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Liver Tissue Characterization Using Dual-Energy Computed Tomography

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Abstract : *The aim of this study was to review the techniques that improve the images in detecting liver lesions using dual-energy computed tomography (DECT). DECT has improved tissue characterization in recent years, which provides extra information such as tissue composition, compared to single-energy computed tomography (SECT). The use of low and high X-ray tube voltages in DECT provided fused images that improved the detection of liver tumors due to the higher contrast-to-noise ratio (CNR) of the tumor compared to the liver. The utilization of the contrast agents in CT scanning improved the image quality by enhancing the CNR and signal–to–noise ratio (SNR) while reducing beam-hardening artefacts. CT imaging visualization and the ability of liver tumor detection can be enhanced using different contrast agents with suitable protocols such as iodine mapping. The use of morphine co-medication in potential donors possibly improved the visualization of the intrahepatic bile ducts after the sphincter of Oddi. Besides that, scanning protocols such as tube current (mAs), collimation, pitch and gantry rotation times were also very important when undergoing CT examination. This also increases the image quality and lesion visibility with lower doses. Furthermore, using the current modulation software such as CARE DOSE 4D, Siemens and SMART MA, GE provided by the manufacturers and low voltage techniques in detecting hyper vascular liver lesions, helped in reducing the dose administered to the patient. The dose in DECT is lower compared to CT perfusion and the conventional SECT, and maintains the image quality at the same time. DECT had shown an encouraging future in improving the characterization and detection of the liver lesions compared to the conventional SECT.*

Keywords: *Dual-energy, contrast, CT, tissue characterization, liver, lesions.*

I. Introduction

The liver is an important organ to humans and it is the only organ which can regenerate itself. The liver functions as a filter in the human body; it will filter blood from the digestive tract before transferring it into systemic circulation. The liver also helps in getting rid of toxins in the human body. Besides this, the liver is important for the digestive system, producing hormones and proteins, blood clotting and other functions which are essential to the human body. A lesion to the liver will affect liver functions and can be fatal for the patient if not acknowledged and treated in time. There are several types of lesions such as hepatic haemangioma, hepatocellular carcinoma (HCC), hepatic metastasis and liver cysts.

HCC is the common primary type of cancer of the liver. This type of cancer starts inside the hepatic cells. Globally, there were more than 1 million deaths due to hepatocellular carcinoma every year. Lung and stomach cancers are the most common type of cancer which causes death, followed by hepatocellular carcinoma. The fifth most common malignancy worldwide is HCC[1]. Thus, it is important to detect the lesion and get the proper treatment in time. Magnetic resonance imaging (MRI), ultrasound imaging and computed tomography (CT) imaging modality are the most commonly noninvasive methods for diagnostic in liver lesion[2]. Comparing CT imaging with ultrasound imaging, CT imaging is more costly and unsafe due to the exposure of ionizing radiation that plays an important role in diagnosing liver lesions[2]. The image quality obtained from the CT scan provides better quality in terms of contrast, noise and ability to characterize the type of lesion, thus encourages the used of CT over ultrasound[2,3]. In addition, scanning with DECT provides extra information in terms of material composition enabling characterization of the type of lesion and at the same time reducing beam-hardening artefacts[4-6]. CT scans are one of the non-invasive methods which are used to detect and diagnose liver lesions. Different types of lesions have tissues that have differences in chemical composition and mass density[7]. Thus, this will result in different attenuation value in different energy levels. The information of the range of CT number obtained can be used while doing image processing for segmentation after the statistical analysis[8,9]. Differentiation and characterization of liver lesion types are very important in diagnosing before the treatment plan is given[2]. Other than the diagnostic value, CT scans for the liver are also very important during liver transplants and treatment, and there were a lot of studies carried out by various researchers on the use of CT[1, 2, 4, 6, 10, 11]. Those researchers carried out the experiment with different protocol settings on the dual energy CT and some performed the scan without contrast agents.

