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Repeatability of quantitative pericoronary adipose tissue attenuation and coronary plaque burden from coronary CT angiography

Technical Report

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Brief title (47/50 characters): Pericoronary adipose tissue and plaque repeatability

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Abstract (191/250 words)

Background

High pericoronary adipose tissue (PCAT) attenuation and non-calcified plaque burden (NCP) measured from coronary CT angiography (CTA) have been implicated in future cardiac events. We aimed to evaluate the interobserver and intraobserver repeatability of PCAT attenuation and NCP burden measurement from CTA, in a sub-study of the prospective SCOT-HEART trial.

Methods

Fifty consecutive CTAs from participants of the CT arm of the prospective SCOT-HEART trial were included. Two experienced observers independently measured PCAT attenuation and plaque characteristics throughout the whole coronary tree from CTA using semi-automatic quantitative software.

Results

We analyzed proximal segments in 157 vessels. Intraobserver mean differences in PCAT attenuation and NCP plaque burden were -0.05HU and 0.92% with limits of agreement (LOA) of ±1.54 and ±5.97%. Intraobserver intraclass correlation coefficients (ICC) for PCAT attenuation and NCP burden were excellent (0.999 and 0.978). Interobserver mean differences in PCAT attenuation and NCP plaque burden were 0.13HU [LOA ±1.67HU] and -0.23% (LOA ±9.61%). Interobserver ICC values for PCAT attenuation and NCP burden were excellent (0.998 and 0.944).

Conclusion

PCAT attenuation and NCP burden on CTA has high intraobserver and interobserver repeatability, suggesting they represent a repeatable and robust method of quantifying cardiovascular risk.

Keywords

Pericoronary adipose tissue; non-calcified plaque; computed tomography angiography; coronary artery disease; repeatability

Abbreviations

CTA	Computed tomography angiography
CP	Calcified plaque
LD-NCP	Low density non-calcified plaque
LMS	Left main stem
NCP	Non-calcified plaque
PCAT	Pericoronary adipose tissue

Word Count: 1224/1500

Introduction

Computed tomography assessment of atherosclerotic plaque subtypes and pericoronary adipose tissue (PCAT) attenuation can identify patients at increased risk of cardiac events.[1, 2] However, to date limited information is available on observer variability of plaque burden or PCAT assessment. Our aim was to evaluate the intraobserver and interobserver repeatability of quantitative measurement PCAT attenuation and non-calcified plaque (NCP) burden in each coronary artery, using a standardized semi-automated method on coronary computed tomography angiography (CTA).

Methods

Study Population and CTA Acquisition

Fifty consecutive patients were included from 3 recruiting sites in the Scottish COmputed Tomography of the Heart (SCOT-HEART) trial.[3-6] All participants underwent CTA using 64-multidetector or 320-multidetector row scanners. CTA was performed following intravenous injection of 50-70 mL of iodine-based contrast medium at a flow rate of 5.5-6.5 mL/sec.

CT Coronary plaque and PCAT analysis

Plaque analysis was performed on CTA data sets by semi-automated software (Autoplaque 2.5, Cedars-Sinai Medical Center) by two independent expert readers. After defining the proximal and distal limits of the vessel segment, semi-automated plaque quantification was performed as described previously.[7, 8] Scan-specific thresholds for NCP and calcified plaque (CP) were automatically generated following a region-of-interest in the aorta, and plaque components were quantified using adaptive algorithms.[8-10]; vessel wall and calcified plaque were edited if required. Low density non-calcified plaque (LD-NCP) was defined as NCP<30 HU.

We performed PCAT and plaque analysis in the proximal 40 mm of the left anterior descending, left circumflex, and right coronary arteries, following a previously described method.[11] We also analyzed the left main stem (LMS) provided that its length was at least 10 mm. PCAT measurement was automated following plaque analysis, and we reported the mean PCAT CT attenuation in Hounsfield units (HU) within a 3 mm radius from the outer vessel wall.[6]

After a minimum of 12 weeks, observers repeated the analyses for all studies in order to examine the intraobserver repeatability and minimize recall bias.

