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A Brief Review of Biomedical Optical Imaging towards Clinical Applications

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Abstract: ***Biomedical optical imaging, recently, has been developed to be useful tools for clinical applications in diagnostics. A number of works based on uses of optical and laser techniques to solve the difficult problems in medical and biological studies were proposed. Under investigation of light propagation in biological tissues, various optical techniques have been demonstrated their capabilities in clinical applications such as diagnostics. The model of light propagation in biological tissues or conversion of light energy to acoustics is beneficial to the imaging reconstruction. These techniques currently employed and replaced conventional techniques in hospital gradually and will be the essential tools for biomedical researches.***

Keywords: Biomedical optics, Vietnam, review, laser, clinical applications..

1. Introduction

Biomedical optical imaging is termed in 90s decade of the last century mentioning to an interdisciplinary field included optical techniques applied to medical and biological research and applications [1]. Since the drawback of the risk from the ionized radiation [2] to the living body and the low resolution [3] in the image generated by the large wavelength waves, the light is highly interested to replace the conventional techniques. The light is known as the physical energy characterized with the low risk of ionization and short wavelength wave, thus provides the good resolution image [4-7] and high safe [8] for investigation of living. However, because of the short wavelength of the light, the scattering phenomenon restricts the penetration of the light into the biological systems, being the cause of the spatial information loss and the difficulties of the reconstruction for optical images as well [1]. To solve this problem, for optical imaging, a number of studies attempted to extract the spatial by photon tagging with modulation or light propagation modelling as well as conversion of the light energy to other physical energy which has lower scattering property than the light [9]. However, in practice, the biomedical optical imaging still strange for medical doctors and biomedical engineers so far, thus their applications to clinical operation do not consider yet. To boost up these techniques to medical and clinical applications, this paper briefly introduce to the principle of optical imaging techniques applied to diagnostic applications. Based on these review of the operating principles of the biomedical optical techniques, the biomedical optical imaging techniques can use for pathology examinations as well as the visualization of biological functions and toward the development for clinical applications in hospitals.

2. Principle of Optical Imaging Techniques

Optical imaging is an interested category in biomedical applications since it provides a visualization of the anatomy organs in living bodies. By the depth of the light propagated in the biological tissues, the images of the tissues benefits to the distribution of optical absorption and reemission light leading to support for the biological functions observation, the useful tool for diagnostics as well. Because of the biological tissues light scattering properties, the photons usually penetrated throughout the biological tissues with zigzag trajectories traced by multiple random walk steps. Since the optical image is the term related to the spatial information of optical objects but the optical paths of the penetrated photons traced as random trajectories, almost of the biomedical optical imaging techniques focus on the efforts of identification or tagging the photons providing the positions of the light sources.

3. Optical Coherence Tomography

One of the methods to extract the position of light source in biological tissue based on optical absorption measurement is firstly proposed by Fercher et al. in 1986 with an optical application system suggested from idea of Michelson interferometer [4, 5]. In 1993, this technique is developed and used to reconstruct the image for retina observation in vivo introduced and termed as optical coherence tomography (OCT) by Fujimoto [6]. The sample is illuminated by the photons from the light source and scattered. In the light scattering processes, there are number of photon return to backward direction called back scattering while the others is traced in forward direction named as forward scattering. For the imaging, the positions of the back scattering photons from the biological samples are identified by interference with a light source from the referent mirror set at a constant distance. The pattern of the interfered light distribution obtained by measurement through a photo-detector present the distribution of optical absorption. Therefore, the light distribution pattern provides the image of the biological tissue layers. The mathematical model of the light interference is expressed by Eq. 1 [10]

$$I(t) = E_{R0}^2 + E_{S0}^2 + 2E_{R0}E_{S0}\cos(\Delta\varphi), \quad (1)$$

where E_{R0}, E_{S0} is the amplitude of electric field of the illuminated light and reflected light and $\Delta\varphi = 2(k_s l_s - k_R l_R)$ with k_S, l_S, k_R, l_R is the wave number and distance measured from the splitting point at the beam splitter to the back reflection surfaces of the light source and sample layer, respectively. The back scattering photon usually occurred with few millimetre depth, thus the parameter k represents the light propagation velocity or refractive index can be neglected. Hence, the Eq. 1 can be reduced to

