Hounsfield Unit Threshold Supportive of Brain Death Diagnosis

Hounsfield unit less than 80 discriminates between clinically significant cerebral perfusion and stasis filling, allowing confirmation of brain death

- M1– 94% sensitive, 100% specific
- A1– 96% sensitive, 100% specific
- BA– 100% sensitive, 100% specific
- ***M1, A1, and BA– 96% sensitive, 100% specific***

Conclusion

- Our results confirm previous reports that absence of cerebral blood flow on CTA is consistent with brain death
  - 100% sensitivity and 100% specificity

Conclusion

- Quantitative analysis of CTA can differentiate between preserved cerebral perfusion and stasis filling for the evaluation of brain death

- We propose that a HU less than 80 for M1, A1, and BA is concordant with no flow on NMPT
  - Indicative of a lack of clinically significant cerebral perfusion
  - Supportive of a diagnosis of brain death

Future Studies

- A large prospective multi-institutional study must be performed to confirm our findings and standardize our defined criteria for the utilization of CTA as an ancillary diagnostic study for brain death

References

1. Memorial Health University Medical Center. *Patient Care Policy: Death determination- Adult.* Savannah, GA: Memorial Health University Medical Center; March 1, 2013.
2. Berenguer C, Davis F, Howington J. Brain death confirmation: comparison of computed tomographic angiography with nuclear medicine perfusion scan. *J Trauma.* 2010;68(3):553-559.
3. Sawicki M, Bohatyrewicz R, Walecka A, Solek-Pastuszka J, Rowinski O, Walecki J. CT angiography in the diagnosis of brain death. *Pol J Radiol.* 2014;79:417-421.
4. Wijdicks EF. The diagnosis of brain death. *N Engl J Med*. 2001;344:1215-1221.
5. Welschehold S, Kerz T, Boor S, Reuland K, Thomke F, Reuland A, Beyer C, Tschan C, Wagner W, Muller-Forell W, Giese A. Computer tomographic angiography as a useful adjunct in the diagnosis of brain death. *J Trauma Acute Care Surg.* 2013;74(5):1279-1285.
6. Escudero D, Otero J, Marques L, Parra D, Gonzalo JA, Albaiceta GM, Cofiño L, Blanco A, Vega P, Murias E, Meilan A, Roger R, Taboada F. Diagnosing brain deah by CT perfusion and multislice CT angiography. *Neurocrit Care.* 2009;11:261-271.
7. Dupas B, Gayet-Delacroix M, Villers D, Antonioli D, Veccherini MF, Soulillou JP. Diagnosis of brain death using two-phase spiral CT. *Am J Neuroradiology.* 1998;19(4):641-647.
8. Frampas E, Videcoq M, de Kerviler E, Ricolfi F, Kuoch V, Mourey F, Tenaillon A, Dupas B. CT angiography for brain death diagnosis. *Am J Neuroradiol.* 2009;30(8):1566-1570.
9. Combes JC, Chomel A, Ricolfi F, d'Athis P, Freysz M. Reliability of computed tomographic angiography in the diagnosis of brain death. *Transplant Proc.* 2007;39(1):16-20.
10. Rieke, A, Regli B, Mattle H, Brekenfeld C, Gralla J, Schroth G, Ozdoba C. Computer tomographic angiography (CTA) to prove circulatory arrest for the diagnosis of brain death in the context of organ transplantation. *Swiss Med Wkly.* 2011;141:w13261.
11. Sawicki M, Bohatyrewicz R, Walecka A, Walecki J, Rowinski O, Solek-Pastuszka J, Czajkowski Z, Guzinski M, Burzynska M, Wojczal J. Computer tomographic angiography criteria in the diagnosis of brain death- comparison of sensitivity and interobserver reliability of different evaluation scales. *Neuroradiology.* 2014;56:609-620.

References (cont)

12. Leclerc X, Taschner CA, Vidal A, Strecker G, Savage J, Gauvrit JY, Pruvo JP. The role of spiral CT for the assessment of the intracranial circulation in suspected brain-death. *J Neuroradiol.* 2006;33(2)90-95.

13. Quesnel C, Fulgencio JP, Adrie C, Marro B, Payen L, Lembert N, El Metaoua S, Bonnet F. Limitations of computed tomographic angiography in the diagnosis of brain death. *Intensive Care Med.* 2007;33(12):2129-2135.

14. Shankar J, Vandorpe R. CT perfusion for confirmation of brain death. *Am J Neuroradiol.* 2013;34:1175-1179.

15. Kramer A, Roberts D. Computed tomography angiography in the diagnosis of brain death: a systematic review and meta-analysis. *Neutocrit Care.* 2014;21:539-550.

16. Taylor T, Dineen RA, Gardiner DC, Buss CH, Howatson A, Pace NL. Computer tomography (CT) angiography for confirmation of the clinical diagnosis of brain death. *Cochrane Database of Systematic Reviews.* 2014;3: CD00969.

17. Welschehold S, Kerz T, Boor S, Reuland K, Thomke F, Reuland A, Beyer C, Wagner W, Muller-Forell W, Giese A. Detection of intracranial circulatory arrest in brain death using cranial CT-angiography. *European Journal of Neurology*. 2013;20:173-179.

18. Flowers WM Jr, Patel BR. Persistence of cerebral blood flow after brain death. *South Med J.* 2000;93(4):364-370.

19. Korein J, Braunstein P, George A, Wichter M, Kricheff I, Lieberman A, Pearson J. Brain death: I. Angiographic correlation with the radioisotopic bolus technique for evaluation of critical deficit of cerebral blood flow. *Ann Neurol.* 1977;2(3):195-205.

20. Kricheff II, Pinto RS, George AE, Braunstein P, Korein J. Angiographic findings in brain death. *Ann NY Acad Sci.* 1978;315:168-183.

21. Sawicki M, Bohatyrewicz R, Safranow K, Walecka A, Walecki J, Rowinski O, Solek-Pastuszka J, Czajkowski Z, Marzec-Lewenstein E, Motyl K, Przybyl W, Czarnecka A. Dynamic evaluation of stasis filling phenomenon with computed tomography in diagnosis of brain death. *Neuroradiology.* 2013;55(9)1061-1069.

22. Bohatyewicz R, Sawicki M, Walecka A, Rowinski O, Bohatyewicz A, Czajkowski Z, Krzysztalowski A, Solek-Pastuszka J, Zukowski M, Marzec-Lewenstein E, Wojtaszek M. Computer tomographic angiography and perfusion in the diagnosis of brain death. *Transplantation Proceedings.* 2010;42:3941-3946.

23. Vassar College. Concepts & Applications of Inferential Statistics – Chapter 14. One-Way Analysis of Variance for Independent Samples – Part 2. http://vassarstats.net/textbook/ch14pt2.html Updated 2013. Accessed October 13, 2014.

