Spectro-angular mapping of localized gold inclusions in Intralipid phantoms

Serge Grabtchaka\textsuperscript{a,b,c}, Tyler J. Palmer\textsuperscript{a} and William M Whelan\textsuperscript{a,d}

\textsuperscript{a}Department of Physics, University of Prince Edward Island, Charlottetown, PEI Canada C1A 4P3, \textsuperscript{b}Department of Electrical and Computer Engineering, Dalhousie University, Halifax, NS Canada B3J 1Z1, \textsuperscript{c}Department of Physics, Dalhousie University, 6310 Coburg Road, Halifax, NS B3H3J5, Canada \textsuperscript{d}Department of Biomedical Sciences, Atlantic Veterinary College, Charlottetown, PEI Canada C1A 4P3

ABSTRACT

We have applied an interstitial radiance-based technique based on a spectro-angular mapping approach to the identification and angular localization of 250-nm and 5-nm Au nanoparticle-based inclusions and non-scattering (water only) inclusions in the Intralipid-1\% liquid phantom. A combination of the point radiance spectroscopy and white light spectroscopy was used to measure angular resolved light distribution in 450-900 nm spectral range in Intralipid-1\% with and without localized inclusions. Characteristic spectro-angular snapshots of the liquid phantom alone and with the localized inclusions were obtained. For liquid phantoms without inclusions, the snapshots demonstrate wavelength dependent light distribution inside the turbid medium. For liquid phantoms with gold inclusions, the approach allows to isolate the spectroscopic signatures of the inclusions from the background, identify locations of the inclusions in the angular domain and show how a presence of water in the inclusion affects spectral identification and angular localization of the target. For liquid phantoms with water-based inclusions, an ability of the inclusion to enhance photon density above reference values and angular dependent signatures were demonstrated. The technique is seen as a potential tool in prostate treatment and diagnostics with gold nanoparticles.

Keywords: spectro-angular mapping, gold nanoparticles, voids, point-radiance spectroscopy, Intralipid, liquid phantoms, interstitial fiber-optic diagnostics, prostate, turbid media

1. INTRODUCTION

Optical diagnostics offers a number of advantages compare with traditional medical modalities: it uses non-ionizing radiation, provides biochemical information via spectroscopic identification, allows controlling light penetration depth in tissues via wavelength selection and (usually) offers more portable and less expensive technical solutions. In some cases, optical diagnostics can be performed in a non-invasive way by confining both illumination and detection to superficial layers. However, even with a few cm-penetration depths some regions in the human body are difficult to reach, and one has to resolve to interstitial illumination and detection while still attempting to minimize invasiveness. Bleeding that may result from interstitial applications can obscure efficient light delivery and strongly affect detected signals. Besides, the nature of light propagation in turbid media significantly complicates the ability to obtain local tissue optical properties of tissues from a single measurement. Hence, much research in the area of biomedical optics is looking to extract as much information as possible from of fewest possible interstitial measurements.

When it comes to interstitial light detection, it can be achieved via either fluence or radiance measurements. Fluence corresponds to light collection from the entire 4\pi solid angle. Radiance on the other hand, resolves the angular distribution of photons impinging from various directions on a selected point. Radiance requires a specially constructed fiber with a small well-defined angular aperture that must be rotated around its axis. The angular coordinate is an additional variable for radiance that is absent in fluence. While a single point fluence measurement produces a single (scalar) intensity value, single point radiance measurements can produce a set of intensity values for an entire 360-degree range (for in-plane measurements). Since radiance carries angular information, radiance set can be thought of as a vector field.

Gold nanoparticles (Au NPs) belong to a class of endogenous chromophores. For cancer applications, the use of Au NPs has advanced along four major fronts: 1) interstitial nanoparticle-mediated laser thermal therapy\textsuperscript{1}, 2) cancer
diagnostics via delineation of cancer affected areas with NPs conjugated to monoclonal antibodies\textsuperscript{2}, 3) enhanced radiation sensitivity and toxicity in prostate cancer cells containing Au NPs\textsuperscript{3}, 4) brachytherapy implants of radioactive \textsuperscript{198}Au NPs placed into a prostate gland to deliver the radiopharmaceutical dose directly to the tumor site\textsuperscript{4}. Whether one uses functionalized NPs with specific binding to tumor sites or non-functionalized NPs with preferential accumulation at tumor sites, the main challenge is “…the inability to visualize or quantify the global concentration or spatial distribution of these particles within the tumors”\textsuperscript{5}. Hence, for all applications an ability to identify, locate and quantify fixed loads of Au NPs in the prostate gland via non-invasive or minimally invasive methods is highly desirable.

