Chapter 5

# Research Status and Prospect for CT Imaging

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**Abstract**

Computed tomography (CT) is a very valuable imaging method and plays an important role in clinical diagnosis. As people pay more and more attention to radiation doses these years, decreasing CT radiation dose without affecting image quality is a hot direction for research of medical imaging in recent years. This chapter introduces the research status of low-dose technology from following aspects: low-dose scan implementation, reconstruction methods and image processing methods. Furthermore, other technologies related to the development tendency of CT, such as automatic tube current modulation technology, rapid peak kilovoltage (kVp) switching technology, dual-source CT technology and Nano-CT, are also summarized. Finally, the future research prospect are discussed and analyzed.

**Keywords:** low-dose CT, spectral CT, dual-source CT, nano-CT, image reconstruction, image enhancement

## 1. Introduction

Computed tomography (CT), also referred to as computerized axial tomography (CAT), is a noninvasive and high-tech medical examination that uses X-ray to produce cross-sectional images of the body. With these cross-sectional images, doctors can visualize anatomical structures and tissues inside the body, like small nodules or tumors, which they cannot see with a plain film X-ray. This does not violate the outer surface of the body, in other words, non-invasively. Since the first practical CT instrument developed in the 1970s by Godfrey N. Hounsfield (he received the Nobel Prize in 1979), X-ray CT technology has developed dramatically and become a standard imaging procedure for virtually all parts of the body in thousands of facilities throughout the world. Nowadays, CT scanners are used for a variety of reasons, for example, diagnostic and treatment planning, therapeutic and interventional purposes.

Generally, X-ray CT go through six generations [1]. The first generation, with parallel-beam geometry, only has single X-ray source and single X-ray detector cell to collect all the data for a single slice. The projection data were acquired in approximately 5 minutes, and the tomographic image was reconstructed in approximately 20 minutes. The second generation scanner uses fan-beam geometry and has multiple detectors, thus multiple projections obtained during each traversal past the patient with the acquisition time for one tomogram 1 minute. Both the first and second generation CT works in a translate/rotate model. In the third generation CT, a fan beam of X-rays is used and a curved detector array consisting of several hundred independent detectors is mechanically coupled to the X-ray source, and both rotate in synchrony, that is, rotate/rotate mode. The fourth generation CT also uses fan-beam geometry but with ring of stationary detections array. Only the X-ray tube revolves around the patient, namely, rotate/stationary mode. For third and fourth generation scanners, acquisition times are similar, less than 10 seconds for one tomogram. In the fifth-generation CT, the detector array remains stationary, while a high-energy electron beams is electronically swept along a semicircular tungsten strip anode. Its scanning time is about 50 ms, which is fast enough to image the beating heart without significant motion artifacts. The sixth generation CT is emerged due to the requirement for faster scan times, and in particular, for fast multiple scans for three-dimensional imaging. Both third and fourth generation fan-beam geometries achieve this using self-lubricating slip-ring technology to make the electrical connections with rotating components. It can produce one continuous volume set of data for entire region.

From the first generation to the sixth generation, CT pursues higher speed, spatial resolution and density resolution. At present, these three aspects are still goals of CT manufacturers, but beyond that low-dose scanning is the fourth aspect that CT manufacturers pay real attention to, and become the development direction of CT technology. Overall, the trend of X-ray CT now is mainly in low-dose CT, ultra-low-dose CT and spectral CT, to obtain clear positioning and qualitative diagnosis using the least X-ray radiation.

## 2. Low-dose CT

The application requirements for CT have almost covered all clinical departments, and have been commonly used in medical institutions. However, by the nature of CT scanning, larger radiation doses are involved compared to conventional X-ray imaging procedures, which may lead to adverse health effects. Many literatures show that X-ray radiation will increase radiation-induced cancer risks in adults and particularly in children. The research published in "New England Journal of Medicine" in 2007 shows that 1.5–2% of the tumors may be due to CT radiation. For example, when the effective dose is 10 mSv in an adult abdominal examination, the risk of cancer will increase 1/2000 [2]. And, more remarkable, children are particularly vulnerable to radiation dose damage [3, 4]. There is a growing concern on the significance of minimizing the radiation dose delivered to patients during X-ray CT. It is worth noting that the relative noise in CT images will increase as the radiation dose is decreased. And a tradeoff should be found between radiation dose and imaging quality. At international conferences on radiology in recent years, such as the radiological society of north American (RSNA), the

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topics of several speakers are related to dose protection. The International Commission on Radiation Protection (ICRP) also recommended that radiation doses should all be kept as low as reasonably achievable (ALARA). This means that radiation dose should be as little as possible on the premise that CT images can meet clinical requirement. "Low-dose" has emerged as one of the important direction of CT development.

