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Abstract. Dynamic perfusion imaging can provide the morphologic details of the scanned organs as well as the dynamic information of blood perfusion. However, due to the polyenergetic property of the x-ray spectra, beam hardening effect results in undesirable artifacts and inaccurate CT values. To address this problem, this study proposes a segmentation-free polyenergetic dynamic perfusion imaging algorithm (pDP) to provide superior perfusion imaging. Dynamic perfusion usually is composed of two phases, i.e., a precontrast phase and a post-contrast phase. In the precontrast phase, the attenuation properties of diverse base materials (e.g., in a thorax perfusion exam, base materials can include lung, fat, breast, soft tissue, bone, and metal implants) can be incorporated to reconstruct artifact-free precontrast images. If patient motions are negligible or can be corrected by registration, the precontrast images can then be employed as *a priori* information to derive linearized iodine projections from the postcontrast images. With the linearized iodine projections, iodine perfusion maps can be reconstructed directly without the influence of various influential factors, such as iodine location, patient size, x-ray spectrum, and background tissue type. A series of simulations were conducted on a dynamic iodine calibration phantom and a dynamic anthropomorphic thorax phantom to validate the proposed algorithm. The simulations with the dynamic iodine calibration phantom showed that the proposed algorithm could effectively eliminate the beam hardening effect and enable quantitative iodine map reconstruction across various influential factors. The error range of the iodine concentration factors ($\text{HU} \cdot \text{ml/mg}$) was reduced from $[-8.01, 14.77]$ for filtered back-projection (FBP) to $[-0.05, 0.08]$ for pDP. The quantitative results of the simulations with the dynamic anthropomorphic thorax phantom indicated that the maximum error of iodine concentrations can be reduced from 1.1 mg/cc for FBP to less than 0.1 mg/cc for pDP, which suggested that the proposed algorithm could not only effectively eliminate beam hardening artifacts but also significantly reduce the influence of the metal artifacts and accurately reconstruct the iodine map regardless of the influential factors. A segmentation-free polyenergetic dynamic perfusion imaging algorithm was proposed and validated via simulations. This method can accurately reconstruct artifact-free iodine maps for quantitative analyses. © 2016 Society of Photo-Optical Instrumentation Engineers (SPIE) [DOI: 10.1117/1.JMI.3.3.033503]

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1 Introduction

In dynamic CT perfusion imaging,^{1–3} an iodinated contrast agent is administered to a patient through intravenous injection as a way to raise the radiopacity and to enhance the visibility of vascular structures and organs.⁴ By recording the change of the CT numbers of the preselected ROIs during the passage of the iodine bolus, time-attenuation curves (TACs), and time-concentration curves (TCCs) can be obtained, from which blood flow, blood volume, and mean transit time can be derived to diagnose different diseases. For example, cardiac myocardial perfusion imaging⁵ can help to detect coronary artery disease (e.g., infarcted or ischemic myocardium), assess left and right ventricular function, and evaluate structural heart disease. Lung perfusion CT^{6,7} can help to identify pulmonary emboli and differentiate between benign and malignant nodules. Researches in breast perfusion imaging^{8–11} show that breast cancers could be distinguished from normal mammary glands based on the perfusion values.

Beam hardening (BH) effect is one of the major influential factors that limit the quality and accuracy of the dynamic perfusion imaging. When x-rays pass through materials, low energy photons are preferentially absorbed, which increase the mean energy of the x-rays. This phenomenon leads to various artifacts in reconstructed images, such as cupping and streaking.^{4,12} In perfusion imaging, the K-edge contrast enhancement agents (such as iodine) can dramatically absorb low-energy photons and cause artifacts stronger than that in noncontrasted CT. For example, in myocardial perfusion imaging,^{2,13} BH artifacts can result in underestimated attenuation of affected tissue that may be misinterpreted as a perfusion defect. The HU deviation due to BH can be as large as 40 HU,¹³ which makes the quantitative evaluation of iodine perfusion challenging.^{14–16}

Currently, the CT perfusion imaging algorithm widely used in clinical practice is based on water-corrected^{17–20} filtered back-projection (FBP) algorithms.^{1,21} This approach requires precalibrated iodine concentration curves^{3,22} across different spectra

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and phantom sizes, so that the errors of measured TACs or TCCs^{2,3} can be reduced. This approach takes the advantage of FBP's fast speed, but is susceptible to streak artifacts induced by high attenuation materials, such as bone, iodine,^{13,23} and metal.

Some efforts have been made to account for the attenuation properties of bone and iodine,^{24,25} but with limited success. For example, Joseph and Ruth²⁴ proposed an image-based BH correction algorithm to incorporate the attenuation properties of water, bone, and iodine in terms of effective density. However, a prerequisite of this method is to accurately segment these three base materials into distinct regions. Stenner et al.²⁵ developed a method to distinguish the three regions by measuring the voxel dynamics, but they used a series of threshold-based segmentation techniques, and the voxels containing low concentration or low dynamic iodinated contrast agent could be potentially misinterpreted as soft tissue or bone minerals. In addition, both of the two methods are limited to myocardial perfusion exam, as they only modeled the attenuation properties of blood-iodine mixture. Errors may arise in other perfusion exams, such as lung or breast perfusion exams (see our simulation results with a dynamic anthropomorphic thorax phantom in Sec. 3.2).

In this paper, a new polyenergetic dynamic perfusion imaging algorithm (pDP) is proposed. Our algorithm does not require segmentation. Assuming minimal or correctable patient motions, precontrast images are used as *a priori* information to derive linearized iodinated projections from postcontrast projections. With the linearized iodinated projections, artifact-free iodine maps can be reconstructed directly. As diverse base materials (e.g., lung, fat, breast, soft tissue, bone, metal implant, and iodine) are incorporated, pDP enables quantitative iodine map reconstruction independent of various influential factors such as iodine location, patient size, spectrum,²⁶ and background tissue type.

2 Methods

2.1 Algorithm

Symbols and definitions used through this paper are summarized in Table 1. The spectra^{26,27} used in this work are plotted in Fig. 1.