24. Tukey JW. Comparing individual means in the analysis of variance. *Biometrics*. 1949;5(2):99-114.

25. Cabrer C, Domínguez-Roldan JM, Manyalich M, Trias E, Paredes D, Navarro A, Nicolás J, Valero R, García C, Ruiz A, Vilarrodona A. Persistence of intracranial diastolic flow in transcranial Doppler sonography exploration of patients in brain death. *Transplant Proc.* 2003;35(5):1642-1643.

Demographics

Demographic Data			
Group	***Study Cohort***	***Control***	***p***
N	60	20	
Age, Mean (years)	36.3	64.4	< 0.001
Age, Median (years)	33.2	64	< 0.001
Male	41 (68.4%)	4 (20%)	0.001
Female	19 (31.6%)	16 (80%)	0.001
Mechanism of Injury			
Hemorrhagic Stroke	7	0	0.155
Motor Vehicle Collision	15	0	0.002
Fall	5	1	0.638
Gun Shot Wound	12	1	0.077
Anoxic Brain Injury	4	0	0.312
Assault	2	0	0.787
Ischemic Stroke	1	7	< 0.001
Ruptured Aneurysm	4	1	0.446
Meningitis	1	0	0.647
Pedestrian vs Auto	5	0	0.073
Motorcycle Collision	1	0	0.481
All-Terrain Vehicle Collision	1	0	0.481
Headache	0	9	< 0.001
Toxic Encephalopathy	0	1	0.394

Study Cohort Homogeneity

- Analysis of demographic and clinical features between the -/-, -/+, and +/+ groups was performed

TABLE 1. Demographic Data For Clinical Examination Brain Death Group

Group	-/-	-/+	+/+	***p***
N	30	23	6	
Age, Mean (years)	40.37	39.96	28.50	.263
Age, Median (years)	38.50	37.00	24.00	.263
Male	23 (76.7%)	14 (60.8%)	4 (66.7%)	.459
Female	7 (23.3%)	9 (39.2%)	2 (33.3%)	.459
Mechanism of Injury				.280
Hemorrhagic Stroke	5	1	1	.361
Motor Vehicle Collision	12	2	1	.030
Fall	2	3	0	.522
Gun Shot Wound	5	4	3	.163
Anoxic Brain Injury	1	2	1	.444
Assault	1	1	0	.871
Ischemic Stroke	1	0	0	.612
Ruptured Aneurysm	1	3	0	.297
Meningitis	1	0	0	.612
Pedestrian vs Auto	1	4	0	.140
Motorcycle Collision	0	2	0	.198
All-Terrain Vehicle Collision	0	1	0	.451
Surgery				
Craniotomy	0	1	0	.451
Craniectomy	1	4	1	.113
Intracranial Pressure Monitor Placed	9	8	4	.230
Status				
Dead	30	23	6	*
Brain dead	30	23	5	.011
Pronounced Dead by				
Neurosurgeon	16	12	3	.988
Surgical Critical Care	13	10	3	.988
Pulmonary Critical Care	1	1	0	.988
Organ Donation:				
Evaluated by Life-Link	23	16	5	.735
Organ Donor	17	15	5	.444
Medical Comorbidities				
Coronary Artery Disease	1	2	0	.710
Hypertension	9	6	1	.787
Diabetes	1	3	0	.480
Hyperlipidemia	3	1	0	.699
Anticoagulation Use	2	1	0	.766

Group	***-/-***	***-/+***	***+/+***	***p***
N	30	23	6	
Mechanism of Injury				.280
Hemorrhagic Stroke	5	1	1	.361
Motor Vehicle Collision	12	2	1	.030
Fall	2	3	0	.522
Gun Shot Wound	5	4	3	.163
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Status				
Dead	30	23	6	*
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Group	**-/-**	**-/+**	**+/+**	***p***
N	30	23	6	
Mechanism of Injury				.280
Hemorrhagic Stroke	5	1	1	.361
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Intracranial Pressure Monitor Placed	9	8	4	.230
Status				
Dead	30	23	6	*
Brain dead	30	23	5	.011

Significant Differences Between Groups

Vessel	*Mean*	*SD*	*n*		*Mean*	*SD*	*n*	*p*
		-/-		*vs.*		-/+		
M1	37.44	12.89	30		64.73	20.86	23	.002
A1	36.80	14.07	30		53.43	17.25	23	.025
BA	35.68	12.42	30		39.74	15.46	23	.778
		-/-		*vs.*		+/+		
M1	37.44	12.89	30		190.74	73.58	6	< 0.001
A1	36.80	14.07	30		171.66	55.52	6	< 0.001
BA	35.68	12.42	30		200.02	57.51	6	< 0.001
		-/+		*vs.*		+/+		
M1	64.73	20.86	23		190.74	73.58	6	< 0.001
A1	53.43	17.25	23		171.66	55.52	6	< 0.001
BA	39.74	15.46	23		200.02	57.51	6	< 0.001
		-/-		*vs.*		***control***		
M1	37.44	12.89	30		634.32	252.35	20	< 0.001
A1	36.80	14.07	30		452.64	182.53	20	< 0.001
BA	35.68	12.42	30		540.67	193.62	20	< 0.001
		-/+		*vs.*		***control***		
M1	64.73	20.86	23		634.32	252.35	20	< 0.001
A1	53.43	17.25	23		452.64	182.53	20	< 0.001
BA	39.74	15.46	23		540.67	193.62	20	< 0.001
		+/+		*vs.*		***control***		
M1	190.74	73.58	6		634.32	252.35	20	< 0.001
A1	171.66	55.52	6		452.64	182.53	20	< 0.001
BA	200.02	57.51	6		540.67	193.62	20	< 0.001

