Ballistic imaging of biological media with collimated illumination and focal plane detection

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Abstract. A simple, affordable method for imaging through biological tissue is investigated. The method consists of (1) imaging with a wavelength that has a relatively small scattering coefficient (1310 nm in this case) and (2) collimated illumination together with (3) focal plane detection to enhance the detection of the ballistic photons relative to the diffusive light. We demonstrate ballistic detection of an object immersed in a 1-cm-thick cuvette filled with 4% Intralipid, which is equivalent to ~1 to 2 cm of skin tissue. With the same technology, a ballistic image of a 1-mm-wide object in 10-mm-thick chicken breast is also presented. © 2015 Society of Photo-Optical Instrumentation Engineers (SPIE) [DOI: 10.1117/1.JBO.20.7.076006]

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1 Introduction
Optical imaging, in general, and optical mammography in particular, are holy-grails of clinical imaging. Visible and infrared (IR) light is safe (as opposed to x rays) and also gives significantly better spatial resolution than ultrasound. Moreover, different types of tissues interact differently with visible light. One of the most useful features is the difference in the absorption coefficient at 700 nm of oxidized and nonoxidized hemoglobin, which can be utilized not only in identifying activated metabolism but also as a tumor detector (see, for example, Refs. 1 and 2). In addition, the scattering coefficient is sensitively dependent upon the cells’ organelles, such as the nucleus and mitochondria. Therefore, visible and near-IR light are extremely useful for diagnosing different anomalies in biological tissue.

The main problem with visible and near-IR radiation is that they undergo significant scattering. In fact, for visible light, the mean free path is <0.1 mm, and therefore, beyond 2 mm, the ballistic component of the light is negligible. For this reason, most optical imaging methods focus on diffusive imaging techniques, such as photon density waves and inverse-scattering solutions of the diffusion equation. Methods that are based on ballistic imaging are only effective for thin scattering media. An important example is optical coherence tomography, which is a leading technology to image skin layers and the retina with micrometer resolution. This technology works in the reflection configuration; therefore, it is useless beyond 1 to 1.5 mm of tissue, where the number of ballistic photons is negligible and the ballistic image is buried in diffusive light.

In 1990, it was demonstrated by Yoo and Alfano that time-resolved streak-camera techniques can be utilized to differentiate between the ballistic and diffusive components of light in diffusive medium. A year later, a similar technique based on an ultrastart optical shutter was used to create a high-resolution image through a 3.5-mm-thick human tissue. Since then, this technology was improved and became an important tool in the research of diffusive media (see Refs. 3 and 4).

It has recently been shown that by applying two simple and well-known modifications, it is possible to substantially extend the ballistic imaging depth of a diffusive medium. This method was based on previous research which demonstrated that the transition point between the ballistic and diffusive regimes depends not only on the scattering coefficient, but on the collection angle of the detection as well.

It is the objective of this work to apply this technology in constructing a ballistic image that can resolve a 1-mm-wide object immersed in 1 to 2 cm (depending on the specific type) of a biological tissue medium.

2 Theory
Photons experience both absorption and scattering while propagating in any medium. However, in biological tissue, scattering is the dominant mechanism for both visible and near-IR light. In many types of tissue, the scattering coefficient can be more than three orders of magnitude larger than the absorption coefficient. In fact, without scattering, most tissues would be almost completely transparent. In such a nonscattering world, all absorbing/blocking structures, such as veins and tumors, would clearly appear in any optical image exactly like bones do in x-ray images. However, since the small cellular organelles that biological tissues consist of have micrometer dimensions, their images. However, since the small cellular organelles that biological tissues consist of have micrometer dimensions, their scattering cross-section (in the visible and near-IR domain) is huge. As a consequence, the amount of ballistic, i.e., non-scattered, light rapidly decreases exponentially. In fact, according to Beer’s law, the dependence of the ballistic light on the longitudinal coordinate $z$ is

$$I_B(z) = I_0 \exp[-(\mu_S + \mu_A)z]. \quad (1)$$

where the subscript $B$ denotes ballistic, $I_0$ is the light intensity entering the medium, and $\mu_S$ and $\mu_A \ll \mu_S$ are the scattering and absorption coefficients, respectively.

The scattered photons, on the other hand, experience a slower decay. However, due to the fact that their optical trajectory is
considerably larger than the ballistic path, they suffer more from absorption. In fact, they obey the diffusion equation

\[ D\nabla^2 I - c\mu_A I = \frac{\partial I}{\partial t}, \quad (2) \]

where \(D \equiv c/3(\mu_s' + \mu_a)\) is the diffusion coefficient, \(\mu_s' \equiv \mu_s(1 - g)\) is the reduced scattering coefficient, and \(g \equiv \langle \cos \theta \rangle\) is the mean cosine of the scattering angle.

