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# Catheter with dielectric optical filter deposited upon the fiber optic end for Raman *in vivo* biospectroscopy applications

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**Abstract.** Raman spectroscopy (RS) is a powerful tool that allows obtaining significant biochemical information from biological tissue. The fiber optic catheter permits applications *in vivo* that present wide clinical employment. This biochemical analysis is developed through a guide light that furnishes to Raman spectroscopy system the data obtained from tissue. These Raman signals represent the modes of vibration of molecular groups that are present in the biological molecules. Raman measurements undergo the optical influence of the material that constitutes the catheter, mainly Raman scattering of the silica that composes the fiber optic, decreasing signal to noise ratio (SNR) of the resultant spectra. In this work, a dielectric optical filter called “bandpass” was deposited upon the surface of the tip of the central fiber optic (distal probe). Indeed, other six fibers without any optical filter are disposed around this central optical fiber with “bandpass”. This prototype of catheter presented significant decrease of the silica Raman scattering when compared with unfiltered catheters. The biomedical applications of this new catheter are auspicious, involving biochemical analysis and diagnosis *in vivo*, since the SNR improvement obtained propitiates a much more informative Raman spectrum.

Keywords: Fiber optic, catheter, optical filter, spectroscopy, *in vivo* applications

## 1. Introduction

The clinical process to assess pathological changes in tissue is currently related to the histopathology. However, the management of biopsy material and the interpretation of the respective analysis are not trivial procedures. The clinical characterization based on these analyses inevitably leads to diagnostic delay and the possibility of taking an unrepresentative sample. Furthermore, this kind of clinical procedure presents high cost and provokes significant patient trauma [1]. Thus, several spectroscopies have been considered as basis for non-invasive and non-destructive measuring systems [2]. In fact, the clinical procedures that are, at least, minimally invasive methodologies present several advantages when compared with the conventional techniques. Among the recent applications of optical spectroscopic methods

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in medicine, we can mention, for instance, the gastrointestinal endoscopy, which is likely one of the most important areas of impact of this biomedical approach [3,4].

In this context, optical catheters have been employed in medicine with excellent perspectives in order to minimize the invasiveness of surgical procedures with a corresponding decrease in risk, time for patient recuperation and cost. Furthermore, the materials for assembling the catheter usually present high resistance to biochemical reactions and sterilization procedures and very low toxicity [5].

The catheter configuration for diagnosis and treatment of the human body depends on the optical technique and the location of the human organ. Thus, efforts have been made in order to elaborate fiber-probes with excellent signal collection capabilities, adequate flexibility to scan different spatial regions of the sample and less background signals generated in probes themselves [6].

Raman spectroscopy is an important technique that permits to obtain precise information about biochemical features from the sample, representing a potential use for diagnostic and therapy medical applications [7,8]. For *in vivo* application, it is necessary that the respective organ presents significant accessibility to the instrumental method of analysis. In this way, the fiber optic catheter has been considered a very convenient device, because it shows adequate mechanical and light characteristics, which allows the guiding of the light from biological tissue until Raman spectroscopy system with laser excitation.

Raman signal from the biological tissue presents very low intensity when compared with laser excitation [8]. Moreover, the Raman scattering from sample is superposed by the intrinsic radiation generated from the probe materials characteristics [5] and also Raman scattering from the silica of the seven optical fibers of catheter. Indeed, these optical influences difficult the detection of the Raman intensity from the sample, therefore, decreasing the signal to noise ratio (SNR) [10]. These difficulties are inherent to the use of catheters associated to the Raman spectroscopy and have limited the widespread and the quality of results of this instrumental technique, especially in biochemical analysis and diagnosis.

Different techniques have been employed to overcome these limitations, improving the SNR of the Raman spectra [11,12]; however, for most of them, the applications are restricted to *in vitro* conditions. One attempt has been made with Raman filtered fiber optic probe which can be used for *in vivo* conditions [13]. However, in this technique, the optical filters are not directed toward the distal tip catheter, i.e., the optical filters are not disposed in the distal end of the catheter, implying that the residual noise generated specifically by the distal region remains emitting significant Raman scattering, which provokes damage in the SNR. Furthermore, this catheter presents great diameter, which limits significantly its flexibility, disfavoring its *in vivo* applications. In fact, these limitations difficult the accessibility of the probe to endoluminal organs, which present small curve radius and diameter [6,14]. In this way, the development of new prototypes of catheter has been considered a relevant contribution to improve the employment of the Raman spectroscopy in biochemical analysis and diagnosis.