Significant Differences Between Groups

Vessel	*Mean*	*SD*	*n*		*Mean*	*SD*	*n*	*p*
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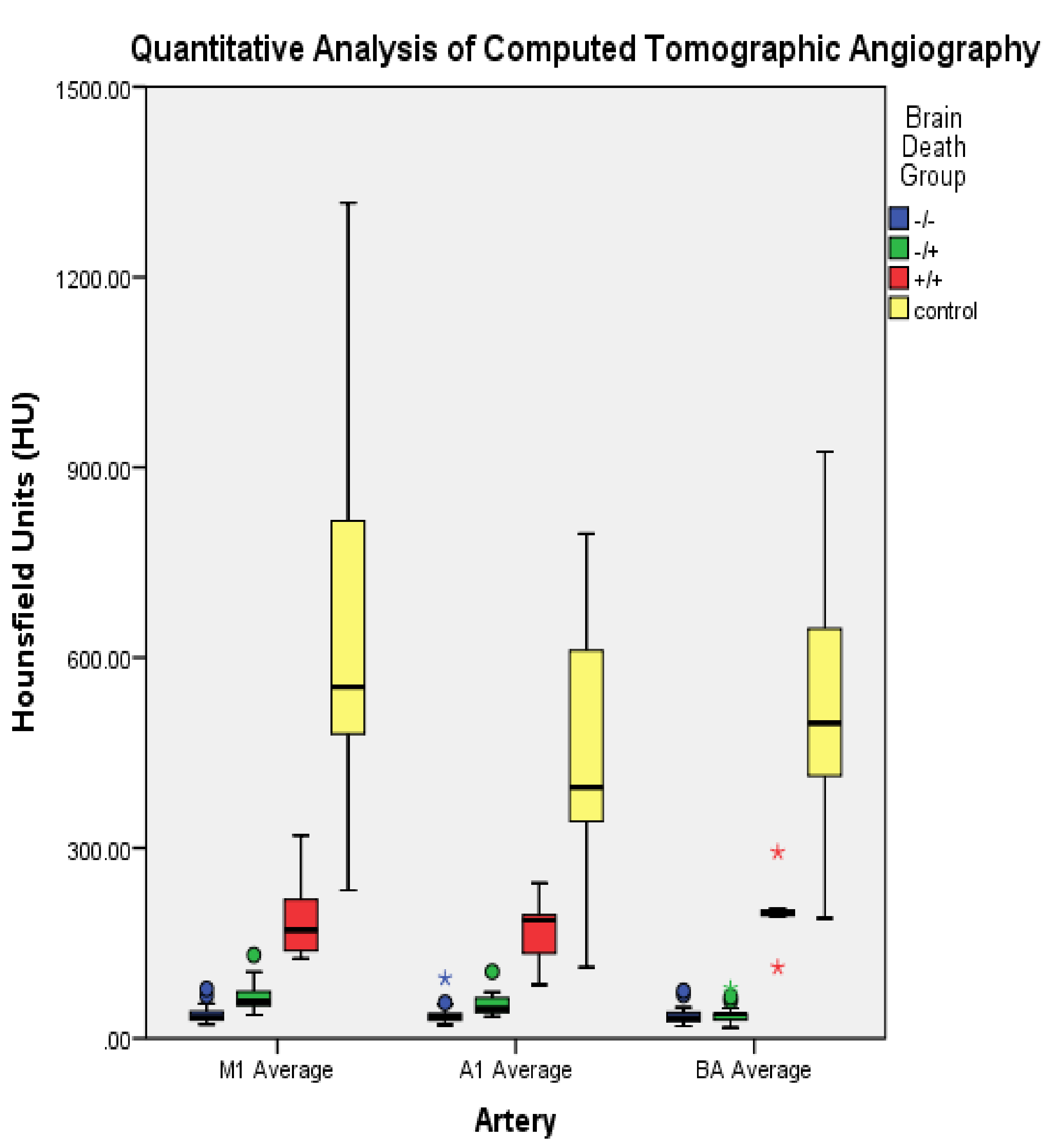
CTA Average Hounsfield Unit Readings

	Group	*n*	*Minimum*	*Maximum*
M1	-/-	30	22.25	78.00
	-/+	23	36.80	131.25
	+/+	6	125.45	320.00
	Control	20	233.40	1317.15
A1	-/-	30	21.25	94.75
	-/+	23	34.21	105.10
	+/+	6	84.20	245.00
	Control	20	111.80	795.45
BA	-/-	30	19.50	75.00
	-/+	23	17.20	78.70
	+/+	6	112.00	293.50
	Control	20	189.40	924.80



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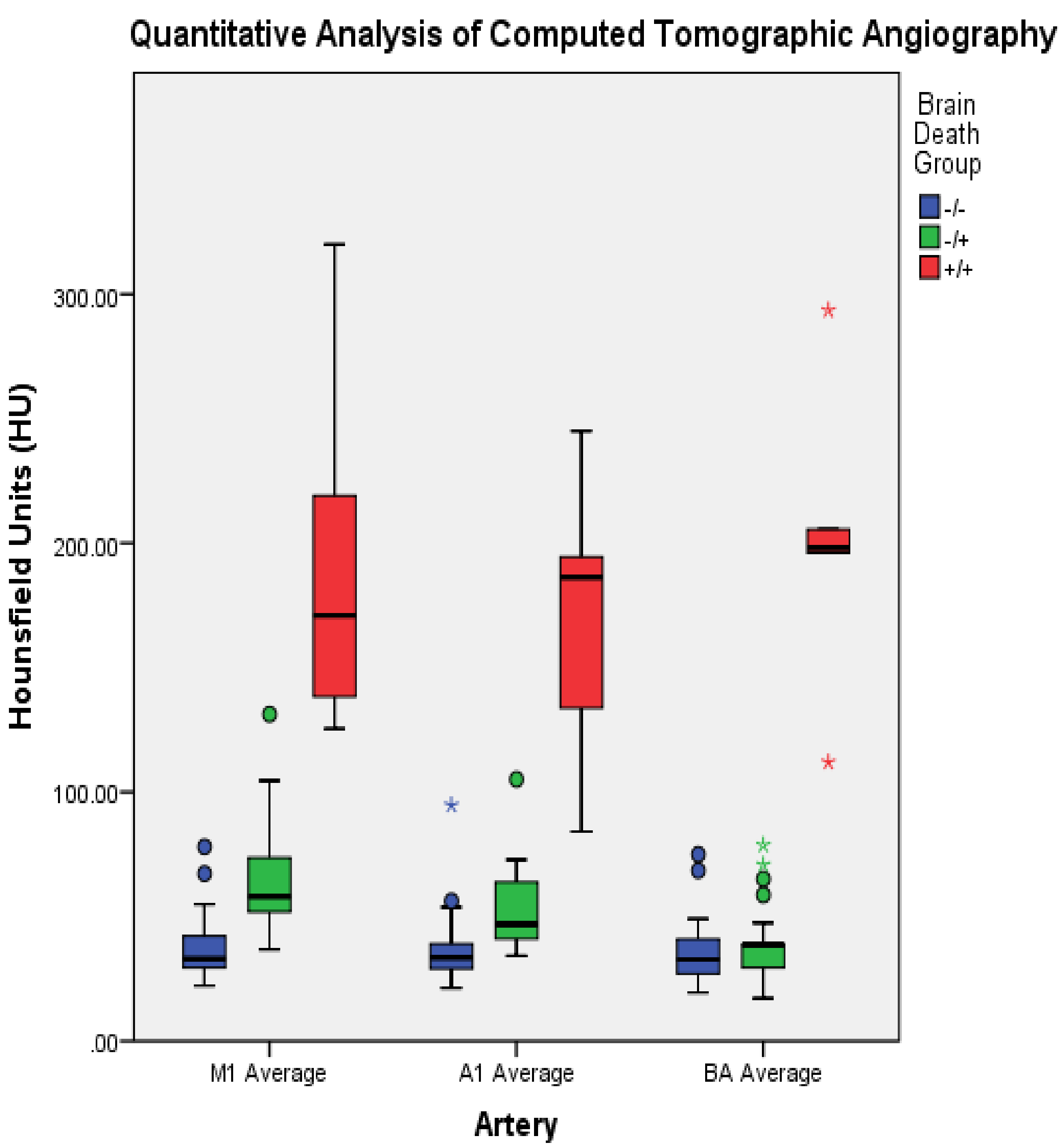

