SOCIETY FOR RADIATION RESEARCH (SRR)

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Registered Office: Advanced Centre for Radiation Oncology

Dr Balabhai Nanavati Hospital, Vile Parle (W), Mumbai 400 056, India

Email: srr1415@yahoo.com **Web page:** www.srrindia.org

A REPORT ON

A Meet of Radiation Researchers

during

International Conference on Radiation Research: Impact on Human Health and Environment (ICRR-HHE 2016) and First Biennial Meeting of SRR, MP Hall, Anushakti Nagar, Mumbai on February 11-13, 2016

International Conference on Radiation Research: Impact on Human Health and Environment (ICRR-HHE 2016) and First Biennial Meeting of SRR was organized at Multi-Purpose Hall, Bhabha Atomic Research Centre (BARC), Anushakti Nagar, Mumbai during February 11-13, 2016 under the aegis of Society for Radiation Research (SRR). This meeting was attended by about 300 students, faculty members, scientists and clinicians from different colleges, institutes and hospitals in India and abroad. Overseas participants were from more than ten countries like USA, Germany, The Netherlands, Republic of Korea, Japan, Italy, Canada, Russia and Thailand. From more than 25 Indian Institutes/Universities, students and faculty Members participated in the Conference. There were three plenary talks and 31 invited talks in addition to **AR Gopal Ayengar Memorial Oration Lecture**. In addition, there were three SRR Young Scientist Award Presentations and ten oral presentations. Out of total 231 accepted abstracts for the Conference about 180 were for poster presentation.

The Inaugural Session of the Conference was started with welcome address by **Dr S. Chattopadhyay**, Associate Director, Biosciences Group followed by Presidential Address by **Dr. Nagraj Huilgol**, President, SRR, Nanavati Hospital, Mumbai. Dr. Huilgol presented a brief overview about the aims and mandates of SRR. On behalf of SRR, he welcomed all the participants including overseas participants. Dr Huilgol emphasized the emerging potential of radiation research in environmental, diagnostic and therapeutic aspects of human health. **Dr A. K. Singh**, Director, Institute of Nuclear Medicine and Allied Sciences (INMAS), DRDO, Delhi delivered Guest of Honor Lecture. Dr Singh highlighted the need of collaborative research amongst various Institutes/Universities in

India to make some fruitful research outcome. **Dr S. Banerjee**, Chancellor, Homi Bhabha National Institute, Mumbai delivered the inaugural address of the Conference. Dr Banerjee mentioned about low dose radiation effects especially in relevance to human health and need to strengthen the results in suitable experimental models.

After that **Dr. K. P Mishra**, Founder President, SRR, Ex-VC, NGBU, Allahabad, Ex-Head, RB&HSD, BARC chaired the **AR Gopal Ayengar Memorial Oration Lecture Session**. Dr Mishra also spoke about the biographical sketch and contributions of Dr AR Gopal Ayengar. AR Gopal Ayengar Memorial Oration Lecture delivered by **Prof. M. J. Atkinson**, Director, Institute of Radiobiology, Germany. Prof. Atkinson discussed about epigenetic based paradigm changes in radiobiology. Prof. Atkinson emphasized that till now the clonal expansion of mutated cells after radiation exposure have been focused for incidence of cancer, which however cannot explain non-cancer health effects of radiation. Prof. Atkinson presented evidences supporting a unifying model for cancer incidence based on mitochondrial function, release of exosomes and epigenetic alterations after radiation exposure.