Low-dose CT was first proposed by Naidich in 1990 and applied to the lung [5]. Their experiments showed that high-quality lung images could be obtained with less radiation doses. But, due to limitations of hardware and software, the image quality are not completely meet the requirements of clinical diagnosis at that moment. Fortunately, the developments of science and technology laid solid foundations for all kinds of low-dose CT technology, and more and more radiologists and researchers have applied themselves to low-dose CT imaging, for example, CT lung screening [6] and CT cardiac screening [7]. In addition, low-dose scan for children has received more attention [8]. On one hand, CT radiation dose reduction is partly dependent on the hardware optimization. On the other hand, it is related to personalized scan parameters, including the number of scans, the tube current and scanning time in milliampere-seconds (mAs), the tube voltage in the kilovolt peaks (kVp), the size of the patient, the axial scan range, the scan pitch (the degree of overlap between adjacent CT slices) and the specific design of the scanner being used.

For any CT scan, the most direct factors that affect the radiation dose are X-ray intensity and exposure time. The clinically common way to achieve the low-dose scan is to lower milliampere-seconds (mAs) or peak kilovoltage (kVp) setting in the scanning protocol, to reduce the intensity of X-ray. **Figure 1** shows a CT phantom reconstruction at standard dose, while lowering the mAs leads to a lower signal-to-noise ratio (SNR) and the decrease of density resolution due to the introduction of noise and streak artifacts [9], such as in **Figure 2**. Thus, it is difficult to distinguish similar density regions. Lowering the kVp causes a worse penetration, greatly reducing SNR. For example, if the tube voltage drops from 120 to 80 kVp, the tube current must be increased by four times to maintain the same SNR [10]. The differences between the two approaches therefore make them used in different applications, for instance, the way of

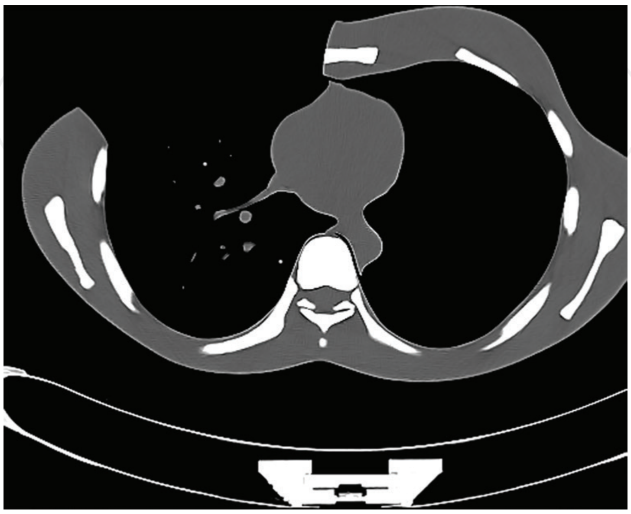

**Figure 1.** CT phantom reconstruction at standard dose (120 kV, 240 mAs).

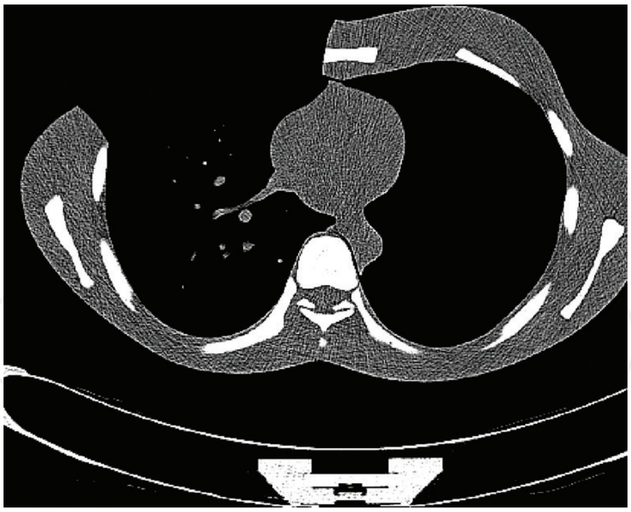

**Figure 2.** CT phantom reconstruction at low dose (120 kV, 30 mAs).

lowering tube current is often used for lesions with high contrast, such as calcifications, while the way of lowering tube voltage is often used for iodine-based contrast imaging [11].

