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CENTERS FOR MEDICARE AND MEDICAID SERVICES
Medicare Coverage Advisory Committee

May 18, 2006

Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, Maryland

Panelists

Chairperson
Alan M. Garber, M.D., Ph.D.

Vice Chairperson
Alexander H. Krist, M.D.

Voting Members
Timothy M. Bateman, M.D.
Douglas D. Bradham, Dr.P.H.
David J. Cohen, M.D., M.Sc.
Carole Redding Flamm, M.D., M.P.H.
Clifford Goodman, Ph.D.
Rita F. Redberg, M.D., M.Sc.
Deborah Shatin, Ph.D.
Richard L. Wahl, M.D.

CMS Liaison
Steve Phurrough, M.D., M.P.A.

Consumer Representative
Charles J. Queenan, III

Panelists (Continued)

Guest Panel Experts
Elliot Fishman, M.D.
David Lu, M.D.
Robert W. Peters, M.D.

Executive Secretary
Michelle Atkinson

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PANEL PROCEEDINGS

(The meeting was called to order at 8:11 a.m., Thursday, May 18, 2006.)

MS. ATKINSON: Good morning and welcome, committee chairperson, members and guests. I am Michelle Atkinson, the executive secretary for the Medicare Coverage Advisory Committee. The committee is here today to discuss the evidence, to hear presentations and public comment, and make recommendations regarding the use of noninvasive imaging technologies versus cardiac catheterization in the diagnosis of coronary artery disease.

The following announcement addresses conflict of interest issues associated with this meeting and is made part of the record. The conflict of interest statutes prohibit special government employees from participating in matters that could affect their or their employer's financial interests. Each member will be asked to disclose any financial conflict of interest during their introduction. We ask in the interest of fairness that all persons making statements or presentations also disclose any current or previous financial involvement in any company that

manufactures diagnostic coronary artery imaging products. This includes direct financial investments, consulting fees, and significant institutional support. If you haven't already received a disclosure statement, they are available on the table outside of this room.
We ask that all presenters please adhere to their time limit. We have numerous presenters to hear from today and a very tight agenda, and therefore cannot allow extra time.
There is a timer at the podium that you should follow. The light will begin flashing when there are two minutes remaining and then turn red when your time is up.
For the record, voting members present for today's meeting are Alex Krist, Timothy Bateman, Douglas Bradham, David Cohen, Carole Flamm, Clifford Goodman, Rita Redberg, Deborah Shatlin, and Richard Wahl. A quorum is present and no one has been recused because of conflict of interest. The entire panel, including nonvoting members, will participate in the voting. The voting scores will be available on our web site following the meeting. Two averages will be calculated, one for the voting members and one for

the entire panel.
Anyone requiring a taxi should sign up at the registration desk during the break. I ask that all panel members please speak directly into the mike, and you may have to move the mikes around. And lastly, please remember to discard your trash in the trash cans located outside of this room. And now I'd like to turn the meeting over to Dr. Steve Phurrough.
DR. PHURROUGH: Good morning. Thank you, Michelle. As an initial comment, let me thank you for your forbearance this morning, as this room was begun to be set up just shortly before we arrived. The Secretary has a meeting with the entire HHS staff this afternoon and that's why we're in this small room, because he has the room next to us. He did have a bit of precedent over us, and this room was busy into the evening last night so it was set up, as you can see, just beginning this morning. Please use the mikes. We have fewer mikes than usual, but just pass them up and down. It's difficult to record this, but we need to, if you're not speaking into the mike.
I want to thank the panelists for

agreeing to be here. We think this is an important topic and we appreciate your willingness to serve. We thank those members of the public who are here to assist us in this conversation, and we do want it to be a conversation and we are interested in your views this morning. We do look forward to a good healthy discussion.
There is some potential around two o'clock that things may get a bit noisy in that the 2,500 to 3,000 people who work here may all be gathering in the room next to us, so we'll sort of play that by ear to see if we need to take a short break at that particular time. The good news is that after that particular discussion between two and three, there are going to be refreshments in the cafeteria, and I'm sure you will be invited. I didn't say that.
Again, thank you, and I will turn it over to Alan.
DR. GARBER: Thank you, Steve. I would like to add to Steve's welcome to the panelists and to the members of the public who have joined us today. I just want to reiterate the necessity of keeping to the schedule, and we're very strict about enforcing the time limits for people who

have speaker slots. And there is, we do have a light here, I will be keeping track with the timer and will cut people off mid-sentence if they go beyond their time. And I apologize for that but it's in the interest of giving everybody a chance to speak, and usually there is more material than we can possibly do justice to in one meeting. So I'll just ask you to respect the time limits, if you would.

I think that in today's meeting in particular, we have a lot of data driven presentations which, I'm sure I speak for many of us, we find very gratifying, because that's the kind of information we really need to consider in a complex set of topics such as the one we're dealing with today. But that's also going to put some demands on the whole process of trying to assimilate the information. There may be a lot of questions for the speakers and so on, so time will be a very important factor in today's meeting and we will try to keep to a very strict schedule.

I just also want to add that some of the panelists have bad backs and may pop up from time to time, standing up behind their seats, and I hope that any speaker who happens to be speaking

at the time doesn't take that personally. Some of us just have a hard time sitting for a long time, so for whatever the reason may be, panelists will be standing from time to time and nothing is meant by that other than they need to stand up. So, thanks once again for joining us today.

And we will be discussing the questions repeatedly today, but I want to make sure that everybody has a copy of the voting questions, which all panelists should have in the little portfolios that you were given. I hope everyone in the audience has them, and there are printed materials just outside the room. Thank you.

Now we need to go through the panel for conflicts of interest and introductions. Please state who you are for the audience, and indicate any conflicts. Carole?

DR. FLAMM: Carole Redding Flamm. I am employed by the Blue Cross Blue Shield Association. I have no personal financial conflicts of interests and have been involved in the past in evaluation of cardiac CT angiography with the technology evaluation center.

DR. COHEN: I'm David Cohen, a cardiologist at Beth Israel Deaconess Medical

Center in Boston, and associate professor of medicine at Harvard Medical School. I have no conflict of interests regarding this topic.

DR. BRADHAM: I'm Doug Bradham. I'm a health economist with the Department of Veterans Affairs involved in large clinical trials and studies in that branch of their research group. I'm also an associate professor at the University of Maryland at Baltimore School of Medicine located here in Baltimore, downtown. And I have no personal finances, so I can't have any conflicts.

DR. BATEMAN: My name is Tim Bateman and I'm a cardiologist in Kansas City. I have no personal financial conflicts. My research group does receive funding from a number of radionuclide companies, and no clinical research support at this time from any CT companies.

DR. KRIST: My name is Alex Krist, I'm with the department of family medicine at Virginia Commonwealth University, and I don't have any conflicts that apply to this topic.

DR. GARBER: Alan Garber. I'm a staff physician with the Department of Veterans Affairs and director of the Center for Health Policy at

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Stanford. I am involved in an ongoing study of CT, cost effectiveness of CT angiography and other aspects of CT angiography but have no financial conflicts.

DR. GOODMAN: Cliff Goodman from the Lewin Group. I have no personal conflicts of interest. As a salaried employee for the Lewin Group, I have worked on various studies involving EB CT, contrasting with pharmaceuticals, and ultrasound imaging. No conflicts of interest of a personal nature.

DR. REDBERG: I'm Rita Redberg. I'm a professor of medicine in the division of cardiology at the University of California San Francisco. I have no personal or financial conflicts of interest. I do serve as the American Heart Association representative on the American College of Cardiology appropriateness technical panel that evaluates CT and MR.

DR. SHATIN: Deborah Shatin. I do have stock in General Electric. No other conflicts.

DR. WAHL: Richard Wahl. I am a professor of radiology and oncology at Johns Hopkins. I have no personal conflicts and no other relevant conflicts on this topic.

MR. QUEENAN: I'm Charlie Queenan, I'm and independent consultant and I have no conflicts to disclose.

DR. FISHMAN: I'm Elliott Fishman, professor of radiology and oncology at Johns Hopkins, and we do get research support in general from Siemens and GE Healthcare, so I guess that's a conflict, and we also get support from the NIH for research on cardiac CT.

DR. LU: David Lu, I'm a cardiologist at the Veterans Administration in D.C., I have no conflicts of interest.

DR. PETERS: Bob Peters. I'm chief of cardiology at the Veterans Administration Medical Center and associate professor of medicine at the University of Maryland at Baltimore. I have no conflicts of interest.

DR. GARBER: Thank you. Next we will proceed with the CMS presentation that will be given by Stuart Caplan.

MR. CAPLAN: Good morning again, everyone, Chairman Garber, panelists, invited guests, members of the public. On behalf of the Centers for Medicare and Medicaid Services, I would like to welcome you again today to the

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Medicare Coverage Advisory Committee meeting on noninvasive imaging for coronary artery disease. The CMS analytic team for today's presentation includes myself, Stuart Caplan as lead analyst, Dr. James Rollins as the medical officer, the MCAC executive secretary, Michelle Atkinson, Dr. Louis Jacques, director of Division of Items and Devices, and Dr. Steve Phurrough, the director of the Coverage and Analysis Group. I would also like to thank my colleagues at CMS who worked diligently to help put our presentation together today.

Today's presentation includes information on coronary artery disease and related imaging technologies, the technology assessment commissioned through the Agency for Healthcare Research and Quality and conducted by the Duke Center for Health Policy Research and presented by Dr. David Matchar, information on Medicare coverage for coronary artery imaging, along with MCAC panel question and discussions. You will also hear presentations from a number of interested parties.

The panel has received the following materials, all of which are publicly available.

The technology assessment provided by AHRQ, copies of all the articles reviewed, the written testimony of scheduled presenters, a summary of evidence that's provided by CMS, and questions to the panel.

According to the national clearing house and the American Heart Association, coronary artery disease is the leading cause of mortality in the United States among the members of every ethnic group. In 2003, coronary artery disease was responsible for approximately 580,000 deaths. In 2003, the death rate for coronary artery disease per 100,000 people was 209 for white men, 241 for black men, 129 for white women, and 164 for black women. The estimated prevalence of coronary artery disease in men is about 6.9 percent in the United States, and among women the prevalence is close to 6 percent. That equates to 7.2 million males and 6 million females with coronary artery disease. The annual cost of coronary artery disease in the United States is approximately $130 billion.

Coronary artery x-ray angiography is the most widely used diagnostic test used in occluded coronary arteries, with the greatest

amount of published peer reviewed evidence on its utility. Angiography is an invasive test for occluded coronary arteries. A catheter is inserted into a peripheral artery, usually the femoral artery, which is then threaded with x-ray guidance to the origin of the coronary arteries. A radiopaque dye is then injected that provides images of the artery's anatomical structure. Other cardiac function can also be evaluated and this test is considered the gold standard against which other diagnostic tests are compared. In the context of this meeting, computed tomography angiography or CTA refers to multislice or multidetector cardiac computed tomography angiography. As an x-ray source and detectors move around the patient, 16, 32, 64 or more slices up to a specified thickness are acquired, and software then reconstructs the images into three-dimensional images. Magnetic resonance angiography, MRA, is a type of magnetic resonance imaging, MRI, and is based upon the phenomenon of nuclear magnetic resonance, whereby a signal can be produced by atomic nuclei. Software then reconstructs these images into anatomic images.

Positron emission tomography is a minimally invasive nuclear medicine procedure used to evaluate glucose metabolism in normal and diseased tissues. Whereas CTA and MRI produce anatomic images, PET produces metabolic images and can detect metabolic function.

EBT, or electron beam tomography, also known as ultrafast computed tomography, can identify calcium in coronary arteries and is being evaluated as a tool to detect coronary artery disease.

This table shows that there are three coverage categories for coronary artery imaging. They are national coverage, national non-coverage, and when Medicare is silent on coverage, coverage is at local contractor discretion to either cover or non-cover a service based on their reasonable and necessary findings. As such, coverage may vary from region to region.

Coronary artery x-ray angiography and cardiac MRA are nationally covered services. CT angiography is currently covered at contractor discretion. FDG PET for evaluating coronary arteries is a nationally non-covered service, but CMS does cover Rubidium 82, an M-13 pneumonia

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for myocardial viability and myocardial perfusion. Electron beam tomography is also being paid at contractor discretion.

Now I would like to move on to the questions for the panel. Question 1: How confident are you that there is sufficient evidence to determine the diagnostic accuracy of the following noninvasive technologies for the detection of obstructive coronary artery lesions: Computed tomography angiography, or CTA; electron beam tomography, EBT; magnetic resonance imaging; or other identified technologies? The voting will be very confident, somewhat confident, unsure, somewhat unconfident, and very unconfident.

Panel Question 2: How confident are you that there is sufficient evidence to determine if these noninvasive technologies can accurately determine the anatomic location of the obstructive coronary artery lesion: CTA, EBT, CMRI, or other identified technologies? Again, the same voting questions, very confident, somewhat confident, unsure, somewhat unconfident, and very unconfident.

The third panel question: How confident are you that there is sufficient

evidence to determine if these noninvasive technologies can accurately detect the relevant morphology, such as size, shape and ulcerations of obstructive coronary artery lesions? Again, the technologies are CTA, EBT, MRI, or other technologies, and the votes will include very confident, somewhat confident, unsure, somewhat unconfident, and very unconfident.

Panel Question 4: How confident are you that the noninvasive imaging identified in Questions 1 through 3 as having sufficient evidence can be used instead of coronary artery catheterization to determine treatment of coronary artery disease? Four continues, if you are confident or very confident, in which populations are you confident that noninvasive imaging can be used without results in adverse health outcomes? Again, the answers will be very confident, somewhat confident, unsure, somewhat unconfident, and very unconfident.

Panel Question 5: If noninvasive imaging identified in Questions 1 through 3 as having sufficient evidence were to be used in addition to coronary artery catheterization: (a), how confident are you that the noninvasive imaging

identified in 1-3 as having sufficient evidence provides an incremental benefit or harm when used before coronary artery angiography? The answers again, very confident, somewhat confident, unsure, somewhat unconfident, and very unconfident.
Panel Question 5(b): How confident are you that noninvasive imaging identified in 1-3 as having sufficient evidence provides an incremental benefit or harm when used after coronary artery angiography? Same answers, very confident, somewhat confident, unsure, somewhat unconfident, and very unconfident.
Panel Question 6: How confident are you that, (a), the diagnostic test characteristics of the technologies that were identified in 1-3 as having sufficient evidence are generalizable to the Medicare beneficiary population? Same answers, very confident, somewhat confident, unsure, somewhat unconfident, and very unconfident.
Panel Question 6, the last part of it: How confident are you that, (b), diagnostic and treatment strategies using noninvasive imaging that were identified in 1-3 as having sufficient evidence of coronary artery disease provide a net

health benefit to Medicare beneficiaries compared to strategies that use invasive imaging. Answers, very confident, somewhat confident, unsure, somewhat unconfident, and very unconfident.
I would now like to introduce Dr. James Rollins, the lead medical officer for this MCAC.
DR. ROLLINS: Good morning. I would like to thank the members of the MCAC as well as the general public for attending today's presentation. In this presentation I would like to discuss the following: Ischemic heart disease and its burden on U.S. population, coronary angiography and its indications as well as its limitations, the frequency of coronary angiography performed in the U.S., potential serious as well as life-threatening complications, and the relative contraindications to this procedure.
As noted on this slide, ischemic heart disease causes significant mortality as well as disability in this country as well as other developed nations. It also causes a significant financial burden. In the year 2000, the American Heart Association estimated that more than 12 million people in the United States had ischemic heart disease. The economic costs approached $120

billion that year. Ischemic heart disease is the most common serious life-threatening illness in the United States. Large increases in the prevalence of ischemic heart disease is projected throughout the world. In the year 2020, ischemic heart disease is likely to become the most common cause of death worldwide.

In the U.S., cardiovascular disease is a leading cause of death in the elderly. As noted on this slide, more than 12 million Americans have ischemic heart disease, more than 6 million angina pectoris, over 7 million have sustained a myocardial infarction secondary due to ischemic heart disease.

Coronary angiography is an invasive investigation which accurately and reproducibly assesses the anatomy of the coronary arteries and is used in the diagnosis and management of patients with known or suspected coronary artery disease. As noted by Stuart earlier, coronary angiography is the standard by which other diagnostic tests are measured.

Though a number of clinicians have proposed that coronary angiography be used as a just-in-time diagnostic tool, its use in this

situation is not practical because of the following. Number one, it is difficult to predict which vulnerable plaque will progress to clinically significant coronary artery events. Number two, most plaque that will cause a myocardial infarction are clinically insignificant up until the day of the clinical event. And number three, over 25 percent of patients with coronary artery disease will have their first symptom be a myocardial infarction or sudden cardiac death.

There are a number of indications for coronary angiography. These include, number one, patients with markedly positive noninvasive tests. Number two, patients at high risk for coronary artery disease in whom a course of empirical anti-anginal therapy has failed. Number three, patients with unstable or post-infarction angina. Number four, patients with contraindications to exercise or pharmacologic stress testing. And number five, patients with equivocal results on noninvasive stress testing when the diagnosis of coronary artery disease remains unclear.

And though coronary angiography testing does have its indications, it also has its

limitations. Two of its limitations include its inability to determine the functional significance of coronary artery stenosis and which coronary plaque are likely to rupture and result in acute coronary syndrome. As with all invasive procedures, there is the potential for harm, and though coronary angiography has a small potential for adverse events, there are some serious as well as potentially life-threatening complications. These include arrhythmias, strokes, coronary artery dissection, access site bleeding, exposure to radiation, blood clots, infections, myocardial infarctions, trauma to the catheterized vessels, as well as perforation of the heart or vessel. When looking at all potential complications, the mortality rate is less than two percent. According to the ACC/AHA guidelines, cardiac catheterization was performed in over a million patients in 1993, making it the second most frequent in-hospital operative procedure performed in the United States. In the general population from 1979 to 2000, the number of coronary angiographies increased by 341 percent. Approximately 48 percent of all catheterizations are performed on patients 65 and older and the use

of catheterization is expected to grow. Given the predicted growth in population and age of the population, it is possible that by the year 2010, three million procedures will be performed annually here in the United States.

The striking variation in use of coronary angiography in the United States has led to concerns about its appropriateness. A number of studies have evaluated this issue and results suggest that the incidence of inappropriate use of coronary angiography is relatively low, ranging between 4 and 18 percent, but if guidelines are available which include indications for the procedure, why should there be variations in the use of this procedure?

And finally, there are a number of relative contraindications to coronary angiography, which include uncontrolled ventricular irritability, uncontrolled hypokalemia or digitalis toxicity, uncontrolled hypertension which predisposes the heart to mild coronary ischemia and/or heart failure during angioplasty, intercurrent febrile illness, anticoagulated state, severe allergy to radiographic contrast media, and severe renal insufficiency and/or

anuria, unless dialysis is planned to remove fluids and radiographic contrast load.

So, in summary, despite these shortcomings, the extent and severity of coronary artery disease in conjunction with the measurement of left ventricular function by left hard catheterization are powerful predictors of clinical outcomes. Thank you.

DR. GARBER: Next, we have a team presentation now from the Duke team.

DR. MARK: Thanks, Dr. Garber, panel members, guests. On behalf of the Duke Evidence-Based Practice Center, I am pleased to be here to be able to share with you the results of our technology assessment for noninvasive direct imaging of coronary artery disease. My name is Dr. Daniel Mark, I am a clinical cardiologist and director of the outcomes research group at ECRI. I will be joined on the podium here by Dr. Manesh Patel, who is joining our faculty in interventional cardiology, and Dr. Lynne Hurwitz, who's a member of the radiology department in the cardiothoracic imaging division. This slide shows our disclosures.

So, we have broken up our presentation

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into the following general sections. Acknowledging the somewhat diverse background of the people here today, we will start with a brief overview of the diagnostic evaluation of coronary disease in general, and that will be presented by me. Dr. Hurwitz will then discuss the three methods available for direct imaging of the coronary arteries and give examples. Dr. Patel will then present our methods for our technology assessment literature review, and the findings of our report on the first three questions of the six that Mr. Caplan shared with you a few moments ago, and then I will come back to finish with the last three questions and a wrap-up.

So as far as background, just very general stuff, but I think important in understanding some of the difficulties in working in this particular area. We're dealing basically with atherosclerotic disease which takes the manifestation of plaques or specific accumulations of cholesterol and other material in the inner lining of medium and large-sized arteries throughout the body and particularly the coronary arteries. And these plaques can cycle through phases, which include periods of quiescence where

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the plaque does nothing, and sometimes periods of rapid growth which can result from or lead to clinical syndromes. The growth in particular is often due to the rupture of so-called vulnerable plaques and this process of rupture and healing may actually lead to further growth and expansion of the plaque with additional narrowing of the coronary artery. Paradoxically, the plaques that are the ones that we focus on clinically, the ones that cause symptoms and the ones that bring most of our attention when we're doing diagnostic testing are those that narrow the arterial lumen by more than 50 percent diameter, whereas most of the clinical events in our current understanding of the pathophysiology of this disease appear to be caused by plaques that are less than or equal to 50 percent diameter stenosis on the antecedent angiogram when such data are available. You have already seen this slide from Dr. Rollins, just emphasizing the fact that there are many patients who present initially with rupture of a plaque and an irreversible clinical event, so it is a disease that is not always progressing in an orderly fashion.

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So why do we use diagnostic tests just as a general concept? I think it's important to keep in mind, however, that the ultimate goal is not to find some diagnosis but it is to improve the outcome to patients, and so it's the ability of the diagnostic tests to actually translate into some sort of information that the clinicians can use to improve the outcomes to patients that gives them their power. Tests that do not change management but perhaps are used for other purposes are certainly at least much harder to value. There is an interesting paradox, if you will, in diagnostic testing. That is that we can ask two different sorts of questions of our diagnostic tests. We can ask, and I use diagnostic tests here in a generic sense. We can ask whether the patient in a coronary disease situation has significant or severe disease, however we choose to define it, an anatomic question essentially. Or we can ask the prognostic question, what's the risk that this patient is going to die or have a major irreversible cardiac event in the next six to 12 months after my clinic visit with him or her. The paradox in this is that the

diagnostic perspective and the prognostic perspective don't always align, in fact they may not align particularly well. So that considering the example, hypothetical, of a patient with three-vessel coronary artery disease was able to go nine minutes on the Bruce protocol treadmill with no evidence of ischemia, no ST segment depression, no angina. From a diagnostic perspective this testing is just wrong, it's a false negative test and it represents a flaw in the test performance. From the prognostic perspective, however, the test tells you something very important, and that is that the patient is in a relatively lower risk stratum for that particular type of disease.

Now there are a number of tests which we're not going to discuss in any detail this morning that are used to indirectly assess the coronary circulation and look for the presentation of CAD, all falling in the general heading of stress testing, and these exercise or pharmacologic stress studies are used to examine patterns of either blood flow to the heart muscle, that is perfusion, or patterns of ventricular contraction at rest and during exercise stress.

And the imaging techniques that can be used along with the stress includes such things as echocardiography to look at left ventricular contraction patterns, or SPECT myocardial perfusion or MR perfusion to look at blood flow patterns. And the literature on these types of tests include both types of evaluations that I referred to a moment ago, that is diagnostic correlations with coronary angiography and evaluations of incremental prognostic value. I will mention that the literature that we're going to be examining in our technology assessment only includes the former type of evaluation so far, that is diagnostic correlations.

Just a word about EBT and calcium scores. As you heard a few moments ago, the EBT test is used to identify primarily coronary calcium burden, and there are in fact a number of studies correlating the diagnostic and prognostic significance of calcium burden incrementally to other clinical factors. However, our evaluation found that the spatial resolution of this technology is fairly limited for coronary anatomy and for that reason it is not included in our

direct assessment technology list to evaluate the coronary lumen. And finally, the calcium score burden increases with age, which is relevant to some things we will get to in a few moments. Just a word about the amount of evidence that's available on other types of assessments in coronary artery disease, and this is from the recent ACC/AHA literature review. You can see that the literature now includes about 24,000 patients that have been studied in an evaluative way with standard exercise and ECG testing, although there's only about 2,400 patients that have been studied under the more strictly defined context of limiting workup bias. There's about 28, 29,000 patients that have been studied evaluating perfusion scintigraphy, over 5,000 patients studied using exercise echocardiography, and the EBT work that I referred to a moment ago involves over 3,700 patients. So, our evaluation is going to focus on direct assessment, that is direct imaging of the coronary artery anatomy, and there are three options for doing this. There is the gold standard that you heard about, x-ray angiography, and then there are the two newer noninvasive

technologies, CTA and MRA, and Dr. Hurwitz is going to come up and take you through those technologies.

DR. HURWITZ: So, I'm going to discuss a little bit about traditional coronary angiography and CT and MRA. The discussion will be limited to native coronary artery assessment. As has been alluded to by the previous speakers, there are current clinical indications for doing diagnostic coronary angiography. Those include patients with known or suspected coronary artery disease or symptoms or patients with abnormal stress studies, acute coronary symptoms, evaluation post-coronary revascularization for a patient with symptoms or abnormal stress tests, pre-operative evaluation before non-cardiac surgery or for valvular surgery or congenital heart surgery, as well as evaluation in patients with congestive heart failure, systolic dysfunction, and patients previously having cardiac arrest.

