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CARDIOVASCULAR IMAGING: A GLIMPSE INTO THE FUTURE

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Abstract

In a relatively short span, technological developments in cardiovascular imaging have infiltrated every aspect of practice, with noticeable improvements in diagnosis and impact on patient management. All imaging technologies have undergone continual improvements since their inception to a point that imaging has become essential in both clinical practice and research. This article provides a glimpse into the future of cardiovascular imaging and highlights areas of imaging that still need improvement, with a view towards improving the practice of health care, where efficiency and value are becoming ever more dominant criteria throughout the continuum of care.

A Half-Century of Change and More to Come

It was not that long ago that the only tools available to physicians to assist in the diagnosis of cardiovascular conditions were a stethoscope and a simple electrocardiogram. In a relatively short span of about 50 years, technological developments in cardiovascular imaging have infiltrated every aspect of practice, with noticeable improvements in diagnosis and outcome for patients. The ability of current imaging modalities to reveal details of various cardiac structures and physiology has made them an essential component of training and practice of cardiovascular professionals (Figure 1).

As other articles in this issue detail, all imaging technologies have undergone continual improvements since their inception. Transformations in technical capabilities, spatial and temporal resolution, and processing speed have led to new applications for echocardiography, nuclear imaging, computerized tomography (CT), and cardiac magnetic resonance (CMR) imaging in research and clinical practice. In nuclear imaging, the newer cameras with CZT detectors have improved both sensitivity and efficiency; newer positron emission tomography (PET) agents enable better measurements of blood flow. CT imaging has increased both the number of slices that can be obtained simultaneously to cover a larger area of the heart as well as temporal resolution that is crucial in cardiac imaging, thus allowing imaging with much lower radiation and better accuracy. In CMR, newer sequences have allowed quantitation of collagen, scar burden, and its distribution, which can be fused with perfusion imaging and anatomy. Echocardiography has evolved from the early days of M-mode and 2-dimensional (2D) imaging to encompass Doppler, transesophageal studies, 3-dimensional (3D) real-time acquisition, and tissue Doppler and speckle tracking technologies.

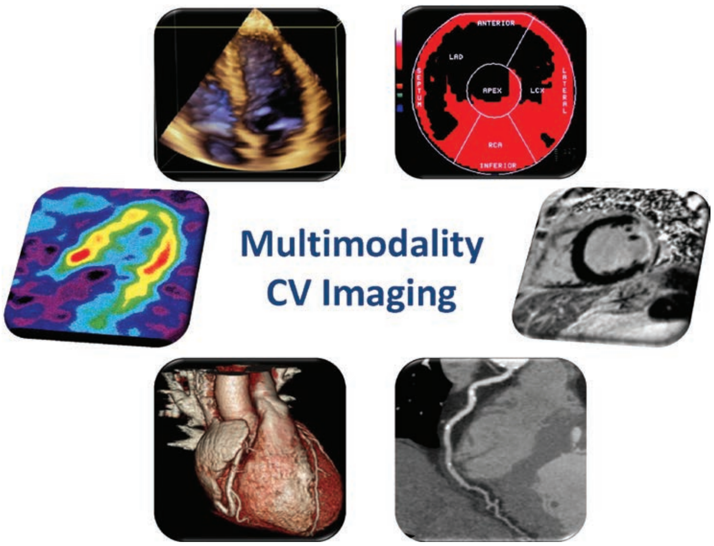

Figure 1. Various imaging modalities currently used for diagnosis and management of cardiovascular disease.

With such rapid progress, we might be forgiven for taking the future of imaging for granted (Table 1). Better temporal and spatial resolution of real-time 3D echocardiography, which would improve efficiency and the reproducibility of measurements, is already on the horizon. Refinements in technology should foster miniaturization of ultrasound and electrocardiography into small, pocket-size devices along with the latest in computer gadgetry and "apps." We can particularly look forward to the fusion of multiple

· 3-dimensional proliferation in echocardiography
· Automation: quantitation of chamber size and cardiac function
· Tissue characterization: viability, scar, collagen, and infiltration
· Improvement in protocols and technology aimed at reduction in radiation
· Miniaturization, hand-held devices
· Multimodality imaging integration and fusion

