SOCIETY FOR RADIATION RESEARCH (SRR)

(Registration No.: Maharashtra State, Mumbai 2280, 2014 GBBSD)

Registered Office: Advanced Centre for Radiation Oncology

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2019 5 Years of Serving Radiation Researchers!!

A Report on

SECOND INTERNATIONAL SCHOOL ON RADIATION RESEARCH (ISRR-2020)

Theme: Radiation Induced DNA Damage Response:

Mechanisms and Human Health Implications

September 6-20, 2020

MODE: E-CONFERENCE **(GOOGLE MEET)**

SRR has taken initiative to organize International Schools with specific theme related to radiation research. These Schools are aimed (i) to educate/train the young researchers/students about theme area and (ii) encourage/facilitate the young researchers (in India and abroad) to build their career in radiation research. In this series, the **First International School on Radiation Research (ISRR-2017) theme: Radiation Carcinogenesis-Mechanisms and Experimental Models** was organized during Feb 2-4, 2017 at Annamalai University, Chidambaram. In this series, the **Second International School on Radiation Research (ISRR-2020)** was organized as **E-Conference** mode during **Sept. 6-20, 2020** under global pandemic situation of Covid-19. The School was participated by about 45 registered participants from India and abroad. A range of topics were covered through talks/special lectures by eminent faculties from India and abroad (Japan, USA, Germany, UK, Austria, Canada, Hungary, Singapore).

During inauguration session of the School on Sept. 6, 2020, **Dr Shyam Kishore Shrivastava (**Former Head, Dept. of Radiation Oncology, TMH, Mumbai**,** Director, Radiation Oncology, Apollo Hospitals, Navi Mumbai, President, SRR) delivered a welcome note to all delegates and participants of the School on Radiation Research. Dr Shrivastava also mentioned about the use of radiation for the human healthcare as well as the adverse heath effects of radiation on human health especially on DNA damage.

The brief introduction about the SRR and ISRR-2020 was given by **Dr K. P. Mishra (**Ex-Head, RB&HSD, BARC, Mumbai, Ex-VC, NGBU, Allahabad, Founder President, SRR). He has provided a brief information about goals, recent activities of the Society. He discussed about, how this Society has grown with a huge success in the field of radiation research, with the contribution of all radiation biologists, radiation oncologists in conducting different activities, seminars, conferences and workshops to explore the radiation biological research.

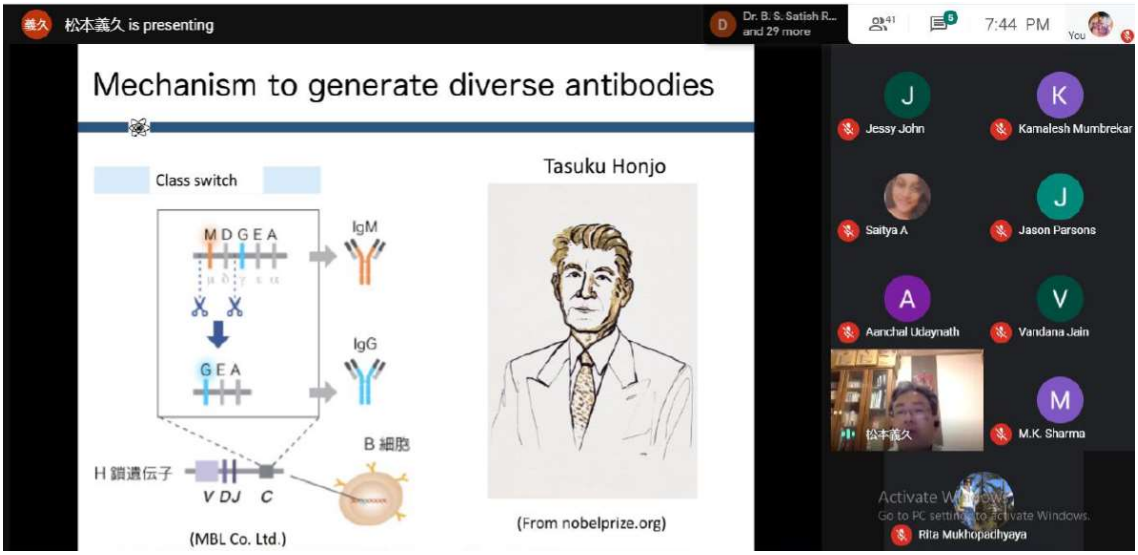
During the Inaugural Session of the School **Dr J. P. Mittal (**Former, Director, Chemistry and Isotope Group, Bhabha Atomic Research Centre, Distinguished Professor and Chairman, Academic Board, Centre for Excellence in Basic Sciences, DAE-University of Mumbai) delivered inaugural address. Dr Mittal highlighted the importance of radiation biology, chemical and molecular effects of radiation on the human health. He also clearly explained the chemical phenomenon behind it. Dr Mittal emphasized the need for collaborative research amongst radiation biologists and radiation chemists for better understanding of the radiation effects.

Dr B. Paul Thaliath (Director, Regional Cancer Centre, Kamala Nehru Memorial Hospital, Allahabad) delivered a special lecture on **"Radiotherapy of Cancer"**. Dr Thaliath highlighted the emerging concepts of radiotherapy and the recent advances in cancer treatment, and how advancement in biophysical techniques is helping in novel radiotherapies of cancer.

Dr B. N. Pandey (Convenor of ISRR-2020, Head, RSCBS, RB&HSD, BARC, Mumbai) has given vote of thanks to all the dignitaries for the inaugural session and for informative introductory lectures. Dr Pandey thanked all the participants, SRR Office bearers, Members and other colleagues of BARC for their whole hearted support to organize the School. Dr Pandey also thanked Mr Deepak Naik for helping to maintain the SRR website and ISRR 2020 online registration process. Dr Pandey thanked sponsor of the School.

