Introduction

The use of multiple imaging modalities (x-ray, ultrasound, optical, magnetic resonance, nuclear) in the diagnosis and treatment of cardiovascular disease (CVD) has grown in popularity in recent years. The rationale for a combined approach is to draw upon the strengths of each imaging modality in order to improve visualization and characterization of CVD. Multimodality approaches are useful for both early detection of CVD and guiding percutaneous cardiovascular interventions (PCI) that require insertion of a catheter into the vasculature. During PCI, x-ray fluoroscopy is almost exclusively used to guide catheters through the vasculature to the target tissue; however ultrasound, optical, electrophysiological and magnetic resonance (MR) methods are useful for soft tissue assessment when necessary.

In November 2006, the Schulich Heart Centre at Sunnybrook Health Sciences Centre in Toronto announced the opening of the Imaging Research Centre for Cardiac Intervention (IRCCI). The new state-of-the-art research centre will use a combined approach of x-ray, ultrasound, optical and MR methods for diagnosis and treatment of CVD. The facility features a combined X-ray / MR imaging (XMR) unit which consists of an x-ray fluoroscopy unit attached via a moving patient table to a GE 1.5 Tesla MRI scanner in the adjacent room (Figure 1). The XMR interventional unit represents a significant advancement in multimodality image-guided therapy. X-ray fluoroscopy offers high spatial and temporal resolution of the vascular lumen, while MR imaging allows visualization of the surrounding soft tissue anatomy during percutaneous procedures.

Abstract

Percutaneous cardiovascular interventions (PCI) that require insertion of a catheter into the vasculature are among the leading treatment options for a variety of cardiovascular diseases. High-resolution imaging modalities such as intravascular ultrasound (IVUS), optical coherence tomography (OCT), and cardiac magnetic resonance imaging (CMRI) are emerging as important complimentary tools to traditional x-ray angiography, as they provide inherent soft tissue contrast and improved spatial resolution at the region of interest. The use of multiple imaging modalities is safer for the patient due to improved image-guidance, and the lack of ionizing radiation and nephrotoxic contrast agents. IVUS provides a detailed cross-sectional view of the vascular lumen and layers of the arterial wall, ideal for imaging coronary artery pathology. OCT is capable of distinguishing tissue composition with detail similar to histological examination (axial resolution of 3-15 µm) for a limited depth. MRI can provide image contrast based on soft tissue, functional and molecular characteristics, which is useful for both vascular and myocardial interventions. Applications of multimodality image-guidance discussed in this article include traversing chronic total occlusions (CTO), regeneration of infarcted myocardium, catheter-based ablation procedures and various pediatric cardiovascular interventions.
Catheter guidance. Combined with ultrasound and optical imaging techniques, it will provide the potential for greater safety, speed and efficacy during difficult cardiovascular interventions. In this article, we review the standard and emerging imaging modalities under investigation at IRCCI and explore several novel applications in cardiovascular intervention.

CARDIOVASCULAR IMAGING

X-Ray Fluoroscopy: Advantages and Limitations

Invasive x-ray angiography remains the current gold standard for image-guided cardiovascular intervention. The use of angiography has been described as “lumenology” since the image represents a two-dimensional planar projection of the vascular lumen that has been injected with radiopaque dye (Figure 2a). The operator gains a three-dimensional understanding of the anatomy by repeatedly injecting contrast agent and visualizing the arteries at different oblique angles. The spatial resolution (less than 0.2 mm) and temporal resolution (less than 0.1 s) represent the greatest strengths of x-ray angiography. These are essential for imaging moving structures such as the coronary arteries in vivo in order to avoid motion-induced image artifacts and for receiving immediate feedback regarding the position of the interventional device.

Since x-ray angiography only provides a view of the patent
Figure 4. (a) Three imaging modalities visualizing a CTO. X-ray fluoroscopy often cannot visualize past the occlusion; (b) IVUS image of a CTO, including the IVUS catheter (IVUS), occluded lumen (OL) and media (M) and adventitia (Ad) layers of the vessel wall; (c) MRI angiogram of a CTO imaging the proximal and distal end of the occlusion as well as collateral circulation.

Figure 5. A volumetric OCT image of an occluded anterior tibial artery is shown on the left. Image segmentation was used to isolate the media wall (red) and the endoluminal microchannel (yellow). Corresponding histology (Movat) is shown on the right.
vascular lumen, lack of soft tissue contrast is a clear disadvan-
tage.5,7 This includes the inability to characterize athero-
sclerotic plaques, vascular wall pathology and myocardial disease.
Soft tissue contrast is also useful for orienting the operator
anatomically with respect to the location of the catheter tip
during an intervention.

