Alternative Isotope Options for Amyloidosis Imaging: A Technologist's Perspective

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The recent pyrophosphate shortages can limit the availability of ^{99m}Tc-pyrophosphate scans for cardiac amyloidosis. However, another radiotracer is available: ^{99m}Tc-hydroxymethylene diphosphonate (HMDP). ^{99m}Tc-HMDP, widely available in the United States for bone scanning, has effectively been used in Europe to diagnose transthyretin amyloidosis. ^{99m}Tc-HMDP and ^{99m}Tc-pyrophosphate have comparable blood clearance and sensitivity. The imaging protocols for ^{99m}Tc-HMDP and ^{99m}Tc-pyrophosphate are similar, except ^{99m}Tc-HMDP is imaged 2–3 h after injection and whole-body imaging is optional. The interpretation is also essentially the same; however, caution is needed because of the high soft-tissue uptake with ^{99m}Tc-HMDP, which can affect heart–to–contralateral-lung ratios.

Key Words: cardiac amyloidosis; ^{99m}Tc-pyrophosphate; ^{99m}Tc-PYP

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Over the past few years, shortages and limited supplies have affected every aspect of our world. Unfortunately, this scarcity has spilled over into the nuclear medicine world with regard to the unavailability of ^{99m}Tc-pyrophosphate. ^{99m}Tc-pyrophosphate is the most commonly used nuclear cardiology radiopharmaceutical for cardiac amyloidosis imaging in the United States.

WHY IS THERE A SHORTAGE? IS THERE AN ESTIMATE ON WHEN THIS TRACER WILL BE BACK?

Before the coronavirus disease 2019 pandemic, supply chain shortages (or interruptions) were intermittent, and the impact on nuclear medicine labs was minor. However, with the recent pandemic, industrial supply chains have seen unprecedented disruptions in production due to lockdowns, lack of availability of raw materials, and limited workforce. Specific to ^{99m}Tc-pyrophosphate, the major suppliers (Curium Pharma and Sun Radiopharma) reported interruptions in supply due to the materials used to make the product. At the time of this writing, it is unclear when production will return to normal.

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IS THERE ANOTHER ISOTOPE OPTION?

Research and the recent American Society of Nuclear Cardiology (ASNC) information statement demonstrate the availability of a viable alternative: ^{99m}Tc-hydroxymethylene diphosphonate (HMDP). ^{99m}Tc-HMDP is also commonly called ^{99m}Tc-HDP or ^{99m}Tc-oxidronate, and all 3 names refer to the same compound (*1*). ^{99m}Tc-HMDP has been widely used in Europe, with a body of literature to support its efficacy. In the United States, ^{99m}Tc-HMDP is approved by the Food and Drug Administration for skeletal imaging of adult and pediatric patients. It is marketed under the trade name TechneScan HDP (Mallinckrodt). Although research demonstrates favorable results using ^{99m}Tc-HMDP as an alternative radiopharmaceutical for cardiac amyloidosis imaging, it is not Food and Drug Administration–approved explicitly for this indication.

The dosing and protocol parameters are very similar between the 2 isotopes.

WHY DOES ^{99M}TC-HMDP WORK AS A SUBSTITUTE FOR ^{99M}TC-PYROPHOSPHATE?

Although the mechanism of ^{99m}Tc-pyrophosphate and ^{99m}Tc-HMDP uptake in myocardial transthyretin amyloid is not defined, it is believed that the phosphate in these radiotracers binds to the calcium in amyloid deposits (*2*).

IS ^{99M}TC-HMDP THE SAME THING AS ^{99M}TC-MDP?

^{99m}Tc-HMDP and ^{99m}Tc-methyl diphosphonate (MDP) are not the same and are not interchangeable for amyloidosis imaging. Although both ^{99m}Tc-HMDP and ^{99m}Tc-MDP are phosphate analogs that form complexes with the crystalline hydroxyapatite in bone mineral, their blood pool clearance and sensitivity for amyloid disease differ (*3*). ^{99m}Tc-MDP has a lower blood pool clearance and lower sensitivity. As a result, ^{99m}Tc-MDP is not recommended for cardiac amyloidosis imaging. Both ^{99m}Tc-pyrophosphate and ^{99m}Tc-HMDP have similar blood pool clearance rates and sensitivity.

IS THERE A DIFFERENCE IN HOW THE PATIENT IS IMAGED USING ^{99M}TC-HMDP VS. ^{99M}TC-PYROPHOSPHATE?

There is no need to purchase new equipment or software, as the acquisition protocols used for ^{99m}Tc-HMDP and ^{99m}Tc-pyrophosphate are very similar, according to the ASNC (*4*).

Table 1 describes the ^{99m}Tc-HMDP protocol for cardiac amyloidosis imaging. The only difference in the acquisition when using ^{99m}Tc-HMDP is to image at 2–3 h after injection, and whole-body imaging is optional.

