# Endoscopically compatible near-infrared photon migration probe

**Carmalyn Lubawy and Nirmala Ramanujam**

*Department of Biomedical Engineering, University of Wisconsin—Madison, 1550 Engineering Drive, Madison, Wisconsin 53706*

Received March 10, 2004

We have developed a 2.3-mm-diameter fiber-optic probe for near-infrared photon migration spectroscopy that can be inserted into the body through an endoscope or biopsy needle. This probe is specifically designed to be inserted into a core biopsy needle to facilitate optical sampling of lesions during breast needle biopsy. This probe was tested on tissue phantoms containing heterogeneities (to stimulate breast lesions) of various sizes and optical properties. Under the conditions tested, the probe can measure the absorption coefficient to within 30% for heterogeneities with radii as small as 10 mm. © 2004 Optical Society of America

*OCIS codes:* 170.4580, 170.5280, 170.6510.

Photon migration spectroscopy (PMS) is a technique in which near-infrared photon density waves are launched into a medium and are collected as much as several centimeters away from the source, permitting measurement of scattering and absorption several centimeters below the source–detector plane.[1] PMS has been used to monitor and image brain and muscle oxygenation[1] and to noninvasively detect changes in hemoglobin oxygenation, vascularity, and water content of breast cancer[2] by use of optical fibers placed perpendicular to the skin directly above the region of interest.[1,2]

PMS probes placed on the skin have a maximum measurement depth of several centimeters, and the measurement is an average of the optical properties of the tissue that the light traverses. Thus the accuracy of transcutaneous PMS is limited if the region of interest is only a portion of the optically sampled tissue volume, and this approach does not provide access to deeply embedded tissues. A small-diameter PMS probe could be used with endoscopes or biopsy needles to more accurately measure the optical properties of regions of interest in deeply embedded organs such as the prostate or the liver or within large tissue volumes such as the breast.

Currently, one million needle biopsies of the breast are performed in the United States annually.[3] Needle biopsies remove only a small amount of tissue, yielding a false-negative rate of as much as 8% (Ref. 4) and thus necessitating repeat biopsies in as many as 7% of patients.[3,5] PMS has the potential to rapidly and nondestructively diagnose the tissue at the tip of the biopsy needle as normal, benign, or cancerous. Thus it can augment an x-ray or ultrasound guided breast needle biopsy by determining if the needle is in the correct position, thus increasing the likelihood that abnormal tissue is sampled. This property should reduce the false-negative rate and the number of women who must endure a repeat biopsy.

Our fiber-optic probe is designed to be inserted into the 2.7-mm-diameter bore of a Mammatome breast biopsy needle (Ethicon Endo Surgery). The needle has a solid tip and a 16-mm-long, 2.5-mm-wide aperture along its side that is used for tissue collection and PMS measurements. Figure 1 is a conceptual picture of the tip of the fiber-optic probe inside the biopsy needle. Overall, the probe consists of side-firing fiber tips encased in a rigid optical quartz cap through which light may be transmitted. These fibers are relayed to the PMS instrument via flexible tubing, which is connected to the cap. This PMS probe was designed by our group and fabricated by Polymicro Technologies.

The first design consideration for this probe was that it will be in contact with the inside of the human body. Thus all materials used in the probe tip (an optical quartz cap, flexible Tygon tubing, and a proprietary epoxy), comply with U.S. Pharmacopoeia class VI standards.

The Mammatome device does not provide straight-line access to the bore of the needle. Geometric calculations have shown that the probe needs to have an effective bend radius of 3 cm or less for insertion into the needle. The two primary factors that affect the bend radius are the length of the quartz cap and the diameter (stiffness) of the largest optical fiber used in the probe. The mean penetration depth of the collected light increases with increasing source–detector separation (SDS), and the SDS determines the minimum length of the cap. Thus the SDS and the fiber diameters were selected to maximize the sampling depth and the throughput, respectively, while an effective bend radius of 3 cm

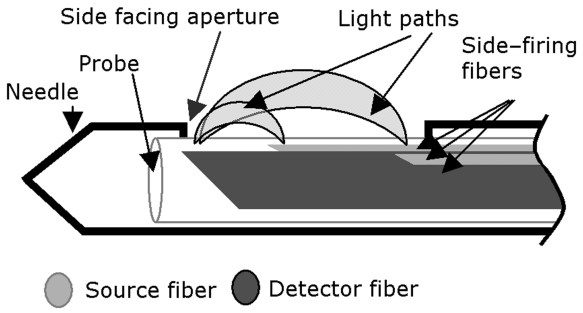


Fig. 1. Conceptual picture of the fiber-optic probe inside the biopsy needle, with the light paths extending into the tissue through the aperture.