As has been noted, coronary angiography is performed with the direct catheterization of the arteries and contrast agent being injected into the arteries. Multiple contrast injections

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are taken and multiple projections are obtained of the different coronary arteries and they are reviewed on several projections and in both streaming and still pictures. These images demonstrate an example case. As you can see, these images give a luminal assessment of the coronary arteries and lay out here for you the main coronary arteries that are evaluated, left main, circumflex, right coronary artery, LAD and their branches. Note that we can see very nicely the very small vessels seen in the coronary arteries with this traditional technique. As has been also noted, there are complications from x-ray angiography, as there are with any procedure performed in the medical field. As you can tell from this slide, overall the total complication rate has stabilized or slightly decreased, and the main complications overall are related to the induction of myocardial infarction, neurologic detriment, arrhythmia, vascular complications, complications related to contrast administration. Radiation risk is one that is not documented and overall, all radiation procedures tend to go by the recommendation of using as low as reasonably achievable to provide diagnostic

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images.
So in contrast to traditional diagnostic angiography, coronary CTA provides for assessment of the coronary arteries through intravenous administration of contrast. So as seen on this patient, the patient is lying on a CT scanner, a large bore IV is placed into the peripheral arm and contrast is administered through a very high rate of injection, usually somewhere between three to six cc's a second.
Prior to the patient being placed on this scanner, assessment of the patient's underlying heart rate and rhythm is needed, and that's because the data has to be acquired in conjunction with the patient's heart rate, and this is because we need to evaluate the condition during the time periods of overall decreased motion of the heart cycle.
To help with that problem, we often utilize beta-blockers to reduce patient's heart rates; that allows for an increase in the overall time of diastole relative to decreased motion of the heart.
Subsequently, the patient is then placed on the CT scanner and x-rays are emitted during the time of contrast administration and an

axial data set is acquired. This data is then reconstructed into cursory formats and direct cross-sectional images of the vessels. MRA uses a similar appearing machine, and may or may not use a contrast through a peripheral IV injection. But in contrast to CT and angiography, radio frequency pulses are applied instead of using x-rays to acquire the images.

So what do these images look like? We've included some examples from both the 16-array multi-detector scanners and the 64. As you can see on this image, these are two cursive formats from the right coronary artery in two different patients and illustrate areas of narrowing and stenosis involving the mid to distal right coronary and the more proximal right coronary on the other patient. What the CT allows for in addition to intraluminal assessment, we can actually look at the walls and actually see these areas of narrowing directly, as well as evaluating for calcified areas.

This is another example of a patient's right coronary artery again coming off the aorta, and in the distal aspect you can see enlargement

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of the vessel, filling in of soft tissues with increased thrombosis. Here's an example of the same patient with a CT angio and a traditional diagnostic angio, and what we're demonstrating here with these arrows is you can see the areas in the coronary CTA in the left coronary artery, the left anterior descending, and you see them again in the same locations on the traditional angiography. So this was just to show you an example of how we can evaluate these areas. This is an example from one of the more newer scanners, 64-slice scanners, and you see we get very nice pictures, laying out the entire anatomy of the coronary artery, even the branches. What you will notice in contrast to the traditional angio images that I showed you a moment ago, is that you can see all the distal branches as the vessels get much smaller. This is an image from an MR, this was performed without intravenous contrast and again, you will see the nice anatomy of the vessels, though you will notice that the edge definition of the vessels is not quite as good as CTA, and this is due to differences in resolution.

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So what are some of the challenges of noninvasive imaging? We've broken it down and two of the biggest problems we have is with cardiac and respiratory motion, and these can really hamper an evaluation of the entire coronary artery or a segment of the coronary artery, as I will elaborate on or illustrate in the next two slides. Additionally troubling is that because of the nature of the coronary arteries, that they are so small and are constantly moving, we're having to fight issues of getting images that are very high spatial resolution. And this is mainly because the coronary arteries are very small, about four millimeters in diameter more proximally, extending down to about .5 millimeters more distally.

Additionally, we need very high temporal resolution to try to acquire the images in a relatively motion-free time period. And methods that we use to do this is we use ECG gating, and this allocates out of the data in correlation with the patient's heart rate and rhythm so that we can image and separate out those data to time periods of least motion. By feeding patients beta-blockers, we can increase this time

of diastole and allow for improved image quality. Additionally, breath holding for respiratory motion or timing with the diaphragm motion on MRA is used to handle the issues related to respiratory motion artifact.

So while some of the images that I showed before are very nicely diagnostic of the examples of stenosis, we not uncommonly will see times when you can see the proximal right coronary artery, and on this slide you can see it very nicely, but right in the mid portion you have one of these stairstep artifacts, and this is all from cardiac motion, and then more distally you can see that the vessel is nicely laid out and you can evaluate it. So this leads to problems with what to do with the areas of cardiac motion and making them uninterpretable.

This is an example of a patient with a respiratory motion artifact. You can see the motion artifact as seen in the chest wall.

And as we talked about with the spatial and temporal resolution, this slide illustrates how the CT technology is progressing. So on one axis we have time in milliseconds, and on the X axis we have labeled out different multi-detector

scanners, so four, 16, 64, compared to electronic beam CT and cardiac cath. The overall temporal resolution and rate of imaging has improved and is getting closer towards cath, and this is mainly due to improvements in gantry rotation times of the CT scanners. With the improvement in temporal resolution and gantry rotation, scan times overall are decreasing. So before when we were imaging for 40 seconds, or 20 to 30 seconds for the 16-slice scanners, we are now down to about eight to ten seconds with a 64-array. And with that, the contrast dose has decreased from 200 cc's to about 80 cc's now of contrast.

Additionally, spatial resolution has improved. Now for the higher quality scanners, the 16 and the 64, we are actually getting near spatial resolution with cardiac cath and also other volumetric imaging.

So now that I've talked a little bit about sort of the technical issues related to the CT technology, some issues come up related specifically to patients, and that has to do with the presence or absence of coronary calcification. When there's a significant amount of calcium burden in the coronary arteries due to partial

volume averaging and beam hardening, evaluations of lumens can be very difficult. Sometimes these areas of calcification can lie eccentrically and even further off from the actual lumen being evaluated, but sometimes they can be very problematic to evaluate the lumen in the region of the calcification. As you see here, this patient has significant amounts of calcification in both the right and left coronary systems. Additionally, timing boluses becomes very important. While studies now suggest that boluses are timed very specifically for everybody's cardiac output, there can be times when the boluses are not optimal and that leads to a poor contrast-to-noise ratio. As you see here, there is more contrast in the pulmonary artery than the left atrium, which leads to very poor assessment of the coronary arteries. Additionally, signal-to-noise becomes a big issue, particularly when looking at very small vessels. As we're imaging with a very small, very fine spatial resolution, we need high signal-to-noise ratio and in order to do that we have to increase our MA or tube current. Especially when dealing with large patients, as you can see here,

there is a significant amount of modeling and a lot of noise, which can hamper evaluation. And finally, while there are benefits and risks for every procedure, the risk for radiation has been brought up repeatedly in the literature with coronary CTA, the recognition that while there are many ways to measure radiation doses, almost all studies have concluded and shown data that overall, coronary CTA has noticeably more radiation exposure to patients than traditional angiography.

DR. PATEL: Thank you. So as Dr. Mark stated, we were going to evaluate the evidence first and then the technologies, and our preliminary evaluation of the literature on noninvasive direct imaging of the coronary arteries was also conducted with two goals, looking at the operating characteristics and the clinical impact. We looked to identify technologies on the horizon also, and in general discussed issues to establish some of the studies and evaluate them.

So let me tell you some of the methods. We identified key articles using indexing terms to generate our search strategy and focus on CT and

MRI/MRA as already mentioned. We then also reviewed the reviews for additional studies to identify emerging technologies in kind of a horizon scan. Of this, we found 114 primary articles and 123 reviews.

So, the inclusion and exclusion criteria for the methodology we reviewed, first of all we looked at, since it's such a rapidly evolving field, for published literature. Certainly within the field of radiology and cardiology, there are many abstracts coming out. So for this we looked throughout the published literature and then also looked at a direct comparison between the direct noninvasive method including CT angiography or MRA angiography, with x-ray angiography. We did an examination for native coronary arteries so that there would be a direct comparison. We excluded congenital coronary anomalies and we also excluded studies that focused only on prior coronary stents or bypass grafts, since the first question was the detection of obstructive coronary disease and this patient population represented patients that already had known obstructive coronary disease. We excluded studies of technology that was less

than 16-slice/detector for CT. In a rapidly evolving field, we felt we had to draw the line somewhere and this seemed appropriate.

So the factors influencing the quality and relevance to the questions, these are some of the things that we looked through. Numerous studies, were they prospective assessments of consecutive patients. In diagnostic imaging, as Dr. Mark has already discussed, the patient sample is obviously very important. We also looked to see if there was a standardized image technique applied, if there was blinded interpretation across the studies, and we wanted to see information on the interpretation of the images. Of course as already mentioned, we looked to make sure there was a comparison with the gold standard, x-ray angiography in this case, and we wanted to see if the assessment was on the patient level, the vessel level, or segmental level. All three were reported with different variables in these studies. Finally, we wanted to see if the patients were representative of the Medicare beneficiaries.

Just a brief review of some key concepts that have already been covered.

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Sensitivity is the proportion of patients with disease in positive tests, the true positives. Specificity is those without disease and negative testing or the true negatives. And prevalence, which I'll come back to in our studies, is an important concept, the proportion of patients that were tested that actually had the disease. Sensitivity and specificity may actually vary according to the population tested depending on that prevalence. Often in imaging studies, there are proof of concept studies that use clinically obvious cases for initial evaluation of diagnostic performance. This may overestimate the performance when applied to clinically relevant populations. In general, increasing test sensitivity typically decreases specificity and vice versa, although there may be arguments against that.

The post-test probability of disease is a direct function of the pre-test probability and the test operating characteristics. We applied Bayes' method of statistical models to come to that. In general, the post-test probability which may be estimated from a data set that's used to estimate sensitivity and specificity shouldn't be

felt to be truly representative because the data set would have to be exactly the same if you retested the population with the same prevalence, the same operating characteristics.
So with those comments, let me tell you what we found with regards to the literature. The literature search identified 29 CTA studies and 13 MRA studies. There are six studies which I'm sure you'll hear about some more today, including our assessment, that used 64-array CTA. All of the MR studies used 1.5 test on magnets. The CTA studies excluded a variable portion of patients due to poor image quality scans and so forth; it would be patients or segments that were excluded due to diagnostic uncertainty due to some of the artifacts that you have seen before. The majority of the MRA studies were unable to visualize the full extent of the major coronary arteries, the distal third in many cases.
So for the noninvasive coronary imaging with 16-slice, this is an example of the four studies that have greater than a hundred patients that are prospective. This is the largest in the literature that we could find. It's consecutive patients, 149 patients using 16-slice. 23 percent

of the coronary segments were of poor quality and 24 percent of the patients had artifacts from motion or calcium. By coronary segment, the sensitivity is listed here as 30, and specificity of 91, and by patient the sensitivity was 86 percent with specificity of 49.

An example of 64, which certainly had better results, is this study by Raff, et al., which took 70 consecutive patients referred for invasive angiography. 41 of these patients had coronary artery disease. This tends to be the case with most of these studies because invasive angiography is the gold standard, and the population tends to be a population that's being referred for angiography, and CT angiography is done in concert with that. They had limited exclusions, analyzed all vessels, and found that 88 percent of the segments were analyzable. By segment, the sensitivity was, as you can see, improved to 86 percent with specificity of 95 percent. By patient, the sensitivity was 95 percent and specificity 90 percent.

So the results, this is the results for MRA, we thought this was fairly representative, potentially one of the higher quality articles.

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This was 109 patients from seven institutions enrolled from 6/99 to 10/00, and this study using MR angiography, so a multicenter study looking at noninvasive angiography. They were referred for coronary angiography, again, for suspected CAD. 84 percent of the proximal and middle segments were interpretable by MRA, 68 percent for example for the mid circumflex and 93 percent for proximal RCA. The distal segments were not evaluable, almost in the majority of these patients. The sensitivity was 93 percent and specificity was 42 percent in this study.

So having reviewed some of the general literature for Question 1, the ability to detect obstructive coronary artery disease with CTA, we found as I stated, 29 total studies, four studies with CTA that used 16 slices with greater than a hundred patients. Six studies with 64-array MDCT, all with less than a hundred patients, a total of 397 patients studied in published literature to date. Reportedly, of these 397, one of the studies didn't tell you how many patients actually had coronary artery disease, but the prevalence looks to be somewhere around 50 percent, if not higher, around 54 percent. The total reported

sensitivity and specificity of these studies with knowledge that the 64-slice seemed to be performing better, were 85 to 100 percent, and specificity was 49 to 98 percent, and this is based on a patient level. On a segmental level, you can see the numbers you have up there varying from 30 to 99 percent.

With regard to the same question for MRA, there is a meta analysis in the literature, as there is for CT angiography, that identified 28 studies of 980 patients. In this group of studies, only four studies had more than 50 patients, and we could find only one that enrolled consecutive patients. We reviewed 13 studies for the present report. The largest was the Beth Israel study. In the meta analysis, when non-evaluable segments were included, the pooled sensitivity was 58 percent and sensitivity was 70 percent.

How about the anatomic location of the obstructive lesions? Well, the evidence suggests better performance for both modalities for more proximal portions of the coronary tree than distal portions. There have been literature statements about vessels less than 1.5 millimeters versus

greater than 1.5 millimeters, and 64-slice has improved the (inaudible) that's covered in the 16-slice. The studies reviewed seems to be biased by exclusion of coronary segments of inadequate quality so that they were not included in the sensitivity and specificity analysis. There were fewer inevaluable segments in the 64-slice studies. We felt it was not possible to reliably estimate test performance by anatomic location based on that literature.

Question 3, morphology of obstructing lesion, what is the morphology of the obstructive lesion? We found five studies with noninvasive technology versus intravascular intracoronary ultrasound. All had 50 or 60 or fewer patients and usually examined one artery, and usually in segments without obstructing lesions.

DR. MARK: So, the first three questions address rather technical issues about the performance of these technologies. The second three questions evaluated the translation of those technical characteristics into clinical applications. I'm not going to repeat the questions.

But Questions 4 and 5 when pooled, they

basically deal with the question of using these noninvasive direct imaging techniques to look at coronary arteries instead of or in addition to the gold standard of x-ray angiography. The bottom line here is there is no direct data for native coronary arteries allowing us to make any statement about this.

And then Question 6 applies to the issue of generalizability of the findings to Medicare beneficiaries specifically. Of the studies we reviewed, only one had subjects with a mean age greater than 65. We found no studies that provided appropriate subgroup analysis by age, and the problem of extrapolating data from younger patients to older patients is made difficult by the fact that calcium deposits are substantially more likely to appear in older patients, and based on the data that we were presented if we were to decrease test specificity, so we just, again, don't have sufficient data.

On the issue of the horizon scan looking forward to see what may be coming down the pike in the next five to ten years in this area, our assessments from looking at the literature that we reviewed was that CTA and MRA are the

current likely near to medium term technologies that will be used for this application. And further down the horizon, our conclusion was that the main thing that's going to happen is further technological improvements in these two technologies and work to evaluate combinations of these technologies with these so-called functional exercise or stress studies.

So to summarize our findings, first of all, we found that both CTA and MRA provide anatomic information about the coronary circulation but are currently less accurate than x-ray angiography. Second, the test performance cannot be assessed definitively at this time due to substantial limitations in the current published studies and the rapid evolution of these technologies is continuing.

Both CTA and MRA do eliminate the specific risks associated with having an intraarterial catheter placed. MRA, in addition, does not involve any radiation exposure or exposure to iodinated contrast. On the other hand, compared to x-ray angiography, CTA does involve the same basic contrast risks and somewhat higher radiation exposure, as was discussed by

Dr. Hurwitz before. The rates and types of unintended consequences of using these technologies such as incidental findings that have to be worked up with additional tests, perhaps in the lung or other parts of the thorax needs to be defined. The literature from EBT suggests that this is a substantial issue, it may not always be in the patient's interest, and certainly deserves further study. There was no information available for these technologies on this point that we were able to identify. And there are yet no empirical data related to the availability, convenience, resource implications and other health services considerations regarding these technologies. Finally, there is no evidence that CTA or MRA can currently replace x-ray angiography prior to performance of PCI or bypass surgery. There is no evidence that these noninvasive technologies provide a useful adjunct to x-ray angiography for native coronary artery evaluation. And the test performance in the Medicare-aged population remains to be defined. Thank you.

DR. GARBER: Thank you, Dr. Mark, and to the rest of the presenters from Duke. At this point, I would like to remind the panelists that

we can ask questions of the presenters at a period that's currently scheduled for after lunch, but I would welcome questions now that are purely of a factual nature related to any lack of clarity or any clarification you might need with the presentation you just heard. So that type of question now, we'll get into further questioning later. Yes, Richard.

DR. WAHL: Just one comment to the previous presentation. You commented that none of the mean ages were over 65, but could you comment as to what the fraction of the patients in those studies were over 65, because I suspect there would be a moderate fraction that would be relevant, and the clinical mean would be less relevant than the total who are 65 and over.

DR. MARK: Again, I think we attempted to try to parse out some of that, but the problem that we had is that the studies are not generally reported in sufficient detail to allow one to confidently make that assessment. You might get within a standard deviation or something, but trying to figure out what that translates into in proportion to Medicare-aged patients just seemed a little too speculative for us.

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DR. GARBER: Cliff.
DR. GOODMAN: Thanks. In the literature review, you went back only to 2005 and 2006, except went to review articles as far as back as 2002. I just want to confirm that you're confident that that covers the literature sufficiently for these types of technologies, yes?
DR. MARK: I think we actually looked at articles that were potentially further back. In the tables, there may be one or two articles that we felt confident that the 64-slice was undergoing rapid change, and our literature review covers all the 64-slice published articles.
DR. GOODMAN: So you felt you went back far enough to capture things relevant to our questions today?
DR. MARK: Yes.
DR. GOODMAN: Okay. I just wanted to confirm as well, you identified absolutely no studies that evaluated the clinical impact of diagnostic strategies for these technologies, there is not a single study you found that told you anything about how information from these studies informed the treatment decision or further downstream, health outcomes; is that correct?

DR. MARK: Yes, for native coronary arteries, that's what we focused on.

DR. GARBER: Could I ask a quick question about that last part? Does that mean also that there was no follow-up on people, say, who were false negative on CTA or MRA in the following sense? The studies as you analyzed them used angiography as the gold standard and the question is, there is a claim sometimes made about some of these noninvasive tests that angiography may not be perfect. And so, was there any follow-up that enabled you to say for example, somebody who was negative on angio but was positive on MRA or CTA ended up having an event later?

DR. MARK: We haven't found anything in the published literature. There are studies I think that are percolating through various meetings, abstracts, I've seen some unpublished data prognostic, but nothing that has actually hit the peer reviewed literature currently.

DR. GARBER: All right.

DR. BATEMAN: Just to follow up on Alan's question, the coronary angiogram is virtually assessed for 50 percent severity, is

notoriously variable, and I just wondered in these proof of principal studies, whether any of them used quantitative coronary angiography and if the threshold was varied, 75, 90, so forth, did you find any difference in the comparisons?

DR. PATEL: That's a good question. I should have mentioned that in order to meet the gold standard was an invasive coronary angiography with a greater than 50 percent stenosis. Some of the studies varied, a fair number of studies used quantitative data for that determination. Some of the studies also report the sensitivity and specificity for greater than 70 percent stenosis, and then also anatomic location, proximal versus distal. For the purpose of doing one single analysis to compare the studies, we presented data on greater than 50 percent stenosis.

As regards the variability in interpretation on the CT angiography side, many of the studies report one or two readers or observers. We didn't find it in the latest literature, and a lot of data on variability for multiple years at different centers.

DR. GARBER: Elliott, did you have a question?

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DR. FISHMAN: Just, I think one issue in viewing the current literature in something as quickly changing as CT is that in doing the literature search, you have some articles published in the last two months that aren't listed, so that's one thing. So, you know, I always like to say particularly with this coronary, this is not so much state of the art as much as state of the moment. I would look through them, but I think a number of speakers will show that later.

The other comment in regard to incidental findings, there have been articles published on that. I know we've published, so the rate of three to five percent, and following those patients up, if you use very strict guidelines, the American Thoracic Society, following up lung articles, you do pick up a percent of patients with incidental lung cancers. So in some ways as long as you follow strict criteria, you do get additional information that can be very valuable to the patient's health from a CT scan, beyond the findings.

DR. GARBER: David.

DR. LU: Most of the studies give you

excellent sensitivity and specificity for by patient analysis rather than by segment. In order to compare CT angio versus coronary angiography, should the panel base their decision more on the patient or by segment analysis?

DR. MARK: I think both are going to be relevant to different parts of the questions that are being examined. If your question is does the patient have atherosclerotic disease or do they have any significant disease, finding one may be sufficient to trigger some further decisions, if that's the decision allegory that you're working with. You just need to find that there is evidence, and then you're going to do whatever you plan after that. If you're mapping out a specific therapy strategy, say eventually you're going to be able to move directly to interventional procedures from this noninvasive technology, you would want to know the detailed very specific and very accurate information about what you've got, so you make the right changes of both therapy and interventions.

DR. GARBER: I think we may want to save this issue of how to use the information for our later discussion, but we will certainly want

to return to that. Rita.
DR. REDBERG: I just wanted to follow up on the comment on incidental findings, because there may be the rare lung cancer, but I think more commonly there are other findings of unknown significance that certainly end up with a lot more procedures, a lot more recommendations for further tests, and a lot of anxiety, patient anxiety knowing about those things they don't know what to do with, and we have to get a handle on it.
DR. GARBER: So, we will return to that, and this will be the last question. Tim.
DR. BATEMAN: I wondered, a fair percentage of stress imaging is done after catheterization to resolve uncertainties in the cath lab. I wonder if you saw very much in the literature that would pertain to that issue, using CTA to clarify the significance of stenosis in different areas.
DR. MARK: We didn't see too much with regards to that. We saw more specific studies with equivocal results that then went to CT angio, where a CT angiograph was potentially planned. We had a few studies that seemed to revolve around that question but it is of unclear significance.

DR. GARBER: Okay. Thank you. Next, Elliott Fishman will be presenting. What I'm going to propose we do is have our break right after Elliott's presentation, and it will only be a ten-minute-exactly break, that means we start at ten minutes, not ten meaning 15 or 20, okay?
DR. GOODMAN: Alan, could I ask, one of our guest panelists making a presentation, is that a little unusual or is that okay?
DR. PHURROUGH: No, we've used that in the past. Most of our guest panelists commonly have, we have them as guest panelists because they have certain knowledge levels that we are interested in, and it's not uncommon that we have them present too.
DR. GOODMAN: And they're non-voting members of the panel?
DR. PHURROUGH: Correct.
DR. GOODMAN: Thank you.
DR. FISHMAN: You had me scared for a second, that I'd have to drive back to Owings Mills without getting my per diem. It's a pleasure to be here. I will apologize in advance that I am about to use a PC which I never use, and I have this really good

working thing on the MacIntosh that allows me to move all my slides around interactively so I can respond to prior speakers, but everything is in there so hopefully I won't have to skip too much. There is no doubt the hardest thing in looking at a topic such as this is the fact that things are rapidly changing. You can see how, even the interest of the public in Time magazine, and one could ask why the panel is meeting now and why, since cardiac CT has been around for a long time, why everything is of interest now. And that's surely because of changes in technology and really, 64-slice CT I think is really what's drawing the interest, both in the lay public but also within radiology and cardiology, and medicine in general. When you look at doing CT scanning, the challenge really is in the heart. You need a system that provides high spatial resolution, high temporal resolution, and provides true volume data sets.

When you look at this chart, this is really where CT has gone, where CT is, but it's not just telling you where CT is going. Right now, 64-slice scanners basically rotate three times a second, so you get 200 images per second,

a slice thickness in the range of about 25 millimeters. We can scan or reconstruct as close as we want to within a range of about 25 millimeters, and we get literally hundreds of thousands of slides per patient. The number of slices of course is not related to radiation dose, it's how we process the data. The average number of slices we get in cardiac CTA is about 3,500 slices.

Because we can deliver contrast rapidly and because now we can scan very quickly, it is very easy for us to be at a specific point in time, which is the optimal visualization of vessels. Because of this high temporal resolution and high spatial resolution, the data sets we get now are isotropic, which means that the data in the X, Y and Z axes has the same spatial resolution so when we go to process data, even though we acquire images in the axial plane, regardless of how we look at the position, the resolution is the same.

Now the other important aspect of doing CT with cardiac is not just the scanner, but truly on the work stations, so a lot of what I will show you to try to bring everybody to the same point is

thinking about getting the scan, and then you have to process the data and display the data, and that becomes very critical. Now when looking at the literature, and with all respect to the Duke group, it's a very difficult thing to do.

If I looked at this article which was published in December '04, you might say well, cardiac CT is so-so, it has lots of problems. But if you read this article carefully, you were on a four-slice scanner and in fact that's pretty impressive. And if you look at this incredible article from Johns Hopkins we wrote, which was published in May 2005, you can see I resisted the editor making the change to how we do it in 2005, because by the time this article was published, which was analysis of how we do it and how we use it, this was on 16-slice CT, and when the article came out, we hadn't used 16-slice CT for eight months. So even the literature trying to keep up to date is very difficult.

There are a range of applications of course with cardiac CT and we are speaking only about the coronaries, and the important thing from a patient perspective, the study is a relatively easy study, the actual exam itself takes less than

five minutes, most of the work is on the prep of the patient and then the post-processing side. CT has been around a long time and we know about calcium scoring, it was mentioned, the visibility of the presence of calcium structure over 130 calcial units, and that provided lots of information, but again, could give you no information as to vessel patency. Calcium scoring could be done in four-slice scanners, could be done in 16-slice scanners, but really for doing coronary CTA, 16-slice was at best, I would say, you could get some reasonable results, but it was really proof of concept that it really worked. Now one of the things that shows that cardiac CT is becoming more mainstream is the fact that protocols are becoming fairly standardized. We looked across a range of centers and they are becoming pretty much well defined. From a patient perspective, the patient requires about ten seconds of cooperation to do the study. It's a single breath hold, single injection of contrast material. We do premedicate the patient. At this point everyone agrees with a heart rate of between 60 and 65, so we end up beta-blocking about 85 percent of all our cases, patients arrive about an

hour before the study and typically that works out very nicely.