In order to remove noise and artifacts mentioned above, researchers studied a lot of reconstruction algorithms based on the existing CT equipment, hoping to improve the image quality by designing the appropriate algorithm under the limited hardware conditions. Based on this, many techniques have been proposed to remove noise and artifacts in low-dose CT [12]. They are generally categorized into three major types such as projection restorations, iterative reconstruction (IR) and post-processing methods.

### 2.1. Projection restorations

Since the advent of the CT system, the analytic reconstruction algorithm, represented by filtered back projection (FBP), is the mainstream algorithm for two-dimensional CT system and the Feldkamp-Davis-Kress (FDK) algorithm is still the first selection of three-dimensional CT system. This is because the analytic algorithms are simple, thus fast and easy to realize. However, in a low-dose scanning, the projections are contaminated with excessive quantum noise, while the analytic algorithms lack effective ability for noise suppression; this makes the reconstructed images from a low-dose scan that are severely degraded with noise and artifacts. In order to solve this problem, some researchers treat the projection data as an image (called sinogram) and suppress excessive quantum noise in it by kinds of methods, making the projection data close to that at standard dose. Thus, reconstructions with suppressed noise and artifacts can be reconstructed from the denoised projections by analytical reconstruction methods. To cope with the excessive quantum noise in projection data, researchers have proposed different techniques to restore noise-corrupted projections. Hsieh modeled the noise in projection data and proposed an adaptive filtering to achieve streak artifact reduction in CT reconstruction [13]. In the study of Elbakri, the detected photon numbers are considered to follow a Poisson distribution plus a background Gaussian noise with zero mean, and then a penalized Poisson likelihood maximization algorithm was then proposed [14, 15]. Li statistically analyzed the large sample of projection data and considered that noise in the low-dose CT sinogram after logarithm transform and calibration could be modeled as a signal-dependent variable and the sample variance depended on the sample mean by an exponential relationship [16]. Then Wang proposed several penalized weighted least-squares (PWLS) approaches on the noisy sinogram based on this model to adaptively remove non-stationary noise [17–19]. Ma designed a generalized Gibbs prior that exploited nonlocal information of the projection data and used the FBP method to finish the final CT reconstruction [20]. To obtain a more accurate model, Zhang studied the property of the projection data and found an important character that isolated noise points may exist in some areas of the sinogram [21]. Soon he proposed a noise reduction scheme which includes isolated data removal and segmentation-based filtering [22]. Denoising techniques based on wavelet transformation are also applied to projection restorations. Sahiner and Yagle showed how to restore noisy projections in wavelet domain (using wavelet transformation) [23]. Wang proposed wavelet coefficient local adaptive (WCLA) for the noisy sinogram and their method was proved to be effective in removing noise while maintaining the diagnostic image details [24]. Mahmood proposed a graph-based sinogram denoising method, which makes the sinogram as an ideal candidate for graph-based denoising since it generally has a piecewise smooth structure [25]. In addition, many sophisticated denoising techniques are used and improved for projection space denoising, for example, bilateral filtering [26–28], nonlocal means filtering [29, 30] and fuzzy filter [31, 32].

In this category, filtering process and reconstruction process are independent of each other, thus it is well facilitated for system integration. Furthermore, the calculation amount is usually far less than iterative reconstruction and advantages on computing speed is obvious. Projection denoising takes noise properties in projections into account, this makes filters restore the projection data effectively, yet has the potential disadvantage that the definition of edge in projection data is not definite, resulting in sharpness loss in image domain.

