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Research paper

Coronary computed tomography angiography-based SYNTAX score for comprehensive assessment of advanced coronary artery disease

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A R T I C L E I N F O

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Anatomic SYNTAX score
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Complex coronary artery disease

A B S T R A C T

Background: Since the initial attempt to adapt the anatomical SYNTAX score (aSS) to coronary computed tomography angiography (CCTA), CCTA imaging technology has evolved, and is currently used as a "decision-maker" for revascularization strategy in complex coronary artery disease (CAD) and has rendered necessary some updating of the aSS to the CCTA modality.

Objectives: The aim is to provide updated definitions of the aSS derived from CCTA in patients with complex CAD undergoing CABG.

Methods: The modifications of CCTA-aSS are the following; (i) updated definition and detection criteria of total occlusion (TO) in CCTA based on length assessment, (ii) inclusion of scoring points for serial bifurcations located in one single coronary segment. (iii) inclusion of weighing score points for lesions located distal to a TO, not visualized on conventional coronary angiography, but visible in CCTA, (iv) removal of thrombus and bridging collateral items from the weighing score, considering the limited diagnostic capability of CCTA in detecting these specific lesion characteristics.

Results: the updated CCTA-aSS was tested in a first-in-man study using the sole guidance of CCTA for the planning and performance of bypass surgery in complex CAD (n = 114). An interobserver analysis showed excellent reproducibility (ICC = 0.96, 95 % confidence interval 0.94–0.97).

Conclusion: The updated CCTA-aSS was implemented in a cohort of patients with complex CAD undergoing CABG with the sole guidance of CCTA and FFR_{CT} and the Inter-reproducibility of the analysis of the updated score was found excellent. The prognostic value of the modified CCTA-aSS will be examined in future studies.

Abbreviations: 3VD, three-vessel disease; CAD, coronary artery disease; CCTA, coronary computed tomography angiography; ICA, invasive coronary angiography; LM, left main; MPR, multi-planar reconstructions; SS, SYNTAX score; TO, total occlusion.

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1. Introduction

The anatomical SYNTAX score (aSS) was developed originally to quantify the anatomical extent and complexity of coronary artery disease (CAD) on conventional invasive coronary angiography (ICA). In the analysis of the SYNTAX trial, aSS demonstrated its prognostic impact on mid and long-term outcomes of patients undergoing percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG).[1,2] Since then, the aSS has been endorsed in international guidelines for the assessment of lesion complexity before revascularization; ESC/EACTS (Class 1, Level B),[3] ACC/AHA/SCAI (Class 2b, Level B),[4] and JCS/JSCVS (Class 1, Level B).[5]

In the ICA-aSS, each stenotic lesion was scored according to the severity of luminal diameter narrowing and the theoretical amount of blood flow supplied to the myocardium by the coronary segment in which the lesion is located, the so-called "myocardial weighing score" introduced by Leaman in 1981.[6] After coronary segmentation and calculation of the "myocardial" weighing score, additional scoring

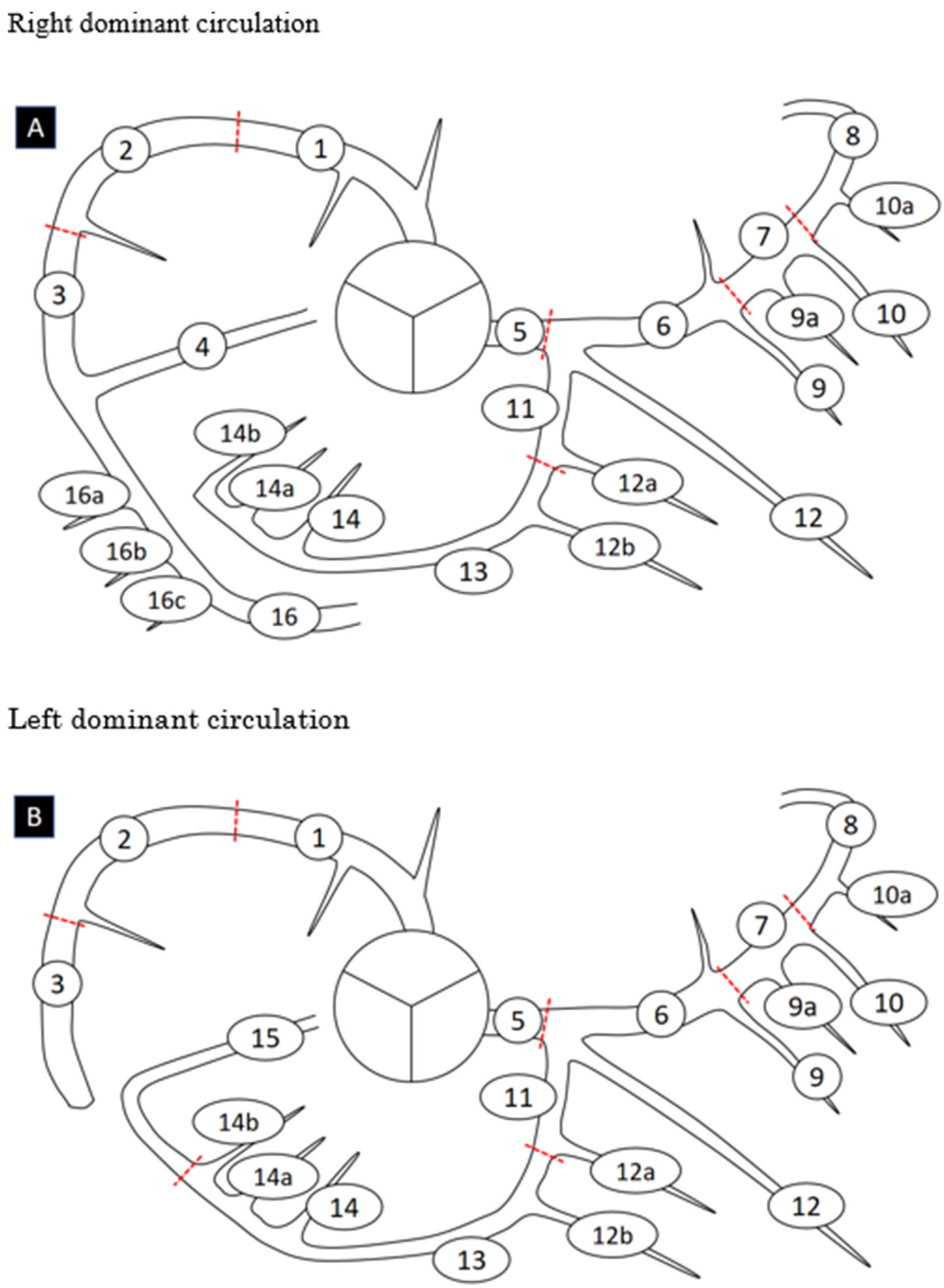

Fig. 1. Segment division and numbering in CCTA-anatomic SYNTAX score (CCTA-aSS). Segment division and numbering in updated CCTA-aSS in right dominant system (A) and left dominant system (B). See Appendix for the definition of the coronary segment written in the text.

points are attributed to the lesion's complexities such as bifurcated/-trifurcated, long lesion, severely calcified lesion, tortuous, and diffuse lesion, etc.

Since the initial attempt in 2013 to adapt the aSS to CCTA.[7] the technology of CCTA imaging has evolved, resulting in greater feasibility of assessment of complex CAD by reducing motion artefacts and blooming artefacts. Therefore, the current CCTA-aSS calculator needed to be updated.

This paper aims to provide a practical update on the CCTA-aSS, and its impact on calculation, and to ascertain the inter-reproducibility of the adapted CCTA-aSS.

2. Methods

First, the coronary system is classified as a right-dominant or left-dominant circulation based on the origin of the posterior descending