Safety concerns regarding x-ray angiography include the
patient exposure to ionizing radiation and the potential
nephrotoxicity of contrast agents.8-11 For example, the UK
National Radiation Protection Board has estimated that the
average risk of developing a solid tumor from a single cardiac
catheterization procedure is approximately 1 in 2,500.9 The
radiation concern is especially important in younger chil-
dren, as their lifetime risk for malignancy is much higher and
procedures for congenital heart disease often require longer
x-ray exposure.10 Contrast-medium induced nephrotoxicity is
a dose-related phenomenon whose rate is substantially
increased in patients with pre-existing renal impairment,
especially in those with diabetes mellitus. The risk for nephro-
toxicity could be reduced by the use of alternative imaging
techniques that do not require injection of iodinated contrast
medium.11

Ultrasound: Outside-In and Inside-Out

Ultrasound techniques such as transthoracic echocardiog-
raphy (TTE), transesophageal echocardiography (TEE) and
intra-vascular ultrasound (IVUS) are important complemen-
tary tools for visualizing soft tissue during cardiovascular
interventions. TTE represents the standard approach for
echocardiography where the imaging transducer is placed on
the chest wall over an intercostal space. TTE transducers
normally operate between 2.0 and 5.0 MHz, depending on the
depth of the region of interest. Higher transducer frequen-
cies provide greater spatial resolution, yet reduce the effective
imaging depth.12 TTE is used as a non-invasive first-line
approach for visualizing valvular disease, myocardial patholo-
gy, and obtaining estimates of blood flow patterns. Assessment
of the left ventricle represents one of the greatest
strengths of echocardiography.13

In TEE, the ultrasound transducer is inserted into
the esophagus and images of the heart are acquired through
the esophageal wall. TEE operates using a higher transducer
frequency range (3.5–7.0 MHz) than TTE and thus it is capable
of acquiring higher resolution images.14 The transducer can
operate at these higher frequencies since the imaging device
is closer to the cardiac structures and the air-filled lungs do
not obstruct the view from this vantage point. TEE is a more
invasive ultrasound modality than TTE and it usually requires
the use of local anaesthesia and intravenous sedation. TEE is
often used during percutaneous mitral valvuloplasty and
pediatric interventions such as atrial or ventricular septal
defect (ASD, VSD) closure.15

IVUS represents a new standard technique for examining
atherosclerotic plaques and vascular wall pathology during
cardiovascular intervention. In IVUS, the ultrasound tran-
ducer is mounted on a catheter tip and inserted into the vas-
culature. IVUS displays a 360 degree cross-sectional view of
the arterial wall (intima, media and adventitia) and the vas-
cular lumen typically up to a depth of 10 mm (Figure 2b).
The transducer operates at frequencies between 15-50 MHz,
which provides much higher axial resolution (100 µm) than
TTE or TEE at the cost of imaging depth.16,17 Applications of
IVUS include the evaluation of coronary artery stent deploy-
ment in order to prevent restenosis, visualizing atherosclerot-
ic changes in the vessel wall and assessing changes in plaque
volume and composition.

Optical Imaging Methods

Optical coherence tomography (OCT) is a relatively new
microscopic imaging technique with tremendous potential in
the field of image-guided procedures. OCT acquires cross-
sectional images by examining the interference of light
backscattered from tissue. OCT is often considered to be the
optical equivalent of ultrasound. OCT’s high axial resolution
(3-15 µm) is ideal for evaluating the thickness of arterial lay-
ers and the fibrous cap of plaques.18,19 Images are acquired
through an optical fiber in a catheter. The catheter is insert-
ed into the vasculature and then guided to the region of
interest. The fiber is rotated at high speeds (<30 Hz) and
pulled back to allow for volumetric imaging at microscopic
resolution over several centimeters.20 Current frequency-
domain OCT systems based on wavelength tunable lasers are
able to acquire such pull-backs in less than 15 seconds. OCT
can also differentiate between tissue types and identify specific
tissue composition with detail similar to histological examina-
tion (Figure 2c). Groups have also reported being able to
quantify macrophage content within the arterial wall using
OCT; thus giving a potential imaging modality to assess arte-
cial inflammation in vivo. Functional extensions of OCT such
as Doppler OCT21 and polarization-sensitive OCT may also
provide further insight into the progression of vessel wall dis-
ease.

