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Use of perturbation Monte Carlo for Measurement of Optical Properties in an Extended Epithelial Tissue Model

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Abstract: A pMC based inverse solution for the determination of optical properties in an extended epithelial tissue model is experimentally validated.

OCIS codes: (100.3190) Inverse problems; (170.3660) Light propagation in tissue; (170.3880) Medical and biological imaging; (170.4580) Optical diagnostics for medicine; (170.5280) Photon migration; (170.7050) Turbid media

1. Introduction

The determination of optical properties of heterogeneous tissues on spatial scales comparable to a transport mean free path (l^*) has been a significant interest in biomedical optics. Radiative transport on this length scale, usually termed the 'transport regime', is especially important because it cannot be fully described by current analytic light transport models. Although conventional Monte Carlo (MC) methods can be used to model light transport in this regime, it is typically not implemented within inverse problem solutions because of high computational cost. Furthermore, the fact that epithelial tissues whose thickness is generally less than 500 μm are known to be the origin of cancer development is demanding a new approach to diagnose small tissue volumes with precision and speed.

To address the inverse problem within the transport regime, we have proposed a method that determines the optical properties of heterogeneous volumes based on a set of spatially resolved reflectance measurements [1]. For fast inversion, the method combines conventional Monte Carlo to generate a background photon biography file. Perturbation Monte Carlo (pMC) is then used to determine the change in the detected signal based on heterogeneous changes in optical property. This capability combined with differential Monte Carlo (dMC) and a gradient-based non-linear optimization algorithm determines the optical properties in a heterogeneous tissues. Here, we focus on the experimental validation of this approach using spatially-resolved diffuse reflectance (SRDR) of layered tissue phantoms for epithelial tissues.

2. Method

We used optical phantoms meant to reproduce the spatial and optical properties of the normal cervical tissue as observed by Hornung and co-workers [2]. The cervical tissue we consider is composed of a thin (0.5 mm) epithelial layer above a much thicker stromal layer. The homogeneous background tissue possesses optical properties of μ_a = 0.034/mm, μ_s = 6.11/mm, g = 0.9, and l^* = 1.55 mm. However, due to the difficulty in consistent production of a two-layered phantom with a 0.5 mm top layer thickness, we adopted an extended cervical tissue phantom model whose dimensions are roughly double in size to real cervical tissue while (μ_s'/μ_a) is kept identical to normal cervical epithelia. Thus, in the extended cervix model, the thickness of the top layer is 1 mm, equivalent to 0.5 mm epithelial layer, and homogeneous background media (simulating the underlying stroma) have optical properties of μ_s' = 0.284/mm, μ_a = 0.016/mm, and l^* = 3.33 mm. These background optical properties are used for the generation of a background biography of the photon history from conventional MC run. Perturbation to the absorption coefficient varied in the

range of 50%–400% while the scattering perturbation is varied in the range of 50%–150%. In the experiment, only one optical parameter is perturbed in one of the two layers to test the effectiveness to tracking changes in a single parameter within the two parameter inversion algorithm. In principle, the basic algorithm is capable of performing simultaneous perturbation and recovery of both μ_a and μ_s.

Fig. 1(a) shows a schematic of the experimental setup for SRDR measurements. A cylindrical container of 8 cm in diameter and 10 cm in height was filled with optical turbid medium composed of Intralipid, Nigrosin, and de-ionized water. The container was composed of two compartments, with the top and bottom layer separated by 100 μm thick clear transparency film. A He-Ne laser (JDS Uniphase, Mountain View, CA) emitting at λ = 632.8 nm was coupled to a multi-mode optical fiber with 200 μm diameter through collimating lens. In order to block specular reflectance near the source and prevent saturation of CCD pixel due to high intensity from the source, a custom made fiber optic illuminator (Fiberguide, Stirling, MA) was designed and fabricated. In the housing of the illuminator, right angle prism was placed at the tip of the illuminator to deflect light 90 degree from the fiber. A sample was placed at the focal point of a 35 mm photographic lens (Nikon, Japan) attached to the thermoelectrically-cooled CCD camera (Photometrics, Tucson, AZ). The CCD was equipped with a 16-bit analog-to-digital converter, and a field of 3.7 $\times$ 3.7 cm in dimension is imaged onto the 1024 $\times$ 1024 pixels of the CCD. To convert the measured intensity to an absolute measurement of reflectance, we employed the calibration procedure outlined by Pham and co-workers [3].