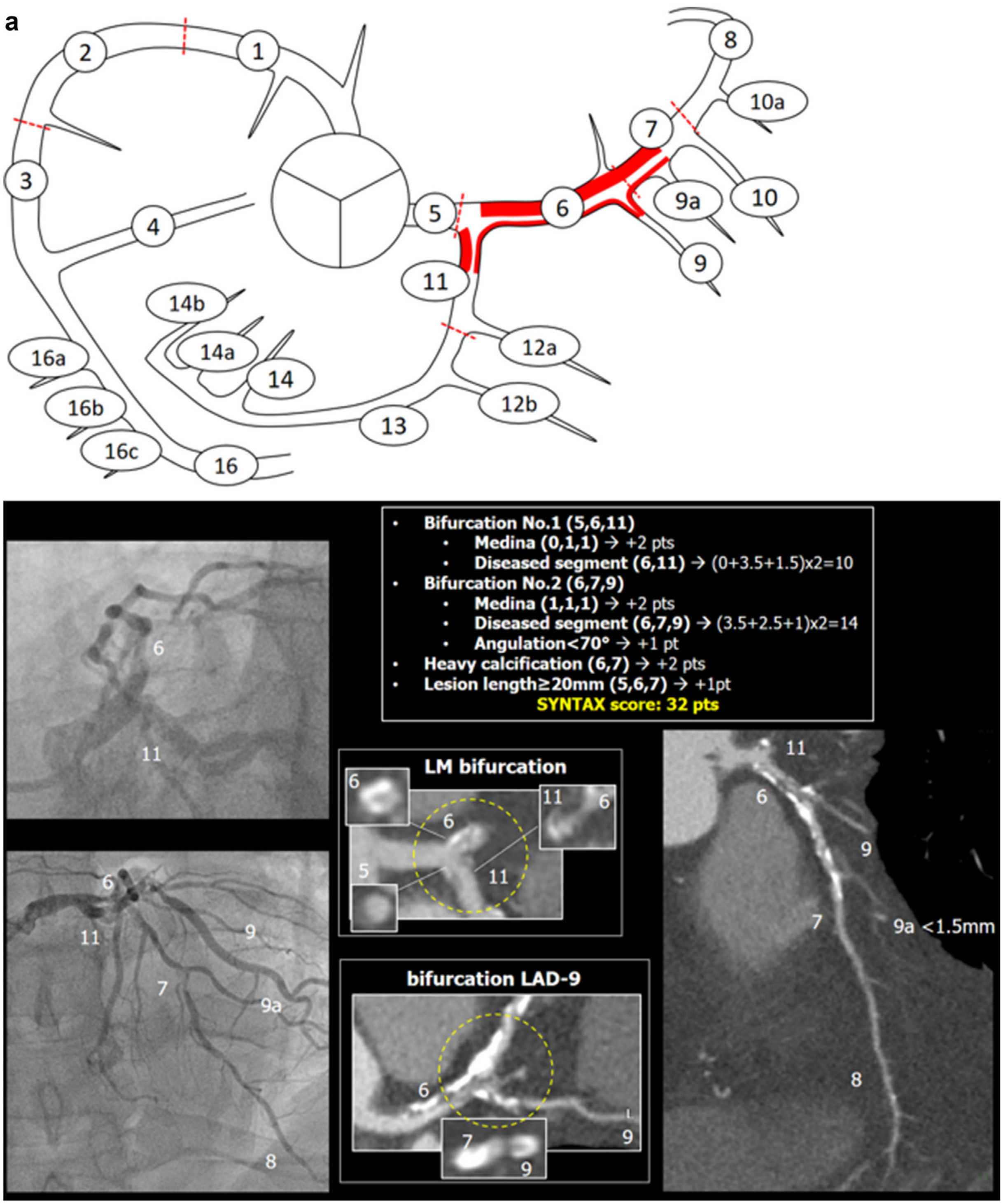

Fig. 2a. An example of 2 serial diseased bifurcations, First, the score for the diseased segments of the left main bifurcation (5,6,11; Medina 0,1,1) is calculated, then segment weight points for the diseased segments (6,7,9) of the bifurcation LAD/diagonal (1,1,1). Finally, other lesion characteristics (angulation, calcification) are considered. Left lower panel shows the ICA of the patient. Abbreviations: LM, left main; LCX, left circumflex; ICA, invasive coronary angiography.

artery.[1] Segment division is defined based on Journal of Cardiovascular Computed Tomography guideline applying the same segment numbering as the original aSS (Fig. 1, Text A).[8] Each coronary lesion with ≥50 % luminal obstruction in vessel diameter of more than 1.5 mm is visually and individually scored; (a) each lesion in a specific coronary segment is weighted by a specific factor based on the amount of myocardium subtended by that segment according to the score of Leaman et al.,[6] and (b) additional score points are attributed to complex morphologic features such as total occlusion, bifurcation/trifurcation, aorto-ostial lesion, long lesion, severe tortuosity, severe calcification, thrombus, and diffuse disease/small vessel as tabulated in Table A. The overall SS summed up all the score points.

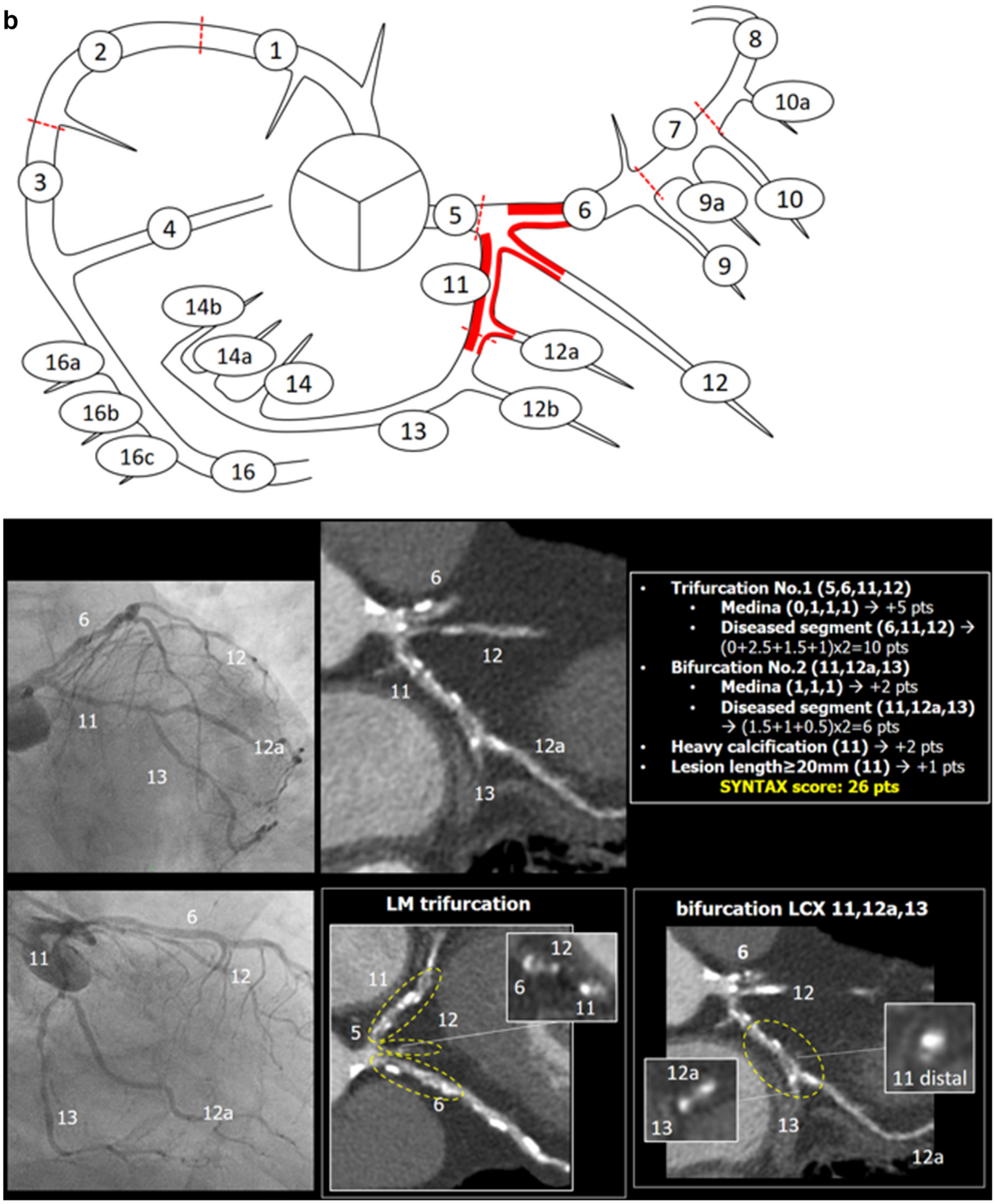

Fig. 2b. An example of serial trifurcation (5.6,12,11) and bifurcation (11,12a,13). First, segment weight points for the diseased segments are calculated. Then, additional points for the LM trifurcation, (Medina 0,1,1,1), subsequently the second bifurcation involving segments 11,12a,13; bifurcation points are added. Finally, other lesion characteristics are considered. Left lower panel shows the ICA of the patient. Abbreviations: LM, left main; LCX, left circumflex; ICA, invasive coronary angiography.

The following changes were made to apply aSS to CCTA:

1) The presence of TO in CCTA is further characterized by length criteria that improve the accuracy of detection with respect to conventional ICA.
2) The CCTA score accounts for narrowings of more than 50 % involved in serial bifurcation/trifurcations and multiple TOs in the same coronary segment.
3) Lesions located behind a TO assessable on CCTA are included in the score, whilst they are usually not scored on conventional invasive coronary angiography since they are not reliably visualized. In conventional cine angiography the duration of injection, the amount of contrast medium injected and the duration of cine filming may impact the visualization of the distal bed due to incomplete opacification through collaterals.
4) Omission of scoring of intra-coronary thrombus and ipsilateral bridging collateral not reliably detected on CCTA.

The comparison of the ICA-SYNTAX score definition (2009) and conventional and new CCTA-SYNTAX score definitions (2013 and 2023) are summarized in Table B.

2.1. *Definition and characterization of TO in CCTA*

TO, -in conventional ICA-, is defined as an occluded coronary artery with a Thrombolysis In Myocardial Infarction (TIMI) flow zero.[9] No

