AUTOMATED QUANTIFICATION OF SYSTEMIC AMYLOID BURDEN IN CARDIAC AL AND ATTR AMYLOIDISIS PATIENTS USING ^{124}I-EVUZAMITIDE, A NOVEL PAN-AMYLOID RADIOTRACER

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BACKGROUND

Characterization of light chain (AL) and transthyretin (ATTR) amyloid deposits in the heart and other anatomic sites is currently challenging. This study aims to assess the utility of a novel PET radiotracer, ^{124}I-evuzamitide, for quantifying extra-cardiac amyloid burden in organs of patients with AL and ATTR cardiac amyloidosis (CA) using an automated whole-body segmentation algorithm.

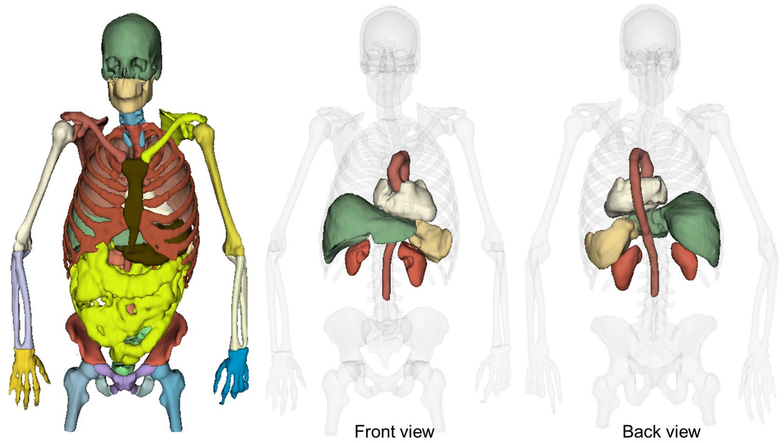
METHODS

This study included 95 CA patients (*n*=37 AL-CA and *n*=58 ATTR-CA) and 16 healthy volunteers, pooled from four independent clinical studies. All subjects underwent ^{124}I-evuzamitide PET/CT imaging at 5 hours post-injection. The 3-dimensional volumes of the liver, spleen, kidneys, heart, pancreas, and adrenals were segmented in the CT data using an automated trained deep learning algorithm (AIQ Solutions). Mean standardized uptake value (SUV) was calculated for each organ and normalized by the average blood pool radioactivity in the aortic arch, resulting in an SUV ratio (SUVR). Uptake of the radiotracer in an organ for a patient was defined a priori as an SUVR at or above a threshold set at the mean+1.96 standard deviations for that organ in the control cohort.

RESULTS

Based on the automated quantitation of radiotracer distribution, ^{124}I-evuzamitide uptake was observed: in the liver in 15 of the *n*=37 (41%) AL patients and 5 of the *n*=58 (9%) ATTR patients; in the spleen in 22 (59%) AL and 9 (16%) ATTR patients; in the kidney in 18 (49%) AL and 3 (5%) ATTR patients; in the pancreas in 25 (68%) AL and 18 (31%) ATTR patients; and in the adrenals in 27 (73%) AL and 13 (22%) ATTR patients. Extracardiac uptake of the radiotracer was seen in maximum intensity projection (MIP) and PET/CT images. ^{124}I-evuzamitide uptake in extracardiac organs, in patients with a diagnosis of cardiac amyloidosis, suggests that amyloid deposits may be more widespread and have clinical consequences. Amyloid in these organs has previously been described in autopsy reports.