II. General information about SECT and DECT

CT was invented by Allan Macleod Cormack and Godfrey Newbold Hounsfield from London and became commercial in the early 1970's[12, 13]. Before this, in the year 1961, Olendorf had already carried out some experiments which had similar a concept with the Allan and Godfrey idea[13, 14]. However, he was not aware of the usefulness of his work and so the image reconstruction technique was not established at that time[13].

X-rays used in CT were to acquire two-dimensional images of the body in cross section. The rapid rotation of the X-ray tube along the gantry in 360 degrees around the patient allowed image production. The detectors located around the gantry would measure the transmitted radiation. These measurements would be used to reconstruct the final image from multiple X-ray projections. In the past, computed tomography was only able to obtain images in a single slice at a time. The significant improvement and development in the technology during the 1980s had brought out the invention of slip ring technology. The invention of the slip ring allowed the X-ray tube to rotate in one direction continuously. This invention has been added to the development of the helical scan in computed tomography.

Single energy computed tomography (SECT) is also known as conventional tomography. SECT scanner performs the scanning at a fixed voltage with a single X-ray tube. Meanwhile, DECT scanner performs the scanning with a low and high voltage. There are several types of approaches for acquiring the dataset in DECT. The first type is the scanner with 2 X-ray tubes and 2 sets of detectors. Each X-ray tube operates at different voltage levels and paired with dual source-detector. The second type is a single X-ray tube with a single detector. The X-ray tube provides rapid alternation between low and high energy in a single gantry rotation. This was followed by the single-source detector and dual-layer detectors. The material of this detector can distinguish between low and high energy photon. Lastly, single source-detector paired with tube voltage switching between sequential gantry rotations[15, 16]. The design of the X-ray tubes and the detectors that acquire the images differ between scanner models and manufacturers[15, 17].

When the X-ray beams penetrate matter, the intensity of the X-ray will reduce due to the absorption or scatter of photons. The atomic number of the subject and the tube voltage will affect the reduction or the attenuation rate of the photons. The attenuation value or CT number (HU) is represented on a grayscale. The CT number differs between different types of materials[7, 16]. Thus, the useful structural information of material would be shown in conventional CT images. Compared with conventional CT, dual energy CT provides more information than single energy CT and this information can be used to determine the composition of materials, bone subtractions and iodine mapping[4, 5, 18]. The iodine mapping provided by DECT corresponds well with static CT perfusion images for lung and heart. Other than this, the iodine mapping technique has been known to have latency in the evaluation of the relative vascularity of pulmonary nodules.

Using the image datasets obtained from the DECT and deriving the 80 kVp which is the accession value in detecting hyper-vascular and hypo-vascular liver lesions, or improving the quality of images for the virtual non-enhanced CT images had been emphasized in most studies of liver[1, 2]. Furthermore, the contrast of the imaging for the abdomen was enhanced with the use of DECT[19]. The perfusion CT has the ability to measure the parameters for tissue hemodynamics and enabling it to provide a qualitative diagnosis of liver lesions. The clinical value in this was high but the use of it in clinical practice was limited due to the high radiation dose. DECT had shown an encouraging future in improving the characterization and detection of the liver lesions with comparing with the conventional SECT[1].

III. Results

3.1 Scanning parameters of liver with DECT

The CT examination performed with DECT contained two X-ray tubes on high energy (140 kVp) with tint (Sn) filter and lower energy (80 kVp)[5, 11, 20]. The tube currents (mAs) which are 96 mA was used for higher energy and 404 mA for lower energy had been used to generate spectral images datasets. The field of view is 26 cm for the smaller detector[5, 11]. The beam collimation and the pitch was 64 × 1.2 mm and 0.55 respectively. The rotation speed for the gantry was 0.5 s[5, 11].

3.2 Potential tube voltage and potential tube current in imaging

The use of low voltage technique not only provides higher CNR and better lesion conspicuity[5, 20]. Moreover, it helps to reduce the dose delivered to the patient[1]. The acquisition of the low and high energy or tube current can achieve at the same time and the disparity of the time was insignificant with the dual-source, dual-energy CT scanner. An average weighted image similar or likely to be 120 kVp was reconstructed from 80 kVp and 140 kVp images with the ratio of 3 to 7[1, 5, 18].

