Non-invasive procedure to calculate Fractional Flow Reserve in patients with coronary artery disease and its comparison with the gold standard

Manuel Insúa-Villa¹ Alberto Otero-Cacho^{1,2,3}, Alberto P. Muñuzuri^{2,3}, Vicente Pérez-Muñuzuri⁴,

Diego López-Otero^{5,6}, María Bastos-Fernández^{5,6}, Brais Díaz-Fernández^{5,6}, and J.R. González-Juanatey^{5,6}

¹FlowReserve Labs S.L., Edificio Emprendia, 15782 Santiago de Compostela, Spain

²Group of Nonlinear Physics. University of Santiago de Compostela, 15782 Santiago de Compostela, Spain

³CITMAga, Santiago de Compostela, Spain

⁴Institute CRETUS, Group of Nonlinear Physics, University of Santiago de Compostela, Santiago de Compostela, Spain
⁵Cardiology and Intensive Cardiac Care Department, University Hospital of Santiago de Compostela, Santiago de Compostela, Spain
⁶Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares (CIBERCV), Madrid, Spain

Cardiovascular diseases are the leading cause of death in developing countries. The most common cause of cardiovascular disease is coronary artery disease. These are formed by the deposition of plaque on the walls of the endothelium, which produce a reduction in the blood supply and thus oxygen, increasing the risk of ischemia [1]. Fractional flow reserve (FFR) is a physiological measure that expresses the severity of a lesion caused by stenosis. It is an invasive procedure in which a pressure guidewire is introduced inside the arteries under hyperemic conditions. Numerous studies have been carried out comparing FFR, the gold standard procedure, with other procedures such as PCI (percutaneous coronary intervention). These conclude that the use of the FFR technique reduces the mortality rate and myocardial infarction [2].

Thanks to advances in technology, it is now possible to perform an FFR using CFD (computational fluid dynamics)[3]. This tool makes it feasible to simulate, in a virtual environment, the dynamics of the blood inside the heart. To do this, CT (computed Tomographic) cardiac images of individual patients and accurate boundary conditions, that simulate the normal functioning of the heart, are required [4]. This technique has been validated in studies comparing it against the invasive procedure (FFR) [5].

The main advantage of performing a FFR using CFD technology, is that it is a non-invasive test. In addition, it allows multiple variables to be measured, such as Wall Shear Stress (WSS). In particular, this variable is related to the appearance and growth of atherosclerosis plaque. Studies have shown how measuring the levels of WSS can help prevent the detachment of atherosclerosis plaques[6, 7].

In conclusion, the use of CFD techniques applied to the heart provides multiple advantages, including the elimination of the risks associated with invasive procedures, as well as broadening the spectrum of parameters that can be measured.

A comparison of the FFR calculation procedure between a coronary CFD model and its invasive counterparty will be presented.

- Bairey Merz, C., Pepine, C., Walsh, M., Fleg, J., Camici, P., Chilian, W., Clayton, J., Cooper, L., Crea, F., Di Carli, M. & Others Ischemia and no obstructive coronary artery disease (INOCA) developing evidence-based therapies and research agenda for the next decade. *Circulation.* 135, 1075-1092 (2017)
- [2] Pijls, N., Fearon, W., Tonino, P., Siebert, U., Ikeno, F., Bornschein, B., Veer, M., Klauss, V., Manoharan, G., Engstrm, T. & Others Fractional flow reserve versus angiography for guiding percutaneous coronary intervention in patients with multivessel coronary artery disease: 2-year follow-up of the FAME (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation) study. *Journal Of The American College Of Cardiology*. 56, 177-184 (2010)
- [3] Min, J., Leipsic, J., Pencina, M., Berman, D., Koo, B., Van Mieghem, C., Erglis, A., Lin, F., Dunning, A., Apruzzese, P. & Others Diagnostic accuracy of fractional flow reserve from anatomic CT angiography. *Jama*. **308**, 1237-1245 (2012)
- [4] Otero-Cacho, A., López-Otero, D., Insúa-Villa, M., Díaz-Fernández, B., Bastos-Fernández, M., García-Campos, A., Pérez-Muuzuri V., P. Muuzuri, A., González-Juanatey, J.R. Non-invasive assessment of coronary lesions by computer tomography fractional flow reserve compared to the invasive technique under hyperaemic and basal conditions. PLOS ONE. Submitted (2022)
- [5] Nakazato, R., Park, H., Berman, D., Gransar, H., Koo, B., Erglis, A., Lin, F., Dunning, A., Budoff, M., Malpeso, J. & Others Noninvasive fractional flow reserve derived from computed tomography angiography for coronary lesions of intermediate stenosis severity: results from the DeFACTO study. *Circulation: Cardiovascular Imaging.* 6, 881-889 (2013)
- [6] Michel, J., Delbosc, S., Ho-Tin-Noé, B., Leseche, G., Nicoletti, A., Meilhac, O. & Martin-Ventura, J. From intraplaque haemorrhages to plaque vulnerability: biological consequences of intraplaque haemorrhages. *Journal Of Cardiovascular Medicine*. 13, 628-634 (2012)
- [7] Lee, J., Choi, G., Koo, B., Hwang, D., Park, J., Zhang, J., Kim, K., Tong, Y., Kim, H., Grady, L. & Others Identification of high-risk plaques destined to cause acute coronary syndrome using coronary computed tomographic angiography and computational fluid dynamics. *Cardiovascular Imaging*. **12**, 1032-1043 (2019)