Multi-grid finite element method used for enhancing the reconstruction accuracy in Cerenkov Luminescence Tomography

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ABSTRACT

Cerenkov luminescence tomography (CLT), as a promising optical molecular imaging modality, can be applied to cancer diagnostic and therapeutic. Most researches about CLT reconstruction are based on the finite element method (FEM) framework. However, the quality of FEM mesh grid is still a vital factor to restrict the accuracy of the CLT reconstruction result. In this paper, we proposed a multi-grid finite element method framework, which was able to improve the accuracy of reconstruction. Meanwhile, the multilevel scheme adaptive algebraic reconstruction technique (MLS-AART) based on a modified iterative algorithm was applied to improve the reconstruction accuracy. In numerical simulation experiments, the feasibility of our proposed method were evaluated. Results showed that the multi-grid strategy could obtain 3D spatial information of Cerenkov source more accurately compared with the traditional single-grid FEM.

Keywords: Cerenkov luminescence tomography (CLT), finite element method, multi-grid strategy, multilevel scheme adaptive algebraic reconstruction technique (MLS-AART).

1. INTRODUCTION

Cerenkov luminescence imaging (CLI) as a sensitive and noninvasive imaging technique, has yielded a wide range of applications in both preclinical and clinical research in recent years.\textsuperscript{1,2} Cerenkov luminescence (CL) which emitted by charged particle can potentially be used for cancer diagnostic and therapeutic.\textsuperscript{3} Because many radionuclides (e.g. \textsuperscript{131}I, \textsuperscript{18}F) have approved by the FDA for clinical, CLI can overcome the limitation that few available imaging agents can be applied to preclinical.\textsuperscript{4,5} However, CLI is a straightforward planar imaging method lacks of 3D structural and depth information.\textsuperscript{6} Thus, three-dimensional imaging optical technique-Cerenkov luminescence tomography (CLT) can provides more precise spatial distribution and information about the radionuclides and diseases in preclinical and clinical research.\textsuperscript{7}

Building a system matrix and solving the inverse ill-posedness problem as two of important problems have been most extensively studied in CLT.\textsuperscript{8} Firstly, the system matrix is a mathematical description of the cerenkov light transport in biological tissue. Presently, most light propagation models are derived from radiative transfer equation (RTE) and based on the finite element method (FEM) framework.\textsuperscript{9} The most attractive feature of FEM is its ability to handle complicated geometries with relative convenience.\textsuperscript{10} However, the quality of FEM mesh grid is still a vital factor to restrict the accuracy of the light propagation model.\textsuperscript{11} Secondly, because of the strong scattering property of biological tissues and the limited boundary measurements with noise, the inverse cerenkov source reconstruction is severely ill-posed.\textsuperscript{12} In pervious study, the \textit{hp}-finite element method (\textit{hp}-FEM) and permissible source region method-based algorithm were utilized to reduce the ill-posedness of inverse source reconstruction.\textsuperscript{9} Zhong et al. incorporated the CT anatomic structural information of imaged animals into the CLT inverse problem to improve the quality of source reconstruction, coupling with a multi-modal \textit{in vivo} imaging system.\textsuperscript{13} Besides that, single photon emission computed tomography (SPECT) validation strategy and an adaptive \textit{hp}-finite element method (\textit{hp}-FEM) were utilized to accurately locate the Na\textsuperscript{131}I radioactive source.\textsuperscript{9} However these research were all based on single-grid FEM. To some degree, multi-grid FEM can reduce...
the mesh discretization error and improve the stability of the CLT reconstruction results. Thus, multi-grid FEM framework can provide an effective approach to improve the accuracy of CLT.\textsuperscript{14}

In this paper, we proposed a multi-grid FEM framework to enhance the reconstruction quality of CLT. Combined with the multilevel scheme adaptive algebraic reconstruction technique (MLS-AART), multi-grid strategy can obtain more abundant structural information and improve the accuracy of reconstruction essentially. In numerical simulation experiments, the feasibility and effectively of our proposed method were evaluated. Results showed that the multi-grid strategy can obtain much more 3D spatial information and accurate Cerenkov source distribution compared with the traditional FEM based on single-grid.

2. METHOD

2.1 Cerenkov radiation and Diffusion approximation

When a charged particle ($\alpha, \beta$) travels through a dielectric medium with the speed exceeds the velocity of light, Cerenkov light was emitted and penetrate into biological tissue. In biophotonics, there are several popular mathematics models to describe the photon propagation process, including: the radiative transfer equation (RTE), the simplified spherical harmonics ($\text{SP}_N$) approximation and a low-order approximation named diffusion equation (DE). Considering the Cerenkov light with low-absorbing and high-diffusive optical tissue properties at near-infrared wavelengths, we adopted the DE to describe Cerenkov light transport in scattering media.