The current work is devoted to applying an interstitial radiance-based technique based on a spectro-angular mapping approach to identification and angular localization of Au NP-based inclusions in the Intralipid-1\% liquid phantom. We present spectroscopic signatures of 250- and 5-nm Au NPs coloids by identifying Au and water presence and show how a presence of water in the target affects angular localization of a two-component target. By performing measurements on a target containing water only, we show what is a spectroscopic signature of water in water-based liquid phantoms. We demonstrate that the angular position of the water-based target can either increase or decrease photon density in Intralipid-1\% and analyze how it affects an ability to localize a non-scattering inclusion in the turbid medium. Intralipid-1\% was chosen as a background medium because its scattering properties are close to those of prostate.

2. EXPERIMENTAL

A detailed description of the experimental set-up has been published elsewhere\textsuperscript{6}. A blackened, 18 cm sided Lucite box was filled with Intralipid-1\%. A tungsten halogen white light source (20 W) was connected to a fiber terminated with an isotropic spherical diffuser. The total power output from the spherical diffuser was estimated to be ~18 mW. A side firing fiber (Molex/Polymicro Technologies) with a well-defined angular acceptance window (~10 degrees in water) served as a radiance detector. The side firing fiber was mounted on a computer-controlled rotation stage ensuring a full 360-degree rotation with a 2-degree step. The output of the radiance detector was connected to a spectrometer (USB 4000, Ocean Optics) for spectral acquisition. Signal averaging was based on four measurements at each angular step requiring approximately 10 minutes to acquire a single complete angular profile. Positions of both fibers and the tube were independently controlled in the X,Y-plane by three translation stages with a sub-mm positioning accuracy.

The positioning of the fibers/tube in the Intralipid-1\% phantom was chosen to mimic a prostate application in which the radiance detector is placed in the urethra, the diagnostic white light source is placed in the rectum and the Au NPs target is located at a peripheral zone of the prostate. This represents an idealized, minimally invasive approach to radiance-based detection in prostate, but at the same time, the extreme separations between the radiance detector and the Au NPs target (~2.5 cm) and between the white light source and the detector (~3 cm) corresponds to the most challenging scenario in terms of target detectability due to limited optical penetration in tissues.

Intralipid-1\% served as a background optically turbid medium. It was prepared by a volume dilution of Intralipid-20\% (Sigma-Aldrich) stock solution. While the scattering properties of the Intralipid-1\% are similar to those of human prostate, the absorption coefficient of Intralipid-1\% in the VIS-NIR range is in 0.01-0.1 cm\textsuperscript{-1} range that is somewhat lower than the absorption coefficient of human prostate. Two types of Au NPs were used: water-based 5-nm diameter Au colloid with a stock concentration of 5x10\textsuperscript{13} particles/mL and 250-nm diameter Au colloid with a stock concentration of 3.8x10\textsuperscript{8} particle/mL (Ted Pella). An inclusion was formed by filling a 3.5-mm diameter quartz capillary tube with ~0.7 mL of the solution and immersing the tube into the Intralipid solution. The immersion length was ~6 cm. Thus, the estimated maximum number of Au NPs contributing to the signal was ~3x10\textsuperscript{13} and ~4x10\textsuperscript{7} for 5-nm and 250-nm Au NPs correspondingly.

3. RESULTS

3.1 Spectro-Angular Mapping of Light Distribution in Intralipid-1\%

While angular light distribution in Intralipid-1\% has been discussed briefly in Ref.7 and in more details in Ref.8, we present here a succinct description that is essential for understanding first, the difference in the information content of spectro-angular maps of a homogenous medium and of a medium with a localized inclusion, and second, spectral signatures of the water based inclusion in Intralipid-1\% discussed in part 3.3. Spatial distribution of light inside turbid media is a wavelength-dependent quantity based on absorption and scattering by individual chromophores.