If you look to the future, of course, there are new scanners that are being introduced now, these dual source scanners which instead of having a scan time of 160 milliseconds temporal resolution, are now down to 83 milliseconds, and so beta-blocking will be something that probably will be eliminated in the future.

Now in terms of timing, as mentioned before, we do define a specific time for each case. You can't just preset timing, we use a test bolus, we use IV contrast, but in CT, the average volume of contrast study depending on the site is between 80 and 100 cc's. Particularly in the Medicare-aged patient, the lower volume the better, because there always is the potential of contrast toxicity, so we tend to be very careful on that.

Protocols are defined here. We try to minimize the dose, radiation dose is something we're very much aware of. There are many different scans now that reduce the dose 40 percent. The newest scanners will reduce dose by 50 percent routinely and the average dose will be

in the range of five to six millicuries, which should be very satisfactory for study. It's typically a study done from about the level of tracheal bifurcation to the base of the heart, roughly typically about 13 centimeters.

One of the key things in terms of the accuracy of cardiac CT is how you do the study. I will agree that one of the things that has been weak in the literature is really an analysis of multiple readers, as well as analysis of the varying techniques you can use. If you're looking at a structure that's four millimeters or less and you're trying to define it, and you look at these schematic diagrams, it becomes clear that what you need to do is really look at the vessels in as many planes as possible. So just to show you a typical cardiac CT scan, if you look at the axial images, that's how we acquire the data, and here's the LAD for example, and then you take that information and go beyond that into other planes. What we're trying to do, of course, is follow each of the vessels.

Now using classic axial planes or coronal planes or sagittal planes, that would be very difficult, so then we switch things into

different types of reconstruction. So we're able to use things like volume rendering, which gives you a global perspective of the vessel relative to the chambers of the heart. We can use volume or we can use MIP, maximum intensity projection, and each of these techniques has certain advantages and disadvantages.

And you can see one of the key advantages, of course on the CT, although I'm showing you static images, when we do the work back home, everything is on a work station, so we have an infinite number of views, unlike cardiac cath which has a set view, we have infinite views. So if I want to look at this patient and look at the right coronary artery, yes, you see it in cross-section, and yes, you can follow it a bit here and you can follow it there. What we would simply do is look at things in different planes and cross-sections, and then use the 3-D imaging to lay out the vessel.

Again, the use of MIP in this example, volume rendering allows us to look at the vessel in its entirety and look at it from a range of perspectives, and so when we're trying to determine the presence or absence of stenosis,

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presence or absence of disease, we don't rely on any one point of perspective or any one rendering technique. And you can see the visualization of the structures. You can see for example at 64, you routinely get the branch vessel and you have a good visualization. You also of course have the advantages of CT of being able to see the individual chambers, myocardial enhancement, also the ability to look at the aortic valves. You can see from this one schematic looking at the right coronary, how the visualization of this patient with some mild plaque and no stenosis will change based on visualization.

Now one of the things that's often very important in terms of being about being able to use this in a practical basis is the speed to diagnosis, particularly to use this in an emergency setting. So one of the things that we're seeing now is new software for developing that, so I'll just show you a series of images. Here is the axial plane again, looking at the left anterior and the left main coronary artery. And then you can see it here, the right coronary in two perspectives. And now we switch to look at the volume display, again, now looking at it in a

more classic angiographic perspective. Then switching over to a MIP display, which shows the vessel in its entirety. We're able to look again with MIP and volume display, again, simply changing the axis of rotation to be able to visualize the space to evaluate for lack of any disease.

We're also able now with current planar reconstruction, these little red lines here, to simply choose the beginning and end of the vessel. The computer is automatically drawing the vessel and we are then able to rotate around the center axis, so you're able to really look at the vessel from literally any perspective. And when we use coronary angiography as the gold standard, one thing to remember is that an advantage of CTA is that you can look at things from any plane or perspective, which can be of tremendous advantage.

There is also the issue of calcification, particularly in this aged population. One of the things, of course, that was initially said was that when calcification appears nicely on this patient's LAD, is that calcification maybe should be a contraindication for doing this study. But if you start looking,

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particularly at 64, the calcifications really aren't quite as problematic, because you're able to lay out each of the vessels. You can see in this case the calcification at that point would not be narrowing the lumen. We can use color mapping, we can use different perspectives going through the vessel to really define whether or not that calcification is indeed causing narrowing or is simply just on the vessel.

You can see here, this narrows the lumen but not quite at 50 percent and again, being able to analyze that with a closer range of planes and perspectives. You can see the ability with 64-slice to see soft plaque. At 16-slice, it is very hard to see soft plaque routinely; at 64-slice, you can see these studies literally done last week, and you can see soft plaque very nicely. And again, in areas of calcified plaque, the ability to separate the calcified plaque and outline the soft plaque becomes very much possible, again depending upon the rendering techniques. And again, taking those same vessels, right coronary, minimal calcified plaque, and then laying out the LAD, and I can't point, but you can see the soft plaque just proximal to the calcified

plaque, causing narrowing in a ratio of 30 to 40 percent.

So one of the key things in terms of looking at this technology is really looking at its capabilities and functionality. And you can see just one more example in that patient, and this patient actually is 64 years of age, so not meeting the 65 age criteria. So that patient was 64. And you can see very nicely, this patient was under medication, underwent cholesterol stress tests and the like.

You also can see in this example very much extensive calcification, but again, you can see in this case a critical stenosis of the RCA, so that becomes very very important, to show that even with the presence of a calcium score of roughly 900, we were able to make a very specific diagnosis. This patient was cathed, had a stent placed and did fine, but again, we can do different renderings to show you that visualization there and there.

One last example, this is a patient. Literally, this patient is 63, I apologize for him not being older. Vague chest pain, normal stress test, extensive calcification, coronary aggregate

score of 1300. Look at the LAD. Here's stenosis right here, over 70 percent stenosis. This patient as an outpatient had a stent placed about six hours later, and you can see just with the range of perspectives confirming specifically where we're able to visualize.

I think that I will try to move forward in my slides to make the point that if you think about where we stand with cardiac CT and making decisions of what is the right thing to do, I think a key thing to really look at is the technology. I would say looking at the question before, looking at the literature before 2002, I think it's hard to look at the literature before 2006. I think things are rapidly evolving, I think the technology is really changing how we can do things, whether it's the technology on the acquisition side or whether it's the technology on the processing side. So in deciding whether or not cardiac CT as a study is acceptable at the present time, I think those are the questions that need to be answered, how we do the study, on what systems we do the study, and how we require people to analyze the study, because when all is said and done, the results that will be published and are

being published really are dependent on those questions. So I will stop there and thank you for your attention.

DR. GARBER: Thank you, Elliott.

Again, any quick factual questions about the presentation? Yes, David.

DR. COHEN: A simple question. For the current scans with the 80 to 100 cc's of contrast that you mentioned, do those always provide information on ventricular function, wall motion as well, in the same study with that contrast load?

DR. FISHMAN: Yeah. Basically what we do is, since all these scans are dated, what we're doing with every patient is we reconstruct the images at ten percent of the R values, you have ten sequences, and then we use the computer to simulate motion. So we routinely look at every patient's wall motion and routinely look at valve motion. And there is an article that will be published next month from us stating that 95 percent of the time you get a good valve visualization. So you do get a lot of additional information, and one of the things that is a very important point is there is additional information

far beyond the coronaries that you get on the CT.
DR. GARBER: Tim, and then Rita.
DR. BATEMAN: I was really intrigued by one of the slides you put up on the importance of post-processing. And recognizing the differences in acquisition and timings and different challenges and so forth, I wondered what your thoughts were about these differences that we've seen and the accuracy between 16 and 64-slice, and if this latest breed of post-processing software was used on 16-slice data, would the 16-slice data look substantively better than was published.
DR. FISHMAN: There is no doubt that as software gets better, it makes things easier. We did CTA at 16 and 64, and the best way I can say it about 16 is if you have the perfect patient, and the sun and moon and stars line up, you can get a good study. That's not going to happen in 70 percent of the cases. In our practice doing cardiac CT, we get an excellent study in 95 percent of the cases. And it's not that everything needs to be perfect, so I think that is the big difference. There is no question that the software now is better, but it's just the data, the best work station is still limited by initial

data. What are the limitations? I read cardiac CTs besides Hopkins, we perform CTs at other sites in the Hopkins network, and one of the things you do learn is that your ability and your accuracy is dependent on your acquisition. If your acquisition is not perfect acquisition, your accuracy will suffer.

DR. GARBER: Rita.

DR. REDBERG: On the picture you showed with LAD stenosis and then the patient got a stent six hours later, did the patient get the stent directly after the CT or did they have an angiography after the CT scan?

DR. FISHMAN: No. The patient, one of the things that we have found, and it's in my latest slides, is that it is having a major impact. One of the things I've noticed both from a cardiologist perspective and internal medicine perspective is that physicians truly believe the images that they see on the cardiac CT. That patient basically was treated by what I would say was the best cardiologist at Hopkins. I called him on the phone and said here's the bottom line, the patient is sitting with me, and you know, he scheduled the cath right there, put in the stent.

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DR. REDBERG: Did they have an angiogram?
DR. FISHMAN: Not before, no. They had an angio to put the stent in.
DR. REDBERG: They shot the dye and put the stent in?
DR. FISHMAN: Well, they would always have to do that.
DR. REDBERG: Right, to see it, to put a stent there, do you have to do an angiogram?
DR. FISHMAN: The thing is with the stent you're doing an angiogram. You're injecting -- well, no one puts a stent anywhere before injecting contrast right before they put the stent in, that's true for an aortic stent, that's true for a renal stent, you know, people inject ten cc's of contrast at the time you do it. But they were not doing it in the sense of a diagnostic angio, that patient went to angio to get the stent placed.
DR. LU: I'm concerned now, that's the exact thing I'm worried about. You have the best Hopkins cardiologist following the patient, and I assume he had some symptoms, or he didn't have symptoms and suddenly he's reacting to a study

that shows stenosis, what happened to his clinical findings?

DR. FISHMAN: The patient's history was that he had some vague chest pains, (inaudible) previous period, so he went to the cardiologist, had a stress test, the stress test was negative, borderline cholesterol. In fact he came to see us for a CT scan of his chest to rule out other noncardiac causes of his chest pain. And he was a friend of mine, he looked pathetic, he looked really bad, so I said why don't we just do the coronary at the same time, and that's how it started, so in a sense, but --

DR. LU: So there was some clinical --

DR. FISHMAN: There was no clinical suspicion, but what ended up happening was --

DR. PETERS: Was it a pharmacologic stress test or an exercise test?

DR. FISHMAN: A treadmill.

DR. LU: You also mentioned that the technology is improving very quickly, and you know, they now have 128 and even 256. Should our decision be based on the 64-slice, and then will it change as the technology comes in? I read something to the effect that you really don't get

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that much more by going up to 256.
DR. FISHMAN: Yeah. I mean, we are doing some analysis on the 128, but one of the inventors has a 256-slice scanner. One of the issues, of course, is the 256 is incredible radiation, that's one thing, so that's not going to be practical at least in the short term. But I think 64 is kind of a critical point in time where it allows you to do excellent quality studies. I think when you look at this new dual source scanner, the two x-ray tubes, it's still basically a 64-slice scanner. The biggest thing is your beta-blockers, you have better, you know spatial temporal resolution. But I think things will always get better. I have no doubt that if you look five years from now, the scanner will not take eight or ten seconds but will take one second to do a study, so it will be one heartbeat or less. So I think things will progress, but I think we're at a critical point now.
DR. KRIST: I have a quick question, it's for Elliott or the Duke center, and it ties into the cases that you explained. In some of the cases you didn't get to, Elliott, that I saw in the handout that you mentioned, patient selection

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in 2006, you list examples like patient with unexplained chest pain without coronary artery disease, patients with intermediate cardiac risks without incidence of coronary artery disease, and your case example builds on that. The technology assessment, all the data that we had was for people with coronary artery disease, higher risk individuals going in and having a cath already. My question is, I'm just interested in the state of the evidence for these other populations, where is the evidence at for our considerations for later today?

DR. FISHMAN: I can answer personally, I guess, but what I meant to put on there, I realized there was more in my handout than I was going to get through today, so I wanted to give people background. What I did when I looked at a lot of the literature and a lot of the presentations at meetings, recognized there were presentations at meetings running about 12 to 18 months ahead of the literature, and those were the things that people were suggesting were good recommendations. That's in literature from the American College of Cardiology, American College of Radiology, so those are some of the

populations. There is also, I think when you look at the tracking codes now, those are some of the scenarios that track relatively well.

DR. KRIST: A lot of the scenarios came up in the assessments too, so I'm partly interested, is there any published evidence on those populations and studies on those populations?

DR. PATEL: I think the question you're asking is clinically very relevant to what's going on. The published literature is six studies of 64-slice CT angiography of patients who are all going to coronary cath, where the prevalence of obstructive coronary artery disease is about 50 to 54 percent of that patient population. At the American College of Cardiology meetings and at the radiology meetings, there has been presented abstracts of randomized trial of patients in the emergency room undergoing 64-slice angiography. There's an effort in cardiology to do a multicenter emergency room study using CT angiography for ruling out patients, but that patient population where the prevalence may be between ten or less percent of obstructive coronary artery disease has not been published

that I'm aware of.
DR. FISHMAN: But they are in the pipelines.
DR. GARBER: Okay, thank you. We're going to take a break now. According to my watch it's about 9:43. We'll resume in ten minutes.
(Recess.)
DR. GARBER: We're going to get started now, if I could ask everybody to take their seats. The next speaker is John Hodgson, from the Society for Cardiovascular Angiography and Interventions.
DR. HODGSON: Thank you very much, and it's a pleasure to be here on behalf of the society. In terms of the disclosures, I just got this form this morning. You should know that in terms of financial interests, I have had some, I have been involved in intravascular ultrasound since 1984. I've had financial conflicts with both EndoSonics and now their current owner, Volcano. I have received financial support in terms of a speakers bureau from General Electric. We get grant support from General Electric for educational projects, and the society has had educational meeting support from everybody, GE,

Siemens, Toshiba, Vital Imaging, and Terra-Recon. The society has paid my expenses for coming to the meeting. I have served on another board of sorts, I have been on the American College of Cardiology appropriateness committee, as well as the committee evaluating the competency issues for interpretation of these types of studies. And I was contacted by other parties, my fellow colleagues at the society as well as at the American College of Cardiology, to discuss this meeting previously.

With that said, the society that I'm here representing was formed in 1978 by Doctors Judkins and Sones, very familiar names to all of you, and our mission has been to promote excellence in invasive and interventional cardiovascular medicine through physician education, representation in the advancement of quality standards which would enhance patient care.

My name is John Hodgson. As I mentioned, I'm the past president of the society from several years ago. I am currently a full-time employee of Catholic Healthcare West as an academic cardiologist, and I have really

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dedicated my entire professional career to the study of coronary anatomy and physiology, with many works in the range of Doppler and flow studies both in animals and humans, as well as the study of coronary anatomy with both angiography and intravascular ultrasound, and now cardiac CT. We are going to limit our comments to the cardiac CT angiography rather than the other technologies under discussion this morning, and we believe this is because it's a natural extension of the base of traditional coronary angiography that we have been performing and studying for well over 40 years now.

There are some fundamentals that have already been gone over by a number of the previous speakers that primarily take somewhat of an issue with the concept that everything we need to know to treat coronary artery disease depends on the finding of, quote, obstructive lesions. And one of the facts that made it difficult to fully analyze these questions was that we were not presented with any type of clinical scenario on which the assumption was that we were dealing with symptomatic patients who presented to a physician for evaluation of some sort of symptom, and

clearly I don't believe we were talking about looking at asymptomatic patients, so we assumed that there was sort of symptoms involved here. And also, obstructive lesions was really not defined, and clearly obstruction could be 10 percent or it could be 100 percent. And as you know from the previous speakers and especially the Duke group, many of the studies have used an arbitrary 50 percent by cath definition of obstruction, and I hope in the next few minutes to indicate that we don't believe that that's all you need to know about a coronary artery or about a patient in order to effectively manage them. Obviously the knowledge of their functional status, the state of their symptoms, the nature of their symptoms, and their functional capacity in terms of the stress testing is also critically important in the management of patients who may have symptoms that suggest coronary artery disease. The other point I want to make early on is that diagnostic cardiac catheterization has many other uses for structural heart disease or valvular disease, for the evaluation of hemodynamics and again, to lump all diagnostic caths into a category that would be compared to

cardiac CT or MR or any other technology would be inappropriate. So we are limiting our comments and in the written comments that you have really, to try to focus on those diagnostic catheterizations that were performed solely to evaluate the status of coronary obstructions. Finally, the degree of coronary obstruction is only roughly correlated with the presence of flow limitation or ischemia, and this has been shown in many, many studies documenting that there is a large intermediate zone variably between 30 to 40 percent and 70 to 80 percent diameter stenosis narrowing by cardiac angiography that may or may not be functionally important. In other words, patients with stenosis in that range might have a positive stress test and beginning ischemia from that lesion, or they might not. And so the arbitrary selection of a 50 percent cut point is exactly that, it is arbitrary, but obviously for these studies, you need to pick something.

A couple of other background issues, and this has already been mentioned as well. There are really two important questions and we need to be clear which of these questions that we

are asking when we are presented with a patient. First of all, is the patient symptomatic or asymptomatic, and we're going to assume that the patient has come with some sort of symptoms. And then we are trying to decide two important things, do they have coronary disease or not. This is purely a function, or excuse me, an anatomic issue. In other words, is there atherosclerotic plaque in the wall of their vessel that will make the diagnosis of coronary artery disease? And that fact alone will have important implications for how we're going to treat the patient. Secondly, is there the presence of ischemia due to presumably a flow obstruction, and I will exclude those very few patients who have so-called syndrome X where they may actually be getting ischemia due to microvessel disease which none of these technologies, including cardiac cath, can image. The vast majority of patients who have ischemia have it because of a flow-limiting obstructive lesion in the coronary artery. So if that is the question at hand, then obviously the types of work-up that we need to do are somewhat different.

So I think it's important as we

evaluate these technologies to keep in mind what our fundamental question is and what is the nature of our patient population. As you heard from Dr. Mark, the pretest likelihood and applying the whole phase theorem situation is critically important in how we utilize and evaluate these tests.

So with regard to the first question, can CT accurately identify coronary obstructions, as you've already heard multiple times now, there are six studies with the more recent current generation 64-slice scanners and you have already seen all of this data. I just want to highlight that for really basically a first generation set of studies, these sensitivities and specificities are actually quite good. And I want to especially highlight the negative predictive value of that. It has not been mentioned before but it is in the table of my handout and a number of the other technical assessments.

So the negative predictive value, in other words, when you say a test is normal, it really is normal, is extremely important for the type of patients that we're asked to see. A patient comes to us with unusual symptoms, we have

a suspicion, probably relatively low, that the patient might or might not have coronary disease, and the ability to tell them with certainty that they do not have coronary artery disease is extremely important. And the finding of any coronary disease obviously puts patients at risk for all the nasty things we saw in the first couple of slides, sudden death, acute myocardial infarction, unstable syndromes, all of this sort of end-stage manifestations of disease. And if we can tell someone you do not have the substrate for that, that of course is a very important thing for them and so I think the negative predictive value of these tests is extremely important to keep in mind.

There are obviously some unevaluable segments, and we talked about that, but I would argue that if you are missing a small lesion in a one-millimeter vessel, that would have very little therapeutic implication, none of us would do bypass surgery or stenting on anybody with a lesion of that sort, and the chance that they would only have a single atherosclerotic lesion in a one-millimeter vessel and nothing else on the cardiac CT would be very unlikely. So even

subclinical atherosclerosis we would not miss in those patients. So I think, again, that's sort of an arbitrary cut point. We do not stent or bypass vessels of that size, so in terms of guiding our therapeutic decision, that is really in my mind not a patient management limitation as much as just a technical fact at this point.

The question is whether CT can in fact define the location, this really gets to Question 2, and as Dr. Fishman nicely showed for you now, we get isotropic vessels which have very nice spatial resolution, and you can see here a comparison from the Hoffman study of the coronary angiogram on your right and the coronary CT on the left, and it very faithfully reproduces the anatomy that is represented on the CT.

This question was a little bit confusing. Clearly we can see where the lesions are and it is very anatomically correct, so we are very confident that you can define where these stenoses are. And again, the limitation of very small vessels, as I mentioned previously, would not change our patient management decisions.

The important point, I think, is that in all of these studies the negative predictive

value is extremely important, so as you're evaluating patients, the ability to tell them you do not have coronary disease will be critically important, and I think is in some ways a more important measure of how this test might be useful than the absolute sensitivity and specificity in these tiny vessels.

I just want to highlight this slide as well. Dr. Fishman mentioned this, that the processing and interpretation skills are critically important. The society, along with many others, have focused heavily on competency statements, providing educational opportunities and trying to further the software capabilities so that we can accurately and easily interpret these studies. Here on your right you see a cross-section through that yellow part of the longitudinal image that shows a section of the coronary with some calcium with two different window level settings. On the top one, obviously you see a lot of calcium which might lead you to overestimate its clinical importance. Then the bottom, with just some adjustments in the window level, you can see that actually the lumen is quite well preserved and the calcium is all in the

vessel wall. So again, a focus on appropriate interpretation, excellence in clinical interpretation and training for the folks who will be interpreting these things is also very important.

The third question has to do with, can it identify relevant coronary morphology, and this one really was a bit confusing to me. Clearly as you can see from this study from Leber's study, or this picture from Leber's study, it very accurately defines this complex proximal circumflex lesion, but really cath and CT are looking at two different things. Whereas the cath can only look at the lumen, the CT as you can see, can also look into the vessel wall. So in addition to seeing a narrowing in the lumen, you can also evaluate what is causing that narrowing, whether it is calcified plaque or non-calcified plaque, where the lumen is traversing through that plaque, is it eccentric or concentric, and this information may be very useful in the future, and we have not been able to get this accommodation. Obviously, we've been able to do this with all this, and as we've talked about already, I believe there are a number of studies correlating this

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with others and showing a good correlation, but we're finding now that we're getting different information. So certainly we can see morphology, but really the two are not directly comparable because you get additional information on the cardiac CT that is just technically impossible on a cath.

Can it be used instead of CT angiography? This really hinges on the point of whether we manage people based on the 50 percent lesion or not. We believe that in many cases CT angiography could be used instead of conventional angiography. This is where this pretest likelihood becomes critical. I've reproduced for you one of the tables from an exercise, a guideline document from the ACC, and in many cases with low probability of CAD, we believe that cardiac CT can be performed instead, or replacing diagnostic CT for a diagnosis. In cases of very high CAD probability, then obviously cardiac CT would not be the optimal choice because we would like to take those patients directly to cardiac catheterization where the therapeutic intervention could be performed. So you want to try to use this on patients with a low likelihood of needing

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an invasive treatment modality such as angioplasty or bypass surgery so that we can try to send only those patients to the cath lab who need that kind of procedure, and we can in many cases rule out coronary disease very effectively with the cardiac CT and thereby avoid an invasive procedure.

So let me just summarize, that we believe that noninvasive CT angiography is really a significant advance, and I would argue a very significant advance in our capacity to diagnose and plan the treatment of patients suspected of coronary disease. I think it should be considered complementary to invasive angiography and if it's applied appropriately, and we are very much in favor of appropriate application, it should allow us to triage patients who are likely to need intervention into the cath lab for further invasive and possibly therapeutic intervention.

And finally, we haven't really talked about this, but it can detect subclinical atherosclerosis, the actual anatomic substrate for all of the bad things that happen to patients, and this finding may fundamentally alter the way we treat patients. We've already seen that very effective risk factor modification can alter

clinical prognosis for the patients, and we believe that this is why this will be a paradigm shift in technology allowing us to evaluate patients who actually have the disease and not just the end-stage manifestation of the disease with an MI or an ischemia-producing lesion. Thank you.

DR. GARBER: Thank you. Just very brief, any clarifying questions? Okay. Thank you very much. Next, Kim Allan Williams, from the ACC.

DR. WILLIAMS: On behalf of the American College of Cardiology, I am pleased to be here addressing the Medicare Coverage Advisory Committee today. As you may know, the ACC is a 33,000-member non-profit medical society and teaching institution whose mission really is to advocate for quality cardiovascular care through educational programs, research development, application of standards and guidelines, and to influence in a positive way health care policy. The college represents over 90 percent of the cardiologists practicing in the United States today.

My name is Kim Williams. I am

currently a professor of medicine in radiology in the department of cardiology and nuclear medicine at the University of Chicago, and I direct the nuclear cardiology laboratory. I will be speaking today on behalf of the ACC, but by way of disclosure, I am immediate past president of the American Society of Nuclear Cardiology, and I am an active member of other organizations who will be testifying here today, including the American College of Radiology, the Society for Cardiovascular Computed Tomography, and the Society for Cardiovascular Magnetic Resonance. On a personal basis, I have the disclosure of being an advisor to GE, particularly in regards to nuclear cardiology, but I will not be making any proprietary remarks today. My travel was paid by the ACC.

The ACC's testimony today is really to give some perspective and overview about the issues brought up by CMS rather than scoring the individual questions, which will continue to be addressed by our colleagues from other organizations. As an overall comment, the ACC is really committed to insuring that cardiovascular imaging services are used appropriately to enhance

the diagnosis and treatment of patients with cardiovascular diseases. We have devoted a significant amount of resources to developing tools to help physicians gain the skills necessary to provide these imaging services and to select tests appropriate for their patients.

