The Research Grants Council of Hong Kong NSFC/RGC Joint Research Scheme ______Joint Completion Report___

(Please attach a copy of the completion report submitted to the NSFC by the Mainland researcher)

Part A: The Project and Investigator(s)

1. Project Title

A comprehensive functional ultrasound imaging framework: the assessment of vascular mechanics for the diagnosis of cardiovascular diseases

	Hong Kong Team	Mainland Team
Name of Principal	Dr. Wei-Ning Lee	Dr. Jianwen Luo
Investigator (with title)		
Post	Associate Professor	Professor
Unit / Department /	Electrical and Electronic	Biomedical Engineering/
Institution	Engineering/The University	Tsinghua University
	of Hong Kong	
Contact Information	wnlee@eee.hku.hk	luo_jianwen@mail.tsinghua.e
	+852-39172703	<u>du.cn</u>
Co-investigator(s)	N.A.	Professor Yanping Cao
(with title and		(Engineering Mechanics/
institution)		Tsinghua University)
		Dr. Linxue Qian (Sonography/
		Beijing Friendship Hospital)

2. Investigator(s) and Academic Department/Units Involved

3. **Project Duration**

	Original	Revised	Date of RGC/ Institution Approval (must be quoted)
Project Start date	2016/01/01	N.A.	
Project Completion date	2019/12/31	N.A.	
Duration (in month)	48	N.A.	
Deadline for Submission of Completion Report	2020/12/31	N.A.	

Part B: The Completion Report

5. Project Objectives

5.1 Objectives as per original application

1. Develop a comprehensive functional ultrasound imaging framework to quantify and map vascular anisotropy and mechanics.

2. Establish a computational model of the vessel with material anisotropy to validate the proposed imaging framework.

3. Validate the framework in vessel-mimicking phantoms in vitro.

4. Investigate the feasibility of the framework in normal and pathological human vessels in a clinical setting.

NSFC/RGC 8 (Revised 01/18)

5.2 Revised Objectives

Date of approval from the RGC: <u>N.A.</u>

Reasons for the change: N.A.

6. Research Outcome

Major findings and research outcome (maximum 1 page; please make reference to Part C where necessary)

- (1) Shear waves, whether induced by acoustic radiation force or other vibration sources, propagate in a guided mode along different radii at different speeds due to the unique geometry of the artery (i.e., thin-walled hollow cylinder in normal cases). Therefore, a geometric correction method was proposed (Part C: Guo et al. 2017). In addition, the shear wave propagation in the thin arterial wall was found to be significantly modified by the surrounding media (Parc C: Lee et al. 2018).
- (2) Multi-directional shear moduli of the arterial wall were estimated and provided to estimate the degree of arterial anisotropy in a completely non-destructive way for the first time (Part C: Guo et al. 2018).
- (3) Arterial wall was found to stiffen during systole (artery expansion) and soften during diastole (recoil). The degree of stiffening and softening is described as mechanical nonlinearity. We proposed a novel graphical representation for this nonlinearity by a strain-shear modulus loop. For the first time, such a loop was established as a qualitative and quantitative measure for arterial functional analysis (Part C: Wang et al. 2019).
- (4) Fluid-structure interaction modeling and 3D-printed vessel-mimicking phantoms were established for anisotropic artery with branches. These two altogether serve as a versatile tool to investigate blood flow and arterial wall behavior comprehensively (Part C: Dong et al. 2020).
- (5) Noninvasive estimation of luminal pressure changes with our derived mathematical equations realized by the proposed imaging framework is demonstrated to be feasible and accurate (Part C: Wang and Lee 2020).
- (6) A new type of spontaneous wave propagating along the longitudinal axis of the arterial wall due to blood ejection from the left ventricle into the arterial network via aorta was discovered. Wave theory, computational modeling and experimental data analysis from human subjects were all done (Part C: Ran et al. 2020). Complementing existing indices, this may serve as a new indicator of arterial health.

Potential for further development of the research and the proposed course of action *(maximum half a page)*

The research has great potential in both basic science and commercialization. In terms of basic science, nonlinearity of the artery was scarcely examined, not to mention its noninvasive assessment. Whether degree of anisotropy and degree of nonlinearity of the arterial wall are more sensitive than arterial wall deformation, stiffness, and blood pressure, to detect early arterial malfunction in a multitude of arterial pathologies, e.g., hypertension, atherosclerosis, aging, and diabetes, should be investigated. This requires continuous and

closer collaboration with the Mainland team as we have complementary strengths and resources.