---

Downloaded from SPIE Digital Library on 14 May 2012 to 137.149.227.104. Terms of Use: http://spiedl.org/terms
Figure 1. a) Surface plot of $I_{\text{air0}}/I_{\text{Intralipid}}$ demonstrating extinction of Intralipid relative to air, b) same as a contour plot (both in log scale).

For radiance, spatial distribution is mapped in the angular domain. Individual spectral profiles of radiance measured every 2 degrees over 360 degrees, were combined into the Intralipid spectro-angular matrix $I_{\text{Intralipid}}(r, \theta, \lambda)$ with columns corresponding to wavelengths from 400 nm to 950 nm and rows corresponding to angles from -178 to 178 degrees. In a similar way the air matrix $I_{\text{air0}}(r, \theta, \lambda)$ was assembled in which the same spectrum of radiance measured at 0 degree in air was replicated for all rows (i.e., angles) with the subscript “0” emphasizing it. Constructing a ratio of these two matrices eliminates spectral responses from the white light source and illuminating and detecting fibers. This procedure is similar.
to referencing to a blank in spectroscopic measurements. While flipping the ratio will not change the referencing, it shifts the focus to different physical quantities. The ratio of $I_{\text{Intralipid}}(r, \theta, \lambda)/I_{\text{air0}}(r, \theta, \lambda)$ focuses on transmission properties of Intralipid, has a clear physical definition and corresponds to relative radiance that can be converted to the absolute value with a proper normalization coefficient. The ratio of $I_{\text{air0}}(r, \theta, \lambda)/I_{\text{Intralipid}}(r, \theta, \lambda)$ emphasizes attenuation of light in Intralipid, and is referred to in this study as the radiance extinction ratio. The ratio $I_{\text{air0}}(r, \theta, \lambda)/I_{\text{Intralipid}}(r, \theta, \lambda)$ is presented in Fig. 1 via surface (a) and contour (b) plots in a logarithmic scale for a 12-mm source-detector separation. In both plots regions of high extinction are marked by red color and low extinction by the blue. Fig. 1(a) demonstrates how the extinction varies with angle in Intralipid-1% with a clear visualization of the spectral content. In the spectral domain, the observed shape of the extinction ratio results from a combination of factors including Mie scattering in Intralipid and wavelength dependent absorption by lipid particles and water. In the diffusion approximation, these effects are combined in the effective attenuation coefficient.

Characteristic water absorption features a peak at 740 nm and a rising slope toward 1000 nm as clearly seen in Fig. 1(a). In the angular domain, the minimum of the extinction ratio occurs at a 0 degree angle that corresponds to the detector facing the source. Since Intralipid is well approximated as a homogenous medium with isotropic distribution of particles, the minimum of the extinction ratio is caused by the higher density of photons propagating in the forward direction (the anisotropy factor of Intralipid-1% varies from 0.87 to 0.64 in 400-900 nm range) and is not related to a presence of some structural inhomogeneity in the selected direction. Fig. 1(b) is a spectro-angular snap shot of light distribution in Intralipid-1% at a selected source-detector separation where contour lines of equal photon density delineate valleys and peaks.

![Figure 2. Spectro-spatial plot of variation (log scale) of $I_{\text{air0}}/I_{\text{Intralipid}}$ with distance at 0-degree normalized to the corresponding value at shortest source-detector separation (6.5 mm). Transparency window is shown by arrows.](image)

