

## In this issue

I am pleased to introduce the ‘in this issue’ for the first issue of the *Journal of Radiotherapy in Practice* for 2018. In this issue there are 16 original articles on a range of topics and a Letter to the Editor.

In the first paper, Rosas, Barbosa and Couto, present their study to compare intensity-modulated radiation therapy (IMRT) and volumetric-modulated arc therapy (VMAT) regarding plan quality and healthy lung sparing, in stage III non-small cell lung cancer (NSCLC) patients.

The plans of 60 patients were allocated either to the IMRT ( $n=30$ ) or the VMAT ( $n=30$ ) group. The dose prescribed to the planning target volume (PTV) was evaluated at the 95% level and the mean lung dose and the healthy lung receiving 5, 10 and 20 Gy (V5, V10 and V20, respectively) were analysed. The normal tissue complication probability for radiation pneumonitis was calculated with the Lyman–Kutcher–Burman model. The authors conclude that both techniques are suitable for NSCLC treatment, but IMRT presented better results regarding lung sparing thus being beneficial in reducing the risk of radiation-induced pneumonitis.

In the next paper, O’Neill, McAleer, McCarty, Clarke, Drake, Hurwitz et al. present their study, a randomised-controlled trial, to compare the ‘Precision Plus Micropigmentation System’ (PPMS) to permanent skin tattoos in radical breast radiotherapy patients.

Accurate and reproducible patient positioning is a critical step in radiotherapy for breast cancer. This has seen the use of permanent skin markings becoming standard practice in many centres. Permanent skin markings may have a negative impact on long-term cosmetic outcome, which may in turn, have psychological implications in terms of body image. The aim of this study

was to investigate the feasibility of using a semi-permanent tattooing device for the administration of skin marks for breast radiotherapy set-up.

This study was designed as a phase II double-blinded randomised-controlled study comparing standard permanent tattoos with the PPMS device method. Patients referred for radical breast radiotherapy were eligible for the study. Each study participant had three marks applied using a randomised combination of the standard permanent and PPMS methods and was blinded to the type of each mark. Follow up was at routine appointments until 24 months post radiotherapy. Participants and a blind assessor were invited to score the visibility of each tattoo at each follow-up using a Visual Analogue Scale. Tattoo scores at each time point and change in tattoo scores at 24 months were analysed by a general linear model using the patient as a fixed effect and the type of tattoo (standard or research) as covariate. A simple questionnaire was used to assess radio-grapher feedback on using the PPMS. In total, 60 patients were recruited to the study, of which 55 were available for follow up at 24 months.

The authors conclude that the PPMS presents a safe and feasible alternative to permanent tattooing method. An extended period of follow up is required to fully assess the extent of semi-permanent tattoo fade.

In the next paper, Hutton, Callender, Hutton, Wong and Syndikus, present their feasibility study for the introduction of micro-enema to improve organ consistency in patients receiving radiotherapy for urinary bladder cancer. The aim of this study was to assess the effectiveness of implementing micro-enemas in achieving rectal consistency for the planning and treatment of radiotherapy for urinary bladder cancer. The treatment cone beam computed tomography (CBCT) images from patients receiving

radiotherapy for bladder cancer were retrospectively assessed. CBCT datasets from nine patients treated without intervention (97 CBCT), and 13 patients (134 CBCT) treated following micro-enema use prior to planning and treatment were evaluated. CBCT were compared with the planning CT for rectal status, rectal diameter and presence of gas. Authors conclude that the use of a micro-enema prior to planning scan and each fraction was well tolerated and proved effective in managing and reducing inter-fraction variations in rectal volume and contents.

The subject of the next paper is the dosimetric impact of manual adjustments following automated registration in prostate image-guided radiotherapy (IGRT), by ElBeltagi, Harper and Coleman. Although manual adjustment of automatic CBCT matching may improve the target coverage in certain points of interest, concerns exist that this may lead to dosimetric uncertainties which would negate the theoretical benefit of this approach. The objective of this study was to evaluate the dosimetric impact of manual adjustments made after automatic bony registration on CBCT in prostate patients.

In total, 50 CBCT datasets of ten high-risk prostate cancer patients were randomly chosen. Each CBCT dataset was registered three times. Method (A): automatic registration, Method (M1): manual adjustment carried out by two experienced radiation therapists, Method (M2): manual adjustment carried out by different radiation therapists with varying levels of experience. The clinical target volume, PTV, the bladder and the rectum were subsequently contoured on each CBCT dataset by a radiation oncologist blinded to the registration methods. The absolute difference of various dosimetric parameters were then analysed and compared with the original planning doses. A comparison of the three matching methods employed was also carried out.

