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Spectroscopic View of Life and Work of the Nobel Laureate Sir C.V. Raman

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ABSTRACT

Raman spectroscopic and microscopic techniques have been used for nondestructive characterization of tissues and to differentiate benign and malignant tissues. The discovery of the principles of spectroscopy is credited to Sir C.V. Raman of India, who in 1930 brought the Nobel Prize in Physics to the East side of Suez. We present the life and work of Sir C.V. Raman with brief review of the uses of Raman spectroscopy in urology.

INTRODUCTION

THE DISCOVERY of the principles of spectroscopy is credited to Sir C.V. Raman (1888–1970). Raman spectroscopy is being used increasingly in the field of urology, most often to differentiate benign and malignant tissues. Currently, it is being evaluated *in vitro* for the diagnosis of prostate and bladder cancer. The principles of this technology are also used in urolithiasis and other benign conditions affecting the urinary tract. The future may see the use of Raman microprobes with endoscopic and laparoscopic resections of benign and malignant tumors. We present the life and work of Sir C.V. Raman, who was awarded the Nobel Prize in Physics in 1930.

MATERIALS AND METHODS

Articles pertaining to the life and work of Raman were reviewed. Personal communications with his biographers were undertaken. Original articles published by Raman also were reviewed. Published studies utilizing Raman spectroscopy in the field of urology were obtained from a MEDLINE search.

BIOGRAPHY OF RAMAN

Chandrasekhar Venkata Raman was born in Tiruchinapalli, a small town in southern India, on November 7, 1888. He was the second child of Chandrasekharan Iyer, a professor of mathematics, and Parvathi Ammal. At the age of 11, he finished his school matriculation and moved to the Presidency College in Madras. At 15 years of age, he finished his Bachelor's degree with a gold medal conferred on him in physics. He received his Masters in physics in 1907 at the age of 17. During his graduate study, he published research on the diffraction of light and also on surface tension of liquids in London's *Philosophical Magazine*.[1]

As the opportunities for Indians for a career in the scientific arena were scarce before independence, Raman chose a career in accountancy, following in the footsteps of his elder brother. After passing the Financial Civil Service (FCS) examination in 1907, he was offered the post of Assistant Accountant General in Calcutta. Although he was working for the British Government in the finance sector, his quest for research in science led him to the Indian Association for the Cultivation of Science. His passion for research was such that Raman rented a house adjoining the Association, and a door was provided between his house and a laboratory where he started experimenting on the acoustics of musical instruments. He was a keen violin player himself. He worked on the excitation of string vibrations; motion of the bowed point; the effect of the bridge in coupling the motion of the string to the body of the violin; vibration phenomena of the piano, veena, and sitar; and also the harmonic overtones of Indian drums. In fact, he designed mechanically played instruments, contributing to the beginnings of robotic musical instruments.[2] He took the lead in bringing out the as-

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FIG. 1. Portrait of Sir C.V. Raman.

sociation *Bulletin* and *Proceedings*. In 1926, the latter was renamed the *Indian Journal of Physics*.

In 1917, when he was 29, Raman was appointed a professor at the University of Calcutta. Raman undertook his first foreign trip, representing his university at the British Empire Universities Congress at Oxford, in 1921 (Fig. 1). It was during this voyage, that his interest in the blue color of the sea led to a series of experiments on the diffraction of light, the findings of which were published in the esteemed journal *Nature* under the title "The Colour of the Sea."[3] Until then, it had been believed that the blue color of the sea was attributable to reflection of the sky and to absorption of the light by the particles suspended in the water. Further research carried out at University of Calcutta on the scattering of light led to the discovery of the Raman effect in 1928. The effect is the change in the frequency of monochromatic light after scattering. The spectrum of the scattered light gives clues to the molecular structure of the material under study, thereby helping to understand its properties.

Raman researched the scattering of light by various materials but mainly liquids. In April 1923, Raman and his associate Ramanathan noticed a weak secondary radiation, shifted in wavelength, along with normally scattered light, which was attributed to "fluorescence." Further research was carried out on the scattering of light in liquids, and in January 1928, Raman and Venkateswaran noticed that pure glycerin did not appear blue under sunlight but instead radiated a strong polarized green light. On February 28, 1928, Raman and Krishnan further refined this experiment by using a mercury arc as the light source and deduced the theory behind the Raman effect. On March 16, Raman reported his results to the Indian Science Association at Bangalore.[4] This secondary radiation showed several lines shifted toward longer wavelengths (the extent of the shifts being characteristic of the substance used) and indicated the absorption of energy by the scattering molecule. Ernest Rutherford described the finding of the Raman effect as "among the best three or four discoveries in experimental physics of the decade." Following this landmark discovery, Raman was awarded the prestigious Hughes Medal of the Royal Society of London (1930), and the Matteucci Medal of the Societa Italiana delle Scienze (1928), was knighted by King George V of Great Britain to attain the title of Sir (1929), and received honorary degrees from universities all around the globe. In 1930, he received the Nobel Prize in Physics "for his work on the scattering of light and for the discovery of the effect named after him."

