A spectral X-ray CT simulation study for quantitative determination of iron

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ARTICLE INFO

ABSTRACT

Iron is an essential element in the human body and disorders in iron such as iron deficiency or overload can cause serious diseases. This paper aims to explore the ability of spectral X-ray CT to quantitatively separate iron from calcium and potassium and to investigate the influence of different acquisition parameters on material decomposition performance. We simulated spectral X-ray CT imaging of a PMMA phantom filled with iron, calcium, and potassium solutions at various concentrations (15–200 mg/cc). Different acquisition parameters were considered, such as the number of energy bins (6, 10, 15, 20, 30, 60) and exposure factor per projection (0.025, 0.1, 1, 10, 100 mA s). Based on the simulation data, we investigated the performance of two regularized material decomposition approaches: projection domain method and image domain method. It was found that the former method discriminated iron from calcium, potassium and water in all cases and tended to benefit from lower number of energy bins for lower exposure factor acquisition. The latter method succeeded in iron determination only when the number of energy bins equals 60, and in this case, the contrast-to-noise ratios of the decomposed iron images are higher than those obtained using the projection domain method. The results demonstrate that both methods are able to discriminate and quantify iron from calcium, potassium and water under certain conditions. Their performances vary with the acquisition parameters of spectral CT. One can use one method or the other to benefit better performance according to the data available.

1. Introduction

Iron is a micronutrient essential for adequate erythropoietic function, oxidative metabolism and cellular immune response to bacterial infection. Disorders in iron, such as iron deficiency or overload, are important risk factors for heart diseases such as coronary artery disease and heart failure [1,2]. There are different methods for the evaluation of tissue iron content, which can be classified into two categories: invasive techniques and noninvasive techniques. Invasive techniques include biopsy and serum ferritin level. Noninvasive techniques include superconducting quantum interference device (SQUID) and magnetic resonance imaging (MRI) [3,4]. However, these existing techniques all have their own limitations. Biopsy is an invasive procedure that may cause bleeding from the incision site, pain and infections, also it is limited by sampling errors since iron is not uniformly distributed inside organs [5]. Serum ferritin test is less invasive, but it can be easily influenced by many factors such as inflammation, infection, hepatic dysfunction, ascorbate deficiency, hemolysis, and ineffective erythropoiesis [6]. SQUID is particularly more accurate for liver iron content (LIC) determination but not for other organs [7]. MRI is a

useful imaging tool for the diagnosis of iron deposition, but has very long scan time and inability to quantify iron concentration greater than 300 μ mol/g due to susceptibility and rapid signal decay artifacts [4,8]. Therefore, it is necessary to develop new techniques for tissue iron content determination.

X-ray computed tomography (CT) is a well known important non-invasive medical imaging tool. The conventional CT with single X-ray tube and energy integrating detector is unable to quantitatively discriminate specific components in mixtures. In the past years, numerous technologies of dual-energy computed tomography (DECT) and spectral CT were developed, their clinical applications were increasingly investigated [9]. DECT has limited ability in material decomposition by producing two datasets corresponding to two different X-ray spectra of the same anatomic region [10]. The potential of using DECT to detect the distribution of iron in tissues was investigated [8,11–13]. Hazirolan et al. applied DECT to the detection of myocardial iron deposition in Thalassaemia patients; the measured myocardial DECT density values showed strong negative correlation with MRI T2* values [11]. Luo et al. also proved the diagnostic potential of DECT in LIC determination using virtual iron content imaging with fifty-six patients suspected of having

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liver iron overload [12]. However, DECT is unable to give the accurate concentration of iron except for the correlated Hounsfield Unit (HU) values and usually requires relatively high dose levels.

Unlike DECT, spectral CT employs photon counting detectors (PCDs) and is able to obtain spectral information of several energy bins with single acquisition. It is capable to improve X-ray CT by reducing dose, enable artifacts correction [14,15], permit K-edge imaging using high-Z contrast agents [16–24] and provide quantitative material decomposition [25–28]. In [16], Roessl et al. proposed a K-edge imaging method that considered the attenuation coefficient as the combination of photo-electric absorption, Compton scattering and K-edge components, and gadolinium was discriminated from normal tissues in the thorax phantom in their simulation study. Their results were further validated by CT system experiments where the contrast agents (gadolinium and iodine) were well quantified [17]. There is less research about the quantification ability of lighter materials that lack K-edge properties within the detection energy range, which is more challenging. Le et al. proposed a calibrated least squares fitting technique to decompose hydroxyapatite and iodine by a simulation study [25]. Based on this work, Alessio et al. made further improvement and their decomposition results with carotid endarterectomy specimens suggested the presence of water, lipid, and calcium deposits in the plaque walls [26]. For the detection of iron, Zainon et al. used small animal spectral micro-CT with Medipix3 detector (thresholds: 10, 16, 22 and 28 keV) to scan the carotid atherosclerotic plaque; water-like, calcium-like and lipid-like tissues were well separated according to histology comparison, but iron was not distinguished from calcium [27].

To summarize the literature survey, various methods exist for iron content evaluation, but with different limitations. At the same time, many material decomposition methods have been proposed and different experimental systems are under development for spectral CT. However, there is a lack of feasibility analysis and method comparison for the use of spectral CT for iron content determination. Therefore, the present study aims to investigate the ability of spectral CT to quantitatively separate iron from other elements like calcium and potassium, by using two regularized decomposition methods: projection domain method and image domain method. The former, also called pre-reconstruction decomposition method, decomposes projection data into several desired components, and then applies independent reconstruction to each component to obtain the distribution of materials. The latter, also known as post-reconstruction method, operates on conventionally reconstructed CT images of multi-energy bins to obtain the concentration of target materials using linear matrix inversion. Both methods have their advantages and disadvantages depending on different situations. To set up the study, a poly(methyl methacrylate) (PMMA) phantom filled with iron, calcium, and potassium solutions at different concentrations is first simulated for spectral CT scanning. Different acquisition parameter settings are then considered with the combination of the number of energy bins ($B = 6, 10, 15, 20, 30, 60$) and the exposure factors per projection in milliamp-seconds (mA s) ($D = 0.025, 0.1, 1, 10, 100$ mA s).