### 2.2. Iterative reconstruction

With rapid advances in computing power and the reduction in costs for that power, all the major CT vendors now offer iterative reconstruction (IR). It benefits from Shepp and Vardi who introduced maximum likelihood expectation maximization (MLEM) into the field of reconstruction [33]. Nowadays iterative reconstruction algorithm has been a hot issue in the field of CT reconstruction with one important reason that IR enables diagnostic image clarity on low-dose scans [34–36]. An IR algorithm first establishes a statistical model of Gaussian or Poisson distribution based on the physical model of the imaging system and statistical characteristics of projection data. Then, the corresponding energy equation is solved in the image space by an iterative algorithm. The reconstructed image quality is better than that reconstructed by the traditional analytic method. Another important algorithm, maximum a posterior (MAP) [37, 38], is very popular and frequently used in IR. MAP is based on Bayesian theory, and introduces the prior information of image space as a penalty term, thus can effectively suppress noise and keep the edge. MAP improves the quality of reconstruction obviously and is far superior to analytical reconstruction algorithms on scattering noise and artifacts elimination, so it is very suitable for low-dose CT reconstruction. How to design an efficient prior is the key point of MAP and has been one of the research hotspots of iterative reconstruction algorithm. The traditional iterative reconstruction algorithm usually uses the neighborhood correlation of image space to construct a Markov field prior model [39, 40]. In this model, noise suppression is greatly affected by the noise level of projection data, and the constraint ability is declined when the projection data is seriously noisy. While some prior constructed by non-convex potential function may introduce additional staircase artifacts [41]. Bian proposed a total variation minimization low-dose CT reconstruction method based on a divergence constraint, which eliminates the block artifacts of the traditional total variation priors [42]. Chen considered the excellent denoising capability of nonlocal algorithm and proposed an adaptive-weighting nonlocal prior statistical reconstruction approach [43]. The proposed prior imposes an effective resolution-preserving and noise-removing regularization for reconstructions, and specially has a good recovery ability for region of gradated density. Zhang explored an adaptive Markov random field (MRF)-based penalty term which utilizes previous normal-dose scan to obtain the MRF coefficients and incorporated it into the PWLS image reconstruction framework [44]. Li proposed a hybrid nonlocal means regularization model for iterative reconstruction of low-dose CT perfusion to overcome the limitation of the conventional prior-image-induced penalty [45].

However, IR techniques such as algebraic reconstruction technique (ART) always have high computation loads (e.g., up to several hours per data set), which have prevented fast clinical applications. It is urgent to improve the reconstruction speed and researchers have proposed a variety of methods to speed up the convergence rate of IR algorithms, for example, ordered-subsets image reconstructions [46–48]. However, the practical application of IR is still limited by hardware level. Fortunately, the development of parallel computing technology has played an important role in the application of IR. The computation time of IR can be greatly reduced by using the graphics processing units (GPUs) [49–51]. It is worth noting that IR techniques require access to the raw projection data (projection restoration also has this problem) and are highly dependent on special scanner model, that is, requiring more detailed information such as scanning geometry, photon statistics, data-acquisition, correction physics, thus highly dependent on specific scanner models. Its limitation appeals a more broadly used denoising method that can perform on different systems, and leads us to think more about denoising after reconstruction.