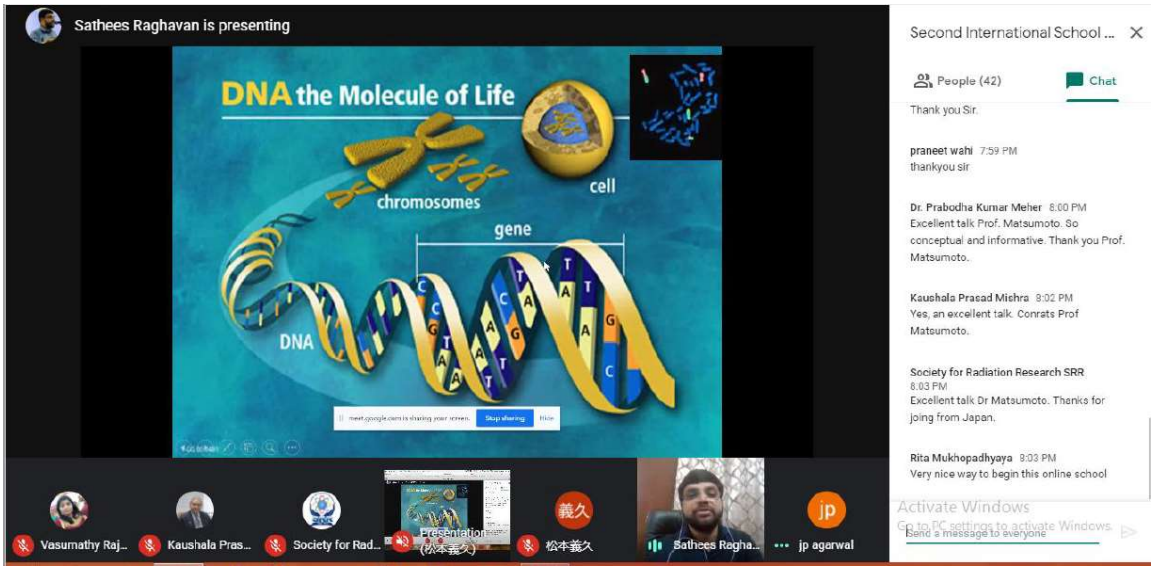
DNA Damage and Repair Mechanisms

The first scientific session was chaired by **Dr J.P. Agrawal** (Head, Department of Radiation Oncology, Tata Memorial Hospital, Mumbai). In this session, **Dr Yoshihisa Matsumoto (**Tokyo Institute of Technology, Tokyo, Japan) delivered a lecture on the basic mechanisms for DNA double-strand break repair. In this lecture, he mentioned that double-strand break is the most difficult type of DNA damage and is also occur as biological effects of radiation. He mentioned different types of DNA damages induced by radiation. DSBs are most commonly detected by immunostaining of 53BP1, γH2AX etc., which accumulates around DSBs. DSBs are mostly repaired through NHEJ (non-homologous end joining) and HR (homologous recombination). NHEJ and HR have merits and demerits over each other but importance of NHEJ is especially prominent in vertebrates. Although it is not accurate as that of HR, still NHEJ plays a key role in diversification of vertebrates such as immune system diversification.



Scientific Session 1: Dr Yoshihisa Matsumoto delivering his online talk

Dr Sathees Raghvan, Indian Institute of Science, Bangalore, India delivered a lecture on DSB Repair mechanisms and its relevance in Cancer therapy. In this lecture, he highlighted that DNA is the only biological macro-molecule that is repaired, all other gets replaced. More than 100 genes are required in DNA repair, even in organism with very small genome. He mainly focused on the role of DNA damage and repair mechanism in cancer development and cancer therapy. He said that cancer is the consequence of inadequate DNA repair. He highlighted the importance of both DNA polymerase and DNA ligase in both replication and repair process. In this lecture he also emphasized that how modulation of DNA double stranded repair act as a strategy to improve precise genome editing. He also discussed the detailed mechanism of non-homologous end joining NHEJ (Non-homologous end joining), HR (Homologous recombination) and microhomology based end joining in DNA double stranded repair pathway. Further he described the mechanism of how efficiency of DNA non-homologous end joining varies among different somatic tissues despite of similarity in mechanism.



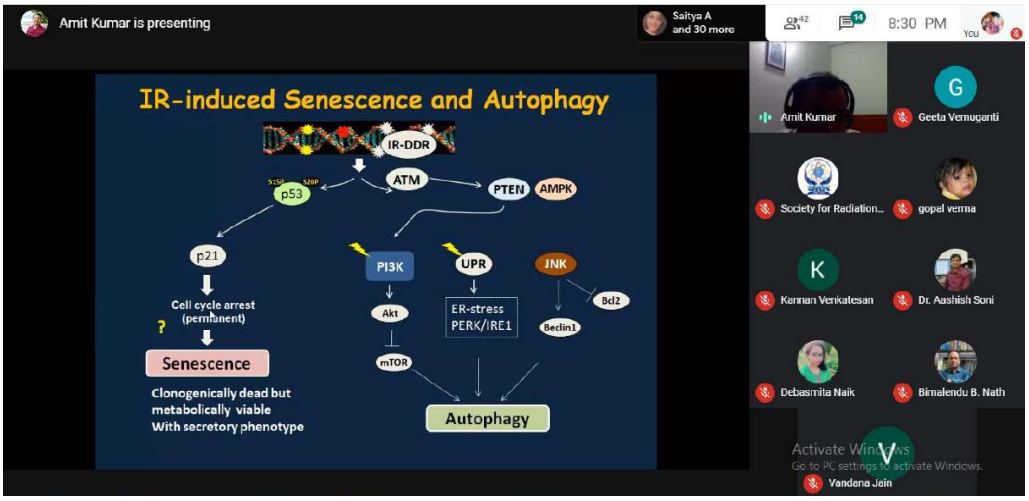
Scientific Session 1: Dr Sathees Raghvan delivering his online talk

Radiation Induced DNA Damage Signalling

Dr Aashish Soni, University of Duisburg-Essen Medical School, Germany delivered a lecture on distinct roles of Double strand breaks repair pathways on the repair of chromosomal DSBs in G2 phase of the cell cycle. In this lecture, he describes how DNA double stranded break affects genomic instabilities in cells and how failure of DNA double stranded break repair pathway leads to different consequences like chromosomal aberration, genomic instability and tumorigenesis. He also described the details of chromosome type aberrations and chromatid type aberrations and how they are produced by irradiating the cells in different phases of cell cycle such as pre-replication and post-replication phases, respectively.

