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Fast Analytical Approach of Application Specific Dose Efficient Spectrum Selection for Diagnostic CT Imaging and PET Attenuation Correction

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Abstract

Computed Tomography (CT) has been used for a variety of applications, two of which include diagnostic imaging and attenuation correction for PET or SPECT imaging. Ideally, the X-ray tube spectrum should be optimized for the specific application to minimize the patient radiation dose while still providing necessary information. In this study, we proposed a projection-based analytic approach for the analysis of contrast, noise, and bias. Dose normalized contrast to noise ratio (CNRD), inverse noise normalized by dose (IND) and bias are used as evaluation metrics to determine the optimal X-ray spectrum. Our simulation investigated the dose efficiency of the X-ray spectrum ranging from 40 kVp to 200 kVp. Water cylinders with diameters of 15cm, 24 cm, and 35 cm were used in the simulation to cover a variety of patient sizes. The effects of electronic noise and pre-patient copper filtration were also evaluated. A customized 24 cm CTDI-like phantom with 13-mm diameter inserts filled with iodine (10 mg/ml), tantalum (10 mg/ml), water, and PMMA was measured with both standard (1.5 mGy) and ultra-low (0.2 mGy) dose to verify the simulation results at tube voltages of 80, 100, 120, and 140 kVp. For contrast-enhanced diagnostic imaging, the simulation results indicated that for high dose without filtration, the optimal kVp for water contrast is approximately 100 kVp for a 15 cm water cylinder. However, the 60 kVp spectrum produces the highest CNRD for bone and iodine. The optimal kVp for tantalum has two selections: approximately 50 and 100 kVp. The kVp that maximizes CNRD increases when the object size increases. The trend in the CTDI phantom measurements agreed with the simulation results, which also agree with previous studies. Copper filtration improved the dose efficiency for water and tantalum, but reduced the iodine and bone dose efficiency in a clinically-relevant range (70 to 140 kVp). Our study also shows that for CT-based attenuation correction applications for PET or SPECT, a higher-kVp spectrum with copper filtration is preferable. This method is developed based on filter back projection and does not require image reconstruction or Monte Carlo dose estimates; thus, it could potentially be used for patient-specific and task-based on-the-fly protocol optimization.

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1. Introduction

Computed Tomography (CT) is widely used in various clinical applications for disease diagnosis, such as cardiac imaging, colonography, angiography and urology (Jiang 2009, Fleischmann and Boas 2011, Prokop *et al* 2003). CT scans are also used in positron emission tomography (PET-CT) and single photon emission computed tomography (SPECT-CT) imaging, primarily for anatomical localization but also for attenuation correction (Townsend *et al* 2004, Tsukamoto and Ochi 2006, Willowson *et al* 2008). The number of CT scans performed every year has dramatically increased, resulting in an increase in total radiation dose delivered to general population (Brenner and Hall 2007, W.A. Kalender 2014). This dose increase has led to concerns within the medical community (Brenner *et al* 2001, Brody *et al* 2007). Technologies have been developed to optimize image quality and minimize patient dose, through improved hardware, scan protocol design, and image reconstruction algorithms (Elbakri and Fessler 2003, Thibault *et al* 2007). Dose reduction techniques such as tube-current modulation and low-voltage protocols have been developed and implemented on commercial CT systems (Gies *et al* 1999, Kalender *et al* 1999, Dougeni *et al* 2012). Moreover, a computer-assisted scan protocol and reconstruction (CASPAR) method has been proposed to achieve the optimal tradeoff between radiation dose and image quality for task- and patient-specific conditions (Sperl *et al* 2010).

Scan protocol design ideally selects the optimal spectrum. Clinical CT systems typically operate at peak X-ray tube voltage (kVp) in the range of 70 to 140 kVp. For diagnostic CT imaging, contrast-enhancing material such as iodine is often injected into the patient to enhance image contrast in the vasculature and blood-perfused soft tissue. Several studies investigated the selection of the optimal kVp based on the contrast material and patient size (Huda *et al* 2004, Kalender *et al* 2009, Yu *et al* 2010). For imaging using iodine-based contrast agents (CA), lower kVp is preferred (Boone *et al* 2003, Funama *et al* 2005, Schueller-Weidekamm *et al* 2006). In order to evaluate contrast, noise, and dose in images, image reconstruction and Monte Carlo dose simulations are usually performed; these are both computationally expensive and time consuming to perform across a multitude of scenarios. In this study, we developed a fast analytical approximation approach, which uses analytical estimates of contrast, noise and dose in the projection domain. This algorithm can be used for a quick screening of a set of spectra in the prediction of optimal spectrum given tasks. In parallel, several alternatives to iodine as a contrast-enhancing element have been investigated (Gamsu 1974, Nowak *et al* 2011). Of these, tantalum is a promising choice (Torres *et al* 2012, Bonitatibus *et al* 2010, 2012), and the dose efficient spectrum can potentially be evaluated using the analytical approach mentioned above.

The evaluation metrics used for kVp selection in the previous studies were mostly based on the analysis of contrast-to-noise ratio normalized by dose (CNRD), which is relevant for diagnostic CT. However, CT scans used to provide a CT-based attenuation correction (CTAC) map for PET reconstruction (Kinahan *et al* 1998) have different requirements than diagnostic CT scans. For PET image reconstruction, the attenuation coefficients at 511 keV must be calculated from CT data acquired at 70–140 kVp (Townsend *et al* 2004). Noise and errors in the CTAC values propagates to PET images, resulting in artifacts which may affect

clinical diagnosis. Therefore, it is important that the CTAC image have low noise and bias, whereas contrast is of less importance. Thus, the desired goal is high accuracy at the lowest radiation dose, which can be significantly lower than diagnostic CT (Rui *et al* 2015). There are few studies focusing on the optimal spectra for CTAC acquisition, but one study observed that using a high kVp spectrum and filtering the X-ray beam through a thin layer of copper improved the CTAC maps, thus providing improved PET images (Xia *et al* 2012). Our study further investigates and explains the selection of the X-ray spectrum for CTAC and provides insights for application-based protocol design.

