^{18}F NaF PET/CT and Conventional Bone Scanning in Routine Clinical Practice

Comparative Analysis of Tracers, Clinical Acquisition Protocols, and Performance Indices

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KEYWORDS

• Bone scan • F-18 fluoride • PET/CT • Whole body SPECT

KEY POINTS

- Conventional planar and SPECT bone scintigraphy is an established technique.
- F-18 fluoride PET/CT has the potential to become the gold standard in functional bone imaging.
- A thorough comparison of both techniques, including advantages and disadvantages are discussed.
- Future directions of both modalities are analyzed.

INTRODUCTION

Bone scintigraphy (BS) was one of the earliest examinations performed in nuclear medicine. F-18 sodium fluoride (NaF) is a bone-scanning agent that was first introduced in 1962.[1] The high 511 keV energy annihilation photons emitted by F-18 could be imaged at that time with rectilinear scanners equipped with thick crystals. For present day standards, the images obtained were of poor quality. With the advent of the first technetium-99m (Tc)-based phosphonates in 1971 followed by methylene disphosphonate (MDP)[2] and the development of the Anger camera, fluoride bone scanning was replaced. BS has become one of the most common procedures, widely used in the evaluation of malignant and benign diseases of the skeleton. The advent of single-photon emission tomography (SPECT) and eventually SPECT/computed tomography (CT) has further increased the diagnostic accuracy of BS and its clinical applications.[3] Over the past few years, with the rapidly increasing implementation of PET/CT devices and F-18, there has been a reemergence of interest and use of NaF.

There are now 2 excellent bone-scanning agents available, and the nuclear medicine community is faced with the dilemma of which one to adopt in routine clinical use. Tc-MDP has withstood the test of time, is easily available from generators even in remote locations, and can be used with the easily accessible gamma cameras that currently

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outnumber PET/CT devices. On the other hand, PET/CT devices are becoming readily available worldwide, together with cyclotrons and distribution networks for ^{18}F-fluorodeoxyglucose (FDG), and this has facilitated as well the use of NaF in routine clinical work. Although there are a number of advantages to the use of NaF, which will be described in this article, do the excellent pharmacokinetic properties of this tracer and superior resolution of PET/CT devices translate to clinical benefits?

PHARMACOKINETICS AND UPTAKE MECHANISM

Comparison of the pharmacokinetics of Tc-MDP and NaF offer a theoretical advantage for NaF. First-pass clearance of Tc-based phosphonates is approximately 64%.[4] Protein binding of Tc-MDP is 25% to 30% immediately after injection and approximately 50% at 4 hours.[5] It does not bind to red blood cells (RBCs). Imaging with Tc-MDP requires a 2-hour to 4-hour uptake time after injection, when 40% of the tracer is found in skeleton, 40% in urine, 10% in soft tissues, and only 5% in the blood stream, which results in improved target-to-background ratio and better image quality.[2] NaF undergoes more rapid blood clearance, with first-pass clearance close to 100%,[6] as it has negligible protein binding. Approximately 30% of the injected dose is in RBCs, which does not interfere with bone uptake, as NaF freely diffuses across the cell membrane.[7] Plasma clearance is very rapid. Approximately 50% of the injected NaF is taken up in bone,[8] with the remainder excreted by the kidneys by 6 hours after tracer administration.[9] These properties permit a shorter uptake time of NaF with earlier start of imaging (**Table 1**).

Bone is composed of two-thirds mineral and one-third collagen, extracellular matrix, and a variety of bone-lining cells. The mineral matrix is composed of calcium hydroxyapatite, Ca10(OH)2(PO4)6, containing calcium phosphate that can be exchanged with phosphonates present in MDP.[2]

Tc-MDP uptake in bone is considered to be mainly related to chemisorption of the disphosphonate onto the surface of hydroxyapatite, followed by incorporation into the crystal. Bone uptake of Tc-MDP is related to increased blood flow and capillary permeability, as well as to increased bone turnover with osteoid formation. Uptake of Tc-MDP in immature collagen has also been described.[2] Uptake of NaF has a similar mechanism to Tc-MDP. Following chemisorption of fluoride ions onto the surface of hydroxyapatite, they exchange with the hydroxyl (OH^-) ions in the crystal, forming fluoroapatite.[4]

Table 1
Comparison of pharmacokinetic properties of Tc-MDP and NaF

	MDP	NaF
Urinary excretion	70% after 6 h[4]	50% after 6 h[9]
Protein binding	50% at 4 h[5]	Negligible[7]
RBC binding	Negligible[5]	30%[7]
First-pass clearance	~64%[4]	Nearly 100%[6]
% bone uptake	35%–50%[2]	50%[8]

Abbreviations: MDP, methylene disphosphonate; NaF, sodium fluoride; Tc, technetium.

Imaging Protocols

Requisition and history

Requisition for BS and NaF PET/CT by the referring physician should ideally be accompanied by a concise summary of the patient's history with a pertinent clinical question. The following points are very important for accurate interpretation of the examination, depending on the clinical indication.

- History of malignancy
- Date of recent chemotherapy
- Previous fractures or recent trauma
- Previous orthopedic surgery and relevant dates
- Previous infection and its location
- Urinary diversion procedures
- Location of any bone pain.

Previous bone scintigraphy, as well as other relevant imaging studies, should be available for comparison.[10]

Patient preparation

The preparation of patients referred for BS and NaF PET/CT is essentially the same. Patients should be well hydrated before the study and during the uptake period between the time of tracer injection and imaging. This enhances renal excretion, resulting in improved target-to-background ratio and reducing radiation exposure of the patients. Patients are also encouraged to drink more frequently for the remainder of the day. Immediately before image acquisition, patients are asked to empty their bladders. Any metal objects should be removed to prevent attenuation artifacts.[10]

Radiopharmaceutical, injected activity, and uptake time

BS using Tc-MDP (other phosphonate-based tracers are also available, such as di-carboxy