Uptake of Iodine (^{124}I) Evuzamitide in Patients with AL and ATTR Amyloidosis and Correlation with Echocardiographic Parameters

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BACKGROUND

Iodine-124-evuzamitide, is a novel radiotracer for the detection of systemic amyloidosis by PET/CT imaging. Semi-quantitative data on organ-specific amyloid load can be obtained from the images. The relationship between cardiac uptake of ^{124}I-evuzamitide and echocardiographic parameters in patients with amyloid cardiomyopathy is of particular interest. We have evaluated the uptake of ^{124}I-evuzamitide and contemporaneous echocardiographic parameters in nine AL (*n*=9) and ten ATTR (*n*=10) patients from the repeat imaging study (NCT05968846)

METHODS

Patients received 1 or 2 mCi ^{124}I-evuzamitide with PET/CT imaging at ~5 h post injection. A manual 2D analysis of radiotracer uptake in the heart was performed by three reviewers. Whole organ cardiac uptake was assessed by automated segmentation (AIQ Solutions) and standard uptake value ratios (SUVRmean) were calculated. Contemporaneous transthoracic echocardiography was performed, and correlation analyses were used to test for associations between variables.

RESULTS

The intraclass correlation coefficient (ICC) for the three image reviewers was excellent (ICC = 0.985, p<0.001). In patients with AL amyloidosis (*n*=9), the SUVRmean correlated strongly with LV thickness (r_P=0.82, p=0.006) and GLS (%) (r_P=0.73, p=0.025), but not the IVS thickness (r_P=0.56, p=0.116). In patients with ATTR amyloidosis (*n*=10), a moderate significant correlation between SUVRmean and LV thickness (p=0.037), and IVS (p=0.016) was observed. The correlation between manual and automated cardiac evaluations was highly significant (r_P=0.66, p=0.002, *N*=19).

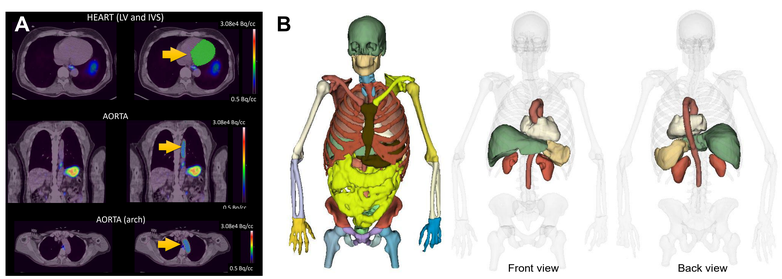


Figure 1. Quantifying cardiac uptake of ^{124}I-evuzamitide in patients with systemic amyloidosis. (A) Manual 2D region of interest (ROI) was used by placing the ROI over the left side of the heart, which included the LV lumen, LV wall and IVS. The blood pool, used as a reference to calculate SUVR was assessed from the lumen of the aorta. (B) Fully-automated 3D segmentation used CT data to map ROIs on to the PET data to generate SUVRmean and SUVRmax (the maximum voxel intensity in the ROI).

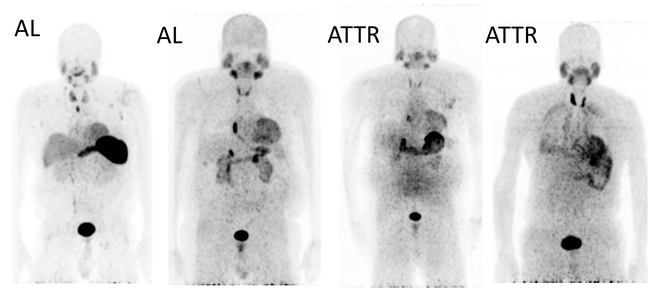
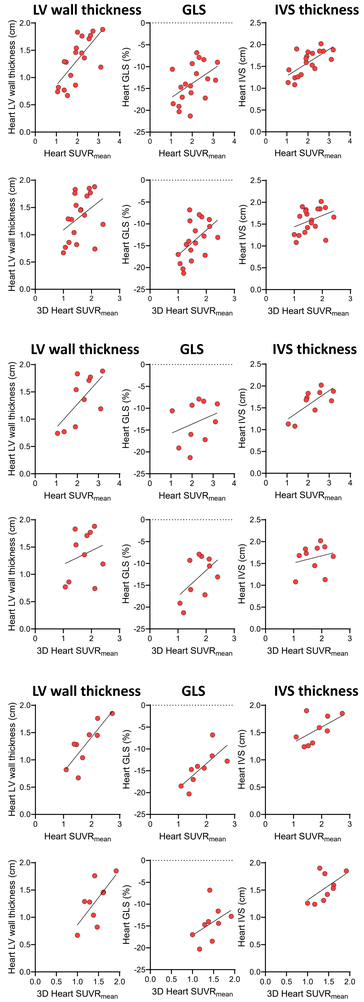


