MEDICAL PHYSICS GAZETTE

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Editorial

Medical Physics for Sustainable Healthcare

In December 2021 the 76th session of the United Nations General Assembly proclaimed the year 2022 to be the International Year of Basic Sciences for Sustainable Development. The announcement underlined that the application of basic sciences were important for the advancement in medicine, industry, agriculture, water resources, energy planning, environment, communication and culture. Keeping this in mind the International Organization for Medical Physics (IOMP) which has started celebrating 7th November, the birthday of Marie Sklodowska Curie as International Day of Medical Physics (IDMP) since 2013, declared the theme of IDMP-2022 as “Medical Physics for Sustainable Healthcare”. Sustainable development, in general, and “sustainable healthcare” in particular has caught the attention and interest of healthcare industry lately. In the message on the eve of IDMP-2022, the IDMP Coordinator Dr. Ibrahim Duhaini identifies three important pillars for quality healthcare services in the form of advanced technology, qualified and trained professional and an intellectual system linking these two to provide sustainable healthcare services. Sustainability has been defined as “meeting our own needs without compromising the ability of future generation to meet their own needs”. Sustainability is said to stand on three pillars of the Economy, the Society and the Environment. These three pillars are also informally referred as 3 Ps of Profit, People and Planet. Global population has grown from 1.8 billion about 100 years ago to about 3 billion in 1960 to 7.8 billion in 2020. Population needs resources to survive and prosper and this strains the resources of the earth. Wealth and consumption are not evenly distributed geographically and socially and so is the man-mode impact on the environment. Some of the examples of sustainability are renewable energy and conserving water resources, environment protection, smaller carbon foot-print of technology, construction etc. A sustainable healthcare is a healthcare system which delivers quality healthcare without impacting the environment adversely and is affordable now and in future and brings positive social impact. Though limited number of medical physicists is engaged in development of the technology, most of us are the prime users of the technology for the precise and safe treatment of cancer and diagnosis of other disease. We must keep it mind that technological development should be affordable and with minimum ecological footprint. We may take care of this in our day-to-day work as well by minimizing the power wastage in leaving equipment 'on' longer than required, segregation of waste, encouraging the use of mass transport, use of tele-medicine for follow-up, by use of solar panels, encouraging re-use and re-cycle of the equipment, by decreasing the use of paper etc. Larger devices (like PC) use much more power than laptop. Cloud storage facilities use power and server space in an efficient way. Pollution or environmental crisis is closely linked with human health and in turn, with the load on healthcare system. Somehow, the healthcare systems have not been enough sensitized towards its carbon foot-print (or ecological impact) though they consume enormous amount of materials, energy, water, chemicals, papers etc. National Health Service (NHS), UK has introduced a workshop on sustainable healthcare and Institute of Physics and Engineering in Medicine (IPEM) has organized a talk on sustainable healthcare in its annual event. Healthcare education and training (including that of Medical Physics) may incorporate this upcoming and up-ticking aspect of sustenance as well.

Pratik Kumar

MEDICAL PHYSICS EDUCATION, TRAINING, ACCREDITATION, CERTIFICATION, AND RECOGNITION – INDIAN PERSPECTIVE

Prof. Arun Chougule, President AFOMP, Chair ETC IOMP, Chairman IOMP Accreditation Board and Member Board of Directors IMPCB. arunchougule11@gmail.com

Medical Physics is one of the most challenging and rewarding application of physics to human health care programme and is mainly concerned with use of ionizing radiation in diagnosis, therapy, and research in health care. Medical physicists working in clinical environment should have required competency and therefore undergo structured education program and residency under experienced medical physicist from recognized institution. The need for a well-structured, high-quality education, and training program for a clinical medical physicist who can work independently as a specialist without the supervision and can take the appropriate technical and clinical decisions toward his professional activities. Looking to the growing need of trained medical physicists, our visionary scientist and planners took early steps and one-year postgraduate Diploma of Radiological and hospital physics [Dip. R. P.] course was started in BARC in 1962, the first structured course for training of medical physicists in Asia. Since then, starting of M. Sc in Medical Physics at Anna University Chennai in 1982, a medical physics education outside of BARC started. Presently India has 21 institutes/Universities running master's in medical physics/Radiation Physics program and producing over 200 medical physicist per year.

According to IAEA, a clinically qualified medical physicist [CQMP] must have (1) A university degree in physics, engineering, or equivalent physical science, (2) Appropriate academic qualifications in medical physics (or equivalent) at the postgraduate level, (3) At least two years (full time equivalent) structured clinical in-service training undertaken in a hospital. The IAEA also states that "It is emphasized that the holder of a university degree in medical physics without the required hospital training cannot be considered clinically qualified." Further this education and training should be recognized by a national accreditation body. The present question is whether all the medical physicists trained by various universities/institutions in India fulfil these expectations? Whether the medical physicists trained by different universities/ institutions are competent enough to discharge the duty of unsupervised clinical medical physicists? AERB has stipulated a curriculum for medical physics education and the medical physicists trained in AERB approved courses are only eligible to work as medical physicists. However, a lot needs to be done to ensure the quality of education and training, some institutes/universities imparting master's in medical physics do not have sufficient well qualified medical physics faculty nor have equipment/labs to train appropriately. Further the students coming out of these institutes/universities are struggling to undergo residency program which is mandatory to work as medical physicists. In addition, the residency programs need to be of two years full time duration as per IAEA recommendation. All the residency programmes offered in India are for radiotherapy and no exclusive residency program for other subspecialty of medical physics. The admission process to masters in medical physics needs to be streamlined and based on competency based entrance test so as attract good students in these streams is requirement of time. None of the medical physics education program in India is accredited to ascertain the standard and quality of education. For certification of medical physicists, the College of medical physics of India [CMPI] is conducting regular examination for certification of medical physicists, however CMPI do not have legal framework and therefore the CMPI certification is not mandatory to work as clinical medical physicists. Efforts need to be done to authorise/recognise CMPI as national certification board by the government agency as is in many countries including Asia. This legalised framework to CMPI will boost the credibility, acceptability, and popularity of CMPI certification. In addition to national certification and accreditation, for globalisation, we need to collaborate with international certification and accreditation board.