To avoid the impact of electronic noise, a frequently-stated requirement in previous studies is that the electronic noise must not be higher than half the magnitude of the maximally expected quantum noise (Kalender 2005). When the dose is reduced, electronic noise cannot be neglected and it impacts the selection of the spectrum. For 'ultra-low dose' levels, i.e. those with radiation dose levels an order of magnitude below current low-dose protocols, the effect of electronic noise can dominate image quality. In this study, we evaluated the selection of the optimal spectrum in the presence of electronic noise, especially at ultra-low dose. Pre-patient filters can be used to reduce the dose delivered to the patient. It is common for clinical CT systems to use a "bowtie filter" which is a pre-patient attenuator to spatially modulate the flux of the fan beam (J. Hsieh, 2009). Additional high Z metal filters such as copper and gold could be used to further improve dose efficiency (Nowak *et al* 2011, Xia *et al* 2012). We explored the possibility of adding extra copper filtration to the X-ray beam, and analyzed its impact on both diagnostic CT scans and CT scans for CTAC.

In this study, we used a fast analytical approximation approach to estimate dose efficiency with respect to the X-ray spectra for diagnostic CT imaging, contrast-enhanced CT imaging with iodine and tantalum, and CTAC for PET. We also performed phantom scans with inserts containing water, PMMA, iodine, and tantalum, and compared the trends in the measurement results with the predictions provided by our analytical method.

2. Material and Methods

We first describe the projection-domain analysis method and the simulations performed to evaluate the dose efficiency associated with a broad range of X-ray spectra. We then use the projection-domain method to identify the optimal spectra for diagnostic CT and for CTAC. To evaluate the validity of the trends in our simulation results, we performed CT scans of a representative CTDI phantom, including various contrast material samples relevant to diagnostic CT scanning.

2.1 Projection domain simulation method

2.1.1 Analysis for diagnostic CT imaging—The method developed in this section considers a linear reconstruction algorithm only, namely filtered backprojection (FBP) (Kak and Slaney 1999). In contrast to iterative reconstruction algorithms, the noise and contrast on the FBP reconstructed images are approximately linearly related to the noise and contrast in the projection measurement (Sperl *et al* 2010). Here we developed methods for estimating each of these parameters using analytical calculations in the projection domain. We applied

these methods to a single projection of computational phantoms representing circular water cylinders of various sizes.

For a polychromatic X-ray spectrum, the incident photon count is a random number I_o with a mean value of $N_o = \int N_0(E) dE$. After attenuation by an object, the mean value of the transmitted photon count at energy E is $N_k(E) = N_0(E) e^{-\sum_k \mu_k(E) l_k}$, and the transmitted photon count is a Poisson random number I_t with mean and variance of

$$N_t = \int N_0(E) e^{-\sum_k \mu_k(E) l_k} dE, \quad (1)$$

where l_k is the intersection length of the projection ray with the object for material k , and $\mu_k(E)$ is the attenuation coefficient. The variance of Poisson noise in the transmitted X-ray photon count is:

$$\sigma_t^2 = N_t. \quad (2)$$

For an ideal energy-integrating detector, the energy of all transmitted X-ray photons is absorbed by the detector and converted to electrons. The electronic noise in the data collecting system needs to be considered. Therefore, the variance of the noise in the transmitted measurements I_{tm} is

$$\sigma_{tm}^2 = \int g^2 E^2 N_0(E) e^{-\sum_k \mu_k(E) l_k} dE + \sigma_e^2, \quad (3)$$

where g is the conversion factor from energy to electrons, E is the energy of the X-ray photon and σ_e^2 is the variance of electronic noise associated with each detector cell, and is in units of electrons.

Typically, a negative logarithm operation is performed to obtain the projection value:

$$p = -\log \frac{I_{tm}}{I_{0m}}, \quad (4)$$

where I_{0m} is the measurement without attenuating object by the energy-integrating detector. The variance of the projection value p can be related to the variance of pre-log measurement I_{tm} based on linearizing the log operation using a Taylor Series expansion:

$$\sigma_p^2 \approx \left| \frac{\partial p}{\partial I_{tm}} \right|^2 \sigma_{tm}^2 = \frac{\int g^2 E^2 N_0(E) e^{-\sum_k \mu_k(E) l_k} dE + \sigma_e^2}{\left(\int g E N_0(E) e^{-\sum_k \mu_k(E) l_k} dE \right)^2}. \quad (5)$$

We used projection domain contrast in our analysis. It is defined as the difference in attenuation when an object of interest is inserted and replaces the background attenuation. In

the simulation, along the path of the projection ray, a small amount of the contrast material (Δl) is inserted at the center of the water cylinder in place of the background material (typically, water is used as a background material in this simulation). For a given energy E , the material contrast $C(E)$ is defined as follows (Eq (6) ~ (9)).

Water contrast in projection (a surrogate for soft-tissue contrast) is defined as a small perturbation of the attenuation based on the water background, which is:

$$C_w(E) = ((1 + \delta)\mu_w(E) - \mu_w(E))\Delta l, \quad (6)$$

where δ is a small constant. Iodine contrast is defined as:

$$C_i(E) = (\mu_i(E) - \mu_w(E))\Delta l. \quad (7)$$

For a polychromatic beam, the material contrast C for a given material with attenuation coefficient of $\mu(E)$ at given energy E , in projection, is defined as the transmitted photon flux-weighted average of the monochromatic contrast,

$$C \equiv \frac{\int C(E)N_t(E)dE}{N_t} = \frac{\Delta l \int (\mu_i(E) - \mu_w(E))N_0(E)e^{-\sum_k \mu_k(E)l_k}dE}{N_t} \quad (8)$$

Since Δl is only a scale factor, it can be dropped, and the contrast in projection can be defined as

$$C \equiv \frac{\int (\mu_i(E) - \mu_w(E))N_0(E)e^{-\sum_k \mu_k(E)l_k}dE}{N_t}. \quad (9)$$

Accurate dose calculation typically uses the Monte Carlo method, which is computationally costly and time consuming. In the projection domain analysis method, we use total energy released per unit mass (Terma) as a surrogate for the absorbed dose. Terma, D_t , has been well corrected and shown to have a linear relationship with absorbed dose (Tian *et al* 2013), and is simply the difference between the incident energy and the transmitted energy:

$$D_t = \int EN_0(E)(1 - e^{-\sum_k \mu_k(E)l_k})dE = \int EN_0(E)dE - \int EN_t(E)dE. \quad (10)$$

Thus D_t can be used as a relative dose measurement.