A flow chart of the proposed pDP algorithm is shown in Fig. 2. Here, $r = 1, \dots, N_R$ is the r 'th ray from the x-ray source to the detector element, $v = 1, \dots, N_V$ is the v 'th voxel of the target volume, and N_R and N_V are the total numbers of the x-ray paths and target voxels, respectively. With the precontrast measurements p_r^{pre} , the precontrast images t_v^{pre} are first reconstructed using polyenergetic iterative FBP (piFBP).²⁸ Note that the derivation of the iodine map reconstruction in Sec. 2.1.2 relies on the theory, symbols, and equations, previously detailed for piFBP.²⁸ Here we provide a summary of these materials for the sake of completeness.

With the postcontrast measurements p_r^{post} , intermediate postcontrast images $\tilde{t}_v^{\text{post}}$ are reconstructed as references to register precontrast images t_v^{pre} as a way to offset patient motions and to obtain motion-free precontrast images $\tilde{t}_v^{\text{pre}}$, with which the accumulated effective lengths $l_{r,m}^{\text{post}}$ of all body tissues are computed based on the acquisition parameters of p_r^{post} and are used as *a priori* information to derive the linearized iodine projections ($l_{r,7}^{\text{post}}$). Here, $m = 1, \dots, N_M$ is the base material index, N_M is the total number of the base materials, and the material index of

iodine is $m = 7$. In this way, the linearized iodine projections $l_{r,7}^{\text{post}}$ can be reconstructed into artifact-free iodine maps (t_v^{iodine}) by a standard FBP algorithm. Section 2.1.2 describes the postcontrast iodine map reconstruction method in detail.

2.1.1 Precontrast image reconstruction

The forward projection model for the polyenergetic x-ray beam²⁹ is given as

$$\bar{p}_r^{\text{pre}} = -\ln\left(\int I(\varepsilon) \exp\left[-\int_{L_r} \mu(\vec{x}, \varepsilon) d\ell\right] d\varepsilon\right), \quad (1)$$

where $\bar{p}_r^{\text{pre}}$ ($r = 1, \dots, N_R$) is the estimated logarithmic measurement along the r 'th ray line L_r in the precontrast phase, $I(\varepsilon)$ is the spectrum (normalized to unit area), and $\mu(r, \varepsilon)$ is the unknown spatial- and energetic-related attenuation map of the object. In order to reduce the free degrees of the attenuation map $\mu(r, \varepsilon)$ and to quickly evaluate this nonlinear double integral, we propose the following adaptive base material decomposition method.

We assume that the object is comprised of N_M known base materials, and the mixture in each voxel can be decomposed to iodine and two other base materials. The base material set can be chosen based on the CT exams. For example, in the thorax perfusion CT exam, the base material set can include air ($m = 0$), lung ($m = 1$), fat ($m = 2$), breast ($m = 3$), soft tissue ($m = 4$), bone ($m = 5$, 1920 mg/cc water-calcium solution), metal implant ($m = 6$, e.g., titanium), and iodine ($m = 7$). The attenuation coefficient curves³⁰ of the base materials in the precontrast phase are plotted in Fig. 3. In previous literatures,²⁹ body tissues such as lung, fat, and breast are usually approximated with water,^{29,31,32} but because of the differences in attenuation property, their CT numbers can deviate significantly from the real values. In contrast, our base material set contains a wide range of base materials, so that gradation of attenuation coefficients for various tissue types can be broadly sampled. As a common biocompatible metal implant material,³³ titanium is also selected as a base material in this work to test the metal artifact reduction ability of the proposed algorithm. In a previous project, a stepwise addition of base material demonstrated the importance of incorporating a wide range of base materials in the scanned objects.²⁸

For the convenience of incorporating the base material set into the forward projection process, we define each indexed voxel of t_v^{pre} ($v = 1, \dots, N_V$) as the attenuation coefficient at a reference monoenergetic energy of ε_0 (e.g., $\varepsilon_0 = 70$ keV). Based on the value of t_v^{pre} , each voxel of mixture is adaptively decomposed to two adjacent base materials. Note that in the precontrast phase, iodine does not exist, so the base material indices are only limited to $m = 0, \dots, 6$. For example, if t_v^{pre} (the circle in Fig. 3) is within the bone interval, i.e., $[\mu_4(\varepsilon_0), \mu_5(\varepsilon_0)]$, where $\mu_m(\varepsilon_0)$ is the attenuation coefficient of the m 'th base material at the reference energy ε_0 , the attenuation coefficient curve for the v 'th voxel can be estimated as

$$\mu(t_v^{\text{pre}}, \varepsilon) = \frac{\mu_5(\varepsilon_0) - t_v^{\text{pre}}}{\mu_5(\varepsilon_0) - \mu_4(\varepsilon_0)} \mu_4(\varepsilon) + \frac{t_v^{\text{pre}} - \mu_4(\varepsilon_0)}{\mu_5(\varepsilon_0) - \mu_4(\varepsilon_0)} \mu_5(\varepsilon). \quad (2)$$

As the base material bone (1920 mg/ml) used here is the mixture of water and calcium element, the bone density in the v 'th voxel can be computed as^{27,28,34}

Table 1 Symbols and definitions.

