A DECISION-THEORETIC APPROACH TO TRANSILLUMINATION IMAGING IN BIOLOGICAL MEDIUMS

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ABSTRACT

The tradeoffs between ballistic imaging (time-gated imaging of first-arrival, unscattered photons) and conventional imaging for resolving tumors in biological scattering media are examined. For ballistic imaging, closed form expressions are derived to characterize the resolvability using five degrees of freedom (laser intensity, scattering coefficient, thickness of medium, false alarm rate, and number of observations). For conventional imaging, a numerical approximation is used to find the asymptotic resolution using the scattering and absorption coefficients of the medium. Using the characterizations of both approaches, a decision-theoretic approach to determining the minimum resolvable object size is developed, which provides clear guidelines as to when time-gated ballistic imaging methods offer advantages over conventional imaging. The theoretical predictions are validated through a realistic simulation of tumors in breast tissue.

Index Terms— Transillumination Imaging, Decision Theoretic, Resolution, Ballistic

1. INTRODUCTION

Ballistic photon imaging is a promising methodology for studying highly scattering media such as human tissue. Recent advances allow for the time-gating of early arriving photons introduced into a scattering (turbid) medium. This allows for the ability to separately detect unscattered or ballistic photons that exit the medium. Due to the lack of scattering, these photons will retain the spatial information of the medium. A tradeoff occurs, as the number of ballistic photons decays exponentially fast as the thickness/depth of the turbid medium increases. This results in an observation from ballistic photons that offers a high resolution but low SNR.

The basic imaging model considered here is a single laser point source and a single photon detector placed on either side of a turbid (scattering) medium. We assume that the source and detector can be positioned at arbitrary points, to allow probing through any desired set transects through the medium. A turbid medium can be considered any scattering material, and in this specific analysis we assume it to be a homogeneously scattering section of human tissue. This scattering material will be parameterized by the number of scatters per unit length (μ_s^m), the fraction of absorptions per length (μ_a^m), and the length of the medium (d^m). At certain points between the source and detector in the medium there may exist an occluder of interest. The occluders, which are assumed to be opaque, represent tumors embedded in tissue for a biomedical imaging application. We assume that the occluders are located at the mid-point of the medium being probed, as this is the point in the medium where the variance of the scattering will be at a maximum [1,2]. To completely define the environment, one must take into consideration the scattering properties of the occluding tumor (μ_a^t, μ_s^t), and the physical properties of the occluding tumor (depth = d^t, width = w^t).

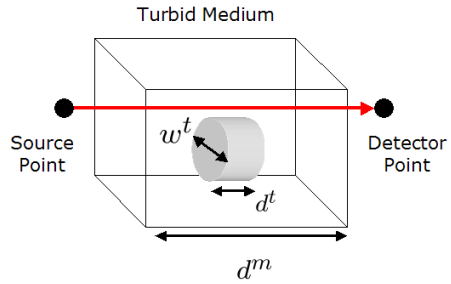

Figure 1. Turbid Medium Model Example

To create an observation of the environment, the source and detector pair will make a raster scan of the field of view to create an estimated cross-section of the environment. Our goal is to find, given the parameters of the medium and the occluder, lower bounds on the width and depth of the occluder (d^t, w^t) that can be reliably resolved in the medium. Two imaging regimes will be considered, the ballistic regime where only early arriving photons are detected using high-speed gating mechanisms, and the conventional imaging regime, where all the photons arriving at the detector are utilized (i.e., no time-gating). The advantage of the ballistic photons is that they are not scattered, providing very high spatial resolution. The limitation of ballistic imaging is that very few photons will propagate through the medium without scattering, resulting in a very poor signal-to-noise ra-

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tio (SNR). Conventional imaging uses all photons (scattered and unscattered) and thus provides a complementary trade-off (lower resolution but higher SNR). A decision-theoretic technique is then derived to determine which technique should be used for a given parameterized scattering medium in order to resolve small tumors.

