Guest Editorial
Low-Dose CT: What Has Been Done, and What Challenges Remain?

I. Introduction

THE introduction of computed tomography (CT) in 1972 was among the most significant development in medical imaging since the discovery of X-rays in 1895. In addition, the innovation of computationally reconstructing tomographic images from projection data significantly influenced the development of other medical imaging modalities, such as magnetic resonance imaging and single photon and positron emission tomography. With the advent of helical and multi-detector-row CT (MDCT) scanners in the 1990s and 2000s along with innovations in cone-beam CT (CBCT) in many forms, CT gained unmatched speed and adaptability for volumetric imaging, leading to widespread use for diagnostic imaging, emergency examination, image-guided interventions, treatment planning, and monitoring of therapeutic response.

As the use of CT has grown, so has concern about the associated radiation dose [item 1) in the Appendix]–[item 4) in the Appendix], and while the biological risk associated with low (mSv) levels of radiation is not established, the concern is sufficient to motivate major efforts from academic, government and industrial researchers to develop methodologies for producing clinically useful images at the lowest doses possible, hereafter called low mSv or low-dose CT (LdCT) [item 5) in the Appendix]. This special issue aims to bring together the expert opinions of CT researchers to review what has been done in the past and what challenges await in the future for LdCT.

II. Review of Past Effort for LdCT Development

For the purpose of simplifying the presentation of the following sections, descriptions will be based on the flowchart of Fig. 1 (left), which outlines the signal or information processing in a typical CT system of Fig. 1 (right) from the X-ray tube or emission source through to the output images.

Typical intermediate stages from the X-ray emission source to the final output images may include the followings. (1) The X-ray energy spectral shaping filter or an attenuating plate, which aims to alter the X-ray tube output energy spectrum for a specific clinical application [item 6) in the Appendix], [item 7) in the Appendix]. (2) The X-ray flux modulator (e.g., the bowtie filter) [item 8) in the Appendix], which aims to alter the X-ray flux for a particular body anatomy part such as the head, chest, abdomen, etc. (3) Automatic adjustment of the X-ray tube current (mAs) and/or the X-ray tube voltage (kVp) values during the X-ray tube rotates around the body [item 9) in the Appendix], [item 10) in the Appendix]; which aims to deliver an adequate amount of X-ray energy at a particular angle during the rotation according to the body anatomy, e.g., more energy at the horizontal direction and less energy at the vertical direction for the body shape in Fig. 1 (right). (4) The scatter estimator on the transmitted photons from the body toward the detector which can be a grid plate hardware with holes allowing the X-rays from the tube toward a detector bin on a straight line path or a computer algorithm. (5) The detector array, which converts the X-ray energy into electrical signals. (6) System calibration, which ensures all the detector bins respond to input X-ray energy uniformly, characterizes system electronic background noise and outputs adequate X-ray transmission data (also called pre-log projection data). (7) Additional system calibration, mainly the operation of log transform from the pre-log projection data to post-log projection data, also called sinogram data, which reflect the line integral of attenuation coefficients through the body, i.e., the well-known Radon transform. And (8)

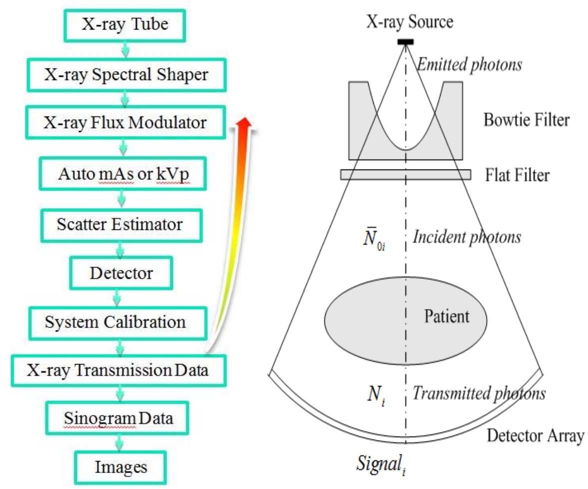

Fig. 1. A simplified flowchart showing the X-ray signal generation, modulation and detection, as well as the processing of the acquired data toward the output of the final CT images. The big arrow indicates that the advancement of detection systems (e.g., the auto mAs or kVp protocol, non-circular orbit rotation, sparse view data acquisition, limited field-of-view data acquisition, etc.) will trigger research efforts to develop corresponding image reconstruction algorithms, and vice versa the innovation in image reconstruction strategies will provide insights to lead the design of new detection systems.

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tomographic reconstruction from the sinogram data, or inverting mathematically the Radon transform, for CT images; where the classic filtered back-projection (FBP) reconstruction is a common choice in the situation when the sinogram data are nearly noise free (high mSv dose level) and sampled adequately around the patient, particularly for volumetric imaging in MDCT or CBCT.

In the early development of CT, research efforts mainly focused on acquiring complete and consistent line-integral sinogram data around the patient, allowing for the inversion of the Radon transform while achieving the highest image quality possible. CT technology evolved through several generations, ultimately allowing fast acquisition of single and then multiple patient slices, providing adequate diagnostic images in real time for almost every vital organ inside the human body.

