

# FULLY AUTOMATED 3D SEGMENTATION AND QUANTITATION OF THE AMYLOIDOPHILIC RADIOTRACER IODINE EVUZAMITIDE (<sup>124</sup>I-p5+14, <sup>124</sup>I-AT-01) IN THE HEART OF PATIENTS WITH SYSTEMIC AMYLOIDOSIS AND HEALTHY SUBJECTS

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## BACKGROUND

Systemic amyloidosis associated with the deposition of immunoglobulin light chains (AL) and transthyretin (ATTR) protein fibrils often involves cardiac deposition, which is the primary cause of morbidity and mortality. Iodine evuzamitide (<sup>124</sup>I-p5+14 or <sup>124</sup>I-AT-01) is a radioiodinated, pan-amyloid-reactive peptide that is being developed as a PET radiotracer to detect diverse forms of amyloid. The peptide binds amyloid deposits via electrostatic interactions with two ubiquitous components of amyloid – the proteinaceous fibrils and hypersulfated heparan sulfate glycan (PMID: 25923515).

Here, we present a method for fully automated 3D quantification of iodine-124 evuzamitide in patients with cardiac amyloidosis who participated in a Phase 1/2 first-in-human clinical trial (NCT 03678259). The method uses TRAQinform IQ technology (AIQ Solutions). The automated approach is compared with a 2D manual method of quantification performed by an experienced reader

## METHODS

A total of 50 patients, including 25 AL and 20 ATTR with a diagnosis of systemic amyloidosis, and five healthy subjects completed the study. All subjects were >18 years of age. PET/CT images were acquired ~5 hours post injection of <2 mg of evuzamitide (≤2 mCi I-124). The heart and aorta were automatically segmented on the CT data using a 3D pretrained convolutional neural network. The contours were applied to the PET data for quantitation of mean standardized uptake value, which was normalized using the mean aorta lumen radioactivity resulting in a 3D mean uptake value ratio (SUVR<sub>mean</sub>). Separately, a manual 2D region of interest analysis was performed on a single representative transaxial image encompassing the interventricular septum, left ventricular lumen, and left ventricular wall of the heart and normalized to the aorta lumen, resulting in a 2D SUVR<sub>mean</sub>. Correlation coefficients (r) were calculated between automated 3D SUVR<sub>mean</sub> and manual 2D SUVR<sub>mean</sub> values.

## RESULTS

In the 20 ATTR and 25 AL patients, automated 3D SUVR<sub>mean</sub> and manual 2D SUVR<sub>mean</sub> yielded excellent positive correlations for the heart, with r = 0.93 and p < 0.0001. For cardiac AL and ATTR patients, the correlation coefficient was r<sub>p</sub> = 0.93 (p < 0.0001) and r<sub>p</sub> = 0.94 (p < 0.0001), respectively. The uptake of iodine evuzamitide in the heart of five healthy subjects was significantly lower than ATTR (p=0.049) and AL (p=0.01) patients.

## CONCLUSION

Detection and quantification of amyloid burden in the heart is an unmet clinical need for patients with diverse forms of systemic amyloidosis. Given the heterogeneous presentation of cardiac disease in this patient population, if the evuzamitide radiotracer is approved for clinical use, this automated approach to image analysis could be an invaluable tool for novice readers, especially to quantify amyloid burden longitudinally without introducing reader bias.

<sup>124</sup>I-AT-01 is a novel PET imaging agent which detects systemic amyloidosis.

AIQ Solutions' TRAQinform IQ technology provided a fast and automated approach for quantifying cardiac uptake in <sup>124</sup>I-AT-01 PET/CT images.