Dr Amit Kumar, Bhabha Atomic Research Centre, Mumbai, India talked on radiation induced DNA damage and its significance in cancer cell death and carcinogenesis. In this lecture, he described the detailed mechanism of ionizing radiation induced DNA damages by both direct and indirect mechanism. He described how gamma/x-ray induce clean DSBs however alpha and other heavy ions causes clustered DSBs. He stated that magnitude of IR induced DNA damage determines cell death, cell survival or survival with mutation. Type of IR induced cell death depends on radiation factors, cell/tissue types, P53/ATM status and micro-environment. The detailed mechanism of IR induced apoptosis, necrosis and autophagy has been studied. However, other forms of cell death are equally relevant for cancer treatment. Depending on the magnitude of DNA damage, decision for cell death/survival is determined by P53. Chromosomal aberrations, point mutation and epigenetic alterations lead to inactivation of tumour suppressor genes and activation of oncogenes which finally results in multi-step radiation carcinogenesis. Human cancer genome sequencing data identified 140 genes as a driver of tumorigenesis, which can be classified into 12 signalling pathways that regulate three core cellular processes such as cell

fate, cell survival and genomic maintenance. He also mentioned the wider implications of research on radiation induced DNA damages such as in radiation carcinogenesis, cancer radiotherapy, nuclear toxicology, diagnosis, food irradiation, environment, space and nuclear agriculture and mutation breeding.



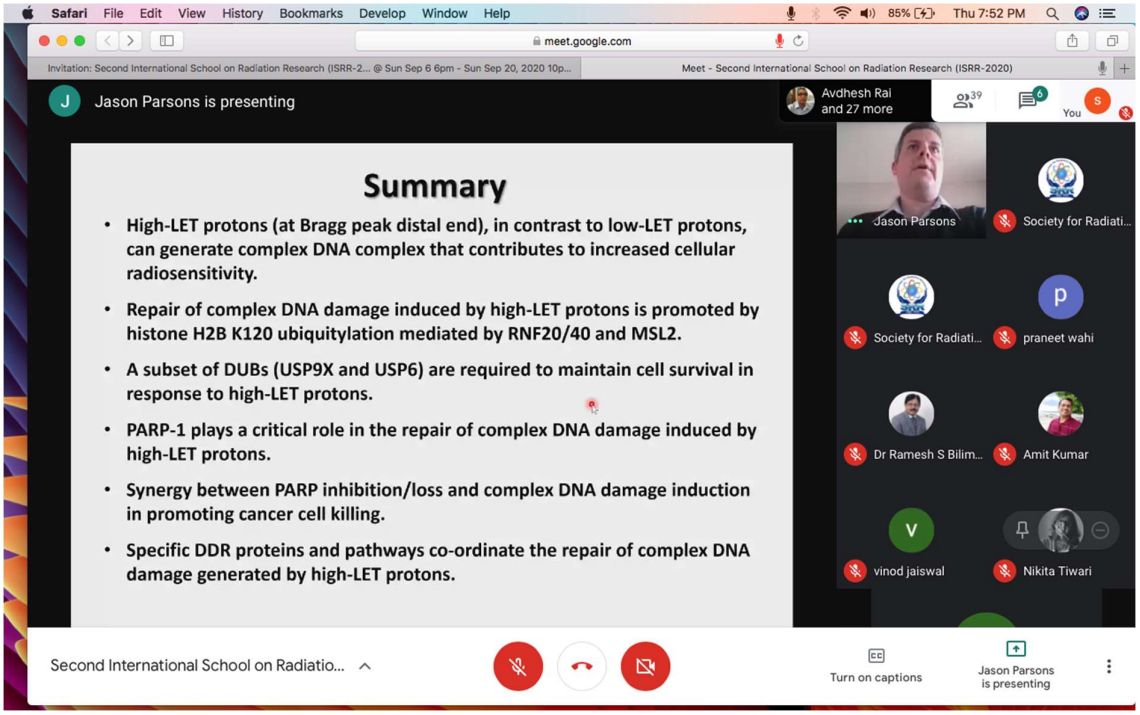
Scientific Session: presented by Dr Amit Kumar

DNA damage and Low Dose Radiation Biology

Dr Edward J. Calabrese, University of Massachusetts, Amherst, USA delivered his first talk about Linear No Threshold (LNT) Dose Response: Historical Foundations and Its Widespread Risk Assessment Implications and another lecture on Hormesis: A Central Concept in Biology and Medicine. In his lecture, he described the LNT Dose Response model and its limitations in the risk assessment. He stated that Muller was eventually proved wrong later with new measurement techniques. Many notable geneticists disputed Muller on this topic. He said that Muller's gene mutation claim was now proven incorrect. LNT single hit model is based on Muller's incorrect interpretation. Muller and Stern misrepresented Manhattan project findings to promote LNT model. He said that self-interest and scientific misconduct lead to the success of LNT. LNT being a wrong model succeeded because of massive project /influence Manhattan project.

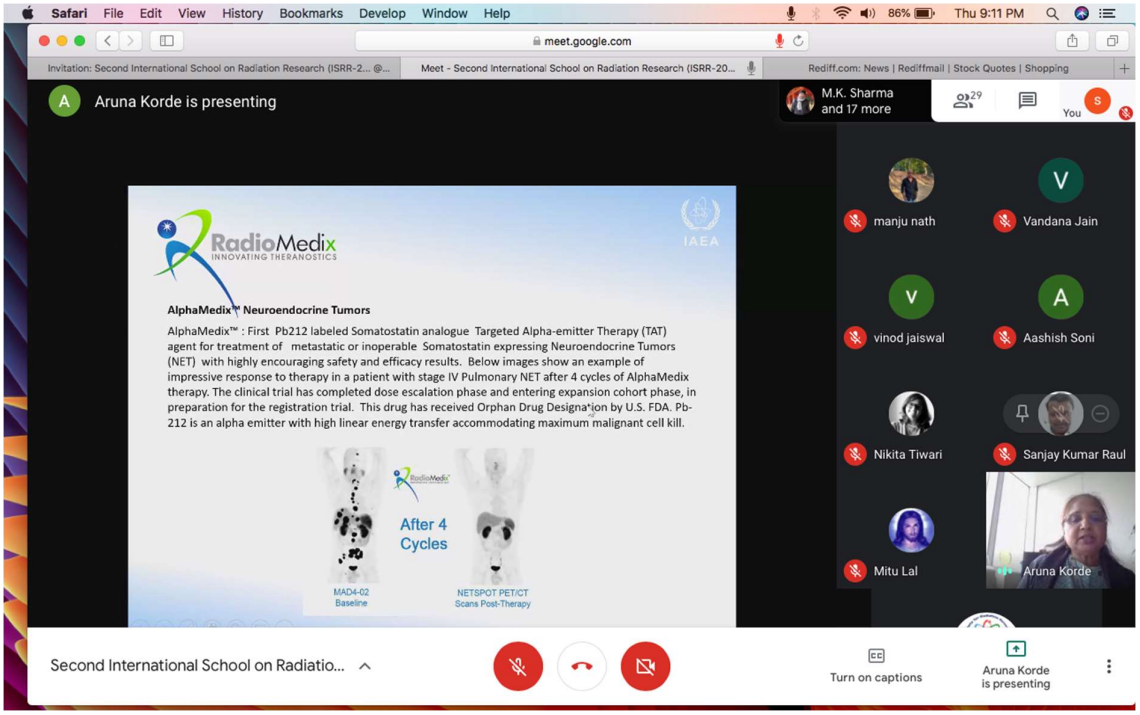
High LET Radiation Induced DNA Damage in Cancer Therapy

Dr J.L. Parsons, University of Liverpool, UK delivered his lecture on the cellular response to complex DNA damage induced by high-LET radiation. He briefly discussed the mechanism of proton beam therapy in radiobiology. In comparison to classical x-ray, proton beam therapy can deliver energy within finite region which can directly target cancer cells. This limits radiation dose to proximal normal tissues. There is still significant biological uncertainty because relative biological effectiveness is variable. Low energy protons cause decrease in cell survival compared to high energy proton.



