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LAMINAR OPTICAL TOMOGRAPHY (LOT)-A NEW REVOLUTION.

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ABSTRACT

Laminar optical tomography (LOT) is an optical imaging technique capable of making depth- resolved measurements of absorption and fluorescence contrast in scattering tissue. The technique combines a non-contact laser scanning geometry, similar to a low magnification confocal microscope, with the imaging principles of diffuse optical tomography (DOT).

KEYWORDS: Tomography, Optical, Confocal, Microscopy, Imaging.

INTRODUCTION

The ability of light to probe biological materials stems from the numerous interactions light undergoes with its environment. In biological tissues, these interactions include, among others, absorption, scattering, and fluorescence. While scattering can be used as a source of optical contrast, it also presents a significant challenge to optical imaging as it limits the penetration depth of optical techniques by attenuating light and introducing uncertainty in the path that the light travels. In the past few decades, advanced

optical imaging techniques have been developed to exploit the value of optical contrast while maximizing resolution and penetration depth. Techniques such as confocal microscopy offer increased resolution and contrast (compared to conventional fluorescence microscopy) by rejecting out of focus light while techniques such as diffuse optical tomography push the penetration depth of optical imaging through innovative instrumentation and advanced tomography algorithms.

Laminar optical tomography (LOT) was developed to record depth sensitive measurements of light in order probe optical properties of tissues beyond the depths of conventional microscopy and with resolution exceeding that of diffuse optical techniques. The technique relies upon scattering to collect backscattered light and is sensitive to absorption and fluorescence contrast.

As light travels through biological tissues, several light-tissue interactions may occur, including absorption, scattering, and fluorescence. The degree to which these interactions occur is governed by the optical properties of the tissue with local differences in optical properties serving as the source of contrast in optical imaging.[1]

Optical imaging provides unparalleled sensitivity to functional parameters such as hemoglobin oxygenation, membrane potential and metabolic processes. In-vivo optical imaging of superficial tissues using CCD cameras has provided valuable insights into the underlying physiology of both healthy and diseased tissues. Laminar optical tomography is a new optical imaging modality which allows high-resolution, depth-resolved optical imaging of tissue to depths of >2mm, with resolution of 100- 200 microns, at the frequency of approximately 8 Hz frame rate.[1] It is a completely non-contact technique so additional imaging or point measurement can be made simultaneously such electrophysiology recordings or speckle flow imaging. LOT measures light that has emitted from the tissue at some distance offset from the source position. Confocal Microscopy measures ballistic light, limiting its penetration depth but allowing high resolution imaging.[2] DOT detects diffuse light, allowing it to probe deeper into the depths but with poorer resolution. The light measured by LOT is from the region in tissue in which light has multiply scattered but is not yet diffuse. By measure this light, LOT offers a compromise between the two techniques: providing proper penetration than confocal microscopy and higher resolution than the DOT.[3]

OPTICAL DESIGN

LOT uses a system similar in design to a confocal microscope, raster scanning a focused laser beam over the surface of the tissue being imaged. It detects both confocal and multiply scattered light. Light that emerges light that has been multiply scattered emerges a distance away from the focus of the scanning spot. The further away that the light emerges, the deeper on average it has travelled. LOT measures the scattered light at 7 different distances away from the scanning point.[4] LOT has seven different pieces of information for each spot scanned, each with differently weighed depth sensitivity. These measurements are combined with an image reconstruction algorithm which incorporates a mathematical model of light propagation in scattering to convert raw measurements into 3D IMAGES. In the confocal type design light from one of the two lasers is emitted from the optical fiber and collimated. This light passes through a polarizing beam splitter and onto galvanometer scanning mirrors which steer the collimated beam through a scan lens. The scan lens focuses the beam at an intermediate image plane, which is imaged onto the surface of the tissue using an objective lens. Light being remitted from the tissue then passes back through the objective, through the scan lens and is de-scanned by the galvanometers. Since the incident laser lights are strongly polarized, specular reflections from optics and from the surface of the tissue will maintain this polarization.[5]

OCT is an important tool for depth- resolved imaging of living tissue, and is capable of penetrating beyond a millimeter into the scattering tissue with very high resolution. It suffers from poor sensitivity to absorption contrast, and cannot be used to measure fluorescence contrast. This is because OCT deliberately isolates only coherently backscattered light.[6] LOT can image both absorbing and fluorescent contrast and is hence strongly sensitive to parameters such as haemoglobin oxygenation and can be used to image molecular and environment sensitive fluorescent probes.[5]

