In the past 3 years, immense progress has been made in the development of a new non-invasive diagnostic technique for the evaluation of coronary artery disease – coronary CT angiography. The current *IMAJ* issue includes two original studies that evaluate this new and promising imaging modality in patients with suspected CAD [1,2].

The principles of computed tomography were first investigated in the mid-1950s, but it was not until 1972 that the first generation of CT scanners was introduced. Invented by British engineer Godfrey Hounsfield of EMI Laboratories, England, the first CT scanner required several hours to acquire the raw data for a single scan or "slice," and days to reconstruct a single image from these raw data. Hounsfield was later awarded the Nobel Peace Prize for his contributions to medicine and science. The first clinical CT scanners were installed between 1974 and 1976. At that time, approximately 5 minutes were needed to acquire one tomographic image. Initial scanners were only suitable for head examinations because the opening in the gantry was small. Improvements in components of the scanners and techniques allowed scanning of any part of the body, and in 1976 whole-body scanners became available. By the early 1980s CT technology was used widely.

The last 20 years have seen the development of several generations of CT scanners. The most important was the introduction of the "spiral" technique in the early 1990s. With this technique (also known as ‘volumetric scanning’), the X-ray point source and the detector array are placed on opposite sides of the patient on a ring-like structure called the gantry. The patient on the table is moved continuously through the scan field in the z direction while the gantry performs multiple rotations around the patient. The X-ray thus traces a spiral around the body and produces a data volume. This large data volume is then sent to a computer that can reconstruct multiple overlapping axial slices, as much as needed, with no additional "cost" of ionizing radiation exposure to the patient. Overlapping axial images enable the reformation of various types of high quality three-dimensional images on a post-processing station. The introduction of spiral CT also enabled the faster acquisition of larger body parts. When coupled with a bolus of intravenous contrast injection, the enhanced arteries could be scanned in a short time, thus allowing the introduction of CTA.

Image post-processing continued to improve with the advance in computer technology, allowing enhanced display of various vascular pathologies, such as dissections or emboli throughout the entire vascular system, including small branches. During the mid-1990s, CTA gained popularity as a reliable non-invasive alternative for angiography of the aorta and its main branches (including the carotid arteries, renal, mesenteric, and iliac arteries) as well as the pulmonary arteries – becoming an important daily examination for patients with suspected pulmonary embolism.

In the late 1990s, CT was still not suitable for cardiac imaging. Its temporal resolution was too low for such a fast moving structure, and its spatial resolution was insufficient for the small caliber of the coronary arteries. The introduction of the multi-row detector scanners in the early 2000s – known also as “multi-detector” or “multislice” scanners – was a major technological breakthrough for cardiac imaging. These scanners use several parallel rows of detectors that enable significant reduction in scan time and reduction in slice width (down to 0.625 mm), resulting in improved spatial resolution – a crucial factor for imaging small vessels such as the coronary arteries. An additional important advance is the shorter rotation time of ~0.4 sec (the time interval needed for a complete 360° rotation of the tube-detector system around the patient), resulting in an improved temporal resolution. A computerized coupling of the acquired scanning data with electrocardiographic tracing enables “freezing” of heart motion in different phases of the R-R interval. Cardiac imaging began to be used in the early 2000s with 4, 8, and 16-slice scanners, but in 2005 all companies pro-

**Key words:** coronary artery disease, computed tomography angiography, multi-detector computed tomography

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**CAD** = coronary artery disease  
**CTA** = coronary CT angiography
Coronary Computed Tomography

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lipid-rich core and thin fibrous cup. The resultant thrombotic
of one or more vulnerable plaques generally characterized by a
unstable angina. This syndrome is related to fissure or rupture
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suggest that coronary CTA might be indicated whenever other
performed due to technical limitations, or when the resulting
indicated in cases where coronary catheterization cannot be
intermediate pretest probability of obstructive coronary artery
determination of coronary artery stenosis exceeding 50% were in the
range of 73–85% and 76–93% respectively, however, as many as
30% of coronary artery segments have been excluded because of
motion artifacts. More recent reports using the 16-slice scanner
showed that in most series better results were achieved, with
sensitivity, specificity, positive and negative predictive values in the
range of 59–95%, 86–97%, 61–80%, 87–97% respectively [7–
10]. Both series in the current IMAJ issue, presented by Blinder
and Gaspar and their teams [1,2], are encouraging and demon-
strate comparable results.

Owing to the lack of large outcome study results, a consen-
sus statement on the role of CTA in the current cardiac eval-
uation algorithm is not yet available. There are no universally
accepted absolute indications for cardiac CTA, but the high
egative predictive value found by most studies suggests that this
examination might be most helpful for patients with a low-
intermediate pretest probability of obstructive coronary artery
disease. It is widely accepted that coronary CTA is clinically
indicated in cases where coronary catheterization cannot be
performed due to technical limitations, or when the resulting
information from coronary catheterization is insufficient. Others
suggest that coronary CTA might be indicated whenever other
non-invasive cardiac studies (such as stress test) are equivocal.

Another promising clinical application of coronary CTA is the
ability to diagnose acute or subacute occlusions (generally of
thrombotic origin) and to reliably differentiate them from nor-
mal arteries. These occlusions clinically manifest as acute coro-
nary syndrome, sudden death, acute myocardial infarction, or
unstable angina. This syndrome is related to fissure or rupture
of one or more vulnerable plaques generally characterized by a
lipid-rich core and thin fibrous cup. The resultant thrombotic
occlusion determines the clinical consequence by the degree of
lumen obstruction. Most of these occlusions are minor and the
patient remains asymptomatic. Subtotal occlusion manifests as
unstable angina, and total thrombotic occlusion results in acute
myocardial infarction or sudden death. The patients who may
benefit from coronary CTA for this indication are those who
presented to the emergency room, internal departments or in-
tensive care unit with acute or subacute chest pain and/or ECG
changes suggesting an acute or recent coronary event, but with
equivocal clinical presentation and uncertain indication for in-
vasive (therapeutic) coronary catheterization.