In the present work, we have deposited an optical filter denominated “bandpass” upon the tip surface of the central optic fiber of a very thinner catheter in order to improve its SNR as well as its accessibility in organs with small cavities. Therefore, this new catheter presents interesting characteristics, such as little diameter, in order to be applied in several kinds of clinical studies. The data obtained with this original “coating” procedure are discussed in agreement with recent reports of the literature.

## 2. Materials and methods

Upon the polished end of the silica fiber optic a “bandpass” optical filter was deposited. The filter was centralized in 830 nm, where 22 layers of dioxide of titanium ($TiO_2$) and dioxide of silicon ($SiO_2$)

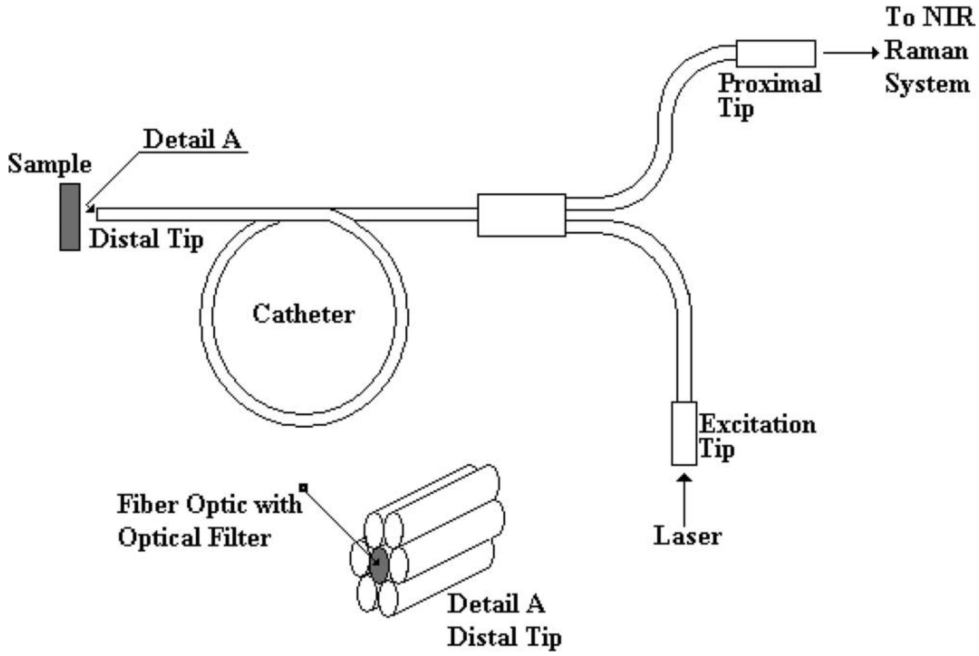


Fig. 1. Set up NIR Raman system to obtain spectra measurements from catheters.

were deposited at convenient sequence. The deposition system utilized was the Leybold-L560. It was also employed a Perkin Elmer $\lambda$20 spectrometer with adaptive fiber optic device, which allowed to verify the optical filter spectrum deposited upon the polished tip of the silica optical fiber. Two Raman fiber optic catheters were assembled with seven fibers each, and the fiber optic with optical filter was positioned in the central part of the distal tip of the first catheter (Fig. 1), while the second catheter remained without any coating. In order to compare these catheters, it was utilized the near infrared Raman (NIR) set up that presents µLS (USA) diode laser with $\lambda = 830$ nm model L48305-115-TE, which was used as an excitation source. This NIR laser radiation focuses onto the catheter excitation tip and goes until the distal tip to excite the sample. The Raman scattering from the sample is collected by the six collection fibers and goes to spectrograph (Chromex, USA, model 250IS)/detector/computer system. A CCD detector (deep-depleted version, Princeton Instruments, USA, model LN/CCD-1024-EHR1), with liquid nitrogen cooling, was used for signal detection. A detailed description of the equipment can be found elsewhere [15,16]. The silica fibers utilized in this work have core, clad and coating protection (polyamide) diameters of 0.200/0.220/0.250 mm, respectively, where the N.A. for all the fibers was 0.28. These optical guides were removed from the same bobbin.

