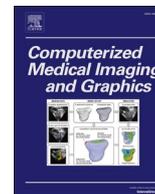




Contents lists available at ScienceDirect

# Computerized Medical Imaging and Graphics

journal homepage: [www.elsevier.com/locate/compmedimag](http://www.elsevier.com/locate/compmedimag)

## Editorial

### Recent advances in artificial intelligence for cardiac imaging



#### 1. Introduction

In recent years, major advancements have been made in Artificial Intelligence (AI), which are rising in sophistication, complexity and autonomy. A continually veritable and explosive data growth with a rapid iteration of the innovation of computer hardware provides a turbo boost for AI development. AI is an overarching term in computer science and an umbrella concept that provides means to imbue machines with human-like “general” intelligence with minimal human intervention. It encompasses a wide variety of research studies, from computer vision, natural language processing, and robotics to medical data analysis, including both theoretical and practical development of machine learning and newly rebranded and prosperous deep learning.

Cardiovascular disorders are the leading cause of death and morbidity worldwide. AI approaches, in particular, deep learning, are especially suited to solving the problems of scalability and high data dimensionality and are showing great potential in the research of cardiac imaging. Recent advances include automated coronary artery calcium score analysis from non-contrast cardiac-gated CT scans (Zhang et al., 2021a, b), multitask learning for estimating multitype cardiac indices in MRI and CT (Yu et al., 2021), diagnosis of chronic myocardial infarction on non-enhanced cardiac Cine MRI (Zhang et al., 2019), direct quantification of coronary artery stenosis (Zhang et al., 2020), diagnosis of coronary cardiac disease using intravascular ultrasound (Cao et al., 2020), segmentation and quantification of scars of atrial fibrillation (Li et al., 2020a; Yang et al., 2020), post-processing and segmentation for *in vivo* cardiac diffusion tensor MR (Ferreira et al., 2020), echocardiographic sequences segmentation (Li et al., 2020b), and multimodal whole heart segmentation (Shi et al., 2018; Zhuang et al., 2019). In addition to computer-aided diagnosis, anatomical and lesion segmentation, recent studies also include investigations in fast cardiac imaging (Schlemper et al., 2018; Seitzer et al., 2018).

In this Special Issue, we have carefully gleaned the state-of-the-art AI powered cardiac imaging research studies, which have addressed outstanding methodological issues as the area transitions from pilot studies to widespread clinical deployment, from one-dimensional global descriptors to high-resolution patient-specific representations of both whole heart and regional structural and functional analysis.

A total of twenty-two papers submitted underwent two to three rounds of rigorous peer review. In this Special Issue, thirteen papers were eventually chosen for publication. Each paper was closely reviewed by 3–4 experts and went through a thorough phase of revision, usually consisting of at least two rounds of revision. There were a few excellent papers that, unfortunately, due to space constraints and reviewers’ feedback, could not be included in the Special Issue.

#### 2. Special issue papers

Below we summarised the major contributions of the papers selected for this special issue in the order of acceptance date.

Ciusdel et al. (Ciusdel et al., 2020), in their paper entitled “Deep Neural Networks for ECG-free Cardiac Phase and End-Diastolic Frame Detection on Coronary Angiographies”, proposed a solely image-based workflow that relied on deep neural networks (DNN) for fully automatic cardiac process and end-diastolic frame (EDF) detection from coronary angiographies. The first DNN, equipped to identify coronary arteries, was used to preselect a subset of frames in which coronary arteries were well evident. The second DNN forecasted the cardiac phase labels for each frame. The networks were trained on 56,655 coronary angiographies from 6820 patients and evaluated on 20,780 coronary angiographies from 6261 patients. The proposed image based workflow could potentially obviate the need for manual frame selection and ECG acquisition with high precision and recall for EDF prediction.

Ding et al. (Ding et al., 2020), in their paper entitled “CAB U-Net: an End-to-end Category Attention Boosting Algorithm for Segmentation”, reported an end-to-end 3D U-Net framework that combined the deep network calculation graph with the category attention boosting (CAB) module for the whole heart segmentation. The proposed framework leveraged a multi-scale paradigm with the optimised gradient flow in the network and made full use of the low resolution feature information. This could enhance the information of coarse segmentation without increasing computation costs significantly. By validation on the HVSMR 2016 Challenge and MM-WHS 2017 CT datasets, the method showed promising results compared to other state-of-the-art segmentation methods.

