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Advancements in Optical Technologies for Medical Imaging and Diagnosis

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Abstract

Biomedical optics has emerged as a dynamic field encompassing a range of optical devices and technologies, including light sources, lasers, sensors, optical fibers, and optical processing principles. Its impact on medical engineering and clinical applications has been profound, leading to advancements in laboratory practices, optical fibers, biosensing, imaging, radiation grading, absorption spectroscopy, and polarization sensing. This article examines the historical progression of biomedical optics, highlighting its contributions to medical imaging and diagnosis. It focuses particularly on computed tomography, fluorescence imaging, optical molecular imaging, spectroscopy, near-infrared tomography, and optical coherence techniques.

Biomedical optics' development has transformed medical science by enabling non-invasive diagnosis, improving treatment planning, and enabling specific therapy. The positive outcomes of these advancements underscore the significance of biomedical optics in promoting progress in the field of medicine. The paper discusses optical technologies and their clinical implications, including spectroscopy, near-infrared tomography, optical coherence tomography, computed tomography, fluorescence imaging, and molecular imaging.

Keywords: Biomedical Optics, Optical Devices, Light Sources, Laser Sensors, Optical Fibers, Medical Engineering, Clinical Applications, Radiation Grading, Absorption Spectroscopy, Polarization Sensing.

1- Introduction:

The use of optical technologies has recently emerged as a powerful tool for medical diagnosis, as they offer non-ionizing radiation and the capability to detect biological, chemical, and molecular properties. There have been many applications in medical imaging because of this development [1]. In the past, researchers faced challenges studying the absorption spectra of biological samples due to their opacity and dispersion. In this case, however, it was possible to detect absorption spectra using double-beam spectrometers that used visible light wavelengths [2]. This represented a crucial turning point in using optics in human investigations. The invention of the pulse oximeter in 1972 made it possible to monitor changes in arterial blood volume and measure arterial haemoglobin oxygen saturation [3]. This innovative method made it possible to detect oxygen saturation despite the drawbacks of neglecting light scattering in tissues [4]. In the 1940s, Glenn Milliken experimented with filtering green and red light to monitor light transmission and measure oxygen levels in living tissues [5]. Later, in 1977, Franz Jobs successfully applied near-infrared (NIR) light to living tissues, demonstrating its potential for measuring haemoglobin,

mitochondrial chromophore, and cytochrome [6]. This breakthrough led to the development of NIR technology for histology and the measurement of oxidation and reduction states in living tissues. Further advancements included the use of continuous wave (CW) technology to measure haemoglobin saturation in tissues by separating the dispersion coefficient from the absorption coefficient.

In 1993, time-dependent spectroscopy (TRS) devices were developed as quantitative tools for measuring chemical concentrations in living tissue [7]. These techniques have found extensive applications in both research and medical contexts [8]. By integrating NIR with frequency domain (FD) technology, it became possible to calibrate quantization rates, determine absorption coefficients, and obtain scattering coefficients in tissues [9]. The integration of optical technologies into medical diagnosis has revolutionized the field, offering new insights and capabilities [10]. Non-invasive optical techniques have proven valuable in studying biological and chemical properties, enabling more accurate and efficient diagnosis [11]. Continued advancements in optical technologies hold great promise for further improvements in medical imaging, diagnosis, and treatment.

The development of NIRS technology led to the design of a multi-channel system capable of achieving tissue imaging. This imaging process, known as diffusion optical topography (DOT), or tomographic reconstruction technique, involves the utilization of back-projection and interpolation algorithms to reveal tissue source information and generate images [12]. The primary objective was to estimate the 2D spatial distribution of optical properties [13]. NIR spectroscopy and optical diffusion imaging techniques have found extensive use in various clinical applications. These include detecting and characterizing breast cancer, functional imaging of the brain, and the study of skeletal connectivity in muscle tissue [14]. These applications have greatly advanced our understanding and capabilities in medical diagnostics and treatment planning.

2- Diagnosis of Breast Tumors by NIR:

The identification and staging of breast cancer have been considerably improved due to the development of MRI and ultrasound techniques, which eliminate the need for invasive treatments like positron emission tomography (PET), which involves the injection of external radionuclides [15]. Light therapy for breast cancer has historically sparked the interest of researchers. The development of optical breast imaging techniques has attracted interest due to advances in the understanding of light sources, light detectors, and models of how light travels through tissues [16]. The progression of tumors in breast tissue is associated with increased vascularization and decreased partial pressure of oxygen. Near-infrared (NIR) technology, sensitive to chromophores such as oxygenated and deoxygenated hemoglobin, water, and lipids, can provide physiological information for breast cancer diagnosis [4]. In 1994, NIR internal contrast imaging of the breast revealed parameters such as blood volume and oxygen saturation, which showed significant differences between normal and tumor regions [17].

Optical properties also differ in breast tissue, making these examinations essential for assessing disparities and distinguishing between healthy and diseased tissues [18]. Dispersion coefficients, related to tissue structure, organelle concentration, and size, have been used clinically to detect tumors before menopause, reducing the need for invasive procedures like biopsies. The sensitivity of optical imaging in distinguishing malignant tumors from healthy breast tissue can reach up to 96%. Results from experiments correlated well with clinical diagnostic ultrasound [19].

