The Philosophy of Laser Imaging

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Abstract. The philosophy of laser imaging first thought by the idea of visualizing the photon trajectories which are even seen by naked eyes when anybody looks inside to the photon diffusing object. If white light beams onto the imaging tissue, blood vessels can be seen by the naked eye from the tissue surface, roughly. One of the important biomedical molecular macroscopic imaging technique is the laser imaging. Most of the works cover research infrastructures, laboratories, and hospitals for diffuse optic laser imaging. Naturally, in most of the clinical applications, near infrared (NIR) laser is being used, since the main motivation trial is the cancer case, obviously. NIR laser helps to figure out hemoglobin content which uses the blood absorption maxima wavelength, hence in most of diffuse optic tomography (DOT) research, NIR laser is used. Most of the diffuse optic laser imaging technique are using low energy incident collimated isotropic un-polarized gaussian beam which is generated by semiconductor laser diode. Applied power is usually less than 10 mW/cm^2. At the beginning of the laser diffuse optic imaging (DOI) research era, most of the researchers have jumped into the research without reading and understanding the limitations of the modality. Low energy light has some restrictions, the most important is the scattering nature of the light depend on the tissue type. However, some tissue types such as cerebrospinal fluid has low optic scattering coefficients. Another important factor besides the scattering, caused by low energy, hence photons are penetrating only superficially. Photons are scattering much and penetrating only superficially. On the other hand, if x-ray bremsstrahlung photons were used, it would go deeper tissue layers, nevertheless it becomes ionized radiative light. The philosophy of laser diffuse macroscopic molecular imaging modality is covering scattering of light, therefore device concept should be thought according to this phenomenon, source and detector placement should be arranged based on this truth. In this review paper, the philosophical concept will be evaluated for laser imaging.

Keywords: Biomedical Imaging; Diffuse optic tomography (DOT) technique; transmission through; back-reflected; cylindrical ring; Continuous Wave (CW); Frequency Domain (FD); Time Resolved (TR).

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1. INTRODUCTION

Light penetrates inside the tissue under the natural rule of the universe. Two basic properties of tissue-light interaction are the key factors depend on the light's penetration ability. In our case, the actor is the low energy, low power, un-polarized collimated isotropic gaussian semiconductor laser diode specific wavelength beam. White light is covering all the visible spectrum between 350 - 750 nm wavelength. Light penetration from tissue surface can be defined based on the physical formulas. The two basic properties of the photon-tissue interactions are absorption ($\mu_{a)}$ and scattering (μ_s) coefficients, which are the key elements that affect the light's penetration ability. Depending on the tissue type, light will scatter more or less. For example, light scatters less in cerebrospinal fluid (CSF) than many other types of tissue. At the beginning of the diffuse optic imaging (DOI) research era, illumination using by an electrical white light bulb was performed for breast imaging [1]. In the history of the DOI technique, important developments for optical source and detector technology were done, however these technologies are still not reliable. It has low level imaging spatial resolution and accuracy. On the other hand, researchers are always interested to work in the field of DOI techniques, since it is possible to make it easy-to-transport, cheap, low-energized, light handheld imaging devices and it is not harmful to body as the other techniques that could be producing harmful ionization effects. Besides advantages, DOT or DOI techniques have been struggling for lack of technological improvements and novel philosophical ideas. New technologies are needed to overcome scattering problem of low-energized laser photons. Some researchers focused on mathematical solutions [2-5]. Positron emission tomography (PET) and other nuclear imaging techniques, x-ray imaging are still superior over light imaging technique, since it is not reliable because of very low level of imaging contrast. On the other hand, researchers are always interested to work in the field of DOI techniques, since it is possible to make it easy-to-transport, cheap, low energy consuming, light handheld imaging devices and it is also not harmful to body, because it is non-ionizing imaging technique. Beside the lots of these advantages, DOT and DOI techniques struggle for lack of improvement and novel philosophical ideas. Novel technological developments are needed to overcome scattering and low energy nature of existing imaging systems.

Without thinking the real disadvantageous of penetrating light, some researchers have spent their more than two decades, just for trying to solve DOT problem by mathematical methods such as in [2-6]. Some others tried to solve the DOT imaging problem by using statistical methods, they called the methodology's name statistical high-density method, since they were using too many source and detector couplings [7]. The real scattering problem was sitting over there, and they were just moving around it. They are waiting for novel technological developments. However, the existing works, are mostly connected to breast and fetal or newborn brain imaging studies. This review is not covering the microscopy such as two photon or multiphoton microscopy, nor optical coherence tomography (OCT) techniques. Because these methods are exempting scattering events, and they are only effective for imaging the superficial layers. The photon-tissue interactions have been studied and investigated for depth analysis, since the scattering events start

beyond the 1-1.5 mm, diffuse optic imaging (DOI) modality is suffering for low spatial resolution and depth analysis. If researchers want to work for DOI methods, he/she should accept that scattering event will dominate his/her research and spatial resolution or image contrast will have low quality. They want to keep working in this area without attempting to discover novel ideas or philosophies, new engineering approaches, technological developments. Theoretical works in area of philosophical aspects of physical thoughts might help them to solve problem and it can give them scientific opportunity for new inventions.