As the use of CT increased, the associated X-ray radiation exposure gradually became a concern, and so attracted more research efforts seeking to reduce the radiation exposure level while retaining high image quality [item 2) in the Appendix], [item 3) in the Appendix], [item 5) in the Appendix], [item 11) in the Appendix]. The research efforts have been increased significantly in the past two decades, particularly due to the demonstrated effectiveness of CT in screening [item 12) in the Appendix], [item 13) in the Appendix] and in pediatric imaging [item 1) in the Appendix], [item 11) in the Appendix], [item 14) in the Appendix]. While a complete survey of the literature cataloging these efforts is beyond the scope of this Editorial, we employ two broad categories of work aimed at reduction of CT dose: (1) dose-optimized CT detection system design; and (2) dose-optimized image reconstruction algorithm development, where the former will be briefly reviewed and the later will be described in more detail.

A. Dose-Optimized CT Detection System Design

A typical CT detection system includes, see Fig. 1 (right), three major components: X-ray source, X-ray modulator (for spectral shaping, flux adaptive to body anatomy, scatter elimination, etc.), and X-ray detector. The first task for dose-optimized CT detection system design is to obtain an adequate X-ray energy spectrum from the X-ray tube for a particular clinical application. Given an X-ray tube, many X-ray spectral shaping filters have been designed to yield a desired energy spectrum [item 6) in the Appendix], [item 7) in the Appendix]. In this special issue, Makeev and Glick report an example of using filter plates to optimize the spectral output of an X-ray tube for fully three-dimensional (3D) breast imaging [*Low-dose contrast-enhanced breast CT using spectral shaping filters: An experimental study*]. In this report, many spectral-shaping methods are cited and more spectral-shaping research efforts are expected in the future to achieve dose-optimized patient-specific clinical tasks.

The next task for dose-optimized CT detection system design is to obtain an adequate X-ray flux across the detected field of view (FOV), adaptive to the body shape by the use of the bowtie filter. Recent advancements for this patient-specific, dose-optimization detection system design can be seen from the reports [item 15) in the Appendix], [item 16) in the Appendix]. A similar approach to achieve the same task is to modulate the X-ray tube mAs and/or kVp according to the body shape when the X-ray tube is rotating around the patient, so called automatic mAs/kVp [item 9) in the Appendix], [item 10) in the Appendix]. Extending in-plane modulation to the z-axis is further investigated in [item 17) in the Appendix] and [item 18) in the Appendix]. In addition to these efforts toward system design optimization, Gang, Siewerdsen and Stayman have further refined the corresponding image reconstruction strategy to realize the gain in dose reduction, as reported in this special issue [*Task-driven optimization of fluence field and regularization for model-based iterative reconstruction in CT*].

At the typical kVp levels used in clinical CT, Compton scatter contributes noticeably and negatively to the acquired data, particularly for fully 3D volumetric CT imaging [item 19) in the Appendix]. The third task for dose-optimized CT detection system design is to improve the anti-scatter grid to reject the scattered counts and/or develop an effective scatter estimation algorithm. Examples of this effort are reported in [item 20) in the Appendix] and [item 21) in the Appendix]. It is expected the reconstruction strategy of Gang *et al.* in this special issue can be further adapted to realize the gain in dose reduction after the use of optimal system design for scatter rejection.

While there are many other strategies for dose-optimized CT detection system design, the most fruitful direction likely involves the design of the X-ray detector, including new detector materials (e.g., for photon counting) [item 22) in the Appendix], new detector assemblies (e.g., axial multi-band array, varying bin size for optimal sampling across the FOV), and new detector geometries (e.g., flat panel, etc.) [item 23) in the Appendix]. It is a challenge to cover this task in a limited space and a brief review can be found in [item 8) in the Appendix].

In addition to the efforts for improvement of each individual component performance above, an innovative integration of all the components for a particular clinical application will also be an important task. Furthermore, the motion of each of the hardware components or a combination of the components can also reduce the dose while accomplishing a specific clinical task [item 24) in the Appendix]. Two examples are reported in this special issue: one is the work of Shamul and Joskowicz [*Radon space dose optimization in repeat CT scanning*] and the other is the work of Medan and Joskowicz [*Reduced-dose imageless needle and patient tracking in interventional CT procedures*].

B. Dose-Optimized Image Reconstruction Algorithm Development

Approaches for dose-optimized image reconstruction algorithm development can be reviewed according to how the data were acquired: (1) low-mAs and/or kVp data acquisition; (2) sparse-view data acquisition. Other data acquisition strategies, such as limited FOV for reconstructing a small region and limited angle for compensating metal insert inside the body, are beyond the scope of this special issue and, therefore, will not be included here. The following presentation will focus on the last three stages of Fig. 1, i.e., from the X-ray transmission data and sinogram data to the output images.