In terms of commercialization, our developed ultrasound imaging framework is compatible with state-of-the-art ultrasound systems and programmable. Offline processing can be packaged into a software application for user-interactive data analysis. This will greatly aid clinicians' diagnosis and even monitoring of arterial conditions. Publicity of our developed framework and talking with prominent ultrasound system manufacturers will be indispensable.

7. The Layman's Summary

(describe <u>in layman's language</u> the nature, significance and value of the research project, in no more than 200 words)

The research project aims at developing an ultrasound imaging framework that can make comprehensive assessment of the arterial health in a completely noninvasive and quick way. This is both a fundamental and translational research project. We have revealed and analyzed unique and complex elastic wave behaviors in the arterial wall which has a hollow cylindrical structure and is surrounded by soft biological tissues. The analysis permits us to quantify arterial stiffness in the circumferential direction accurately and unprecedentedly. We have proposed and examined a novel graphical indicator of arterial nonlinearity for better sensitivity to arterial health condition. We have discovered a new fast elastic wave that propagates in the artery once every heartbeat and demonstrated its direct association with the longitudinal wall stiffness in full scope from wave theory to computational models and living carotid arteries in healthy human subjects. The research overall has advanced our understanding of dynamic arterial properties and realized a safe ultrasound imaging framework that not only assesses arterial anisotropy, deformation, stiffness, nonlinearity, and luminal pressure change, but is also compatible with state-of-the-art ultrasound imaging systems to aid clinical diagnosis and prognosis.

Part C: Research Output

8. Peer-reviewed journal publication(s) arising directly from this research project

(Please attach a copy of each publication and/or the letter of acceptance if not yet submitted in the previous progress report(s). All listed publications must acknowledge RGC's funding support by quoting the specific grant reference.)

The Latest Status of Publications			Author(s)	Title and	Submitted	Attached to	Acknowledged	Accessible	
Year of	Year of	Under	Under	(bold the	Journal/ Book	to RGC	this report	the support of	from the
publication	Acceptance	Review	Preparation	authors	(with the	(indicate	(Yes or No)	this Joint	institutiona
	(For paper		_	belonging to	volume, pages	the year		Research	l repository
	accepted but		(optional)	the project	and other	ending of		Scheme	(Yes or No)
	not yet			teams and	necessary	the		(Yes or No)	
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				author with an	specified)	report)			
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2018 UN. Lee* Stiffness Estimation in Vascular Shear Wave Imaging: A Simulation and Phantom Study," Applied Physics Letters, vol. 110, 193701, 2017. No Yes Yes 2018 Y. Guo, Y. Vang, E. JH. Chang, estimation of and WN. Lee* 'Multi-direct Yes (2018) No Yes 2018 Y. Guo, Y. Vang, E. JH. Chang, guided wave imaging (VGWI) with geometry correction," Ultrasound in Medicine and Biology, vol. 44, No. 4, pp. 884-896, 2018. No Yes Yes 2018 WN. Lee* "Experiment Wang Yes Yes Yes 2018 WN. Lee*, Vang, F. JH. Chang, Y. Guo, and Y. Yes Yes Yes 2018 WN. Lee*, Vang "Experiment In Soft Modia in Various Couping," Ultrasound in Medicine and Biology. Yes Yes	2017		Y. Guo, H.	"Transmural	Yes	No	Yes	Yes
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2019				Y. Wang, H.	"Bidirection	Yes	No	Yes	Yes
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					1184-1196,				
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2019				Y. Zhang, H.	"Imaging	No	Yes	Yes	Yes
				Li, WN.	Heart				
				Lee*	Dynamics				
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2020		Y. Wang and WN. Lee*	"Non-invasi ve Estimation of Localized Dynamic Luminal Pressure Change by Ultrasound Elastography in Arteries with Normal and Abnormal Geometries," <i>IEEE Trans.</i> <i>Biomedical</i> <i>Engineering</i> (early access)	No	Yes	Yes	Yes
2020		J. Dong, Y. Zhang, and WN. Lee*	"Walled vessel-mimi cking phantom for ultrasound imaging using 3D printing with a water-solubl e filament: design principle, fluid-structur e interaction (FSI) simulation, and experimental validation," <i>Physics in</i> <i>Medicine</i> <i>and Biology</i> , vol. 65, 085006, 2020.	No	Yes	Yes	Yes
2020	1	Y. Zhang, J. Dong, Z. Zhen, SY. Liao, HF. Tse, K. H. Yiu, and WN. Lee*	"Ultrasound Angiography with Tissue Echoes Filtering and Adaptive Image Formation," <i>IEEE Trans.</i> <i>Ultrason.</i> <i>Ferroelectr.</i> <i>Freq.</i> <i>Control</i>	No	Yes	Yes	No

