Coronary Physiologic Assessment and Imaging

Assessing Computational Fractional Flow Reserve From Optical Coherence Tomography in Patients With Intermediate Coronary Stenosis in the Left Anterior Descending Artery

Jinyong Ha, PhD*; Jung-Sun Kim, MD*; Jaeyeong Lim, BS; Gihoon Kim, BS; Seungwan Lee, MS; Joon Sang Lee, PhD; Dong-Ho Shin, MD; Byeong-Keuk Kim, MD; Young-Guk Ko, MD; Donghoon Choi, MD; Yangsoo Jang, MD; Myeong-Ki Hong, MD

**Background**—Intravascular optical coherence tomography (OCT) imaging provides limited information on the functional assessment of coronary stenosis. We evaluated a new approach to OCT image–based computing modeling, which can be used to estimate the fractional flow reserve (FFR) in patients with intermediate coronary stenosis.

**Methods and Results**—Ninety-two patients with intermediate diameter stenosis in the left anterior descending artery underwent both FFR measurement with pressure wires and OCT examination. Using the OCT data, a computational fluid dynamics algorithm was used to calculate the computational FFR (FFR_{OCT}). The diagnostic performance of the FFR_{OCT} was assessed based on the pressure wire–based FFR. The median FFR and FFR_{OCT} values were 0.86 (0.79–0.89) and 0.89 (0.82–0.94), respectively. The average diameter stenosis in quantitative coronary angiography and area stenosis in OCT were 58.1±13.4% and 67.5±13.5%, respectively. The FFR_{OCT} was better correlated to the FFR than were the anatomic variables (r=0.72; P<0.001 versus r=0.46; P=0.001 for minimal luminal diameter on quantitative coronary angiography or r=0.57; P<0.001 for minimal lumen area on OCT). When functionally significant stenosis was defined as an FFR cutoff value of ≤0.8, FFR_{OCT} resulted in 88.0% accuracy, 68.7% sensitivity, and 95.6% specificity. The positive and negative predictive values were 84.2% and 89.0%, respectively.

**Conclusions**—The computation of FFR_{OCT} enables assessment not only of anatomic information, but also of the functional significance of intermediate stenosis. This measurement may be a useful approach for the simultaneous evaluation of the functional and anatomic severity of coronary stenosis. (Circ Cardiovasc Interv. 2016;9:e003613. DOI: 10.1161/CIRCINTERVENTIONS.116.003613.)

**Key Words:** coronary artery disease ▪ coronary stenosis ▪ coronary vessels ▪ fractional flow reserve, myocardial ▪ tomography, optical coherence

Coronary revascularization is often performed using only angiographic assessment of luminal narrowing; however, both functional and anatomic assessments of coronary stenosis severity are clinically useful for coronary revascularization. Functional assessment, in particular, is required in intermediate (40%–70%) stenotic lesions in which angiographic assessment is unreliable for determining the presence of myocardial ischemia. Pressure wire–based fractional flow reserve (FFR) is used for functional assessment and clarification of the optimal revascularization strategy. Therefore, it is a useful supplement to angiography. Currently, the FFR is considered the gold standard for assessing the functional significance of lesions with intermediate stenosis. Several studies have demonstrated that FFR-guided coronary intervention leads to favorable clinical outcomes and reduces unnecessary revascularization without increasing adverse cardiac events. Intravascular ultrasound or optical coherence tomography (OCT) has been used for accurate anatomic assessment of coronary stenosis. The image resolution of the coronary arteries is 10x better using OCT than it is with intravascular ultrasound. As computational flow dynamics (CFD) has been applied to cardiac computed tomography for FFR estimation (FFR\textsubscript{CT}), OCT-derived CFD simulation has proven useful for assessing the local shear stress distribution, but direct FFR estimation has

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From the Department of Electrical Engineering, Sejong University, Seoul, Korea (J.H., J.L., G.K., S.L.); Severance Cardiovascular Hospital, Yonsei University Health System, Seoul, Korea (J.-S.K., D.-H.S., B.-K.K., Y.-G.K., D.C., Y.J., M.-K.H.); Cardiovascular Research Institute (J.-S.K., D.-H.S., B.-K.K., Y.-G.K., D.C., Y.J., M.-K.H.) and Severance Biomedical Science Institute (Y.J., M.-K.H.), Yonsei University College of Medicine, Seoul, Korea; and Department of Mechanical Engineering, Yonsei University, Seoul, Korea (J.S.L.).

