Automatic quantification of AL and ATTR amyloidosis disease burden using [124]I-evuzamitide, a novel radiotracer

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Background

Amyloidosis is a heterogeneous disease that results from the abnormal deposition of beta-sheet fibrillar protein aggregates in various tissues. The two main forms of amyloidosis with significant cardiac involvement are transthyretin amyloidosis (ATTR) and immunoglobulin-light-chain related amyloidosis (AL). While recent therapeutic advancements have improved outcomes in cardiac amyloidosis, characterization of AL and ATTR amyloid deposits in the heart and systemic organs remains challenging. This study evaluates the novel PET radiotracer [124]I-evuzamitide for quantifying AL and ATTR amyloid burden in the heart and systemic organs.

Method

The study included 24 patients (12 AL, 12 ATTR) and 16 healthy controls who underwent [124]I-evuzamitide PET/CT at 5 hours post-injection (median 0.98 mCi). The liver, spleen, kidneys, heart, pancreas, and adrenal glands were automatically segmented using a trained deep learning algorithm (AIQ Solutions). Mean standardized uptake value (SUV) in each organ was normalized by the average aortic arch uptake to obtain ratio SUVR measurements. Abnormal uptake was defined as mean+1.96SD in the controls.

Table 1
Baseline Characteristics of Study Participants

Characteristic	Data
Age (y)	69.9 +/- 8
Male/Female	33/7
ATTR-CA	12
AL-CA	12
Control	16
Height (m)	1.74 +/- 0.10
Weight (kg)	81.7 +/- 13.4
eGFR (mL/min/1.73 m²)	67.3 +/- 24.2

Figure 1: Example organ segmentations produced by the deep learning algorithm on a randomly selected patient.

Result

[124]I-evuzamitide demonstrated excellent sensitivity in detecting cardiac amyloidosis, identifying 24/24 patients. It also identified abnormal uptake in the liver (3/12 AL and 1/12 ATTR), spleen (5/12 AL), kidneys (4/12 AL), pancreas (7/12 AL), and adrenal glands (6/12 AL and 1/12 ATTR) (Table 2). Compared to the International Society of Amyloidosis criteria for organ involvement in AL, [124]I-evuzamitide identified more patients with hepatic involvement and fewer patients with renal involvement (2/5, 40%). Notably, it detected abnormal renal uptake in two patients without biochemical signs of renal involvement.

Table 2

Heat map of SUVR by organ, with corresponding 24-hr urine protein and alkaline phosphatase for AL patients

Patient ID	Diagnosis	Liver	Spleen	Kidneys	Pancreas	Heart	Adrenals	24-hr urine protein (g), > 0.5 g abnormal	Alkaline Phosphatase:ULN, ratio > 1.5 abnormal
Cut-off values		1.31	1.21	1.88	1.40	1.19	1.35		
02	AL	0.94	1.04	1.43	1.36	1.93	0.87	0.08	0.76
03	AL	1.14	1.15	2.06	1.71	1.94	1.51	1.86	0.46
05	AL	1.04	1.64	1.58	0.92	2.29	0.95	0.10	0.81
07	AL	1.65	16.24	1.96	2.71	1.79	4.41	0.24	0.96
08	AL	0.88	0.63	1.29	1.20	1.50	1.33	0.17	0.47
09	AL	0.95	1.02	2.14	1.58	1.39	0.90	0.14	0.75
14	AL	1.25	1.70	1.67	2.06	2.32	1.77	3.08	0.48
15	AL	1.01	1.00	1.17	1.20	1.78	1.35	0.22	0.87
17	AL	1.08	0.87	1.76	1.19	1.60	1.06	0.55	0.55
44	AL	10.52	3.82	1.88	2.76	3.14	2.63	0.92	1.52
46	AL	1.04	1.19	1.33	1.43	1.40	1.30	0.06	0.88
48	AL	1.39	21.10	2.36	2.01	1.33	1.53	2.48	1.09
01	ATTR	6.90	0.79	1.56	0.85	1.57	1.41		
04	ATTR	1.04	0.92	1.44	1.40	2.02	1.06		
10	ATTR	0.85	0.79	1.19	1.03	1.63	0.78		
11	ATTR	1.12	0.86	1.40	0.83	1.92	0.95		
12	ATTR	1.01	0.88	1.11	0.90	1.52	0.92		
13	ATTR	0.91	0.87	1.28	1.16	1.84	0.83		
16	ATTR	0.93	0.92	1.04	1.04	1.58	1.06		
20	ATTR	1.21	1.05	1.62	1.01	1.42	1.09		
25	ATTR	1.28	0.90	1.33	1.03	1.72	1.04		
32	ATTR	0.76	0.85	1.21	0.73	1.58	0.73		
41	ATTR	0.93	0.74	1.32	0.78	1.48	0.79		
45	ATTR	0.80	0.90	1.12	0.75	1.61	0.67		

Red cells denote values greater than organ-specific cut-off values defined as mean + 1.96SD in healthy controls, and green cells denote values less than organ-specific cut-off values. SUVR: standardized uptake value ratio, defined as mean SUV for each organ normalized by the average uptake in the aortic arch. ULN: upper limit of normal. To determine amyloid involvement, cut-off values of each quantitative metric in each organ were defined as the 95th percentile of the corresponding value in the healthy controls (mean + 1.96SD). The number of patients with values above this normal range was quantified for each metric and organ.
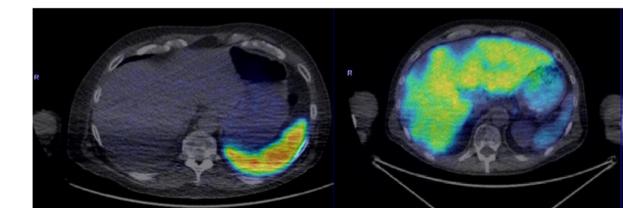
Figure 2: High [124]I-evuzamitide uptake in the spleen and liver in two patients with AL-CA
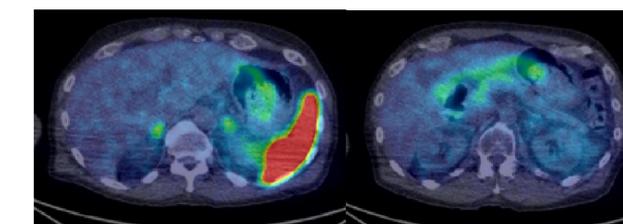
Figure 3: High [124]I-evuzamitide uptake in the adrenal glands and pancreas in a patient with AL-CA

Conclusion

[124]I-evuzamitide PET/CT is highly sensitive for detecting amyloid deposits in the heart and systemic organs, providing a novel noninvasive approach for characterizing cardiac and systemic organ amyloid burden. The novel findings of abnormal pancreatic and adrenal uptake indicate [124]I-evuzamitide's potential for early amyloidosis detection in these organs.

Acknowledgements

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