In one study, it was also mentioned that the fused image of 120 kVp was reconstructed at the weights of 0.5 and 0.6[21]. In all those weights, it also has the same similarity which all provided better image quality compared with the 140 kVp and 80 kVp itself. The image obtained from 80 kVp has better contrast but lower SNR whereas the image obtained from 140 kVp has better SNR but lower contrast. The fused weighted image resolved these problems and provided the images in better contrast and lower noise[5, 18].

Concluding from the study of Zhang et al of an animal rabbit model with Vx2 liver tumor with DECT, the result shows that DECT iodine mapping provided higher tumor-to-liver ratio compared to the average weighted 120 kVp images. There is some potential of using the iodine mapping images derived from the images obtained with DECT in improving the detection of hyper-vascular liver tumors[1].

The study of Park et al was conducted to evaluate the assessment of detection for HCC in liver-transplant patients in a weighted average 120 kVp images by adding the 80 kVp images with the use of dual-source had increased the result in better stratification for liver lesion and at the same time the duration used to interpret the CT images also improve[5].

In another study carried out by Jijo Paul, namely the Microwave Thermal Ablation study, showed that the conspicuity of the ablation region during microwave thermal ablation is higher for the images obtained at 80 kVp datasets. However, for the images dataset reconstruction at 0.5 weighted had higher SNR and CNR ratio. The precision of analysis for microwave thermal ablation by the dual-energy CT images is essential. In clinical practice for the real patient during microwave thermal ablation treatment, the ablated volumes or dimensions achieved is based on the temperature expended within a certain time[5]. Besides this, there were several other studies which made use of the dual energy technology which used high and low tube voltages that showed promising results in terms of providing better liver transplantation procedures, diagnosis, and overall treatment[10, 19-22].

3.3 Image enhancement with the help of contrast agents and morphine co-medication

The use of contrast agents in CT scan will improve the image quality by enhancing the contrast-to–noise (CNR) and signal–to–noise ratio (SNR). Although this improved the image quality, it also impaired with increasing the scanning dose to the patient in certain organs using iodinated contrast agents[23]. There is a risk of impaired renal function when using the contrast agents especially for patients with pre-existing kidney disease. Clinical research is done on the liver using contrast agents when scanning the abdomen to detect liver lesion and followed-up after the treatment plan[7, 24-26, 29]. All contrast agents injected into patients follow the injection protocol. The amount of contrast medium given to a patient is calculated accordingly with the BMI of each patient[1, 5, 11, 25, 27, 28]. All contrast mediums were injected by an automatic double-head power injector with a fixed flow rate. The study of Anzidei et al showed that the use of iodinated contrast agents in DECT scans improved the detection and diagnosis of HCC lesions. The X-ray photon attenuation increased in the presence of contrast agents and this will help in increasing the visibility to detect the lesion (Figure 1)[19, 25, 26, 28]. From the increase of the iodine attenuation resulting the increasing of visibility for the hepatocellular carcinoma (HCC) in the mixed reconstruction at 80 kVp refer to Figure 1(b) and Figure 1(c) pointed with arrowheads was initially hardly visible and had been wrongly interpreted as benign at 140 kVp in both wash-outs in portal and delayed phases (Figure 1(a)).

