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Vessel-specific coronary perfusion territories using a CT angiogram with a minimum cost path technique and its direct comparison to the American Heart Association 17-segment model

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Abstract

Objectives—This study compared the accuracy of an automated, vessel-specific minimum cost path (MCP) myocardial perfusion territory assignment technique as compared with the standard American Heart Association 17-segment (AHA) model.

Methods—Six swine (42 ± 9 kg) were used to evaluate the accuracy of the MCP technique and the AHA method. In each swine, a dynamic acquisition, comprised of twenty consecutive whole heart volume scans, was acquired with a computed tomography scanner, following peripheral injection of contrast material. From this acquisition, MCP and AHA perfusion territories were determined, for the left (LCA) and right (RCA) coronary arteries. Each animal underwent

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Conflict of interest Sabee Molloi, Ph.D., has previously received grants from Canon America Medical Systems and Philips Medical Systems. The remaining authors Shant Malkasian, Logan Hubbard, Ph.D., Pablo Abbona, M.D., Brian Dertli, and Jungnam Kwon, M.D., do not have any conflict of interest to disclose.

Statistics and biometry No complex statistical methods were necessary for this paper.

Informed consent Approval from the institutional animal care committee was obtained.

Ethical approval Institutional Review Board approval was not required because this was an animal study, although approval from the institutional animal care committee was obtained.

Study subjects or cohorts overlap The six animals used in this manuscript submission were also used for a previous study for validation of the myocardial assignment technique. However, there is no overlap in the data presented in this submission with the previous study.
In the previous report, reference standard and minimum cost path perfusion territories for the left and right coronary arteries were validated for the whole heart (both left and right ventricles). In the present study, these previously determined whole heart perfusion territories were cropped to a common left ventricle myocardial segmentation and compared with the AHA 17-segment model. Data regarding the coronary perfusion territories of the left ventricle coronary perfusion territories in the present study has not been published.

Methodology

- Retrospective
- Experimental
- Performed at one institution

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additional dynamic acquisitions, consisting of twenty consecutive volume scans, following direct intracoronary contrast injection into the LCA or RCA. These images were used as the reference standard (REF) LCA and RCA perfusion territories. The MCP and AHA techniques' perfusion territories were then quantitatively compared with the REF perfusion territories.

Results—The myocardial mass of MCP perfusion territories (M_{MCP}) was related to the mass of reference standard perfusion territories (M_{REF}) by $M_{MCP} = 0.99M_{REF} + 0.39$ g ($r = 1.00$; $R^2 = 1.00$). The mass of AHA perfusion territories (M_{AHA}) was related to M_{REF} by $M_{AHA} = 0.81M_{REF} + 5.03$ g ($r = 0.99$; $R^2 = 0.98$).

Conclusion—The vessel-specific MCP myocardial perfusion territory assignment technique more accurately quantifies LCA and RCA perfusion territories as compared with the current standard AHA 17-segment model. Therefore, it can potentially provide a more comprehensive and patient-specific evaluation of coronary artery disease.

Keywords

Cardiovascular disease; Computed tomography angiography; Coronary artery disease; Cardiac imaging techniques

Introduction

Accurate assessment of coronary artery disease (CAD) requires both morphological and physiological data to adequately evaluate the severity of disease [1–6]. The existing imaging modalities used to assess the physiological severity of CAD, i.e., single-photon emission computed tomography (SPECT), positron emission tomography (PET), cardiac magnetic resonance (CMR), and computed tomography (CT) perfusion, are unable to accurately provide patient-specific morphological data, such as the myocardial mass and location of each coronary perfusion territory. The American Heart Association 17-segment (AHA) model provides a general population-based solution. Specifically, the AHA model estimates the mass and locations of the coronary perfusion territories based on the average coronary anatomy and perfusion territories of 102 healthy human subjects [7]. While the AHA model has been shown to be clinically useful, many studies have demonstrated that it misassigns coronary perfusion territories as it cannot account for variations in coronary morphology between patients. For example, the AHA model often misassigns coronary perfusion territories for right-dominant versus left-dominant circulations or in patients with a ramus intermedius [8–13].

Advances such as multidetector CT imaging systems allow for concurrent acquisition of both physiological and morphological data [14, 15]. Therefore, there is a clinical need to better integrate the morphologic and physiologic data by providing patient-specific coronary perfusion territories to account for coronary anatomic variability, which has the potential to improve treatment planning.

A minimum cost path (MCP) technique was previously validated ex vivo [16] and in vivo [17], to assign vessel-specific perfusion territories for the left and right coronary arteries, in the whole heart, i.e., the left and right ventricles. The MCP technique uses coronary artery centerlines from a CT angiogram to determine vessel-specific perfusion territories. While

many studies have suggested alternative methods to quantify vessel-specific perfusion territories in the left ventricle [18–20], the MCP technique can provide quantification of coronary perfusion territories for both left and right ventricles [17]. However, the MCP technique has not been compared with the standard AHA 17-segment model.

The purpose of this study was to directly compare the accuracy of the MCP technique with the AHA 17-segment model, which is widely accepted as a clinical standard in estimating coronary perfusion territories.

Methods

This study was approved by the Animal Care Committee and Institutional Review Board for the Care of Animal Subjects. All data was acquired from seven male Yorkshire swine (42 ± 9 kg) between December 2014 and July 2016, with a mean heart rate and arterial pressure of 84 ± 10 beats per minute and 77 ± 9 mmHg, respectively. The data from the first six swine were from one previous study [17], while data from the seventh swine was from a separate study [15]. Specifically, the first six swine had a right-dominant coronary circulation, where the posterior descending artery (PDA) originated from the right coronary artery (RCA). In these swine, the AHA and the MCP techniques were compared quantitatively with the corresponding reference standard (REF) LCA and RCA perfusion territories. The seventh swine had a left-dominant circulation, where the PDA originated from the left circumflex artery (LCx). Only AHA and MCP perfusion territories were determined for the left-dominant animal.

Each of the six right-dominant swine from the study underwent one intravenous contrast injection CT acquisition, used to derive AHA and MCP perfusion territories. Specifically, one MCP (LCA_{MCP} and RCA_{MCP}) and one AHA (LCA_{AHA} and RCA_{AHA}) perfusion territory pairs for the LCA and RCA were determined in each case, respectively. Additionally, each animal underwent CT acquisition to obtain reference LCA and RCA perfusion territories (LCA_{REF} and RCA_{REF}) following intracoronary contrast injection. Repeat LCA_{REF} and RCA_{REF} measurements were made in all but one of the six animals, resulting in a total of fifteen LCA_{REF} and RCA_{REF} perfusion territory pairs in the six animals. Finally, the seventh left-dominant animal only underwent one intravenous contrast injection CT acquisition, used to derive AHA and MCP perfusion territories. Intracoronary contrast injection was not performed as that was not part of the previous study [15]; hence, no REF perfusion territories were derived. A summary of the study design is shown in Figs. 1 and 2.

Animal preparation

Anesthesia was induced via intramuscular injection of Telazol (4.4 mg/kg), ketamine (2.2 mg/kg), and xylazine (2.2 mg/kg). After intubation (Covidien), anesthesia was maintained through ventilation (Highland Medical Equipment) with an oxygen-air mixture containing 1.5–2.5% isoflurane (Baxter). Catheter sheaths (AVANTI®, Cordis Corporation) were placed in both femoral veins and in the right carotid artery. Fluid and drugs were administered via the right femoral vein, while peripheral contrast injections were made via the left femoral vein.

