

Letter to the Editor

Letters to the Editor will be published, if suitable, as space permits. They should not exceed 1000 words (typed double-spaced) in length and may be subject to editing or abridgment.

Letter by Baumann et al Regarding Article, “Fractional Flow Reserve and Coronary Computed Tomographic Angiography: A Review and Critical Analysis”

To the Editor:

With interest we read the review of Hecht et al¹ in the July issue of *Circulation Research*. The authors present the technical principles and prerequisites of fractional flow reserve derived from computed tomography (CT-FFR) as a novel noninvasive technique using computational fluid dynamics to calculate FFR from standard coronary computed tomography angiography data sets without the administration of a pharmacological stress agent or repeat CT acquisitions. In several large trials, the feasibility of CT-FFR has been proven with promising results. It was demonstrated that the technique primarily improves the specificity and positive predictive value of CT, while the test’s traditionally high sensitivity and negative predictive value are preserved. A substantial correlation with invasive FFR has also been shown.

Although the technique was approved by the Food and Drug Administration in late 2014, the exact use and benefit of this approach remain unclear, and it is still perched on the verge between a research application and a clinical tool. To date, the data sets require transfer to an external supercomputer to create a patient-specific 3-dimensional pressure map of the whole coronary artery tree. The whole process remains time consuming ($\approx 3\text{--}7$ hours), which limits its clinical practicability. For this reason, simplified on-site workstation-based calculations of CT-FFR represent an interesting and fast alternative (<1 hour) with promising initial results as conveyed by the review.^{2,3}

We would like to complete the references of the excellent review by adding a few important landmark and other studies using the fast on-site CT-FFR algorithm. The retrospective, single-center study by Coenen et al⁴ included 189 vessels of 106 patients and showed an improvement of the specificity from 37.6% (95% confidence interval, 28.5%–47.4%) for coronary computed tomography angiography alone compared with 65.1% (95% confidence interval, 55.4%–74.0%) by CT-FFR. Similar results were presented in a smaller Swedish study with 21 patients, demonstrating CT-FFR a specificity of 76% per lesion 80% per patient.⁵ Furthermore, Yang et al⁶ performed the first head-to-head comparison of this on-site CT-FFR software with stress CT myocardial perfusion in patients with coronary artery disease with a per-vessel specificity of 66% for coronary computed tomography angiography, 77% for CT-FFR, and 91% for CT myocardial perfusion, respectively. The diagnostic performance of coronary computed tomography angiography (area under the curve=0.856) was significantly improved by combination with CT-FFR (area under the curve=0.919; $P=0.004$) or CT myocardial perfusion (area under the curve=0.913; $P=0.004$).

The use of local, reduced-order computed fluid dynamics and machine-learning-based CT-FFR validated against invasive FFR is currently being evaluated in the Machine Learning Based CT

angiography derived FFR: a Multi-center (Machine) registry (ClinicalTrials.gov ID: NCT02805621) with an estimated enrollment of 352 patients in 5 centers to determine the actual diagnostic performance of this technique. This development could be the next step in establishing the feasibility for the routine application of a game-changing one-stop-shop approach.⁷

The authors are to be congratulated for their review, as it covers a highly topical and frequent subject of discussion that will likely be of great interest to readership.

Disclosures

U.J. Schoepf receives institutional research support from Astellas (Deerfield, IL), Bayer (Wayne, NJ), Bracco (Princeton, NJ), GE Healthcare (Little Chalfont, Buckinghamshire, UK), Medrad (Warrendale, PA), and Siemens Healthcare (Malvern, PA) and received consulting fees from Guerbet (Roissy, France). M. Renker receives consulting fees/honoraria from Symetis (Ecublens, Switzerland). The other authors report no conflicts.

