Material elemental decomposition in dual and multi-energy CT via a sparsity-dictionary approach for proton stopping power ratio calculation

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Purpose: Accurate calculation of proton stopping power ratio (SPR) relative to water is crucial to proton therapy treatment planning, since SPR affects prediction of beam range. Current standard practice derives SPR using a single CT scan. Recent studies showed that dual-energy CT (DECT) offers advantages to accurately determine SPR. One method to further improve accuracy is to incorporate prior knowledge on human tissue composition through a dictionary approach. In addition, it is also suggested that using CT images with multiple (more than two) energy channels, i.e., multi-energy CT (MECT), can further improve accuracy. In this paper, we proposed a sparse dictionary-based method to convert CT numbers of DECT or MECT to elemental composition (EC) and relative electron density (rED) for SPR computation.

Method: A dictionary was constructed to include materials generated based on human tissues of known compositions. For a voxel with CT numbers of different energy channels, its EC and rED are determined subject to a constraint that the resulting EC is a linear non-negative combination of only a few tissues in the dictionary. We formulated this as a non-convex optimization problem. A novel algorithm was designed to solve the problem. The proposed method has a unified structure to handle both DECT and MECT with different number of channels. We tested our method in both simulation and experimental studies.

Results: Average errors of SPR in experimental studies were 0.70% in DECT, 0.53% in MECT with three energy channels, and 0.45% in MECT with four channels. We also studied the impact of parameter values and established appropriate parameter values for our method.

Conclusion: The proposed method can accurately calculate SPR using DECT and MECT. The results suggest that using more energy channels may improve the SPR estimation accuracy. © 2018 American Association of Physicists in Medicine [https://doi.org/10.1002/mp.12796]

Key words: dictionary, dual- and multi-energy CT, elemental decomposition, proton therapy, sparsity, stopping power ratio

1. INTRODUCTION

Proton therapy has been increasingly used for cancer treatment due to its capability of delivering a highly focused radiation dose to a target region, while sparing normal tissue.^{1–3}

As a proton beam travels through a patient, it deposits most of its energy at the end of its range, forming the so-called Bragg peak. By adjusting the Bragg peak position, it is possible to precisely target the tumor at a certain depth, while completely sparing the organ distal to the target and delivering a low dose to the organ proximal to the target. Because of this property, calculating proton range is a crucial task at the treatment planning stage: errors in the range calculation result in significant overdose to the critical structure and/or underdose to the target.^{4,5} Since the range is determined by

stopping power ratio (SPR) relative to water of those voxels on the beam path, it is of central importance to precisely calculate the SPR to improve the accuracy of proton therapy treatment planning.

In current clinical practice, SPR is typically derived from a treatment planning CT image. A simple method is to generate a CT number calibration curve by scanning tissue substitutes with known density and compositions to establish the relationship between the SPR and the CT number. A stoichiometric calibration method has been proposed to determine the calibration curve based on the calculated SPR and CT numbers of standard human tissues.⁶ This method has also been extended to orthovoltage CT applications to improve accuracy.⁷ However, the SPR of a voxel depends on both density and material composition. It is challenging to

accurately derive the SPR value from a single CT number. To overcome this challenge, dual-energy CT (DECT)-based SPR calculation approaches have been developed. The two CT numbers of a voxel can provide more information to determine voxel density, material composition, and therefore the SPR. In fact, the use of DECT for precise determination of tissue properties has been explored in the photon therapy regime, for example, to estimate photon cross sections at low energy in the range of 20–1000 keV for accurate radiotherapy dosimetry.⁸ When it comes to the problem of SPR calculation, a spectrum of novel algorithms via estimating effective atomic number and mean excitation energy have been developed over the years, with the benefits of DECT over conventional CT clearly demonstrated.^{9–22} For instance, Hünemohr et al.¹⁹ established a method to convert DECT to electron density relative to water and effective atomic number (Z_{eff}). The latter was further converted to mean excitation energy using a parameterized curve. With these quantities derived, SPR was calculated for tissue surrogates with a root-mean-square (RMS) error of 0.65% (range in 0.2–1.0%) using 80/140Sn kVp DECT images. Bourque et al.¹⁸ used a dual-energy index that only depends on effective atomic number. They developed a scheme for the DECT-based stoichiometric calibration to estimate electron density and effective atomic number simultaneously, which can be used to calculate proton SPR. Several methods extracting elemental compositions from DECT images have also been proposed recently. Landry et al.²³ developed a method that mapped DECT numbers to Z_{eff} and rED, which were further converted to carbon and oxygen concentrations. Hünemohr et al.²⁴ put forward a method considering the DECT-based parameterization of Z_{eff} and rED. Elemental mass fraction was obtained via a fitted function.²⁵ More recently, Lalonde et al.²⁶ presented a tissue characterization approach suitable for DECT and multi-energy CT (MECT). The solution was constrained on the principal component basis that was obtained by applying principal component analysis on fractional weights of known tissues.

One method that may potentially further improve calculation accuracy is to incorporate prior knowledge on tissue composition via a dictionary approach. Clinical applications always deal with tissues that are relevant to human or a few other types, such as metal. It is expected that incorporating the tissue type information *a priori* is beneficial to SPR estimation. Another possible direction to improve accuracy is to incorporate more energy channels, that is, MECT.²⁶ In this paper, we propose a new method to derive tissue composition and electron density which has a unified structure to handle different number of energy channels, and hence can

accommodate both DECT and MECT. In our method, a dictionary consisting of known material compositions of tissue types relevant to human is constructed as the prior knowledge. Determination of tissue composition and density is subject to a constraint that the resulting composition is a linear combination of only a few tissues in the dictionary. Such a dictionary idea has also been widely applied in many other decomposition problems with great successes, such as hyperspectral imaging.^{27–29}

