Advertisement for Incubation of Technology

Title of the technology	**Portable Raman spectroscopy system for oral cancer detection**

Current state of Technology

BARC has developed a portable, indigenous Raman spectroscopic system with custom designed piston grip Raman probe for oral cancer detection. It consists of suitable laser source to excite the target sample for Raman shift and advanced optical module to collect the low intensity Raman spectrum with minimum artifacts. Data acquisition module and software have been developed to process the capture Raman data for spectral identification. Test set up has been developed to carry out the preliminary experiments on clinical samples. BARC is building high quality spectral database of thousands of known spectra of patients with the assistance of doctors (under collaboration with TMC). AI based deep learning algorithms will be developed to identify molecular patterns among cancer types.

General Information

Oral cancer is a major problem in India due to the wide spread abuse of tobacco products. The diagnosis of oral cancer needs clinical as well as pathological expertise and lack of these has contributed to absence of successful screening programs in the country. Recently, Raman spectroscopy has emerged as a promising bio-sensing technology to find out molecular information, identifications and characterization of cancerous and non cancerous cells. The Raman system and spectra obtained from biological samples are complex and diverse and commercial available systems are costly and imported.

Portable Raman spectroscopy system for oral cancer detection is made of following important sub-units:

a) **Miniaturized fiber optic based Raman probe**

b) **Control board for Raman probe**

c) **Wavelets and deep learning based algorithms for data processing and characterization**

d) **Control software for spectral identifications, visualization and detection**

Features of the system

- Light weight and handheld
- Pistol grip Raman probe for safety and easy operation
- Custom design of probe can manually change the throughput and resolution
- Raman spectrum acquisition with custom settings like interval time, single shot or continuous
- Signal filtering, normalization and signal correction (Baseline, horizontal, vertical)
- Multiple spectra viewer
- Peak analysis algorithm
- Database searching with peak matching algorithms for spectral identification
- Database creation allowing custom databases to be created and used for searching

Specification of the current system

Specification of Portable Raman Spectroscopy System

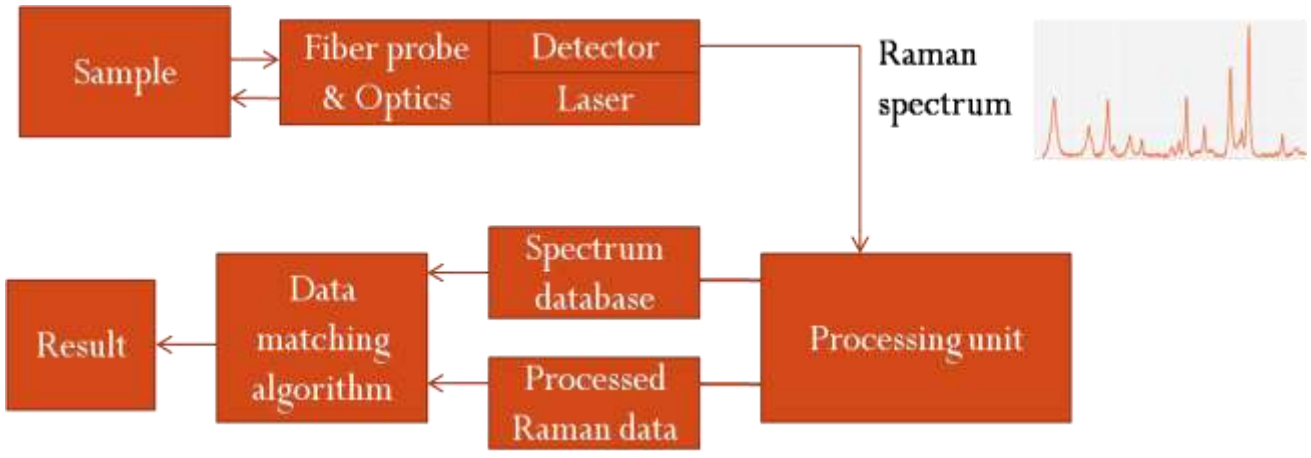
a) **Laser wavelength**: 785nm; **laser Power:** Max. 500mW (Variable 0 to 100%); **Narrow spectral line width**: < 0.15nm
b) **Resolution**-6 cm^{-1}; **Spectral range**: 150 cm^{-1} to 3200 cm^{-1} ; CCD resolution:2M ; Signal to Noise ratio: 350:1; dynamic range: 3700, Integration time: 1.1ms - 10 minutes
c) Compatible stainless steel pistol grip fiber probe with interlocks for patient safety; fiber cable length:1.5m
d) VGA port with 7inch display
e) **Weight of Raman probe approx.**: 300gm
f) **Portable and battery operated**

