COMMENTARY

Image-guided radiation therapy: what is our Utopia?

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The manuscript entitled 'Schedule for CT image guidance in treating prostate cancer with helical tomotherapy' [1] addresses an interesting question from a number of angles in contemporary radiotherapy. At the time of writing, the widespread use of image guidance is realistically still in its infancy. Many groups are considering how it may be utilised to effect the ultimate goal of adaptive radiotherapy. The work presented here is related to a specific (helical tomotherapy) treatment device designed for image-guided radiotherapy (IGRT), but the same concepts and considerations are relevant to the variety of image-guided solutions available. A comprehensive review of this topic is found elsewhere [2–4].

Beldjoudi et al [1] took historical data from 20 patients who underwent daily imaging as part of their treatment regime and analysed it to simulate an alternative imaging strategy that employed fewer imaging fractions. This retrospective approach has an obvious benefit in that hypothetical questions relating to the effects of terminating the imaging early in the treatment are completely removed. Indeed the authors were able to provide a measure of the difference between their 'predicted' and 'observed' interfraction motion as a quality control. This study should form an interesting basis for work in many groups who could perform similar retrospective analyses or plan prospective studies that would help inform the issue further.

Image guidance

The underlying reason for utilising IGRT is to ensure that the proposed treatment is delivered accurately and to reduce the irradiation of normal surrounding tissue, thus reducing 'collateral damage'.

The majority of contemporary treatment planning is based upon three-dimensional image data sets. These planning scans are snap-shots of the tumour presentation,

its relational anatomy (to the organs at risk (OARs)) and the patient's shape and position on the treatment couch. They define a model of the patient that is used by the treatment plan. The resultant dose calculation is used as a surrogate for the effectiveness of the treatment and is assumed to represent each fraction of treatment. The impact of inter- and intrafractional changes to the composite delivered dose is minimised (or risk managed) by the application of appropriate localisation devices and planning target volume (PTV) margins [5, 6]. Conventionally, re-planning occurs only if observed gross deviations are beyond predetermined tolerances.

The utilisation of daily image guidance allows us to assess the geometric accuracy of the 'patient model' as the course of treatment is delivered. This can be effected by assessing deviations of the anatomy from that in the treatment plan or by using this information to update the dosimetric assumptions.

Obtaining this information opens up a number of correction strategies from daily repositioning (to rigidly register the patient to the assumed plan) to recalculating the treatment delivery in real-time to reflect the patient's presentation. This philosophy of re-evaluating treatment, to take into account how the actual patient anatomy deviates from the snap-shot treatment plan, is known as adaptive radiotherapy. The two examples given here represent the ends of a spectrum of possible strategies that are currently under investigation.

The ultimate aim of IGRT is to be able to re-evaluate, and if necessary re-define, treatment as it evolves in order to 'keep it on track' with regard to the original intent. In the future we might also consider the titration of radiation dose to best effect or against side effects, as is coming into consideration with other modalities [7].

To make any of these suggested end-point strategies possible, there are a number of pragmatic limitations and concerns that need to be addressed. The computing power

required to realise the more technologically exciting solutions (daily adaptation of the treatment delivery) is currently beyond that of the typical hospital organisation. Even for the 'simplest' approach (daily repositioning based on real-time rigid registration of images) we can argue that availability of qualified, experienced treatment staff is a limitation. The spectrum of other scenarios raise a number of considerations, including quality control when making changes to treatments, the training of staff to make 'go'/'no go' decisions, the need for better algorithms, and the need for further research and understanding together with the commercial development. These various considerations all increase the time required to develop IGRT [8], thus reducing capacity. The above list is not considered exhaustive, but merely illustrates that which schemes IGRT utilising imaging at a less than daily frequency, must almost certainly be considered for the majority of departments.

A further concern regarding concomitant imaging, raised by Beldjoudi et al [1] and many others, is that of the dose given to the OARs [9]. This topic is broad and not considered in detail here. It is sufficient to recognise that there are considerations beyond workload issues to suggest that the short-, medium- and even long-term future of IGRT should not necessarily involve daily imaging schedules.

A recent joint publication by UK professional bodies [10] provides an excellent review of the current clinical status of IGRT. The document provides recommendations on the best evidence-based practice and guidelines for implementation. It stresses the need for geometric verification processes to be undertaken within a clearly defined structure and under locally defined protocols. Checks must be in place to detect and correct gross errors at the start of each course of treatment. Systematic errors must be identified and minimised. The study described by Beldjoudi et al [1] nicely reflects these guiding principles and provides an excellent example of how local protocols can be determined. Of course, the author of a commentary can claim that the evidence of best practice needed to back his assertions relating to future scenarios is yet to be determined!

In practice: should we, or do we need to, image every day of treatment?