1) Low-mAs or kVp Data Acquisition: This approach is a relatively straightforward attempt to directly reduce the X-ray radiation exposure, given an available CT scanner configuration and image reconstruction algorithms, such as the well-established FBP algorithm. By carefully performing the above system design tasks and modulating the mAs and/or kVp parameters for each individual patient and clinical application, the FBP reconstruction can generally yield clinically useful images at reduced radiation dose. However, when the radiation exposure is further reduced to reach sub-mSv dose level [item 5) in the Appendix], the images reconstructed by FBP are not only noisy but also include structural artifacts, where the artifactual structures in the noisy images can bring much higher interpretation risks than the noise [item 25) in the Appendix], [item 26) in the Appendix] . To solve the associated noise and artifact problems in the FBP reconstruction, great efforts have been devoted to explore and develop alternative iterative algorithms to achieve desired image quality. Many of these algorithms predate FBP, but computational and algorithmic improvements have allowed them to find clinical use in recent years. Recent efforts are not limited to the iterative solution of the linear systems in the past, such as algebraic reconstruction techniques (ART) [item 27) in the Appendix] or its variants, e.g., simultaneous ART [item 28) in the Appendix] and maximum likelihood (ML) expectation maximization [item 29) in the Appendix], but also introduce many knowledge-based models for both the acquired data and the to-be-reconstructed images. In the following, two models are reviewed within the framework of Bayesian statistics inference, one is a data-fidelity model and the other is a prior-knowledge model constraining the to-be-reconstructed image. A reconstruction outcome within the Bayesian framework is frequently called penalized ML solution (pML), or simply penalized likelihood (PL). Other reconstruction methods for a different framework solution will not be included here and are referred to the reports [item 5) in the Appendix], [item 8) in the Appendix], [item 11) in the Appendix].

The data-fidelity model typically includes both the X-ray counting noise and the system electronic background noise in both the pre-log X-ray transmission space [item 30) in the Appendix], [item 31) in the Appendix] and the post-log attenuation line-integral sinogram domain [item 32) in the Appendix], [item 33) in the Appendix], where in order to construct a numerically tractable data fidelity function, the statistical distribution of the X-ray counts of a compound Poisson nature [item 34) in the Appendix] is approximated by the Poisson process and the background noise is usually modeled by the Gaussian distribution [item 30) in the Appendix]. Further approximation is made to replace the summation of the Poisson and Gaussian distributions by a shift-Poisson distribution for a numerically tractable data fidelity function [item 35) in the Appendix]–[item 37) in the Appendix]. Despite the approximations, image reconstruction in the pre-log transmission space is still quite computationally intensive [item 38) in the Appendix], [item 39) in the Appendix], compared to the reconstruction in the post-log line-integral sinogram domain [item 40) in the Appendix], [item 41) in the Appendix]. In this special issue, Wang, Zhou, Yu, *et al.* developed a hybrid image reconstruction to take advantages of each of the pre- and post-log data fidelity models respectively [*Hybrid pre-log and post-log image reconstruction for CT*].

The most widely cited prior model for the to-be-reconstructed images is reported in the classic paper of Geman and Geman [item 42) in the Appendix], where a neighborhood system of Markov random field (MRF) is specified using pixel-by-pixel representation to encourage reconstruction of a piece-wise smooth image. Expansion from the previous pixel-by-pixel presentation to patch-by-patch description with application to LdCT by the use of the non-local mean (NLM) descriptors is detailed in the review paper [item 43) in the Appendix]. Further exploration to include tissue-specific structural and textual information from previous diagnostic scans into the MRF framework is reviewed in [item 44) in the Appendix] and [item 45) in the Appendix]. There are many other prior models, e.g., those which are constructed based on the image total variation (TV) minimization [item 46) in the Appendix]. Inspired by recent advancements, machine learning was also adapted in the prior-model construction for LdCT. Two examples of adapting the machine learning are reported in this special issue: one is the work of Bai, Yan, Jia, *et al.* [*Z-index parameterization for volumetric CT image reconstruction via 3D dictionary learning*], and the other is the work of Wu, Kim, El Fakhri, *et al.* [*Iterative low-dose CT reconstruction with priors by artificial neural network*].

In addition to the reconstruction strategies from the acquired data in either the pre-log data space or the post-log data domain, another reconstruction strategy has also been attracting significant research interest. This strategy aims to restore the ideal line integral sinogram from the pre-log data with consideration of the X-ray Poisson distribution and the electronic background Gaussian noise, as well as other factors such as X-ray tube size, detector bin crosstalk, etc. It is followed by a computationally efficient method for tomographic image reconstruction from the restored line integral sinogram, such as a FBP or ART type algorithm [item 31) in the Appendix], [item 32) in the Appendix]. A straightforward approach is to filter the sinogram noise, followed by a FBP image reconstruction [item 47) in the Appendix], [item 48) in the Appendix]. Examples of this alternative strategy, in this special issue, are the work of Xie, Zeng, Zhao, *et al.* [*Robust low-dose CT sinogram preprocessing via exploiting noise-generating mechanism*] and the investigation of Liu, Ma, Zhang, *et al.* [*Discriminative feature representation to improve projection data inconsistency for low-dose CT imaging*].

While the image reconstruction strategies in either the pre- or the post-log domain have shown a noticeable dose reduction with adequate image quality for several clinical applications, as seen from the above mentioned studies, further research efforts on the reconstructed images by the use of sophisticated image restoration methods in the image domain have demonstrated variable gains in dose reduction with adequate image quality for some specific clinical tasks [item 49) in the

Appendix], [item 50) in the Appendix]. Of particular note are the machine learning contributions of Zhang, Rong, Lu, *et al.* [*Low-dose lung CT image restoration using adaptive prior features from full-dose training database*], Chen, Zhang, Kalra, *et al.* [*Low-dose CT with a residual encoder-decoder convolutional neural network*], and Wolterink, Leiner, Viergever, *et al.* [*Generative adversarial networks for noise reduction in low-dose CT*].