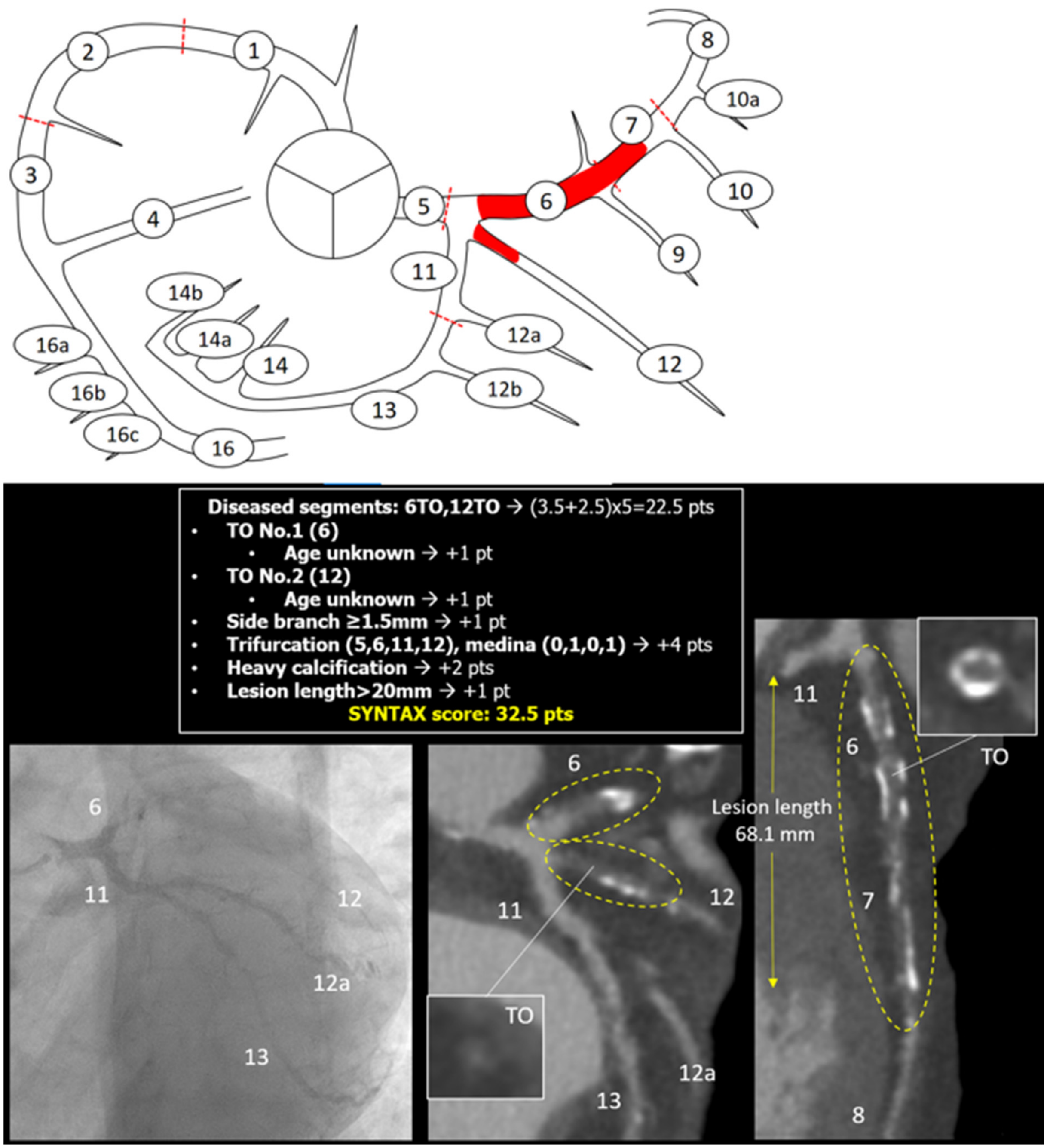

Fig. 3. One example of a trifurcation lesion that includes 2 TOs. First, are calculated the segment weight points for the 2 TOs that are part of the trifurcation (5,6,11,12; Medina 0,1,0,1) since both branches are located within ≤4 mm from the POB. Then, additional points for each TO were added. Finally, other lesion characteristics are considered. Left lower panel shows the ICA of the patient. Abbreviations: TO, total occlusion; POB, point of bifurcation; ICA, invasive coronary angiography.

special CCTA definition is mentioned in the expert consensus[10] or guidelines,[8] although von Erfa et al. reported that >9 mm length of TO in CCTA corresponded to a specificity of 100 % and sensitivity of 70 % in detecting TO in ICA.[11] Measuring the length of the TO lesions is a unique capability of CCTA, which cannot be always determined in ICA. Among 114 patients of the FAST TRACK CABG trial who underwent both CCTA and ICA before CABG, 86 vessels were diagnosed as TO in CCTA whereas 45 were confirmed as TO in ICA. The Youden index of receiver operating characteristics curve for agreement on the presence of TO in CCTA and ICA is 5.5 mm in terms of TO length in CCTA (area under the curve 0.78, sensitivity 91.1 %, specificity 61.1 %, Figure B). Therefore a 6 mm length of occlusion with a complete luminal absence of contrast media in consecutive cross-sections in multi-planar reconstructions (MPR) of CCTA was adopted as the definition of TO in the modified CCTA-aSS. Table B summarized the diagnostic ability of TO in ICA from CCTA, based on von Erfa criteria and current trial criteria. In addition, Garcia-Garcia et al. reported the relation of the length of TO in ICA and CCTA in ICA-defined 124 consecutive TOs.[12]

2.2. *Scoring of serial bifurcation lesions in the same coronary segment*

A bifurcation lesion is defined as a coronary stenosis adjacent to and/or involving either the mother branch or/and a daughter side branches of ≥1.5 mm in diameter with a stenosis equal to or of more than 50 %.[1,7,13] The minimum lumen diameter (MLD) in the bifurcation (3 branches)/trifurcation (4 branches) must be located ≤4 mm from the point of bifurcation (POB) of the 3/4 branches according to the consensus of the Bifurcation Academic Research Consortium (Bif-ARC, Figure A).[14] The Medina classification for trifurcation is also adapted from the Bif-ARC consensus. As mentioned above, CCTA-aSS algorithm takes into account the score points of the two serial bifurcations/trifurcations lesions located in the proximal and distal parts of the same coronary segment connecting the two bifurcations; (i) includes all the lesions involved in the connecting segment, (ii) provides Medina classification and angulation (<70° or not) for each individual bifurcation/trifurcation, (iii) and considers other morphologic features classically recorded in the ICA-aSS. Fig. 2 shows 2 examples of dual serial bifurcation/trifurcation lesions. Of note, each bifurcation should be primarily named according to the main mother branch, no matter whether the main branch is diseased or not. For instance, bifurcation 1 in Fig. 2a should be viewed as LM bifurcation (segment 5), although the LM itself does not have significant stenosis). As a consequence of this approach, the stenotic lesion located in the proximal segment 6, as the daughter branch of the bifurcation 5,6,11 will also as the mother branch of the bifurcation 6,7,9 be scored a second time as a stenotic lesion in the distal part of segment 6.

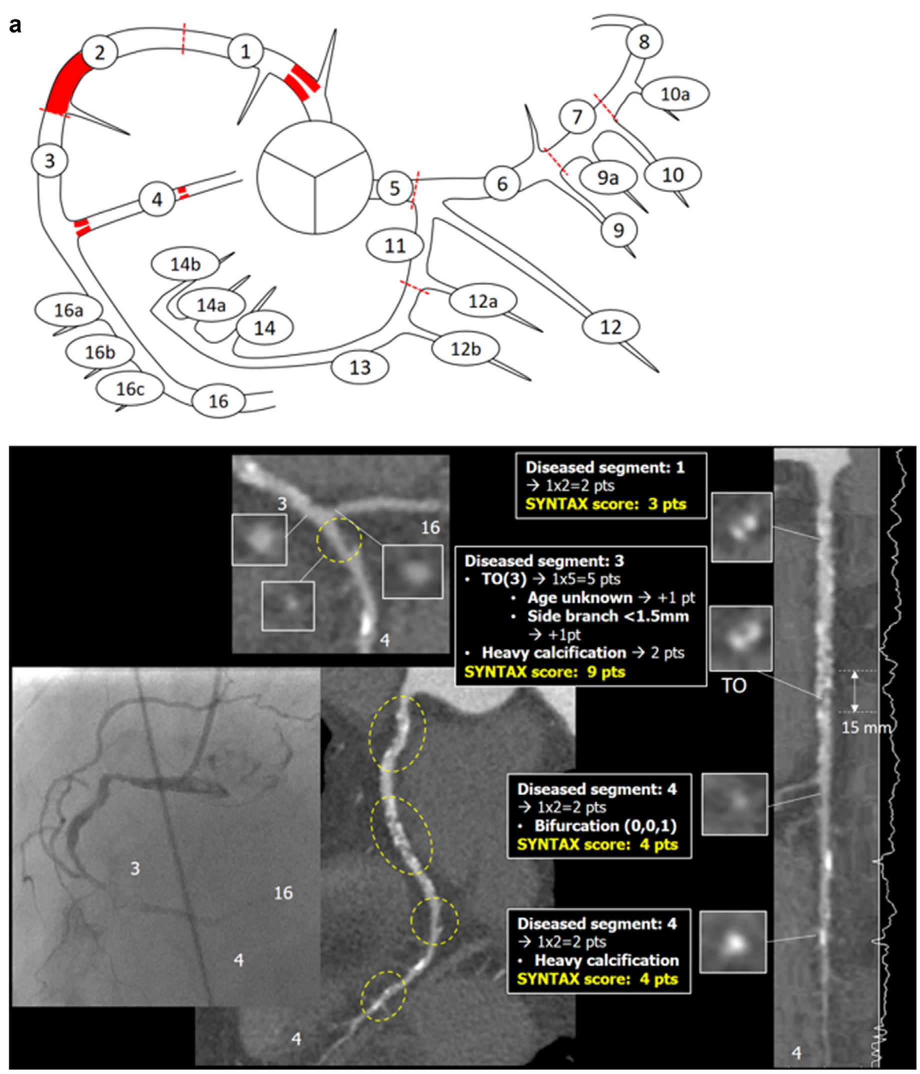

Fig. 4a. One example of serial lesions distal to a TO in RCA. There are 4 serial lesions including a total occlusion in the RCA. In segment 3, there is a 15 mm long total occlusion (complete absence of contrast media in the luminal cross-sections) in MPR. Left lower panel shows the ICA of the patient with a narrowing in segment 1 and a total occlusion in segment 3. Abbreviations: TO, total occlusion; MPR, multiplanar reconstruction; ICA, invasive coronary angiography.

2.3. TO involved in bifurcation

The CCTA-aSS calculation may report in its new version 2 TO in the same coronary segment and the new algorithm allows the combined scoring of bifurcations/trifurcations and total occlusion. Fig. 3 shows 1 example of 2 TOs in 1 trifurcation lesion.

2.4. Lesions scored distally to a total occlusion

Assessment of stenotic lesion distal to is usually feasible in CCTA through reliable contrast opacification of the vascular bed distal to the TO whilst opacification of the distal bed is variable and inconsistent with ICA.[10] Whenever visible on CCTA, lesions distal to are scored.