2.1.2 Analysis for CT attenuation correction (CTAC)—Since PET requires 511 keV CTAC, the CT projection needs to be converted to projection values at 511 keV. In our simulation, a water cylinder is used as the object, and the projection value at 511 keV can be written as

$$p_{511} = \mu_{w511} l \quad (11)$$

where μ_{w511} is the attenuation coefficient for water at 511 keV, and l is the intersection length.

A polychromatic X-ray beam is typically used for CT imaging. As the X-ray photons are attenuated by the object, low-energy photons are preferentially absorbed; therefore, after logarithm conversion, the projection p is not linearly proportional to the thickness (Brooks and Di Chiro 1976). The “hardening” of the X-ray beam can result in artifacts in the reconstructed images, and is often corrected by a non-linear function; for example, a polynomial correction can be applied (Herman 1979, Hsieh *et al* 2000).

The CT projection p that we obtained from the polychromatic X-ray beam measurement needs to incorporate the beam-hardening correction and then be converted to the 511 keV projection

$$p_{511} = f(p(l)) \quad (12)$$

where function f is a non-linear function that performs the beam-hardening correction and converts the corrected projection value to a 511 keV projection value, and l is the thickness of the material, assuming that only one material exists along that projection path. From equation (4), we can derive

$$\frac{\partial p}{\partial l} = \frac{\int \mu_w(E) N_0(E) e^{-\mu_w(E)l} dE}{\int N_0(E) e^{-\mu_w(E)l} dE} \triangleq \mu_{w\text{eff}}, \quad (13)$$

where $\mu_{w\text{eff}}$ is defined as the effective water attenuation coefficient for a given polychromatic spectrum. Therefore,

$$\frac{\partial p_{511}}{\partial p} = \frac{\partial p_{511}}{\partial l} \frac{\partial l}{\partial p} = \frac{\mu_{w511}}{\mu_{w\text{eff}}} \triangleq a, \quad (14)$$

This process implicitly takes into account the beam hardening correction for the projection with polychromatic spectrum, which is inherited in the factor a . With this direct conversion of the projection measurement, at a given path length of water, the variance from the original projection can be calculated as:

$$\sigma_{p_{511}}^2 = \left(\frac{\partial p_{511}}{\partial p} \right)^2 \sigma_p^2 = a^2 \sigma_p^2. \quad (15)$$

If multiple materials need to be included in the analysis, when converting the original CT images to the 511 keV CTAC maps, a bilinear conversion or possibly trilinear conversion can be applied (Kinahan *et al* 2003). The propagation of the variance can be derived similarly as well.

For diagnostic CT images, dose-normalized contrast-to-noise ratio (CNRD) is often used as the evaluation metric (Kalender *et al* 2009). However, for CTAC analysis, besides the variance, bias in the data at 511 keV is also critical. We performed simulations for different spectra to analyze the bias in the projection data. The noise in the pre-log projection data has two components: quantum noise, which has a Poisson distribution, and electronic noise, which has a Gaussian distribution. We simulated the two different noise processes separately. For energy E , the attenuated photon count is

$$N_t(E) = \text{Poisson}(N_0(E)e^{-\sum_k \mu_k(E)l_k}). \quad (16)$$

For an energy-integrating detector, the Gaussian distributed electronic noise is added to the signal collected, which is an energy weighted integral of the attenuated photon counts.

$$S = \text{Gaussian}(\int E N_t(E) dE, \sigma_e^2). \quad (17)$$

If the attenuated photon count becomes very low, the signal with electronic noise can become a negative signal.

Before performing the logarithm operation, negative numbers must be converted to small positive numbers, which introduces bias in the measurement. We replaced non-positive signals with a small positive number ϵ .

The original CT projection value is converted to the 511 keV projection value using the same conversion factor a described in the previous section. The bias in 511 keV projections is then calculated as:

$$\text{Bias}_{511} = E[p_{\text{noisy}511}] - p_{\text{no-noise}511}, \quad (12a)$$

where the $p_{\text{noisy}511}$ represents the projection at 511 keV converted from simulation with Poisson and electronic noise, and $p_{\text{no-noise}511}$ represents the projection at 511 keV converted from the electronic-noise-free projection simulation.

2.1.3 Simulation studies—We chose a circular water cylinder as our simulation subject. For the contrast analysis, a small region at the center (1 mm diameter) was replaced by the contrast material to introduce a small perturbation in the projection value. Three water cylinder diameters were used: of 15 cm, 24 cm and 35 cm to represent pediatric, small adult and adult abdomen scans. Four different types of contrast material were evaluated in the simulation, including water, bone, iodine and tantalum. To evaluate the impact of electronic noise, three dose levels were simulated. The dose levels were normalized to the dose of

using 100 kVp spectrum at 1, 10, and 100 mA (referred as dose-1mA, dose-10mA and dose-100mA, in Table 1.). We used spectrum files in the CatSim software package (De Man *et al* 2007), which were generated by the XSPECT package. We simulated the geometry of a GE LightSpeed VCTTM scanner and traced one projection ray through the object center. We evaluated spectra with X-ray tube voltages ranging from 40 kVp to 200 kVp, with 10 kVp step size. Each spectrum is represented by 0.5 keV energy bins. Poisson noise, electronic noise, and detection efficiency were included in the simulations. We performed simulations with and without a 1-mm copper (Cu) filter in the X-ray beam. The simulation conditions are summarized in Table 1. For bias simulation, 1 million simulations were performed to obtain robust statistics.