Table 1. Current Trends in Imaging

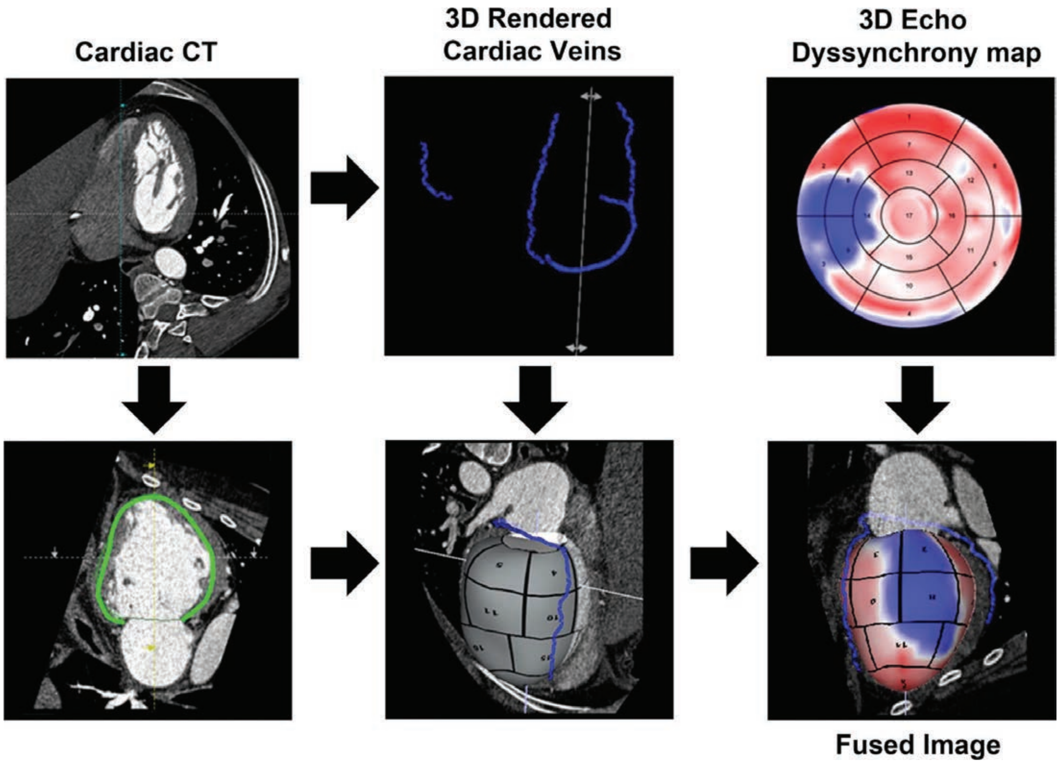

Figure 2. Fusion of cardiac computed tomography, imaging of cardiac veins, and echocardiographic imaging with a dyssynchrony map (courtesy of Dr. Roberto Lang). This could optimize the localization of biventricular pacing leads in patients with heart failure and ventricular dyssynchrony.

imaging modalities, particularly in assessing structural heart disease and in the interventional arena (Figure 2).

The world of health care is changing, even as the population of patients at cardiovascular risk keeps expanding. In this article, I will highlight areas of imaging that still need improvement with a view to improving health care practice,[1] where efficiency and value are becoming ever more dominant criteria throughout the continuum of care—from early detection and prevention of cardiovascular disease to treating advanced illness.

Advances in Evaluation of Cardiac Function

A major determinant of prognosis is cardiac function. The two primary modalities for assessing function are echocardiography and cardiac MRI (CMR), which provide structural imaging and good temporal resolution. Cardiac MRI is the current standard for quantitation of cardiac chambers and ejection fraction of both right and left ventricles. Its characterization of myocardial tissue is unique among imaging technologies in that it is the only one that can image scar tissue through the use of delayed gadolinium enhancement. Newer methodologies are aimed at refining quantitation of diffuse scarring or increases in collagen content, which would complement investigations on diastolic function. Software for automation of such quantitative parameters is currently being enhanced.

Progress in two areas of echocardiography should soon greatly aid the assessment of cardiac function. First, high volume rate imaging with 3D echocardiography, with real-time image capture in a single beat, will facilitate quantitation of ventricular volumes and ejection fraction. Second, automated quantitation of flow at valve annular sites, arising from combined 3D annular size without geometric assumptions and from 3D flow maps at the same site, should soon become a clinical reality.[2] This information will be particularly useful in the quantitation of valvular regurgitant lesions.