For 3D optical tomography, the DE and the Robin-type boundary condition at a specific wavelength $\lambda$ can be expressed:\textsuperscript{15} \begin{equation}
\begin{cases}
-\nabla \cdot (D(r, \lambda)) + \mu_a(r, \lambda) \Phi(r, \lambda) = q(r, \lambda), (r \in \Omega) \\
\Phi(r, \lambda) + 2\kappa(r, \lambda) D(r, \lambda)(\nu(r, \lambda) \cdot D(r, \lambda)) = 0, (r \in \partial \Omega)
\end{cases}
\end{equation}
Where $\Phi(r, \lambda)$ is the photon flux at position $r \in \Omega$, wavelength $\lambda$. $q(r, \lambda)$ provides the isotropic source energy distribution of the internal Cerenkov source, $D(r, \lambda) = 1/3(\mu_a(r, \lambda) + (1 - g)\mu_s(r, \lambda))$ is the optical diffusion coefficient with $\mu_a(r, \lambda)$ being the optical absorption coefficient, $\mu_s(r, \lambda)$ is the scattering coefficient, and $g$ is the anisotropy coefficient. $\kappa(r, \lambda)$ is the boundary mismatch factor accounting for different refractive indices across the boundary $\partial \Omega$, $\nu(r)$ denotes the unit outer normal. A linear relationship between the Cerenkov source inside the biological medium and the surface photon fluence can be established by the finite element method:

$$[K + C + B]\Phi = M\Phi = X$$ \hfill (2)

If $\psi$ denotes the basic function, every elements of $K$, $C$, $B$, $X$ can be expressed as:

$$\begin{cases}
K_{i,j} = \int_{\Omega} D(r)(\nabla \psi_i(r)) \cdot (\nabla \psi_j(r))dr \\
C_{i,j} = \int_{\Omega} \mu_a(r)(\nabla \psi_i(r)) \cdot (\nabla \psi_j(r))dr \\
B_{i,j} = \int_{\partial \Omega} \nu(r) \cdot (\nabla \psi_i(r))dr \\
X_i = \int_{\Omega} q_i(r) \psi_i(r)dr
\end{cases}$$ \hfill (3)

In Eq.(2) $M$ denotes the positive definite matrix. $\Phi$ is the measured light flux at the boundary. $X$ is the Cerenkov source distribution. If removing the nonmeasurable entries in $\Phi$ and corresponding row in $M^{-1}$, a new linear relationship can be established:

$$AX = \Phi^m$$ \hfill (4)

where $A \in R^{m \times n}$ and $\Phi^m$ is the boundary measurement. $m$ and $n$ are correspond to the node number of whole organism and the surface detector.

2.2 Multi-grid FEM

Multi-grid FEM requires several separate meshes to merge into a uniform mesh grid. As a example, a square geometry was divided into separate FEM meshes mesh 1, mesh 2 as Fig 1(a) and (b) shown. It’s a difficult issue to new-built some additional cross nodes and tetrahedrons based on the new spatial relationship. In order to generate a multi-grid system as (c) shown and build the corresponding matrix, the mesh nodes, elements of tetrahedron, and the surface triangles need to be extracted and reordered base on the spatial distribution. And the system matrix of the multi-grid FEM was generated by building the spatial mapping relationships based
Figure 1. The basic ideal of mutil-grid FEM. (a) the coarse mesh; (b) the fine mesh; (c) the mutil-grid mesh.

on two grid distribution. For mesh 1, the mass matrix of \( M_1 \) has dimensions of \( n_1 \times n_1 \), whereas the mass matrix of \( M_2 \) is \( n_2 \times n_2 \) for mesh 2 according to Eq. (2). \( n_1 \) and \( n_2 \) are correspond to the node number of two meshes. Firstly, these two mass matrices were combined into one block diagonally matrix \( M_{all} \) with dimensions of \( (n_1 + n_2) \times (n_1 + n_2) \) to allow the solution of multi-grid FEM, as shown in:

\[
M_{all} = \begin{bmatrix}
M_1 & M_{1,2} \\
M_{2,1} & M_2
\end{bmatrix}
\]  

(5)