2. MATERIALS AND METHODS

2.A. Forward model of CT numbers

We used the forward model that maps relative electron density with respect to water (rED) and elemental composition (EC) into a CT number^{30,31} as

$$f = \rho(K^{PE}\tilde{Z}^{3.62} + K^R\hat{Z}^{1.86} + K^C), \quad (1)$$

where f is the shifted CT number ($f = \frac{\mu}{\mu_w}$) at a voxel of interest with μ being the linear x ray attenuation coefficient of this voxel and μ_w being that of water. K^{PE} , K^R and K^C are constants characterizing contributions of photoelectric effect, coherent Rayleigh scattering and incoherent Compton scattering, respectively. They are parameters specific to a CT scanner and a scan protocol. ρ is rED of the voxel relative to water. $\tilde{Z}$ and $\hat{Z}$ only depend on the EC of the voxel

$$\tilde{Z} = \left(\sum_i \lambda_i Z_i^{3.62} \right)^{\frac{1}{3.62}}, \quad (2)$$

$$\hat{Z} = \left(\sum_i \lambda_i Z_i^{1.86} \right)^{\frac{1}{1.86}}. \quad (3)$$

Z_i is the atomic number of the i -th chemical element and λ_i is the fraction in number of electrons for this element, satisfying $\sum_i \lambda_i = 1$. Let us write the element fractions using a compact row vector $\lambda = (\lambda_1, \dots, \lambda_N)$, where N is the total number of elements considered. Then Eq. (1) can be expressed as

$$f = \rho(\lambda K + K^C), \quad (4)$$

where K is a column vector $K = (K^{PE}Z_1^{3.62} + K^RZ_1^{1.86}, \dots, K^{PE}Z_N^{3.62} + K^RZ_N^{1.86})^T$.

When it came to CT numbers of multiple energy channels, we used a row vector $F = (f_1, f_2, \dots, f_M)$ to denote the CT numbers of a voxel at M different energy channels. Since the constants K^{PE} , K^R and K^C depend on energy channel, we labeled them with a subscript of energy channel and hence generalized the previously defined vector K into a matrix form:

$$K = \begin{pmatrix} K_1^{PE}Z_1^{3.62} + K_1^RZ_1^{1.86} & K_2^{PE}Z_1^{3.62} + K_2^RZ_1^{1.86} & \dots & K_M^{PE}Z_1^{3.62} + K_M^RZ_1^{1.86} \\ K_1^{PE}Z_2^{3.62} + K_1^RZ_2^{1.86} & K_2^{PE}Z_2^{3.62} + K_2^RZ_2^{1.86} & \dots & K_M^{PE}Z_2^{3.62} + K_M^RZ_2^{1.86} \\ \vdots & \vdots & \ddots & \vdots \\ K_1^{PE}Z_N^{3.62} + K_1^RZ_N^{1.86} & K_2^{PE}Z_N^{3.62} + K_2^RZ_N^{1.86} & \dots & K_M^{PE}Z_N^{3.62} + K_M^RZ_N^{1.86} \end{pmatrix}, \quad (5)$$

and defined

$$K_3 = (K_1^C, K_2^C, \dots, K_M^C). \quad (6)$$

With these terms, the mapping from EC and rED to CT numbers can be written into a compact form

$$F = \rho(\lambda K + K_3). \quad (7)$$

2.B. Construction of a dictionary

To impose prior knowledge on tissue composition into the decomposition problem, we built a dictionary that contained EC for materials that are commonly encountered in a human body. The dictionary was represented as a matrix A with N_D rows and N columns. Each row of the matrix corresponded to one material in the dictionary. The N elements in a row were the known fractions of the chemical elements for this material. With this dictionary matrix, composition of an actual material that is a mixture of those materials in the dictionary can be expressed as $\lambda = \alpha A$. Here $\alpha = (\alpha_1, \dots, \alpha_{N_D})$ is a vector specifying the contribution of each dictionary material.

A few remarks are in order. First, elements existing in a human tissue include Hydrogen (H), Carbon (C), Nitrogen (N), Oxygen (O), Phosphorus (P), Calcium (Ca) and a few other elements with small fractions.²⁵ In our study, we considered those elements with small fractions as Ca when generating the dictionary. Second, we constructed the dictionary A based on the 71 tissues listed in Schneider et al.²⁵ which includes one lung tissue, 49 soft tissues, and 21 bone tissues. Since the tissue composition for a real patient may be slightly different from the nominal composition listed in the paper, we further enlarged the dictionary by utilizing the method proposed in Yang et al.¹² Specifically, for each type of lung tissues, we randomly perturbed the fraction of H with a Gaussian random number. The mean of the random number was zero, and the standard deviation was determined based on a literature search.¹² Once the perturbed H fraction was determined, the fractions of the remaining five elements, C, N, O, P, and Ca, were adjusted by an equal amount, such that fractions of the six elements summed up to unity. In this way, we generated 49 additional materials based on the lung tissue listed in Schneider et al.²⁵ Similarly, for each of the soft tissues and bone tissues, we randomly perturbed the H and Ca fractions, respectively, to generate four additional materials. The reason for generating more additional materials for the lung tissue group was to increase the weight of the lung tissue group in the dictionary, as the number of lung tissue in Schneider et al.²⁵ was much smaller than those of the other two groups. This approach enlarged the original 71 tissues into 400 for building the dictionary. The number of tissues in the dictionary determines its comprehensiveness. We have investigated this issue and found 400 materials in the dictionary are sufficient, as will be presented in Sections 2.E.2 and 3.B.

2.C. Proposed decomposition model

When determining the EC of a voxel, it is our assumption that the unknown EC can be represented by a sparse non-negative linear combination of the ECs of those materials in the dictionary. We formulated the decomposition model as a constrained optimization problem:

$$\begin{aligned} \min_{\rho, \alpha} & \frac{1}{2} \|F - \rho(\alpha A + K_3)\|_2^2, \\ \text{s. t.} & \|\alpha\|_0 \leq s, \quad \alpha_i \geq 0, \quad \sum_i (\alpha A)_i = 1. \end{aligned} \quad (8)$$

Here, $\|X\|_2 = \sqrt{\sum_i X_i^2}$ is the l_2 norm of a vector X and $\|X\|_0$ is the l_0 norm, which gives the number of non-zero elements in X . The objective function ensures fidelity of the determined ρ and α to the CT numbers based on Eq. (7) with $\lambda = \alpha A$. The first constraint enforces sparsity of α by requiring the number of non-zero elements in α less than a parameter s . The second and third constraints are imposed to ensure the non-negativity of the coefficients and the property that they sum to unity. Note that $\sum_i A_{j,i} = 1$ for $j = 1, 2, \dots, N_D$, because each row of the matrix A corresponds to one dictionary material and the fractions of elements add up to unity. It follows that $\sum_i (\alpha A)_i = \sum_i \sum_j \alpha_j A_{j,i} = \sum_j \sum_i \alpha_j A_{j,i} = \sum_j \alpha_j$. Therefore, the constraint $\sum_i (\alpha A)_i = 1$ is equivalent to $\sum_i \alpha_i = 1$.