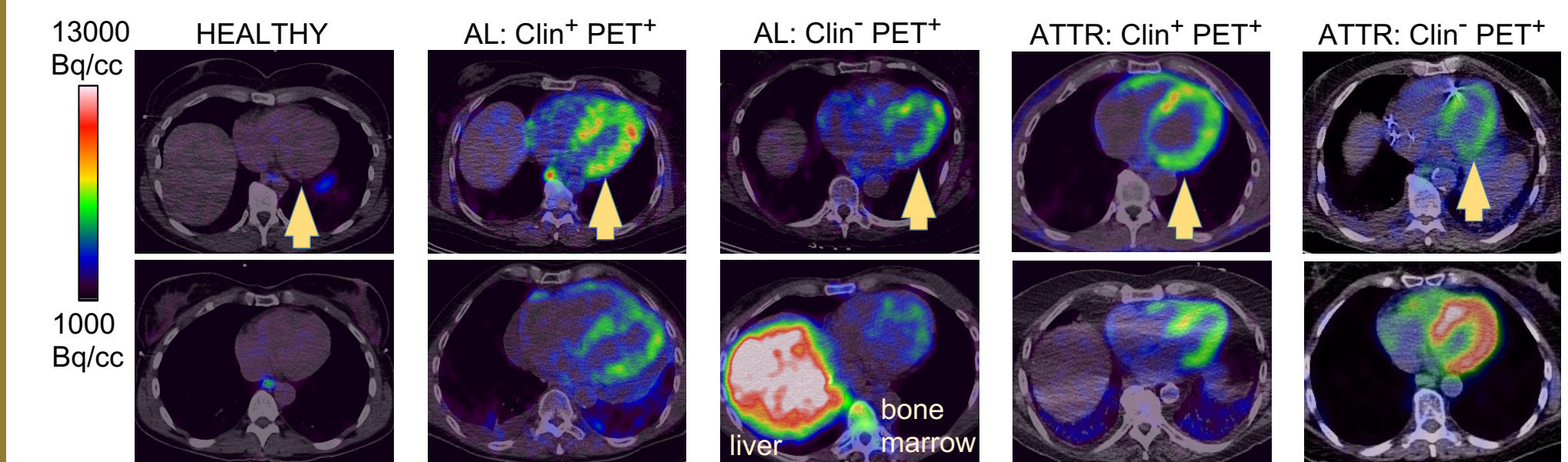
Cardiac uptake of <sup>124</sup>I-AT-01 was significantly higher in patients with systemic amyloidosis compared to healthy patients.

A combination of <sup>124</sup>I-AT-01 PET/CT imaging and TRAQinform IQ technology would be an invaluable tool for quantifying cardiac amyloid burden.

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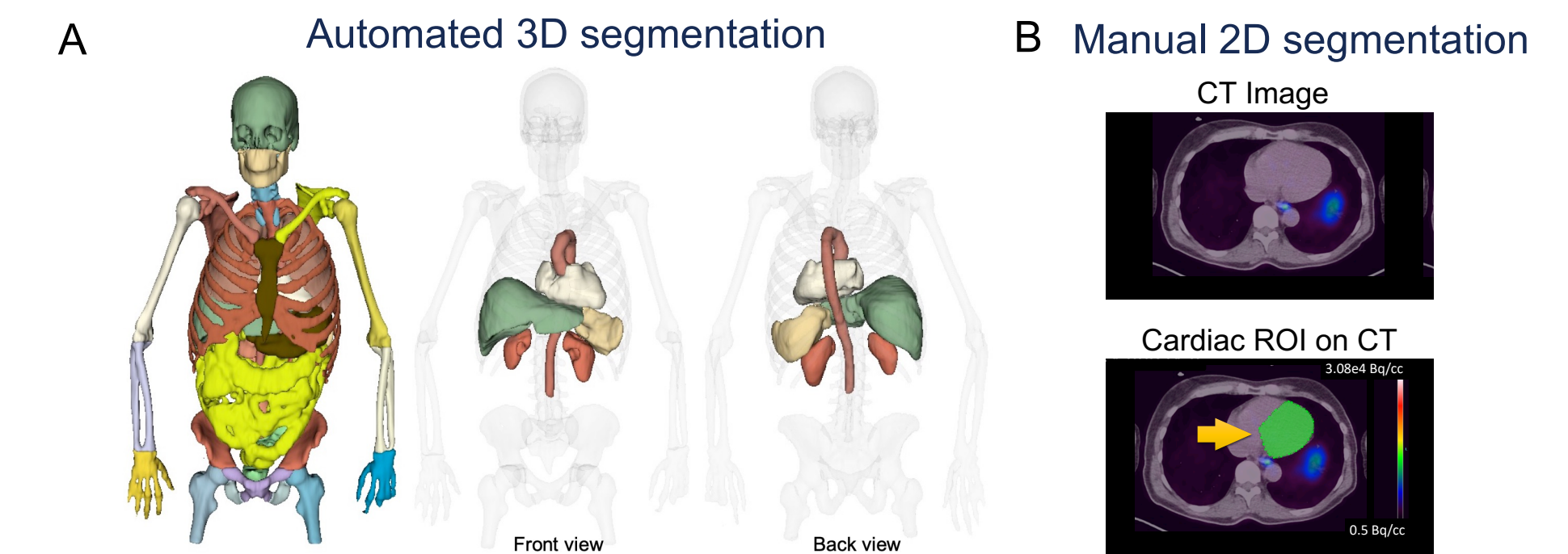
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FIGURE 1