Injection protocol

Peripheral intravenous contrast injection was performed via the left femoral vein (Isovue 370 mg/mL, 1 mL/kg, 5 mL/s) during dynamic CT acquisition.

Coronary catheter (Judkins right guide catheter, Cordis Corporation) introduction was achieved using the right carotid sheath. Intracoronary contrast injections were made into the LCA or RCA during dynamic CT imaging (Isovue 50 mg/mL, 15 mL, 2 mL/s). The imaging protocol is detailed in Fig. 1.

Imaging protocol

Prospective ECG-gated dynamic CT image datasets were acquired using a multidetector CT scanner (Aquilion One, Canon Imaging). Each dynamic dataset consisted of 20 volume scans, with an estimated effective dose of 26.4 mSv, as determined based on a similar study [15]. Reconstructed images were then registered to the peak enhancement volume acquired during intravenous contrast injection [21] to reduce motion artifacts. Successive acquisitions were at least 10 min apart, to allow for contrast clearance from the blood pool. Imaging parameters are shown in Table 1.

American Heart Association 17-segment model measurement

Two readers used a Vitrea workstation (Vitrea fX version 6.0, Vital Images, Inc.) to semi-automatically obtain AHA perfusion territories, using the image with the best contrast enhancement acquired during peripheral intravenous contrast injection. Each reader also performed semi-automated left ventricle segmentation using the Vitrea workstation. MCP and REF perfusion territories for the whole heart were cropped using the left ventricle segmentation, as shown in Figs. 1 and 2. Segments 1, 2, 5, 6, 7, 8, 11, 12, 13, 14, and 17 defined the LCA_{AHA}, while segments 3, 4, 9, 10, and 15 defined the RCA_{AHA} territory based on the AHA 17-segment model [7]. Reader 1 (P.A.) is a radiologist with over 16 years of experience, while reader 2 (S. Malkasian) has over 5 years of experience conducting radiology research.

Minimum cost path measurement

The MCP LCA (LCA_{MCP}) and RCA (RCA_{MCP}) perfusion territories were determined using a maximum-projection image of the peripheral intravenous contrast injection CT acquisition, for the whole heart [17]. The MCP technique automatically assigns every voxel of myocardial tissue to the closest coronary artery branch. To implement the MCP technique, whole heart myocardial segmentation and coronary artery centerline extraction were performed semi-automatically using a Vitrea workstation. Left anterior descending coronary artery (LAD), LCx, and RCA centerlines were extracted to second-generation branches. The MCP technique used the fast-marching algorithm to create a distance map of each coronary artery, constrained to the morphology of the myocardium. Each distance map was compared to determine LAD_{MCP}, LCx_{MCP}, and RCA_{MCP} perfusion territories by assigning each voxel to the coronary artery branch with the shortest distance [17]. LAD_{MCP} and LCx_{MCP} were combined to yield LCA_{MCP} perfusion territories since only LCA_{REF} perfusion territories were available for comparison. The left ventricular component of each MCP territory was then isolated, as shown in Figs. 1 and 2.

Reference standard measurement

Whole heart LCA_{REF} and RCA_{REF} territories were determined following selective intracoronary contrast injection. For each intracoronary contrast injection acquisition, a maximum intensity projection image was created. Region-growing segmentation of each maximum intensity projection image was then used to yield two discrete whole heart perfusion territories—a territory of "blushed" myocardium and a territory of "non-blushed" myocardium—representing the reference perfusion territories, where the details have previously been reported [17]. The left ventricular component of each reference LCA_{REF} and RCA_{REF} perfusion territory was then isolated, as shown in Figs. 1 and 2.

Myocardial mass correspondence

The myocardial mass of the AHA and MCP territories were compared with the myocardial mass of reference territories via linear regression, Bland-Altman analysis, root-mean-square error (RMSE), adjusted R^2, Lin's concordance correlation coefficient (CCC) [22], and Pearson's r (r). Ninety-five percent confidence intervals (CI) for adjusted R^2, CCC, and r were provided as (CI_{lower}, CI_{upper}). Myocardial mass was estimated by multiplying the volume of AHA, MCP, or reference territory by the mean density of myocardial tissue (1.053 g/mL).

Spatial correspondence of the myocardium

To evaluate spatial correspondence between AHA and MCP with reference coronary perfusion territories, Dice's similarity coefficient and mean minimum Euclidean distance were computed, as previously described [17, 23]. Dice's similarity coefficient is a spatial overlap index and a reproducibility validation metric. Its value ranges from 0, indicating no spatial overlap between two sets of binary segmentation results, to 1, indicating complete overlap. For the six right-dominant animals, reference territories of each coronary artery that were acquired from the same animal were averaged together. This yielded a total of twelve reference perfusion territories, six LCA and six RCA reference territories. Thus, a total of twenty-four measurements were made, twelve for each reader.

Per-segment relative mass root-mean-square error analysis

For the six right-dominant animals, within each of the 17 segments of the AHA method, the assigned mass of AHA and MCP perfusion territories was compared with the mass of LCA_{REF} and RCA_{REF} perfusion territories, respectively. Average root-mean-square error for each of the 17 segments of the AHA method was calculated, across all six animals, and normalized to the mean mass of the corresponding AHA segment, to yield the per-segment relative root-mean-square error for AHA and MCP perfusion territories. The means of both readers' per-segment relative mass root-mean-square error were calculated, for each of the 17 segments of the AHA model.

MCP application in a left-dominant case

A comparison of AHA and MCP perfusion territory mass distributions was performed in one left-dominant animal. For this comparison, AHA perfusion territories were only segmented by reader 2 (S. Malkasian). A single intravenous contrast injection acquisition was used to

derive LAD_{MCP}, $LCx_{MCP,}$ RCA_{MCP}, LAD_{AHA}, LCx_{AHA}, and RCA_{AHA} perfusion territories [15].

Inter-observer analysis of the AHA technique

LCA_{AHA} and RCA_{AHA} perfusion territories from each reader were also compared with measure inter-observer variability. Mass correspondence, Dice's similarity coefficient and mean minimum Euclidean distance were measured between corresponding AHA perfusion territories from readers 1 and 2.

Statistical analysis

A two-tailed paired *t* test was used to compare differences between the mass of AHA or MCP perfusion territories with the mass of REF perfusion territories. A one-tailed paired *t* test was used to compare differences in spatial correspondence metrics and per-segment root-mean-square error, between AHA and MCP perfusion territories. Further, a two-tailed paired *t* test was also used to compare differences between AHA perfusion territories determined by the two readers. Statistical significance for this study was defined as p value < 0.05. Unless stated otherwise, all data are presented as mean ± standard deviation.

Results

Myocardial mass correspondence

The mean left ventricle mass from CT images for all animals was measured to be 53.33 ± 7.25 g. The mean LCA_{AHA}, LCA_{MCP}, and LCA_{REF} masses were 39.63 ± 5.58 g (p value < 0.05), 42.40 ± 5.65 g, and 42.52 ± 5.91 g, respectively. The mean RCA_{AHA}, RCA_{MCP}, and RCA_{REF} masses were 13.70 ± 1.89 g (p value < 0.05), 10.93 ± 2.43 g, and 10.81 ± 3.07 g, respectively. Mass correspondence using linear regression analysis is further detailed in Table 2 and Fig. 3. Each reader's individual mass measurements and linear regression analysis are shown in Supplemental Tables 1 and 2.