We would like to comment on the sparsity assumption. This assumption means that the vector α has only a few non-zero elements. This can be understood as following. Sparsity is a condition naturally satisfied in the limit of a large number of tissues in the dictionary. In the ideal case with a complete dictionary that contains every possible tissue composition, the solution would be that there is one and only one tissue selected from the dictionary. This naturally leads to a sparse solution: the α vector is 1-sparse, namely containing only one non-zero entry. In this limit the dictionary size is large and so is the length of the vector α . In a realistic situation using an incomplete but sufficiently comprehensive tissue dictionary, it is expected that a few number of the dictionary tissues can be selected to represent majority of the tissue composition. The residual part can be captured by several other dictionary tissues. In this context, the solution vector α is still sparse given the long length of this vector and the relatively small number of non-zero elements, although it is not one-sparse anymore. It is this fact that supports the use of sparsity as a prior knowledge. The purpose of using this sparsity dictionary is to constrain the solution of elemental composition. As the dictionary is over-complete, naively using the dictionary without any additional constraint would lead to infinite many possible solutions. The sparsity constraint is served as an additional regularization that has to be satisfied by the true solution due to the way that we constructed the dictionary. It helps to restrict the solution space and therefore to obtain the correct solution. In a certain sense, this is similar to the principal component analysis approach employed

by Lalonde et al.^{26,32}, where the principal components of human tissues are used to define a sub-linear space to constrain the solution.

2.D. Numerical algorithm

To solve the proposed model in Eq. (8), we developed a two-loop iterative alternating minimization scheme. At the outer loop, we simply split the problem into two sub-problems, such that we tackled the original problem by alternatively updating ρ and α as following

$$\begin{cases} \alpha_t = \arg \min_{\alpha} \frac{1}{2} \|F - \rho_{t-1}(\alpha \Lambda K + K_3)\|_2^2 + \delta_+(\alpha), \text{ s. t. } \|\alpha\|_0 \leq s, \sum_i \alpha_i = 1 \\ \rho_t = \arg \min_{\rho} \frac{1}{2} \|F - \rho(\alpha_t \Lambda K + K_3)\|_2^2. \end{cases} \quad (9)$$

Here t is an index for the iteration step. $\delta_+(\alpha)$ is an indicator function: $\delta_+(\alpha)$ is zero, when all the entries in α are non-negative, and infinity otherwise.

The sub-problem with respect to ρ is convex for a given α_t and can be solved explicitly as

$$\rho_t = \frac{\sum_i f_i(\alpha_t \Lambda K + K_3)_i}{\sum_i (\alpha_t \Lambda K + K_3)_i^2}, \quad (10)$$

The sub-problem of α is more complicated and does not have an explicit solution. It is non-convex due to the presence of the sparsity constraint $\|\alpha\|_0 \leq s$. Our idea was to utilize alternating direction method of multipliers (ADMM)^{33–38} to further split the problem into multiple sub-problems, such that the objective function could be minimized in these sub-problems at inner-loop iterations. More specifically, we introduced an auxiliary variable z and integrated the linear constraint into the objective function by incorporating Lagrangian multipliers:

$$\begin{aligned} L_{\beta_1 \beta_2}(\alpha, z, \Gamma_1, \Gamma_2) = & \frac{1}{2} \|F - \rho_t(\alpha \Lambda K + K_3)\|_2^2 + \delta_+(z) \\ & + \frac{\beta_1}{2} \|\alpha - z\|_2^2 + \langle \Gamma_1, \alpha - z \rangle \\ & + \frac{\beta_2}{2} \|\alpha \mathbf{1}_M - 1\|_2^2 + \langle \Gamma_2, \alpha \mathbf{1}_M - 1 \rangle, \end{aligned} \quad (11)$$

and the sparsity constraint was replaced by $z_0 \leq s$. $\mathbf{1}_M$ is a vector of length M with all the entries being unity. With this new formulation, we were able to update α , z , Γ_1 and Γ_2 sequentially by

$$\begin{cases} \alpha^p = \arg \min_{\alpha} L_{\beta_1 \beta_2}(\alpha, z^{p-1}, \Gamma_1^{p-1}, \Gamma_2^{p-1}), \\ z^p = \arg \min_z L_{\beta_1 \beta_2}(\alpha^p, z, \Gamma_1^{p-1}, \Gamma_2^{p-1}), \text{ s. t. } \|z\|_0 \leq s \\ \Gamma_1^p = \Gamma_1^{p-1} + \beta_1(\alpha^p - z^p), \\ \Gamma_2^p = \Gamma_2^{p-1} + \beta_2(\alpha^p \mathbf{1}_M - 1), \end{cases} \quad (12)$$

where p indicates the iterative index for the inner-loop. For the first sub-problem

$$\begin{aligned} \alpha^p = \arg \min_{\alpha} & \frac{1}{2} \|F - \rho_{t-1}(\alpha \Lambda K + K_3)\|_2^2 + \frac{\beta_1}{2} \|\alpha - z^{p-1}\|_2^2 \\ & + \langle \Gamma_1^{p-1}, \alpha - z^{p-1} \rangle + \frac{\beta_2}{2} \|\alpha \mathbf{1}_M - 1\|_2^2 \\ & + \langle \Gamma_2^{p-1}, \alpha \mathbf{1}_M - 1 \rangle, \end{aligned} \quad (13)$$

the objective function is of a quadratic form. If we define,

$$G^p = (\rho_{t-1})^2 (\Lambda K + K_3)(\Lambda K + K_3)^T + \beta_1 I_N + \beta_2 \mathbf{1}_M \mathbf{1}_M^T, \quad (14)$$

$$\begin{aligned} b^p = & \rho_{t-1} F (\Lambda K + K_3)^T + \beta_1 z^{p-1} + \beta_2 \mathbf{1}_M^T - \Gamma_1^{p-1} \\ & - \Gamma_2^{p-1} \mathbf{1}_M^T, \end{aligned} \quad (15)$$

where $I_N \in \mathbb{R}^{N \times N}$ is the identity matrix, the solution can be expressed as

$$\alpha^p = b^p (G^p)^{-1} \quad (16)$$

Next, for the sub-problem corresponding to z ,

$$\begin{aligned} z^p = \arg \min_z & \frac{\beta_1}{2} \|z - \alpha^p\|_2^2 + \langle \Gamma_1^p, \alpha^p - z \rangle \\ & + \delta_+(z), \text{ s. t. } \|z\|_0 \leq s, \end{aligned} \quad (17)$$

it is equivalent to

$$z^p = \arg \min_z \frac{1}{2} \left\| z - \alpha^p - \frac{\Gamma_1^{p-1}}{\beta_1} \right\|_2^2 + \delta_+(z), \text{ s. t. } \|z\|_0 \leq s. \quad (18)$$

