Metrological reliability of optical coherence tomography in biomedical applications

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Abstract. Optical coherence tomography (OCT) has been proving to be an efficient diagnostics technique for imaging in vivo tissues, an optical biopsy with important perspectives as a diagnostic tool for quantitative characterization of tissue structures. Despite its established clinical use, there is no international standard to address the specific requirements for basic safety and essential performance of OCT devices for biomedical imaging. The present work studies the parameters necessary for conformity assessment of optoelectronics equipment used in biomedical applications like Laser, Intense Pulsed Light (IPL), and OCT, targeting to identify the potential requirements to be considered in the case of a future development of a particular standard for OCT equipment. In addition to some of the particular requirements standards for laser and IPL, also applicable for metrological reliability analysis of OCT equipment, specific parameters for OCT's evaluation have been identified, considering its biomedical application. For each parameter identified, its information on the accompanying documents and/or its measurement has been recommended. Among the parameters for which the measurement requirement was recommended, including the uncertainty evaluation, the following are highlighted: optical radiation output, axial and transverse resolution, pulse duration and interval, and beam divergence.

1. Introduction

Optical technology has an extended application in medicine and biology, dating back to the 18^{th} century with the use of microscope. Relatively new, the application in the medical field of optical instruments that take advantage of the coherent properties of light is rising. One technique that has emerged is the optical coherence tomography (OCT), an important and successful application of interferometry in the biomedical sciences. Measuring the reflected light, this technique is capable to provide non-invasive high-resolution cross-sectional images of the internal structures of living tissue.

Originally, due to its low scattering characteristics, OCT was developed for transparent tissue imaging [1]. Later on, the equipment has evolved, allowing the generation of images of non-transparent tissue [2]. Its first clinical application occurred in ophthalmology and the first commercial OCT was released in 1996. Since then, it advanced as a diagnostic and therapeutic technique for different areas. However, risks of adverse events from the use of these technologies are always present. These risks can be avoided with periodical evaluation concerning safety and appropriate performance of the equipment for the referred application, protecting the patient and the medical staff [3].

Every medical electrical equipment must comply with the International Standard published by the International Eletrotechnical Commission (IEC), IEC 60601-1 (Medical electrical equipment - Part 1: General requirements for basic safety and essential performance), and possible existing particular standards. In spite of its established clinical usage, to the present day there is not a specific technical standard published to evaluate optical coherence tomography equipment's conformity to essential safety and performance requirements for biomedical imaging.

Therefore, the present work analyses the IEC particular international standards published for safety and performance evaluation of laser and IPL (Intense Pulsed Light) to identify the parameters also applicable for metrological reliability analysis of OCT equipment. Additionally, specific parameters for OCT evaluation that were not mentioned in these standards were identified, aiming at contributing for the complete list of parameters to be recommended for a possible future development of a specific standard for the non-invasive high-resolution imaging technique by optical coherence tomography.

2. Optical Coherence Tomography

Optical coherence tomography (OCT) is a signal acquisition technique based on the interference between an low-coherence optical field that is divided and later recombined after reflecting back from multiples layers within the sample. The heart of the system is Michelson interferometer illuminated by a low-coherent light source.

One of its advantages is the possibility of non-invasive generation of high resolution imaging of tissue's internal structures, which is of great relevance to the biomedical field. Different from confocal microscopy, which depends on numerical aperture of the optical system, OCT's axial resolution relies only on the coherence of light from the source. This characteristic allows *in vivo* deep tissue measurements non-invasively[4, 5].

Information about the structure of the sample is obtained from the interferogram, the light intensity measured by the photodectetor. Refractive index variations between layers within the sample represent intensity peaks on the interference pattern [6].

3. Parameters for OCT metrological reliability evaluation

This section briefly describes the parameters identified as important to assure metrological reliability of biomedical equipment based on OCT. The suggestions indicated for each evaluation parameter included their measurement and/or the insertion of information of their values in the device's accompanying documents (Table 1). Some of the recommended parameters are already mentioned in the published standards for laser and IPL, as indicated.

3.1. Beam diameter and divergence

IEC 60825-1 standard (Safety of laser products - Part 1: Equipment classification, requirements and user's guide) defines beam diameter as the diameter of the smallest circle which contains 63% of total laser output power. As the laser beam propagates, the beam diameter increases [7]. The IEC 60825-1 standard defines beam divergence as the far field plane angle formed by the beam diameter.

The guarantee that the beam is focused only on the intended area for diagnostic/treatment of the biological tissue is vital to a safe use of the equipment. Therefore, it is suggested to measure the beam divergence of OCT devices. It is recommended to inform the value of the beam diameter on the device's accompanying documents.