Symbols	Definitions
$\mathcal{B}$	FBP operator
$\mathcal{F}(\mathcal{F}_w)$	Logarithmic polyenergetic forward projection operator (with water correction)
I_e	X-ray photon intensity at the e 'th energy bin
$I(\varepsilon)$	X-ray photon intensity at energy level ε
N	Total number of the voxels in the measured ROI
N_E	Total number of the spectrum energy bins
N_M	Total number of the base materials
N_R	Total number of the x-ray paths from x-ray source to detector modules
N_V	Total number of the voxels of the volume
$\mathcal{S}$	Smoothing operator
Y_{rs}	CT Measurement through the r 'th x-ray with the s 'th incident spectrum
a_{vr}	Contribution of the v 'th voxel to the r 'th ray
e	Index for spectrum energy bins
$l_{mr}^{\text{pre}}/l_{mr}^{\text{post}}$	Accumulated effective length of the m 'th material along the r 'th ray in the pre-/postcontrast phase
m	Index for the base materials
$\bar{\mathbf{p}}^{\text{pre}}(\bar{\mathbf{p}}_w^{\text{pre}})$	Column vector of estimated logarithmic polyenergetic measurements (after water correction) in the precontrast phase
$p_r^{\text{pre}}/p_r^{\text{post}}$	Logarithmic measurement along the r 'th ray in the pre-/postcontrast phase
$\bar{p}_r^{\text{pre}}/\bar{p}_r^{\text{post}}$	Estimated logarithmic measurement along the r 'th ray in the pre-/postcontrast phase
r	Index for the x-ray paths
$\mathbf{t}^{\text{pre}}$	Column vector of voxels of the target volume in terms of the attenuation coefficient at ε in the precontrast phase
$t_v^{\text{pre}}/t_v^{\text{post}}$	Attenuation coefficient of the v 'th voxel at reference energy ε_0 in the pre-/postcontrast phase
t_v^{iodine}	Iodine map in the postcontrast phase
$\tilde{t}_v^{\text{pre}}$	Intermediate precontrast image obtained by registering t_v^{pre} to t_v^{post}
$\tilde{t}_v^{\text{post}}$	Intermediate postcontrast image reconstructed from postcontrast projections as motion correction reference
$t(\bar{\mathbf{x}})$	Attenuation coefficient at location $\bar{\mathbf{x}}$ at reference energy ε_0
v	Index for the voxels
ε	Energy level within the spectrum range

Table 1 (Continued).

Symbols	Definitions
ε_0	Reference energy, at which the monoenergetic image will be reconstructed
$\mu(\bar{\mathbf{x}}, \varepsilon)$	Attenuation coefficient at location $\bar{\mathbf{x}}$ at reference energy ε
μ_{me}	Attenuation coefficient of the m 'th base material at the e 'th energy bin
$\mu_m(\varepsilon)$	Attenuation coefficient of the m 'th base material at energy ε
ρ_m	Density of the m ' base material
ρ_v	Density of the v 'th voxel

$$\rho_v = \frac{t_v^{\text{pre}} - \mu_4(\varepsilon_0)}{\mu_5(\varepsilon_0) - \mu_4(\varepsilon_0)} \times 1920 \text{ mg/cc.} \quad (3)$$

The above adaptive decomposition strategy can be applied to the other intervals {i.e., $[\mu_i(\varepsilon_0), \mu_{i+1}(\varepsilon_0)]$, $i = 1, 2, 3$ } to account for the gradual changes of the attenuation coefficient curves. Therefore, a general decomposition equation for the v 'th voxel can be expressed as

$$\mu(t_v, \varepsilon) = \sum_{m=0, \dots, 5} \chi_{[\mu_m, \mu_{m+1})}(t_v^{\text{pre}}) \left[\frac{\mu_{m+1}(\varepsilon_0) - t_v^{\text{pre}}}{\mu_{m+1}(\varepsilon_0) - \mu_m(\varepsilon_0)} \mu_m(\varepsilon) + \frac{t_v^{\text{pre}} - \mu_m(\varepsilon_0)}{\mu_{m+1}(\varepsilon_0) - \mu_m(\varepsilon_0)} \mu_{m+1}(\varepsilon) \right], \quad (4)$$

where the step function $\chi_{[a,b)}$ is defined as

$$\chi_{[a,b)}(t) = \begin{cases} 1 & t \in [a, b) \\ 0 & t \notin [a, b) \end{cases}. \quad (5)$$

For easy observation, the interpolated attenuation curves along the 70 keV reference energy line with Eq. (4) is plotted in Fig. 3 with a gray gradient color. Elabakri and Fessler²⁹ used tissue fraction to incorporate the attenuation properties of water and bone and to approximate the attenuation properties of the other body tissues. In this study, more base materials were incorporated in the material decomposition [Eq. (4)].

Note that the choice of the reference energy does not affect the reconstruction accuracy. That is because the reference

Fig. 1 Plot of the spectra used in this work.

Fig. 2 Flow chart of the proposed pDP algorithm.

energy is only used to compute the composition fractions of the base materials in each voxel and the composition fractions are energy independent. This has been verified in a convergence test in our previous published paper.²⁸

To reduce the computational time, the base material interval indices and the corresponding effective lengths for every voxel can be calculated and stored in matrices before each iteration, with which the accumulated effective lengths of all base materials can be computed through one forward ray tracing as

$$\int_{L_r} \mu[t(\vec{x}), \varepsilon] dL \approx \sum_{v=1, \dots, N_v} a_{rv} \mu(t_v^{pre}, \varepsilon) = \sum_{m=0, \dots, 6} l_{rm}^{pre} \mu_m(\varepsilon), \quad (6)$$

where a_{rv} denotes the elements of the system matrix, and l_{rm}^{pre} denotes the accumulated effective length of the m 'th material for the r 'th ray

$$l_{rm}^{pre} = \sum_{v=1, \dots, N_v} a_{rv} \chi_{[\mu_m, \mu_{m+1})}(t_v^{pre}) \times \begin{cases} \frac{\mu_{m+1}(\varepsilon_0) - t_v^{pre}}{\mu_{m+1}(\varepsilon_0) - \mu_m(\varepsilon_0)} & m = 0 \\ \frac{\mu_{m+1}(\varepsilon_0) - t_v^{pre}}{\mu_{m+1}(\varepsilon_0) - \mu_m(\varepsilon_0)} + \frac{t_v^{pre} - \mu_{m-1}(\varepsilon_0)}{\mu_m(\varepsilon_0) - \mu_{m-1}(\varepsilon_0)} & m = 1, \dots, 5, \\ \frac{t_v^{pre} - \mu_{m-1}(\varepsilon_0)}{\mu_m(\varepsilon_0) - \mu_{m-1}(\varepsilon_0)} & m = 6 \end{cases} \quad (7)$$

Fig. 3 The attenuation coefficient curves of the base materials for chest CT exam. (a) A plot with large attenuation coefficient range [0.0, 2.5] to facilitate the appreciation of the relative relationship between the high attenuation curves and the low attenuation curves. (b) A plot with small attenuation coefficient range [0.0, 1.0] to facilitate the appreciation of the relative relationship of the low attenuation curves. The gray gradient indicates the interpolated attenuation curves along the 70-keV reference energy line.