*Drs Ha and J.-S. Kim contributed equally to this work.


Correspondence to Myeong-Ki Hong, MD, Division of Cardiology, Severance Cardiovascular Hospital, Yonsei University College of Medicine, Yonsei-ro 50–1, Seodaemun-gu, Seoul, 03722, Korea. E-mail mkhong61@yuhs.ac

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WHAT IS KNOWN

• Fractional flow reserve (FFR) is considered the gold standard for assessing the functional significance of lesions with intermediate stenosis.
• Intravascular ultrasound or optical coherence tomography (OCT) has been used for accurate anatomic assessment of coronary stenoses.
• The resolution of image to assess the coronary arteries is 10× better using OCT than it is with intravascular ultrasound.

WHAT THE STUDY ADDS

• The simple and fast computation of FFR using OCT lumen contour–based 3D coronary models (FFROCT) enables simultaneous assessment of the functional significance and anatomic information of lesions with intermediate stenosis.
• This technique may be a useful approach for evaluating the simultaneous functional and anatomic severity of coronary stenoses.

not been reported. Recently, 3-dimensional (3D) quantitative coronary angiography (QCA)–based FFR evaluation (FFRQCA) proved to be a promising tool for evaluating the functional significance of intermediate coronary stenosis during diagnostic coronary angiography. The objective of this study was to present a new approach for estimating invasive FFR using OCT lumen contour–based 3D coronary models (FFROCT) and CFD algorithms. In addition, the clinical usefulness of FFROCT was evaluated with pressure wire–based FFR in patients with ambiguous intermediate diameter stenosis in the left anterior descending artery.

Methods

A total of 100 consecutive patients who underwent both OCT and FFR evaluation of intermediate stenosis in the left anterior descending artery between November 2013 and January 2015 were retrospectively enrolled. Eight patients were excluded because of poor reconstruction of the 3D OCT images. A total of 92 patients were finally included in the analysis. The inclusion criteria included (1) clinical presentation of angina, (2) intermediate diameter stenosis (40%–70%) in de novo lesions proximal to the mid-portion of the left anterior descending artery, and (3) visual angiographic lesions of <20 mm in length. The exclusion criteria included: (1) clinical presentation of acute myocardial infarction, (2) previous history of myocardial infarction, (3) presence of regional wall motion abnormality in the territory of the left anterior descending artery, (4) significant stenosis (>50% diameter stenosis) distal to the target lesion, (5) angiographic thrombus, and (6) contra-indication to adenosine. This study was approved by the institutional review board at our institution. Written informed consent was obtained from all patients.

An off-line quantitative coronary angiographic system (CAAS system; Pie Medical Instruments, Maastricht, Netherlands) was used to perform QCA analysis in an independent core laboratory (Cardiovascular Research Center, Seoul, Korea). Using the guiding catheter for magnification calibration, the reference vessel diameter and minimum luminal diameter (MLD) were measured from diastolic frames in a single, matched view showing the smallest MLD (Figure 1A).

OCT Imaging and Reconstruction of 3D Coronary Artery Geometry

Target lesion imaging was performed using a frequency-domain OCT system (C7-XR OCT imaging system; LightLab Imaging, Inc./St. Jude Medical, St. Paul, MN). The OCT cross-sectional images were generated at a rotational speed of 100 frames/s. The fiber probe was withdrawn at 20 mm/s within the stationary imaging sheath. All OCT images were analyzed at the core laboratory (Cardiovascular Research Center) by analysts who were blinded to patient and procedural information. The minimal luminal area (MLA) was identified at the segment with the smallest lumen area by OCT analysis. Area stenosis was calculated as follows: [(mean reference lumen area–minimum lumen area)/mean reference lumen area]×100. The reference lumen area was the region within the same segment as the lesion with the largest lumen. These reference areas were proximal or distal to the stenotic area (and usually within 10 mm of the stenosis without major intervening branches). The minimal lumen area defining functional stenosis in the OCT criteria was 1.96 mm².