Raman was associated with Mahatma Gandhi (Fig. 2) in the Indian freedom struggle from British imperialism. After receiving the Nobel Prize, Raman wrote "It is celebrated with much pomp and dignity. There were about ten thousand persons in the assembly. The Swedish king was in the chair. Five persons had to receive the prizes. All of them were seated in their chairs flanked by their countries' flags. I was sorry to see that I was under the British flag. India was still under British rule. The Civil Disobedience Movement was in full swing and Mahatma Gandhi was in jail. I was overcome by emotion when my name was called and I went up to receive the prize from royal hands." He also believed in self-reliance and the importance of educating the population and said "The true wealth of a Nation consists not in the stored-up gold in its coffers and the banks, not in the factories, but in the intellectual and physical strength of its men, women and children."

In 1933, Raman was made the Director of the Indian Institute of Science in Bangalore. In 1937, because of differences with the management, he had to resign the post but remained as the Head of the Department of Physics (1933–1948). He con-

FIG. 2. Raman standing behind Mahatma Ghandhi.

FIG. 3. Indian postage stamp in honor of Raman.

tinued his work on the diffraction of light, mainly by crystals, and encouraged many juniors to enter the field of physics.

In 1948, Raman set up the Raman Research Institute and became its first director. He was appointed the first National Professor by the government of a newly independent India in 1948.

Raman passed away on November 21, 1970, in Bangalore and was cremated in his beloved rose garden at the Raman Institute. In India, even today, February 28, the date on which Raman's discovery was reported, is observed as National Science Day, and a postage stamp was released to honor this great scientist (Fig. 3).

RAMAN SPECTROSCOPY AND ITS USE IN UROLOGY

Raman spectroscopy is an optical technique that utilizes molecule-specific, inelastic scattering of light photons to interrogate biological tissues.[5] When tissue is illuminated with laser light, photons interact with intramolecular bonds within the tissue. The photon donates energy to or receives energy from the bond, producing a change in the bond's vibrational state. When it subsequently exits the tissue, the photon has an altered energy level and, therefore, a different wavelength from the original laser light. This change in the photon's energy is known as the "Raman shift" and is measured in wave numbers. Photons interacting with different biochemical bonds within the tissue undergo different Raman shifts, which, taken together, form the "Raman spectrum," a plot of intensity against Raman shift in wave numbers. As the Raman shift is inversely proportional to the change in the photons' wavelength, wave numbers are expressed in units of centimeters. The Raman spectrum is a direct function of the molecular composition of the tissue and can therefore give a truly objective picture of the pathology.[5]

Several changes occur during the transformation of normal to neoplastic tissue. Loricz and colleagues[6] demonstrated the nondestructive method of using Raman spectra to distinguish tissues and its potential value in the clinical diagnosis. Art historians have utilized Raman spectroscopic and microscopic techniques for nondestructive characterization of archaeological artefacts.[7]

The laser Raman microprobe has been used for the characterization and identification of renal lithiasis.[8,9] The microprobe can differentiate the monohydrate and the dihydrate forms of calcium oxalate inclusions in tissue sections that could be a potential adjunct in diagnostic pathology.[10] Presmasiri and associates[11] studied the components of human urine using both normal Raman and surface-enhanced spectroscopic methods for qualitative and quantitative analysis.

Raman spectroscopy has demonstrated that testicular microliths are composed of hydroxyapatite and located in the seminiferous tubules. These microliths were associated with glycogen deposits in germ-cell neoplasms.[12] Grubisha and coworkers[13] demonstrated the low-level simultaneous determination of many complexed forms of prostate specific antigen using surface-enhanced Raman scattering. For first time, Prieto et al[14] were able to obtain spectra from different depths through both the prostate gland and the bladder using Kerr-gated Raman spectroscopy. They showed the potential use of Raman spectroscopy to identify a small focus of adenocarcinoma in an otherwise-benign gland and also to stage bladder cancers by assessing the base of the tumor after resection.[14]

In other parts of the body, Raman spectroscopy has been reported to show promising results for the diagnosis of Barrett's esophagus, oral lesions, brain-tumor margins, cervical intraepithelial neoplasia, and skin cancer. Parekh and coworkers[15] demonstrated the accurate differentiation between normal human renal tissues and renal-cell cancers using combined fluorescence and diffuse reflectance spectroscopy in an *ex-vivo* setting. In the future, this technology could aid in margin detection and tissue discrimination during laparoscopic and open nephron-sparing surgery.[15]

Raman spectroscopy has been successful in identifying the grade and the stage of bladder cancer *in vitro* (Fig. 4). It has the potential to provide immediate pathological diagnoses during transurethral resection of bladder tumors.[16] *In vitro*, Raman spectroscopy has been used to differentiate the layers of the bladder wall. It is predicted that this technology can be applied *in vivo* by a thin, flexible fiberoptic catheter for analysis of the molecular composition of the normal and pathological bladder