To access and standardise the medical physics education and profession, IOMP has started accreditation of medical physics education program. For accreditation of national certification boards and individual certification of medical physicists, International Medical Physics Certification Board [IMPCB] has started accreditation of certification boards and certification of individual medical physicists. To help member state to establish the certification and registration of medical physicists as health professional IAEA has brought out Training Course Series TCS 71 document in February 2021 on "Guidelines on certification of Clinically Qualified Medical Physicists". This document is endorsed by IOMP and IMPCB. [TCS71]. Accreditation is important because it helps determine if an institution meets or exceeds minimum standards of quality and helps students determine acceptable institutions for enrollment in addition employers often require evidence that applicants have received a degree from an accredited school or program. For the public, accreditation promotes the health, safety, and welfare of society by assuring competency of public health professionals. IOMP is dedicated to improving medical physics worldwide by disseminating systemized knowledge through education and training of medical physicists, to advance the practice of physics in medicine by fostering the education, training, and professional development of medical physicists. The institutes/universities India conducting master's in medical physics can take advantage of IOMP accreditation. To accomplish the goals, IOMP Accreditation Board [AB] has been set up to ensure that accredited medical physics programs satisfy the highest standards established by IOMP in collaboration with other international organizations.

The IOMP accreditation board accredits medical physics degree/Post graduate programs, medical physics education and training institutions/centers and education and training events.

Benefits of IOMP accreditation:

- Reputation of accredited programs and courses which will result in more demand for these education and training activities.
- Provision of an international dimension to an education event that will attract participants from other countries.
- Evidence of highest teaching standards and best preparation of medical physicists for the work environment
- Publication of accredited programs and courses on the IOMP website

The IOMP Accreditation Board accredits Medical Physics degree/Postgraduate programs, Medical Physics education and training institutions/centers, Medical Physics residency program and education and training events. Why is the official recognition of medical physics education of so much importance? Because it opens the door to a change of the status of the medical physics profession, the introduction of the education, training and accreditation programme and the establishment of appropriate qualification framework for medical physicists working in the clinics. These changes are not possible without recognition of medical physics as a healthcare profession.

AFOMP has studied the status of medical physics education and profession in AFOMP countries and is tabulated in Table 1. It is evident from the table that the number of medical physicist per million population varies from 0.56 to 20.0 with India at 1.16 MP/Million population. Further most of the medical physicists work in radiotherapy. In India less than 1 % medical physicists exclusively work in radiology as compared 69.8 % MP in Indonesia are working in Radiology. Countries like Indonesia, Thailand, Malaysia has regulation/acts/laws which mandates services of radiation protection experts/medical physicists in radiology. In India no such act/law/regulates mandating services of medical physicists in radiology. The regulatory authorities and professional organization in India need to work in this direction and the services of medical physicists in the postgraduate institutes offering MD /DNB Radiology must be made mandatory exclusively for radiology. This not only will increase the quality of education, radiation safety and increased opportunity where medical physicists can work.

Table 1 Number of medical physicis and population in AFOMP countries

Country/NMO	Number of Medical Physicists (Approx)	Physicists in radiotherapy		Physicists in Radiology		Population million	Medical Physicists/ million population
Australia	500	300	60.00	140	28.00	25	20.00
Bangladesh	200	70	35.00	00	0.00	170	1.18
Peoples Rep. of China	4000	3500	87.50	50	1.25	1400	2.86
Hong Kong	120	85	70.83	32	26.67	7	17.14
India	1600	1590	99.75	15	0.94	1380	1.16
Indonesia	438	114	26.03	306	69.87	273	1.60
Iran	310	250	80.65	45	14.52	84	3.70
Japan	2000	850	42.50	50	2.50	126	15.87
S. Korea	360	209	58.06	10	2.78	51	7.06
Malaysia	275	128	46.55	53	19.27	32	8.59
Mongolia	10	10	100.00	00	0.00	3	3.33
Myanmar	30	30	100.00	00	0.00	54	0.56
Nepal	18	17	94.44	00	0.00	29	0.62
New Zealand	90	65	72.22	10	11.11	4.8	18.75
Philippines	130	70	53.85	24	18.46	109	1.19
Singapore	65	39	60.00	09	13.85	5.8	11.21
Republic of China, Taiwan	350	200	57.14	10	2.86	23	15.22
Thailand	200	137	68.50	29	14.50	69	2.90
Vietnam	155	115	74.19	00	0.00	97	1.59
Pakistan	150	120	80.00	15	10.00	220	0.68
Sri Lanka	50	40	80.00	05	10.00	22	2.27
	11051	7852	71.05	800	7.24	~4140	2.67

Table 2 gives comparison of number of medical physicists per million population in various regions of the world.

Table 2 Number of Medical Physicists in AFOMP compared with other regions of IOMP

Sr. No	Regional organization/ Region	Population (million)	Number of medical Physicists [MP] (approx.)	MP/Million population
01	USA & Canada	330+38= 368	9000	24.5
02	EFOMP	750	9000	12.0
03	FAMPO	1300	1000	0.77
04	ALFIM	700	1400	2.0
05	MEFOMP	400	1100	2.75
06	AFOMP	4300	11000	2.56

The number of medical physicists per million population in AFOMP region of 2.67 is far below as compared to USA-Canada [24.5] or EFOMP [12.0] region and in comparison, India is at 1.16 MP/Million population, a long way to go. Further, IAEA has brought out the Technical Series Document TCS 56 for model Postgraduate medical physics academic programme in 2013. Since them lot of technological developments in healthcare delivery system and increased professional competency requirement of CQMP has taken place and therefore the training and educational curriculum needs to be tuned with the requirement to produce the competent CQMP not for the present but also for the future needs. Furthermore, the major outcome of the academic programme is to provide the students with a thorough grounding in medical physics, critical thinking, scientific rigor, and adequate professional ethics, to facilitate the integration of the graduates in a healthcare profession, where the benefit of the patient is at the centre of all activities. Medical physics is facing significant changes, particularly with quick development of biological sciences, more complex research requiring interdisciplinary teams and strong need for translational research. The changes towards personalized medicine are opening new avenues for medical physicists like molecular imaging and extending beyond radiation therapy. To prepare medical physicists for the future, education and training should be properly adjusted including more basic non-physical sciences, particularly biology, more imaging, especially molecular imaging, and with more interdisciplinary and translational research components. AFOMP has taken imitative and formed a task group to revise the curriculum and syllabus to train the CQMP for the need of AFOMP region. Similarly, IOMP and IAEA have undertaken the revision of TCS 56 document.