With the accumulated effective length l_{rm}^{pre} , the polyenergetic forward projection equation [Eq. (1)] can be easily calculated as

$$\begin{aligned} \bar{p}_r^{\text{pre}} &= -\ln \left(\int I(\varepsilon) \exp \left[- \int_{L_r} \mu(t(\vec{x}), \varepsilon) dl \right] d\varepsilon \right) \\ &\approx -\ln \left(\sum_{e=1, \dots, N_E} I_e \exp \left[- \sum_{m=0, \dots, 6} l_{rm}^{\text{pre}} \mu_{me} \right] \Delta e \right), \end{aligned} \quad (8)$$

where I_e denotes the e 'th energy bin ($e = 1, \dots, N_E$) of the x-ray spectrum and N_E is the total number of the discrete energy bins. For simplicity, Eq. (8) can be expressed in a vector notation as

$$\bar{\mathbf{p}}^{\text{pre}} = \mathcal{F} \mathbf{t}^{\text{pre}}, \quad (9)$$

where $\bar{\mathbf{p}}^{\text{pre}}$ is the column vector of the estimated logarithmic polyenergetic detector values, $\mathbf{t}^{\text{pre}}$ is the column vector of the target volume in terms of the attenuation coefficient at reference energy ε_0 , and $\mathcal{F}$ is the logarithmic polyenergetic forward projection operator.

With the polyenergetic forward projection operation described earlier, the piFBP algorithm with a smoothing operator (piFBP) can be written as

$$\begin{cases} \mathbf{t}^{\text{pre}(0)} = \mathcal{B} \mathbf{p}_w^{\text{pre}} \\ \mathbf{t}^{\text{pre}(k+1)} = \mathbf{t}^{\text{pre}(k)} + c \mathcal{S} \mathcal{B} (\mathbf{p}^{\text{pre}} - \mathcal{F} \mathbf{t}^{\text{pre}(k)}), \end{cases} \quad (10)$$

where $\mathcal{B}$ is the filtered back-projection (FBP) operator, $\mathbf{p}_w^{\text{pre}}$ is the column vector of the water corrected logarithmic polyenergetic measurements, k is the iteration index ($k \geq 0$), and c is the relaxation parameter. In this work, the relaxation parameter c was set to one. As BH artifacts are mainly low frequency signals, a smoothing operator $\mathcal{S}$ was added to suppress the noise of the correction volume and to improve the convergence stability. In this work, a smoothing kernel of 5×5 pixels Gaussian low pass filter (mean = 0 and sigma = 1.05) was favored to provide sufficient noise suppression. Based on our previous experiments,²⁸ the relative errors in terms of attenuation coefficient can be reduced to 0.3% for all body tissues after four iterations. Therefore, we use four iterations for all the experiments in this study.

2.1.2 Postcontrast iodine map reconstruction

The enhancement of the postcontrast projections with respect to the precontrast ones is mainly due to the introduced iodine contrast agent. As the attenuation property of the iodine solvent is similar to that of soft tissue or blood, we can simply assume the increase of the voxel values is only caused by iodine element, i.e.,

$$t_v^{\text{post}} = \tilde{t}_v^{\text{pre}} + t_v^{\text{iodine}}, \quad (11)$$

where $\tilde{t}_v^{\text{pre}}$, t_v^{iodine} , and t_v^{post} are the v 'th voxel values of the motion corrected precontrast images, the iodine maps, and the postcontrast images, respectively. With Eqs. (4) and (11), the energy-dependent attenuation coefficient for the v 'th voxel of the postcontrast images can be expressed as

$$\begin{aligned} \mu(t_v^{\text{post}}, \varepsilon) &= \sum_{m=0, \dots, 5} \chi_{[\mu_m, \mu_{m+1})}(t_v) \left[\frac{\mu_{m+1}(\varepsilon_0) - \tilde{t}_v^{\text{pre}}}{\mu_{m+1}(\varepsilon_0) - \mu_m(\varepsilon_0)} \mu_m(\varepsilon) \right. \\ &\quad \left. + \frac{\tilde{t}_v^{\text{pre}} - \mu_m(\varepsilon_0)}{\mu_{m+1}(\varepsilon_0) - \mu_m(\varepsilon_0)} \mu_{m+1}(\varepsilon) \right] + \frac{t_v^{\text{iodine}}}{\mu_7(\varepsilon_0)} \mu_7(\varepsilon). \end{aligned} \quad (12)$$

With the above equation, the linear integral along the r 'th ray can be approximated by the accumulated effective lengths (l_{rm}^{post} , $r = 1, \dots, N_R$) of the base materials ($m = 0, \dots, 7$) as

$$\begin{aligned} \int_{L_r} \mu[t(\vec{x}), \varepsilon] dl &\approx \sum_{v=1, \dots, 7} a_{rv} \mu(t_v^{\text{post}}, \varepsilon) \\ &= \sum_{m=1, \dots, 6} l_{rm}^{\text{post}} \mu_m(\varepsilon) + l_{r,7}^{\text{post}} \mu_7(\varepsilon). \end{aligned} \quad (13)$$

As l_{rm}^{post} ($m = 1, \dots, 6$) can be calculated with $\tilde{t}_v^{\text{pre}}$ [Eq. (7)] based on the postscan acquisition parameters, the proposed method does not require the postcontrast projections to be geometrically identical to the precontrast projections. The effective length of iodine ($l_{r,7}^{\text{post}}$) is defined as

$$l_{r,7}^{\text{post}} = \sum_{v=1, \dots, N_V} a_{rv} \times \frac{t_v^{\text{iodine}}}{\mu_7(\varepsilon_0)}. \quad (14)$$

With l_{rm}^{post} ($m = 1, \dots, 6$) and p_r^{post} , the accumulated lengths of iodine ($l_{r,7}^{\text{post}}$) can be numerically computed by solving the following nonlinear equations using bisection method:³⁵

$$\begin{aligned} p_r^{\text{post}} &= -\ln \left(\int I(\varepsilon) \exp \left\{ - \int_{L_r} \mu[t^{\text{post}}(\vec{x}), \varepsilon] dl \right\} d\varepsilon \right) \\ &\approx -\ln \left\{ \sum_{e=1, \dots, N_E} I_e \exp \left[- \sum_{m=1, \dots, 6} l_{rm}^{\text{post}} \mu_m(\varepsilon) - l_{r,7}^{\text{post}} \mu_7(\varepsilon) \right] \Delta e \right\}. \end{aligned} \quad (15)$$

