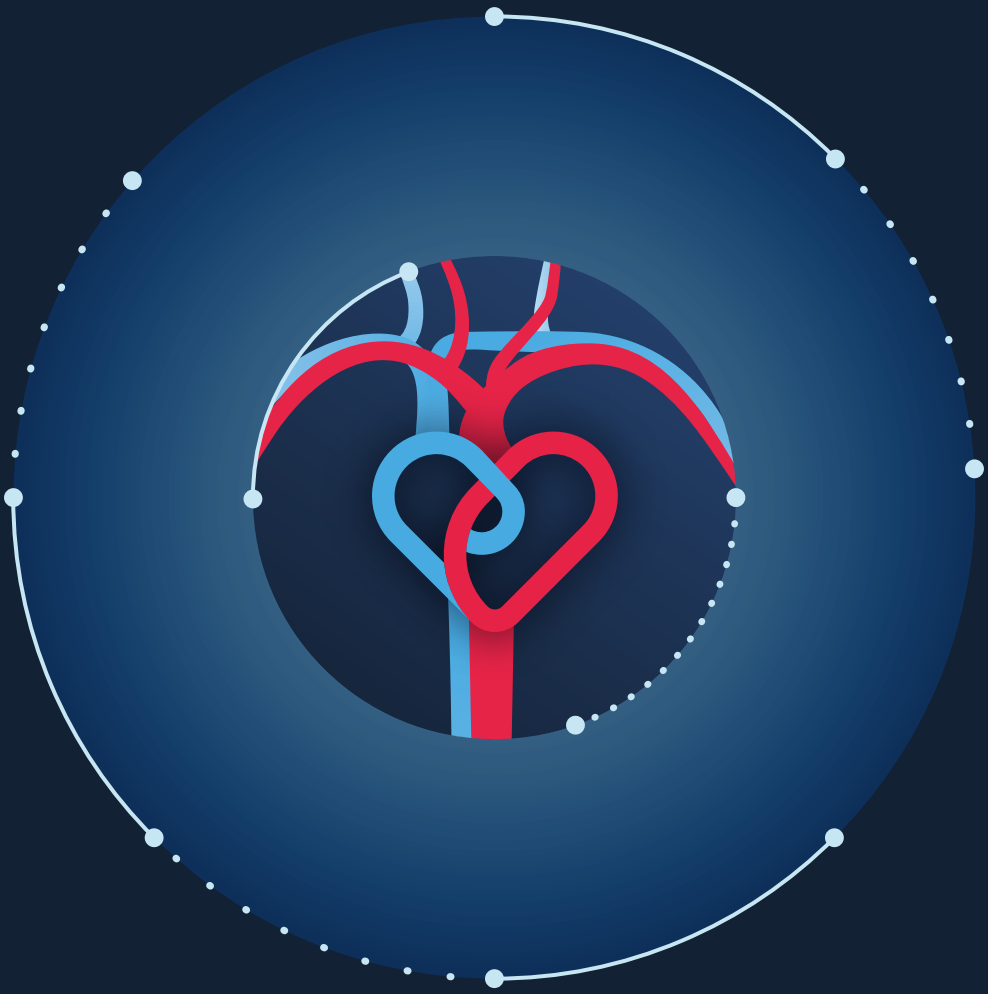
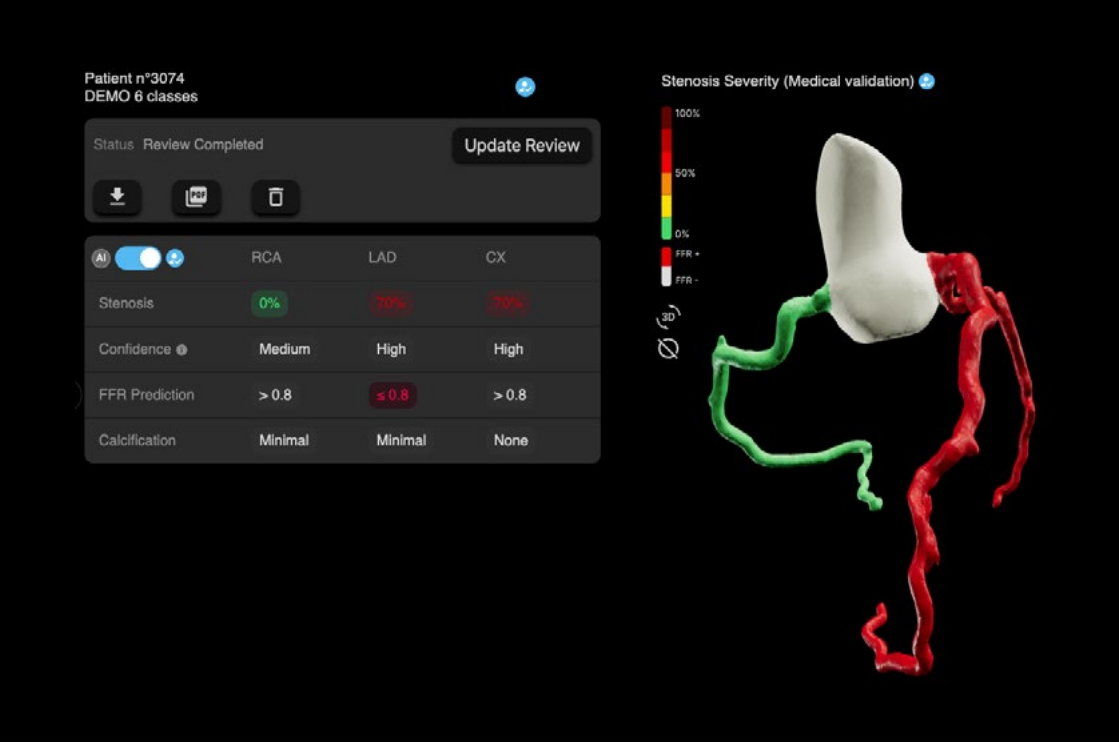