Working of the system

A portable system is a handheld tool used to characterize/identify the biological/patient samples for oral cancer detection. It consists of suitable laser source to excite the target sample for Raman shift and collected light by advanced optics & detector in the probe creates a spectrum that is used to identify the samples. A Raman spectroscopy control software is developed for real-time and offline applications for processing and analysis of Raman spectra. The software contains modules for baseline correction, vertical/horizontal line correction, and signal noise filtering and spectrum identification from known databases. Some of the features are listed below:

1) Raman spectrum acquisition and laser control

Spectrum acquisition module is developed for acquisition of Raman spectrum. User can give/edit the value of integration time, no of averages and smoothing pixel as per requirements of the samples. Spectrum can be captured either in single shot or continuous shots. Laser can be on/off by pressing the button in the toolbar. User also has the option of changing the laser power for desired results.

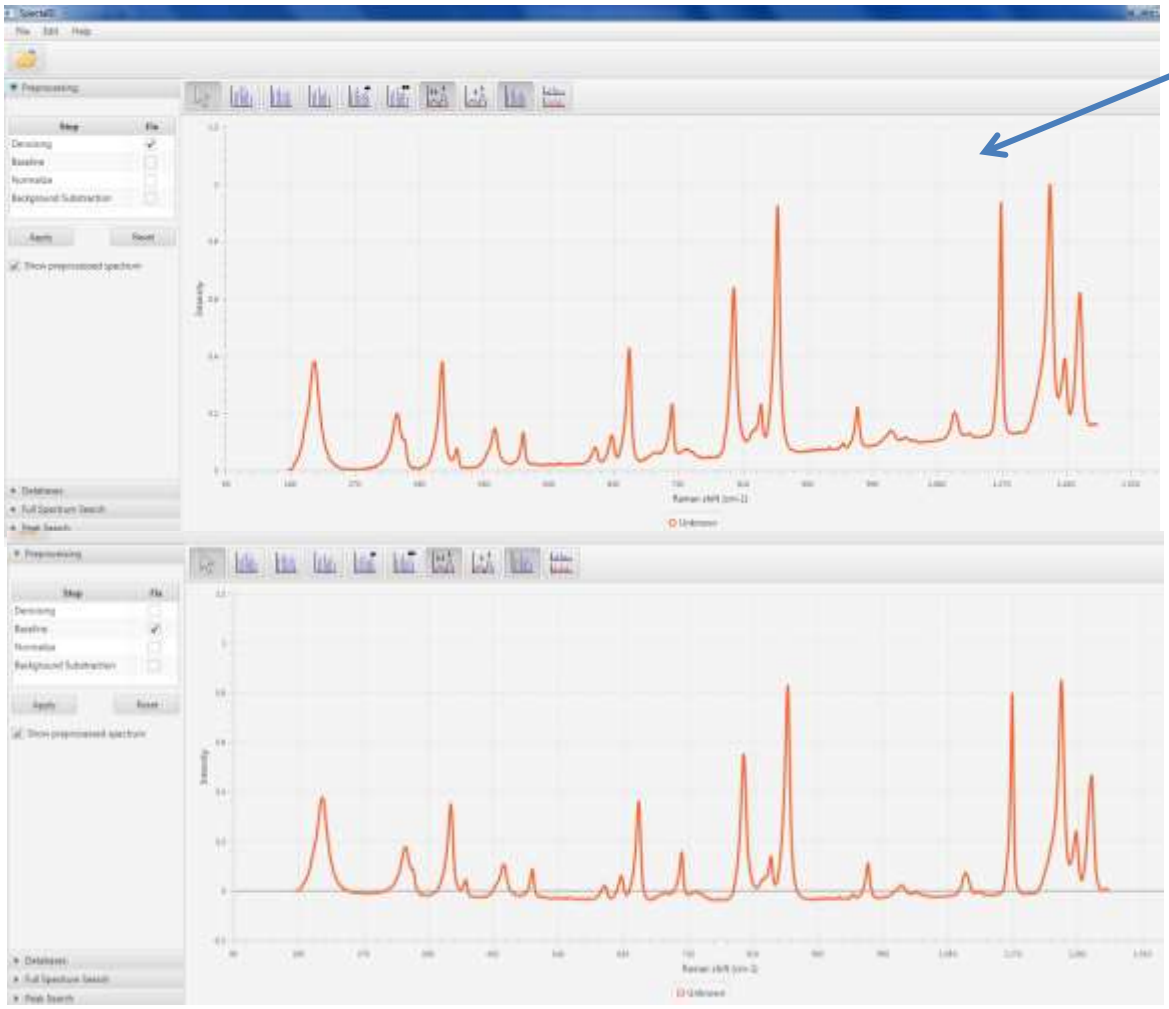


Block diagram of Raman Spectroscopy System

