REPORTS OF PRACTICAL ONCOLOGY AND RADIOTHERAPY 16 (2011) 203–206

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Editorial

Recent developments in brachytherapy

Brachytherapy has a long and illustrious history in the treatment of cancer dating back to the early 20th century. Although its popularity has fluctuated in response to the emergence of newer treatment modalities, brachytherapy has persisted over time. Although it is not the predominant radiotherapy modality, this treatment modality continues to play an important role in cancer therapy, even now, more than a 100 years after it was first introduced. Today, it is most commonly used in prostate, gynecological, and breast cancer, although technological developments in recent years have opened up several new treatment possibilities.

Brachytherapy tends to “fly under the radar” when compared to external beam radiotherapy (EBRT). However, numerous important – though perhaps under-appreciated – advances in brachytherapy have been made in the last two decades. This therapeutic modality has several important advantages, particularly the fact that it allows for high-doses of radiation to be delivered to the tumor with a high degree of precision, thus minimizing damage to healthy tissue. For this reason, it is important that efforts be made to remind all cancer care professionals of the continuous improvements in this technique and the value of brachytherapy in the cancer treatment toolkit.

In the last few years, our journal, Reports of Practical Oncology and Radiotherapy (RPOR), has been publishing cutting-edge research into new developments in the field of brachytherapy, particularly in improved dosimetric techniques, imaging, and treatments. In this editorial, we take a closer look at a few of these advances through some of the more relevant papers published in our journal over the past 3 years. We believe that these important papers help to reveal the value and progress that is being made in the field, and we are proud to be able to help disseminate this important research to a wide audience.

1. Imaging

Functional imaging for brachytherapy is an area in which great improvements have been made. The range of imaging tools, many which can now be used in real-time, have greatly expanded the possibilities of brachytherapy. These include ultrasound, power doppler imaging, positron emission tomography (PET), and magnetic resonance imaging (MRI). The combination of functional imaging with intraoperative dose calculation and optimization opens new horizons for brachytherapy.

Thanks in large part to advances in computer technology, treatment planning, intraoperative navigation, and dose delivery have all improved. Powerful new computers able to process images in real-time have made image-guided brachytherapy (IGBT) the technique of choice to achieve excellent conformal radiation therapy. IGBT allows for accurate dose delivery to small volumes under direct image visualization.

1.1. *An example of IGBT is the paper published in RPOR in 2008 with the following title: “Real-time brachytherapy for prostate cancer – implant analysis”*[1]

This article evaluated the use of real-time techniques to carry out seed implants in prostate BT. The authors discuss how high-dose rate brachytherapy (HDR-BT) has become one of the more popular methods in early-stage prostate cancer because dwell times inside the catheter can be individually selected (optimized) for better targeting while sparing normal tissue and organs at risks. In their study, the authors used transrectal ultrasound guidance for continuous visualization of the prostate during treatment planning. However, as the authors point out, precision of catheter implantation based on the preplanned needle positioning and patient anatomy is essential. This research is important because, as the authors state, few studies have addressed the subject of needle displacement and possible adverse consequences. The authors suggest steps that can be taken during the needle insertion procedure to improve the quality of the final dose distribution.

2. Dosimetric research

RPOR has a strong tradition in the physics of radiation therapy, and numerous articles have been published in this journal over the years on this subject. Below, we discuss some of the most important reports.

2.1. *Application of Monte Carlo calculations for validation of a treatment planning system in high dose rate brachytherapy*[2]

In 2009, Neseri and Mezbahi reported the results of their study which investigated the use of Monte Carlo calculations to validate a treatment planning system in HDR-BT. In that article, the authors discuss the importance of accurately calculating the absorbed dose distribution in a patient before treatment, which is particularly important in HDR due to the high dose rate and dose per session as any inaccuracies in dose distributions can have severe consequences on healthy tissue. The authors wanted to verify the accuracy of algorithms used in HDR BT treatment planning for 3 different ^{60}Co sources of the GZP6 afterloading brachytherapy system. They found that dose calculations of the TPS were accurate and so validated using the Monte Carlo method. The agreement (<2%) between TPS and MC calculated dose distributions was good and this study confirmed the accuracy of TPS calculated dose distributions for clinical use in HDR brachytherapy.