2020	1		D. Ran, J. Dong, H. Li, and WN. Lee*	"A N Spontaneo Mechanic. Wave for Vivo Assessme of Arte Wall Anisotrop American Journal Physiolog 2020 (Manuscri #: H-00756-2 20)	New 1 ous cal cal cal cal cal cal cal cal cal cal	No	Yes	Yes	No
		1	J. Dong and WN. Lee*	"Guideling for computati al modell of fluid-struct e interact for anisotropi artery"	ion ling ctur tion ic	No	No	Yes	No

9. Recognized international conference(s) in which paper(s) related to this research project was/were delivered (Please attach a copy of each delivered paper. All listed papers must acknowledge RGC's funding support by quoting the specific grant reference.)

Month/Year, Place	Title	Conference Name	Submitted to RGC (indicate the year ending of the relevant progress report)	Attached to this report (Yes or No)	Acknowledged the support of this Joint Research Scheme (Yes or No)	Accessible from the institutional repository (Yes or No)
Oct/2016/Ver mont, USA	"Bi-Plane Arterial Wall Stiffness Estimation Using Shear Wave Imaging: A Simulation and Phantom Study"	International Tissue Elasticity Conference, Vermont, New England, USA, Oct 16-19, 2016.	Yes	No	Yes	No

April/2017/M elbourne, Australia	"Shear Wave Elastography for the Characterization of Arterial Wall Stiffness: A Thin-Plate Phantom and Ex Vivo Aorta Study"	Proc. In IEEE International Symposium on Biomedical Imaging, Melbourne, Australia, April 18-21, 2017.	Yes	No	Yes	Yes
May/2017/Ei ndhoven, The Netherlands	"MEMS pressure sensor array wearable for Traditional Chinese Medicine pulse-taking"	2017 IEEE 14th International Conference on Wearable and Implantable Body Sensor Networks (BSN). IEEE, 2017, 59-62.	Yes	No	Yes	Yes
September/20 17/ Washington DC, USA	"Estimation of arterial transverse stiffness using vascular guided wave imaging (VGWI) in comparison with pulse wave imaging (PWI)"	IEEE International Ultrasonics Symposium, Washington D.C., U.S.A., Sep 6-9, 2017.	Yes	No	Yes, on the poster	No
September/20 17/ Washington DC, USA	"Multi-plane estimation of the third- and fourth-order elastic constants of soft material"	<i>IEEE International</i> <i>Ultrasonics Symposium</i> , Washington D.C., U.S.A., Sep 6-9, 2017.	Yes	No	Yes, on the poster	No
September/20 17/ Washington DC, USA	"Experimental investigation of Shear Wave Imaging in Thin Soft Media in Various Coupling Conditions"	<i>IEEE International</i> <i>Ultrasonics Symposium</i> , Washington D.C., U.S.A., Sep 6-9, 2017.	Yes	No	Yes, on the poster	No
December/20 17/Hong Kong	"Assessment of Direction-depend ent Strain-Stiffness Relationship of Physiologically Pressurized Artery Using Ultrasound Elastographic Imaging"	5 th International Conference on Biomedical Ultrasound, Hong Kong, Dec 2-4, 2017.	Yes	No	Yes	No