2. DOI IN CLINICAL APPLICATIONS

2.1. INSTRUMENTATION

DOI imaging became a routine undeveloped scientific research tool for researchers and clinicians in entire academic world. Device instrumentation of DOI constitutes electronic, optic, and mechanical parts. Different device types were made [8-31]. The second part of DOI modality is the mathematical inverse problem solution algorithms or image reconstruction [32-45]. In clinic, laser imaging has been used, mostly to detect breast and newborn brain blood hemoglobin (Hb), and oxyhemoglobin (HbO_2) concentration differences over homogeneous tissue types. In general form, name of the differences is usually called by perturbation. Perturbation is the natural logarithmic of the division of two different experimental measurements with inclusion and non-inclusion, with blood and non-blood for brain imaging, with carcinoma and non-carcinoma for breast imaging. For brain imaging Hb and HbO_2 change is the interested change by measuring absorption coefficient (μ_a) differences between two different imaging geometry. Sometimes fingering activation is requested from patient. Between two consecutive event which first one is sitting, waiting and the second one is the fingering causes blood level oxygenation; thus, the perturbation measurement data occur between two consecutive events. Measurement system is the instrumentation device which might use different running procedure modes such as Continuous Wave (CW), Time Resolved (TR) or Frequency Domain (FD) modalities. In all of these experimental measurement setups, sources and detectors are located around circular ring, rectangular back-reflected plane, or rectangular slab transmission geometry. They can also be arranged like rotated fan-beam projectory shape. Rotation procedure is increasing the number of source-detector matches. Some researchers are curious to make DOT system more sophisticated and high density. But the meaning of high-density is not the real meaning of it, since the obscuring problem is still there and sitting which was previously mentioned is scattering event, and of course superficial low energy photons are affected much. More source-detector matches bring more equation in the forward problem model. For example, if you had an experimental measurement device setup, which has 63 sources and 63 detectors, then this system would produce 63*63=3969 equations in mathematical forward problem model. If someone can rotate this device by 1 degree in circular ring mode, the device will produce 360*3969=1428840 equations

unless they overlap previous source-detector matches. Forward problem model is the summarization of the diffuse photon behavior for specific tissue imaging medium which has definite number of source-detector couplings (with rotating procedure or not). Basically, weak energy collimated isotropic unpolarized gaussian beam photons are behaving based on the physical radiative transport equation (RTE), or diffusion equation (DE) which connects first order time derivative of concentration to second order distance derivative term of concentration. DOT imaging is divided into two different groups; these are forward and inverse problems. In the forward problem model, photon fluence distributions are calculated for specific source and detector matches and related instrumentation geometry. RTE defines light distribution. It is not possible to solve RTE equation by differentially. It should be solved by analytic methods. For the simplicity, diffusion approximation to RTE is used. For the diffusion approximation source-detector distance (SDS) should be minimum 3 mm, and scattering coefficient (μ_s) should be at least second order greater than absorption coefficient (μ_a). To linearize second order diffusion equation, Rytov or Born approximation is applied to DE. Finally, Green function makes the equation system linear and numerical.

$$\begin{bmatrix} \phi_{sc}(r_{s1}, r_{d1}) \\ \phi_{sc}(r_{s1}, r_{d2}) \\ . \\ . \\ \phi_{sc}(r_{si}, r_{dj}) \end{bmatrix} = \begin{bmatrix} w_{1,1;1} & w_{1,1;2} & . & . & . & .w_{1,1,n} \\ w_{1,2;1} & w_{1,2;2} & . & . & . & .w_{1,1,n} \\ . & & & & & \\ . & & & & & \\ w_{i,j;1} & w_{i,j;2} & . & . & . & .w_{i,j,n} \end{bmatrix} \begin{bmatrix} \delta\mu_a(r_1) \\ \delta\mu_a(r_2) \\ . \\ . \\ \delta\mu_a(r_n) \end{bmatrix} \qquad \text{Eq. 1}$$