WHITE PAPER

Automated CAD-RADS classification and prediction of the Fractional Flow Reserve using CorEx

Spimed-AI

In this white paper:



I. Intended use of CorEx

CorEx is a standalone software that is intended to be used for viewing and analyzing cardiac Computed Tomography angiography (CCTA) data in support to the evaluation of coronary artery disease (CAD).

This software post processes CT images obtained using any Computed Tomography (CT) scanner with cardiac imaging capabilities (i.e. ECG gating).
The software provides visualization of CT scan images, classification of coronary lesions according to their degree of severity (using the international CAD-RADS classification) and can, in the event of a lesion, infer their functional character by estimating the coronary flow reserve using artificial intelligence (FFR_{AI}).

The results of this analysis are provided to assist in the evaluation and assessment of coronary artery disease. The results of CorEx are intended to be used by qualified clinicians in conjunction with the patient's clinical history, symptoms if any, and other diagnostic tests, as well as the clinician's professional judgment.

II. Principle of operations

CorEx software allows the user to:

- Upload and display CT scan curved MPR images (cMPR) for each main coronary artery, using 9 images 40° apart around the centerline
- Automatically classify arteries using CAD-RADS and provide FFR assessment;
- Generate a medical report that can be downloaded as a PDF file and directly send to the PACS.

Automatic Segmentation - CorExtract NEW

- Obtain segmented arteries in less than 10 minutes
- Accelerate physician workflow
- Easily correct centerlines if needed
- Zero-click solution

III. Studies involving CorEx

To date, 11 clinical studies have been conducted to evaluate the safety and performance of CorEx. These studies are focused on CAD-RADS and/or FFR.

All studies founded high NPV for both 50% stenosis detection and FFR ≤ 0,8 prediction, showing that CorEx could be used safely as a gatekeeper tool for diagnosis and management of CAD.

STUDIES TABLE

1. **Evaluation of a deep learning model on coronary CT angiography for automatic stenosis detection.**
JF. Paul, A. Rohnean, H. Giroussens, T. Pressat-Laffouilhere, T. Wong, 2022.

2. **Artificial intelligence-based opportunistic detection of coronary artery stenosis on aortic computed tomography angiography in emergency department patients with acute chest pain.**
C. Glessgen, M. Boulougouri, JP. Vallée, S. Noble, A. Platon, PA. Poletti, JF. Deux, JF. Paul, 2023.

3. **CAD Evaluation in TAVR Work-Up using Photon-Counting and Artificial Intelligence.**
JM. Brendel, J. Walterspiel, F. Hagen, J. Kübler, JF. Paul, K. Nikolaou, M. Gawaz, S. Greulich, P. Krumm, M. Winkelmann, 2024.