Spatial correspondence of myocardium

The mean Dice similarity coefficient for all AHA perfusion territories, when compared with corresponding reference perfusion territories, was 0.82 ± 0.13 (p value < 0.05). The mean Dice similarity coefficient for all MCP perfusion territories, when compared with corresponding reference perfusion territories, was 0.92 ± 0.06 (p value < 0.05). Further, the mean minimum Euclidean distance for all AHA perfusion territories, when compared with corresponding reference perfusion territories, was 5.04 ± 1.80 mm (p value < 0.05). The mean minimum Euclidean distance for all MCP perfusion territories, when compared with corresponding reference perfusion territories, was 2.88 ± 0.89 mm (p value < 0.05). A perfect mean minimum Euclidean distance would be 0 mm. Spatial correspondence for LCA and RCA perfusion territories is shown in Table 3. Each reader's individual spatial correspondence measurements are shown in Supplemental Table 3.

Per-segment relative root-mean-square error

The overall relative RMSE for the AHA and MCP techniques were 16.24 ± 18.25% and 6.08 ± 6.38%, respectively. The relative RMSE was lowest in segment 1 for both the AHA and MCP techniques. The relative RMSE was highest in segments 4 and 17 for the AHA and MCP techniques, respectively. Per-segment relative RMSE is shown in Fig. 4.

MCP application in a left-dominant case

For the left-dominant animal, the masses of the LAD_{AHA}, LCx_{AHA}, and RCA_{AHA} perfusion territories were 24.66, 20.61, and 22.44 g, respectively. The results for masses of the LAD_{MCP}, LCx_{MCP}, and RCA_{MCP} perfusion territories were 25.45, 36.63, and 5.63 g, respectively. The left-dominant comparison is summarized in Fig. 5.

Inter-observer analysis

The mean mass of LCA_{AHA} perfusion territories was 48.22 ± 5.12 g for reader 1 and 54.37 ± 4.53 g for reader 2. The mean mass of RCA_{AHA} perfusion territories was 21.26 ± 2.63 g for reader 1 and 22.20 ± 2.45 g for reader 2. The spatial correspondence between reader 1 and reader 2 for LCA_{AHA} and RCA_{AHA} perfusion territories were related by a Dice similarity coefficient of 0.77 ± 0.14. Further inter-observer analysis is shown in Table 4.

Discussion

In this study, coronary perfusion territories created using the MCP technique and the current clinical standard AHA model were directly compared with reference standard LCA and RCA perfusion territories. The main findings of this study are as follows: (1) the MCP technique demonstrated better correspondence with reference standard perfusion territories than the AHA model, and (2) both techniques demonstrated relatively decreased correspondence with reference standard perfusion territories in the inferior and inferoseptal wall.

For the MCP technique, segments 17, 10, 4, 15, and 9 showed the highest relative root-mean-square error. Similarly, for the AHA technique, segments 4, 17, 10, 15, and 9 showed the highest relative root-mean-square error, in agreement with previous findings [8, 10, 12]. Further, the AHA method systematically over-estimated the RCA perfusion territory, in agreement with Chung et al [24]. The slight discordance of the MCP technique in the inferior and inferoseptal walls could be improved with more extensive coronary centerline extraction. In the inferoseptal wall, extraction of intraseptal coronary branches would likely improve the performance of the MCP technique, although these branches are difficult to visualize using CT imaging [11, 12].

The results of this study suggest that extensive coronary centerline extraction is important for accurate quantification of coronary perfusion territories using the MCP technique. This is particularly true in the inferior and inferoseptal wall. Furthermore, another CT-based technique [19] has recently been shown to provide prognostic value in the assessment of CAD [6]. All CT-based techniques are expected to show a decreased performance in the inferior wall.

Occlusion or partial occlusion of coronary arteries imparts high morbidity and mortality. Previous studies have shown that the most important determinant of infarct size is the myocardial mass distal to the occlusion [25–28]. Therefore, information about the myocardial mass at risk can be used to determine the potential infarct severity of a coronary artery occlusion. This is particularly important in the case of a more proximal lesion. Several studies have demonstrated the short-comings of the AHA model [8–12]. Furthermore, many studies have demonstrated the prognostic value of CT-based subtended myocardium when assessing CAD [6]. Ultimately, the results of this study are clinically impactful as the MCP technique has the potential to provide more accurate patient-specific coronary perfusion territories, in contrast to the generalized population-based AHA model. In addition to coronary CT angiography, in imaging modalities such as myocardial CT perfusion imaging or hybrid SPECT/CT imaging, where physiological and morphological data are acquired simultaneously, the MCP technique could be used to accurately attribute perfusion defects to a specific coronary artery stenosis.

This study has several limitations. First, the study lacks left-dominant subjects for analysis and comparison. Unfortunately, the prevalence of left-dominant circulations in swine is about 5% [29]; hence, a very large sample size will be necessary for future validation of the MCP technique in left-dominant circulations. Future studies with a larger sample size, including left-dominant subjects, are necessary. Additionally, this study utilized a swine animal model, while the AHA method was developed for human use. However, swine coronary vasculature is well-documented to be similar to that of humans [29, 30]. Further investigation using human subjects must be pursued. Another limitation is that the influence of superimposed CAD on the performance of the MCP technique as compared with that of the AHA technique was not assessed. Specifically, coronary centerlines at least to second-generation branches are necessary for the accurate performance of the MCP technique. The accuracy of the MCP technique could be reduced if severe CAD or poor CTA quality prevents proper visualization and extraction of coronary centerlines. Yet, the majority of patients undergoing noninvasive functional assessment of CAD have intermediate severity disease, as patients with indications of acute coronary syndrome will not typically undergo cardiac CT imaging [31]. Thus, contrast enhancement distal to a stenosis of interest remains adequate, especially with nitroglycerin administration to increase vessel caliber during imaging. Although, in patients with chronically obstructed CAD and collateral circulation, adequate coronary centerline extraction may be possible via retrograde collateral contrast flow [32]. Further studies are necessary to better understand the effects of collateral circulation on the MCP technique. Additionally, in patients with rapid heart rates, the use of beta blockers is known to reduce motion artifact and improve CT angiographic quality [33], to ensure extensive coronary centerline extraction.

Other limitations are that the accuracy of LAD and LCx perfusion territory assignment, as well as myocardial mass at-risk distal to a stenosis, calculated by the MCP technique, remains to be validated. Future studies should perform selective intracoronary contrast injections into the LAD or LCx to validate the accuracy of the MCP technique for measuring LAD and LCx perfusion territories. Lastly, inter-observer analysis showed that the application of the AHA technique was moderately variable. The AHA method is semi-automated; its application still relies on user input, making the application of the AHA

model vulnerable to user error [34]. Similarly, the MCP technique is also semi-automated, requiring the extraction of vessel centerlines and myocardial wall segmentation. That said, automation of vessel centerlines [35] and myocardial segmentation [36] could help eliminate the associated intra- and inter-observer variability of the MCP technique.

