MITA
MEDICAL IMAGING
& TECHNOLOGY ALLIANCE
A DIVISION OF NEMA

1300 North 17th Street ▪ Suite 900
Arlington, Virginia 22209
Tel: 703.841.3200
Fax: 703.841.3392
www.medicalimaging.org

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U.S. Food and Drug Administration
Office of the Commissioner
10903 New Hampshire Avenue
Building 32, Room 4254
Silver Spring, MD 20903-0002

RE: Docket No. FDA-2013-N-0816

Dear Sir/Madam:

This letter represents the comments of the Medical Imaging & Technology Alliance (MITA) in response to the request for submission of comments to the FDA Joint Gastroenterology-Urology Panel and Radiological Devices Panel for the Joint Panel ("Joint Panel") meeting on September 9, 2013.[1] The Joint Panel meeting is being convened to discuss the risks and benefits of computed tomography colonography (CTC) with respect to the screening of asymptomatic patients for colorectal cancer.

The Medical Imaging & Technology Alliance (MITA) is the leading U.S. trade association and collective voice of manufacturers and developers of medical imaging and radiation therapy equipment, and radiopharmaceuticals. MITA is in a unique position to have in-depth knowledge of the significant benefits to the health of patients that medical imaging provides, while also collectively working to enhance those benefits and mitigate risks through ongoing innovation. In addition, MITA is best able to comment on the substantive technology innovations to computed tomography (CT) systems in the past several years that have the ability to decrease radiation doses delivered to patients while preserving diagnostic image quality.

In the comments that follow, MITA will provide 1) general background on CTC and 2) specific comments on the significant technological innovations and other important initiatives which have been implemented with respect to CTC.

1. <u>General Background on CTC</u>

[1] 78 Federal Register 41937

Clinical Efficacy

Close to 150,000 people in the United States are diagnosed with colorectal cancer every year with nearly 50,000 dying because it is detected too late,[2] despite the low cost of fecal occult blood tests (FOBT) and wide availability of colonoscopy for colorectal cancer screening. Colorectal cancer is the third most frequently diagnosed cancer and the second leading cause of cancer death in both men and women in the United States.[3] MITA is keenly interested in bringing solutions to bear that can reduce those numbers, and we believe that CTC is one of those solutions.

CTC has advantages over other colorectal cancer screening. Unlike FOBT, which can only detect lesions that are actively bleeding, CTC can identify both bleeding and non-bleeding tumors as well as the clinically significant adenomatous polyps that could progress to cancer. CTC can consistently provide both 2D and 3D advanced visualization of the entire colon even in tortuous segments where instrumentation with colonoscopy frequently cannot be accomplished.

Like colonoscopy, CTC can detect clinically significant polyps. Published clinical trials comparing CTC to colonoscopy[4, 5] have demonstrated, and the United States Preventive Services Task Force (USPSTF) and the Centers for Medicare & Medicaid Services reviews of data[6,7] have noted, that CTC is able to identify clinically significant polyps (≥10 mm) in asymptomatic screening patients as equally well as colonoscopy. However, unlike colonoscopy, CTC is does not require sedation and the procedure is minimally invasive.

CTC has the potential to encourage and accomplish screening in many people who have not utilized other screening options. In a large prospective trial assessing colorectal cancer screening participation, in which randomized invitations for primary screening by either colonoscopy or CTC were sent to the general population, a higher participation rate was seen for CTC (34%) than for colonoscopy (22%).[8] Additionally, data collected by the National Naval Medical Center demonstrates that access to CTC raises screening levels. When given the option, 40 percent of

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[2] American Cancer Society, 2012. http://www.cancer.org/cancer/colonandrectumcancer/moreinformation/five-myths-about-colorectal-cancer

[3] American Cancer Society. Cancer Facts and Figures, 2012. http://www.cancer.org/acs/groups/content/@epidemiologysurveilance/documents/document/acspc-031941.pdf

[4] Pickhardt PJ, Choi JR, Hwang I, Butler JA, Puckett ML, Hildebrant HA, et al. Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults. N Engl J Med. 2003;349:2191-200.

