applied sciences

Editorial

Biomedical Imaging Technologies for Cardiovascular Disease

Julio Garcia [1,2,3,4,5]

[1] Department of Radiology, Cumming School of Medicine, University of Calgary, Calgary, AB T2N 1N4, Canada; julio.garciaflores@ucalgary.ca
[2] Department of Cardiac Sciences, Cumming School of Medicine, University of Calgary, Calgary, AB T2N 1N4, Canada
[3] Libin Cardiovascular Institute, University of Calgary, Calgary, AB T2N 1N4, Canada
[4] Alberta Children's Hospital Research Institute, University of Calgary, Calgary, AB T2N 1N4, Canada
[5] Stephenson Cardiac Imaging Centre, University of Calgary, Calgary, AB T2N 1N4, Canada

1. Introduction

Non-invasive biomedical imaging technologies for investigating the heart's physiology, performance, function, and structure have increased in number and diversity over the past several years. The standard-of-care imaging techniques include echocardiography, X-rays, computed tomography, nuclear scans, magnetic resonance imaging (MRI), and catheterization. Each imaging technique provides specific information, with its own characteristics, advantages, and limitations. Important improvements in precision, sensitivity, accuracy, and refinement have been possible thanks to the technological advances in software and hardware. Better assessments of cardiovascular disease, hemodynamics, and biomarkers have aided the stratification of patient risk and therapy. The recent integration of artificial intelligence and machine learning have also supported novel approaches for personalized image-based diagnosis. Furthermore, image-based computation-assisted diagnosis is a promising means of uncovering key insights into disease progression and personalized solutions.

This Special Issue on Biomedical Imaging Technologies for Cardiovascular Disease collected the most recent progress in biomedical imaging technologies for cardiovascular disease. The original articles and reviews cover a wide range of subjects that can be classified into the following topics: (I) advances in Doppler echocardiography; (II) advances in magnetic resonance imaging; (III) specialized reviews.

check for updates

Citation: Garcia, J. Biomedical Imaging Technologies for Cardiovascular Disease. *Appl. Sci.* **2023**, *13*, 2209. https://doi.org/10.3390/app13042209

Received: 4 February 2023
Accepted: 7 February 2023
Published: 9 February 2023

2. Topic I: Advances in Doppler Echocardiography

Doppler echocardiography remains the primary imaging technique for the assessment of cardiovascular disease. This non-invasive imaging technique has a low cost, is easily accessible, and can be used in standard-of-care primary cardiovascular evaluations. The classification and monitoring progression proposed by the current AHA/ACC includes four stages that consider the factors that influence clinical decision making: severity status, irreversible consequences in the left and right ventricles, structural and functional changes in the whole heart, changes in cardiac pressures, development of cardiac arrythmias, and the presence of symptoms.

Heart failure (HF) is the most common cardiovascular disease worldwide affecting > 25 million people in industrialized countries [1]. The most widely used device-based therapy for the treatment of heart failure with a reduced ejection fraction (HFrEF) and a QRS duration > 150 ms is cardiac resynchronization therapy. Cardiac contractility modulation (CCM) has been available for patients with a narrow QRS and persistent symptoms or frequent HF hospitalization re-admissions. CCM improves the cardiac performance and reverses left ventricular (LV) remodeling. In this Special Issue, Contaldi et al. [2] analyzed the effects of CCM on right ventricular (RV) systolic function and RV–pulmonary artery (PA) coupling. They reported that HF patients who underwent CCM therapy showed a reduction of the RV diameters and improved RV systolic function, PA systolic pressure, and

RV–PA coupling after six months of follow-up. The latter findings remark on the potential benefit of CCM as device-based therapy for HF patients.

