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. 

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.¹²

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.³⁴

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 technological 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-
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\(^7\) (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.\(^8\)

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).\(^3\)

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.\(^12\)

### 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).\(^2\)

### Promising applications

**Plaque imaging**

Several studies have shown that CCTA can detect calcified and non-calcified plaques and especially in the proximal vessel segments.\(^16\) However, with the current technique, differentiation of the character of various pla-

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

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

TTE: transthoracic echocardiography, 3 MHz probe, conventional setting, SPECT: single photon emission computerized tomography, technetium-sestamibi (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

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**Table 2. CT angiography applications in a clinical context**

<table>
<thead>
<tr>
<th>Indications</th>
<th>Class*</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessment of obstructive disease in asymptomatic patients</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Work-up for known or suspected coronary anomalies</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Follow-up after bypass surgery</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>Follow-up of percutaneous coronary intervention</td>
<td>III</td>
<td>C</td>
</tr>
<tr>
<td>Asymptomatic persons as a screening test for atherosclerosis</td>
<td>III</td>
<td>C</td>
</tr>
<tr>
<td>Assessment of non-calcified plaque</td>
<td>III</td>
<td>C</td>
</tr>
</tbody>
</table>

*: AHA evidence-based scoring system
In CTO cases, CCT can allow the operator to plan per-
nephropathy.\textsuperscript{18} cutaneous revascularization and reduce the procedure
intermediate risk of coronary artery disease
of stay for only those patients having a clinically low or
unnecessary admissions and possibly reduce the length
approach to ACP in the limited cases; this can reduce
Screening in asymptomatic population: a troubleshooter
Debating applications
Chronic total occlusion(CTO)
CCT may be used to optimize the therapeutic strategy.
In CTO cases, CCT can allow the operator to plan per-
cutaneous revascularization and reduce the procedure
times, the radiation exposure and the risk of contrast
nephropathy.\textsuperscript{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 sub-
jects had hemodynamically significant stenosis. A secon-
dary 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 secon-
dary test was the severity of stenosis on CCTA (OR: 19.5). Even for the asymptomatic population, and espe-
cially for the high-risk group, CCTA had a significant
impact on the screening and managing strategy. How-
ever, CCTA had no impact on and might be harmful,
when considering the radiation hazard, to those patients
with a low to intermediate risk.\textsuperscript{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 parame-
ters with CCT correlated and agreed with those obtai-
ned by MR imaging. Functional analysis with CCT was
more accurate than that with using two-dimensional echocardiography or cardiac gated nuclear scanning. How-
ever, 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.\textsuperscript{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 re-
liably identified under a resting condition in patients
with myocardial infarction.\textsuperscript{21}

Recent Advances of CMR Techniques
Magnetic resonance systems consist of 3 major com-
ponents: magnets, radiofrequency (RF) coils (to excite
nuclei in a gravitational field) and gradient coils (addi-
tional magnetic fields to localize the signals).
First of all, the development of various MR sequen-
ces makes MR applicable to many different cardiac di-
seases. 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 assess-
ment 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 navig-
ator, whereby the diaphragm is monitored in real-time.
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 disease22)23)

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

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...
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 than 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

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

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

MDCT: multidetector computerized tomography

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**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.
with these new modalities, the optimal solution requires merging of several individual areas of expertise.\textsuperscript{20} 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).\textsuperscript{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 evolution 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\textsuperscript{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?

**REFERENCES**