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BY ELECTRONIC DELIVERY

William Larson, MA
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Centers for Medicare and Medicaid Services
7500 Security Boulevard
Mail Stop C1-09-06
Baltimore, Maryland 21244

Re: NCA Tracking Sheet for Screening Computed Tomography Colonography (CTC) for Colorectal Cancer (CAG-00396N)

Dear Mr. Larson:

On behalf of Philips Healthcare ("Philips"), I am delighted to have the opportunity to submit these comments in support of Medicare's National Coverage Assessment (NCA) for Screening Computed Tomography Colonography (CTC) for Colorectal Cancer (CAG-00396N). Philips operates in five main business areas: Diagnostic Imaging Systems, Clinical Solutions, Healthcare Information, Customer Services and Home Healthcare Solutions. Our product line includes best-in-class technologies in X-ray, ultrasound, magnetic resonance, computed tomography, nuclear medicine, PET, radiation oncology systems, patient monitoring, information management, personal emergency response systems, and resuscitation products.

Colorectal cancer is the third most common cancer and second leading cause of cancer death in the United States, and screening is recommended[1] for men and women over 50. Unfortunately, compliance is relatively low, at approximately 43% of the target population[2], resulting in more limited treatment options and lower survival rates. In fact, a study published in the January 15, 2008 issue of CANCER[3], a peer-reviewed journal of the American Cancer Society, show that only 25 percent of Medicare patients received recommended screening during the study period. The low overall screening rates are consistent with previous studies.

In September, 2007, the long-awaited preliminary results of the American College of Radiology Imaging Network (ACRIN) #6664 screening trial of more than 2500 patients were announced. The ACRIN trial[4] involved 15 centers and 2531 asymptomatic patients over age 50, using several multi-slice CT scanners (all with at least 16 detector rows). In almost all cases, colonoscopy was performed immediately after the CTC. The results indicate that CTC is comparable to optical colonoscopy for intermediate to large adenomas, with 90% sensitivity and 86% specificity for adenomas 1 cm or larger. Performance characteristics remained high in smaller sized polyps, with 84% sensitivity in lesions 7 mm or bigger. Specificity remained high (86% to 89%) across all relevant lesion sizes.

Based on the ACRIN trial results and a large body of clinical literature, the American Cancer Society (ACS) recently updated its colorectal screening guidelines[5] and added CTC to the list of options: In fact, the new ACS guidelines for the first time divide the available screening methods into two categories: Tests that find both polyps and cancer and those that mainly find cancer. CTC (with re-testing every five years, in the absence of specified risk factors) is added to the first, and preferred, category.

In order to facilitate CMS review of this issue, we thought that it might be helpful for us to respond to a number of the questions that have been raised with respect to screening CTC:

Question: Isn't CTC inferior to optical colonoscopy for the detection of small lesions?

Response: The main purpose of ACRIN #6664 was a comparison of CTC with Optical Colonoscopy (OC)). In this trial, all patients underwent a CTC followed by a same-day segmentally unblinded OC. The results of the two techniques were compared and it was found that for all clinically significant lesions that CTC was equal to or better than OC. Similar blinded studies performed in Europe[6] have achieved almost identical results to ACRIN #6664, with sensitivity and specificity of 90% and 86% for lesions 10mm and greater. The use of 3D as well as 2D images for reading the CTC exam means that regions of the colon which may be difficult to view by OC, because they are hidden on the "wrong side" of a fold in the colon wall, are easily observed, and, in a typical CTC protocol, each region of the colon is inspected 6 times, whereas in a OC many regions are only properly observed once, while the colonoscope is withdrawn. This probably contributes to the slightly better performance of CTC as a screening test as shown by Kim et al.

Question: Isn't CTC duplicative, since detection of a lesion using CTC may trigger the need for an optical colonoscopy and surgical intervention, while lesions can be simply removed contemporaneously with the performance of an optical colonoscopy?

