Synthesis of ^{99m}Tc-labeled Peptide p5+14 for Detection of Cardiac Amyloidosis – Preclinical Studies in a Mouse Model

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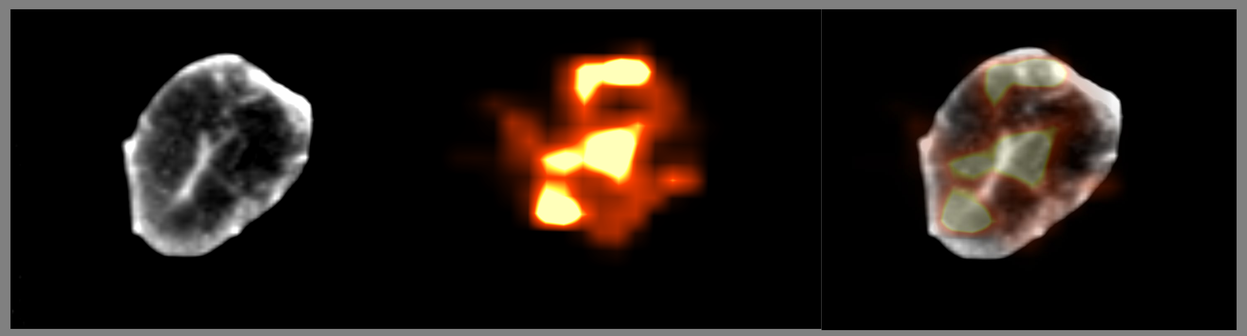
Introduction

Systemic amyloidosis is a rare but invariably fatal disorder resulting from the deposition of protein fibrils in organs and tissues which ultimately results in organ dysfunction. The major forms of amyloidosis, which account for more than 85% of the cases diagnosed in the US, result from the aggregation and deposition of monoclonal immunoglobulin light chains (AL amyloidosis) or, mutant or wild type, transthyretin (ATTR amyloidosis). The majority of patients with AL and ATTR present with cardiac amyloid deposits; however, due to the heterogeneous presentation of symptoms in these patients, a rapid and accurate diagnosis of disease is challenging. Peptide p5+14 is a pan-amyloid binding reagent that we have labeled with technetium-99m using a novel facile kit method for the specific detection of cardiac amyloid deposits.

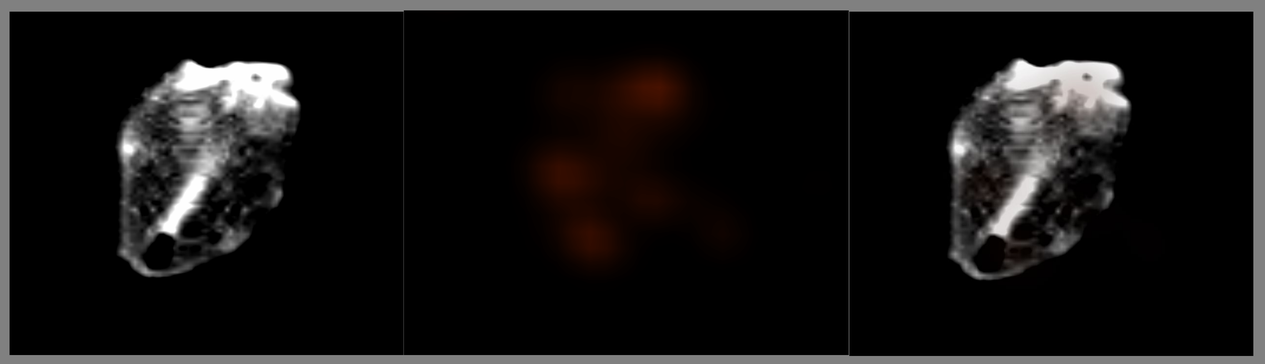
Materials and Methods

Peptide p5+14 was labeled using a facile kit method. Peptide (100 μg) and 20 μg of stannous chloride were dried from a solution of dilute sodium hydroxide. The labeling was accomplished by addition of 1-2 mCi [^{99m}Tc] pertechnatate in 100 μL of saline. The radiolabeled peptide was purified by size-exclusion chromatography and the bioactivity assessed using a synthetic fibril pulldown assay. Mice with systemic inflammation-associated (AA) amyloidosis, notably in the liver and spleen, but with modest cardiac amyloid deposition received ~150 μCi of ^{99m}Tc-p5+14 or ^{99m}Tc-PyP, a bone seeking agent that has been shown to bind AA amyloid. SPECT/CT imaging was performed using an Inveon trimodality platform.

Tc-99m-p5+14



Tc-99m-PYP



Results

The ^{99m}Tc-p5+14 peptide was readily labeled using the kit method with a radiochemical yield of >90%. The purified product was >95% pure with a bioactivity of ~95% (binding to synthetic amyloid fibrils). Extracardiac amyloid uptake in the liver and spleen in AA mice resulted in 10% ID/g and 7% ID/g, respectively. SPECT/CT imaging of the excised heart revealed significantly higher uptake of ^{99m}Tc-p5+14 as compared to ^{99m}Tc-PyP.

Conclusions

The production of ^{99m}Tc-labeled peptides for amyloid imaging has been previously described by our laboratory; however, we have now developed a facile kit-based method for generating a radiotracer that is optimally suited for the detection of cardiac amyloid deposits by SPECT imaging.

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