Stefan Baumann

Heart & Vascular Center
Medical University of South Carolina
Charleston, SC

First Department of Medicine-Cardiology
University Medical Centre Mannheim
Mannheim, Germany

DZHK (German Centre for Cardiovascular Research)
Partner Site Heidelberg/Mannheim
Mannheim, Germany

Christian Tesche

Heart & Vascular Center
Medical University of South Carolina
Charleston, SC

Department of Cardiology and Intensive Care Medicine
Heart Center Munich-Bogenhausen
Munich, Germany

U. Joseph Schoepf

Heart & Vascular Center
Medical University of South Carolina
Charleston, SC

Ibrahim Akin

First Department of Medicine-Cardiology
University Medical Centre Mannheim
Mannheim, Germany

DZHK (German Centre for Cardiovascular Research)
Partner Site Heidelberg/Mannheim
Mannheim, Germany

Martin Borggrefe

First Department of Medicine-Cardiology
University Medical Centre Mannheim
Mannheim, Germany

DZHK (German Centre for Cardiovascular Research)
Partner Site Heidelberg/Mannheim
Mannheim, Germany

Matthias Renker
 Heart & Vascular Center
 Medical University of South Carolina
 Charleston, SC
 Kerckhoff Heart and Thorax Center
 Department of Cardiology
 Bad Nauheim, Germany

References

1. Hecht HS, Narula J, Fearon WF. Fractional flow reserve and coronary computed tomographic angiography: a review and critical analysis. *Circ Res.* 2016;119:300–316. doi: 10.1161/CIRCRESAHA.116.307914.
2. Renker M, Schoepf UJ, Wang R, Meinel FG, Rier JD, Bayer RR 2nd, Möllmann H, Hamm CW, Steinberg DH, Baumann S. Comparison of diagnostic value of a novel noninvasive coronary computed tomography angiography method versus standard coronary angiography for assessing fractional flow reserve. *Am J Cardiol.* 2014;114:1303–1308. doi: 10.1016/j.amjcard.2014.07.064.
3. Kruk M, Wardziak Ł, Demkow M, Pleban W, Pręgowski J, Dzielińska Z, Witulski M, Witkowski A, Rużyłło W, Kęпка C. Workstation-based calculation of CTA-based FFR for intermediate stenosis. *JACC Cardiovasc Imaging.* 2016;9:690–699. doi: 10.1016/j.jcmg.2015.09.019.
4. Coenen A, Lubbers MM, Kurata A, Kono A, Dedic A, Chelu RG, Dijkshoorn ML, Gijzen FJ, Ouhlous M, van Geuns RJ, Nieman K. Fractional flow reserve computed from noninvasive CT angiography data: diagnostic performance of an on-site clinician-operated computational fluid dynamics algorithm. *Radiology.* 2015;274:674–683. doi: 10.1148/radiol.14140992.
5. De Geer J, Sandstedt M, Bjorkholm A, Alfredsson J, Janson M, Engvall J, Persson A. Software-based on-site estimation of fractional flow reserve using standard coronary CT angiography data [published online ahead of print December 20, 2015]. *Acta Radiol.*
6. Yang DH, Kim YH, Roh JH, Kang JW, Ahn JM, Kweon J, Lee JB, Choi SH, Shin ES, Park DW, Kang SJ, Lee SW, Lee CW, Park SW, Park SJ, Lim TH. Diagnostic performance of on-site CT-derived fractional flow reserve versus CT perfusion [published online ahead of print June 28, 2016]. *Eur Heart J Cardiovasc Imaging.*
7. Itu L, Rapaka S, Passerini T, Georgescu B, Schwemmer C, Schoebinger M, Flohr T, Sharma P, Comaniciu D. A machine-learning approach for computation of fractional flow reserve from coronary computed tomography. *J Appl Physiol (1985).* 2016;121:42–52. doi: 10.1152/jappphysiol.00752.2015.

Circulation Research

JOURNAL OF THE AMERICAN HEART ASSOCIATION



Letter by Baumann et al Regarding Article, "Fractional Flow Reserve and Coronary Computed Tomographic Angiography: A Review and Critical Analysis"
Stefan Baumann, Christian Tesche, U. Joseph Schoepf, Ibrahim Akin, Martin Borggrefe and Matthias Renker

Circ Res. 2016;119:e106-e107

doi: 10.1161/CIRCRESAHA.116.309680

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Copyright © 2016 American Heart Association, Inc. All rights reserved.

Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://circres.ahajournals.org/content/119/6/e106>

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Circulation Research* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the [Permissions and Rights Question and Answer](#) document.

Reprints: Information about reprints can be found online at:
<http://www.lww.com/reprints>

Subscriptions: Information about subscribing to *Circulation Research* is online at:
<http://circres.ahajournals.org/subscriptions/>