4. **Deep Learning to Exclude Coronary Stenosis on Coronary CT Angiography in TAVI Patients: Diagnostic Performance vs. Invasive Coronary Angiography.**
B. Mehier, K. Mahmoudi, A. Veugeois, A. Masri, N. Amabile, C. Del Giudice, JF. Paul, 2024.

5. **Invasive Fractional Flow Reserve prediction by coronary CT angiography using artificial intelligence vs. computational fluid dynamics software in intermediate-grade stenosis**
B. Peters, JF Paul, R. Symons, W M.A. Franssen, A. Nchimi, O. Ghekiere, 2024.

6. **Diagnostic performance of a new coronary CT Deep Learning Model for the prediction of invasive Fractional Flow Reserve.** [Submitted]

7. **Artificial intelligence for Automated classification of coronary LEsions fRom Computed Tomography Coronary Angiography scans (ALERT).**
VA Verpalen, CF Coerkamp, J P.S Henriques, JF Paul, I. Isgum, RN Planken, 2025.

8. **Artificial intelligence-based CT-derived fractional flow reserve (FFR_{AI}) for the detection of hemodynamically significant coronary artery disease: a comparative study with dynamic stress CT myocardial perfusion imaging.** [Submitted]

9. **Artificial intelligence-enhanced detection of subclinical coronary artery disease in athletes: diagnostic performance and limitations.**
J. Kübler, JM. Brendel, T. Küstner, J. Walterspiel, F. Hagen, JF Paul, K Nikolaou, S. Gassenmaier, I. Tsifikas, C. Burgstahler, S. Greulich, MT. Winkelmann, P. Krumm, 2024.

10. **Validation of a deep learning model for computed tomography-derived Fractional Flow Reserve.**
V. Pham, F. Picard, S. Monnot, P. Garrigoux, A. Jegou, G. Dambrin, JF Paul, 2025.

11. **Coronary artery disease detection using deep learning and ultrahigh-resolution photon-counting coronary CT angiography.**
J.M. Brendel, J. Walterspiel, F. Hagen, J. Kübler, A.S. Brendlin, S. Afat, JF Paul, T. Küstner, K. Nikolaou , M. Gawaz, S. Greulich, P. Krumm, MT. Winkelmann, 2024.

1. AI based CAD-RADS Study (3 grade classification)

Evaluation of a deep learning model on coronary CT angiography for automatic stenosis detection.

This study aimed to determine the performance of CorEx in classifying patients into CAD-RADS categories.

Main finding: The Deep Learning Model (DLM) detected ≥ 50% stenosis with performance similar to those achieved by senior radiologists.

Ref: Paul JF, Rohnean A, Giroussens H, Pressat-Laffouilhere T, Wong T. Diagn Interv Imaging. 2022 Jan 25; S2211-5684(22)00004-3.

2. AI based CAD-RADS: Acute Chest Pain Emergency Study

Artificial intelligence-based opportunistic detection of coronary artery stenosis on aortic computed tomography angiography in emergency department patients with acute chest pain.

This study aimed to evaluate the performance of CorEx in automatically classifying coronary artery stenosis in emergency department patients with acute chest pain, with suspicion of aortic dissection.

Main finding: A DLM demonstrated high NPV for significant coronary artery stenosis in patients with Acute Chest Pain (ACS). All patients with ACS and stenoses by ICA were identified by the DLM.

Ref: CG. Glessgen, M. Boulougouri, JP. Vallée, S. Noble, A. Platon, PA. Poletti, JF. Deux, JF. Paul, et al. Eur Heart J Open. 2023 Sep

3. TAVR Study using FFR

CAD Evaluation in TAVR Work-Up using Photon-Counting and Artificial Intelligence.

This study aimed to evaluate the performance of CorEx in classifying coronary artery stenosis in patients eligible for Transcatheter Aortic Valve Replacement (TAVR), using photon-counting CT.

Main finding: The deep learning-based photon-counting FFR_{AI} evaluation, (1) improves the accuracy of CCTA ≥ 50% stenosis detection, (2) reduces the need for ICA, and (3) may be incorporated into the clinical TAVR work-up for the assessment of CAD.