Whole-body imaging helps identify shoulder and hip ^{99m}Tc-HMDP uptake, which is a specific sign of systemic transthyretin amyloidosis. Whole-body imaging also helps identify soft-tissue uptake in the extremities, another sign of systemic transthyretin amyloidosis (*5*). SPECT imaging is necessary with both ^{99m}Tc-pyrophosphate and ^{99m}Tc-HMDP. To help localize uptake in the myocardium, CT attenuation is also recommended if SPECT/CT is available. For cadmium-zinc-telluride cameras, the ASNC states that further validation is needed before widespread use because of the inability to accurately display bone and lung uptake (*4*).

IS IMAGE INTERPRETATION DIFFERENT WHEN ^{99M}TC-HMDP IS USED?

There is no significant difference in image interpretation between ^{99m}Tc-HMDP and ^{99m}Tc-pyrophosphate. The anterior and lateral planar images and SPECT views are reviewed, and the uptake patterns are categorized similarly as absent, focal, diffuse. Cardiac uptake of ^{99m}Tc-HMDP is evaluated using the same semiquantitative visual scoring method, comparing with bone (rib) uptake.

However, it is critical that administration of ^{99m}Tc-HMDP instead of ^{99m}Tc-pyrophosphate be properly documented because there are differences in the heart–to–contralateral-lung ratio. With ^{99m}Tc-HMDP, there is increased background noise due to uptake in the soft tissues (i.e., muscles, in gluteal, shoulder, chest, abdominal wall, liver, skeletal muscle, and lung tissue) (*5–8*). More information about interpretation of ^{99m}Tc-HMDP and ^{99m}Tc-pyrophosphate scans can be found in the ASNC information statement (*4*).

WHAT ABOUT BILLING? ARE THERE DIFFERENCES WHEN ^{99M}TC-HMDP IS USED?

Several current-procedure-terminology billing codes are available, the selection of which is based on whether the study is performed with planar imaging only (78800), with SPECT imaging with/without planar imaging (78803), or with SPECT/CT imaging with/without planar imaging (78830) (*1*). Planar-only imaging for cardiac amyloidosis is

TABLE 1
^{99m}Tc-HMDP Cardiac Amyloidosis Protocol (*1*)

Protocol	Parameter	Recommendation
Prescan		
Preparation	No specific preparation; no fasting required	
Scan	Rest scan	Standard
Dose	370–740 MBq (10–20 mCi) ^{99m}Tc-HMDP intravenously	Standard
Time from injection to acquisition	2 or 3 h	Standard
General imaging parameters		
Field of view	Heart or chest	Standard
	Whole-body	Optional
Image type	Planar	Standard
	SPECT if planar is positive	Required
Position	Supine	Standard
	Upright	Optional
Energy window	140 keV, 15%–20%	Standard
Collimators	Low-energy, high-resolution	Standard
Matrix	Planar: 256 × 256 (minimum, 64 × 64)	Standard
	SPECT: 128 × 128 (minimum, 64 × 64)	Standard
Pixel size	3.5–6.5 mm	Standard
Planar parameters		
Views	Chest: anterior and lateral	Standard
	Whole-body: from head to toe	Optional
Detector configuration	90°	Recommended
Image duration (count-based)	Planar: 750,000	Standard
	Whole-body: 20 cm/min	Optional
Magnification	1.46	Standard
SPECT parameters		
Angular range	180°	Standard
	360°	Optional
Detector configuration	90°	Standard
	180°	Optional
Electrocardiographic gating	Off; nongated imaging	Standard
Number of views/detector	40/32	Standard
Time per stop	20 s/25 s	Standard
Magnification	1.46 (180° angular range) or 1.0 (360° angular range)	Recommended

recommended only when the planar images can immediately be reviewed by the interpreting physician and determined to be Perugini grade 0. The ASNC recommends that all patients receive SPECT or SPECT/CT imaging.

Regarding billing for the radiopharmaceutical, ^{99m}Tc-HMDP is equivalent to ^{99m}Tc-oxidronate. Category II code A9561 (^{99m}Tc-oxidronate, diagnostic, per study dose, up to 1,110 MBq [30 mCi]) in the Healthcare Common Procedure Coding System should be used to bill for ^{99m}Tc-HMDP.

KEY POINTS

QUESTION: Is an alternate radiotracer available for cardiac amyloidosis imaging during times of pyrophosphate shortage?

PERTINENT FINDINGS: ^{99m}Tc-HMDP and ^{99m}Tc-pyrophosphate have similar blood pool clearance and sensitivity to detect cardiac amyloidosis. Only minor protocol modifications are needed to use ^{99m}Tc-HMDP. Physicians interpret scan results using the same methods but accounting for increased soft-tissue uptake with ^{99m}Tc-HMDP and its potential effect on the heart–to–contralateral-lung ratio.

IMPLICATIONS FOR THE PATIENT: Patient access to cardiac amyloidosis imaging during ^{99m}Tc-pyrophosphate shortage should not be limited, because an acceptable, alternate radiotracer, ^{99m}Tc-HMDP, is available.

CONCLUSION

The shortage of ^{99m}Tc-pyrophosphate does not hinder the ability to provide cardiac amyloid imaging. ^{99m}Tc-HMDP is a reasonable alternative because of its comparable imaging quality and diagnostic performance. ^{99m}Tc-HMDP is approved for use in the United States and has been endorsed by the ASNC for cardiac amyloidosis imaging.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

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