In conclusion, the minimum cost path (MCP) myocardial perfusion territory assignment technique was able to more accurately quantify the left and right coronary artery perfusion territories than the existing AHA model. Hence, the technique has the potential to provide accurate patient-specific coronary perfusion territories, making comprehensive morphological and physiological assessments of CAD more realizable for patients in need.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

AHA	American Heart Association
CAD	Coronary artery disease
CCC	Concordance correlation coefficient
CI	Confidence interval
CMR	Cardiac magnetic resonance
CT	Computed tomography
LCA	Left coronary artery
LCx	Left circumflex coronary artery
MCP	Minimum cost path
PDA	Posterior descending artery
PET	Positron emission tomography
RCA	Right coronary artery
REF	Reference standard
RMSE	Root-mean-square error
SPECT	Single-photon emission computed tomography

References

1. Davies RF, Goldberg AD, Forman S et al. (1997) Asymptomatic Cardiac Ischemia Pilot (ACIP) study two-year follow-up: outcomes of patients randomized to initial strategies of medical therapy versus revascularization. Circulation 95:2037–2043 [PubMed: 9133513]
2. Madsen JK, Grande P, Saunamaki K et al. (1997) Danish multicenter randomized study of invasive versus conservative treatment in patients with inducible ischemia after thrombolysis in acute myocardial infarction (DANAMI). DANish trial in Acute Myocardial Infarction. Circulation 96:748–755 [PubMed: 9264478]
3. Hachamovitch R, Hayes SW, Friedman JD, Cohen I, Berman DS (2003) Comparison of the short-term survival benefit associated with revascularization compared with medical therapy in patients with no prior coronary artery disease undergoing stress myocardial perfusion single photon emission computed tomography. Circulation 107:2900–2907 [PubMed: 12771008]
4. Shaw LJ, Berman DS, Maron DJ et al. (2008) Optimal medical therapy with or without percutaneous coronary intervention to reduce ischemic burden: results from the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial nuclear substudy. Circulation 117:1283–1291 [PubMed: 18268144]
5. Topol EJ, Nissen SE (1995) Our preoccupation with coronary luminology. The dissociation between clinical and angiographic findings in ischemic heart disease. Circulation 92:2333–2342 [PubMed: 7554219]
6. Kang SJ, Kim YH, Lee JG et al. (2019) Impact of subtended myocardial mass assessed by coronary computed tomographic angiography-based myocardial segmentation. Am J Cardiol 123: 757–763 [PubMed: 30545479]
7. Cerqueira MD, Weissman NJ, Dilsizian V et al. (2002) Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart. A statement for healthcare professionals from the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association. Circulation 105:539–542 [PubMed: 11815441]
8. Javadi MS, Lautamaki R, Merrill J et al. (2010) Definition of vascular territories on myocardial perfusion images by integration with true coronary anatomy: a hybrid PET/CT analysis. J Nucl Med 51:198–203 [PubMed: 20080895]
9. Ortiz-Perez JT, Rodriguez J, Meyers SN, Lee DC, Davidson C, Wu E (2008) Correspondence between the 17-segment model and coronary arterial anatomy using contrast-enhanced cardiac magnetic resonance imaging. JACC Cardiovasc Imaging 1:282–293 [PubMed: 19356440]
10. Pereztol-Valdes O, Candell-Riera J, Santana-Boado C et al. (2005) Correspondence between left ventricular 17 myocardial segments and coronary arteries. Eur Heart J 26:2637–2643 [PubMed: 16183694]
11. Thomassen A, Petersen H, Johansen A et al. (2015) Quantitative myocardial perfusion by O-15-water PET: individualized vs. standardized vascular territories. Eur Heart J Cardiovasc Imaging 16: 970–976 [PubMed: 25944051]
12. Donato P, Coelho P, Santos C, Bernardes A, Caseiro-Alves F (2012) Correspondence between left ventricular 17 myocardial segments and coronary anatomy obtained by multi-detector computed tomography: an ex vivo contribution. Surg Radiol Anat 34:805–810 [PubMed: 22569833]
13. Cerci RJ, Arbab-Zadeh A, George RT et al. (2012) Aligning coronary anatomy and myocardial perfusion territories: an algorithm for the CORE320 multicenter study. Circ Cardiovasc Imaging 5: 587–595 [PubMed: 22887690]
14. Hubbard L, Ziemer B, Lipinski J et al. (2016) Functional assessment of coronary artery disease using whole-heart dynamic computed tomographic perfusion. Circ Cardiovasc Imaging 9:1–8
15. Hubbard L, Lipinski J, Ziemer B et al. (2018) Comprehensive assessment of coronary artery disease by using first-pass analysis dynamic CT perfusion: validation in a swine model. Radiology 286:93–102 [PubMed: 29059038]
16. Le H, Wong JT, Molloi S (2008) Estimation of regional myocardial mass at risk based on distal arterial lumen volume and length using 3D micro-CT images. Comput Med Imaging Graph 32:488–501 [PubMed: 18595659]

17. Malkasian S, Hubbard L, Dertli B, Kwon J, Molloi S (2018) Quantification of vessel-specific coronary perfusion territories using minimum-cost path assignment and computed tomography angiography: validation in a swine model. J Cardiovasc Comput Tomogr 12:425–435 [PubMed: 30042078]
18. Carlsson M, Saeed M (2008) Intracoronary injection of contrast media maps the territory of the coronary artery: an MRI technique for assessing the effects of locally delivered angiogenic therapies. Acad Radiol 15:1354–1359 [PubMed: 18995187]
19. Kurata A, Kono A, Sakamoto T et al. (2015) Quantification of the myocardial area at risk using coronary CTangiography and Voronoi algorithm-based myocardial segmentation. Eur Radiol 25:49–57 [PubMed: 25173626]
20. Ide S, Sumitsuji S, Yamaguchi O, Sakata Y (2017) Cardiac computed tomography-derived myocardial mass at risk using the Voronoi-based segmentation algorithm: a histological validation study. J Cardiovasc Comput Tomogr 11:179–182 [PubMed: 28431861]
21. Modat M, Ridgway GR, Taylor ZA et al. (2010) Fast free-form deformation using graphics processing units. Comput Methods Programs Biomed 98:278–284 [PubMed: 19818524]
22. Lin LI (1989) A concordance correlation coefficient to evaluate reproducibility. Biometrics 45:255–268 [PubMed: 2720055]
23. Taha AA, Hanbury A (2015) Metrics for evaluating 3D medical image segmentation: analysis, selection, and tool. BMC Med Imaging 15:29 [PubMed: 26263899]
24. Chung MS, Yang DH, Kim YH et al. (2017) Myocardial segmentation based on coronary anatomy using coronary computed tomography angiography: development and validation in a pig model. Eur Radiol 27:4044–4053 [PubMed: 28342101]
25. Lowe JE, Reimer KA, Jennings RB (1978) Experimental infarct size as a function of amount of myocardium at risk. Am J Pathol 90:363–377 [PubMed: 623206]
26. Reimer KA, Ideker RE, Jennings RB (1981) Effect of coronary-occlusion site on ischemic bed size and collateral blood-flow in dogs. Cardiovasc Res 15:668–674 [PubMed: 7326685]
27. Koyanagi S, Eastham CL, Harrison DG, Marcus ML (1982) Transmural variation in the relationship between myocardial infarct size and risk area. Am J Physiol 242:H867–H874 [PubMed: 6282144]
28. Lee JT, Ideker RE, Reimer KA (1981) Myocardial infarct size and location in relation to the coronary vascular bed at risk in man. Circulation 64:526–534 [PubMed: 7261285]
29. Weaver ME, Pantely GA, Bristow JD, Ladley HD (1986) A quantitative study of the anatomy and distribution of coronary arteries in swine in comparison with other animals and man. Cardiovasc Res 20:907–917 [PubMed: 3802126]
30. Sahni D, Kaur GD, Jit H, Jit I (2008) Anatomy & distribution of coronary arteries in pig in comparison with man. Indian J Med Res 127:564–570 [PubMed: 18765875]
31. Taylor AJ, Cerqueira M, Hodgson JM et al. (2010) ACCF/SCCT/ACR/AHA/ASE/ASNC/NASCI/SCAI/SCMR 2010 appropriate use criteria for cardiac computed tomography. A report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, the Society of Cardiovascular Computed Tomography, the American College of Radiology, the American Heart Association, the American Society of Echocardiography, the American Society of Nuclear Cardiology, the North American Society for Cardiovascular Imaging, the Society for Cardiovascular Angiography and Interventions, and the Society for Cardiovascular Magnetic Resonance. J Am Coll Cardiol 56:1864–1894 [PubMed: 21087721]
32. Choi JH, Kim EK, Kim SM et al. (2014) Noninvasive evaluation of coronary collateral arterial flow by coronary computed tomographic angiography. Circ Cardiovasc Imaging 7:482–490 [PubMed: 24700691]
33. Pannu HK, Alvarez W Jr, Fishman EK (2006) Beta-blockers for cardiac CT: a primer for the radiologist. AJR Am J Roentgenol 186: S341–S345 [PubMed: 16714607]
34. Zakkaroff C, Biglands JD, Greenwood JP et al. (2016) Patient-specific coronary blood supply territories for quantitative perfusion analysis. Comput Methods Biomech Biomed Eng Imaging Vis 3:1–18

