# Spleen visualization in both TTR and AL amyloidosis during $^{99m}$Tc-DPD scintigraphy. Do we have to deal with a different than the myocardial uptake mechanism?

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**Abstract**
Technetium-99m-diphosphono-1,2-propanodicarboxylic acid ($^{99m}$Tc-DPD) is currently used in Europe for the diagnosis of cardiac amyloidosis, being able to distinguish light chain (AL) from transthyretin (TTR) type [1, 2]. We are reporting obvious spleen visualization in two patients suffering the first from proven TTR and the second from AL type of cardiac amyloidosis, with myocardial uptake-as anticipated-only in the first one. We raise the hypothesis that a common uptake mechanism exists for the spleen amyloid regardless of the type of the disease (AL or TTR), and is possibly different than the cardiac uptake mechanism.

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## Introduction

Extraosseous accumulation of bone-seeking radiopharmaceuticals is not an uncommon finding during scintigraphic workup of patients due to different kind of malignancies [3-5], as well as for excluding or establishing the diagnosis of TTR cardiac amyloidosis [2]. For the latter, the preferred bone agent in Europe is nowadays technetium-99m 3,3-diphosphono-1,2-propanodicarboxylic acid ($^{99m}$Tc-DPD) [1, 2].

Even though the exact mechanism of non-osseous uptake of bone-seeking agents in amyloidosis is not clearly understood, it has been presumed that soft tissue microcalcification, that could not be detected radiographically, may play a major role. Microscopic deposits of calcium ions within a crystalline structure similar to that of hydroxyapatite in infiltrated or necrotic cells might be the main mechanism of $^{99m}$Tc-methyl diphosphonate (MDP) uptake [6, 7].

Spleen and liver are two organs that show avid amyloid deposit; therefore, it is expected, at least in the cases of TTR amyloidosis, a variable amount of the radiotracer to be accumulated at these organs [8, 9].

## Case presentation

### Patient Number 1

A 78-year-old man, who was been evaluated for possible TTR myocardial amyloidosis, as he met all the criteria for possible cardiac amyloidosis. In the whole body scintigraphy that followed 2 hours after the intravenous administration of 22mCi (815MBq) $^{99m}$Tc-DPD, obviously increased uptake of the radiopharmaceutical was observed throughout the area of the left and right ventricle. Furthermore, clear appearance of the spleen was noted (Figure 1). The ratio of the left to the right hemithorax was calculated 1.77, and SPECT confirmed the accumulation of $^{99m}$Tc-DPD at almost the entire area of the left ventricle (Figure 2).

Subsequently, the patient underwent myocardial biopsy, which confirmed the presence of TTP amyloidosis; he was considered a suitable candidate for therapy and was enrolled to the tafamidis treatment protocol.

