Beyond Radiation Induced Double Strand Breaks - a New Horizon for Radiation Therapy Research

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Recent advances in cancer research have shed new light on the complex processes of how therapeutic radiation initiates changes at cellular, tissue, and system levels that may lead to clinical effects. These new advances may transform the way we use radiation to combat certain types of cancers. For the past two decades many technological advancements in radiation therapy have been largely based on the hypothesis that direct radiation-induced DNA double strand breaks cause cell death and thus tumor control and normal tissue damage. However, new insights have elucidated that in addition to causing cellular DNA damage, localized therapeutic radiation also initiates cascades of complex downstream biological responses in tissue that extend far beyond where therapeutic radiation dose is directly deposited. For instance, studies show that irradiated dying tumor cells release tumor antigens that can lead the immune system to a systemic anti-cancer attack throughout the body of cancer patient; targeted irradiation to solid tumor also increases the migration of tumor cells already in bloodstream, the seeds of potential metastasis. Some of the new insights may explain the long ago discovered but still unexplained non-localized radiation effects (bystander effect and abscopal effect) and the efficacy of spatially fractionated radiation therapy (microbeam radiation therapy and GRID therapy) where many "hot" and "cold" spots are intentionally created throughout the treatment volume. Better understanding of the mechanisms behind the non-localized radiation effects creates tremendous opportunities to develop new and integrated cancer treatment strategies that are based on radiotherapy, immunology, and chemotherapy. However, in the multidisciplinary effort to advance new radiobiology, there are also tremendous challenges including a lack of multidisciplinary researchers and imaging technologies for the microscopic radiation-induced responses. A better grasp of the essence of these advances in cancer biology research will give medical physicists a new perspective in daily clinical physics practice and in future radiation therapy

technological development. Furthermore, academic medical physics should continue to be an integral part of the multidisciplinary cancer research community, harnessing our newly acquired understanding of radiation effects, and developing novel cost-effective treatment strategies to better combat cancer. Learning objectives are 1) Understand that localized radiation can lead to non-localized secondary effects such as radiation-induced immune response, bystander effect, and abscopal effect; 2) Understand that the non-localized radiation effects may be harnessed to improve cancer treatment; 3) Learn examples of physics participation in multidisciplinary research to advance cancer biology; and 4) Recognize the challenges and possibilities of physics applications in cancer research.