Liao et al. (Liao et al., 2020), in their paper entitled “MMTLNet: Multi-modality Transfer Learning Network With Adversarial Training for 3D Whole Heart Segmentation”, designed a generative adversarial networks (GAN) based *transfer learning* architecture (MMTLNet), which transferred from the source domain (e.g., from MRI domain) to the target domain (e.g., to the CT domain) by reconstructing the MRI images with a generator network and optimising the reconstructed MRI images with a discriminator network. Channel attention and spatial attention were also incorporated. This design could well fuse the MRI with CT data to fully explore the useful information from both domains to facilitate the multimodal whole heart segmentation. Compared to other recently proposed methods, this MMTLNet would achieve superior results.

Xue et al. (Xue et al., 2020), in their paper entitled “Left Ventricle Quantification With Sample-level Confidence Assessment via Bayesian Neural Network”, investigated a novel left ventricle quantification method with a sample-level confidence assessment via the Bayesian

<https://doi.org/10.1016/j.compmedimag.2021.101928>

Available online 3 May 2021

0895-6111/© 2021 Elsevier Ltd. All rights reserved.

neural network. Two types of uncertainty, i.e., model uncertainty and data uncertainty, were analysed for the quantification performance and contributed to the sample-level confidence. Experimental studies on a dataset consisting of 145 subjects showed improved quantification performance and the sample-level confidence could provide an uncertainty measurement to draw clinicians' attention.

Budai et al. (Budai et al., 2020), in their paper entitled "Fully Automatic Segmentation of Right and Left Ventricle on Short-axis Cardiac MRI Images", demonstrated a regression-based fully automated method for the right and left ventricle segmentation. This regression-based framework could use a smaller network design because there was no need for deconvolutional layers in the second half of the network. The proposed method was lightweight, fast to train and required a relatively small amount of GPU resources. The results of ADCD datasets achieved similar performance to human observers.

Xiao et al. (Xiao et al., 2021), in their paper entitled "A New Deep Learning Method for Displacement Tracking From Ultrasound RF Signals of Vascular Walls", presented a new approach focused on deep learning to track the displacement of the vessel wall from ultrasound radiofrequency signals, which was a key technique for quantitative estimation of vascular biomechanics. Compared to conventional approaches, both simulation findings and experimental carotid artery evidence showed that this deep-learning approach obtained better precision for the motion tracking of the arterial walls. The proposed deep learning based method can potentially be applied to predict early pathology of the cardiovascular system.

Zhou et al. (Zhou et al., 2020), in their paper entitled "Pyramid Attention Recurrent Networks for Real-time Guidewire Segmentation and Tracking in Intraoperative X-ray Fluoroscopy", investigated a novel and powerful network architecture called Pyramid Attention Recurrent Networks (PAR-Net) for real-time segmentation and tracking of the guidewire. The proposed PAR-Net comprised three main components, namely the Pyramid Attention Module, the Recurrent Residual Module, and the Pre-Trained MobileNetV2 Encoder. In their PAR-Net, both reinforced focal loss and Dice loss were introduced to help resolve class imbalance problems and misclassified instances. Quantitative and qualitative analyses of clinical intraoperative images demonstrated that this PAR-Net significantly outperformed the baseline and previously reported results for tackling this task.

Candemir et al. (Candemir et al., 2020), in their paper entitled "Automated Coronary Artery Atherosclerosis Detection and Weakly Supervised Localization on Coronary CT Angiography With a Deep 3-Dimensional Convolutional Neural Network", developed a fully automated deep learning system to enable screening of a Coronary Computed Tomography Angiography (CCTA) examination for confident detection of the presence or absence of coronary artery atherosclerosis. The system first extracted the coronary arteries and their branches from CCTA datasets and represented them with multiplanar reformatted volumes. A 3D Convolutional Neural Network (3DCNN) was then implemented to model pathological changes (e.g., atherosclerotic plaques) in coronary vessels with pre-processing and augmentation techniques to increase the robustness and generalisation capability of the system. The evaluation of the developed system was performed on 247 patients with atherosclerosis and 246 patients without atherosclerosis. The developed system would be potentially useful to assist interpreting physicians to exclude coronary atherosclerosis in patients with acute chest pain.