The OCT cross-sectional images generated at 0.2-mm intervals resulted in reliable 3D coronary geometry models. To make accurate OCT-derived models for blood flow simulation, lumen contours of the OCT cross sections were extracted with semiautomated procedures using a developed software. A simple 3D coronary model was created by eliminating the side branches in the bifurcations of the target lesions. Therefore, the overall lumen contour was extracted by estimation of the mother vessel lumen. The lumen contour data were then used to generate a 3D coronary geometry using 3D CAD design software (SOLIDWORKS; Dassault Systèmes SOLIDWORKS Corp., Waltham, MA; Figure 1B; see Data Supplement).

CFD Simulation With OCT

The reconstructed 3D model was processed using finite element analysis software (ADINA; ADINA R&D, Inc., Watertown, MA). Anisotropic meshes with tetrahedral elements were generated. Blood flow simulation was performed by solving the Navier–Stokes equations. Blood was modeled as an incompressible Non-Newtonian fluid with a viscosity of 0.00345 Pa·s and density of 1060 kg/m³. A no-slip boundary condition was used to calculate the interaction between the vessel wall and blood flow. To perform steady state CFD analysis, the mean flow velocity was obtained by averaging the velocities on coronary angiography using the Thrombolysis in Myocardial Infarction frame count. The mean blood pressure was calculated by averaging the mean pressure acquired at the guiding catheter tip in 37 lesions (retrospective group). Next, 55 of 92 patients were prospectively evaluated with the mean flow velocity and pressure calculated from the retrospective group. The calculated mean flow velocity as a boundary condition at the inlet and mean blood pressure at the outlet were 0.273 m/s and 93.2 mm Hg (12427 Pa), respectively. The FFRQCA values from 55 patients were independently simulated and blindly compared with the FFR. It should be noted that coronary flow measurement was performed at nonhyperemia, as opposed to that of FFRQCA. FFROCT was calculated as the mean pressure at the outlet divided by the mean pressure at the inlet. It was then compared with pressure wire–based FFR values.

FFR Measurement

Coronary pressure was measured using a 0.014-inch pressure guidewire (St. Jude Medical, Minneapolis, MN). After the equalizing process, the pressure guidewire was positioned distal to the target lesion. Intravenous adenosine was administered at 140 μg/kg per minute via an antecubital vein to induce maximal hyperemia. FFR was calculated using the following formula: mean hyperemic distal coronary pressure/mean aortic pressure. Stenosis was considered functionally significant when FFR was ≤0.80.

Statistical Analysis

Statistical analyses were performed using SPSS (version 20.0.0; IBM, Armonk, NY). Data are expressed as mean±SD, median (quartiles),
or number (%). Pearson correlation was used to evaluate the correlation between FFR and FFR\textsubscript{OCT} and between FFR and parameters of QCA or OCT. The comparisons between correlation coefficients were performed using MedCalc (version 16.4.3; MedCalc Software BVBA, Ostend, Belgium). The performance of FFR\textsubscript{OCT} in predicting functionally significant stenosis was assessed using accuracy, sensitivity, specificity, positive predictive value, and negative predictive value. Receiver-operating characteristic curve analysis was used to assess the QCA and OCT parameters that predicted functionally significant stenosis. Inter- and intraobserver agreement with regard to FFR\textsubscript{OCT} measurement was assessed using intraclass correlation coefficients with 20 randomly selected cross-sectional images. The images were assessed by 2 independent analysts and by the same analyst at 2 separate time points. A 2-sided \( P \leq 0.05 \) were considered statistically significant.

## Results

Baseline clinical characteristics are summarized in Table 1. Coronary angiographic and OCT findings are shown in Table 2. Both OCT and FFR procedures were successfully performed without any complications. There were bifurcation lesions of the side branch of \( \geq 2.5 \) mm in diameter in 19 patients (20.7%). Functionally significant stenosis was observed in 24 patients (26.1%). Median FFR at baseline and maximal hyperemia was 0.95 (quartiles, 0.93–0.96) and 0.86 (quartiles, 0.79–0.89), respectively. FFR\textsubscript{OCT} was 0.89 (quartiles, 0.82–0.94). A representative example of FFR\textsubscript{OCT} computation is shown in Figure 1C. FFR\textsubscript{OCT} was well correlated with FFR (correlation coefficient, \( r = 0.72; P < 0.001 \) and mean difference, \( -0.03 \pm 0.08 \); Figure 2).