To confirm the accuracy of continuous-wave (CW) DOT systems, the organic dye indocyanine green (ICG) is injected into the breast, and external mechanical pressure is applied to record oxygen saturation and hemoglobin concentration. Malignant tumors exhibit slower absorption and flow rates compared to healthy conditions,

enabling the formation of a pharmacokinetic profile through DOT. Statistical differences in rates have been found between the tumor area and surrounding tissue, suggesting that breast ICG pharmacokinetics can be used as a diagnostic tool for differentiating between benign and malignant tumors [20].

Advancements in CW systems have led to the development of the DYNOT (dynamic near-infrared optical tomography) system, which allows bilateral breast imaging synchronized with breast hemodynamics [21]. The hybrid CW/frequency-domain system combines chemical treatment capabilities with the quantitative nature of frequency-domain techniques for breast imaging. Malignant cancer shows increased hemoglobin concentration and dispersion compared to normal tissues, and quantitative distributions can aid in distinguishing between benign and malignant tumors. Such systems have also been used to monitor the effects of chemotherapy on tumors [22].

The development of time-domain DOT systems using time-correlated single-photon counting (TCSPC) technology has been a pursued goal. By combining simultaneous MRI and DOT imaging using contrast agents like ICG, a success rate of 80%-85% has been achieved, making it a model DOT system. Optical imaging, particularly NIR DOT, can effectively differentiate between benign and malignant tumors. Integration with other imaging modalities such as CT, X-rays, and MRI can provide high-resolution tissue maps and aid in the reconstruction of DOT images. Multimodal imaging systems combining DOT with mammography, MRI, ultrasound, and frequency-domain imaging have also been designed [23].

3- Studying the Brain using NIR:

Researchers in the 1990s used nuclear magnetic resonance (NMR) to identify variations in the deoxyhemoglobin signal. Since then, there has been a rise in interest in using near-infrared (NIR) light to study brain functions. Measuring HbO2 and Hb

concentration using NIR can detect changes in blood volume and oxygen saturation that are related to brain activity. NIR diffusion optical imaging is a helpful tool for understanding brain function in many clinical settings [24][25].

DOI technology can monitor brain activity and treat neurological disorders without the need for invasive methods. We have used it for the diagnosis and monitoring of brain diseases such as stroke, epilepsy, traumatic brain injury, and post-traumatic stress disorder. Early bleeding detection and distinguishing between ischemic and hemorrhagic strokes are possible with DOI visual technology [26].

Continuous-wave (CW) brain imaging systems have been developed using phototopography, where laser avalanche photodiodes operating at wavelengths of 780 nm or 830 nm detect signals. These systems encode multiple channels at different frequencies ranging from 1 to 6.5 kHz. They have been applied to study various aspects of healthy brain function, including linguistic processing, emotional responses to external stimuli, functional connectivity, brain development in infants, epilepsy, post-accident disorders, and cognitive dysfunction. Empirical studies have demonstrated the success of these systems in mapping brain activity, particularly in covering different areas of the adult brain and synchronizing optical signals from the frontal, sensory, and visual cortices [27].

By using these systems, researchers have been able to explore spatiotemporal patterns of physiological signals in living organisms under normal conditions. Algorithms have been developed to recognize functional activation signals, allowing the system to operate with high performance. This has enabled the mapping of relaxation-state networks in the living brain and the understanding of functional connectivity between different cortical areas. It has been observed that high-intensity signals make the DOI device a practical tool for brain mapping. Frequency-domain DOI has the capability to measure slow blood circulation rates that coincide with

optical signals and are modulated by neural activity [28]. Rapid neural signals, associated with changes in neuronal scattering, introduce a delay in photon capture. The frequency-domain imaging system measures the phase delay, which provides information about light signals related to neural events [23].

A 3D field optical tomography system designed for imaging the brains of newborns has successfully reconstructed measurements of the average photon flight time. This system has been used to image the brains of premature infants with cerebral hemorrhage and monitor changes in blood volume and oxygenation in brain tissue [11].

4- Muscle Imaging using NIR:

Since the 1930s, light has been utilized for non-invasive monitoring of muscle tissue. New imaging techniques can examine muscle function in different conditions. Researchers have utilized high-density continuous-wave (CW) imaging systems to capture images of blood volume and oxygen changes in the peroneal muscles before and during exercise quickly. By comparing these spatial differences within muscles before and after exercise, valuable insights into muscle physiology can be gained [29].

The near-infrared (NIR) frequency-domain optical tomography system has played a crucial role in mapping variations in hemoglobin concentration during exercise in muscles such as the extensor digitorum. By utilizing a hybrid system that combines frequency-domain diffusive reflectance spectroscopy and diffusive correlation spectroscopy, synchronized monitoring of muscle hemodynamics and blood flow has become possible. This enables the quantification of total hemoglobin amount, hemoglobin concentration, and oxygen saturation, as well as the assessment of relative blood flow in deep tissues. These hybrid systems provide a means to evaluate muscle microcirculation and metabolism within the body. Information on

oxygenated hemoglobin (O2Hb), deoxygenated hemoglobin (HHb), and myoglobin has also been recorded. The time domain has been extended to capture changes in absorption and response of finger muscles before and after exercise [30].