Interactions of photons with individual chromophores (lipid particles and water) under multiple scattering conditions make the spectro-angular plots distance dependent. As oppose to spectroscopic measurements of a purely absorptive sample, increasing the geometrical distance between the source and the detector under multiple scattering conditions leads to a nonlinear increase in the effective optical path and, as a result, drastic changes in a spectro-angular plot. A series of spectro-angular plots similar to the one shown in Fig. 1(a) were acquired at different source-detector separations (from 6.5 to 30.5 mm with a step of 5 mm). To assess distance effects, multiple spectra collected at selected angles were combined into spectro-spatial contour plots. An example of such a plot corresponding to $I_{\text{air0}}(r, \theta, \lambda)/I_{\text{Intralipid}}(r, \theta, \lambda)$ for 0 degree angle is shown in Fig. 2. For clarity, all data were normalized to the spectrum measured at the shortest source-detector separation (6.5 mm). Contour lines demonstrate a continuous spectral evolution with distance. The plot illustrates that the ratio of two spectra taken at different distances can produce quite different spectral content. With increasing the source-detector separation, photons interact with a larger volume of the medium.
that leads to an increase in absorption and scattering and as result, the overall radiance extinction ratio. In Fig. 2, a region of lowest extinction is within 500-700 nm and is called the transparency window (marked by arrows on the plot).

3.2 Spectro-Angular Mapping of 250-nm Au Inclusion in Intralipid-1%

The spectro-angular mapping approach introduced in the current work can be fully appreciated when applied to media with inclusions. Spectro-angular mapping doesn’t require \textit{a priori} knowledge of spectral characteristics of a localized chromophore, as opposed to our earlier approach\textsuperscript{6}. Instead, spectral properties of the inclusion in the presence of a background are visualized in the entire VIS-NIR range. In particular, radiance can localize the Au-based inhomogeneity via an extinction ratio approach that effectively cancels a contribution from the turbid medium and ensures that any constructed from the ratio signal must come from the presence of the Au NPs.

![Figure 3](image)

Figure 3. a) Raw non-corrected radiance measured in Intralipid (no target); b) raw non-corrected radiance measured in Intralipid with 250-nm Au NPs target at 0 degree; c) contour plot of radiance extinction ratio of 250-nm Au NPs target in Intralipid positioned at 0 degree; d) surface plot of plot radiance extinction ratio of 250-nm Au NPs target in Intralipid. All: source-detector separation 12 mm, detector-target separation 6 mm.

The extinction ratio approach relies on obtaining two data sets, for the phantom without the inclusion and for the phantom with the inclusion. In the first example the inclusion was 250-nm Au NPs in a 3.5-mm capillary tube positioned 6 mm away from the detector at one of selected angles (0, 45, 90, 135 and 180 degrees) when the source-detector separation was 12 mm. Data from radiance measurements in the phantom without inclusion were assembled into the Intralipid matrix, $I(r, \theta, \lambda)$ with columns corresponding to wavelengths and rows to angles. Raw matrix data (in counts per second, cps) are presented as a contour plot in Fig. 3(a). The detector registers the maximum signal (red
color) when it faces the source that corresponds to 0 degree on the plot. The spectrum seen on the plot is a result of a spectral response of the white light source modified by transmission of the illuminating and detecting fibers in addition to the optical absorption and scattering of Intralipid. Placing the target at a 6-mm distance from the detector along a 0 degree angle and repeating the measurements yields the Intralipid+target matrix, $I_{target}(r, \theta, \lambda)$ that is presented as a contour plot in Fig. 3(b). Because of a large dynamic range of raw signals (from ~200 to 56,000 cps), it is difficult to isolate the contribution of Au colloid in Fig. 3(b). However, taking a ratio $I(r, \theta, \lambda)/I_{target}(r, \theta, \lambda)$ eliminates contributions from Intralipid, white light source, illuminating and detecting fibers and produces a signal originated from the target (Fig. 3(c)). Hence, Fig. 3(c) represents a spectro-angular signature of a localized inclusion of Au colloid in Intralipid. Presenting such as the radiance extinction ratio in a form of a surface plot as on Fig. 3(d) visualizes the spectral content that allows for a clearer identification of 250-nm Au colloid absorption spectrum (see corresponding spectrum in Ref.6). As was discussed earlier, scattering from the background turbid medium overcomes scattering from Au NPs leaving absorption as the only detectable signature.

![Figure 4](image_url)  

Figure 4. Contour plot of radiance extinction ratio of 250-nm Au NPs target in Intralipid positioned at: a) 45 degrees; b) 90 degrees; c) 135 degrees; d) 180 degrees. All: source-detector separation 12 mm, detector-target separation 6 mm.