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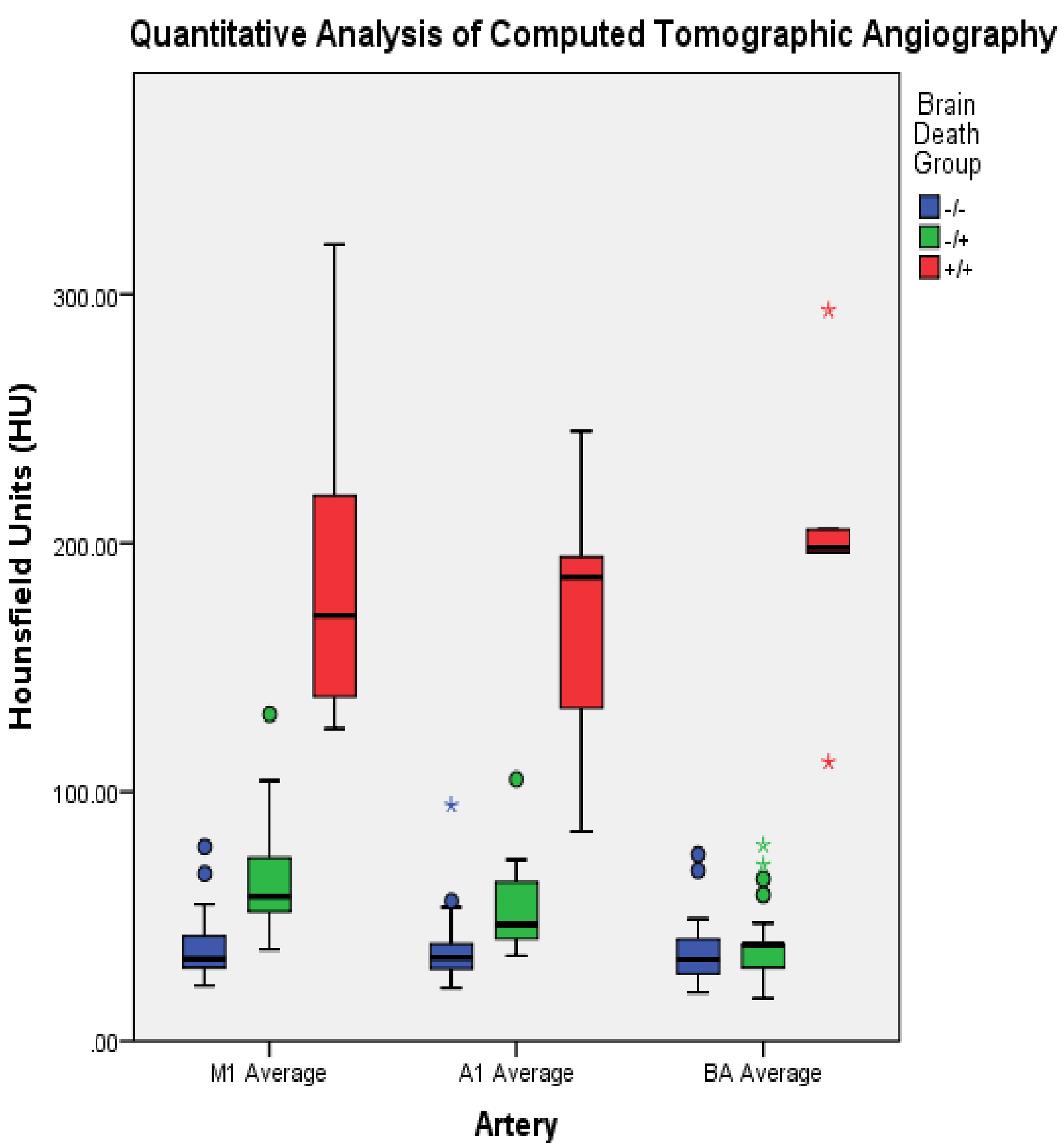

