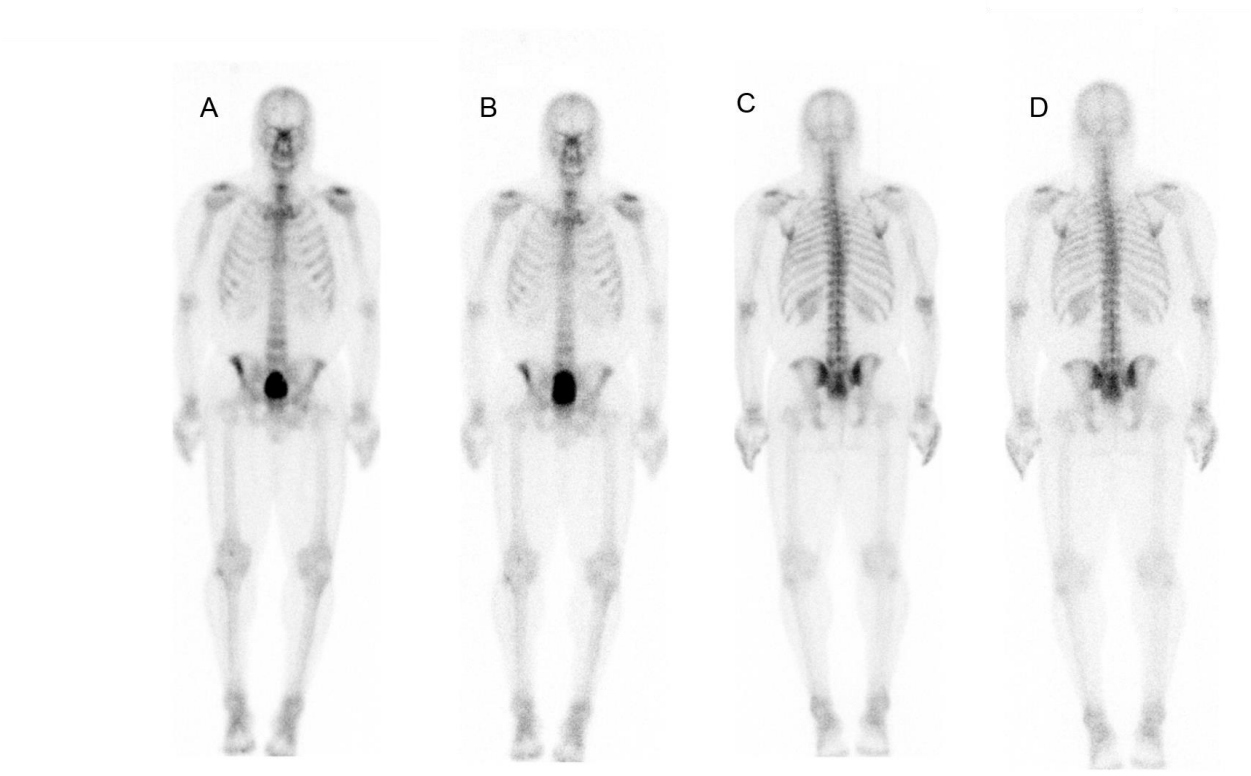
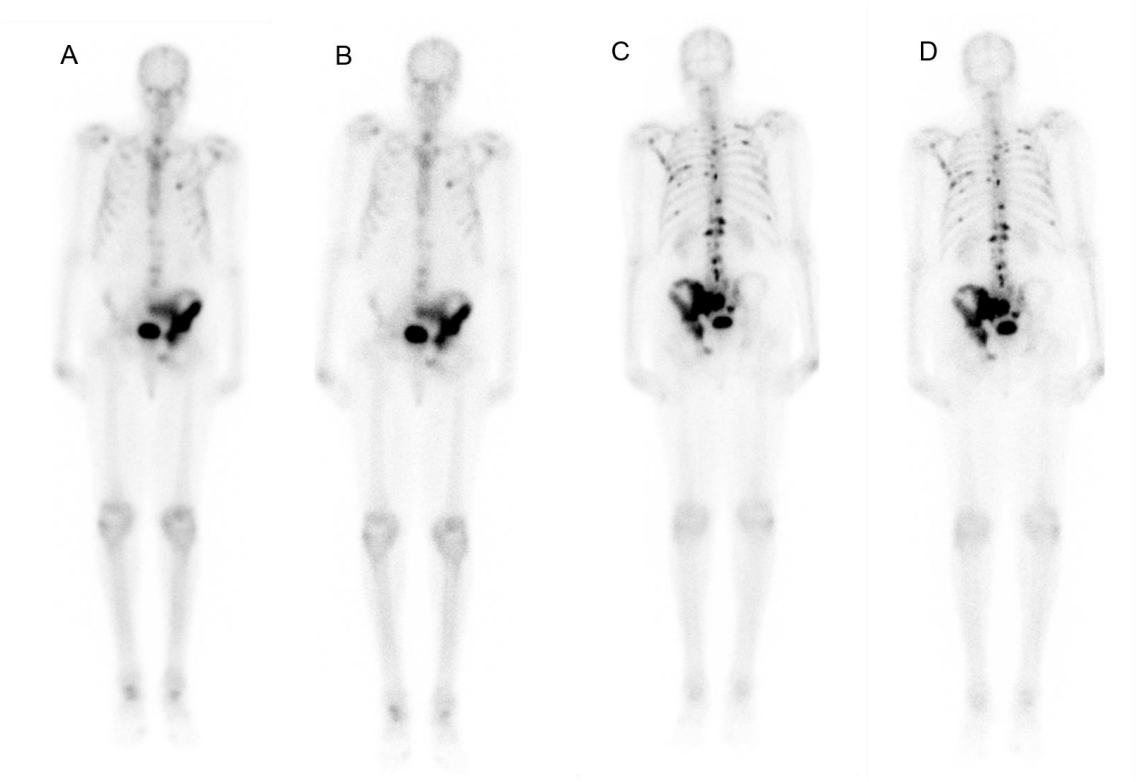
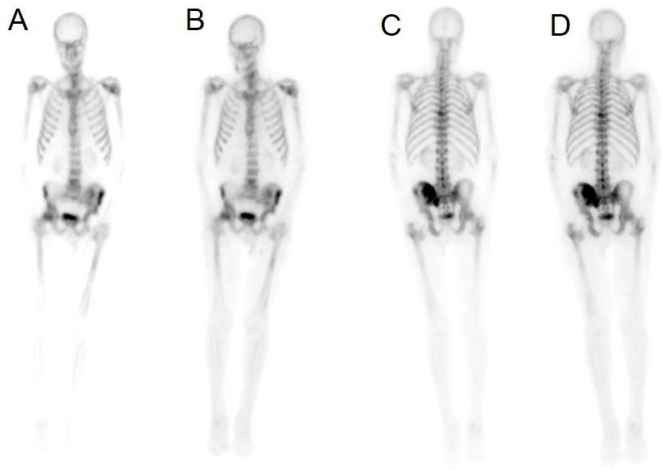


Figure 2.

Planar scintigraphic images of the skeleton of a different patient from Figure 1, also being evaluated for prostate cancer metastasis. Planar anterior (A) and posterior (C) whole body images are obtained with the Standard Protocol. Planar anterior (B) and posterior (D) whole body images are obtained with the Half Time protocol. There is uptake throughout the left iliac bone and within multiple ribs and vertebral bodies better seen on posterior views, in a pattern likely representing osseous metastasis. Degenerative uptake is noted in the shoulders, ankles and knees.



Graphical Abstract



Planar images of a bone scan on a patient evaluated for osseous metastasis. Images A and C , anterior and posterior views, were acquired with the **Standard protoc**ol and images B and D where acquired with the **Half time protocol**. The diagnostic quality of the images does not change with half the amount of imaging time. Focal tracer activity on the left iliac bone and thoracic spine area likely metastatic lesions seen on posterior views. Anterior left femoral shaft uptake is also noted on both protocols. Other lesions are also present.