Mini-Symposia Title:

Coronary physiology assessment in coronary artery disease

Mini-Symposia Organizer Name & Affiliation:

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Mini-Symposia Speaker Name & Affiliation 1:

Bon-Kwon Koo, Seoul National University Hospital, Republic of Korea

Mini-Symposia Speaker Name & Affiliation 2:

Chee Yang Chin, National Heart Centre Singapore, Duke-NUS Medical School. NUS. Singapore

Mini-Symposia Speaker Name & Affiliation 3:

Eun Bo Shim, Kangwon National University, South Korea

Mini-Symposia Speaker Name & Affiliation 4:

Liang Zhong, National Heart Centre Singapore, Duke-NUS Medical School. NUS. Singapore

S Mini-Symposia Speaker Name & Affiliation 5:

Mini-Symposia Speaker Name & Affiliation 6:

🜔 03. Micro/ Nano-bioengineering; Cellular/ Tissue Engineering &

O 4. Computational Systems & Synthetic Biology; Multiscale modeling

- 05. Cardiovascular and Respiratory Systems Engineering
- 🔘 06. Neural and Rehabilitation Engineering
- n 07. Biomedical Sensors and Wearable Systems
- 08. Biorobotics and Biomechanics
- O9. Therapeutic & Diagnostic Systems and Technologies
- 10. Biomedical & Health Informatics
- 11. Biomedical Engineering Education and Society
- C 12. Translational Engineering for Healthcare Innovation and Commercialization

Mini-Symposia Synopsis- Max 2000 Characters

Coronary artery disease (CAD) (also known as coronary artery disease, CAD) is defined as the blockage of coronary, due to a build-up of plaque inside the coronary artery. The plaque narrows the artery and impacts the blood supply to the heart and causes a damage of the heart muscle. CAD is a common disease, affecting 6% of adult general population, and up to 20% in age > 65 years old. The prognosis of CAD is poor. Revascularization of coronary territories with demonstrable myocardial ischemia, rather than anatomical stenoses per se, is imperative both for symptom reduction and outcome benefits. Invasive coronary angiography (ICA) with fractional flow reserve (FFR) measurement has emerged as the gold standard for assessment of coronary flow physiology, and hence, coronary territory ischemia. However, its measurement involves invasive procedure. CT coronary angiography (CTCA) is emerging as firstline of investigation of CAD. However, CTCA alone does not

determine whether a stenosis causes ischemia. Non-invasive FFR determination is an alternative approach using computational fluid dynamics (CFD) applied to coronary computed tomography coronary angiography (CTCA) images. Computation of FFRCT requires construction of an anatomical model of the coronary arteries; mathematical modeling of coronary physiology to derive boundary conditions representing cardiac output, aortic pressure, and microcirculatory resistance; and numerical solution of physical laws governing fluid dynamics.

Non-invasive FFR technology could be incorporated effectively into a clinical management pathway for patients with suspected or known CAD, and assist cardiologists in diagnosing ischemiacausing lesion and assisting their decision-making in the care of patients (i.e. medical treatment or stent treatment). We have invited several speakers from various disciplines

Theme:

O1. Biomedical Signal Processing

O2. Biomedical Imaging and Image Processing

CT-derived hemodynamic assessment: Past, present and future

Bon-Kwon Koo, M.D., Ph.D, Seoul National University Hospital, Republic of Korea

Abstract—

Invasive measurements of coronary artery blood flow and pressure can be used to assess whether atherosclerotic disease is causal of ischemia. Fractional flow reserve (FFR) is defined as the ratio of flow in the diseased vessel divided by the flow that would be attained in the vessel in the hypothetical case where the vessel was normal. FFR can be derived from pressure measurements assuming that the resistance to flow downstream of the measurement location would be the same in the hypothetical normal case. Non-invasive CT-derived computed FFR (FFR_{CT}) is a novel technology that enables non-invasive assessment of the functional significance of lesions from computational fluid dynamics (CFD) applied to coronary computed tomography angiography (cCTA). Since FFR_{CT} technology enabled non-invasive methods to model patient specific coronary geometry and physiology, this technology is applicable to plan the revascularization strategy and to the analysis of various hemodynamic parameters related with plaque progression and rupture.

