Three Dimensional Diffuse Optical Spectroscopic Imaging (DOSI) of Breast Tumor in Reflectance Geometry

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Outlines

• Motivation
• Background information
• Simulation results
• Summary
• Future work
Magnetic Resonance Spectroscopic Imaging of Prostate Diffuse Optical Spectroscopic Imaging of Breast

Importance of Optical Spectrum

Cancer

\[
[\text{HHb}] + [\text{O}_2\text{Hb}] > [\text{HHb}] + [\text{O}_2\text{Hb}]
\]

\[
[\text{H}_2\text{O}] > [\text{H}_2\text{O}]
\]

\[
[\text{Lipid}] < [\text{Lipid}]
\]

\[
[\text{O}_2\text{Hb}]/([\text{HHb}] + [\text{O}_2\text{Hb}]) < [\text{O}_2\text{Hb}]/([\text{HHb}] + [\text{O}_2\text{Hb}])
\]

Diffuse Optical Spectroscopy (DOS)
Diffuse Optical Imaging (DOI)

Diffuse Optical Spectroscopy
- Spectrally rich
- Spatially limited

More field of views

Parametric image reconstruction

Diffuse Optical Imaging
- Spatially rich
- Spectrally limited

Physiological constraints

Three dimensional spatially localized diffuse optical spectroscopic imaging, using reflectance geometry
Frequency Domain Measurement

\[ \phi(\omega, \rho, \mu_a, \mu'_s) \]

\[ A(\omega, \rho, \mu_a, \mu'_s) \]

Mathematical Background

- Diffusion Equation & Boundary condition

\[
\begin{cases}
    i\omega \frac{\Phi(r, \omega)}{v} - \nabla \cdot \frac{1}{3\mu'_s(r)} \nabla \Phi(r, \omega) + \mu_a(r) \Phi(r, \omega) = q(r, \omega) \\
    \Phi(r, \omega) + 2\Lambda \cdot \frac{1}{3\mu'_s(r)} \frac{\partial \Phi(r, \omega)}{\partial n} = 0
\end{cases}
\]

Arridge SR Inverse Problem (1999)

- Physical Quantity
  - Energy density \( \Phi(r, \omega) \) or fluence rate \( \Phi(r, \omega) \)
  - Source term \( q(r, \omega) \)

- Physiological Quantities
  - Absorption coefficient \( \mu_a(r) \)
  - Reduced scattering coefficient \( \mu'_s(r) \)
Forward Problem

Given optical properties, find signals measured by detectors

• Signal detected

\[ y = \begin{bmatrix} \text{Re}(\log[\Phi(\mathbf{r}_{\text{detectors}}, \omega)]) \\ \text{Im}(\log[\Phi(\mathbf{r}_{\text{detectors}}, \omega)]) \end{bmatrix} \]

\[ y = (y_{11}, y_{12}, \ldots y_{ij}, \ldots y_{SD})^T \]

Yalavarthy Phd Thesis 2007

• Forward operator

\[ y = F[\mu_a(\mathbf{r}), \mu'_s(\mathbf{r})] \equiv F[\mathbf{x}] \]

• Methods to solve
  – Analytical solutions: only possible for simple geometries
  – Numerical solutions: FDM/BEM/FEM
Inverse Problem

Given noisy signals measured by detectors, find optical properties.

Initial parameters $x^{(0)}$

Set $k=0$

Calculate forward solutions $F_x^{(k)}$

Calculate objective functional $\Omega$

Convergence?

Calculate the update $\Delta x^{(k+1)}$

$x^{(k+1)} = x^{(k)} + \Delta x^{(k+1)}$

$k = k+1$

STOP

Least Square

Generalized Least Square

REGULARIZATION:

$x_0$ is an estimated parameters

$\Gamma_x$ is an estimated covariance matrix of parameters

Arridge SR et al. Inverse Problem 2005

$$\Delta x^{(k+1)} = \left( J^T \Gamma_n^{-1} J + \Gamma_x^{-1} \right)^{-1} \times \left\{ J^T \Gamma_n^{-1} \left( y_{\text{measured}} - F[x^{(k)}] \right) - \Gamma_x^{-1} \left( x^{(k)} - x_0 \right) \right\}$$