## 3. Results

Figure 2a shows a spectrum obtained from the “bandpass” optical filter, deposited upon the polished surface end of the silica optical fiber. The filter is centered in approximately 12,048 cm$^{-1}$(830 nm), with 10 nm of Full Width at Half Maximum (FWHM) (Fig. 2b). This optical filter allows removing significant intensity of the Raman scattering from the fiber optic silica, also permitting to transmit the specific laser excitation. In the wavelength range between 10,000 and 12,300 cm$^{-1}$, which corresponds to the spectral

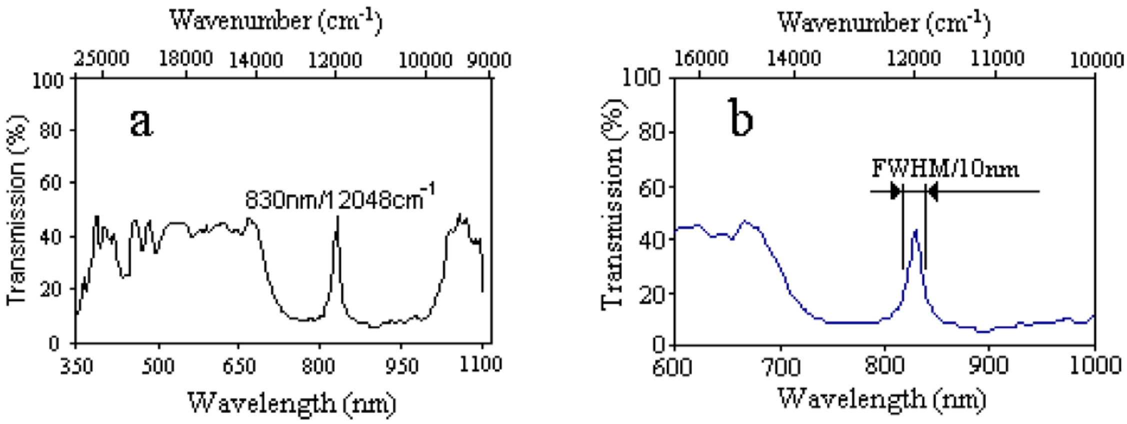


Fig. 2. Spectrum measured from the optical filter ("bandpass") deposited upon polished surface of the fiber optic tip.

region of the Raman scattering generated by the optical fiber, it is observed a significant attenuation of the Raman scattering intensity of the optical fiber. This Raman scattering intensity was reduced to approximately 10% of the value that corresponds to the catheter without optical filter. Therefore, this result demonstrates the efficiency of the "bandpass" optical filter in to decrease the Raman scattering of the optical fiber.

After the elaboration of this fiber optic with "bandpass" filter, it was assembled a Raman catheter with this fiber with "bandpass" as a central fiber positioned together with other six fibers without any optical filter. Other unfiltered fibers optic probe was also assembled constituting a second catheter to be used as a reference to evaluate the efficiency of the catheter with optical filter.

Figure 3 presents the spectra corresponding to the probes without contact with biological sample, being utilized in this measurement a metallic aluminum foil to be employed as reference. The first spectrum (a) is generated by a catheter without optical filter, while the second graph (b) is originated from a catheter with "bandpass" optical filter. Figure 3 permits to verify the efficiency of the optical filter in attenuate the Raman scattering from optical fiber. Indeed, the intensity of Raman scattering from the silica optical fibers was significantly decreased. It is possible to note in these spectra that the optical signal extends to 1100 $cm^{-1}$, and it consists of a number of broadened lines, which corresponds to different types of glass lattice vibrations of the quartz [17].

Figure 4 presents two spectra that permit to compare the effect of the presence of the optical filter in the catheter in contact with a sample of naphthalene. It was chosen this organic compound as sample due to the fact of its Raman signals are obtained in a large range of wavelength. In this way, we can to evaluate the signal to noise ratio (SNR) in the wide range of wavelength that corresponds to the intrinsic Raman scattering of the optical fiber. Thus, Fig. 4a represents the spectrum of a traditional catheter without filter, while Fig. 4b presents the spectrum from a catheter where the central fiber optic has a "bandpass" optical filter. It is possible to note the decrease of the Raman scattering intensity from the silica fibers in the catheter with optical filter. Therefore, it is clear that the optical filter was very effective in the attenuation process of the background of the Raman scattering of the optical fiber.