CT-cholangiography was performed before the living-related liver transplantation to obtain images of the biliary system. The accuracy of the images acquired from the examination of the biliary system is very important for potential liver donors before the living-related liver transplantation. Comparing the images from the conventional CT with the reconstructed images from dual-energy CT-cholangiography, DECT had a better result for both the contrast-optimized images and pure iodine images (refer Figure 1). Use of morphine would result in spasm in the sphincter of Oddi. The visualization of the intrahepatic bile ducts might improve after the sphincter of Oddi. In cholescintigraphy, the use of morphine had shown a superior result (refer Figure 2). In the past, the biliary ability and the vitalization did not improve after the use of morphine in CT-cholangiography. The improvement of the biliary visualization with intravenous morphine co-medication in potential donors for living-related liver transplantation was carried out in the Sommer et al. study. Patients were divided into 2 groups which were named control group (CG) and morphine group (MG) while undergoing CT cholangiography. There were 20 patients in each group. A hepatobiliary contrast agent was infusion over 40 min. Control group patients were injected with normal saline while morphine group patients were injected with morphine sulfate 20 minutes after the contrast infusion. DECT images of the liver were acquired 45 minutes after the initial injection of the contrast agent. In Figure 2, the delineation of bile duct was clearly visible for morphine groups (Figure 2(B) and Figure 2(D)) compared to control groups (Figure 2(A) and Figure 2(C)) [19].

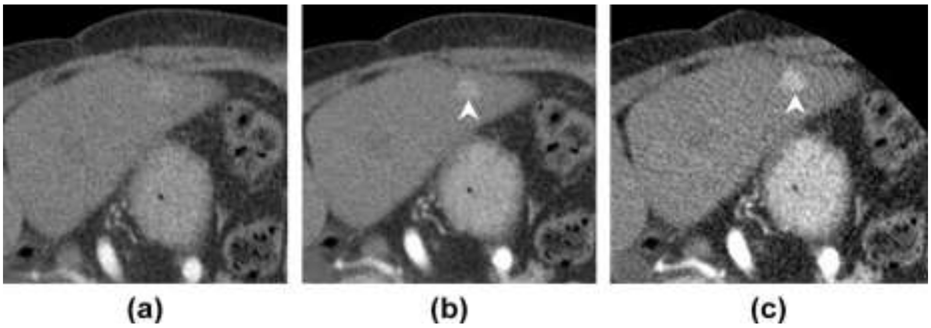
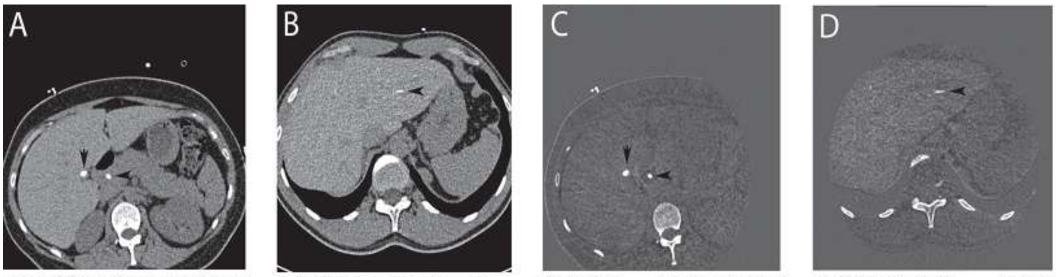


Figure 1. Case for a male patient at 69 years old which had hypervascular lesion in the left liver lobe (Anzidei, M. et al, 2015). (a) Nodule was barely visible and interpreted as benign and did not show a clear wash-out in portal or delayed phase. (b) The lesion was sufficiently delineated in the mixed reconstruction. (c) The increasing of the iodine attenuation resulting the increment of visibility for the hepatocellular carcinoma (HCC) at 80 kVp.



A	B	C	D
Weighted image without morphine co-medicine.	Weighted image with morphine co-medicine.	Standard reconstructed image without morphine co-medicine.	Reconstructed image without morphine co-medicine.

Figure 2. Images for with and without morphone co-medicine (Sommer et al, 2012).

3.4 Imaging of the temperature change during MTA with DECT (Jijo Paul et al)

An experiment was carried out ex vivo to evaluate the correlation between temperature and the CT number of fluids with different densities using CT imaging by Jijo Paul showed that the correlation between the CT number and temperature is highly tissue specific. He carried out the experiment ex vivo in the porcine liver to investigate the temperature changes during the MTA therapy with DECT image data. The DECT imaging for the ex-vivo porcine liver was obtained at 80 kVp and 140 kVp (with tint filter) during the microwave thermal ablation experiments and the images were reconstructed at 0.5-weighted. The weighted image reconstruction in Jijo Paul study was different from other studies [5, 10, 18, 19, 22, 23]. The conspicuity of the ablation region during microwave thermal ablation is higher for the images obtained at 80 kVp datasets but the signal-to-noise ratio and the contrast-to-noise ratio were higher with the reconstruction for 0.5 weighted average images datasets. The DECT datasets and the sensitivity of tissue with microwave thermal were inversely linear.