Time-resolved (TR) diffuse optical tomography (DOT) systems have been developed to image the forearm during the Hand grip test, demonstrating their ability to capture images in a time-sensitive manner. Building upon this, a fast and compact multi-channel TR DOT system has been designed to image leg muscle tissue and assess hemoglobin content during dynamic plantar flexion exercises [9]. These findings confirm the role of DOT in understanding the spatial and temporal characteristics of muscle physiology. Despite the challenge of separating the contributions of hemoglobin and myoglobin to muscle, NIR diffuse optical imaging is expected to be widely utilized in the future for imaging muscle functions and diagnosing muscle-related diseases [12].

5- Endoscopy and the Development of Optical Coherence Tomography (OCT):

Medical imaging has been transformed by optical coherence tomography (OCT), which enables the real-time visualization of tissue microstructure. OCT offers comprehensive imaging similar to conventional biopsies or histopathology without the requirement for tissue samples, with a resolution of 1-10 micrometers and a depth penetration of 1-2 mm [31]. Similar to ultrasound imaging, OCT utilizes the measurement of time delay and intensity of reflected or scattered light instead of sound waves. It can be performed using optical fibers, making it suitable for portable sensors, endoscopes, catheters, laparoscopes, and minimally invasive procedures to visualize the internal structures of the body [32].

OCT measurements are based on a Michelson interferometer setup. One arm of the interferometer directs light onto the tissue, and the reflected light is collected either by the sample arm or the reference arm. By introducing a time delay in the reference path of the interferometer, data is collected and analyzed only when the optical delays match the wavelength of the light source. This technique is known as time-domain wavelength interferometry. Another variation of OCT is frequency-domain OCT (also known as Fourier domain OCT), where the position of the reference mirror is fixed, and the light echoes are obtained by Fourier transform or interference spectrum transform. This technique allows for simultaneous measurement of signals from different depths along the axial scan, resulting in improved sensitivity and speed compared to time-domain OCT. Fourier domain OCT has advanced the field of medical detection and imaging, particularly in terms of enhancing performance and enabling 3D imaging [33][34].

Spectroscopic/Fourier domain OCT and source domain/Fourier-OCT are two techniques that have been developed for OCT imaging. These techniques have demonstrated their effectiveness in diagnosing diseases and have been utilized for in vivo imaging of biological tissues. Miniature devices such as catheters/endoscopes have been employed for intraluminal and angiographic imaging. Furthermore, laparoscopes and needle imaging devices have been specifically designed for organ imaging. In recent years, there has been significant development in OCT imaging sensors, leading to a wide range of applications [35].

6- Clinical Applications:

6-1 Clinical OCT:

Clinical applications of OCT have gained significant momentum since its introduction in 1991 [31]. Distinct from other biomedical imaging modalities, OCT

provides cross-sectional images of tissues and microstructures. Its spatial resolution is higher compared to ultrasound and closer to that of pathological anatomy devices, enabling real-time and spatial visualization of tissue structures. This non-invasive technique is particularly valuable in situations where biopsy procedures are either impossible or pose risks, thereby avoiding the drawbacks associated with excisional biopsy sampling. As a result, OCT has found increasing use in various clinical fields [36].

Ophthalmology is one of the prominent areas where OCT has been extensively applied. The technique offers valuable insights into ocular structures and has revolutionized the diagnosis and management of ophthalmic conditions [37]. Additionally, OCT has proven beneficial in cardiology for imaging the heart and blood vessels [38]. It has also been employed in gastroenterology for evaluating gastrointestinal abnormalities, dermatology for assessing skin conditions, dentistry for examining oral tissues, urology for investigating urological disorders, and gynaecologic for studying gynaecological diseases, among other clinical applications. The use of OCT has been instrumental in these fields, allowing for improved diagnostics and monitoring of various conditions, including tumors [39-43].

Overall, OCT has emerged as a versatile tool in clinical practice, enabling non-invasive imaging and providing valuable information for diagnosis and treatment planning in a wide range of medical specialties.

6-2 Eye Imaging:

OCT has emerged as a valuable tool for ocular imaging, providing significant clinical benefits in ophthalmology. Its high-resolution capabilities enable the visualization of detailed structures within the eye that cannot be easily observed with conventional

ophthalmoscopes. By utilizing cross-sectional imaging, OCT has proven effective in evaluating various retinal diseases and conditions [44].

The development of high-speed OCT, particularly in the spectral domain/Fourier domain, has led to the creation of numerous OCT devices specifically designed for ophthalmology. These advancements have significantly enhanced the efficiency and performance of clinical procedures [35]. The exceptional axial resolution of OCT makes it particularly well-suited for imaging the layers of the retina, vitreous interface, macular edema, macular holes, central serous chorioretinopathy, age-related macular degeneration, and choroidal neovascularization. Additionally, OCT enables the measurement and imaging of the nerve fiber layer thickness, providing valuable information for early glaucoma detection and assessing optic nerve structure and function [37].