### 2.3. Post-processing method

Image post-processing techniques, working on the image space alone, are retrospectively applied and relatively simple to implement without access to the raw projection data. Since post-processing methods directly enhance the existing CT images, they do not need to improve or replace the existing equipment, thus easy to be used and promoted. The main difficulty comes from the non-stationary mottle noise and streak-like artifacts, which often distribute over the whole CT image. These mottle noise and streak artifacts are caused by the back-projection process within the FBP algorithms, and are difficult to remove because they do not obey to specific distribution models. Various sophisticated techniques, considering the strong structural and statistical properties of objects in image space, have been proposed for improving the quality of low-dose CT images. In [52, 53], the low-dose CT reconstruction images are filtered by nonlinear or anisotropic filters, which can smooth the image effectively meanwhile preserve edges to some extent. But this kind of algorithms is easy to reduce the image contrast and blur the image edge. Furthermore, since such filters are usually defined in small scale regions, it is impossible to suppress high-frequency noise in projection data, typically with almost no effect on metal artifacts. Wavelet-based method to a certain extent can remedy the defects of small scale spatial filtering, and effectively preserve the texture information while suppressing high-frequency noise [54, 55]. Zhong presented wavelet coefficient magnitude sum (WCMS) and experiments showed that 60% of the noise could be removed [56]. Borsdorf proposed a correlation-based wavelet method for noise reduction in low-dose CT images [57]. Large-scale nonlocal mean filter is another commonly used post-processing algorithm, which carry out the nonlinear filtering correction in the current position by searching the matching information according to the self-similarity of the tissues under various doses in a large scale. This method has good performance in noise elimination and edge preservation. Chen proposed a large-scale nonlocal means (LNLM) filter to improve abdomen low-dose CT images by exploiting large-scale structure similarity knowledge, which was further combined with a multiscale directional diffusion scheme to reduce the streak artifacts in thoracic CT images [58]. Ma proposed a new nonlocal mean algorithm by combining nonlocal mean and the results obtained from previous normal-dose scans to deal with low-dose CT, and the image artifacts are solved in a certain extent by means of image guidance techniques [59]. In [60], feature knowledge in available CT database is incorporated into weight update in LNLM strategy, and a notable image quality enhancement was reported. Dictionary learning and sparse representation were also used for reconstruction and enhancement for low-dose X-ray imaging [61–64]. The dictionary technique studies from normal-dose CT images (feature extraction) guide the low-dose CT image processing. Dictionary technology combines the advantages of large-scale nonlocal filtering and image guidance technology, and has very good extendibility. However, they have the limitation of computation time. Recently, the deep learning technology is popular and shows great potential in image denoising. Chen trained a deep convolutional neural network (CNN) to transform low-dose CT images toward normal-dose CT images, patch by patch and visual and quantitative evaluation demonstrates a competing performance of the proposed method [65]. Wu proposed a cascaded training network for low-dose CT image denoising, where the trained CNN was applied on the training dataset to initiate new trainings and remove artifacts [66]. Wolterink proposed to train a CNN jointly with an adversarial CNN to estimate routine-dose CT images from low-dose CT images and hence reduce noise [67]. Kang applied a CNN to wavelet coefficients of low-dose CT images and showed that wavelet domain CNN was efficient in removing the noises from low-dose CT compared to an image domain CNN [68, 69].

In addition to X-ray intensity, to shorten scanning time can also reduce the radiation dose dramatically, which can be achieved by reducing projection angles (sparse angles or incomplete angles) in acquisition process. Due to the projection, data of CT systems usually have high redundancy, under the condition of less sampling angles, the missing data can be repaired to get a complete projection data set, and the reconstruction quality can be improved using the repaired data. In the decade, dictionary learning and TV (total variance) constraint are two effective techniques to estimate the missing projection data [70–76]. Recently, the convolutional neural network was also performed in sparse-view reconstruction (down to 50 views) on parallel-beam X-ray CT [77].

### 2.4. ATCM technology

In addition to adjusting scanning parameters, GE, Philips, Siemens and Toshiba introduced automatic tube current modulation (ATCM) to realize low-dose CT scanning. ATCM is based on differences of attenuation characteristics of human anatomy structure, and adjusts the tube current automatically according to the X-ray attenuation change. ATCM controls the tube current by using a certain algorithm and an optimized mode in the X-Y plane or along the scanning direction (Z-axis), thereby radiation doses are reduced in unnecessary projection direction. Another way, ATCM can achieve imaging with the minimum radiation dose by setting the image quality that meets certain criteria in advance. For example, the anteroposterior diameter of the chest and pelvis is significantly smaller than its right-and-left diameter. The anteroposterior tissue is thinner and the X-ray attenuation is lower, while the side is thicker and the X-ray attenuation is higher. Studies have shown that the total radiation dose can be reduced by 29.4% by using the ATCM technique for full-body scan, and the abdominal radiation dose can be reduced by 29.7% [78]. At the annual conference on radiology in North America in 2008, some manufacturers introduced selective shielding techniques that would allow the closure of X-ray when it rotates to the direct irradiation position of sensitive organs, such as eyes, thyroid and breast, thereby to avoid direct exposure to sensitive organs [79]. In addition, an asymmetric shielding acquisition system, called adaptive dose shield (ADS), can shield the invalid X-ray at the beginning and end of the Z-axis scan. Furthermore, it reasonably distributes the irradiation area with a cardiac bowtie. The radiation doses of cardiac scan are therefore reduced without increasing noise.