Secondly, the relationship and interaction effect between the mesh 1 and mesh 2 were taken into consideration. And two correlation matrix \( M_{1,2} \) and \( M_{2,1} \) were introduced to built the system matrix \( M_{all} \) based on multi-grid FEM, as shown in:

\[
M_{all} = \begin{bmatrix}
M_1 & M_{1,2} \\
M_{2,1} & M_2
\end{bmatrix}
\]  

(6)

where \( M_{1,2} \) has dimensions of \( n_1 \times n_2 \), whereas the mass matrix of \( M_{2,1} \) is \( n_2 \times n_1 \). In Eq.(6), \( M_1 \) and \( M_2 \) can be calculated by Eq.(2 and 3). Referring to Eq.(3), subscript \( i, j \) correspond to the number index of mesh node with a specific coordinates. In single-grid FEM, \( i \) and \( j \) fell into the same mesh system. However, to multi-grid FEM, \( i \) and \( j \) were no longer belong to the same mesh system. So we can’t calculate \( M_{1,2} \) and \( M_{2,1} \) directly by tradition FEM framework. Let \( i \) belongs to mesh 1, meanwhile \( j \) is the node of mesh 2 and the node number \( n_1 < n_2 \). To node \( i \), we can find the corresponding nearest node \( index_i \) in mesh 2. More important, the value of the element \( M_{i,j} \) can be approximated as \( M_{i,\text{index}_i,j} \). i.e. \( M_{i,j} \approx M_{i,\text{index}_i,j} \). Because \( \text{index}_i \) and \( j \) were all belong the mesh 2. \( M_{i,\text{index}_i,j} \) can be calculated by the tradition FEM framework based on mesh 2. Obviously \( M_{1,2} \) and \( M_{2,1} \) can regard as a series of column vectors \([C_1,...,C_i,...,C_{n_1}]\) and a series of row vectors \([R_1,...,R_i,...,R_{n_2}]^T\). Meanwhile, the column vectors \( C_i \) and row vectors \( R_i \) can be approximated as \( M_2(\text{index}_i) \) and \( M_2(\text{index}_i,\cdot) \), respectively.

Different from single-grid FEM, we can get multi-group surface photon fluence, and \( \Phi_{all} = [\Phi_1, \Phi_2]^T \). So a linear relationship between the Cerenkov source inside the biological medium and the multi-group surface photon fluence can be established:

\[
M_{all} \Phi_{all} = X
\]  

(7)

where \( X \in R^{(n_1+n_2)} \) denotes the multi-gride Cerenkov source distribution. Corresponding to single-grid FEM, if removing the nonmeasurable entries and corresponding row in \( M_{all}^{-1} \), a new linear relationship can be established:

\[
G X = \Psi
\]  

(8)

2.3 Inverse reconstruction

As mentioned in introduction part, the inverse problem of CLT is an ill-posed problem and can be regard as a minimization problem. In this study, the multilevel scheme adaptive algebraic reconstruction technique (MLS-AART) was utilized to solve the iterative minimization problem and get the solution \( X \). In the \( j \)-th iteration
of MLS-AART, the solution is updated as follows:

\[
\begin{align*}
X^j &= \min \|X^j - X^{j-1}\|_{X^{-1}} \text{ subject to } G_i \cdot X^j = \Psi_i \\
\|S^2\|_{X^{-1}} &= X^T \cdot \text{diag}(1/S) \cdot X
\end{align*}
\]

where \(i\) is the \(i\)-th element of \(\Psi\). We can use Lagrange multipliers yields to solve \(X^j\) as:

\[
\begin{align*}
X^{(j)} &= X^{(j-1)} - \xi_{i,j} \cdot (G_i \cdot X^{(j-1)} - \Psi_i) \\
\xi_{i,j} &= (S^{(j-1)} \cdot G_i) / (G_i \cdot S^{(j-1)} \cdot G_i^* ) \\
S^{(j-1)} &= \text{diag}(X_1, X_2, ..., X_n)
\end{align*}
\]

3. EXPERIMENT AND RESULT

In order to testify the performance of our proposed method, a group of numerical simulations were conducted. The commonly used digital mouse model was employed, and only the torso section of the mouse with a height of 35 mm was selected as the region to be investigated. Including muscle, heart, liver, lungs, stomach, and kidney, six organs were segmented and shown in Fig. 2(a). At the wavelength of 650 nm, the absorption coefficient \(\mu_a\), the scattering coefficient \(\mu_s\), and the anisotropy coefficient \(g\) of these organs were also listed in Table 1. A spherical Cerenkov source with a 1 mm radius was placed in the liver with center at (18 mm, 7.5 mm, 15.5 mm), and the intensity of the source was set to be 10 nanowatt. Two meshes with different size were generated: mesh1 including 7802 nodes and 39,396 elements; mesh2 including 9004 nodes and 47,219 elements. Fig. 2(b) shows the surface light flux calculated by Molecular Optical Simulation Environment (MOSE).