Statistical methods

Statistical analysis was performed using R (Version 1.2.1335) and SPSS (IBM Corp. Released 2016. IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp). Continuous parametric variables were expressed as mean ± standard deviation (SD) and non-parametric data were presented as median (interquartile range [IQR]). Categorial variables were reported as frequencies (in percent). Intraclass correlation coefficients (ICC) were calculated using the two ways mixed effects model. The repeatability coefficient was defined as 1.96×the standard deviation of the absolute differences of each measure. A paired two-sided t-test or Wilcoxon ranksum test was used to test for statistically significant differences. Two-sided P values less than 0.05 were considered to be statistically significant. Bland–Altman analysis and the repeatability coefficient were used to assess for intraobserver and interobserver repeatability.

Results

Of the 50 patients, 35 (70%) were male. The median [IQR] age was 59 [53-64] years. Mean (SD) BMI was 29.02 ± 4.20. We analyzed 157/200 vessels; 43 vessels did not meet the criteria of length and diameter. A detailed quantitative and qualitative analysis of all vessels is presented in Table 1.

Intraobserver Repeatability

There was excellent intraobserver correlation of the PCAT attenuation (HU) and NCP plaque burden (%) (Figure 2 A and C). Intraclass correlation coefficients for PCAT attenuation and NCP burden values were 0.999 (95% confidence interval: 0.998 to 0.999; $p<0.0001$) and 0.978 (95% confidence interval: 0.954 to 0.989; $p<0.0001$) respectively. Bland-Altman plots of PCAT attenuation and NCP burden are illustrated in Figure 2 B and D. The mean absolute differences between the two examinations for PCAT attenuation and NCP burden were -0.05 (limits of agreement: -1.59 to 1.49) HU and 0.92 (limits of agreement: -5.06 to 6.89) %. The repeatability coefficients for PCAT attenuation and NCP burden were 1.36 HU and 4.62% and the coefficients of variation were 0.87% and 5.73% respectively.

Interobserver Repeatability

There was excellent interobserver correlation of the PCAT attenuation and NCP burden for all vessel analysis ($r = 0.9956$, and $r = 0.8446$ respectively; Figure 3 A and C). Bland-Altman plots for interobserver analysis of PCAT attenuation and NCP burden are shown in Figure 3 B and D. Intraclass correlation coefficients for PCAT attenuation and NCP burden were 0.998 (95%

confidence interval: 0.997 to 0.998; p<0.0001) and 0.944 (95% confidence interval: 0.923 to 0.959; p<0.0001) respectively. The mean absolute differences between the two examinations for PCAT attenuation and NCP burden were 0.13 (limits of agreement: -1.54 to 1.80) HU and -0.23 (limits of agreement: -9.84 to 9.38) %. The repeatability coefficients for PCAT attenuation and NCP burden were 1.27 HU and 5.55%, and the coefficient of variation were 0.80% and 6.81% respectively.

Discussion

Our data suggest excellent NCP and PCAT repeatability. We have previously demonstrated the excellent correlation between the quantification of plaque components from coronary CT angiography, compared with intravascular ultrasound (IVUS).[12, 13] To the best of our knowledge, this is the first study to systematically investigate simultaneously the interobserver and intraobserver agreement in measuring PCAT attenuation and coronary plaque burden using semi-automated software in a “real-world” trial. We are also the first to perform PCAT and plaque analysis in the LMS, which confirmed a similarly excellent repeatability compared to the other coronary arteries. Between observers, PCAT attenuation and NCP burden showed excellent correlation and small mean differences (0.13 HU and 0.23%).

Our study is not without limitations. We performed only interobserver and intraobserver reproducibility; the interscan repeatability of plaque burden measurement has been well described in two previous studies.[10, 14] Further, agreement with invasive IVUS has also been shown before. [12, 13] While the number of patients in our study is small, we have demonstrated excellent reproducibility both at an interobserver and intraobserver level with no significant outliers.

Conclusion

PCAT attenuation and NCP burden on CTA has high intraobserver and interobserver repeatability, suggesting they represent a repeatable and robust method of quantifying cardiovascular risk.

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Figure Legends

Figure 1: A) Observer 1 and observer 2 plaque measurement (red is non-calcified plaque, yellow is calcified plaque) and 3D plaque composition (orange is low density non-calcified plaque, yellow is calcified plaque) in the left anterior descending artery. NCP burden was 34.13% and 37.83% for observer 1 and 2, respectively. B) Observer 1 and observer 2 PCAT quantification of the left anterior descending artery. PCAT attenuation was -79.54 HU and -79.77HH for observer 1 and 2, respectively.