These efforts for dose-optimized, task-dependent approaches have been expanded to the case of multi-frame dynamic scans in functional CT perfusion studies and image-guided intervention, where the dose level can be very high [item 2) in the Appendix]. Two examples of dynamic CT imaging in this special issue are the low-dose cerebral perfusion CT of Zeng, Xie, Cao, *et al.* [*Low-dose dynamic cerebral perfusion CT reconstruction via intrinsic tensor sparsity regularization*] and the low-dose myocardial perfusion CT of Li, Speidel, Francois, *et al.* [*Radiation dose reduction in CT myocardial perfusion imaging using SMART-RECON*].

2) Sparse-View Data Acquisition: Another approach for reducing X-ray radiation exposure is acquiring a smaller number of projections, while retaining relatively high mAs/kVp parameter setting for each projection, i.e., sparse-view data acquisition. Such approaches maximize the signal-to-noise ratio (SNR) in each view and reduce the total amount of electronic readout noise in the dataset. The ability to reconstruct images from sparse views is inspired by developments in compressive sensing (CS) field for reconstruction of signals that can be sparsely represented in some basis [item 51) in the Appendix]–[item 53) in the Appendix]. While the mathematical theory behind CS does not necessarily apply directly to CT reconstruction, in practice many of the algorithmic approaches from CS field produce visually high-quality images in CT. A typical implementation realizing the potential of sparse-view reconstruction for LdCT is the algorithm called TV-POCS (total variation – projections on to convex sets) [item 54) in the Appendix], [item 55) in the Appendix], where each of the POCS forward- and back-projection cycles imposes a subspace of feasible solutions in the image domain, where all the possible feasible solutions in the sub-space satisfy the constraints of the line integral projection data. The selection of the TV solution among the feasible solutions in the sub-space yields a unique reconstruction.

While the TV-based LdCT image reconstruction showed impressive results, staircase or patch artifacts are sometimes observed in subsequent investigations and some possible solutions for reduction of the artifacts were suggested [item 56) in the Appendix]–[item 59) in the Appendix]. Among these possible solutions, the theoretical TV-stokes model in [item 60) in the Appendix] and [item 61) in the Appendix] is interesting in the sense that it can explicitly consider the high sampling rate across the detector elements (or bins) at each projection view to recover any possible missing information between two adjacent sparse views (from low sampling rate), thus its robust performance is expected [item 62) in the Appendix], [item 63) in the Appendix]. This special issue includes three examples of adapting TV optimization for (1) regional LdCT reconstruction by Zhang, Song, Chen, *et al.* [*Limited-range and detector few-view CT method for ROI reconstruction in solitary lung nodules follow-up examination using historical image*], (2) dual-energy LdCT image reconstruction by Lee, Lee, Kim, *et al.* [*A feasibility study of low-dose single-scan dual-energy cone-beam CT in many-view under-sampling framework*], and (3) prior penalty model construction to eliminate unnecessary radiation in radiation oncology by Liu, Li, Xiang, *et al.* [*Low-dose CBCT reconstruction based on Hessian Schatten penalty with different orders*].

III. Challenges in the Future for LdCT

While significant progress has been made in the past decades by the efforts reviewed above, challenges remain for the long-term objective of low-mSv or LdCT to achieve dose-optimized, clinical task-dependent and patient-specific personal healthcare. The challenges may be reviewed along the information processing path of X-ray signal generation, data acquisition, and image reconstruction of Fig. 1.

A. X-Ray Signal Generation and Data Acquisition

As reviewed above, both the X-ray spectral-shaping filter plate and flux-modulating bowtie filter play an important role for dose-optimized, application-dependent, patient-specific CT imaging. To achieve a real-time dynamic modulation of the spectral shaping and flux profile at each projection angle around the body remains a challenging task. The challenge for real-time dynamic modulation also exists for the automated mAs and/or kVp modulation operation during data acquisition, although significant progress has been made. In addition, for fully 3D volumetric MDCT and CBCT, the photon scatter remains a major cause of degrading image quality and a challenge for dose reduction.

It is clearly seen that more significant progress at the data-acquisition stage relies on detector optimization [item 23) in the Appendix]. Photon-counting detectors [item 22) in the Appendix], for example, have the potential to eliminate the electronic readout noise.

B. Image Reconstruction

The challenges for LdCT image reconstruction may be reviewed along the following steps, starting from the output of the detector array.

1) Reconstruction from Pre-Log Transmission Data Model: It is desirable to start the image reconstruction from the output of the detector where all the factors affecting X-ray photons traversing the body and interacting with the detector can be modeled by a mathematical formula. At present time, the output data noise is modeled as comprising X-ray counting statistics and electronic background noise. While the system electronic background noise can be characterized as Gaussian distribution (which is numerically tractable), the X-ray counting statistics was shown to follow a compound Poisson distribution [item 34) in the Appendix], which is numerically intractable and remains a challenge so far. It is hoped that the advent of photon counting detector will eliminate this challenge and the effect of the background noise as well.

By the above mentioned approximations, which simplifies the two parts of the detector output as Poisson statistics for the X-ray counts and Gaussian statistics for the electronic background, the pre-log transmission data can be modeled as the so-called shifted Poisson statistics [item 35) in the Appendix]–[item 39) in the Appendix]. Despite the simplification, this data fidelity model is still a severely non-linear function of the line integral of the attenuation coefficient. Great numerical challenges in calculating the optimal solution are observed in the reports [item 38) in the Appendix], [item 39) in the Appendix].