Figure 2. ^{124}I-evuzamitide PET/CT imaging provides high resolution data on the distribution of systemic amyloid, including the heart. Representative maximum intensity images from patients with AL or ATTR show cardiac uptake (as well as other anatomic sites).



r values

ALL (*N*=19)	ROI method	LV wall (cm)	GLS (%)	IVS (cm)	Troponin T	NTproBNP
Pearson	2D SUVRmean	0.706	0.470	0.677	0.443	0.637
Pearson	3D SUVRmean	0.386	0.505	0.355	0.316	0.406
Pearson	3D SUVRmax	0.080	0.250	-0.202	0.006	0.030

r values

ALL (*N*=19)	ROI method	LV wall (cm)	GLS (%)	IVS (cm)	Troponin T	NTproBNP
Spearman	2D SUVRmean	0.761	0.535	0.679	0.458	0.688
Spearman	3D SUVRmean	0.416	0.516	0.361	0.390	0.402
Spearman	3D SUVRmax	0.221	0.247	-0.091	-0.059	0.214

p values

ALL (*N*=19)	ROI method	LV wall (cm)	GLS (%)	IVS (cm)	Troponin T	NTproBNP
Pearson	2D SUVRmean	0.0007	0.0423	0.0015	0.0753	0.0034
Pearson	3D SUVRmean	0.1028	0.0274	0.1364	0.2172	0.0845
Pearson	3D SUVRmax	0.7461	0.3024	0.4074	0.9832	0.9027

p values

ALL (*N*=19)	ROI method	LV wall (cm)	GLS (%)	IVS (cm)	Troponin T	NTproBNP
Spearman	2D SUVRmean	0.0002	0.0182	0.0014	0.0661	0.0011
Spearman	3D SUVRmean	0.0766	0.0238	0.1293	0.1219	0.0882
Spearman	3D SUVRmax	0.3631	0.3072	0.7102	0.8221	0.3789

r values

ATTR (*n*=10)	ROI method	LV wall (cm)	GLS (%)	IVS (cm)	Troponin T	NTproBNP
Pearson	2D SUVRmean	0.663	0.303	0.730	0.535	0.579
Pearson	3D SUVRmean	0.244	0.529	0.223	0.167	0.285
Pearson	3D SUVRmax	-0.120	0.493	-0.222	-0.197	-0.010

r values

ATTR (*n*=10)	ROI method	LV wall (cm)	GLS (%)	IVS (cm)	Troponin T	NTproBNP
Spearman	2D SUVRmean	0.721	0.406	0.673	0.405	0.721
Spearman	3D SUVRmean	0.103	0.382	0.200	-0.095	0.321
Spearman	3D SUVRmax	0.055	0.467	0.152	-0.119	0.321

p values

ATTR (*n*=10)	ROI method	LV wall (cm)	GLS (%)	IVS (cm)	Troponin T	NTproBNP
Pearson	2D SUVRmean	0.0366	0.3952	0.0165	0.1719	0.0794
Pearson	3D SUVRmean	0.4975	0.1161	0.5359	0.6923	0.4243
Pearson	3D SUVRmax	0.7411	0.1479	0.5371	0.6404	0.9773

p values

ATTR (*n*=10)	ROI method	LV wall (cm)	GLS (%)	IVS (cm)	Troponin T	NTproBNP
Spearman	2D SUVRmean	0.0234	0.2475	0.0390	0.3268	0.0234
Spearman	3D SUVRmean	0.7850	0.2788	0.5837	0.8401	0.3679
Spearman	3D SUVRmax	0.8916	0.1786	0.6821	0.7930	0.3679

r values

AL (*n*=9)	ROI method	LV wall (cm)	GLS (%)	IVS (cm)	Troponin T	NTproBNP
Pearson	2D SUVRmean	0.824	0.730	0.562	0.255	0.809
Pearson	3D SUVRmean	0.685	0.423	0.554	0.307	0.722
Pearson	3D SUVRmax	0.404	-0.203	-0.195	0.126	0.121

r values

AL (*n*=9)	ROI method	LV wall (cm)	GLS (%)	IVS (cm)	Troponin T	NTproBNP
Spearman	2D SUVRmean	0.783	0.900	0.500	0.433	0.783
Spearman	3D SUVRmean	0.683	0.533	0.533	0.417	0.633
Spearman	3D SUVRmax	0.517	-0.050	-0.167	-0.083	0.300