The FFR_{CT} solution encompasses pressure and velocity fields and thus wall shear stress (WSS) or traction can be easily derived for the quantification of total plaque force or stress. Non-invasive assessment of those hemodynamic parameters can provide valuable information on the possibility of plaque progression and on the identification of rupture prone plaques.

Clinical application of these non-invasive hemodynamic indices will provide additional insight in understanding the patient's vulnerability and its association with hemodynamic indices. In a recently performed EMERALD study, addition of non-invasive hemodynamics derived from CT angiography significantly improved the ability to predict the risk of ACS. The results were the same even in non-obstructive lesions. Ongoing EMERALD II study will validate this concept.

Biographical sketch of the Speaker:

Dr. Bon-kwon Koo is a professor of Seoul National University, director of cardiovascular center and chair in Cardiology Division of Seoul National University Hospital, Seoul, Korea. Dr. Koo is an interventional cardiologist and his main research interest is imaging and physiology of coronary artery disease. Dr. Koo is a principal investigator of many domestic and international studies. He has published more than 400 papers in major journals. He was a course director of TCT-AP and is a course co-director of ENCORE course. He has performed series of studies on bifurcation lesions and coronary physiology/imaging which provided important insights in this field. His recent researches on noninvasive hemodynamic assessment using coronary CT angiography and computational fluid dynamics enables the assessment of FFR without invasive procedures and has started a new chapter in the diagnosis of coronary artery disease. This innovation has now been expanded to noninvasive treatment planner and non-invasive assessment for the risk of acute coronary syndrome

ACKNOWLEDGMENT

None

REFERENCES

- Koo BK, Erglis A, Doh JH et al. Diagnosis of ischemia-causing coronary stenoses by noninvasive fractional flow reserve computed from coronary computed tomographic angiograms. Results from the prospective multicenter DISCOVER-FLOW (Diagnosis of Ischemia-Causing Stenoses Obtained Via Noninvasive Fractional Flow Reserve) study. J Am Coll Cardiol 2011;58:1989-97.
- [2] Kim KH, Doh JH, Koo BK et al. A novel noninvasive technology for treatment planning using virtual coronary stenting and computed tomography-derived computed fractional flow reserve. JACC Cardiovasc Interv 2014;7:72-8.
- [3] Park JB, Choi G, Chun EJ et al. Computational fluid dynamic measures of wall shear stress are related to coronary lesion characteristics. Heart 2016;102:1655-61.
- [4] Lee JM, Choi G, Koo BK et al. Identification of High-Risk Plaques Destined to Cause Acute Coronary Syndrome Using Coronary Computed Tomographic Angiography and Computational Fluid Dynamics. JACC Cardiovasc Imaging 2019;12:1032-1043.

Physiology Guided PCI: what is the matter with clinician

Chee Yang Chin, MBBS, National Heart Centre Singapore; Duke-NUS Medical School, National

University of Singapore

Abstract—

The introduction of invasive physiology indices in the functional assessment of coronary artery disease has revolutionised the way clinical decisions are made whether or not to treat a coronary artery lesion by percutaneous coronary intervention (PCI). The fractional flow reserve (FFR) was introduced over 3 decades ago as a user friendly wire-based index using intra-arterial pressure gradients as a surrogate measurement for coronary blood flow. Over the last 15 years, the number of trials involving FFR has increased exponentially with robust data consistently supporting the superiority of an FFR-guided versus angiography-guided approach to PCI. It follows that FFR now receives the top level of recommendation from many international Cardiology societies as a required step before PCI is performed in patients with stable coronary artery disease. More novel indices have since been developed, namely the wire-based resting indices including the instantaneous wave free ratio (iFR), which overcome some of the main limitations of FFR such as the need for a hyperaemic drug agent which increases procedure time and affects patient comfort. Yet more novel tools available for use in the cardiac catheterisation laboratory include non-wire-based indices such as the quantitative flow reserve (QFR), which utilises computational fluid dynamics to estimate changes in flow based on angiographic findings. In this paper, we discuss the pivotal trial data supporting the use of these physiologic indices and their rise in prominence from mere research devices to real-world clinical tools for decision making.