We also performed a Monte Carlo study using the GEANT4 toolkit (Agostinelli *et al* 2003) and compared our numerical model to the Monte Carlo simulation. We simulated the scenario of a pencil beam with polychromatic spectrum at 80 kVp interacting with a rectangular prism of water. The size of the water prism was 40 cm in width, 24 cm in height, and 40 cm in length. We simulated the geometry of the GE LightSpeedTM VCT system with a scanning protocol of 1.0 s rotation, 984 views at two dose levels: 100 mAs and 10 mAs. The central ray from the large bowtie was simulated with 10^5 events for each dose level. Figure 12-A shows a schematic overview of the Monte-Carlo simulation. The probability distribution of the total energy deposited on the detector was obtained from both our Monte Carlo simulation and our numerical model.

2.2 CTDI phantom studies

To verify the simulation results, we scanned a 24-cm diameter, modified CTDI phantom (made from a commercial 32 cm CTDI phantom) with a material sample (water, iodine solution tantalum solution, or PMMA) inserted at the center (Figure 1. (A)). The circumference of the 32-cm CTDI phantom is 40 inches, which corresponds to a water cylinder with a circumference of 47 inches given the PMMA density (1.18 g/cm^3). It therefore represents an overweight-obese patient. To better represent a normal adult abdomen, we cut down the CTDI phantom diameter to 24 cm, which corresponds to a water cylinder with a circumference of 35 inches. Scans were performed on a 64-slice clinical CT scanner (LightSpeedTM VCT, GE Healthcare). Scan parameters are shown in Table 2, using axial mode with a 1-second rotation time and 10-mm collimation. The narrow collimation was chosen to reduce the effect of scatter. The tube current was selected to achieve approximately the same dose level as shown in Table 2. Scans were performed in service mode, which allows fine tuning of the tube current in 5 mA steps to allow approximately equal dose at the different tube voltage settings. For each scan, sixteen images were reconstructed using a filtered back projection (FBP) algorithm with the standard kernel and a 500 mm FOV.

The concentrations of the iodine and tantalum solutions were both 10 mg active element / mL. The sample was installed in a vial inserted in the center of the phantom. The vial provided a 13-mm-diameter cross-section of the sample, of which a 10-mm-diameter sample ROI (ROI 1, Figure 1 (C)) was used. Image contrast was determined as the difference in the average HU between the contrast materials inserts and water inserts in the sample ROI. We

defined a “noise” ROI (ROI 3, Figure 1 (C)) as an annulus with 130-mm inside diameter and 150-mm outside diameter. The noise was determined as the variance in the noise ROI. We defined a “background” ROI (ROI 2, Figure 1 (C)) as an annulus with 20-mm inside diameter and 40-mm outside diameter for contrast analysis. For ultra-low dose measurement, the bias for each ROI region was obtained by calculating the difference between the mean of the ROI in the ultra-low dose measurement and the corresponding standard dose measurement at the same kVp. For each phantom, measurements were averaged for sixteen images from the same scan. The large ROIs and averaging over images were intended to provide robust statistics.

2.3 Evaluation metrics

For diagnostic CT imaging, the contrast-to-noise ratio (CNR) is an essential metric to evaluate the image quality. To make the metric independent of mA, the dose efficiency can be represented by the dose-normalized contrast-to-noise ratio (CNRD) (Kalender *et al* 2009):

$$\text{CNRD} = \frac{C}{\sigma \sqrt{D}}. \quad (19)$$

For CTAC analysis, the attenuation map at 511 keV is required. The constant between any given materials at this single energy remains constant, so we set the contrast to 1 and use inverse noise normalized by dose (*IND*) in our CTAC analysis:

$$\text{IND}_{511} = \frac{1}{\sigma_{p511} \sqrt{D}}. \quad (20)$$

Bias in the measurement is also used as an important evaluation metric for CTAC analysis. The definitions of contrast (*C*), noise (σ), bias, and dose (*D*) for simulation and phantom measurement can be found in the description in the previous sections. Note that in the simulations, contrast, noise and bias are defined in the projection domain, but for the phantom measurements, these metrics are measured in image domain. The dose is represented by Terma (*D_t*) in the simulations and by the CTDI measurement in the phantom scans.

3. Results

3.1 Simulations for assessment of diagnostic CT imaging

The CNRD curves for water (representing soft tissue), bone, iodine and tantalum are shown in Figure 2-A (15-cm phantom), Figure 2-B (24-cm phantom), and Figure 2-C (35-cm phantom) for the case without electronic noise. The CNRD represents dose efficiency, where the highest dose efficiency is found at the highest CNRD. For easier plotting, the CNRD curves for each material were normalized to the maximum CNRD value for that material in the condition of no filtration.

When no filtration is used, for the 15-cm phantom, the CNRD curve for water is relatively flat, and decreases below 80kVp. As the subject size increases, water contrast is more dose-efficient at higher kVp. For the 24-cm phantom, the optimal kVp for water is greater than 140 kVp. For the 35-cm phantom, the water contrast again prefers higher kVp for better dose efficiency – in this case the highest dose efficiency for water was found at 200 kVp, the highest kVp in our simulation. For bone and iodine contrast, lower kVp settings are more dose efficient. For the 15-cm phantom, the 60-kVp spectrum produces the highest dose efficiency for bone and iodine. The optimal kVp for tantalum occurs at two tube voltages: one is around 50 kVp, the other is around 100 kVp. The most dose-efficient kVp increases for these contrast materials when subject size increases. For the 35-cm phantom, the optimal kVp for iodine and bone contrast is around 80 kVp. For tantalum, the most dose-efficient kVp increases to 120 kVp.

With the 1-mm-Cu filter added, despite the phantom size, the dose efficiency decreased for bone and iodine above 100 kVp. There is improvement in the iodine and bone dose efficiency with filtration at extremely low kVp (less than 60 kVp). The dose efficiency for water and tantalum increases with filtration at high kVp.