Table 1. Optical Parameters of the Mouse Organs for 650 nm.

<table>
<thead>
<tr>
<th>Tissue</th>
<th>(\mu_a (\text{mm}^{-1}))</th>
<th>(\mu_s (\text{mm}^{-1}))</th>
<th>(g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle</td>
<td>0.12</td>
<td>15.58</td>
<td>0.97</td>
</tr>
<tr>
<td>Heart</td>
<td>0.08</td>
<td>10.07</td>
<td>0.90</td>
</tr>
<tr>
<td>Lungs</td>
<td>0.26</td>
<td>31.56</td>
<td>0.93</td>
</tr>
<tr>
<td>Liver</td>
<td>0.47</td>
<td>10.00</td>
<td>0.93</td>
</tr>
<tr>
<td>Kidneys</td>
<td>0.09</td>
<td>23.59</td>
<td>0.90</td>
</tr>
<tr>
<td>Stomach</td>
<td>0.10</td>
<td>17.00</td>
<td>0.90</td>
</tr>
</tbody>
</table>

Figure 2. The results of the forward simulation: (a) The digital mouse used to simulate the forward model. (b) The surface Cerenkov luminescence fluxes simulated by MOSE.

For better evaluate the proposed method, the tradition single-grid FEM was compared and some quantitative indexes were utilized to evaluate the performance. The reconstructed results were shown in Fig. 3. Where (a) and (d) were the results based on mesh1; (b) and (e) were the reconstructed results based on mesh2; (c) and (f) were the reconstructed result based on our multi-grid FEM method. (a)-(c) were the isosurface view of the reconstructed results, where the red spherical and the black mesh area denoted the real Cerenkov source and reconstructed source area with node values greater than 10% of the maximum value, respectively. (d)-(f) were...
the transverse views of the reconstruction at \( z = 15.5 \text{mm} \) plane, where the black circle presented the actual source. The reconstructed source center, reconstructed intensity, location error (LE), and relative intensity error (RIE) were presented in Table 2. LE was the Euclidean distance between the centers of the reconstructed and the actual source. RIE presented the relative intensity deviation between the reconstructed Cerenkov source intensity \( I \) and the real source intensity \( I_0 \): \( \text{RIE} = \frac{\|I-I_0\|}{I_0} \times 100\% \); It’s obviously that the location error of the multi-grid FEM was 0.59mm, meanwhile the relative intensity error was 7\%, which was superior to the results of single-gride FEM based on mesh1 and mesh2.

Figure 3. The reconstruction results of the simulation experiment. (a)-(c) The isosurface view of the results; (d)-(f) The transverse view of the reconstruction at \( z = 16.5 \text{mm} \); (a) and (d) were the results based on the first group mesh; (b) and (e) were the reconstructed results based on the second mesh; (c) and (f) are the reconstructed result based on our multi-grid FEM method.)

<table>
<thead>
<tr>
<th>Mesh</th>
<th>Recon.Source Center (mm)</th>
<th>Recon.Source intensity (nw)</th>
<th>LE (mm)</th>
<th>RIE(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mesh1</td>
<td>(17.87, 8.06, 14.96)</td>
<td>1.33</td>
<td>1.04</td>
<td>33</td>
</tr>
<tr>
<td>Mesh2</td>
<td>(18.05, 7.82, 16.37)</td>
<td>1.11</td>
<td>0.97</td>
<td>11</td>
</tr>
<tr>
<td>mutilig-grid</td>
<td>(18.15, 8.06, 15.37)</td>
<td>1.07</td>
<td>0.59</td>
<td>7</td>
</tr>
</tbody>
</table>

4. DISCUSSION AND CONCLUSION

In this research, a multi-grid FEM framework was proposed to reduce the mesh discretization error and improve the quality of the CLT reconstruction. Compared with tradition single-grid FEM, this strategy could obtain more abundant structural information and improve the accuracy and stability of reconstruction. Beside that, the multilevel scheme adaptive algebraic reconstruction technique (MLS-AART) was also utilized to improve the accuracy of the inverse solution. According to the properties of the data and constraints of Cerenkov imaging, MLS-AART could get unbiased stable solutions with high location accuracy and fast convergence speed. The numerical simulation results showed that the multi-grid FEM could obtain 3D spatial distribution information of the placed Cerenkov source more accurately.
5. ACKNOWLEDGMENTS
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