New research directions

Most of medical physicists are currently involved in radiation therapy of cancer. Consequently, future developments in radiation oncology will have the strongest impact on most medical physicists. Medical physicists are good at developing and refining technology, which should remain our focus. Medical physicists are good at interacting with physicians and other basic scientists, but it is essential to become much better at it. Finally, medical physicists have knowledge and skills to attack the problems of modern medicine but should not be shy at embarking on new territories. Diversity of medical physics as well as the strong connection to other similar disciplines, like biomedical engineering might bring other areas into the focus. Major areas of focus are personalization of therapy, molecular imaging, molecular targeted therapies, particle therapies, clinical trials, translational research, simulations of complex systems and artificial Intelligence and data mining. Future focus of MP research must be inter- and trans-disciplinary with much more interaction with physicians as well as other basic scientists. We will have to have do, in addition to clinically relevant, also biologically relevant research. Rather than base programs on the traditional medical physics curricula, special care should be taken to incorporate enough imaging, biological and translational research components into the programs. Rather than preparing medical physicists for the present, the programs should prepare them for the future. One of the problems is that all dedicated medical physics programs, as well as other educational programs from where people enter the field of medical physics, have typically a very limited biological training. The knowledge of biology is most often limited to 'high school' training. Medical physics is facing significant changes, particularly with quick development of biological sciences, more complex research requiring interdisciplinary teams and strong need for translational research. The changes towards personalized medicine are opening new avenues for medical physicists like molecular imaging and extending beyond radiation therapy. To prepare medical physicists for the future, education and training should be properly adjusted including more basic non-physical sciences, particularly biology, more imaging, especially molecular imaging, and with more interdisciplinary and translational research components. Medical Physicists should expand their horizon beyond the traditional boundaries [dosimetry, QA/QC etc] and be a part of exciting multidisciplinary research team. The major outcome of the academic programme is to provide the students with a thorough grounding in medical physics, critical thinking, scientific rigor, and adequate professional ethics, to facilitate the integration of the graduates in a healthcare profession, where the benefit of the patient is at the center of all activities. The authorities and the responsible organizations/agencies in India need to think and tune the medical physics education program for the present and future requirement without losing the precious time.

In Summary, it is important that the medical physics education program/curriculum needs to be revised and tuned to requirement of present and future. Medical physics education and training programs become accredited. Medical physicists become certified by certifying agency approved/endorsed by govt. Medical physicists are registered / licensed by agency approved/endorsed by govt.

WHO'S WHERE

Dr. Kanan Jassal have joined Inlaks and Budhrani Hospital, Pune as Chief Medical Physicist.

Dr.Vindhyavasini Prasad Pandey Joined Hind Institute of Medical Sciences, Barabanki as Assistant Professor & Head Medical Physics on 9th Sept 2021.

FLOWERING OF CONSCIOUSNESS

Dr. M.R. Raju, Managing Trustee, Mahatma Gandhi Memorial Medical Trust, PedaAmiram, Bhimavaram, AP - 534204.

If you are conscious you cannot do anything wrong.

Be alert in what so ever you are doing, Just do it watchfully and consciously.

You can get rid of all insanity in just by being a simple witness of your thought process.

As you become more and more deeply rooted in witnessing, thoughts disappear.

Discontinuity with the past, living in the present will bring transformation.

When the mind is utterly empty, you become unconditioned; thereby you are really free human being. That is the moment of enlightenment.

Enlightenment simply means an experience of your consciousness unclouded by thoughts, emotions, sentiments, etc. When the consciousness is totally empty, there is something like an explosion, atomic explosion. Your whole insight becomes full of light. It remains.

Man has evolved out of the animals. Animals are in a deep sleep, but they don't know that they are. No animal is aware of himself. Man also has been always asleep (kumbakarna!)

Only a few individuals in the whole history of man have been awakened. The moment you are awakened, ego has no function, it is useless.

Enlightenment is the ultimate *flowering of consciousness.*

(…Adapted from Osho)

RAMAN SPECTROSCOPY AND ITS APPLICATION IN CANCER DETECTION

Arun Chougule, Gourav Kumar Jain, Department of Radiological Physics, SMS Medical College and Hospitals, Jaipur. arunchougule11@gmail.com)