Scientific Session: presented by Dr. Parsons

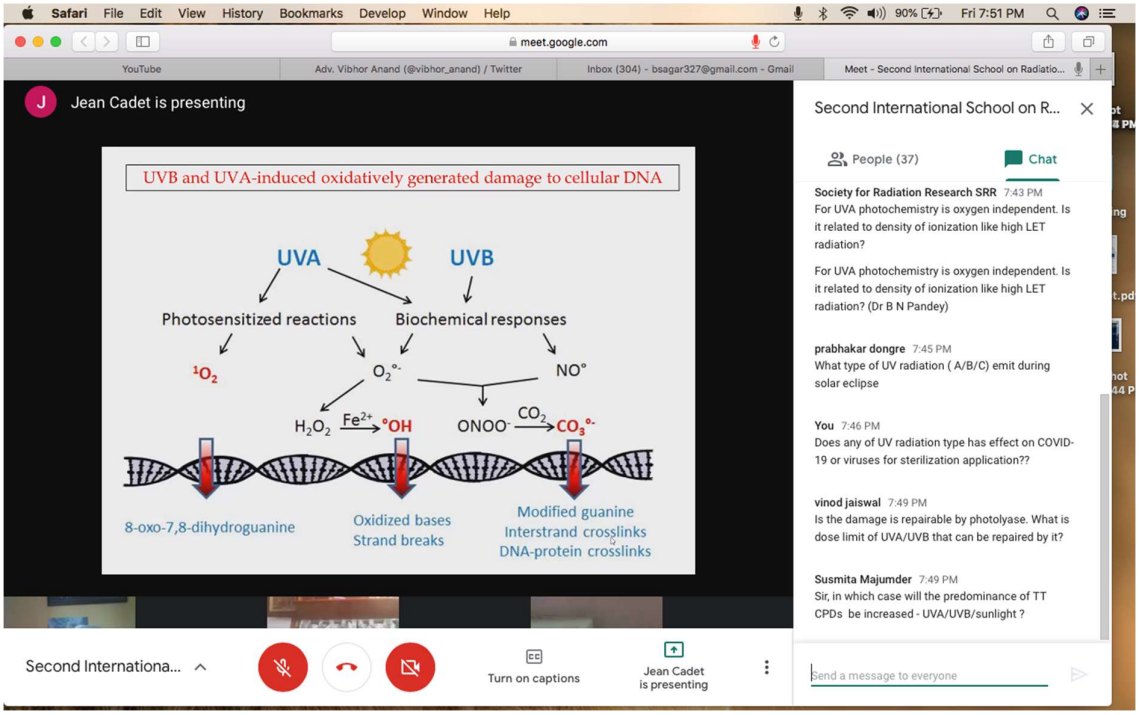
Dr Aruna Korde, International Atomic Energy Agency, Vienna, Austria emphasized on the concept of alpha emitting radionuclides for therapy. In this talk, she gave brief introduction about radiopharmaceuticals which are suitable for both therapeutic and diagnostic purposes. Radiopharmaceuticals should be designed for pharmacokinetic pattern which will allow minimum dose to the non-target tissues, desired accumulation/retention in the target tissue and faster clearance from the non-target tissue. She briefly described about alpha emitters and their therapeutic potential.



Scientific Session: presentation by Dr. Aruna Korde

UV Induced DNA Damage and Repair

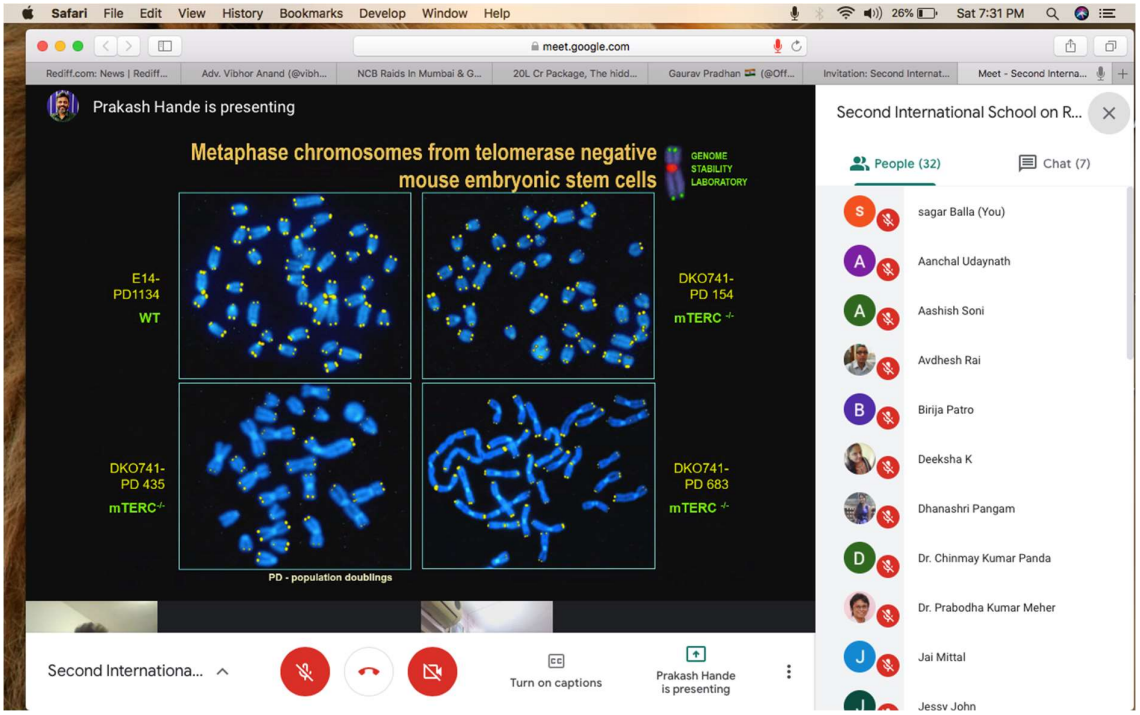
Dr Jean Cadet, University of Sherbrooke, Canada talked about UV Induced DNA Damage and Repair and Mutagenic and Carcinogenic Effects of UV radiation. In this lecture, he described the photochemistry of nucleic acid such as low intensity UVC, UVB and UVA photochemistry, high intensity UV laser photochemistry and photosensitized reactions. He described different mass spectroscopic measurement of dimeric pyrimidine photoproduct in DNA. C-T or CC-TT transversion act as a molecular signature for UV radiation.