So earlier this year, ACC, along with the Duke University, held a think tank that generated a commitment from multiple stakeholders in the imaging area to further enhance the quality of imaging through the development of various standards and tools, including appropriate criteria, accreditation, standardization of reports, performance measures and outcome evaluation.

The college is really committed to providing assistance to policy makers and health plans as they try to make informed decisions about the array of services to be covered, so working with CMS to extend and improve Medicare coverage is one of the things that is a priority for the ACC. The ACC's efforts are of particular relevance today in terms of developing cardiac imaging guidelines and more recently, appropriateness criteria for cardiac imaging

modalities. Together these documents provide a summary of the evidence supporting the use of these services and guidance for physicians about when these services are useful and when they're likely not to be generally useful.

Last fall the ACC and the ASNC published the myocardial perfusion SPECT appropriateness criteria. The ACC is partnering with several other cardiovascular organizations to develop CT and MR appropriateness criteria, and those should be published within the next few months. Hopefully we will go on to do echocardiography and coronary angiography within the next year.

In approaching the topic before you today, the ACC would sort of like to ask that the MCAC remain mindful of several key principles, one of which has been brought up already today. One is that physicians use a variety of imaging techniques to evaluate patients who present with symptoms of CAD and some of these techniques, particularly echo, radionuclide imaging, and cath, have a long history. Other modalities that are on topic today are here because their history is fairly short, they continue to be defined, refined

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and developed, and they have enormous potential, but the best uses of these technologies is really not known yet, and we would like to emphasize that at this time you cannot consider them as substitutes for one another. Physicians caring for Medicare patients really should have access to the full array of appropriate diagnostic tools in order to help the individual patient.

Now the application of CT and MR for cardiac indications, as I said, are developing and as new clinical evidence come on it becomes outdated, and as Dr. Fishman said, it's really about 2006, because the technology is improving continuously. So the college is in the process of planning for revision of each of the guidelines and each of the appropriateness criteria, and we expect that after publication of the CT/MR appropriateness criteria, that we will be revising it within 12 months. So we encourage CMS to take that sort of attitude as well, that the noninvasive imaging for coronary artery disease will have to be reevaluated over the next several years and probably several times. If the Medicare patients are going to benefit from these advances, we have to remain flexible in terms of payment, in

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terms of understanding the body of knowledge and the clinical utility.

Now before beginning to respond to the specific questions that CMS has set up for the panel, I'd like to make a few comments about those questions. First of all, in terms of CT, MR and EBCT, we really wouldn't want to talk about them necessarily to the exclusion of the other imaging modalities that have been mentioned today. I would just like to emphasize the importance of physiologic imaging, particularly in its complementary role to anatomic imaging and the fact that some studies indicate that the prognostic capabilities of the physiologic parameters are actually superior to anatomic variables, and so that really can help the physician make the right choices and optimize cost expenditures.

Secondly, these questions really assume that the primary utilization of these tests is to try to define who's going to have interventions such as bypass surgery and coronary percutaneous stenting, et cetera, but one of the best uses of the test, particularly the physiologic one, is to figure out who's going to benefit from the medical

therapy and does not need coronary angiography. Third, we would like do emphasize that it's really important as we accumulate more knowledge about this, to identify the coronary artery disease that's not going to be apparent. As noted earlier by several of the speakers, the majority of myocardial infarctions occur on vulnerable plaques that have stenoses that are significantly less than 50 percent narrowed. Therefore, we anticipate that there would be a much greater role for the tests that can look at degree and function and functional significance of extraluminal and intraluminal plaque formation. So CMS has asked the panel to evaluate whether the evidence is sufficient to determine the diagnostic accuracy of noninvasive imaging technology for detecting obstructive coronary lesions. Each of the cardiovascular imaging modalities has some strength and some weakness in this regard. Based on the evidence thus far, we believe that MDCT can be a valuable diagnostic tool when ordered by a physician and used in selected patients in a careful way. It's rapidly evolving and the evidence continues to grow, and the accuracy really, as you heard today, depends

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on image quality and the expertise of the physician performing the study, as well as patient selection and patient preparation.

The major strength of CTA is going to be that the diagnosis of coronary disease gives us a high negative predictive value and that is particularly true in patients with a low to intermediate likelihood of significant coronary disease. In terms of EBCT without contrast, it's very sensitive for coronary calcium and that has been very helpful prognostically over the years. It's true now that you probably will not see much in terms of development of CT angiography with this low resolution technique. It also is true that the MDCT has taken over this capability and has been shown to match the coronary calcium scoring that we saw with EBCT.

Cardiovascular MR has the ability to look at a wide variety of things, cardiac, vascular structures, function, as well as perfusion. We can look at the late enhancement of gadolinium to detect myocardial viability, which is very helpful. It can look at stress perfusion defects. In terms of MRA, however, we have somewhat more limited data than a CT angiography,

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but it has been shown to be at least equivalent to the 16-slice CT scan. CMS has questioned the capability of these noninvasive technologies for the evaluation of morphology of obstructions and we would say that with CTA, this is something that is becoming more and more robust, although it has been less robust than the evidence for the evaluation for stenosis. But what is clear is that we are able to distinguish calcified from noncalcified plaque, as you saw earlier, and we're hoping to get to the point where you can actually look at lipid-rich versus high risk plaque, and that should be around the corner. The evidence of coronary angiography, as Dr. Hodgson pointed out, is actually limited in this regard, and so we would like to focus on the fact that the ability to look at vulnerable plaque probably will be afforded to us by the newer technologies rather than coronary angiography. In terms of whether noninvasive imaging technologies can be effective instead of catheterization to determine treatment, it's clear that CTAs have a high negative predictive value in patients with a low or intermediate probability of coronary artery disease. It really can help us

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identify people who do not need to go forth for cardiac catheterization because it's not likely that they're going to need revascularization. People can be treated, therefore, with medical therapy as appropriate, or other modalities. There is less experience with MR in this regard, but for patients who have symptoms and have significantly higher risks for CAD, those patients probably should go to catheterization, and CT angiography will offer little if any additional benefit, while increasing both the risks in terms of iodinization, iodinated contrast and radiation exposure. Both CT and MR have some uses after catheterization in occasional circumstances, particularly locating anomalous coronary arteries, which can be very difficult invasively, trying to do selective catheterization of unusual locations, and looking at the patency of coronary artery bypass grafts. And so as we see these cases, we know that this is something that we expect to increase over time. Using CTA for stent occlusion, on the other hand, is something that will need further development, although you have some initial literature suggesting that can be

done.
CMS is also interested in whether we can appropriately generalize this information to the Medicare population. As noted earlier, the CTA population that's been studied is very similar to the Medicare population, but that really hasn't been tested specifically.
So in closing my remarks, I want to sort of leave you with some observations of how this is sort of evolving as a person who actually does all these techniques on a daily basis. A patient recently was referred to my clinic because he had gone to my nuclear lab and was felt to have a very mildly abnormal perfusion scan, the kind that you would normally just treat with medication. However, there was one high risk finding, that is the presence of transient ischemic dilation of the ventricle which typically occurs when you have high risk multi-vessel disease or left main coronary artery stenosis. If you're going to have proximal disease, you can actually do a pretty good job of detecting that with CT angiography, so that was a choice that we were able to make, as opposed to a year or year and a half ago where we would have had to send

that patient to coronary angiography to be certain about the anatomy. The CTA confirmed that he had mild calcification, minimal stenoses, and no proximal significant left main disease. So we really felt like we saved that patient the expense and risk of a cardiac catheterization.

And as time goes on, you will find that there are more and more scenarios that are just like that. So I would predict with time, we will refine these techniques and understand many more scenarios that will allow us to do noninvasive imaging in preference to invasive testing, and the invasive testing, as many speakers have said today, will go more towards preparing people for immediate coronary interventions.

So I thank you for the opportunity to address you today and will be happy to respond to any questions that you have.

DR. GARBER: Thank you. Unless there is some burning question, why don't we defer the questions until we have the questioning period from the panel, because I think a lot of the speakers have touched on some of the same issues.

Now we turn to the open public comments. I'm sorry, the scheduled public

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comments, and the first speaker is Michael Poon, to be followed -- I would like each speaker to come up toward the front before, while the other person is speaking, and next will be Cathleen Biga.

DR. POON: Good morning. My name is Michael Poon. I'm chief of cardiology at the Cabrini Medical Center New York, and associate professor of medicine at the Mount Sinai School of Medicine. I'm currently president-elect and chair of the efficacy committee of the Society of Cardiovascular CT. I'm on the scientific advisory board of Siemens Medical, (inaudible) and Chase Medical, Inc., and I'm currently holding a research grant from Siemens Medical on the study and growth of multi-detectable CT in early detection of coronary artery disease.

Today CT coronary angiography using at least 16-slice multi-detectable CT permits high resolution imaging of the coronary arteries as seen here in this slide. However, the (inaudible) testing remains a key clinical parameter for determination or prognosis, and any further need of diagnostic testing and therapeutic intervention. For example, coronary

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echocardiology and nuclear cardiology imaging are commonly being used in everyday clinical practice to assess the association between cardiac symptoms and associated pathophysiology, even though they are not directly visualized through the coronary arteries or accurately determined as the anatomical location of the obstructed coronary artery lesions.

Over the past 12 years, we have seen a dramatic improvement in the technical side of the CT technology both in the spatial resolution, that is the ability to see smaller and smaller pathology in greater detail with the multi-detectable CT from the early days of EBCT as shown on the far left here. At the same time, the multi-detectable CT has also improved in its temporal resolutions very quickly over the last two years, approaching that of the EBCT, but there is still a way to go. With the introduction of the new source, that gap is getting smaller and smaller. And the whole point of having better temporal resolution is to be able to freeze the motion of the beating heart, which is the most challenging aspect of cardiac CT.

Today's CT technology can detect

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coronary lesions as shown in this slide very much similar to what you see on x-ray angiography, and this is a particular example showing the strength of cardiac CT which is able to see lesions, particularly those noncalcified ones, to be almost exactly like what you see with x-ray angiography. In fact, CT can show you the tissue characteristics, which is information which is not available on the conventional x-ray angiography, and then they provide very important pathobiology of the disease process.

Coronary CTA can also be used to detect patency of bypass graft as shown in this pair of images. Occlusion and patency of bypass grafts can be assessed with very high accuracy. However, the detection of coronary stenosis at the MI site and even in native coronary arteries after the bypass surgery graft remains difficult. Rarely, coronary CT may be used following x-ray angiography to show if the graft had been missed during the prior invasive coronary angiography.

The major limitation of this bursting imaging technology are due to artifacts caused by motions of the beating heart or extensive calcification, as shown in the panels on the left

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and center here. These artifacts can severely impair the evaluability of a study. With a modern scanner with at least 16-slice multi-detector CT and aggressive premedication with heart wave lowering agents, the percent of unevaluable segments are infrequent.

Due to the artifacts caused by the high density of metal, the assessment of stents concerning in-stent stenosis by CT is substantially more difficult than the assessment of native coronary arteries or bypass grafts, as shown in the far right here. The visualization of stent lumen can be impaired by these artifacts and are influenced essentially both by the scanner technology as well as size and type of stent.

There is not yet sufficient evidence to support the use of CT angiography to routinely follow up patients after coronary stent implantations.

To date, more than 15 scientific reports, all published in reputable peer reviewed journals, show that accuracy of coronary CTA in comparison with that of conventional x-ray angiography to be very very good. This slide shows the most recent reports on the latest 16-slice technology, with another six reports on

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the latest 64-slice CT scanner. It reports similar accuracy in both sensitivity, specificity, negative predictive value, and percent unevaluable segments.

Similarly, the accuracy of multi-detectable CT to detect patients with at least one significant coronary stenosis is equally high. This is commonly referred to as per-patient analysis, as shown in this slide. With the exception of one study, as pointed out by other speakers, that this study used the earliest CT scanner technology, all of the studies basically showed that the 16-slice technology is comparable to that of 64-slice in terms of its accuracy on a per-patient analysis basis.

The currently available body of evidence demonstrated that coronary CTA can reliably rule out the presence of significant coronary artery disease in patients with low to intermediate probability of having coronary artery disease, and can reliably achieve a high degree of diagnostic accuracy and technical performance necessary to replace conventional angiography.

Severe form of calcification is a reason for impaired evaluability of CT coronary

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angiography due to partial volume effects which are a consequence of limited spatial resolution. The overall rate of an unevaluable study has been lowered with recent technology, but CTA may have a somewhat higher rate of unevaluable study and lower accuracy in the Medicare beneficiary population due to the increase in coronary calcifications. However, that fact is not likely to be of significant magnitude. In fact, it has been shown that age alone does not have an influence on the accuracy of CT coronary angiography for the detection of coronary artery stenosis.

As shown in this patient, an 83-year-old with atypical chest pain, equivocal stress perfusion test, and on CTA showed absolutely no obstructive coronary artery disease, and saved this patient from having unnecessary and potentially dangerous invasive procedures.

Another patient, a 72-year-old scheduled for surgery of a benign cardiac tumor, and CTA showed normal coronary and the surgeon accepted the patient for surgery without additional invasive coronary catheterization.

And these are just some of the examples

to show what the CTA can achieve and potentially avoid some of the complications associated with an invasive test. Even for the younger population, for example this patient, a 43-year-old with congenital bicuspid aortic valve and dilated descending aorta, CTA also ruled out the presence of significant coronary artery disease and eliminated the need of a pre-op coronary artery catheterization.

And there are times that the patients may not be able to go through a further invasive test because of other complications associated with the vascular structure, and CTA will be able to show, as this case, the bypass graft, which is very difficult to show on conventional x-ray angiography but shows very nicely on the CTA.

DR. GARBER: Thank you very much.

Next, Cathleen Biga. She will be followed by Jason Cole.

MS. BIGA: Good morning. My name is Cathy Biga, I'm the president and CEO of Cardiovascular Management of Illinois and am here representing my two private practice groups that consist of 50 cardiologists, as well as the Cardiology Advocacy Alliance. The Cardiology

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Advocacy Alliance is a consortium of 3,500 practicing cardiologists in private practice. My disclosure statement is that I do do extensive lecturing on the operationalizing and economic impact of CT angiography across the United States, and I'm also on GE's speakers bureau.

I would like to take this opportunity to share with you the clinical and administrative experiences that exist with multi-slice CT angiography. With the advent of 64-slice CT scanning, we entered a new diagnostic era. It's realized rapidly increasing acceptance within the cardiology and radiology communities as a scientifically accurate and complementary modality.

It should be noted that we believe there is a distinction between the 64-slice scanners and the previous multi-slice scanners, specifically in the visualization of stents, post-CABG grafts, and the ability to detect subclinical atherosclerosis, as several of the other speakers have already identified.

Obstructive coronary artery disease can indeed be reliably diagnosed using 64-slice scanning. If the detection of any amount of coronary

atherosclerosis is our goal, i.e., for effective management, we believe that the CTA has no peer. CTA angiography detects atherosclerosis much earlier than other modalities, except perhaps intercoronary ultrasound. In regards to detecting a hemodynamically significant lesion, one that would land a patient in the cath lab, for instance, the sensitivity and specificity for both approach the upper 90s, as you've already seen in several slides. Equally important is the negative predictive value, which we have shown in our studies to be between 97 and 99 percent; no other modality comes close to this.

With this growing experience, the sensitivity in detecting the existence of coronary atherosclerosis could surpass and then exceed stress echo and stress nuclear imaging. Anatomical location, as you have seen, is very easy with a coronary CT with the multiple resolutions we get from these scanners. There is no question or doubt as to the location of the particular lesion, whether it be a calcified lesion or noncalcified lesion. And like the prior speakers, we have sent several patients directly to surgery without having to undergo a cardiac

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catheterization. All other imaging modalities lack the ability to detect the size, shape, ulceration and other aspects of morphology that coronary CT can and will continue to improve on. Until now, imaging modalities have offered neither the sensitivity nor the specificity to be reliably compared to cardiac catheterization, the current gold standard. Indeed, many patients most likely would have gone untreated or undertreated because of the relative high false negative rates with the existing imaging modalities. We believe that coronary CT can begin to breach this gap. Many normal cardiac caths have actually shown mild nonobstructive disease on 64-slice coronary CTAs and yet, we have seen a decrease in our normal coronary catheterization rate from an 18 percent to an 11 percent rate. These patients are often mislabeled as normal on a cardiac cath and miss out on potentially life-saving therapies such as stents, anti-platelets, life-altering events, smoking cessation, weight loss, et cetera. Cardiac cath gives us an indirect view of the lumen, which shows nothing of the outside of the lumen. Coronary CT angiography not only

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shows the lumen but its surrounding structures. CT angiography would provide a tangible benefit to patients by identifying those patients who would not need a cardiac cath. It would save those patients the risk and inconvenience of an invasive procedure, the additional contrast, loss of work, and hospitalization. Coronary CT angiography would be an effective gatekeeper for the cath labs.

There would be little use for coronary angiography, CT angiography after a cardiac cath, with the exception perhaps of a bypass evaluation of grafts not found in cath. This use could help reduce the risk of stroke or bypass surgery.

Of the newer technologies, coronary CT angiography, EBCT and MR, only coronary CT angiography is generalizable to the Medicare beneficiary population. We believe that EBCT is less compelling to the Medicare population because of its calcium scoring. 37 to 40 percent of our patients are in the Medicare population.

In closing, I would just like to say that while I have not presented any of our case studies, some of the initial case studies that we have, specifically a 77-year-old with unexplained

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chest pain, a negative nuclear stress test, showed on coronary CT angiography that he had significant right coronary lesions and had the stent a few hours after the coronary CTA.

An analysis of our database and registry for our 1,300 coronary CTAs, we have determined that if coronary CTAs are ordered appropriately following narrowly defined and appropriate clinical indicators, they are clinically useful in determining treatment plans, has resulted, as I already mentioned, in a decrease in our normal cath rate, has not become a third test. In fact, our first 250 cases showed only 3.7 percent of patients come back for a third test, and in our first thousand patients, 6 percent only went on for a third test. It's excellent in determining state patency and post-CABG graft patency.

It's an important modality in the diagnosis and treatment of coronary disease when used appropriately with good patient selection criteria, patient preparation including beta blockers the night before and the morning of, gating, contrast dosing, performed by a skilled technician and supervised by a credentialed

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interpreting physician, resulting in high quality studies. Thank you.

DR. GARBER: Thank you. Next will be Jason Cole, to be followed by Harvey Hecht.

DR. COLE: Thank you very much for the chance to talk. My name is Jason Cole, I am a cardiologist with a 25-person private practice cardiology group in Mobile, Alabama, and I'm speaking today on behalf solely of myself and my partners, as well as the cardiology alliance. I do have relationships with GE Healthcare in that I've served on their speakers bureau, their medical advisory board, and do have some research support for CT angiography and cath relation studies from GE Healthcare. My transportation here was paid by our practice.

There really are three points that I want to make relatively briefly and directly. The first one is that there are enormous questions related to this technology to come out in terms of how generalizable is it. There are studies that have reduced, can it be done, can it be reproduced in a practice setting, and I'm here to tell you that absolutely it can because we're doing it. We have been practicing with a 64-slice

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CT angiogram for the past, a little over the past year. We have done over 1,500 studies. We have maintained the data prospectively in a database and we have gotten excellent results of well over 90 to 95 percent of the patients that we imaged, we were able to image. There is certainly some amount of a learning curve that goes along with it, but it can be very well controlled. We paid tremendous attention to the data that's already out there.

We had initially three physicians who were trained to read this. We have been able to learn a large number of things about how the studies can be read. The issues related to coronary calcification are certainly there, as they have been shown to you today, but as you get the ability to read these and you develop the ability to read a cross-sectional analysis, and understand exocytic calcium versus calcium that intrudes into the lumen. These are very easy things to overcome. There certainly are some patients who cannot be imaged adequately because their calcium scores are extremely high. It is very simple to put in place processes so that those patients solely get an initial low dose

screening x-ray and then can be screened out from needing to go on to further CT angiography.

The second thing I wanted to address is the question of how do we use this test. How is this test actually being used in practice when it's able to be used? We have focused, as you've begun to hear as the drum rolling theme, focusing on the negative predictive value of the test. We believe in that as an extremely strong point. The numbers that have been shown are 90 to 99 percent negative predictive value, and remembering that there were some issues raised by the fact that those studies have been derived from patients who were going into catheterization and may have a 50 percent prevalence of coronary disease, as we look at low to intermediate risk patient populations, it's important to recognize that that negative predictive value will be even higher. We have enormous confidence in using this technology to avoid using catheterizations.

We have also used it to identify coronary artery disease in patients who we otherwise wouldn't know, and we considered some of the other noninvasive imaging technologies and that's the important initial point of comparison,

because really this is being compared to other noninvasive ways of looking at the coronaries. You can identify early coronary atherosclerosis, things that are truly transforming, and we have a number of case examples of patients, both patients 65 years of age and older and younger patients, who have had a very similar experience where other diagnostic tests don't show disease, they have this test and it picks up disease. This is an important, very clinically relevant point. The third thing that I want to say is based on our own data and using this test appropriately, we can identify patients and target their care directly. One of the questions that has been raised is, you know, do these patients still require invasive catheterizations? Well, certainly as far as an original procedure, they do. But it shapes the way that you think; this is the closest correlation to our pathophysiologic understanding of coronary atherosclerosis, because we see it. If we go directly to catheterization, everything including choosing the guide and catheter that's used based on the angle at which the artery is taking off is an extremely valuable tool.

We have identified in our database a particular niche for this use in patients who have the equivocal or low risk nuclear studies, and this is our data that we've derived and has been presented at national meetings, so far published only in abstract form. But what we have shown is that in a carefully selected group of individuals, certainly less than 10 percent of the patients undergoing nuclear perfusion studies in our practice, we found that we can get adequate studies to avoid having to go to catheterization in 60 to 65 percent of these individuals. So in an appropriate patient population, we can then use this test to make a decision. And it's a big deal for a patient when they don't have to go through catheterization, they avoid the risks that are there. The preliminary cost analysis that we did also showed that this was a cost saving technique. So number one, this test can absolutely be used in clinical practice, it can be done. Training is important, it is available, and doctors can learn to use it. We use it focusing on the negative predictive value, that's the reason to use this test, because when it's negative and it's negative enough, you know that

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you don't have to proceed. If you've got mild disease, you also know to treat that medically in a way you had to do before, and in many cases you can actually target what you do in an interventional lab, and you can also identify patients who truly would have otherwise gone on for invasive procedures who don't need to. It's an exciting technology and as we work with it, it becomes integral in the way that we take care of patients. It's enormously valuable to us as well as to all of our Medicare patients that we're caring for. Thank you.

DR. GARBER: Thank you. Next, Harvey Hecht, to be followed by Greg Thomas.

DR. HECHT: Thank you. My name is Harvey Hecht, I am the director of cardiovascular CT at the Heart and Vascular Institute in New York, and formerly professor of medicine at the Albert Einstein College of Medicine. My conflict of interest disclosure is that I have research grants from Philips and indeed, Philips did pay my transportation down here.

Let me assure you I'm not going to go over the same territory that has been done before and the presenters have done a superb job.

However, what I will do is elaborate on a few of those themes and perhaps generalize it. And I would start off by showing you an example of a patient who has minimal abnormalities on his CTA, a patient who we evaluated for atypical chest discomfort. There is a little bit of narrowing in the proximal LAD but there is clearly nothing obstructive. Does this patient need to have a stress test, and the answer is obviously no. He has nothing close to obstructive disease on this test, his symptoms are atypical, he was low to intermediate likelihood of disease to enter, so he does not need a stress test and certainly he does not need an angiogram.

The next patient, low to intermediate risk of disease on entering, atypical pain, and he's got calcified plaque there in the proximal LAD and there is noncalcified plaque as well. If you try to measure the stenosis, it will come out somewhere in the 50 to 70 percent range perhaps, and this is an indication where you do need to do a stress tress to determine the functional significance of this abnormality. You would not send the patient directly to the cath lab just on the basis of the CTA, you would do the stress

test. If the stress test were significantly abnormal, then you would send the patient for a cath; if it were not, then again, you would not do an invasive procedure.

Finally, we have a patient here again with atypical pain post-bypass surgery, and we did a CTA and there was a critical left main stenosis which was not adequately revascularized because they did not vascularize the circumflex, which was jeopardized by the left main. You are not going to go ahead and do a stress test on this patient clearly, you're going to go straight to the angiogram.

So we're talking about this, then, in the context of triaging patients for the cath lab, and avoiding procedures, both noninvasive and invasive. I mean, how has this played out in practice? Well, the best example so far is the one that Tracy Callister has presented at numerous meetings. In his two-year experience with CTA in a large practice, international, the number of normal caths in his practice declined by 40 percent; the number of nuclear stress tests declined by 33 percent, and he did not own the CTA. So the trust in the CTA as the first test to

do in the evaluation of these patients was validated by the results clinically in terms of utilization of other resources which, unnecessary utilization was dramatically decreased.

So to put it in a greater context, we were told at the beginning of this session that there are 1.8 million catheterizations in the country. If you look at the national level, I think it's fair to say that there are probably 18 to 20 percent of these that reveal no significant obstructive disease, and how you define that is probably less than 50 percent stenosis. If you had a noninvasive test, which by virtue of the extraordinary sensitivity and specificity could accurately diagnose those patients and save 95 percent of them from entering the cath lab, well, 95 percent of 1.8 million is about 350,000 diagnostic caths that could have been prevented. We were told that the mortality rate for diagnostic cath is one out of a thousand, .1 percent, so that's 350 deaths. The major adverse event rate is 2 percent; that's about 7,000 adverse events that could have been prevented by CTA. The cost of the procedure to the government, to Medicare, to the payers, to the patient in

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terms of time off from work, to society, is enormous, and the cost saving consequently is also enormous.