To increase the details viewed in the reconstructed images, modeling (1) the finite sizes of X-ray tube and detector bins, (2) the effect of beam hardening, (3) the detector cross talk, etc. [item 31) in the Appendix], into the image reconstruction may become necessary.

2) Reconstruction from Post-Log Line-Integral Sinogram Data Model: One way to get around the numerical challenges is the use of a sinogram-restoration strategy [item 31) in the Appendix]. Other alternatives are to take only the most important first- and second-order statistical moments into consideration and ignore higher orders [item 32) in the Appendix], [item 33) in the Appendix].

Since the models in both (3.2.1) and (3.2.2) sections require iterative means to approach optimal reconstructions, the associated computation can be a very costly burden.

3) Incorporation of Prior Knowledge Model for Dose-Optimized LdCT Image Reconstruction: While a piece-wise smooth image constraint in the prior models for the to-be-reconstructed images can reduce the dose significantly while retaining the image's SNR and edge sharpness by the widely-cited pixel-based MRF Huber model [item 64) in the Appendix] and the patch-based NLM expansion [item 43) in the Appendix], image texture is gaining more attention as a source of clinical information [item 65) in the Appendix], [item 66) in the Appendix]. Recent advancements in incorporating tissue textures from previous high-quality images into current LdCT image reconstruction demonstrated great potential to achieve dose-optimized LdCT image reconstruction [item 45) in the Appendix]. It is expected that recent research interest in machine (deep) learning will rapidly progress the extraction of the texture information from previous high-quality images into current LdCT image reconstruction. However, severe challenges are expected.

4) Restoration of Reconstructed Images in the Image Domain: Filtering images is a well-established field, and various point spread functions and noise-filtration methods have been explored to restore a desired image from a distorted and noise-contaminated image. The approach continues to attract attention for LdCT because of its high speed and the convenience of working with readily available reconstructed images as opposed to the less accessible sinogram data [item 67) in the Appendix], [item 68) in the Appendix]. As mentioned before, the photon starvation streak artifacts are very hard to remove, although filtering the random noise could be less challenging [item 26) in the Appendix].

5) Modulation of Multiple Scans for Dynamic Study and Image-Guided Applications: As CT is expanded rapidly into multiple scans for dynamic function studies and image-guided interventional operations, innovation in data acquisition and image reconstruction is clearly desired [item 69) in the Appendix]. Examples of this kind of innovations are illustrated by the dynamical cerebral perfusion CT studs of Zeng, *et al.*, the myocardial perfusion study of Li, *et al.*, and the two reports from Joskowicz's group in this issue.

6) Spectral LdCT Image Reconstruction: X-ray energy plays an essential role in modulating the image contrasts in CT imaging, particularly among soft tissues. Since the clinically-desired image textures heavily depend on the contrasts, accurate reconstruction of a series of images at different energy intervals will have significant impact on expansion of LdCT applications to more clinical tasks. This would open a new path to explore computer-aided detection and diagnosis in a low-dose CT setting for screening many cancer precursors in the colon, lung and other vital organs [item 70) in the Appendix]. With advancement of photon counting detection system, reconstructing a series of spectral LdCT images will become more feasible, although challenges await on the path ahead.

IV. Conclusion and Outlook

The objective of this special issue is to bring the expert opinions of CT researchers together to review what has been done in the past development of low-mSv or LdCT and what challenges await in the future for further advancement of LdCT. While the authors of the papers in this special issue contributed their original research materials, the reviewers added great insights in polishing the research ideas and refining the experimental outcomes. We, the guest editors and the editor-in-chief of this great journal of IEEE Transactions on Medical Imaging, believe the hard work of the reviewers and the authors have made a successful achievement to the objective, and the hard work is greatly appreciated.

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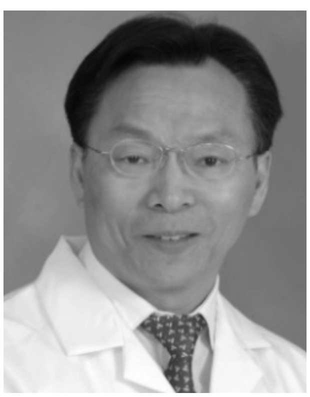
Appendix
Related Work

