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BRACHYTHERAPY

Brachytherapy 17 (2018) 1–6

Treatment Delivery Verification in Brachytherapy

Treatment delivery verification in brachytherapy: Prospects of technology innovation

Any radiotherapy modality is associated with uncertainties and deviations between planned and delivered dose. Brachytherapy is characterized by steep dose gradients and is most often delivered in hypofractionated schedules. Potential errors or uncontrolled uncertainties in brachytherapy may therefore have considerable clinical consequences. This thematic issue of the *Brachytherapy Journal* addresses brachytherapy uncertainties/events and their prevention through novel treatment verification methods and technologies.

Patient safety is highly prioritized, and several authorities and societies worldwide are focusing on radiation safety and medical events. In 2005, the International Commission of Radiation Protection (ICRP) published an analysis of 500 radiation events in brachytherapy (ICRP 97 report) (1). This investigation and others (2–4), have shown that a significant share of radiation events are caused by human errors related to manual procedures. The brachytherapy workflow is indeed associated with many manual processes as for example implantation of catheters, reconstruction of catheters during treatment planning, manual connection of afterloader with guidetubes, and so forth. In 2013, the US Nuclear Regulatory Commission therefore emphasized the importance of treatment verification in an information notice on brachytherapy, stressing the ''importance of verification of treatment parameters for high-dose-rate remote afterloader administrations'' (5).

Historically, quality management methods in radiation oncology have focused on technical aspects, such as verification of the proper functioning of a device or software. Quality assurance methodologies have been established for each technology, and regular verification of the device and software performance vs. established tolerances is performed. More recently, quality management has started focusing also on process and workflow. Although initially the focus has been to reactively analyze safety events that have occurred through root cause analysis, the AAPM Task Group 100 (TG100) report (6) described the translation of three proactive risk assessment tools used in industry and engineering (process mapping, failure mode and effect analysis, and fault tree analysis) to the practice of radiotherapy. The use of these tools has now been demonstrated by both academic institutions (7) and community practices (8). Process mapping and failure mode and effect analysis have been described for high-dose-rate (HDR) brachytherapy in general (9), and more specifically for gynecologic brachytherapy (10, 11), ocular brachytherapy (3), and skin brachytherapy (12). A proactive, process-focused approach to HDR gynecologic treatments has also been described (13). Yet, wide adoption for TG100 methodologies or other proactive approaches is still limited by the time commitment required, the need for an interdisciplinary team committed to these tasks, and the lack of training in the use of these analysis tools for medical professionals. Another important tool for improving patient safety is the collection of events impacting patient safety at the level of individual institutions (14) and on the national scale (15). These event reporting and learning systems can be used both reactively (pointing at specific weaknesses that led to single events) and proactively as a tool for process improvement. Although the adoption of nonpunitive reporting systems is common in large institutions, its effectiveness as a learning system depends on the specific implementation and on the use of the provided information. In this issue, a review of the potential limitations of these learning systems is presented by Richardson *et al.* (16), while Felder *et al.* (4) underlines the usefulness of these systems to highlight key safety messages.

Significant investments and progress in technologies have enabled considerable progress in treatment delivery verification in external beam radiotherapy (EBRT). Important examples are patient-specific intensity modulated radiotherapy pretreatment quality assurance (17) as well as *in vivo* dosimetry based on electronic portal imaging (EPID) or detectors placed on/in the patient (18). Furthermore, the development of onboard anatomical imaging with cone beam CT (CBCT) has significantly improved the possibilities to secure monitoring and control of target motion during EBRT. The latest developments on linear accelerators combined with MRI provide excellent prospects for verification of target location and offer possibilities to perform daily adaptation through rapid replanning.

Image guidance in brachytherapy has become state of the art in the most frequent indications for brachytherapy (prostate, gynecological, and breast cancer) and has led to a high level of navigation for implantation and of individual dose adaptation (19). However, the state of the art in brachytherapy treatment delivery verification is currently less