IMAGE RECONSTRUCTION

The probable paths travelled by light in scattering tissues can be stimulated using radiative transport equation. Diffuse optical tomography is an established technique for imaging large volumes of scattering tissue using near infrared light. LOT uses similar image reconstruction approaches as DOT with main difference that LOT cannot use diffusion approximation to RTE, since the length scales considered are comparable to the scattering length of the tissue, and at visible wavelengths, absorbtion is more higher than NIR wavelengths.[7]

LOT has lower resolution than conventional scanning microscopy methods and OCT, it has the advantage that there are no significant physical limit to its depth sensitivity. It also has the advantage of being highly sensitive to both absorption and fluorescence contrast.[4]

INSTRUMENTATION

The incident light is shown as solid lines originating from an optical fiber. The light is collimated and passed through a beam splitter before being reflected by a set of galvanometer mirrors (Figure 1). These mirrors are computer controlled to raster scan the beam. The beam then passes through a scan lens, collimator detector lens detector image plane x-galvanometer y-galvanometer scan lens mirror microscope objective intermediate image plane sample plane beam splitter laser photodetectors which convert the angular deviation of the collimated light into lateral translation of the scanning spot.[8]

LOT was the first demonstrated in 2004 by Hillman et al where it was shown that the technique could allow high- resolution 3D imaging in a scattering medium over depths of 0-2.5 mm. it was limited in its speed, signal to noise, and was unable to image multiple wavelengths and florescence in parallel.[5]

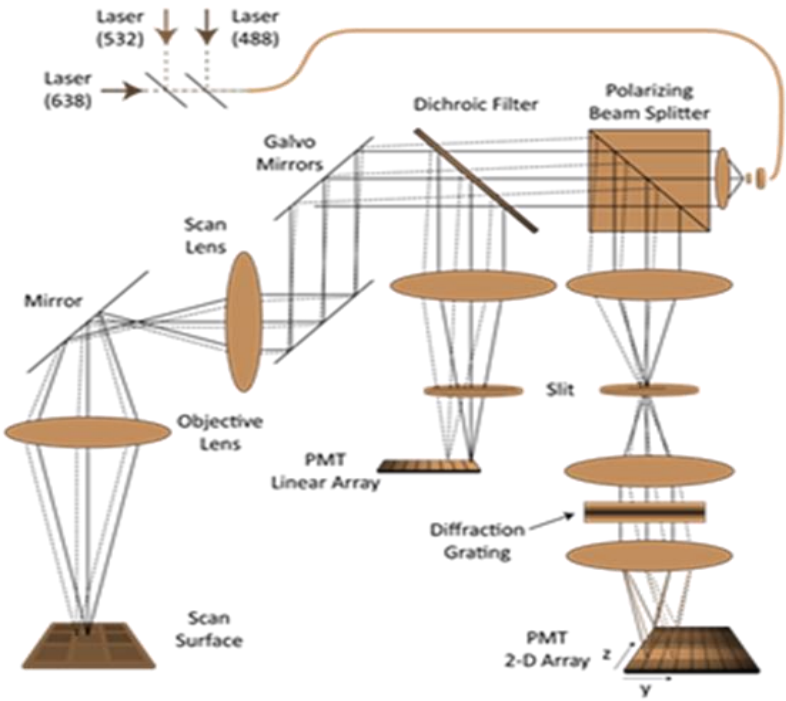

Figure 1: Basic design of an LOT system-Galvanometer mirrors raster scan a focused spot over the sample plane. On axis and off-axis light are de-scanned by the galvanometer mirrors and measured using multiple detectors.

APPLICATIONS OF LAMINAR OPTICAL TOMOGRAPHY

The advances made to LOT overcame the shortcomings and improves upon many other aspects of the system including faster acquisition rate, larger field of view, and higher measurement density. It is better suited for in vivo imaging as it can capture faster responses, measure additional sources of contrast and have fewer motion artifacts.[9]

LOT imaging of skin cancer could provide valuable information for skin cancer screening and treatment planning. The ability of LOT to probe beyond the dermal epidermal junction could reveal changes in vasculature beneath lesions which could help deter dermal invasion has occurred or assist in the excision margin determination. The depth sensitive measurement could help determine the lesion depth, an important prognostic factor and parameter for surgical planning. Further it can be used for selecting a region to biopsy within larger lesions.[10]

CONCLUSION

LOT is a new technique for medical imaging, allowing high resolution imaging to depths much greater than possible with microscopy, and with enhanced sensitivity to absorption and fluorescence compared to OCT. Currently the studies of vascular dyanamics using a self-built video rat two photon microscopy systems are being extended.[11] In addition studies are being performed to allow the comparison of these results with those functional MRI to investigate the impact of our observations on interpretation of high blood oxygen level dependent signal. Plans are being made to extend these studies by investigating neurovascular coupling in 3D.[12]

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