Introduction

Living biological systems are immensely complex, they are at the same time highly ordered and compactly put together in a remarkably efficient way. Such systems store the information and means of generating the mechanisms required for repetitive cellular reproduction, organization, control, and so on. However, infection or mutation in the biological mechanisms leads to progression of disease. Amongst these are worldwide leading causes of mortality are cardiovascular diseases and cancer. There is an urgent need for finding point of care procedures and techniques for the correct diagnosis for diseases with ease of use. Different physical effects are used and various techniques are applied to achieve diagnostic information that is not directly visible. Spectroscopy and imaging technologies have potential for non- or minimally-invasive use in a wide range of clinical applications. Spectroscopy has always benefitted from its involvement with developing sciences. It is a well-established, well recognized subject. The use of spectroscopy is recent and fast-growing in detection of cancer[1-3]. The inelastic scattering of photons of light, named the Raman effect after its experimental discoverer C.V. Raman. The Raman effect was discovered in Calcutta, India in 1928 while studying the scattering of sunlight, made quasimonochromatic by the use of a filter, by liquids.[4] The interest in this discovery was such that by the end of that year, some 70 papers had already been published on the subject. By 1939, over 1800 papers had been published on the Raman effect, showing its wide-ranging applications. This phenomenon, which later bore Raman's name, was characterized in his own words as “excessive feebleness,” due to the low efficiency of inelastic scattering, hence necessitating intense excitation light. This is why it was not until the emergence of lasers in the 1960s that Raman spectroscopy [RS] was popularized. Raman spectroscopy has now become an indispensible tool for reporting molecular vibrational frequencies and chemical analyses in industrial and research laboratories. However, the phenomenon was not reported for biomedical applications until 1970 [5]. Subsequent improvements in light sources and signal detection have made possible the emergence of RS techniques across a wide range of biological applications. Over the last decade, Raman spectroscopy has gained more and more interest in research as well as in clinical laboratories. Substances can be identified and molecular changes can be observed with high specificity through specific spectral patterns. Because of a high spatial resolution due to an excitation wavelength in the visible and near-infrared range, Raman spectroscopy combined with microscopy is very powerful for imaging biologicalsamples. Individual cells can be imaged on the subcellular level. In vivo tissue examinations are becoming increasingly important for clinical applications. Raman spectroscopy allows study of the structure of individual groups of atoms and provides information on the conformational changes taking place in macromolecules. Recent advances in instrumentation and spectral analysis have substantially improved the clinical feasibility of RS in a wide range of cancer types and locations, as well as for non oncological conditions.

The burden of cancer is expected to increase in the coming decades including in the developing world where access to affordable, point-of-care medical technology is problematic. Current diagnostic methods for cancer typically involve the use of histopathology of biopsied or resected tissue (or cytology of blood in the case of hematological malignancies) and radiological imaging modalities such as magnetic resonance imaging (MRI), ultrasound (US), and computed tomography (CT), and gamma-ray imaging and positron emission tomography. However these methods are expensive, can be time consuming, may not be optimal for intraoperative use and often fail to fully characterize the extent of cancer or detect smaller tumors. Hence, there remains an urgent need for improved cancer detection, characterization and localization technologies. The interest and excitement in the field of spectroscopy of biological tissues are increasing rapidly as both the clinical and nonclinical researchers are recognizing that the vibrational spectroscopic techniques have the potential to become noninvasive tissue diagnostic tools.[6]

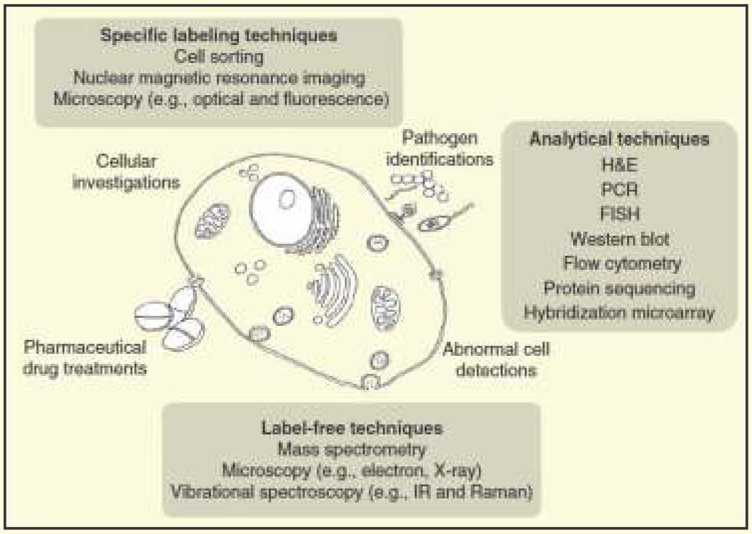

Figure 1: Common optical and biochemical methodologies for the analysis of biological samples with and without labels. H&E: Hematoxylin and eosin; IR: Infrared. Adopted from [7]

Raman techniques for disease detection

Spontaneous Raman spectroscopy (SpRS)

A molecule scatters most of the light elastically at the same frequency under beam illumination at a given frequency. The molecule, initially in the ground state, is promoted to a virtual state and reemits a photon of the same frequency to return to its initial state (Rayleigh scattering). Inelastic Raman scattering produces a shift in frequency proportional to the difference of energy between the vibrational states of the molecule. The molecule promoted to a virtual state can move from a vibrational state to the ground state, or move from the ground state to a vibrational state. These are referred to, respectively, as the anti-Stokes transition where the scattered light is at higher frequency (lower energy) and the Stokes transition where the scattered light at lower frequency (higher energy) than the incident photon. In 'conventional' spontaneous RS, the Stokes signal is detected under continuous wave (CW) illumination, typically from a diode laser with high spectral stability. The optimal optical windows for SpRS in tissue are between 700 and 900 nm and around 1064 nm. The choice of wavelength typically involves a trade-off between signal intensity and tissue autofluorescence and depend on the particular tissues involved and the application.

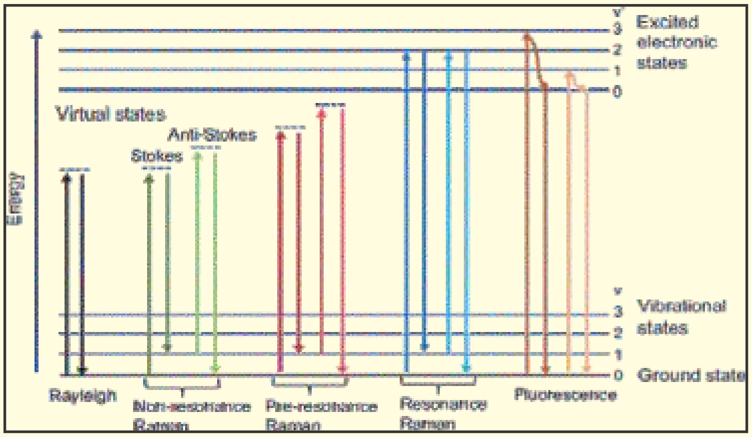

Figure 2: Energy level diagram for Rayleigh scattering, Raman scattering, and fluorescence. Adopted from [8]

Confocal Raman spectroscopy

SpRS can also be implemented in confocal configuration to provide optical depth sectioning,by spatially filtering the collected RS light with a pinhole or an optical fiber to block out-of- focus signal. This also improves the lateral and axial resolutions to as low as ~2 µm. However, the acquisition time per point is usually >5 s and increases with focal depth in the tissue. Confocal Raman probes can achieve acquisition times as low as 1 s but only with significant loss in lateral resolution. Confocal Raman probes have been used mainly for ex vivo and in vitro studies.