When the target is placed between the source and the detector, the greatest optical attenuation is expected to occur at a 0 degree angle (target’s location marked with a dashed line). However, the target is actually composed of two components (i.e., Au+water) with distinctly different properties not only from each other but from Intralipid-1%. Now 250-nm Au NPs have a characteristic absorption band around 500 nm with a scattering signature that has a maximum at 600 nm. Water is a non-scattering and weakly absorbing medium, while Intralipid-1% is a highly scattering medium that has absorption signatures of lipid particles and water. Water in the target leads to an increase in photon density behind the sample, while the presence of Au NPs leads to a decrease in photon density. Because the signal from the target is present in the denominator of the radiance extinction ratio, water would decrease and Au would increase the ratio.
relative to unity. (Note, that the extinction values <1 correspond to an increase of the signal relative to the reference.) When the contributions are approximately equal, the response will be almost flat on the angular axis as is seen in Fig. 3(c, d) when tracking the wavelengths in the vicinity of 500 nm. It makes problematic the accurate angular localization of the target. However, for wavelengths where the contribution of plasmonic absorption becomes almost negligible, the water signature is seen more clearly as a valley developing along 0 degree for 650-900 nm. It corresponds to a deep blue pattern in both Fig. 3(c) and (d) and allows for more quite accurate localization of the target around a 0 degree angle. In addition, the presence of water in the target is manifested via a characteristic feature at ~740 nm clearly seen in the spectral domain (Fig. 3(d)).

Fig. 4 (a, b, c, d) demonstrates spectro-angular contour plots of the radiance extinction ratio for the Au target located at 45, 90, 135 and 180 degree, respectively, while keeping the source-detector separation at 12 mm and the target-detector separation at 6 mm. The target location is marked with a dashed line on all plots. There is a good correspondence between the position of the line and the region identified by high extinction ratios. Water contribution no longer interferes with the angular localization of the target. Although a relatively broad angular signature and a shifted toward 0 degree light-green region seen in Fig. 4(a) for a 45 degree target location result from a residual water effect. Therefore, the angular location of the sample inside scattering medium can be identified even though multiple scattering is manifested via angular broadening of the inclusion’s signature.

3.3 Spectro-Angular Mapping of Water Inclusion in Intralipid-1%

The effect of water as a non-scattering component leads to a reduction in scattering and as result, an increase in photon density in this region. It is manifested as a dip or valley along 0-degree relative to backscattered photons. When water replaces the equivalent volume of Intralipid, it acts as an optical clearing agent or as a (non-scattering) void region. To isolate effects of water in the gold colloid, the experiments were performed with the target being a water-filled capillary. All other parameters and locations of the target were kept the same as in section 3.2. Contour and surface plots of the radiance extinction ratio for the water target located at 0 degree are shown in Fig. 5(a, b) correspondingly. The extinction ratio now spans a range from ~0.8 to ~0.95. It indicates that the radiance signal measured with the water inclusion inside Intralipid is always higher than the one measured for the blank Intralipid-1%. From the symmetry pattern of Fig. 5(a) it is evident that a possible ~10 degree sample misalignment or a backlash likely occurred during the scan. Note, that while the sample’s location corresponds to a 0 degree angle marked by a dashed line, the maximum extinction ratio is reached in the backscattering direction. Introducing the void region inside the scattering medium increases the photon density in all directions, however the biggest increase happens in the direction of the inclusion. It appears that one can achieve at least 8% photon density increase confined to the direction of the sample in the transparency window (500 nm - 700 nm).
Figure 6. Contour plots of radiance extinction of water target in Intralipid positioned at: a) 45 degrees; b) 90 degrees; c) 135 degrees; d) 180 degrees. All: source-detector separation 12 mm, detector-target separation 6 mm.