1) W. Huda and A. Vance, "Patient radiation doses from adult and pediatric CT," *Amer. J. Roentgenol.*, vol. 188, no. 2, pp. 540–546, 2007.
2) A. J. Einstein, M. J. Henzlova, and S. Rajagopalan, "Estimating risk of cancer associated with radiation exposure from 64-slice computed tomography coronary angiography," *J. Amer. Med. Assoc.*, vol. 298, no. 3, pp. 317–323, 2007.
3) D. J. Brenner and E. J. Hall, "Computed tomography—An increasing source of radiation exposure," *New England J. Med.*, vol. 357, no. 22, pp. 2277–2284, 2007.
4) W. A. Kalender, "Dose in X-ray computed tomography," *Phys. Med. Biol.*, vol. 59, no. 3, pp. 129–150, 2014.
5) C. H. McCollough *et al.*, "Achieving routine submillisievert CT scanning: Report from the summit on management of radiation dose in CT," *Radiology*, vol. 264, no. 2, pp. 567–580, 2012.
6) P. Spanne, "X-ray energy optimisation in computed microtomography," *Phys. Med. Biol.*, vol. 34, no. 6, pp. 679–690, 1989.
7) M. Shleifer, F. A. Dilmanian, F. A. Staicu, and M. H. Woodle, "Mechanical design of a high-resolution tunable crystal monochromator for the multiple energy computed tomography project," *Nucl. Instrum. Methods Phys. Res. A, Accel. Spectrom. Detect. Assoc. Equip.*, vol. 347, nos. 1–3, pp. 356–359, 1994.
8) J. Hsieh, *Computed Tomography: Principles, Design, Artifacts, and Recent Advances*. Bellingham, WA, USA: SPIE, 2003.
9) M. Gies, W. A. Kalender, H. Wolf, C. Suess, and M. T. Madsen, "Dose reduction in CT by anatomically adapted tube current modulation. I. Simulation studies," *Med. Phys.*, vol. 26, no. 11, pp. 2235–2247, 1999.
10) W. A. Kalender, H. Wolf, and C. Suess, "Dose reduction in CT by anatomically adapted tube current modulation. II. Phantom measurements," *Med. Phys.*, vol. 26, no. 11, pp. 2248–2253, 1999.
11) C. Suess and X. Chen, "Dose optimization in pediatric CT: Current technology and future innovations," *Pediatric Radiol.*, vol. 32, no. 10, pp. 729–734, 2002.
12) D. J. Brenner and M. A. Georgsson, "Mass screening with CT colonography: Should the radiation exposure be of concern?" *Gastroenterology*, vol. 129, no. 1, pp. 328–337, 2005.
13) D. Aberle *et al.*, "Reduced lung-cancer mortality with low-dose computed tomographic screening," *New England J. Med.*, vol. 365, no. 5, pp. 395–409, 2011.
14) S. Singh *et al.*, "Dose reduction and compliance with pediatric CT protocols adapted to patient size, clinical indication, and number of prior studies," *Radiology*, vol. 252, no. 1, pp. 200–208, 2009.
15) S. S. Hsieh and N. J. Pelc, "The feasibility of a piecewise-linear dynamic bowtie filter," *Med. Phys.*, vol. 40, no. 30, p. 031910, 2013.
16) F. Li, Q. Yang, W. Cong, and G. Wang, "Dynamic bowtie filter for cone-beam/multi-slice CT," *PLoS ONE*, vol. 9, no. 7, p. e103054, 2014, doi: 10.1371/journal.pone.0103054.
17) M. K. Kalra, M. M. Maher, T. L. Toth, R. S. Kamath, E. F. Halpern, and S. Saini, "Comparison of Z-axis automatic tube current modulation technique with fixed tube current CT scanning of abdomen and pelvis," *Radiology*, vol. 232, pp. 347–353, 2004.
18) S. Bartolac, S. Graham, J. Siewerdsen, and D. Jaffray, "Fluence field optimization for noise and dose objectives in CT," *Med. Phys.*, vol. 37, no. 7, pp. S2–S17, 2011.
19) M. Endo, T. Tsunoo, N. Nakamori, and K. Yoshida, "Effect of scattered radiation on image noise in cone beam CT," *Med. Phys.*, vol. 28, no. 4, pp. 469–474, 2001.
20) L. Zhu, Y. Xie, J. Wang, and L. Xing, "Scatter correction for cone-beam CT in radiation therapy," *Med. Phys.*, vol. 36, no. 6, pp. 2258–2268, 2009.
21) J. Wang, W. Mao, and T. Solberg, "Scatter correction for cone-beam computed tomography using moving blocker strips: A preliminary study," *Med. Phys.*, vol. 37, no. 11, pp. 5792–5800, 2010.
22) K. Taguchi and J. S. Iwanczyk, "Vision 20/20: Single photon counting X-ray detectors in medical imaging," *Med. Phys.*, vol. 40, no. 2, p. 100901, 2013.
23) E. Shefer *et al.*, "State of the art of CT detectors and sources: A literature review," *Current Radiol. Rep.*, vol. 1, pp. 76–91, 2013.
24) S. Ouadah, M. Jacobson, J. W. Stayman, T. Ehtiati, C. Weiss, and J. H. Siewerdsen, "Task-driven orbit design and implementation on a robotic C-arm system for cone-beam CT," *Proc. SPIE*, vol. 10132, p. 101320H, Mar. 2017, doi: 10.1117/12.2255646.
25) C. McCollough *et al.*, "Degradation of CT low-contrast spatial resolution due to the use of iterative reconstruction and reduced dose levels," *Radiology*, vol. 276, no. 2, pp. 499–506, 2015.