3.2. Pulse duration

According to the IEC 60825-1 standard, the pulse duration is the time increment measured between the half peak points of a pulse. The pulse duration must respect the maximum continuous tissue exposure limit, which varies according to each application.

Therefore, in case of a pulsed source, it is recommended not only the pulse duration evaluation but also the inclusion of its value in the accompanying documents.

3.3. Optical radiation output

By the definition on laser's particular standard (IEC 60601-2-22), the output laser can be either the laser energy or the laser power. The laser power is the radiant flux of the work beam and the laser energy is the radiant energy, both incident on the working area [8].

Following the same recommendations of the particular standards for laser and IPL, this parameter should be evaluated for OCT equipment. The accuracy of the radiation output is fundamental to assure successful device-tissue interaction. It is also important to inform the maximum radiation emitted by the light source on the accompanying documents.

3.4. Pulse interval

The interval between pulses is the time from the end of one pulse and the beginning of the next, measured at 50% trailing and leading edges respectively, as the definition of IEC 60601-2-57 states [9].

For devices using pulsed sources, it is suggested to measure and inform the pulse interval value on the accompanying documents.

3.5. Number of pulses in pulse train

A pulse train is a series of pulses where the total pulse time in a solely exposure does not exceeds 0.25 s in the wavelength region between 400 nm and 700 nm. For other wavelengths, this total pulse time exposure changes to 10 s.

As for the other parameters related to pulses, it is suggested to evaluate and inform the value on the device's manual.

3.6. Spectral irradiance

The irradiance (E) is defined by the IEC 60825-1 standard as:

$$E = \frac{d\Phi}{dA} \qquad [W/m^2], \tag{1}$$

where dΦ is the radiant flux incident on an element and A the element's area [7]. For all possible configurations of the device, the spectral irradiance varies according to different wavelengths.

It is recommended to inform the spectral irradiance on the OCT documents, as it is already required by the particular standard for IPL (IEC 60601-2-57).

3.7. Concentricity between aim beam and work beam

The aim beam indicates the area of work and the work beam is the radiation beam emitted by the output laser. The concentricity between them must have a sufficiently small tolerance as to avoid undesirable effects. The maximum lateral displacement allowed between both centers must not be over 50% of the biggest diameter [8].

The concentricity between aim beam and work beam has the same importance as the diameter and divergence of the work beam. To assure the aim marks the real spot where the electromagnetic radiation is applied means guaranteeing the treatment/diagnostic occurs on the correct region. Thus, the measurement of this parameter is recommended to attest the equipment's reliability.

3.8. Exposure time and limit

The exposure time is the duration of continuous laser radiation (or pulse, in case of pulsed sources) incident upon the human body. This value varies according to the application and the type of exposed tissue [9]. As for the exposure limit, the IEC 60601-2-57 particular standard for IPL defines it as the maximum level of eye or skin exposure where adverse biological effects are not expected.

Both these parameters should be known by manufacturers and users to ensure safe application of the equipment in their respective areas. Hence, it is suggested the inclusion of this information in the documentation.

3.9. Ocular and/or skin hazard distance

The particular standard for IPL (IEC 60601-2-57) defines as the distance from the emission aperture where the irradiance in a certain exposure time is equal to the limit exposure value of the eye and skin, respectively, for the parameters ocular and skin hazard distance.

Considering that OCT has ophthalmological and dermatological applications, it is recommended to inform these values on the accompanying documents, according to the equipment's application.

3.10. Central wavelength

The emission wavelength (nominal wavelength) and the source's power determine OCT's depth penetration [4, 5]. The depth penetration of the light is limited by the optical properties of biological tissues, depending on absorption and scattering. In the visible region of the spectrum (400 nm to 700 nm), light absorption by biological tissue is higher compared to the near infrared region (approximately from 800 nm to 2500 nm). The reason for this behavior in the near infrared region is the fact that the wavelength is too long to result in a high number of electrons transitions, but too short to induce vibrational transitions in the water. All biological risks are evaluated around these wavelength values.

In that, it is recommended to inform this parameter on the OCT system's documentation.

3.11. Axial resolution

The axial resolution is an important specification for OCT systems. In most biomedical applications, high axial resolution is necessary to distinguish boundaries and differentiate types of tissue. Also known as longitudinal resolution, it is related to the coherence length of the light source, but also depends on absorption and scattering properties of tissue. This relation with the coherence length is due to the broadband nature of the light, where the interference between optical fields is only observed when the lengths of the optical path on both reference and sample arms correspond to the coherence length of the light [5].