Response: Research carried out in December 2007 has shown that one of the main reasons that patients do not receive appropriate screening for colorectal cancer is the distaste for stool based tests and the invasiveness of optical colonoscopy A minimally invasive test such as CTC was found to be more acceptable to patients and is likely to lead to a greater uptake of colorectal cancer screening by the target population and likely to lead to better rates of follow-up screening. In addition, Optical Colonoscopy has some associated risk of bowel perforation and requires a sedative or anesthesia, which also have associated risks; These risks can be avoided by using CTC as the primary screen because the majority (>87%)[7] of all people tested will be found to have no clinically significant lesions. In an optimal clinical setup, those patients in whom lesions are found and who require a therapeutic colonoscopy can receive an OC on the same day. Even where this is not possible, people who have been screened using CTC will now be motivated to undergo the OC by the sure knowledge that they have lesions to be removed whereas previously they might never have been screened at all. It is our belief that giving patients the option of CTC screening will encourage those who currently ARE NOT being screened to do so, the primary goal being to reduce the incidence and subsequent cost of CRC. If the primary goal of CMS is to reduce healthcare costs and save lives then adopting a preventative-health CTC screening program makes sense, regardless of whether therapeutic intervention takes place during the same patient encounter.

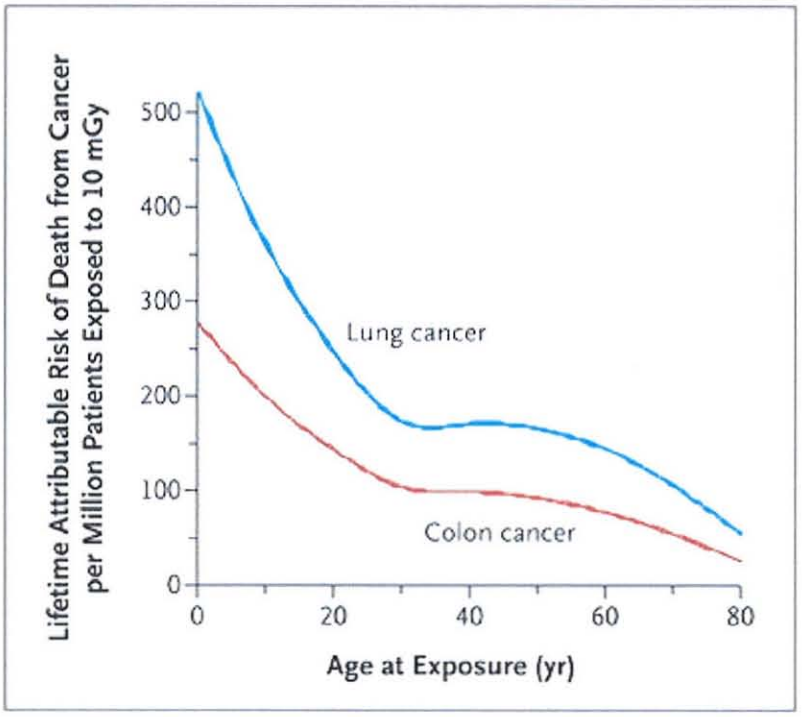
Question: What about the radiation risk involved in CTC?

Response: Preliminary information presented from the ACRIN study showed an average dose of only ~5 mSv. The ACRIN trial was performed with a low-dose CT technique yielding a total dose of about 5 mSv per exam, an amount the Health Physics Society considers a risk that is either nonexistent or "too small to be measured". To demonstrate that a very minimal risk is associated with this dose, we would like to mention that:

- Average background radiation dose the general population receives in a year is about 3 mSv/year.
- The allowed radiation dose for radiation workers (like technologists) = 5 mSv/year.

We should also note the following:

- The risk from radiation exponentially decreases with age, as shown in the graph below. This is significant because candidates for VC screening are over 50 years of age and those candidates who are likely to be covered by the Medicare Program are generally 65 years of age or older. Moreover, because the risk of finding colorectal cancer **increases** with age, while the risk from radiation **decreases**[8] with age which makes the additional risk from a second or third screening CTC even less significant.



- More than 87% of patients will receive only one scan every five year. This was demonstrated in a large-cohort study done by Kim et al in which 87.1% of patients were negative.

The following Table shows a variety of things we do in our lives; each of the listed activities has the equivalent one-in-a-million risk of death or disease associated with it, which is in the range of the radiation risk typically posed by the use of CTC for colon cancer screening:

One-in-a-Million Risks of Death	Cause or Nature
Being male, aged 60 for 20 minutes	heart disease, cancer
Living 2 days in New York	air pollution
Living 2 months in Denver	cancer caused by cosmic radiation
Drinking Miami water for 1 year	cancer caused by chloroform
Traveling 6 minutes in a canoe	accident
Riding a bicycle for 10 miles	accident
Driving in a car for 300 miles	accident
Traveling in an airplane for 1000 miles	accident
Spending 1 hour in a coal mine	black lung disease
Working 10 days in a factory	accident
Smoking 1.4 cigarettes	heart disease, cancer
Drinking liter of wine	cirrhosis
Drinking 30 12 oz cans of diet soda	carcinogens
Eating 40 tablespoons of peanut butter	liver cancer due to aflatoxin

Question: How much training should be necessary for radiologist or gastroenterologist to read CTC?