35. Yang G, Kitslaar P, Frenay M et al. (2012) Automatic centerline extraction of coronary arteries in coronary computed tomographic angiography. Int J Cardiovasc Imaging 28:921–933 [PubMed: 21637981]

36. Zhu L, Gao Y, Appia V et al. (2013) Automatic delineation of the myocardial wall from CT images via shape segmentation and variational region growing. IEEE Trans Biomed Eng 60:2887–2895 [PubMed: 23744658]

Key Points

- The minimum cost path (MCP) technique accurately determines left and right coronary artery perfusion territories, as compared with the American Heart Association 17-segment (AHA) model.
- The minimum cost path (MCP) technique could be applied to cardiac computed-tomography angiography images to accurately determine patient-specific left and right coronary artery perfusion territories.
- The American Heart Association 17-segment (AHA) model often fails to accurately determine left and right coronary artery perfusion territories, especially in the inferior and inferoseptal walls of the left ventricular myocardium.

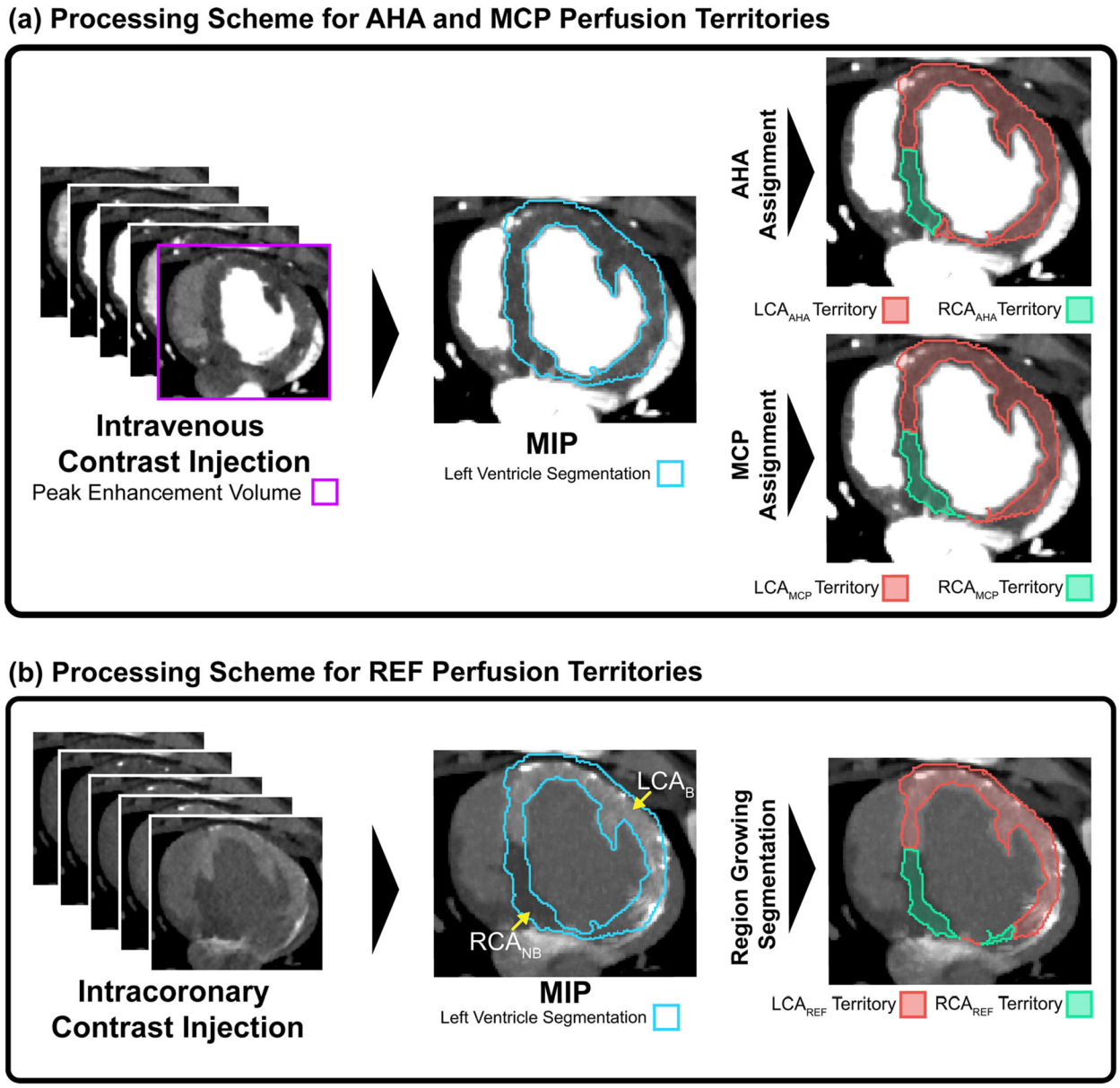

Fig. 1.