Moving to a slightly different topic, the cross-sectional aspects of CTA have been emphasized in terms of it being (inaudible) equivalency, and yes, there is not an enormous amount of data on this, but all of us who use CTA are constantly astounded by our (inaudible) views that we have of the coronary arteries by use of CTA. We see noncalcified plaque, we see very very low density noncalcified plaque. Is this the tip of the thin cath fiber atheroma, can we put it in correlations of (inaudible) to find out? We are using it, as previously alluded, CTA on a daily basis to change, to transform the way we do interventions at Lenox Hill. We are guided by the results on CTA. We have avoided going through significant left main stenoses that have not been appreciated on conventional angiogram because of the limited views en route to dilating LAD stenosis, so the information that you obtain beforehand can very profoundly affect the way you do your interventions.

On coronary calcium, in our laboratory

now there is no coronary calcium score that excludes the patient from having a CTA, for the reasons that have been given. Dr. Hodgson showed a beautiful example of a very heavily calcified plaque that diminished in size when you adjusted the leveling in the window, and this can routinely happen. It's a rare plaque that you cannot interpret whether or not it's obstructive. And equally important, it is usually not the calcified plaque that's responsible for obstruction anyhow, and it's the rare patient who has significant calcification and in whom you cannot detect a significant stenosis in the area of a noncalcified plaque when it's there.

Finally, I would like to talk a little bit about radiation because the Duke group talked about it, and yes, there is radiation from CTA. It has been put in the perspective of invasive angiography, but radiation from CTA is going to decline over the years as the technology improves, but also keep it in the perspective of other tests that are being used to evaluate patients. It's safe to say that the radiation from CTA is at worst equal to, and in fact according to most studies, significantly less than that of a nuclear

stress test, and we rarely consider radiation load on a routine basis for nuclear stress testing. So in summary, I would ask you perhaps to change the focus of this discussion really not to ask the question, can CTA replace invasive angiography. We're not saying that. We're saying what is the role of CTA in the comparative diagnostic paradigm, can CTA be the gatekeeper, can it be the triage or entry into the catheterization laboratory, and the answer is an unequivocal resounding yes. Thank you.

DR. GARBER: Thank you. Next, Greg Thomas.

DR. THOMAS: Well, after three hours of testimony, it's kind of like following the late night talk show hosts, so I've got to think of some things new to say. I don't have a monologue or a top ten, but I do have a top five, and I'd like to bring up some new points. My name is Greg Thomas, I'm currently president-elect of the American Society of Nuclear Cardiology and a clinical assistant professor at the University of California, Irvine.

ASNC is a 5,000-member professional society to foster, or develop and foster nuclear

cardiology in terms of training, education, accreditation or certification, and more recently added cardiovascular CT as a complementary anatomic evaluation to go along with the well-documented prognostic and diagnostic value of the physiologic tests.

One of the comments Dr. Rollins made was in terms of the cath rate, and obviously as we're looking at where does this test come, are we going to save lives, are we going to save tests. The cath rate interestingly last year did go down. I think you mentioned, Dr. Rollins, maybe three million in 2010, but as you may know, the more recent data from Medicare is that in 2005 the cath rate, diagnostic cath rate went down 15 percent. So in the past it was rising, then leveling, and now it's down 15 percent, so I don't see that continuing to go up.

Also in terms of statistics, we're looking, we haven't talked about costs, but underlying a lot of what we're thinking about and particularly as we look at the cost evaluation, the value to the public of this test will become very important. And I think to look at the cost in the global context with other cardiology

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testing, cardiology technology, I want to bring up how well we've done in cardiology. With cardiologists taking care of the patients, along with the internists and family physicians, since 1970 we have had an annual three percent average decrease in mortality for cardiac disease, so the diseases of the heart according to the CDC comparing 1970 to now is down by two-thirds. In fact it's accelerated over the last several years such that between 2003 and 2004, the death rate for cardiac disease went down 3.5 percent. And lastly, it was announced that cardiac disease, the age-adjusted death rate went down 6.5 percent between 2003 and 2004. So I think we're getting a great deal of bang for the buck with our technological evaluation for diagnosing disease, treating disease, with a 9.5 percent drop in age-adjusted mortality just in the last two years, for example.

As well as, if you compare the causes of death between 1999 and 2004, disease of the heart was 40 percent in 1999. Disease of the heart last week, according to the CDC data, was 33.5 percent. So the money we're spending in cardiology, which is substantial, I think we're

giving the public a great deal of value for that, and I don't want us to limit new technology such as CT, such as MR, because of the cost of it and because it will require more tests, because I think we are getting a great deal, again, a bang for the buck, for this technology we've used and technology to come, and if we don't allow promising technology to develop, it's unlikely we will see this continued drop in heart disease.

One of the things brought up was the prognostic studies, and again, none of them have seen the light of day as Dr. Mark suggested, in terms of peer reviewed literature. There are two articles, one accepted, one in review, looking at the prognostic with some very nice slides, as you would expect. For example, looking at the decrease in the mortality based on the number of vessels, one-vessel disease like this based on CT, two-vessel like this, three-vessel like this, and the same for severity based on CT. So very soon we will be seeing that data as well as other data that's still in review.

So what I would suggest based on this and based on the fact that it has been well stated, we don't have clinical utility studies,

I'd suggest that the MCAC panel not develop a national coverage determination and that in fact you allow this technique to develop and to be evaluated on a state-by-state basis using the LCD process. As you know, 33 percent of states now have LCDs either approved or in draft form and some, like in California, have a generous set of indications, some elsewhere have a less generous set of indications. So it's a moving target for something that is, as Dr. Fishman mentioned, state of the moment rather than state of the art. I would suggest you allow these national experiments to occur on the LCD basis rather than coming out with a national coverage decision which will require a higher level of evidence. I see an NCD as potentially decreasing access to care and decreasing their ability to further develop that clinical utility data. One of the other comments raised was the 16-slice scanners, and in the evidence review from Duke only four of the studies were included. Bachs and colleagues published a meta-analysis about a year ago looking at studies that were commonly done prior to 2005 and if you just included the 1.5-millimeter vessels which are

likely to be fixed, the sensitivity and specificity are very good. In fact, the sensitivity is 88 percent using a weighted average for 16-slice CT using, again, 1.5 millimeters or greater, and 96 percent specificity. So 16-slice, while harder to read, as Dr. Fishman pointed out, still has excellent negative predictive value in particular, and it is also a moving target. The 16-slice scanners now can spin often at 375 milliseconds, whereas in the past they were spinning at much slower rates, so I think that we don't want to stop that technology, the evaluation by 16-slice, which are about $500,000 cheaper as well.

And as I sum up to talk about the Medicare population, the specific Question 6, looking at a study by Paul Rogge, the mean score for calcium scoring is not particularly high in older patients. Comparing those who are 50 to 55, men and women, compared to those who are 65 to 70, the average woman has a zero calcium score in the younger group and a score of only 24 in the older group. As far as men, we have a score averaging 41 in the population 50 to 55 and a score of only 151 in those 65 to 70. So I suggest that the test

will perform well in that Medicare population. It may decrease specificity a little bit because of the calcification, but because of the higher pretest likelihood of disease in that population, the sensitivity would be expected to go up compared to a more middle-aged population. Thank you very much.

DR. GARBER: Thank you. Now we move to the open public comments. I believe nobody has signed up. Is there somebody who wishes to address the committee before we move on to questions for the presenters? Okay. Thank you very much.

Just for everybody in the room, the plan is to do the questions to presenters. I would like us to try to finish by 11:30, have an early lunch, and then return here at about noon. So, I would like to open it to the panelists for questions to the presenters. Rita.

DR. REDBERG: Just in thinking about who CT angiography would be used for, I think one of the presenters said low to moderate probability of coronary disease. But first of all, I divide my patients into asymptomatic and symptomatic, and certainly when talking about low, that can be

asymptomatic with some differentiation. So for asymptomatic people, the only thing we have is risk factor reduction, which is really powerful, but certainly not something that we need to have any kind of a CT angiography to do risk factor reduction. You know, the only, PCI doesn't, hasn't been shown to make people live longer and it's certainly not going to make an asymptomatic person feel better. So to me it's hard to argue that in an asymptomatic population, there could be any benefit from coronary artery imaging by catheterization, CT angiography or any other way, and we can certainly do risk factor reduction, but none of that would be based on any kind of testing except for risk factor assessment.

Then if we start looking at low to moderate probability of coronary disease, assuming that we're talking a symptomatic population, that's the population that usually would start out with functional testing, and I think many of the presenters mentioned that we can't predict who's going to have an MI on the basis of anatomic findings, but I think the Duke group mentioned we do get some prognostic information from functional testing. So I guess in my mind, that's a

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population where I would be thinking about functional testing, not about taking anyone to the cath lab if they have a low to moderate probability of coronary disease. So when I think about who would I use this test for I'm having, you know, a hard time seeing a low to moderate probability where there's been some functional assessment for the risk reduction, assuming they're symptomatic. Assuming they're asymptomatic, I think the data we have is all in favor of risk factor reduction, and there's not any data that I know of that would suggest there is any improvement in patient outcomes. So I guess what I'm thinking about, I'm trying to thin who is it that could theoretically benefit. I know we don't have any data on actual patient benefit, but who is it that would theoretically benefit and how would we use those data?

DR. GARBER: Elliott.

DR. FISHMAN: I guess if you looked at just some of the work on calcium scoring alone, it would seem that provides an added benefit in terms of risk analysis, so I think the calcium scoring portion is sort of step one. There have been several articles, an article from, several

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articles from Lou Bechter at Hopkins on similar studies looking at the population, particularly in women where there would be 30 percent of the population they evaluated were in a clinically moderate to high risk category rather than low risk based on calcium scoring.

DR. REDBERG: But there isn't any data to suggest improved patient benefit based on that calcium score.

DR. GARBER: I don't believe there is any direct data. Maybe I could just follow up on that. Elliott, I think it was in your presentation that you had said that this is really -- well, several presenters said it was a good test for ruling out and that it avoided cath. I think in your case it was a calcium low risk person. And it might have been in Dr. Hodgson's presentation on the question, though, what do you mean by low risk? In the sense that there is pretest risk before they've had any testing, a patient comes in, atypical chest pain, maybe it's a woman, or a young woman in more typical chest pain perhaps. Pretest probability may be around 25 percent, and the question is, is that kind of person a candidate for CT angiography or are they

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a candidate for another noninvasive test as the first step, or do you mean low risk after a noninvasive test, which is really a different ballpark?

DR. FISHMAN: There are several articles now looking at the population with atypical chest pain in the ER setting, for example. There is a publication by White from the University of Maryland, and I heard a presentation, though it's not published yet, from Ellis Casoverde at the University of Michigan. At the University of Michigan they evaluated all patients at a chest pain center in the ER setting. And because of the high negative predictive value of CT, they looked at the cost analysis, and they would basically save $3 million a year by simply being able to triage patients where if the CT was negative, you know, they would be discharge patients.

So, I think a few of the other speakers mentioned if you look at all literature, whether it's things from Steffan Achenbaugh or it's things from Russo, Becker, all those articles, basically the one thing they all came down very strong on was there was a 99 percent, or close to 99 percent

negative predictive value, so a quality study basically excludes the presence of disease, so that might be a very good situation.

DR. GARBER: And would you generalize the office setting then? Somebody comes in, you're suggesting it would be a replacement potentially for noninvasive tests, not necessarily just cardiac cath?

DR. FISHMAN: Right. These studies basically looked at cost analysis and it's based on all tests.

DR. GARBER: Someone, one of the speakers.

DR. WILLIAMS: Yes. I just wanted to put Rita's question in perspective. As people have noted, there is a lot of data in prognosis in coronary calcium. We can actually model this and there was published a study with the Framingham risk factor scoring in asymptomatic populations. With this, we could actually put people into quartiles, and it turns out that the lower quartile, coronary calcium scoring even at the highest level, would not put them at a risk of eight to ten percent, which people sort of draw a line in the sand and say that's where you would

start doing things more aggressively, more testing, more therapy, you couldn't get in either the low or the low to intermediate group. Similarly, in the high probability group, that was already defined as high, distinguishing those groups based on calcium didn't get them below that eight to ten percent.

But that third tercile, where you actually had the high to intermediate group, that's where a high coronary calcium score really would push you over and change your management. An so this actually had been done. When you look at studies, they're always mixed in terms of populations, but there have been publications from Tracy Callister's group and more recently from the St. Francis group that having coronary calcium data will actually allow you to look therapeutically. And we haven't seen regression, which is what we would all like to see, but perhaps that's not something that's going to happen because it's basically an osteoplasty type of activity. But what it does show is that therapy can slow down the progression, and that becomes a therapeutic target. Now once we have CT angiography data that has prognostic data like

that, then we can actually do that kind of modeling again, but it's going to be a while.

DR. REDBERG: I think that's interesting with calcium scoring and looking at prognosis, there isn't any data showing that any calcium score will improve patient outcome. And the data on progression as we know from the recent studies that came out observing high dose tests, or low dose tests, they didn't show a change in coronary calcium, so they were not following progression. But I actually didn't think we were talking so much about coronary calcium per se.

DR. GARBER: Okay. Dr. Hecht and then Cliff.

DR. HECHT: In response to the questions about who should have the test, two populations are emerging, the asymptomatic patient and the symptomatic patient. The ACC-AHA guideline for stress testing in the asymptomatic population is restricted to those with multiple risk factors and whom the stress testing is to be done for prognostic value. This is unfortunately a group of patients in whom there is a well-defined percentage of false positives, because the specificity of nuclear stress testing

or stress cardiography is not that high, and these patients then up in a cath lab. So using the stress testing as the evaluation tool, which is ACC-AHA recommended, I don't think is the best way to go because it will result in unnecessary procedures. I would suggest that CTA be substituted for stress testing in that subset of patients.

In a symptomatic patient, as I mentioned in my talk, we have the same conundrum, 20 percent of the diagnostic caths in this country, we deal with no significant obstructive disease, and it would be to everybody's benefit to utilize CTA in this group of patients to determine, A, is there a further need for stress testing? And a lot of these patients are going to have perfectly normal coronaries or no clear-cut evidence of significant obstruction, some will have peripheral disease and we will take them straight to the cath lab, and the intermediate group can then have stress tests done. So it's hard for me actually, except for the high risk patients, the high risk symptomatic patients, to think of patients who would not benefit from having a CTA.

In response to the coronary calcium issue, I think that there is no sense in really debating this anymore. The vast majority of people in this country firmly believe that coronary calcium adds to prognostic value, and there is no doubt that it will shortly be incorporated into recommendations for evaluation of risk and treatment of the intermediate risk patient.

DR. GARBER: Cliff.

DR. GOODMAN: Thank you. I hope, I'm wondering if someone can disabuse me of the following impressions I've gotten. Various speakers have said that CTA is great for ruling out the need for coronary angiography, and although I understand that intuitively, I'm pretty sure I haven't seen a single published study that offers that. I also heard, I think it was Jason Cole, and I was glad to hear this, he said, because I'm wondering about how CTA or these other modalities help decide treatment, and he said that CTA, I think if it's mild to positive, helps you to decide about medical therapy, maybe about risk factor reduction. I think he also said, no one else said this, that a positive CT might even help

you choose the catheter or the angle of the problem or help you choose the kind of instrument, which all sounds plausible and interesting, and I'm pretty sure I haven't seen any published data on that whatsoever.

Harvey Hecht said that CTA can profoundly affect the care of these patients and that CTA, yes, is unequivocally a gatekeeper for the triage. And these all make intuitive sense to me. I'm puzzled, as I asked the Duke people earlier, why there isn't a single published peer reviewed article showing that.

John Hodgson made a nice presentation where he showed his slides side by side and asked if the CT can detect morphology, and on the left side he had coronary angiography that seemed to show stenosis and then on the right side he had CT angio that also showed stenosis, but I think it also showed some plaque. And I'm wondering, faced with those two pictures, why these patients would get any different treatment. Aren't you going to pop a stent no matter what, whether you've got the right picture or the left picture?

So, a lot of these claims that we're hearing are certainly plausible. We've heard

people make comments about how they do it in their clinic, we've heard a lot of anecdotal stories about how it might have changed physician behavior. We have nothing about outcomes, by the way. But I'm puzzled why there isn't a single published article showing this, and if I were CMS or a payer, I would certainly want to see a little bit of something in the published literature about this and I'm wondering why. Is the technology, are they so new that people haven't built up enough data to show this. And if that's the case, maybe they're all investigational technologies, and I'm pretty sure payers don't go out of their way to pay for investigational things unless there is some other arrangement to pay partially for data, additional coverage and all that, but I would like to hear somebody say that there's some published data on any of these technologies, and for me that would be a little bit more persuasive.

DR. GARBER: Go ahead, Dr. Hodgson, and then Dr. Thomas.

DR. HODGSON: Well, I can't say that there is any published data because as you've appropriately noted, this technology is relatively new and there just hasn't been enough time for

outcomes data, although as you heard from Dr. Fishman, it is being presented, it's in review and it will be forthcoming. But I don't think it's fair to say this is a totally experimental technology. This is a technology which is a natural outgrowth of a very long history with CT, so we understand a lot about CT, and also a natural outgrowth of the injection of radio iodinated contrast into coronary arteries which we have been doing for well over 40 years.

So this is a technology which is not so much new or investigational, it's just now technically possible. So I think it's not a great leap of faith to say that whether we can see the stenosis by directly injecting dye into the artery and taking x-ray pictures of it, or injecting dye into the vein and taking x-ray pictures of it is a great difference. And that's I think what we have been trying to present this morning, is that they are very similar technologies, iodinated contrast x-ray producing an image of the vascular structures.

And the advantage of CT now is that you can also view the vessel wall. And so yes, those two pictures, either of those two pictures that

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you just mentioned could lead to placing a stent, but that really wasn't the question. The question was, can you identify, quote, relevant morphology, which again, I don't know what that is. As a practicing interventionalist, some things are relevant, some things aren't relevant. In fact to me, the more relevant thing is is there any calcium in the vessel wall, and it has been shown that cardiac CT can be more accurate at that. But I don't think this is a fundamentally different technique. In fact, I think it's a natural outgrowth of two techniques which have been very well developed and because of technological advances now, can come together and provide a noninvasive x-ray-based angiographic view of the vessels.

DR. GOODMAN: When I think about how medical professional societies establish evidence-based practice guidelines or how third-party payers set criteria, such as Blue Cross Blue Shield, or even Medicare's own criteria for making coverage decisions, the body of evidence presented so far doesn't seem quite ready to close that gap to meet those criteria, and I'm wondering about that. I fully appreciate the need

to continue to evolve these technologies and to collect data as we're going, and to help guide further research and so forth, but there remains a yawning gap between the claims that are made here and the kind of base of evidence that is typically required for practice guidelines and informed payer decisions.

DR. GARBER: Greg?

DR. THOMAS: Yeah, Dr. Goodman, I concur, and that's why I suggest that we allow the state process or LCDs to continue in some states where I think Harvey wants to use this as a gatekeeper in New York, and elsewhere it's going to be much more restricted. Again, that's part of Medicare.

And I think it's an appropriate point in terms of asymptomatic, I agree as well, that this would uncommonly be done in someone. Another thing to think about is the potential in terms of the prognostic parts. I can refine risk stratification and so, if someone comes in, for example, a symptomatic patient to the ER with chest pain, we can send them home and they do well, but I would like to see the studies evolve so we can see if there is a difference between

someone who had a normal nuclear test and someone who has a CT scan which has no disease, and at that time they can be restudied. I understand what you're talking about, but I think that the bottom line, this is our opportunity for the technique to flourish and these --

DR. GARBER: Can I just interrupt for a second? I think one of the great difficulties is what exactly would you change about risk factor management, would it just be based on calcium score, or shift the ROP curve up a little bit because you have some slides indicating that? And this doesn't only apply to the EBCT, there's many tests for which these kind of claims are being made. How exactly -- I haven't seen a paper, by the way, that modeled out what you would do and what effect that would have on outcomes. There was some well-known cardiologists who said we should put statins in the water supply. I find it a little hard to believe that many cardiologists would stay their hands to prescribe a statin in someone who otherwise seems to be elevated risk on the basis of any one of these tests.

But, are you aware of some studies, and I invite anybody else to answer this question,

that show how outcomes are improved by using the added risk prediction from EBCT to any other tests in this kind of setting, that is, it's really primary prevention here we are talking about?

DR. THOMAS: I was one of those that voted for statin in the water. In a cardiovascular review a year and a half ago, I suggested that many above, or men at 30 and women at menopause consider, the physicians consider adding the drug for them. But I think that actually a more precise way to do it, and this is theoretical, hopefully someone will do this, perhaps you, but can we instead of in the water, can we have it in the water for those with positive calcium scores, for example? You can ask a group of cardiologists, say, are you taking a statin or not? If I ask, and I've done this a number of times, out of ten of them, say nine, or eight will be taking a statin, okay? And I'll say, and I bet you guys have a negative calcium score, and you know what, that's almost always what happens. So we're voting with our feet, but we don't have the data yet. But again, that's what's so exciting about cardiology and being able to decrease that death

rate further and further.
DR. GARBER: Well, I have to point out that if you do the numbers, the people who are not taking the statin on the basis of the calcium score are probably making a mistake, unless you think that the statins have significant toxicity, because -- and you look at those ROC curves, that's also a mistake, unless you think there is toxicity of the statin that would make it not worth taking. But it's not, it's simply none of these individual variables are enough of a predictor to allow you to do that.
DR. GARBER: Yeah, Dr. Poon was next.
DR. POON: I just had a comment maybe about some of the lack of outcome data from the CT field, and I think that it's an evolving field, as Dr. Fishman has eloquently mentioned before, and the technology keeps changing every few months. And this year for the first time, we see two different vendors going in different directions in terms of the way that they design the scan, so it makes it very hard to design a study in multicenter trials.
And being a former molecular cardiologist, I would love to control every

molecule as precisely as possible and look at the changes, but that doesn't mean that we shouldn't do more studies. We are all working very hard from the society standpoint and with the college to have more outcome studies, and I think the first group of outcome studies that you will see will be a cost effectiveness analysis and to do CT in the ER situation for the assessment of new chest pain.

But we also have to do some of the clinical judgment. As a cardiologist who does a lot of, I used to do a lot of interventional procedures and I do see many complications from cath, which is real. Mortality may not be as great as what we quote, one in a thousand, but morbidity is certainly very common with groin complications and so on and so forth. And right now the debate we have is on CT's accuracy in comparing with the x-ray angiography, and it's very impressive and we cannot deny that or ignore that data. That is real data and is published, peer reviewed, and we have to combine it with clinical judgment.

And being an angiographer, when I see a patient that I suspect certain diagnosis, the CT

will be much better. For example, congenital anomaly would be a very good one. Trying to prove that in a multicenter trial would take you years and years, and that may never be proven, that CT is better. But as a clinician and as an imager, I think all of us would agree that CT gives you a phenomenal image of congenital anomalies that perhaps angiography is not able to show you. So if you use a gold standard which is really not the gold standard to compare, and I don't think that would be fair here.

So I think we really need to look at the science and the clinical practice and how should we use it for the patient's interests, and that's why we have this discussion and that's why we would like to show you from the clinical standpoint how this clinical modality can affect our management of many of these cardiac patients.

DR. GARBER: Dr. Hecht?

DR. HECHT: I'd like to address some of the issues that were raised by Doctors Goodman and Garber regarding, yes, all this data seems possible but where are the studies, where are the outcome data that the technology affects prognosis or affects treatment. Well, let's put it in the

perspective of all the technology that we have available in cardiology. We do electrocardiograms, and is there a single study, randomized controlled study, one group of patients have an EKG, another group of patients don't have an EKG, and then look at those outcomes? We have echocardiographs in patients with congestive heart failure; is there a single study that shows if you used echocardiography in one randomized group and you don't use it in the other, it affects the outcomes of these patients? The same applies to nuclear cardiology. The kind of trial that you're asking for has not been done in a satisfactory rigorous scientific fashion for any of the technologies that we employ. But yet, they are still valuable. Nobody would argue that echocardiography is not a superb tool for cardiac anatomy and function, nor that nuclear cardiology is not a superb tool for evaluating myocardial perfusion. So I think perhaps the more appropriate question is do we think that CTA is an excellent and readily acceptable tool for defining atherosclerosis. And if is, then it should be used to define atherosclerosis, for which there is

ample prognostic data. The more atherosclerosis you have, the worse the prognosis; the less atherosclerosis, the less the prognosis. And that's the answer to the critique of coronary calcium, and it's the same thing for CTA. Can CTA effectively define the cardiac anatomy? Can it distinguish between significant and nonsignificant obstructive disease? And if you can, as the data, albeit preliminary because it is a very new technology, suggest that you can with a sensitivity and specificity in the mid-90s for both, then yes, this is a tool that should be used.

The prognostic studies can be applied to particular uses perhaps in certain populations but the question, that's not the question we're thinking of. Should CTA be used to evaluate atherosclerosis? If you think atherosclerosis is important to evaluate, then that's your decision, but I think we all agree that it is, and now we have a tool to do it better than our preexisting tools.

DR. GARBER: Thank you. I wanted to clarify one thing. Speaking for myself and I believe probably for Cliff, I don't think anybody

was asking for an RCT. But to suggest that there are studies, observational studies to establish what's available for some of the other noninvasive modalities, that's the question. And what we've seen suggests far less is known about these, and that seems to be quite clear from the Duke report. But let me, Dr. Redberg and then Dr. Cohen.

DR. REDBERG: Right. And I certainly agree that we don't have all the data we'd like about EKG, although I think the Duke study shows 24,000 patients for stress testing, so we're certainly looking at a lot more data than the few hundred we're looking at here in the CT studies. But that was also all done and came into being at a time when, you know, health care spending was probably six percent of GDP and we're now at 18 percent of GDP. And so I think we're just in an era where we really need to see a lot more data. We may be seeing some of the same kind of data, but I don't think we can really compare, because the studies we saw today were interesting, but they were all single center studies with less than a hundred patients.