2. BALLISTIC ANALYSIS

The ballistic imaging regime consists of probing points in a Field-of-View (FOV) and acquiring a count of the number of ballistic photons that arrive at each point in the FOV. These photons traverse in a straight line-of-sight between the source point and the detector, and therefore retain the spatial characteristics of the occluding objects in the turbid medium. Due to their direct line-of-sight characteristics, these photons will travel the shortest length and will arrive at the detector before any scattering photons. In order to collect only ballistic photons, time-gating is performed to restrict the observation to only early arriving photons (i.e. photons with no scattering events). If a perfect occluder is in the line-of-sight between the source and detector, then no ballistic photons will arrive at the detector. Therefore, the detection of ballistic photons indicates a "clear" line-of-sight and the absence of a tumor along the given transect. However, a problem occurs – as the turbidity of the medium increases, the less likely a photon is to arrive at the sensor having no scattering events. As a consequence, the total number of ballistic (non-scattering) photons for a medium might be very low. In addition, stray "noise" photons from other sources corrupt the observed signal, resulting in an observation that has high spatial resolution, but low SNR.

2.1. Ballistic Imaging - Single Point

The detected time-gated photons are ballistic photons from the source or stray "noise" photons arriving during the time-gate interval from other ambient light sources. The problem of determining whether or not a tumor lies along the line-of-sight can be cast as a statistical hypothesis test, as follows. Given a received photon count X at the sensor, one must choose between two possible situations. The first situation, is that no occluding tumors exist in the path between the laser and the sensor ($\mathcal{H}_0$). The alternative is that there is an occluding tumor along the line-of-sight between the laser and the sensor ($\mathcal{H}_1$). Tumors can be considered to be significantly more turbid scattering medium than the healthy tissue [3], and therefore the detector will collect an attenuated number of ballistic photons (compared to $\mathcal{H}_0$) along with the noise photons.

We define the number of noise photons that will arrive at the detector as $\mathcal{P}\left(t\lambda_0\right)$ (where $X \sim \mathcal{P}(\lambda)$ is a Poisson distributed random variable with mean = λ, and where t is the duration of photon acquisition time-gating). The ballistic photons traveling through only healthy tissue will be $\mathcal{P}\left(t\lambda_{L(tissue)}\right)$ (where $\lambda_{L(tissue)} = \lambda_L\left(\exp\left(-\mu^m d^m\right)\right)$), while the ballistic photons traveling through both healthy tissue and tumor will be $\mathcal{P}\left(t\lambda_{L(tissue+tumor)}\right)$ (where $\lambda_{L(tissue+tumor)} = \lambda_L\left(\exp\left(-\left(\mu^m d^m - \mu^m d^t + \mu^t d^t\right)\right)\right)$, with λ_L is the expected number of photons sent through the medium by the laser per unit time, $\mu^m = \mu_s^m + \mu_a^m$, and $\mu^t = \mu_s^t + \mu_a^t$).

This can be expressed as a hypothesis test with the null hypothesis (only tissue) defined as $\mathcal{H}_0 : X \sim \mathcal{P}\left(t\left(\lambda_0 + \lambda_{L(tissue)}\right)\right)$ and the true hypothesis (tissue and tumor) defined as $\mathcal{H}_1 : X \sim \mathcal{P}\left(t\left(\lambda_0 + \lambda_{L(tissue+tumor)}\right)\right)$. As the mean of the Poisson distribution grows, the probability distribution tends to a Gaussian. Averaging repeated trials (i.e. averaging of multiple laser pulses) therefore results in a Gaussian distributed statistic. Using the Anscombe Transformation [4], we obtain the following relationship (where $X \sim \mathcal{N}\left(\mu, \sigma^2\right)$ is a gaussian distributed random variable with mean = μ and variance = σ^2) then $X \sim \mathcal{P}\left(\lambda\right) \Rightarrow 2\sqrt{X + \frac{3}{8}} \sim \mathcal{N}\left(2\sqrt{\lambda}, 1\right)$. Defining a new variable representing the Anscombe Transformed statistic $X' = 2\sqrt{X + \frac{3}{8}}$ the hypothesis test becomes:

$$\mathcal{H}_0 : X' \sim \mathcal{N}\left(2\sqrt{t\left(\lambda_0 + \lambda_{L(tissue)}\right)}, 1\right) \quad (1)$$

$$\mathcal{H}_1 : X' \sim \mathcal{N}\left(2\sqrt{t\left(\lambda_0 + \lambda_{L(tissue+tumor)}\right)}, 1\right) \quad (2)$$

The decision test is now defined as $\left(X' \lessgtr_{\mathcal{H}_0}^{\mathcal{H}_1} \gamma'\right)$. Using the test, a user-specified false alarm rate (α) determines the value of the threshold (γ') such that $P\left(X' < \gamma' \mid \mathcal{H}_0\right) \leq \alpha$.

