Computational Model of OCT in Lung Tissue

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ABSTRACT
Lung research may have significant impact on human health. As two examples, recovery from collapse of the alveoli and the severe post surgery declines in forced vital capacity in patients under the effects of anesthesia are both poorly understood. Optical imaging is important to lung research for its inherently high resolution. Microscopy and color imaging are fundamentals of medicine, but interior lung tissue is usually viewed either endoscopically or ex vivo, stained slices. Techniques such as confocal microscopy and optical coherence tomography (OCT) have become increasingly popular in medical imaging because of their sectioning and depth penetration. Since OCT has the ability to achieve higher depth penetration than confocal it is more widely used in lung imaging, despite the difficulty of interpreting the images due to the poor numerical aperture (NA). To understand light propagation through the highly reflective and refractive surfaces of the lung, we developed a Finite-Difference Time Domain (FDTD) simulation. FDTD solves a discrete approximation to Maxwell’s equations. Initial simulations have shown that structure up to $30 - 40 \mu m$ below the surface is clearly visible. Deeper structures are hard to interpret, because of light scattering, compounded by speckle associated with coherent detection. Further simulations and experimental imaging may lead to improved collection and processing of images at deeper levels.

1. MOTIVATION
Little is known about the internal structure of the lung in vivo since the structure collapses under biopsy. Imaging techniques such as bronchoscopy are only able to image surfaces exposed to airways, leaving much of the deeper structure of the lung still unknown. Currently there are concurrent investigations looking at the surfactant covering the lung to determine its involvement with the compression and expansion of the lung while under normal conditions and more importantly with regards to pulmonary atelectasis. The biomedical community is interested in the mechanisms regarding atelectasis but have only had limited success with imaging sub-surface structure. Since the interior surfaces make up the majority of the lung, bioengineers need images at deeper levels than what is currently available in order to understand the behavior of the mechanical structure of the lung.
2. RELEVANT IMAGING MODALITIES

Currently there are several microscopy modalities used to image animal tissue. Confocal reflectance microscopy (CRM) has become increasingly popular because it has the ability to section discrete planes of tissue in order to recreate the three-dimensional structure of the tissue. Since CRM has a high NA, it is able to achieve high depth resolution of approximately $2 - 4\mu m$ and a slightly higher lateral resolution of approximately $0.5 - 2\mu m$. A disadvantage to CRM is that it is only able to image to a limited depth of approximately $100\mu m$, in skin images.\(^2\) The lung provides much greater discontinuities of index-of-refraction at the many tissue-air boundaries which is closer to $0.33$, while skin contrast is an order of magnitude less. The limited depth can be attributed to the aberrations of the focused beam by the tissue’s heterogeneity over the large input beam. Since the structure of the human lung consists of alveoli each with a diameter of approximately $225\mu m^3$ and structure of several millimeters in depth, CRM cannot accurately image deep enough to gain useful information about the structure of the lung. Optical Coherence Tomography (OCT) is the preferred method for imaging at greater depths, which has been used for imaging to depths of up to $2mm$.\(^4\) OCT has a relatively low NA, and sectioning is obtained through temporal gating of the detected light. A disadvantage due to the low NA is that the lateral and depth resolution are severely limited to approximately $30\mu m$.\(^5\) Currently, OCT is only able to resolve masses of $500\mu m$ in the lung using available techniques.\(^5\) We need to be able to resolve individual alveoli of diameters between $75 - 250\mu m$, depending on species. The way that OCT is able to section the image and provide good depth resolution is by time-gating the incident wave, however, lateral resolution is still poor and does not provide an adequate image to resolve the alveolar structure. In order to gain useful information on the alveolar structure, we look at histologic images taken from euthanized animals seen in Figure 1. These images are sliced from a removed lung, and while they may be different from the lung of the living species, they give the most accurate data we can use to construct the initial model.

![Figure 1: These are two histologic images of alveoli.\(^6,7\) We try to duplicate this structure when creating our simulation model.](image)

3. MODEL

As mentioned earlier, our computational model is roughly based on histologic images taken of tissue *ex vivo*, which can be seen in Figure 1. We believe these images provide the closest
resemblance to the structure of the lung in vivo. A cross section of the lung resembles amorphous ellipsoids packed into a confined area; mouse lung alveoli are approximately $58 \pm 4 \mu m$ in diameter.\textsuperscript{3}

Figure 2: This is the computational model which is based upon the histologic image in Figure 1.

Using this information we created the model, which is shown in Figure 2. In order to solve Maxwell’s equations accurately we must know the index of refraction of the tissue and cells that make up the lung. For our initial modeling, we chose to make the tissue homogenous in order gain insight on the effects of the large alveolar structure instead of the small cellular structure. We then increase the heterogeneity of the tissue with the presence of red blood cells, which are shown in Figure 2. Once we know more about how these large structures affect the propagation of light, we may adjust the model in many ways, including increasing the heterogeneity of the tissue by adding more complexity to the alveolar structure and lung tissue.

4. FDTD SIMULATION

The Finite-Difference Time Domain simulation was developed in 1966 by Kane Yee, but did not become a popular method of solving Maxwell’s equations for over 20 years due to the limitations concerning computational resources.\textsuperscript{8} FDTD treats continuous space as a discretely sampled region; Maxwell’s equations are then calculated across this region over discrete time intervals.

