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Era of Multimodality Imaging: Where do We Stand?

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ABSTRACT

With the recent technological advancement, the field of cardiac imaging is riding the tide of change not only for the long-standing traditional imaging procedures like echocardiography and nuclear cardiology, but also for the emerging cardiac computed tomography (CCT) and cardiac magnetic resonance (CMR) imaging. Among them, CCT and CMR are already entering the early phase of the technology being adopted for use by the majority of hospitals and physicians, and a period of rapid growth awaits as users better understand and acquire the technology. In this review, we tried to summarize the recent technical advancements, the altered recommendations and potential risks of imaging procedures with focusing to CCT and CMR, and we speculate on how change will happen in our field in the near future. With the progress that's happened in the past generation, the development of these new technologies has brought with them new roles for the cardiovascular specialist, and this has changed the pattern of clinical practice. Unfortunately, the appropriateness of performing cardiac imaging is still extraordinarily low. Imaging specialist, therefore, should be aware of the elementary physical basis, the evolving clinical indications, the differential costs, the radiation doses and the long term risks of different imaging modalities. **(Korean Circulation J 2006;36:717-722)**

KEY WORDS : Heart ; Tomography, spiral computed ; Magnetic resonance imaging.

Introduction

A renaissance of cardiac imaging came about in the 1980s. The medical imaging market has expanded to several billion tests per year worldwide since then; of these, at least one third are cardiovascular procedures.[1)2)]

The field of cardiac imaging has experienced major growth and technological advances in recent years with respect to the long-standing traditional cardiac imaging procedures of echocardiography and nuclear cardiology, and with the emergence of cardiac computed tomography(CCT) and cardiac magnetic resonance(CMR) imaging in clinical practice.

Echocardiography, due to the major advantages such of their utilization as wide availability, short examination time and low cost, has played a pivotal role in the evaluation and follow-up of patients with cardiac diseases. However, there are also some drawbacks that have to be cleared up. Echocardiography is highly dependent on the experience of the observer and the image quality; therefore, the interobserver and inter-study variability are thought to be inherent limitations of this modality.[3)4)]

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With a recent evolution of technology, several new technologies have allowed the non-invasive description of cardiac function, perfusion and metabolism in a more objective and clear fashion. Among them, CCT and CMR are already entering the early user phase of technologal adoption and a period of rapid growth is anticipated as users better understand and acquire the new technology.[5)]

Therefore, in this review, we tried to summarize the recent technical advancements, the altered recommendations and the potential risks of imaging procedures with focusing on CCT and CMR, and we then speculate on the changes that will happen in our field in the near future.

Recent Advance of CCT Techniques

The important technical prerequisites for cardiac applications of CT are higher temporal and spatial resolution and faster scan times.

During the past decade, the speed of gantry rotation (the tube and opposing detectors rotate within the gantry) has been accelerated, which improve the temporal resolution of the system for obtaining motion-free imaging of the heart. Also, an increased number of detectors (slices), which is different from single detector-row helical or spiral CT systems, are now configured to simul-

Table 1. Comparison of the 'State-of-the Art' commercial imaging modalities

	TTE	Cardiac gated SPECT	MDCT	CMR	CAG
Spatial resolution	1 mm (axial)/2.5 mm (lateral)	>6 mm	0.4 mm	0.7 mm (coronary: 1.0 mm)	0.2 mm
Temporal resolution	30 ms	100ms	83-165 ms	30-40 ms	10 ms
Iodinated contrast agent	(-)	(-)	80 mL	(-)	80 mL
Radiation dose	(-)	10 mSv	13-18 mSv	(-)	4-6 mSv
Cost	1 (as a cost comparator)	3.27x	3.1x	5.51x	19.96x
Charge (in case uncovered by NHI) (Won)	80,000-200,000*	216,218 (stress: 518,261)	273,982	400,000-700,000	350,000-400,000

TTE: transthoracic echocardiography, 3 MHz probe, conventional setting, SPECT: single photon emission computerized tomography, technetium-sesatmibi (rest), MDCT: multidetector computerized tomography, 64 slice, CMR: cardiac magnetic resonance imaging (rest), CAG: coronary angiography, uncomplicated case, NHI: national health insurance, *: survey of the Korean Society of Echocardiography

taneously acquire multiple adjacent sections (i.e. multidetector CT: MDCT) and the unit thickness of the detector has been decreased to improve spatial resolution. As a result, the overall duration of data acquisition and the necessary amount of contrast agent can be decreased in a stepwise fashion by increasing the number of slices such as 4-, 16- or 64- MDCT[6)7)] (Table 1, comparison with respect to the different imaging techniques).