[5] Johnson CD, Chen MH, Toledano AY, Heiken JP, Dachman A, Kuo MD, et al. Accuracy of CT colonography for detection of large adenomas and cancers. N Engl J Med. 2008;359:1207-17.

[6] Screening for Colorectal Cancer: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med. 2008; 149(9):627-637.

[7] Centers for Medicare & Medicaid Services. Decision Memo for Screening Computed Tomography Colonography (CTC) for Colorectal Cancer (CAG-00396N). May 12, 2009 http://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=220&ver=14&NcaName=Screening+Computed+Tomography+Colonography+(CTC)+for+Colorectal+Cancer&bc=BEAAAAAAEAAA&&fromdb=true Accessed August 24, 2013

[8] Stoop EM, de Haan MC, de Wijkerslooth TR, et al. Participation and yield of colonoscopy versus noncathartic CT colonography in population-based screening for colorectal cancer: a randomised controlled trial. *Lancet Oncol* 2012; 13:55–64

patients chose to undergo CTC.[9] Moreover, 37 percent of patients who underwent colon cancer screening said they would not have been screened without CTC.

Innovation

MITA member companies have made significant investments over the last two decades that have brought unprecedented improvements to medical imaging in general and CT in particular. These advancements have revolutionized the ability to rapidly resolve diagnostic dilemmas, diagnose and stage disease, and give clinicians greater information to use in making treatment decisions with their patients.

One of those innovations two decades ago called helical technology revolutionized how CT images are captured, and opened up new opportunities of non-invasive, high resolution imaging of patient anatomy. Helical technology directly made possible the advent of virtual colonoscopy, now generally called CTC, which provides 3D fly-through visualization of the colon that mimics the views seen with colonoscopy. In the early days of CTC, the success of the tool in identifying polyps was somewhat variable. As adoption and use of CT increased, imaging techniques were refined, and technological advancements were made, with the result that CTC became a more robust and practical screening option.

In 2008, the USPSTF examined CTC for the purpose of assessing its role as a screening option for colorectal cancer. USPSTF accepted that the procedure was comparable to colonoscopy in its ability to detect clinically significant polyps (≥10 mm) in a screening cohort. However, USPSTF concluded that the evidence was insufficient at that time to adequately assess the net benefits compared to risks of screening CTC. A particular concern was the unknown potential for patient harm from exposure to radiation during the exam.

Since the time of the USPSTF statement, and with a desire to keep radiation dose as low as possible in all imaging procedures, MITA member companies have developed a number of ways to address and mitigate the delivered dose in screening CTC, while continually improving the ability of these technologies to aid physicians in recommending treatment options to their patients. These new dose reduction strategies reflect a collaborative industry-wide imperative to innovate, develop, and implement additional patient protection features for CT equipment, and demonstrate industry commitment to the "As Low As Reasonably Achievable" (ALARA) principle.

2. Specific Comments

Technology Innovations in CT Systems to Mitigate Radiation Dose

Dose efficiency and dose reduction have been important design considerations for CT for many years. The focus on these design considerations has grown and intensified in more recent years, and has yielded a variety of new and innovative hardware and software features that directly help physicians both reduce and monitor dose for CT exams, including CTC. These features have built upon each other such that what may have once been an 8-10 mSV CTC exam is now

9 Cash Brooks D.Stamps Kathryn, McFarland Elizabeth G.Spiegel Andrew R.Wade Sally W.. Clinical Use of CT Colonography for Colorectal Cancer Screening in Military Training Facilities and Potential Impact on HEDIS Measures. Journal of the American College of Radiology (2013) 10:1, 30-36

possible at doses in the 1 mSv range. These newly obtainable lower doses compare favorably to the 3 mSv of background radiation a person is typically exposed to, and serve to make the risk vs. benefit equation significantly more favorable.