The major highlights of Conference during the various theme topics were as following:

Radiation Oncology and Radiotherapy: Biology to Clinics

Dr Rajiv Sarin (ACTREC, Navi Mumbai) in his talk emphasized about developing assays which can predict the toxicity and response for a given radiotherapy protocol. He showed that influence of germline and somatic mutations in radiation toxicity, disease free and overall survival in oral cancer patients. It was found that mutations in arachidonic acid metabolic pathways genes showed significant association with clinical outcome in these patients. **Prof RP Hill** (Princess Marget Cancer Centre, Toronto, Canada) showed effect of combined treatment of Plerixafor (a CXCL12/CXCR4 inhibitor) with radiation, which caused enhanced tumor growth delay, reduced metastasis and improved overall survival in the xenograft tumor model. **Dr Supriya Chopra** (TMH, Mumbai) showed a correlation of expression of cancer stem markers like SOX-2, OCT-4, Nanog, CD44 and podoplanin and local control in cervical cancer patients after chemo-radiation and brachytherapy. **Prof. T. Kamada** (NIRS, Chiba, Japan) shared his experience of carbon ion radiotherapy (CRIT) at NIRS-HIMAC facility. As of March 2015, a total of 9,021 patients were treated with CIRT at HIMAC and even patients with locally advanced tumors and tumors with non-squamous cell types responded well to this therapy. He emphasised the need of next generation CRIT system with the spot scanning beam delivery and the compact superconducting magnet mounted rotating gantry. **Dr V. Monaco** (University of Torino, Italy) delivered his talk on control of dose distribution in charged particle therapy. The need to evaluate the biological effect of a complex radiation field, using detailed and fine tuned physical and radiobiological

models was emphasized and presented. **Dr Sung-Kee Jo** (KAERI, Republic of Korea) showed the combinatorial effect of HemoHIM (a herbal formulation) and cisplatin on radio-sensitization in tumor bearing mice. It also reduced the liver toxicity and increased the activity of NK and Tc cells. In a preliminary clinical study in 85 patients diagnosed with breast or uterine cervix cancer, HemoHIM administration showed fewer cases of severe leucopenia (<3,000 leukocytes/mm) but it was more evident in the breast cancer patients. **Dr Deepak Sharma** (BARC, Mumbai) showed that exposure of lymphoma cells to plumbagin led to inhibition of total and specific phosphatase activity, increased total protein S-glutathionylation and induced glutathionylation of dual specific phosphatase-1 and 4 (MKP-1 and MKP-2). The *in vivo* anti-tumor efficacy of plumbagin was demonstrated using a mouse model. On the contrary, plumbagin prevented radiation induced apoptosis in normal lymphocytes. **Prof. Geeta Vemuganti** (Central University Hyderabad, Hyderabad) talked about post-radiotherapy ophthalmic complications like dry eye syndrome and approaches to overcome the same using stem cell approach. She highlighted about establishing the human lacrimal gland cultures from the post-radiotherapy samples. The 3D lacrispheres showed presence of stem cells and secretory acinar cells. The stem cells were identified as CD117 positive, ALDH high and high clone forming ability. The most promising evidence of its secretory function was seen in the presence of tear substances like lysosymes, lactiferrin, and scIg A in the conditioned media of the lacrimal gland cultures. **Dr Binod Kumar** (The Johns Hopkins University School of Medicine, Baltimore, USA) identified a series of miRNAs that affect androgen receptor signalling signaling in prostate cancer cells. A large percentage of miRNA were found to increase cellular radiosensitivity, while a smaller percentage of them showed protective effect. Two of the most potent radio-sensitizing miRNAs, miR-890 and miR-744-3p, significantly delayed radiation induced DNA damage repair, while intratumoral delivery of miR-890 mimetics prior to radiotherapy significantly enhanced radiotherapeutic efficacy. **Dr Tanuja Teni** (ACTREC, Navi Mumbai) showed proteomics profile of three radio-resistant oral cancer cell lines; 70Gy-AW13516, 70Gy-AW8507 (Tongue-SCC) and 70GySCC029B (Buccal-SCC). Mass Spectrometry identification showed differential expression of 106 proteins like GRP78, STIP1, PGP, PKM2, GRP94, PDIA3, HSP70-1A/B and HSPA8 among three parental/radio-resistant cell lines. Pathway analysis revealed genes related to PI3K, P38 and Wnt signalling. **Prof. P. Vaupel** (University Medical Center, Mainz, Germany) talked about role of hypoxia-driven adenosine accumulation during radiotherapy, which induced anti-tumor immune response.