The current state-of-the-art MDCT scanner is 64-slice MDCT. Dual-source CT allows the upper limit of the heart rate at which motion artifacts can be consistently minimized to be 97 beats per minute. The entire CCT procedure can be performed in approximately 10 minutes with using <80 mL of contrast volumes. Furthermore, advanced workstations for the post-processing, such as for evaluation of cardiac function, makes the study immediately available for final interpretation.[8)9)]

A growing number of studies have suggested that 64-slice coronary CT angiography (CCTA) is highly accurate for the exclusion of significant coronary artery stenosis (>50% luminal narrowing), with negative predictive values (PV) of 97-100%, as compared with invasive selective coronary angiography (CAG).[10)]

Our study that included those; <1.5mm vessel diameter, a calcium score above 400 Agaston U and a higher heart rate, also demonstrated a sensitivity, specificity, positive PV and negative PV of 95%, 80.6%, 90.5% and 89.3%, respectively. The accuracy did not significantly deteriorate even in the presence of severe calcification and at higher heart rates (>80 bpm). On the evaluation of diagnostic accuracy according to the clinical status, there was no significant difference according to the Framingham risk score (FRS) or the clinical impression of the patients, including diagnosing those patients who were suffering with acute coronary syndrome (ACS).[11)]

Although the applications of CCT are promising, there is still room for further technical improvements due to the relatively low spatial and temporal resolution as compared with conventional CAG. Image degradation by motion artifacts or calcium deposits may also lead to under- or overestimation of luminal narrowing when using CCTA, and this is due to the insufficient spatial resolution. Because of similar effects, metal objects such as coronary stents or surgical clips can also interfere with the evaluation of underlying coronary stenosis (blooming artifacts). Developments are currently underway to use 256 detector technology (256-slice MDCT) that will cover the entire coronary anatomy in a single cardiac phase (less than 1 second) with high spatial resolution (0.2 mm) that is identical to invasive CAG, and this might overcome several limitations of the current technology.[12)13)]

Table 2. CT angiography applications in a clinical context[10)]

Indications	Class*	Level of* evidence
Assessment of obstructive disease in symptomatic patients	IIa	B
Work-up for known or suspected coronary anomalies	IIa	C
Follow-up after bypass surgery	IIb	C
Follow-up of percutaneous coronary intervention	III	C
Asymptomatic persons as a screening test for atherosclerosis	III	C
Assessment of non-calcified plaque	III	C

*: AHA evidence-based scoring system

Clinical Indications for CCT

Accepted indication

Considerable technical and practice advances have been made in the past several years and the clinicians' level of interest in this field is unprecedented. Yet there are only a few indications for this type of imaging that have been supported by a substantial body of literature because of safety issues, with respect to the competing imaging techniques (e.g., echocardiography)(Table 2).[10)]

Promising applications

Plaque imaging

Several studies have shown that CCTA can detect calcified and non-calcified plaques and especially in the proximal vessel segments.[14)15)] However, with the current technique, differentiation of the character of various plaque characters is a large grey zone and the ability of CCTA to quantify the size and volume of a plaque is still limited. Leber et al.[15] reported that 64-slice MDCT has a tendency to overestimate the volume of calcified plaque, whereas the volume of non-calcified and "mixed" plaques were systematically underestimated with using CCTA.

Acute chest pain(ACP)

Triple rule-out (ACS, aortic dissection, pulmonary embolism) by MDCT may improve the early, accurate triage of patients presenting with ACP at the emergency department (ED).

Different CCTA patterns between patients with and without ACS may provide incremental information on the traditional risk factors and clinical risk assessment for predicting the risk of ACS among patients who present with ACP to the ED.[16]

However, the prospective randomized clinical trials done by our group revealed CCT to be a first diagnostic approach to ACP in the limited cases; this can reduce unnecessary admissions and possibly reduce the length of stay for only those patients having a clinically low or intermediate risk of coronary artery disease (CAD).[17]

Chronic total occlusion(CTO)

CCT may be used to optimize the therapeutic strategy. In CTO cases, CCT can allow the operator to plan percutaneous revascularization and reduce the procedure times, the radiation exposure and the risk of contrast nephropathy.[18]

Debating applications

Screening in asymptomatic population: a troubleshooter or troublemaker?

