Evaluation of image quality and radiation dose using gold nanoparticles and other clinical contrast agents in dual-energy Computed Tomography (CT): CT abdomen phantom

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Abstract. The aim of this study was to evaluate the image quality and radiation dose using commercial gold nanoparticles and clinical contrast agents in dual-energy Computed Tomography (CT). Five polymethyl methacrylate (PMMA) tubes were used in this study, where four tubes were filled with different contrast agents (barium, iodine, gadolinium, and gold nanoparticles). The fifth tube was filled with water. Two optically stimulated luminescence dosimeters (OSLD) were placed in each tube to measure the radiation dose. The tubes were placed in a fabricated adult abdominal phantom of 32 cm in diameter using PMMA. The phantom was scanned using a DECT at low energy (80 kV) and high energy (140 kV) with different pitches (0.6 mm and 1.0 mm) and different slice thickness (3.0 mm and 5.0 mm). The tube current was applied automatically using automatic exposure control (AEC) and tube current modulation recommended by the manufacturer (CARE Dose 4D, Siemens, Germany). The contrast-to-noise ratio (CNR) of each contrast agent was analyzed using Weasis software. Gold nanoparticles has highest atomic number (Z = 79) than barium (Z = 56), iodine (Z = 53) and gadolinium (Z = 64). The CNR value of each contrast agent increases when the slice thickness increases. The radiation dose obtained from this study decreases when the pitch increases. The optimal imaging parameters for gold nanoparticles and other clinical contrast agents is obtained at pitch value of 1.0 mm and slice thickness of 5.0 mm. Low noise and low radiation dose obtained at these imaging parameters. The optimal imaging parameters obtained in this study can be applied in multiple contrast agents imaging.

1. Introduction
Computed tomography (CT) is one of diagnostic tool that is applied in clinical and preclinical applications. This is because CT has high diagnostic efficiency which provides anatomical information of tumor and good accessibility. Conventional CT uses a wide energy spectrum and digital integrating sensor¹,². However, conventional CT cannot distinguish the tissues because the attenuation of x-ray is not at a specific energy but it is over the broad energy for all tissues within the voxel. The contrast resolution for soft tissues do not adequate for conventional CT ¹,³. Thus, innovation in CT imaging technology has overcome this limitation with the use of an advanced imaging technique known as a dual-energy CT (DECT) imaging.
In this study, the DECT with single source was used with applied energies of 80 kV and 140 kV. These two tube voltages will be fast switched to obtain the CT images. Different types of tissues that have similar density with different composition of element are able to distinguish by DECT. This is because DECT can differentiate the tissues according to their atomic number and electron density differences. The higher atomic number of material are more preferable for contrast agent. This is because the beam hardening which the effect of photon starvation is less worse than the contrast agent with low atomic number. The use of multiple contrast agents simultaneously are possible in diagnostic imaging which may reduce the drug dose, diagnosis time, radiation dose, and improve specificity and sensitivity. Nevertheless, the conventional CT is unable to differentiate between the multiple contrast agents with wide range of concentrations and atomic numbers when they use simultaneously. This limitation can be overcome by using DECT as two different energies are applied which can differentiate the contrast agents with different atomic numbers.

Thus, DECT with multiple clinical contrast agents and new contrast agent were used in this study. Barium (Ba), iodine (I), and gadolinium (Gd) are the clinical contrast agents that were used in this study. The atomic numbers (Z) of Ba, I and Gd are 56, 53, and 64 respectively. A new contrast agent, gold nanoparticles (AuNPs) have higher atomic number (Z=79) than current used clinical contrast agents. Gold nanoparticles have all the properties and features of the contrast element. The circulation time for gold is up to 15 hours which is longer than iodine (less than 10 minutes). Gold also easy to fabricate into nanoparticles with variety shapes and sizes. The contrast-to-noise ratio (CNR) of CT image increases with the presence of gold at certain dose or the dose will be decreased without diminishing the CNR when using high atomic number contrast agent.

In the previous study, there is no measurement on the radiation dose obtained from multiple contrast agents scanning. Most of the studies only evaluated CT image quality when the contrast agents were applied. Thus, in this study, the evaluation of radiation dose using gold nanoparticles and other clinical contrast agents in DECT was proposed by applying different pitch and slice thickness. The optimum imaging parameters obtained from this work were proposed when applying barium, iodine, gadolinium and gold nanoparticles for DECT. The optimum imaging parameter is obtained when the radiation dose is lowest at an optimal image quality. Thus, the dose-weighted contrast-to-noise ratios (CNRD) were calculated to determine the optimum imaging parameters when using multiple contrast agents simultaneously in DECT.

