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A digital system of fluorescence visualization for antibacterial photodynamic therapy in dentistry

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Abstract

In the present work, a novel compact system for visualizing the spatial intensity distribution of the photosensitizer fluorescence for antibacterial photodynamic therapy in dentistry is suggested. The compact intraoral system includes a visible imaging camera and a violet laser diode. The wavelength of laser radiation is matched to the short-wavelength absorption peak of Photoditazin, so the effective excitation of its fluorescence is ensured. The built-in spectral-selective optical filter allows the camera to detect only the spatial distribution of the fluorescence intensity while the excitation radiation is blocked. Intraoral fluorescent images obtained with the suggested system can be used for diagnosis of residual amount of pathogens.

Keywords: Dentistry; Antibacterial photodynamic therapy; Fluorescence visualization; Intraoral camera.

1. Introduction

The photodynamic therapy (PDT) is currently rapidly developing as a method for treating cancers of various sites. This method is based on generating active oxygen as a result of a photochemical reaction at a cellular level using a photosensitizer. The pharmacokinetics of the photosensitizer determines its selective accumulation in mitochondria and membranes of pathological cells. When photosensitized tissues are exposed to optical radiation, non-toxic triplet oxygen is transformed into a singlet form that has a pronounced cytotoxic effect leading to the disruption of cellular membranes in tumor cells [1,2].

The efficiency of PDT is largely due to the physicochemical, the pharmacodynamical and the pharmacokinetic properties of the photosensitizer. There are currently several groups of photosensitizing compounds, in particular, those based on porphyrins and chlorins. Photosensitizers based on the derivatives of chlorin e_6, including the commercially available Russian compound Photoditazin® [3], are among the most

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viable due to their biomedical, optical and physical properties.

At the same time, the efficiency of the PDT method depends to a great extent on the spectral content of the optical radiation exciting the photochemical reaction of the photosensitizer. Obtaining agreement between the spectral content of the radiation and the absorption spectrum of the photosensitizer could significantly improve the efficiency of the photosensitizer's optical excitation and reduce the side effects from the irradiation of healthy tissues. The recent advances in semiconductor optoelectronics allow to reach this agreement for virtually any photosensitizer, as cheap compact high-power sources of laser radiation based on semiconductor laser diodes have been developed [4].

One of the significant advantages of the PDT method is the fact that the photochemical reaction is accompanied by the fluorescence of both the photosensitizer and the singlet oxygen produced as a result of the reaction. The fluorescence analysis allows to perform *in situ* diagnostics, i.e., directly during photodynamic therapy; additionally, this offers opportunities for early cancer detection. Primary imaging of the photochemical reaction proceeding is possible from the analysis of the singlet oxygen photoluminescence intensity and its spatial distribution. However, its fluorescence spectrum is located in the near-infrared range with the maximum at a wavelength of 1270 nm [5,6]. The systems previously developed for imaging the photoluminescence of oxygen used near-infrared sensitive cameras based on InGaAs and spectrally selective filters [5,6]. However, these systems are rather expensive and are used mainly in fundamental studies.

In contrast to the luminescence spectrum of singlet oxygen, the spectral features of Photoditazin's fluorescence lie in the visible region where photosensitive Si-based CCD and CMOS arrays can be successfully used for imaging; these are considerably cheaper than the InGaAs-based devices. The studies carried out using a two-channel imaging system for the visible and the infrared regions [5] have revealed a correlation between the photoluminescence intensities of singlet oxygen and of the photosensitizer, which allows performing photoluminescence diagnostics of the photosensitizer in the visible area. This system includes a monochrome silicon camera, a diode illuminator, and software for imaging and analyzing the spatial distribution of Photoditazin's photoluminescence; it has already been devised [7,8], has successfully passed clinical trials as a means of diagnosing malignant tumors presenting externally, and is authorized for use in the Russian Federation [9].

Even though the PDT method was initially developed to treat malignant tumors presenting externally, recently it has found application in other areas of medicine, e.g., in dentistry, as an anti-aging therapy in aesthetic medicine, etc. The type of PDT used in dentistry is antibacterial photodynamic therapy (APT) that allows to combat pathogenic bacterial flora in the oral cavity. Lately, a number of studies reported having successfully used APT for treating inflammatory periodontal diseases [10], and for photoactivated decontamination in endodontics and periodontology [11]. However, no data could be found in literature on using the main advantage of photodynamics, i.e., the fluorescent diagnostics for control during APT, since the currently existing imaging systems for PDT [5–7] cannot be used in dentistry due to their large sizes.

The present study proposes a new original compact system for imaging photochemical reactions; the system can be used in dentistry for fluorescent diagnostics during antibacterial photodynamic therapy.

2. The optical properties of Photoditazin

Photoditazin was chosen as a photosensitizer for the system of fluorescent diagnostics during APT in dentistry that we have developed on the strength of the compound's overall properties. Its optical characteristics, and, in particular its optical absorption spectrum, are well-known. Photoditazin has an absorption line at a wavelength of 653 nm, a number of weak features in the 500- and 600-nm regions, and a strong absorption line with a maximum at 403 nm. The fluorescence spectra of Photoditazin when excited by radiation of various wavelengths were measured and discussed in detail earlier in Ref. [12]. The results of this study are shown in Fig. 1 as the absorption spectrum of a Photoditazin solution and the spectra of its photoluminescence when excited by light at 650- and 405-nm wavelengths.

One of the important parameters of PDT in oncology is the penetration depth of the exciting radiation into biological tissues. The Photoditazin absorption line at the 653-nm wavelength is typically used for the above-described purposes, as radiation with this wavelength has a fairly substantial penetration depth. Rather stringent requirements are imposed on the optical elements performing the spectral filtering of the useful photoluminescence signal from the spurious signal of the scattered exciting radiation. For example, when using optical bandpass filters to block the exciting radiation, the variation in optical density in the narrow (about 10 nm) spectral range between the