distribution or active migration of injected agents. The last may be the most important, because the nature of the recipient tissue and the capacity of cells to attach to, and resist detachment from, native cells or extracellular matrix are major determinants of transplanted cell survival (4). It is here that the C-Cathez, by increasing myocardial dispersion, may have its greatest impact on biologic efficacy.

The use of the C-Cathez in CHART-1 is the largest and most detailed experience with intramyocardial injection and demonstrates 2 key attributes for adoption into the clinical arena: ease of use and efficiency of biologics retention (5). We have developed a method using common imaging modalities for this novel transendocardial device, thus providing a platform for the administration of biologics in patients with myocardial disease.

Warren Sherman, MD
***Jozef Bartunek, MD, PhD**
Dariouch Dolatabadi, MD
Ricardo Sanz-Ruiz, MD
Branko Beleslin, MD, PhD
Wojtek Wojakowski, MD, PhD
Guy Heyndrickx, MD, PhD
Jose Zefu Kimpalou, MSc
Scott A. Waldman, MD, PhD
Gerrit J. Laarman, MD, PhD
Aymeric Seron, PhD
Atta Behfar, MD, PhD
Jean-Pierre Latere, PhD
Andre Terzic, MD, PhD
William Wijns, MD, PhD
for the CHART Program

*Cardiovascular Center
Onze-Lieve-Vrouwziekenhuis OLV Hospital
Moorselbaan 164
B-9300 Aalst
Belgium
E-mail: jozef.bartunek@olvz-aalst.be

https://doi.org/10.1016/j.jcin.2017.10.036

Please note: This study was sponsored by Celyad. Dr. Sherman was employed by Celyad during the time CHART-1 was conducted and is now a paid consultant. Dr. Bartunek is a member of an institution that has been a shareholder of Celyad. Dr. Dolatabadi was a study proctor for Celyad and received compensation in that role. Dr. Sanz-Ruiz was a study proctor for Celyad and received compensation in that role. Dr. Beleslin was a study proctor for Celyad and received compensation in that role. Dr. Wojakowski was a study proctor for Celyad and received compensation in that role. Dr. Heyndrickx was a study proctor and is a past consultant to Celyad. Dr. Seron and Mr. Kimpalou were employed by Celyad during the time CHART-1 was conducted. Dr. Waldman was the chair of the data safety and monitoring board for the CHART-1 trial and received compensation from Celyad for that role. Dr. Laarman was a consultant to Celyad and received compensation in that role. Dr. Behfar has received Mayo Clinic-administered research grants from Celyad. Dr. Latere is employed by Celyad. Dr. Terzic has received research grants, administered by the Mayo Clinic, from the Marriott Foundation, the Michael S. and Mary Sue Shannon Family, the Russ and Kathy VanCleve Foundation, the Leducq Fondation, the Florida Heart Research Institute, Celyad, and the National Institutes of Health. The Mayo Clinic has rights to future royalties from Celyad. Dr. Wijns has received institutional grants and support for research from Celyad. Cardiovascular Research Center Aalst was a cofounder of Cardio3Biosciences, now Celyad. Dr. Wijns is a shareholder and nonexecutive board member of Argonauts and Genae and a past board member and past shareholder of Cardio3Biosciences. Cardiovascular Research Center Aalst has received research grants on behalf of Dr. Wijns from several medical device companies (outside the submitted work). Drs. Sherman and Bartunek contributed equally to this work.