This may open interesting applications of void engineering by positioning artificial void regions in strategic locations inside turbid media that would support higher dosages of light delivery to targeted areas. For prostate applications, it would be interesting to explore the effect of small volume (<1 mL) interstitial saline injections on light distribution inside the organ. Fig. 6(b) emphasizes the spectral content of the contour plot. Because water is present both in the target and the background, it cannot be completely excluded in the ratio. Therefore, the ratio of two slightly different spectral profiles would exhibit a spectral profile similar to one obtained from a division of two spectra measured at different distances inside Intralipid, as in Fig. 2. Therefore, the spectroscopic signature of a localized water-based target inside water containing Intralipid-1% resembles a spectrum of Intralipid-1%, and it will vary with distance in a similar way as was discussed in section 3.1.

When the water inclusion is positioned off-axis, the effect of the enhanced transmission is not observed and the effect of the non-scattering target on the measured radiance extinction ratio becomes similar to the absorbing target. (Strictly speaking, the effect is still there but it has to be detected behind the target when the source, the target and the detector are on a straight line). In both cases the number of photons detected in the direction of the target is reduced due to locally reduced scattering or locally increased absorption. The spectro-angular snap shots of the water inclusion positioned at 45, 90, 135 and 180 degrees in Intralipid-1% are shown in Fig. 6 (a, b, c, d) correspondingly (all other parameters are the same as in the section 3.2). Let’s start from considering the plot corresponding to a 90 degree target location (Fig. 6(b)). The position of the sample marked with a dashed line coincides with the area of the maximum extinction. Since the main difference between the target and the background is in the reduction of scattering, this reduction will be manifested as an increase in the extinction ratio. Note, that the scale for the extinction ratio extends now to values >1 as for the absorptive Au NPs based inclusion. While translating the inclusion toward 180 degree position, the region of maximum extinction follows the location of the sample. Placing the water inclusion at a 45 degree
angle corresponds to some intermediate case between 0 and 90 degree snap shots. When moving the target from 0 to 90 degree position, the valley surrounded by two maxima has to transform to a single maximum in the direction of the sample which is quite a complex transformation. Hence, a 45 degree position corresponds to a case when two maxima are disappearing but the extinction along the sample’s direction hasn’t assume the maximum value yet. Such an intermediate target location presents a difficulty in identifying the angular position of the target.

3.4 Spectro-Angular Mapping of 5-nm Au Inclusion in Intralipid-1%

Even though an individual 5-nm Au NP has higher absorption efficiency than a 250-nm Au NP, the size difference is also responsible for orders of magnitude higher stock concentrations that translate to larger values of the absorption coefficient. Spectro-angular signatures of 5-nm Au NPs were detected using the same geometrical arrangements as described earlier. Positioning 5-nm Au NPs based inclusion 6 mm away from the detector at 0-degree angle resulted in contour and surface plots shown in Fig. 7(a, b). Because of higher concentration of 5-nm Au NPs, the effect of water was significantly reduced near the plasmon resonance (~520 nm). A clear maximum in the radiance extinction ratio was observed at 0 degree allowing unambiguous identification of the inclusion’s position. Still, the water effect is manifested as an appearance of the valley for wavelengths >650 nm with corresponding radiance extinction ratio values reduced to <1. An interesting transformation from a peak to a valley occurs along a 0 degree angle. Similar to 250-nm Au NP results, presence of water in the sample is identified via a feature at 740 nm in the spectral domain (Fig. 7(b)).

Contour plots for all other angles (-45, -90, -135 and -180 degrees) are shown in Fig. 8(a, b, c, d), respectively. One can notice a systematic up to ~30-degree offset between the position of the sample (marked by the dashed line) and the angle of the highest extinction ratio. This is the blurring effect caused by multiple scattering. The ratio approach used in the current work compares photon distributions in the vicinity of the sample with the one in Intralipid-1% with sample absent. Placing the sample inside Intralipid extends the perturbation beyond the physical dimensions of the sample. Photons that cross sample’s area (with the sample absent) can be found in a large volume around it. Introducing the absorption inhomogeneity is equivalent to tagging photons with nanoparticles by scavenging them from the cloud they would normally be present and forming the area of a lower photon density that is perceived as blurring or a shadow. Overall, even with the blurring effect one can identify a presence of Au NPs by their spectroscopic signature and locate their angular position in the angular domain. Also, the effect of water in skewing the symmetry pattern relative the angular position of the target is clearly seen for an intermediate angle of -45 degrees (Fig. 8(a)) while diminishing for all other angles.