There is a paucity of information on the role of CCTA in the asymptomatic population. We collected data on 1,165 asymptomatic subjects (mean age: 49.1 ± 9.5 years, 63% men and a FRS of 7.4 ± 6.6%) who underwent CCTA as a part of health check-ups. 5.7% of the subjects had hemodynamically significant stenosis. A secondary test after CCTA, including CAG, was done in 6.4% patients. CAD was detected on invasive CAG in 1.9%, and 1.1% had undergone revascularization therapy. The most powerful predictor of referring patients for a secondary test was the severity of stenosis on CCTA (OR: 19.5). Even for the asymptomatic population, and especially for the high-risk group, CCTA had a significant impact on the screening and managing strategy. However, CCTA had no impact on and might be harmful, when considering the radiation hazard, to those patients with a low to intermediate risk.[19] This is a particularly important issue for the diagnostic tests that will be given to healthy individuals as part of a disease-screening or risk stratification program.

Evaluation of cardiac function

The measurements of various LV functional parameters with CCT correlated and agreed with those obtained by MR imaging. Functional analysis with CCT was more accurate than that with using two-dimensional echocardiography or cardiac gated nuclear scanning. However, the lower temporal resolution limits acquiring images at the right moment of the cardiac cycle, and the radiation hazard makes CCT application debatable in routine clinical practice.[20]

Myocardial perfusion and viability

The infarct size determined by delayed enhanced (DE)-CCT and DE-MRI showed good correlation with the infarct size found on pathology in an animal model. However, CCT can detect myocardial infarction in most of the cases, but ischemic perfusion defects are not reliably identified under a resting condition in patients with myocardial infarction.[21]

Recent Advances of CMR Techniques

Magnetic resonance systems consist of 3 major components; magnets, radiofrequency (RF) coils (to excite nuclei in a gravitational field) and gradient coils (additional magnetic fields to localize the signals).

First of all, the development of various MR sequences makes MR applicable to many different cardiac diseases. An MR pulse sequence is a combination of RF pulses and magnetic field gradient on-and-offs, and this can be imagined as a musical score instrumented by the scanner and conducted by the scanning computer.

Spin echo (for multi-slice anatomical imaging, a.k.a., the 'black' blood technique), gradient echo and steady state free precession (SSFP) (for the physiological assessment of function through cine acquisitions, a.k.a., the 'white' blood technique) and echo-planar imaging (EPI) sequences are most commonly used for CMR in signal read-out).

Pre-pulses as a prelude, can also be added to sequences to change the appearance of the contrast. For example, an inversion recovery pre-pulse is typically used for infarct/viability imaging, where the myocardium is nulled to be black, the infarct white and blood is an intermediate grey.

The performance of the gradient system (the gradient coil and amplifier) determines how fast MR acquisition can be done. With modern scanners, many sequences are now performed during a 4-20 seconds breath-hold and this reduces image artifacts from respiratory motion. Respiratory motion is also reduced by using a navigator, whereby the diaphragm is monitored in real-time.

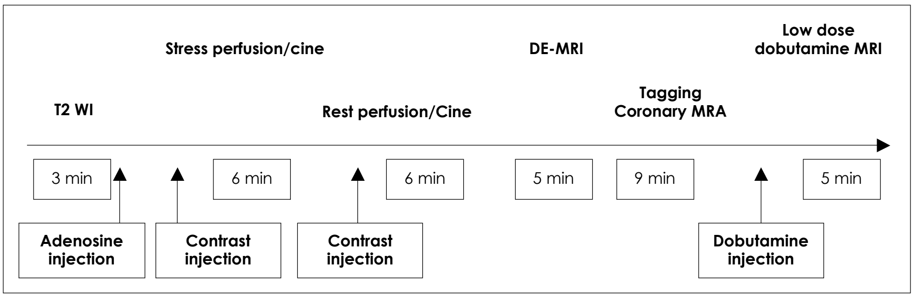

Fig. 1. MRI protocol of SNUBH for the assessment of ischemic heart disease. T2 WI: T2 weighted image, DE-MRI: delayed enhancement-MRI, MRA: MR angiography.

The contrast agent gadolinium has 7 unpaired electrons in its outer shell, which hastens T1 relaxation, and this usually increases the signal in the area of interest. Myocardial perfusion CMR is based on the effect of a first pass of an i.v. bolus of gadolinium through multiple planes of the myocardium with using ultra-fast sequences such as SSFP or EPI.[22)23)]

CMR is on the brink of a change in magnetic field strength to 3.0T (tesla). On the basis of the high signal to noise ratio, it will decrease the imaging time, improve image quality and can detect ischemia directly with using spectroscopy. However, this technology is still under investigation.