$$I(t) = E_{R0}^2 + E_{S0}^2 + 2E_{R0}E_{S0}\cos\left(4\pi\frac{n\Delta l}{\lambda_0}\right) \quad (2)$$

where λ_0 is the wavelength of the illuminated light and reflected light as well, n is the refractive index of air or vacuum approximately and $\Delta l = l_s - l_R$. Because of the identification by the interference, the light source illuminated to the biological sample should be coherence. With each layer of the sample, present a distance l_R, therefore images of multilayer of the biological sample can be observed. This explains why the optical imaging named as optical coherence tomography.The OCT can be measured in both time domain and frequency domain and called as time-domain optical coherence tomography (TD-OCT) and fourier-domain optical coherence tomography (FD-OCT), respectively. In the case of measurement in time domain, Eq. 2 will be used while in the FD-OCT applications, the Eq.2 is transferred to frequency domain by fourier transform to be [11]

$$I(k) = E_{S0}^2(kc) \times \times \left(1 + 2\int_{-\infty}^{+\infty} cos\left(2k(n_S\Delta l)\right)dl_s + \left|\int_{-\infty}^{+\infty} e^{i2kl_S n_S} dl_s\right|^2\right) \quad (3)$$

where $k = \frac{\omega}{c}$ with c is the light velocity in the media. The TD-OCT and FD-OCT provide the information of the optical absorption values and the optical path length of each reflected sources in the biological tissues since the measurement in time and frequency domain can return the amplitudes and phases of the reflected photon streams. Beside the optical absorption property, the optical polarization property of the biological tissue also characterizes the abnormality of the biological tissues and cells, therefore benefits to diagnosis as well. To solve this problem, a development called Mueller OCT was proposed by Wang et al. in 2000 (ref). The reconstructionfor the image is calculated with use of Stoke vector. The OCT technique provide very high resolution image because of the interference pattern in light wavelength thus called microstructure visualization, however, since the light penetrated into the biological tissues scattered and highly lost spatial information after few millimetres tracing. Therefore, this technique is applicable for observation of the intravascular or soft tissue with few millimetres depth from the outer surfaces of epidermises such as retina examinations.

4. Diffuse Optical Tomography

Because of limitation of the penetration depth in OCT technique, the investigations applied to deep soft tissues are not able to be satisfactory. To solve the problem of identification for the photons in the high coefficient light scattering of the biological tissues, the mathematical model of the light propagation in turbid media can be considered. Based on this idea, in 1992, O'Leary et al. proposed a model of light propagation in biological tissues with a consideration of the light propagation processes similar to the heat transfer derived and termed as radiative transfer equation (RTE) as [12].

$$\frac{\partial L(\vec{r},\hat{s},t)}{c\partial t} == -\hat{s}\nabla L(\vec{r},\hat{s},t) - (\mu_a + \mu_s)L(\vec{r},\hat{s},t) + \mu_s\int_{4\pi} L(\vec{r},\hat{s},t)P(\hat{s'},\hat{s})d(\Omega) + S(\vec{r},\hat{s},t) \quad (4)$$

where $L(\vec{r},\hat{s},t)$and $S(\vec{r},\hat{s},t)$ represent the radiance and photon sources in direction $\hat{s}$ at position $\vec{r}$ and time point t; the μ_a and μ_s are the optical absorption and scattering coefficients, respectively; the term $P(\hat{s'},s)$ is the phase function mentioning to the scattering direction or the deflection between $\hat{s'}$ and $\hat{s}$. However, there are six independent variables appeared in this equation leading to difficulties of the equation solving. To solve this equation, a number of the independent variable reduced by the assumption of isotropic media and the time for photon traverse is neglected, thus, with the application of Fick law, the RTE equation is reduced to Helmholtz equation as [13]

$$\frac{\partial\Phi(\vec{r},t)}{c\partial t} + \mu_a\Phi(\vec{r},t) - \nabla\left[\frac{1}{3(\mu_a+\mu_s)}\nabla\Phi(\vec{r},t)\right] = S(\vec{r},t) \quad (5)$$