1538-4721/$ - see front matter
https://doi.org/10.1016/j.brachy.2017.12.003

developed than in EBRT in terms of commercially available systems which fit well into the clinical workflow. Except for certain clinical workflows with US-guided prostate brachytherapy inside a shielded room, imaging is not available in the treatment delivery bunker in many institutions, and it is often not possible to perform onboard imaging as is done in EBRT with two-dimensional X-ray, cone beam CT, or even MRI. Organ movement may lead to uncertainties in recording of dose to organs at risk (20, 21), and verification of delivered dose through recalculation on images acquired directly before treatment may improve dose assessment and recording. On top of dose recalculation in volumetric images, *in vivo* dosimetry is the most direct way of verifying delivered dose. However, current commercial *in vivo* dosimetry systems are affected with measurement uncertainties of >20% and are only sensitive to gross errors (22). Furthermore, commercial systems provide only posttreatment evaluation and do not facilitate treatment interruption, in case of errors. Owing to limited confidence in error detection with these systems, *in vivo* dosimetry is currently not systematically performed. A large European patterns of care study reported that *in vivo* dosimetry was available in <20% of centers in 2007 (23), and preliminary results from ongoing surveys within GEC-ESTRO activities indicate that less than 10% of clinics perform *in vivo* dosimetry, whereas the majority are interested in an implementation, if a relevant system had been available (24). With limited monitoring of treatment delivery, a significant number of errors may go unnoticed, and current reports are likely underestimating the frequency of BT errors. Till date, only one large-scale study (>2000 brachytherapy fractions) has systematically monitored BT during treatment and reported an incidence of treatment delivery errors in 0.1% of fractions and 0.5% of patients (25). The latest years have fortunately shown promising developments of brachytherapy technologies. Imaging, *in vivo* dosimetry, and electromagnetic tracking are technologies with significant potential to improve guidance, automation, geometric treatment verification, and plan adaptation in brachytherapy.

Six articles in this special issue investigate the use of repeated imaging to assess anatomical variations and catheter movements in bladder, breast, ocular, gynecological, and prostate brachytherapy. The articles address the need for replanning and the added value of additional imaging. Bus *et al.* performed daily position verification with CT for interstitial bladder brachytherapy (26). It is a unique study for this type of treatment and proves the need for position verification for subsequent fractions. The study also contains a margin analysis, which could potentially reduce the number of position verifications. It will become state of the art to allow margins between clinical target volume and planning target volume of 0 mm or with a defined value larger 0 mm for brachytherapy, where each margin value is linked to different needs for verification. If margins are used, the implant geometry is of major interest as geometric variations occur not to the same extent in all directions. Needle shifts are dominant in the direction of the needle path and almost not present in lateral direction. Furthermore, the use of margins has to be based on the dose gradients and spatial dose distribution of the application (27). Zoberi *et al.* used MRI for intraocular melanoma brachytherapy treatment planning and for dose delivery verification (28). They proved that MRI is a feasible method to perform preplan and postplan dosimetric evaluations. Such elaborated methods can provide better possibilities for assessing the quality of the implant and will become important for documenting dose and volume data needed to perform dose-response curves for target and organs at risk. Altman *et al.* performed a verification CT for breast brachytherapy with a strut-adjusted volumetric implant device (29). Around one-third of cases were identified to need replanning, which underlines the need for an optimal workflow and technology for verification for this device. Three articles in this special issue and another recent article in *Brachytherapy* investigated the magnitude and impact of catheter migration in interstitial HDR brachytherapy. Buus *et al.* evaluated catheter migration between treatment planning scan and directly before/after treatment in MRI-guided HDR whole gland prostate brachytherapy (30). They found that considerable needle migration occurred frequently during 1–2 h after the planning scan, and concluded that assessment of needle position directly before treatment was of importance. Rink *et al.* found minor caudal migration and minor dosimetric impact of swelling in whole gland/focal/salvage HDR prostate brachytherapy when patients were under general anesthesia throughout the entire brachytherapy process (31). Maenhout *et al.* also found limited catheter migration in focal HDR prostate brachytherapy, and the dosimetric impact of catheter migration and anatomical changes was in general small, although for individual patients considerable (32). Catheter migration in interstitial gynecologic HDR brachytherapy was found to be limited even across fractions delivered across several days (33), which is very different from results in prostate brachytherapy (34, 35). Thresholds for acceptable migration were found to be 3 mm for prostate (30) and gynecologic implants (33), which have also previously been recommended in prostate brachytherapy (36). Van der Ende *et al.* demonstrated the need for adaptive treatment planning in endorectal brachytherapy. (37). This technique allows highly conformal partial volume treatments in case of targets limited to parts of the rectal wall. The contralateral part can be spared in an optimal way. However, variations of the organ filling and applicator motions result in deviations from the prescribed plans. Without adaptations of the initial plan for subsequent fractions, 12/22 fractions reached the planning aim. This could be increased by preplanning to 14/22. For the remaining fractions, corrections of the applicator position and organ filling status would be necessary to fulfill the optimal criteria. This article shows that ‘‘replanning’’ is not necessarily linked to the calculation of dose distributions and