The therapeutic cross-link between urology and cardiovascular disease has been well reported and recognized. For example, the inhibitors of phosphodiesterase type 5 (PDE5i) are a common treatment for erectile dysfunction and are used to treat pulmonary hypertension. PDE5i holds back the breakdown of nitric oxide-driven cyclic guanosine monophosphate (cGMP) in smooth cells of the vascular bed, resulting in a potent vasodilator. cGMP signaling is abnormal in HF, and it has emerged as potential therapeutic option [3]. Crocetto et al. investigated whether tadalafil, a long-acting PDE5i, could also improve the diastolic function as assessed by echocardiography [4]. A total of 23 patients underwent the echocardiography assessment at the baseline, after 3 months, and after 6 months. This prospective study showed that after 6 months of erectile dysfunction therapy for secondary to radial prostatectomy, a positive effect was observed for the diastolic function by improving the E/e′ ration and peak velocity of the tricuspid jet. These findings suggest that a further investigation could be performed to assess the role of tadalafil as a treatment and to prevent diastolic dysfunction.

Tissue motion annular displacement (TMAD) is a well-known speckle-tracking-derived echocardiographic parameter that tracks the annular tissue towards the ventricular apex. TMAD is an angle-independent parameter that is commonly measured at the mitral and tricuspid valves and used for the assessment of ventricular function. In this Special Issue, Muntean et al. investigated the prognostic value of TMAD of the tricuspid valve in children with pulmonary arterial hypertension (PAH) [5]. PAH is a severe and progressive disease that causes RV disfunction over time in children. Its timely characterization and detection can improve pediatric PAH treatments. In this study, twenty PAH patient and twenty sex- and age-matched controls were enrolled at the baseline and after one year of follow-up. By comparing the healthy and poor PAH groups with the controls, the TMAD indices were significantly lower in the PAH groups ($p = 0.010$ and $p = 0.018$, respectively). These findings suggest that TMAD could be a good parameter to include in the assessment of pediatric PAH patients.

3. Topic II: Advances in Magnetic Resonance Imaging

The magnetic field properties of non-invasive MRIs cause the body's hydrogen atoms to align temporarily. Radiofrequency pulses are then applied to stimulate the protons out of equilibrium. The frequential response signal is collected and used to reconstruct an image of the region of interest. Cardiovascular MRIs provide detailed images to examine the heart's function, structure, cardiac motion, and tissue damage of the cardiac muscle. An additional advantage is the lack of radiation and use of iodine contrast.

Left ventricular hypertrophy (LVH) is presented in between 15% and 20% of the population. LVH is more frequent in patients with hypertension and obesity and in Afro-American people. Cardiac MRIs provide a comprehensive assessment of myocardial hypertrophy. Cardiac MRI has become the gold standard for ventricular volume quantification. Accurate measurements of the wall thickness, hypertrophy pattern, chamber size, and ventricular function are necessary for the proper characterization of LVH. These measurements often require the delineation of the region of interest in a large number of images per patient. In recent years, machine learning (ML) methods have been used to accelerate the segmentation of the ventricles for LV function quantification. In this Special Issue, Budai et al. aimed to automatically detect LVH in cardiac MRI scans by applying ML methods [6]. The authors developed an ensemble model based on a 3D ResNet. The study included 428 patients with LVH under various conditions and 234 healthy controls without any known cardiovascular diseases. The developed model achieved a 92% F1 score and 97% recall using the testing dataset, which are similar to those of expert reports. This study is an excellent example of the clinical cardiac applications of ML.

Standard-of-care cardiac MRI protocols typically use 2D phase contrast (PC) to assess heart hemodynamics. However, 2D PC only acquires the through-plane velocity for the flow quantification in the region/vessel of interest. A whole heart 3D hemodynamic acquisition of the velocity field can be achieved using a 4D-flow MRI. This Special Issue collected four studies investigating the clinical applications, validation, and novel approaches for 4D-flow MRI. The study by Hong et al. [7] aimed to investigate the hemodynamic changes within the PA and its association with ventricular remodeling and vascular architecture. This study included 33 patients with PAH and 17 healthy controls. The patients presented alterations in the PA, showing larger distances of PA bifurcation. In addition, the wall shear stress (WSS), kinetic energy (KE), and energy loss (EL) values decreased further in the PAH patients compared to those of the controls. The PA 4D-flow derived velocities were associated with RV ejection fraction. This study illustrated the potential usefulness of 4D-flow MRI for the hemodynamic assessment of the right heart, which is often more challenging to assess than the left heart.