The increasing influence of OCT in clinical medicine has spurred rapid advancements in OCT imaging techniques, resulting in improved clinical imaging performance, and facilitating comprehensive evaluations of the latest ophthalmic OCT techniques. These developments, particularly in axial accuracy and retinal imaging, have had a significant positive impact on ophthalmology applications. The layered structures of the retina are enhanced, allowing for precise diagnosis of diseases. The axial resolution of OCT is inversely proportional to the bandwidth of the light source, meaning that higher bandwidth results in greater axial resolution. With advancements such as ultra-high-resolution (UHR) OCT systems, super-resolution imaging of approximately 2-3 μm has been achieved, surpassing the capabilities of standard OCT systems that use Super Luminescent Diodes (SLD). UHR OCT has demonstrated exceptional imaging of all retinal layers, particularly the inner and outer photoreceptor segments [45].

Numerous studies addressing conditions such as age-related macular degeneration, central serous chorioretinopathy, foveal neoplastic dystrophy, Stargardt's dystrophy, and retinitis pigmentosa have been conducted as a result of the application of OCT technology [46]. High-speed OCT, in particular, enables the acquisition of three-dimensional images, facilitating the analysis of retinal structures. Rapid three-dimensional imaging has had a positive impact on clinical research, allowing for quantitative measurements of retinal layers for early disease diagnosis, such as glaucoma or diabetic retinopathy, and assessment of disease progression and treatment response. Spectroscopic OCT systems operating at 1000 nm have also been utilized to obtain clearer views of placental tissue [47][48].

Other OCT technologies, such as Doppler OCT and spectral domain/Fourier domain OCT with Doppler flow imaging, have enabled the measurement of blood flow velocity in tissues and the visualization of blood vessels in the retina. Functional OCT methods, incorporating polarization sensors to study light refraction in deep tissues and assess scattering properties, have provided additional information on the retinal nerve fiber layer, and enhanced the diagnostic capabilities of OCT. The combination of OCT scattering signals and functional responses of the retina has contributed to a deeper understanding of visual physiology [49].

In summary, OCT has emerged as a powerful tool in ophthalmology, enabling non-invasive imaging and precise evaluation of various eye conditions. Its high-resolution imaging, speed, and functional capabilities have significantly advanced clinical diagnostics and research in the field.

6-3 Cardiovascular Imaging:

OCT technology has been utilized for the diagnosis and screening of heart diseases for the past decade. Compared to intravascular ultrasound, OCT has demonstrated impressive volumetric imaging capabilities, allowing for the visualization of fine

structures within the luminal walls. With technological advancements such as catheterization, high-speed OCT imaging, and the use of small-diameter fiberoptic catheters, OCT has successfully imaged blood vessels from within. By diluting the blood with saline solution, OCT can detect signals and record data from the artery within a short period of time, highlighting the importance of high-speed imaging in Fourier OCT [50].

OCT has emerged as a valuable method for diagnosing vascular diseases and guiding endovascular interventions in real-time. Its ability to reveal microscopic details of atherosclerotic lesions allows for the detection of vulnerable plaques and distinguishes between different plaque types, such as fibrous, fatty, and calcified plaques. In experimental research, OCT has shown promise in identifying clinical structures within the plaques, including fibrous coverings, fat-laden pools, and calcifications. The specific features of each plaque type can be determined through histological correlation.

The advantages of OCT imaging in plaque characterization are significant. Fibrous plaques exhibit homogeneous areas with high signals, while calcified fibrous plaques display low-signal areas with sharp edges. Fat plaques are characterized by numerous low-signal areas with spreading borders. The detection sensitivity of the OCT system for different plaque types is high, with 98% for fibrous plaques, 97% for calcified fibrous plaques, and 92% for lipid-rich plaques. These results confirm the accuracy of intravascular OCT imaging and the clear interpretation of intracoronary OCT images obtained in clinical settings. Studies using a 1 mm (3.0 F) catheter for coronary artery angiography have demonstrated OCT's ability to understand coronary artery plaques and characterize different types of coronary atherosclerotic plaques [38][51].

OCT imaging of blood vessels enables the diagnosis of vulnerable plaques. Identifying vulnerable plaques is crucial for implementing advanced therapeutic strategies, predicting treatment response, and monitoring structural changes after interventions. OCT also aids in determining the presence of activated macrophages in the body. Studies have found a correlation between OCT measurements and histological measurements of the fibrous cap and the density of macrophages, suggesting that OCT has the ability to characterize the fibrous cap and identify vulnerable plaques in patients [52].

Quantitative analyses using OCT technology, such as signal attenuation and layer thickness changes, have been employed to characterize coronary artery plaques histologically. By studying attenuation and backscatter characteristics, OCT enhances contrast and enables deep tissue characterization, opening doors to future computer-aided plaque diagnosis, atherosclerosis treatment, and improved detection of thin fibrous caps. Furthermore, OCT contributes to the monitoring of treatment and surgical interventions, including stent deployment. It provides a clear view of stents and their positioning in relation to the arterial wall, allowing doctors to evaluate stent placement, tissue subsidence, and wall anatomy [53].

6-4 Tumor Imaging:

OCT technology has been successful in imaging cancer and has been widely used in the identification of structural abnormalities in various tissues. It has shown accuracy comparable to standard biopsy and histopathology, making it a valuable tool for optical biopsy in diseases affecting tissues [18]. OCT has been employed in several domains in addition to ophthalmology, cardiology, and cancer imaging. It has been utilized for dentistry imaging, kidney transplant evaluation, and neurosurgical guiding for visualizing cartilage pathology. In the field of histopathology, OCT has been utilized for excisional biopsy and sampling to detect structural changes

associated with malignancies in different areas such as the breast, bladder, brain, digestive system, respiratory system, reproductive system, skin, larynx, oral cavity, and genital tract [36-42].