26) I. Mori, Y. Machida, M. Osanai, and K. Iinuma, "Photon starvation artifacts of X-ray CT: Their true cause and a solution," *Radiol. Phys. Technol.*, vol. 6, no. 1, pp. 130–141, 2013.
27) R. Gordon, R. Bender, and G. T. Herman, "Algebraic reconstruction techniques (ART) for three-dimensional electron microscopy and X-ray photography," *J. Theor. Biol.*, vol. 29, no. 3, pp. 471–476, 1970.
28) A. H. Andersen and A. C. Kak, "Simultaneous algebraic reconstruction technique (SART): A superior implementation of the art algorithm," *Ultrason. Imag.*, vol. 6, no. 1, pp. 81–94, 1984.
29) K. Lange and R. Carson, "EM reconstruction algorithms for emission and transmission tomography," *J. Comput. Assist. Tomogr.*, vol. 8, no. 2, pp. 306–316, Apr. 1984.
30) J. Xu and B. M. W. Tsui, "Electronic noise modeling in statistical iterative reconstruction," *IEEE Trans. Image Process.*, vol. 18, no. 6, pp. 1228–1238, Jun. 2009.
31) P. J. La Rivière, J. Bian, and P. A. Vargas, "Penalized-likelihood sinogram restoration for computed tomography," *IEEE Trans. Med. Imag.*, vol. 25, no. 8, pp. 1022–1036, Aug. 2006.
32) J. Wang, S. Wang, L. Li, H. Lu, and Z. Liang, "Virtual colonoscopy screening with ultra low-dose CT and less-stressful bowel preparation: A computer simulation study," *IEEE Trans. Nucl. Sci.*, vol. 55, no. 5, pp. 2566–2575, Oct. 2008.
33) J. Ma *et al.*, "Variance analysis of X-ray CT sinograms in the presence of electronic noise background," *Med. Phys.*, vol. 39, no. 7, pp. 4051–4065, 2012.
34) B. R. Whiting, P. Massoumzadeh, O. A. Earl, J. A. O'Sullivan, D. L. Snyder, and J. F. Williamson, "Properties of preprocessed sinogram data in X-ray computed tomography," *Med. Phys.*, vol. 33, no. 9, pp. 3290–3303, 2006.
35) D. L. Snyder, A. M. Hammoud, and R. L. White, "Image recovery from data acquired with a charge-coupled-device camera," *J. Opt. Soc. Amer. A, Opt. Image Sci.*, vol. 10, no. 5, pp. 1014–1023, 1993.
36) D. L. Snyder, C. W. Helstrom, A. D. Lanterman, M. Faisal, and R. L. White, "Compensation for readout noise in CCD images," *J. Opt. Soc. Amer. A, Opt. Image Sci.*, vol. 12, no. 2, pp. 272–283, 1995.
37) M. Yavuz and J. A. Fessler, "Statistical image reconstruction methods for randoms-precorrected PET scans," *Med. Image Anal.*, vol. 2, no. 4, pp. 369–378, 1998.
38) L. Fu *et al.*, "Comparison between pre-log and post-log statistical models in ultra-low-dose CT reconstruction," *IEEE Trans. Med. Imag.*, vol. 36, no. 3, pp. 707–720, Mar. 2017.
39) Y. Xing, J. Rong, H. Zhang, H. Lu, and Z. Liang, "Ultralow dose CT image reconstruction with pre-log shifted-poisson model and texture-based MRF prior," in *Proc. Int. Conf. Fully 3D Image Reconstruction Radiol. Nucl. Med.*, Xi'an, China, Jun. 2017.
40) T. Li *et al.*, "Nonlinear sinogram smoothing for low-dose X-ray CT," *IEEE Trans. Nucl. Sci.*, vol. 51, no. 5, pp. 2505–2513, Oct. 2004.
41) J. Wang, T. Li, H. Lu, and Z. Liang, "Penalized weighted least-squares approach to sinogram noise reduction and image reconstruction for low-dose X-ray CT," *IEEE Trans. Med. Imag.*, vol. 25, no. 10, pp. 1272–1283, Oct. 2006.
42) S. Geman and D. Geman, "Stochastic relaxation, Gibbs distributions, and the Bayesian restoration of images," *IEEE Trans. Pattern Anal. Mach. Intell.*, vol. PAMI-6, no. 6, pp. 721–741, Nov. 1984.
43) H. Zhang, D. Zeng, H. Zhang, J. Wang, Z. Liang, and J. Ma, "Applications of nonlocal means algorithm in low-dose X-ray CT image processing and reconstruction: A review," *Med. Phys.*, vol. 44, no. 3, pp. 1168–1185, 2017.
44) H. Zhang, J. Ma, J. Wang, W. Moore, and Z. Liang, "Assessment of prior image induced nonlocal means regularization for low-dose CT reconstruction: Change in anatomy," *Med. Phys.*, vol. 44, no. 9, pp. e264–e278, 2017.
45) H. Zhang *et al.*, "Extracting information from previous full-dose CT scan for knowledge-based Bayesian reconstruction of current low-dose CT images," *IEEE Trans. Med. Imag.*, vol. 35, no. 3, pp. 860–870, Mar. 2016.
46) M. Defrise, C. Vanhove, and X. Liu, "An algorithm for total variation regularization in high-dimensional linear problems," *Inverse Problem*, vol. 27, no. 6, p. 065002, 2011.
47) H. Lu, I. Hsiao, X. Li, and Z. Liang, "Noise properties of low-dose CT projections and noise treatment by scale transformations," in *Proc. Conf. Rec. Nucl. Sci. Symp. Med. Imag.*, vol. 3. Nov. 2001, pp. 1662–1666.
48) O. Demirkaya, "Reduction of noise and image artifacts in computed tomography by nonlinear filtration of projection images," *Proc. SPIE*, vol. 4322, pp. 917–923, Jul. 2001.