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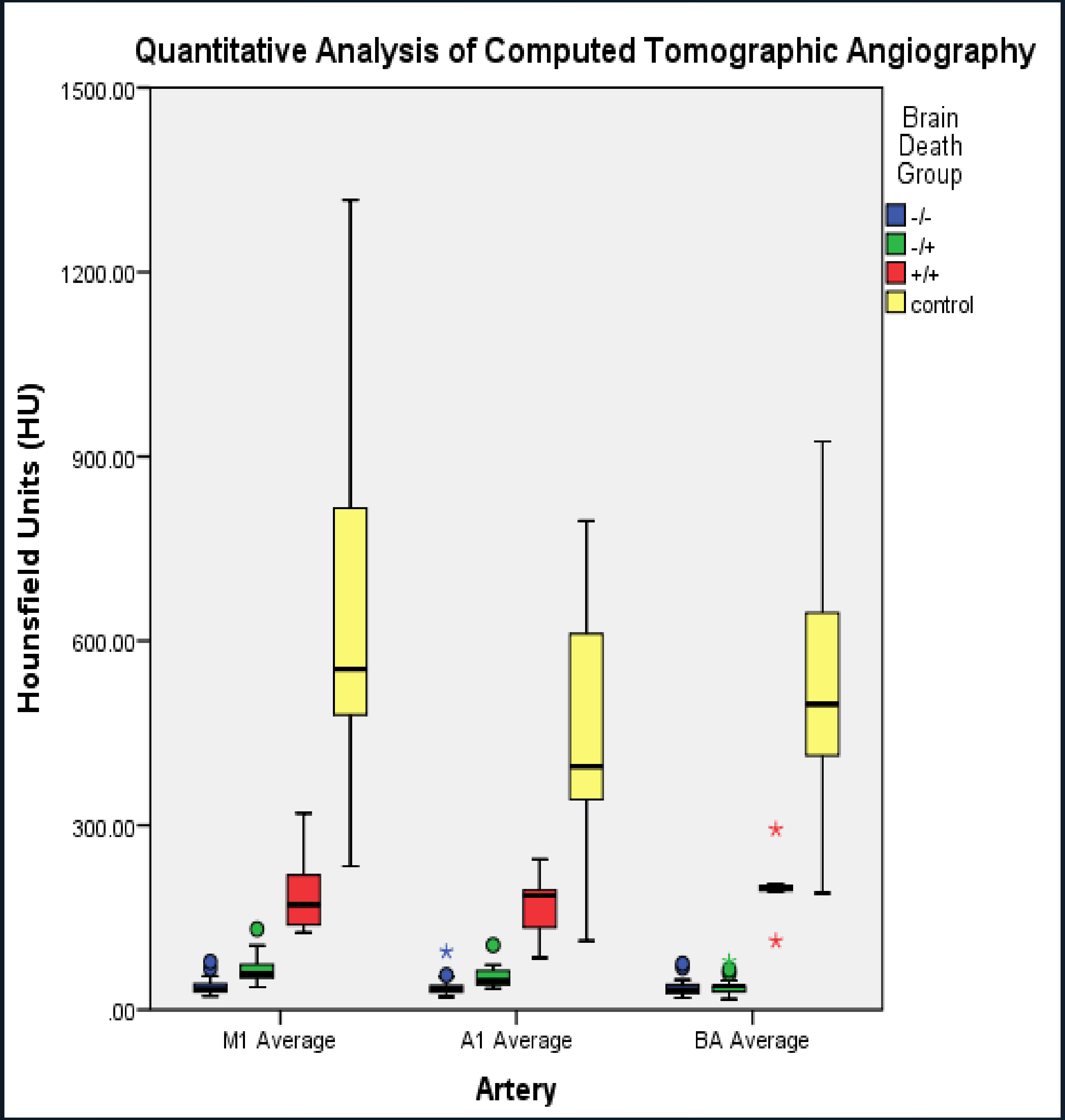
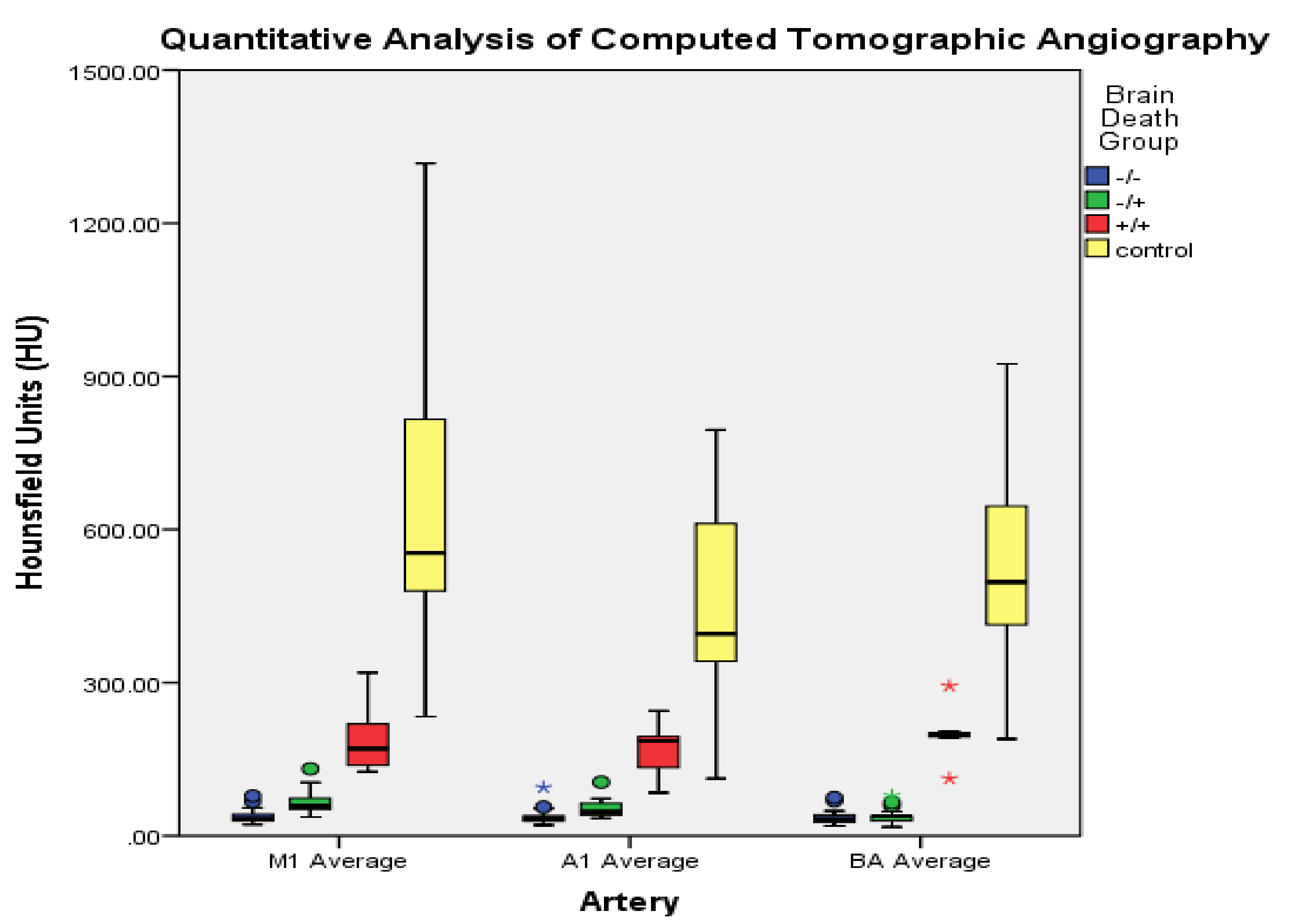
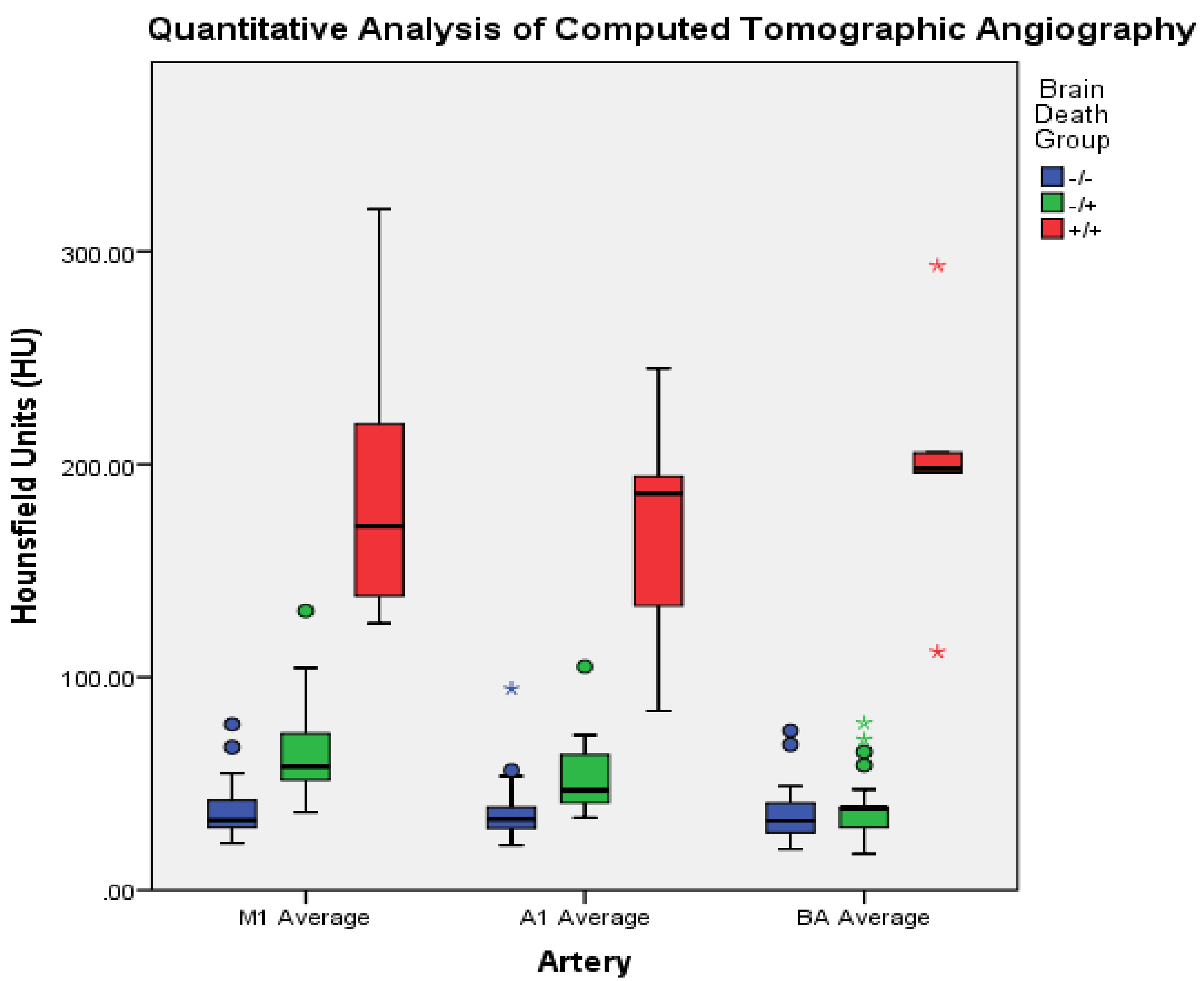