To suppress noise, we apply a projection space denoising operation to $l_{r,7}^{\text{post}}$ by using a 5×5 pixels Gaussian low pass filter (mean = 0, sigma = 0.8). As $l_{r,7}^{\text{post}}$ is linearly related to t_v^{iodine} [Eq. (14)], standard FBP algorithm can be used directly to reconstruct the iodine map. The iodine concentration of the v 'th voxel can be further computed as

$$c_v = \frac{t_v^{\text{iodine}}}{\mu_7(\varepsilon_0)} \times 4933 \text{ mg/cc}, \quad (16)$$

where 4933 mg/cc is the density of the iodine element. With $\tilde{t}_v^{\text{pre}}$ and t_v^{iodine} , synthesized postcontrast images can then be computed by Eq. (11). As the attenuation curve of iodine is incorporated, the BH effect due to iodine can be effectively eliminated.

Note that the previous algorithms^{2,3,24,25} are limited to myocardial perfusion, as they assume that iodine can only be mixed with blood. In contrast, by allowing for any types of tissue-iodine mixtures, our method can be applied to other organ perfusion exams, such as in lungs or breasts. By choosing suitable base materials, we can further extend the proposed algorithm to cerebral, renal, and hepatic perfusion exams. For example, for the cerebral perfusion imaging exams, the base materials can

include fat, white matter, gray matter, bone, and tooth. This adaptive base material selection method can be readily implemented based on the CT exam type and organ segmentation techniques.^{36,37} Thus, accurate artifact-free precontrast images can be reconstructed and used as *a priori* information to linearize the iodine projections.

2.2 Validations

We simulated a fan beam with an equiangular arc detector. The simulation parameters are listed in Table 2. Quantum noise corresponding to 4.0×10^5 photons per detector pixel was added to the projection data. In this work, no inhomogeneous bow-tie filtering and scattering were taken into consideration. All simulations were conducted on Duke Blue Devil GPU Cluster with NVIDIA Tesla C1060 GPUs, which consists of 30 multiprocessors (each with eight SIMD processing cores) and 4 GB of memory. The precontrast phase takes 28 s for four iterations of piFBP, and the postcontrast phase takes about 7 s.

2.2.1 Dynamic iodine calibration phantom

A size-variable dynamic iodine calibration phantom (Fig. 4) was designed to compare the conventional FBP-based perfusion algorithm and the proposed pDP algorithm. In the precontrast phase [Fig. 4(a)], this phantom was composed of uniform soft tissue. In the postcontrast phase [Fig. 4(b)], five groups of iodine inserts with different concentrations (2, 6, 10, 14, and 18 mg/cc) emerged from the soft tissue background. For each group, five iodine inserts with the same concentration were positioned at different radial distances. The size of this phantom was scaled to 16, 23, 30, and 37 cm diameters to simulate patients of different sizes. With this phantom, three tests, i.e., an iodine location test, a phantom size test, and an x-ray spectrum test, were performed to investigate the reconstruction stability of the algorithm. The parameters used in the three simulation tests are summarized in Table 3.

2.2.2 Dynamic anthropomorphic thorax phantom

In order to further validate our reconstruction algorithm, real CT data from the database of The Cancer Imaging Archive (TCIA, Ref. 38) were used to create a more complex and realistic dynamic anthropomorphic thorax phantom (Fig. 5). The phantom was assumed idealized for tissue registration and contrast enhancement.

In the precontrast phase [Fig. 5(a)], this phantom was composed of diverse materials, i.e., (1) lung, (2) fat, (3) breast,

Fig. 4 Definition of the dynamic calibration phantom (1024 × 1024 pixels). (a) In the precontrast phase, this phantom was only composed of uniform (1) soft tissue. (b) In the postcontrast phase, this phantom was composed of (1) soft tissue, (2) 2 mg/cc iodine insert group, (3) 6 mg/cc iodine insert group, (4) 10 mg/cc iodine insert group, (5) 14 mg/cc iodine insert group, and (6) 18 mg/cc iodine insert group.

(4) soft tissue, (5) bone (1000 mg/cc), and (6) metal implant (titanium). In the postcontrast phase [Fig. 5(b)], iodine perfusion resulted in different tissue-iodine mixtures, i.e., (7) lung-iodine mixture, (8) fat-iodine mixture, (9) breast-iodine mixture, and (10) soft tissue-iodine mixture. In order to simulate the dynamic wash-in and wash-out kinetics, a gamma-variate function³⁹ (Fig. 6) was employed to govern the concentration changes of the iodinated contrast agent as

$$c(t) = c_{\max} (t/t_{\max})^a \exp[a(1 - t/t_{\max})]. \quad (17)$$

The parameter a affects the rise and fall times of the function and was set to 1 in this work; the peak time $t_{\max}$ was set to the 8 s for all tissues; the maximum iodine concentration $c_{\max}$ at the peak time was set to 14 mg/ml for all tissues. In addition, a common set of regions of interest surrounding the left chamber (Fig. 7) was used to assess the effect of BH artifacts induced by iodinated contrast agent in both heart chambers and the aorta. With this dynamic anthropomorphic thorax phantom, polyenergetic projections were simulated from 0 s to 20 s with a 2-s interval.²⁵ The projections were reconstructed by the conventional FBP algorithm and the proposed pDP algorithm. The simulation results were compared quantitatively.

Note that as this dynamic phantom was mainly used to validate the proposed algorithm, a single TAC was applied to

Table 2 Simulation parameters used in the simulations.

Parameter name	Value
Source-to-detector distance	1085.6 mm
Source-to-object distance	595.0 mm
Number of detector bins	736
Detector size at iso-center	$0.60 \times 0.60 \text{ mm}^2$
Total photon number per detector bin	4.0×10^5 photons
Number of projections	2304 projections

Table 3 Parameter summary of the simulation tests for the dynamic iodine calibration phantom.