Diastolic function assessment has relied on Doppler echocardiographic techniques, which offer high temporal resolution. Noninvasive assessment of diastolic function and ventricular filling pressure currently requires a combination of Doppler mitral inflow dynamics and tissue Doppler at two mitral annular sites (septal and lateral). The limitation of this approach is its focal, regional nature, which is not representative of total diastolic myocardial function and properties. In the future, improved 3D time resolution will enable an evaluation of global diastolic function that is more representative of cardiac function than currently inferred from limited interrogation of annular sites.

The advent of speckle tracking technology has allowed current measurements of strain and strain rate using 2D approaches to quantitate regional and global function.[3,4] With expected improvements in the technology and standardization of the methodologies among industry vendors, application of speckle tracking to 3D echo will further enhance the accuracy of strain and strain rate measurements without assumptions of deformation in the 3D space. This will make quantitation of regional and global function even more robust.

Imaging in Coronary Artery Disease

The gold standard for detecting ischemia with noninvasive imaging techniques has been during stress testing with echocardiography and nuclear perfusion techniques. Cardiac MRI is gradually making its mark in this field as well. In the future and with more competitive pricing going forward, one can foresee an important role for CMR, especially in patients with depressed ventricular function, since it can provide a comprehensive evaluation of cardiac function, assess the extent of previous infarction along with residual viability, and determine the extent of peri-infarct or distant ischemia all in the same setting. In fact, CMR has an edge in ascertaining myocardial viability, as it is currently the only methodology that can image a scar directly with good spatial resolution.

· Clinical risk factors (age, gender, symptoms, smoking, hypertension, cholesterol, diabetes, etc.)
· Cardiac phenotype
– Coronary calcifications
– Left ventricular hypertrophy
– Left ventricular global/regional dysfunction
– Diastolic properties/left atrial volume
· Exercise tolerance
· Stress-induced ischemia and extent
· Vascular atherosclerosis imaging

Table 2. Towards Identifying Total Cardiovascular Risk

While stress echocardiography and stress nuclear techniques can identify low- and high-risk individuals and help select patients for medical or invasive management in the vast majority of patients, there are some challenges in the evaluation of coronary artery disease that require better approaches. The presence of left bundle branch block presents a difficulty for both stress echo and nuclear imaging. Recent investigations with CMR suggest that it may have an edge in this situation by providing a comprehensive evaluation of stress wall motion, perfusion, and late gadolinium enhancement. Assessment of the inferior base can present difficulties for wall motion techniques or nuclear imaging, and left ventricular hypertrophy presents a challenge for detecting wall motion abnormalities, particularly during dobutamine stress and with perfusion techniques. Lastly, poor detection of balanced ischemia in patients with multivessel disease remains an underappreciated weakness of nuclear techniques, whereas a hypertensive response during exertion poses specificity concerns for echocardiography and other wall-motion-based techniques. In some of these equivocal situations, one usually proceeds to further imaging with either CT or invasive coronary angiography to delineate the presence or absence of coronary artery disease, depending on the clinical scenario and findings.

Going forward, we need to shift the focus from ischemia detection to addressing total cardiovascular risk for a particular individual. Identifying and decreasing total cardiovascular risk has been highlighted in the recent ACC/AHA guidelines on the treatment of hypercholesterolemia.[5] Imaging can enhance this risk assessment by identifying the phenotype (e.g., coronary calcifications or atherosclerosis) in addition to detecting ischemia and other cardiovascular changes that portend an adverse outcome, such as left ventricular hypertrophy and diastolic dysfunction (Table 2). This has been substantiated in recent investigations using a coronary calcium score in individuals with normal stress nuclear techniques; patients with higher calcium scores despite a normal stress nuclear test were at incrementally higher risk of cardiovascular events because of a higher burden of coronary atherosclerosis.[6] This approach may also be applied to vascular imaging. Thus, we should aim to identify total cardiovascular risk, which encompasses clinical risk factors, the cardiac phenotype as defined by cardiac imaging, exercise tolerance, stress-induced ischemia, and the extent of vascular atherosclerosis with imaging. Studies are needed to substantiate this approach and thus improve our prevention strategies.