A key element for any dose reduction feature is that diagnostic quality must not be compromised; all of the features mentioned below uphold this principle. The ability to record and monitor dose is also an important aspect of any radiation safety program. Here too, the CT industry has developed new features that enable both the dose to be displayed prior to scanning, and to alert operators to potentially higher than expected doses, as well as enabling electronic recording of the CTC dose in the patient record. These features are important for both the patient as well as facilities, since they provide facilities with the ability to compare the dose of their CTC protocols and establish optimized reference values.

The dose monitoring/reduction features described below play a significant role in helping to reduce the dose for CTC exams, while maintaining diagnostic quality and the capability to report and record dose. As noted in the list below, many of these features are now standard on CT systems without additional charges. Many of these features are also available as upgrades to existing system so that older CT's can achieve the benefits of the latest innovations in dose reduction.

For example:

- Automatic Exposure Control helps optimize dose for each patient for the given diagnostic task. This feature adjusts the exposure to use only what is needed to maintain a constant image quality. This feature is now standard on CT systems.
- Wider coverage detectors minimize the amount of x-ray that falls outside of the active detector region, thereby reducing dose to the patient without impacting image quality. Systems are now available in a range of wide coverage designs.
- "Shutter" modes block unused x-ray at the beginning and end of helical scans and therefore do not degrade image quality. This feature is now standard on many CT systems and is "built in" to each helical acquisition.
- Advanced electronics in data acquisition systems result in better imaging performance and less noise, thereby enabling equal performance at a lower dose.
- First generation CT iterative reconstruction results in a significant dose reduction potential, while maintaining diagnostic image quality, and is well suited to CTC studies. Iterative reconstruction is available on new systems and also as an upgrade to many installed base systems.
- More advanced second generation CT iterative reconstruction provides even further dose reduction potential, where some expert users are able to achieve some exams approaching 1 mSv levels for combined supine and prone CTC scans, while still maintaining diagnostic image quality. This feature is becoming widely available on new systems.
- The DICOM Dose Structured Report allows the exam dose to be electronically captured with the patient record. This feature is now standard on all new CT systems and has also been implemented on newer installed base systems.

CTC Radiation Dose

CTC is a low dose procedure. A review of the current data on CTC concluded that state-of-the-art techniques used in CTC can reduce dose to about 3 mSv or less (similar to annual background radiation levels in the United States). [10] The authors further noted that three different radiation physics professional societies now discourage the calculation of risk below 50-100 mSv because risk is too small to estimate with any accuracy. One society, the American Association of Physicists in Medicine, states that the risks of medical imaging at effective doses below 50 mSv for a single procedure, or 100 mSv for multiple procedures, over short time periods are too low to be detectable and thus the risks may be non-existent. [10]

Due to low dose and high clinical efficacy, CTC has a high benefit-to-risk profile. A benefit- to-risk analysis on radiation used in screening CTC used three micro-simulation models to assess the radiation dose used in the ACRIN National CT Colonography Trial. [11] The goal of the study was to compare the benefit – to - risk ratio of CTC by projecting the number of lives saved from CTC screening and comparing this projection to the deaths from cancer induced by the radiation used in the CTC procedure. In the study, the investigators calculated that CTC screening would be performed every five years from age 50 to age 80 years, and they included the radiation that would be employed in subsequent investigation of extra colonic findings that were identified during the CTC exams. The investigators concluded that the benefit – to - risk ratio substantially favored CTC by ratios from 24:1 to 35:1.

Industry Standards

MITA leads industry efforts to coordinate and establish standards to mitigate radiation dose. Adoption of these standards benefits patient dose. MITA's approach builds upon existing manufacturer safety measures – including equipment safety standards, protocol development, quality and safety checks, provider education programs and physician-developed medical guidelines – to minimize radiation dose as much as possible, and to provide even greater degrees of coordination, transparency and reporting in the delivery of medical radiation. Recent examples of MITA standards which have addressed dose include:

- NEMA XR 25-2010, *Computed Tomography Dose Check*. This standard introduced two novel features to assist the imaging team in providing better patient care: dose notifications and dose alerts. Dose notifications are designed to provide a clear indication to health care providers when the parameters for a CT scan will result in a dose higher than the facility's pre-determined dose threshold for routine use. Dose alerts are designed to prevent dose levels for a complete exam from exceeding pre-determined thresholds that are deemed excessive by the facility. This feature can be configured to prevent equipment operation. These protections help the operator and ultimately the physician to better understand dose implications of protocol choices, and should significantly reduce exposure due to inappropriate scan parameter settings.