## 3. Ultra low-dose CT

In the decades, ultra low-dose CT, defined as a radiation dose ≤1.9 mSv, was studied and used [80, 81]. Accordingly, researchers pay attention to the reconstruction algorithms for high-quality ultra low-dose CT. Yu proposed a previous scan-regularized reconstruction (PSRR) method for ultra low-dose CT of lung perfusion [82]. His study demonstrated that approximately 90% reduction in radiation dose is achievable using PSRR without compromising quantitative computed tomographic measurements of regional lung function. Xu compared the effect of different reconstruction algorithm applications for ultra low-dose CT on image quality improvement using a phantom study [83]. Rob investigated whether ultra low-dose CT and low-dose CT KUB (kidney, ureters and bladder) for acute renal colic impacted upon the specificity, sensitivity and detection of urolithiasis, and found that both ultra low-dose CT and low-dose CT yield comparable results against standard-dose CT KUB in detecting alternative diagnoses (they may not be as effective in detecting stones <3 mm in size or in patients with a body mass index of >30 kg/m$^2$) [84]. For the foreseeable future, ultra low-dose CT with the tendency of CT development and more commonly used in clinical, especially for several months baby, and pregnant female. In a word, CT technologies have entered into low-dose imaging times.

## 4. Spectral CT

CT manufacturers have tried their best to improve the hardware for the improvement of reconstructed image quality for low-dose CT. For example, they improved the detection efficiency to increase the SNR of acquired data and sequentially reduced the noise in CT images. They also designed wide-detector CT to improve time resolution and improved the detector material. One study reported that the wide-detector revolution CTA with 70 Kv tube voltage and prospective ECG-gated technique can provide high accuracy for assessment of congenital heart disease (CHD) in infants and children, which can keep good image quality, with the low radiation dose [85]. More significantly, it is the appearance of spectral CT, which can achieve high time resolution and high intensity resolution.

Advances in multi-detector technology, photon counting energy dispersive detectors and computer-processing technology have made spectral CT imaging possible [86–94]. Spectral CT can convert the X-ray absorption coefficient of any material to absorption coefficient of any two base material and achieve the same attenuation effect. On the basis of the improvement of X-ray tubes and X-ray detectors, spectral CT can obtain two images at different levels of energy at the same time and at the same phase to reconstruct high-definition and monochromatic images from 40 to 140 keV and even generate three materials decomposition images, virtual non-contrast images and specific spectrum curve. Thanks to innovations on the tube ball and detectors, spectral CT not only achieves high resolution, high-definition images in the case of low radiation dose, but also uses the spectral imaging technology for the first time. Spectral CT uses different X-ray spectra and certain chemical elements to detect changes in the shape and function of the whole body, and can realize single photon imaging and physical separation, thus fundamentally changes the traditional way of CT imaging based on a single CT value and provides reliable information to diagnose disease earlier and more accurately, showing a great advantage in imaging. As a new method of clinical application, spectral CT can be developed rapidly in the qualitative, quantitative diagnosis and prognosis evaluation of systemic diseases. Nowadays, it is a promising technique with clinical application potential and has become another direction of CT technology. At present, there are two clinical kinds of spectral CT equipment. One takes the rapid kVp switching as the core technique and another is the dual-source CT (DSCT).

The rapid kVp switching technology is first launched by GE, that is, Discovery CT750 HD [95], it has a double energy system but only with a single source, as shown in **Figure 3**. This system is composed of a special X-ray source which can switch kVp in a very short time (0.5 ms) and detectors can detect the high-energy and low-energy photons, thus obtaining two projection data sets. Discovery CT750 HD adopt gemstone as the detector materials (that has more stability than traditional materials), rapid kVp switching and adaptive statistical iterative reconstruction (ASIR) technology, spectral grating imaging technology and so on, makes it has high resolution imaging with low radiation dose. Detectors made of gemstone ensure each image in a whole body scan reconstructed in a low-dose case from hardware. More importantly, ASIR is the key technology to achieve high resolution and low radiation dose at the same time. It can achieve the limit of 0.23 mm spatial resolution around the body, and find small lesions that cannot be found using a conventional CT scan, greatly improve the detection rate of the lesions and the identification of tumorous diseases [96]. Besides an approximate 50% reduction in radiation dose is achieved compare to routine dose.