Spatially offset Raman spectroscopy

SORS is similar to SpRS, but collects Raman signal from deeper regions in tissue by spatially offsetting the detection and excitation fibers. The detected photons will then have been elastically scattered multiple times and traverse some distance from the illumination source.

Collecting the Raman signal at different offsets effectively samples different layers in the tissue. SORS enables the collection of Raman spectra from several millimeters beneath the surface of turbid media, in contrast to conventional Raman spectroscopy which only measures to a depth of a few hundred microns. In SORS, Raman scattered photons generated at greater depths propagate further through the medium and spread apart due to diffuse scattering before they reemerge from the sample surface. Thus, the greater the offset between excitation and collection positions, relatively more Raman signal from photons generated deeper in the sample can be collected, though at the cost of reduced Raman intensities.

Coherent Raman spectroscopy

Coherent Raman spectroscopy (CRS) refers to nonlinear Raman processes and broadly categorized into Coherent Anti-Stokes Raman Scattering (CARS) and Stimulated Raman Scattering (SRS) are the best known. CARS successfully bypasses the limitations of measuring weak anti-Stokes Raman signals generated via spontaneous Raman scattering. This is achieved by a four-wave mixing process consisting of pump, probe and Stokes fields, which together interact with the sample and generate an anti-Stokes field. CARS offers the advantage of much higher signal intensities and signal-to-noise ratios compared to spontaneous Stokes and anti-Stokes Raman scattering, as all the molecules of interest are 'coherently' excited to a stable eigenstate before returning to the ground state. However, the drawback of this method is the complex instrumentation needed, including multiple pulsed lasers, the quadratic dependence on pump laser intensities, and specialized spectral preprocessing. A further limitation of CARS is the presence of a significant non-resonant background that adds coherently with the resonant signal. This is particularly an issue in tissue since water has a large non-resonant signal. Moreover, CARS spectra can differ from spontaneous Raman spectra due to the non-resonant background, and because the CARS signal varies non-linearly with molecular concentration. Among the challenges for in vivo translation of coherent RS techniques are to achieve efficient light delivery and collection using optical fibers, and to miniaturize the optical components for endoscopic or contact-probe use.

Stimulated Raman scattering

SRS is a technique allowing for rapid acquisition of Raman spectral information from one or a few wavenumbers and uses pico- to femtosecond laser pulses. SRS uses two beams, one at a pump frequency and the other at a Stokes frequency. When the difference in frequency between the two beams matches the frequency of a molecular vibration, it results in amplification of the Raman signal from that vibrational mode. Unlike CARS, the signal intensity is linear with respect to analyte concentration and laser intensities. This facilitates preprocessing, chemometric analysis, and data interpretation. Like CARS, the main drawback is that a very limited range of Raman shifts can be probed at one time – however this is useful in applications where information from a small spectral region is sufficient to characterize the sample.

Surface-enhanced Raman spectroscopy

Low signal intensity is clearly a major limitation of RS. An alternative to coherent amplification of the signal is to use nanoparticles and chemical amplification. The metal nanoparticles are usually the dominant factor; under an incident electromagnetic field metal nanoparticle generate a localized surface resonance that enhances the illumination at the pump frequency and the Raman signal at the Stokes frequency. This enhancement of 10 to 12 orders of magnitude is known as surface-enhanced Raman spectroscopy that produces ultrahigh sensitivity enabling, for example, trace biomolecular analysis. The chemical enhancement is much weaker and is due to wavelength-specific resonance with the charge transfer between the nanoparticles and the molecule. There have been two main approaches to SERS in biomedical applications. The first is to coat an optical fiber probe with metal nanoparticles that is then placed on or in the biological sample and amplifies the intrinsic Raman signature. The second is to administer metal nanoparticles that have been coated with reporter molecules of known Raman spectra. The nanoparticles may then be targeted to specific biomarkers, for example, using antibodies or peptides, acting as nanotags. Limitations of SERS for clinical applications are that it depends on knowledge of sensitive disease biomarkers and the availability of corresponding targeting moieties, as well as potential toxicity and the need for regulatory approval of the contrast agent. SERS possess potential for disease detection from Raman sensitive blood biomarkers and body fluids present in human body to develop point of care and ease of use technology.

Instrumentation and raman spectra

Figure 3 shows a schematic of a Raman probe. Light from the laser transverses through an optical fiber and through a laser line cleanup filter that is internal to the probe. This filter suppresses unwanted signals including those that can arise from the fiber itself. The laser light is then focused onto the sample with an internal lens (or assembly of lenses). Backscattered light is collected via the lens and directed through an edge filter (internal in the probe) that allows only the Raman signal to pass though. The Raman scattered light is then coupled into a second fiber or assumedly of fibers that connect to the spectrometer at the slit.

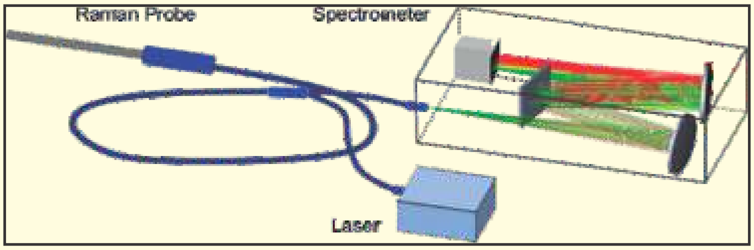

Figure 3: Raman probe assembly. Represented from [8]

Application for cancer detection

The potential use of RS in various diagnostic applications are discussed below.