March/2018/ New York, USA	"Assessment of Direction-depend ent Strain-Stiffness Relationship of Physiologically Pressurized Artery Using Ultrasound Elastographic Imaging"	2018 American Institute of Ultrasound in Medicine (AIUM) Convention, New York, USA, March 24-28, 2018.	Yes	Yes	Yes, appeared in the presentation slides	No
Sep/2018/ Avignon, France	"A comparison study of mapping stiffness distribution of partially stiffened porcine aorta,"	International Tissue Elasticity Conference, Avignon, France, Sep 9-12, 2018.	No	Yes	Yes, appeared in the presentation slides	No
Oct/2018/ Kobe, Japan	"Bi-directional Ultrasound Assessment of Nonlinear Mechanical Behavior of Physiologically Pressurized Artery in Both Normal and Hardening Conditions"	IEEE International Ultrasonics Symposium, Kobe, Japan, Oct 22-25, 2018.	No	Yes	Yes, on the poster	No
Oct/2019/ Glasgow, Scotland	"Non-invasive estimation of localized intraluminal pressure in the artery by an ultrasound elastographic imaging framework"	<i>IEEE International</i> <i>Ultrasonics Symposium</i> , Glasgow, Scotland, Oct 6-9, 2019.	No	Yes	Yes, on the poster	No
Oct/2019/ Glasgow, Scotland	"Influence of blood vessel wall nonlinearity on flow velocity: a fluid-structure interaction (FSI) simulation study with in vitro validation"	<i>IEEE International</i> <i>Ultrasonics Symposium</i> , Glasgow, Scotland, Oct 6-9, 2019.	No	Yes	Yes, on the poster	No
Oct/2019/ Glasgow, Scotland	"Noninvasive Coronary Angiography with Ultrafast Cascaded-wave Ultrasound"	<i>IEEE International</i> <i>Ultrasonics Symposium</i> , Glasgow, Scotland, Oct 6-9, 2019.	No	Yes	Yes, appeared on the poster	No

Dec/2019/ San Diego, California	"Computational and ultrafast ultrasound assessment of arterial bi-directional stiffness from spontaneous pulsatile waves"	178th Meeting of the Acoustical Society of America, San Diego, California, U.S.A., Dec 2-6, 2019 (Student Travel Award)	No	Yes	Yes, appeared in the presentation slides	No
Sep/2020/ Las Vegas, USA	"Wrist-side Pulse Sensing: Pilot Comparison between Ultrasound Imaging and a Wearable Pulse-taking Sensor"	<i>IEEE International</i> <i>Ultrasonics Symposium</i> , Las Vegas, USA, Sep 6-11, 2020.	No	Yes	Yes, on the poster	No
Sep/2020/ Las Vegas, USA	"Quantitative Assessment of Arterial Anisotropy by Spontaneous Pulsatile Waves"	<i>IEEE International Ultrasonics Symposium</i> , Las Vegas, USA, Sep 6-11, 2020.	No	Yes	Yes, on the poster	No

10. Student(s) trained (*Please attach a copy of the title page of the thesis.*)

Name	Degree registered for	Date of registration	Date of thesis submission/ graduation
Yuexin Guo	PhD	2013/09/01	2017/11 (graduation)
Yahua Wang	PhD	2016/09	2020/11 (graduation)
Jinping Dong	PhD	2016/09	2021/01 (submission)
Dan Ran	PhD	2017/09	2021/06 (submission)
Enoch JH. Chang	BEng	2013/09/01	2017/05 (graduation)
Ho Yuen Lo	BEng	2013/09/01	2017/05 (graduation)

11. Other impact (*e.g. award of patents or prizes, collaboration with other research institutions, technology transfer, etc.*)

This is a collaboration project with Tsinghua University in Beijing, China. Mr. Dong was awarded as a finalist at the 2018 International Tissue Elasticity Conference, a leading conference in our research field. Mr. Ran received a student travel grant from American Society of Acoustics, a leading acoustical society. Mr. Chang received an undergraduate student thesis prize in 2017.

12. Statistics on Research Outputs (*Please ensure the summary statistics below are consistent with the information presented in other parts of this report.*)

	Peer-reviewed	Conference	Scholarly books,	Patents awarded	Other research
	journal	papers	monographs and		outputs
	publications		chapters		(Please specify)
No. of outputs	7 published;	16	0	0	2 (student
arising directly	2 under review;				awards)
from this research	1 under				
project [or	preparation				
conference]					