Clinical Indications of CMR

CMR can evaluate the cardiac morphology and function, the myocardial perfusion, viability and metabolism and the coronary status etc. It has frequently been claimed that CMR can provide virtually all of the information needed to assess heart disease. CMR is considered the gold standard for diagnostic evaluation in usual.

An, "one-stop examination" however for all of the information needs a relatively long (~1 hour) scan time, which limits performing one-stop examinations in routine clinical practice (Fig. 1). Therefore, clinicians should know what should be evaluated with using CMR in individual situations.

A consensus panel of established experts has recommended the updated indications for CMR based on the evidence compiled from the literature and clinical experience. These indications, also endorsed by The Society for Cardiovascular Magnetic Resonance (SCMR), and The Working Group on Cardiovascular Magnetic Resonance of the European Society of Cardiology (ESC), are extended with time (e.g., Table 3 in coronary artery disease).[22)23)]

However, this classification is not meant to equate with the AHA/ACC/ESC consensus documents. It should also be kept in mind that the classification system for imaging technologies is not easily compared with that of therapeutic trials because the number of subjects is smaller in therapeutic trials, multi-center trials are not common and randomized controlled trials are rare. The experts with the clinical experience of CMR applications are also limited. Nonetheless, CMR is now at the stage where it could be routinely applied clinically for most cardiac diseases.

Table 3. Evolving indications of CMR for coronary artery disease[22)23)]

Indications	98'	04'
1. Assessment of global ventricular function and mass	III	I
2. Detection of CAD		
Regional LV function at rest and during dobutamine stress	III	II
Assessment of myocardial perfusion	Inv	II
Coronary MRA (CAD)	Inv	III
Coronary MRA (anomalies)	Inv	I
Coronary MRA for bypass graft patency	III	II
MR flow measurements in the coronary arteries	Inv	Inv
Arterial wall imaging		Inv
3. Acute and chronic myocardial infarction		
Detection and assessment	IV	I
Myocardial viability	II	I
Ventricular septal defect	III	III
Mitral regurgitation (acute MI)	III	III
Ventricular thrombus	II	II
Acute coronary syndromes		Inv

Class I: provides clinically relevant information and is usually appropriate, may be used as the first line imaging technique and is usually supported by substantial literature. Class II: provides clinically relevant information and is frequently useful, other techniques may provide similar information, supported by limited literature. Class III: provides clinically relevant information, but is infrequently used because the information from other imaging techniques is usually adequate. Class Inv: potentially useful, but still investigational. CMR: cardiac magnetic resonance, CAD: coronary artery disease, LV: left ventricle, MRA: MR angiography, MI: myocardial infarction

Safety Issues

The dose-response curve for radiation-induced cancer is assumed to be linear at low doses, with no minimum threshold. In contrast to echocardiography and magnetic resonance imaging, the amount of radiation exposure during CT angiography has been escalated with the technological advances. The radiation dose and the risk associated with some common imaging examinations are

Table 4. Radiation doses and the estimated cancer risk from common radiological examinations and isotope scans

Type of test	Effective radiation dose (mSv)	Equivalent period of natural back-ground radiation	Lifetime additional risk of cancer/exam	Lost life expectancy	Equivalent n. of chest X-rays
Chest radiograph	0.01	A few days	Negligible risk	2 minutes	1
Lung isotope scan	1	A few months to a year	Very low risk (1 in 10,000 to 1 in 100,000)	3 hrs	50
Cardiac gated study	10	A few years (4 years)	Low risk (1 in 2,000)	2 days	500
MDCT angiography (64 slice)	13-18	A few years (6 years)	Low risk (1 in 1,500)	3 days	750
Thallium scan	20	(8 years)	(1 in 1,000)	4 days	1000