Radiopharmaceuticals and hyperthermia in cancer radiotherapy

Dr J. Crezee (Academic Medical Centre, The Netherlands) discussed about development

of models for thermoradiotherapy planning for combination of hyperthermia and radiotherapy. These models were applied to evaluate the effective hyperthermic dose for combined radiotherapy and hyperthermia treatment for prostate and cervical cancer. Hyperthermic dose escalation was temperature dependent and equivalent to ~10 Gy for clinically realistic hyperthermia temperatures for prostate cancer and cervical cancer patients treated with radiotherapy and hyperthermia. **Dr Nicolaas Franken** (University of Amsterdem, The Netherlands) showed mechanism of hyperthermia induced radio-sensitization in papiloma positive tumors from cervical cancer patients. Combined treatments were found to increase DNA-DSB, decrease BRCA2 level and degradation of E6 and thereby prevention of E6-p53 complex formation. **Dr Tapas Das** (BARC, Mumbai) presented results about radiopharmaceuticals developed at BARC which have successfully reached to clinical domain. Striking similarity observed between the post-therapy scans obtained with ^{177}Lu-EDTMP and ^{99m}Tc-MDP in patients, suffering from skeletal metastases, indicate the possibility of using low-dose preparation of ^{177}Lu-EDTMP for the diagnostic imaging of such patients.

Radiation Signalling: DNA damage and repair

Dr Sateesh Raghavan (Indian Institute of Science, Bangalore) presented results about Scr7, a chemically synthesized and characterized inhibitor of Ligase IV (SCR7) for non-homologoud end joining. SCR7 treatment inhibited progression of breast adenocarcinoma in mice models and a significant increase in life span on these animals. SCR7 could also reduce the effective dosage of gamma-radiation from 2 to 0.5 Gy, in cancers derived from breast cancer, colon cancer and B-ALL. **Dr B. S. Patro** (BARC, Mumbai) showed that WRN-deficient cell lines were hyper-radiosensitive to CHK1 pharmacologic inhibition. Interestingly, silencing CTIP, a HR-protein required for RAD51 loading, significantly abrogated the CHK1i mediated radio-sensitivity in WRN-deficient cells. Results presented to show that WRN and CTIP together play a complementary role in executing DNA end resection during HR-mediated repair of radiation-induced DSBs. **Dr Sanjay Gupta** (ACTREC, Navi Mumbai) presented about G1-phase specific decrease of H3 serine10 phosphorylation (H3Ser10P) in response to DNA damage, which was coupled with chromatin compaction in repair phase of DNA damage repair. The loss of H3Ser10P during DNA damage showed an inverse correlation with gain of γH2AX from a same mono-nucleosome in a dose-dependent manner. **Dr B.S. Satish Rao** (Manipal University, Manipal) showed about the prediction ability of expression kinetics of DSB repair kinetics genes like XRCC3, LIG4, NBN, CD44, RAD9A, LIG3, SH3GL1, BAXS, XRCC1, MAD2L2 in head and neck cancer, and breast cancer patients. **Dr H. S. Misra** (BARC, Mumbai) presented about characterization of an antioxidant and DNA damage inducible eST/YPK (RqkA) and its role in repair of radiation induced DSB in *Deinococcus*

radiodurans.

Low dose radiobiology and dosimetry

Dr Venkatachalam Perumal (SRU, Chennai) presented results on low dose radiation exposure during medical exposure conditions. Chromosomal aberration frequency in subjects who had undergone CT imaging procedures (n = 27; 0.009 ± 0.01) and personals involved in interventional radiological procedures (n=26; 0.0105 ± 0.001) was compared with that obtained from age and sex equivalent healthy volunteers (0.004 ± 0.001). **Dr Nagesh Bhat** (BARC, Mumbai) presented results about dicentric chromosomal aberration assay, which was developed as gold standard for biodosimetry in the range of 0.1-5 Gy. The assay has advantage of very high specificity to radiation, stability over several months and very low background.