Cardiovascular MRI: Thinking “Outside the Lumen”

Magnetic resonance imaging (MRI) represents a powerful
technology for imaging cardiovascular morphology and func-
tion. Over the past decade, significant advances in MRI have
included developments in real-time MR imaging, MR angiog-
draphy and assessment of hemodynamics and myocardial func-
tion. Several advantages of MRI include the inherent soft tis-
sue contrast, high-quality four-dimensional (three spatial
dimensions over the dimension of time) imaging, lack of ion-
izing radiation and the dynamic nature of MR pulse
sequences (Figure 3a). For example, MR pulse sequences can
provide image contrast based on anatomical structures, tissue
perfusion, rates of intracardiac and intravascular blood flow,
molecular features and cardiac wall mechanics. The limita-
tions of MR technology include the cost, lack of portability
and contraindication to certain implanted devices (especially
vascular clips and pacemakers).

With the emergence of MR fluoroscopy techniques, MRI
now includes the potential to guide a variety of cardiovascu-
lar interventions. In interventional MR, high-resolution
(>500 µm) static MR images are merged with real-time data
catheter tracking to produce accurate soft tissue visualiza-
tion. Real-time MRI is capable of updating one or two imaging
planes at a rate of 15-30 frames per second (Figure 3b).
Local imaging coil techniques, where the MR signal is
received from a small (< 2 mm) solenoid coil on the distal tip
of the catheter, are used to increase the signal quality during
intravascular imaging to obtain high resolution images over a small field of view. For instance, when working at high-field (3 Tesla scanner) with local imaging coils, MR can reasonably achieve a spatial resolution of 100-200 µm in-plane and about 1 mm through-plane.22 The image quality obtained with local imaging coils is crucial in imaging small structures such as occluded coronary arteries in-vivo.

APPLICATIONS IN IMAGE-GUIDED CARDIOVASCULAR INTERVENTION

Chronic Total Occlusions: A Shot in the Dark

Chronic total occlusion (CTO) represents a major problem facing traditional image-guided intervention. A CTO, defined as a complete vascular occlusion for a period greater than 3 months,23 is one of the most common reasons for referral for coronary artery bypass graft, as opposed to PCI.24 The main difficulties arising from CTO are both the inability to image beyond the proximal end of the lesion using x-ray contrast and the inability to cross the CTO using a standard guidewire.25 X-ray fluoroscopy provides almost no information regarding the geometry of CTOs since the vessel must first be opacified with contrast medium for visualization to occur (Figure 4a). CTO crossing with an interventional guidewire is believed to be impeded by collagen-rich extra-cellular matrix deposition within the CTO. Several promising studies have identified the presence of microchannels (generally 100-200 µm) throughout CTOs which may provide an alternative route for crossing them.19,22,25

In recent years, MRI, IVUS and OCT have been investigated for the potential to safely guide the recanalization of CTOs. MRI provides a detailed view of the regional anatomy, including the composition of the occlusion and the distal portion of the vessel (Figure 4c). Elements of the atherosclerotic plaque such as thrombus, lipid, fibrous tissue and calcification can be differentiated based on T1-, T2- and proton-density weighted images.22 IVUS and OCT provide a detailed intravascular view of the atherosclerotic plaque by placing the transducer directly proximal to the CTO. The images are acquired millimeters ahead of the probe in cross-section by using a “forward-looking” imaging technique. IVUS is capable of differentiating between lipid, necrosis and thrombus (low echogenicity) and fibrous plaque (intermediate echogenicity) in the CTO (Figure 4b). Calcified plaque poses a problem for IVUS imaging due to the acoustic shadow beyond the calcified portion.26 OCT imaging allows visualization of the composition in the CTO, similar to histological examination, up to a depth of 2-3 mm.18 Volumetric imaging of microchannels is easily identified on OCT, which is an exciting prospect for safely crossing CTOs (Figure 5).

Myocardial Interventions: Potential for Stem Cell, Drug and Biological Therapy

Myocardial regeneration is currently under investigation for patients who have suffered ischemic damage from infarction. Some proposed regeneration techniques include injection of mesenchymal stem cells (MSCs),27 local drug delivery28 and biological therapies such as cell products, plasmids and viral vectors.29 X-ray fluoroscopy is a limited technology with respect to these procedures since they require an imaging modality that can differentiate between infarcted and viable tissue. MRI is considered the leading technology in guiding myocardial regeneration since it provides excellent soft tissue contrast and physiological information, even without the use of contrast agents.27-29 For instance, successful injection of MSCs into the myocardium post-infarction requires visualization of the border between normal and infarcted tissue. This landmark is important since MSCs assume fibroblast-like characteristics in infarcted tissue and cardiomyocyte-like characteristics at the border of infarction.30 MRI has been successful in the past in visualizing and injecting MSCs in the infarct border, thus potentially providing a suitable medium for regeneration of functional myocardium.30 Ultrasound and electrophysiological methods have been used for similar injection systems with less spatial precision.31,32