where the $\Phi(\vec{r},t)$ denote the intensity of the photon stream. Based on this equation with consider the measurement in time or frequency domain as well as continuous modes, the light scattered intensity pattern can be visualized. The Eq. 4 also called the forward problem model of the light propagation in biological tissues. With the optical absorption and scattering coefficients are constant the map of light intensity distributed in biological tissues will be extracted. If the light intensity values can be measured by optical device, the map of μ_a and μ_s values distributed in biological tissues can be estimated as well. Therefore, this solution might be applicable to optical imaging technique to observe the optical properties such as optical absorption and scattering coefficients. Assuming the photon densities measured from a point $\vec{r}$ to $\vec{r}_S$of an infinite media can be decomposed to be $\Phi(\vec{r},\vec{r}_S) = \Phi_0(\vec{r},\vec{r}_S) + \Phi_{SC}(\vec{r},\vec{r}_S)$, the optical properties can be solved through the equation expressed as [14]

$$\Phi_{SC}(\vec{r}_D,\vec{r}_S) = \int \frac{\delta D(\vec{r})}{D_0} \nabla G_0(\vec{r}_D,\vec{r}) \nabla \Phi(\vec{r},\vec{r}_S) d\vec{r} - \int \frac{\delta \mu_a(\vec{r})}{D_0} G_0(\vec{r}_D,\vec{r}) \Phi(\vec{r},\vec{r}_S) d\vec{r} \quad (6)$$

where the term $D(\vec{r}) = D_0 + \delta D(\vec{r})$ mention to the term $\frac{1}{3(\mu_a(\vec{r})+\mu_s(\vec{r}))}$ in Eq. 4, the $G_0(\vec{r})$ is the Green function of the boundary of the media, and $\mu_a(\vec{r}) = \mu_{a0} + \delta\mu_a(\vec{r})$ in which the $\vec{r}_S$ or $\vec{r}_D$ are the positions of sources and detectors, respectively. Equation 5 is termed as the inverse problem and solvable if and only if the number of $\Phi_{SC}(\vec{r}_D,\vec{r}_S)$are greater than the number of variables $\delta D(\vec{r})$ and $\delta\mu_a(\vec{r})$. It means the resolution of the optical image generated by diffuse optical tomography (DOT). This technique provides the image of soft tissue in deep biological tissues, however the requirementof number of couples source-detector limiting the measurement arrangement.

5. Photo-Acoustics Tomography

Another approach to solve the photon determination for light propagated in light scattering media is efforts of conversion the light energy to other energy which has the less scattering than the light. Acoustic is one of the energy. The wavelength of acoustic wave usually ranged on few hundred micrometers to few centimetres, much larger than the biological cell components, leading to the low scattering coefficient. I idea of the conversion light energy to the acoustics came from proposal of Graham Bell in 1880 when attempt to invent the "photophone". This effect suggested to Grinvald et al. for an idea to image a layer of biological soft tissues. When a photon stream hits a substance volume, a heat induced leading to generation of a pressure p_0 expressed as [9]

$$p_0 = \Gamma \eta_{th} A_e = \Gamma \eta_{th} \mu_a \Phi, \quad (7)$$

where Γ is Grueneisen parameters representing the conversion of heat to volume for a substance, η_{th} is the percentage that photon stream converted to heat, and A_e is the specific optical absorption. The model of the acoustic wave transferred from photon is derived to be [9]

$$\left(\nabla^2 - \frac{1}{v_s^2}\frac{\partial^2}{\partial t^2}\right) p(\vec{r},t) = -\frac{\beta}{k v_s^2}\frac{\partial^2 T(\vec{r},t)}{\partial t^2}, \quad (8)$$

with v_s is the sound speed in biological tissue, k and β are the isothermal compressibility and thermal coefficient of volume expansion. In the forward problem the pressure propagated in biological tissues can be solved as [9]

$$p(\vec{r},t) == \int_{-\infty}^{t} dt' \int d\vec{r}' G(\vec{r},t;\vec{r}',t') \frac{\beta}{k v_s^2} \frac{\partial^2 T(\vec{r}',t')}{\partial t'^2}.$$