Atherosclerosis assessment will drive technological development in two more areas over the coming years: molecular imaging for earlier detection, and methods to characterize and predict plaque instability and acute coronary syndromes.[7,8] The evolution of imaging techniques, particularly with PET/CT fusion and more recently CMR/CT fusion, will enhance the diagnostic

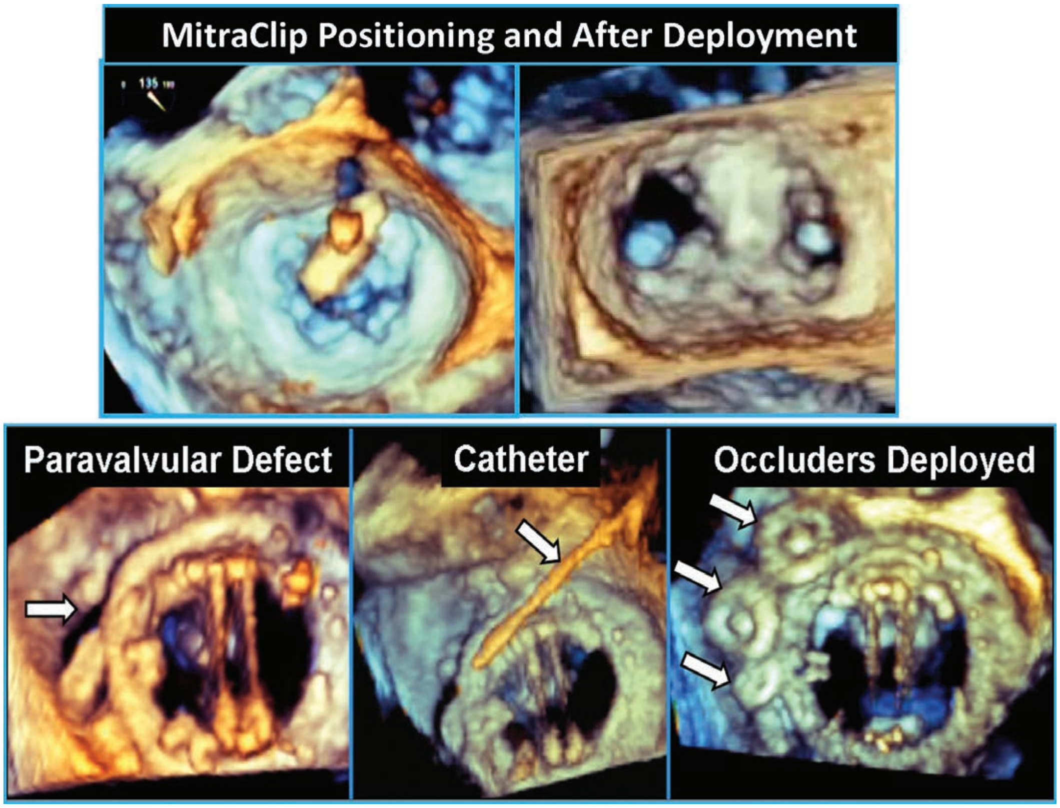

Figure 3. Interventional imaging in the catheterization laboratory. Upper panels: positioning of a MitraClip for repair of mitral regurgitation with 3-dimensional echo transesophageal guidance and images of the valve after deployment. The lower panels show guidance of occluder devices in a patient with paravalvular prosthetic mitral regurgitation.

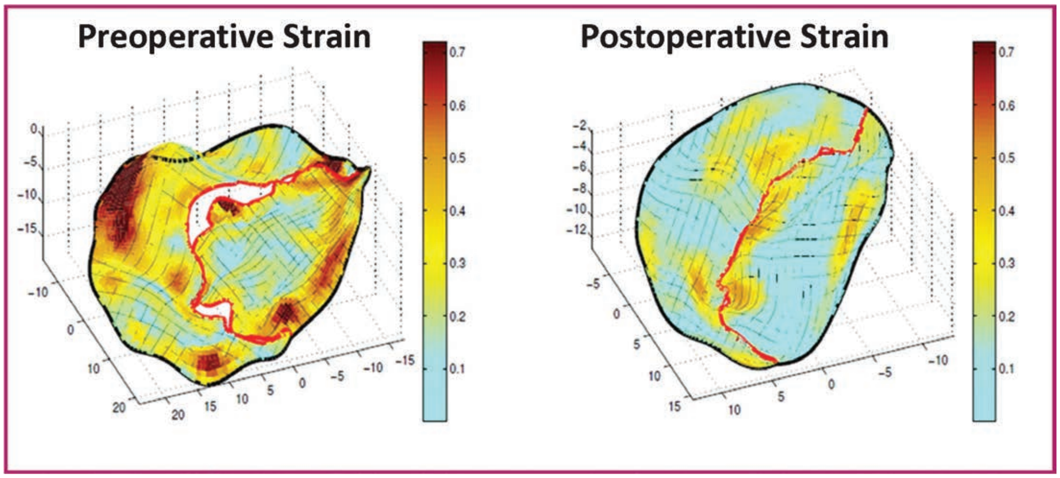

Figure 4. A depiction of mitral valve strain in a patient with mitral regurgitation prior to mitral valve repair and after surgical repair. With obliteration of the area of noncoaptation (defect) and adequate surgical repair, a significant decrease in the strain pattern is seen postoperatively.

power of imaging and may unravel dynamic changes that lead to earlier detection and prediction of the unstable patient.