The authors' findings are that CBCT-based manual adjustments of automated bony-based registrations during the IGRT verification of prostate cancer patients can improve PTV coverage without impacting negatively on the doses received by the organs at risk.

In the next paper, Al-Hajri, Isfahanian, Samant, Alyamani, Atallah, Choan et al. present their study to determine the outcome of patients with locally advanced cervix cancer treated with curative intent using external beam radiotherapy (EBRT), without brachytherapy. A chart review was performed of all patients with cervix cancer who received EBRT alone at their centre from 2000 to 2010. Overall survival and local control were evaluated using Kaplan–Meier survival curves. In total, 22 patients were identified. The median age and follow up were 56 years and 65 months, respectively. The stage included IB to IVB. Main histology was squamous cell carcinoma (82%). Median tumour size was 5.5 cm. Majority were treated with three-dimensional (3D) conformal techniques and nine patients (41%) were treated with IMRT. In all, 14 patients received doses of  $\geq 65$  Gy. Most patients (73%) received weekly concurrent *cis*-platinum. The major reason for not receiving brachytherapy was locally extensive tumour (59%). The 5-year relapse-free survival and overall survival rates were 57 and 50%, respectively. Seven patients (32%) had a component of loco-regional failure, mainly within the cervix. There was a better outcome among the nine patients treated with IMRT to a median dose of 66 Gy with a loco-regional control of 78%.

Authors conclude that patients who cannot have brachytherapy may still achieve acceptable rates of loco-regional disease control if high radiation doses ( $>65$  Gy) was delivered.

In the next paper, Osei, Maraghechi, Davis, Badu, Darko and Fleck, present their retrospective analysis of portal dosimetry pre-treatment quality assurance (QA) of prostate VMAT plans. Electronic Portal Imaging Device (EPID) offers high-resolution digital image that can be compared with a predicted portal dose image. A very common method to quantitatively compare a measured and calculated dose distribution that is routinely used for QA of VMAT and IMRT treatment plans is the evaluation of the gamma index. The purpose of this work was to evaluate the gamma passing rate (%GP), maximum gamma ( $\gamma_{\max}$ ), average gamma ( $\gamma_{\text{ave}}$ ), maximum dose difference ( $DD_{\max}$ ) and the average dose difference ( $DD_{\text{ave}}$ ) for various regions of interest using Varian's implementation of three absolute dose

gamma calculation techniques of improved, local and combined improved and local. The study analysed 232 portal dose images from 100 prostate cancer patients' VMAT plans obtained using the Varian EPID on TrueBeam Linacs.

The results of this study can be used to establish stricter action levels for pre-treatment QA of prostate VMAT plans. A stricter 3%/3 mm improved gamma criterion with a passing rate of 97% or the 2%/2 mm improved gamma criterion with a passing rate of 95% can be achieved without additional measurements or configurations.

In the paper by Shah, Ahmad, Ahmad, Khattak, Javed, Shah et al. investigate the treatment of non-melanoma superficial skin cancer with custom made wax moulds using Iridium-192 HDR brachytherapy source. In non-melanoma skin cancer (NMSC), that is basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), brachytherapy treatment can be preferred over surgical excision due to cosmetics reason and acceptability preference of patients. A mould is prepared of wax that represents the size of lesion and represents the area of the dose in treatment planning.

A total 85 patients were treated both of SCC and BCC, all of these patients were classified on the basis of age, gender and tumour origin. Patients were treated with 39 Gy in 13 fractions (BED = 50.7 Gy).

The authors found that treatment outcomes not only improve their confidence on the use of brachytherapy treatment but also improve the patient's feedback satisfaction over the cosmetic results and curative output, while avoiding surgical procedures for NMSC.

In the next paper authors Ahmad, Ahmad, Khattak, Shah, Javed, Shah, Shaheen et al. undertake a comparative study into postoperative single versus multiple fraction high-dose rate Iridium-192 surface mould brachytherapy for keloid treatment. In developing countries like Pakistan the cost effectiveness and patient convenience in any treatment modality is a question of major concern. The purpose of this study was two-fold; first to report their experience of using a high-dose rate Iridium-192 surface mould brachytherapy

treatment of keloid scars after surgical excision, using different radiation treatment regimens and second to establish the most convenient and cost-effective treatment protocol having no compromise on the treatment outcomes.