Ref: JM. Brendel, J. Walterspiel, F. Hagen, J. Kübler, JF. Paul, K. Nikolaou, M. Gawaz, S. Greulich, P. Krumm, M. Winkelmann, National Library of Medicine, 2024 Feb. 16.

4. TAVI Study using CAD-RADS

Deep Learning to Exclude Coronary Stenosis on Coronary CT Angiography in TAVI Patients: Diagnostic Performance vs. Invasive Coronary Angiography.

This study aimed to evaluate the performance of CorEx in classifying coronary artery stenosis in patients eligible for Transcatheter Aortic Valve Implementation (TAVI), making it possible to avoid unnecessary invasive coronary angiography.

Main finding: CorEx was found to have a 100% negative predictive value in detecting ≥ 50% stenosis, making it possible to avoid invasive coronary angiography in 36% of patients.

Ref: B. Mehier, K. Mahmoudi, A. Veugeois, A. Masri, N. Amabile, C. Del Giudice, JF. Paul, 2024 Mar 25. DOI: 10.1007/s10554-024-03063-5.

5. FFR_{AI} versus FFR_{CT}

Invasive fractional-flow-reserve prediction by coronary CT angiography using artificial intelligence vs. computational fluid dynamics software in intermediate-grade stenosis.

This proof-of-concept study aimed to compare the performance of FFR prediction between an Artificial Intelligence solution and a Computational Fluid Dynamics (CFD)-based software.

Main finding: Prediction of FFR ≤ 0.80 intermediate-grade stenosis yielded comparable diagnostic values between FFR_{AI} and FFR_{CT}, suggesting FFR_{AI} may become a similar non-invasive imaging tool to guide patient management as FFR_{CT}.

Ref: B. Peters, JF Paul, R. Symons, W M.A. Franssen, A. Nchimi, O. Ghekiere, Int J Cardiovasc Imaging, 2024 March 01.

6. FFR_{AI} validation in a multicenter Study [Submitted]

Diagnostic performance of a new coronary CT Deep Learning Model for the prediction of invasive Fractional Flow Reserve.

This large multicenter study involving 282 patients aimed to compare the performance of an AI solution for FFR prediction with invasive physiological measurements.

Main finding: FFR_{AI} has a high diagnostic performance for the diagnosis of ischemia in vessels with intermediate-grade stenosis compared to invasive physiological assessments. FFR_{AI} accuracy was comparable in two centers with different CT-scanners and readers with different levels of experience. The high sensitivity and negative predictive value indicate FFR_{AI} might reliably exclude intermediate-grade lesions responsible for ischemia.

7. AI-based CAD-RADS study II (6 grade classification)

Artificial intelligence for Automated classification of coronary Lesions from Computed Tomography Coronary Angiography scans (ALERT)

This study aim to evaluate the diagnostic performance of a DLM for quantifying coronary stenosis on computed tomography coronary angiography (CTCA) using the Coronary Artery Disease-Reporting and Data System (CAD-RADS).

Main finding: Ruling out obstructive CAD (stenosis >50%) by the DLM is safe, considering the 100% NPV. The DLM yielded promising results in CAD-RADS classification (0-5). Further studies need to determine the potential of this DLM as an assisting tool for clinical CTCA reading.

Ref: VA. Verpalen, CF. Coerkamp, JPS. Henriques, JF. Paul, RN. Planken, European Radiology, 2025 Jan. 10.

8. FFR_{AI} versus dynamic stress CT [Submitted]

Artificial intelligence-based CT-derived fractional flow reserve (FFR_{AI}) for the detection of hemodynamically significant coronary artery disease: a comparative study with dynamic stress CT myocardial perfusion imaging.

The aim of this study was to evaluate the diagnostic performance of a deep-learning model of CT-derived FFR_{AI} for the detection of hemodynamically significant coronary artery disease compared to CT myocardial perfusion imaging.

Main finding: FFR_{AI} provides high sensitivity and NPV for identifying hemodynamically significant CAD among patients with coronary stenosis ≥ 50%.
FFR_{AI} could be used as a filter to avoid a subsequent CT-MPI and reduce radiation exposure as well as contrast reinjection.

9. Screening coronary artery disease in Athletes with CorEx

Artificial intelligence-enhanced detection of subclinical coronary artery disease in athletes: diagnostic performance and limitations.

