

Radiopharmaceutical Name	Na ¹⁸ F, Sodium fluoride Abbreviations: NaF, NaF-18 sodium fluoride	
Radiopharmaceutical Image Normal 	Normal Biodistribution After injection, Na ¹⁸ F rapidly equilibrates within the extracellular fluid space and fluorine is extracted and incorporated into hydroxyapatite crystals forming fluoroapatite. First-pass extraction from bone capillaries is about 100%. Approximately 20% is then excreted through the kidney in the urine in the first 1-2 hours (Czernin et al.)	Radiopharmaceutical Structure $\text{Na}^+ - {}^{18}\text{F}^-$
Radionuclide	¹⁸ F Half-life 109.7 minutes	
Emission	Emission positron: Emax 0.634 MeV	
MICAD	Not referenced (as of December 2012)	
Molecular Formula and Weight	Na ¹⁸ F 40.99 g atom mole ⁻¹	
General Tracer Class	Clinical Diagnostic PET Radiopharmaceutical	
Target	Bone-seeking agent to image skeletal abnormalities. The target is the bone surface where the fluoride ions are incorporated within the bone matrix, with a greater uptake in the axial skeleton than in the appendicular skeleton, and greater uptake in the bone around joints than the shafts of long bones.	
Molecular Process Imaged	Incorporation of fluoride ions into the bone matrix at the bone surface preferably in sites of newly mineralizing bone, such as during growth, infection, malignancy (primary or secondary), after trauma or during inflammation.	
Mechanism for in vivo retention	Incorporation of fluoride ions in the bone matrix to form crystals of fluoroapatite.	
Metabolism	Fluoride ions are deposited in the bone matrix and reflect: (1) bone remodeling and (2) blood flow. The uptake of fluoride ions is better in osteoblastic processes, while purely osteolytic processes have a lower uptake, or even no uptake at all. The target organ is bone, but approximately 20% is excreted through the kidney in the urine in the first 1-2 hours.	
Radiosynthesis	Proton bombardment of ¹⁸ O-water in commercial cyclotrons, where Na ¹⁸ F is the chemical precursor to produce ¹⁸ F-fluorodeoxyglucose and is therefore readily available.	
Availability	Due to the short half-life, it must be delivered within 2-3 half-lives from a producing cyclotron (similarly to ¹⁸ F-fluorodeoxyglucose). Requires a site with an IND, NDA or ANDA filed with the Food and Drug Administration (FDA) for the radiopharmaceutical (IND = investigational new drug application, NDA = new drug application, ANDA = amended new drug application).	

Status with USP / EuPh	Drug was approved by the FDA in 1972 but then withdrawn in 1975 because less expensive ^{99m} Tc-based tracers were available. It became approved again in February 2011 for PET bone scans in time of the ⁹⁹ Mo shortage. It is listed in USP and EuPh. Status in US is the same as other PET radiopharmaceuticals (requires an IND, NDA or ANDA for use).
Recommended Activity and Allowable mass	DOSAGE AND ADMINISTRATION (Segall et al.) IV administration, typically 185-370 MBq (5-10 mCi) as a bolus. Pediatric activity should be weight based with 2.1 MBq/kg (0.06 mCi/kg).
Dosimetry	The effective dose (ED) is estimated to be 0.024 mSv/MBq (0.089 rem/mCi) for adults. The dose-critical organ is the bladder in adults, which receive 0.22 mGy/MBq (0.81 rad/mCi) for adults (<i>ICRP Publications 80 and 106</i>).
Pharmacology and Toxicology	After intravenous injection, ¹⁸ F is rapidly cleared from the blood stream in a bi-exponential fashion (T _{1/2} = 0.4h and 2.6h) and essentially all ¹⁸ F delivered to bone capillaries and the extracellular space is trapped. One hour after injection, only 10% remain in the blood and in patients with normal kidney function an average of 20% is cleared through the kidney and excreted in the urine by 2 hours post-injection.
Current Clinical Trials	The NIH clinical trials registry (www.clinicaltrials.gov) should be consulted for a list of current trials using. As of December 2012, eleven clinical trials were open (7 in United States/Canada).
Reference Site / Person	The best reference at this time is the SNMMI Procedure guideline, which includes interpretation criteria (Segall et al.)
Imaging Protocol	The SNMMI has published a procedure guideline on [¹⁸ F]-NaF PET/CT imaging (Segall et al.) <ul style="list-style-type: none"> • No specific patient preparation is needed besides good hydration (see below); the patient does not need to fast and may take all his/her medication • 185-370 MBq (5-10 mCi) as a bolus through a catheter inserted into a large peripheral vein. • Start imaging 45-60 minutes after the injection and acquire images for a total of 10-20 minutes in 2- or 3-D mode with 2–5 min per bed position depending on PET camera. • Patients should be encouraged to void immediately prior to imaging the lumbar spine and bony pelvis. • To reduce the radiation dose to the bladder, hydration (min >500mL) should be encouraged prior to and after administration of [¹⁸F]-NaF, and the patient should void 30 minutes after the administration and as frequently as possible thereafter. <p>When high-quality imaging of the extremities is needed, it is recommended to wait 90–120 minutes. Recent work indicates that starting imaging less than 30 min after injection may limit the reproducibility for oncology imaging; optimal imaging time would be 60±30 minutes (Kurdziel et al.). It is important to scan at same time when repeat imaging is done.</p>
Human Imaging Experience	Listed below are selected references for [¹⁸ F]-NaF PET in the evaluation of bone disease. <p>Bridges RL, Wiley CR, Christian JC, Strohm AP. An introduction to Na(18)F bone scintigraphy: basic principles, advanced imaging concepts, and case examples. <i>J Nucl Med Technol.</i> 2007; 35:64-76; quiz 78-69.</p> <p>Czernin J, Satyamurthy N, Schiepers C. Molecular Mechanisms of Bone 18F-NaF Deposition. <i>Journal of Nuclear Medicine.</i> 2010; 51:1826-1829.</p> <p>Grant FD, Fahey FH, Packard AB, Davis RT, Alavi A, Treves ST. Skeletal PET with 18F-Fluoride: Applying New Technology to an Old Tracer. <i>Journal of Nuclear Medicine.</i> 2007; 49:68-78.</p> <p>Kurdziel KA, Shih JH, Apolo AB, et al. The kinetics and reproducibility of 18F-sodium fluoride for oncology using current PET camera technology. <i>J Nucl Med.</i> 2012; 53:1175-1184.</p> <p>Li Y, Schiepers C, Lake R, et al. Clinical utility of (18)F-fluoride PET/CT in benign and malignant bone diseases. <i>Bone</i> 2012;</p>

50:128-139.

Segall G, Delbeke D, Stabin MG, et al. SNM Practice Guideline for Sodium 18F-Fluoride PET/CT Bone Scans 1.0. *Journal of Nuclear Medicine*. 2010; 51:1813-1820.

Radiation dose to patients from radiopharmaceuticals (addendum 3 to ICRP Publication 53): ICRP publication 106, approved by the Commission in October 2007. *Ann ICRP*. 2008; 38:1-197.

Radiation dose to patients from radiopharmaceuticals (addendum 2 to ICRP publication 53): ICRP publication 80, approved by the Commission in September 1997. *Ann ICRP*. 1998; 28:1-126.

[Molecular Imaging and Contrast Agent Database \(MICAD\) http://www.ncbi.nlm.nih.gov/books/NBK5330/](http://www.ncbi.nlm.nih.gov/books/NBK5330/)

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