And certainly, I have a lot of concerns about how this would play out in the Medicare

population. I think the Duke report points out that these are kind of proof concept, they are very selective, a lot of them had significant bias in the population. And now you're talking about a Medicare population which is over 65, has a lot of morbidity, certainly will have more calcium, I can't imagine them holding their breath for 20 or 25 seconds. I think that we barely have the data to look at the middle-aged healthy population from these studies, and I don't think we have data to evaluate it for the Medicare population.

DR. GARBER: We will have more discussions in the committee deliberations. David, and then Tim.

DR. COHEN: My question builds a little bit on what Rita mentioned which, again, brings us back to the Medicare question. I think that virtually all the presenters and all the data that I have seen raises the issue of, if the optimum current application of this technology is going to be exclude coronary disease maybe for those who are relatively low risk in the ER setting or the office setting through whatever mechanism, and my question is, what proportion of patients do you think this applies to who are actually Medicare

patients? My perception is this is sort of, you know, a 30-to-40-year-old kind of patient type of tool, and most patients who fall into that low risk category are not 70 to 75, which is the typical age for a Medicare patient. Does anybody have an answer to that from the studies that have been done?

DR. GARBER: Dr. Williams, did you want to respond to that?

DR. WILLIAMS: If I understand what you're saying, it's that you're concerned that this is going to be something that's going to be employed mostly to younger people, and I think that's really true for the coronary calcium. But for CT angiography, these are people who typically have some demonstration of abnormality and they're going to go on, and the conventional thinking is that you don't want to be invasive with peripheral vascular disease, so there are some high risk people who end up going to CT angiography to try to avoid the invasive demonstration. But for the most part, these are the routine coronary disease populations.

DR. COHEN: I know just in my own experience as a coronary angiographer, most of the

patients in whom I do catheterizations that turn out to be normal are not 65 or older, that's the point I'm trying to make.

DR. WILLIAMS: That's correct.

DR. GARBER: Dr. Hodgson, did you want to comment?

DR. HODGSON: Well, the question about people getting the cath now are highly selected, but if you just go back to the table I presented here about the pretest probability, and the oldest group they have is 60 to 69, which gets us into this range. With the exception of definite angina pectoris in men and women, everyone else is either low or immediate risk. So at least by the published standards, you're going to have a large proportion of those people who are exactly what we're talking about, atypical or funny chest pain who would fall into the category where the test should be performed less.

DR. COHEN: I don't deny that there are some patients, I just notice that that table doesn't tell us anything about what proportion of patients may fall into those risk categories, that is what I was really trying to drive at.

DR. GARBER: Let me just do a quick

time check question, if I might. We've got two more questions from the panelists and Dr. Cole would like to speak. It is now about 11:35. There are some significant advantages of getting to the cafeteria fairly soon. So, first of all, do you want to do your questions right now? Because as long as the presenters are willing to stick around, we can continue with questions to presenters after the lunch break. So, will the presenters all be here after lunch? Okay. So just real quickly, Tim -- actually, why don't we let Dr. Cole answer, he's been waiting for a long time.

DR. COLE: Just real quickly, actually I will address that issue. I think the information that you get from the data, once again, I'm looking at negative and positive predictive values that are out there that are based on pretest likelihood of probably 50 percent coronary disease. So that's the evidence basis on which I'm clinically practicing, and I can tell you from a clinical practice standpoint, it is an enormously valuable test in these patients because it's true they have a higher prevalence of coronary disease.

DR. HODGSON: But the other thing that hasn't been mentioned is there's no obligation to do invasive catheterization if you document that a patient has single vessel coronary disease and then you can manage them medically. You know that, you absolutely know that with CT angiography.

And then a very brief point that has been raised earlier in terms of, you know, who the right patients are for the test and evidence. I mean, we are responding. We are still participating in multicenter studies to hopefully get to the multicenter correlation data that you want. But based on the overwhelming list of 16 and 64-slice studies, there is evidence for negative predictive value for these tests, so as we use that, we are using it in an evidence basis. And who do you choose? Well, if you choose a low to intermediate risk patient population and you do this test, you know if you get an adequate study whether or not they have coronary disease, and you don't know that with any other diagnostic test.

DR. REDBERG: Just to clarify, are you telling me that a patient in your practice ended up in a cath lab or stress test, whatever, and

they had single vessel disease, you would not stent, you would treat it medically?
DR. HODGSON: I'm telling you that I believe actually, and this is actually true clinical experience, they are much more likely to get a trial of medical therapy after a CT angiogram than they are after a cath, because if you're already in the cath lab, it's very difficult to restrain putting a stent into that vessel, but if you're doing CT angiogram and you see clear single vessel coronary disease, their symptoms seem to have abated, you can be very comfortable treating that patient medically. So there has been actual clinical experiences where I have actually not done catheterizations where I might have otherwise.
DR. REDBERG: So if you see single vessel on CTA, you might not --
DR. HODGSON: If I see single vessel on CTA and it's not proximal or left main disease.
DR. GARBER: We're going to have to move on real quickly. David?
DR. LU: Just a comment following up on Dave Cohen. Isn't the final decision more than juts what a physician does? A lot of times the

patient plays a part in this. If the patient knows they have a single vessel disease, they're going to push their physician to do something, and it has happened many, many times, so I think there are many factors to that.

I will get to my questions after lunch.

DR. GARBER: Are they long or short?

DR. LU: Well, I guess as all physicians, we base our care on angiography to identify atherosclerosis, you know, with the patient's symptoms and physical studies. And you know, some of the studies show that most of the physicians perform the tests appropriately and the ACC-AHA guidelines would be very important. I'm just sort of concerned about what's happened in the real world. The group from Illinois who had 50 cardiologists where they did CT angio and six percent went to cath, so my question is, what happened to the other 90 to 95 percent? Are they ordering the tests appropriately? Why are we seeing so many tests when only six percent go to cath.

MS. BIGA: I think I can say this quickly and then we can all go eat. What I said was six percent went on for an additional third

test, meaning that they -- one of the big concerns we had with our Blue Cross carrier is that we wouldn't order a nuclear test after a coronary CTA, and in fact that's not true. In the first thousand patients, 27 percent of them went for a cath and then of those, 50 percent were stented, 50-some-plus percent were stented, and 17 percent went on for a CABG, and the rest were medically managed.

DR. LU: So it's pretty similar to the published data?

MS. BIGA: Yes. And as I think Dr. Cole mentioned, I think that the economic impact papers that we're looking at doing some longitudinal studies, that will get us back to the evidence base and give us some of that data that people are looking for.

DR. GARBER: Tim.

DR. BATEMAN: Well, just, you know, I'm one of these guys in private practice so I'm a scientist at nighttime but a clinician during the daytime, and I don't know how much science that you really need once you have some of this diagnostic accuracy type data. Every day I see many, many Medicare patients who I really don't

want to see go to the cath lab, you know, I work hard to try to keep them out of the cath lab. And one patient population that I see a lot of is the one that Dr. Williams brought up with an abnormal nuclear scan that may be very high risk, but may be absolutely nothing and in fact, with what the data says, probably only about 10 or 20 percent of those people actually have any disease. If we can answer that question with a noninvasive test, I'm sure they're not going to worry about radiation exposure in a 70 or 75-year-old person.

It just seems to me that maybe we should be carving out certain indications where it just seems obvious, you must go on and do another test in that type of patient, and you've only got two choices, you've got invasive angiogram and there isn't a lot of data there either, or you can rule out disease with CTA. So I just wanted to kind of refrain some of this. We could have hierarchical science for some things but we still have to answer questions for patients, and when we have a lower-risk simpler and cheaper procedure with demonstrated accuracy, I don't think you have to do a large prospective randomized study to

convince me that it has a place.
DR. GARBER: Okay, thank you. It's now 11:45. We will resume this discussion at 12:15.
(Luncheon recess.)
DR. GARBER: First I will recognize Alex, who has been waiting very, very patiently to ask his question.
DR. KRIST: Actually I don't have as much of a question, it's more, I had a response and had an opposite opinion to Dr. Bateman, that he made right before our lunch break. He was saying that he was impressed with the sensitivity and specificity data and in many ways we heard some speakers say that for comparing some techniques that seem somewhat similar, I think we could suggest that the sensitivity and specificity is equal, that they're pretty comfortable with this.
The more I've been listening to the group, the more I've actually been thinking, well, we really do need to have not just prognostic information, we need outcomes information. Because I'm hearing people saying more and more that they're changing what they're doing based on what they're going to start off with. For

example, if you're starting off with the CT, you know, there is this potential that people aren't going to have a cath, you might defer a cath, you might defer an opportunity to have a stent. Maybe that's a good thing, and from the data that we're hearing about negative predictive value, there are some positive things. We're also hearing people talk about deferring medical therapy, you have a normal CT and you stop the statin, you stop being more aggressive with your blood pressure and some of your primary prevention measures.

Conversely, there is a possibility which we've sort of been skirting around here about false positives. So people go and they have the CT scan, there's going to be some element of false positives, we haven't talked as much about the positive predictive value, but people will go on to caths and other interventions that they may not get otherwise.

We've been talking about which patients are going to be indicated for having this procedure. There is a natural barrier for doing a cath, it's an invasive procedure, a lot of patients don't want to do it and clinicians don't want to do it. That barrier will go away. If

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it's a CT, there's a benefit that some of the invasiveness is not there. But there is also a possibility to extend this to other patient populations, patients who you wouldn't normally do some type of imaging technique and know their anatomy in the coronary arteries, and that does have potential to lead to harms with positive predictive value.

We talked about identifying subclinical disease and the benefits with that, and there are some benefits. As a family physician, what I struggle with every day is getting people to do the things that we already know are indicated. And I have people come to me with their coronary calcium scores, and about all that happens is I'm finally able to get them on the therapy that they should be on. I haven't had a scenario yet where I say well, you're on maximum medical therapy, let's now move your statins to get your LDL from 100 to 70. I haven't had that, I know it can happen.

But there is this case too on the negative end that we identify more subclinical disease and then there's a set of things that people are talking about doing different, and

doing those things different have their associated potential benefits and potential harms. And so I'm actually in a position different than Dr. Bateman. The more I hear people talk, the more I want to see some outcomes data, and not just sensitivity and specificity data.

DR. GARBER: Thank you. I wanted to ask the Duke team if they would be willing to address some of the questions that were addressed during the preceding session, especially about where we have evidence and where we don't. A lot of this was already answered in the report, but I wonder if you might want to expand on that.

DR. MARK: So, I just want to take a moment to add a few comments perhaps to stir the pot a little more, and I'll let my colleagues add anything if I've forgotten to say something that I should have said. It seems like part of this discussion is being driven around the question of what the nature of this technology is and whether we're dealing with a technology that's substantially similar to other technologies that we already have in place so that we can, by borrowing or extrapolation, really assume that we know a great deal about it and how it performs and

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what it does and what it means. It's like we're saying this is a knife, we have other knives in our armamentarium, we know what a knife is, we know what it looks like, we know approximately how to tell what its properties are, and therefore, what, do we need to do a lot of large fancy outcome trials or randomized trials to figure out, yes, this is in fact a knife? But the question is, is it in fact a knife, does it cut meat the same as it cuts bread, does it cut ripe tomatoes, does it perform the same under different circumstances, and can we assume that we actually understand how it performs under all those clinically relevant different circumstances. There has been a lot of discussion about the negative predictive value of CTA. I think a lot of confusion probably attends to the use of the word predicted value. If you think of it as a post-test probability of disease instead of predicted value, you would realize it's not a feature of the test at all, that predictive value isn't a characteristic of the test, it is a function of the sensitivity, specificity and prevalence. It's a calculated value. It just so happens people tend to calculate it in the papers

where they also calculate sensitivity and specificity. And journal editors don't edit that out, which is what they should do, or at least add the caveat that this is relevant only to this population and substantially similar populations. So we don't know what the predictive value is or the post-test probability. We can calculate it, but that assumes we know the prevalence in the new target population and we know the appropriate sensitivity and specificity in that population, which we would have to assume can be extrapolated from the populations that have been studied. Because what I'm hearing is that people have intentions to study populations with this that are not representative of the patients that have been studied in the literature so far. For example, the emergency room setting, an interesting population to study. I think it's important to keep in mind, though, and this is a good example of one of the problems with a new technology, is that there is a lot of information that we already have about those patients, and we actually do pretty well managing those patients. Harry Selter had a paper a few years ago, a multicenter trial looking at over

10,000 patients coming in to rule out coronary disease using a predictive instrument that he developed. And he showed that basically with simple clinical tools without even a troponin test, you could basically, you had a two percent rate of people going home from the emergency room with an MI, so a very low risk of making the wrong decision if the concern was sending somebody home who's got a diagnosis that may be potentially life-threatening.

So in that context, how are you going to be able to actually show that you're going to do substantially better? You may change the mix of how you're going to do the test or the risk stratification tests, but I think some of the calls for outcomes simply suggested one of the features of the noninvasive imaging of coronary arteries is that it lowers the bar for evaluating coronary arteries. You don't have to pay that little price of sticking a catheter into the artery and potentially causing a catastrophe in that way, even though the risk is small.

But there may be, as I said before, unintended consequences of getting that information. One of the things that I think is

hard to evaluate from the literature right now is how many patients are going to have those intermediate risk lesions, the thing that looks like something but I can't quite tell, and I'm not comfortable just ignoring it, maybe I ought to get an angiogram. So I study a patient that I wasn't intending to study with invasive study, with a noninvasive study that leads me to get an invasive study just to clarify it, and then while I'm here, maybe I should do a PCI procedure on it. I'm not saying that's necessarily the most likely scenario, but I'm saying what should happen or what would be logical and most likely will happen is the difference between the theoretical considerations that we've heard this morning, and outcome data that actually show us what the truth is when you put this thing into play in large practical scenarios. Guys, anything to add? Thanks.

DR. GARBER: Thank you, Dan. Do the panelists have questions?

DR. PETERS: I just found out yesterday that one of the big private practices in Baltimore decided to make electron beam CT for calcium scoring free for anybody who walks in. Now these

people are businessmen, they are not doing this to help humanity, and I doubt that Baltimore is too different from any other city. The people who presented today are the best possible people you want doing this, they're here for that reason. Otherwise they'd be out making money, they wouldn't be here.

So before we throw these techniques out to the wolves and let people just use them indiscriminately, I think we need very very specific data and information as to what to use them for. Once an office gets 64-slice CT, you know they're going to use that on every single patient because it's going to have to pay for itself, and that's the problem. It's not you guys in here, I would trust you guys to do what is right. But at least in Baltimore, these things are run as businesses, and these people are as good at business as we are at medicine, and that's what they're trying to do. And I'm afraid that's what we're going to wind up doing unless we are very, very careful with these new and very, very promising techniques., .

DR. REDBERG: I agree. I have been told by more than one hospital physician executive

that they offer EBCT as a loss leader because it will generate so much downstream testing for the cath lab for nuclear testing. I don't know what Steve was going to volunteer, but just from what Dan was just mentioning, I think, I just did a back of the envelope calculation, and if you change the prevalence of CAD from 50 percent, as it was in these studies that we looked at, to 10 percent, the false positive rate goes up to about 40 or 50 percent, so clearly the false positive rate is going to be a lot higher in the low risk kind of population. And I would just comment that I know at UCSF where we offer it but I don't see it being used much clinically, but the big surges have been after Oprah goes on TV and talks about it, the Time magazine cover that you showed, Elliott, shows a CT image and says this test can prevent a heart attack. Well, I would like to know how that test can prevent a heart attack and that's what I think we have to be mindful of. We don't have the data that this test can prevent a heart attack, or any test can prevent a heart attack, but we're going to have a lot of demand for it. And we're now talking about this test plus all of the downstream testing, and I think we

really need some data or decision models at least.
DR. GARBER: John, go ahead.
DR. HODGSON: I just want to address
Dr. Peters' comments. I think we have to stay
above the fray of what unscrupulous people might
be doing. We're here to evaluate this
scientifically as people who are interested in the
public's best health care, and whether you're
talking about having your car fixed or going to
Burger King, there are people out there trying to
make money and doing things that aren't
necessarily appropriate.
So, I don't think anybody here would
advocate anybody using these tests
inappropriately, which is why myself and many
others in the room are working diligently to have
appropriateness criteria and to be sure people are
adequately and appropriately trained, and then
labs are accredited, physicians are certified,
et cetera, et cetera. So we would share your
concern that any technology, whether it's EKG,
nuclear scan, echo, whatever, can be abused, and
we would strongly dissuade that and are working
diligently to try to prevent that from happening.
DR. FISHMAN: I can speak up to defend

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Baltimore. I mean, the same, it is always going to be an issue, and I was guessing the wrong hospital, but one of the other hospitals in a very similar thing with lung cancer screening, that was kind of the rage a couple years ago where they said okay, free lung cancer screening, or was it $25, something like that. And one of the things of course is to require, a typical situation is they allow people to come off the street and just show up and get the scan.

I mean, whether it was screening CT or anything else in terms of cardiac, we would never have a patient come in without being referred by a doctor, so there have to be some rules. And people will always find the lowest denominator of getting through, and I agree that is potentially an issue.

I think in terms of the other comments related to when we start using a more general population, how will it change things in terms of management, I think that's a valid point. One of the things which is probably no great surprise is we've run CT on everything from the adrenal to the kidney and to the heart. When they are 55 years old, it's not the same thing as coming with the

original equipment when you're 20 years old. So when you read articles presented on whole body screening, the people in California, nothing against California, said that, Eisenberg wrote an article that 80 percent of all the patients who came for screening CT were positive. Now it's impossible for 80 percent of healthy people to be abnormal. But of course we know that if you go for a CT scan of your whole body at age 55, you're going to have scars in your lung, 80 percent, 50 percent will have a nodule under five millimeters. The same thing with cardiac, the more patients you scan in that population, you will see minimal disease, and as the scanners get better, with the 16-slice, I would think you didn't see the little soft plaques or things like that, but with 64 you do see a lot of minimal disease. So I think people will need to be in some ways recalibrated as to what is significant disease and what is not. But it is a true point that the more people get screened and the better technology gets, the more you will pick up subclinical disease or very minimal disease.

DR. KRIST: Well, I was just going to say, with all these examples as a primary care doc

dealing downstream with it, and all those false positives that you mentioned, they're not insignificant. I mean, people come in with their abnormal CAT scan for their lung cancer finding and then for years afterwards, even after you've done tests to say it's okay, even after you've done risk factor modification and you're dealing with all the consequences of this abnormal test and how often do you repeat things and what do you do. And that's where I just think that that outcomes data is important, because that will at least capture some of those downstream unintended consequences that are significant, they are real for the patients, they're real for the clinicians who are left to interpret and try to deal with the results.

And I'll even take, Bob, what you were saying one step further. You were concerned about it being used unscrupulously. I have concerns about it being used with the best intentions because there is an allure for information. I mean, that's one of the reasons it's on the cover of Time magazine, because this is a great source of information and people like information. And it's very easy for a clinician to say well, we're

going to do a test and we're going to find this out; it's much harder to use clinical judgment, risk stratification and those other things, and so it just becomes easier. And so even if there is not business and money generating overuse, there are other natural tendencies with good intentions that increase the use as well.

DR. GARBER: I would like to change to a different subject that's also for you, Elliott, and I would like to invite the other speakers to respond to this. One of the things that I think we have to grapple with is an issue you raised in your presentation and other people have also raised, which is that this technology is improving constantly. And it sounds like there was, we heard varying views about the differences between 16 and 64-slice, but clearly 64 seems to be better. And the question I have is, with any technology that's evolving, at some point you have to say we're going to evaluate it now, what it is now. We know it's probably going to be better in the future, we know it was worse in the past, but what is it that we're really evaluating. And CMS is in the position, having to make a decision based on the evidence that we have today, which is

for a mixture of technologies.
So, the first part of the question is, should we assume that 16 and 64-slice and different ways of doing it are similar enough that it's all one technology and that's what we're evaluating, or should we split them up and take one of them? What do we do then about the very limited data, and for which purposes can we lump or split these different variants? One of the things I'm disturbed by are the claims that this is getting better which, based on what I've heard today and what I've read in the literature, I have no doubts about that, and I also suspect that we're going to end up using this pretty widely at some point, but that's partly based on optimism of our future technological change. We need to advise CMS about what to do based on the evidence at hand. So is this a good time for us to take a look at the technology, or is it premature because it's going to be a lot better in six months or a year, or we'll have better evidence? Is this the right time? And should we treat this all as one thing? And by the way, I'm only referring to CT angiography, we haven't really discussed MRA today, but is this a good time to look and should

we treat these separately or the same?
DR. FISHMAN: I would say it is a good time. The way I kind of look at deciding what's a good time, I mean, recognizing that things will always change, it's kind of the equivalent of never buying a computer, because the next Apple will always get better. The reason I think that the time is right is because if you look at the percent successes of doing a good study, that really to me is the magic number, and if you're in a situation where 70 percent of the studies are adequate, then you say well, that technology is not really there. When you look around and you easily can get in the high 90s for doing an excellent study patient after patient, not, you know, excluding patients because they didn't meet this criteria or that criteria, just taking consecutive patients, to me that means the study is ready for prime time.
I think also, I mentioned both the technology side from the scanners to the post-processing. I think one of the great variabilities in any type of imaging is the reading of the study, for instance, is there a single reader or are they read by multiple people,

you know. I think now with a lot of very dedicated software -- initially cardiac CT was read with the same software that the aorta was read with and everything else, so you really didn't have slope or design for four-millimeter vessels. Now every vendor is providing cardiac-specific software, so I think that that makes it for the common man much easier to do the study and to make the study results more reproducible.

In saying that 64 versus 16, Hopkins runs a number of courses, so if I surveyed the audience, I would say at this point a show of hands typically, and this is general practice radiologists, I think, roughly about 30 percent have access to 64-slice technology. And then if you ask the question, how many people are going to have it within six to nine months, almost everybody else raises their hand. It has become almost a consensus on the grassroots level, it seems to me, that if you want to do cardiac CT and do it well, you need to be at 64. Yes, there's some articles that are very good at 16, the Duke group presented those, but in looking at what we've done and what we do, and in looking at what

people are doing across the board, I think everyone who is really taking cardiac CT very seriously and putting an effort into it is doing it at 64, and I think that's really where the standard has to be.

And I think the data is just substantial. I mean basically, again, we can argue about the patient selection and everything, but article after article is impressive. The presenters today were speaking about, as I said, 99 percent negative predictive value, positive predictive value at 88 to 92 percent. That's very strong numbers taking all comers. So I think really, the time is here. You know, we can say dual source energy, flat panel, everything that's going to come along, but I think for a good period of time we're at really a sweet spot, this is going to be the technology that will be, the Medicare patients will be able to get on a routine basis, and I think it's a very stable technology.

DR. GARBER: Yes.

DR. WILLIAMS: I think you're asking a good question, and this was sort of the basis of our comments from the ACC, that it really is a moving target and that's why we're having to do

the guidelines over and over again. But to amplify that a little bit, we hear some very different things about, there are some new technologies available that will make this a little better than it is now, but we're also hearing from some experts that with the 128 and the 256-slice machines, that the radiation exposure is higher, and that's the price you pay for thinner slices, so that we may have 64 slices for quite a while. And to the extent that that's true, this is a good time to evaluate them, as long as we take the attitude that this will have to be reevaluated at some point in the near future.

I wanted to mention, in that same regard, something that Dr. Hecht said about nuclear and putting it on the list of things where there wasn't data. Well, nuclear cardiology actually came up at a time where there was a lot of demands for competing tests. And there is data randomized to do the test or don't do the test, or do the test but don't tell the doctor, look at the outcomes. And there is outcomes data showing that it's cost effective and useful. But I wanted you to understand that all this data was collected

after people like Dr. Bigman had put together guidelines and there were organizations to solidify how the test should be done so all the manufacturers had come together, there was software available, so people really had a stable thing that they could actually do long-term outcome studies on, and the studies were all being paid for at that time.

So I think, you know, you have to sort of put the data in that kind of perspective to get that history, but you're going to have to put up with the fact that it will have to develop and it will have to be supported until it can stand on its own.

DR. GARBER: Dr. Poon.

DR. POON: I just find it a little confusing when we are looking for an evidence base to discuss but when we look at the literature, the 16 and the 64-slice technology are very comparable and there is a lot more published data on the 16, probably three times, to show that the accuracy is very similar. I grew up in a four-detector generation and I have to say four-detector is impossible to do, but once in a while we were able to do a couple patients on a four-detector. 16

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was really the technology that changed the entire way that we look at the heart. And when 64 came along, I thought that it was easier, and I think maybe for the radiologists who are not comfortable with using a heart rate lowering regime, 64 definitely is an easier technology to handle and you don't have to spend as much time preparing the patient.

But from a cardiologist's standpoint, I really did not see a dramatic difference in terms of the image quality compared to the 16-slice data, particularly when we're looking at the negative predictive value or the specificity of the tests. I thought that if you have a normal coronary, it doesn't matter whether it's 16 or 64, they look very similar. It's only when you have tough lesions that the 64 really gives you that .2-millimeter resolution improvement that may help, and it cuts down the loss due to calcification, but for the strength of CT, I don't see the advantage in my everyday clinical practice. So I just think that since there is a lot of 16-slice already out there and people who use this technology know it very well, to just have to raise the bar because of the ease of use,

I just don't think that that is a good enough reason.

DR. GARBER: Yes, Dave Lu.

DR. LU: I think the people who work on MBCT are making the negative predictive value very high, and that's the major thing that they are stressing, but that's not going to affect the outcomes of a patient. What we're looking for the patients affecting impact is the positive predictive value. And so you're pushing this technology as far as negative predictive value, and yet the patient will not get a cardiac cath, but what's going to happen to the positive value with that technology?