49) M. Kachelrieß, O. Watzke, and W. A. Kalender, "Generalized multi-dimensional adaptive filtering for conventional and spiral single-slice, multi-slice, and cone-beam CT," *Med. Phys.*, vol. 28, no. 4, pp. 475–490, 2001.
50) M. K. Kalra *et al.*, "Can noise reduction filters improve low-radiation-dose chest CT images? Pilot study," *Radiology*, vol. 228, no. 1, pp. 257–264, Jul. 2003.
51) E. J. Candès, J. Romberg, and T. Tao, "Robust uncertainty principles: Exact signal reconstruction from highly incomplete frequency information," *IEEE Trans. Inf. Theory*, vol. 52, no. 2, pp. 489–509, Feb. 2006.
52) D. L. Donoho, "Compressed sensing," *IEEE Trans. Inf. Theory*, vol. 52, no. 4, pp. 1289–1306, Apr. 2006.
53) E. Candés and M. B. Wakin, "An introduction to compressive sampling," *IEEE Signal Process. Mag.*, vol. 25, no. 2, pp. 21–30, Mar. 2008.
54) E. Y. Sidky, C.-M. Kao, and X. Pan, "Accurate image reconstruction from few-views and limited-angle data in divergent-beam CT," *J. X-Ray Sci. Technol.*, vol. 14, no. 2, pp. 119–139, 2006.
55) E. Sidky and X. Pan, "Image reconstruction in circular cone-beam computed tomography by constrained, total-variation minimization," *Phys. Med. Biol.*, vol. 53, no. 17, pp. 4777–4807, 2008.
56) J. Tang, B. E. Nett, and G. H. Chen, "Performance comparison between total variation (TV)-based compressed sensing and statistical iterative reconstruction algorithms," *Phys. Med. Biol.*, vol. 54, no. 19, pp. 5781–5804, 2009.
57) X. Han *et al.*, "Algorithm-enabled low-dose micro-CT imaging," *IEEE Trans. Med. Imag.*, vol. 30, no. 3, pp. 606–620, Mar. 2011.
58) Y. Liu, J. Ma, Y. Fan, and Z. Liang, "Adaptive-weighted total variation minimization for sparse data toward low-dose X-ray computed tomography image reconstruction," *Phys. Med. Biol.*, vol. 57, no. 23, pp. 7923–7956, 2012.
59) A. S. Khaled and T. J. Beck, "Successive binary algebraic reconstruction technique: An algorithm for reconstruction from limited angle and limited number of projections decomposed into individual components," *J. X-Ray Sci. Technol.*, vol. 21, no. 1, pp. 9–24, 2013.
60) T. Rahman, X.-C. Tai, and S. Osher, "A TV-Stokes denoising algorithm," in *Proc. 1st Int. Conf. Scale Space Variational Methods Comput. Vis. (SSVM)*, 2007, pp. 473–483.
61) Y. Liu *et al.*, "Total variation-Stokes strategy for sparse-view X-ray CT image reconstruction," *IEEE Trans. Med. Imag.*, vol. 33, no. 3, pp. 749–763, Mar. 2014.
62) Y. Liu, H. Zhang, W. Moore, P. Bhattacharji, and Z. Liang, "A clinical evaluation of total variation-Stokes image reconstruction strategy for low-dose CT imaging of the chest," *Proc. SPIE*, vol. 9412, p. 94123S, Mar. 2015, doi: 10.1117/12.2081614.
63) Y. Liu, H. Zhang, W. Moore, and Z. Liang, "A new look at signal sparsity paradigm for low-dose computed tomography image reconstruction," *Proc. SPIE*, vol. 9783, p. 97834H, Mar. 2016, doi: 10.1117/12.2216536.
64) P. J. Huber, *Robust Statistics*. New York, NY, USA: Wiley, 1981.
65) E. J. Stern and M. S. Frank, "CT of the Lung in Patients with Pulmonary Emphysema: Diagnosis, quantification, and correlation with pathologic and physiologic findings," *Amer. J. Roentgenol.*, vol. 162, no. 4, pp. 791–798, 1994.
66) T. Win *et al.*, "Tumor heterogeneity and permeability as measured on the CT component of PET/CT predict survival in patients with non–small cell lung cancer," *Clin. Cancer Res.*, vol. 19, no. 13, pp. 1–9, 2013.
67) J. Ma *et al.*, "Low-dose computed tomography image restoration using previous normal-dose scan," *Med. Phys.*, vol. 38, no. 10, pp. 5713–5731, 2011.
68) J.-B. Thibault, C. A. Bouman, K. D. Sauer, and J. Hsieh, "A recursive filter for noise reduction in statistical iterative tomographic imaging," *Proc. SPIE*, vol. 6065, p. 60650X, Feb. 2006.
69) J. W. Stayman, J. L. Prince, and J. H. Siewerdsen, "Information propagation in prior-image-based reconstruction," in *Proc. Int. Conf. Image Formation X-Ray CT*, 2012, pp. 334–338.
70) Z. Liang, "Computer-aided detection and diagnosis in CT colonography," in *Computer-Aided Detection and Diagnosis in Medical Imaging*, Q. Li and R. Nishikawa, Eds. New York, NY, USA: Taylor & Francis, 2015.



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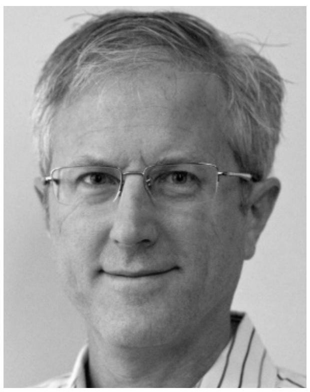

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