The CT number were influenced more by the temperature changes in the heating phase than in the cooling phase. When the temperature increases the ablation-region-conspicuity and the ablation-region were also increased. DECT was used to evaluate the effects of temperature on ex-vivo porcine liver during microwave thermal ablation for both heating and cooling phases. Throughout the microwave thermal ablation process, the thermal sensitivity of the liver tissue was feasible to obtain accurately with the dual-energy CT-based thermometry. The delineation for the final ablated margin in MTA is important because the effectiveness of the treatment and the recurrence of the local tumor will be determined by this. There were no reports during microwave thermo-ablation MTA with DECT regarding the changes of the temperature correlated with hepatic tissue. The experiment showed that the DECT image datasets provided better sensitivity, visibility and lesion detection than SECT. This experiment was carried ex vivo and is impossible to be done in the body. The changing of the CT number reflected the changes of the temperature. The experiment raised some suspicion on the result of whether it affects the CT number when increasing the temperature of the phantom because the experiments were performed at the room and body temperature (about 37 degrees Celsius). This study may draw the attention of other researchers to study further to figure out how the change of the CT numbers correlates with the changing of the temperature.

3.5 The used of material decomposition in liver

Different materials might show different or similar CT numbers in CT image. The attenuation value is depending on the materials' densities[7, 30-34]. DECT provides extra data set than SECT as it provides two sets of measurements at high and low energy level in a single scan. These measurements were used for determining the composition of the materials [30-34]. Material decomposition is the technique that used to define the concentration of constituent materials in a mixture. In late 1970, although a lot afford was put in the algorithms and clinical application of material decomposition imaging by using DECT this technique was not completely attained due to certain limitation in the earlier CT system[34]. Nowadays, a lot of study had been carried out in term of applied material decomposition technique in quantifying the iron and fat in the liver. Two materials can be accurately disintegrated from DECT measurement. But in a lot of clinical and industrial applications they require three or more component images. It is very challenging to apply material decomposition in human body as the organs and tissues can be a combination of various materials which contain of blood, fat, water, air, bone and contrast agent. This is a harsh obstacle to various material decomposition method, whichever can distinguish between two or the most three materials at the time. In order to solve three sets of unknowns from two sets of measurement volume conservation, mass conservation or q combination of both is required.

In Liu et al study, they applied the principle of mass conservation. The mass fraction of any chemical element in a three-material mixture of solution can be measure without the requirement of volume conservation. The study of Liu et al able to decompose a mixture into three constituent material by using reconstructed images without the presence of volume conservation. This could be used to quantify the concentration of iron in a fatty liver as the iron deposit basically considers "in solution"[34]. In Yong Long et al study, they proposed another technique (flexible image-domain (ID) multi-material decomposition) instead of using volume conservation and mass conservation as a third constraint. This method assumed that each pixel in the image contains at most three materials out of numerous possible materials and decomposes a mixture pixel by pixel[33]. Paulo et al extended the triplet material decomposition study into multi-material decomposition (MMD). This method able to solve the limitation for the current material decomposition technique and able to distinguish more than three materials. In clinical application for liver-fat quantifying, we need to distinguish between four materials: liver tissue, blood, fat, and contrast agent.

In Mendonca et al study, the working mechanism of his algorithm is based on by making the assumption that the mixing of constituents and tissue types in the human body has the physiochemical properties of an ideal solution. The mass attenuation curve of every voxel in the image is predictable underneath this model and instantly resulting in a material-decomposed image triplet. Figure 3 is the example of material triplet library for MMD for air, fat, blood and contrast agent which commonly used while perform CT image (Omnipaque 300). The system will select adequate triplets from an application-specific material library and perform the decomposition processes. This process able to carry out automatically.