Simulation tests	Varying parameters	Fixed parameters	Individual parameters
Iodine location test	Radial distance of the iodine inserts	Spectrum: 80 kVp Phantom size: 30 cm	FBP: water correction pDP: $\epsilon_0 = 70 \text{ keV}$
Phantom size test	Phantom size: 16, 23, 30, and 37 cm	Spectrum: 80 kVp	FBP: water correction pDP: $\epsilon_0 = 70 \text{ keV}$
X-ray spectrum test	X-ray spectrum: 80, 100, 120, 140 kVp	Phantom size: 30 cm	FBP: water correction pDP: $\epsilon_0 = 70 \text{ keV}$

Fig. 5 Definition of the dynamic anthropomorphic thorax phantom (2048×1400 pixels, 0.15×0.15 mm²). (a) In the precontrast phase, this phantom was composed of (1) lung, (2) fat, (3) breast, (4) soft tissue, (5) bone (1000 mg/cc), and (6) metal implant (titanium). (b) In the postcontrast phase, iodine perfusion resulted in different iodine–body tissue mixtures, i.e., (7) lung–iodine mixture, (8) fat–iodine mixture, (9) breast–iodine mixture, and (10) soft tissue–iodine mixture. The TAC of those different body tissue–iodine mixtures is defined in Fig. 6.

all the body tissues. This choice enabled the comparison of the impact of iodine on the reconstruction values across different background tissues.

3 Results

3.1 Dynamic Iodine Calibration Phantom

Figure 8 shows the reconstruction results of the dynamic iodine calibration phantom in the postcontrast phase. The images in the first column were reconstructed by FBP (70 keV). Because of the monoenergetic spectrum, BH artifacts were not noticeable. The bright or dark borders around the edges of the iodine inserts are due to the partial volume effect. The images in the first column were used as benchmarks for the rest of the comparisons. The percent relative difference image in the second row shows uniform zero values. The iodine map shown in the last row was obtained by subtracting the postcontrast image from the precontrast image, and it correctly retrieved all iodine inserts.

The postcontrast images reconstructed by FBP (80 kVp) are shown in the second column of Fig. 8. Dark streak artifacts were readily visible. The percent relative difference image in the second row shows that iodine inserts were constantly overestimated

for all concentrations, which affects the accuracy of the quantitative perfusion assessment. By subtracting the postcontrast image from the precontrast image, we obtained the iodine map as presented in the last row. The BH artifacts were prominent in a narrow window level (0 HU/40 HU). As expected, the strength of the artifacts was positively correlated with the iodine concentration but inversely correlated with the distance between the iodine inserts. In addition, the strength of the artifacts was also positively correlated with the radial distance. For instance, for the 10 mg/cc iodine inserts, the shape of the iodine inserts near the center was round, but when approaching the phantom border, the shape was gradually deformed to an ellipse, the long axis of which was parallel to the shortest intersection line between the x-ray path and the phantom. This phenomenon was due to the cupping effect.⁴ For the iodine inserts close to the center, the x-rays from different directions were equally attenuated, so that the BH effect was isotropic and the shape of the iodine inserts could be preserved. However, for the iodine near the phantom boarder, BH effect was no longer isotropic. The directions with shorter intersection lines between the x-ray path and the phantom could induce stronger BH artifacts,

Fig. 6 The TAC of the different body tissue–iodine mixtures. The iodine concentration scale was added to the right y-axis for reference. Ten time points were sampled from 0 s to 20 s with 2 s interval.

Fig. 7 Anatomical structures in the heart region. A set of ROIs (i.e., apical, septal, basal, and lateral) was used to evaluate the BH artifacts induced by iodine in both heart chambers and aorta.

Fig. 8 Reconstruction results of the dynamic iodine calibration phantom. The images from the first column to the third column were reconstructed by FBP (70 keV), FBP (80 kVp), and pDP (80 kVp), respectively. The images from the first row to the third row were post-contrast images (50/100), relative difference images (0%/20%), and iodine maps (0/40), respectively.

because of the large amount of unattenuated low energy photons. Water correction could not effectively eliminate this iodine-induced cupping effect.

The images in the last column of Fig. 8 were reconstructed by pDP (80 kVp). In comparison with FBP (80 kVp), the streaks caused by the iodine inserts were totally eliminated in the post-contrast image. The relative difference image in the second row had uniformly negligible values. The iodine map in the last row was nearly identical with the iodine map obtained by FBP (70 keV).

Figure 9 shows the location test results of the dynamic iodine calibration phantom (30 cm and 80 kVp). To facilitate comparison, the CT numbers of the iodine inserts in the same concentration group were subtracted from the value of the innermost iodine insert to yield the relative CT numbers, which were

then plotted against the radial distance. For FBP [Fig. 9(a)], the maximum intragroup difference of the iodine inserts was more than 50 HU. With regard to algorithm pDP, the maximum intragroup difference was reduced below 3 HU, which indicated that the cupping effect was eventually eliminated.

In the phantom size test, by varying the phantom size (16, 23, 30, and 37 cm) under the same spectrum (80 kVp), a series of projection datasets were simulated and then reconstructed by FBP and pDP. For each reconstructed image, the CT numbers of the iodine inserts in the same group were averaged and plotted against their corresponding theoretical iodine concentrations (Fig. 10). Ideally, the theoretical iodine concentration curve should be $y = 26.46x + 58.33$, where x (mg/ml) represents the iodine concentration, 26.46 (HU · ml/mg) is the iodine concentration factor, 58.33 (HU) is the CT number of unenhanced soft tissue, and y (HU) represents the CT number. The theoretical curve was plotted in solid line as a reference. The FBP results were plotted in dashed line. Due to the BH effect, all the iodine concentration curves tended to be overestimated and the slopes of those curves increased with decreased phantom size. In comparison, the curves derived from the pDP algorithm (dotted line in Fig. 10) perfectly overlapped with the theoretical curve. Linear regression method was performed to compute the iodine concentration curves with a correlation coefficient of greater than 0.999 (Table 4). The high agreement of our proposed algorithm indicated our algorithm was independent of the patient size.

By varying the x-ray spectrum (80, 100, 120, and 140 kVp), iodine concentration curves for algorithms FBP and pDP were computed and plotted in Fig. 11. For FBP, only the curve derived from the 100 kVp spectrum was close to the theoretical trend and that was only for the phantom at 30 cm diameter. In comparison, the curves derived from pDP accorded with the theoretical curves very well across x-ray spectrum. The accuracy of the agreements can be further quantitatively reflected by the linear regression results in Table 4.