The development of laparoscopic OCT has enabled the visualization of raised cancers in internal organs. OCT has been effective in detecting cancers in the intestine, Barrett's esophagus, and inflammatory bowel disease. In Barrett's esophagus, OCT has achieved a sensitivity of 83% and a qualitative efficiency of 75% in detecting dysplasia and cancer within the mucosal region. A digital recording system based on surface maturation has proved highly effective in recording data on glandular geometry, with a sensitivity of 68%, specific efficiency of 82%, and accuracy of 78% in detecting dysplasia in Barrett's esophagus [54].

Ultra-resolution endoscopic OCT (UHR) imaging systems with high axial resolution have been successful in clinical imaging, providing clear cross-sections of tissues. OCT has been able to visualize the stratified structure of normal esophagus and identify glandular structures and dysplasia in Barrett's esophagus. The irregular and distorted glandular structure characteristic of dysplasia is clearly visualized in OCT images, which show good correlation with histological architecture [55].

Bladder cancer has also been detected using OCT in conjunction with endoscopy and real-time imaging. OCT has shown high sensitivity and specificity in determining the stages of bladder cancer, with a sensitivity of 100% and specificity of 90% compared to estimates of muscle tumors. OCT imaging has also been successful in detecting cancer in solid organs such as glands, lobules, ducts, prostate, kidney, and cervix. Spectroscopic analysis using OCT has shown the ability to identify tumor boundaries in the cervix. OCT imaging combined with other techniques has been used for colon imaging and monitoring the development of colorectal tumors [56].

7- NIR and Medical Fluorescence:

Fluorescence techniques in medical imaging utilize the properties of internal molecules, known as autofluorescence, or external dyes to assess the biochemical status of diseases, particularly in histology. In this technique, tissues are stimulated with light, causing the fluorophore molecules present within the tissues to absorb and gain light energy. To learn more about the tissue, information is obtained and analyzed from the fluorescence light that is released, which typically has longer wavelengths than the excitation light [57].

Collagen, elastin, coenzymes like NADH reductase, flavin adenine dinucleotide (FAD), flavin mononucleotide (FMN), and heme by-products linked to recognized biosynthetic processes involving porphyrins are all examples of endogenous fluorophores that can be found in tissues. The clinical application also includes external dyes such as aminolaevulinic acid (5-ALA) and indocyanine green (ICG) [58].

The three primary categories of fluorescence systems are computed tomography, wide-field imaging, and point spectroscopy. Studying the optical characteristics of tissues at particular spatial places is the focus of point spectroscopy. A light source, an optical fiber probe containing both excitation and collection fibers, a spectrometer, and a detector make up the equipment used in optical spectroscopy [59-60].

8- Conclusions and Recommendations:

Further clinical studies are warranted to explore the accuracy of OCT in detecting early neoplastic lesions across various clinical domains.

In conclusion, A flexible analytical method that offers valuable insights into the chemical makeup and structure of many biological materials is near-infrared (NIR)

spectroscopy. By using infrared light to observe functional group interactions in chemical compounds, infrared spectroscopy can produce distinctive vibrations that act as a unique fingerprint for the chemical and biological components found in cells and tissues. This makes it an effective and independent technique in numerous medical research settings.

As stated in this study, fluorescence and near-infrared (NIR) tomography allow fluorescent contrast agents that can be stimulated at wavelengths feasible with readily available equipment. Additionally, these methods use detectors that gather data from backscattered light at particular wavelengths that may be analysed further.

This work clearly shows that medical optics is a multidisciplinary subject that includes researchers from Medical Physics, Biomedical Engineering, and other related fields. As a result, we suggest that the University of Tobruk's Faculty of Medical Technology establish a Biomedical Optics Research Laboratory (BORL). This facility would aid in the training of medical engineers with expertise in biomedical technology like near-infrared spectroscopy.

References:

1. Evan, P., Stater., Magdalena, Skubal., Ryo, Tamura., Jan, Grimm. (2019). The Present and Future of Optical Imaging Technologies in the Clinic: Diagnosis and Therapy. Doi: 10.1007/7355_2019_84
2. Marco, Ferrari., Karl, H., Norris., Michael, G., Sowa. (2012). Guest editorial: Medical near-infrared spectroscopy 35 years after the discovery. Journal of Near Infrared Spectroscopy, Doi: 10.1255/JNIRS.982
3. Claude, A., Piantadosi. (2007). Early development of near-infrared spectroscopy at Duke University, Journal of Biomedical Optics, Doi: 10.1117/1.2804925