The solution is a vector that keeps the s largest non-zero entries in $\alpha^p + \frac{\Gamma_1^{p-1}}{\beta_1}$ unchanged, while setting the remaining entries zero. Specifically,

$$z_i^p = \begin{cases} \left(\alpha^p + \frac{\Gamma_1^{p-1}}{\beta_1} \right)_i, & \text{if } i \in S_{\max}; \\ 0, & \text{otherwise} \end{cases} \quad (19)$$

where $S_{\max}$ is a set of indices for the s largest elements in the vector $\alpha^p + \frac{\Gamma_1^{p-1}}{\beta_1}$. After alternatively updating α^p , z^p , Γ_1^p and Γ_2^p until the inner-loop iterations converge, we set converged α^p to α_t . We then exit the inner loop and move on to the next step of the outer loop.

In summary, our algorithm to solve the problem in Eq. (8) is presented in Table I.

2.E. Evaluation studies

2.E.1. Scanner calibration

As mentioned previously, K^{PE} , K^R and K^C are scan protocol-dependent parameters. Therefore, before evaluating the

TABLE I. Numerical algorithm to solve the problem in Eq. (8).

Algorithm 1	
Input:	$\Lambda, K, K_3, \rho^0, \alpha^0, z^0, \Gamma_1^0, \Gamma_2^0, \beta_1, \beta_2, s$ and a stopping criterion ϵ
Output:	ρ^{opt} and α^{opt}
Procedure:	
1.	Set $t = 1$;
2.	Set $p = 1$;
	(a) Compute α^p according to (14), (15) and (16);
	(b) Compute z^p according to (20);
	(c) Compute Γ_1^p, Γ_2^p according to (12);
	(d) If $\frac{\ \alpha^p - \alpha^{p-1}\ _E}{\ \alpha^p\ _F} < \epsilon$, set $\alpha_t = \alpha^p, z^0 = z^t, \Gamma_1^0 = \Gamma_1^p, \Gamma_2^0 = \Gamma_2^p$; otherwise, set $p = p + 1$ and go to Step a);
3.	Compute ρ_t according to (10);
4.	If $\frac{\ \alpha_t - \alpha_{t-1}\ _F}{\ \alpha_t\ _F} < \epsilon$ and $\frac{\ \rho_t - \rho_{t-1}\ _F}{\ \rho_t\ _F} < \epsilon$, set $\alpha^{opt} = \alpha_t$ and $\rho^{opt} = \rho_t$; otherwise, set $t = t + 1$, go to Step 2.

performance of our decomposition algorithm, we first conducted a calibration study to determine these parameters for each energy channel. Because we do not have access to DECT or MECT scanners, we performed proof-of-principle studies by scanning the phantom repeatedly under different kVp levels. Specifically, we scanned an RMI-467 tissue characterization phantom (Gammex, Middleton, WI) in a GE LightSpeed QX/I scanner with four energy channels: 80, 100, 120 and 140 kVp. For each channel, at least three materials with known rED and EC were needed to determine the three unknown parameters K^{PE} , K^R and K^C . For the sake of robustness, we used six materials for calibration, namely lung (LN450), adipose tissue (AP6), solid water, brain (SR2), mineral bone (B-200) and 50% CaCO_3 (CB2-50%), which covered a wide range of tissue types. To reduce the impact of noise, CT numbers of these materials in corresponding regions of interest (ROIs) were averaged. Let us write the CT number of these six materials in a column vector F_{cal} and define a matrix

$$U = \begin{pmatrix} \rho_1 \tilde{Z}_1^{3.62} & \rho_1 \hat{Z}_1^{1.86} & \rho_1 \\ \rho_2 \tilde{Z}_2^{3.62} & \rho_2 \hat{Z}_2^{1.86} & \rho_2 \\ \vdots & \vdots & \vdots \\ \rho_6 \tilde{Z}_6^{3.62} & \rho_6 \hat{Z}_6^{1.86} & \rho_6 \end{pmatrix}. \quad (20)$$

Then according to Eq. (1), the vector $K_{cali} = (K^{PE}, K^R, K^C)^T$ satisfies $F_{cal} = UK_{cali}$. This is an over-determined linear system with six linear equations and three unknowns. Hence, the solution was obtained as $K_{cal} = U^\dagger F_{cal}$, where $U^\dagger$ indicates pseudo-inverse of the matrix U .

After that, we examined accuracy of the forward CT number model. Specifically, we scanned another six materials: namely breast, water, liver (LV1), inner bone, 30% CaCO_3 (CB2-30%) and cortical bone (SB3). For the 12 materials, we computed their CT numbers using Eq. (1) based on their known EC and rED, as well as the calibration parameters K^{PE} , K^R and K^C . The calculated CT number f_{cal} was compared with the experimental value f_{true} and accuracy was quantified by the relative difference $e_f = |f_{cal} - f_{true}| / f_{true}$.

2.E.2. Impact of sparse dictionary-based prior knowledge

The prior knowledge imposed by both dictionary and sparsity is an essential component in the proposed method. The validity and effectiveness of this approach should be tested. For this purpose, we generated tissues with compositions close to the real Gammex materials via the same technique used to enlarge the dictionary.¹² In total, we generated 100 lung tissues, 100 soft tissues and 100 bone tissues for testing. All these tissues were different from those in the dictionary.