Zhuang et al. (Zhuang et al., 2020), in their paper entitled "Cardiac VFM Visualization and Analysis Based on YOLO Deep Learning Model and Modified 2D Continuity Equation", utilised a YOLO based deep learning model and 2D continuity equation for visual analysis of the cardiac Vector Flow Mapping (VFM). The analysis contained the following steps: (1) the radial velocity values of blood particles were obtained, (2) the YOLO model was combined with the improved block matching algorithm to position and track the myocardial wall, (3) the azimuth velocity of the myocardial wall was obtained, and (4) the

nonlinear weight function was used to obtain the vortex diagram in the cardiac flow field. The experiments showed that the proposed method improved the accuracy of the cardiac VFM and could provide a new evaluation for the cardiac function.

Wu et al. (Wu et al., 2020), in their paper entitled "Left Ventricle Automatic Segmentation in Cardiac MRI Using a Combined CNN and U-Net Approach", devised a composite model combining CNN (ROI localisation) and U-Net (delineation) to accurately segment the left ventricle. The proposed method was validated using the cardiac MRI datasets extracted from the MICCAI 2009 Left Ventricular Segmentation Challenge. The testing results demonstrated the accuracy and robustness of the proposed model compared to state-of-the-art methods.

Zhao et al. (Zhao et al., 2020), in their paper entitled "Super-resolution of Cardiac Magnetic Resonance Images Using Laplacian Pyramid Based on Generative Adversarial Networks", combined the Laplacian pyramid architecture with Generative Adversarial Network (dubbed LSRGAN) to create cardiac MR images with superior perceptual image quality and increased peak signal-to-noise ratio in order to improve clinical diagnosis and treatment for myocardial ischemia and myocardial infarction.

Kong et al. (Kong et al., 2020), in their paper entitled "Learning Tree-structured Representation for 3D Coronary Artery Segmentation", developed an innovative tree-structured convolutional gated recurrent unit model to delineate the anatomical structure of the coronary artery. Compared to previously proposed tree-structured long short-term memory for semantic relatedness and sentiment classification in natural language processing, the designed tree-structured convolutional gated recurrent unit considered the local spatial correlations in the input data since the convolutions were used for input-to-state and state-to-state transitions; therefore, the proposed method could be more suitable for image analysis. The proposed framework was comprehensively evaluated on four large-scale 3D coronary computed tomography angiography datasets. Experimental results showed promising accuracy and efficiency compared with other coronary artery segmentation approaches.

de Albuquerque et al. (de Albuquerque et al., 2020), in their paper entitled "Fast Fully Automatic Heart Fat Segmentation in Computed Tomography Datasets", employed an advanced machine learning method, i.e., the clustering algorithm named Floor of Log that had a major advantage of processing efficiency for segmenting cardiac fat. More importantly, the method achieved relatively high accuracy for the segmentation task and could be useful as a medical diagnostic aid tool.

### 3. Conclusion

In this editorial, we briefly introduce thirteen exciting AI-based papers selected for this Special Issue, including 12 deep learning based and 1 machine learning based technologies. Among these thirteen studies, 2 used X-ray/Fluoroscopy, 2 used ultrasound/photoacoustic, 3 used CT, 5 used MRI, and 1 was applied for multimodal imaging. We hope that these most up to date and inspiring studies will encourage more groundbreaking ideas for translational science and advance the research of AI in the field of cardiovascular imaging towards precision cardiovascular medicine (Krittanawong et al., 2017) and further development of cardiovascular engineering. Ongoing research and future studies, e.g., on AI powered cardiac imaging-genetics research (de Marvao et al., 2019) and integration of explainable AI (XAI) and trustworthy AI (Yang et al., 2021), will usher in a new era of precision cardiovascular medicine and cardiovascular engineering.

Finally, we would like to thank all the authors who submitted their research studies to be willing to make contributions. Their encouragement and efforts have made this Special Issue a profound success. We would also like to express our gratitude to all the anonymous reviewers for their timely and constructive remarks that made our review efficient and productive even under the special circumstances of COVID-19 pandemic. Finally, we would also like to give our appreciation to the

editorial team, especially to Prof. Stephen Wong (the Editor-in-Chief), Ms. Jacqueline Zhu (Senior Publishing Content Specialist) and Ms. Suganya Dorai (Journal Manager), of Computed Medical Imaging and Graphics. Nothing would have happened without their strong support for this Special Issue.