High axial resolution can be achieved regardless of focus conditions of the beam. Considering a source with Gaussian spectrum distribution, the axial resolution Δl is:

$$\Delta l = \left(\frac{2\ln 2}{\pi}\right)\left(\frac{\lambda^2}{\Delta\lambda}\right), \tag{2}$$

where $\Delta\lambda$ is the source band width and λ is the central wavelength.

It is suggested the evaluation of the axial resolution, a crucial parameter to determine imaging potential of OCT systems. The axial resolution values for air and water should be informed on the accompanying documents.

3.12. Transverse resolution

One advantage of the OCT is the total disassociation between the transverse and axial resolution. The transverse resolution Δx, also known as lateral resolution, in OCT systems is determined by the size of the focal point, as in conventional microscopy [10].

$$\Delta x = \left(\frac{4\lambda}{\pi}\right)\left(\frac{f}{d}\right) \tag{3}$$

where d is the spot size at the lens and f is the focal length. High transverse resolution is achieved using large numerical aperture and focusing the beam in a small spot size.

As for the axial resolution, it is suggested both the measurement and inclusion of the transverse resolution value in the documentation.

Table 1. Parameters recommended for reliability evaluation of biomedical equipment based on OCT. The recommendation for the measurement of the parameter and/or inclusion of its information in the accompanying documents is indicated. * parameter mentioned in the standard IEC 60601-2-22 for laser equipment; † parameter mentioned in the standard IEC 60601-2-57 for non-laser light source equipment.

Parameter	Documentation	Measurement
Central wavelength	✓	
Concentricity between aim beam and work beam		✓
Beam diameter	✓	
Ocular hazard distance and/or skin hazard distance†	✓	
Beam divergence*		✓
Pulse or pulse train duration*†	✓	✓
Pulse interval†	✓	✓
Spectral irradiance†	✓	
Exposure time	✓	
Exposure limit	✓	
Number of pulses in pulse train†	✓	✓
Axial resolution	✓	✓
Transverse resolution	✓	✓
Optical radiation output*†	✓	✓

For all the parameters in which measurements are indicated to assess metrological reliability of the optoelectronic equipment, it is recommended to include the estimation of measurement uncertainty.

Considering the necessity of assuring reliable diagnostics and safety during the whole period of biomedical equipment clinical use [3], some of the recommended parameters mentioned on Table 1 should be performed throughout the equipment lifetime, as the concentricity between aim beam and work beam; beam divergence; pulse or pulse train duration; pulse interval; number of pulses in pulse train; axial resolution; transverse resolution; and optical radiation output.

In the literature, it is emphasized another important aspect concerning metrological reliability for this optical technique on continuing expansion in medical diagnostics applications is the method validation, that is currently limited by the lack of comparable techniques and incomplete database regarding optical properties of tissue (refractive index, scattering and absorption of light by the tissue) [11].

4. Conclusion

Although the already well-established clinical use and important perspectives as a diagnostics tool for imaging in vivo tissues, there is no international standard addressed to optical coherence tomography (OCT) for biomedical application.

In this study, the OCT system characteristics are analyzed aiming at identifying parameters that need to be evaluated to ensure metrological reliability for biomedical use of optical coherence tomography devices.

Based on the published particular international standards for laser and non-laser light source equipment intended for biomedical applications [7–9], some common evaluation parameters for OCT and these optical techniques were identified as: ocular and/or skin hazard distance; beam divergence; pulse or pulse train duration; pulse interval; spectral irradiance; number of pulses in pulse train; optical radiation output. Considering the lack of a specific standard for OCT, the evaluation of these parameters in common with other optoelectronic equipment could already be considered for conformity assessment.

Nevertheless, the evaluation of these parameters mentioned in the published standards is not enough to ensure the metrological reliability of OCT. The additional specific parameters, not existent in the laser and IPL standards, but identified in this work as necessary to be evaluated includes: central wavelength; concentricity between aim beam and work beam; beam diameter; exposure time; exposure limit; axial resolution and transverse resolution. The measurement uncertainty estimation is recommended for each measuring parameter suggested.

Considering the great potential of OCT as an imaging technique useful in multiple biomedical applications, it is essential to ensure its metrological reliability. The evaluation parameters suggested in the present work can be a contribution in the case of a future development of a particular standard specifically addressed to the non-invasive imaging technique by OCT intended for clinical applications.

Acknowledgments

This work was financially supported by CNPq and PUC-Rio.

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