Effectiveness of using a dictionary: To test the effectiveness of using dictionary, we formulated and tested the following non-dictionary model:

$$\min_{\rho, \lambda} \frac{1}{2} \|\hat{F} - \rho(\lambda K + K_3)\|_2^2, \quad \text{s.t. } \lambda_i \geq 0, \sum_i \lambda_i = 1, \quad (21)$$

where $\hat{F}$ is the CT numbers generated by the forward model in Eq. (7). We considered two situations. First, assuming the rED ρ was already known or can be accurately estimated, we determined the elemental composition λ by solving a constrained least-square problem. The solution accuracy would largely depend on the mathematical property of the linear system $\lambda K K^T = \frac{F K^T}{\rho} - K_3 K^T$, which is often ill-posed. Second, assuming ρ was unknown, we solved the problem by alternatively updating of ρ and λ . We expected an even worse accuracy than that in the first situation due to the non-convexity of the problem.

Comprehensiveness of a dictionary: Second, we studied the comprehensiveness of a dictionary. For each testing tissue, we investigated how well the dictionary can represent the tissue by solving an optimization problem:

$$\min_{\alpha} \frac{1}{2} \|\alpha \Lambda - \hat{c}\|_2^2, \quad \text{s.t. } \|\alpha\|_0 \leq s, |\alpha|_1, \alpha_i \geq 0, \quad (22)$$

where $\hat{c}$ is the EC of the testing material. This problem was solved by a modified version of Algorithm 1. We used a sparsity level of $s = 20$, the reason of which will be demonstrated in the next test. We expected that the solution accuracy would increase with increased dictionary size, but it would not be significantly improved once the dictionary became large enough. As such, we gradually increased the dictionary size and monitored the solution quality. Specifically, we first formed a large number of tissues. Each time a new material is randomly selected from them and added to the dictionary.

Impact of sparsity: We studied the impact of sparsity by solving the model in Eq. (22) but with a fixed dictionary size under various sparsity level s .

In all the three tests, the agreements between ground truth and the solution were quantified by the following metrics:

$$e_{EC} = \sqrt{\frac{1}{N_M} \sum_i \left(\frac{1}{6} e_i(H) + \frac{1}{6} e_i(C) + \frac{1}{6} e_i(N) + \frac{1}{6} e_i(O) + \frac{1}{6} e_i(P) + \frac{1}{6} e_i(Ca) \right)^2}, \quad (23)$$

Equation (23) represents error in EC. For the i -th material, we computed e_i , the absolute difference in the fraction of the i th element. Equation (23) then computed average error over all the six elements. It then took the root-mean-square error over all tissues in a group, that is, lung, soft tissue, and bone group, where N_M indicates the total number of tested tissues in each group. This metric characterized the accuracy of decomposition in EC for each group.

2.E.3. Simulation studies

We performed simulation studies to evaluate the performance of the decomposition method. We first generated testing materials based on tissues listed in Ref. [25] by perturbing elemental fractions as we did previously in dictionary enlargement. We synthesized 10 testing materials for each lung tissue, two for each tissue in the soft tissue and bone tissue group according to the method suggested in Yang et al.¹² with variations of each element stated in their paper. This led to a total number of 150 materials for testing covering the range of EC variations in human. EC of all the synthesized testing materials were different from those in the dictionary. We computed e_{EC} for all the synthesized testing materials using corresponding materials in the dictionary as references. The average, maximum, and minimum e_{EC} were 0.3%, 1.6% and 0.07%, respectively. Original rED was kept in these synthesized materials. We then computed CT numbers for each material according to Eq. (1) using K^{PE} , K^R and K^C obtained through the calibration process. Note that the setup here did not consider any uncertainty introduced by imaging, calibration or forward CT model.^{27,28} The rational was to examine the effectiveness of the proposed decomposition method in an ideal context. This would allow us to gain confidence on the model before moving on to experimental studies where various uncertainties would be included.

After that, the calculated CT numbers were fed to the proposed algorithm to determine the rED and EC. Finally, SPR of the material was calculated using Bethe Equation³⁹

$$SPR = \rho \cdot \frac{\ln\left(\frac{2m_e c^2 \beta^2}{I_m(1-\beta^2)}\right) - \beta^2}{\ln\left(\frac{2m_e c^2 \beta^2}{I_w(1-\beta^2)}\right) - \beta^2}. \quad (24)$$

The mean excitation energy of the material I_m and that of the water I_w were computed based on the EC as $I_m = \exp(\sum_i \lambda_i \ln I_i)$, where I_i is the excitation energy of the i -th element. The SPR was calculated for a 200 MeV proton beam. We used e_{EC} defined above to evaluate accuracy of EC. To quantify the accuracy of rED, and SPR, we considered

$$e_{rED} = \sqrt{\frac{1}{N_M} \sum_i \sigma_i(\rho)^2}, \quad (25)$$

$$e_{SPR} = \sqrt{\frac{1}{N_M} \sum_i \sigma_i(SPR)^2}. \quad (26)$$

In Eqs. (25) and (26), $\sigma_i(\rho)$ and $\sigma_i(SPR)$ are relative difference between the calculated and the ground truth rED and SPR for the i -th material, respectively. For the evaluation of SPR estimation accuracy, we computed SPRs according to estimated rEDs and ECs of all the six elements and made comparisons with theoretical SPRs computed based on ground truth EC of all the elements.

All the studies were conducted under different settings: DECT with 80 and 140 kVp, MECT (three energy channels) with 80, 100, and 140 kVp, and MECT (four energy channels) with 80, 100, 120, and 140 kVp. Since the main idea of using multiple channels is to get information along energy dimension, spectral separation between channels is crucial. Hence, we selected channels with large separations to minimize the effects of overlapping spectrums.

2.E.4. Experimental studies

Finally, we performed experimental studies to evaluate the accuracy of decomposing these materials using the proposed method and calculating SPR. The study procedure followed what was described in the simulation study expected that experimentally measured CT numbers of the Gammex phantom were used as input to the algorithm. Comparison studies regarding SPR accuracy were carried out with respect to two state-of-the-art methods developed by Bourque et al.¹⁸ and Hünemohr et al.¹⁹

2.E.5. Parameter selection

Since the proposed model in Eq. (8) is non-convex, different selections of the initial guess (ρ^0 in Algorithm 1) and sparsity level s could lead to different solutions due to the existence of local minimizers. To investigate the effect of parameter selection and determine appropriate parameter values, we repeated simulation and experimental studies with different parameter values.