[10] Yee J, Keysor KJ, Kim DH. The Time Has Arrived for National Reimbursement of Screening CT Colonography. AJR 2013; 201:73-79

[11] Berrington de González A, Kim KP, Knudsen AB, et al. Radiation Related Cancer Risks From CT Colonography Screening: A Risk-Benefit Analysis. AJR 2011; 196:816-823

- NEMA standard XR 26 - 2012, *Access Controls for Computed Tomography: Identification, Interlocks, and Logs.* This standard requires software features that ensure only an authorized operator can alter the controls of CT equipment. This industry-wide standard requires the institutionalization of administrative privileges, access levels, and the recording of clinical protocols to ensure safe and appropriate use.
- NEMA standard XR 27 - 2012, *X-ray Equipment for Interventional Procedures User Quality Control Mode*. This standard helps imaging facilities conduct quality testing and monitoring of X-ray equipment used for interventional procedures.
- NEMA standard XR 29 - 2013, *Standard Attributes on Computed Tomography (CT) Equipment Related to Dose Optimization and Management*. This standard, known also as MITA "*Smart Dose"*, is the fourth dose-related standard to be released by MITA since 2010. This standard includes four components:
    1. DICOM Dose Structured Reporting – This enables the recording of post-exam dose information in a standardized electronic format. This information can be included in the patient record, promoting the establishment of diagnostic reference levels, as well as facility dose management and quality assurance.
    2. Pediatric and adult reference protocols – These are a set of pre-loaded protocols on a CT system that serve as a baseline for a variety of clinical tests.
    3. CT Dose Check – CT Dose Check incorporates two features—dose notifications and dose alerts that can inform operators and physicians when dose exceeds established thresholds.
    4. Automatic Exposure Control (AEC) – AEC automatically adjusts the amount of radiation used based on the size, shape and composition of the patient, in order to achieve a specified level of image quality. Studies of AEC procedures have demonstrated dose optimizations and reductions when used properly.

Education

Manufacturers provide comprehensive applications training on new CT scanners that includes robust instruction on the latest techniques and best practices to tailor radiation dose to the lowest level needed to capture diagnostic quality images.

Member companies provide educational grants to support a wide variety of Continuing Medical Education (CME) programs for radiologists/technologists. Programs include optimizing and minimizing dose during CT exams, most of which are offered at no cost or minimal cost through a wide array of sources, to maximize the number of providers who are aware of the latest cutting edge strategies for dose modulation.

Appropriateness

MITA advocates the development and use of physician-developed appropriateness criteria to guide treatment decisions and training of hospital and imaging facility personnel who perform medical imaging exams. In order to provide optimal care and prevent medical errors, physicians and technologists must account for the patient's individual needs, including adjusting dose levels based on these needs and characteristics. By providing proper training and adhering to these standards and initiatives, physicians can limit unnecessary radiation exposure and ensure that patients receive the life-saving benefits of medical imaging technology.

Conclusion

In summary, since the 2008 USPSTF statement on CTC was issued, almost 750,000 people in the United States have been diagnosed with colorectal cancer, and approximately 250,000 people have died from the disease.[12] MITA supports the value of CTC as a frontline tool that can provide a viable, alternative screening option for people who are currently resistant to customary colorectal cancer screening modalities, and may otherwise avoid colorectal cancer screening altogether.

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MITA appreciates the opportunity to share its views with you. If you have any further questions, please feel free to contact me. I can be reached at (703) 841 – 3235, or by email at grodriguez@medicalimaging.org.

Respectfully,

Gail Rodriguez, Ph.D.
Executive Director, MITA

[12] American Cancer Society. Cancer Facts and Figures http://www.cancer.org/research/cancerfactsstatistics/allcancerfactsfigures/index Accessed August 29, 2013