3.2 Dynamic Anthropomorphic Thorax Phantom

The reconstruction results of the dynamic anthropomorphic thorax phantom are shown in Fig. 12. The images reconstructed by FBP with monoenergetic spectrum (70 keV) are presented in the first column as benchmark results. The images reconstructed

Fig. 9 Location test results of the dynamic iodine calibration phantom (30 cm and 80 kVp). For the iodine inserts within the same group, their relative CT numbers with respect to the iodine insert nearest to the phantom center were plotted against the radial distance for algorithms (a) FBP and (b) pDP.

Fig. 10 Attenuation-concentration curves derived from the phantom size test. By varying the phantom size (square: 16 cm; circle: 23 cm; star: 30 cm; triangle: 37 cm), iodine concentration curves were plotted for different reconstruction algorithms (solid line: FBP; dotted line: pDP). All simulations in this test used the 80 kVp spectrum.

Fig. 11 Iodine concentration curves derived from the spectrum test. By varying the x-ray spectrum (square: 80 kVp; circle: 100 kVp; star: 120 kVp; triangle: 140 kVp), iodine concentration curves are plotted for different reconstruction algorithms (solid line: FBP; dotted line: pDP). All simulations in this test used the 30-cm-diameter phantom.

by FBP and pDP from the same polyenergetic projection dataset (80 kVp) are presented in the second and third columns, respectively. The reconstructed images and relative difference images of the precontrast phase are shown in the first two rows; the reconstructed images and relative difference images of the postcontrast phase with the peak iodine concentration are shown in the third and fourth rows. The iodine maps are shown in the last row.

In the first column of Fig. 12, due to a monoenergetic spectrum, the images reconstructed by FBP (70 keV) were free of BH artifacts in the pre- and postcontrast images. The second column depicts the reconstruction results of FBP (80 kVp), where BH artifacts severely deteriorated the image quality. For instance, the metal implant in the precontrast image resulted in strong streaks in the heart region and obscured the heart detail. Bones around thoracic cage resulted in visible artifacts to the neighboring soft tissue. In the postcontrast images, other than the mentioned artifacts, the iodinated inserts lowered the attenuations of the breast tissue and the high concentrations of contrast in the left chamber blood pool and descending aorta severely impacted the attenuation density in myocardium. The relative images of the pre- and postcontrast images visually show the error distributions. Fat and breast tissues tended to be underestimated, but bones and iodinated regions tended to be overestimated. The iodine map in the last row was contaminated

by the bright and dark streaks, and the shape of some iodine inserts were not correctly reconstructed.

The images in the last row were reconstructed by pDP (80 kVp). In comparison with FBP (80 kVp), the artifacts induced by the bones, the metal implant, and the iodinated contrast agent were completely eliminated in both pre- and postcontrast images. The image appearance was almost the same with that reconstructed by FBP (70 keV). The relative difference images yielded uniformly negligible values. The iodine map in the last row correctly reflected the iodine distribution.

Figure 13 depicts the CT number error profiles of the iodine TACs/TCCs in different iodinated regions, i.e., lung, fat, breast, and heart. For FBP [Fig. 13(a)], as the average diameter of the dynamic anthropomorphic thorax phantom was ~30 cm, iodine concentration curve $y = 35.99x + 63.69$ (Table 4) was applied to reduce the errors of the CT numbers and the iodine concentrations. However, only the error profile of the iodinated heart was close to zero values, which benefited from the same background tissue with the iodine calibration phantom. Because the shape and the structure of the thorax phantom were different from those of the iodine calibration phantom, discrepancies were still observable. Among all the body tissues, as the attenuation property of the lung tissue deviated most from that of soft tissue, the error profile of lung tissue yielded highest deviations. The error profile of breast tissue also had a similar error magnitude

Table 4 Linear regression results of the attenuation-concentration curves derived from the phantom size test and spectrum test. The parameters x (mg/ml) and y (HU) represent the iodine concentration and the CT number, respectively.

Simulation tests	Spectrum/phantom size	FBP	pDP
Phantom size test	80 kVp/16 cm	$y = 41.23x + 64.43$	$y = 26.41x + 58.06$
	80 kVp/23 cm	$y = 38.59x + 64.48$	$y = 26.47x + 58.08$
	80 kVp/30 cm	$y = 35.99x + 63.69$	$y = 26.51x + 57.61$
	80 kVp/37 cm	$y = 34.45x + 63.98$	$y = 26.54x + 57.31$
Spectrum test	80 kVp/30 cm	$y = 35.99x + 63.69$	$y = 26.51x + 57.61$
	100 kVp/30 cm	$y = 27.12x + 62.09$	$y = 26.50x + 58.15$
	120 kVp/30 cm	$y = 21.97x + 61.28$	$y = 26.51x + 58.40$
	140 kVp/30 cm	$y = 18.45x + 60.87$	$y = 26.50x + 58.67$

Fig. 12 Reconstruction results of the dynamic anthropomorphic thorax phantom. The images from the first column to the third column were reconstructed by FBP (70 keV), FBP (80 kVp), and pDP (80 kVp), respectively. The images from the first row to the last row are precontrast images (−70/130), relative difference images (0%/20%) of the precontrast images, postcontrast images (−70/130), relative difference images (0%/20%) of the postcontrast images, and iodine maps (0/40), respectively.

Fig. 13 CT number error profiles of the TACs/TCCs for the iodine inserts in lung (square), fat (circle), breast (star), and heart (triangle) as defined in the dynamic anthropomorphic thorax phantom [Fig. 5(b)] for (a) FBP and (b) pDP.

Fig. 14 CT number error profiles due to BH enhancement in the four ROIs as defined in Fig. 7 in the dynamic anthropomorphic thorax phantom for algorithms (a) FBP and (b) pDP.

with that of lung, which was caused by the cupping effect [Fig. 9(a)]. If iodine concentration curves were not applied, those curves would have had even larger errors. For FBP, the maximum error was more than 40 HU, i.e., 1.1 mg/cc in iodine concentration. Improvement in the error profiles was evident by using pDP algorithm, and all error profiles were close to zero values.