4. Takafumi, Hamaoka., Kevin, K., McCully. (2019). Review of early development of near-infrared spectroscopy and recent advancement of studies on muscle oxygenation and oxidative metabolism. Journal of Physiological Sciences, Doi: 10.1007/S12576-019-00697-2
5. Johanna, Paulsson. (2014). Time of Flight Spectroscopy of Photon Migration in Turbid Media.
6. Nicholas, R., Trefiak., Jack, A., Barnes., Fiona, Rask., Daniel, G., Courtney., Richard, Walford., Runkai, Li., Richard, D., Oleschuk., Hans-Peter, Loock. (2005). Absorption Measurements in Microfluidic Devices Using Ring-Down Spectroscopy. Doi: 10.1117/12.629756
7. K., Ajito., Masahito, Nakamura., T., Tajima., Yuko, Ueno. (2017). Terahertz Spectroscopy Methods and Instrumentation. Doi: 10.1016/B978-0-12-409547-2.12092-X
8. Amira, C., Padilla-Jiménez., William, Ortiz-Rivera., Carlos, Rios-Velazquez., Iris, Vazquez-Ayala., Samuel, P., Hernández-Rivera. (2014). Detection and discrimination of microorganisms on various substrates with quantum cascade laser spectroscopy. Optical Engineering, Doi: 10.1117/1.OE.53.6.061611
9. Francesco, Banfi., Claudio, Giannetti., Gabriele, Ferrini. (2014). A multimodal approach to time-resolved optical spectroscopy for biomolecular detection. Doi: 10.1109/LO.2014.6886367
10. Irving, J., Bigio., Judith, R., Mourant., Gerrit, Los. (1999). Elastic-scattering spectroscopy for quantitative measurement of chemotherapy and PDT drug concentrations in vivo. Doi: 10.1117/12.336840

11. Zeinab, Hajjarian., Seemantini, K., Nadkarni. (2020). Tutorial on laser speckle rheology: technology, applications, and opportunities. Journal of Biomedical Optics, Doi: 10.1117/1.JBO.25.5.050801

12. Jhao, Ming, Yu., Liang, Yu, Chen., Min, Cheng, Pan., Ya, Fen, Hsu., Min, Chun, Pan. (2015). Implementation of 3D prostrate ring-scanning mechanism for NIR diffuse optical imaging phantom validation. Proceedings of SPIE, Doi: 10.1117/12.2080282

13. Hideyuki, Shinzawa., Kimie, Awa., Yukihiro, Ozaki., Hidetoshi, Sato. (2009). Near-Infrared Imaging Analysis of Cellulose Tablets by a Band Position Shift. Applied Spectroscopy, Doi: 10.1366/000370209788964584

14. Zhen, Yuan., Huabei, Jiang. (2013). Diffuse Optical Tomography for Brain Imaging: Theory. Doi: 10.1007/978-1-4614-4978-2_4

15. Chun, Yang., Zhiguo, Shi. (2019). Research in Breast Cancer Imaging Diagnosis Based on Regularized LightGBM. Doi: 10.1007/978-981-15-1925-3_35

16. Michel, Herranz., Álvaro, Ruibal. (2012). Optical imaging in breast cancer diagnosis: the next evolution, Journal of Oncology, Doi: 10.1155/2012/863747

17. Nioka, S., Miwa, M., Orel, S., Shnall, M., Haida, M., Zhao, S., & Chance, B. (1994). Optical imaging of human breast cancer. *Oxygen Transport to Tissue XVI*, 171-179.

18. Ken, Y., Foo., Kelsey, M., Kennedy., Renate, R., Zilkens., Wes, M., Allen., Qi, Fang., Rowan, W., Sanderson., James, D., Anstie., Benjamin, F., Dessauvagie., Bruce, Latham., Christobel, Saunders., Lixin, Chin., Brendan, F., Kennedy. (2021). Optical palpation for tumor margin assessment in breast-conserving surgery, Biomedical Optics Express, Doi: 10.1364/BOE.415888

19. Maximilian, Eisel., Stephan, Ströbl., Thomas, Pongratz., Herbert, Stepp., Adrian, Rühm., Ronald, Sroka. (2018). Investigation of optical properties of dissected and homogenized biological tissue. Journal of Biomedical Optics, Doi: 10.1117/1.JBO.23.9.091418

20. Venugopal, Vivek, and Xavier Intes. "Recent advances in optical mammography." *Current Medical Imaging* 8.3 (2012): 244-259

21. C. H. Schmitz, D. P. Klemer, R. Hardin, M. S. Katz, Y. Pei, H. L. Graber, M. B. Levin, R. D. Levina, N. A. Franco, W. B. Solomon, and R. L. Barbour, "Design and implementation of dynamic near-infrared optical tomographic imaging instrumentation for simultaneous dual-breast measurements," Applied optics 44, 2140-2153 (2005).

22. Xin, Gao., Binlin, Wu. (2019). Breast cancer diagnosis using fluorescence spectroscopy with dual-wavelength excitation and machine learning. Doi: 10.1117/12.2509147.

23. Intes, Xavier. "Time-domain optical mammography SoftScan: Initial Results1." *Academic radiology* 12.8 (2005): 934-947.

24. B. Chance, Z. Zhuang, C. UnAh, C. Alter, and L. Lipton, "Cognition-activated low-frequency modulation of light absorption in human brain," Proceedings of the National Academy of Sciences of the United States of America 90, 3770-3774 (1993).