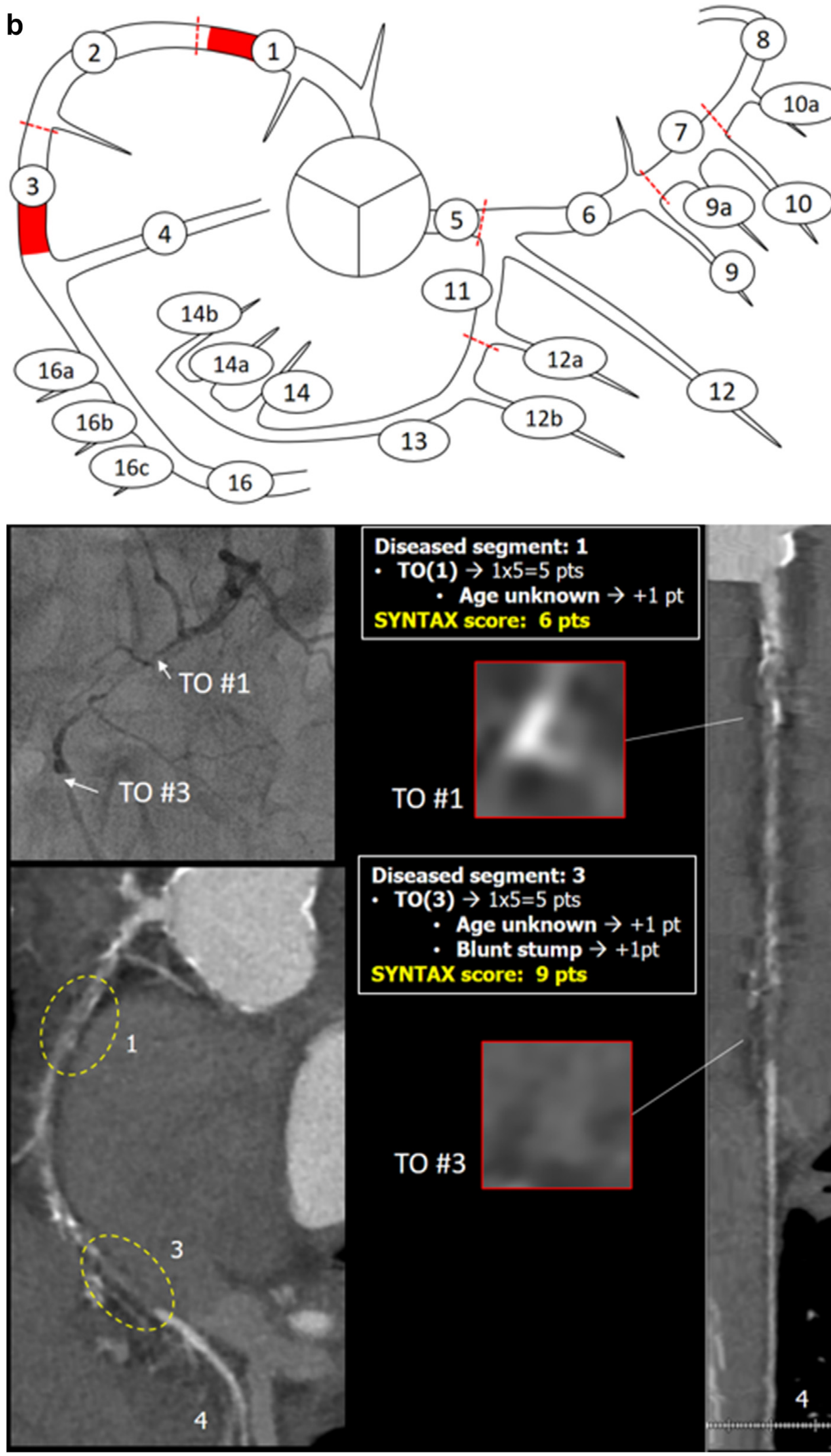

Fig. 4b. One example of sequential two TOs in RCA. In segment 1 and 3, there are 2 serial total occlusions (complete absence of contrast media in the lumen in cross-sections) in MPR (length of TO: 6 mm and 21 mm, respectively). Left upper panel shows the ICA of the patient. Abbreviations: TO, total occlusion; MPR, multiplanar reconstruction; ICA, invasive coronary angiography.

The new CCTA-aSS algorithm also allows us to include weighing score of lesions located distally to a TO. Fig. 4a shows one example of multiple lesions detected distally to a TO. Also, sequential TOs in one vessel can be scored, although it is not so frequently observed (Fig. 4b).

2.5. Omission of thrombus and bridging collateral in CCTA

In CCTA, thrombus has more or less the same level of Hounsfield unit as a soft plaque (Fig. 5). It is difficult to distinguish thrombus from plaque except on special occasions.[15] It is evident that CCTA does not detect thrombus and thereby underestimates the aSS, although the frequency of intra-luminal thrombus is low in the FAST TRACK CABG trial (2 lesions scored in ICA and both of them were undetected in CCTA).[16] Also, detection of bridging collaterals in CCTA is unreliable compared to ICA. None of the guidelines or expert consensuses recommends the report of ipsilateral bridging collateral in CCTA.[8,10] Therefore, we excluded the items -thrombus and bridging collaterals-from the CTA-aSS.

2.6. Diffuse disease

At variance with ICA-aSS, CCTA-aSS could differentiate genuine small vessels from small but diffusely diseased vessels since the imaging modality can detect and quantify the plaque, whereas angiography can only assess a luminogram, which does not distinguish genuine small vessels from diffusively diseased vessel with plaques.

In the ICA-aSS, diffuse disease is defined as atherosclerotic narrowings involving more than 75 % of the length of coronary segments while in CCTA-aSS the presence of plaques with cross-sections $\geq$1 mm^2 specifically characterizes diffuse disease.[1] Thus, in the CCTA-aSS small vessels without plaque should not be given any weighing score point.

3. Results-reproducibility of new CT SYNTAX score

We assessed the reproducibility of CCTA-aSS in 114 consecutive patients in the FASTTRACK CABG trial who were diagnosed with complex CAD by CCTA (Table D).[17] Among them, CCTA-aSS was obtained in 113 subjects. Two CCTA experts performed an interobserver reproducibility analysis. Means and standard deviations (SD) in the CCTA-aSS reported by observers A and B were 42.6 $\pm$ 15.4 and 42.8 $\pm$ 14.3, respectively. Excellent interobserver interclass correlation (ICC) was reported (ICC = 0.96, 95 % confidence interval 0.94–0.97, $p < 0.001$, Bland-Altman plot is presented in Figure C. The mean difference was 0.03 and the boundaries of agreement were 8.43. Cohen's Kappa showed almost perfect agreement ($\kappa = 0.82$) between analysts when concordance of classification into low (<22), intermediate ($\geq$22, $\leq$33), and high (>33) CCTA-aSS was analyzed (also see Figure D and Table E).

4. Discussion

Since the initial description of CCTA-aSS in 2013, more than 45 reports have been published focusing on CCTA-aSS. Recently deep learning has rekindled the interest in an automated assessment of the score.[18] These publications aimed to unravel the resemblance or dissimilitude between the ICA-aSS and CCTA-aSS with the ultimate goal of predicting cardiac events and mortality solely with non-invasive CCTA data combining CCTA-aSS and clinical characteristics.[19] Nowadays, more complex CAD patients are examined by CCTA as a first line of diagnosis. It was felt opportune to review critically the CCTA-aSS and make necessary changes over certain points of methodology. For the appropriate diagnosis, it must be emphasized that CCTA must be performed under the supervision of trained radiologists based on precise acquisition protocol (Text C).

First, the reproducibility of the updated CCTA-aSS score is important. In the ICA-aSS, a weighted kappa of 0.61 has been reported for tertile partitioning of aSS.[1] The intraobserver variability of the original CCTA-aSS tertiles showed almost perfect agreement ($\kappa = 0.80$).[7] The updated CCTA-aSS showed comparable agreement among 2 CCTA experts ($\kappa = 0.82$). In order to have the same level of reproducibility in daily clinical practice, attempts to apply deep learning to CCTA-aSS are currently ongoing.[18]

At a vessel level analysis, serial lesions detected distally to and stenosis $\geq$50 % involving serial bifurcations in the same coronary segment

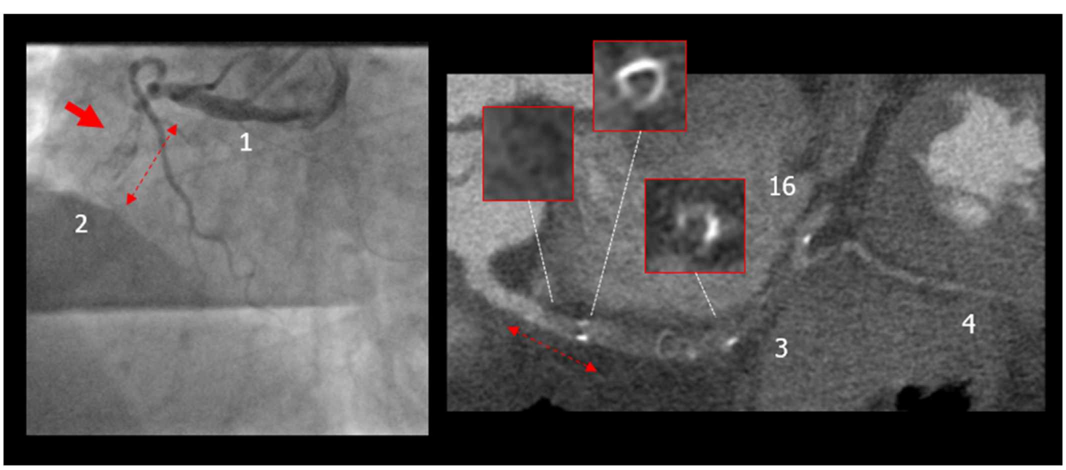

Fig. 5. One example of coronary artery thrombus in segment 2 in ICA and CCTA. In the ICA projection, ovoid and irregular intraluminal filling defect or lucency surrounded by contrast medium detected distal to the coronary stenosis (red arrow in the left panel). The corresponding location in the CCTA-MPR is presumably indicated with a dotted line with two red arrows. The thrombus is not visible on CCTA. Also, it is difficult to distinguish texture of the thrombus-related occlusion from the texture of the rest total occlusion due to a similar level of Hounsfield unit (left and middle cross-sections and right cross-section in the right panel). Abbreviations: CCTA, coronary computed tomography angiography; AM, acute marginal branch; ICA, invasive coronary angiography; MPR, multiplanar reconstruction. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

are the two critical modifications in the updated CCTA-aSS. The capability of assessing and scoring stenoses located distally to and CCTA-aSS of serial bifurcations located at the origin and the extremity of the same coronary segment tends to increase numerically the overall score at least in 13 out of 113 cases in the FAST TRACK CABG trial with average increase of 6 points.

Shortly, it is expected that an increasing number of patients will be assessed on the appropriateness of surgical or percutaneous revascularization with CCTA rather than ICA. The aSS had provided evidence that the patient's prognosis following PCI or CABG can be predicted, and it is desirable to extend that prognostic capability to CCTA-aSS.