Figure 2: Intraobserver PCAT attenuation (HU) correlation and NCP burden (%) (A, C) and Bland-Altman plots (B, D) by all vessel analysis.

*NCP: non-calcified plaque, LOA: limits of agreement, PCAT: pericoronary adipose tissue

Figure 3: Interobserver PCAT attenuation (HU) correlation and NCP burden (%) (A, C) and Bland-Altman plots (B, D) by all vessel analysis.

*NCP: non-calcified plaque, LOA: limits of agreement, PCAT: pericoronary adipose tissue

Table 1: Quantitative analysis of all vessels between observer 1 and observer 2.

Plaque and Lesion Characteristics	All Vessels (N=157)		
	Observer 1	**Observer 2**	**P-value**
Total plaque burden (%)	43.39 (36.13-53.28)	42.58 (35.79-52.88)	0.92
CP burden (%)	0.24 (0-2.57)	0 (0-2.878)	0.42
NCP burden (%)	40.35 (34.99-46.92)	41.11(14.32-47.92)	0.77
LD-NCP burden (%)	5.17 (3.73-7.92)	5.40 (3.83-7.59)	0.67
Intermediate density NCP burden (%)	20.85 (16.94-25.37)	20.60 (16.12-25.65)	0.64
High density NCP burden (%)	14.83 (9.11-18.80)	14.73 (8.50-19.01)	0.82
Plaque length (mm)	39.86 (9.92-39.94)	39.86 (10.01-39.94)	0.69
Remodeling index	1.1 (1.01-1.28)	1.07 (1.01-1.25)	0.33
Stenosis (%)	28.17 (21.67-40.19)	29.24 (21.20-40.44)	0.90
Contrast density difference (%)	11.97 (2.86-21.09)	11.22 (3.77-25.11)	0.92
PCAT attenuation (HU)	-80.16 ± 9.05	-80.28 ± 9.09	0.90

*CP: calcified plaque, LD-NCP: low density non-calcified plaque, NCP: non-calcified plaque, PCAT: pericoronary adipose tissue

** Mean ± SD are included for continuous variables.

Figure 1

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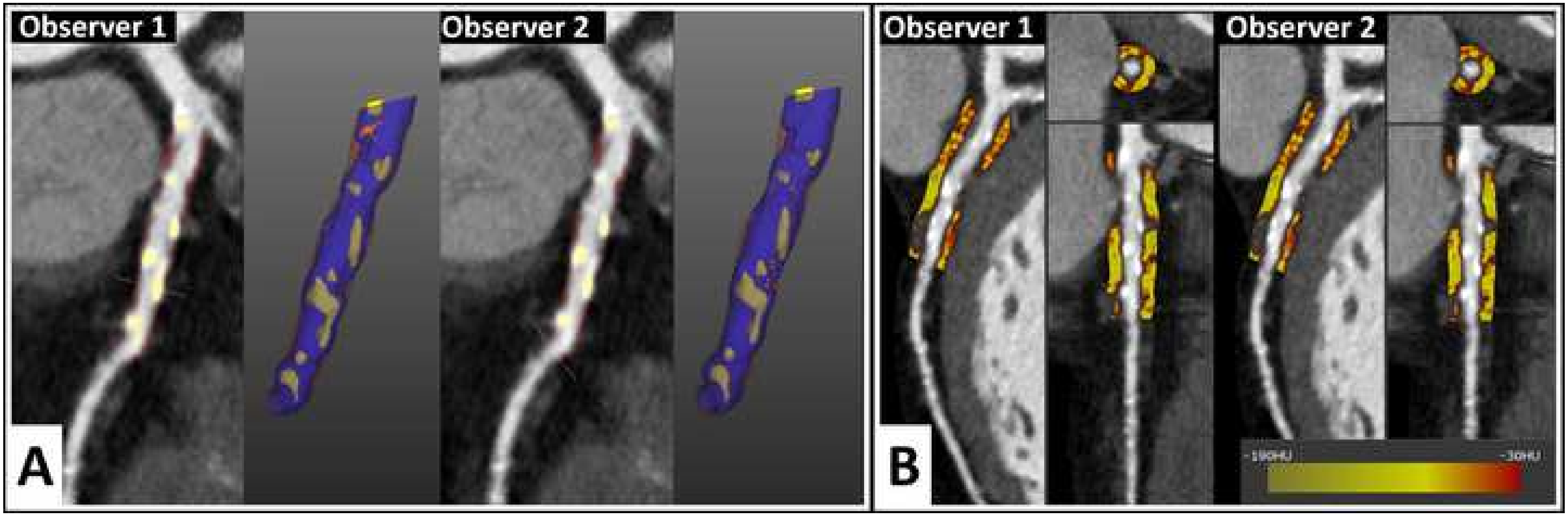