Here, the $\vec{r}$, $\vec{r}'$, t, t' mention to the source of the acoustic wave and a sound pressure at a point in biological tissue. For the imaging, the inverse problem solution is written as [9]

$$p_0(\vec{r}) = -\frac{2}{\Omega_0} \nabla \int_{S_0} \vec{n_0^2} dS_0 \left[\frac{p(\vec{r_0},\bar{t})}{\bar{t}}\right], \quad (9)$$

where $\bar{t} = |\vec{r} - \vec{r_0}|$ mention to the time fly when the acoustic wave propagated from the source of p_0 to $p_0(\vec{r})$, S_0 is surface of which the acoustic detector scanning, Ω_0 is the solid angle subtended by the entire surface S_0, and $\vec{n_0^2}$ represents normal vector of pointing inward. The photoacoustic tomography (PAT) technique allows reconstruction of image with deep tissue up to 7 centimetres with high resolution depending on the scanning step resolution. However, it is limited by the low signal to noise of the weak acoustic waves.

6. Conclusions

The biomedical optical imaging benefits to clinical application such as medical diagnosis. Although they are is limited in some requirements of applications, the advantages of these techniques provide to clinical applications which the conventional techniques are obtained difficultly. In hospital, these techniques still strange to almost of medical doctors and biomedical engineers. With these beneficial of the biomedical optical imaging and development of the technologies, these techniques believed to be useful tools for biomedical researches and applications.

References

[1] T. Vo-Dinh, *Biomedical Photonics Handbook*, chapter 2, CRC Press, New York, NY, USA, 2003.
[2] Brenner DJ, Hall EJ. "Computed tomography:an increasing source of radiation exposure." *N Engl J Med*.357(22):2277-2284, 2007.
[3] Thulborn KR, Waterton JC, Matthews PM, Radda GK, "Oxygenation dependence of the transverse relaxation time of water protons in whole blood at high field". *Biochim. Biophys. Acta***714** (2): 265–70, (1982).
[4] A. F. Fercher and E. Roth, "Ophthalmic laser interferometry. Proc. SPIE vol. 658, pp. 48-51. 1986.
[5] Fercher, AF; Mengedoht, K; Werner, W (1988). "Eye-length measurement by interferometry with partially coherent light.".*Optics letters***13** (3): 186–8.
[6] Swanson, E. A.; Izatt, J. A.; Hee, M. R.; Huang, D.; Lin, C. P.; Schuman, J. S.; Puliafito, C. A.; Fujimoto, J. G. (1993). "In vivo retinal imaging by optical coherence tomography". *Optics Letters***18** (21): 1864–6.
[7] Drexler, Wolfgang; Morgner, Uwe; Ghanta, Ravi K.; Kärtner, Franz X.; Schuman, Joel S.; Fujimoto, James G. (2001). "Ultrahigh-resolution ophthalmic optical coherence tomography". *Nature Medicine***7** (4): 502–7.
[8] IARC, "IARC Classifies Radiofrequency Electromagnetic Fields As Possibly Carcinogenic To Humans", (31 May 2011).
[9] L. V. Wang, "Ultrasound-mediated biophotonic imaging: A review of acousto-optical tomography and photo-acoustic tomography", *Disease Markers* 19 (2-3/2004), 123-138, 2004.
[10] Bouma BE and Tearney GJ, *Handbook of Optical Coherence Tomography*, Marcel Dekker, New York, 2002.

[11] Cense B and Nassif NA, "Ultrahigh-resolution high-speed retina imaging using spectral-domain optical coherence tomography", *Opt.Express* 12(11), 2435-2447, 2004.
[12] O'Leary MA, Boas DA, Chance B, and Yodh AG, "Refraction of diffuse photon density waves", *Phys.Rev.Lett*. 69(18), 2658-2661,1992.
[13] RC Haskell et al. "Boundary conditions for the diffusion equation in radiative transfer". *Journal of the Optical Society of America A* 11 (10): 2727–2741, 1994.
[14] Arridge SR, "Optical tomography in medical imaging", *Inverse Problem* 15(2), R41-R93, 1999.