The ability to identify and locate inclusions of Au NPs was tested at the most unfavorable conditions when the source-detector separation was increased up to 30 mm and the target was moved with 5-mm increments at -90 degree angle from 5 mm to 25 mm. In prostate geometry it would correspond to illuminating through the rectal wall and having the inclusion located at a periphery of the prostate. The evolution of spectro-angular snap shots included a gradual shift of the angle of the maximal extinction ratio from -90 degrees to -120 degrees, lowering the extinction ratio with distance...
and broadening the contour lines in the angular domain. The characteristic features are presented in Fig. 9 as a spectrospatial plot for -90 degree angle where spectral changes with distance are manifested via contour lines.

![Contour plots of radiance extinction ratio of 5-nm Au NPs target in Intralipid positioned at: a) -45 degrees; b) -90 degrees; c) -135 degrees; d) 180 degrees. All: source-detector separation 12 mm, detector-target separation 6 mm.][1]

Contour lines follow the spectrum of Au NPs that can be easily identified along Y-axis. This is an important because in contrast to Intralipid-1% and water-based localized inclusion, the spectral signature of Au NPs doesn’t change much with distance and can be considered as a distance-invariant feature. Contour lines are labeled with numbers that correspond to values of the radiance extinction ratio. Detectability can be evaluated by constructing a contrast or signal-to-noise ratio from the maximum and the minimum extinction ratio values in the angular domain for the selected wavelength. Translating the target from 5 to 25 mm with 5 mm steps at -90 degree caused the following changes in contrast values for 520 nm: 5 mm - 47%, 10 mm -11%, 15 mm - 4.8%, 20 mm - 2.1%, 25 mm -1.1%. Increasing the distance spreads photons over a larger angular range and increases a portion of backscattered light leading to lower contrast values. For comparison, the contrast values for 250-nm Au NPs discussed in section 3.2 are about 5% for 6-mm detector-target separation. The major difference is caused by a higher concentration (3x10^{13} particles/mL vs. 3.8x10^8 particle/mL) of 5-nm Au NPs in the target. The range of concentrations falls well within the clinically relevant values. For example, 100 μL of 2.4x10^{11} particle/mL were injected intravenously in hyperthermia treatment in mice. Given a size difference, the payload to canine and human prostate would always exceed this amount. We’d like to stress that the minimally detectable number of nanoparticles should be always considered in conjunction with a value of contrast achieved at a particular depth in a specific tissue.
4. CONCLUSIONS

We have introduced a radiance-based spectro-angular extinction ratio approach that is applied to study light distributions in both homogenous turbid media (Intralipid-1%) and turbid media with localized inclusions of Au NPs. When applied to homogenous turbid media, spectro-angular mapping demonstrates wavelength dependent light distribution in Intralipid-1% medium, visualizes the transparency window and illustrates a distance-variant spectroscopic signatures of Intralipid-1%. When applied to Intralipid with Au NPs inclusions, the spectro-angular approach isolates spectroscopic signatures of the inclusions from the background and maps them in the angular domain. Both 5-nm and 250-nm Au NPs can be identified by their characteristic plasmon absorption. For homogenous phantoms with an absorptive type localized inclusions (i.e., Au NPs), positions of high extinction regions in the angular domain map the angular location of the absorptive inclusion for all possible angular positions of the inclusion. For homogenous phantoms with a void type localized inclusions (i.e., water) at 0 degree, void’s signature is a region with a lowest extinction ratio (opposite to absorptive targets) that is responsible for up to 8% increase in photon density in the direction of the void. The detectability of Au NPs inclusions can be quantified by the contrast value or signal-to-noise ratio formed in the angular domain from the maximum and the minimum radiance values. The contrast value depends on a distance between the inclusion and the detector and can vary from 47% at 5 mm to ~1% at 25 mm in the Intralipid medium. The proposed method can be employed for in vivo prostate diagnostics and treatment.

REFERENCES