Skin

Zhao et al measured in vivo Raman spectra on 289 patients presenting 9 different lesion types including BCC and SCC and achieved 91% sensitivity and 75% specificity for differentiating cancers from benign lesions, and 97% sensitivity and 78% specificity for distinguishing malignant melanoma from pigmented benign lesions.[9] Schleusener et al were unsuccessful in differentiating cancerous form benign skin lesions but were able to discriminate malignant melanoma from pigmented nevi in vivo with 87% sensitivity and 94% specificity.[10]

Commercially available skin cancer detection instrument (Verisante Technology, Inc.) as shown in Figure 4.

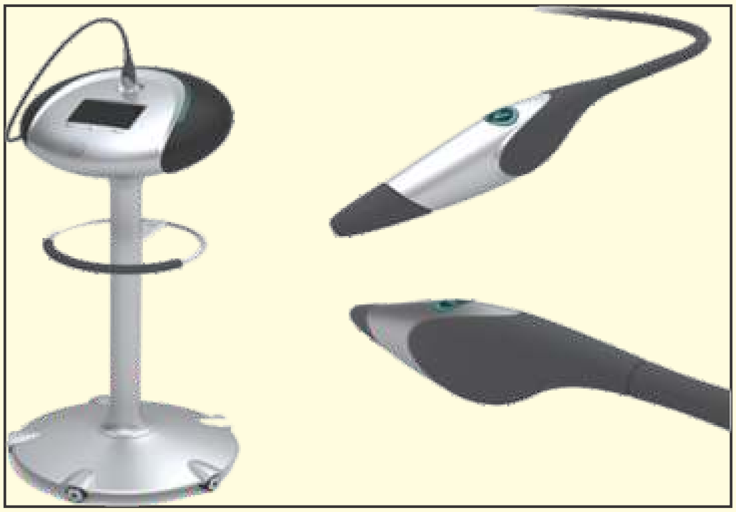

Fig. 4. Verisante Commercial device Aura, a non-invasive imaging and spectroscopy system, offers a more reliable way to diagnose skin cancer, which is currently done by visual examination, followed by a biopsy. [Courtesy of Verisante Technology, Inc.]

Breast

Standard margin assessment using frozen sections is time consuming, labor intensive and is not sufficiently accurate. There are numerous studies on the application of RS to breast cancer diagnosis, mostly using ex vivo human tissue samples or animal models. Bhattacharjee et al used transcutaneous in vivo RS in a mouse and achieved a classification accuracy of 99% with a 15 s integration time [11]. The first in vivo RS study, using <1 s integration time, in patients was reported by Haka et al in 9 patients undergoing partial mastectomy and claimed 100% accuracy in classifying tissue as tumor versus non-tumor. However, the statistical significance of this result was limited.[12] Three years later, the same group published a prospective analysis on ex vivo samples showing 83% sensitivity and 93% specificity.[13] RS may address the need for rapid and robust intraoperative breast cancer margin assessment.

Gynecology

Cervical cancer is one of the leading causes of death in women in developed countries. There are several research studies evident of use of RS in detection of gynecological cancers. Krishna et al looked at healthy, benign and malignant formalin-fixed ovarian tissue from surgical resections and found that benign and healthy tissue spectra are similar, and are clearly differentiated from the malignant tissue spectra [14]. Maheedhar et al achieved 100% sensitivity and specificity for detecting ovarian cancer in 72 spectra from 15 patients on freshly excised ovaries, with acquisition times of several minutes per spectrum [15]. Boca-Farcau et al reported a more specific marker: silver nanotriangles that were both SERS labeled and folic-acid conjugated [16]. Since foliate receptors are known to be overexpressed in most ovarian epithelial cancers, these nanoparticles have potential to target ovarian cancer in the surgical field with higher specificity. Borel et al using spectrally-resolved confocal Raman microscopy showed 92% sensitivity and 85% specificity to distinguish between normal and malignantly-transformed ovarian epithelial cells, a model for high-grade serous ovarian cancer [17].

Oral

Head and neck cancers are most common cancer in developing countries. Oral cancers include lesions of the tongue, hard palate and floor of the mouth. Several optical techniques have been investigated to diagnose oral cancer and guide surgical resection [18]. Guze et al acquired in vivo Raman spectra from 7 different sites in the mouth of 51 healthy patients with 1 s integration time in the 1500–3100 cm^{-1} band [19]. Classification yielded mixed results, with the accuracy ranging from 60% to 100%. The best results were obtained in the 2800–3100 cm^{-1} region. Krishna et al used in vivo RS for the detection of normal oral mucosa, squamous cell carcinoma, submucosa fibrosis and leukoplakia achieving accuracies of 85%, 89%, 85%, and 82%, respectively. Distinguishing normal from abnormal (pooling the other 3 types) resulted in 94% sensitivity and specificity [20].

Brain

Gliomas represent 80% of adult malignant brain tumors and aggressively invade into normal brain.[21] The standard for surgical resection is visual inspection through a neurosurgical microscope along with navigational guidance from magnetic resonance imaging (MRI). However, the full extent of tumor infiltration is often not detected, leading to residual tumor and recurrence. Moreover, the removal of normal tissue can cause permanent neurological deficits. RS has the potential to be useful for neurosurgical guidance by increasing the ability to detect residual tumor in vivo and extend safe resection. Many groups have investigated the spectral differences between normal and cancerous tissue using ex vivo human tissue or rodent glioma models and have revealed important biochemical differences.[22-23] A system using a hand-held RS probe was developed and optimized for intraoperative use during brain tumor resection with 0.2 s acquisition time.[24-25] The system was used in vivo on 17 patients with grade 2–4 gliomas for a total of 161 spectra, yielding 93% sensitivity and 91% specificity for distinguishing normal brain from dense cancer and low-density tumor infiltration.