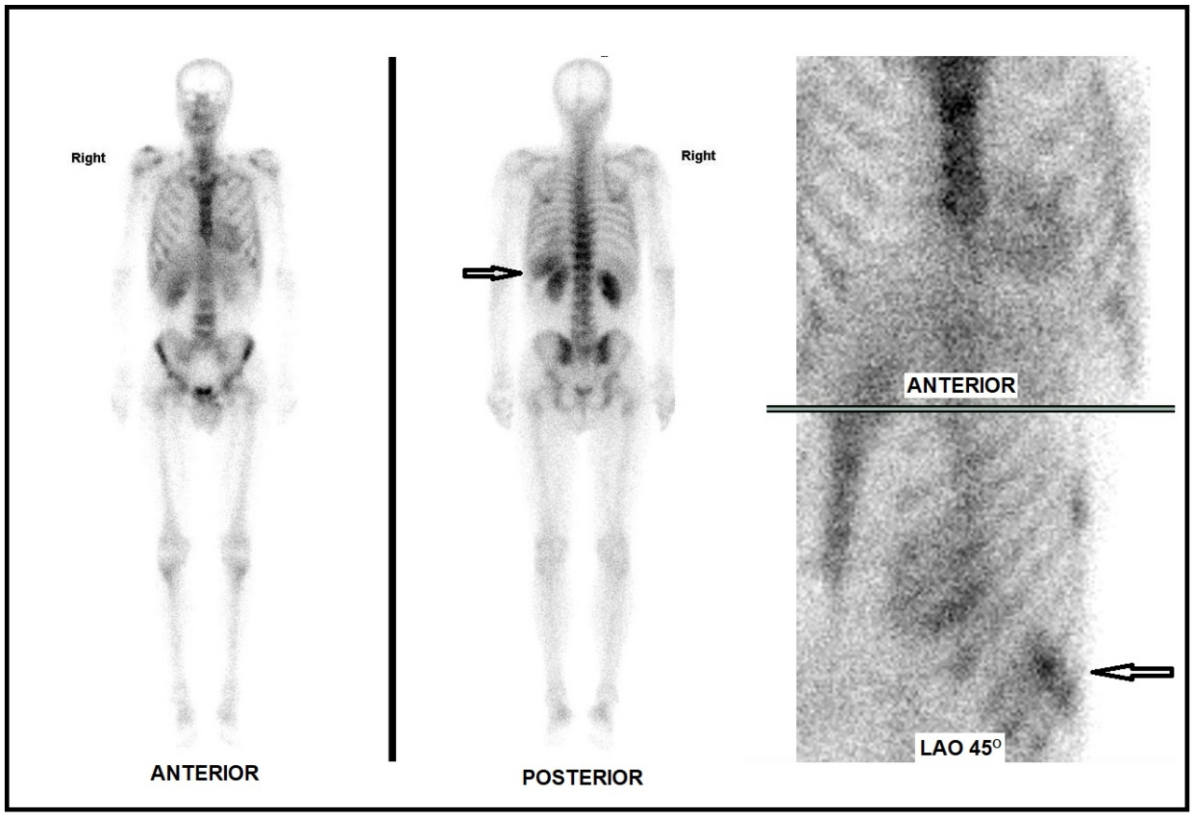



**Figure 1.** Patient's 1 total body, planar Anterior and LAO 450 views, 2 hours after iv administration of 22mCi (815MBq) $^{99m}$Tc-DPD. Cardiac and spleen uptake (arrow) is clearly evident.