Image acquisition and processing scheme. The complete image dataset of one animal is shown. The six right-dominant swine underwent at least two dynamic computed tomography (CT) volume acquisitions following this image processing scheme. Each dynamic CT volume acquisition was comprised of twenty consecutive volume scans. **a** During the first dynamic CT acquisition, contrast was injected intravenously. The American Heart Association 17-segment (AHA) model and the minimum cost path (MCP) technique were applied to this acquisition. **b** During subsequent dynamic CT acquisitions, the left or right coronary artery (LCA and RCA) was cannulated and intracoronary contrast injection was performed. In this case, an LCA intracoronary contrast injection was performed. Blushed and non-blushed myocardium was automatically segmented, using region-growing segmentation, to derive reference standard (REF) LCA and RCA perfusion territories. AHA,

American Heart Association 17-segment model; B, blushed myocardium; CT, computed tomography; LCA, left coronary artery; MCP, minimum cost path; MIP, maximum intensity projection; NB, non-blushed myocardium; RCA, right coronary artery; REF, reference standard

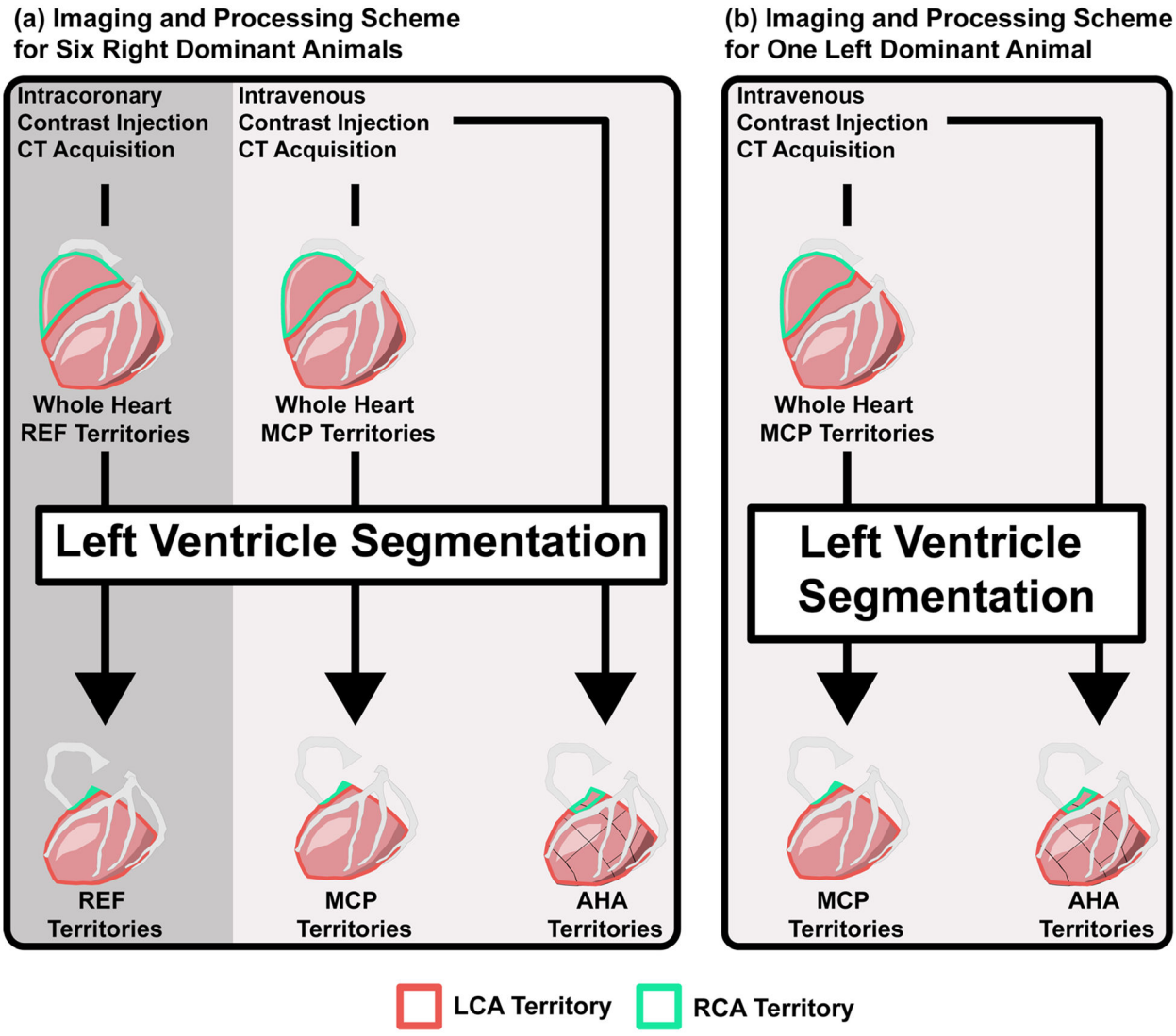

Fig. 2.

Experimental workflow. **a** The six right-dominant animals underwent at least one intracoronary contrast injection computed tomography acquisition, from which whole heart reference standard (REF) perfusion territories were determined for the left and right coronary arteries (LCA and RCA). Additionally, each right-dominant animal underwent an intravenous contrast injection CT acquisition, used to determine whole heart minimum cost path (MCP) and American Heart Association (AHA) perfusion territories for the LCA and RCA. Each reader performed a left ventricle segmentation on the six right-dominant animals, used to isolate left ventricle MCP and REF perfusion territories from the respective whole heart perfusion territories. Each reader also applied the AHA technique. Thus, for each of the right-dominant animals, two sets of AHA, MCP, and REF perfusion territories for the LCA and RCA were determined; one set for each reader's left ventricle segmentation and AHA model application. Whole heart REF and MCP perfusion territories were determined in a previous study [17]. **b** The single left-dominant animal only underwent one intravenous contrast injection CT acquisition, as this animal image data was used from a

previous study where intracoronary contrast injections were not performed [15]. Consequently, only MCP and AHA perfusion territories were determined. Whole heart MCP perfusion territories were isolated to a left ventricle segmentation, as described previously. Only reader 2 applied left ventricle segmentation and determined AHA perfusion territories for the left-dominant animal. AHA, American Heart Association 17-segment model; LCA, left coronary artery; MCP, minimum cost path; RCA, right coronary artery; REF, reference standard