### Table 1. Baseline Clinical Characteristics

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total (n=92)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y, mean±SD</td>
<td>62.7±9.6</td>
</tr>
<tr>
<td>Sex, male, n (%)</td>
<td>58 (63.0)</td>
</tr>
<tr>
<td>Unstable angina, n (%)</td>
<td>27 (29.3)</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>20 (21.7)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>54 (58.7)</td>
</tr>
<tr>
<td>Dyslipidemia, n (%)</td>
<td>64 (69.6)</td>
</tr>
<tr>
<td>Current smoker, n (%)</td>
<td>12 (13.0)</td>
</tr>
<tr>
<td>Multivessel disease, n (%)</td>
<td>22 (26.8)</td>
</tr>
</tbody>
</table>
of the 38 lesions (19 lesions) with anatomic significance (OCT-measured MLA <1.96 mm²) were functionally significant (FFROCT ≤0.8). There were no statistically significant differences in the correlation with regard to the presence of bifurcation (r=0.76 versus r=0.76; z statistic 0; P=1.00; Figure 3). When functionally significant stenosis was defined as a pressure wire–based FFR cutoff value of ≤0.8, FFROCT resulted in 88.0% accuracy, 68.7% sensitivity, 95.6% specificity, 84.2% positive predictive value, and 89.0% negative predictive value. The performance of FFROCT was comparable between retrospective and prospective groups (accuracy, 91.9% versus 85.5%; sensitivity, 87.5% versus 56.3%; specificity, 93.1% versus 97.4%; positive predictive value, 77.8% versus 90.0%; and negative predictive value, 96.4% versus 84.4%).

The area under the receiver-operating characteristic curve to predict functionally significant stenosis was similar or better in FFROCT than in the anatomic parameters (0.93 versus 0.83 in MLD and 0.90 in % diameter stenosis in QCA and 0.93 in MLA and 0.90 in % area stenosis in OCT; Figure 4). The inter- and intraobserver agreement with regard to FFROCT were acceptable (intraclass correlation coefficient, 0.94; 95% confidence interval, 0.86–0.97; mean difference, 0.01±0.01 and intraclass correlation coefficient, 0.94; 95% confidence interval, 0.86–0.98; mean difference, 0.01±0.05, respectively).

The overall analysis lasted <10 minutes owing to semiautomated lumen detection. The overall construction time with 3D rendering was also minimized because the side branches were removed in the 3D coronary model. The same meshing scheme was applied to all cases, resulting in an average of 14,239 to 105,101 cells per case. It took ≈10 seconds to generate the interior meshes after 3D coronary reconstruction and 40 seconds for CFD simulation on a workstation with a quad-core Intel i7-4770 processor (Intel Corporation, Santa Clara, CA; 3.40 GHz) and 8 GB of RAM. Most analysis time was spent setting up simulation values for the CFD simulation.

**Discussion**

We have developed a new approach to OCT image–based computation of virtual FFR in patients with intermediate diameter stenosis in the left anterior descending coronary artery. There were several main findings of this study. FFROCT was well correlated and in agreement with FFR (correlation coefficient, r=0.72; P<0.001 and mean difference, 0.03±0.08). In addition, FFROCT was more strongly correlated with FFR than it was to anatomic angiographic and OCT variables. This approach is superior to the angiographic assessment. When functionally significant stenosis was defined as a FFR cutoff value of ≤0.8, FFROCT had an accuracy of 88.0%, sensitivity of 68.7%, specificity of 95.6%, positive predictive value of 84.2%, and negative predictive value of 89.0%. These findings indicate that FFROCT may be applied to assess functionally significant stenosis in lesions with intermediate diameter stenosis.

![Figure 2](https://example.com/figure2.png)

**Figure 2.** Correlation and agreement between fractional flow reserve (FFR) and FFROCT. Between FFR and FFROCT (A) the correlation was good and (B) agreement was acceptable. FFROCT indicates computational FFR by optical coherence tomography (OCT).
and be more useful for excluding significant stenosis than for predicting hemodynamic significance.