From January 2012 to April 2015 a total 51 patients with 65 keloid lesions underwent post-operative Iridium-192 HDR surface mould brachytherapy. The dose regimen used was 8 Gy in a single fraction, 10 Gy in a single fraction, 15 Gy in three fractions and 18 Gy in three fractions. The median follow-up period was 33 months (range 15–53 months).

The authors conclude that the results of this study show that a dose regimen of 10 Gy (BED<sub>10</sub> = 20 Gy) in a single fraction have comparable results with a dose regimen of 15 Gy in three fractions or 18 Gy in three fractions. 10 Gy in a single fraction is therefore the most convenient and cost-effective dose regimen for the management of keloid scars in developing countries like Pakistan, while 8 Gy in a single fraction is considered suboptimal and discouraged in practice.

In the next paper, Osei, Maraghechi, Davis, Mitchell, Shah, Fleck et al. investigate the sensitivity of single- and multi-gamma criteria techniques to detect multi-leaf collimator (MLC) positioning errors using the Varian TrueBeam Electronic Portal Imaging Device™ (EPID) dosimetry and the ArcCHECK™ device.

All active MLC positions of seven intact prostate patients' volumetric-modulated radiotherapy plans were randomly changed with a mean value of 0.25, 0.5, 1 and 2 mm and a SD of 0.1 mm on 25, 50, 75 and 100% of the control points. The change in gamma passing rates of six gamma criteria of 3%/3 mm, 3%/2 mm, 3%/1 mm, 2%/2 mm, 2%/1 mm and 1%/1 mm were analysed individually (single-gamma criterion) and as a group (multi-gamma criteria) as a function of the simulated errors. We used the improved and global gamma calculation algorithms with a low-dose threshold of 10% in the EPID and ArcCHECK software, respectively. The changes in the PTV dose distributions and the organs at risk due to the MLC positioning errors were also studied.

Authors conclude that the Varian TrueBeam EPID dosimetry shows a higher sensitivity in detecting MLC positioning errors compared with the ArcCHECK regardless of using the single- or the multi-gamma criteria techniques. Higher sensitivity was observed using the multi-gamma criteria technique compared with the single-criterion technique when using the EPID.

In the next paper, Armpilia, Harpidou, Kalaitzi, Tsapas, Tsagouli, Gkiozos et al. present their study to review the results of applying a hypofractionated radiotherapy schedule for locally advanced inoperable lung cancer in patients who have received chemotherapy. Lung cancer and especially NSCLC is prone to accelerated repopulation and shorter treatment schedules in the form of accelerated radiotherapy have been shown to improve treatment outcome.

In all, 29 patients with inoperable lung cancer (stage II, IIIa, b, IV) were treated with accelerated hypofractionated 3D conformal radiotherapy. All patients received a dose of 55 Gy in 20 fractions (daily dose of 2.75 Gy). The median age was 65.5 years, 87% of patients had stage III–IV disease, 93% of patients received sequential chemotherapy with their radiotherapy. Median follow up of patients was 36 months.

Authors conclude that, although their study limitation is the small number of patients, these data suggest that the efficacy of this hypofractionated schedule could be considered as alternative option to the conventional regimen of 66 Gy given in 33 fractions.

In the next study, Iqbal examines the dosimetric properties of GafChromic<sup>®</sup> EBT3 film and IMRT QA.

Beams characteristics dosimetric properties and 20 IMRT plans were created and irradiated on Varian dual-energy DHX-S Linac for 6 and 15 MV energies. EBT3 films were analysed using 'film Pro QA 2014' software.

The author concludes that the results advocate that the film can be used not only for dosimetric assessment but also as a reliable IMRT QA tool.

In the next paper Iqbal undertakes a dosimetric characterisation of anthropomorphic PRESAGE<sup>®</sup> dosimeter and EBT2 film for partial breast radiotherapy. In whole breast EBRT results significant reduction in the risk of breast cancer death, but this may be offset by an increase in deaths from other causes and toxicity to surrounding organs. Partial breast irradiation techniques is an approach that treats only the lumpectomy rather than the whole breast. QA in the radiation therapy treatment planning process is essential to ensure accurate dose delivery to the patient. For this purpose this article compares the results of anthropomorphic PRESAGE<sup>®</sup> dosimeter, radiation treatment planning system and GafChromic<sup>®</sup> EBT2 film.

A breast dosimeter was created and three fields partial plan was generated in Pinnacle3 treatment planning system. Dose distribution comparisons were made between Pinnacle3 treatment planning system, GafChromic<sup>®</sup> EBT2 film and PRESAGE<sup>®</sup> dosimeter. Dose–volume histograms (DVHs), Gamma maps and line profiles were used to evaluate the comparison.