DSCT is first launched by Siemens, at the moment, there are two clinical, commercially available DSCT scanners: the SOMATOM Definition (the first generation DSCT, launched in 2005) and the SOMATOM Definition Flash (the second generation DSCT, launched in 2019). Each of them contains two X-ray tubes and two detectors which are mounted so that the X-ray

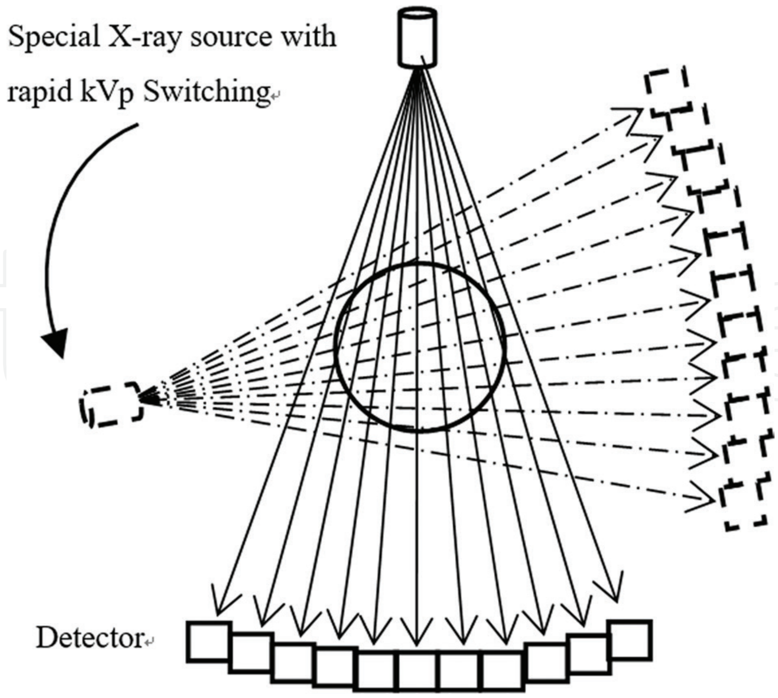


**Figure 3.** Diagram of discovery CT750 HD system.

beams are approximately perpendicular to each other, as shown in **Figure 4**. DSCT has two working model, that is, single source model and double source model. It works like an ordinary CT when using the single source model, while two acquisition systems work simultaneously when using the double source model. Thus one can obtain two independent sets of images, mainly used for separation of bones and calcification, tissue and collagen component,

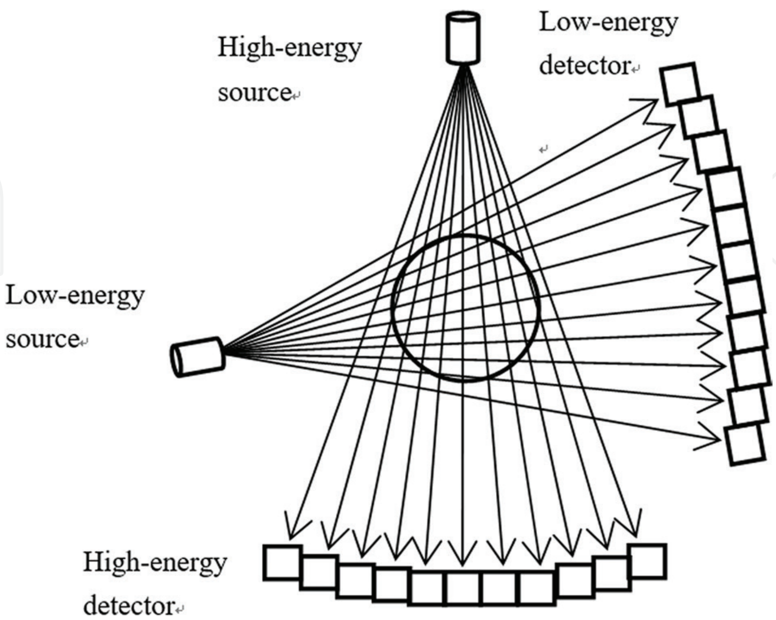


**Figure 4.** Diagram of DSCT system.

etc., or one set of fusion image reconstruction, mainly used for high time resolution requirements such as the cardiac workup. DSCT has advantages on time resolution, only 83 ms in SOMATOM Definition and 75 ms in SOMATOM Definition Flash, thus lead to a low radiation dose. In a word, DSCT provides faster scanning speed and lower radiation dose, and completely broke the traditional idea of CT technology, leading to a new revolution in CT history.