2. Materials and methods

2.1. Projection domain decomposition method

The detector absorption efficiency is denoted as $D(E)$ and we assume that the photon counting detector allows energy-resolving measurements in N energy bins with ideal energy resolution. According to Beer–Lambert law, the expected number of photons λ_i, in energy bin B_i ($i = 1, 2, \ldots, N$) can be expressed as

$$\lambda_i = \sum_{E=E_s(i)}^{E_f(i)} D(E)N_0(E)exp[-\int \mu(\vec{x}, E)\,\mathrm{d}s], \tag{1}$$

where $E_s(i)$ and $E_f(i)$ denote the start and final energies of bin B_i; $N_0(E)$ is the number of photons in the initial spectrum at energy E; $\mu(\vec{x}, E)$

represents linear attenuation coefficient of the object at location $\vec{x}$ and energy E. It is noticed that there is a location-dependent integral and an energy-dependent sum in this formula, which correspond respectively to the two variables $\vec{x}$ and E on which $\mu(\vec{x}, E)$ depends. Therefore, if we transform $\mu(\vec{x}, E)$ into the sum of the products of energy-dependent term $f_\alpha(E)$ and location-dependent term $a_\alpha(\vec{x})$, it will be easier to calculate the integral and the sum separately [29]. We then write

$$\mu(\vec{x}, E) = \sum_{\alpha=1}^{M} a_\alpha(\vec{x})f_\alpha(E), \tag{2}$$

where M denotes the number of terms in use. Generally, $a_\alpha(\vec{x})$ describes the physico-chemical or quantity property (depending on the concrete formulation of Eq. (2)) of the unknown object and $f_\alpha(E)$ is a known function that varies with energy. In the work of [16], $\mu(\vec{x}, E)$ is taken as the combination of photo-electric absorption, Compton scattering and extra K-edge components if there is any K-edge material in the object, making Eq. (2) into

$$\mu(\vec{x}, E) = a_{ph}(\vec{x})f_{ph}(E) + a_{Co}(\vec{x})f_{KN}(E) + \sum_{\alpha=1}^{M-2} \rho_\alpha(\vec{x})\mu_{m\alpha}(E), \tag{3}$$

where $a_{ph}(\vec{x})$ and $a_{Co}(\vec{x})$ represent location dependency of photo-electric absorption and Compton scattering, respectively. $f_{ph}(E)$ denotes the cross section of photo-electric absorption that can be approximated by E^{-3} [30]. $f_{KN}(E)$ is the cross section of Compton scattering that was first deduced by Klein and Nishina, namely Klein–Nishina function [31]. $\rho_\alpha(\vec{x})$ denotes the density of K-edge material α at point $\vec{x}$ and $\mu_{m\alpha}(E)$ the mass attenuation coefficient of K-edge material α at energy E. ($M - 2$) represent the number of K-edge materials inside the object.

This method was proved to be capable for K-edge imaging. Contrast agent like gadolinium and gold were well quantified from other elements. However, lighter atoms, such as iron, calcium and potassium, usually have much lower K-edge energy that is beyond the detection energy range. In this situation, K-edge imaging method cannot distinguish them, nor give any quantitative information since their attenuations are all included and mixed in photoelectric absorption and Compton scattering.

Therefore, in the present study, we consider another version of Eq. (2) which describes linear attenuation coefficient by the contributions of a basis of M materials:

$$\mu(\vec{x}, E) = \rho_1(\vec{x})\mu_{m1}(E) + \rho_2(\vec{x})\mu_{m2}(E) + \cdots + \rho_M(\vec{x})\mu_{mM}(E)$$
$$= \sum_{\alpha=1}^{M} \rho_\alpha(\vec{x})\mu_{m\alpha}(E), \tag{4}$$

where $\rho_\alpha(\vec{x})$ denotes the density of material α at point $\vec{x}$. Material α is not exclusive to K-edge materials, but also applicable for lighter materials. $\mu_{m\alpha}(E)$ designates the mass attenuation coefficient of material α at energy E, which is in NIST database [32]. M should be smaller than or equal to N, otherwise the problem will be under-determined and an infinite number of solutions exist if there are no other equality constraints. The types of materials chosen for decomposition depend on the application and prior knowledge of the scanned objects. Substituting Eq. (4) into Eq. (1), we then have

$$\lambda_i = \sum_{E=E_s(i)}^{E_f(i)} D(E)N_0(E)exp[-\int \sum_{\alpha=1}^{M} \rho_\alpha(\vec{x})\mu_{m\alpha}(E)\,\mathrm{d}s]$$
$$= \sum_{E=E_s(i)}^{E_f(i)} D(E)N_0(E)exp[-\sum_{\alpha=1}^{M} \mu_{m\alpha}(E)\int \rho_\alpha(\vec{x})\,\mathrm{d}s]$$
$$= \sum_{E=E_s(i)}^{E_f(i)} D(E)N_0(E)exp[-\sum_{\alpha=1}^{M} \mu_{m\alpha}(E)P_\alpha(sx, sy)], \tag{5}$$

with

$$P_\alpha(sx, sy) = \int \rho_\alpha(\vec{x})\,\mathrm{d}s, \tag{6}$$