Figure 14 depicts the CT number error profiles of the four ROIs as defined in the dynamic anthropomorphic phantom (Fig. 7). For FBP [Fig. 14(a)], large deviations caused by BH effect could be observed in the basal wall of the left heart chamber and the maximum deviation was as large as -42 HU. The lateral wall also had relative large deviation, which was probably due to the metal artifacts. The BH enhancement of the other two ROIs was relatively small. By contrast, the BH across all ROIs disappeared with the case of pDP [Fig. 14(b)].

4 Discussion

In this study, we developed a segmentation-free pDP. There are four important features that distinguish our algorithms from the previous work^{24,25}

1. The proposed algorithm can model the attenuation properties of diverse base materials (e.g., lung, fat, breast, soft tissue, bone, implant metal, and iodine) in the reconstruction process. Because the attenuation properties of the tissue mixtures are computed by interpolating two predefined base materials [Eq. (4)], the proposed method does not result in ill-posed problems or unstable solutions, but can improve reconstruction accuracy and stability as shown in our previous studies^{28,34} via a base material transition test.
2. For each postcontrast phase, the iodine projections can be obtained by linearization and be used directly to reconstruct artifact-free iodine maps. As the reconstructed iodine maps can realistically reflect the iodine concentrations, it is not necessary to precompute the iodine concentration curves for different spectra and different sized phantoms.

3. The methodology is not limited to blood-iodine mixtures. The proposed perfusion algorithm can be applied to organ-based perfusion exams as well (e.g., lung, fat, and breast). Note that if certain patient anatomical information or material distribution information are reasonably assumed, adaptive base material decomposition³⁴ can be employed to better decompose the tissue mixtures. For example, the breast tissue can be confined only in the breast region, and the base material set for this region can include fat, breast, soft tissue, and calcifications only. Doing so, the fat-soft tissue mixtures would not be misinterpreted into breast-related mixtures in the other body regions.
4. As no segmentation is required in our method, misinterpretations of the voxel types due to the threshold-based segmentation method can be avoided.

In this work, two phantoms were used to validate the proposed algorithm, i.e., a dynamic iodine calibration phantom and a dynamic anthropomorphic thorax phantom. The dynamic iodine calibration phantom was used to investigate the reconstruction stabilities of the iodinated contrast agent in terms of various influential factors (i.e., iodine location, phantom size, and x-ray spectrum). The simulation results showed that, for the widely used FBP-based perfusion algorithm, the errors of the iodine concentration factor (HU · ml/mg) were in a large range (i.e., $[-8.01, 14.77]$), which indicated that the iodine concentration curve highly depended on these influential factors, making it necessary to apply the precalibrated iodine concentration curve to reduce the errors. In contrast, the proposed method accurately modeled the attenuation properties of iodine, so that the error range was reduced to $[-0.05, 0.08]$, effectively eliminating the BH effect.

A realistic dynamic anthropomorphic thorax phantom was utilized to further investigate the reconstruction performance of the proposed algorithm. The simulation results showed that, for FBP, the reconstructed images suffered from severe BH artifacts caused by bone, iodine, and metal implant. The strong artifacts seriously affected the accuracy of the CT numbers. For example, the deviation of the TACs of the soft tissue around the left heart

chamber was as large as -40 HU. Though iodine concentration curve was applied to the iodine inserts, the errors of the voxel values were still larger than 40 HU, which was equivalent to a 1.1 mg/ml deviation in iodine concentration. There are two major reasons for this large discrepancy. First, the strong cupping artifacts could significantly affect the iodinated tissues near the periphery of the patient body. Second, as the iodine concentration curves were mainly derived from iodinated blood or soft tissue, the errors could be introduced when applying those curves to other iodinated tissues. For pDP, the BH artifacts, due to bone and iodine, were completely eliminated, and the metal artifacts were also greatly reduced. The quantitative results showed that the TACs of both soft tissue ROIs and different iodinated tissues could be accurately derived.

For the iodine map reconstructed by the proposed method (Fig. 12), the values of the voxels originally containing bones were slightly less than zero (i.e., the darker region in the bone locations), which is due to the iteration cutoff in the pre-contrast image reconstruction. Because of only using four iterations, the bone inserts in the precontrast reconstructed images were about 0.1% overestimated.²⁸ This overestimation, after being magnified by the large attenuation of bone, systematically decreased the accumulated lengths of iodine [$l_{r,7}^{\text{post}}$ in Eq. (15)] and thus caused a negative bias in the iodine map images. This negative bias can be corrected by reconstructing more accurate precontrast images using more iterations.

One limitation of the proposed algorithm is that the scanned organs should be relatively stationary. Therefore, in the image acquisition process, it is important to minimize patient motion, and/or additional techniques^{40–45} can be employed to reduce the influence of motions. For example, the respiratory motion and the cardiac motion can be minimized by the respiratory-gating technique,^{40,41} the ECG-gating technique,^{42–44} and the deformable image registration algorithms.⁴⁵

The effect of scatter was not considered in our work, which can affect the accuracy, robustness, and material discrimination ability of the proposed method. One way to resolve this issue is to combine the proposed method with Monte Carlo-based scatter correction methods⁴⁶ and to iteratively estimate the scatter distribution and the reconstructed volume.

Two smoothing kernels were used in this work. In this study, it was not necessary to optimize these filters, as the purpose of this work was to eliminate BH effect and not to improve the noise properties of the images as affected by the choice of the smoothing kernels. In the future, we intend to utilize adaptive smoothing kernels to reduce image noise while keeping sharp edges or anatomical structures intact. Furthermore, we plan to statistically model the Poisson distribution of the quantum noise^{19,29,30} into the reconstruction algorithm to further suppress image noise.

5 Conclusions

We have presented a pDP. Simulation results show that the proposed algorithm can effectively eliminate BH artifacts and accurately reconstruct the iodine map regardless of the phantom size, spectrum, location, and background tissue type. Future work will include noise reduction potentials of the proposed algorithm. Other beam-hardening reduction algorithms^{17–20,24,25} and clinical data will be included to further investigate the effectiveness of the proposed method. In order to relax the “adjacent base materials” assumption, adaptive approaches will also be explored.

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