Quantitative Analysis of Computed Tomographic Angiography
1500.00
1200.00
900.00
600.00
300.00
.00
Hounsfield Units (HU)
M1 Average
A1 Average
BA Average
Artery
Brain Death Group
-/-
-/+
+/+
control



Quantitative Analysis of Computed Tomographic Angiography
Hounsfield Units (HU)
300.00
200.00
100.00
.00
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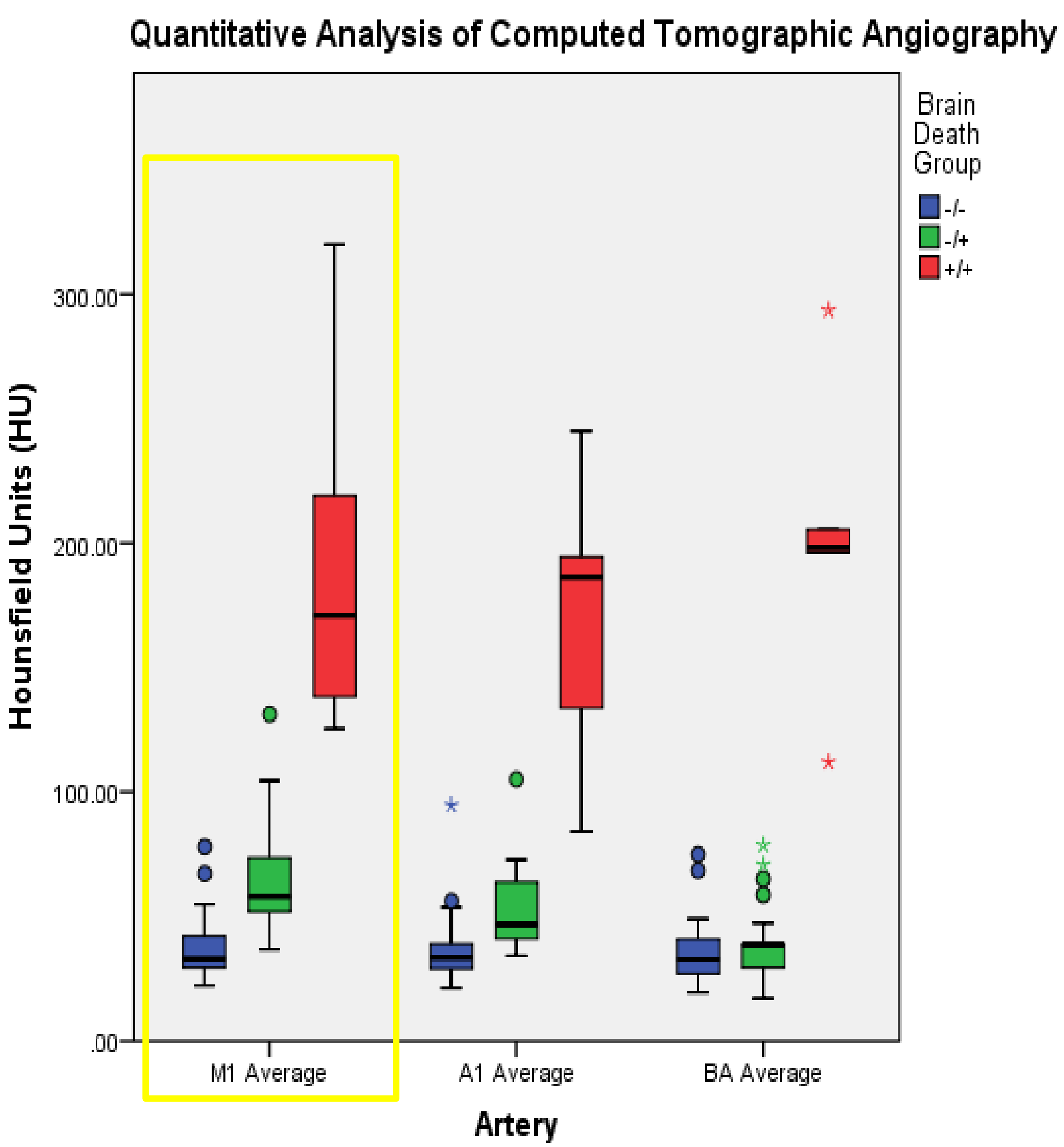