Scientific Session: presented by Dr. Jean Cadet

Radiation Induced DNA damage Response and Telomere Maintenance

Dr Prakash Hande, National University of Singapore, Singapore delivered a lecture on Telomere dysfunction and DNA repair deficiency: Markers of sensitivity to radiation and other mutagens. He emphasized the structural and functional perspective of telomeres in detailed, which is having cap like structure and containing repetitive simple non coding DNA sequences, variable in size and responsible for chromosomal stability, protect the chromosomes from end-to-end fusion and exonuclease degradation. He also emphasized on telomere hypothesis of cell ageing and immortalization. He vividly explained how telomere dysfunction leads to DNA repair deficiency. In another talk, he also explained the major scientific misconduct in biomedical research in the entire world with example and how it leads to scientific disaster.



Scientific Session: presented by Dr. Prakash

Radiation Induced DNA Damage Quantification Techniques-I

Dr T. Konishi, National Institutes for Quantum and Radiological Science and Technology, Chiba, Japan has delivered a lecture on advances in microbeam technology for single cell radio-biology. In his lecture he described the detailed investigation on the radiation induced bystander effect in targeted and nontargeted area relevant to cancer therapy. Induction of DSBs of cyto-targeted irradiation was result of cytoplasmic damage triggered signalling. Cyto-damage triggered cellular signals may also activate DSBs repair mechanism(s).

Dr Nagesh Bhatt, Bhabha Atomic Research Centre, Mumbai, India has delivered a talk on biological indicators of DNA damage by radiation, tools for medical application, research and radiation protection. He explained the structure of DNA and the sources of DNA damage in detail. He explained the concept of triage simulation in bio dosimetry and explained different bio-dosimetry techniques based on radiation induced DNA damages.

Radiation Induced DNA Damage Quantification Techniques-II

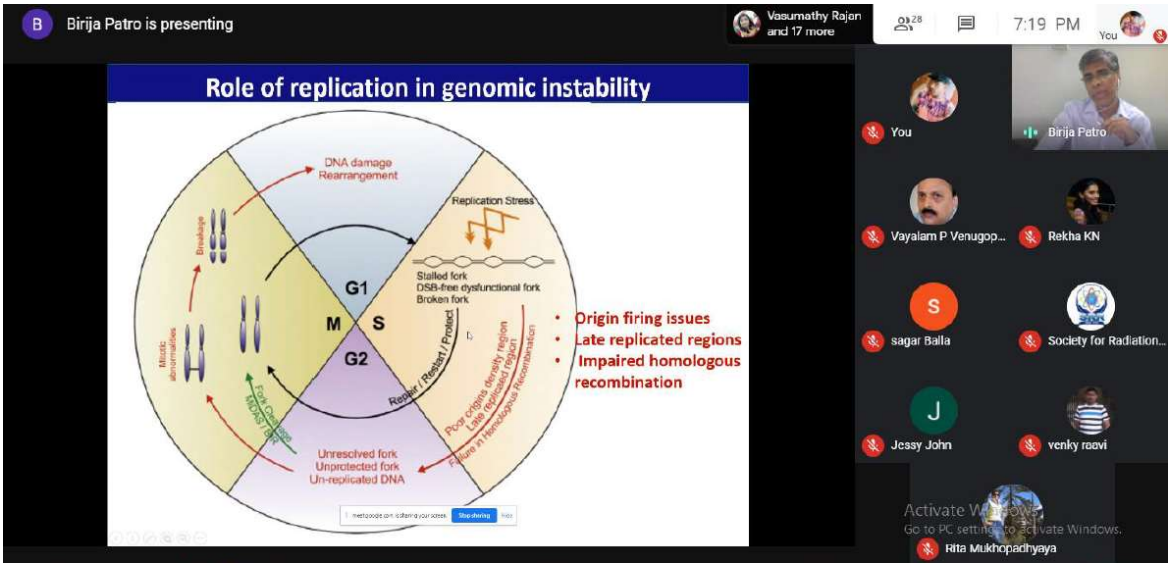
Dr Y. S. Rajpurohit, Bhabha Atomic Research Centre, Mumbai, India, talked about radiation-induced DNA injury and damage detection. He stated that DNA is the primary target of many DNA damage causing agents like UV radiation, ionizing and non-ionizing radiations, DNA alkylators, certain environmental carcinogens, oxidative stress and certain chemotherapeutic drugs. Variety of DNA repair mechanism(s) could repair the damaged DNA. Repair enzymes may function as important biomarkers for predicting the response of tumours to genotoxic stress and for prognosis purpose. He emphasized on the strategies for DNA damage detection, which includes molecular

strategies, fluorescent strategies, chemiluminescent strategies and analytical strategies and briefly describes different techniques and assays for detection of DNA damage.

N. R. Prasad, Annamalai University, Chidambram, India has delivered a lecture on UV radiation-induced DNA damages in human and various analytical methods for its detection. He briefly discussed the UV radiation induced DNA damage response pathways and the model systems for its experimentation.

Radiation Induced DNA Damage Quantification Techniques-III

Dr B. S. Patro, Bhabha Atomic Research Centre, Mumbai, Indiahas delivered a brief lecture on emerging concepts of replication dynamics in the genome instability. He briefly described about replication fork repair, different mechanism of replication fork repair, replication fork repair and its correlation with genomic instability, different methods to study replication repair, live cell imaging for double stranded break repair and assessment of different repair proteins at replication fork.