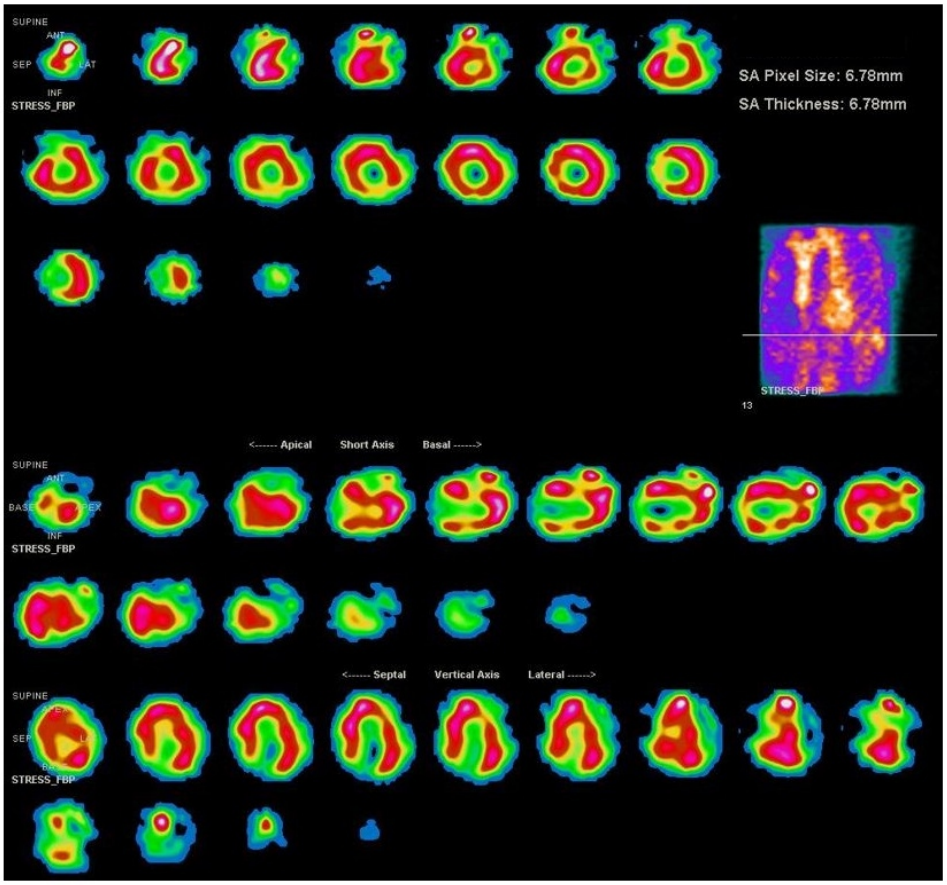



**Figure 2.** Patient's 1 Cardiac SPECT. Almost the entire area of the left ventricle is clearly seen.

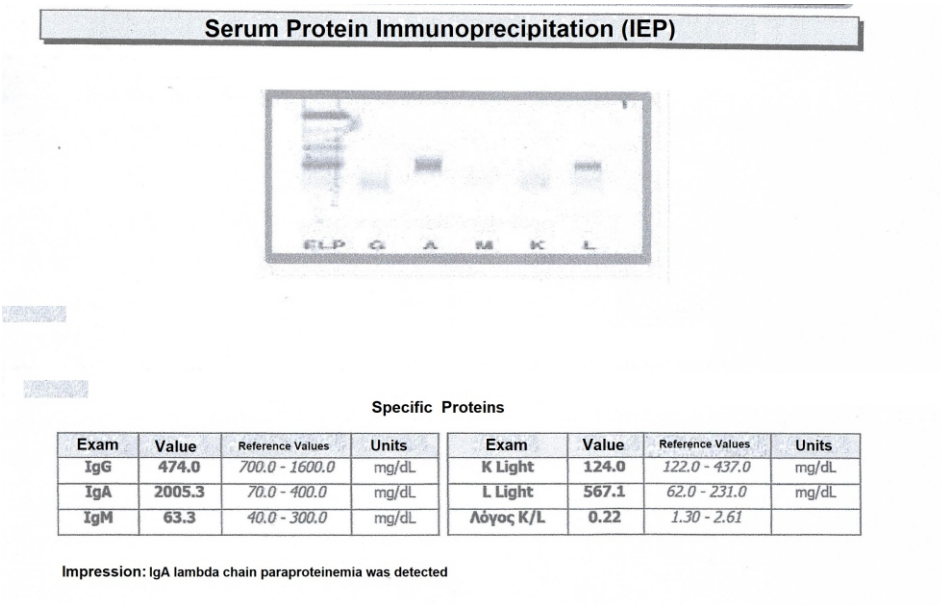
## Patient Number 2

He was a 72-year-old male, who presented with symptoms of heart failure (lower limb edema, dyspnea on exercise, cardiomegaly, bilateral pleural effusion and splenomegaly). Laboratory evaluation revealed hypofibrinogenemia, while Serum protein immunoprecipitation (IEP) revealed IgA lambda chain paraproteinemia (Figure 3), a finding that was also demonstrated after bone biopsy, which was positive for plasmocytic type clgλ+ marrow infiltration, a finding compatible with plasmocytic infiltrating disease.