The findings of this study demonstrated the feasibility of PRESAGE<sup>®</sup> to be in the form of anthropomorphic phantom and laid the foundation for researches in PRESAGE<sup>®</sup>/optical-CT 3D dosimetry with the most complex anthropomorphic phantoms.

In the next paper, Lenko and Peterlin, examine and quantify set-up errors in patient positioning in head-and-neck radiotherapy and to investigate the impact of the choice of reference isocentre—on the patient neck or patient skull—on the magnitude of set-up errors.

Set-up position corrections obtained using online kV 2D/2D matching were recorded automatically for every treatment fraction. In total, 3,413 treatment records for 117 patients treated with VMAT during 2013 and 2014 on a single treatment machine in our clinic were analysed. In 79 treatment plans the reference isocentre was set to the patient skull, and in 47 to the neck.

Results: standard deviation of group systematic error in the vertical, longitudinal and lateral direction and the couch rotation were found to

be 2.5, 2.1, 1.9 mm and 0.43° (skull) and 2.5, 1.8, 1.7 mm and 0.49° (neck). Random error of the vertical, longitudinal, lateral and rotational position correction was 1.8 mm, 1.5 mm, 1.6 mm and 0.62° (skull) and 1.9 mm, 1.6 mm, 1.5 mm and 0.60° (neck). Positional shifts in different directions were found to be uncorrelated.

The authors conclude that neither reference isocentre set-up shows a clear advantage over the other in terms of inter-fraction set-up error.

In the next paper, Nithiyantham, Mani, Raju, Velliangiri, Paramasivam, Palaniappan et al. present their study to characterise small photon beams using the Monte Carlo dose calculation algorithm for small field ranges in a heterogeneous medium.

An in-house phantom constructed with three different mediums, foam, polymethyl methacrylate and delrin resembling the densities of lung, soft tissue and bone, respectively, was used in this study. Photon beam energies of 6 and 15 MV and field sizes of 8 × 8 mm, 16 × 16 mm, 24 × 24 mm, 32 × 32 mm and 40 × 40 mm using X-ray voxel Monte Carlo (XVMC) algorithm using different detectors were validated. The relative output factor was measured in three different mediums having six different tissue interfaces, at the depth of 0, 1, 2 and 3 cm. The planar dose verification was undertaken using gafchromic films and considered dose at the lung and bone medium interfaces. For all the measurements, 104 × 104 mm was taken as the reference field size. The relative output factor for all other field sizes was taken and compared with planning system calculated values.

Authors conclude that the accuracy of dose calculations for small field sizes in XVMC-based treatment planning algorithm was studied in different inhomogeneous mediums. It was found that the results correlated with measurement data for field size 16 × 16 mm and above. Noticeable deviation was observed for the smallest field size of 8 × 8 mm with interfaces of significant change in density. The observed results demands further analysis of work with smaller field sizes.

The last original article in this issue is by authors Tharavichitkul, Rugpong, Chawapun and Galalae, on their study aims to clarify the influence of overall treatment time (OTT) on the efficiency of combined chemo-radiotherapy in cervical cancer.

This retrospective study enrolled 122 cervical cancer patients who had squamous cell carcinoma and had undergone definitive chemo-radiotherapy from 2009 to 2013. All patients received whole pelvic radiotherapy (WPRT) with the dose of 50 Gy in 25 fractions (with central shielding after 44 Gy) plus intracavitary brachytherapy with the dose of 28 Gy in four fractions. During WPRT, all patients received concurrent chemotherapy with weekly platinum-based regimen. The data of patient characteristics, OTT, treatment results and toxicities were collected and evaluated. Results: the mean follow-up time was 36 months. The mean age of patients was 52 years old; 68% of patients were stage IIB related to FIGO staging. Pelvic control (PC), distant metastasis-free survival (DMFS), disease-free survival (DFS) and overall survival (OS) rates did not differ significantly in the data-derived cut points of 55.8 and 53 days. No statistically significant difference in treatment results between the two groups of OTT <49 and OTT ≥ 62 days was observed.

Authors conclude that their data-derived cut point, OTT did not influence to PC, DMFS, DFS and OS. The influence of OTT on treatment results may be found in longer periods.

To complete the research reported in this issue, there is a paper on the subject of 18-FDG-PET metabolic response of NSCLC to chemo-radiotherapy with long-term follow-up, by authors Ampil, Caldito and Richards.

To complete this issue, there is a letter to the Editor in response to 'caution in comparing keloid treatment regimen through linear quadratic model' by Misbah Ahmad and Habib Ahmad.

*Professor Angela Duxbury*