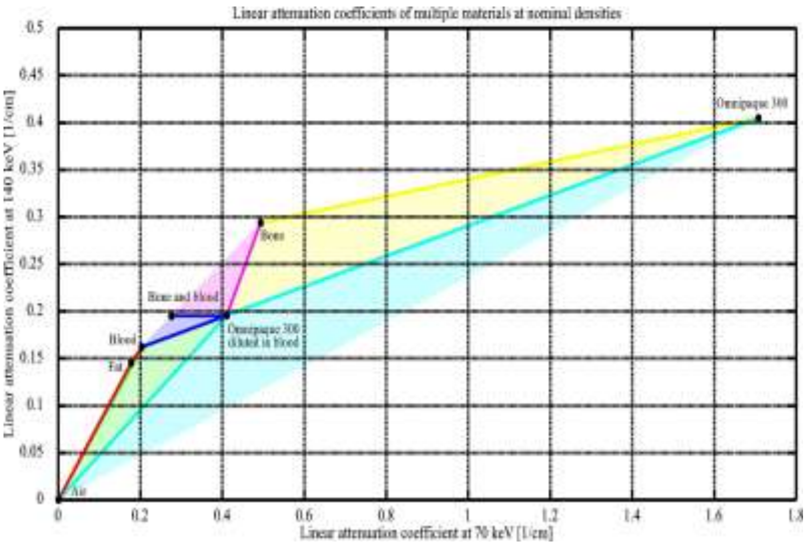


Figure 3. Eexample material triplet library for multi-material decomposition (Mendonca et al, 2014).

Figure 4 illustrates the steps of multi-material decomposition based on virtual unenhanced (VUE) and liver fat quantification (LFQ) algorithm in Paulo et al study. VUE stage is a pre-processing step of LFQ. In this stage the algorithm will replace the volume of contrast agents with its equal volume in blood. After that the system will proceed to quantify the concentration of fat in the liver. The arrow that pointing from "VUE" to

"Healthy Liver" in this figure is indicating the LFQ process. The VUE stage can help to reduce the dose delivered to the patient. The result of LFQ for Paulo research was shown in Figure 5. The LFQ algorithm result is consistent in every phase of imaging.

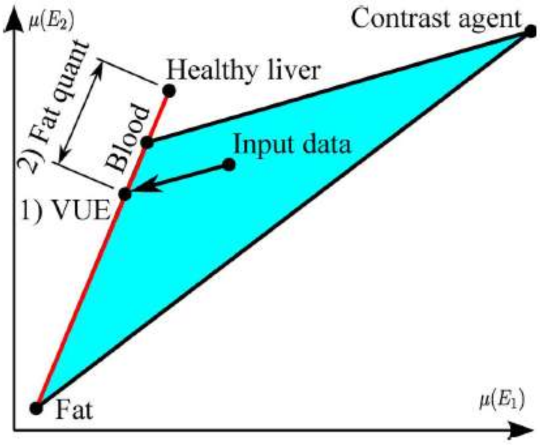


Figure 4 Stages of Multi-material based virtual unenhance (VUE) and liver fat quantification (LFQ) algorithm (Mendonca et al, 2014).