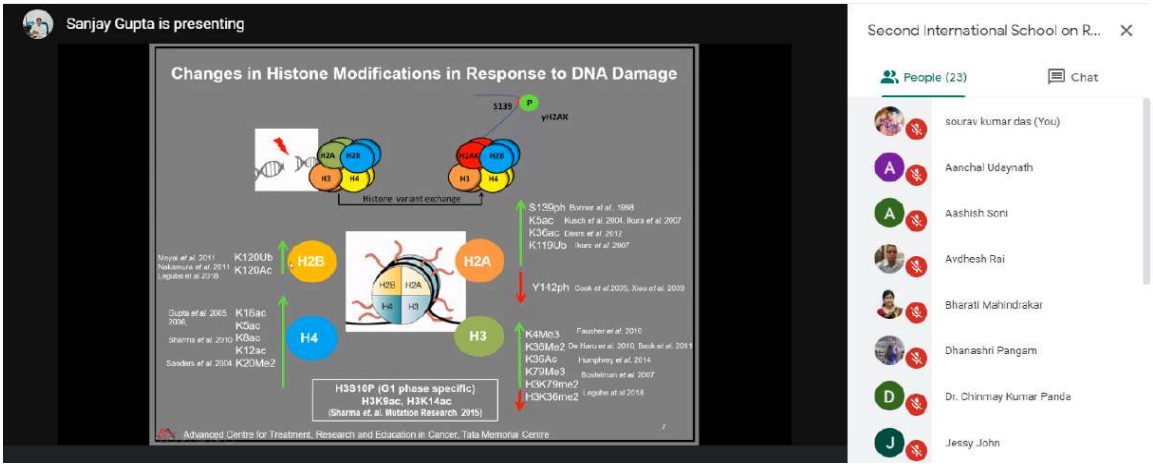


Scientific Session: presented by Dr B. S. Patro

Dr Senthil Karunakaran, Merck Life Sciences, India delivered a technical talk on proximity ligation assay to detect and visualize DNA damage-induced Protein Complexes

Epigenetics and Chromosomal Aberrations in Radiation Induced DNA Damage Response

Dr Sanjay Gupta, Advanced Centre for Treatment Research and Education in Cancer, Navi Mumbai, India discussed about the dynamic alterations of histone H3 phospho-acetylation correlate with radio-sensitivity of mitotic cells during DNA damage. He described the role of epigenetics in cell cycle regulation, DNA damage and repair pathways. He stated the various types of histone modification in response to DNA damage response and described the role of different chromatin modifiers in DNA damage response. He mentioned about the chromatin organization, differential phosphorylation of H3 histone in G0/G1 and G2/M cells and cell survival mechanism.

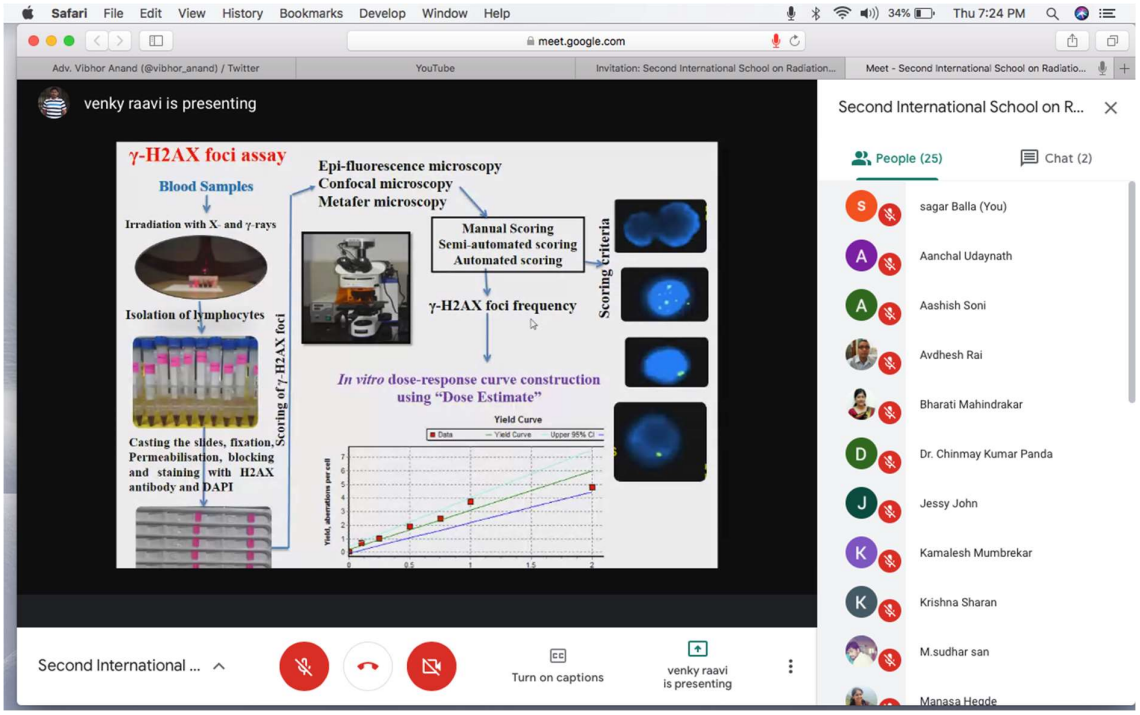


Scientific Session: presented by Dr Sanjay Gupta

Dr V. Perumal, Sri Ramachandra Institute of Higher Edu. & Res., Chennai, India delivered a lecture on Radiation Induced Chromosomal Aberrations and Health Implications. In this lecture, he provided information about different types of chromosomal aberrations in response to radiation and its detection methods. He also described different cytogenetic markers and molecular markers to detect radiation induced DNA damages.

DNA Damage as Biomarker and Cancer

Dr V. Raavi, Sri Devaraj Urs Academy of Higher Education and Research, Kolar had delivered a lecture on Gamma H2AX, Gene and miRNA expression as Biomarkers of Radiation Induced DNA Damage. He briefly discussed about the mechanism of gamma H2AX as a marker of DSBs and its determination techniques. Apart from γH2AX, and other gene-based marker and miRNA-based markers are used as biomarker of radiation exposure. He briefly discussed the mechanism of these markers in the detection of radiation induced DNA damage.