Biographical sketch of the Speaker:

Asst Prof Chin is cardiologist consultant. He graduated from the University of Edinburgh (UK), in 2006 with both a Bachelor of Medicine and a Bachelor of Surgery. He obtained Membership of the Royal College of Physicians (UK) in 2009 and completed his basic medical training in the UK. In 2014, he completed his Advanced Specialist Training in Cardiology at the NHCS. For further training in Interventional Cardiology, he underwent a fellowship in Intravascular Coronary Imaging and Physiology at the Cardiovascular Research Foundation and Columbia University Medical Center in New York, USA, from 2015-2016. Asst Prof Chin is also active in clinical research and has multiple publications in major international peer-reviewed journals. Asst Prof Chin has a special passion for teaching and medical education, and he attained his Master of Science in Clinical Education degree in 2014. He actively participates in, and drives initiatives to enhance the training of junior doctors and medical students, including the introduction of online learning modules that has led to significant positive clinical impact. He holds several official teaching positions and is also a Core Faculty Member of the SingHealth Internal Medicine Residency Programme and a Physician Faculty Member of the SingHealth Cardiology Senior Residency Programme.

A novel Q-method for CT based fractional flow reserve

Eun Bo Shim, PhD, Kangwon National University& AI Medic Inc., Korea

Abstract—

Fractional flow reserve (FFR) is a hyperemic pressure ratioderived index to estimate stenosis severity in coronary artery as gold diagnostic standard. In spite of recent progresses in patients specific method of computed FFR (CT-FFR), there are still many unresolved problems. Especially, complicated model structure to compute patient specific model of CT-FFR is a typical example. The aim of this study is to propose a simple and efficient method of CT-FFR based on Q-method approach. This method couples computed tomography (CT)derived 3D computational fluid dynamics (CFD) model with Q-method based lumped parameter models (LPM).

In this work, steady flows were simulated to obtain noninvasively the coronary FFR values by using a multi-scale coronary modeling coupling CFD with the LPM of the cardiovascular system. The simulations of the multi-scale modeling were performed using a Navier-Stokes solver based on a segregated finite element scheme [1-3]. Inlet boundary condition for CFD model employed measured blood pressure data and we couple CFD outlet and LPM of microvascular system of coronary system for specification of outlet boundary condition of CFD model. To calculate the LPM parameters such as resistances and capacitances, we employed the novel scheme of Q-method. Here, resistance and capacitance values in this method were not initially set and iteratively adjusted according to the model geometry of coronary arteries.

Biographical sketch of the Speaker

Dr. Eun Bo Shim is Professor of Mechanical & Biomedical Engineering at the Kangwon National University in South Korea and Director, National Research Laboratory on Biosystems Engineering. He finished undergraduate course at Dept. of Mechanical Engineering of Seoul National University and received two PhDs; a PhD degree in Mechanical Engineering from the Korean Advanced Institute of Science and Technology in 1994 and a PhD degree in physiology from Kyoto University School of Medicine (Japan) in 2008. He is the director of the National Research Laboratory (NRL) on Biosystems Engineering funded by the Korean Government. He has served as General Secretary of the Korean Physiome Society, which is the leading Korean professional society to address mathematical modeling in physiology. From 2017 to 2018, he was the president of Bioengineering division of Korean Society of Mechanical Engineers. His major research interest is computational modeling of cardiovascular hemodynamics. He developed the CT-FFR simulation system based on coronary vessel-lengths and Q-method whose clinical performance were successfully

validated. He founded AI medic Inc (Seoul, Korea) and is now the CEO of AI Medic.

ACKNOWLEDGMENT

None.