DR. GARBER: Carole.

DR. FLAMM: Well, I just wanted to make a few comments in relation to this discussion of the 16-slice technical performance issues. In the published studies and as reviewed in the technology assessment, the rate of patients who had some technical limitation in their images, some blurring, some inadequate evaluative value, were up to a quarter of the patients. And I think if we're using this test for its negative predictive value for ruling out significant CAD,

giving them a clean bill of health, we have to see all their vessels well. And if any one of their vessels are not well seen, you can't exclude a lesion in that area.

And also, I think that 16-slice studies in particular focus on the larger caliber spectrum of vessels that are 1.5 millimeters or greater, and so you're not really seeing the smaller vessels, some of which may have some implications, not a complete clean bill of health. So if we're using this for ruling out CAD, taking people off of medical management and giving them a clean bill of health, the 16-slice imaging may not be adequate for that in a robust reliable fashion across the country.

DR. GARBER: Yes.

DR. HODGSON: I guess I'm a little confused about where this conversation is going. The test at hand was to determine whether these technologies could find obstructive lesions in the coronary arteries vis-a-vis invasive cardiac cath. Now all of a sudden we're talking about, you know, finding subclinical disease in minor vessels that nobody is going to do anything about. So we should probably try to focus, unless we're going

to change the question. And if the question is, can cardiac CT exclude subclinical atherosclerosis, but I don't think that was the question that was posed to the panel, and I think we simply need to focus, because we're wandering all over the place here as a group.

DR. GARBER: I would like to -- yes, go ahead.

DR. WAHL: I just wanted to wander a little further about the data on this. I do think that to answer these questions, one concern I have is a lot of the discussions had to do with low prevalence patient populations, and these specificity figures for 16-slice are really low. And I am concerned, as was pointed out, that if you have a lot of people who don't have disease and you have a test with low specificity, you're going to generate a lot of false positives. The impact of those false positives is going to be to do downstream medical testing of a variety of types which may not in any way benefit society, they won't benefit the patient, and they certainly will raise costs.

So, costs aren't supposed to be part of our discussion, but I am concerned that the one

study that the Duke group pointed out with a sensitivity of 30 percent, specificity of 49 percent on a patient basis, I mean, that level of specificity could really result in a high frequency of false positives with 16-slice. I have access to a couple 16-slice CT machines that are hybrid devices as far as our nuclear medicine program, and because of some of these issues we limit our use of these CTA devices because the other technology does seem to be better. So I do think it's appropriate to worry about what the effects would be of performance characteristics which are potentially, or which appear to be worse with less, with older technology.

Further, the selection bias in terms of introducing the studies, I mean, the fact that the patients had to be able to hold their breath for 20 to 25 seconds, and even with that you have a 20-plus percent frequency of failure to study in some technical manner, or near failure, that suggests to me that there are major issues with applying that technology to a patient population that would be the ones hardest to take the cath. So I think that discussion is appropriate, and I do think I feel far more comfortable discussing

technology that has a lower failure rate, a higher frequency of including the entire population, and a lower false positive rate, and I think that would be 64 or more, just from what I see in this literature. I would have to look at all the literature before I make a decision, but I'm concerned that there are differences.

DR. LU: Let's narrow down the question. Is the CT angio, is it equivalent to or is it going to replace cardio cath? CT angio unfortunately (inaudible) greater than 50 percent. There are very few centers that have used CT angio at greater than 75 percent, which may be clinically much more significant than 50 percent. Since neither of these studies can really (inaudible) determine which ones are (inaudible), so let's just stay with the lesion severity. Do you think that the lesion severity with the CT is as good as cardiac cath, narrowing it down to that question.

DR. HODGSON: Well, I want to point out that evaluation of lesion severity has been attempted even with cath for years and is notoriously variable, as you know. The fundamental question here is can we use cardiac CT

to determine the trigger point for a patient, and I believe the answer to that is yes. And whether that's a 70 percent or 69 percent or 73 percent doesn't influence me. Does it influence you, 73 versus 69?

DR. LU: Again, taking (inaudible).

DR. HODGSON: Well, sure. This is an anatomic test, it has to be applied by a physician to the specific situation that the patient presents with, which is what we really all are talking about. What is the right population to do this in? We've all said low to intermediate probability; nobody is going to suggest this for somebody who comes in with an HDL of 25, clutching their chest with a cigarette in their mouth, no, we're going to send them to the cath lab. Those are very high probability patients, but these other folks -- and these angio comparison criticisms are fundamentally an issue because those patients got in the study because they were going to have a cath, so they are already on the way to the cath lab, and then they also had a CT to do the comparison on.

The lowest prevalence in any of those studies is in the 30s, and if we extrapolate back

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to 10 percent, then you're right, there will be some potentially false positive studies, but a whole lot of people who were spared additional tests. And you really have to choose, are you going to use a different test as a first one? In other words, let's say you wanted to pick a stress test, what's the sensitivity and specificity for that test, is it really better? I don't think so. Will it lead to downstream testing? You work in a cath lab, you know very well there are a lot of patients referred for an equivocal stress test. And then also, the alternative is to do a cath on everybody. Then you have subjected a lot of people to potentially a morbid or mortal procedure who may not have needed it.

So, obviously we all would like to have a perfect test, 100 percent sensitivity, 100 percent specificity, works the same in any patient population. We don't have any of those, but I think given the armamentarium that we do have, for an appropriate physician in an appropriate patient, this test can be very helpful in discriminating who needs additional workup and who doesn't.

DR. GARBER: Could I just ask you, if I

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heard you correctly, you're saying that the studies say that the best population for this test is the low to intermediate probability population. The test has been studied in intermediate and high risk populations, so we have to make one extrapolation to --

DR. HODGSON: I'm not sure it has been studied in a high risk population because we don't really know the risks in most of those studies. Maybe the Duke group can answer that. Was there a clear listing of what we're talking about, calculated for those patients?

DR. GARBER: There is a prevalence in all --

DR. HODGSON: Well, prevalence isn't risk. Prevalence is knowing what the cath showed.

DR. GARBER: That's what I mean. So you're saying its design --

DR. HODGSON: They may all have been low risk patients for all I know, in terms of their pretest likelihood. Obviously a lot of them had disease but --

DR. GARBER: Well, this gets to the second part of my question. So the studies, and Manesh may correct me if I'm wrong, the studies

are done primarily in an intermediate and high probability population, of having angiographic coronary disease; is that correct?

DR. PATEL: Right, but let me just make sure this point is clear. I don't think, none of the studies published what the TIMI risk or whatever chest pain risk score is for the patient going in. However, the studies tell you that the reasons were that someone suspected coronary artery obstructive disease and were referring the patient for coronary angiography, invasive angiography, so the physician suspected coronary artery disease, or the patient in some of the studies had no coronary artery disease with a stent or bypass, few of those are included in these studies, or the patients had a positive functional study or stress study before this that then led them to go to an invasive coronary angiography and got a CT angio. Unfortunately, in these six 64-slice CT, you cannot tease out the population and say what was the clinical indication for every single patient. And you're right, there is no risk score applied to all patients.

DR. GARBER: What was the prevalence of

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the angiograph coronary disease?
DR. PATEL: The prevalence, one study does not report it, the weighted prevalence seems to be about 54 percent.
DR. GARBER: Right. So intermediate to high probability, and we're talking about using it in pretest risks that are low to intermediate probability. The difference between this test and some of the other noninvasive tests is that they have been validated, the other tests have been validated prognostic tests. So although they appear to have inferior test performance characteristics of predictive angiographic disease, they are validated as prognostic tests, so there is an important difference, but we're lacking some data and don't have direct tests of test performance in the relevant population, nor do we have information about their prognostic implications. Is that a fair statement about the state of the literature? Yes.
DR. HECHT: I think the question here is not a prognostic question. We're not doing this test, CT angio, to determine what the patient's prognosis is, we're doing it to determine whether or not he needs to go to the

cath lab for a possible intervention. We don't take patients to the cath lab for prognostication, we do it to see if there's an obstructive lesion, and if we have sufficient evidence, then we go ahead and we fix it. So it's nice to have prognostic data, but then you'd be talking about using it as a prognostic tool, but that's really not the issue.

The second thing I would like to mention is since I was up here before, I was updated. We did query the ACC national cardiac data registry in terms of what percentage of the 366,000 patients in the database had indeed non-obstructive disease. I gave a number of 18 to 20 percent, that number is 35.8 percent, so the magnitude of the problem is far greater than we appreciated.

DR. GARBER: Thank you. Rita.

DR. REDBERG: I would say that in the low to medium probability that we're talking about, I don't think we're talking about taking people to the cath lab to decide what to do, because that's a population where medical therapy is going to be better than anything else we could do based on the cath lab. So, I still think we're

back to the situation we talked about that we need a test that's going to give you some information about events, and I think patients are interested in not so much whether or not they have a blockage but whether or not they're going to have a heart attack or die, and that information we do have from functional testing to base treatment on, among other things.

DR. GARBER: This leads to the question I have for Dr. Williams, actually. We've heard a variety of possible uses for CT angiography which includes this question of going to cath, but it also includes the question of should somebody be put on an aggressive risk factor modification program. And I earlier asked the question about the technical characteristics of the test, how it's changed over time, and it seems to me we're hearing some evidence today that there are some different views about its role in management. Do you see the management algorithms that incorporate CT angiography as undergoing change? And I think in your talk you did suggest that and that's part of the reason to keep revisiting the guidelines and updating them.

DR. WILLIAMS: Right. And I think if

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you're asking from a clinical point of view, I'm going to give you an evidence-based answer that no one else would agree with.

Number one is if you take, you brought up the topic of single vessel disease. There really is no evidence that you're going to improve the person's prognosis in single vessel disease by taking them to the cath lab and doing a revascularization. Perhaps in proximal LAD that's questionable, definitely in left main nobody even has randomized data, you just get revascularized. But for the rest, there is really no value in that. And so who do you really need for angiogram, who do you really need for revascularization, that's a real valid question, and so far, you know, the data is relatively small.

Most people are going to benefit from medical therapy, from an exercise program, from excessive diet therapy that is evidence-based and most people ignore, and those are tried and true things. So to that end, you can actually do a lot. You can actually bring a test on line like CT angiography that can rule out -- you know, everyone is talking about 1.5 millimeters, but

give me a 4 to 6-millimeter left main that you can see clearly, and a 5-millimeter LAD and circumflex that you can see clearly in the proximal portion and show me there's not evidence of disease there. And I think you've got, obviously you will have to test this to satisfy that side of the table, but these are things that as a clinician you can use in a robust way to say this is going to affect patient management.

DR. GARBER: Yes, Dr. Hodgson.

DR. HODGSON: I go back to your point a moment ago about the prevalence. Going to this table compiled by Givens, et al., intermediate prevalence is defined as 10 to 90 percent, so certainly the 50 falls right in there.

(Laughter.)

DR. HODGSON: And other schemes are similar to this, so high prevalence is really high, and intermediate is relatively wide.

DR. GARBER: That's one definition, but some of the others use different definitions of intermediate.

Are the panelists ready to move on to the voting questions? And I should add that if you feel you need to ask more questions to

presenters, you're open to do that during this period of discussion, but for the most part if you know you have some questions, now is the time. Yes, Charlie?

MR. QUEENAN: Did we come to a conclusion, or are we going to come to a conclusion with the panel vis-a-vis the question you asked a little while ago, that started the discussion about the difference between 16 and 64, whether we will look at those separately.

DR. GARBER: Well, I think that, my intent was for us to pursue that in the context of the questions, but it may be a good thing to discuss now, since it will cut across questions. Do we want to restrict our considerations to the 64-slice for some or all of the questions, or do we want to lump it together, or for some indications look at both? There are many ways to go with this. The idea is so that this will have some clarity about how we assessed the evidence base. Well, that was a resounding thud.

DR. COHEN: It sounds like from what we heard earlier that even if we include 16 in our assessment today, everybody is going to have 64 by the time this sees the light of day anyways, so I

wonder if it's so important, and I think, I guess what that means is we are probably implicitly going to 64 because that's where it's headed.

DR. FISHMAN: You know, I think, again, in terms of where things are, you're right. In terms of the marketplace, that's definitely true. And we're not going to have some technology that is limited to a few sites, and create rules that nobody can execute. I think if you look at the Duke group, their presentation, or look at Blue Cross Blue Shield's analysis of 16, I mean everyone has basically said that based on the literature, no one would approve 16-slice CT as a technology for reimbursement. So I think maybe it's almost like beating a dead horse. So you really have to say, you know, the question you had before, should we wait for the next technology, which would result in never getting anything done, which is the flip side of the question.

I think 64 is the state of technology. There's a big difference between 64 and what's going to follow, and there's a very practical reason. If you look at CT scanning cost of purchase, in 1980 to buy a scanner that took 10 seconds a slice, it was 1.1 to 1.3 million. The

first spiral scanner cost 1.1 to 1.3 million in 1989. The 4-slice in 1993 cost 1.1 to 1.3. The 16-slice in 1999, 1.1 to 1.3. The 64-slice, 1.1 to 1.3. The dual source and following, 2.5 to 4 million. So there is a substantial difference, basically a minimum of twice the cost. I think that's going to be a major limitation of that technology regardless of how much better it is in theory, if it is better. 64, as I think I said, in terms of distribution across the country for big hospitals, small hospitals, community, academic, small city, big city, it is becoming the state of the art.

DR. GARBER: Let me ask, I'm not in a position to make a motion or anything of the sort as chair, but I would ask if this is a reasonable way to approach this. Assume that 64 is what we're interested in. When we look at data on 16, we might assume that the data that we're lacking on 64 will be at least as good as for 16, in other words, sensitivity, specificity, indeterminate rate and so on. So in that sense we might want to consider the evidence on 16, assuming that the data on 64 will be at least as good. And that's, I think I've summarized what you've said, but go

ahead.
DR. FISHMAN: If you just look at, there is no way than you can do worse than a 64, hopefully. I mean, you're basically getting a scanner that spins a minimum as fast with improved spatial resolution.
DR. REDBERG: I think concerns were raised about specificity and I think that's what I worry about, especially in the low prevalence population, that we're going to see things that really aren't anything.
DR. GARBER: Maybe I could ask the Duke people, because this is always a tough question, the variance across studies within one technology versus across two. Did you think that the specificity was clearly worse for the 64-slice, or is this within the range of variation within a technology?
DR. PATEL: I just want to make sure I understand the question. Was the variance in 64 different than 16?
DR. GARBER: Basically, is the specificity different for 64 than 16?
DR. PATEL: We didn't do formal testing. Inherently when you look at the studies,

there's more 16-slice studies.
DR. GARBER: Yeah, so it's narrower.
DR. PATEL: The numbers are narrower and they do seem to be higher for 64, but there are six 64 and many more 16, I think in the range of 13 or 16, so since there's more studies, there's more variance.
DR. GARBER: Okay.
DR. HODGSON: This isn't going to be horribly scientific, but obviously the 16 provided the learning curve for the 64, so many of you learned how to read these better on a 16. There were advances on the cardiac software but fundamentally, and Dr. Fishman can correct me if I'm wrong, many of the 16-slice scanners have the same width and rotation speed as the 64s. What you get on a 64 is a larger field of view over the area that can be covered, and therefore you can scan the heart in less time, allowing less time for heart rate variability and less time for the patient to move or breathe. And that's where a lot of the gains come in, is that they don't have as much time to move or breathe or have an arrhythmia or whatever. But the technical aspects of it, maybe some small changes in the tube

current and stuff like that, but the slice thickness and the gantry rotation speed are pretty similar in a lot of those.

So I would actually favor a current 16, a 16 today, not even three years ago, but a 16 today with the current software and what we've learned about reading them, I think in many patients can give very acceptable studies.

DR. FISHMAN: I think the statement is what you said in the last line, for many patients. I think particularly in the Medicare population where it is not as easy to hold your breath for 20-plus seconds, it's a lot easier to do it for eight or ten seconds, so the chance of a study succeeding, as Dr. Flamm said, I think is significantly greater. The reality is technology is different, the spatial and temporal resolutions are far superior in 64, but the chance of executing an acceptable study I think goes from probably 70 percent to 95 percent. And those little things in an older population who have calcification, 64 has less issue with blooming, and I think makes a significant difference.

DR. GARBER: Okay. I think it's time for us to move on to the voting questions, and I'm

not sure we're going to be able to resolve 16 versus 64 much more completely than we have now. So now everybody -- do you want to explain the cards? Does every panelist have their numbers? So we are going to discuss each question one by one on this confidence scale of one to five, five being very confident and one being very unconfident, diffident, whatever term you want to use.

The first one is going to be about CT angio, electron beam CT, MRI, that being MR angiography, and other identified technology which I think, if I understand, to be the other commonly accepted noninvasive tests for coronary disease. Is that the intent? Well, since there is no contradiction, I'll assume that's the case.

So let's open discussion on number one. How confident are you that there is sufficient evidence to determine the diagnostic accuracy of the following noninvasive technologies for the detection of obstructive coronary artery lesions? You are only voting not on how good they are or anything of the sort, just how good the evidence base is, do you feel confident that you have enough information to judge. Discussion? No.

DR. COHEN: Alan, for the other identified technology, are we supposed to assume something, or specify what they are, do we care what they are?

DR. GARBER: I think as I understood the question, and Steve will promptly contradict me, I'm sure, we have some idea about the evidence base, I think for treadmill tests, for the various variations of the nuclear scans and for echo, stress echo, so I think that's kind of what we have in mind. Is there good evidence about these other types of tests.

DR. FISHMAN: You mean not tests.

DR. GRABER: This says noninvasive technologies.

DR. HODGSON: I'm just not sure where that definition came from. I interpreted it as saying other tests that somebody in the panel or maybe the Duke people identified as an up and coming noninvasive mechanism for evaluating obstructive disease. Is that different? Because now if you've just thrown in all nuclear, echo stress, everything else into this fourth category, that was never discussed anywhere.

DR. PHURROUGH: D was to include other

things that would do what these are doing, if any were identified in this meeting.
(Unintelligible colloquy.)
DR. GARBER: We haven't discussed anything else, so D is moot.
DR. PATEL: I thought D from our perspective was a horizon scan to see if there were other technologies that would soon be able to do something like this, and we didn't find any other technologies that would be able to do the ones we discussed.
DR. GARBER: Yeah, so that means if we didn't discuss them today, that we don't need to vote on this one.
DR. PHURROUGH: You don't need to vote on D.
DR. GARBER: Okay. Charlie.
MR. QUEENAN: I'm still confused on the 16 versus 64, but the only suggestion I would make is you call for a vote on the two separately, because it sounds like some people may assign different rankings to a 16 versus 64.
DR. GARBER: I think that's a really good suggestion, so just a straw vote. Do people want to consider them as two distinct technologies

or would you want to lump them together the way I have suggested? So how many people would like to consider them separately.
(Hands raised.)
DR. GARBER: So we've got, I think six. And how many people would rather lump them together?
(Hands raised.)
DR. GARBER: Five. We're going to consider them separately. Okay. CT angiography -- oh, Richard?
DR. WAHL: Just to clarify, we didn't spend much time discussing EBCT or MRI, I would suggest that we not, that B and C might be moot as well, but I just wanted to put that out there to lessen the numbers we have to vote on.
DR. PHURROUGH: I'm sorry, Richard, we're not going to let you do that. Particularly for Question 1, I think it's important to answer B and C, and if the answer to B and C is such that you think there is no evidence, then you couldn't answer the rest of the questions, so I think that's how you would handle B and C.
DR. GARBER: So first, I would like your votes on CT angiography in the 16-slice

variant. So put up your numbers.
(Members displayed votes.)
DR. GARBER: And remember, this is about adequacy of evidence, this is 16 right now, adequacy of evidence, not how good it is.
DR. KRIST: I think that concept doesn't come across.
DR. GARBER: Well, in other words, let me just point out, there are more studies for 16-slice than 64-slice, so unless you think the studies are better for 64-slice, you probably shouldn't give a higher confidence rating for 64-slice. So we're only talking about the evidence, not how good you think the test is. Okay, everybody's comfortable.
Now, CT angiography, 64-slice version.
(Members displayed votes.)
DR. GARBER: Electron beam computer tomography. This is for detection of obstruction of coronary lesions, so how good is the evidence.
DR. FISHMAN: This only means you know what the results are, right?
DR. GARBER: Yeah, it doesn't mean you think it's good as a test. The question is, do you think there is a good evidence base from which

you can draw conclusions.
(Members displayed votes.)
DR. GARBER: Now, MR angiography, MRI.
(Members displayed votes.)
DR. GARBER: Thank you. You folks are fast. Good form too. Okay. Number two. This is the thing I think you were waiting for.
How confident are you that there is sufficient evidence -- I'm sorry, this is not the one. This is the same question about, can you accurately determine the anatomic location of obstructive coronary artery lesions, can you accurately determine the location. Again, this is about your confidence in the evidence, not do you think the test is good for this. So first we'll ask about 16-slice CT.
(Members displayed votes.)
DR. GARBER: 64-slice CT.
(Members displayed votes.)
DR. GARBER: Electron beam CT.
(Members displayed votes.)
DR. GARBER: MRI.
(Members displayed votes.)
DR. GARBER: Okay. Question 3. How confident are you that there is sufficient

evidence to determine if these noninvasive technologies can accurately detect the relevant morphology, size, shape, et cetera, of obstructive coronary artery lesions? So we're still on the adequacy of the evidence issue here. 16-slice CT.
(Members displayed votes.)
DR. GARBER: 64-slice CT.
(Members displayed votes.)
DR. GARBER: Electron beam CT.
(Members displayed votes.)
DR. GARBER: MRI.
(Members displayed votes.)
(Dr. Garber and Dr. Phurrough conferred privately.)
DR. GARBER: Let me just explain what Steve just said. Because the next questions are phrased as for which there is sufficient evidence, in other words, what are the results if you think there is sufficient evidence, we're going to need to quickly tally what the evidence ratings were.
MR. QUEENAN: Alan, while they're doing that, could I ask a question that relates to these?
DR. GARBER: Sure.
MR. QUEENAN: You asked a follow-up

question when we talked about 16 versus 64, and then also sort of what clinical practice was in mind or what protocol was in mind when one evaluated that, and I wonder if we may need some clarification when we get to this set of questions, so we have a common understanding of what that background practice would be.

I have my own suggestion for that, which would be without trying to be specific because it doesn't sound like we could be specific, without giving many, many variations that, you know, there is a presumption that it is, to try to define that, and I'm not the one to do it, but to try to define that in terms of what common practice is today for people who are using 16 or 64.

DR. GARBER: Charlie, I think that's a really excellent point. I guess my interpretation of this question is that you have at least some way in mind. Take number four, that it might be used instead of coronary angiography, x-ray angiography, that there is some specific use, and I think it would be useful for the panelists to discuss which situation they think that might be, or situations, so that we have some common idea.

We don't necessarily have to reach agreement, there just has to be an understanding that there is some study in which it could be used to replace it, but it would be useful to find out what those situations might be from the panelists' point of view. So I think they might want to address that, if they feel it does have a use. David.

DR. COHEN: I think as we've heard, several, even most of the purported uses at least on the CT side are areas where there is generally a suspicion that coronary angiography adds little already, and that avoiding an invasive procedure is a good idea, so some of the suggestions such as emergency room uses for patients who are suspected of not having obstructive coronary disease, or patients who currently undergo catheterization prior to valve or other heart surgery, where it's being done as the gold standard, but because there is a low prevalence of disease and relatively high sensitivity in tests such as CT angio, those might be two applications where I can perceive that you might truly be able to avoid catheterization. And I think those are the ones that we have heard the most about. There are obviously others, but there are certainly at least those two.

DR. GARBER: Any other comments, agreement, disagreement, additions? Okay. Yes, Deborah.
DR. SHATIN: For this Question 4, is it relevant for each (inaudible).
DR. GARBER: Well, yeah, there's two possible voting mechanisms. One is based on the individual ratings and the other is the group was over some number. I think probably, do you want to use --
DR. COHEN: Because otherwise, the people who voted low don't get counted in this vote. So you have to use the group, because otherwise, if you said you were unconfident of the evidence, then you're silent on the voting in this process.
DR. GARBER: Yeah. I mean, the other option would be to reject what was -- what David is saying is people who said they weren't confident might also give it a relatively negative grading, it's a different sample than the people who said they were confident, so it's not an accurate reflection of the panelists' views. So that's one reason to do it. An alternative procedure would be to rephrase the question and

allow everybody to vote on this regardless of the evidence, but there is a logical problem. If you think the evidence is no good, to then say what the evidence show and what conclusions you draw, but other than that, it's inconclusive.
So you know, I think what David is saying is pretty sensible, even though it means we don't have a vote from the people who thought that there was no confidence.
MR. QUEENAN: So we're going to exclude people who --
DR. GARBER: No, no. What David suggested, and we can vote on the procedure too, and if there's disagreement, we probably should. The procedure that David proposed is that we say who, what's the average vote on confidence, and if the average vote turns out not confident, and there is a second question here, what numerical score means we're not confident, which we will have to resolve. But if we decide we don't have confidence in these questions, that means there is no vote for Questions 4, 5 and 6, they're moot. So let me ask, are people comfortable with that voting mechanism? Charlie?
MR. QUEENAN: I mean, I think we need

to hear the tallies, this is anticipating the answer, but my guess is we should vote on 16 and 64, and we should knock out the rest. I think there are enough, my suspicion is there will be enough people that individually thought there was adequate evidence on 16 and 64 that it would be worth having follow-on votes for that, whereas I doubt that was the case for all the rest of these. Well, let's wait for the numbers.

DR. GARBER: Cliff, did you have a comment you wanted to make?

DR. GOODMAN: So you're talking about voting on each one for 16 and 64?

MR. QUEENAN: Yes.

DR. GARBER: Does anybody want to suggest what cutoff we should use for being confident versus not confident?