0146-9592/04/172022-03$15.00/0 

was maintained. The resultant probe specifications are as follows: two source fibers with a core diameter of 200 $\mu$m and a numerical aperture of 0.22, a detector fiber with a core diameter of 600 $\mu$m and a numerical aperture of 0.22, an optical quartz cap with a length of 15 mm and an outer diameter of 2.4 mm, and a maximum SDS of 10 mm (the extra cap length seals the tip and joins the cap to the Tygon tube). A second source fiber was incorporated at a SDS of 5 mm. All fibers were polished at an angle of 43° and radially oriented such that the light from each fiber was normal to the circumference of the quartz cap, minimizing specular reflection into the detector fiber. We fixed the relative placement and orientation of the fiber tips by gluing the fibers together. Epoxy at the junction of the rigid cap and the Tygon tube fixed the fibers inside the cap. The outer diameter of the cap was stepped down such that it fit inside the Tygon tube to provide strength at the junction and to make the junction smooth for easy insertion and removal of the probe. The rest of the probe was fabricated by standard construction techniques. Figure 2 shows a top-down photograph of the tip of the probe.

The instrument to which the probe is coupled is a frequency-domain system that is similar in design to one described in the literature.[6] It consists of a laser diode driver, a network analyzer, three laser diodes (811, 849, and 905 nm), an optical switch, an avalanche photodiode, and a 19-dB amplifier. The 811-nm laser was used for the experiments presented in this Letter. The average power delivered at the probe tip was approximately 6 mW. For each measurement, 101 data points were collected over the frequency range 50–150 MHz. At a bandwidth of 15 Hz (resulting in a measurement sweep time of 8 s), the signal-to-noise ratio of the instrument and the probe was greater than 300:1 over the measurement range in a representative liquid phantom. This instrument records phase and amplitude data at both SDSs. These data were fitted to a diffusion equation for an infinite medium. For homogenous media the multifrequency, two-SDS method and the multifrequency single-SDS method provide similar results, but the two-SDS method was used in subsequent analyses because it obviated the need for calibration phantoms.[6]

First, the accuarcy of the probe for measuring the optical properties of semisolids that are representative of normal and diseased tissue was characterized.[1,2] Agar tissue phantoms with a reduced scattering coefficient ($\mu_s'$) of 10 cm$^{-1}$ and absorption coefficients ($\mu_a$) that ranged from 0.02 to 0.20 cm$^{-1}$ were constructed with Intralipid (scatterer) and India ink (absorber).[7]

Figure 3 shows the measured $\mu_a$ as a function of the theoretical $\mu_a$ of the homogeneous phantom. It can be seen that the retrieved $\mu_a$ is very accurate from 0.02 to 0.15 cm$^{-1}$. At a value of $\mu_a$ of 0.20 cm$^{-1}$ there is some roll-off. We believe that this roll-off is caused by light leaking directly from the source to the detector fiber without exiting the probe, swamping the signal detected from the darker phantoms. The measured $\mu_s'$ was within 30% of theoretical with no discernable trend with varying absorption coefficients.

Next, semisolid tissue phantoms that simulate breast tissue with a lesion were created. Figure 4 shows a drawing of the test setup. Phantoms made from agar, Intralipid, and ink were constructed with cylindrical heterogeneities that were approximately as tall as they were wide. The background phantom was representative of normal breast tissue with values of $\mu_a$ and $\mu_s'$ of 0.05 and 10 cm$^{-1}$, respectively.[1] The cylindrical heterogeneities had optical properties representative of malignant breast tissue with $\mu_a$ values of 0.10, 0.15, and 0.20 cm$^{-1}$ and a constant $\mu_s'$ of 10 cm$^{-1}$.[1,2] The probe tip was approximately at the bottom of the heterogeneity.