FFR and intravascular ultrasound/OCT have been adopted as complementary modalities to provide critical information on the functional or structural status of coronary lesions. Many clinical trials have estimated FFR indirectly from anatomic imaging data. In the FIRST study (Fractional Flow Reserve and Intravascular Ultrasound Relationship Study), there was a moderate correlation between intravascular ultrasound–derived data such as MLA and ischemic FFR values.\textsuperscript{17} OCT has the advantage of high resolution (10–15 μm) to provide more accurate information of the lumen’s contour in a coronary artery. Therefore, OCT may be suggested as a better potential imaging modality to estimate the functional significance of coronary artery stenosis. In one study, OCT volumetric assessment based on blood flow resistance derived from OCT lumen profiles showed a stronger linear correlation with FFR measurements than QCA and OCT-derived MLA, but this study was exploratory in nature and limited by the small number of patients.\textsuperscript{13} Recent studies have suggested that OCT may be better than intravascular ultrasound or coronary angiography for assessing the functional significance of intermediate coronary stenosis.\textsuperscript{18–20} In the present study, OCT variables were also better correlated than were those of angiography (0.44 in MLD and −0.47 in % diameter stenosis in QCA and 0.58 in MLA and −0.61 in % area stenosis in OCT). Compared with previous studies, FFROCT and MLA on OCT had better diagnostic value of the area under the curve. This finding might be explained by the fact that our study included only lesions of the left anterior descending artery, which is already known to have good correlation between anatomic and functional indices.\textsuperscript{13,19,21,22} In addition, the present study

**Figure 3.** Correlation between fractional flow reserve (FFR) and FFROCT, according to anatomic parameters. A, Diameter stenosis (≤50% vs >50%; r=0.75 vs r=0.70, respectively) and (B) presence of bifurcation (presence vs absence: r=0.76 vs 0.76, respectively). FFROCT indicates computational FFR by optical coherence tomography (OCT).

**Figure 4.** Receiver-operating characteristic curve for assessment of functionally significant stenosis based on fractional flow reserve (FFR). Area under the receiver-operating characteristic curve for the prediction of FFR ≤0.8 by FFROCT, indices of quantitative coronary angiography (QCA) and optical coherence tomography (OCT). AUC indicates area under the curve; MLA, minimal luminal area by OCT; and MLD, minimal luminal diameter by QCA.
showed that FFR_{OCT} was better at discriminating the functional significance than were the anatomic parameters of QCA; it was also slightly better than those of OCT. These findings may be explained by the application of mean flow velocity, which was obtained by averaging velocities on coronary angiography using the Thrombolysis in Myocardial Infarction frame count and the mean blood pressure. When the CFD simulation was added, the correlation improved when compared with the anatomic angiographic and OCT variables. These findings imply that, in lesions with intermediate stenosis, adding CFD simulation to anatomic indices improves the accuracy of the functional significance.

FFR_{OCT} Versus FFR_{QCA} and FFR_{QCA}c

FFR_{QCA}c is a noninvasive method of predicting the functional significance of stenosis based on coronary computed tomographic data. In intermediate stenosis, several studies showed that the sensitivity, specificity, positive predictive value, and negative predictive value were 83% to 88%, 78% to 86%, 61% to 74%, and 92% to 95%, respectively.10,23,24 FFR_{QCA}c was reported to be well correlated with FFR (Pearson correlation coefficient, 0.82; P < 0.001).24 However, overall, 13% of patients were not included in analysis of FFR_{QCA}c because of nonvaluable coronary computed tomographic angiographic images.24 Another promising approach is FFR_{QCA}c simulated by 3D angiography. The accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of this method were reported to be 88%, 78%, 93%, 82%, and 91%, respectively.14 Accurate reconstruction of the lumen contour is an essential component of creating an image-based computation model; reconstruction is totally dependent on the resolution of each imaging modality. Despite the noninvasive nature of FFR_{QCA}c, the applicable population for FFR_{QCA}c is more limited than that for FFR_{QCA} because of the lower resolution of computed tomographic angiography (600 μm) compared with that of conventional angiography (200 μm).11