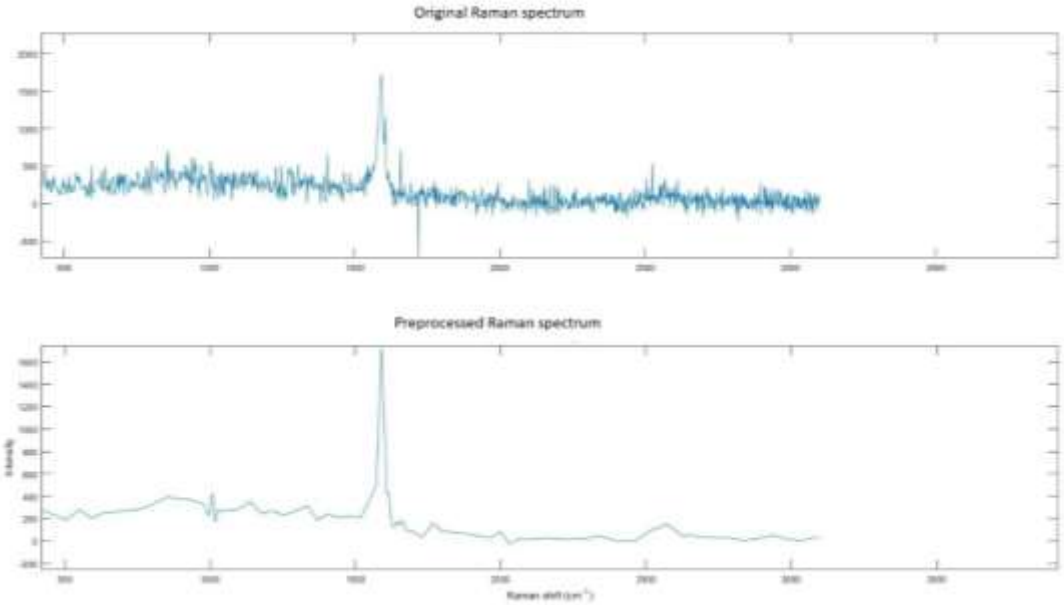
2) Advanced algorithms for Raman spectrum pre-processing

Raman signal is an inherently weak and owing to low signal to noise ratio (SNR), the captured spectrum is noisy and needs to be pre-processed for further processing. We have provided three

different methods for pre-processing of signal to improve the spectra. First method is de-noising to remove the unwanted noisy components from the signal, thereby increasing the SNR ratio. We have implemented the Savitzky-Golay (SG) and Wavelet method. SG filter smooths the signal by fitting sub signal with a low degree polynomial by the method of least squares. We have also implemented non sub-sampled wavelet-based filtering and found that results were superior as compared to other filters. Second pre-processing method is spectrum normalization for enhancing the matching accuracy. Third pre-processing method is baseline correction. Baseline in the spectrum signal can induce uneven amplitude shifts across different wave numbers and lead to inaccurate results. Therefore, these amplitude shifts should be compensated before further analysis. Automatic baseline correction algorithm has been developed to correct the baseline prior to spectrum identification.