Size is decided by columns of $J$

## Jacobian

The Jacobian matrix, denoted as $J$, is defined as the matrix of all first-order partial derivatives of a vector-valued function $F(x)$ with respect to the vector $x$.

$$
J = \begin{bmatrix}
\frac{\partial y_{11}}{\partial x_1} & \frac{\partial y_{11}}{\partial x_2} & \cdots & \frac{\partial y_{11}}{\partial x_N} \\
\frac{\partial y_{12}}{\partial x_1} & \frac{\partial y_{12}}{\partial x_2} & \cdots & \frac{\partial y_{12}}{\partial x_N} \\
\vdots & \vdots & \ddots & \vdots \\
\frac{\partial y_{1D}}{\partial x_1} & \frac{\partial y_{1D}}{\partial x_2} & \cdots & \frac{\partial y_{1D}}{\partial x_N} \\
\frac{\partial y_{21}}{\partial x_1} & \frac{\partial y_{21}}{\partial x_2} & \cdots & \frac{\partial y_{21}}{\partial x_N} \\
\frac{\partial y_{22}}{\partial x_1} & \frac{\partial y_{22}}{\partial x_2} & \cdots & \frac{\partial y_{22}}{\partial x_N} \\
\vdots & \vdots & \ddots & \vdots \\
\frac{\partial y_{2D}}{\partial x_1} & \frac{\partial y_{2D}}{\partial x_2} & \cdots & \frac{\partial y_{2D}}{\partial x_N} \\
\vdots & \vdots & \ddots & \vdots \\
\frac{\partial y_{S1}}{\partial x_1} & \frac{\partial y_{S1}}{\partial x_2} & \cdots & \frac{\partial y_{S1}}{\partial x_N} \\
\frac{\partial y_{SD}}{\partial x_1} & \frac{\partial y_{SD}}{\partial x_2} & \cdots & \frac{\partial y_{SD}}{\partial x_N}
\end{bmatrix}
$$

The Jacobian matrix can be partitioned into sections for each source and detector pair.

- **Source #1, different detectors**
- **Source #2, different detectors**
- **Source #S, different detectors**

The size of the Jacobian matrix is $(S \times D) \times N$ where:

- $S$: Number of sources
- $D$: Number of detectors
- $N$: Number of parameters

The Jacobian matrix $J$ is given by:

$$
J = \frac{\partial F[x]}{\partial x}
$$

For any specific row $i$, column $j$, and parameter $k$,

$$
J(i, j, k) = \frac{\partial y_{ij}}{\partial x_k}
$$

The row index $i$ corresponds to the source ID, the column index $j$ corresponds to the detector ID, and $k$ corresponds to the parameter ID.
\[ x = (\mu_a(r), \mu'_s(r)) = (\mu_{a1}, \mu_{a2}, \ldots, \mu_{aN}, \mu'_{s1}, \mu'_{s2}, \ldots, \mu'_{sN}) \]

\[ x = (\mu_a(r), \mu'_s(r)) = (x_1, x_2, x_3, \ldots) \]
Physiologically realistic model for tumor optical properties

Tumor Gridscan

Tumor Linescan

Measured

Carcinoma
US size: 15x12x11 mm³; Depth 11 mm

• High contrast between lesion and normal tissue regions (100% increase)
• FWHM of linescan is larger than the ultrasound dimension (FWHM 26 mm)
Physiologically realistic model for tumor optical properties

Tumor Simulation (FEM)

Tumor Linescan

Measured
Simulated (confined)

Confined ellipsoid
size: 15x12x11 mm; Depth 11 mm
Absorption Coefficient: 0.025 mm\(^{-1}\)*

* Wells WA etc. Anal Quant Cytol Histol 2004
Physiologically realistic model for tumor optical properties

Tissue Simulation (FEM)

Tumor Linescan
- Measured
- Simulated (confined)
- Simulated (distributed)

Optical absorption property can be modeled as a 3D Gaussian distribution

Li A. et al. JBO (2008)
Mathematical Formulation

• Forward Problem
  – Lesion Absorption Model:
    \[ \mu_a(r) = A \cdot \exp \left(-\frac{(x-x_0)^2}{\text{FWHM}_x^2} - \frac{(y-y_0)^2}{\text{FWHM}_y^2} - \frac{(z-z_0)^2}{\text{FWHM}_z^2}\right) + A_{\text{background}} \]
  – Parameters: \( x = (x_0, y_0, z_0, \text{FWHM}_x, \text{FWHM}_y, \text{FWHM}_z, A) \)
    \[ y = F[\mu_a(r), \mu'_s(r)] \equiv F[x] \]
  – Solution: FEM with linear basis functions