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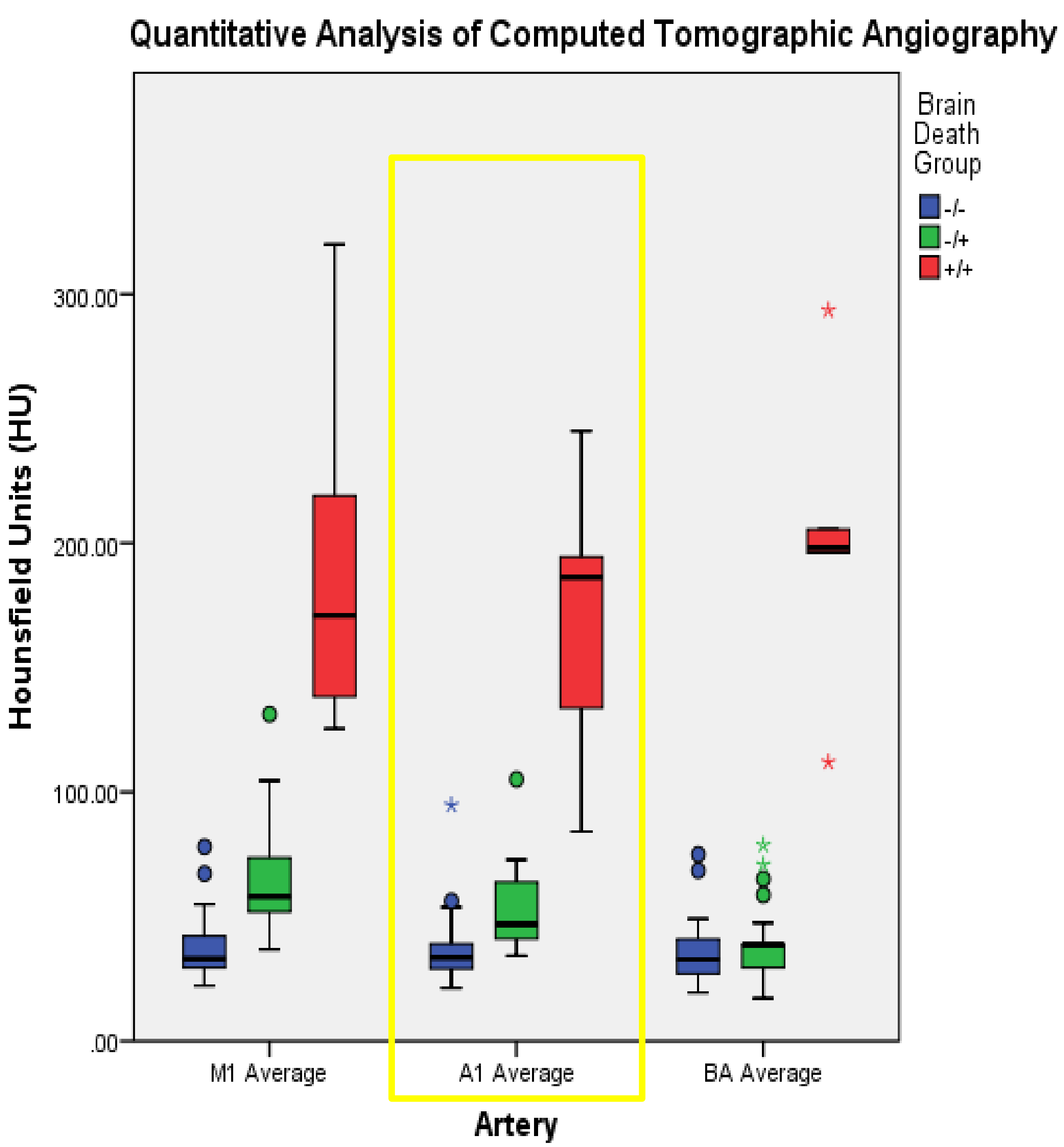

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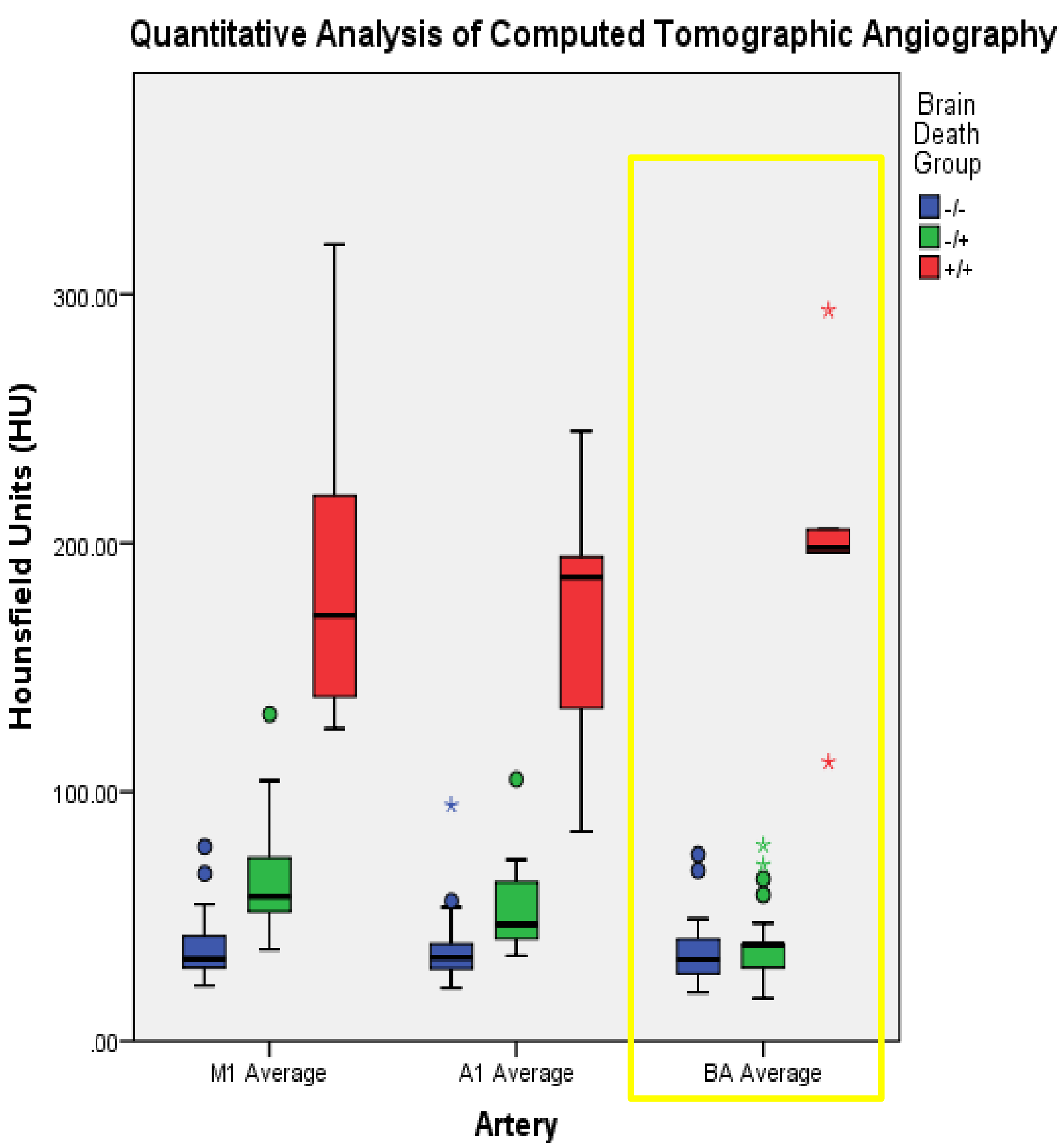

Evaluation of CTA Induced Contrast Nephropathy in Brain Death Evaluation

43 patients with clinical criteria of brain death, all patients underwent CTA and then cerebral angiography

- total of 160ml IV contrast received
- No statistically significant difference identified between the pre- and post-contrast creatinine levels (87.9μmol/L vs 120μmol/L respectively)

Combes et al. Transplantation Proceedings. 2007;39:16-20.