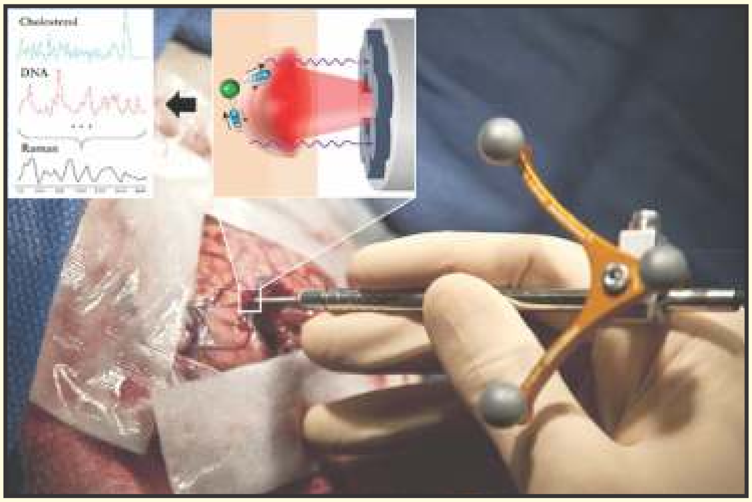

Fig. 5. The handheld Raman spectroscopy probe (EmVision LLC) being used during surgical resection. A schematic illustration shows the excitation light from the probe interacting with molecular species in the brain tissue, which give rise to the measured Raman spectra. Adopted from [25]

Gastrointestinal (GI) tract

The GI tract consists of a number of organs including the pancreas, esophagus, stomach and intestines. For many GI cancers, early detection is critical for reducing mortality rates. Due to the prevalence of endoscopy for GI diseases diagnosis, a number of groups have developed endoscopic RS systems. However long acquisition times and the need to miniaturize fiber-optic components are some of the primary challenges for implementing RS in this manner. While there has been a great deal of in vitro work done by Teh et al 2008, Widjaja et al 2008, Kawabata et al 2011 [26-28]. Bergholt et al have developed in vivo RS endoscopy systems with <1 s acquisition times, and achieved 85% sensitivity and 96% specificity to detect adenocarcinoma in gastric tissue in vivo during endoscopy.[29] This group has also distinguished between normal mucosa, benign and malignant ulcerous lesions in the stomach with sensitivities of 91%, 85%, 82% and specificities of 94%, 95%, 95%, respectively.[30] The Wilson group assessed both in vivo and ex vivo tissue in the colon for distinguishing adenomatous and hyperplastic polyps, with 100% sensitivity and 89% specificity for in vivo samples, with 30 s acquisition time.[31] They also reported detecting high-grade dysplasia in Barrett's esophagus with ~90% sensitivity and specificity.[32] Combining high-wavenumber with fingerprint RS in vivo, Wang et al detected esophageal squamous cell carcinoma with 97% sensitivity and specificity, using acquisition times of 0.1–0.5 s.[33] This body of in vivo work that has achieved high classification performance indicates the diagnostic potential for endoscopic RS in the GI tract. This may also be applicable in lung cancer; a recent study used endoscopic RS in vivo for early detection of lung cancer. In 280 samples from 80 patients, they achieved 90% sensitivity and 65% specificity for the detection of high grade dysplasia and malignant lung lesions, with an acquisition time of 1 s.[34]

Biofluids

RS has also seen increased use to measure biofluids such as blood, urine and saliva for the detection of disease and as a prognostic indicator for treatment monitoring. Biofluids are rich in chemical information, motivating the application of RS. Many standard-of-care tests for disease lack the desired specificity for effective screening. For example, the prostate-specific antigen (PSA) test is commonly used for prostate cancer screening but only ~25% of men who undergo biopsy due to elevated PSA level have prostate cancer.[35] RS has potential for a highly-specific, low-cost and non-invasive optical test to complement or replace existing procedures. It is common to use SERS for the analysis of biofluids, due to the full surface coverage and improved signal detection. Feng et al used SERS with an integration time of 1 s to analyze blood plasma for colorectal cancer and adenomatous polyps, achieving 86% sensitivity and 80% specificity.[36] This group also recently used SERS on saliva to differentiate healthy subjects from subjects with benign and malignant breast tumors, reporting sensitivities of 75%, 72% and 74% and specificities 94%, 81% and 86%.[37] Elumalai et al achieved 99% sensitivity and 87% specificity for detection of oral cancer using urine-based RS, with 90 s integration time.[38] It has also been used for Alzheimer's disease diagnosis based on blood serum, with >95% sensitivity and specificity, using two 10 s acquisitions per spectrum.[39] While the reported sensitivities and specificities of biofluid-based RS detection are still somewhat limited for many applications, there is a great deal of potential for improvements to current standard-of-care cancer screening, particularly to supplement existing diagnostic methods.

Summery

Vibrational spectroscopy can yield a wealth of molecular information from biological tissue, which can be used to discover and quantify new intrinsic biomarkers associated with disease. The strength of RS lies in the high biochemical information content of the spectra, that characteristically show an array of very narrow peaks associated with specific chemical bonds. This results in high sensitivity and specificity, for example to distinguish malignant or premalignant from normal tissues. The true value of Raman spectroscopy unquestionably lies in its versatility and non-destructive nature. The ability to make near real-time measurements is important for in vivo interventional applications. Raman spectroscopy in particular is seeing increased clinical investigation as the instrumentation and spectral analysis techniques improve. RS has potential to develop as diagnostic tools for real time for in vivo interventional applications. However, choosing the most practical and accurate technology often involves trade-offs between field-of-view, spatial resolution, spectral resolution and acquisition time. There is frequently a trade-off between spatial and spectral resolution, and more detailed studies evaluating the most relevant information for different applications are required. The Raman techniques has a number of implementation challenges, requiring interdisciplinary contributions from clinicians and biologists as well as engineers, mathematicians and physicists. As our understanding of the molecular basis of disease improves, this information can be incorporated into the optimal design of Raman systems. Disease progression is typically associated with molecular changes, motivating the use of RS for detection of cancer. RS can be used in place of or in combination with existing clinical practices such as biopsy, histopathology and radiologically-based surgical guidance. Signal detection remains one of the primary challenges facing the use of RS for clinical diagnostics. The contribution from intrinsic auto-fluorescence background in tissue often dominates the relatively small Raman signal, and other factors such as noise, instrument response, and ambient light further confound the problem. While sophisticated spectral analysis and pre-processing techniques can mitigate some of the confounding factors, signal detection is still the key limitation. Many approaches such as CARS, SRS, and SERS aim to address this issue, and evaluating the trade-offs of these approaches in the context of different oncology applications will be critical to enabling clinical translation, particularly regarding acquisition time and spectral/spatial resolution. 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.