Interventional Imaging

As imaging has evolved, so has the catheterization laboratory with the arrival of interventional cardiology and catheter-based techniques for repair of structural heart disease. These currently include tools or devices for atrial and ventricular septal defects, transcatheter aortic valve replacement (TAVR), mitral valve clip or other novel devices for mitral repair, occluders for repair of paraprosthetic valvular regurgitation, and, more recently, left atrial appendage occluder devices (Figure 3). Many of these procedures need imaging guidance for accurate deployment and evaluation of immediate results.[9] Thus has the hybrid field of "interventional imaging" gradually evolved. Interventional imaging holds the promise of improving patient care and outcome with less invasive procedures, but to fulfill the promise we need to provide this service with appropriate resources, training, and skill. The field is slated for impressive growth with a cohesive "Heart Team" approach, in which the imager is an integral member.[10]

Valvular Heart Disease

One of the great strengths of echocardiography has been in the evaluation of valvular heart disease. In fact, echocardiography has evolved over the years to become the first-line diagnostic modality for the assessment of native and prosthetic valves.[11,12] Echocardiography is quite robust at assessing the structure and significance of valvular lesions, particularly those with stenosis. More recently, 3D echocardiography, particularly with the transesophageal approach, has allowed us to see valve structure and motion in exquisite detail.

Nevertheless, evaluation of valvular regurgitation, particularly of the mitral valve, remains a challenge and accounts for significant variability among interpreters. Although guidelines have proposed a few parameters,[11] they require integration of several findings and thus are amenable to variability. Future developments would aim at more robust, automated quantitation of valvular regurgitation. This could be from comparative volumetric 3D flow through the mitral valve and a systemic valve[2] and/or determination of vena contracta using 3D color Doppler or other novel methods.[13] While flow convergence using 2D technology has been helpful in this assessment, limitations of this technique are evident in eccentric jets and in crescent-shape regurgitant orifices as seen in functional mitral regurgitation.[13]

The advent of catheter-based valve implantation or repair has presented new challenges in the assessment of valvular regurgitation. In the case of TAVR, paravalvular regurgitation may occur because of focal asymmetrical valve calcification or inadequate seating of the valve. Paravalvular regurgitation is quite variable (single or multiple sites; circular or crescent shapes) and has proven difficult to evaluate with conventional 2D Doppler. Similarly, the use of the mitral valve clip for repair of mitral regurgitation not infrequently results in residual 1-2 jets from the two created mitral orifices, complicating the assessment and quantitation of regurgitation severity. Future validation of quantitative methods and recommendations on how to approach these lesions will be helpful. Along these lines, a few lingering questions are worth pursuing: How best to evaluate the severity of valvular regurgitation in eccentric or multiple jets? What is the role of cardiac MRI in valvular regurgitation (native or prosthetic) since it is quite accurate in quantitation of flow, and when should it be used?

Another area for future technological development is that of 3D dynamic and automated mapping of valve motion. Software is being developed for better geometric assessment and, importantly, for quantitation of valve strain and stress. Early data show that the distribution of strain is much higher in organic valvular regurgitation and improves significantly after mitral valve repair (Figure 4).[14] Further quantitation of stress and strain could provide more insight into the pathophysiology and natural history of valve disease and possibly improve mitral repair techniques that aim at preserving the mitral valve apparatus while at the same time reducing strain and stress for longer durability.