Figure 3 shows the CNRD curves for water (A), bone (B), iodine (C) and Tantalum (D) at three different dose levels with and without filtration for the 24 cm phantom simulation. Electronic noise is included for the simulation. Similar results were expected for other phantom sizes, so we picked up the 24-cm phantom to represent the analysis. For easier plotting, the data were normalized to the maximum CRND values for each material without filtration at dose-100mA. For a given spectrum, when dose is reduced from dose-100mA to dose-1mA, the dose efficiency reduces due to the impact of electronic noise for same spectrum. At low dose, where electronic noise has a substantial contribution, the optimal kVp for contrast imaging increases. For water contrast, when dose decreases from dose-100mA to dose-1mA, the optimal kVp increases from around 140 kVp to around 200 kVp. For bone contrast, the optimal kVp increases from 60 kVp to 140 kVp. For iodine contrast, the optimal kVp increases from 60 kVp to 100 kVp. For tantalum contrast, the optimal kVp increase from 100 kVp to 150 kVp. The impact from Cu filtration is similar at low dose when compared to the case of high dose. In the clinically-relevant kVp range, which is typically from 70 kVp to 140 kVp, the filtration improves the dose efficiency for water and tantalum but decreases the dose efficiency for bone and iodine.

3.2 Simulations for assessment of CTAC

For CTAC analysis, the dose efficiency of the spectrum is evaluated based on noise and bias. The IND curves for 511-keV CTAC are shown in Figure 4. Electronic noise was included in this simulation. For easier plotting, for each phantom size, the IND curves were normalized to the maximum IND value without filtration at dose-100mA. Considering noise, without Cu filtration, for the 15-cm phantom, the most dose-efficient kVp is around 100 kVp. As the phantom size increases, higher kVp was found to be more dose efficient. At low dose (dose-10mA and dose-1mA), the dose efficiency for a given kVp decreases due to the impact of the electronic noise, resulting in higher dose efficiency at higher kVp. With the filtration, the dose efficiency for a given spectrum improves at all dose levels. The optimal kVp with

filtration is around 60 kVp for the 15-cm phantom, and around 100 kVp for the 24-cm phantom. For the 35-cm phantom, the highest dose efficiency was found at 200 kVp, the highest kVp in our simulation.

The results for bias simulation are shown in Figure 5. The bias increases when the dose decreases. At low dose, the bias was substantially lower with higher kVp versus lower kVp at the same dose. With filtration, especially at low dose, the bias is reduced.

3.3 Phantom scans for diagnostic CT imaging

Images from the phantom scans are shown in Figure 6, Figure 7, Figure 8, and Figure 9 for iodine, tantalum, PMMA, and water inserts respectively. For standard dose, iodine contrast visually decreases as kVp increases from 80 kVp to 140 kVp (Figure 6). The tantalum, water and PMMA contrast are visually similar for the four kVp scanned. The mean and variance for each ROI are reported in Table 3 and Table 4 for standard and ultra-low-dose scans respectively. Contrast, noise, CNRD, IND and bias were calculated and reported (Table 3 and Table 4). The CNRD curves for iodine, tantalum and water at standard dose are plotted in Figure 10. For iodine, the dose efficiency decreases quickly as the tube voltage increases. The water CNRD curve increased slightly, with highest dose efficiency at 140 kVp. For tantalum, 100 kVp is the optimal tube voltage.

For the ultra-low-dose scans, the contrast measurements (based on ROI 1 and ROI 2) were affected by the ring artifacts. There is significant bias in these two regions (Table 4 and Figure 11). The variance of these two ROIs at ultra-low dose measurement is substantially higher than that in standard-dose images (Table 4). Therefore, the contrast measurement is not reliable at this dose level.

3.4 Phantom scans for CTAC

We evaluated the noise and bias in the ultra-low dose CT scans which could be used for CT attenuation correction. For ultra-low dose, the noise in the low-kVp images is visually higher compared to the images acquired at higher kVp. The variance and bias in each ROI at ultra-low dose are reported in Table 4. The bias at ultra-low dose in different regions is also plotted in Figure 11. In the ultra-low dose measurements, ring artifacts become visible at the center and are more substantial at lower kVp. Despite the high bias for different contrast material inserts, the average bias in the uniform region of ROI 2 increases as the kVp decrease. For ROI 3, it is located at the edge of the phantom which is away from the region affected by artifacts. The bias in ROI 3 is within 2 HU, and slightly decreases with increasing kVp (Table 4). The noise measurement is also based on ROI 3. The averaged IND curves calculated from ROI 3 for ultra-low dose measurements are plotted in Figure 11. We found that higher kVp provides higher IND, which indicates higher dose efficiency considering noise only.

3.5 Monte-Carlo simulation

We used the GEANT 4 simulation toolkit to perform a Monte-Carlo simulation, and compared those results with the results using the analytical model. The probability distribution of the total energy deposited on the detector is shown in Figure 12.-B. The

results obtained from the Monte-Carlo simulation agree with the results from the numerical model at both dose levels of 100 mAs and 10 mAs.

4. Discussion

4.1 Diagnostic CT imaging

As a first-order approximation, the CNRD values for water can be treated as surrogates for dose efficiency of imaging unenhanced soft-tissue, since soft tissues are predominantly composed of elements that result in effective atomic numbers that are similar to that of water. Our simulation shows that for soft-tissue imaging with small subject sizes, the optimal kVp is around 100 kVp; and with increasing subject size, this value increases.

In order to apply the most dose-efficient spectrum, we can select the most dose-efficient kVp, and filters can also be applied in order to shape the spectrum. Different high-Z-material filters have been investigated previously, including Al, Cu, Au, and so on (Nowak *et al* 2011, Ay *et al* 2013). Jennings has shown that Cu can be used as an efficient filter for the clinically-used X-ray energy range (Jennings 1988). A previous study has demonstrated that, with various Cu filter thicknesses, spectra with more high-energy photons are more dose efficient for CTAC (Xia *et al* 2012); therefore, in our simulation, a 1 mm Cu filter was applied. The filter removes low-energy photons in the spectrum which is beneficial for soft-tissue imaging, but decreases image contrast for bone and iodine. Therefore, for high-dose contrast-enhanced imaging of bone and iodine, filtration reduces the CNRD for the clinically-relevant kVp range, which is between 70 to 140 kVp for contemporary clinical CT scanners. It is also expected that other high-Z-material filters could effectively remove the low energy photons in the spectrum and have a similar effect as a Cu filter.