3. RESULTS

3.A. Scanner calibration

The relative differences between calculated and measured CT numbers e_f for all the tissues with different energy channels were less than 3%, as shown in Table II. Note that for

six materials that were used for the calibration of the CT number model, the reported values were indeed the residual error when solving the linear system $F_{cal} = UK_{cal}$. For the remaining six materials, the values represented the accuracy of the forward CT number model.

3.B. Impact of sparse dictionary-based prior knowledge

We have considered two different setups in solving the non-dictionary model in Eq. (21). In the first situation, the rED ρ was fixed to be the ground truth. Due to the ill-posed problem, we were not able to obtain accurate ECs and both errors were $\sim 10\%$. When it came to a more challenging situation with ρ to be determined, the errors were further amplified, that is, more than 15% in e_{EC} and 20% in e_{rED} . This study demonstrated the necessity of including a dictionary in the decomposition problem.

Regarding the comprehensiveness of the dictionary, the top subfigure of Fig. 1 shows e_{EC} as a function of the dictionary size. It was found that, as the number of materials in the dictionary was increased, the errors generally decreased initially and then saturated to a constant level at ~ 400 materials. Therefore, we used the dictionary size of 400 in the rest of this study.

Finally, for the test on sparsity level, the bottom subfigure of Fig. 1 depicts results when solving the model in Eq. (22) with different levels of sparsity. Starting from $s = 1$, with the increasing sparsity levels, the errors decreased at first until an optimal level around $s = 20$. After that, the errors started to increase with s and then saturate to a constant level. The degraded quality of solution with s after $s > 20$ can be ascribed to overfitting. With a large s value, there are a large number of degrees of freedom to fit the targeted elemental composition

using dictionary materials. While the residual fitting error can be reduced, the solution may not be deviated from the exact one, which could yield a relatively large error in EC. On the basis of this observation, in the rest of this paper, we used this sparsity level of $s = 20$, unless stated otherwise.

3.C. Simulation study

Table III presents different quantities of interest for tissues in the lung, soft tissue, and bone groups. It was observed that the maximum RMS error of the estimated SPR was 0.27%, 0.21%, and 0.13% for DECT, MECT (3 energy levels) and MECT (4 energy levels), and the average error was 0.22%, 0.16%, and 0.12% for the three groups, respectively.

3.D. Experimental studies

We report errors in the experimental study in Table IV. Except for liver (LV1) in DECT case and brain (SR2) in MECT with three energy channels, the resulting relative errors for SPR and rED were all less than 1%. In Table V, we summarized errors for the three tissue groups. Averaging over all materials, the RMS errors in rED for DECT, MECT (three energy levels) and MECT (four energy levels) were 0.61%, 0.47%, and 0.32%, respectively. The RMS errors in SPR were 0.70%, 0.53%, and 0.45% compared with 0.83% achieved by Hünemohr's method¹⁹ using DECT and 0.76%

TABLE II. Relative difference between calculated and measured CT numbers.

	Relative difference e_f (%)			
	80 kVp	100 kVp	120 kVp	140 kVp
Calibration materials				
LN-450	2.57	1.81	1.49	0.81
Adipose (AP6)	0.83	0.53	0.36	0.20
Solid water	0.27	0.20	0.24	0.16
Brain (SR2)	1.04	0.99	0.94	0.91
B-200	1.69	1.36	1.27	1.18
CB2-50%	0.89	0.67	0.60	0.48
Average	1.22	0.93	0.82	0.62
Testing materials				
Breast	1.33	1.76	1.09	1.07
Water	0.76	0.47	0.32	0.01
Liver (LV1)	0.63	0.67	0.68	0.61
Inner bone	0.95	0.71	0.66	0.58
CB2-30%	1.86	1.68	1.31	1.10
Cortical bone	1.80	1.55	1.37	1.25
Average	1.22	1.14	0.91	0.77

FIG. 1. Top: e_{EC} as a function of number of materials in the dictionary at a fixed sparsity level of $s = 20$. Bottom: e_{EC} as a function of sparsity level s for a fixed dictionary size of 400 tissues. [Color figure can be viewed at wileyonlinelibrary.com]

TABLE III. Accuracy of EC, rED, and SPR for different tissue types in simulation study.

	e_{EC} (%)	e_{rED} (%)	e_{SPR} (%)
Lung tissues			
DECT (2 energy channels)	3.20	0.10	0.24
MECT (3 energy channels)	2.53	0.08	0.13
MECT (4 energy channels)	2.47	0.02	0.10
Soft tissues			
DECT (2 energy channels)	1.59	0.13	0.17
MECT (3 energy channels)	1.61	0.14	0.17
MECT (4 energy channels)	1.29	0.06	0.13
Bone tissues			
DECT (2 energy channels)	0.63	0.08	0.27
MECT (3 energy channels)	0.67	0.05	0.21
MECT (4 energy channels)	0.55	0.02	0.12
Average over all tissues			
DECT (2 energy channels)	1.86	0.11	0.22
MECT (3 energy channels)	1.65	0.09	0.16
MECT (4 energy channels)	1.48	0.04	0.12

by Bourque's method.¹⁸ In addition, it also implied that the overall SPR estimation accuracy could be improved by utilizing more energy levels in our method.

3.E. Parameter selection

3.E.1. Impact of sparsity level

The effect of sparsity levels was studied in the simulation case and the results are shown in the left column of Fig. 2. $s = 20$ was found to be a good choice for all the three tissue types, as the error achieved a minimal level at this choice. The same study was performed for the experimental study with results shown in the right column of Fig. 2. Although the advantages of $s = 20$ was not as obvious as in the simulation studies, especially for the lung tissue group, this

parameter value still seemed to be reasonable. Hence in all the studies in Sections 3.C and 3.D, the parameter value $s = 20$ was used.

3.E.2. Impact of initial value

The impacts of initial value ρ^0 are presented in the two columns of Fig. 3. Overall speaking, bone tissues and soft tissues are robust to different initial selections compared to the lung tissues. Hence, we used $\rho^0 = 1.0$ for them in this paper. For lung tissues, it seemed that the estimation accuracy is higher with $\rho^0 < 1.0$, especially in the experimental studies. This is reasonable since the ground truth rEDs for lung tissues should always be smaller than 1.0. Therefore, we used $\rho^0 = 0.1$ as initial guess for lung tissues.