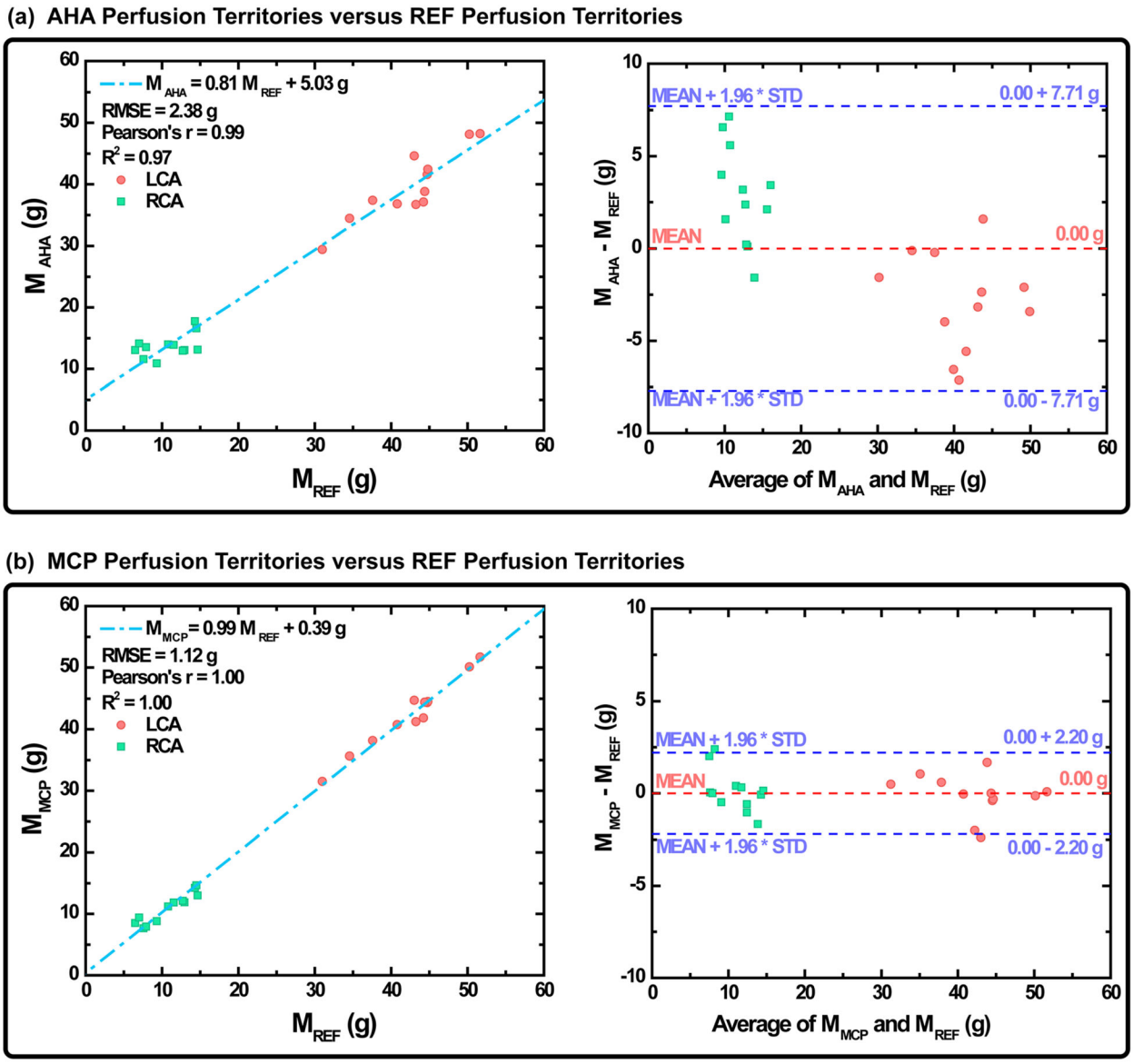

Fig. 3.

Linear regression mass correspondence and Bland-Altman analysis of the American Heart Association 17-segment (AHA) model and minimum cost path (MCP) perfusion territories with reference standard (REF) perfusion territories. Linear regression analysis and Bland-Altman analysis were performed to assess mass correspondence of left and right coronary artery (LCA and RCA) perfusion territories discerned using the American Heart Association 17-segment (AHA) model and the vessel-specific minimum cost path technique (MCP), compared with reference standard (REF) coronary perfusion territories. This analysis was performed on the six right-dominant animals. **a** Linear regression and Bland-Altman analyses of AHA perfusion territories, as compared with those of reference perfusion territories, are shown. **b** Linear regression and Bland-Altman analyses of MCP perfusion territories, as compared with those of reference perfusion territories, are shown. Analysis was performed by combining the AHA, MCP, and REF perfusion territories from readers 1

and 2; thus, a total of 24 samples were assessed for LCA and RCA perfusion territory correspondence. Linear regression analysis is also shown in Table 2. A breakdown of linear regression analysis on a per-reader and per-vessel basis can be found in Supplemental Table 2. AHA, American Heart Association 17-segment model; LCA, left coronary artery; MCP, minimum cost path; RCA, right coronary artery; REF, reference standard; RMSE, root-mean-square error

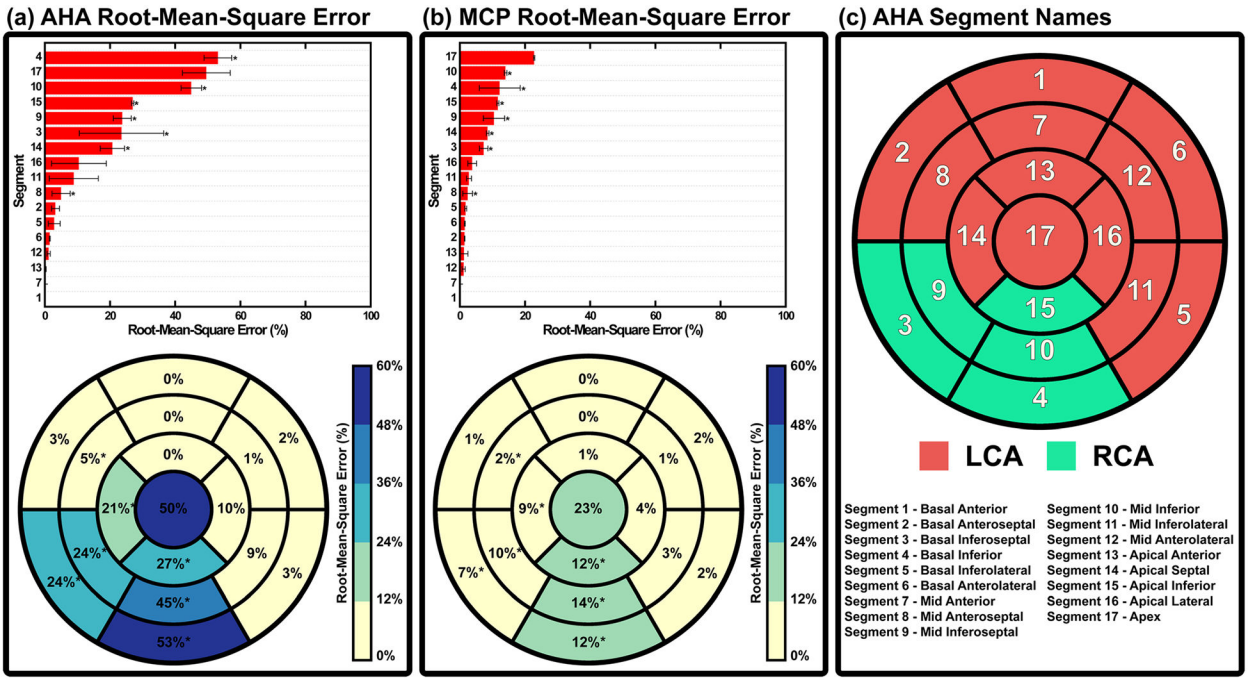

Fig. 4.