Imaging and the Digital Revolution

At the bedside, we have consistently relied on the stethoscope, essentially a 200-year-old technology. Studies in the late 1990's showing less than 30% accuracy of cardiac diagnoses at the bedside with a stethoscope are sobering[15]; the rate is likely similar or worse at present. While there are worthwhile discussions to be had about whether we are losing important skills, advances in miniaturization and digital technologies may soon make such discussions moot. Smartphones and tablets now carry apps for auscultation, heart rate and rhythm, and heart rate variability, not to mention health tips for patients. Although "hand-held" ultrasound devices have been produced over the years, miniaturization of echocardiography has only very recently provided us with a portable machine that truly fits in one's pocket. I believe this is the beginning of a true revolution in bedside

· Improves CV examination and delivery of care
· Needs further education and training
· Selective Ultrasound use: questionable murmurs, follow-up pericardial effusion, heart failure…
· Better triage for more advanced imaging & faster medical decisions
· Adoption predicated on ease of use, impact & payment models

Table 3. Incorporation of Imaging at the bedside in CV Examination

diagnostics, as one can foresee a combination of ultrasound with other devices that are important to the healthcare professional such as an electronic stethoscope and electrocardiogram, among other tools.[16,17] Empowering the physician and healthcare professional at the bedside with simple yet powerful diagnostic tools allows earlier and more accurate diagnosis and management of patients and improved workflow. Even more importantly, bedside diagnostics through portable devices restores the conversation between the physician and patient; instead of test results being reported much later through third parties, the patient receives direct attention from the doctor and a prompt discussion of test results. Physicians in the emergency department and other clinical settings could easily use such devices to determine whether or not patients need further, more costly, imaging.

In order for cardiologists to optimize the use of these technologies in practice, however, we will need studies on the impact of such devices as well as proper education and training (Table 3). Ideally, hand-held devices will be integrated into high-end healthcare systems so that findings are immediately incorporated into the electronic health record (Figure 5). Such devices are not just for wealthy healthcare systems, however; in underdeveloped countries where the equipment is used in rural settings, such devices would afford quick and accurate diagnoses in the field and assist busy healthcare professionals in population risk assessment.

The Future of Cardiovascular Imaging: Opportunities and Challenges

The past few decades have witnessed significant improvements in cardiovascular imaging, which is all to the benefit of better diagnosis, management, and early prevention of cardiovascular disease.[1] Going forward, I expect the observed growth and refinements in imaging technology and applications to continue unabated, from high-end equipment of CT, nuclear, CMR, 3D echocardiography, and molecular imaging to miniaturization with hand-held devices. The future promises an unprecedentedly wide spectrum of opportunities (Table 4). Early detection of disease and assessment of the cardiac phenotype at early stages is paramount in preventing cardiovascular disease and particularly relevant in inherited diseases where genetic markers are not yet available and conventional risk factors are absent. There is also the possibility of using imaging for novel drug development and as a surrogate to patient outcome, where appropriate.