Response: Clinicians who volunteered as "Readers" were required to take a competency test before they were allowed to participate in the ACRIN #6664 trial. Assuring appropriate physician training was the most critical component in the success of the study. According to the study authors, more than half of the readers had to go under additional training in order to pass the initial CTC certification exam, which indicates that CTC requires appropriate training. Both the ACR and AGA are in the process of setting guidelines for such training, and it is our belief that clinicians who read CTC examinations should be trained according to the guidelines set by the relevant specialty societies.

Question: What should be the minimum specifications for the scanner to be used for screening CTC?

Response: Most modern CT systems are capable of performing a CT colonoscopy, which requires a multi-slice scanner capable of 16 slices or more. Importantly, CTC should be able to carry out each of the two scans currently required in 10 seconds or less, to help keep breathholds short and radiation dose low. The interpretation software should have both 2-D and 3-D visualization capability. The goal is to ensure image quality is such that no repeat examinations are needed due to patient motion or failed breathholds. It is worth noting that all the scanners in the ACRIN trial included scanners 16-slice and above.

In our view, the ACRIN trial results, which will be published in a peer-reviewed journal in the near future, in combination with the recent modifications of the ACS colon screening guidelines,

unequivocally indicates that CTC meets colon cancer screening coverage criteria without the need for any additional data. This conclusion is supported by the results from several European trials and some earlier North American trials that are referenced in this letter.

However, in the unlikely event that CMS determines that additional data is needed, we urge CMS to adhere to the *"Guidance for the Public, Industry, and CMS Staff; National Coverage Determinations with Data Collection as a Condition of Coverage: Coverage with Evidence Development [CED]"*("Guidance Document") which was issued on July 12, 2007and to characterize any data collection activities that are required under the provisions of the Guidance Document that are applicable to Coverage with Appropriateness Determinations (CADs) , rather than to those applicable to Coverage with Study Participation (CSPs) . CADs are more appropriate, where, as here, there is adequate evidence to determine that an item or service is covered, but that additional clinical data is needed that is not routinely available on claims forms to ensure that the item or service is being provided appropriately. When an NCD requires CAD, only items or services for patients who are included in the data collection are covered; accordingly, a number of the CEDs that mandate participation in a registry as a precondition of coverage are CADs. By contrast, a CSP may be appropriate for less developed technologies for which the evidence is not adequate to support coverage, but where additional data gathered in the context of a controlled clinical trial would be helpful. Thus, a CSP requires a provider to participate in a CMS-funded clinical study as a precondition of coverage of an otherwise uncovered technology. In light of the significant body of clinical literature indicating that CTC is as effective as optical colonoscopy in the detection of clinically significant polyps, we believe that, IF CMS determines that unconditional coverage of CTC is inappropriate at this time, any additional data collection requirements should be developed in accordance with the procedures that have been used in the past by registries, and not limited to patient participation in more limited clinical trials.

We hope that these comments are helpful.

Sincerely yours,

Peter Martin, Ph.D.
Director, Colorectal Care Cycle
Philips Healthcare

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[1] http://www.cdc.gov/cancer/colorectal/basic_info/facts.htm

[2] http://www.cdc.gov/cancer/colorectal/statistics/screening_rates.htm

[3] "Association of Insurance with Cancer Care Utilization and Outcomes" Elizabeth Ward, Michael Halpern, Nicole Schrag, Vilma Cokkinides, Carol DeSantis, Priti Bandi, Rebecca Siegel, Andrew Stewart, and Ahmedin Jemal CA Cancer J Clin 2008 58: 9-31.

[4] "The National CT Colonography Trial: **ACRIN 6664**", **Johnson CD** et al, ***In Press***

[5] "Screening and Surveillance for the Early Detection of Colorectal Cancer and Adenomatous Polyps, 2008: A Joint Guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology", Bernard Levin, MD, David A. Lieberman, MD, Beth McFarland, MD, Robert A. Smith, PhD, Durado Brooks, MD, MPH, Kimberly S. Andrews, Chiranjeev Dash, MD, MPH, Francis M. Giardiello, MD, Seth Glick, MD, Theodore R. Levin, MD, Perry