Per-segment root-mean-square error. For each right-dominant animal, assigned left coronary artery (LCA) and right coronary artery (RCA) territories derived using the American Heart Association 17-segment (AHA) model were compared with the minimum cost path (MCP) territories, within each of the 17 segments comprising the AHA method. Root-mean-square error was calculated by comparing the amount of correctly assigned MCP or AHA mass within each of the 17 segments with the reference standard (REF) perfusion territory mass within the corresponding segment. Root-mean-square error was then normalized to the total mass of the corresponding AHA segment. The mean root-mean-square error, normalized to the mean mass of each AHA segment, for LCA and RCA perfusion territories derived using the (**a**) AHA method and (**b**) the MCP method is shown. Panel c depicts the standard AHA model segments with corresponding segment names and coronary artery assignment. Error bars in each bar graph represent the standard deviation of the relative root-mean-square error between readers 1 and 2, for each segment. Beneath each bar graph, a bullseye plot with a colored representation of the percent root-mean-square error for each AHA segment is also shown. Corresponding *p* values for illustrating statistically significant differences between AHA and MCP parameters are shown in Supplemental Table 4c. AHA, American Heart Association 17-segment model; LCA, left coronary artery; MCP, minimum cost path; RCA, right coronary artery; REF, reference standard. The single asterisk indicates statistically different per-segment root-mean-square error between respective AHA and MCP assignment, as indicated by a *p* value of < 0.05

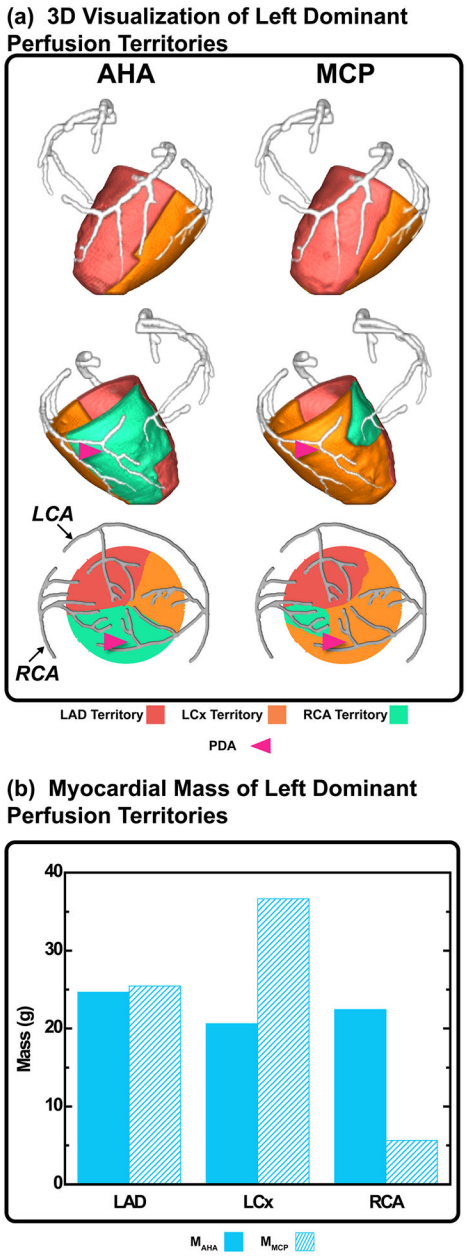

Fig. 5.

Assessment of the left-dominant case. American Heart Association 17-segment (AHA) model and minimum cost path (MCP) coronary perfusion territory distributions were compared in a left-dominant animal. Right and left dominance was determined based on the origin of the posterior descending artery (PDA) from either the left or the right coronary artery. **a** Left ventricular coronary perfusion territories derived using the AHA and MCP techniques are shown superimposed with coronary artery centerlines. In the left-dominant animal, the PDA originates from the left circumflex coronary artery (LCx). Coronary perfusion territories for the left anterior descending coronary artery (LAD), LCx, and RCA, derived using the AHA and MCP techniques, are shown. Additionally, bullseye plots of left perfusion territories are shown, superimposed with coronary artery centerlines. **b** Coronary

perfusion territory mass distribution in the left ventricle was also assessed for AHA and MCP techniques. AHA, American Heart Association 17-segment model; LAD, left anterior descending coronary artery; LCx, left circumflex coronary artery; MCP, minimum cost path; PDA, posterior descending coronary artery; RCA, right coronary artery; REF, reference standard; RMSE, root-mean-square error

Table 1

Computed tomography imaging parameters

Parameter	
Model and vendor	Aquilion One, Canon Imaging
Energy	100 kVp
Current	200 mA
Detector collimation	320 × 0.50 mm
Gantry rotation speed	0.35 s
Effective dose of dynamic acquisition	26.4 mSv
Reconstruction interval	75% of R-R interval
Reconstruction kernel	FC03
Reconstruction voxel size	0.79 × 0.79 × 0.50 mm to 0.43 × 0.43 × 0.50 mm (depending on field of view)

Table 2

Linear regression analysis of the American Heart Association 17-segment (AHA) model and minimum cost path (MCP) coronary perfusion territory mass correspondence with reference standard (REF) coronary perfusion territories

Method (*N*)	SLOPE	Intercept	R^2	Pearson's *r*	CCC	RMSE
AHA (24)	0.81* (0.75, 0.87)	5.03* (3.12, 6.94)	0.97* (0.96, 0.98)	0.99* (0.98, 0.99)	0.98* (0.97, 0.99)	2.38
MCP (24)	0.99* (0.96, 1.01)	0.39* (−0.51, 1.29)	1.00* (0.99, 1.00)	1.00* (1.00, 1.00)	1.00* (1.00, 1.00)	1.12

Where applicable, values are represented as value (95% CI_{LOWER}, 95% CI_{UPPER})

95% *CI*, 95% confidence interval; *AHA*, American Heart Association 17-segment model perfusion territories; *CCC*, Lin's concordance correlation coefficient; *LCA*, left coronary artery; *MCP*, minimum cost path perfusion territories; *RCA*, right coronary artery; *RMSE*, root-mean-square error

*Indicates non-overlap of the 95% CI, i.e., significant differences between corresponding AHA and MCP parameters

Table 3

Spatial correspondence of the American Heart Association 17-segment (AHA) model and minimum cost path (MCP) left and right coronary artery (LCA and RCA) perfusion territories compared with that of reference standard (REF) LCA and RCA perfusion territories

Vessel (*N*)	DSC_{AHA}	DSC_{MCP}	MMD_{AHA} (mm)	MMD_{MCP} (mm)
LCA (12)	0.92 ± 0.03 *	0.97 ± 0.01 *	4.99 ± 1.82 *	2.50 ± 0.39 *
RCA (12)	0.73 ± 0.08 *	0.86 ± 0.05 *	5.08 ± 1.85 *	3.26 ± 1.30 *
LCA + RCA (24)	0.82 ± 0.13 *	0.92 ± 0.06 *	5.04 ± 1.80 *	2.88 ± 1.02 *

All values are presented as mean ± STD

AHA, American Heart Association 17-segment model perfusion territories; *DSC*, Dice's similarity coefficient; *MCP*, minimum cost path perfusion territories; *LCA*, left coronary artery; *MMD*, mean minimum Euclidean distance; *RCA*, right coronary artery; *R1*, measurements made using reader 1 AHA perfusion territories and left ventricle segmentation; *R2*, measurements made using reader 2 AHA perfusion territories and left ventricle segmentation

* Indicates p value < 0.05, i.e., significant differences between corresponding AHA and MCP parameters

Table 4

Inter-observer analysis of mass (M) for the American Heart Association 17-segment model perfusion territories from readers 1 (R1) and 2 (R2)

Vessel (*N*)	M_{R1} (g)	M_{R2} (g)	DSC	MMD (mm)
LCA (6)	48.22 ± 5.12	54.37 ± 4.53	0.80 ± 0.10	1.68 ± 0.85
RCA (6)	21.26 ± 2.63	22.20 ± 2.45	0.73 ± 0.17	2.21 ± 1.41

All values are presented as mean ± STD

AHA, American Heart Association 17-segment model; *DSC*, Dice's similarity coefficient; *LCA*, left coronary artery; *MMD*, mean minimum Euclidean distance; *R1*, reader 1 AHA perfusion territories; *R2*, reader 2 AHA perfusion territories; *RCA*, right coronary artery; *STD*, standard deviation