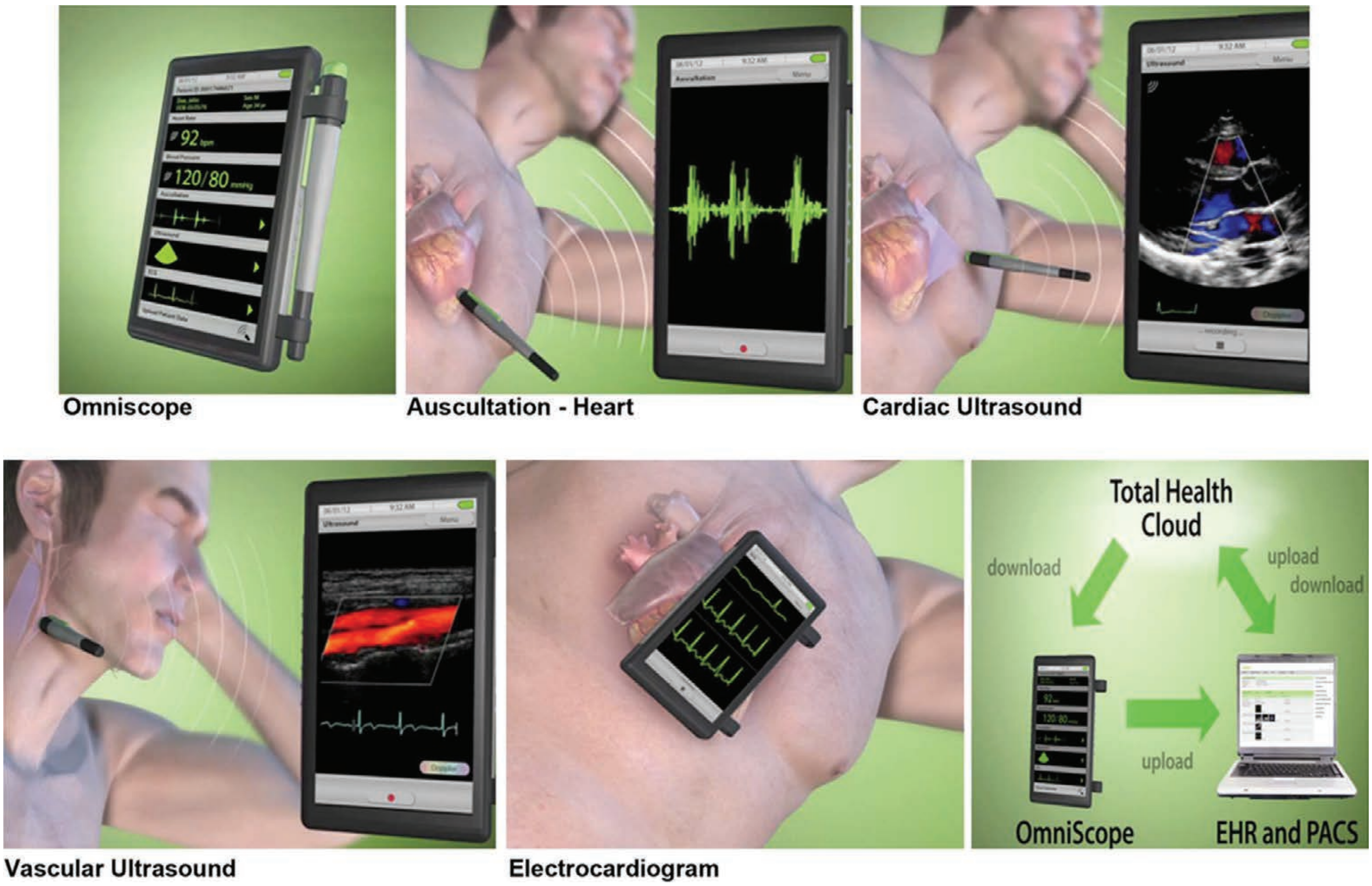

Figure 5. A rendition of a proposed futuristic small hand-held device (Omniscope™) developed by the author, incorporating vital signs, electronic auscultation, ultrasound, electrocardiographic rhythm strip, and other features that would also synchronize with electronic health records.[17]

· Imaging is crucial in cardiovascular health care delivery
· Multimodality imaging ranges from High-end, molecular imaging to Hand-Held devices
· Allows detection of early disease, identification of the cardiovascular phenotype
· Possible use for novel drug development and as surrogate to patient outcome
· Multimodality imaging: adding complexity, looking for value, appropriate use, comparative effectiveness
· Novel technologies need to demonstrate value: impact on efficiency, patient care & outcome
· Health care providers need to avoid layering of testing with various imaging modalities and use the least radiation
· Research is needed to identify best and cost-effective approaches to disease detection and management in a Digital & Multimodality Imaging world

Table 4. The Future of Multimodality CV Imaging: *Opportunities & Challenges*

Imaging will always be an integral part of clinical cardiovascular medicine. With new realities in health care emphasizing quality and cost-effectiveness, future technologies will need to demonstrate value through greater efficiency and efficacy of care and/or patient outcomes. Greater emphasis will be placed on appropriate utilization of technology and resources, including imaging.[1,18,19] It is therefore imperative to avoid layering of multiple tests in individual patients; we need to address both cost and safety in the context of patient-centered care. Ultimately, we need to identify, through research, the best approaches to disease detection and management with a focus on providing the best care to the patient.