To evaluate the validity of the trends in our simulation results, CTDI phantom measurements were performed for water, iodine and tantalum. The trends in the results from scanning agree with the simulation results reasonably well. The general trends of the CRND curves for bone, water and iodine are also consistent with previous studies in the literature (Dougeni *et al* 2012, Kalender *et al* 2009).

We applied our analysis to tantalum nanoparticles, which is a new contrast agent technology under development. Tantalum has K-edge at 67 keV, which is reflected as a sharp dip in the CNRD curves at this energy. Therefore the optimal spectrum can have two choices with one below 60 keV (around 50 kVp) and one above 60 keV (100~120 kVp). The later one can also provide sufficient soft-tissue imaging. In fact, as reported in the previous study, the spectral response of tantalum at such energy is very close to that of water (Bonitatibus *et al* 2010). Therefore, unlike iodine, a dose efficient scan can be performed for both contrast and non-contrast enhanced imaging if tantalum is used as the contrast material. With added filtration, the dose efficiency for both tantalum and soft-tissue imaging can further be enhanced. Our analysis for tantalum also agrees with the recent phantom study (FitzGerald *et al* 2015).

4.2 CT-based attenuation Correction (CTAC)

At ultra-low dose, a higher kVp provides less noisy measurements compared to a low-kVp spectrum. When filtration is applied, the spectrum after filtration is harder compared to the original spectrum, which further reduces the noise in the projection measurements. When CT is primarily used for CTAC, a lower dose compared to typical diagnostic scan can be applied. As noise and bias are more critical than contrast for accurate PET reconstruction, despite subject sizes, high kVp with Cu filtration improves CTAC image quality. This result is also consistent with the previously reported analysis (Xia *et al* 2012). When dose becomes low, the impact of the electronic noise cannot be neglected. At ultra-low dose, the electronic noise can produce negative detected signals, which then must be converted to small positive values before the negative log operation. This can introduce a bias in the projection data. Since the penetration rate for low-energy photons is low, this bias is more significant at low kVp. Our simulation results show that this impact is more significant at ultra-low dose. However, for the phantom scans, the lowest dose we can scan is constrained by the system. We observed some bias from electronic noise for the average bias calculated based on ROI 3 which is away from the artifacts region, but the impact is not significant.

There is another source of bias which is caused by artifacts in the images when the dose becomes very low. The images acquired at ultra-low dose have obvious ring artifacts which becomes more severe at lower kVp, which could relate to the non-uniformity performance of the detector pixels (Kyriakou *et al* 2009). All of these observations indicate that for ultra-low dose scanning, higher kVp may be preferred considering the noise, bias and artifacts in the measurement.

4.3 Projection-domain fast analytical method

The projection-domain analysis method presented in this paper can rapidly screen over numerous variables for specific applications, and provide guidance for selecting the optimal spectrum. Compared to time-consuming Monte-Carlo simulations, this method could potentially be used in real time, to select an optimal spectrum for a given patient and clinical task. This method is not intended to provide absolute, quantitative agreement with results obtained from actual scans, but rather to predict the general trend that would be obtained with scanning. In this paper, we demonstrated that this method can be used for different applications such as non-contrast-enhanced CT scans, contrast-enhanced CT scans using conventional iodinated agents or novel contrast elements such as tantalum, or CT scans for PET attenuation correction.

Clinical CT systems are complicated, and the analytical approach we propose in this paper intends to provide a fast estimation of system performance rather than to accurately model all the aspects of the system. For example, bowtie filter is typically used to balance the flux across the detector channels to reduce the dose applied to the patient. In our analysis, we focus on the central ray where the bowtie filter is thin and has limited impact. The shape of the bowtie filter and its indication to the dose reduction are not taken into account in this analysis. The power constraint of the X-ray tube is also not considered in the simulation. For certain applications such as the diagnostic imaging of iodine or calcium, the optimal kVp can be quite low (e.g. 40 kVp or 60 kVp). To match the image quality at tube voltages

typically used today (e.g. 100 kVp or 120 kVp), the tube power required at the optimal kVp may not be available with today's tube technology. Therefore, this analysis provides an entitlement for the spectral optimization and the potential dose saving for a given spectrum. The spectrum that is actually applied in the scan should be subject to the X-ray tube power constraints. For transmission tomography with energy-integrating detectors, the statistical models need to include effects such as X-ray tube current fluctuation, scatter, scintillation process, electronic noise and so on (Nuyts *et al* 2013). The electronic noise is known to follow normal distribution (Xu and Tsui 2009, Hsieh 2009). From previous studies, the "Poisson+Gaussian" model is developed as a reasonable and popular model to approximate these random processes (Snyder *et al* 1995, Ma *et al* 2012) which we adopted in our analytical model. Even more sophisticated models such as Compound Poisson models have been proposed but remain difficult in practice (Whiting *et al* 2002, Ma *et al* 2012). The analytical method we developed based on the "Poisson+Gaussian" model agrees with the phantom measurements and the results from previous studies, which provide a sufficient estimate of the optimal spectrum selection. This noise model has its limitations, especially at very low dose; a more sophisticated model such as Compound Poisson distributions has been proposed, but remains difficult in practice (Whiting *et al* 2002, Ma *et al* 2012). We observed artifacts in our ultra-low-dose measurement which have a negative impact on diagnostic imaging and CTAC. However, these artifacts are difficult to re-produce in the simulation scheme since they depend on the system performance and calibration. The evaluation of image quality (IQ), especially the definition of a quantitative IQ metric for CT images can be complicated. Conducting an observer study is an established way to evaluate IQ given a specific imaging task, for example, lesion detection (Christianson *et al* 2015). To quantify the IQ, a number of evaluation metrics are established by the research community such as noise magnitude, CT number accuracy, image uniformity, noise-to-contrast ratio (CNR), signal-to-noise ratio (SNR), modulation transfer function (MTF), noise power spectrum (NPS) (Pahn *et al* 2016). Recently, task-based IQ metrics such as the d' indicator were proposed, combining resolution, noise texture, diagnostic task and viewing conditions (Richard and Siewerdsen 2008). Among these metrics, CNR is widely accepted to determine the relative dose efficiency of scanning protocols as it can be measured relatively quickly and easily (Gramer *et al* 2012, Christianson *et al* 2015). Therefore, in our study, we chose CNR as the evaluation metric to perform our screening study. A comprehensive evaluation of the IQ and the interpretation of its diagnostic value requires more sophisticated metrics as mentioned above, especially in the case of non-linear reconstruction algorithms, and is beyond this study.

