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## ISRS President's Note

# Personal perspectives on the evolution of radiation therapy and future outlook for SRS

It is my great honour to humbly accept the presidency of the ISRS, and to write the very first presidential letter from a physicist. I hope to live up to the trust that ISRS members have placed in me. We live in interesting times. In the 28 years that I have been involved in radiation therapy many previously precious concepts have been turned on their head. I mention three examples below.

Firstly, I did not lose my job in my first decade due to the imminent chemotherapeutic cure for cancer, as I was reminded that I would be many times. In the early 1990s, medical oncologists were buoyed with confidence following the discovery of oncogenes and the significant advances being made in the arena of cancer biology. When I first joined the oncology community, no drug had reversed an oncogene's activation or a tumour suppressor's inactivation. However, within a year of my first appointment, the oncogene inactivated by trans-retinoic acid (a "miracle cure" for acute promyelocytic leukaemia), was identified.[1] In the same year, the monoclonal antibody trastuzumab was isolated and used to switch off the human epidermal growth factor receptor-2 (HER2) oncogene in HER2 positive breast cancer.[2] The era of onco- and tumour suppressor genes promised a brave new world of chemotherapeutic cures. Radiation therapy was relegated by some to a stopgap, to be used in the meantime until all cancers would be cured by targeted therapies. Almost three decades later, and while our patients are benefiting more and more from the increasingly cunning arsenal of chemotherapeutic agents, ionizing radiation is still needed, perhaps more than ever. Almost 50% of all cancer patients are now treated with radiation therapy,[3] despite using around 10% of the total oncology budget, and just 5% in the UK.[4,5] Chemotherapy agents still get the lion's share.

Secondly, the absolute necessity for fractionation, that was taught to me on day 1 with dogmatic certainty, is now being questioned, thanks to the surprisingly excellent results of single session radiosurgery. The assumption that the alpha/beta ratio of every tumour is 10 and of normal tissue is 3 (the classic values used to explain and justify fractionation) has been abandoned. Values for melanoma, prostate, some breast cancers, not to mention a host of benign tumours have all been shown to have values close to that of normal tissue.[6,7,8] Fractionation, which was justified due to the differential repair rates of tumour versus normal tissue, is now known to contribute little towards enhancing the therapeutic ratio for many treatments. The advantages of normal tissue avoidance with stereotactic radiosurgery, however, is now suspected to be much more important.

Lastly, the recent advent of an immunological rationale to explain why we get such good results with radiosurgery redefines what our treatment is doing.[9] Via the abscopal effect, tumours do not even need to receive radiation in order to exhibit a response.[10] Hypofractionation schedules have to some extent abandoned the linear-quadratic model in pursuit of maximizing the immunological effect. We would be wise to revisit the rich radiobiology archive from the 1960s to the 1980s that contains a wealth of knowledge, as large doses per fraction were often used for practical reasons in those experimental studies.

Indeed, everything has been turned upside down. When I moved from conventional radiation therapy to intracranial radiosurgery 20 years ago I was warned, by some previously supportive radiation oncologists, that I was getting involved with an unproven and dangerous technique, particularly in relation to the "neurosurgical application" of single fraction treatments to the brain. Many of the doubting radiation oncologists have now joined the radiosurgery bandwagon, but some still find it difficult to drop the concepts of margins and fractionation. For treatments of benign disease in the brain, I do not believe that either are essential and there is little evidence, if any, that they are beneficial.[11,12,13] Nowadays, many conventional radiation therapy treatment plans look more like radiosurgery plans. Even the unconverted have unintentionally moved their practice closer to radiosurgical principles, reducing margins and geometrical uncertainty while increasing dose per fraction.

I recently heard a fellow physicist describe radiosurgery as "bad radiobiology saved by good physics." The

more I look into the latest radiobiology research, this really could not be further from the truth. It is in this area of radiobiology that the radiosurgical world has a considerable amount of catching up to do. Correcting the potentially large differences in the biologically effective dose delivered to patients receiving the same physical dose, will increase the dosimetric precision of our treatments tremendously. The growing contribution from radiobiologists and radiation oncologists in this area has been very positive.[14]

What all of this means is that we have to keep questioning ourselves and remain open to learning from others. This was the primary reason why the ISRS was started as the leading forum where neurosurgeons, radiation oncologists and physicists could meet up and exchange ideas. This still has a way to go. No one has a monopoly on the truth and what is now considered to be truth may be later shown to be dogma. The ISRS forms a melting pot of disciplines, which all of us should be proud of, while striving to do better.

With every new generation of radiosurgery equipment released, potential conformity is improved and gradients are increased, leading to a greater sparing of normal tissue and an enhancement in the therapeutic ratio. With the advent of particle therapy, this may continue further. I invite fellow members to submit work to our newly PubMed-indexed journal, actively participate in the subcommittees to enhance our reach, invite new members to participate, and be creative in the preparation for successful meetings in Rio de Janeiro, Brazil in 2019 and in Brisbane in 2021.

As the new president, my vision is to create a strong, far-reaching, and vibrant society that functions year-round by bringing to the radiosurgical community webinars, educational courses, coordination of research, working groups, and opportunities for credentialing. I expect all of these activities to become a reality in the next 2 years. I am enthusiastic about the opportunity to serve your society along with my fellow officers and board members. We intend to guide the society forward, better serving those who use these excellent treatments; both now and those yet to be imagined in the future. We will educate, encourage and advance together.

Ian Paddick
President ISRS
London, UK
ian@physicsconsulting.co.uk

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