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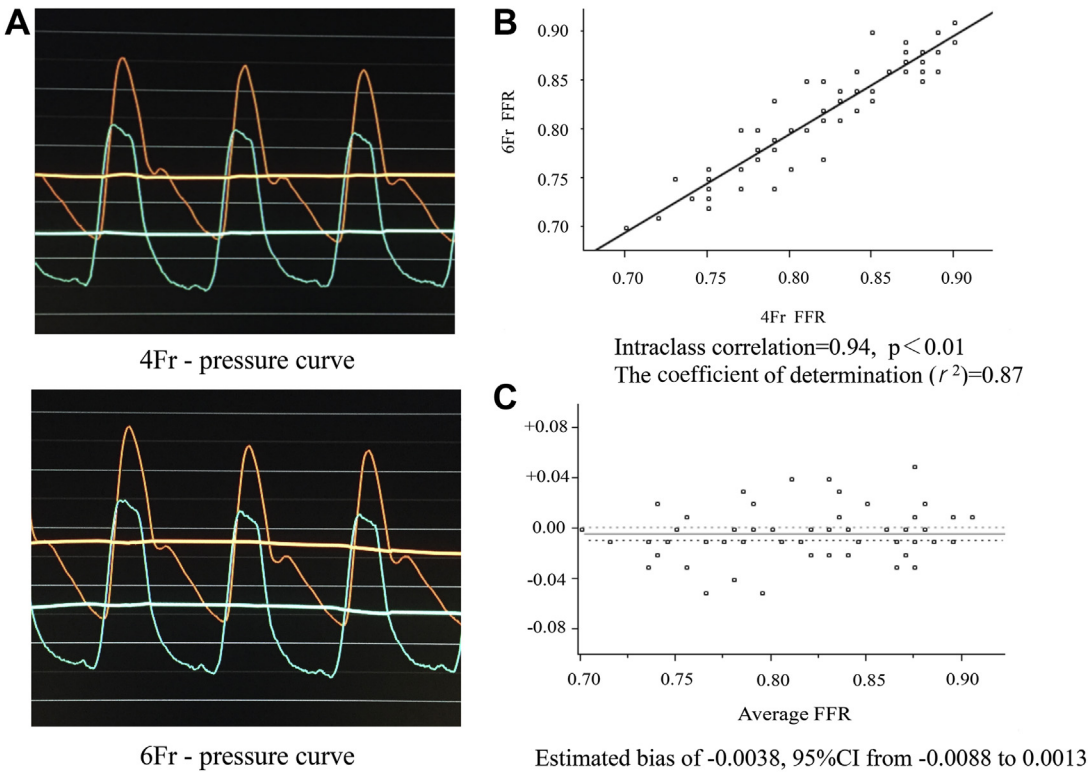
RESEARCH CORRESPONDENCE

The COFFEE Trial (COmparison of Fractional Flow Reserve Measurements through 4 FrEnch versus 6 FrEnch Diagnostic Catheter)

Fractional flow reserve (FFR) measurement is a well-established pressure wire-based procedure that is used to assess the functional severity of coronary lesions (1). Various randomized trials have demonstrated that FFR-guided revascularization improves clinical outcomes in patients with ischemic heart diseases (2,3). On the other hand, transradial access (TRA) is widely performed worldwide and has become the main access method. A clinical benefit to TRA, including less vascular complications and improved patient comfort, compared with the transfemoral approach, has been previously revealed (4,5). Therefore, in the TRA era, a less invasive procedure needs to be established. Although 5-F or 6-F catheter-based FFR is routinely performed, the use of much smaller catheters has not been established. Furthermore, the standard approach for measuring FFR throughout the

FIGURE 1 FFR Analysis via 4-F and 6-F Catheters



(A) A typical fractional flow reserve (FFR) recording. Pressure curves obtained via a 4-F diagnostic catheter are comparable to those obtained via a 6-F diagnostic catheter. Accurate pressure tracing is obtained via a 4-F diagnostic catheter. **(B)** Linear regression analysis of FFR measurements comparing FFR measured via a 4-F catheter with that via a 6-F catheter. There was a strong and linear correlation between both FFR measurements (i.e., 4-F FFR [x-axis] vs. 6-F FFR [y-axis]). **(C)** Bland-Altman analysis of the 2 sets of measurement to allow easier visualization of the direction of data. CI = confidence interval.

world is still using a guiding catheter. The aim of this study was to compare the accuracy of FFR measurement via 4-F diagnostic catheters compared with that via 6-F in the same coronary lesion.