Figure 2

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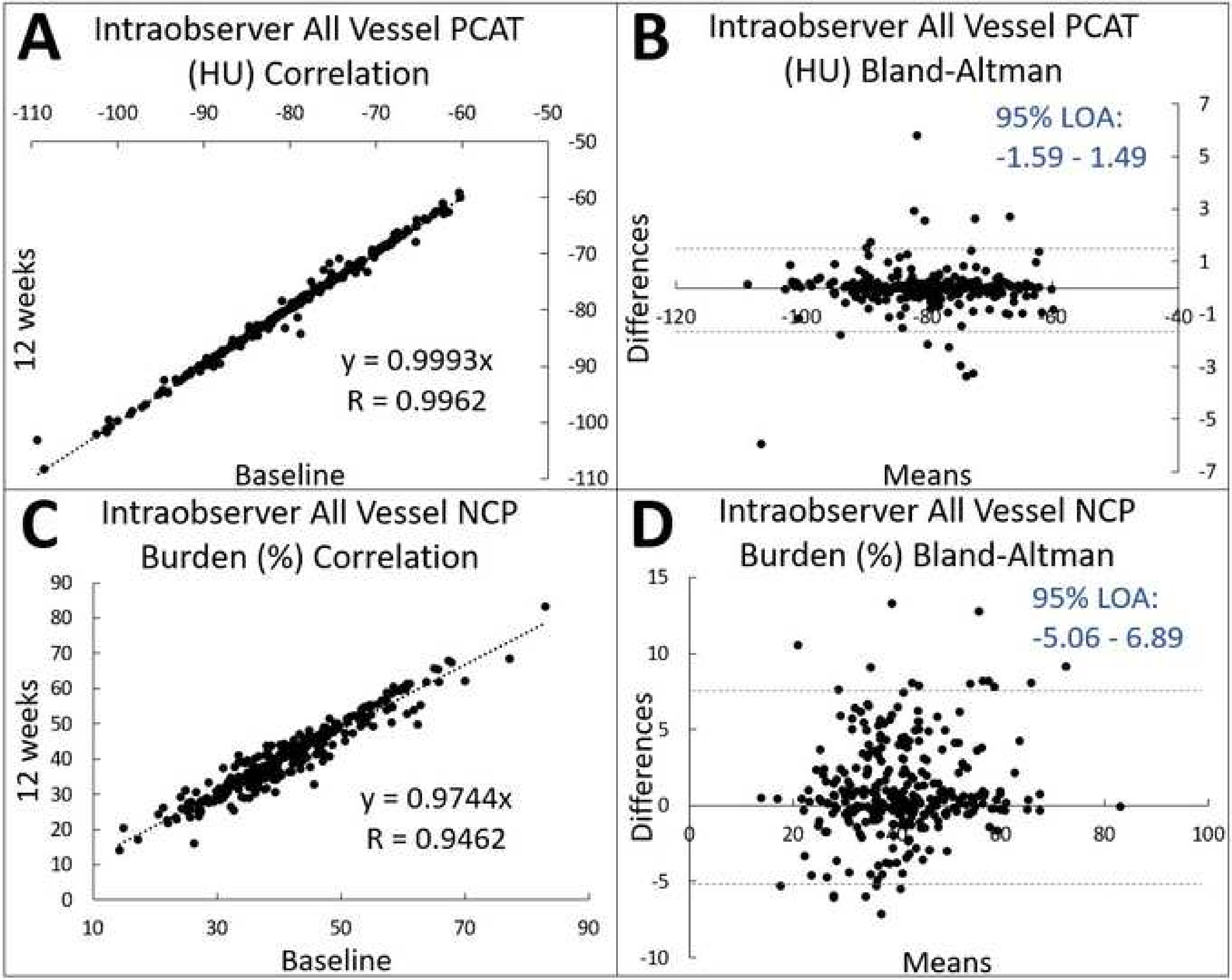