## 5. Nano-CT

In addition to technologies mentioned above, CT contrast agents that often used for distinguishing subtle changes of soft tissues with similar densities, also makes, or rather, requires a low kVp, that is, low-dose radiation. Studies have shown that a lower kVp can improve the enhancement degree of contrast agent and thus improve the contrast between different tissues [97]. Especially in turn, using this low-dose CT, one can obtain good images with a low contrast agent dose, because contrast agent is harmful to human health. For example, often used contrast agent in angiography imaging, iodinated compounds, have relatively short circulation times in vivo and its rapid renal clearance may lead to serious adverse effects. Therefore, a variety of CT contrast agents are required to be developed.

A long-sought-after CT contrast agent is the nanoparticle, which has tunable composition, shape and size, and can be readily attached to bioconjugates with interesting biofunctionalities on their surface [98, 99]. Nano-sized iodinated CT contrast agents have been developed that can increase the circulation time and decrease the adverse effects [100]. The classical nanoparticulate iodine-containing contrast agents include liposomal contrast agents, nanosuspensions, nanoemulsions, nanocapsules and polymeric nanoparticles [101]. Despite prolonged in vivo circulation time as compared to iodinated molecules, iodine-conjugated nanoparticles are still limited by iodine loading through surface covalent conjugation [102]. Moreover, iodinated agents cannot be used for those patients who are iodine hypersensitive. These appeals to new CT contrast agents using nanoparticles composed of other elements with higher X-ray attenuation. In 2006, Hainfeld first introduced gold nanoparticles (AuNPs) as CT contrast agent [103], and caused a lot of attention since gold has a higher atomic number than iodine, and thus, has a larger X-ray attenuation. Moreover, the size and shape of gold nanostructures can be easily controlled, and their surface can be modified with various functional groups [102]. Besides, it has good biotolerability and nontoxicity. All of these make AuNPs attract intense interest as CT contrast agents. Over the past few years, many studies on Au nanoparticle design techniques are reported and show good significant CT image enhancement [104–108]. In addition to iodine and gold, other nanoparticles based on heavy atoms such as lanthanides, Bismuth and tantalum Bismuth-based contrast agents, have been used as more efficient CT contrast agents [109, 110].

With the progress of micro-nano processing technology, nano-ray source, micron grade CCD with nanoscale resolution, precise optical focusing imaging device, synchronous radiation source with high brightness, CT is being extended to the nanoscale, that is, nano-CT, bringing us startlingly accurate pictures of objects [111]. Nano-CT is derived from micro-CT but with higher resolution. At present, it has been widely used in many fields such as biology imaging, pathological examination, integrated circuit testing and so on, and it is believed to have broad application prospects. For example, the phoenix nanotom® m, which is a nanoCT® system, has been used in industry and realized a unique spatial and contrast resolution on a wide sample and application range. Nano-CT also has been developed at the European synchrotron radiation facility (ESRF) to image bone tissue at the nanoscale [112].

## 6. Summary

In recent years, CT has been developing steadily and the scope of clinical application has been continuously expanded. Now we pay more attention on utility-driven CT instead of algorithm-driven CT. Low-dose CT, ultra low-dose CT and spectral CT are representative directions of CT application, and the rapid development of the hardware provides substantial support. The future development of CT equipment is spectral CT, low-dose CT and even harmless CT. It is believed that with the progress of the ball tube and detector technology, the X-ray dose problem will be completely solved 1 day. The promotion of low-dose CT, combining the enhancement of time resolution, spatial resolution and density resolution, will make CT under the condition of safety and low-dose radiation, achieve more quickly in a clearer image display, making the disease more early and more clearly diagnosed. CT themselves will play an effective role clinical diagnosis and evaluation for more disease in such a high level of display. CT vendors shall stand to win in the fierce market competition if they step up such developments and win praise from the medical community and the whole people.

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