2.2. Ballistic Imaging - K Points

The problem now is modified to trying to image a fixed square array of ($\sqrt{K}$ x $\sqrt{K}$) points. This results in a multiple hypothesis testing problem (K tests), and for large K it is difficult to control the overall probability of false-alarm (i.e., false tumor detection at one or more point). A standard technique is to increase the acquisition time (t) for each point, but by the setup of the problem increasing t will increase not only the number of signal photons, but also the number of noise photons. This puts a lower bound on the SNR of the observation. To boost the SNR, one could use spatial aggregation by averaging over a number of observation points. This modifies the problem to averaging neighborhoods of points in an area measuring $\sqrt{M}$ x $\sqrt{M}$, $M < K$, effectively reducing the spatial resolution of the detection map (image). By decreasing the spatial resolution, this also decreases the variance at each point, modifying the decision test to:

$$\mathcal{H}_0 : X' \sim \mathcal{N}\left(2\sqrt{t\left(\lambda_0 + \lambda_{L(tissue)}\right)}, \frac{1}{M}\right) \quad (3)$$

$$\mathcal{H}_1 : X' \sim \mathcal{N}\left(2\sqrt{t\left(\lambda_0 + \lambda_{L(tissue+tumor)}\right)}, \frac{1}{M}\right) \quad (4)$$

This test is under the assumption that the averaging window will contain either no occluder points or all occluder points. In reality, the averaging filter will result in an observed point: $X'' \sim \mathcal{N}\left(\rho E\left[X'|\mathcal{H}_0\right] + (1-\rho)\, E\left[X'|\mathcal{H}_1\right], \frac{1}{M}\right)$ (where ρ is the fraction of the window containing non-occluders). Our goal is to find the lower bound on the value of M that will guarantee an overall false alarm rate of less than α, we consider the ideal case (all occluders or non-occluders) in our calculations in order to obtain closed-form solutions.

2.2.1. Bonferroni Correction

The Bonferroni Correction approach is a conservative method of controlling the false alarm rate for a detection problem under multiple i.i.d. tests [5]. The correction adjusts the threshold for each individual test in order to satisfy a lower (per test) false alarm rate value ($\frac{\alpha}{K}$) such that each of the fixed number K-points in the array (and M-point averaging filter) satisfies $\left(P\left(X < \gamma' | H_0\right) \leq \frac{\alpha}{K}\right)$. With $\Phi(x)$ as the cumulative distribution function of the $\mathcal{N}(0,1)$ density at the point x, this results in $\left(\gamma' \leq \frac{1}{\sqrt{M}}\Phi^{-1}\left(\frac{\alpha}{K}\right) + 2\sqrt{t\left(\lambda_0 + \lambda_{L(tissue)}\right)}\right)$. To give a satisfactory observation, we also bound the miss probability for detecting a ballistic photon by the same modified value ($\frac{\alpha}{K}$) such that $\left(P\left(X > \gamma' | H_1\right) \leq \frac{\alpha}{K}\right)$. Using the miss bounds, we determine the lower bound on the necessary averaging window size (M) to image a fixed K-point array.

$$M \geq \left(\frac{\frac{1}{2\sqrt{t}}\left(\Phi^{-1}\left(1-\frac{\alpha}{K}\right) - \Phi^{-1}\left(\frac{\alpha}{K}\right)\right)}{\left(\sqrt{(\lambda_0 + \lambda_{tissue})} - \sqrt{(\lambda_0 + \lambda_{tissue+tumor})}\right)} \right)^2 \quad (5)$$

The minimum width of the occluding tumor ($w^t_{ballistic}$) that can be reliably resolved for a given parameterized turbid medium can now be derived. Using the lower bound for M found in Eqn 5, we can solve for the lower bound on the width using $w^t_{ballistic} = \sqrt{\frac{FOV*M}{K}}$. Due to M being a function of the tumor depth d^t, we can also numerical solve for the minimum tumor depth possible for a parameterized system.