2. Materials and methods

2.1. Phantom
A fabricated polymethyl methacrylate (PMMA) phantom with diameter size of 32 cm as shown in figure 1 was used in this study to mimic an adult human abdomen. This phantom contains five cylindrical tubes which four of them filled with barium (EZ-CAT), iodine (OMERON 350), gadolinium (MultiHance), and gold nanoparticles (SIGMA ALDRICH) while one of the tubes filled with water. The concentration of these contrast agents are similar with clinical used which are 4.9187 % w/v (4.6 % w/w), 350 mg/ml and 1.220 g/mL for barium (Ba), iodine (I), and gadolinium (Gd), respectively. The concentration of commercial gold nanoparticles (AuNPs) was used (2.15 x 10⁻⁷ g/ml). The volume of each contrast agent used in this study was 100 ml. There is a slot in the middle of each contrast agent tube to be inserted with the optically stimulated luminescence dosimeter (OSLD). Two OSLDs were inserted in each tube to measure the radiation dose and the average dose was computed. These contrast agents were scanned simultaneously using single-source CT scan (Somatom Definition; Siemens AG, Wittelsbacherplatz Muenchen, Germany).
2.2. Scanning Parameters and Image Analysing
The phantom filled with water and contrast agents was scanned at 80 kV and 140 kV for DE scanning. The tube current was set automatically using CARE Dose 4D software. The pitches were set at 0.6 mm, and 1.0 mm and the slice thickness were set at 3.0 mm, and 5.0 mm. CT scanner used in this study is single source. Thus, three set images were obtained from DE scanning; where two images were acquired from 80 kV and 140 kV, and the third one was obtained from fused image.

The images obtained were analyzed using Weasis and Matlab softwares. The contrast-to-noise ratio (CNR) was calculated based on equation (1).

$$\text{CNR} = \frac{|S_A - S_B|}{\sigma_B}$$ (1)

where $S_A$, $S_B$, and $\sigma_B$ are mean value of contrast agent (HU), mean value of background (HU), and standard deviation of background respectively. Dose-normalised contrast-to-noise ratio dose (CNRD) was calculated to determine the optimum scanning parameters for gold nanoparticles and other clinical contrast agents using DECT[11]. CNRD was calculated using equation (2).

$$\text{CNRD} = \frac{\text{CNR}}{(\text{Dose})^{1/2}}$$ (2)

3. Results and Discussion
3.1. Contrast-to-Noise Ratio
There are three set of images were obtained from each scanning as the single source DECT (80 kV and 140 kV) was used in this study. These images obtained were at 80 kV, 140 kV and fused image. The fused image from DECT was obtained after the scanning is assumed to be similar with the images that taken at energy of 120 kV in single-energy CT (SECT)[12,13]. All the images obtained were analyzed using Weasis and Matlab softwares to measure the CT number of the contrast agents. Then, the CNR of the contrast agent was calculated. Three regions-of-interest (ROIs) were chosen for contrast agents and background.

The CNR values obtained from DECT images were shown in figure 2. The highest CNR was obtained using DECT imaging. This is due to reduction of image noise during image reconstruction of the fused image using sharp convolution Kernel. Moreover, the image obtained was the output of quick removal of beam hardening errors as each dataset pair is obtained at the same point along the route through the patient[14,15]. The applied tube voltage of 140 kV shows higher CNR compared to CNR obtained at tube voltage of 80 kV for iodine, gadolinium and gold nanoparticles. This is because...
more radiation dose were exposed and less image noise produced at higher tube voltage applied\textsuperscript{11}. However, tube voltage of 80 kV shows higher CNR than 140 kV for barium as shown in figure 2. This is because barium has higher attenuation at low tube voltage. Therefore, the contrast of the image was brighter when the attenuation of x-ray beam is high. In general, iodine gives high CNR at DECT imaging compared to other clinical contrast agents. This is due to high concentration of iodine was used which gave more attenuation occurred in iodine. The x-ray attenuation was affected by concentration and atomic number. The pattern of CNR against tube voltage for 0.6 mm pitch and 3 mm slice thickness was similar to figure 2.

![Figure 2. The CNR of different contrast agent against tube voltage at pitch of 1 mm and slice thickness of 5 mm.](image)

Figure 3 shows the CNR of fused image for all contrast agents. The CNR was evaluated with different slice thickness at pitch of 1 mm. The CNR of all contrast agents increase when the slice thickness increases. The beam width and the voxel size changed when changing the slice thickness\textsuperscript{16}. Bigger beam width and voxel size were produced when applying large slice thickness which captured more photons. These captured photons produced the contrast of the image. The gold nanoparticles shows the lowest CNR compared to other contrast agents as shown in figure 3. The CNR of gold nanoparticles was up to 0.6 slightly similar to water. This finding contradicts from other studies due to lower concentration of the gold nanoparticles used. The concentration of gold nanoparticles from other studies\textsuperscript{10,17,18} were between 2.0 mg/ml to 13.6 mg/ml while this study used 2.15 \times 10^{-7} g/ml. This low concentration reduced the x-ray attenuating atom per agent as low particles number found in gold nanoparticles\textsuperscript{7}. Thus, the CNR for gold nanoparticles is lowest than other contrast agents as its concentration is lowest. The CNR pattern of all contrast agents when applying 0.6 mm pitch also increased with slice thickness.