The analytical approach derived in this study is based on a linear reconstruction algorithm, namely, filtered back projection (FBP). Statistical iterative reconstruction algorithms have been demonstrated clinically to offer improved noise and resolution properties for CT imaging. These nonlinear algorithms change the characteristics of the nonstationary noise as well as the resolution, especially when spatially-variant prior information is incorporated (Stayman and Fessler 2000; Fessler and Rogers, 1996). Therefore, it is not straightforward to directly apply the methodology we developed in this study to iterative reconstruction. However, a protocol that results in improved CNR with FBP could also potentially benefit iterative reconstruction. It is still possible to derive the approximate analytical expression for

the noise and impulse response for iterative reconstruction (Qi *et al* 2000, Gang *et al* 2014). More complicated methods involve forward and back projections (Zhang-O'Connor and Fessler 2010). These could be the topic of extensive future studies and fall outside of the scope of the current paper.

5. Conclusion

We proposed a fast analytical spectral optimization method intended for screening scanning protocol designs. Projection domain analysis was used to select the optimal X-ray spectrum for CT scans performed for different subject sizes and clinical tasks. Tube voltage, X-ray filtration, electronic noise, patient size, and dose levels were all considered in the evaluations. For contrast-enhanced diagnostic imaging for bone and iodine contrast agent, low kVp is in general more dose efficient, as previously reported. For soft-tissue imaging with small subject sizes, the optimal kVp is around 100 kVp; and with increasing subject size, this value increases. Over the clinically-relevant kVp range, the most dose-efficient kVp for tantalum contrast agent was found to be around 100 kVp. This value is similar to that for soft tissue contrast; therefore, X-ray techniques could be used that are more optimal for both soft tissue and tantalum-based contrast agent, as compared with iodine as contrast agent. We demonstrated that when CT scans are used for CTAC, higher kVp with Cu filtration reduces the noise and bias in the measurement, especially for low-dose cases. Considering noise in the measurement, for a 15-cm diameter water phantom, the optimal kVp is around 100 kVp. The optimal kVp increases with increasing subject size. When the dose is further reduced, higher kVp is more dose efficient for CTAC. The bias introduced by the electronic noise is substantial, especially for ultra-low dose CT scans. As dose decreases, a higher-kVp spectrum is preferred because it introduces less bias. Added Cu filtration is effective in further improving the dose efficiency and reducing the bias in the projection measurements. CTDI phantom measurements matches well with our simulations from the fast analytical approach we developed. This simulation approach is developed based on FBP reconstruction. It has the advantage of projection-domain analytical calculations, which requires minimal computation cost. Meanwhile, it provides sufficient accuracy for the screening of optimal spectrum selection across various variables for different applications.

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(A)

(B)

(C)

Figure 1.

(A) In-house manufactured 24 cm CTDI-like phantom with contrast material insert. (B) Example cross-section image for a scan of the phantom with iodine insert in the center. Display window is $40 + [-400\ 400]$ HU. (C) ROI regions to be applied to images for measurement analysis, indicated by ROI1 (blue): 10-mm diameter circular ROI centered on the contrast sample vial; ROI2 (purple): inner background annulus ROI located closely surrounding the contrast sample with 20-mm inside diameter and 40-mm outside diameter;

ROI3 (green): outer background ROI located in the uniform region of the phantom away from center with 130-mm inside diameter and 150-mm outside diameter.

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Figure 2.

Simulation results for the normalized CNRD curves with different object sizes. These data do not include electronic noise; therefore, the dose levels do not impact the simulation results. Water, bone, iodine and tantalum were evaluated. (A), (B), and (C) show the CNRD curves for 15-cm, 24-cm, and 35-cm water cylinders respectively. The CNRD curves for each contrast material are normalized to the maximum CNRD value without filtration for that contrast material.

Figure 3. Simulated CNRD curves at three different dose levels for (A) water, (B) bone, (C) iodine and (D) tantalum, using a 24-cm water cylinder with electronic noise. The CNRD curves for each contrast material are normalized to the maximum CNRD value without filtration at dose-100mA for that contrast material.

Figure 4. Simulated IND curves for three different dose levels with and without 1-mm Cu filter, for (A) 15-cm, (B) 24-cm, and (C) 35-cm water cylinders. Electronic noise is included in the simulation. The IND curves are normalized to the maximum IND value without filtration at dose 100mA.

(A)

(B)

Figure 5.

Bias (% error) in the 511 keV projection. (A) is for analysis with and without electronic noise. (B) is for analysis with and without 1mm Cu filter, including electronic noise. X-ray quantum noise is included in all simulations.

Figure 6.

Images from scans of a 24-cm CTDI-like phantom using an iodine insert at two equal dose levels for different kVp settings. The top row shows the images from the ultra-low-dose scans. The bottom row shows the images from the standard-dose scans. From left to right are the images acquired using 80, 100, 120, 140 kVp. The display window is $[-100\ 300]$ HU.

Figure 7.

Images from scans of a 24-cm CTDI-like phantom using a tantalum insert at two equal dose levels for different kVp settings. The top row shows the images from the ultra-low-dose scans. The bottom row shows the images from the standard-dose scans. From left to right are the images acquired using 80, 100, 120, 140 kVp. The display window is $[-100\ 300]$ HU.

Figure 8.

Images from scans of a 24-cm CTDI-like phantom using a PMMA insert at two equal dose levels for different kVp settings. The top row shows the images from the ultra-low-dose scans. The bottom row shows the images from the standard-dose scans. From left to right are the images acquired using 80, 100, 120, 140 kVp. The display window is $[-100 \ 300]$ HU.

Figure 9.

Images from scans of a 24-cm CTDI-like phantom using a water insert at two equal dose levels for different kVp settings. The top row shows the images from the ultra-low-dose scans. The bottom row shows the images from the standard-dose scans. From left to right are the images acquired using 80, 100, 120, 140 kVp. The display window is $[-100\ 300]$ HU.