• Inverse Problem

\[ \Omega = (y_{\text{measured}} - F[x])^T \Gamma_n^{-1} (y_{\text{measured}} - F[x]) + (x - x_0)^T \Gamma_x^{-1} (x - x_0) \]
Preliminary Probe Design

Source-detector Set-up

Measurement Geometry
Reconstruction Based on Simulated Data

• Generation of simulated data
  – Data is generated by using a FEM model with cubic shape functions
  – Random noises are added to the simulated data

• Scenarios
  – Fixed noise level and Gaussian absorbing targets
  – Fixed noise level and non-Gaussian absorbing targets
Fixed noise level (1%) and Gaussian absorbing targets

(1) Peak optical absorption coefficient is 0.025/mm, 5x the background value
(2) In x-y plane, the center of the target is at (0, 5)mm

<table>
<thead>
<tr>
<th>Size (mm)</th>
<th>Depth (mm)</th>
<th>Reconstructed parameters</th>
<th>Relative RMS error</th>
</tr>
</thead>
<tbody>
<tr>
<td>(15 12 10)</td>
<td>-10</td>
<td>(x,y) mm: 0.297, 5.94</td>
<td>-10.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dep(mm): -10.3</td>
<td>Size (mm): 14.4, 14.8, 11.0</td>
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<tr>
<td></td>
<td>-18</td>
<td>(x,y) mm: -0.138, 6.45</td>
<td>-18.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dep(mm): -18.1</td>
<td>Size (mm): 15.4, 14.8, 11.6</td>
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<tr>
<td>(20 20 20)</td>
<td>-10</td>
<td>(x,y) mm: 0.242, 4.86</td>
<td>-11.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dep(mm): -11.1</td>
<td>Size (mm): 19.9, 20.6, 19.2</td>
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<td></td>
<td>-18</td>
<td>(x,y) mm: 0.116, 5.44</td>
<td>-16.7</td>
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<td></td>
<td></td>
<td>Dep(mm): -16.7</td>
<td>Size (mm): 19.9, 21.0, 17.1</td>
</tr>
</tbody>
</table>

Relative RMS error = \left( \frac{\text{mean} \left( \frac{\|x_{real} - x_{reconstructed}\|^2}{\|x_{real}\|^2} \right) }{\text{mean} \left( \frac{\|x_{real}\|^2}{\|x_{real}\|^2} \right) } \right)^{1/2}
Fixed noise level (1%) and non-Gaussian absorbing target

\[ \mu_a(r) = 0.015 \left[ \left( -\frac{(x)^2}{7.5^2} - \frac{(y-5)^2}{7.5^2} - \frac{(z+10)^2}{6.5^2} + \frac{x(y-5)}{10^2} + \frac{(y-5)(z+20)}{16^2} + \frac{x(z+20)}{12^2} \right) \leq 1 \right] + 0.005 \]

Volume Contrast: \( VC = \int \mu_a(r) \, dr \)

Irregular Object: 27 mm\(^2\)
Reconstructed Gaussian: 33 mm\(^2\)
Fixed noise level (1%) and non-Gaussian absorbing target

\[ \mu_a(\mathbf{r}) = 0.015 \cdot \left[ \left( \frac{(x)^2}{7.5^2} + \frac{(y-5)^2}{7.5^2} \right) \leq 1 \right] \cdot [-20 \leq z \leq -12] + 0.005 \]

Volume Contrast:

Cylindrical absorbing target: 22 mm²
Reconstructed Gaussian target: 18 mm²
Summary

• Diffuse optical spectroscopic imaging (DOSI) is a model-based technique
• DOSI is capable of non-invasive characterization of subsurface tissue structures and functions
• Optical absorption property of breast tumor can be modeled as a 3D Gaussian distribution
• The parametric DOSI is robust to both measurement noise and model-misspecification
Future work

• Other parameterization of tumor optical properties
• Reduced scattering coefficient distribution
• Spectral images with optical properties at multiple wavelengths
• Direct reconstruction on chromophore concentration and distribution
• Optimal probe design