During the workup of the patient, and in order to rule out metastatic bone disease, a bone scan was ordered. Twenty mCi (740MBq) of $^{99m}$Tc-DPD was administered and 3 hours later, whole-body planar and tomographic scintigraphy was performed (Figures 4, 5).

As expected, no cardiac uptake of $^{99m}$Tc-DPD and no signs of metastasis was evident, but as in the pervious case, there was clear visualization of the spleen.

The patient was considered to have AL type amyloidosis, and the splenic uptake was attributed to amyloid deposition in that organ, since marrow infiltration from plasmocytic type clgλ+ was already been proven.




| Exam | Value | Reference Values | Units | Exam | Value | Reference Values | Units |
|---|---|---|---|---|---|---|---|
| IgG | 474.0 | 700.0 - 1600.0 | mg/dL | K Light | 124.0 | 122.0 - 437.0 | mg/dL |
| IgA | 2005.3 | 70.0 - 400.0 | mg/dL | L Light | 567.1 | 62.0 - 231.0 | mg/dL |
| IgM | 63.3 | 40.0 - 300.0 | mg/dL | Λόγος K/L | 0.22 | 1.30 - 2.61 | |

**Figure 3.** Patient's 2 Serum Protein Immunoprecipitation (IEP). IgA lambda chain paraproteinemia was detected.

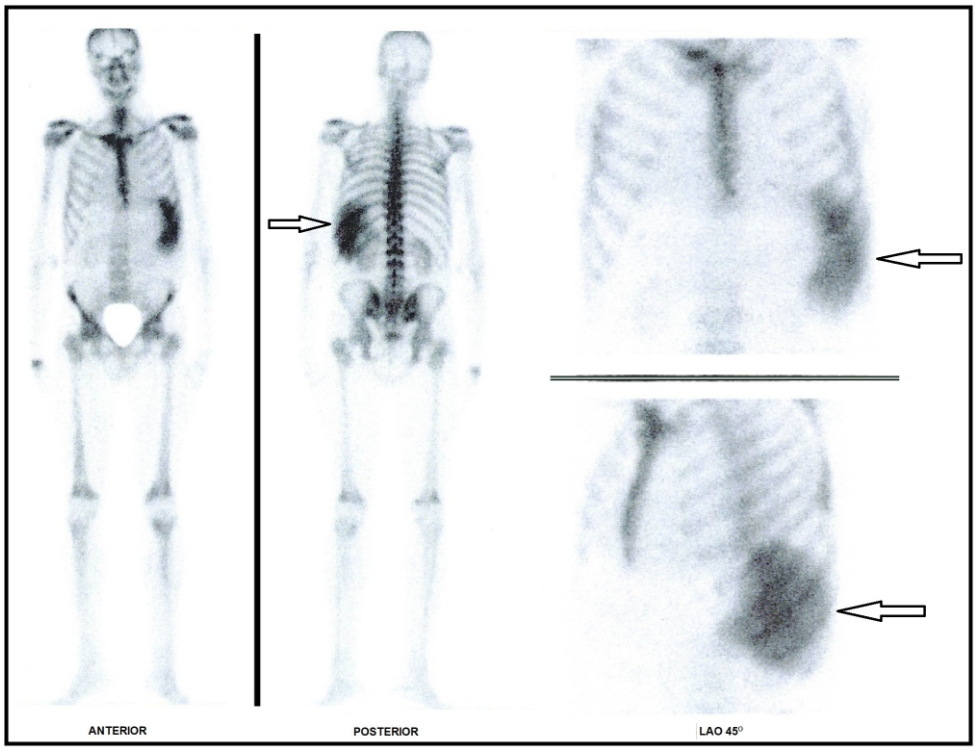



**Figure 4.** Patient's 2 total body, planar Anterior and LAO 45° views, 2 hours after iv administration of 20mCi (740MBq) $^{99m}$Tc-DPD. Spleen uptake (arrow) is clearly evident, but no cardiac visualization.