2.2. *Dosimetric verification of dose optimisation algorithm during endovascular brachytherapy of the peripheral vessels*[3]

In this study, Zwierzchowski et al. performed a dosimetric verification of dose optimization algorithm during endovascular brachytherapy following angioplasty. Endovascular brachytherapy has long been used to treat recurrent vessel narrowing due to restenosis following angioplasty. The aim of endovascular brachytherapy in these case is to prevent inward remodelling and increase the lumen area. As the authors point out, endovascular brachytherapy has been shown to significantly reduce the risk of restenosis if the irradiation is planned and delivered accurately. The difficulty lies in dose verification, which is difficult because endovascular *in vivo* dose checks are practically impossible. As an alternative, the authors designed and constructed a phantom which allowed for reliable and repeatable dosimetric verification (using thermoluminescent detectors and Gafchromic films). The results confirmed the accuracy of the calculation algorithm in endovascular brachytherapy conditions. Importantly, the end result of this study was the creation of indices that can be used to describe dose homogeneity around the applicator in endovascular brachytherapy. Through optimization, the authors were able to increase dose homogeneity by 30% at the edges and by 7% in the middle of the treated volume.

2.3. *Dosimetric verification of the dose calculation algorithms in real time prostate brachytherapy*[4]

In this study, Mocna and Zwierzchowsky evaluated 3 optimization algorithms [geometric optimization (GO), inverse optimization (IO) and blind inverse optimization (BIO)] used to modulate dwell times and source positioning in real time prostate brachytherapy. This study was important because dwell times and source positioning have a direct impact on dose distribution and, therefore, therapeutic indices. In their study, the authors used a phantom for the dosimetric verification. They compared doses measured by semiconductor detectors and calculated doses and found differences ranging from 0.10 Gy in the urethra for IO and BIO and up to 2.46 Gy for GO. Differences in the rectum were much smaller, ranging from 0.32 and 0.66 Gy. The authors concluded that the use of a phantom ensures repeatable geometric relations between the needles, the treated volume, and the corresponding organs at risk and also makes dose distribution verification possible. The important “take-away” conclusion is that it is essential to understand the limitations of optimization algorithms to make proper clinical decisions during real-time brachytherapy of the prostate.

2.4. *Verification in the water phantom of the irradiation time calculation done by the algorithm used in intraoperative radiotherapy*[5]

In this study, the authors evaluated dose calculations used in intraoperative radiation therapy (IORT) for breast-conserving treatment. According to the authors, although irradiation time is usually determined manually in IORT, automation of irradiation time calculation is essential. They used a water phantom to evaluate the accuracy of the Generalized Gaussian Pencil Beam (GGPB) algorithm which is part of the Varian TPS. The authors conclude that the GGPB algorithm is a tool that can be used for IORT, not just for conventional radiotherapy. Results calculated automatically were more reliable as well as easier and faster to obtain.

2.5. *Differential dose contributions on total dose distribution of 125I brachytherapy source*[6]

In this study, a group of researchers from Turkey assessed how differences in source geometry and internal construction affect total dose distribution. According to the authors, source models are highly manufacturer-specific and vary from one another in weld thickness and type, radioactivity carrier construction, presence of radio-opaque material (sharp or rounded edges), presence of silver (which produces characteristic X-rays that modify the photon spectrum), and capsule wall thickness. All of these properties can affect the dosimetric characteristics of the source, and, as the authors argue, the angular and radial dose distributions of the implanted source are clinically relevant. The authors used a Monte Carlo simulation because dose information of inner geometrical structure of a brachytherapy source cannot be acquired by experimental methods.

2.6. *The histopathologic evaluation of soft tissue changes in rabbit extremity after different dose-fractionation schemes of interstitial high dose rate (HDR) brachytherapy*[7]

In this trial, the authors note that although HDR is the modality of choice in soft tissue sarcoma, there is a paucity of prospective randomized clinical trials to investigate how various HDR dose-fractionation schemes affect normal tissue damage. The trials in the literature are retrospective with limited number of patients and heterogeneous therapies. After using three different fractionation schemes on 3 groups, the authors found that fractionated interstitial HDR resulted in a lower toxicity rate and less severe toxicity compared to a single high dose fraction. As a result, the authors suggest that radiation oncologists need to be aware of the increased morbidity related to irreversible early toxicity or progressive late toxicity before using a single fractionated regimen in the clinic.