The relationship between CCTA-aSS and ICA-aSS has been affected by the newly introduced modifications, which resulted in some systematic score discordance in vessels and patients that have extensive lesions involving serial bifurcations in the same coronary segment and stenotic lesions distal to total occlusions. Ultimately, the regional myocardial blood flow in the absolute value of each diseased coronary segment (ml/min/g) supplying the various parts of the left ventricle can be computed and an actual specific weighting score can be attributed to each diseased vessel in each patient (Figure E).

CCTA-aSS calculation is more time-consuming including the image reconstruction part compared to ICA-aSS. Moreover, three-dimensional measurement of lesion length and judgement of bifurcation angulation and tortuosity is more complicated than two-dimensional luminography. It is strongly recommended to apply artificial intelligence (AI) for using CCTA-aSS in daily clinical practice to secure reproducibility and for time savings. AI-based scoring allows to quantify all the important parameters like diameter stenosis, lesion length, spacious angle, plaque volume and composition and to apply an ideal threshold.

4.1. Limitation

Blooming artefacts from calcified plaque also contribute to overestimation.[20] Merging potential solutions such as photon-counting detectors, high-resolution CT reconstruction, subtraction techniques and post-processing techniques, with a special emphasis on deep learning techniques could contribute to circumventing the current drawback.[20,21] Conversely, bridging collateral and intracoronary thrombus only detected in ICA could contribute to the underscoring of the CCTA-aSS compared to ICA-aSS, but these components were proved to be a minor incidence in the FAST TRACK CABG trial.

5. Conclusions

In view of the specific and extra diagnostic capabilities of CCTA in patients with complex anatomy, further adaptations were defined in CCTA-aSS based on ICA-aSS. The measurement of CCTA-aSS is reasonably reproducible. These modifications in the CCTA-aSS should reinforce the prognostic value of the score and ongoing implementation of AI in the CCTA-aSS should promote its use in clinical practice.

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Appendix

Text A. Definition of the coronary segment

- 1. Right coronary artery (RCA) proximal: From the ostium to one half the distance to the acute margin of the heart.
- 2. RCA mid: From the end of first segment to acute margin of heart.
- 3. RCA distal: From the acute margin of the heart to the origin of the posterior descending artery.
- 4. Posterior descending artery (PDA): Running in the posterior interventricular groove.
- 16. PL branch from RCA: Posterolateral branch originating **from the RCA distal.**
- 16a PL branch from RCA a: First branch from segment 16.
- 16b PL branch from RCA b: Second branch from segment 16.
- 16c PL branch from RCA c: Third branch from segment 16.
- 5. Left main: From the ostium of the left coronary artery through bifurcation into left anterior descending (LAD) and left circumflex (LCx) branches.
- 6. LAD proximal: From end of left main to **the first large septal or first diagonal (>1.5 mm in size) whichever is most proximal.**
- 7. LAD mid: From end of LAD proximal to **one half the distance to the apex of the heart.**
- 8. LAD apical: **From end of mid LAD to the apex.**
- 9. First diagonal: The first diagonal originating from segment 6 or 7.
- 9a First diagonal a: Additional first diagonal originating from segment 6 or 7, before segment 8.
- 10. Second diagonal: Originating from segment 8 or the transition between segment 7 and 8.
- 10a Second diagonal a: Additional second diagonal originating from segment 8.
- 11. Proximal LCX: Main stem of circumflex from its origin of left main and including origin of first obtuse marginal branch.
- 12. Intermediate/anterolateral artery: Branch from trifurcating left main other than proximal LAD or LCX. It belongs to the LCX territory.
- 12a Obtuse marginal (OM) a: First side branch of LCX running in general to the area of obtuse margin of the heart.
- 12b OM b: Second additional branch of LCX running in the same direction as 12.
- 13. Distal LCX: The stem of the LCX distal to the origin of **12a**, and running along the posterior left atrioventricular groove. Calibre may be small or artery absent.
- 14. Left posterolateral: Running to the posterolateral surface of the left ventricle. May be absent or a division of OM branch.
- 14a Left posterolateral a: Distal from 14 and running in the same direction.
- 14b Left posterolateral b: Distal from 14 to 14 a and running in the same direction.
- 15. Posterior descending: Most distal part of dominant LCX when present. It gives origin to septal branches. When this artery is present, segment 4 is usually absent.

Table A: Definitions of words used in modified CCTA-anatomic SYNTAX scoring

Factors	Definition
Dominance	a) Right dominance: the posterior descending coronary artery is a branch of the right coronary artery (segment 4). b) Left dominance: the posterior descending artery is a branch of the left coronary artery (segment 15). Co-dominance does not exist as an option at the SYNTAX score.
Target lesion	Serial stenosis which plaque edges from 2 stenoses ≤4 mm apart. It should be scored as 1 lesion.
Total occlusion	No contrast media can be seen in consecutive intra-luminal cross-sections (6 mm).
Bridging collaterals	Not available in CCTA in general.
Trifurcation	A division of a main branch into three branches. Trifurcations are only scored for the following segment junctions: 3/4/16/16a, 5/6/11/12, 11/12a/12b/13, 6/7/9/9a and 7/8/10/10a.
Bifurcation	A bifurcation is defined as the division of a main, parent, branch into two daughter branches (with a minimum diameter of 1.5 mm). Bifurcations are only considered for the following segment junctions: 5/6/11, 6/7/9, 7/8/10, 11/13/12a, 13/14/14a and 3/4/16 and in case of left dominance 13/14/15. The MLD in at least 1 of the 3 segments is located ≤4 mm from the point of bifurcation (POB) or ≤3 mm from the polygon of confluence (POC). Bifurcation/trifurcation lesions are classified according to the Medina classification. Multiple counts are admitted in 1 lesion.
Aorto-ostial	A lesion is classified as aorto-ostial when it is located immediately at the origin of the coronary vessels from the aorta (≤4 mm). (applies only to segments 1, 5, 6 and 11).
Severe tortuosity	One or more bends of 90° or more, or three or more bends of 45°–90° proximal to the diseased segment.
Long lesion	Estimation of the length of that portion of the stenosis that has ≥50 % reduction in luminal diameter in the projection where the lesion appears to be the longest. (In case of a bifurcation lesion at least one of the branches has a lesion length of >20 mm).
Heavy calcification	Maximum encircling of peripheral calcification≥180° or >50 % CSA (i.e., calcium occupies more than half of the cross-sectional area at the point of CTO maximum calcification).
Thrombus	Not available in CCTA.
Diffuse disease	More than 75 % of the length of the segment(s) proximal to the lesion, at the site of the lesion or distal to the lesion having diameter stenosis ≥50 % or lumen diameter <2 mm due to the plaque. Existence of the plaque is defined as a plaque area ≥ 1 mm^2 at the cross-section.

Table B: Difference of definition between ICA, previous and new CCTA-SYNTAX score

Original (ICA) SYNTAX score definition (2009)	Previous CCTA-SYNTAX score definition (2013)	New CCTA-SYNTAX score definition (2023)
Dominance Right dominance: the posterior descending coronary artery is a branch of the right coronary artery (segment 4) Left dominance: the posterior descending artery is a branch of the left coronary artery (segment 15). Co-dominance does not exist as an option in the SYNTAX score.	**Dominance (unchanged)** Right dominance: the posterior descending coronary artery is a branch of the right coronary artery (segment 4) Left dominance: the posterior descending artery is a branch of the left coronary artery (segment 15). Co-dominance does not exist as an option in the SYNTAX score.	**Dominance (slight change)** Right dominance: the posterior descending coronary artery is a branch of the right coronary artery (segment 4) Left dominance: the posterior descending artery is a branch of the left coronary artery (segment 15). Co-dominance does not exist as an option in the SYNTAX score. Coronary segment division is based on SCCT guidelines.
Total occlusion No intra-luminal antegrade flow (TIMI 0) beyond the point of occlusion. However, retrograde opacification beyond the total occlusion might be maintained partially or totally by "bridging collaterals "(Small channels running in parallel to the vessel and connecting proximal vessel to distal and being responsible for the ipsilateral collateralization) and/or contra collaterals.	**Total occlusion (slight change)** No intra-luminal antegrade flow (TIMI 0) beyond the point of occlusion; it is visualized as the non-contrast enhanced segment of the vessel. Bridging collaterals and/or ipsi collaterals can only be measured by conventional angiography.	**Total occlusion (changed)** Defined as ≥6 mm length of occlusion with a complete luminal absence of contrast media in consecutive cross-sections of MPR of CCTA. Omission of ipsilateral bridging collateral scoring. Stenotic lesions located beyond a total occlusion but assessable on CCTA are included in the anatomic SYNTAX score.
Stump Defined as the entry site of the occlusion that has either a tapered- (central or eccentric) or a blunt appearance.	**Stump (unchanged)** Defined as the entry site of the occlusion that has either a tapered- (central or eccentric) or a blunt appearance.	**Stump (unchanged)** Defined as the entry site of the occlusion that has either a tapered- (central or eccentric) or a blunt appearance.
Segment numbers beyond the total occlusion Specify the first that is visualized by antegrade or retrograde contrast.	**Segment numbers beyond the total occlusion (unchanged)** Specify the first that is visualized by antegrade or retrograde contrast. (unreliable opacification)	**Segment numbers beyond the total occlusion (unchanged)** Specify the first that is visualized by antegrade or retrograde contrast. (reliable opacification)
Caliber of branch at the origin of the occlusion Specify whether this is smaller or at least 1.5 mm diameter.	**Caliber of branch at the origin of the occlusion (unchanged)** Specify whether this is smaller or at least 1.5 mm diameter.	**Caliber of branch at the origin of the occlusion (unchanged)** Specify whether this is smaller or at least 1.5 mm diameter
Trifurcation A trifurcation is a division of a main branch into three branches of at least 1.5 mm. Trifurcations are only scored for the following segment junctions: 3/4/16/16a, 5/6/11/12, 11/12a/12b/13, 6/7/9/9a and 7/8/10/10a.	**Trifurcation (unchanged)** A trifurcation is a division of a main branch into three branches of at least 1.5 mm. Trifurcations are only scored for the following segment junctions: 3/4/16/16a, 5/6/11/12, 11/12a/12b/13, 6/7/9/9a and 7/8/10/10a.	**Trifurcation (changed)** A trifurcation is a division of a main branch into three branches of at least 1.5 mm. Trifurcations are only scored for the following segment junctions: 3/4/16/16a, 5/6/11/12, 11/12a/12b/13, 6/7/9/9a and 7/8/10/10a. MLD's at least in 1 of the 4 trifurcated segments, located ≤4 mm from POB or ≤3 mm from POC determine the Medina classification (JACC 2022; 80 (1):63–88). Serial trifurcations located in the same segment and lesion characteristics of these serial trifurcations are additively accounted for in the new CCTA-SYNTAX score.