## Acknowledgements

This work was supported in part by the British Heart Foundation (Project Number: TG/18/5/34111, PG/16/78/32402), in part by the European Research Council Innovative Medicines Initiative on Development of Therapeutics and Diagnostics Combating Coronavirus Infections Award “DRAGON: rapiD and secuRe AI imaging based diaGnosis, stratification, follow-up, and preparedness for coronavirus paNdemics” [H2020-JTI-IMI2 101005122] and in part by the AI for Health Imaging Award “CHAI MELEON: Accelerating the Lab to Market Transition of AI Tools for Cancer Management” [H2020-SC1-FA-DTS-2019-1 952172].

## References

- Budai, A., Suhai, F.I., Csorba, K., Toth, A., Szabo, L., Vago, H., Merkely, B., 2020. Fully automatic segmentation of right and left ventricle on short-axis cardiac MRI images. *Comput. Med. Imaging Graph.* 85, 101786 <https://doi.org/10.1016/j.compmedimag.2020.101786>.
- Candemir, S., White, R.D., Demirel, M., Gupta, V., Bigelow, M.T., Prevedello, L.M., Erdal, B.S., 2020. Automated coronary artery atherosclerosis detection and weakly supervised localization on coronary CT angiography with a deep 3-dimensional convolutional neural network. *Comput. Med. Imaging Graph.* 83, 101721 <https://doi.org/10.1016/j.compmedimag.2020.101721>.
- Cao, Y., Wang, Z., Liu, Z., Li, Y., Xiao, X., Sun, L., Zhang, Y., Hou, H., Zhang, P., Yang, G., 2020. Multiparameter synchronous measurement with IVUS images for intelligently diagnosing coronary cardiac disease. *IEEE Trans. Instrum. Meas.* 1 <https://doi.org/10.1109/TIM.2020.3036067>.
- Ciusdel, C., Turcea, A., Puiu, A., Itu, L., Calmac, L., Weiss, E., Margineanu, C., Badila, E., Berger, M., Redel, T., Passerini, T., Gulsun, M., Sharma, P., 2020. Deep neural networks for ECG-free cardiac phase and end-diastolic frame detection on coronary angiographies. *Comput. Med. Imaging Graph.* 84, 101749 <https://doi.org/10.1016/j.compmedimag.2020.101749>.
- de Albuquerque, V.H.C., de A Rodrigues, D., Ivo, R.F., Peixoto, S.A., Han, T., Wu, W., Rebouças Filho, P.P., 2020. Fast fully automatic heart fat segmentation in computed tomography datasets. *Comput. Med. Imaging Graph.* 80, 101674 <https://doi.org/10.1016/j.compmedimag.2019.101674>.
- de Marvao, A., Dawes, T.J.W., O'Regan, D.P., 2019. Artificial intelligence for cardiac imaging-genetics research. *Front. Cardiovasc. Med.* 6, 195. <https://doi.org/10.3389/fcvm.2019.00195>.
- Ding, X., Peng, Y., Shen, C., Zeng, T., 2020. CAB U-Net: an end-to-end category attention boosting algorithm for segmentation. *Comput. Med. Imaging Graph.* 84, 101764 <https://doi.org/10.1016/j.compmedimag.2020.101764>.
- Ferreira, P.F., Martin, R.R., Scott, A.D., Khaliq, Z., Yang, G., Nelles-Vallespin, S., Pennell, D.J., Firmin, D.N., 2020. Automating in vivo cardiac diffusion tensor postprocessing with deep learning-based segmentation. *Magn. Reson. Med.* 84, 2801–2814. <https://doi.org/10.1002/mrm.28294>.
- Kong, B., Wang, X., Bai, J., Lu, Y., Gao, F., Cao, K., Xia, J., Song, Q., Yin, Y., 2020. Learning tree-structured representation for 3D coronary artery segmentation. *Comput. Med. Imaging Graph.* 80, 101688 <https://doi.org/10.1016/j.compmedimag.2019.101688>.
- Krittanawong, C., Zhang, H., Wang, Z., Aydar, M., Kitai, T., 2017. Artificial intelligence in precision cardiovascular medicine. *J. Am. Coll. Cardiol.* 69, 2657–2664. <https://doi.org/10.1016/j.jacc.2017.03.571>.
- Li, L., Wu, F., Yang, G., Xu, L., Wong, T., Mohiaddin, R., Firmin, D., Keegan, J., Zhuang, X., 2020a. Atrial scar quantification via multi-scale CNN in the graph-cuts framework. *Med. Image Anal.* 60, 101595 <https://doi.org/10.1016/j.media.2019.101595>.
- Li, M., Wang, C., Zhang, H., Yang, G., 2020b. MV-RAN: Multiview recurrent aggregation network for echocardiographic sequences segmentation and full cardiac cycle analysis. *Comput. Biol. Med.* 120, 103728 <https://doi.org/10.1016/j.combiomed.2020.103728>.
- Liao, X., Qian, Y., Chen, Y., Xiong, X., Wang, Q., Heng, P.-A., 2020. MMTLNet: multi-modality transfer learning network with adversarial training for 3D whole heart segmentation. *Comput. Med. Imaging Graph.* 85, 101785 <https://doi.org/10.1016/j.compmedimag.2020.101785>.
- Schlemper, J., Yang, G., Ferreira, P., Scott, A., McGill, L.-A., Khaliq, Z., Gorodetzky, M., Roehl, M., Keegan, J., Pennell, D., Firmin, D., Rueckert, D., 2018. Stochastic deep compressive sensing for the reconstruction of diffusion tensor cardiac MRI. *International Conference on Medical Image Computing and Computer-Assisted Intervention (MICCAI)* 295–303.