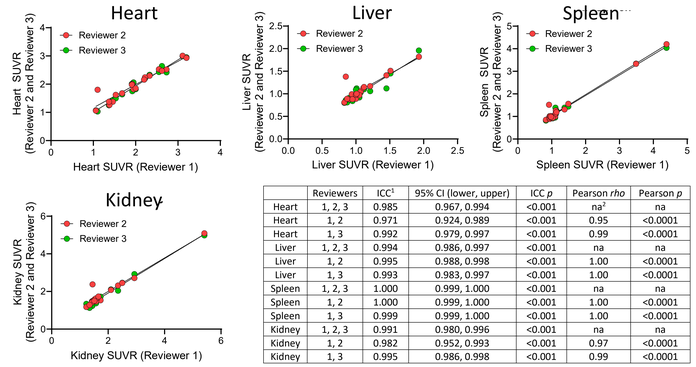
p values

AL (*n*=9)	ROI method	LV wall (cm)	GLS (%)	IVS (cm)	Troponin T	NTproBNP
Pearson	2D SUVRmean	0.0064	0.0254	0.1152	0.5087	0.0083
Pearson	3D SUVRmean	0.0416	0.2562	0.1215	0.4222	0.0280
Pearson	3D SUVRmax	0.2812	0.5996	0.6144	0.7470	0.7572

p values

AL (*n*=9)	ROI method	LV wall (cm)	GLS (%)	IVS (cm)	Troponin T	NTproBNP
Spearman	2D SUVRmean	0.0172	0.0020	0.1777	0.2499	0.0172
Spearman	3D SUVRmean	0.0503	0.1475	0.1475	0.2696	0.0760
Spearman	3D SUVRmax	0.1618	0.9116	0.6777	0.8432	0.4366

Figure 3. Correlation of manual and 3D automated quantitation of ^{124}I-evuzamitide uptake in the heart with contemporaneous (same day) echocardiographic parameters (red=high correlation and significance; blue=low).



	Reviewers	ICC[1]	95% CI (lower, upper)	ICC *p*	Pearson *rho*	Pearson *p*
Heart	1, 2, 3	0.985	0.967, 0.994	<0.001	na[2]	na
Heart	1, 2	0.971	0.924, 0.989	<0.001	0.95	<0.0001
Heart	1, 3	0.992	0.979, 0.997	<0.001	0.99	<0.0001
Liver	1, 2, 3	0.994	0.986, 0.997	<0.001	na	na
Liver	1, 2	0.995	0.988, 0.998	<0.001	1.00	<0.0001
Liver	1, 3	0.993	0.983, 0.997	<0.001	1.00	<0.0001
Spleen	1, 2, 3	1.000	0.999, 1.000	<0.001	na	na
Spleen	1, 2	1.000	0.999, 1.000	<0.001	1.00	<0.0001
Spleen	1, 3	0.999	0.999, 1.000	<0.001	1.00	<0.0001
Kidney	1, 2, 3	0.991	0.980, 0.996	<0.001	na	na
Kidney	1, 2	0.982	0.952, 0.993	<0.001	0.97	<0.0001
Kidney	1, 3	0.995	0.986, 0.998	<0.001	0.99	<0.0001

Figure 4. 2D manual quantitation of ^{124}I-evuzamitide in abdominothoracic organs by three independent reviewers (one experience [1], two novice [2 and 3]) was assessed by intraclass correlation coefficient and linear correlation analysis. [1]ICC, intraclass correlation coefficient; [2]na, not applicable.

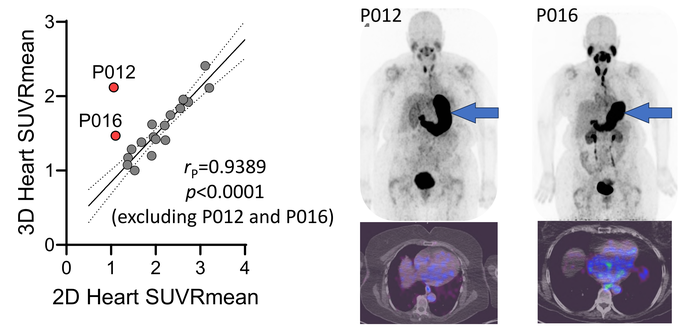


Figure 5. The correlation between cardiac uptake of tracer by 2D manual and automated 3D analysis was excellent. Disagreement in two patient images, with low cardiac uptake was likely due to spillover from radioactivity in the stomach (arrow).

CONCLUSION

^{124}I-evuzamitide imaging is a promising technique for detecting cardiac amyloidosis. Cardiac amyloid load, based on PET imaging, correlated well with cardiac structure and function and may have prognostic value.

DISCLOSURE

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.
EBM and AS: Founding shareholder in Attralus Inc.
SJK: Founding shareholder in Attralus Inc. Patent rights in peptides used for amyloid imaging, licensed to Attralus.

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