The fundamental difference in the 3 different approaches (FFR_{QCA}, FFR_{QCA}c, and FFR_{OCT}) used to solve the Navier–Stokes equations is in the boundary conditions. For the assessment of coronary flow, the FFR_{QCA} was used to estimate the total rest coronary flow relative to ventricular mass. It was assumed that microcirculation would react predictably to the maximal hyperemic condition. In contrast, FFR_{QCA}c calculated the hyperemic flow during hyperemia, using 3D QCA and frame count directly on the angiographic projections.14 In the present study, FFR_{QCA}c used a generic, simplified one-size-fits-all approach to boundary conditions in CFD models.25 To determine the boundary conditions of the CFD models, the blood flow velocity acquired from Thrombolysis in Myocardial Infarction frame count analysis was determined at nonhyperemia states apart from FFR_{QCA}. The applied mean flow velocity and pressure were 0.273 m/s and 93 mmHg, respectively. In general, 3D reconstruction of coronary cross sections including bifurcations can be used for realistic flow simulation. Although lesions with side branches were disregarded in imaging assessment using OCT, the extraction of the lumen allowed for the most accurate anatomic CFD model. A recent study explored a method for coregistration and fusion of 3D OCT and 3D x-ray angiography including side branches and then discussed the feasibility and accuracy of shear stress and virtual FFR calculations. This study may provide a solution to the present difficulties surrounding clinical application in lesions including side branches.26 In this study, the simulation time of meshing after 3D rendering and CFD was <10 minutes, including semi-automated OCT lumen detection. Therefore, an OCT-derived virtual FFR approach may be valuable in clinical practice.

Potential Clinical Implications of FFR_{OCT}

FFR is a gold standard method of assessing the functional significance of coronary stenosis. However, the method has some limitations with regard to evaluating the morphological features and predicting the presence of vulnerable plaques. Using a single tool to simultaneously assess the morphological and functional features is more valuable and promising in daily clinical practice than is using 2 different tools. A single tool can reduce procedural time and additional costs. Although FFR_{OCT} showed moderate correlation with pressure wire–based FFR, the present study found that OCT alone can be used to simultaneously collect anatomic and functional information from coronary artery segments with intermediate diameter stenosis.

Limitations

This study has several limitations. The study population was relatively small and retrospectively analyzed. The study also only included patients with lesions in the left anterior descending artery. Therefore, more data will be required to expand this application to other coronary vessels. FFR is influenced by several variables including the amount of supplying myocardium and reference vessel size. Previous studies reported better correlation between anatomic and functional parameters in the left anterior descending artery compared with other coronary arteries. Based on previous observations, we assessed the clinical relevance of FFR_{OCT} in lesions of the left anterior descending artery to minimize possible confounding factors.21,22 Another limitation to application in clinical practice is the rather low sensitivity of FFR_{OCT}. However, its high specificity could provide clinically useful information for exclusion of functionally significant ischemia. To improve the diagnostic accuracy, further investigation of patient-specific and lesion-specific boundary conditions should be performed under physiologically hyperemic conditions. In addition, CFD models of side branches using coregistration and fusion of 3D OCT and 3D x-ray angiography may enhance the accuracy of FFR_{OCT}.26 One technical limitation of this study is that side branches were disregarded to simplify the numeric solutions to the Navier–Stokes equations. However, lesions with side branches and those without were not significantly different in the current study. Furthermore, the impact of the size of side branches in 3D reconstructions on FFR calculations should be investigated and the cutoff value for side branch diameter. In addition, the steady flow was imposed at the inlet boundary instead of the pulsatile flow in nature. This resulted in a less realistic blood flow simulation. Therefore, a prospective study with a large population is needed to provide more accurate FFR_{OCT} via simulation of side branches using fusion with 3D angiography and patient- and lesion-specific boundary conditions under physiologically hyperemic conditions.
Conclusions
The computation of FFR\textsubscript{OCT} enables simultaneous assessment of the functional significance and anatomic characteristics of lesions with intermediate stenosis. This technique may be a useful approach for evaluating the simultaneous functional and anatomic severity of coronary stenosis.

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Disclosures
None.