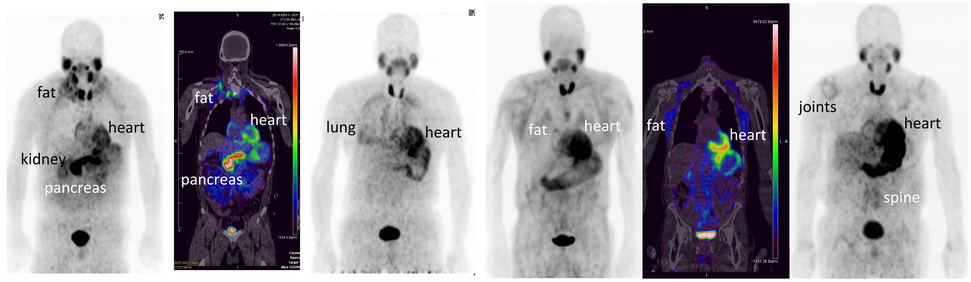
FIGURE 1



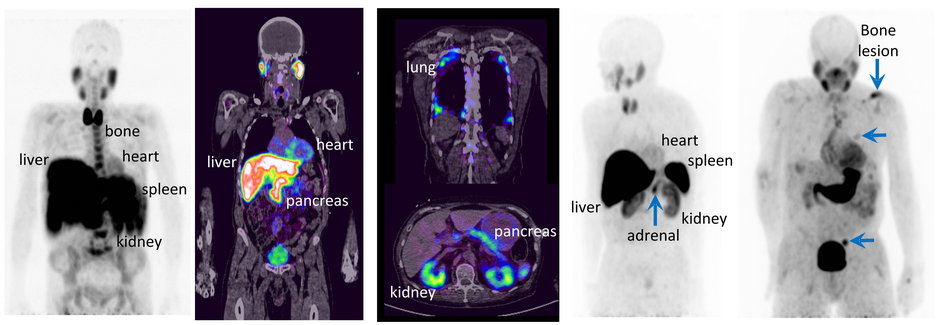
Volume rendering image showing the output of anatomic segmentation which includes more than 20 organs and tissues, represented by individual colors (AIQ Solutions software; left). Center and right images highlight 3D-rendered whole organ segmentation of the liver, spleen, kidneys, heart, and aorta (right).

FIGURE 2

Cardiac and extracardiac Uptake of ^{124}I-evuzamitide in patients with ATTR amyloidosis

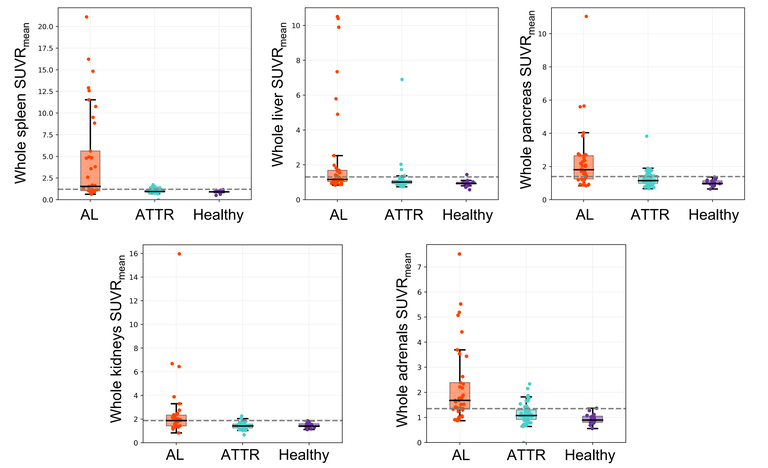


Cardiac and extracardiac Uptake of ^{124}I-evuzamitide in patients with AL amyloidosis



^{124}I-evuzamitide is taken up avidly in the heart of patients with ATTR or AL cardiac amyloidosis. In addition to cardiac uptake, PET/CT and MIP images revealed uptake of the radiotracer in extracardiac sites including, liver, spleen, kidneys, pancreas, adrenal gland, lungs, adipose tissue, spine and joints, and bone lesions in a patient with light chain amyloidosis secondary to multiple myeloma

FIGURE 3



Box plots of $SUVR_{mean}$ values for each of the organs, separated by AL, ATTR, and healthy volunteers, with all individual data points plotted. Gray dashed lines indicate the mean + 1.96 x standard deviation of the values from the healthy volunteers.

TABLE 1

Mean SUV values were calculated and normalized using the blood pool (aorta lumen) as the reference tissue to yield an SUV_{mean} ratio (SUVR). Positive uptake of the radiotracer in each organ was based on $SUVR_{mean}$ values that were at, or above, the mean+1.96×SD (97.5th percentile) of the organ in the control cohort.

Organ	AL Patients (*n*=37)	ATTR Patients (*n*=58)
Liver	15 (41%)	5 (9%)
Spleen	22 (59%)	9 (16%)
Kidneys	18 (49%)	3 (5%)
Pancreas	25 (68%)	18 (31%)
Adrenal glands	27 (73%)	13 (22%)

DISCUSSION

^{124}I-evuzamitide PET/CT imaging is a sensitive, quantitative method for identifying amyloid deposits in the heart and other thoracoabdominal organs. This new radiotracer affords a novel noninvasive approach to characterize cardiac and extracardiac organ amyloid burden. Additionally, the novel findings of abnormal uptake in the pancreas and adrenal glands highlight ^{124}I-evuzamitide's potential for early detection of amyloidosis in these organs.

DISCLOSURE INFORMATION

JSW: Co-founder, interim CSO, and shareholder in Attralus Inc. Research funding from Attralus Inc. Patent rights in peptides used for amyloid imaging, licensed to Attralus. SG: Co-founder, COO, and shareholder in Attralus Inc. SD: Research funding from Attralus Inc. AW: Employee of AIQ Solutions. OFC has a research grant from Pfizer, travel expense coverage by Spectrum Dynamics. AJE reports consulting for Artrya, authorship fees from Wolters Kluwer Healthcare—UpToDate, and serving on scientific advisory boards for Axcellant and Canon Medical Systems USA; his institution has grants/grants pending from Alexion, Attralus, BridgeBio, Canon Medical Systems USA, GE HealthCare, Intellia Therapeutics, Ionis Pharmaceuticals, Neovasc, Pfizer, Roche Medical Systems, and W. L. Gore & Associates.