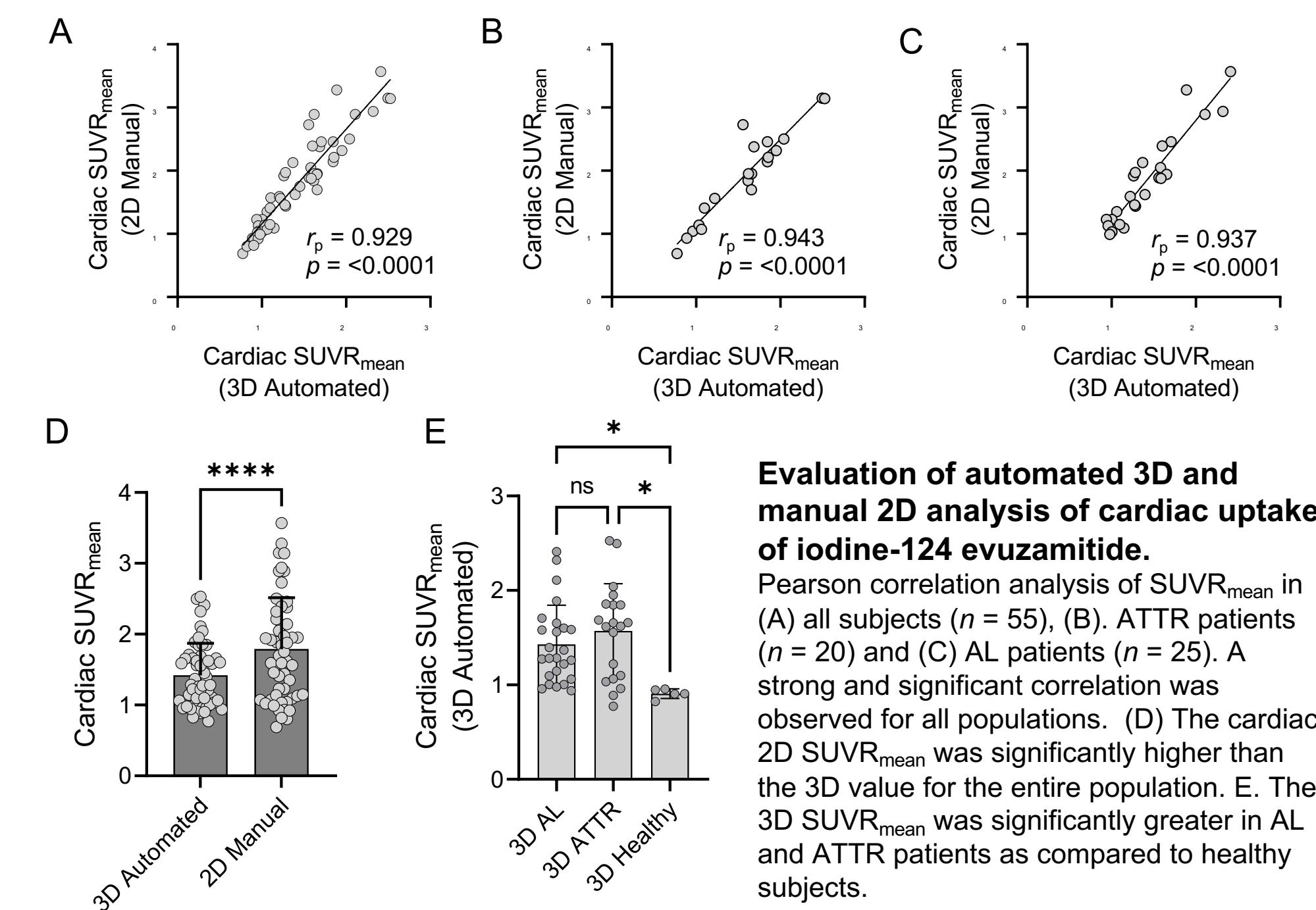
Representative transaxial PET/CT images of the heart in healthy subjects, AL and ATTR patients with clinically positive (Clin+) or negative (Clin-) cardiac amyloidosis.

FIGURE 2



Automated 3D (A) and manual 2D (B) methods of organ quantitation of AT-01 PET/CT images.

FIGURE 3



## DISCLOSURE INFORMATION

JSW is founder, shareholder and interim CSO of Attralus and receives research funding from Attralus. He holds patent rights in amyloid-reactive peptides. EBM is a founder and shareholder of Attralus. DB is a founder and CEO of Adaptive Research. AJW and TP are employees of AIQ Solutions. SJK is a founder and shareholder of Attralus and holds patent rights in amyloid-reactive peptides.