![Figure 3. The CNR of contrast agent obtained at 80/140 kV DECT against 1 mm pitch.](image)
3.2. Radiation Dose

The average measured radiation dose obtained from OSLD was shown in figure 4. The accumulated radiation dose from 80 kV and 140 kV imaging in DECT is corresponding to the radiation dose from the fused image. From figure 4, the radiation dose of the contrast agents and water decreases with the increasing of the pitch. In multislice CT (MSCT), pitch is defined as table distance traveled in one 360° gantry rotation divided by total thickness of all simultaneously acquired slices. The radiation exposure to the contrast agents were reduced when high table speed applied. The measured radiation dose using OSLD decreases when pitch and slice thickness increases. Christner et al. 19 also found a large percentage of dose reduction for high pitch while Srivastava et al. 20 found that the dose reduced with increasing the slice thickness.

The use of CARE Dose 4D for tube current allows optimal tube current to give the adequate radiation dose and image quality. The highest radiation dose was obtained with Ba followed by gold nanoparticles and gadolinium. The low concentration of Ba causes less x-ray photon absorbed and allows more x-ray photon to pass through the Ba which measured by OSLD. Although that the concentration of the gold nanoparticles is lower than the barium, it shows a slightly lower radiation dose than barium. This is due to higher atomic number of gold nanoparticles compared to barium. The concentration and atomic number of the contrast agent affects the attenuation of the x-ray. The lowest radiation dose was obtained in this study with the use of iodine. The same pattern of radiation dose was obtained in this study with the use of slice thickness of 3 mm and 5 mm. In clinical application, saline solution is injected after contrast agent. The saline is not used in this study as the phantom is fixed with the region of interest.

![Figure 4](image)

*Figure 4.* The graph of radiation dose against pitch at slice thickness of 5 mm for 80/140 kV DECT image.

The optimum scanning parameters for gold nanoparticles and other clinical contrast agents in DECT were determined by calculating CNRD as shown in equation 2. The maximum CNRD represents the minimum radiation dose that measured for a given image quality. The values of CNRD of all contrast agents and water were listed in table 1. The maximum values of CNRD were obtained from high pitch of 1 mm and slice thickness of 5 mm for barium, gadolinium, and gold nanoparticles. Iodine shows maximum CNRD at pitch of 0.6 mm and slice thickness of 5 mm. The maximum CNRD for barium, iodine, gadolinium, and gold nanoparticles were 7.08, 64.30, 26.00, and 0.23 respectively.
5. Parameters

Thus, the use of higher kV. The tube voltage, slice thickness of 5 mm was evaluated in this study. The overall optimum imaging parameters for multi contrast agent imaging obtained from this study were at 1 mm pitch and 5 mm slice thickness. The maximum slice thickness for DECT imaging was up to 10 mm. The slice thickness of 5 mm is an acceptable slice thickness that has less diminished in image resolution.

4. Conclusion

The image quality and radiation dose using commercial gold nanoparticles and clinical contrast agents in DECT were evaluated in this study. The attenuation of barium and iodine are higher when applying low tube voltage because both contrast agents have lower atomic number compared to gadolinium and gold nanoparticles. The high concentration of iodine used causes more attenuation at tube voltage 120 kV. The tube voltage, slice thickness, and pitch affect the image quality and radiation dose to patient. Thus, the use of higher tube voltage and slice thickness gives high contrast-to-noise ratio (CNR). The DECT gave highest CNR on the fused image. Low radiation dose was obtained with the use of high pitch. Thus, pitch of 1 mm and slice thickness of 5 mm were recommended as the optimum scanning parameters for simultaneous multiple contrast agents imaging with DECT.

5. References

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**Table 1.** The CNRD of gold nanoparticles and other clinical contrast agents using DECT for different pitch and slice thickness.

| Pitch (mm) | Slice thickness (mm) | Ba | I | Gd | Au | Water |
|-----------|----------------------|----|---|----|----|-------|
| 0.6       | 3                    | 6.25 | 61.50 | 18.49 | 0.15 | 0.06  |
|           | 5                    | 6.93 | 64.30 | 25.58 | 0.10 | 0.02  |
| 1         | 3                    | 5.48 | 33.32 | 25.21 | 0.15 | 0.01  |
|           | 5                    | 7.08 | 63.67 | 26.01 | 0.23 | 0.07  |
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