Future outlook

Raman spectroscopy with other techniques provides for multimodal approaches with extended capabilities. The molecular information from RS can be combined with complementary information from other modalities to improve diagnosis or for treatment planning and guidance. While in some cases the achieved in vivo sensitivities and specificities with RS may be sufficient for clinical translation, there are many diagnostic applications that could benefit from complementary biomarkers. For example, metabolic (tissue fluorescence) and morphological (optical coherence tomography) information can serve as quantitative diagnostic biomarkers, and potentially improve the sensitivity and specificity. A great deal of progress has been made for the use of multimodal imaging and spectroscopy to complement the molecular detection of RS. The recent surge in machine-learning research has benefitted RS, making available sophisticated classification algorithms that can optimally utilize the spectral information. While surgical guidance is one of the primary avenues for clinical use of RS, the increased portability, convenience and affordability of RS technology also makes it increasingly viable for screening and point-of-care, extending Raman techniques into a wider clinical user community. The key for effective RS spectral analysis is combining it with machine learning and artificial intelligence for extraction of important feature from spectral information to support accurate clinical decision making. A number of companies have already developed in vivo systems for clinical use of RS, such as: Verisante (Canada) for skin cancer, Endofotonics (Singapore) for endoscopic cancer detection and ODS Medical (Canada) for brain cancer. RS has also seen increased use for disease detection via the measurement of biofluids such as blood, saliva, and urine, with several companies developing toolkits and microscopes for this purpose, e.g. RiverD (The Netherlands). Thus number of hand-held tools have been developed specifically for in vivo Raman spectroscopy. The recent extensive research work in this direction strongly suggests that RS will find its well-deserved place for disease detection into clinics in coming decade.

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THREE CHEERS

Dr. Ngangom Robert, Medical Physicist, Department of Radiotherapy, PGIMER, Chandigarh has been awarded PhD in Physics by National Institute of Technology (NIT), Krurkshetra in July 2021. The topic of the PhD thesis was "**Analysis of dose reporting in radiation therapy treatment planning and its dosimetry system**". Congratulation!

Prof Arun Chougule has been awarded prestigious Prof L.S. Ramaswamy Memorial Oration award 2022 by the Indian Society for the Study of Reproduction and Fertility (ISSRF) for his research contribution in Radiobiology. Congratulations!

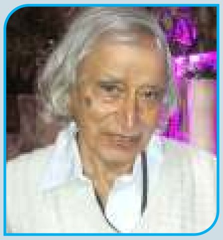
Dr. Suresh Yadav has been promoted to Associate Professor (Medical Physics), Department of Radiation Oncology, Gandhi Medical College, Bhopal, Madhya Pradesh in December 2021. Congratulations!!

Mr. Pradeep Goswami has been promoted to Scientist E, Institute of Nuclear Medicine & Allied Sciences (INMAS), DRDO, New Delhi in July 2021. Congratulations!!

Dr. A. Saravana Kumar has received the Junior Associate Award of ICTP, Italy for the Year 2023-2028. Also, He has been promoted to Head, Medical Physics, PSG Institute of Medical Sciences Research and Hospitals, Coimbatore, Tamil Nadu. Congratulations!!

Dr.Vindhyavasini Prasad Pandey, Asstt. Professor, Hind Institute of Medical Sciences, Barabanki received Dr.M.S.Aggarwal Young Investigator Award for outstanding research contribution at AMPICON-2021 at Bangalore. He also received APSIG Elekta Award to attend EPSM-2021 virtual conference, Australia. Congratulations!

OBITUARY



Late Dayal C Aurora

Shri Dayal C Aurora, retired Chief Physicist & HOD of Medical Physics, The Gujarat Cancer & Research Institute (GCRI), Ahmedabad, Gujarat, passed away on 13th August 2022 at the age of 84 after a brief illness. Fondly known as Dayal Babu among his peers and colleagues, he was one of India's pioneering medical physicists. He was an alumnus of the 2nd batch of DRP, BARC, Mumbai, India. Shri Dayal C Aurora always advocated the advancement of Medical Physics in India such as the use of linear accelerators, advanced treatment planning software, IGRT, IMRT, and others. He was also instrumental in helping set up a modern infrastructure for Medical Physics at GCRI, Ahmedabad during his tenure there. Shri Dayal C Aurora was a man with a simple outlook and a completely dedicated attitude towards the field of Medical Physics in India. He was a true and sincere Karmyogi and lived a disciplined and principled life. He dedicated his entire life to the advancement of Medical Physics and the service of humanity in the country. May God grant him Sadgati and eternal peace.

MEDICAL PHYSICS PHOTO CONTEST

Medical Physics Gazette (MPG), the newsletter of the Association of Medical Physics of India (AMPI) invites entries from AMPI members for Medical Physics Photo Contest. One contestant may send one entry only. The camera clicked photo in the format JPG and JPEG should not have any identification mark (like name, place, title etc.) in the photo. The entry must demonstrate or involve the situation / concept / procedure / life or message related with medical physics and medical physicist. The contestant must write a title for the entry. The contestant may add an optional description for the entry in maximum 50 words. Kindly write your name, designation, affiliation, AMPI Membership No., mobile and email address. The title, optional description and the particulars regarding the contestant may be sent in a word file. The entry into the contest is free. MPG reserves the right to select the winner, hold, modify or cancel the contest any time. The decision taken by MPG regarding this contest would be final and binding.

Kindly send the entry to drpratikkumar@gmail.com by 31st January 2023.

There are three prizes of Rs. 3000/-, Rs. 2000/- and Rs. 1000/- for this contest sponsored by M/S MEX India.

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