REFERENCES

- Kwon SS, Chung EC, Park JS, Kim GT, Kim JW, Kim KH, Shin ES, Shim EB. A novel patient-specific model to compute coronary fractional flow reserve. Prog Biophys Mol Biol 2014;116:48e55.
- [2] Lee KE, Kim GT, Lee JS, Chung JH, Shin ES, Shim EB. A patientspecific virtual stenotic model of the coronary artery to analyze the relationship between fractional flow reserve and wall shear stress. Int J Cardiol. 2016 Nov 1;222:799-805.
- [3] Chung JH, Lee KE, Nam CW, Doh JH, Kim HI, Kwon SS, Shim EB, Shin ES, Diagnostic Performance of a Novel Method for Fractional Flow Reserve Computed from Noninvasive Computed Tomography Angiography (NOVEL-FLOW Study), American Journal of Cardiology 2017;120:362e368

A novel non-CFD based method for fractional flow reserve

assessment

Liang Zhong, PhD; National Heart Centre Singapore; Duke-NUS Medical School, National University of Singapore

Abstract:

Coronary artery disease (CAD) is a very common cause of heart failure affecting millions of people worldwide. Detection of ischemia - producing coronary stenosis is a critical component of clinical practice. Despite with established fractional flow reserve (FFR) from invasive coronary angiography (ICA), it is invasive and not without its own inherent risks. There is therefore a need for additional imaging technique for this important condition. Computed coronary tomographic angiography (CCTA) is a noninvasive test for diagnosis of anatomic coronary stenosis. Mathematical computational modeling applied to CCTA images, enables computation of FFR (CT-FFR) and other hemodynamic parameters [1-4]. In this talk, we will discuss CFD-based CT-FFR, our developed non-CFD method of CT-FFR_B, and the comparisons of existing methods with metaanalysis [5].

Non-CFD based CT-FFR will yield a quicker diagnosis test for the diagnosis of lesion specific ischemia in patients with CAD, which would be accessible to wide population.

Biographical sketch of the speaker:

Dr. Liang Zhong is Principal Investigator at the National Heart Centre Singapore (NHCS) and Associate Professor at Duke-NUS Medical School, National University of Singapore. He heads Cardiovascular Bioengineering Theme, Cardiovascular Image Processing Lab and Computational Cardiology Lab. Dr. Zhong has interest in the cardiovascular biomechanics, non-invasive cardiac imaging, and coronary circulation in health and disease, and medtech research. He has published more than 150 peer-reviewed articles in international journals, 18 book chapters. Dr. Zhong is the chairman of Engineering in Medicine and Biology Society (EMBS) Singapore Chapter, committee member of ISMRM Singapore Chapter and member of European Society of Cardiology, Currently, he has led in the development of noninvasive fractional flow reserve from computed tomography coronary angiography (CTCA) and computational fluid dynamics (CFD) in coronary artery disease (NCT03054324), and computational platform for right heart-pulmonary circulation in congenital heart disease (INITIATE multicentre study) (NCT03217240).

ACKNOWLEDGMENT

The study was supported by National Medical Research Council Singapore (NMRC/BnB/0017/2015; MOH-000358).

REFERENCES

- [4] Zhang JM, Zhong L, Luo T, et al. Numerical simulation and clinical implications of stenosis in coronary blood flow. *Biomedical Research International* 2014(2014), Article 514729, 10 page
- [5] Zhang JM, Zhong L, Yap JS, et al. Perspective on CFD studies of coronary artery disease lesions and hemodynamics – A review. *International Journal of Numerical Methods in Biomedicine*; 2014;30(6):659-680
- [6] Zhang JM, Zhong L, Luo T, et al. Simplified models of non-invasive fractional flow reserve based on CT images. *PLOS ONE* 2016;11(5):e0153070
- [7] Zhang JM, Shuang D, Baskaran L, et al. Advanced analyses of computed tomography coronary angiography can help discriminate ischemic lesions. *International Journal of Cardiology* 2018:267:208-214
- [8] Tan XW, Zheng QS, Shi LM, et al. Combined diagnostic performance of coronary computed tomography angiography and computed tomography derived fractional flow reserve for the evaluation of myocardial ischemia: A meta-analysis. International Journal of Cardiology 2017;236:100-106.

^{*}Research supported by National Medical Research Council Singapore (NMRC/BnB/0017/2015 and MOH-000358).

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