Electrophysiology

Prior to recent advances in image-guided technology, defective electrical tissue causing cardiac arrhythmia was managed either medically using long-term drug therapy or surgically via cryoablation (freezing) or radiofrequency ablation. Surgical ablation therapy has been traditionally performed with a full thoracic opening; however more recently, percutaneous cardiac catheter ablation has become the gold standard in the management of arrhythmias. For instance, catheter ablation has been successful in 91-99% of cases of paroxysmal atrial fibrillation – thus eliminating the need for open-heart surgeries or long-term drug therapies.33,34,35 Catheter-based ablation techniques, however, possess critical limitations. Image guided cardiac catheter ablation often depends on a three-dimensional electroanatomical mapping (EAM) system to aid in defining the geometry of the atrial or ventricular chambers. The use of the EAMs is problematic, however, due to technical difficulties and the amount of time required to obtain sufficient mapping information.36 The addition of MRI in cardiac ablation is a relatively novel concept and has proven to be quite successful in clinical research trials for the treatment of arrhythmias. High spatial resolution obtained in MR imaging will provide tremendous assistance in visualizing atrial or ventricular anatomy. Furthermore, it is capable of distinguishing normal cardiac tissue from chronically infarcted tissue with sub-millimeter spatial resolution which is particularly valuable in treating arrhythmias in post-myocardial infarction patients.37,38 Combined MR imaging, x-ray guidance and electrophysiological data for cardiac catheter ablation is a prime example of the utility of multi-modal technology.

Pediatric Cardiovascular Interventions

In spring 2007, the Hospital for Sick Children in Toronto is scheduled to open the Cardiac Diagnostic and Interventional Unit (CDIU), a new $25 million clinical cardiovascular centre. The centre will feature two cardiac catheterization labs and an integrated Siemens MR unit, which are dedicated for the purpose of diagnosis and treatment of congenital heart disease. Congenital cardiovascular malformations (CCVMs) affect 3-12 per 1000 live births, representing the most common form of birth defect.39 In the field of pediatric cardiology, cardiac catheterization is a defin-
itive diagnostic modality, providing anatomic, hemodynamic and electrophysiological data crucial to patient care. It is important to note that imaging cardiovascular structures in a fetus, infant, or child is especially challenging when compared with adults due to the smaller anatomic structures, increased heart rate, restless patients and a wide spectrum of congenital anomalies. As such, pediatric interventional procedures are often longer and more complicated than adult procedures. Imaging modalities that provide high-resolution anatomic information without prolonged exposure to ionizing radiation, such as TEE and more recently real-time MR, are therefore more desirable for pediatric patients than traditional x-ray fluoroscopy.10

TEE has been used for many years as a standard imaging modality for pediatric cardiovascular interventions such as the treatment of atrial and ventricular septal defects (ASD, VSD), and percutaneous valvuloplasty, angioplasty and other stenting procedures.41,42 TEE is suitable for cardiovascular intervention since it offers high resolution soft tissue contrast; however it must be used in combination with x-ray fluoroscopy.10

The use of multiple imaging modalities provides more information regarding anatomy, physiology and pathology during cardiovascular intervention than x-ray angiography alone. The advances in ultrasound, optical and magnetic resonance techniques discussed in this article will provide the framework for safer and more effective percutaneous treatments for cardiovascular disease. Reducing x-ray exposure and improving soft tissue contrast are integral for performing more complex procedures such as traversing CTOs, catheter-based electrophysiological ablation, myocardial regeneration and CCVM interventions. As more imaging modalities become routinely used in clinical practice, there will be a reduction in morbidity and mortality related to cardiovascular procedures and the possibility for novel image-guided interventions will continue to expand.

Conclusion

The use of multiple imaging modalities provides more information regarding anatomy, physiology and pathology during cardiovascular intervention than x-ray angiography alone. The advances in ultrasound, optical and magnetic resonance techniques discussed in this article will provide the framework for safer and more effective percutaneous treatments for cardiovascular disease. Reducing x-ray exposure and improving soft tissue contrast are integral for performing more complex procedures such as traversing CTOs, catheter-based electrophysiological ablation, myocardial regeneration and CCVM interventions. As more imaging modalities become routinely used in clinical practice, there will be a reduction in morbidity and mortality related to cardiovascular procedures and the possibility for novel image-guided interventions will continue to expand.

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References