The obvious question to ask is whether, given the considerations put forward above, imaging on limited fractions (and therefore capturing only a sampling of the potential information that we could collect) would affect our ability to establish the real picture. Would such schemes risk not using the equipment to its fullest capability? Alternatively, we could ask whether restricting the frequency of imaging would result in a poorer gain in overall accuracy than might otherwise be achieved, therefore reducing the potential benefit of implementing IGRT.

The case presented in the highlighted study

The study by Beldjoudi et al [1] seeks to determine whether an optimal number of imaging sessions could be

suggested by historical data sets collected during initial experience with their IGRT system. Their clinical correction strategy was to reposition the patient (presumably from a controlled position) in accordance with the information derived from the registration of the daily megavoltage MV-CT data and the planning CT.

In summary, the work shows that four imaging fractions would have been sufficient to establish a modified (corrected) set-up position, such that the residual positional uncertainty for the remaining fractions was within (predetermined) tolerance. The authors conclude that this imaging overhead, over the entire treatment, is an acceptable trade-off for the gain in accuracy.

The authors performed an analysis on the residual set-up discrepancies to calculate individualised margins for each patient, based on observations and corrections drawn from the first four fractions. On a patient-specific basis, they computed the difference between the predicted daily offsets from the modified set-up utilised in the simulated scheme and the actual daily positions that were observed and recorded. This was presented as an estimate of interfractional uncertainty in the predicted set-up correction and was found to be 3 mm. The sum of the individual predicted daily offset from the modified set-up (determined from the first four fractions) and this uncertainty was cited as the interfractional uncertainty. Furthermore, an intrafractional uncertainty of 4 mm was assumed [11]. These uncertainties were used to compute individualised PTV expansion margins. In the case of the two example patients, these PTVs were used to recompute the dose distributions representing the entire treatment. It would seem that there were some small differences between the planned (*i.e.* original plan adjusted by actual daily corrections) doses and those based on the simulated scheme.

Summary

The results provided by Beldjoudi et al [1] would seem to suggest that the proposed IGRT scheme could work in practice. In actual fact, it reflects the common practice of imaging on the first few days of treatment, during which we expect the magnitude of initial set-up errors to 'dampen down' as the patient gets used to their treatment. It is probably important to stress that the dosimetric evaluation of the simulated scheme is comparable to that achieved by the daily correction strategy. Little change in the OAR dosimetry is an indication that the scheme has merit.

My conclusion is that there is no need to image every day of treatment. At least, this seems to be the case in the short or medium term considering the practical limitations that we face in contemporary clinical situations. However, we need to reflect that the 21st century is still young and not even into its teenage years. Increasing the pool of experienced staff is something that we must continue to promote, but it is inevitable that computer hardware will improve and that the algorithms necessary to achieve 'instant' anatomy matching/recognition and instantaneous dose recalculations will eventually become mainstream, as will the database systems needed to manage all the information sufficiently quickly.

Therefore, in the longer term, daily imaging may become a viable and valuable strategy. The aim of IGRT and adaptive therapy is not really to find the simplest pragmatic implementation, but an aspirational goal of improving the therapeutic ratio. In any debate over the results obtained from treatment planning studies, we need to remember that the dose distributions are still only surrogates to the real end-points of interest: survival and toxicity. To truly estimate the toxicity to OARs (which may change shape and position), we need to follow the dose to the organ. This demands that the contours of the OARs are somehow generated on each occasion, which would demand very sophisticated modelling or *imaging on each day of the treatment*. In the case of prostate treatments, the size and shape of the target organ does not vary (although its positions may), but target volumes for other clinical sites (e.g. head and neck) may change during the course of a treatment, and would therefore also benefit from ongoing reassessment.

A question posed earlier was whether reduced imaging schemes reduce the potential benefit of the IGRT implementation. Within the proposed scheme presented by Beldjoudi et al [1], the PTV expansion margin was created using data derived from the analysis and an intrafractional component from the literature. An obvious benefit of daily imaging is that the interfractional uncertainty can be eliminated. Furthermore, if we assume that this imaging snap-shots the 'targets' during their intrafractional meanderings, then we can also build up a bespoke understanding of this component of positional uncertainty. An 'extreme IGRT' philosophy has been adopted by some investigators, who are advocating that the process should include interlaced or simultaneous imaging and treatment delivery, proposing the use of MR imaging [12, 13] to circumvent the issue of concomitant dose. Clearly, such bold assertions need to be backed up by a model for constructing the associated adaptive therapy PTV. Nevertheless, we can see in principle how imaging on each treatment day could provide benefits in reducing the expansion margins and therefore reducing the tissue irradiated to tumoricidal doses.

Final thought

The proposed scheme presented by Beldjoudi et al [1] is a pragmatic approach and the analysis contained

therein is very useful in understanding its ramifications. For the near future, such schemes have merit for a number of practical considerations. Software and hardware technology will continue to improve and our understanding and training will evolve. Hence, we should not lose sight of the ultimate IGRT/adaptive therapy goal.

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