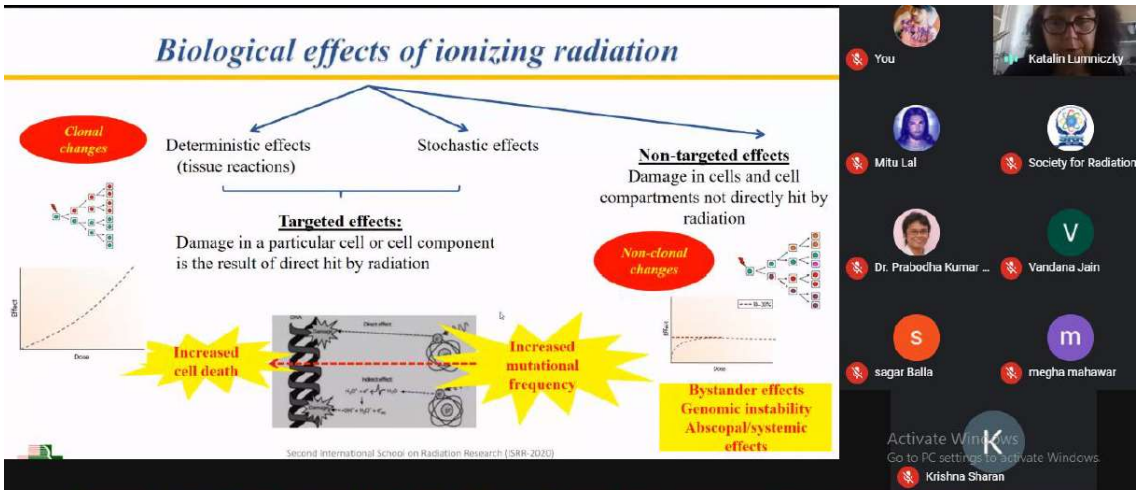


Scientific Session: presented by Dr Raavi

Dr. Krishna Sharan, Kasturba Medical College, Manipal had briefly described about Radiation-Induced DNA Damage in Cancer Radiotherapy and how it can be further exploited in improvement of cancer therapy.

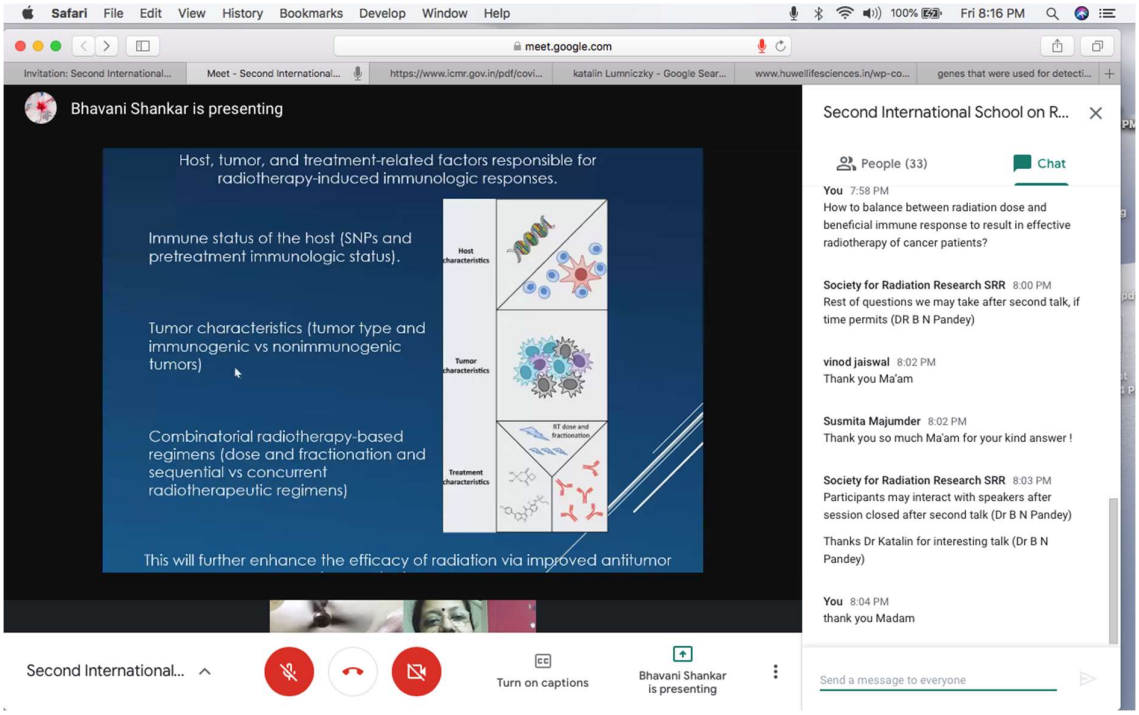
Interplay of Immune Response in Radiation Induced DNA Damage

Dr K. Lumniczky, National Public Health Center, Budapest, Hungary delivered a brief lecture on Ionizing radiation effects on the immune response. She explained the biological effects of ionizing radiation which comprises of deterministic effects, stochastic effects and non-targeted or bystander effects. Both deterministic and stochastic effects are targeted effects which results in damage in particular cell or cell components is the result of direct hit by radiation. She discussed the different types of changes in immune parameters like, increased frequency of chromosomal aberrations, oxidative stress, inflammation and release of immune modulatory factors, activation of radiation responsive signal transduction pathways, increased mutational frequency and increased cell death.



Scientific Session: presented by Dr K. Lumniczky

Bhavani Shankar, Bhabha Atomic Research Centre, Mumbai, India talked about Synergistic effects of radiotherapy and immunotherapy and its underlying principles and challenges. In her lecture, she described the importance of radiotherapy in cancer treatment. High precision techniques are available, making treatment delivery safer and more effective, sparing normal healthy tissue. According to the central dogma of traditional radiobiology, cytotoxic effects of radiation on tumor cells are primarily due to the production of DSBs followed by cell death. The major mode of action of radiation directed on tumor cells is the cytotoxic effect, that can result in cell death by different modes like; apoptosis, autophagy, necroptosis, pyroptosis etc.