Figure 2a represents the spectrum obtained from an optical filter (bandpass type) deposited upon the fiber optic tip. In this spectrum, the optical filter with centered peak in 12,048 $cm^{-1}$, which corresponds to 830 nm in wavelength, only allows the transmission from the laser diode of a narrow band, attenuating the intrinsic Raman scattering of the silica optical fiber (Fig. 2b). It can be noted that the signal

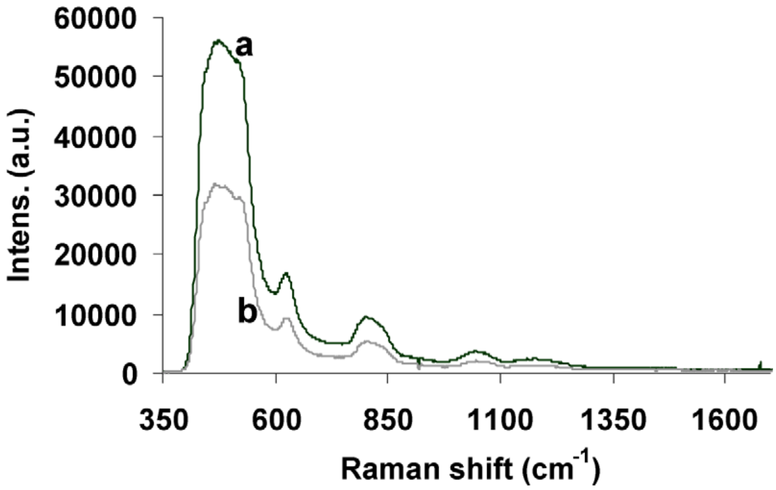


Fig. 3. Raman spectra obtained from catheters with and without optical filter. Spectrum a presents unfiltered catheter with fiber optic while the spectrum b is originated from catheter with optical filter. Distal tip was positioned in front of aluminum foil reflector. Diode laser output power from the probe is 42 mW with time of exposition at CCD detector of 20 s.

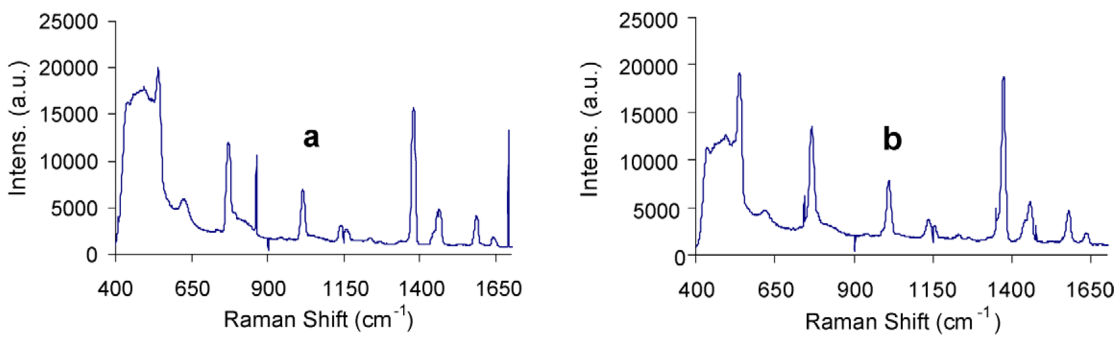


Fig. 4. Raman spectra utilizing two fibers optic catheters: (a) traditional catheter without filter; (b) catheter where the central fiber optic has a "bandpass" optical filter and other six fibers unfiltered. Both spectra measurements were made with diode laser power 42 mW, and detector CCD with time exposition of 20 s. Naphthalene was the sample used in this analysis.