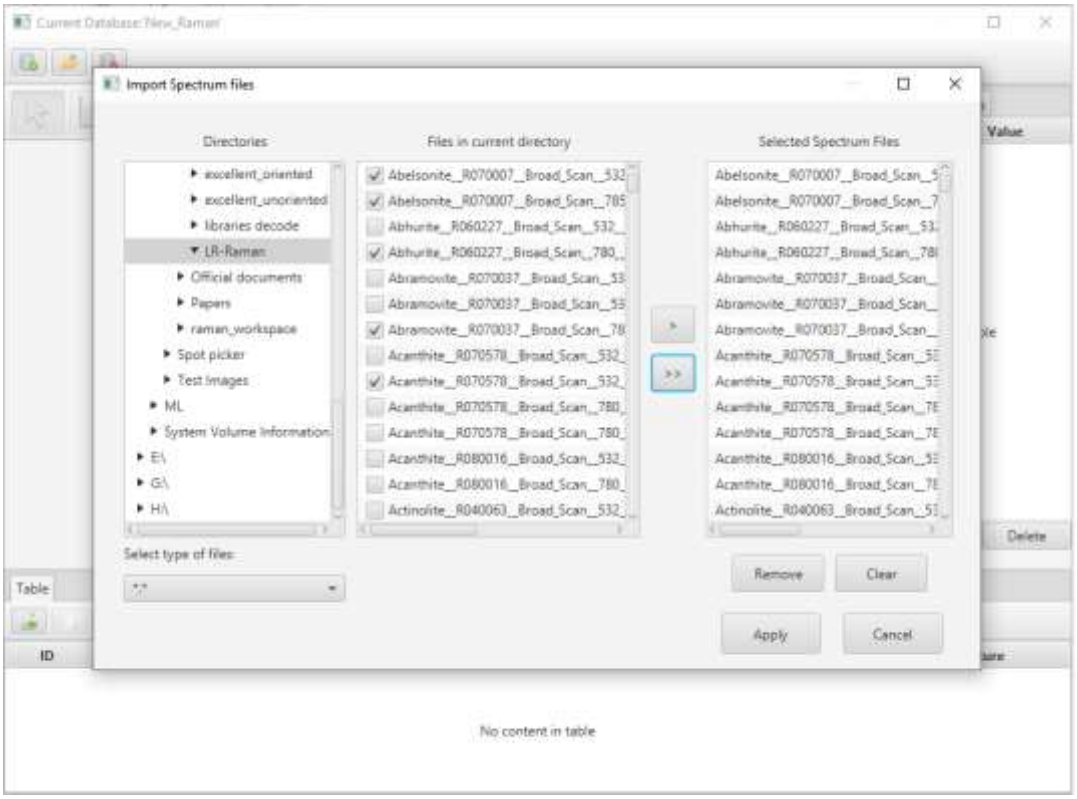
Baseline correction of Parcetamol spectrum



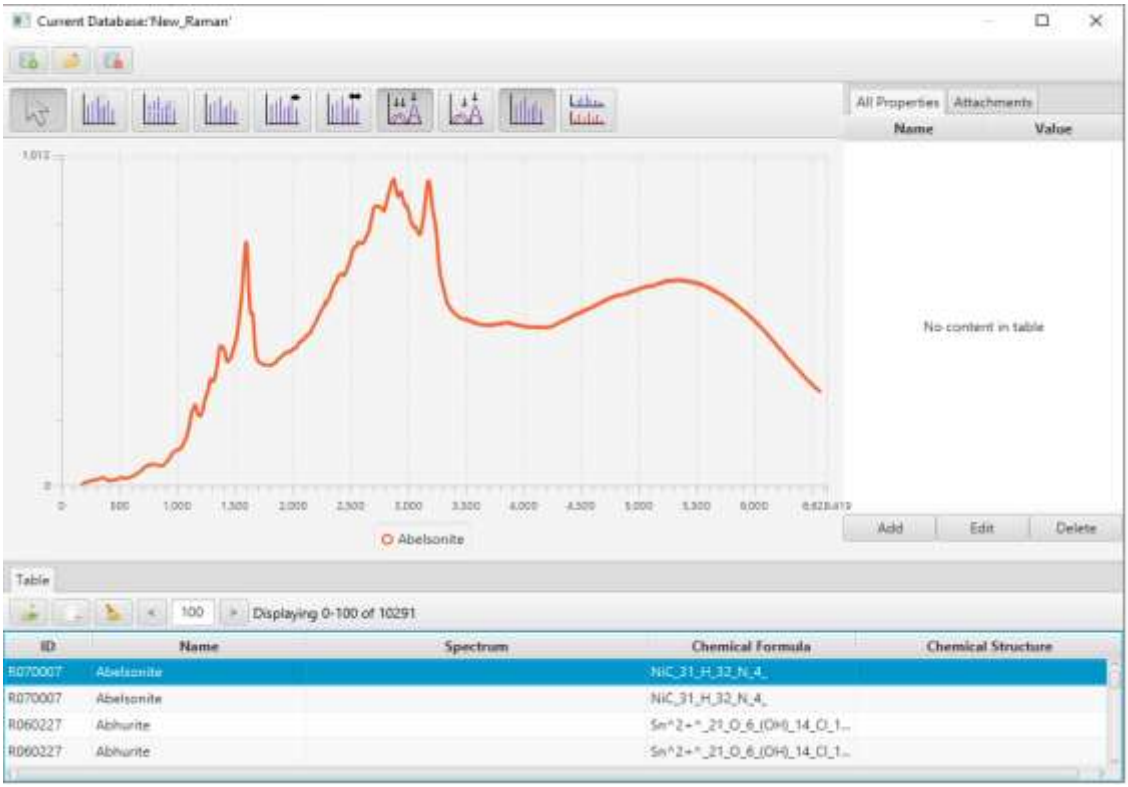
Pre-processed Raman spectrum of carbon nano tube (CNT) wool