25. Sergio, Fantini., Blaise, deB., Frederick., Angelo, Sassaroli. (2018). Perspective: Prospects of non-invasive sensing of the human brain with diffuse optical imaging. Doi: 10.1063/1.5038571

26. Matthew, B., Applegate., Raeef, Istfan., Samuel, Spink., Anup, Tank., Darren, Roblyer. (2020). Recent advances in high-speed diffuse optical imaging in biomedicine. Doi: 10.1063/1.5139647

27. E. Watanabe, A. Maki, F. Kawaguchi, K. Takashiro, Y. Yamashita, H. Koizumi, and Y. Mayanagi, "Non-invasive assessment of language dominance with near-infrared spectroscopic mapping," Neurosci Lett 256, 49-52 (1998).

28. B. W. Zeff, B. R. White, H. Dehghani, B. L. Schlaggar, and J. P. Culver, "Retinotopic mapping of adult human visual cortex with high-density diffuse optical tomography," Proceedings of the National Academy of Sciences of the United States of America 104, 12169-12174 (2007).

29. G. A. Millikan, "Experiments on Muscle Haemoglobin in vivo; The Instantaneous Measurement of Muscle Metabolism," Proceedings of the Royal Society of London B: Biological Sciences 123, 218-241 (1937).

30. T. Hamaoka, K. K. McCully, V. Quaresima, K. Yamamoto, and B. Chance, "Near-infrared spectroscopy/imaging for monitoring muscle oxygenation and oxidative metabolism in healthy and diseased humans," Journal of Biomedical Optics 12, 062105 (2007).

31. J. G. Fujimoto, M. E. Brezinski, G. J. Tearney, S. A. Boppart, B. Bouma, M. R. Hee, J. F. Southern, and E. A. Swanson, "Optical biopsy and imaging using optical coherence tomography," Nature medicine 1, 970-972 (1995).

32. Z. Yaqoob, J. Wu, E. J. McDowell, X. Heng, and C. Yang, "Methods and application areas of endoscopic optical coherence tomography," J Biomed Opt 11, 063001 (2006).

33. M. A. Choma, M. V. Sarunic, C. H. Yang, and J. A. Izatt, "Sensitivity advantage of swept source and Fourier domain optical coherence tomography," Optics Express 11, 2183-2189 (2003).

34. J. F. de Boer, B. Cense, B. H. Park, M. C. Pierce, G. J. Tearney, and B. E. Bouma, "Improved signal-to-noise ratio in spectral-domain compared with time-domain optical coherence tomography," Optics letters 28, 2067-2069 (2003).

35. R. Leitgeb, C. K. Hitzenberger, and A. F. Fercher, "Performance of Fourier domain vs. time domain optical coherence tomography," Optics Express 11, 889-894 (2003).

36. J. Walther, M. Gaertner, P. Cimalla, A. Burkhardt, L. Kirsten, S. Meissner, and E. Koch, "Optical coherence tomography in biomedical research," Anal Bioanal Chem 400, 2721-2743 (2011).

37. M. R. Hee, J. A. Izatt, E. A. Swanson, D. Huang, J. S. Schuman, C. P. Lin, C. A. Puliafito, and J. G. Fujimoto, "Optical coherence tomography of the human retina," Arch Ophthalmol 113, 325-332 (1995).

38. M. E. Brezinski, G. J. Tearney, B. E. Bouma, S. A. Boppart, M. R. Hee, E. A. Swanson, J. F. Southern, and J. G. Fujimoto, "Imaging of coronary artery microstructure (in vitro) with optical coherence tomography," The American journal of cardiology 77, 92-93 (1996).

39. M. V. Sivak, Jr., K. Kobayashi, J. A. Izatt, A. M. Rollins, R. Ung-Runyawee, A. Chak, R. C. Wong, G. A. Isenberg, and J. Willis, "High-resolution endoscopic imaging of the GI tract using optical coherence tomography," Gastrointest Endosc 51, 474-479 (2000).

40. J. Welzel, C. Reinhardt, E. Lankenau, C. Winter, and H. H. Wolff, "Changes in function and morphology of normal human skin: evaluation using optical coherence tomography," Br J Dermatol 150, 220-225 (2004).

41. L. S. de Melo, R. E. de Araujo, A. Z. Freitas, D. Zezell, N. D. Vieira, J. Girkin, A. Hall, M. T. Carvalho, and A. S. Gomes, "Evaluation of enamel dental restoration interface by optical coherence tomography," J Biomed Opt 10, 064027 (2005).

42. M. J. Manyak, N. D. Gladkova, J. H. Makari, A. M. Schwartz, E. V. Zagaynova, L. Zolfaghari, J. M. Zara, R. Iksanov, and F. I. Feldchtein, "Evaluation of superficial bladder transitional-cell carcinoma by optical coherence tomography," Journal of Endourology 19, 570-574 (2005).

43. 165. S. A. Boppart, A. Goodman, J. Libus, C. Pitris, C. A. Jesser, M. E. Brezinski, and J. G. Fujimoto, "High resolution imaging of endometriosis and ovarian carcinoma with optical coherence tomography: feasibility for laparoscopic-based imaging," British journal of obstetrics and gynaecology 106, 1071-1077 (1999).

44. C. A. Puliafito, M. R. Hee, C. P. Lin, E. Reichel, J. S. Schuman, J. S. Duker, J. A. Izatt, E. A. Swanson, and J. G. Fujimoto, "Imaging of macular diseases with optical coherence tomography," Ophthalmology 102, 217-229 (1995).