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Original (ICA) SYNTAX score definition (2009)	Previous CCTA-SYNTAX score definition (2013)	New CCTA-SYNTAX score definition (2023)
Bifurcation A bifurcation is a division of a main, parent, branch into two daughter branches of at least 1.5 mm. Bifurcation lesions may involve the proximal main vessel, the distal main vessel and the side branch according to the Medina classification. The smaller of the two daughter branches should be designated as the 'side branch'. In case of the main stem either the LCX or the LAD can be designated as the side branch depending on their respective calibers. Bifurcations are only scored for the following segment junctions: 5/6/11, 6/7/9, 7/8/10, 11/13/12a, 13/14/14a, 3/4/16 and 13/14/15.	**Bifurcation (unchenged)** A bifurcation is a division of a main, parent, branch into two daughter branches of at least 1.5 mm. Bifurcation lesions may involve the proximal main vessel, the distal main vessel and the side branch according to the Medina classification. The smaller of the two daughter branches should be designated as the 'side branch'. In case of the main stem either the LCX or the LAD can be designated as the side branch depending on their respective calibers. Bifurcations are only scored for the following segment junctions: 5/6/11, 6/7/9, 7/8/10, 11/13/12a, 13/14/14a, 3/4/16 and 13/14/15.	**Bifurcation (changed)** A bifurcation is defined as the division of a main, parent, branch into two daughter branches (with a minimum diameter of 1.5 mm). Bifurcations are only considered for the following segment junctions: 5/6/11, 6/7/9, 7/8/10, 11/13/12a, 13/14/14a and 3/4/16 and in case of left dominance 13/14/15. MLD's at least in 1 of the 3 bifurcated segments, located ≤4 mm from POB or ≤3 mm from POC determine the Medina classification (JACC 2022; 80 (1):63–88). Serial bifurcations located in the same segment and lesion characteristics of these serial bifurcations are additively accounted for in the new CCTA-SYNTAX score.
Aorto-ostial A lesion is classified as aorto-ostial when it is located immediately at the origin of the coronary vessels from the aorta (applies only to segments 1 and 5, or to 6 and 11 in case of double ostium of the LCA).	**Aorto-ostial (unchanged)** A lesion is classified as aorto-ostial when it is located immediately at the origin of the coronary vessels from the aorta (applies only to segments 1 and 5, or to 6 and 11 in case of double ostium of the LCA).	**Aorto-ostial (changed)** A lesion is classified as aorto-ostial when located immediately at the origin of the coronary vessels stemming from the aorta (≤4 mm). (applies only to segments 1, 5; 6 and 11 in case of double ostium of the LCA).
Severe tortuosity One or more bends of 90° or more, or three or more bends of 45°–90° proximal of the diseased segment.	**Severe tortuosity (unchanged)** One or more bends of 90° or more, or three or more bends of 45°–90° proximal of the diseased segment.	**Severe tortuosity (slight change)** One or more bends of 90° or more, or three or more bends of 45°–90° proximal of the diseased segment 3D spatial angle is available on commercial software.
Length >20 mm Estimation of the length of that portion of the stenosis that has ≥50 % reduction in luminal diameter in the projection where the lesion appears to be the longest. (In case of a bifurcation lesion at least one of the branches has a lesion length of >20 mm).	**Length >20 mm (unchanged)** Estimation of the length of that portion of the stenosis that has ≥50 % reduction in luminal diameter in the projection where the lesion appears to be the longest. (In case of a bifurcation lesion at least one of the branches has a lesion length of >20 mm).	**Length >20 mm (slight change)** Estimation of the length of that portion of the stenosis that has ≥50 % reduction in luminal diameter in the projection where the lesion appears to be the longest. (In case of a bifurcation lesion at least one of the branches has a lesion length of >20 mm). 3D length quantification is assessable on commercial workstations.
Heavy calcification Multiple persisting opacifications of the coronary wall visible in more than one projection surrounding the complete lumen of the coronary artery at the site of the lesion.	**Heavy calcification (changed)** Severe calcification was defined as the presence of calcium that occupies more than 50 % of the vessel cross-sectional area at any location within the lesion.	**Heavy calcification (changed)** Maximum encircling of peripheral calcification≥180° or >50 % cross-sectional area. Tissue characterization and calcified plaque volume quantification can be considered as well as deblooming software or use of photon CT scanner.
	Thrombus (changed) It is difficult for CCTA to distinguish thrombus from plaque; therefore this feature was no longer scored.	**Thrombus (unchanged)** It is difficult for CCTA to distinguish thrombus from plaque; therefore this feature was no longer scored.
Diffuse disease Present when at least 75 % of the length of any segment(s) proximal to the lesion, at the site of the lesion or distal to the lesion has a vessel diameter of <2 mm.	**Diffuse disease (unchanged)** Present when at least 75 % of the length of any segment(s) proximal to the lesion, at the site of the lesion or distal to the lesion has a vessel diameter of <2 mm.	**Diffuse disease (changed)** More than 75 % of the length of the segment(s) proximal to the lesion, at the site of the lesion or distal to the lesion having diameter stenosis ≥50 % or lumen diameter <2 mm due to the plaque. Existence of the plaque is defined as a plaque area ≥ 1 mm^2 at the cross-section. Diameter and area function, plaque burden assessment are currently available in conventional workstations and in AI software (Pack et al. Vis Comput Ind Biome. 2022 Dec 9; 5 (1).).

Abbreviations: ICA, invasive coronary angiography; CCTA, coronary computed tomography angiography; TIMI, Thrombolysis In Myocardial Infarction; POB, point of bifurcation; POC, polygon of confluence; LAD, left anterior descending artery; LCX, left cirumflex artery; LCA, left coronary artery; MPR, multi-planar reconstruction; AI, artificial intelligence.

Table C: Concordance of detecting TOs between ICA and CCTA

Publication/trial	Threshold of TO in CCTA	Ability to detect TO in ICA from CCTA by using criteria
Von Erfa et al.	9 mm	A lesion length of 9 mm or more was 100 % specific (95 % CI 0.80–1.0) and 70 % sensitive (95 % CI 0.46–0.87) for a complete occlusion: six occlusions had a length of less than 9 mm.
Garia-Garcia et al.		In total 142 consecutive CTOs defined by ICA, mean length was 16.6 ± 12.8 mm in ICA and 27.1 ± 19.4 mm in CCTA.
FAST TRACK CABG	5.5 mm	Area under the curve of ROC = 0.78, sensitivity 91.1 %, specificity 61.1 %.

Abbreviations: TO, total occlusion; CCTA, coronary computed tomography angiography; ICA, invasive coronary angiography; CI, confidence interval; ROC, receiver operative characteristics.

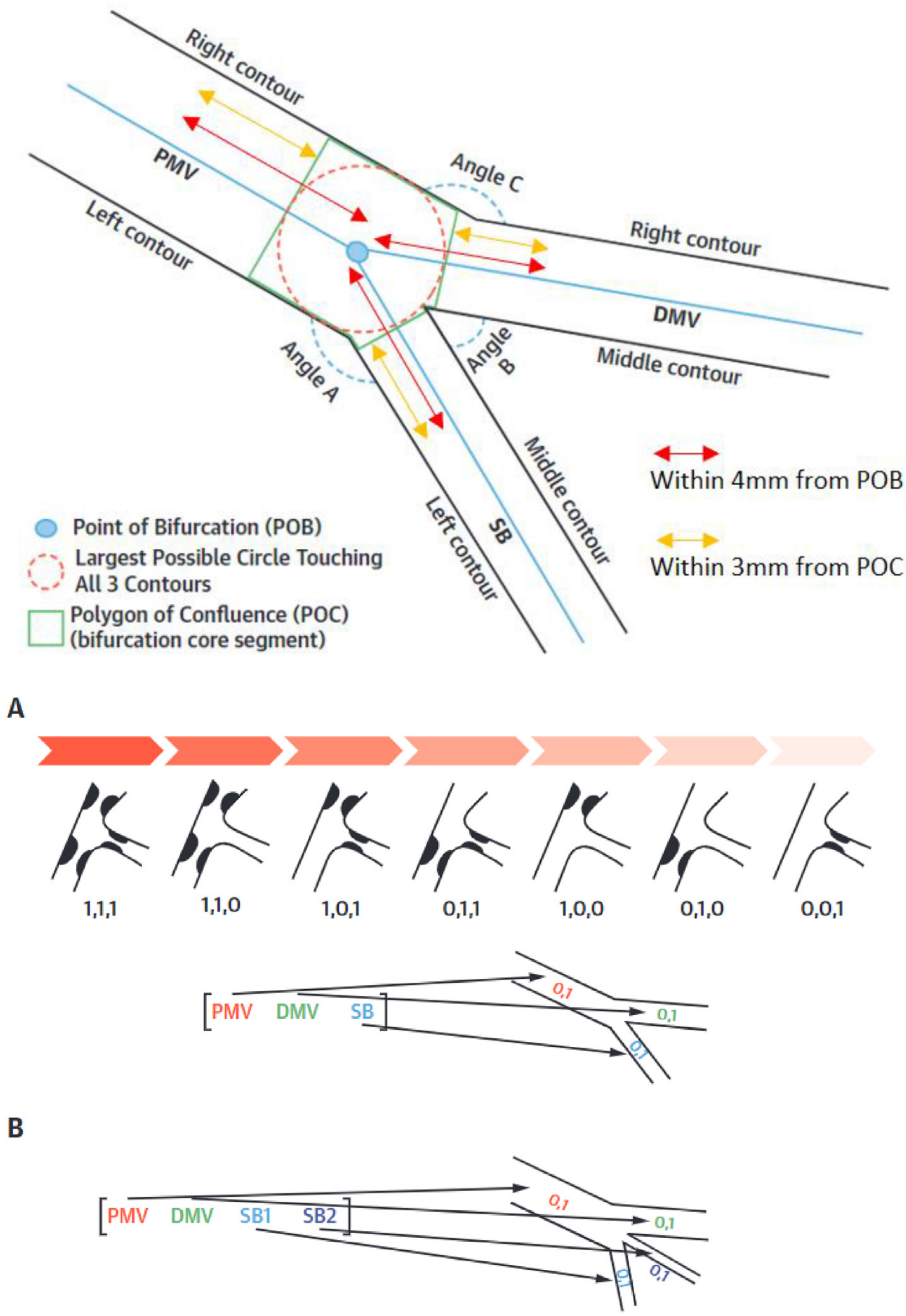

Fig. S1. Consensus of the definition of coronary bifurcation composition and medina classification, These figures are reproduced from (Lunardi M et al. Definitions and Standardized Endpoints for Treatment of Coronary Bifurcations. J Am Coll Cardiol. 2022; 80(1):63–88.) with copyright permission and modified.