3) Generation of Raman spectrum database

We have developed a database module for storing the high-quality Raman spectrum. User can also import spectrum files to existing database from disk. Database creation allows custom databases to be created and can be used for searching the required samples.



Database creation window

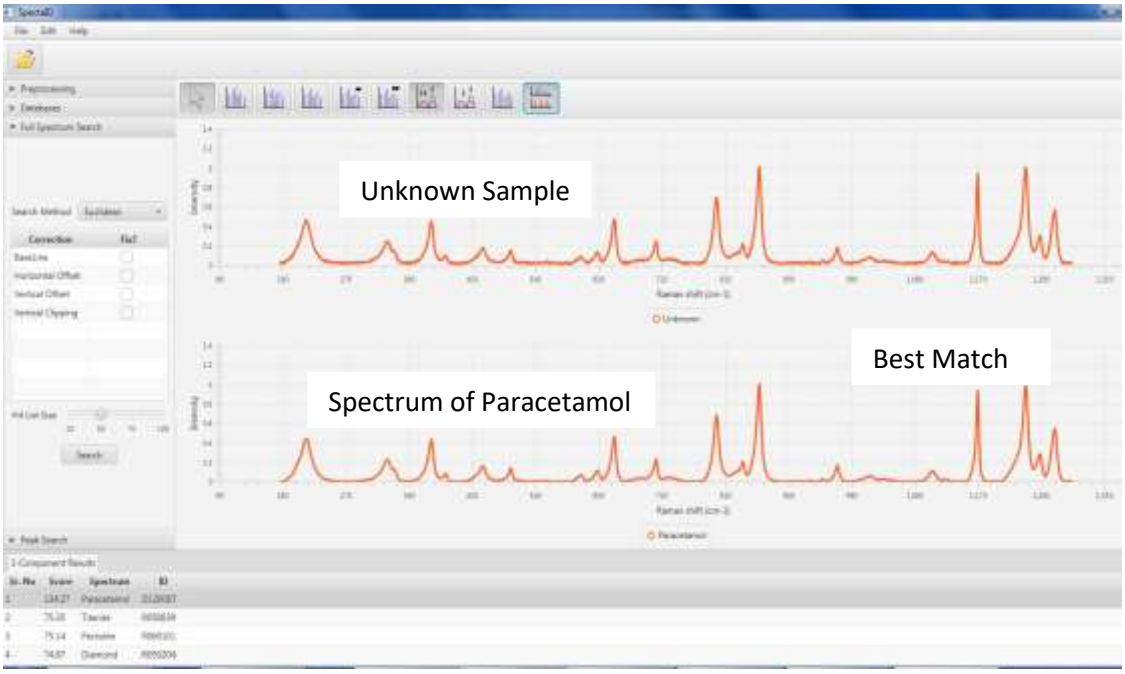


Import spectrum window

4) Raman spectral searching/identification

The user can find out the spectral identification of unknown spectrum. The software will automatically perform the single component searches, multiple component searches, peak searches and summarizes the results on a single window to give a complete view of all possibilities for the unknown spectrum. Unknown spectra may contain noise and pre-processing is required to attenuate the noise. Spectra needs to be normalized, corrected for baseline, horizontal and vertical offset prior to identification. These steps along with spectral database provide fastest and accurate answers possible to the user for identifying unknown spectra.The matched spectra are ranked by how closely they resemble the query spectrum. Spectrum matching results for paracetamol Raman spectrum as shown in the figure.