4. DISCUSSION AND CONCLUSIONS

In this paper, we proposed a novel approach to estimate rED and EC for human tissue using DECT and MECT images aiming at accurate calculation of SPR for proton therapy treatment planning. A sparsity dictionary-based method was proposed. It formulated the decomposition problem as a non-convex optimization problem, which was solved by an iterative algorithm. The simulation study was performed to demonstrate the effectiveness of the proposed algorithm in an ideal setup that neglected uncertainty in calibration and forward CT model. Success in such an ideal simulation context motivated us to move on to experimental studies, in which an end-to-end test of the proposed method was carried out. The results showed the advantage of the proposed method in SPR estimation compared to the state-of-art methods. Impacts of parameters in the model were also investigated and appropriate parameter values were determined.

Inside the algorithm, there are two parameters β_1 and β_2 . Because of the non-convex nature of our algorithm, their values can also impact the resulting accuracy. In a real clinical application, it is clearly impractical to tune these two

TABLE IV. Accuracy of EC, rED, and SPR for different tissue types in experimental study.

Materials		DECT			MECT (3 energy channels)			MECT (4 energy channels)		
		e_{EC} (%)	e_{rED} (%)	e_{SPR} (%)	e_{EC} (%)	e_{rED} (%)	e_{SPR} (%)	e_{EC} (%)	e_{rED} (%)	e_{SPR} (%)
Calibration materials	LN-450	5.07	0.55	0.68	6.31	0.38	0.33	4.87	0.20	0.30
	Adipose (AP6)	3.24	0.37	0.26	3.55	0.22	0.28	3.23	0.15	0.45
	Solid water	3.83	0.71	0.77	4.09	0.28	0.39	4.17	0.11	0.50
	Brain (SR2)	4.09	0.87	0.85	3.48	0.91	1.08	3.29	0.78	0.83
	B-200	3.92	0.43	0.52	2.56	0.62	0.51	2.39	0.32	0.05
	CB2-50%	6.74	0.65	0.97	4.66	0.38	0.69	4.87	0.56	0.85
Testing materials	Breast	3.51	0.17	0.21	2.83	0.10	0.32	3.06	0.32	0.73
	Water	4.23	1.05	0.99	3.52	0.59	0.70	3.20	0.05	0.25
	Liver (LV1)	4.47	1.30	1.25	3.06	0.92	0.98	2.46	0.45	0.24
	Inner bone	2.20	0.30	0.07	2.17	0.35	0.10	2.28	0.22	0.18
	CB2-30%	3.26	0.13	0.37	3.13	0.02	0.23	2.95	0.20	0.36
	Cortical bone	6.48	0.44	0.73	4.89	0.58	0.86	4.62	0.33	0.60

TABLE V. Accuracy of EC, rED, and SPR for different tissue types in experimental study, and accuracy SPR from two other relevant studies.

System		e_{EC} (%)	e_{rED} (%)	e_{SPR} (%)	e_{SPR} (%) Hünemohr's method	e_{SPR} (%) Bourque's method
Lung Tissues	DECT (2 energy channels)	5.07	0.55	0.68	1.44	1.14
	MECT(3 energy channels)	6.31	0.38	0.33	—	—
	MECT(4 energy channels)	4.87	0.20	0.30	—	—
Soft Tissues	DECT (2 energy channels)	3.89	0.84	0.80	0.84	0.52
	MECT(3 energy channels)	3.42	0.60	0.70	—	—
	MECT(4 energy channels)	3.24	0.40	0.55	—	—
Bone Tissues	DECT (2 energy channels)	4.52	0.43	0.61	0.70	0.96
	MECT(3 energy channels)	3.48	0.44	0.55	—	—
	MECT(4 energy channels)	3.42	0.35	0.50	—	—
Average over all tissues	DECT (2 energy channels)	4.49	0.61	0.70	0.83	0.76
	MECT(3 energy channels)	4.40	0.47	0.53	—	—
	MECT(4 energy channels)	3.84	0.32	0.45	—	—

FIG. 2. Effect of sparsity levels in SPR estimation in simulation study (left) and experimental study (right). Three rows are for different tissue groups. [Color figure can be viewed at wileyonlinelibrary.com]

FIG. 3. Effect of initial value in SPR estimation in simulation study (left) and experimental study (right). Three rows are for different tissue groups. [Color figure can be viewed at wileyonlinelibrary.com]

parameters for each tissue. Hence, it is an important task to decide robustness of the algorithm with respect to these parameters and establish appropriate values of them. In our study, we have finely tuned parameters β_1, β_2 in the algorithm for each group of tissues to yield the best accuracy. It was found that the proper parameter values depend on tissue group, but not on each specific tissue within a group. From application point of view, using tissue-group specific parameter values is expected to be practical. The studies presented in Sections 3.C and 3.D were all performed using the established parameters. Meanwhile, the optimal parameter values may depend on other factors that have not been explored in this study, such as patient geometry or imaging uncertainties due to image artifacts. This will be an important aspect to be explored in the future.

Our method is naturally applicable to DECT and MECT with different numbers of energy channel. This provided us a common ground to evaluate the benefit of incorporating more energy channels for SPR estimation. Based on our study, the benefit of MECT over DECT has been observed in both simulation and experimental studies. The RMS error in SPR estimation for all the testing materials in simulation study has been reduced from 0.22% in DECT to 0.16% in MECT with 3 energy channels, and further to 0.12% in MECT with 4 energy channels. These reductions of error were small, as the simulation study was conducted in a relatively simple setting and SPR calculation was accurate even with DECT. In experimental study, which was more clinically relevant, the RMS errors of SPR were 0.70% in DECT, 0.53% in MECT with three energy channels, and 0.45% in

MECT with four channels, respectively. In particle therapy, SPR uncertainty is a major factor affecting range uncertainty. Going from single energy CT to DECT reduces SPR uncertainty substantially. However, as expected, the gain with each additional energy channel becomes diminishing. In a clinical setting, the overall range uncertainty is determined by the combined effects of many factors including SPR uncertainty.⁴ Although it may be possible to use more energy channels to continuously reduce SPR uncertainty, this may not be always needed, as the overall range uncertainty would be limited by other factors. The current paper focused on the development of a novel sparse dictionary-based method that is suitable for different number of energy channels, which allowed the evaluation of using different energy channels for SPR calculation on a common ground. The exact number of channels to be used in clinic for SPR calculation is under active exploration by many groups^{32,40,41} and is beyond the scope of this current study.