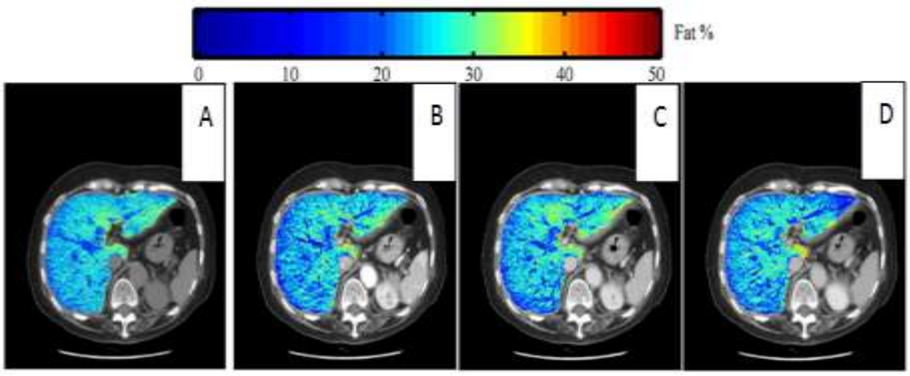


Figure 5 Result of LFQ for (A) contrast free phase (B) Arterial phase (C) Portal venous phase and (D) delayed phase (Mendonca et al, 2014).

3.6 Image quality analysis

Contrast-to-noise ratio calculated based on the formula below in several studies[1, 5, 21, 28]. The mean attenuation represented with ROI_{HCC}, while the mean attenuation of the normal liver parenchyma represented with ROC_{liver} and SD_{noise} are used to represent the image noise[1, 5, 23].

$$\text{CNR} = \frac{|ROI_{HCC} - ROC_{liver}|}{SD_{noise}}$$

3.7 Radiation Dose

During the perfusion CT scan of the liver, the radiation dose delivered to the patient is high disabling it from being applied widely in clinical practice[1, 9]. The total dose delivered to the patient is still considered high although the perfusion CT already used a low tube voltage and current techniques[1]. Thus, the planning of perfusion CT imaging studies for hepatic tumors must take account of both diagnostic and follow-up stages. Staging CT for liver scans applied in a lot of studies[1, 2, 9, 26]. The effective dose for abdominal and pelvic staging CT scans was significantly lower than the abdominal perfusion CT studies. In Wang et al study which used staging CT, the effective dose was 7.21 mSv while the effective dose for perfusion CT was 28.7 mSv[1, 9]. Besides this, the effective dose delivered was about 5.5 mSv and 6.5 mSv in bi-phase or dual phase dual-energy CT in another study[1, 22]. For quadruple-phase dual-energy CT liver protocol, the effective dose delivered was 17.2 mSv while the radiation doses for SECT imaging was 12.1 mSv. Park et al. claimed that the results obtained from this study were consistent with the studies prior to this. From those study, we can conclude that the radiation dose delivered by the perfusion CT was significantly higher than SECT and staging CT.

The lower radiation dose delivered and the potential in the evaluation of tumor angiogenesis without the use of contrast agents had made DECT easier to incorporate into the routine liver CT examinations or studies[1]. The tumor vascularity evaluation as well as treatment efficacy monitoring throughout the anti-angiogenic therapies for the treatment of the liver tumors also was possible to be done with DECT without the use of the contrast agents[1]. For the patients who underwent CT-base thermometry to monitor the tumor ablation, the overall radiation doses received was high due to the multiple scanning required during the treatment. The radiation dose in standard imaging protocol for single energy CT was higher than dual energy CT[1]. Other than lower radiation dose, the reconstruction of multiple image datasets into single imaging in DECT could eliminate the misregistration artefacts[5]. In certain special conditions, whereby the single-energy CT was unable to be achieved due to unique advantages of DECT allowed, it to be used although the radiation doses from it were high. In certain special conditions, where the SECT is unable to be achieved, due to unique advantages of DECT such as characterization of lesion types and determining the composition of urinary stones in non-invasive methods allowed it to be used although the radiation doses from DECT were high[5].

IV. Conclusion

A lot of studies have already shown potentials and advantages of incorporation of dual-energy CT in routine liver scanning for diagnostic purposes, overall treatment and recurrent follow-ups in liver disease. DECT provides extra information compared to the SECT and this information can be used to determine tissue composition and help to determine and characterize the type of lesions for further treatment planning. The iterative reconstruction algorithm in DECT increases the image quality by reducing the noise, artefacts and provides better lesion visibility with lower dose at the same time[22, 28]. To conclude, dual-energy base CT had shown an encouraging future in improving the characterization and detection of the liver lesions compared to the conventional CT.

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