User can choose the search method (like Euclidean etc.) and various optimization parameters (baseline, horizontal/vertical correction, clipping) for accurate matching of own spectrum with spectral database. A report generation facility also developed for easy exporting of Raman spectrum in csv format.



Spectrum identification of pharmaceutical drug (Paracetamol)- By prototype Raman spectroscopy system developed at BARC

Picture/Photo of the System

Portable Raman Spectroscopy System

Whether the parent product/ technology/ process is patented: No

Justification for incubation

Tata Memorial Centre (TMC) registers more than three thousand patients with OSCC every year and we have a great opportunity to explore the possibility of developing multiple tools for oral cancer

detection. In this collaborative project with TMC, they will provide a screening and selecting confirmed oral cancer samples that will help to refine the tools and finally evaluate their performance in clinical setting. As indigenous development, the production of these tools is not costly and can provide an affordable solution for the above-mentioned problem. A commercial version of the portable Raman spectroscopy system needs to be developed using incubation procedure. The commercial version needs to be evaluated by several doctors (oncologist) for its acceptance in the industry. The industrial collaboration is required & necessary for packaging of overall system as per medical & safety standards.

Improvement proposed through incubation

1. The technology will have to be **transformed to a commercial product** by

(a) Standardising the probe, cables, control board, etc. to enable easy deployment in the hospital.

(b) Upgrading the cosmetic aspect of the system to appear as a gentle medical device without compromising the functionality.

2. **Validation and testing in various healthcare facilities across TMC hospitals** to build a Raman database for accurate detection of oral cancer.

3. The **safety features** to satisfy medical guidelines and protocol have to be considered. Methods of **sterilization/draping** of various hardware components of the Raman probe have to be formulated and developed.

4. The **end tip of Raman probe** needs to be modified based on the feedback from the doctors.

5. A **GUI enhancement** would be incorporated based on the feedback from doctors for enabling seamless operation of the system for detection of oral cancer.

6. **Automation and customization of a patient station** having desired translations and orientations of Raman probe and patient for acquiring best spectra without noise and artifacts.

7. **Progressively evolving techniques and methods**, which provide simple and qualitative enhancement in the Raman spectroscopic system, will be undertaken.

Facility and infrastructure requirements

Title Head	To be provided by BARC	To be provided by Incubatee
Manpower/expertise	Technology for components of Portable Raman Spectroscopy System: • Design of customized Raman probe • Control board for Raman probe. • Software for baseline correction, vertical/horizontal line correction, signal noise filtering and spectrum identification from known databases.	• Experience and knowhow in manufacturing, evaluating, certification and commissioning of laser based medical devices. • Experience and capability to get valuable feedback from doctors for clinical trials. • Capability of manufacturing, assembling of high precision components. • Mechanical engineer for design, analysis, CAD modelling, inspection and calibration of assembly. • Personnel having degree in Computer science and expertise in C++ / Java, python languages for software up-gradations & modifications. • Personnel having degree in Electrical/Electronics for dealing with motion control aspects.
Machinery and		• Clean room facility for component storing,

Equipment		handling and assembly. • Assembly facilities like small size press, assembly kits, external/internal circlips pliers, bearing fitting kit, etc. • Design, drawing and drafting with latest 3D solid modelling software's facility. • Software packages for modification and up-gradation. • Electrical wiring, cabling and testing facilities along with qualified personnel. • Computing facilities to check and validate the functionality of the system.

Note: As per in-house technology incubation policy, the incubatee should be a licensee of the existing technology. Alternatively, the applicant will be required to take the license of the existing technology before entering incubation agreement.

If interested in Incubation, kindly ***download -> fill -> scan -> send*** the application form to -

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