45. W. Drexler, U. Morgner, R. K. Ghanta, F. X. Kärtner, J. S. Schuman, and J. G. Fujimoto, "Ultrahigh-resolution ophthalmic optical coherence tomography," Nature medicine 7, 502-507 (2001).

46. M. R. Hee, C. R. Baumal, C. A. Puliafito, J. S. Duker, E. Reichel, J. R. Wilkins, J. G. Coker, J. S. Schuman, E. A. Swanson, and J. G. Fujimoto, "Optical coherence tomography of age-related macular degeneration and choroidal neovascularization," Ophthalmology 103, 1260-1270 (1996).

47. N. A. Nassif, B. Cense, B. H. Park, M. C. Pierce, S. H. Yun, B. E. Bouma, G. J. Tearney, T. C. Chen, and J. F. de Boer, "In vivo high-resolution video-rate spectral-domain optical coherence tomography of the human retina and optic nerve," Optics Express 12, 367-376 (2004).

48. B. Povazay, B. Hermann, A. Unterhuber, B. Hofer, H. Sattmann, F. Zeiler, J. E. Morgan, C. Falkner-Radler, C. Glittenberg, S. Blinder, and W. Drexler, "Three-dimensional optical coherence tomography at 1050 nm versus 800 nm in retinal pathologies: enhanced performance and choroidal penetration in cataract patients," J Biomed Opt 12, 041211 (2007).

49. Z. Chen, T. E. Milner, D. Dave, and J. S. Nelson, "Optical Doppler tomographic imaging of fluid flow velocity in highly scattering media," Optics letters 22, 64-66 (1997).

50. R. Bhindi, S. M. Munir, and K. M. Channon, "Images in cardiovascular medicine. Optical coherence tomography in the setting of an acute anterior myocardial infarction," Circulation 116, e366-367 (2007).

51. I. K. Jang, B. E. Bouma, D. H. Kang, S. J. Park, S. W. Park, K. B. Seung, K. B. Choi, M. Shishkov, K. Schlendorf, E. Pomerantsev, S. L. Houser, H. T. Aretz, and G. J. Tearney, "Visualization of coronary atherosclerotic plaques in patients using optical coherence tomography: comparison with intravascular ultrasound," Journal of the American College of Cardiology 39, 604-609 (2002).

52. I. K. Jang, G. J. Tearney, B. MacNeill, M. Takano, F. Moselewski, N. Iftima, M. Shishkov, S. Houser, H. T. Aretz, E. F. Halpern, and B. E. Bouma, "In vivo characterization of coronary atherosclerotic plaque by use of optical coherence tomography," Circulation 111, 1551-1555 (2005).

53. C. Xu, J. M. Schmitt, S. G. Carlier, and R. Virmani, "Characterization of atherosclerosis plaques by measuring both backscattering and attenuation coefficients in optical coherence tomography," J Biomed Opt 13, 034003 (2008).

54. J. A. Evans, J. M. Poneros, B. E. Bouma, J. Bressner, E. F. Halpern, M. Shishkov, G. Y. Lauwers, M. Mino-Kenudson, N. S. Nishioka, and G. J. Tearney, "Optical coherence tomography to identify intramucosal carcinoma and high-grade dysplasia in Barrett's esophagus," Clin Gastroenterol H 4, 38-43 (2006).

55. Y. Chen, A. D. Aguirre, P. L. Hsiung, S. Desai, P. R. Herz, M. Pedrosa, Q. Huang, M. Figueiredo, S. W. Huang, A. Koski, J. M. Schmitt, J. G. Fujimoto, and H. Mashimo, "Ultrahigh resolution optical coherence tomography of Barrett's esophagus: preliminary descriptive clinical study correlating images with histology," Endoscopy 39, 599-605 (2007).

56. S. P. Lerner, A. C. Goh, N. J. Tresser, and S. S. Shen, "Optical coherence tomography as an adjunct to white light cystoscopy for intravesical real-time imaging and staging of bladder cancer," Urology 72, 133-137 (2008).

57. R. M. Cothren, M. V. Sivak, J. VanDam, R. E. Petras, M. Fitzmaurice, J. M. Crawford, J. Wu, J. F. Brennan, R. P. Rava, R. Manoharan, and M. S. Feld, "Detection of dysplasia at colonoscopy using laser-induced fluorescence: A blinded study," Gastrointest Endosc 44, 168-176 (1996).

58. T. Desmettre, J. M. Devoisselle, and S. Mordon, "Fluorescence properties and metabolic features of indocyanine green (ICG) as related to angiography," Survey of ophthalmology 45, 15-27 (2000).

59. D. Roblyer, R. A. Schwarz, and R. Richards-Kortum, "Fluorescence Spectroscopy," in Handbook of Biomedical Optics, D. A. Boas, C. Pitris, and N. Ramanujam, eds. (CRC Press, Boca Raton, FL, 2011), pp. 217-232.

60. R. J. Antcliff, M. R. Stanford, D. S. Chauhan, E. M. Graham, D. J. Spalton, J. S. Shilling, T. J. Ffytche, and J. Marshall, "Comparison between optical coherence tomography and fundus fluorescein angiography for the detection of cystoid macular edema in patients with uveitis," Ophthalmology 107, 593-599 (2000).