that represents the range between 10,000 and 12,300 cm$^{-1}$, coincides with approximately 10% of transmission from optical filter disposed on the fiber optic tip. Considering Fig. 3b, it is possible to infer the Eq. (1) that represents the amount of the scattered Raman signal from the optical fibers of the catheter with optical filter at central fiber:

$$0.23R_{\text{fexc}} + R_{\text{fcol}} = B, \tag{1}$$

where $R_{\text{fexc}}$ represents the Raman intensity scattered from the central fiber optic catheter, which corresponds to the fiber of laser excitation with optical filter. $R_{\text{fcol}}$ is associated to the Raman scattering intensity from the six optical fibers of signal collection disposed around the central optical fiber, which is responsible for the excitation by laser. Figure 3a represents the formulation to quantitative determination of intrinsic Raman intensity scattered from the unfiltered fiber optics catheter, which can be represented by the Eq. (2):

$$R_{\text{fexc}} + R_{\text{fcol}} = A. \tag{2}$$

The $A$ value represent the area of the spectrum of the unfiltered catheter while the $B$ value corresponds to the spectrum area of the filtered catheter. These respective areas were calculated using numerical data obtained in the same wavelength range (420–1200 $\text{cm}^{-1}$), employing the Origin software. This analysis was developed obtaining $R_{\text{fexc}} = 5.8$ and $R_{\text{fcol}} = 4.5$. Thus, the calculations obtained from the spectra presented in Fig. 3, has demonstrated that the distribution of Raman scattering involving the excitation and collection fibers present proximal values, i.e., the Raman intensity scattered from the fiber of excitation by laser and the fibers of signal collection does not have significant difference.

## 4. Discussion

In the present work, we have developed a catheter with small diameter to be used in Raman biospectroscopy. Indeed, for this employment, the catheter needs some specific properties. Thus, in the process of elaboration of the probe, several aspects must be considered, such as probe caliber. Actually, for this kind of use, the optical fibers require small diameter, which is associated to significant catheter flexibility for *in vivo* applications.

It is important to notice that the methodology of coating deposition in very small surface is an auspicious interdisciplinary area. Our group has worked with small surfaces, which corresponds to approximately 0.250 mm of diameter, constituting in an excellent prototype of probes to several *in vivo* biological applications, such as diagnosis of atherosclerosis. In fact, $SiO_2$ and $TiO_2$ have demonstrated adequate compatibility with the quartz of the optical fiber, allowing the formation of a very stable thin film on the surface of the fiber tip. Really, this coating presents high mechanical resistance and excellent adherence on the silica surface, propitiating significant durability to the film. Moreover, it is well-established that $SiO_2$ and $TiO_2$ are biocompatible compounds used in various biomaterials, such as prosthesis, illustrating the excellent perspectives regarding this new catheter [18].

This new catheter with optical fiber modified with “bandpass” optical filter could be employed in various biological samples as well as in synthetic compounds used in pharmacology. These compounds of biological relevance present important Raman scattering bands in the wavelength region that coincides with the Raman scattering of the optical fiber. In this way, the fingerprint bands of several biological and synthetic compounds could be identified with more precision with this prototype of catheter, permitting, include, the development of semi-quantitative analysis. For example, we can to mention the typical bands of bones that occur in around 960 $\text{cm}^{-1}$ [19] as well as the characteristic bands of ephedrine, which appear in 1006 $\text{cm}^{-1}$ [14].

Therefore, an optical filter (“bandpass”) was deposited directly on the surface of the polished tip of the central fiber optic, and this filter allowed decreasing the intensity from the Raman scattering in the silica optical fiber. This procedure resulted in improvement of the SNR. It is relevant to notice that the remaining noise is generated from the six fibers of signal collection without optical filter, by the laser light reflected and backscattered from the sample. In near future, we expect to improve the “bandpass” filter deposited directly upon central fiber optic as well as to develop another “longpass” optical filter upon the six optical fibers. Thus, with this methodology of catheter surface modification, we expect to minimize drastically the probe noise. It is interesting to register that in a previous article, our group divulgated a new optical fiber catheter with distal end bending mechanism control [14] that together with the present data will permit a total control of the movements of the catheters in organs and tissues of difficult accessibility, favoring a improvement in the analysis by Raman spectroscopy. In fact, we have applied instrumental tools, such as Raman spectroscopy, in order to improve the methodologies employed in biomedical engineering, allowing, in this way, a significant advancement in the clinical procedures of diagnosis [20,21].

## 5. Conclusions

This article presents the methodology of elaboration and the effective results of a new kind of catheter with interesting properties to biomedical *in vivo* applications. This catheter improved significantly the signal-to-noise ratio (SNR) of the Raman spectra obtained through action of the optical filter fixed on the optical fiber. New studies focused on applications in diagnosis of this new catheter are been developed and auspicious results have been found.

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