Computational efficiency is one important aspect of the algorithm, which determines its clinical practicality. In this study, our algorithm was implemented in MATLAB (R2015b) using a desktop computer equipped with 3.50 GHz Intel (R) CPU E5-1620 v3. Computational time to solve the algorithm ranged in 3.7–8.0 s. For a clinical application, the algorithm needs to be solved for each voxel. The large number of voxels in a real patient case would make the total computation time unaffordable. However, we expect that the computational speed can be substantially improved by coding the algorithm in C++. In addition, because of the computations at different voxels are independent, it is straightforward to conduct parallel processing at voxel level using advanced hardware platform, for example, GPU,⁴² which can further reduce the computation time.

CT numbers can be affected by different types of imaging artifacts such as beam hardening effect and partial volume effect. Hence, the accuracy of a model that derives SPR from CT numbers is also subject to the accuracy of input CT numbers. In this paper, the experimental study was indeed an end-to-end test on the overall accuracy of SPR calculation. In addition, real human tissue composition can be different from normal tissue compositions, for example, those listed in Schneider et al.²⁵ This could lead to uncertainty in SPR calculation, even when an algorithm is well tested in phantom studies.¹² In our method, by enlarging the number of tissues in the dictionary, it is expected that the impact of variation in human tissue composition has been investigated to a certain extent. This was demonstrated in the simulation studies. Although testing tissues were set to have compositions different from nominal compositions, resulting SPR calculation still achieved error of lower than 0.27%. Yet, it is difficult to test this fact in real experiments, which requires phantoms of different compositions.

Some EC decomposition based SPR estimation methods have been proposed recently in literature. For instance, average errors of 0.21% ($Z_{\text{eff}} < 8.2$) and 0.06% ($Z_{\text{eff}} \geq 8.2$) in SPR for DECT were reported in Hünemohr et al.²⁴ In Lalonde and Bouchard,²⁶ SPR estimation error was $\sim 0.11\%$

for soft tissues and $\sim 0.07\%$ for bone tissues. While these results were slightly better than ours (Table III), the studies were conducted using theoretically calculated CT numbers. Performance in realistic settings requires further investigations, as uncertainties in CT numbers due to scanner calibration may affect result accuracy.

Compared to the study of Lalonde et al.^{26,32} which incorporated principal component analysis to represent ECs, the proposed method uses a dictionary constructed by ECs of known materials. Lalonde and Bouchard 2016²⁶ achieved SPR estimation error as low as $\sim 0.11\%$ for soft tissues and $\sim 0.07\%$ for bone tissues using two energy levels in a simulation study. This seems better than our method in simulation study (see Table III.) However, the improved accuracy may be ascribed to the different forward models of CT number in Lalonde et al. and in ours. To study this fact, we have implemented a sparse dictionary-based model but with the forward CT model in Lalonde et al. This approach was able to achieve SPR estimation error of $\sim 0.07\%$ for both soft and bone tissues for DECT, comparable to those reported in Lalonde et al. Yet, for a real problem, the validity of the forward CT number model has to be validated. Residual error in forward CT number model will inevitably cause decomposition error after solving the optimization problem. We fitted the forward CT model in Lalonde et al. using our experimental data and found that the average residual error is $\sim 1.5\%$, slightly higher than that of our model (Table II). This residual error may affect the performance of their decomposition model in real data.

There are several limitations in our study. First, since there is only one lung tissue available in the original database, we synthesized 50 materials based on it to balance the numbers of materials of different types in the dictionary. However, such a strategy is not ideal, since with a large chance, these synthesized materials fail to represent compositions of real human lung tissues due to their strong correlations with each other. In the future study, we will try to find more compositions of real lung tissues and use them as basis to construct the dictionary.

Addition to that, the calibration and validation were performed on the same physical phantom. The calibration step was performed on a subset of inserts and validations were performed on different inserts. It would be necessary to validate the method using different phantoms considering that model accuracy may be affected by many factors such as phantom size and location. However, since we do not have a second phantom that has the ground truth EC and rED information, we had to limit our study in the current form. It is our ongoing work to perform more detailed and comprehensive validations.

Another limitation of this study is that DECT and MECT images in our experiments were simply acquired by scanning the phantom multiple times with different kVp levels, but not using an actual DE or MECT scanner. This choice was made, because we do not have access to a DECT or MECT scanner, and hence the study is only for illustrating principle. At the

moment, DECT scans can be acquired in different approaches using scanners from different vendors, such as rapid kVp switching, dual-source scan, and energy discriminating detection techniques. When comparing DECT realized using multiple scans with that performed on a real scanner, there are two factors to consider. In terms of motion, the actual DECT scan would reduce geometry inconsistency between different scans, which is beneficial to subsequent decomposition calculations. In terms of performance of our method in DECT realized with different scanning approaches, we expect that the performance would be similar in DECT with the kVp switching and dual-source setups, as the underlying forward image models in these two setups are similar to that in a multiple scan-based method. However, the forward imaging model of DECT achieved by a dual-layer detector is different. The validity of our method in this setup would be an interesting study in future. As for MECT, it is still under active research nowadays and the state-of-the-art scanner employs photon-counting detection technique. In this scenario, it probably requires tuning the forward CT number model in Eq. (1), for instance the powers of different terms, to better model different physics contributions. After that, we expect the decomposition model will be still valid.

Another important issue is the impact of noise. This is particularly important since current DE and MECT imaging technique usually end up with higher noise level compared to conventional SECT. This problem may be alleviated by advanced image processing methods that can achieve effective noise reduction for DE and MECT.^{43,44} Other than that, it is also possible to directly tackle the whole problem starting from reconstruction, that is, formulate a simultaneous reconstruction-decomposition model for MECT following the framework given in Ref. [45]. More specifically, the reconstruction-decomposition model integrates two components in a single optimization model. The first part is a tight-frame based iterative reconstruction model which would effectively reduce the noise level by utilizing spatial information in image domain; the second part is the sparse dictionary-based decomposition model which estimates rED and EC from CT numbers at different energy channels as introduced in this paper. This approach effectively incorporate regularizations along spatial and energy dimension, yielding accurate reconstruction results.⁴⁵

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