105 patients with clinical criteria of brain death, all patients underwent CTA

- total of 120ml IV contrast received
- No statistically significant difference was identified between the pre- and post-contrast mean creatinine levels (101.1μmol/L vs 89μmol/L respectively)

Frampas et al. Am J Neuroradiol. 2009;30(8):1566-1570

25 patients with clinical criteria of brain death, all patients underwent CTA

- No statistically significant difference was identified between the pre- and post-contrast mean creatinine levels (max rise was 18μmol/L)

Berenguer et al. Journal of Trauma. 2010; 68(3):553-559.

Previous major studies assessing CTA have proposed three evaluation systems:

10-, 7-, and 4-point scales

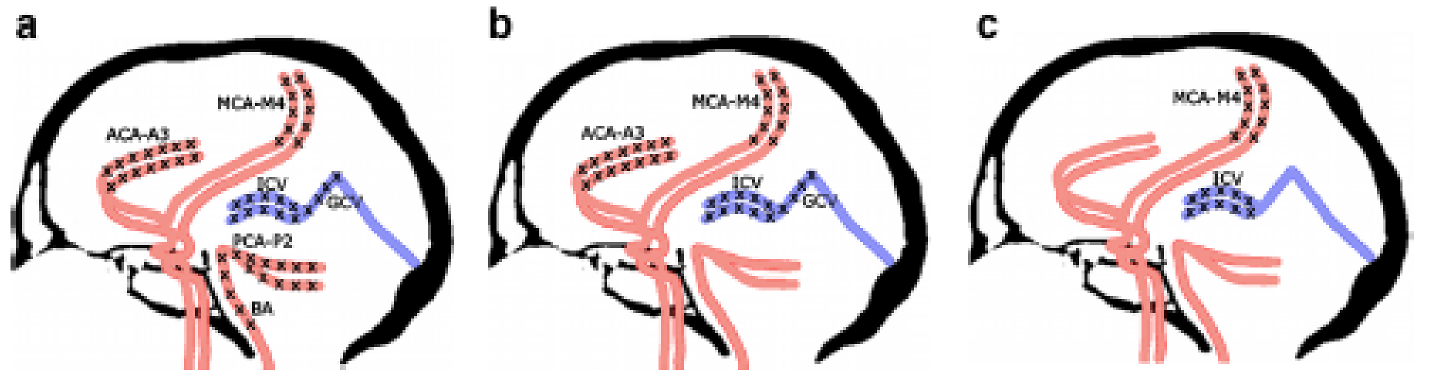

Fig. 1 Different criteria for the diagnosis of BD by CTA: **a** Positive result in the 10-point scale (score=10) confirming the diagnosis of BD was recorded when the following vessels were not opacified: the bilateral PCA-P2, the BA, the bilateral ACA-A3, the bilateral MCA-M4, the bilateral ICV, and the GCV. Scores from 0 to 9 were classified as negative results excluding the diagnosis of BD; **b** In the 7-point scale, positive result (score=7) was recorded with a lack of opacification of the bilateral ACA-A3, the bilateral MCA-M4, the bilateral ICV, and the GCV. Scores from 0 to 6 were classified as negative results; **c** Positive result in the 4-point scale (score=4) was recorded when the bilateral MCA-M4 and the bilateral ICV were not opacified. Scores from 0 to 3 were classified as negative results

Table 1. CTA evaluation scales in the diagnosis of BD.

Criteria	Lack of opacification of
Intracranial non-filling	• ICA beyond the level of the anterior clinoid process • VA beyond their dural penetration • ICV, GCV and the straight sinus
10-point*	• BA • Right and left PCA-P2 • Right and left ACA-A3 (pericallosal artery) • Right and left MCA-M4 • Right and left ICV • GCV
7-point*	• Right and left ACA-A3 (pericallosal artery) • Right and left MCA-M4 • Right and left ICV • GCV
4-point*	• Right and left MCA-M4 ** • Right and left ICV

* One point is noted for each nonopacified vessel in the late phase. Cerebral circulatory arrest is diagnosed with the score of 10, 7, or 4 points, accordingly; ** according to the 4-point scale, opacification of 1 or 2 cortical branches of MCA on the same side does not exclude the diagnosis of cerebral circulatory arrest provided there is no opacification of ICVs.

Sawicki et al. Neuroradiology. 2014;56:609-620.

Sawicki et al. Pol J Radiol. 2014; 79:417-421.

Previous major studies assessing CTA have proposed three evaluation systems:

Table 2. Sensitivity of CTA in the diagnosis of BD.

Study authors and year	No of cases	Sensitivity (%)		
		10-point	7-point	4-point
Combes et al. 2007 [15]	43	70		
Welschehold et al. 2013 [16]	63	54 *		
Dupas et al. 1998 [4]	14		100	
Quesnel et al. 2007 [13]	21		52**	
Frampas et al. 2009 [6]	105		63	86
Rieke et al. 2011 [14]	29		76	93
Leclerc et al. 2006 [7]	15			87
Sawicki et al. 2014 [9]	82	67	74	96

* GCV was not assessed, ** the study included 5 out of 21 patients with anoxic brain injury.

Sawicki et al. Pol J Radiol. 2014; 79:417-421.

Pitfalls of Confirmatory Tests

Cerebral Angiogram

- Image variability with injection of arch or selective arteries
- Image variability with injection and/or push technique
- No guidelines for interpretation

EEG

- Artifacts in intensive care settings
- Information from mostly cortex
- Somatosensory evoked potentials
- Absent in comatose patients without brain death

Transcranial Doppler Ultrasonographic Scan

- Technical difficulties and skill-dependent
- Normal in anoxic-ischemic injury

CT Angiogram

- Interpretation difficulties
- Retained blood flow in 20% of cases
- Possibility to miss slow flow states because of rapid acquisition of images

Nuclear Brain Scan

- Areas of perfusion in thalamus in patients with anoxic injury or skull defect

Wijdicks et al. Neurology. 2010; 75:77-83.