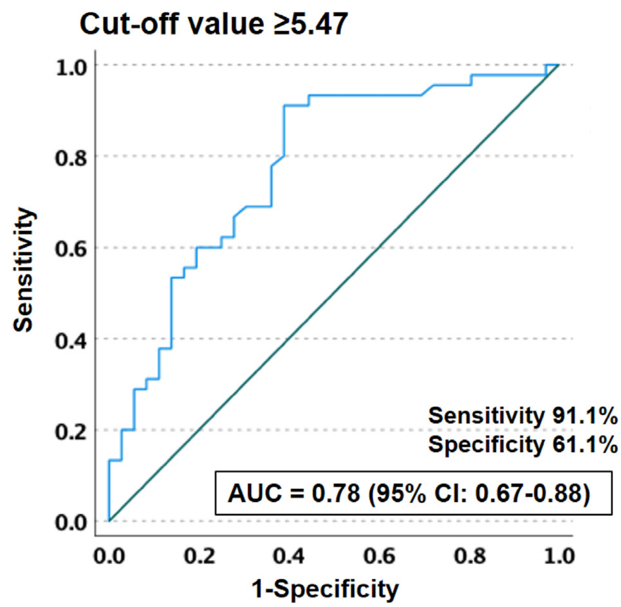

Fig. S2. ROC curve and Youden index for TO length in CCTA to detect TO in ICA in the FAST TRACK CABG trial (n = 114), Among 114 patients of the FAST TRACK CABG trial who underwent both CCTA and ICA before CABG, 86 vessels were diagnosed as TO in CCTA whereas 45 were confirmed as TO in ICA. The Youden index of receiver operating characteristics curve for agreement on the presence of TO in CCTA and ICA is 5.5 mm in terms of TO length in CCTA (area under the curve 0.78, sensitivity 91.1 %, specificity 61.1 %, Figure B). Therefore a 6 mm length of occlusion with a complete luminal absence of contrast media in consecutive cross-sections in multi-planar reconstructions (MPR) of CCTA was adopted as the definition of TO in the modified CCTA-aSS. Abbreviations: AUC, area under the curve; CI, confidence interval.

Table D: Baseline characteristics of the FAST TRACK CABG

Clinical characteristics	N = 114
Age, year (SD)	65·9 (8·7)
Body mass index, kg/m^2 (SD)	26·8 (4·2)
Male, n (%)	101 (87·8 %)
Prior myocardial infarction, n (%)	9/114 (7·9 %)
Prior heart failure, n (%)	4/114 (3·5 %)
Prior stroke, n (%)	4/114 (3·5 %)
Prior revascularization, n (%)	0
Angina status	
Silent ischemia, n (%)	29/114 (25·4 %)
Chronic coronary syndrome, n (%)	69/114 (58·7 %)
Unstable angina, n (%)	7/114 (6·1 %)
Equivalent angina, n (%)	6/114 (5·3 %)
Asymptomatic but history of angina	3 (2·6 %)
Current smoker (%)	26 (22·8 %)
Chronic obstructive lung disease (%)	9 (7·9 %)
Peripheral artery disease (%)	10 (8·8 %)
Creatinine clearance, ml/min	81·2 (20·1)
Hypertension, n (%)	97 (85·1 %)
Systolic blood pressure, mmHg (SD)	126·7 (14·4)
Diastolic blood pressure, mmHg (SD)	77·2 (9·0)
Heart rate, bpm (SD)	67·7 (11·9)
Dyslipidaemia, n (%)	82 (71·9 %)
Medically treated diabetes mellitus, n (%)	38 (33·3 %)
Insulin-dependent, n (%)	3 (2·6 %)
Left ventricular ejection fraction, % (SD)	56·5 (8·7 %)
Coronary anatomy	
Left main disease, n (%)	28 (24·8 %)
Three-vessel disease, n (%)	85 (75·2 %)
Total number of lesions according to the anatomic SYNTAX coronary segmentation	735 (CCTA) 565 (ICA)
Total Occlusion diagnosed by CCTA, n (%)	86/735 (11·7 %)
Total Occlusion diagnosed by ICA, n (%)	74/565 (13·1 %)
Number of lesions per patient according to the SYNTAX coronary segmentation diagnosed by CCTA (SD)	6·51 (4·09)
ICA-derived anatomical SYNTAX Score (SD)	34·0 (12·9)
CCTA-derived anatomical SYNTAX Score (SD)	43·6 (15·3)
FFR_{CT}-derived functional SYNTAX Score (SD)	41·2 (16·5)
Clinical prediction	N = 114

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Clinical characteristics	N = 114
EuroScore II, % (SD) predicted mortality 30 days	1·06 (0·62)
STS score, % (SD) predicted mortality 30 days	0·80 (0·62)

One patient withdrew after informed consent before performing baseline CCTA.
Abbreviation: SD, standard deviation; SYNTAX, The SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery; ICA, invasive coronary angiography: CCTA, coronary computed tomography angiography; FFR_{CT}, computed tomography-derived fractal flow reserve; STS, society of thoracic surgery; SS-2020, SYNTAX Score 2020; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; MACCE, major adverse cardiac and cerebrovascular disease.

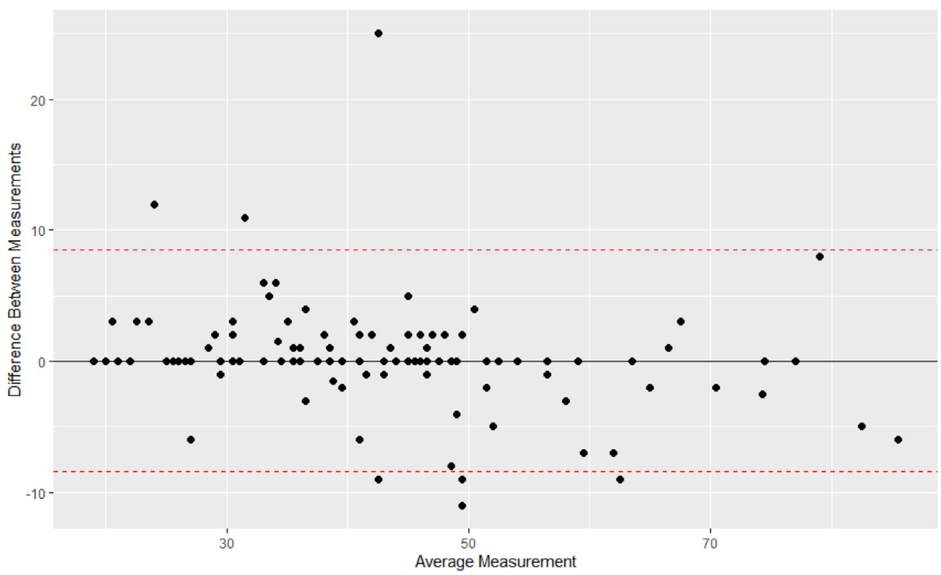

Fig. S3. Bland Altman plot for interobserver agreement of updated CT-SYNTAX score in the FAST TRACK CABG trial (n = 113), Mean = 0.03, boundary of agreement 8.43 (1.96 SD).

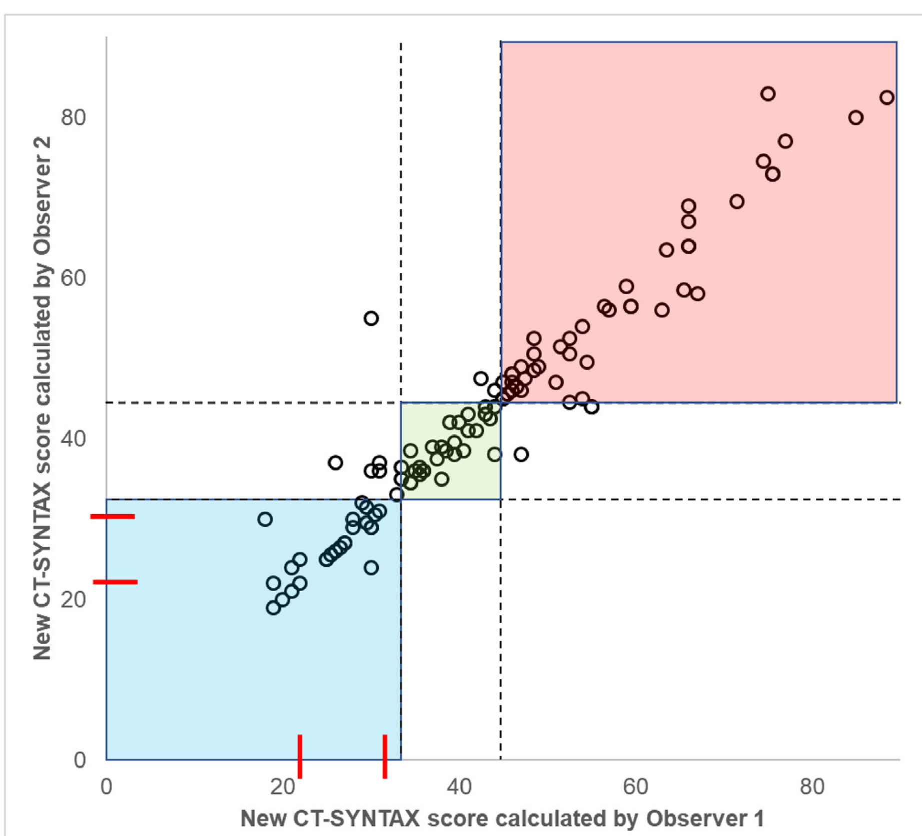

Fig. S4. Correlation plot for the new CT-SYNTAX score interobserver reproducibility, In the FAST TRACK CABG population (n = 113), the aSSLOW, aSSMID, and aSSHIGH tertiles calculated by each observer are represented with blue, green, and pink shaded areas, respectively, on the correlation plot. The traditional SYNTAX score cutoff values (low, <22; intermediate, 23 to 32; high, <33) are also indicated with red marks on each axis. Abbreviation: aSS, anatomic SYNTAX score.