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Reference

1. Zoghbi WA. President's page: cardiovascular imaging: a look to the past, present and future. J Am Coll Cardiol. 2012 Dec 4;60(22):2331-4.
2. Thavendiranathan P, Liu S, Datta S, Rajagopalan S, Ryan T, Igo SR, et al. Quantification of chronic functional mitral regurgitation by automated 3Dimensional peak and integrated proximal isovelocity surface area and stroke volume techniques using real-time 3Dimensional volume color Doppler echocardiography: in vitro and clinical validation. Circ Cardiovasc Imaging. 2013 Jan 1;6(1):125-33.
3. Stanton T, Leano R, Marwick TH. Prediction of all-cause mortality from global longitudinal speckle strain: comparison with ejection fraction and wall motion scoring. Circ Cardiovasc Imaging. 2009 Sep;2(5):356-64.
4. Pirat B, Khoury DS, Hartley CJ, Tiller L, Rao L, Schulz DG, et al. A novel feature tracking echocardiographic method for the quantitation of regional myocardial perfusion: validation in an animal model of ischemia-reperfusion. J Am Coll Cardiol. 2008 Feb 12;51(6):651-9.
5. Stone NJ, Robinson J, Lichtenstein AH, Bairey Merz CN, Lloyd-Jones DM, Blum CB, et al. 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2013 Nov 7. [Epub ahead of print]
6. Chang SM, Nabi F, Xu J, Peterson LE, Achari A, Pratt CM, et al. The coronary artery calcium score and stress myocardial perfusion imaging provide independent and complementary prediction of cardiac risk. J Am Coll Cardiol. 2009 Nov 10;54(20):1872-82.
7. Leuschner F, Nahrendorf M. Molecular imaging of coronary atherosclerosis and myocardial infarction: considerations for the bench and perspectives for the clinic. Circ Res. 2011 Mar 4;108(5):593-606.
8. Rogers IS, Nasir K, Figueroa AL, Cury RC, Hoffmann U, Vermylen DA, et al. Feasibility of FDG imaging of the coronary arteries: comparison between acute coronary syndrome and stable angina. JACC Cardiovasc Imaging. 2010 Apr;3(4):388-97.
9. Zamorano JL, Badano LP, Bruce C, Chan KL, Gonçalves A, Hahn RT, et al. EAE/ASE recommendations for the use of echocardiography in new transcatheter interventions for valvular heart disease. Eur Heart J. 2011 Sep;32(17):2189-214.
10. Holmes DR Jr, Rich JB, Zoghbi WA, Mack MJ. The heart team of cardiovascular care. J Am Coll Cardiol. 2013 Mar 5;61(9):903-7.
11. Zoghbi WA, Enriquez-Sarano M, Foster E, Grayburn PA, Kraft CD, Levine RA, et al.; American Society of Echocardiography. Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography. J Am Soc Echocardiogr. 2003 Jul;16(7):777-802.
12. Baumgartner H, Hung J, Bermejo J, Chambers JB, Evangelista A, Griffin BP, et al.; American Society of Echocardiography; European Association of Echocardiography. Echocardiographic assessment of valve stenosis: EAE/ASE recommendations for clinical practice. J Am Soc Echocardiogr. 2009 May;22(5):442.
13. Little SH, Pirat B, Kumar R, Igo SR, McCulloch M, Hartley CJ, et al. Three-dimensional color Doppler echocardiography for direct measurement of vena contracta area in mitral regurgitation: in vitro validation and clinical experience. JACC Cardiovasc Imag. 2008 Nov;1(6);695-704.
14. Ben Zekry S, Lawrie G, Little S, Zoghbi WA, Freeman J, Jajoo A, et al. Comparative evaluation of mitral valve strain by deformation tracking in 3D-echocardiography. Cardio Eng Tech. 2012 Dec;3(4):402-12.
15. Mangione S, Nieman LZ. Cardiac auscultatory skills of internal medicine and family practice trainees. A comparison of diagnostic proficiency. JAMA. 1997 Sep 3;278(9):717-22.
16. Zoghbi WA. Echocardiography at the point of care: an Ultra Sound Future. J Am Soc Echocardiogr. 2011 Feb;24(2):132-4.
17. Pearlman AS. Echocardiography 2020: opportunities and challenges. J Am Soc Echocardiogr. 2011 Feb;23(8):898-900.

18. Carr JJ, Hendel RC, White RD, Patel MR, Wolk MJ, Bettmann MA, et al. 2013 appropriate utilization of cardiovascular imaging: a methodology for the development of joint criteria for the appropriate utilization of cardiovascular imaging by the American College of Cardiology Foundation and American College of Radiology. J Am Coll Cardiol. 2013 May 28;61(21):2199-206.
19. American College of Cardiology Foundation Appropriate Use Criteria Task Force, American Society of Echocardiography, American Heart Association, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, et al. ACCF/ASE/AHA/ASNC/HFSA/HRS/SCAI/SCCM/SCCT/SCMR 2011 Appropriate Use Criteria for Echocardiography. A Report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, American Society of Echocardiography, American Heart Association, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Critical Care Medicine, Society of Cardiovascular Computed Tomography, and Society for Cardiovascular Magnetic Resonance Endorsed by the American College of Chest Physicians. Douglas PS, Garcia MJ, Haines DE, Lai WW, Manning WJ, Patel AR, Picard MH, Polk DM, Ragosta M, Ward RP, Weiner RB. J Am Coll Cardiol. 2011 Mar 1;57(9):1126-66.