In the stationary case, the equation is reduced to

\[ \nabla^2 I - \mu_{\text{eff}} I = 0, \quad (3) \]

where \(\mu_{\text{eff}} \equiv \sqrt{\mu_s' \mu_a / \mu_A}\) is an effective attenuation coefficient.

In a quasi-one-dimensional model, where both \(x\) and \(y\) directions are degenerate, the solution is approximately

\[ I_D(z) = I_0 \exp(-\mu_{\text{eff}} z), \quad (4) \]

where the subscript \(D\) denotes diffusive.

Since in biological tissue \(\mu_{\text{eff}} \ll \mu_s\), it follows that diffusive photons penetrate the medium over much longer distances. However, since all the photons are initially ballistic, it is clear that their dominance changes (quite dramatically) inside the medium, so that an undistorted ballistic image is transformed into a blurred one during propagation.

Previous work indicated that the critical width of the diffusive medium, beyond which the number of diffusive photons exceeds the photon number of ballistic light, depends on the measurement’s collection angle, or numerical aperture. It was demonstrated that the total intensity can be written as a superposition of the diffusive and the ballistic components, i.e.,

\[ I(z) = I_0 \left[ \exp(-\mu_s z) + \frac{\delta\Omega}{4\pi} \exp(-\mu_{\text{eff}} z) \right], \quad (5) \]

where \(\delta\Omega\) is the collection angle.

A direct consequence of Eq. (3) is the transition width \(z_c\), beyond which the diffusive portion of the light becomes dominant, can easily be extracted

\[ z_c \equiv \frac{1}{\mu_s - \mu_{\text{eff}}} \ln \left( \frac{4\pi}{\delta\Omega} \right). \quad (6) \]

A ballistic image of the medium can only be extracted for a medium thickness smaller than \(z_c\). In Eqs. (3) and (5), it was assumed that the absorption coefficient is negligible in comparison to the scattering coefficient (\(\mu_s \gg \mu_a\)).

If no special measures are taken, then \(z_c \approx \mu_s^{-1}\), which, for visible light, is approximately \(z_c \approx \mu_s^{-1} \approx 0.1 \text{ mm}\). It is clear why the naked eye (or camera) cannot image veins that are \(\lesssim 1 \text{ mm}\) deep. In fact, with the naked eye, one cannot clearly discern any object below the skin layer.

It was demonstrated in Ref. that Eq. (3) gives a roadmap for improving the ballistic image. Any decrease in the scattering coefficient \(\mu_s\) and/or in the collection angle \(\delta\Omega\) will increase the transition width.

Reference suggested to increase the ballistic penetration depth by imaging with 1310 nm light, which has a much larger absorption coefficient than 700 nm; however, it has a smaller scattering coefficient. The ballistic photon attenuation is weaker, and therefore is larger. However, it was further suggested to decrease the collection angle by using an additional collimator for focal-plane detection. Collimators can easily reduce the collection angle to \(\delta\Omega/4\pi \approx 2 \times 10^{-5}\). With these two simple changes, it was shown that the ballistic regime can be increased by at least two orders of magnitude and the goal of optical ballistic imaging turned from unrealistic to tenable. These suggestions are consistent with other work (see Refs. and for the collimator imaging and Refs. for the wavelength selection).

Equation (3) suggests that the image of the medium can be approximated as a superposition of the ballistic image \(M_B(x)\) and the diffusive one \(M_D(x)\), where \(x\) is the transversal coordinate. Whereas \(M_B(x)\) is a shadow image of the medium, is the solution of the diffusion equation at the end of the diffusive medium.

Therefore, when the object is scanned with a detection angle \(\delta\Omega\), the image can be written as a superposition of weighted images, i.e.,

\[ I(z, x) = I_0 \left[ M_B(x) \exp(-\mu_s z) + M_D(x) \frac{\delta\Omega}{4\pi} \exp(-\mu_{\text{eff}} z) \right]. \quad (7) \]

In this work, we evaluate and measure the image of an opaque wire of diameter \(D_0 = 1 \text{ mm}\) embedded within a scattering medium. The ballistic image \(M_B(x)\) can be described as

\[ M_B(x) \equiv [1 - \text{rect}_{D_0}(x)] \ast [C(x) / \Delta], \quad (8) \]

where \(\text{rect}_{D_0}(x) \equiv \left\{ \begin{array}{ll} 1 & |x| < D_0/2 \\ 0 & \text{else} \end{array} \right\}\) is the rectangle function, the asterisk stands for spatial convolution, and the output collimator response, which is a consequence of the collimator’s circular shape, is \(C(\xi) = \left\{ \begin{array}{ll} (2/\pi)^{1/2} \sqrt{1 - \xi^2} & |\xi| \leq 1/\Delta \\ 0 & |\xi| > 1/\Delta \end{array} \right\}\) where \(\Delta\) is the diameter of the collimator. Due to the response function \(C(\xi)\), the image resembles a Gaussian function.