Less common indications for obtaining cardiac CTA include
the evaluation of patients with a suspected aberrant coronary
pathway, evaluation of left atrial anatomy in patients before
ablation of pulmonary vein orifices (for atrial fibrillation), evalua-
tion of pericardial disease, post-surgical complications, and
congenital malformations. Although coronary CTA may demon-
strate myocardial perfusion defects, infarcts and tumors, cardiac
magnetic resonance imaging is a superior technique for demon-
strating these abnormalities.

There is considerable debate regarding the role of coronary
CTA as a primary screening test in asymptomatic patients. The
main goal of screening asymptomatic populations for the pres-
ence of CAD is to diagnose the subclinical stage of the disease
in order to initiate early treatment and to avoid the morbidity
and mortality associated with the advanced stages. Thus, the
target for CAD screening should be the early stages of ather-
sclerosis. These early plaques are located within the wall of
the arteries in the form of lipid-rich fibroplaque, and they can
be identified by coronary CTA. However, adequate methods to
measure soft plaques have not yet been established and are
still under investigation. In general, coronary CTA has to ful-
fill several universal criteria that are required to justify it as a
screening test. It requires high sensitivity, specificity and posi-
tive predictive values, a low complication rate, a low risk/benefit
ratio, and a reasonable cost. Unfortunately, the clinical value of
coronary CTA (especially with the new MDCT scanners) is not
well established. In addition, the risk and complication rate of
coronary CT cannot be underestimated: it exposes the patients
to ionizing radiation that is at least as high as an average diag-
nostic cardiac catheterization, and it requires intravenous injec-
tion of iodinated contrast material. Moreover, the present cost
of coronary CTA is relatively high, ranging between 3,000 and
4,500 shekels ($680–$1,000) in most centers in Israel that cur-
rently offer the examination.

Referring physicians should be aware of the limitations of
cardiac CTA. Heavy calcified plaques, which are frequent in pa-
tients with chronic CAD, might not allow accurate estimation
of the degree of stenosis due to the blooming artifact. Heart
rate of more than 60 beats per minute or significant arrhythmia
might reduce image quality. These limitations are well empha-
sized in Blinder’s study that used a four-slice scanner, but are
still very relevant when using the latest MDCT generations. Pa-
tients should be prepared with beta blockers if no contraindica-
tions exist. Breath-hold difficulties and the inability to remain
supine and motionless are relative contraindications. It is an-
ticipated that in the near future many of these limitations will
be improved due to the rapidly evolving technology.

In summary, coronary CTA is an additional new diagnos-
tic modality that can contribute to the clinical evaluation of

MDCT = multi-detector CT
patients with suspected CAD. Despite the current limitations, MDCT can provide adequate and useful information as long as referring physicians will select the right patient for the right clinical entity.

References


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Capsule

Fibril shape is the basis of prion strains and cross-species prion infection

Although research suggests that prions from one species rarely infect other species, some scientists believe the species barrier was breached when a new version of Creutzfeld-Jakob disease appeared in humans after several recent epidemics of bovine spongiform encephalopathy or “mad cow” disease. Earlier studies identified many “strains” of disease prions across mammalian and yeast species. Researchers thought these strains could be defined by differences in the underlying amino acid sequences of the prions. In this scenario, disease transmission would be more likely between species with similar prion amino acid sequences. In a study published last year in the journal Molecular Cell, Surewicz and colleagues also demonstrated that a “preseeding” process between animals with different prion amino acid sequences could overcome species barriers. For instance, mouse prion fibrils normally infect humans but not hamsters. But when mouse prion fibrils were brought into contact with hamster prion amyloid fibrils, a new strain of mouse fibrils emerged with the ability to infect hamsters but not humans. The new mouse strain had the same amino acid sequence as the original mouse strain but completely different infectious capabilities. With the help of atomic-level microscopic observation of prions in humans, mice, and hamsters, Jones and Surewicz (Cell 2005;121:63) discovered that it is the specific shape of the amyloid fibrils, and not the amino acid sequences, that may allow prions from one species to infect another. In a second Cell study, Jonathan Weissman and co-workers (Cell 2005;121:49) at the University of California, San Francisco came to the same conclusion in their experiments with yeast. They too discovered that the particular shape of a prion amyloid fibril was the determining factor whether one species of yeast could infect another yeast species. Just as in the case with the preseeded mice fibrils, a particular fibril shape in Saccharomyces cerevisiae yeast allowed prion transmission to Candida albicans yeast. The transmission event led to a new strain of Candida prion fibrils that could in turn infect Saccharomyces. Although fibril shape appears to be the deciding infectious factor, amino acid sequence is still important because it defines a set of possible preferred fibril shapes that prions can adopt, Weissman says. Species with similar amino acids sequences share an overlapping set of shapes, which helps explain why species with shared sequences have the ability to infect each other. Surewicz says the next step in their research will be to examine fibril shape differences at much higher resolution. Their experiments also used a shortened version of the mammalian prion protein, so they hope to test the fibril factor in a full-length protein soon. According to Jones and Surewicz, the new findings suggest that repeated cross-species transmission events might eventually create prion fibril strains that can bridge the infection gap between previously separate animals like humans and elk and deer, which suffer from a prion disease called chronic wasting disease. Surewicz stresses that prion infection between species is still rare, because transmission by eating is very ineffective. There have been hundreds of thousands of bovine spongiform encephalopathy cases, and lots of people exposed to tainted beef products, but very few cases of variant Creutzfeld-Jakob.

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