Table E. Inter-observer reproducibility in 5 categories of total anatomic SYNTAX score

		Observer 2					
		≤20	21–40	41–60	61–80	80<	Total
Observer 1	≤20	2	2	0	0	0	4
	21–40	0	44	2	0	0	46
	41–60	0	3	44	0	0	47
	61–80	0	0	3	10	1	14
	80<	0	0	0	1	1	2
	Total	2	49	49	11	2	113

K = 0.83 (95 % CI 0.743–0.919). The inter-observer difference in SYNTAX score calculation at the corelab when the scores are sub-divided into categories of 20 points.

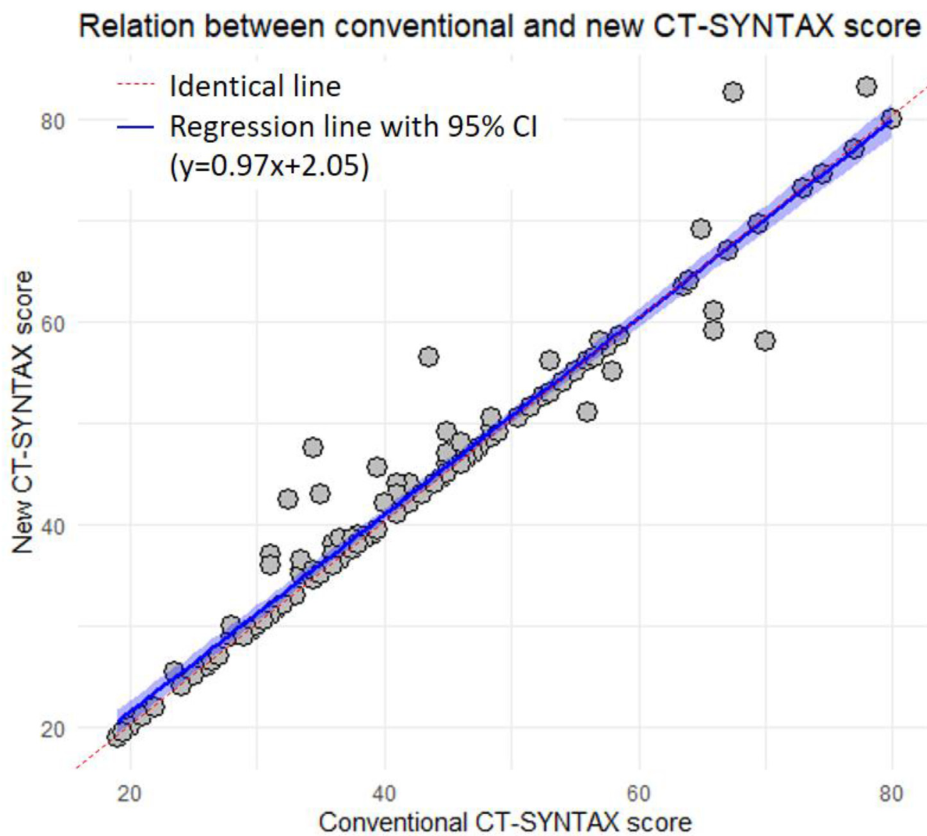

Fig. S5. Correlation of conventional and updated CT-SYNTAX score in the FAST TRACK CABG trial (n = 113), Comparison of previous and New CT-SYNTAX score in the FAST TRACK CABG population. The regression line with a 95 % confidence interval is depicted by a blue line with a surrounding light blue shade. Out of 113 patients, 35 patients evaluated with the new anatomic CT-SYNTAX score are above the identity line whereas 5 have higher anatomic CT-SYNTAX scores with the previous version (2013) of the CT-SYNTAX scoring. Pearson's R = 0.975. Slope 0.97, intercept 2.05.

Text C: Acquisition guideline of CCTA images of the FAST TRACK CABG trial (also presented in this manuscript)

CTA acquisition guidelines for CT prior to CABG.
Introduction.

- Before CABG procedure, CTA is performed to assess the native coronary arteries.

According to the local practice, mammary arteries may be assessed with additional imaging.

- Utilize 256-slice GE Revolution CT Scanner.
- Imaging the entire coronary tree allows for the most accurate FFR_{CT} computation.
- These guidelines also including imaging of the mammary arteries and implications on image reconstruction.
- The full set of image data as well as raw scan data should be saved for each exam.

Preparation.

- Assess heart rate and rhythm. Heart rate control (below 65 beats per minute) reduces motion artefacts.
- Heart rate modulation for heart rates >60/min during breath holding.

Oral: metoprolol tartrate 100 mg, 1 h before the exam. Atenolol 50 mg, 1 h before the exam.

IV: metoprolol 5 mg, repeated up to 5 times.

Contraindications: conduction delays, hypotension, severe asthma, allergy to betablockers, reduced left ventricle ejection fraction.

Consider ivabradin for patients with contra-indications to betablockers (in case of ivabradine the dosage suggested is 5 mg twice a day for at least 3–4 days before the scan).

- Provide full explanation of exam, and practice breath hold. Ensure breath hold time will be sufficient for scan time. Evaluate impact of breath holds on heart rate.

Nitrates and FFR_{CT}.

- Use NTG preferably 3 min prior to CT image acquisition;
- Use 1–2 sprays (0.4mg–0.8 mg)
- Use beta-blocker with it to avoid reflex tachycardia/vasoconstriction
- Additional Beta blockade may be given after nitroglycerin to counteract the reflex tachycardia
- Confirm absence of allergy to contrast media (consider prophylaxis for patients with doubtful or mild reactions to contrast in the past).

Patient installation:

- Attach ECG leads, avoid respiratory muscles, and check signal stability during breath hold.
- Placement of an IV catheter that allows a flow of at least 5 ml/s

Data acquisition:

Overview/scout of the entire chest.

Contrast enhancement:

- ≥300 g/L iodine contrast medium.
- Injection rate: 5–6 ml/s.
- Total amount depends on the patient size, the scan mode and the scan duration.

Contrast-scan timing:

- Test/Timing Bolus: 15–20 ml of contrast is injected, preferably followed by a bolus chaser. Place the localizer line 1 cm below the carina and just above the base of the heart, the optimal location to find the ascending aorta for a timed contrast injection. The time of (maximum) enhancement is used as the delay of the data acquisition after start of contrast injection.
- Bolus tracking/Smart Prep: arrival of the (entire) bolus is monitored in the ascending aorta. To avoid premature triggering of the scan the ROI should be sufficiently large and placed away from the superior vena cava. A saline bolus of ≥50 ml is injected after the contrast medium at the same rate.

Gating and phase acquisition:

ECG-triggered one-beat scan mode should be used. For HR $<$ 65, 75 % of the R–R cycle is appropriate. For HR $>$ 65 or variable heart rates, 40–80 % of the R–R cycle is appropriate with ECG mA modulation. Consider use of Auto-Gating functionality on the system.

Acquisition parameters:

- Thinnest detector collimation.
- Noise Index (NI) of 30 at ASIR-V 50 %. May be adjusted depending on the size of the patient. If fixed tube current (mA) is used, it should be $>$ 500 mA. For patients acquired in standard mode we suggest 100 kVp for BMI$<$25 and 120 kVp for BMI$>$25; for HD mode we suggest 100 kVp for BMI$<$20 and 120 kVp for BMI$>$20. Do not use a kVp less than 100 kVp.
- For patients with BMI $>$25, the x-large focal spot should be preferentially used. This can be achieved by either increasing the NI until the focal spot size change is reflected on the screen, or by switching to a fixed tube current scan mode.
- Additionally, if heart rate is well controlled (HR $<$ 65) in these large patients, gantry rotation time of 0.35sec should be considered. This is pre-configured in the nominal

Autogating profiles if Autogating is being utilized on the system.

- Scan range: from the apex of the lung until the caudal border of the heart. If more than one slab is required, the acquisition should be performed such that first the entire heart is captured in one axial slab, and then the table is moved to capture the remaining range in the cranial direction.
- High Definition Mode should be used preferably except in patients with BMI $>$25

Image reconstruction:

Two sets of reconstructions will be provided – one for assessing the heart and one for assessing the mammary arteries should be provided.

For assessment of the heart:

- 0.625 mm slice thickness

ASIR-, ASIR-V 50 % in all cases should be provided. Additional ASIR-V levels may be provided if ASIR-V 50 % is inadequate.

Field-of-view enclosing the entire heart (cover inferior carina to lower heart border) (approx. 18 × 18 cm).

- Standard kernel reconstructions. Depending on the scan protocol both diastolic and systolic reconstructions should be performed.
- Reconstructions should be optimized for the segments of interest (ROI). In case of suboptimal image quality other phases should be explored.
- Additional high-definition or sharp kernel reconstructions should be provided at the optimal phase(s). If High Definition mode was not performed, then Detail kernel reconstructions should be provided
- If motion artefacts persist in the optimal phase images, the standard and high definition

(or detail) reconstructions should be done with "Temporal Enhanced" enabled and SnapShot Freeze processing should be performed.
For assessment of the mammary arteries:

- 0.625 mm slice thickness
- ASIR-V 50 % in all cases should be provided. Additional ASIR-V levels may be provided if ASIR-V 50 % is inadequate.
- Field-of-view enclosing the entire chest cavity.
- The optimal phase as what was reconstructed for the coronary assessment should be reconstructed.
- Standard kernel reconstruction

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