2.7. *In-air calibration of new high dose rate 60Co brachytherapy sources: results of measurements on a GZP6 brachytherapy afterloading unit*[8]

One of the more interesting advances in brachytherapy is the production of artificial isotopes in recent decades, which, when combined with remote afterloading techniques, has led to the increasing use of HDR techniques that are coming to dominate brachytherapy. According to the authors, the dose distribution within the target volume must be uniform in order to achieve optimal tumor cell killing with uniform clonogenic cell density and to avoid necrosis of healthy cells within the target volume. However this dose uniformity is difficult to achieve in interstitial HDR due to the very high radiation dose in the vicinity of the radiation source. Hence, the tumor control probability (TCP) calculated on the basis of minimum or mean or median target dose would not be appropriate to predict accurate treatment outcome. To solve this problem, the authors used in-air calibration. They conclude that this technique may offer an alternative approach to calculate TCP for HDR implants.

3. Breast cancer

For many years now, the two most important localizations for brachytherapy have been breast and prostate cancer, largely because these are ideal localizations for brachytherapy treatment and because they have a high incidence rate. In the section on dosimetric research above, several of the studies addressed aspects of dosimetry for prostate cancer. In this section, we highlight a few studies that focus on breast cancer.

3.1. *The role of high-dose-rate brachytherapy boost in breast-conserving therapy: long-term results of the Hungarian National Institute of Oncology*[9]

The Hungarian National Institute of Oncology published the results of their long-term study of HDR-BT as a boost following surgery. According to the authors, the use of a boost has traditionally been delivered through low-dose rate (LDR) brachytherapy, electrons or photons. However, HDR-BT has been growing but there is still some controversy still exists regarding the optimal boost technique. For this reason, the authors performed a retrospective analysis of 100 patients who underwent breast-conserving surgery followed by radiotherapy and a HDR-BT boost. The authors concluded that interstitial HDR-BT boost yields a low incidence of late side effects with local tumor control rates that are similar to percutaneous boost techniques.

3.2. *CT-image based conformal high-dose-rate brachytherapy boost in the conservative treatment of stage I–II breast cancer – introducing the procedure*[10]

Similar to the previous study, this trial sought to evaluate HDR boost after surgery for stage I–II breast cancer. The authors evaluated 58 female patients who underwent breast-conserving surgery followed by whole breast irradiation and a 10 Gy boost to the tumor bed with interstitial HDR. The authors conclude that, to reduce the possibility of a geographical miss, CT-guided 3D HDR-BT is especially appropriate for patients with a large breast volume, a deep-seated tumor bed, and in patients at high risk of local relapse. The authors believe that, in selected cases, better local control rates with fewer side effects might be achieved with this technique.

3.3. *Sole conformal perioperative interstitial brachytherapy of early stage breast carcinoma using high-dose rate afterloading: longer-term results and toxicity*[11]

The results of this study provide further support for the use of accelerated partial breast irradiation (APBI) after breast-conserving surgery, though for select cases. The authors carried out a prospective study of 25 patients who underwent lumpectomy followed by HDR-BT for APBI using three-dimensional treatment planning. The results were good: at a median follow-up of 44 months, none of the women had developed in-field breast recurrences, and only one patient had an out-of-field recurrence and another had distant metastasis. There were no regional nodal recurrences. The only treatment complications were hematoma and abscess in the tumor bed after extirpation. All patients rated the overall cosmetic outcome as excellent or good. The authors conclude that this method is suitable alternative to whole-breast radiotherapy for patients with small tumous (<3 cm in diameter) without negative prognostic factors for local recurrence. The authors do caution, however, that local disease control should be compared with standard adjuvant radiotherapy in a randomized clinical study.

3.4. *Optimization in high-dose rate vaginal cylinder for vaginal cuff irradiation*[12]

American Brachytherapy Society guidelines on HDR treatment for endometrial carcinoma suggest that a pre-calculated treatment plan can be used for patient treatment delivery. However, the authors of this study argue that use of a pre-calculated plan excludes the ability to compute the dose to the organs at risk. By optimizing the treatment plan, it is possible to affect the dose to the rectum and bladder. Two different HDR cylinder models, the non-curved dome model (NCDM) and curved dome model (CDM), were studied. The authors found that the CDM results in more uniform dose distribution around the vaginal cylinder than NCDM. Importantly, they conclude that dose distribution for all the vaginal cylinders can be stored as a library plan and the best matched for target geometry can be used for treatment.

4. Conclusion

In conclusion, this journal believes that brachytherapy deserves more attention as a valuable and highly improved technique with unique advantages. The recent advent and integration of sophisticated radiation planning and imaging modalities has improved the quality of brachytherapy treatments, allowing for more conformal radiation delivery. Brachytherapy is an effective therapy for many types of cancer. RPOR is pleased to be at the forefront of publishing meaningful and serious articles on the latest findings in brachytherapy research.

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doi:10.1016/j.rpor.2011.11.003