2.2.2. False Discovery Rate

While the closed form resolution bounds for the Bonferroni Correction were derived, it is a very conservative approach and may obtain a poor reconstruction in order to avoid false alarm errors. To improve the reconstruction, we can increase the resolution by decreasing the M value (averaging filter size), and then use a modified False Discovery Rate (FDR) algorithm [6] for the multiple point test. To obtain the threshold, take the K number of observed signal values and determine the p-value (p_i) under each observed value (X'_i).

$$p_i = P\left(x < X'_i \,|\, \mathcal{H}_0\right) \quad (6)$$

$$= \Phi\left(\sqrt{M}\left(X'_i - 2 * \sqrt{t\left(\lambda_0 + \lambda_{L(tissue)}\right)}\right)\right) \quad (7)$$

To choose the FDR threshold (γ'), take the threshold corresponding to the largest index (n) such that $p_n \leq 1 - (1-\alpha)^{\frac{1}{K+1-n}}$. In practice, False Discovery Rate will result in a less conservative reconstruction, but it cannot be analyzed to obtain closed form bounds.

3. CONVENTIONAL IMAGING ANALYSIS

In the conventional imaging regime, there is no time-gating mechanism and all the photons that reach the detector over a long acquisition time will be observed (acquisition time $\gg \left(\frac{d}{c}\right)$ = direct line-of-sight flight time). Therefore, a large number of photons sent through the medium will be collected by the detector. A problem occurs here, too — while the signal-to-noise ratio is high due to the large number of photons, the average number of scattering events on each photon collected will also be high. As the number of scattering events increases for a photon, the less the photon will retain the spatial resolution of the occluding object. The lack of spatial information results in a blurred observation. Using random walk theory in [2], it is possible to solve for the minimum width of an occluding tumor that is reliably resolved using the conventional imaging regime. The width is found using the photon mean-time-of-flight $\langle \Delta t \rangle$, which can be numerically solved as a function of the parameters of the medium (μ_s^m, μ_a^m). The minimum width is equal to $w^t_{conv} = 0.408\left(\frac{\langle \Delta t \rangle c}{\mu_s^m}\right)^{\frac{1}{2}}$.

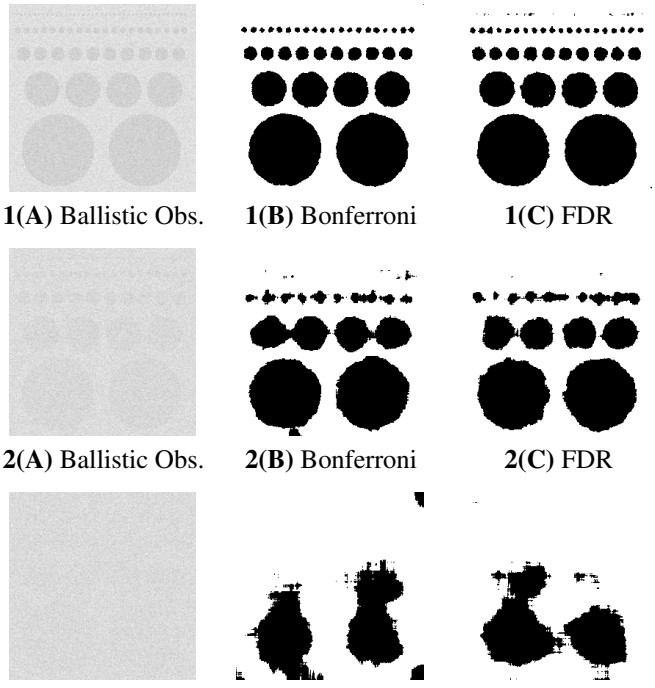
4. OPTIMAL RESOLUTION TRADEOFFS

Ideally, one should choose the imaging system (ballistic or conventional) that reliably resolves the smallest possible object ($w^t = \min\left(w^t_{conv}, w^t_{ballistic}\right)$). The decision test $w^t_{conv} \underset{ballistic}{\overset{conv}{\lessgtr}} w^t_{bal}$, using the minimum resolvable sizes derived above becomes: $0.408\left(\frac{\langle \Delta t \rangle c}{\mu_s^m}\right)^{\frac{1}{2}} \underset{ballistic}{\overset{conv}{\lessgtr}} \sqrt{\frac{FOV*M}{K}}$. Using the lower bound of M from Eqn. 5, one can solve for the critical distance ($d^m = d_{critical}$), the maximum distance at which ballistic still offers superior resolution relative to conventional imaging.

