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TECHNOLOGY NOTE

A novel, patient-tailored method for non-invasive iFR_{CT} measurement

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Coronary artery disease (CAD) is one of the leading causes of mortality worldwide, accounting for about 30% of all deaths [1]. Early diagnosis and correct estimation of the hemodynamic significance of coronary stenoses are crucial to initiate pharmacotherapy and to qualify the patient for possible percutaneous or surgical revascularization.

Currently, invasive pressure-wire-based methods such as fractional flow reserve (FFR) and resting indices, e.g., instantaneous wave-free ratio (iFR), are the standard to assess the significance of coronary stenoses. However, invasive determination of iFR/FFR has disadvantages, including (i) the use of a potentially nephrotoxic contrast agent and ionizing radiation, (ii) vascular access complications in 1.5% of patients, (iii) damage of the atherosclerotic plaque or healthy arterial segment during guidewire passage in 0.5% of patients [2], and (iv) side effects of adenosine administration, required during FFR measurements, in 35% of patients (chest pain, dyspnea, and transient arrhythmias) [2].

The increasing use of computed tomography angiography (angio-CT) to diagnose CAD and plan PCI procedures has triggered the development of novel non-invasive methods for iFR_{CT}/FFR_{CT} evaluation [3–6]. The values of iFR_{CT}/FFR_{CT} can be numerically determined based on the flow simulation and pressure measurements. In the last decade, 4 solutions for non-invasive estimation of the hemodynamic significance of coronary stenoses using FFR_{CT} have become commercially available [7]. However, due to their feasibility only in a central core laboratory necessitating telemedicine and/or high costs, they are not commonly used in clinical practice. To circumvent the disadvantages of FFR, methods to determine iFR_{CT} have also been developed but not yet commercialized [3-6]. Those methods have limitations (Table 1). Therefore, we aimed to assess the effect of simplifications implemented in previous iFR_{CT} software on the estimation of coronary artery stenosis and propose a new method for coronary artery stenosis assessment using iFR_{CT}.

The simplifications in Table 1 yield the following shortages in the methods: lack of information on the vessel complex geometry, lack of blood-wall interaction, non-realistic flow model, and no possible patient comorbidities considered. Those shortages affect reliable estimation of iFR_{CT}.

In contrast to previous solutions (Table 1), our simulations include patient-specific conditions by considering blood pressure, stroke volumes, blood velocities, and heart rate (Fig. 1). This approach makes it possible to incorporate the impact of the patient's comorbidities on the hemodynamic parameters of the flow, enabling the most accurate representation of the physiological coronary blood

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Table 1. Comparison of methods for determining iFR_{CT}

Reference	[3]	[4]	[5]	[6]	Present study
Pearson correlation coefficient	0.65 (iFR_{CT} vs. FFR)	–	0.85 (iFR_{CT} vs. iFR)	0.68 (iFR_{CT} vs. iFR)	–
Geometrical model	3D model	1D model	3D model	3D model	3D model
Flow assumption	Newtonian fluid	Newtonian fluid	Newtonian fluid, laminar	Newtonian fluid	Non-Newtonian fluid, turbulent
Coronary artery wall assumption	Rigid wall	Wall viscosity coefficient	Rigid wall	Rigid wall	Elastic wall
Simulation boundary conditions	Resting correlation	Average data from literature	Correlation of flow and coronary vessel length	Resting correlation	Velocity, Windkessel model