This study aim to evaluate the diagnostic performance of AI-based CCTA for detecting CAD and assessing FFR in asymptomatic male marathon runners.

Main finding: AI-enhanced CCTA is a valuable non-invasive tool for detecting CAD in asymptomatic, low-risk populations. The AI model exhibited high sensitivity and NPV, particularly for identifying significant stenosis, reinforcing its potential role in screening.

However, limitations such as a lower PPV and overestimation of disease indicate that further refinement of AI algorithms is needed to improve specificity. Despite these challenges, AI-based CCTA offers significant promise when integrated with clinical expertise, enhancing diagnostic accuracy and guiding patient management in low-risk groups.

Ref: J. Kübler, Jan M. Brendel, T. Küstner, J. Walterspiel, F. Hagen, JF Paul, K. Nikolaou, S. Gassenmaier, I. Tsifikas, C. Burgstahler, S. Greulich, MT. Winkelmann, P. Krumm, Int J Cardiovasc Imaging, 2024 Sept. 25

10. Validation of a deep learning model for computed tomography-derived fractional flow reserve

This study aimed to evaluate the performance of FFR_{AI} model to predict positive invasive FFR and compare it to invasive FFR.

Main finding: In conclusion, FFR_{AI} exhibits high sensitivity and NPV in identifying hemodynamically significant coronary artery disease among patients with coronary stenosis ≥50% compared with invasive FFR. FFR_{AI} holds promise as a non-invasive, quick tool to rule out unnecessary ICAs and predict potential ischemic stenosis.

Ref: V. Pham, F. Picard, S. Monnot, P. Garrigoux, A. Jegoua, G. Dambrina, JF. Paul, Wolters Kluwer Health, 2024 Oct. 12.

11. CorEx and Photon-Counting CT

Coronary artery disease detection using deep learning and ultrahigh-resolution photon-counting coronary CT angiography

The purpose of this study was to evaluate the diagnostic performance of automated deep learning in the detection of coronary artery disease (CAD) on photon-counting coronary CT angiography (PC-CCTA).

Main finding: Automated deep learning shows remarkable performance for detecting significant coronary artery stenosis using photon-counting CT technology.
For the diagnosis of significant CAD on non-UHR PC-CCTA images, AI pre-reading may be of supportive value to the human reader in daily clinical practice to target and validate coronary artery stenosis using UHR PC-CCTA.

Ref: JM. Brendel, J. Walterspiel, F. Hagen, J. Kübler, A.S. Brendlin, S. Afat, JF. Paul, T. Küstner, K. Nikolaou, M. Gawaz, S. Greulich, P. Krumm, MT. Winkelmann, Diagnostic and Inter. Imaging, 2024 Oct. 04.

IV. Summary table of current studies

N°	Studies with CorEx	Sites	First Author	Status	Number of Patients	Journal
1	CAD-RADS (3 grades)	Paris, France	JF Paul	Published	53	Diagnosis and Interv. Imaging
2	50% stenosis detection / Emergency Dpt	Geneva, Switzerland	C. Glessgen	Published	217	EHJ Open
3	Evaluation in TAVI / PHOTOCOUNTING	Tubingen, Germany	J.M. Brendel	Published	260	Diagnosis and Interv. Imaging
4	CAD-RADS / TAVI	Paris, France	B. Mehier	Published	165	Int J Cardiovasc Imaging
5	FFR_{AI} Vs FFR_{CT}	Hasselt, Belgium	B. Peters	Published	37	Int J Cardiovasc Imaging
6	FFR_{A}I Vs Invasive FFR	Hasselt & Bonheiden, Belgium	B. Peters	Submitted	282	N/A
7	CAD-RADS (6 grades)	Amsterdam, Netherlands	C.F Coerkamp	Published	50	European Radiology
8	FFR_{AI} Vs CT Perfusion	Lille, France	F. Pontana	Submitted	100	N/A
9	Detection of Subclinical Coronary Artery Disease in Athletes: Diagnostic Performance	Tubingen, Germany	J. Kübler	Published	94	Int J Cardiovasc Imaging
10	FFR_{AI} validation	Le Chesnay, France	V. Pham	Published	50	Coronary Artery Disease
11	Stenosis detection with Photocounting	Tubingen, Germany	J.M. Brendel	Published	150	Int J Cardiovasc Imaging

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