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Editorial

Improving radiotherapy through medical physics developments

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This issue contains a handful of highlight medical physics contributions that were presented at the 3rd ESTRO Forum held recently in Barcelona. This tradition was established over recent ESTRO Biennial Physics Conferences (now part of the wider ESTRO Forum conferences), with the highlight papers being published in Radiotherapy & Oncology [1–4]. As for the previous conference selections [5–18], the papers present new and significant findings in some of the many areas where medical physics research and development is essential to improve radiotherapy (RT) planning and delivery, and ultimately outcomes.

Quality assurance in RT – a core medical physics contribution

Quality assurance (QA) continues to be at the core of medical physicists' work (as also reflected in the number of QA-related abstracts submitted to the 3rd ESTRO Forum). It is an essential component for safe, high quality treatments. Results from clinical trials show that poor quality correlates with poor treatment outcomes [19–21]. In parallel with the continuing introduction and development of novel and increasingly complex techniques and technologies, the time needed for QA and dosimetry has increased [2]. Clinical medical physicists necessarily spend a great deal of time on routine QA duties, with potential impact on the time available for other relevant areas such as clinical dosimetry, development and implementation of new techniques, management, and teaching and training [22–23]. Time could be optimised if more of the QA was automated. In the 1950s, automation was seen as a new paradigm that would change society's way of working, minimising routine tasks and freeing more time for creative and higher level work and providing improved work-life balance and quality of life. Unfortunately, more than half a century after the first publications on automation, its application to QA in RT is still very limited. It is also perceived that some of the proposed quality controls (QCs), metrics and tolerance limits proposed are out-dated by RT technology advances or insufficiently effective to detect at least some errors that may have a clinical impact [24–27]. When new technology is being implemented, it is crucial to understand how systems and, in particular, treatment units behave in order to identify failure modes and design quality controls capable of detecting any delivery error. Our principal aim is to ensure the patient receives the dose distribution as planned, and if significant differences are found, these should be reported and if possible re-addressed before the end of the treatment. We also need to widen the scope of the assessment of the results of our QC tests and the decisions taken on their basis, moving from a binary evaluation (pass or fail) to an evaluation of trends (temporary or systematic) using groups of data, applying approaches such as Statistical Process Control [28]. In short, there is a clear need for innovative, efficient and effective QA methods with potential for automation. We have now reached a crossroads where we have to consider whether the original QA paradigms remain appropriate for the new technologies, techniques, priorities and resource availability.

Routine implementation of beam intensity modulation with dynamic treatment techniques such as intensity-modulated RT (IMRT) and volumetric modulated arc therapy (VMAT) has had a considerable influence on QA procedures. International guidelines [29–31] propose specific QCs to ensure safe and accurate delivery of these techniques. They recommend performing intensive machine-specific QA of dynamic beam delivery and verifications of correct data transfer from the TPS to the treatment unit and limiting pre-treatment measurement QC to a number of plans until sufficient confidence in beam delivery is obtained. However, most European centres still perform pre-treatment verification for each patient long after these techniques are implemented. It seems that we still lack confidence in the capabilities of our treatment units regarding dynamic treatment delivery, or in the alternative verification approaches. This practice may potentially limit the number of patients who can benefit from these techniques. It is also worth noting the results of multi-institutional audits on IMRT and VMAT as they show differences in pre-treatment verification results depending on the equipment and metrics used by the institution [9,32–33]. As no consensus has been reached on discontinuing pre-treatment verification [34], several groups have worked on optimising patient-specific verification focusing on efficiency and effectiveness of the tests and also on evaluation metrics and tolerances [24,35]. Along these lines, the use of treatment unit log files [36–38], detector arrays mounted on the treatment head [39–41] and *in vivo* portal dosimetry using electronic portal imaging

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devices [42–45] has been proposed to check accurate delivery of dynamic techniques on each fraction. The log file monitoring approach is very attractive as it can be easily automated and does not need any additional equipment. Defenders of log file monitoring argue that it can replace pre-treatment and *in vivo* dose measurements. Log file analysis, for instance, can verify information transfer integrity and delivery performance for each fraction during patient treatment. Log files can be re-inserted in the TPS and the dose distribution can be re-calculated. Therefore, any difference in the log files can be linked to clinical impact and tolerance thresholds on dose distribution differences could be set. This approach relies on the accuracy of the information on linac parameters as recorded in the log files. It can therefore be an ill-posed problem, relying on the parameters that we want to independently check. In addition, variation in beam profiles, MLC calibration, energy and dose monitor unit equivalence would not be detected by log file analysis. However, coupled with a suitable machine QA programme, log file analysis undoubtedly has a high potential for treatment delivery checking at the machine level [46–49]. Along this line, Pasler et al. show in this issue how log files analysis, after the delivery of a demanding QA plan, can be used for prospective machine QA in dynamic mode [49]. As also stated in their paper, at this stage, log files cannot completely replace *in vivo* dosimetry or pre-treatment dose measurements as patient variability and beam dosimetry are not checked. Even so, log file analysis is an excellent complement to end-to-end QC tests to trace back any detected error.