- Seitzer, M., Yang, G., Schlemper, J., Oktay, O., Wuerfl, T., Christlein, V., Wong, T., Mohiaddin, R., Firmin, D., Keegan, J., et al., 2018. Adversarial and perceptual refinement for compressed sensing MRI reconstruction. *Medical Image Computing and Computer Assisted Intervention (MICCAI)* 232–240.
- Shi, Z., Zeng, G., Zhang, L., Zhuang, X., Li, L., Yang, G., Zheng, G., 2018. Bayesian VoxDRN: a probabilistic deep voxelwise dilated residual network for whole heart segmentation from 3D MR images. *Medical Image Computing and Computer Assisted Intervention (MICCAI)* 569–577.
- Wu, B., Fang, Y., Lai, X., 2020. Left ventricle automatic segmentation in cardiac MRI using a combined CNN and U-net approach. *Comput. Med. Imaging Graph.* 82, 101719 <https://doi.org/10.1016/j.compmedimag.2020.101719>.
- Xiao, C., Li, Z., Lu, J., Wang, J., Zheng, H., Bi, Z., Chen, M., Mao, R., Lu, M., 2021. A new deep learning method for displacement tracking from ultrasound RF signals of vascular walls. *Comput. Med. Imaging Graph.* 87, 101819 <https://doi.org/10.1016/j.compmedimag.2020.101819>.
- Xue, W., Guo, T., Ni, D., 2020. Left ventricle quantification with sample-level confidence estimation via Bayesian neural network. *Comput. Med. Imaging Graph.* 84, 101753 <https://doi.org/10.1016/j.compmedimag.2020.101753>.
- Yang, G., Chen, J., Gao, Z., Li, S., Ni, H., Angelini, E., Wong, T., Mohiaddin, R., Nyktari, E., Wage, R., Xu, L., Zhang, Y., Du, X., Zhang, H., Firmin, D., Keegan, J., 2020. Simultaneous left atrium anatomy and scar segmentations via deep learning in multiview information with attention. *Future Gener. Comput. Syst.* 107, 215–228. <https://doi.org/10.1016/j.future.2020.02.005>.
- Yang, G., Ye, Q., Xia, J., 2021. Unbox the Black-Box for the Medical Explainable AI Via Multi-modal and Multi-centre Data Fusion: A Mini-Review, Two Showcases and Beyond. *arXiv:2102.01998*.
- Yu, C., Gao, Z., Zhang, W., Yang, G., Zhao, S., Zhang, H., Zhang, Y., Li, S., 2021. Multitask learning for estimating multitype cardiac indices in MRI and CT based on adversarial reverse mapping. *IEEE Trans. neural networks Learn. Syst.* 32, 493–506. <https://doi.org/10.1109/TNNLS.2020.2984955>.
- Zhang, N., Yang, G., Gao, Z., Xu, C., Zhang, Y., Shi, R., Keegan, J., Xu, L., Zhang, H., Fan, Z., Firmin, D., 2019. Deep learning for diagnosis of chronic myocardial infarction on nonenhanced cardiac cine MRI. *Radiology* 291, 606–617. <https://doi.org/10.1148/radiol.2019182304>.
- Zhang, D., Yang, G., Zhao, S., Zhang, Y., Ghista, D., Zhang, H., Li, S., 2020. Direct quantification of coronary artery stenosis through hierarchical attentive multi-view learning. *IEEE Trans. Med. Imaging* 39, 4322–4334. <https://doi.org/10.1109/TMI.2020.3017275>.
- Zhang, N., Yang, G., Zhang, W., Wang, W., Zhou, Z., Zhang, H., Xu, L., Chen, Y., 2021a. Fully automatic framework for comprehensive coronary artery calcium scores analysis on non-contrast cardiac-gated CT scan: total and vessel-specific quantifications. *Eur. J. Radiol.* 134, 109420 <https://doi.org/10.1016/j.ejrad.2020.109420>.
- Zhang, W., Yang, G., Zhang, N., Xu, L., Wang, X., Zhang, Y., Zhang, H., Del Ser, J., de Albuquerque, V.H.C., 2021b. Multi-task Learning With Multi-view Weighted Fusion Attention for Artery-specific Calcification Analysis. *Inf. Fusion. In Press*.
- Zhao, M., Liu, X., Liu, H., Wong, K.K.L., 2020. Super-resolution of cardiac magnetic resonance images using laplacian pyramid based on generative adversarial networks. *Comput. Med. Imaging Graph.* 80, 101698 <https://doi.org/10.1016/j.compmedimag.2020.101698>.
- Zhou, Y.-J., Xie, X.-L., Zhou, X.-H., Liu, S.-Q., Bian, G.-B., Hou, Z.-G., 2020. Pyramid attention recurrent networks for real-time guidewire segmentation and tracking in intraoperative X-ray fluoroscopy. *Comput. Med. Imaging Graph.* 83, 101734 <https://doi.org/10.1016/j.compmedimag.2020.101734>.
- Zhuang, X., Li, L., Payer, C., Stern, D., Urschler, M., Heinrich, M.P., Oster, J., Wang, Chunliang, Smedby, O., Bian, C., Yang, X., Heng, P.-A., Mortazi, A., Bagci, U., Yang, Guanyu, Sun, C., Galisot, G., Ramel, J.-Y., Brouard, T., Tong, Q., Si, W., Liao, X., Zeng, G., Shi, Z., Zheng, G., Wang, Chengjia, MacGillivray, T., Newby, D., Rhode, K., Ourselin, S., Mohiaddin, R., Keegan, J., Firmin, D., Yang, Guang, 2019. Evaluation of algorithms for multi-modality whole heart segmentation: an open-access grand challenge. *Med. Image Anal.* 58, 101537 <https://doi.org/10.1016/j.media.2019.101537>.
- Zhuang, Z., Liu, G., Ding, W., Raj, A.N.J., Qiu, S., Guo, J., Yuan, Y., 2020. Cardiac VFM visualization and analysis based on YOLO deep learning model and modified 2D continuity equation. *Comput. Med. Imaging Graph.* 82, 101732 <https://doi.org/10.1016/j.compmedimag.2020.101732>.