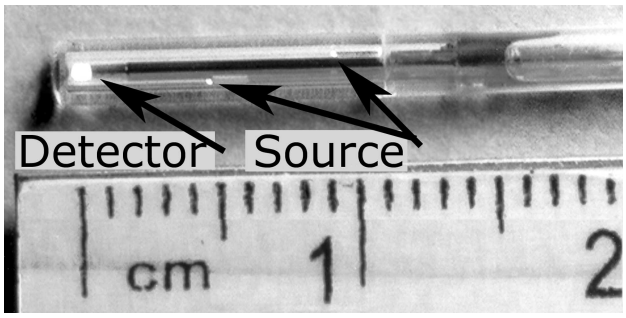


Fig. 2. Photograph of the tip of the PMS probe. There are three side-firing fibers (two source and one detector fiber) fixed inside a quartz cap, which is connected to flexible Tygon tubing.

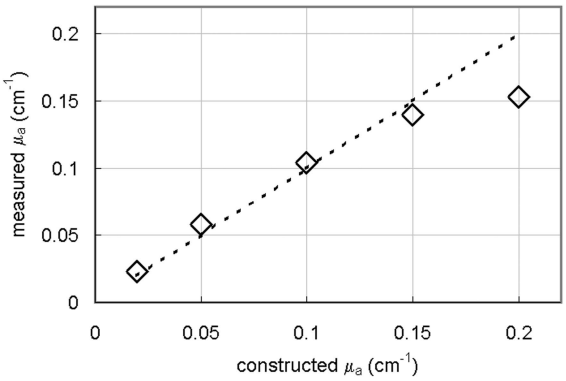


Fig. 3. The measured (diamonds) and theoretical (dashed line) absorption coefficient ($\mu_a$) of the homogeneous agar phantoms for $\mu_a$ from 0.02 to 0.20 cm$^{-1}$ and for a value of $\mu_s'$ of 10 cm$^{-1}$.

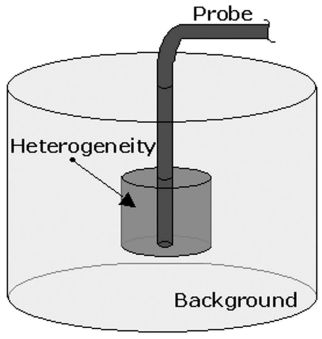


Fig. 4. Test setup in which the probe was used to make PMS measurements of synthetic tissue phantoms that simulate breast tissue with lesions.