In a prospective, single-center study performed between October 2016 and May 2017, we verified the accuracy of FFR results obtained with a 4-F diagnostic catheter compared with those obtained with a 6-F diagnostic catheter. This clinical study was registered with the University Hospital Medical Information Network Clinical Trials Registry (UMIN000025089). All patients had arterial access established before the procedure using a 6-F Glidesheath Slender (Terumo, Tokyo, Japan). The COMET Pressure Guidewire (Boston Scientific, Minneapolis, Minnesota) was used in all cases. In the current study, the cutoff value for clinical significance was 0.80. If FFR measured through the 4-F diagnostic catheter was between 0.70 and 0.90, the measurement through a 6-F diagnostic catheter was evaluated.

Paired (4-F and 6-F diagnostic catheter FFR) recordings taken from 62 vessels in 61 consecutive patients were suitable for this analysis. The mean age was 70.9 ± 8.6 years. Stable angina pectoris was the presentation in 55 (90%) patients. Pressure curves obtained via a 4-F catheter were similar to those via a 6-F catheter (**Figure 1A**). The mean FFR values measured using the 4-F and 6-F diagnostic catheters were 0.82 ± 0.05 and 0.82 ± 0.06, respectively (p = 0.97).

Figure 1B illustrates corresponding steady-state FFR measurements for each lesion as (x, y) coordinates. The line of identity is revealed as a solid line on this graph. The majority of readings lie close to this line, indicating a good agreement between FFR values derived from the 4-F and 6-F catheters

(intraclass correlation = 0.94; $p < 0.001$, $r^2 = 0.876$). Figure 1C shows a Bland-Altman plot of the same data. Many cases were found in which the FFR value was actually lower when measured using a 4-F catheter than when using a 6-F catheter (represented as data points above the x-axis on the graph). There were similarly several other cases in which the converse is true. Formal evaluation of the agreement between these 2 measurements of FFR by Bland-Altman plot analysis indicated an estimated bias of −0.0038 with the 95% limit of agreement extending from −0.0088 to 0.0013, which indicates no evidence for a systemic direction of bias of FFR measurements from the two different catheters.

In this study, aortic wave distortion (loss of the dicrotic notch) was found in 3 cases but only when using the 4-F diagnostic catheters. All 3 cases had a severely tortuous innominate artery via right radial artery approach. This anatomical variation in access route could make the inner lumen of a 4-F diagnostic catheter even narrower. Also, while using a 4-F catheter it is important to carefully inspect the quality of the Pa signal and flush the catheter adequately with saline to remove all contrast.

This is the first study to report the accuracy of FFR assessment using 4-F diagnostic catheters. The quality of the pressure curves through a 4-F catheter was comparable to that observed through a 6-F catheter. This method is particularly suited to the TRA era and may become widely accepted. Larger studies are warranted to further investigate the efficacy of this promising novel method in patients requiring FFR measurement.

***Noriaki Moriyama, MD**
Futoshi Yamanaka, MD
Koki Shishido, MD
Kazuki Tobita, MD
Shohei Yokota, MD
Takahiro Hayashi, MD
Tatsuya Koike, MD
Hirokazu Miyashita, MD
Hiroaki Yokoyama, MD
Takashi Nishimoto, MD
Takuma Takada, MD
Tomoki Ochiai, MD
Shingo Mizuno, MD
Yutaka Tanaka, MD, PhD
Masato Murakami, MD, PhD
Saeko Takahashi, MD
Shigeru Saito, MD

*Department of Cardiology and Catheterization Laboratories
Shonan Kamakura General Hospital
1370-1 Okamoto
Kamakura
Kanagawa 247-8533
Japan
E-mail: e2718nm@gmail.com

https://doi.org/10.1016/j.jcin.2017.12.007

Please note: The authors have reported that they have no relationships related to the contents of this paper to disclose.

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