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Commentary

New technologies in radiation oncology: opportunities, caveats and the way forward
Commentary on "New technology for radiotherapy in paediatric oncology" by Dr. Frank Saran

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Cure is now a realistic goal for most children with cancer. Depending on the specific tumour type, this may be the result of a number of factors including improvements in surgery and chemotherapy, or better integration of all of the various treatment modalities into the therapeutic plan. Although recognised to be a valuable part of the armamentarium, radiotherapy has been perceived as a treatment to be avoided whenever possible because of the risk of morbidity associated with its use in this age group. However, elimination of radiotherapy from the treatment plan may not always be desirable because of a greater risk of local failure and, in some cases, inferior survival.

Developments in radiotherapy over the past decade have been truly exciting. Over this short period of time, the introduction into routine clinical practice of first computerised tomography (CT) simulation for target volume definition, then improved radiotherapy treatment planning computers and better treatment delivery systems has allowed us to move into an era in which treatments that conform to the target volume and spare to a greater extent than previously possible the surrounding uninvolved normal tissues represent the standard of care. In his "Update", Dr. Frank Saran has done a fine job of reviewing these developments and describing 'state-of-the-art' radiotherapy for children with cancer [6].

Opportunities for therapeutic gain as a result of the use of the new technologies are arguably greater in this population of patients than any other. Children are, after all, the prototypic "high-risk" population [1] for whom any additional effort or financial cost would be fully justifiable. In contrast to most adults with cancer, it is not unreasonable to anticipate improvements in survival and/or decreases in morbidity that will be of major clinical relevance.

The use of conformal radiotherapy delivery techniques should result in less morbidity than techniques used in the past. There is persuasive evidence that this is the case, but it will be important to complete planned multicentre studies (e.g., in medulloblastoma) in order to assess the magnitude of the benefit. At least in North America, these studies will allow comparison of delivery techniques, that is, using linear accelerators or more costly modalities such as proton therapy that are available in only a few centres world-wide. Even without any other modification of the therapeutic plan, reduction in morbidity is a worthwhile goal. In addition, we have begun to reintroduce radiotherapy into the treatment plan in circumstances where we had tried to avoid it because of concerns about late effects, for example, in infants and very young children with certain brain tumours and those with retinoblastoma. If treatment is shown to be associated with less acute toxicity and therefore could be given concurrently with chemotherapy, without the need for chemotherapy dose reductions, we can begin to argue for use of radiotherapy earlier in the treatment plan in these and other circumstances. Strategies like these are likely to result in improved local tumour control and, quite possibly, in improved survival. In adult patients, demonstration of reduced treatment-related morbidity has led to dose escalation to part or all of the tumour and to hypofractionation studies. These approaches are probably, in

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general, less relevant in paediatric cancers, but may be of interest in some tumour types under certain conditions – for example, ependymoma with residual macroscopic tumour after surgery – again because of the potential for improved local tumour control.

The above outlines some of the opportunities. Now let me describe some of the caveats. Although precision radiotherapy begins with accurate target volume definition, this is the ''weakest link'' in the chain. In some circumstances, CT simulation performed with the patient in the position that will be used for treatment provides all the information required to ensure coverage of the target volume. In craniospinal radiotherapy for medulloblastoma, for example, where failure in the subfrontal region is still relatively frequent [2] and can be correlated with decreased survival [3], the use of CT simulation with an autoblock function has the potential to eliminate failure in this region and thereby improve survival. However, in most other settings, definition of the target volume is based not on normal anatomy, but on the tumour and potential areas of spread that may or may not be well demonstrated on conventional imaging. The additional information obtained by co-registration with magnetic resonance imaging (MRI) has been very helpful, particularly in the management of brain tumours and tumours of the bone and soft tissues, and nowadays, could be said to be prerequisite for treatment of these tumours, but an important corollary here is that as we have implemented these technologies, we have made other important changes. These include, for example, the use of post-operative rather than ''conventional'' preoperative target volumes for some tumour types, and, in some circumstances, because of greater confidence about the extent of disease, tighter margins. For treatment of an individual patient, we need more than ever before to ensure the accuracy of treatment each day by using optimal immobilisation, on-line treatment verification, and even repeated diagnostic imaging during treatment [4]. The new ''standards'' with respect to target volume definition are evolving and need to be tested. In multicentre studies this mandates very explicit description of the target volume [5], as well as the use of stopping rules for excessive failures.

As Dr. Saran illustrates by the many references to investigators at his own institution, the proper application of the new technologies depends on the availability of a highly skilled team of physicians, physicists and technologists and careful attention to every aspect of the treatment planning and delivery process. The incidental delivery of low dose radiation to a larger volume of normal tissue outside the target, for example, is a particularly important issue in paediatric radiation oncology because of concerns that this may result in an increased risk of functional deficits and/or second malignancies. Careful documentation of the treatment delivered and long-term outcomes is therefore essential. In this regard, the cooperative groups that are able to provide central radiotherapy data review and correlate these data with clinical and imaging findings at diagnosis and at follow-up will certainly play a very critical role.

And the way forward? Well, it is evident that in terms of technology development a plateau has not yet been reached. On the contrary, there are many new developments that open up even more exciting possibilities. Functional imaging using positron emission tomography ((PET), single photon emission computer tomography (SPECT), magnetic resonance spectroscopy (MRS), functional MRI) will allow better targeting (including combined modality approaches that might, for example, specifically target hypoxic cells) and, in the brain, will permit selective avoidance of critical normal structures. Further improved linear accelerators and other treatment delivery tools that provide on-line 3-dimensional (3D) imaging of the tumour and allow for adjustments (breathing control, field placement) to adapt to changes in size, shape or position of the tumour during or between daily treatments are now coming into general use. We need to continue to do what we have a tradition of doing particularly well in paediatric oncology, namely to undertake multicentre national and even international, research studies to evaluate these new treatment approaches and to share knowledge rapidly as data become available. If we can demonstrate that, thanks to these new technologies, it can indeed be given more safely than in the past, it is likely that radiotherapy will remain an important component of treatment and contribute to further improvements in survival rates for children with cancer.

Conflict of interest

None.

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