If the longitudinal thickness of the medium is \(w\), and the object is centered within the medium, then the diffusive image of the object can be approximated as

\[ M_D(x) \equiv 1 - \exp\left[ -\frac{2\mu_{\text{eff}} \sqrt{(w/2)^2 + x^2}}{1 + (2x/w)^2} \right]. \quad (9) \]

This expression can beverified by calculating the product of the probabilities (which are proportional to the solution of the diffusion equation) of migrating from \(z = 0, x = 0\) to \(z = w, x = 0\) via the point \(z = w/2\) for any \(x\).

As a consequence, while in the ballistic image the object’s transversal width is approximately \(\Delta x \approx D_0 \approx 1 \text{ mm}\); in the diffuse image, it is approximately [the FWHM of Eq. (4) when the width of the object is taken into account]:

\[ \Delta x \approx 2 \sqrt{\left( \frac{\ln 2 + w - D_0}{2\mu_{\text{eff}}} \right)^2 - \left( \frac{w - D_0}{2} \right)^2 + D_0}. \quad (10) \]

We therefore expect a very sharp transition (of \(\approx 0.1 \text{ mm}\)) from a ballistic image to a diffusive one.
3 Experiment

In the following experiments, a 1-cm-thick emulsion of Intralipid and water is the turbid medium in which the wire is submerged. Light from a 10 mW, 1310 nm fiber-coupled diode laser is collimated and illuminates the sample in both setups. In the first experiment (Fig. 1), an output lens (an additional collimator) focuses the light into a detector located at the focal plane to reduce the collection angle, whereas in the second setup (Fig. 2), the fiber end is located 18 mm from the medium. In both experiments, we gradually change the density of the Intralipid while monitoring the image (the thickness remains constant at 1 cm).

It is convenient to write the scattering coefficient in terms of the Intralipid density $\rho$ measured in percent of the emulsion, i.e.,

$$\mu_s \equiv \sigma_0 \rho_{\%},$$

(11)

where $\rho_{\%}$ is measured in percent and $\sigma_0$ is the normalized cross-section in $(\text{cm}^{-1})$.

In this case, the critical density, beyond which the image is mainly diffusive, is [from Eqs. (6) and (13)]

$$\rho_c \equiv \frac{1}{\sigma_0} \left[ \frac{2}{w - D_0} \ln \left( \frac{4 \pi}{\Delta z} \right) + \mu_{\text{eff}} \right],$$

(12)

such that for focal plane detection, this leads to

$$\rho_c \equiv \frac{1}{\sigma_0} \left[ \frac{4}{w - D_0} \ln \left( \frac{2}{\text{NA}} \right) + \mu_{\text{eff}} \right],$$

(13)

where NA is the numerical aperture of the collimator.

In the second case, where the bare fiber is used at the detection end, Eq. (1) cannot be applied since the fiber’s core is considerably smaller than the cross-section of the illuminating beam. Instead, the ballistic component is reduced by the ratio between the fiber’s core and the collimator cross-section, i.e.,

$$I(z, x) = I_0 A_{\text{fiber}} A_{\text{coll}} \left[ M_B(x) \exp(-\mu_s z) + M_D(x) A_{\text{coll}} \frac{\delta Q}{A_{\text{fiber}} 4 \pi} \exp(-\mu_{\text{eff}} z) \right],$$

where $A_{\text{fiber}}$ and $A_{\text{coll}}$ are the collecting fiber and collimator cross-sections, respectively.

Hence,

$$\rho_c \equiv \frac{1}{\sigma_0} \left[ \frac{4}{w - D_0} \ln \left( \frac{4 \Delta z}{\Delta} \right) + \mu_{\text{eff}} \right],$$

(14)

where $\Delta z$ is the distance between the medium’s boundary and the fiber, and $\Delta$ is the illuminating collimator (i.e., the first collimator) diameter. Note that the fiber’s diameter is not a parameter in this case.

For $w = 1 \text{ cm}$, we measured $\sigma_0 \equiv 7.2 \text{(cm)}^{-1}$ such that $\mu_{\text{eff}} \equiv 2.4 \sqrt{\frac{\rho_c}{2}}$.