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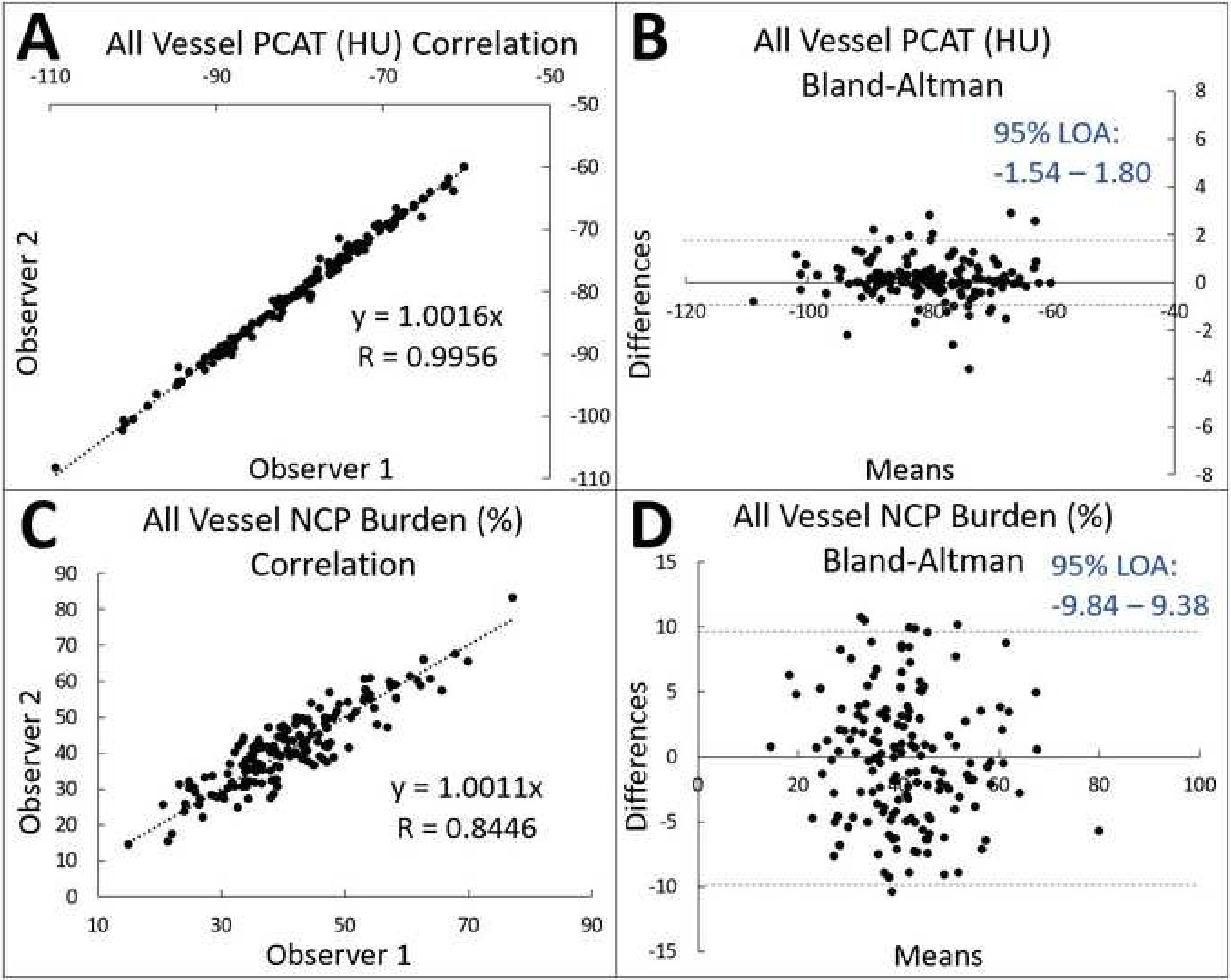

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