Raman Spectroscopy for Cancer Diagnosis

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Abstract

Both Raman spectroscopy and surface enhanced Raman spectroscopy (SERS) are proving to be invaluable tools in the field of biomedical research and clinical diagnostics. The robust, compact, fit-for-purpose Raman spectrometer designs are appropriate for use in surgical procedures to help surgeons assess tumors and allow rapid decisions to be made. Raman systems are also being developed for molecular diagnostic testing to detect and measure human cancer biomarkers. Based on the SERS technique, this approach potentially could change the way bioassays are performed to improve both the sensitivity and reliability of testing. The two applications highlighted in this review, together with other examples of the use of Raman spectrometry in biomedical research areas such as the identification of bacterial infections, are clearly going to make the technique an important part of the medical toolbox, as we continually strive to improve diagnostic techniques and bring a better health care system to patients. Raman spectroscopy is increasingly investigated for cancer diagnosis. As the potential of the technique is explored and realized, it is slowly making its way into clinics. There are more reports in recent years showing promise that it can help clinicians for cancer diagnosis. However, a number of challenges remain to be overcome, especially in vivo cancer diagnosis. In this article, the recent progress of the technique toward clinical cancer diagnosis is discussed from a critical perspective.

In recent years, Raman spectroscopy has gained widespread acceptance in applications that span from the rapid identification of unknown components to detailed characterization of materials and biological samples. Raman spectroscopy is a promising new tool for noninvasive, real-time diagnosis of tissue abnormalities. Here, we show evidence of its application for cancer diagnosis in four distinct tissue types: skin, breast, gastrointestinal tract, and cervix. Multivariate statistical analysis and discrimination algorithms allow for automated classification of the spectra into clinically relevant pathological categories using histology as a gold standard. Although limitations exist, the technique shows every indication of being an exciting prospect in the management of cancer in a clinical setting.

Optical spectroscopy has been around for many years and traditionally has been applied to a number of diverse fields, including analytical chemistry, geology, and even art history. Over the past 20–25 years, the use of optical spectroscopy for biomedical applications has grown significantly. Its attractiveness comes from its ability to provide quantitative information about the biochemical and morphological states of tissue in a minimally invasive or noninvasive manner. Spectra typically are collected with fiber-optic probes and charge-coupled device (CCD) cameras, and diagnostic algorithms have been developed to discriminate between different categories of tissue. Of the many optical spectroscopic techniques, fluorescence spectroscopy was one of the first to be

developed as a diagnostic tool for a variety of diseases including cancers and plaques, as well as other conditions such as burns. However, although fluorescence spectroscopy can differentiate between normal tissue and disease (cancer) successfully, it suffers from a lack of specificity when differentiating between multiple non normal groups. Diffuse reflectance spectroscopy provides valuable structural information by determining tissue optical properties. The lack of information regarding tissue biochemistry makes this method generally insufficient by itself for tissue diagnosis. In recent years, Raman spectroscopy has garnered a great deal of interest in disease diagnosis, particularly cancer, because of its ability to provide molecular specific information about tissues.

Raman scattering is an inelastic scattering process that occurs when an electron enters a virtual excited state due to an incident photon, then falls back to a higher or lower vibrational energy level with accompanying release of a new photon. The energy transfer is proportional to a specific vibrational mode of the molecule, so Raman spectra are independent of excitation wavelength, and the change in energy between the incident and released photon is displayed as relative wave numbers (1/wavelength). Raman spectral peaks tend to be narrow, particularly in the fingerprint region of about 700–2000 cm^{-1} , and each peak can be associated with specific vibrations in molecular bonds. Thus, this technique provides biochemical information about a sample, including conformations and concentrations of constituents with the level of detail that is determined by the instrumentation and the need of the application.

Over the years, different forms of Raman spectroscopy have been developed and used for biological application. The earliest of these is Forier transform (FT)-Raman spectroscopy, a method that measures Raman spectra with high signal-to-noise ratio and minimal fluorescence interference and has been used for many in vitro applications. The typically long integration times and bulky instrumentation negate this technique for in vivo use. Ultraviolet resonance Raman spectroscopy can be used to target specific molecules by selecting excitation wavelength at their resonance, thus yielding strong Raman signals. The high excitation intensities and mutagenicity of UV light prevent the application of this technique for in vivo use. Surface-enhanced Raman spectroscopy (SERS) is an excellent technique that can detect molecular signatures in trace amounts and has been pursued for such applications as biochips. However, the use of silver and other such element for enhancement prevents its implementation in vivo. Thus, near-infrared (NIR) dispersive Raman spectroscopy, in which NIR excitation minimizes fluorescence and absorption by tissue, has been the technique of choice for in vivo applications.

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