DR. KRIST: Above three.

DR. BRADHAM: If we're above a three, we feel like we've got some confidence.

DR. GARBER: Okay. So greater than three, not equal to three.

DR. SHATIN: Before the scores are being read, we're talking about three different questions which may have variations, so is it an

average of one, two and three, or is the first question the most critical, with whatever the score is for that?

DR. GARBER: Well, it depends on whether you want to have a model when Steve comes back. I think for most people, Question 1 is going to be the most important, I could be guessing wrong, about evidence adequacy. But you're right, there are other ways to do it if you take the average over all three questions. But I didn't hear much talk about how the morphology, for example, would be critical in the management algorithm. In fact some people, we had the question about whether morphology really mattered and as I heard the answer, it doesn't at this point clearly affect treatment.

DR. GOODMAN: Alan, a little different tact here. I think there is a fundamental difference between the first few questions and the last couple questions. Even if in the first few questions there is a little bit of evidence, there's not much evidence, you have little confidence in the amount of evidence, you could still, and I think we should still answer the last couple of questions, because even if there is not

much evidence, you may still try to draw some conclusions about the generalizability as in Question 6.A, for instance, and Question 6.B about net health benefit. What it really means, I think, is you can still come up with a score for each of those, but as we know, there's going to be a big fat confidence interval around that because the evidence is kind of limited. So I would rather answer all the questions, and if we didn't think there was a lot of evidence upon which to base those answers. I would just say that there is a lot of overage and underage possibilities for any score you might give. And I really do think if I were in the profession or if I were in industry or if I was another stakeholder, I would want to know what this group thinks about how generalizable they are to Medicare, even if there's not a lot of data, and how much confidence we have about benefits or harm, even if there aren't a lot of data, that would be helpful for me to know.

DR. GARBER: Let me make sure I understand your proposal about 6.A in particular, the one about generalizability. If we conclude that there is not enough data to draw conclusions

about anybody, then the question is, can we generalize this kind of vague thing where we don't know anything to the Medicare population. The way I interpret this is, do you have enough information specifically about the elderly to draw conclusions. You have less data specifically about the elderly than the whole sample. So is the idea to give a signal that, yeah, the studies if they were bigger would do it, or if there were more of them? What would be the interpretation if you were to say we're confident it's generalizable, although we're not all confident that we know anything?

DR. GOODMAN: You may have few studies and/or limited data, but in the real world sometimes, policy-makers here at CMS have to make a decision on a coverage or medical necessity question, payers have to do that all the time in the absence of perfect data. And I will posit that even if I have limited data from these studies, I want to say how I generalize what those few studies with limited data are to the Medicare population, that would be a useful observation.

DR. REDBERG: The American College of Cardiology does this all the time with guidelines,

they have level A if there was good data, level B if there was little, and level C if we gave an opinion. But you know, that's how life is in our world.

DR. GARBER: So, do people want to go through, and I know you're all waiting to find out if this discussion has any point, but do you want, if it turns out that there is not enough evidence, do you want to go through all the questions? I think that's what you were proposing, Cliff. Is that the general sense of the panel?

DR. COHEN: I don't think it's going to hurt, and I think you will factor the confidence level in as you hear the results.

DR. GARBER: Okay. If we do this quickly, you may even get to hear the secretary's talk.

DR. PHURROUGH: So, do you even care now?

DR. GARBER: We're going to go through them all.

DR. PHURROUGH: Do you want to know what the scores are?

DR. BRADHAM: Not if we're going to proceed.

DR. GARBER: Okay. Let's have a vote. Who wants to hear the scores before we vote on the other questions? Okay. I take it the rest of you are nays, okay. Question 4.

DR. SHATIN: I have a question about Question 4. The way it's worded, first it's general and then it goes to a specific population. But if you believe it would be helpful for a specific population, can that be incorporated in terms of what number we give it? In other words, if it can help with a certain population, would that kick it into a higher category?

DR. REDBERG: Does the first part mean that it could be used in any situation, or in one particular key finding?

DR. GARBER: In any situation, and then David has proposed, you gave two examples.

DR. COHEN: They were just examples.

DR. GARBER: Two examples, right, and I asked if anything anybody else wanted to add to that and I didn't hear any.

DR. REDBERG: Well, I could see being in a situation where you really don't know whether the cath is useful or not, but we do it. Like what David suggested, I think preoperative

assessment a lot of times, or someone going for a valve replacement and they often get a routine angiogram, even though they might not otherwise get an angiogram. I think those kinds of situations, there might be enough evidence.

DR. COHEN: I'm still trying to figure out this question. I mean, are we trying to figure out scenarios and then vote on individual scenarios or, I mean, the way the question is written, it sort of goes the other direction. And the other thing is, all the guys here who presented all this stuff from all their practices, none of these areas have been talked about, they're all in the outpatient practice where they're doing thousands and thousands of CT angios, so we're not even voting on all those.

DR. GARBER: As I understand this, and Steve, correct me if I'm wrong, CMS wants to know, are there some scenarios. We would like you to be able to describe them, but we're not going to vote scenario by scenario unless you wanted to do that. I mean, you might care more about that if you had a high rating for the evidence level, right? It would get a little ridiculous to go through scenario by scenario unless you gave it a one, and

I hope I'm not surprising anybody, but the average is not one for any of these questions, as you saw. So I think you have to just be able to give aye votes, we've heard a few possible examples, it's really a question about is there a scenario where you think this could be placed.

SPEAKER: The other data we've heard was not necessarily about Medicare beneficiary, it was more a middle-aged population.

DR. PHURROUGH: Right, and this particular question is on the data. The population, the next question will ask about Medicare. And the question is, can you substitute some noninvasive imaging for coronary catheterization in making the determination of whether you need to intervene in this person's coronary arteries? That's really the question.

DR. KRIST: I was going to say too, for the cases that Rita and David presented, I mean, those are the exceptions cases as opposed to the general stuff we have been considering this whole MCAC. So if you're considering that as a population, I think we would be doing a disservice to what we're here for.

DR. FISHMAN: I would expand that to

say there are certainly things that aren't that controversial. One of them, of course, is comments about aberrant origin of coronary arteries, that's been pretty well documented, so you would add that to the population. I think from a practical basis and what people do on a daily basis, at least what we do, is take patients with indeterminate stress tests, they're very commonly referred to cardiac CT, so there are many more than those. Those are just two examples.

DR. GARBER: So if you believe that that's an appropriate indication, then it's how confident are you that it could replace cardiac catheterization in that setting.

DR. PETERS: Are we asking about all settings combined in this question?

DR. GARBER: This is not restricted to the Medicare population.

DR. PETERS: In other words, if you can think of five different applications where this would be true, you give it a higher score than if you can only think of two, is that what you're saying?

DR. GARBER: No, I think if you're confident in any one.

DR. PETERS: Even though it's a very small percentage?
DR. GARBER: That's what this question is asking. Then we'd have to explain what those populations are as the second part to the question.
DR. COHEN: So in the next go-round, you would ask us what scenarios we think might be qualified.
DR. GARBER: Those of you who are prepared to offer any, yeah. So, are we ready to vote?
DR. LU: The treatment plan, I assume you -- okay.
DR. GARBER: So this is, again, a two-part question. Can we agree that you have to have more than a three on the first one for us to have a discussion about what the scenarios are? I mean less than three in absolute value, to have a discussion about what scenarios you think should replace catheterization. So let's start first with 16-slice CT, how confident are you that it could be used instead of coronary cath to determine treatment of coronary disease, 16-slice?
(Members displayed votes.)

DR. GARBER: It doesn't make it. Okay.
64-slice CT.
(Members displayed votes.)
DR. GARBER: Doesn't make it.
Electron beam CT.
DR. COHEN: What do you mean, it doesn't make it?
DR. GARBER: It means that the evidence, we don't discuss the second part for those.
DR. COHEN: Why?
DR. GARBER: Because it's greater than three, and it has to be less than three in absolute value.
DR. COHEN: You've got it reversed.
DR. GARBER: Oh, I'm sorry.
(Laughter.)
DR. GARBER: Actually, let's discuss them then before we go on to the other technologies. I assume that you all think the indications are the same for 16 and 64, so we don't have to do those separately, so let's go around and hear your reasons. Carole.
DR. FLAMM: Well, I was one of the more uncertain people all along. So let me qualify

that I think for me, I shouldn't go back to Questions 1, 2 and 3, but I have some uncertainties given the limited size and quality of existing studies that sort of color some of my votes. If we took the sensitivity and specificity and talking about just this question, I do think that there are some limited populations such as the ones that have been mentioned that I would be more confident about, but I think my votes were reflecting the overall quality of the evidence. The indications would be things like the pre-op evaluation, the lower risk population, those where you really don't want to do an invasive procedure, so if the patient is at low risk for CAD, you could then do a CT angiogram for other reasons, things like that.

DR. COHEN: I more or less am in agreement with Carole. I think these are patients at this point with CT angiography focused on these patients who are low risk. I am very skeptical as to the value of it for pursuing equivocal stress tests, because I don't know why you would be pursuing those to begin with. I don't think there is a lot of prognostic value that you could ascribe to that, and most of the patients with

equivocal stress tests don't have a lot of symptoms either, so I'm fairly skeptical of that application, which is a fairly large reported application for this technology. But I do think there are clearly areas where it will be valuable even as currently developed, the ones I mentioned earlier, pre-op evaluation of outpatients, patients who you would otherwise send to cath but you think are at low risk for some reason, but are defining your diagnostic abilities.

DR. BRADHAM: I would agree with what David just elaborated on. I think the idea of trying to open this up as a second level test for equivocal treadmill or pharmaceutical stress test is not a great idea at all, that just opens up duplications that are going to be a bad situation downstream.

DR. BATEMAN: I hate to disagree with everybody, but I think I do. I'm most impressed after some of the numbers that we've heard, you know, 50 percent of the caths in the comparative studies turned out to be normal, 37 percent of all the caths in the cardiology database are normal. I think we have a big problem in this country with a $4,000 test that carries morbidity and mortality

numbers, and I think there's a big opening for a test that can identify those patients who are normal and don't need that procedure. So I do think when I reflect on our patient population that a big percentage of those people who do have equivocal stress tests of one type or another, and I do think it's bad medicine when those people are labeled as having coronary disease, I think they are followed differently and I think they do add a lot of cost. So I think that is an important patient population, and certainly the anomalies and the before surgery are populations that are pretty -- it's a simple question we're asking, does a patient have coronary disease or not, and I think this test can address that pretty definitively in those populations.

DR. KRIST: It's good we're sitting next to each other because I also disagree. I gave three, unsure, because I was sticking with the evidence we were reviewing and everything. I want to see the outcomes, that this is going to change outcomes. I think the promise of these tests with the existing specificity data looks impressive, and I got confused there at the end for voting because Elliott and David came up with

cases where I can see where we could do this. But I wanted to stick to the cases in the areas we're talking about and if we're sticking to that and the evidence we're reviewing, I have to say I'm unsure and I need more information before I could say that this could be used to replace catheterization.

DR. PETERS: I agree with a lot of what has been said. There are clearly situations where I think it would be helpful. I was especially impressed with people in the emergency room with chest pain, that's a huge population and a lot of them wind up getting admitted, and this might be helpful. On the other hand, I'm very much afraid if the door is opened as a follow-up to stress test, because there's a whole lot of people with equivocal stress tests and I think this could be very overutilized in that situation.

DR. LU: My feeling is that the CT is good for assessing patients without coronary disease rather than for a patient with coronary disease in terms of management. It's good for patients because it has such highly predictive value. Part of the 30 percent negative cardiac cath, I think is a reflection of both the

defensive medicine and tendency to cath to please a patient, and obviously there are some monetary incentives in that. When you see 20 percent, if not 30 percent or slightly higher than 30 percent, I think ACC should look into this, but when CT comes out, I think that number is going to go higher.

DR. FISHMAN: I will agree with some of the indications and comments before. I think one of the things that makes the question a little tricky, I don't think we're really saying we're doing cardiac CT instead of coronary artery catheterization. I think that's not exactly the question. The question is really more, where does it fit into the workup of a patient. That's why in the situation with a patient with a family history of coronary disease and an indeterminate stress test, it seems to be a great application of the cardiac CT, but it probably wouldn't have been somebody you would just send for an x-ray cath. I think the importance, as mentioned by many speakers today, the difference in the intensity of the study, you know, a study that takes a couple seconds with a low complication rate versus an angiogram which

has the potential of high risk, particularly in older patients, there is a significant difference. Again, there is the issue which I agree with, the danger of course with people abusing it or overusing it. That, you know, with any modality is always an issue.

But I think the thing we ought to focus on is that it provides information that's essentially or almost equivalent, having looked at the data, to a cardiac cath without any of the complications, it's an outpatient procedure, and it basically allows you to confine the risk to that patient or the management of that patient. I think in our practice, the way I see people using it as a way of coming to a definitive answer on the patient's care many times, and I think it's one of the things that provides a lot of certainty, showing a negative side as well as the positive side. So you know, that's why I think there are a range of applications that many of the speakers spoke about that I think really contribute to its strength.

DR. GARBER: Charlie.

MR. QUEENAN: I guess I took a little bit of a different tack, primarily because I don't

feel I'm in a position to answer this question with respect to any specific application, although I certainly believe that's useful and necessary for CMS to look at. But rather from the perspective that this is now used in a variety of different settings, different calculations and, you know, different clinical practices, and each of those clinical practices may think of this question or this protocol in a slightly different way.

So I basically answered the question from the perspective of an amalgam of those, thinking about whether I was unsure, et cetera, as to whether that would result in a, you know, an ability to use this technology as opposed to CA. So from that perspective, I think with respect to the 16, I was unsure, because I think there's some questions there, but with the 64, I was confident.

DR. WAHL: I came to a somewhat confident level and, you know, obviously the database is far from mature, but I consider my practice as being moderately on the cutting edge, and there are cases in which nuclear scans are completely negative but have very good negative predictive value, or are very positive that have

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pretty bad prognostic value unless there is an intervention, but there are some that are in between that, as I think Dr. Bateman pointed out. In some of those cases, I could see that that group of patients could potentially benefit from a quick clarification from a CTA and it might well prevent a cath. And I could see that that group of patients who would be at low to intermediate risk but at a higher than baseline risk, the coronary disease might be at higher risk than the cath. That is, they might be obese, they might have bleeding disorders, there would be some specific reasons. So I don't think it's hard to think there would be specific indications where this would be a very useful test to really risk-stratify patients who still aren't really that well stratified.

I am concerned that the specificity of the test, that is the ability to find small 40 to 50 to 60 percent lesions in a lot of people who are elderly, may result in a lot of false positives if it were used as a first line test routinely. I would be concerned that there would be not such a good positive predictive value to that extent in the Medicare population, and that's

why my thoughts on its use were somewhat limited at the movement until the evidence develops further.

DR. SHATIN: I think it's important to consider the risk/benefit, and therefore the patients that are at relatively low risk and would be at high risk to get cardiac cath, it is important to have this technology available. We also haven't really spoken about the potential increased risk for the elderly population who undergo cardiac cath, so I can envision some of that population, the borderline elderly, where it might be critical to have this available.

DR. REDBERG: I think that our history, particularly with the use of testing, our cardiac imaging volume has gone up about 23 percent a year, and although some people propose this test would be a gatekeeper, I don't actually find from our experience in testing that it would work that way. And I just think it's important for us to understand what the impact would be on patient management and outcomes, and I haven't heard any data today on outcomes or on patient management or benefit, and so I don't see how this is going to help us take better care of our patients, although

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we were certainly given some very beautiful pictures.
I think Harvey pointed out that the normal cath rate has gone up to 30 percent, and I think that if we started using CTA more frequently, we could get an even higher normal cath rate because I think we would be using it in low risk patients that would have more false positives and then get referred to the cath lab. I think that's what happened to cath with primary calcium testing. I certainly have talked to all of my colleagues saying that people who get coronary consults who are pretty low risk for whatever reason, they have an inclination to send them to the cath lab, and so I think that's why we're seeing a lot more normal caths.
And so I think before we enthusiastically embrace another test that currently just gives us a beautiful picture, we have to find out how it's going to help us take better care of our patients and I don't think we have that data. Having said that, I think there are situations like pre-op testing where, you know, perhaps -- personally I don't think people need a test before a stress test, but if you

wanted to do one, that this would be equally beneficial, or if you wanted to do it before an aortic valve replacement where an older person goes for valve replacement, situations like that. But otherwise, I think you're only increasing the volume of caths by opening another gateway to caths.

DR. GOODMAN: Nothing to add.

DR. GARBER: Okay, thank you. Now we're going to the same question for, you asked for this, electron beam CT and MRI. So how confident are you it could be used instead of coronary catheterization to determine treatment of coronary artery disease, for EBCT?

(Members displayed votes.)

DR. GARBER: Okay. Now I think I've got it. And for MRI.

(Members displayed votes.)

DR. GARBER: So we don't have to discuss your reasons for that one.

Now we're on Question 5, if noninvasive imaging were to be used in addition to coronary artery catheterization, how confident are you that noninvasive imaging provides an incremental benefit or harm when used before coronary artery

catheterization?
DR. REDBERG: Are you going to separate those?
DR. GARBER: Yes. So first, 16-slice.
DR. REDBERG: No, benefit or harm, I meant separate benefit or harm.
DR. GARBER: We can change it to net benefit.
DR. COHEN: Can I ask a clarifying question? The way this is worded, so, are we talking about using them both together or are we talking about using them in sequence and potentially avoiding one? That's not clear to me. I think much of what we've been discussing has related to using one as a potential way of avoiding invasive catheterizations, which is, you know, but recognizing that some people still go on to catheterization depending on the findings, but then the other way is as though they come together.
DR. GARBER: So, I thought it was in place of other noninvasive tests.
DR. ROLLINS: This was essentially sequential. In other words, if you decided that you couldn't replace coronary cath with this but

you needed to do both of them together in some way, would you combine them with this before cath, this after cath? We realized that you couldn't literally do them simultaneously, but the time frame separating them in sequence could be as short as a few hours, or it might be years. You know, if you were going to do it before cath, whether that means as a gateway to cath or not is up to the panel to decide, but do you see a role for it in some sort of sequence that includes cardiac cath.

DR. GARBER: But does it include cardiac cath 100 percent of the time for this question?

DR. ROLLINS: Not necessarily for this question.

DR. GARBER: I'm not positive I understand, but one of the things we already considered was using it in place of other noninvasive tests like, in someone who is low risk, you might do this instead of a treadmill or stress treadmill, or perfusion scan, in which case one of the advantages is you much of the time won't have to do a cath, so would we consider that to be one of the --

DR. ROLLINS: Yeah, conceptually if you had a model or algorithm where noninvasive testing was sort of upstream from cath, do you foresee that kind of model being developed?
DR. GARBER: Okay.
DR. COHEN: So that model implies there could be cases where you did it and then decided that the cath wasn't necessary.
DR. GARBER: Right.
DR. COHEN: Okay.
DR. GARBER: Okay. Are people ready to vote? 16-slice CT.
(Members displayed votes.)
DR. GARBER: 64-slice CT.
(Members displayed votes.)
DR. GARBER: Electron beam CT.
(Members displayed votes.)
DR. GARBER: And MRI.
(Members displayed votes.)
DR. GARBER: B. How confident are you that noninvasive imaging provides an incremental benefit or harm when used after coronary artery catheterization? Again, net benefit, and this is where you already have the anatomy from x-ray angiography.

DR. FISHMAN: I guess the question would be what did they do in primary cath, did they put in a stent, or if nothing was done if the cath was normal or had some mild disease, then why would we be going backwards and doing a CT in those situations?

DR. BATEMAN: Or that there was concern about a left main lesion.

DR. FLAMM: And are we considering here things where the technical success of the procedure may have been limited, you couldn't see everything well, suspected coronary anomaly, that sort of thing?

DR. GARBER: Could I ask, did you want to include PCI in this or just diagnostic tests?

DR. ROLLINS: We were really talking more about diagnostic cath, focused on native coronary arteries, so the focus of the question was, is there some paradigm or model where having had a coronary angiogram would not completely eliminate the necessity or possibility of noninvasive testing.

DR. WAHL: Could you specify the time line, like three years later or what?

DR. ROLLINS: Well, I think that is up

to the panel. One of the things that was discussed today was sort of what is the life span of a test result for a noninvasive test. If you're noninvasive this week and you have other symptoms next week, do you get another noninvasive test, or is the one you had this week good enough to last you for three years, five years, whatever, so we did not predefine that. However, if the panel wants to do that, they may.

DR. GARBER: Am I right in assuming you mean in the same episode of care, however that's defined?

DR. ROLLINS: Yes, I mean in general.

DR. LU: Again, incremental meaning any small group or the majority of the patients?

DR. GARBER: Have a case scenario in mind. Is there a scenario for which this provides a net benefit. Okay? Further discussion? Okay. We're voting. 16-slice.

(Members displayed votes.)

DR. GARBER: 64-slice.

(Members displayed votes.)

DR. GARBER: Electron beam CT.

(Members displayed votes.)

DR. GARBER: MRI.

(Members displayed votes.)
DR. GARBER: Everybody doing okay?
Okay, number six. How confident are you that, this is, again, this is the generalizability discussion that we started to have, the diagnostic characteristics of the technologies are generalizable to the Medicare beneficiary population? 16-slice CT.
(Members displayed votes.)
DR. GARBER: 64-slice CT.
(Members displayed votes.)
DR. GARBER: Electron beam CT.
(Members displayed votes.)
DR. GARBER: And MRI.
(Members displayed votes.)
DR. GARBER: Now, 6.B, diagnostic and treatment strategies using noninvasive imaging of coronary artery disease provide a net health benefit to Medicare beneficiaries compared to strategies that use invasive imaging. And I take it this means any strategies. Any discussion?
MR. QUEENAN: Just for clarification, I'm assuming this would be strategies that include the noninvasive imaging, but then the additional step may also include invasive tests.

DR. GARBER: Yeah, it's some kind of management approach that incorporates it.
16-slice CT.
(Members displayed votes.)
DR. GARBER: 64-slice CT.
(Members displayed votes.)
DR. GARBER: Electron beam CT.
(Members displayed votes.)
DR. GARBER: And MRI.
(Members displayed votes.)
DR. GARBER: Congratulations.
MR. QUEENAN: Could we get the answers now?
DR. PHURROUGH: I can give you the answers for the first three questions. The others will take a while to do. Okay. For 16-slice for the three questions averaged together, 3.74. Question 1 was 3.69, Question 2 was 4.15, Question 3 was 3.38. These are for all panel members, not separating out voting members.
For the 64-slice, Question 1 was 3.69, Question 2 was 4.31, Question 3 was 3.54, average was 3.85.
For electron beam, Question 1 was 2.31, Question 2 was 2.38, Question 3 was 2, average

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2.23.
MRI, Question 1, 2.69, Question 2,
2.85, Question 3, 2.77, average 2.77.
Just another piece of interesting
information, I always find how flexible and
entrepreneurial cardiologists are. So, I have a
data run we did earlier this year on the number of
left heart caths paid for by Medicare in 2005.
Since it was done earlier this year, it doesn't
include all cases, some obviously have not been
reported yet, but in this particular run, a bit
over a million left heart caths were paid for. It
gives you a breakdown of where they were
performed. 57 percent in inpatient hospitals, 34
percent in outpatient hospitals, a little over 6
percent in office, that makes up the vast
majority, about 99 percent. But then there were
some interesting ones. Four were done at home.
Two were done at school, school nurse now has a
different connotation. And to demonstrate that
there are other physicians who are homing in on
your jobs, two were done in birthing centers.
DR. GARBER: That's full service
birthing centers.
DR. PHURROUGH: All right. Let me

thank the panel for all their work. As usual, these are invigorating discussions, they are never discussions in which everyone agrees, otherwise we wouldn't have to have this kind of meeting. As usual, the questions are never clear when we get here and discuss them, when they were very clear when we put them together and had our conversations over the phone. So actually, it was much better this time since we didn't have to rewrite all the questions.

Let me give you just sort of a brief discussion of what we plan to do. The purpose of this particular meeting was not to arrive at a recommendation as to what the Agency should do for, in the area of coverage for these particular technologies. We do have MCACs that are part of national coverage determinations where we take the recommendations of the MCAC and let that inform us as to what our potential decision would be for coverage. This was not one of those. The purpose here was to put out in a public forum some discussion of what the current state of evidence is around these particular technologies. And as many mentioned, our expectation is that we will need to do this again sometime in the not too

distant future to reassess again. Whether it will be a year, two years, some of that depends on our ability to budget for these particular MCAC meetings. We are able to have four or five a year. More than that, I have to write a check for, and I tend to not like doing that.

So we will summarize this meeting, we will make that summary public, the transcript will be public, we will have the voting questions summarized and on our web site later tonight or first thing in the morning, so that you can see what the rest of the numbers were.

But I think it is always helpful for us as we try to make sure our decisions around the things that we should be addressing in a national decision, to have these public discussions so that we can be somewhat better informed as to the consensus or lack thereof in a particular technology.

So again, panel, thank you for your time and for your interest, and for those who attended from the public, we appreciate your interest also. And with that, I'll give it back to Alan.

DR. GARBER: I would just like to thank

the panelists for their very thoughtful deliberations. I also wanted to thank CMS staff and the Duke team for their excellent work preparing this. I would also like to thank the outside presenters, who really did a remarkably good job in assisting us in our deliberations. Your presentations were very much focused on the material we needed to know and you were very candid and helpful in the question and answer sessions. I wish I could say it's always this way. It is what we strive for, and I really appreciate that you made the effort to help us out here.

So with that, is there a motion to adjourn?

MR. QUEENAN: So move.

DR. BRADHAM: Second.

MR. GARBER: All in favor?

(Whereupon, the meeting adjourned at 2:20 p.m.)