Radiation Protection and Radiation Countermeasures Approaches

Dr Vijay Singh (AFRRI, USA) showed the radioprotective ability of gamma-tocotrienol (GT3). Pharmacokinetics studies of GT3 in nonhuman primates showed complete prevention of thrombocytopenia at 5.8 and 6.5 Gy total body irradiation. GT3 was found to be dose dependent and more effective at 75 mg/kg than 37.5 mg/kg post 5.8 Gy irradiation. However, high dose of GT3 administration (75 mg/kg) was associated with adverse skin effects (small abscess). **Dr Manju Gupta** (INMAS, Delhi, India) presented about the radioprotective ability of a combination of two herb based compounds (A and C) against lethal dose of radiation. A and C in combination had apparently up-regulated antioxidant, anti inflammatory and DNA damage and repair pathways. Compound C, being an excellent ROS-RNS scavenger, was also showed protective potential to salivary glands in mice administered with lethal/sub-lethal acute/fractionated doses of radiation. **Dr C. Lange** (University Medical Center Hamburg-Eppendorf, Germany) showed and discussed about extracellular vesicles from mesenchymal stromal cells from bone marrow and their potential to protect against radiation damage. Genomic DNA was detected in these extracellular vesicles and they were able to salvage the stem/progenitor cells in vitro from radiation suppression. These vesicles after intravenous administration into lethally irradiated animals co-localize within 2-4 hours with hematopoietic stem cells in the bone marrow, which may be playing role in protection of stem cells against radiation damage.

Environmental radiobiology

Dr B. B. Nath (Pune University, Pune) discussed about effect of gamma radiation on hemoglobin of *Chironomus ramosus* larvae, which was compared with human haemoglobin. Bioinformatics studies showed that the profound tolerance of evolutionarily ancient ChHb to high-dose gamma radiation in contrast to Hu-Hb, which seems to be associated with higher substitution of hydrophilic amino acids in Hu-Hb resulting in their poor electrostatic interaction in the heme cavity. **Dr N. R. Prasad** (Annamalai University, Annamalai Nagar) discussed about role of nutraceuticals and dietary phenolic acids against UVB-mediated cellular damage and associated adverse effects. The intraperitoneal and topical administration of phenolic acids significantly reduced the UVB induced tumor incidence and prevented the UVB-induced hyperplasia, squamous cell carcinoma and dysplastic feature in the mice skin. Furthermore, these phytochemicals potentially interact with PPARγ, an anti-inflammatory transcription factor, and downregulates iNOS, VEGF, TGF-ß thereby reduces tumors multiplicity in the mice skin. Chronic UVB irradiation induces the expression of JAK1 eventually activates the STAT3 leads to the transcription of proliferative and anti-apoptotic markers such as PCNA, Cyclin-D1, Bcl2 and Bcl-xl, respectively. Caffeic acid rather than ferulic acid inhibits JAK-STAT3 signaling thereby induces apoptotic cell death by upregulating Bax, Cytochrome-C, Caspase-9 and Caspase-3 expression in mice skin. In another work, it was shown that UVB exposure for 10 consecutive days showed edema formation, increased lipid peroxidation, decreased antioxidant status with activation of inflammatory molecules such as TNF-a, IL-6, COX-2 and NFκB, which was prevented when caffiec acid (15 mg/kg.b.wt.) administration before each UVB exposure.

Heavy metal radio-nuclide toxicity and decorporation

Dr Amit Kumar (BARC, Mumbai) presented his work about effect of thorium-232 (alpha-emitter) and the potential of novel decorporation strategies. Glycophorin was found as a target of ^{232}Th effects on human erythrocyte. Animal studies demonstrated liver and bone as the major depository organs of ^{232}Th, causing oxidative stress by altering activities of superoxide dismutase/catalase. Microarray studies of liver tissue in mice treated with ^{232}Th revealed the potential of serum amyloid protein A as a biomarker of ^{232}Th toxicity. Results showed the key role of IGF1R in proliferative effect of ^{232}Th in liver cells (HepG2).