CATHETERS EMPLOYED IN DIAGNOSIS AND BIOCHEMICAL ANALYSIS BY RAMAN SPECTROSCOPY

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Abstract
The present review is focused on the advancements in biomedical engineering regarding the elaboration of new prototypes of optical fiber catheters to be applied in spectroscopic analysis, such as Raman and Fluorescence spectroscopies. New prototypes with interesting properties have been developed, such as side-viewing signal excitation and collection, distal tip with bending control and Raman scattering minimization from the optical fiber. In addition, several groups have contributed with new catheters improving other properties of this spectroscopic device. In this work, we revise this topic, analyzing the advancements and limitations of the recent biomedical catheters.
Keywords: optical fibers; Raman spectroscopy; Fluorescence spectroscopy; catheters; biomedical engineering; diagnosis.
Area of Knowlwgement: Biomedical Engeneering

Introduction

In the clinical environment, optical techniques, such as microscope, ophthalmoscope, endoscope and colposcope, have been employed by many years. The integration of spectroscopies has improved the clinical analysis, involving biochemical evaluation and diagnosis. Fiber optic assemblies provide a flexible solution for an adequate optical interface between the spectroscopic device and the biological samples that are evaluated *in situ* [UTZINGER et al., 2004].

Many medical applications require remote sampling by use of optical fibers in which the sizes of the probe and the fiber bundle are strictly limited by anatomic aspects. For example, the ability to clinically evaluate coronary atherosclerosis and breast cancer requires probes with a diameter of ~2 mm or less to be incorporated into standard cardiovascular catheters or configured for optical needle biopsy. Similar constraints are presented with endoscopic employments, in which the probe should be inserted into a narrow-diameter channel. In addition, time of data acquisition must be limited to a few seconds [MOTZ et al., 2004].

Optical catheters, in medicine, minimize the invasiveness in surgical procedures with a corresponding decrease in risk, time for patient recuperation and cost. The catheter configuration for diagnosis and treatment of the human body depends on the optical technique and location of the human organ. Furthermore, the materials for assembling the catheter must show high resistance against biochemical reactions, low toxicity, and high stability when used in sterilization procedures [LIMA et al., 2000].

Utilization of fiberoptic catheters can improve significantly the employment in diagnosis and biochemical analysis of instrumental techniques, such as Raman and fluorescence spectroscopies, becoming these tools very powerful bio-medical diagnostic probes [LIMA et al., 2004].

Material and Methods

A review of the literature was developed, bases on high quality articles, focusing the employment of Raman Spectroscopy and fluorescence and the advances in biomedical applications of these techniques associated to fiberoptic cateters. The articles were selected from pubmed and from the Web of Science databases.

Results and discussion

The practical implementation of Raman spectroscopy in biomedical engineering requires an integrated instrument that can provide, preferentially, real-time spectral analysis and diagnostic information to the clinician. This application needs a catheter system perfectly associated to the Raman spectroscopy instrument in order to furnish the signal of Raman scattering from the biological sample to the Raman spectrometer. Furthermore, it is important to notice the association between Raman spectroscopy and other tools, which have been employed in order to contribute with the physicians in the diagnostic and therapeutic procedures. For example, we can cite the intravascular ultrasound that has been used combined with Raman spectroscopy to localize and quantify cholesterol and calcium salts in atherosclerotic coronary arteries [ROMER et al., 2000].

Catheters made with silica have been developed for application with Raman spectroscopy [SHIM et al., 1999; LIMA et al., 2008]. Fiberoptic near infrared Raman spectroscopy has also been employed for differentiation of colon polyps with high accuracy [CROW et al., 2005].

Raman measurements undergo the optical influence of the material that constitutes the catheter, decreasing signal to noise ratio (SNR) of the resultant spectra. In fact, Lima and co-workers [2008], elaborated a dielectric optical filter called “bandpass”, which has been deposited upon the surface of the tip of the central fiber optic (distal probe). Other six fibers without any optical filter are disposed around this central optical fiber with “bandpass”. This prototype of small caliber catheter presented significant decrease of the silica Raman scattering when compared with unfiltered catheters, being a very auspicious prototype to improve the analytical ability of this methodology [COTHREN et al., 1986]. It is also relevant to mention the article of Ma and Li [1998]. These authors elaborated two types of optical probes, efficiently reducing the interference of the Raman scattering background by the exploiting an optimum spatial distribution of the respective background in each one of them, since the distribution of the background from the silica fiber is highly dependent on the numerical aperture. However, it is important to notice that this methodology is not adequate to *in vivo* applications, since its set-up is not easily adaptive to the biological conditions.

Komachi and co-workers [2006] elaborated a Raman spectroscopic catheter with an outer diameter of 2 mm to be used in diagnosis of atherosclerotic coronary disease. This prototype presents a side-view-type micro-Raman probe, an imaging fiber bundle, a working channel (injection drain) and a balloon, which by inflating allows a disposition close to the inner wall of a modeled blood flow system. Preliminary results obtained demonstrate the possibility of application of this catheter in methodologies of diagnosis of coronary lesions.

Our group described the development of a catheter with side-viewing. The spectroscopic results obtained by this device are very similar to those obtained by the “traditional” front-view catheter.

Raman biospectroscopy has been considered an interesting clinical procedure to biochemical analysis and diagnosis of cardiovascular diseases, such as atherosclerosis. Komachi and co-workers [2006] presented a new prototype of catheter with a kind of balloon coupled in the distal tip. This balloon increases its volume in the moment of signal collection and the Raman scattering is obtained through a lateral optical system [25]. However, this methodology implies in the almost total obstruction of organs and arteries, becoming the clinical procedure of biospectroscopic analysis very difficult in small organs and increasing the inherent risk of this invasive method. On the other hand, the new catheter proposed by Lima and co-workers [2008], which has a diameter much lower than that commonly used, does not present this balloon system, permitting to obtain a very intense signal from the biological sample without causing any obstruction in organs with small endoluminal diameter.

The employment of fluorescence emission spectroscopy has been considered able to differentiate normal and neoplastic human tissue [HAGE et al., 2003]. Indeed, trials involving reflectance spectroscopy using a fiber optic probe in the screening and diagnostic settings in order to detect several diseases, such as cervical neoplasia, have been developed with auspicious results.

Conclusions

The present review is focused on the novel advancements of biomedical engineering with respect to the new prototypes of catheters and their potential employment to improve the applications in biochemical analysis, diagnosis and therapy.

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