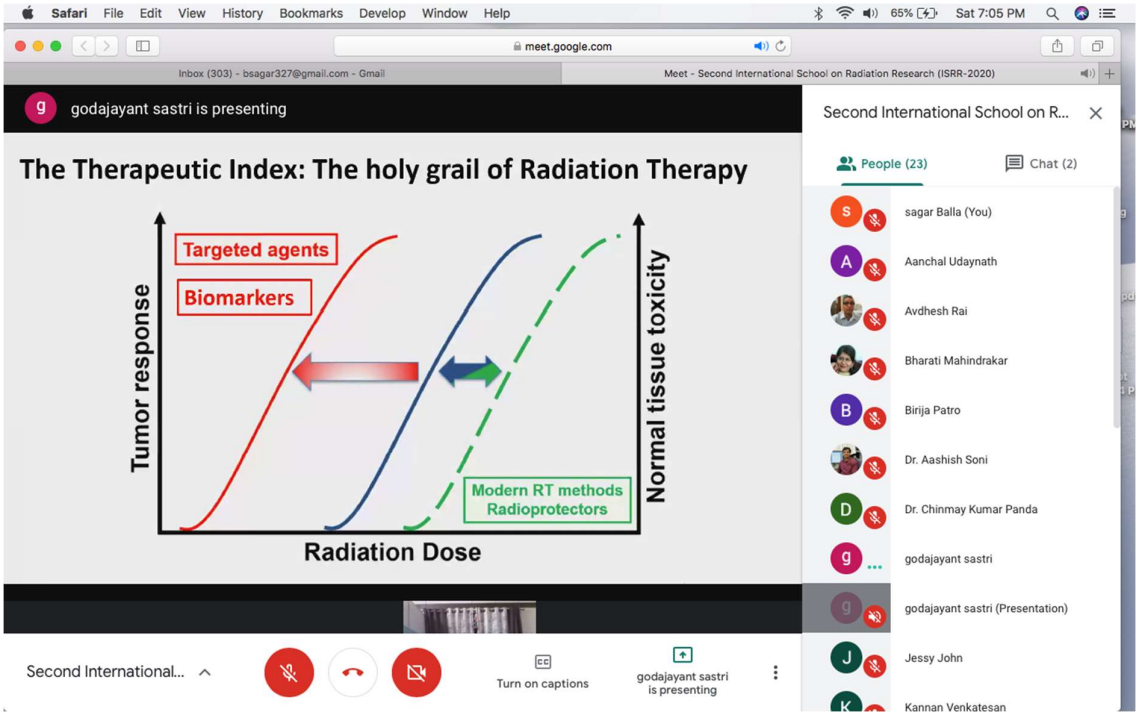


Scientific Session: presented by Dr Bhavani

DNA Damage Response in Cancer Radiotherapy

J. Sastry, Advanced Centre for Treatment Research and Education in Cancer, Navi Mumbai, Indiahas delivered a brief lecture on Diagnostic, Prognostic and Predictive Ability of DNA damage and repair in clinical radiation oncology.

S. Laskar, Tata Memorial Hospital, Mumbai, Indiahas delivered a brief lecture onExcitements and Challenges of Carbon Ion Radiotherapy



Scientific Session: presented by Dr Sastry

Roger Howell, New Jersey Medical School, Cancer Institute of New Jersey, Newark, USA delivered a special lecture on Radiopharmaceutical therapy elicits radiation-induced bystander effects that cause DNA damage and growth delay of tumor cells.

Award and Valedictory Function

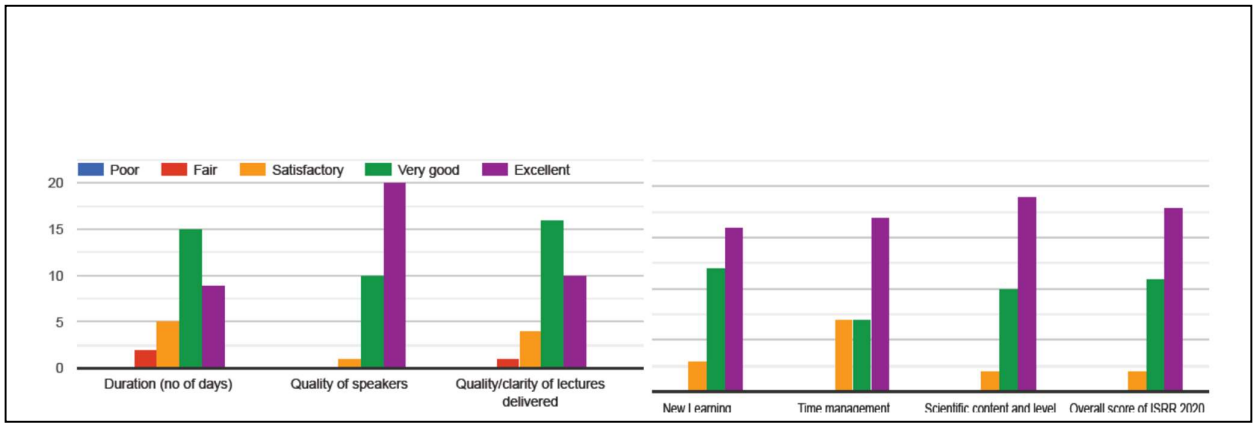
During award and valedictory session, Dr. Nagaraj Huilgol Chief Radiation Oncologist, Dr. Balabhai Nanavati Hospital, Mumbai, **Dr. B. B. Singh,** Ex-Head, RB&BCD, BARC, Mumbai and **Prof Hiroshi Yasuda**, Research Institute for Radiation Biology and Medicine, Hiroshima University, Japan addressed the audience. They appreciated the efforts of SRR to successfully conduct ISRR 2020. The Session was addressed by Chief guest of function Dr. Avinash Pandey, Director, Inter

University Accelarator Centre, New Delhi. Later **Dr. Avinash Pandey**, **Prof. Roger Howell,** and **Prof. K. P. Mishra** distributed the awards. They also highly praised the efforts to conduct such a meeting. **Prof. K. P. Mishra** has invited all of the participants for the 5th Asian Congress on Radiation Research (5th ACRR 2021) to be held in Nov 2021. Best participation awards were selected by a jury which was conferred during award and valedictory function. Vote of thanks was delivered by Dr Chandan Kumar, Bhabha Atomic Research Centre, Mumbai and Treasurer, SRR.

Best Participation Awards

1. **Dr AVDHESH KUMAR RAI,** DBT CENTRE FOR MOLECULAR BIOLOGY & CANCER RESEARCH, DR. B. BOROOAH CANCER INSTITUTE, GUWAHATI
2. **Dr Prabodha Kumar Meher,** Institute of Medical Radiation Biology, University of Duisburg-Essen, Medical School, Essen, Germany
3. **Ms Saitya Raju Amula**, Homi Bhabha National Institute, Mumbai and Indira Gandhi Centre for Atomic Research, Kalpakkam
4. **Ms Rekha K N,** Department of Radiation Biology & Toxicology, Manipal School of Life Sciences, Manipal Academy of Higher Education, Manipal
5. **Ms SUSMITA MAJUMDER,** Dinabandhu Andrews College, Department of Zoology, Kolkata
6. **Mr Vinod Deomani Jaiswal,** Department of Biophysics, University of Mumbai, Kalina, Mumbai

Feedback from the Participants



Report prepared by:

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