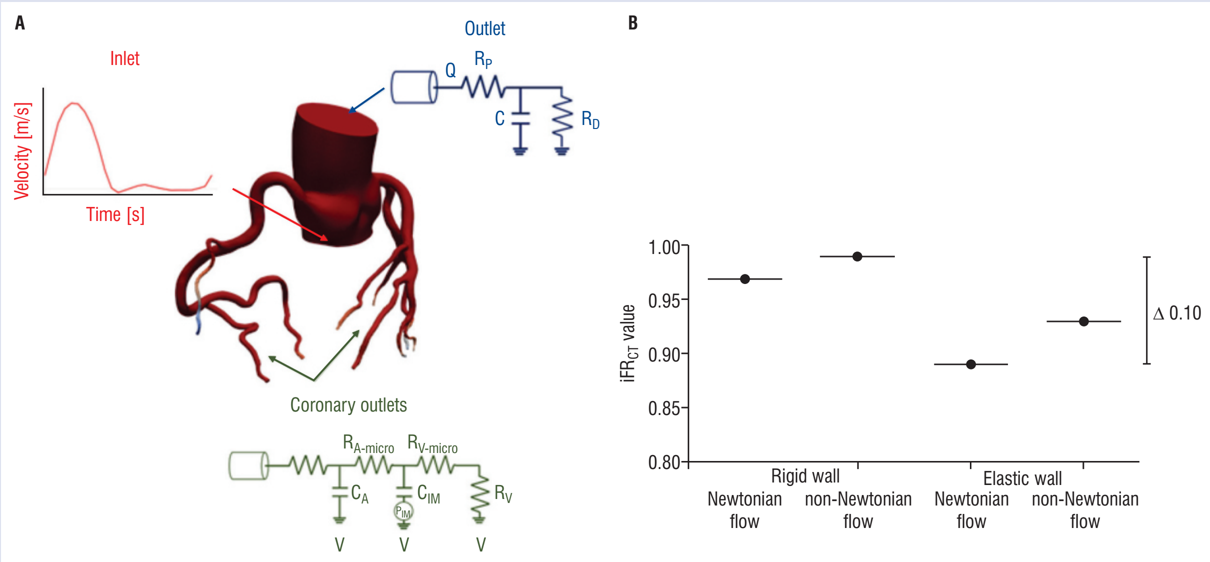

Figure 1. A. Assessment of coronary artery stenosis with patient-specific blood flow parameters; **B.** Effect of different variants of assumptions on the estimation of the iFR_{CT} index, leading to differences in iFR_{CT} value of up to 0.10

flow. Based on CT, 3D models were created, taking into account the branches of the coronary arteries. This issue is important because the number, length, and irregularity of the branches affect the value of the pressure behind the stenosis. Despite the promising results obtained with previous numerical methods for determining coronary artery stenosis, it is necessary to be cautious about the potential underestimation of the calculated values [3–6]. We analyzed the effect of different variants of assumptions on the estimation of the iFR_{CT} index, including (i) rigid wall, Newtonian blood flow, (ii) rigid wall, non-Newtonian blood flow, (iii) elastic wall, Newtonian blood flow, and (iv) elastic wall, non-Newtonian blood flow. The estimated iFR_{CT} indices for the considered cases are: (i) 0.97, (ii) 0.99, (iii) 0.89, and (iv) 0.93, respectively (Fig. 2). Clearly, the differences between the index values are considerable, ranging up to 0.10 units, and potentially changing the decision regarding the need for revascularization. Subsequently, our results show that the assumptions related to coronary artery wall, boundary conditions, and blood flow are fundamental because they can lead to inaccurate clinical decisions.

Our new methodology of non-invasive estimation of the iFR_{CT} index is based on numerical simulations of blood flow in the coronary arteries, whose geometry was generated from CT images. Our simulations showed that the above-listed conditions (iv) yielded the best match of the iFR_{CT} index (0.93) to the invasive examination value of iFR 0.92.

We conclude that the assumptions made in the flow numerical modelling significantly affect the results. To reliably estimate the iFR_{CT} index, numerous factors must be taken into account, i.e., a change in velocity over time as the boundary condition at the aortic inlet, boundary conditions at the truncated ends of the coronary arteries and the aortic outlet determined based on the Windkessel model, and fluid-structure interaction between the blood and the artery walls. The Windkessel model makes it possible to take into consideration very important factors determining the boundary conditions, i.e., the elasticity of blood vessels outside the considered artery system geometry, their possible pathology and complex reactions, and the effect of coronary artery wall material on blood flow. The results and the definition of an appropriate methodology can be the basis for the execution of an algorithm, allowing the determination of the iFR_{CT} index or preoperative planning based on CT images [7–10]. Further studies will include a larger number of patients to further develop a new method to accurately identify the hemodynamic significance of coronary artery stenosis and facilitate revascularization decisions.

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