Guang Yang<sup>a,b,\*</sup>

<sup>a</sup> National Heart and Lung Institute, Imperial College London, London, SW7 2AZ, UK

<sup>b</sup> Cardiovascular Research Centre, Royal Brompton Hospital, SW3 6NP, London, UK

Heye Zhang<sup>\*\*</sup>

School of Biomedical Engineering, Sun Yat-Sen University, Shenzhen, 510006, China

David Firmin<sup>a,b</sup>

<sup>a</sup> National Heart and Lung Institute, Imperial College London, London, SW7 2AZ, UK

<sup>b</sup> Cardiovascular Research Centre, Royal Brompton Hospital, SW3 6NP, London, UK

Shuo Li<sup>a,b</sup>

<sup>a</sup> Department of Medical Imaging, Western University, London, ON, Canada

<sup>b</sup> *Digital Imaging Group, London, ON, Canada*

\* Corresponding author at: National Heart and Lung Institute, Imperial College London, London, SW7 2AZ, UK.

\*\* Corresponding author.

*E-mail address:* [g.yang@imperial.ac.uk](mailto:g.yang@imperial.ac.uk) (G. Yang).  
*E-mail address:* [zhangheye@mail.sysu.edu.cn](mailto:zhangheye@mail.sysu.edu.cn) (H. Zhang).