In the matrix format, equation system has perturbation data on the left hand-side of matrix, *w* forward problem model weight matrix has *i* source and *j* detector, and *n* voxels, and the final column has *n* rows, which has *n* unknowns over homogeneous tissue medium. This is the forward problem model of DOT modality. The $\delta\mu_a$ unknowns are solved by applying mathematical inverse problem solution image reconstruction algorithms. Inverse problem solution algorithms might be back-projection such as iterative algebraic methods, Algebraic Reconstruction Technique (ART), Simultaneous Iterative Reconstruction Technique (SIRT), or subspace methods such as Conjugated Gradient (CG), Singular Value Decomposition (SVD), Truncated Singular Value Decomposition (TSVD) or regularization methods such as Tikhonov & Morozov Discrepancy regularization method. The perturbation data is generally generated in Continuous Wave (CW) mode. In CW mode, low power semiconductor laser diodes are connected to the device instrumentation system, then laser is optically switched between source positions by electro-mechanic optic switches. Some systems are using frequency modulated (FM) laser sources. Some systems are also using very sensitive time resolved (TR) picosecond (ps) or femtosecond (fs) semiconductor laser systems such as Titanium Sapphire (TiSa) lasers. TR systems are using very expensive photo-multiplier

tubes (PMTs) or relatively cheap single photon detecting avalanche photodiodes (SPDAD) and vertical cavity surface emitting lasers (VCSELs).

2.2. IMAGE RECONSTRUCTION ALGORITHMS

Diffuse optic laser imaging systems are many photon systems. It is the macroscopic molecular imaging technique. It does not depend on the single or couple photons like two-photon microscopy, optical coherence tomography (OCT), or optical holographic imaging microscopy systems. These microscopic systems are cellular specific imaging modalities hence; they are imaging superficial layers such as skin tissue imaging. Microscopic imaging systems have real biophotonic pictures, on the other hand macroscopic biomedical imaging modalities such as diffuse optic laser imaging modality has computer-based reconstructed images. First, forward problem model is built, then unknowns are solved by using mathematical inverse problem solution algorithms. Forward problem model has photon fluence distribution multiplications between source and detector positions inside the imaging tissue medium. From the source positions, photons penetrate inside the imaging tissue medium, there are huge number of photons at the beginning of the penetration, then photons are scattered and absorbed by the imaging tissue molecules, less number of photons are left behind when they become close to detector points. However, there exists even less number of photons, the distribution of photons has the same percentage with the around of source positions, since the photons escape the tissue into the detector with the same angles as they penetrate from the source position. After building the forward problem model weight matrix, then mathematical inverse problem solution algorithms should be applied. These are grouped into three subsections. They are all known as inverse problem solution image reconstruction algorithms in literature. The unknowns are tissue absorption differences of heterogeneous tissue voxels over homogeneous tissue voxels. Once the unknowns are solved by mathematical inverse problem solution algorithmic methods, then the voxels are assigned into color codes, and images are reconstructed for semi-infinite imaging tissue medium. First group is the iterative back-projection solution methods, some famous forms are algebraic reconstruction technique (ART), simultaneous iterative reconstruction technique (SIRT) methods. The second group is the sub-space method; most famous of them are Conjugated Gradient (CG), Singular Value Decomposition (SVD), and Truncated Singular Value Decomposition (TSVD) methods. Finally, in the real-world application there are always electrical noises, photonic artefacts and, such that perturbations data, which were generated by experimental measurements, might have been inconsistent. In this situation, mathematical regularization inverse problem solution methods are used, the famous one is Tikhonov & Morozov discrepancy regularization method.

3. RESULTS and DISCUSSION

In this review, general prospectus of diffuse optical laser imaging modality was assessed. In the past 3-4 decades, firstly, researches are accelerated by the academicians and startup companies, but then it has slowed down, since diffuse optic imaging (DOI) modality gave to the researchers more struggling hard time. Scattering nature of low power photons gave obstacles in front of the modality. Despite the fact that there were big difficulties, some researchers insisted to keep go on. In this review, to respect these researchers and search area, diffuse optic laser imaging modality was summarized, based on the philosophy, physics, instrumentation, mathematical solution image reconstruction methods.

4. CONCLUSION

Laser imaging modality philosophical concept was reviewed. Research activity almost stopped, since it needs technological development, and novel ideas. Almost 3-4 decades passed; but no significant research development has been achieved. There is still lack of important achievement. A big gap is showing itself, if someone choose to look inside the DOI modality. However, some clinicians are choosing as a research tool diffuse optic laser imaging tools for their scientific contributions. It is not easy to find practical approach for this field, since basic scientific research achievement is necessary. It will build the new philosophical perspective. Because existing methods are using the same ways and they are all stuck at the same scattering event, unfortunately. New philosophical methods should be established.

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Macroscopic laser imaging device prototypes have been made and research activities are still trying to go on. Novel discoveries and philosophical thoughts are necessary for this area.

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