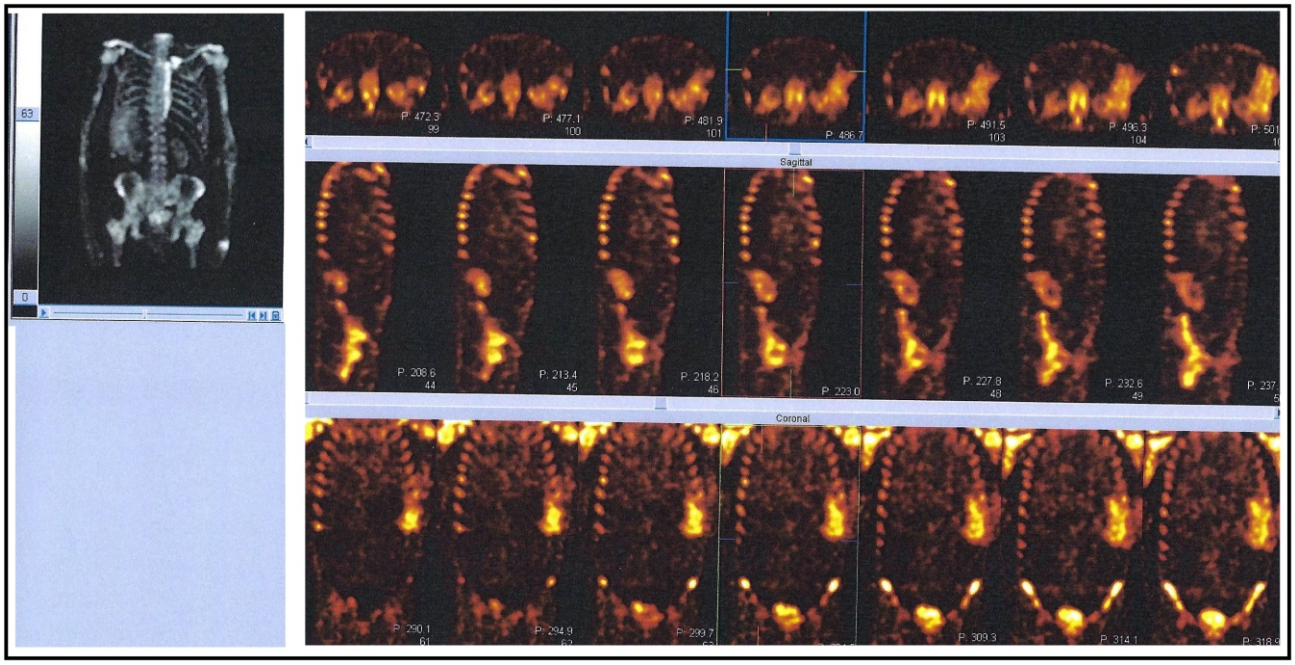



**Figure 5.** Patient's 2 SPECT imaging. Spleen but no cardiac uptake is confirmed.

## Discussion

Bone scintigraphy is the most common nuclear medicine examination in the workup of patients with known or suspected malignancies [10]. Even though is not widely recommended as a method of choice in the cases of multiple myeloma due to the pure osteolytic nature of the lesions and consequently no $^{99m}$Tc-MDP or $^{99m}$Tc-DPD uptake can be seen [11-13], we often perform it, in order to investigate sites of bone pain or to depict other pathologies. On the other hand, extra-osseous uptake of bone-seeking radiopharmaceuticals is frequently observed in a number of conditions and in different organs [6]. The possibility of any mispreparation of the technetium complex is easily excluded, because it will be obvious in all the bone scans performed this specific day.

The possibility of reticuloendothelial system expansion in both patients can also be excluded due to the lack of liver visualization [7, 12]. On the other hand, only in the patient with TTR cardiac amyloidosis there was intense uptake at the myocardium, as expected, whilst in the case of the other patient the only explanation for the spleen uptake is infiltration from AL amyloid [2].