One important aspect in the 4D-flow acquisition planning is the subject's respiratory motion. Respiratory gating is typically used to reduce the effects of respiratory motion and artifacts. Denecken et al. [8] performed a comparison of 4D-flow acquisitions with and without respiratory self-gating and its impact on the 4D-flow derived parameters. This study was conducted with 15 healthy controls. Their findings showed that the acquisition without respiratory self-gating underestimated the values in the aortic arch, the descending aorta, and diaphragmatic aorta. Both the acquisitions with and without respiratory self-gating showed a significant variability in the 4D-flow-derived parameters. However, respiratory compensation provided a more reliable quantification.

Advanced cardiac hemodynamic characterization ideally requires high temporal and spatial resolution datasets. A standard 4D-flow MRI acquisition can have >4000 images with an isotropic spatial resolution of 2–3 mm per voxel and 25–45 ms of temporal resolution. Despite the impressive characteristics of the standard 4D-flow acquisition, given the multidimensional and complex nature of the cardiac flow, it is difficult to assess the hemodynamic phenomena on a small scale. Recent studies applied finite element strategies to achieve computation fluid dynamics simulation characteristics. One application example is the study presented by Franco et al. [9]. In this study, the authors presented a proof of concept for the use of finite element methods in dilated cardiomyopathy (DCM). A total of 25 subjects, 12 controls, and 13 DCM patients were recruited to perform a comprehensive evaluation of the left intra-ventricular hemodynamics. Their approach demonstrated high inter- and intra-observer reproducibility and detected abnormal flow patterns in more detail than standard 4D-flow acquisitions can.

As cardiac MRI technology improves and 4D-flow MRI sequences become more widely used, several investigators have begun to question the inter- and intra-observer reproducibility in the whole heart. Juffermans et al. evaluated this aspect in the thoracic aorta for the most common 4D-flow derived parameters [10]. A cohort of 20 patients with aortic aneurysms were recruited for this purpose. They reported good reproducibility for normalized flow displacement and jet angle, a very good-to-excellent reproducibility for WSS and helicity, and an excellent reproducibility for vorticity.

These four studies in 4D-flow MRI illustrate the impressive technical and clinical application progress that has been made in recent years for this advanced cardiac flow technique.

4. Topic III: Specialized Reviews

This Special Issue included two review articles on positron emission tomography (PET) in coronary heart disease and the emerging use of ultrasmall supermagnetic particles iron oxide (USPIO) in cardiac MRI. De Almeida et al.'s review of PET imaging presented the recent advances in plaque imaging, and the use of 18F-Fluorodeoxyglucose for inflammation imaging, microcalcification imaging using 18F-Sodium Fluoride, myocardial perfusion imaging with Ribidium, 13N-Ammonia, and 15O-water, and viability imaging [11]. Tsampasian et al. presented a great summary of the properties of USPIO, its use in cardiac MRI, clinical applications, and safety parameters [12]. Both of these reviews assembled the state-of-the-art knowledge for PET imaging in coronary disease and USPIO in cardiovascular diseases.

Acknowledgments: This Special Issue would not be possible without the contribution of enthusiastic and talented authors. I would like to express my great gratitude to all of the reviewers. Your extraordinary feedback allowed the authors to improve their manuscripts and sustain the high-quality peer review standards. I would like to recognize the amazing work from the dedicated editorial team of *Applied Sciences* in assembling this Special Issue.

Conflicts of Interest: The author declares no conflict of interest.

