

EDITORIAL

Stereotactic body radiation therapy – A discipline with Nordic origin and profile

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Single fraction treatment procedures have been used ever since the introduction of radiotherapy (RT) around 1900. At that time, radiation was delivered and explored by surgeons as an alternative to the scalpel and other surgical instruments. With time, the field of RT developed, both in terms of its technology and understanding of important radiobiological issues. Fractionated therapy with the use of 1.8–2 Gy fractions over several weeks became an established principle in RT. However, in stereotactic RT (SRT) extreme hypofractionation most often with the use of 1–3 fractions remaining the main type of fractionation primarily for technical reasons. Some have argued that SRT ignored the well-established knowledge of fractionation effects whereas others claim that fractionation is not needed when the volume of normal tissue is spared by use of high-precision technology.

SRT was initially developed by the neurosurgeon Lars Leksell from Karolinska Hospital, Stockholm, Sweden. Being a neurosurgeon, obviously before the RT specialisation had matured with its own societies and scientific periodicals, the papers of Leksell appeared mainly in surgical journals. His seminal paper in 1951 was published in another 'Acta' journal from the Scandinavian countries, the *Acta Chirurgica Scandinavica* [1]. This journal was created in 1920, renamed in 1990 as the *European Journal of Surgery* and in 2002 it merged with *British Journal of Surgery*. Interestingly, a very early idea was to use proton beams in this stereotactic set-up – together with scientists at The Svedberg Laboratory in Uppsala, Sweden; this concept was first published in *Nature* [2] and then in *Acta Radiologica* [3], a pre-runner journal for *Acta Oncologica*. Besides intro-

ducing these concepts of stereotactic targeting when treating tumours within the skull, Leksell also made significant further developments in this field, regarding both delivery technology and clinical applications. The Leksell Gamma Knife was for many years the only available equipment for this application, and in large parts of the world it is still the dominating equipment for SRT of benign brain tumours and brain metastases. The indications for cranial SRT have been widened and the number of patients treated by Gamma Knife and by linear accelerator based systems has increased considerably.

Also the field of stereotactic body RT (SBRT) was introduced in Stockholm, through the joint efforts of scientists and clinicians at Karolinska Institutet. Both the first technology-related paper and the first clinical reports from this collaboration appeared in *Acta Oncologica*, in 1994 [4] and 1995 [5], respectively. These two papers are among the top four most cited papers in *Acta Oncologica* overall, with more than 500 citations together. The stereotactic body frame developed by the Stockholm group was equipped with an external coordinate system which was adopted from cranial SRT and a diaphragm compression system for reduction of the respiratory-related internal motion. Set-up by cone-beam CT scanning has now replaced the coordinate based system in many centres, but stereotactic body frames are still in use.

In the years that have followed, *Acta Oncologica* has contributed to the efforts of bringing SBRT to a higher level of scientific evidence. The journal has published a large body of papers both on technical aspects and on clinical studies of SBRT, as is the case in the present issue of the journal. In 2006, a

dedicated issue of *Acta Oncologica* presented a collection of SBRT papers, compiled in connection with an *Acta Oncologica* symposium on SBRT [6–15]. In this issue we follow-up this tradition, having collected a number of key papers on important clinical studies and on translational research [16–24].

One of the papers presented in this issue is a report of a survey among members of ASTRO, CARO, TROG and ESTRO on the use of SBRT for ablation of liver metastases and on RT for palliation of symptoms related to liver metastases [16]. It reports an increased referral of patients for SBRT by 36% over the past five years. The survey reveals large differences in practice between members of the four societies. The technology differs considerably between members of the societies with IGRT being used in 9–90% of centres offering radical intent radiotherapy for liver metastases. Interestingly, the centres offering SBRT for liver tumours are almost equally divided into academic and non-academic institutions and only two-thirds of the centres have regular multidisciplinary gastro-intestinal or dedicated liver tumour board meetings. Unfortunately, only 8–55% of patients were on a clinical trial and only 32% of the centres entered patients in a database. It is therefore encouraging that US centres have now joined forces in the establishment of a database for recording of patients with primary liver cancer [17]. This example of multicentre collaboration for registration of patients may provide important information for future treatment strategies for SBRT.

The efficacy of local therapies in therapy of metastatic cancer has not been proven and the ranking of the different local therapies such as surgical resection, radiofrequency ablation (RFA) and high-intensity focused ultrasound (HIFU) has not yet been clarified [25]. Even with the large bulk of papers published in scientific journals, a number of important questions remain and the most important of these can only be answered through randomised clinical trials. Acknowledgement of SBRT as an accepted therapy for cancer will need more clinical trial activities. The ROSEL phase III trial (ClinicalTrials.gov: NCT00687986) comparing SBRT and surgical resection in stage IA non-small cell lung cancer was until recently ongoing in the Netherlands. Regretfully, it was terminated due to health care structural issues which resulted in poor recruitment. This was an outstanding study and hopefully comparative studies between SBRT and surgery in lung cancer will be taken up and successfully completed by other groups. Very few prospective studies on SBRT for metastases are active. A phase III trial randomising between SBRT and RFA for liver metastasis is currently under initiation in Sweden, Denmark and the Netherlands (ClinicalTrials.gov: NCT01233544).

SBRT is a playground for new developments in radiation technology. Because of its high-precision nature, it is immediately appealing to develop and test new technologies in the frame of SBRT. A number of technical developments have been introduced through SBRT and are now implemented standard tools in conventional RT. A large number of papers have been published on the physics and technical issues related to SBRT, also in *Acta Oncologica*. These include papers on treatment planning [4,26–30], target motion [31–34], image-guidance [35–38], iso-normal tissue complication probability (NTCP) model dose prescription [39] and accreditation and quality assurance [40]. Recently, also functional imaging of normal tissues has caught the attention [41] and these methods may be utilised for (SB)RT planning and morbidity evaluation [42,43]. Treatment with protons and other heavy ions, which represents the ultimate ability to conform the dose to the target and to spare the normal tissues, has also been covered in papers recently published in the journal [44,45].

These novel technologies represent important progress in the field of SBRT and soon these techniques will also be implemented in conventional RT for the benefit of larger groups of patients. They are all aiming to provide RT with more cures and less side effects. However, therapies should not be offered to patients because they are high-tech, they should be offered because we know that they are efficient. The field should not be driven solely by the technology, but should develop together with clinical trials with the common goal of providing therapies to the patients with favourable therapeutic ratio at a high evidence level.

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