At this point, we would like to raise the question: Why do we have splenic visualization after $^{99m}$Tc-DPD administration as a common denominator for both TTR and AL amyloidosis, while there is no myocardial uptake in the AL amyloidosis, despite the existing signs of heart failure in Patient 2? The only explanation is that a different fixation mechanism in the cardiac and splenic parenchyma exists in these two different kinds of amyloidosis.

The exact mechanism for extraosseous $^{99m}$Tc-DPD uptake in both AL and TTR amyloidosis remains unclear. Many possible hypotheses of radiopharmaceutical fixation exist, but not proven yet [1, 2, 6]. Thus, is not unlikely to have multiple or different mechanisms of radiotracer uptake for each type of tissue. This is already proven for the myocardial tissue with obvious and avid $^{99m}$Tc-DPD uptake in cases of TTR and faint or none in AL cardiac amyloidosis [1, 2]. The spleen, when is affected, probably has a common uptake mechanism in both amyloid types. This exact mechanism should be investigated and elucidated in the future.

## Bibliography

1. Damy T, Kristen AV, Suhr OB et al. Transthyretin cardiac amyloidosis in continental Western Europe: an insight through the Transthyretin Amyloidosis Outcomes Survey (THAOS). *Eur Heart J* 2022; 43(5): 391-400.
2. Gillmore JD, Maurer MS, Falk RH et al. Nonbiopsy diagnosis of cardiac Transthyretin Amyloidosis. *Circulation* 2016; 133: 2404-12.
3. Peller PJ, Ho VB, Kransdorf MJ. Extraosseous Tc-99 MDP uptake: a pathophysiologic approach. *Radiographics* 1993; 13: 715-34.
4. Gentili A, Miron SD, Bellon EM. Nonosseous accumulation of bone-seeking radiopharmaceuticals. *Radiographics* 1990; 10(5): 871-81.
5. Cappelli F, Gallini C, Costanzo EN et al. Lung uptake during $^{99m}$Tc-hydroxymethylene diphosphonate scintigraphy in patient with TTR cardiac amyloidosis: an underestimated phenomenon. *Int J Cardiol* 2018; 254: 346–50.
6. Kula RW, Engel WK, Line BR. Scanning for soft-tissue amyloid. *Lancet* 1977; 1: 92-3.
7. Kaur H, Muhleman M, Balon H. Spleen Uptake on a Bone Scan. *J Nucl Med Technol* 2017; 45: 245-6.
8. Skok P, Knehtl M, Ceranic D, Glumbic I. Splenic rupture in systemic amyloidosis- case presentation and review of the literature. *Z Gastroenterol* 2009; 47: 292-5.
9. Ravanbod MR , Reza Nemati R, Javadi H et al. Diffuse hepatic and spleen uptake of Tc-99m MDP on bone scintigraphy resembling liver-spleen scintigraphy in a patient of plasma cell tumor. *Case Rep Radiol* 2014; 2014: 264904.

10. Krishnamurthy GT, Krishnamurthy S, Thakur ML, McAfee JG. Gopal Subramanian and the Tc-99m bone scan: a continuing benefactor. *Semin Nucl Med* 2001; 31(4): 258-9.
11. Leonard RCF, Owen PJ, Proctor SJ, Hamilton PJ. Multiple myeloma: Radiology or bone scanning? *Clin Radiol* 1981; 32(3): 291-5.
12. Sood A, Seam RK, Sethi, Gupta M. Diffuse hepatic and splenic Tc-99m MDP tracer uptake in case of multiple myeloma. *Indian J Nucl Med* 2010; 25(2): 70-2.
13. Evans JC, Murphy M, Eyes B. Extensive soft tissue uptake of $^{99m}$Tc methylene diphosphonate in a patient with multiple myeloma. *Br J Radiol* 2000; 73(873): 1018–20.