4.1. Simulation Study - Breast Tissue

We now present a simulation study of imaging malignant breast tissue through healthy breast tissue. For this simulation, a 10cm x 10cm FOV (as a K=256^2 point array) is defined with circular occluding objects of diameter 0.2 cm, 0.4 cm, 0.8 cm, 2.0 cm, and 4.0 cm. From [3], we use the scattering and absorption coefficients of the two tissue types. Using a specified depth of the occluding tumor (d^t=0.25cm) and false alarm rate ($\alpha = 0.05$), we solve for the minimum width of the occluding tumor under the ballistic observation

with Bonferroni Correction testing ($w^t_{bal(bon)}$, along with the size of the averaging filter M), and the conventional imaging observations minimum occluding width (w^t_{conv}). To obtain a better observation of the model, a higher resolution ($w^t_{bal(fdr)} = \frac{3}{4} w^t_{bal(bon)}$) observation using the False Discovery Rate (FDR) method was also simulated. Three medium distances ($d^m = 1.6, 1.7, 1.8$ cm) are used to show the effects that the distance of the medium has on the number of ballistic photons received.



1(A) Ballistic Obs. **1(B)** Bonferroni **1(C)** FDR

2(A) Ballistic Obs. **2(B)** Bonferroni **2(C)** FDR

3(A) Ballistic Obs. **3(B)** Bonferroni **3(C)** FDR

Figure 2. Simulations under FOV = 10x10cm, d^t = 0.25 cm (1) d^m = 1.6 cm, (2) d^m = 1.7 cm, (3) d^m = 1.8 cm

d^m	M	$w^t_{bal(bon)}$	w^t_{conv}	$pSNR_{bon}$	$pSNR_{fdr}$
1.6	31	0.217	1.012	15.52	16.34
1.7	301	0.678	1.04	11.27	11.33
1.8	3195	2.21	1.07	5.73	6.21

Table 1. Derived properties of the malignant/healthy breast tissue environment (distances in cm, pSNR in dB)

Figure 2 shows the effect of distance on the resolution of the observed image. One can observe the ballistic observation with Bonferroni Correction testing width size increasing dramatically as $d \rightarrow d_{critical}$ (numerically found here to be =1.73cm), this is due to the Bonferroni Correction being a very conservative estimate. For $d \geq d_{critical}$ one can observe that the conventional imaging observation performs significantly better than the ballistic observation under Bonferroni ($w^t_{bal(bon)} \geq w^t_{conv}$). As stated previous, the Bonferroni Method obtains a lower bound for the resolution of the observation while retaining the false alarm rate. Using the higher resolution False Discovery Rate (FDR) approach, we obtain a higher SNR than the conservative Bonferroni approach while maintaining the false alarm rate. A point of interest is that the filter window will generally contain both occluding and non-occluding points (non-ideal case), but this does not greatly degrade the reconstruction quality.

5. CONCLUSIONS

Using the decision-theoretic analysis approach, it is shown that the resolution of the turbid medium, the smallest reliably resolved object (in terms of the width w^t) for both the conventional imaging and ballistic regimes, can be derived. For the ballistic regime, a trade-off between resolution, distance, laser intensity and confidence level was shown. The ballistic regime was considered under two multiple hypothesis test method, the Bonferroni Correction and False Discovery Rate. Under the conservative Bonferroni Correction, the optimal choice between ballistic and conventional imaging was derived and can be used to find the best reconstruction technique for a given system as a function of the parameters of the medium. Using the False Discovery Rate approach, it was shown how to obtain a higher resolution observation while still maintaining a specified false alarm rate.

6. REFERENCES

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