MDCT: multidetector computerized tomography

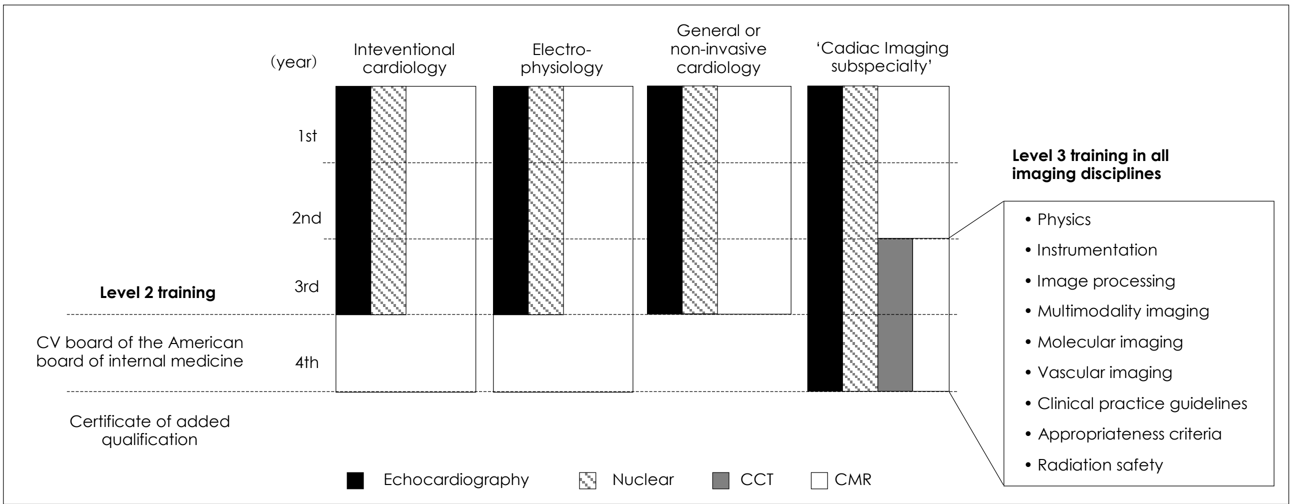

Fig. 2. A proposal for an advanced cardiovascular imaging training track.[27] With respect to the current training paradigm, virtually all cardiology fellows get Level 2 training in echocardiography and most obtain Level 2 training in nuclear cardiology. In the cardiac imaging subspecialty, the fellows interested in cardiovascular imaging achieve Level 3 training in all 4 modalities. CCT: cardiac computerized tomography, CMR: cardiac magnetic resonance imaging, CV: cardiovascular; levels of training, Level 1: minimum of months of training for all cardiology fellows, Level 2: independently supervise and interpret imaging tests, Level 3: direct an imaging laboratory in a clinical setting or to have imaging technology as a focus of an academic career.

expressed in Table 4 as equivalent doses of natural yearly background radiation, the extra-risk of fatal cancer in a lifetime and lost of life expectancy per exam.[24][25]

This small increase in the radiation-associated cancer risk for an individual can become a public health concern if a large portion of the population undergoes an increased number of CT procedures for screening purposes.

CMR is very safe and no long-term detrimental effects have been demonstrated. In contrast with the CT contrast agents, gadolinium-based MR contrast agents (inert extracellular agents) do not affect kidney function. Claustrophobia may be a problem for approximately 2% of patients. Although an artifact related to an implant may be present, metallic implants such as hip prostheses, mechanical heart valves, vascular stents and sternal sutures present no hazard. However, care is required for the patients with cerebrovascular clips. Although there have been occasional reports of success, and there is progress towards creating CMR-compatible devices, patients with electrical stimulators such a pacemakers, implanted cardioverter defibrillators (ICD), and retained permanent pacemaker leads should not be studied because of the risk of causing arrhythmias from the potentials induced in the endocardial wire and also the rapid rhythms that some pulse generators develop in a rapidly changing magnetic environment.[22][23]

Perspectives

Perhaps nowhere is the potential for change in cardiology greater than in the area of noninvasive imaging. As discoveries and progress occurred during the past decade, the development of these new technologies has brought about new roles for the cardiovascular specialist; this has transformed the specialty and how and where it is practiced. The result will be a blurring of the borders between the specialties in many areas, and the cardiovascular specialist will morph into a different specialist other that the one that presently exists. Imaging specialists should also be aware of the elementary physical basis, the differential costs, the radiological doses and the long term risks of different imaging modalities.

While one could argue about who is best suited to deal with these new modalities, the optimal solution requires merging of several individual areas of expertise.[26)]

A recent issue of the Journal of the American College of Cardiology had encouraged a proposal for establishing an advanced cardiovascular imaging training track for physicians (Fig. 2).[27)]

Conclusions

The rapid technical and clinical advances in cardiac imaging will forever change clinical practice. Unfortunately, the appropriateness of performing cardiac imaging is extraordinarily low and both patients and physicians generally have little awareness of the differential costs, radiological doses and long term risks of different imaging modalities.

With the technological evolvement of competing imaging techniques, coupling together the ultrasound and radioisotope procedures with the new CMR and CCT techniques could form the basis for a cardiovascular imaging specialist'[26)]

We are currently riding this exciting wave of change. To properly surf this wave, our team has chosen close collaboration between the cardiologist and the radiologist. Only a fool surfs alone in rough, unknown waters and a "buddy" system between medical specialties might keep you from sinking, so what will your decide to do?

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