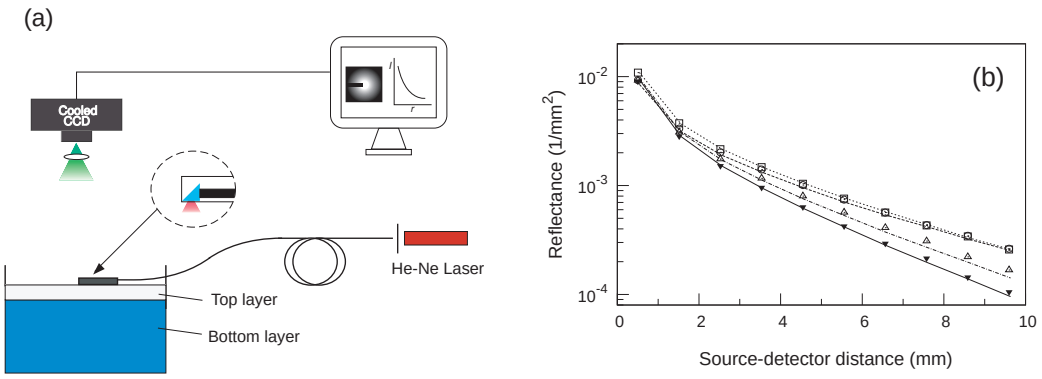

Fig. 1. Experimental setup for the pMC analysis of layered media (a), and reflectance vs. detector position as measured with different perturbed media (b) for the comparison between experimental measurements (symbols) and pMC prediction from the recovered optical properties (lines). Each line and symbol pair represents bottom layer absorption perturbation of 200% (dash dot, triangle), 350% (solid line, filled triangle), top layer scattering perturbation of 80% (dash, circle), and 120% (dot, square) from the background optical properties, respectively.

3. Results

Fig. 1(b) depicts SRDR from experimental measurements and their comparison to reflectance signals predicted by pMC using the recovered optical properties from the pMC inversion algorithm. Ten equispaced detectors placed from 0.05 to 10 mm are used to detect reflectance signal and the reflectance for each perturbed phantom measurements is fed to the inversion pMC procedure to recover optical properties of the perturbed layer. The recovery is then examined by running forward pMC procedure with the recovered properties to compare experimental reflectance measurements. Even though there are four different combinations of perturbation, that is top layer scattering, top layer absorption, bottom layer scattering, and bottom layer absorption, we show the physiologically relevant perturbation case in this literature.

Fig. 2 summarizes pMC inversion results for the SRDR measurements of bottom layer absorption and top layer scattering perturbation. As indicated by Fig. 2(a), the recovered μ_a and μ_s agree quite well with

the expected value over the whole range of perturbations with relative error of less than 20% and 10%, respectively. In the case of top layer scattering perturbation [Fig. 2(b)], recovered scattering coefficients agrees with the expected values in the range of 70%–130% perturbation. However, the recovery of μ_a is not decoupled from scattering properties. This is probably due to small average path-length of the detected photons to recover absorption coefficient. We also tried with various layout of detector positions to optimize sensitivity analysis of cervical tissue model, and it demonstrated that accurate recovery of optical properties is most difficult when top layer scattering perturbations occur.

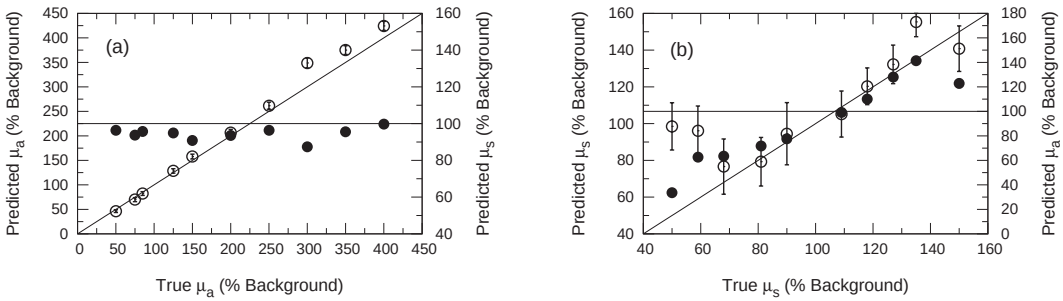

Fig. 2. Experimental results of (a) μ_a perturbation of the bottom layer , and (b) μ_s perturbation of the top layer. Values of μ_a (○) and μ_s (●) shown as predicted by the pMC method. Error bars represent 1σ confidence intervals and are not visible where they are smaller than the symbol.

4. Conclusion

We have developed and validated a novel and efficient method for solving inverse problems to determine optical properties of layers within epithelial tissues. Since this method is purely MC based, the method can be applied even in 'transport regime' or in highly absorbing media. The physiological changes caused by cancer development in epithelial tissues are examined with bottom layer absorption perturbation which may be reflected by increase of blood flow in the stroma, or top layer scattering perturbation which may be represented by morphological change in cellular/sub-cellular structure in the epithelia. Experimental results show great promise that pMC can be applied to accurate, rapid determination of μ_a and μ_s for many heterogeneous tissue structures.

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