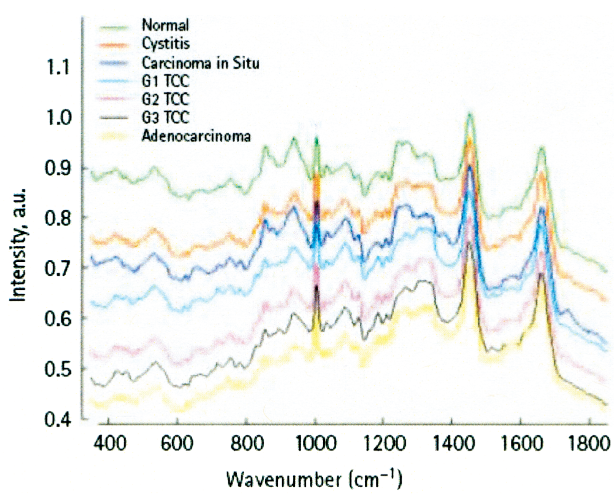

FIG. 4. Raman spectra of various bladder pathologies. (Reprinted with permission from reference 16).

without the need for biopsies.[17] Crow et al[18] constructed a diagnostic algorithm using recorded Raman spectra from both benign and malignant prostate biopsies. The algorithm had an accuracy of 89% in identifying each pathological group.[18] Raman spectroscopy can be used to identify benign prostatic hyperplasia and different grades of prostatic adenocarcinoma *in vitro*. Crow et al[19] demonstrated that the clinical Raman system can provide an accurate and objective method to diagnose prostate and bladder cancer *in vitro*. Because the Raman probe is suitable for use during endoscopic, laparoscopic, or open procedures, this work paves the way for *in-vivo* studies.

CONCLUSION

Raman spectroscopy is used in various disciplines of medicine and is being applied increasingly in urology. Its potential applications may herald a new future in the management of various benign and malignant urologic disorders.

REFERENCES

1. Raman CV. Unsymmetrical diffraction bands due to a rectangular aperture. Philosophical Magazine 1906;12:494–498.
2. Raman CV. Experiments with mechanical mechanically played violins. Indian Association of Cultivation of Science 1920.
3. Raman CV. The colour of the sea. Nature 1921;108:367.
4. Raman CV, Kishnan KS. A new type of secondary radiation. Nature 1928;121:501–502.
5. Mahadevan-Jansen A. Raman spectroscopy for the detection of cancers and precancers. J Biomed Optics 1996;1:31–70.
6. Lorincz A, Haddad D, Naik R, et al. Raman spectroscopy for neoplastic tissue differentiation: A pilot study. J Pediatr Surg 2004; 39:953–956; discussion 953–956.
7. Edwards HG. Probing history with Raman spectroscopy. Analyst 2004;129:870–879.
8. Allegrini I, Febo A, Liberti A. Laser Raman microprobe for the characterization of renal lithiasis. Ann Ist Super Sanita 1983;19: 565–568.
9. Sudlow K, Woolf A. Identification of renal calculi by their Raman spectra. Clin Chim Acta 1991;203:387–393.
10. Pestaner JP, Mullick FG, Johnson FB, et al. Calcium oxalate crystals in human pathology: Molecular analysis with the laser Raman microprobe. Arch Pathol Lab Med 1996;120:537–540.
11. Premasiri WR, Clarke RH, Womble ME. Urine analysis by laser Raman spectroscopy. Lasers Surg Med 2001;28:330–334.
12. De Jong BW, De Gouveia Brazao CA, Stoop H, et al. Raman spectroscopic analysis identifies testicular microlithiasis as intratubular hydroxyapatite. J Urol 2004;171:92–96.
13. Grubisha DS, Lipert RJ, Park HY, et al. Femtomolar detection of prostate-specific antigen: An immunoassay based on surface-enhanced Raman scattering and immunogold labels. Anal Chem 2003;75:5936–5943.
14. Prieto MC, Matousek P, Towrie M, et al. Use of picosecond Kerr-gated Raman spectroscopy to suppress signals from both surface and deep layers in bladder and prostate tissue. J Biomed Opt 2005;10:44006.
15. Parekh DJ, Lin WC, Herrell SD. Optical spectroscopy characteristics can differentiate benign and malignant renal tissues: A potentially useful modality. J Urol 2005;174:1754–1758.
16. Crow P, Uff JS, Farmer JA, et al. The use of Raman spectroscopy to identify and characterize transitional cell carcinoma in vitro. BJU Int 2004;93:1232–1236.
17. De Jong BW, Bakker Schut TC, Wolffenbuttel KP, et al. Identification of bladder wall layers by Raman spectroscopy. J Urol 2002;168:1771–1778.
18. Crow P, Stone N, Kendall CA, et al. The use of Raman spectroscopy to identify and grade prostatic adenocarcinoma in vitro. Br J Cancer 2003;89:106–108.
19. Crow P, Molckovsky A, Stone N, et al. Assessment of fiberoptic near-infrared Raman spectroscopy for diagnosis of bladder and prostate cancer. Urology 2005;65:1126–1130.

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