Managing and adapting for motion in RT – a contemporary medical physics challenge

The technical realisation and subsequent clinical implementation of hybrid beam delivery and imaging systems stimulated research and developments to account for intra- and inter-fraction organ motion, including adaptive RT (ART) approaches. Moreover, these topics have become central in contemporary medical physics research and have eclipsed the more traditional fields of dosimetry, quality assurance and treatment planning [7,32,33,45,50–55]. This movement is well reflected in the physics tracks as well as in the interdisciplinary tracks of recent ESTRO meetings.

The utilisation of cone beam CT (CBCT) technology on linear accelerators has become the main platform for ART developments [56–58], as demonstrated by Tuomikoski et al. [59] and Heijkoop et al. [60] in this issue. Tuomikoski et al. focused on bladder cancer and explored different plan of the day workflow concepts for ART to overcome inter-fraction effects. Their contribution nicely adds to previous publications on plan of the day ART approaches, which are achievable with today's state-of-the-art technology as available in many institutions [61–64]. Heijkoop et al. studied the magnitude of intra-fraction motion of the cervix uterus, as well as volume changes of the bladder and rectum, by analysing daily CBCTs. Both studies are representative of the changing use of volumetric imaging, in that CBCT is used beyond setup corrections, moving towards a next level of clinical implementation and utilisation to enable anatomy-based personalised radiation oncology decisions and treatment.

Lung cancer is clearly another treatment site that continuously motivated medical physics developments to tackle intra-fraction motion challenges [65–70]. Marker-less tumour tracking and subsequent image registration is key in this context. Dhont et al. present their feasibility study on how the upcoming dual energy X-ray imaging can contribute in this context, although further development and adjustments are still needed to make this a mature technology for everyday clinical use [71].

Outcome modelling to guide RT improvements – a promising medical physics research avenue

Although much RT physics research focuses on developing, evaluating and verifying emerging treatment modalities (new photon-based techniques as well as proton and particle therapy), medical physics input is also essential in exploring and understanding outcome data from both earlier as well as present RT techniques [72–75]. Establishing models and their input parameters through analysis of clinical data is an area that is currently receiving increasing attention, for a number of reasons. Technology develops too fast for evidence to be based on (randomised) trials alone [76–80]. At the same time, the input data to our models is increasing in complexity, including predictive/prognostic medical, imaging and molecular factors, with data mining and machine learning methods becoming relevant modelling tools [80–81]. This clearly represents an area where medical physics has an important role to play, cf. the ESTRO Future working group ambitions outlined by Fiorino et al. in the accompanying editorial in the present issue [23].

Two highlight papers on normal tissue outcome modelling that were presented at the 3rd ESTRO Forum are published in respectively the previous [82] and the present [83] issue of the journal. These papers addressed challenges for the key normal tissues in RT of pelvic tumours, the bladder and the rectum. Yahya and colleagues investigated urinary bladder symptoms following RT of a large cohort of (more than 750) patients with prostate cancer [82]. Although there are now several studies published addressing bladder morbidity after RT [84–88], a clear dose response relation has been difficult to establish. Issues such as the large mobility of the organ and the definition of the relevant volume of interest as well as endpoint (e.g. identification of the critical bladder area; bladder- vs. urethra-related symptoms) have probably blurred this relation [89–90]. In their study, Yahya et al. focused on the endpoint definition [82], comparing peak-symptom models with multiple-event and events-counts models [91–92]. They found that including the temporal aspect of the endpoint definitions led to stronger associations between the outcome and the bladder dose surface measures. Surface dose distributions in RT for prostate cancer patients were also the basis for the study of Wortel et al., exploring 2D dose surface maps of the anorectal region [83]. To advance our understanding of normal tissue reactions after RT, there is increasing interest in both imaging of normal tissue function [93–94] and studies such as those considered here [83,87], where differences in the spatial patterns of the dose distributions (e.g. in 2D dose maps as for the unfolded rectum) are compared between patients with vs. without morbidity. In their study, Wortel et al. found considerable differences in the doses received at the cranial and posterior part of the rectum between patients with vs. without morbidity, i.e. at parts of the organ well outside of the high dose area [83]. Further work is needed in this direction, both for the rectum [94] and for other organs, before e.g. spatially defined normal tissue constraints can be established. Overall, much remains to be done in this field, as well-characterised, validated normal tissue dose response relations are still scarce. This is a major challenge for the use of models in RT planning, optimisation and evaluation, including the much-cited Dutch model-based patient selection approach for proton therapy [79].

Medical physics challenges in proton and particle therapy

Proton and particle therapy have always been a rich area for medical physics research and technological developments. While these activities mainly took place in dedicated treatment and/or research centres, this situation has already changed and will certainly continue to change in the near future. The reasons are