Phantom measurement-CNRD-four materials wrt the spectrum (24cm CTDI)

Figure 10.

CNRD from scans using a 24-cm CTDI-like phantom with iodine, tantalum water and PMMA inserts, scanned at equal standard dose.

(A)

(B)

Figure 11.

IND (A) and bias (B) analysis from scans of a 24-cm CTDI-like phantom with a different contrast material insert, at equal ultra-low dose.

Figure 12.

Monte Carlo simulation results. Image (A) shows a schematic overview of the Monte-Carlo simulation using 120 incident X-ray photons. Image (B) shows the probability distribution of the total energy deposited to the detector. The probability distribution obtained using Monte-Carlo simulation with 1 million photons is compared to the numerical model used in our analytical method at two dose levels.

Table 1

Simulation Variables

Tube voltage (kVp) and spectrum	Polychromatic spectrum from 40–200 kVp in 10 kVp steps
Filter	With and without 1-mm Cu filter
Electronic Noise	With and without electronic noise
Terma levels (represent dose)	Three Terma levels which are normalized to the Termas obtained at 100 kVp spectrum without extra filtration, with 1, 10, and 100 mA (referred as dose-1mA, dose-10mA and dose-100mA).
Phantoms	Water cylinders with diameters of 15 cm, 24 cm, 35 cm

Table 2

Phantom Dose Measurements

Tube voltage (kVp)	Tube current (mA)	Dose (mGy)
Standard dose measurement		
80	300	1.536
100	165	1.553
120	105	1.558
140	75	1.561
Ultra-low dose measurement		
80	40	0.205
100	20	0.188
120	15	0.223
140	10	0.208

Table 3

Phantom ROI Measurements (HU) at Standard Dose.

kvp	mean(roi)	var(roi)	mean(roi 2)	var (roi 2)	mean(roi 3)	var (roi 3)	contrast	noise(σ)	CNRD	IND
Water Inserts										
80	1.9	38.1	101.8	37.8	96.1	27.7	99.9	5.2	15.3	0.15
100	2.3	35.1	115.0	34.6	111.1	25.0	112.7	5.0	18.1	0.16
120	0.6	34.5	122.6	33.8	120.8	24.6	122.0	4.9	19.7	0.16
140	0.1	33.2	127.3	34.0	127.4	24.7	127.2	4.9	20.5	0.16
PMMA Inserts										
80	102.3	39.7	102.0	37.9	96.1	27.7	-0.3	5.2	-0.1	0.15
100	117.6	34.8	115.1	34.7	111.1	24.9	-2.5	4.9	-0.4	0.16
120	123.6	35.1	122.7	33.9	120.7	24.6	-0.9	4.9	-0.1	0.16
140	129.1	33.4	127.6	33.9	127.3	24.7	-1.5	4.9	-0.2	0.16
Iodine 10mg/mL Inserts										
80	429.5	41.2	102.7	38.5	96.1	28.0	426.5	5.2	64.9	0.15
100	331	37.2	115.5	34.7	111.1	25.1	328.0	5.0	52.5	0.16
120	266.9	35.1	123.2	34.1	120.7	24.7	265.7	4.9	42.8	0.16
140	225.3	35.4	128.0	34.0	127.3	24.8	224.4	4.9	36.0	0.16
Tantalum 10/mL Inserts										
80	300.8	39.1	102.6	38.0	96.1	27.8	298.0	5.2	45.5	0.15
100	328.1	37.5	115.5	35.0	111.1	25.2	325.1	5.0	52.0	0.16
120	312.4	35.5	122.8	34.2	120.7	24.8	311.5	4.9	50.0	0.16
140	286.8	35.0	128.0	34.3	127.3	24.8	285.8	4.9	45.9	0.16

Table 4

Phantom ROI Measurements (HU) at Ultra-low Dose.

kVp	Mean (roi 1)	Var (roi 1)	Mean (roi 2)	Var (roi 2)	Mean (roi 3)	Var (roi 3)	Noise (σ)	IND	Bias (roi1)	Bias (roi2)	Bias (roi3)
Water Inserts											
80	-15.5	173.4	131.3	155.0	97.6	104.3	10.2	0.22	-17.4	29.5	1.5
100	-3.2	142.7	132.1	127.2	112.3	91.1	9.5	0.24	-5.5	17.1	1.2
120	-4.2	102.0	130.4	99.7	121.2	74.2	8.6	0.25	-4.8	7.8	0.4
140	1.6	99.4	133.0	98.3	128.0	75.0	8.6	0.25	1.5	5.7	0.6
PMMA Inserts											
80	100.4	177.4	130.1	152.2	97.8	105.1	10.2	0.22	-1.9	28.1	1.7
100	120.7	141.9	129.3	125.0	112.0	90.5	9.5	0.24	3.1	14.2	0.9
120	124.7	103.2	129.2	96.6	121.2	73.3	8.5	0.25	1.1	6.5	0.5
140	131.3	100.8	133.0	97.6	128.1	74.8	8.6	0.25	2.2	5.4	0.8
Iodine 10mg/mL Inserts											
80	454.6	195.0	130.0	154.6	97.8	105.3	10.2	0.21	25.1	27.3	1.7
100	337.4	162.0	132.0	128.4	112.4	91.7	9.5	0.24	6.4	16.5	1.3
120	266.9	106.5	129.8	97.8	121.2	74.1	8.6	0.25	0.0	6.6	0.5
140	229.6	104.0	133.5	99.3	127.8	75.4	8.6	0.25	4.3	5.5	0.5
Tantalum 10/mL Inserts											
80	321.3	190.9	131.1	156.0	97.8	104.1	10.2	0.22	20.5	28.5	1.7
100	341.8	156.2	131.8	127.7	112.1	91.2	9.5	0.24	13.7	16.3	1.0
120	312.7	106.2	129.6	97.9	121.2	73.8	8.5	0.25	0.3	6.8	0.5
140	289.2	110.0	133.6	100.6	127.8	75.3	8.6	0.25	2.4	5.6	0.5