Using Maxwell’s equations shown below for a non-conducting medium, we can discretize the equations to solve for the electric and magnetic field at each successive time-step.

$$\nabla \cdot \vec{E} = \frac{\rho}{\epsilon_0}$$

$$\nabla \cdot \vec{H} = 0$$

$$\nabla \times \vec{E} = -\mu_0 \frac{\delta \vec{H}}{\delta t}$$

$$\nabla \times \vec{H} = \epsilon_0 \frac{\delta \vec{E}}{\delta t}$$
Using the discrete differential form shown below we can then calculate the electric field over the entire simulation window, the magnetic field is calculated in a similar way.

\[
\frac{E_{z}^{n+1} - E_{z}^{n}}{\Delta t} = \varepsilon_0 \left[ \frac{H_{y}^{n}(i, j) - H_{y}^{n}(i - 1, j)}{\Delta x} + \frac{H_{x}^{n}(i, j - 1) - H_{y}^{n}(i, j)}{\Delta y} \right]
\]

Starting from an initial electric field zero everywhere except for the source, the incident wave is introduced, causing the simulation to begin. First the magnetic field is calculated across the entire simulation window, and then the electric field; this process continues throughout the simulation period with the effect of propagating the incident beam over the simulation model. This technique has been proven effective at looking at the propagation of light in skin using confocal microscopy.\(^9\) We slightly altered this method by changing the converging beam to a collimated beam that more accurately represents an OCT beam, we also sent out finite time pulses to simulate the time-gating aspects of OCT. It can easily be shown that the accuracy of this simulation technique is limited by the accuracy of the model and the computational limits of the computer running the simulation. The most destructive factor to the simulation is the effect of boundary conditions. The boundaries act as large discontinuities in the medium and thus reflect a significant portion of the light that is incident on these surfaces. In order to deal with this, we have implemented the Mur first-order absorbing boundary conditions, which lessen these effects, but do not eliminate them.\(^10\)

Using the initial model based on histologic samples we ran multiple simulations, one of which can be seen in Figure 3.

It is clearly visible how the propagating light wave is refracted by the alveolar structure as it continues down the screen. These images were created by overlaying the electric field measurements onto the computational model; doing this clearly shows where and how the structure refracts the incident wave. Due to computational limitations, we were only able to achieve depths on the order of 150\(\mu m\) and widths on the order of 50\(\mu m\); for this initial investigation this was sufficient in order to gain a preliminary understanding of the accuracy of the model and structure of the lung. In future work we will be able to move these computations over to a more powerful machine; doing this will increase the model area, decrease spatial and temporal resolution, while also limiting the destructive presence of reflections due to boundary conditions. Figure 3h shows that the absorbing boundary conditions do not work perfectly to avoid reflections at the boundary. This a problem that will be addressed in further investigations.

5. RETURN IMAGE

Once we calculated both the electric and magnetic field over the course of the entire simulation, we then needed to recreate what we would expect to see from the reflected light as it strikes an actual detector. In order to simulate these returned images we calculated the Poynting vector from the electric and magnetic field taken at the top edge of the simulation model.

\[
\vec{S} = \vec{E} \times \vec{H}
\]
Figure 3: This is a sequence of images showing the electric field as the light propagates downward through the tissue. Figures 3g and 3h show waves being reflected by the alveoli wall. 3h shows how there is reflection from the boundaries, which can be seen by the wave now travelling upwards.

This is the signal that would be observed in a pulsed time gated imager. Figure 4 shows both the model, shown in 4a, and the corresponding return image, shown in 4b. The image is the $z$ component of the poynting vector plotted as a function of $x$ and $t$, with the axis scaled to represent depth. Figure 4c shows an image that was calculated similarly to Figure 4b but also multiplied with a reference waveform which represents the coherent interference which would be present in an actual OCT system. The reference introduces some speckle and the image is somewhat harder to interpret than the incoherent image in Figure 4b. The first 30 – 40$\mu$m of structure can be seen in the returned image and this image provides promising results.

The three alveoli which are nearer to the pleural wall are clearly visible in this return image and we find these results very promising. The vertical surfaces between alveoli cause much distortion in the return image and these areas are part of our future investigations. The return image also shows that the red blood cells represented by the red dots seem not to affect the resultant image, and so we hope to concentrate our investigation on the alveolar structure until we feel satisfied with the knowledge gained within that area. We can use the model to optimize the OCT sensor and signal processing algorithms to extract as much information as possible the lung measurements.
Figure 4: 4a shows the model used in simulation, while 4b shows the corresponding return image calculated from the poynting vector. Figure 4c is Figure 4b multiplied by a reference wave that represents the incident pulse, this gives the effect of an actual coherent OCT image.

6. CONCLUSION

In conclusion, we find that the research in increasing the understanding of lung structure using OCT is possible with continued research. We plan to continue imaging different mammalian lungs using different modalities while modifying our model to provide more accurate simulation...
results. We also plan to develop and study the simulation to understand what is happening to the light as it refracts because of the lung structure, which is still poorly understood.

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