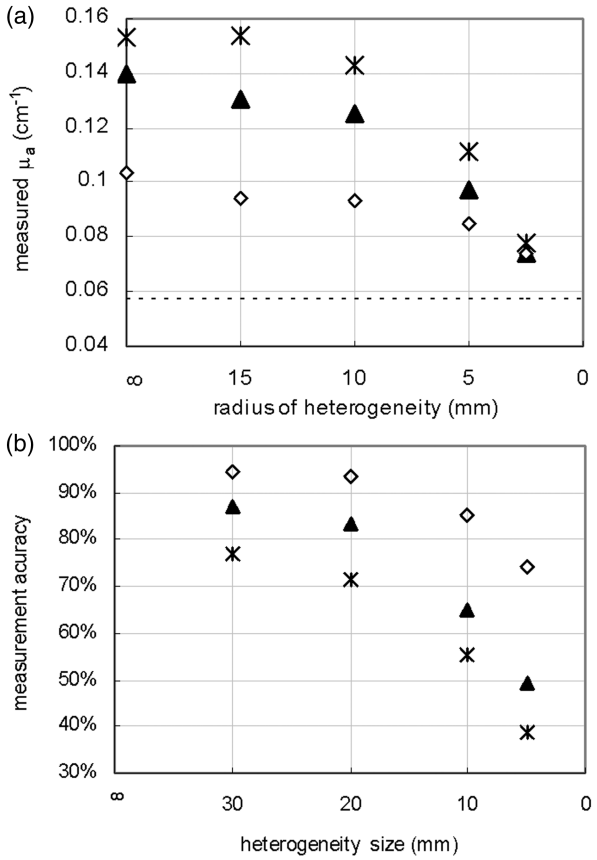


Fig. 5. (a) Measured absorption coefficient ($\mu_a$) of a tissue phantom containing a heterogeneity and (b) measurement accuracy for data presented in (a). The values of $\mu_a$ of the heterogeneities are (⋆) 0.20 cm$^{-1}$, (▲) 0.15 cm$^{-1}$, and (◇) 0.10 cm$^{-1}$. The dashed line in (a) represents the measured $\mu_a$ of the background. The reduced scattering coefficient ($\mu_s'$) of the entire phantom is 10 cm$^{-1}$.

Figure 5 shows the measured absorption coefficients for heterogeneities of various sizes and absorption coefficients, and the accuracy of these measurements. As expected, the measured absorption coefficient is closest to that of the heterogeneity when the heterogeneity comes closer to filling the optical sampling volume. As the size of the heterogeneity decreases, more of the collected light has traversed the background medium, and thus the measured absorption coefficient starts to shift toward the absorption coefficient of the background medium. This shift is exaggerated in darker heterogeneities because of the large difference between the optical properties of the heterogeneity and of the background. In the smaller heterogeneities the photons collected by the smaller SDS have traveled a higher percentage of their flight through the heterogeneity than the photons collected at the longer SDS. In summary, a measurement accuracy of at least 70% was achievable for heterogeneities with a radius comparable to the large SDS, and there is clearly a measurable difference between the background and the heterogeneities with a radius as small as 2.5 mm.

There are several refinements that should improve the accuracy of the PMS probe. Adding a light baffle to the probe to limit the amount of light leaking between the source and the detector fibers may prevent the roll-off in optical properties that is seen with the darker phantoms. Simulations have shown that photons travel a more coherent path at higher modulation frequencies.[8] Thus increasing the modulation frequencies may improve the measurement accuracy of smaller-sized heterogeneities. Additionally, changing the modulation frequency may enable the mean penetration depth for a fixed SDS to be varied.

In conclusion, we have constructed a novel PMS probe that will fit inside the bore of a Mammatome breast biopsy needle. This probe has been demonstrated to measure the optical properties of both homogenous and heterogeneous phantoms that are representative of human breast tissue. Probes of a similar design could be inserted into the body through an endoscope or a catheter, thus enabling the diagnostic capabilities of PMS measurements to be used on parts of the body that are not accessible with transcutaneous PMS methods.

N. Ramanujam's e-mail address is nimmi@engr.wisc.edu.

## References

1. B. J. Tromberg, N. Shah, R. Lanning, A. Cerussi, J. Espinoza, T. Pham, L. Svaasand, and J. Butler, Neoplasia **2,** 26 (2000).
2. T. McBride, B. W. Pogue, S. Jiang, U. L. Osterberg, K. D. Paulsen, and S. Poplack, Opt. Lett. **26,** 822 (2001).
3. L. Liberman, T. L. Feng, D. D. Dershaw, E. A. Morris, and A. F. Abramson, Radiology **208,** 717 (1998).
4. G. Pfarl, T. H. Helbich, C. C. Riedl, T. Wagner, M. Gnant, M. Rudas, and L. Liberman, Am. J. Roentgenol. **179,** 1503 (2002).
5. L. Liberman, D. D. Dershaw, J. R. Glassman, A. F. Abramson, E. A. Morris, L. R. LaTrenta, and P. P. Rosen, Radiology **203,** 151 (1997).
6. T. H. Pham, O. Coquoz, J. B. Fishkin, E. Anderson, and B. J. Troberg, Rev. Sci. Instrum. **71,** 2500 (2000).
7. R. Cubeddu, A. Pifferi, P. Taroni, A. Torricelli, and G. Valentini, Phys. Med. Biol. **32,** 1971 (1997).
8. A. Honar, C. Ricks, and K. Kang, in *Oxygen Transport to Tissue XXIV*, J. F. Dunn and H. M. Swartz, eds., Vol. 530 of *Advances in Experimental Medicine and Biology* (Kluwer Academic/Plenum, New York, 2003), pp. 113–121.