References

1. Savarese, G.; Lund, L.H. Global Public Health Burden of Heart Failure. *Card. Fail. Rev.* **2017**, *3*, 7. [CrossRef] [PubMed]
2. Contaldi, C.; De Vivo, S.; Martucci, M.L.; D'Onofrio, A.; Ammendola, E.; Nigro, G.; Errigo, V.; Pacileo, G.; Masarone, D. Effects of Cardiac Contractility Modulation Therapy on Right Ventricular Function: An Echocardiographic Study. *Appl. Sci.* **2022**, *12*, 7917. [CrossRef]
3. Kong, Q.; Blanton, R.M. Protein Kinase GI and Heart Failure. *Circ. Heart Fail.* **2013**, *6*, 1268–1283. [CrossRef] [PubMed]
4. Crocetto, F.; Cuomo, V.; Santoro, C.; Fiorillo, L.; Barone, B.; Arcaniolo, D.; Fedele, T.; Imbimbo, C.; Esposito, R. New Possibilities in Heart Failure: The Effects of Tadalafil on Diastolic Function in Patients Undergoing Robot-Assisted0 Radical Prostatectomy. *Appl. Sci.* **2022**, *12*, 5629. [CrossRef]
5. Muntean, I.; Melinte, M.; Făgără, A.; Șuteu, C.C.; Togănel, R. A Novel Speckle-Tracking Echocardiography Derived Parameter That Predicts Clinical Worsening in Children with Pulmonary Arterial Hypertension. *Appl. Sci.* **2022**, *12*, 5494. [CrossRef]
6. Budai, A.; Suhai, F.I.; Csorba, K.; Dohy, Z.; Szabo, L.; Merkely, B.; Vago, H. Automated Classification of Left Ventricular Hypertrophy on Cardiac MRI. *Appl. Sci.* **2022**, *12*, 4151. [CrossRef]
7. Hong, Z.M.; Garcia, J. Pulmonary Artery Remodeling and Advanced Hemodynamics: Magnetic Resonance Imaging Biomarkers of Pulmonary Hypertension. *Appl. Sci.* **2022**, *12*, 3518. [CrossRef]
8. Denecken, E.; Sotelo, J.; Arrieta, C.; Andia, M.E.; Uribe, S. Impact of Respiratory Gating on Hemodynamic Parameters from 4D Flow MRI. *Appl. Sci.* **2022**, *12*, 2943. [CrossRef]
9. Franco, P.; Sotelo, J.; Montalba, C.; Ruijsink, B.; Kerfoot, E.; Nordsletten, D.; Mura, J.; Hurtado, D.; Uribe, S. Comprehensive Assessment of Left Intraventricular Hemodynamics Using a Finite Element Method: An Application to Dilated Cardiomyopathy Patients. *Appl. Sci.* **2021**, *11*, 11165. [CrossRef]
10. Juffermans, J.F.; van Assen, H.C.; te Kiefte, B.J.; Ramaekers, M.J.; van der Palen, R.L.; van den Boogaard, P.; Adriaans, B.P.; Wildberger, J.E.; Dekkers, I.A.; Scholte, A.J.; et al. 4D Flow MRI in Ascending Aortic Aneurysms: Reproducibility of Hemodynamic Parameters. *Appl. Sci.* **2022**, *12*, 3912. [CrossRef]
11. de Almeida, J.; Martinho, S.; Gonçalves, L.; Ferreira, M. Positron Emission Tomography in Coronary Heart Disease. *Appl. Sci.* **2022**, *12*, 4704. [CrossRef]
12. Tsampasian, V.; Merinopoulos, I.; Cameron, D.; Garg, P.; Vassiliou, V.S. Ultrasmall Superparamagnetic Particles of Iron Oxide and Cardiac Magnetic Resonance: Novel Imaging in Everyday Conditions. *Appl. Sci.* **2022**, *12*, 6913. [CrossRef]