References


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/content/10/1/e000022.full.pdf

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Correction to: Assessing Computational Fractional Flow Reserve From Optical Coherence Tomography in Patients With Intermediate Coronary Stenosis in the Left Anterior Descending Artery

In the article by Ha et al, “Assessing Computational Fractional Flow Reserve From Optical Coherence Tomography in Patients With Intermediate Coronary Stenosis in the Left Anterior Descending Artery,” which published online August 8, 2016, and appeared in the August 2016 issue of the journal (*Circ Cardiovasc Interv*. 2016;9:e003613. DOI: 10.1161/CIRCINTERVENTIONS.116.003613), a correction is needed.

On page 4, Figure 2, has been replaced.

![Figure 2](http://circinterventions.ahajournals.org/content/9/8/e003613)

Figure 2. Correlation and agreement between fractional flow reserve (FFR) and FFR\textsubscript{OCT}. Between FFR and FFR\textsubscript{OCT} (A) the correlation was good and (B) agreement was acceptable. FFR\textsubscript{OCT} indicates computational FFR by optical coherence tomography (OCT).

This correction has been made to the current online version of the article, which is available at http://circinterventions.ahajournals.org/content/9/8/e003613.
Simulation process of fractional flow reserve (FFR) calculation.

1. Extraction of lumen borders of optical coherence tomography (OCT) images using ImageJ and developed software.

Lumen borders of OCT coronary images were semi-automatically extracted using ImageJ & developed software. The spatial scale of the OCT image was defined and lumen borders in Cartesian coordinates were then extracted and saved as a txt file format.

2. Three-dimensional (3D) reconstruction of coronary artery using SOLIDWORKS 2014.

Extracted lumen borders were smoothed out and a 3D surface image was then generated by a loft boss-base feature. Finally, the 3D model was saved as a Parasolid file format (http://help.solidworks.com/2013/English/SolidWorks/sldworks/c_Parasolid_Files_(x_t_b).htm) to import in finite element analysis software of ADINA.

3. Computational flow dynamics (CFD) simulation using ADINA 9.0.7.

Blood flow simulation was performed by solving the general conservative non-Newtonian Navier-Stokes equations and simulation parameters were set up according to the following steps.
(a) Specifying flow assumption

Blood was modeled as an incompressible and laminar flow. The difference of the wall shear stress would be small, thus the fluid-structure interaction was not considered.

(b) Modeling blood material

Blood was modeled using the Carreau model which relates the viscosity to shear rate (\(\dot{\gamma}\)) as shown in the equation below.

\[
\mu = \mu_\infty + (\mu_0 - \mu_\infty)[1 + (\lambda \dot{\gamma})^2]^\frac{n-1}{2}
\]

where \(\mu_0\) is the low shear viscosity of 0.056 Pa \cdot s, \(\mu_\infty\) is the high shear viscosity of 0.00345 Pa \cdot s, \(\lambda\) is the time constant, which is 3.313 s, \(n\) is the power index of value of 0.3568, constant \(A\) is \(\lambda^2\), which is 10.9759, \(m\) is power law exponent index, that is \(\frac{n-1}{2} = -0.3216\). Blood density was assumed as 1,060 kg/m\(^3\).
(c) Defining body density

Element edge length was 0.5 mm and 4-nod tetrahedral elements of approximately 45,000 were generated for each model.

(d) Choosing solution process

Flow-condition-based-interpolation-center (FCBI-C) formulation of element was selected to have stable solution schemes.
(e) Defining time function and step

Velocity and pressure was defined by time functions from 0 to 1 second and the number of time steps was 10.

(f) Defining special wall condition

A no-slip condition was utilized to calculate the interaction between the vessel wall and blood flow.
(g) Setting the boundary condition

To perform steady-state CFD analysis, the mean flow rate of 0.273 m/s was obtained by averaging the velocities on coronary angiography using the TIMI frame count. The mean blood pressure of 93.2 mmHg (12,427 Pa) was calculated by averaging the mean pressures acquired at the guiding catheter tip in 37 lesions (retrospective group). The mean flow rate was applied as a boundary condition at the inlet and mean blood pressure was applied at the outlet, respectively.

(h) Calculating FFR after simulation

Both the inlet and outlet pressures were obtained by averaging pressure values at multiple points. FFR was then calculated as the mean pressure at the outlet divided by the mean derived pressure at the inlet.

\[ \text{FFR}_\text{OCT} = \frac{P_{\text{inlet}}}{P_{\text{outlet}}} \]
Inlet

0.273 m/s

Outlet

93.2 mmHg