We therefore expect that the width of the image will have the following approximate behavior:

$$\Delta x(\rho) \approx \begin{cases} D_0 & \rho < \rho_c \\ \frac{D_0}{2} & \rho = \rho_c \\ D_0 \left( \ln \frac{w - D_0}{D_0} + \frac{w - D_0}{2} \right)^2 + D_0 & \rho > \rho_c \end{cases}$$

(15)

In the second experiment, the distance from the medium to the collecting fiber was $\Delta z = 18 \text{ mm}$, and since the illuminating collimator core is approximately $\Delta = 3.4 \text{ mm}$, from Eq. (14), we have $\rho_c \equiv 2.2\%$.

Therefore,

$$\Delta x(\rho) \approx \begin{cases} 1 \text{ mm} & \rho < 2.2\% \\ 4.3 \text{ mm} & \rho > 2.2\% \end{cases}$$

(16)

For the first experiment with a numerical aperture $\text{NA} = 8.9 \times 10^{-3}$, according to Eq. (13), $\rho_c \equiv 3.75\%$, and therefore, the transition in the object width should correspond to

$$\Delta x(\rho) \approx \begin{cases} 1 \text{ mm} & \rho < 3.75\% \\ 4.3 \text{ mm} & \rho > 3.75\% \end{cases}$$

(17)

In Fig. 1, the normalized power (normalized to the minimum value) as a function of $x$ is plotted for the two configurations and for two different concentrations: below the concentration $\rho_c = 2.2 \text{ cm}^{-1}$ and above it. This critical concentration represents many types of human tissue. It is clearly seen that below $\rho < \rho_c$, there is no significant difference between the two configurations. With both systems, the width of the image is approximately $\Delta x \equiv 1 \text{ mm}$ as should be expected for the ballistic image. However, above $\rho > \rho_c$, in the two-collimator configuration, there is almost no difference in the width of the image compared to the low-concentration case, i.e., the image remains basically ballistic, while in the one-collimator configuration, the image width is considerably wider.
As can be seen from Fig. 4, these evaluations are consistent with the experimental results. Since it is known that an Intralipid emulsion of 2 to 4% simulates several types of tissue, these results suggest that this simple technique can be utilized in imaging 1 to 2 cm of biological tissue.

In principle, the penetration depth in the one-collimator configuration can be improved by increasing the distance between the medium and the detector; however, to reach $\rho_c \approx 3.75\%$, the distance should be increased 12-fold to $\sim 22$ cm, which, in practice, would decrease the signal to an unacceptably low level. The clear advantage of focal plane detection can be realized from Fig. 5. In this figure, the ratio between the measured power in the two-collimator configuration ($p^{(2\text{ col})}$) and the one-collimator one ($p^{(1\text{ col})}$) is plotted as a function of the transverse coordinate. Since the measurement locations are different in the two experiments, the ratio was calculated between the interpolations of the experimental data (this is the reason that the plots are continuous). In the ballistic regime (i.e., $\rho < 2.2\%$), the sensitivity of the two-collimator method is at least an order of magnitude better; beyond the ballistic regime, there is more than three orders of magnitude improvement.

To illustrate the potential of this technology, the Intralipid emulsion was replaced with a 1-cm-wide cuvette filled with chicken breast. In Fig. 6, a transverse scan of the medium is plotted. The dashed line is the ideal ballistic image of the object, while the solid line represents the measured power (in pW). As can be seen from this plot, not only can the object be detected even in a 1-cm-thick tissue, but the fact that its width is still $\sim 1$ mm indicates that it is indeed a ballistic image.
Since these experiments were carried out using relatively simple equipment, it seems more than reasonable to conclude that by optimizing the wavelength, light power, detection sensitivity, and collecting angle, an extension of this technique to thicker or denser tissue would be feasible.

4 Conclusions
A simple and affordable method was implemented to view an opaque object in a tissue phantom and in chicken breast. The method is based on the premise that to create a ballistic image of a diffusive medium, two requirements must hold: (1) the ballistic portion of the light should be separated from the main diffusive portion, and (2) the ballistic part component should be sufficiently strong to be detected.

To obtain the first requirement, the collecting angle is reduced substantially. The second requirement is achieved by illuminating the medium with a wavelength that has a relatively small scattering coefficient in tissue. In our experiment, the angle reduction was carried out by using focal plane detection, and the scattering coefficient reduction was reached by using 1310-nm light. With these simple modifications, it was possible to detect a ballistic image of a concealed opaque object in 1 cm of ∼4% Intralipid emulsion, which is equivalent to 1 to 2 cm of human tissue. Moreover, the method was implemented in detecting a concealed object in 1 cm of chicken breast with a resolution of ∼1 mm. One application would be in bone age assessment, where an image of the hand bones is necessary.

References