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Clinical Study

Monte Carlo-Based Dose Calculation in Postprostatectomy Image-Guided Intensity Modulated Radiotherapy: A Pilot Study

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Step-and-shoot (S&S) intensity-modulated radiotherapy (IMRT) using the XiO treatment planning system (TPS) has been routinely used for patients receiving postprostatectomy radiotherapy (PPRT). After installing the Monaco, a pilot study was undertaken with five patients to compare XiO with Monaco (V2.03) TPS for PPRT with respect to plan quality for S&S as well as volumetric-modulated arc therapy (VMAT). Monaco S&S showed higher mean clinical target volume (CTV) coverage (99.85%) than both XiO S&S (97.98%, $P = 0.04$) and Monaco VMAT (99.44, $P = 0.02$). Rectal V60Gy volumes were lower for Monaco S&S compared to XiO (46.36% versus 58.06%, $P = 0.001$) and Monaco VMAT (46.36% versus 54.66%, $P = 0.02$). Rectal V60Gy volume was lowest for Monaco S&S and superior to XiO (mean 19.89% versus 31.25%, $P = 0.02$). Rectal V60Gy volumes were lower for Monaco VMAT compared to XiO (21.09% versus 31.25%, $P = 0.02$). Other organ-at-risk (OAR) parameters were comparable between TPSs. Compared to XiO S&S, Monaco S&S plans had fewer segments (78.6 versus 116.8 segments, $P = 0.02$), lower total monitor units (MU) (677.6 MU versus 770.7 MU, $P = 0.01$), and shorter beam-on times (5.7 min versus 7.6 min, $P = 0.03$). This pilot study suggests that Monaco S&S improves CTV coverage, OAR doses, and planning and treatment times for PPRT.

1. Introduction

In the field of radiotherapy, a number of treatment planning systems (TPS) are commercially available and capable of creating treatment plans with a variety of multileaf collimator (MLC) leaf positions, dose rate, and gantry speeds. The Monaco planning system (Elekta-CMS Software, Riverport Drive, Maryland Heights, MO 63043, USA) uses fluence map-based optimization algorithms to optimize fluence maps and take biological tissue properties into account [1].

Image-guided intensity modulated radiotherapy (IG-IMRT) for postprostatectomy radiation therapy (PPRT) has been associated with a lower frequency of acute and late gastrointestinal (GI) and genitourinary (GU) toxicity (using Common Terminology Criteria for Adverse Events (CTCAE) version 3.0) [2]. In the study of Nath et al., Grade 2 acute GI and GU toxicity was observed in 8% and 14% of patients, respectively [2]. Grade 2 late GI and GU toxicity was observed in 2% and 16% of patients, respectively [2]. Grade 3 toxicity was not observed in the acute setting. Only 2% of patients experienced Grade 3 late GU toxicity [2].

Since opening in May 2007, North Coast Cancer Institute (NCCI) has used step-and-shoot (S&S) IG-IMRT for PPRT. All patients in the pilot study were originally planned using the XiO (Elekta-CMS Software, Riverport Drive, Maryland Heights, MO 63043, USA) TPS using a seven- or nine-field technique, superposition dose calculation algorithm and according to eviQ guidelines [3] which are based on the consensus guidelines of the Australian and New Zealand Radiation Oncology Genitourinary Group [4].

The present pilot study compares XiO with the Monaco TPS. The latter employs Monte Carlo-based dose calculations

(MC v1.6 algorithm) and biological modeling of cost functions, for both S&S and volumetric-modulated arc therapy (VMAT). Plan quality was assessed by comparing clinical target volume (CTV) coverage, organ-at-risk (OAR) sparing [5], and treatment delivery time.

2. Methods and Materials

A planning study was conducted on five randomly selected patients who were prescribed 64 Gy or 66 Gy at the isocenter for PPRT. These patients were treated according to plans delivered using XiO (V4.51) and were retrospectively replanned using Monaco (V2.03). Current department protocol for PPRT planning uses 6 MV photon beams with nine fields distributed equally around the patient at 40° apart, starting at 160° and moving anticlockwise to 200°, modeled on our NCCI Elekta Synergy linear accelerators. Two additional plans were generated for each patient: the first using S&S delivery and the second using VMAT with a single 360° arc. Monaco planning was done on the same dataset with the same target and OAR contours. At the time of data collection, Monaco v2.03 offered single arc direction VMAT only; subsequent versions include the option for bidirectional arcs which will be investigated in the future.

All plans were normalized to achieve a minimum 95% of the planning target volume (PTV) covered by 95% of prescribed dose. For each plan, quality was evaluated by comparing CTV coverage and OAR dose sparing according to the eviQ [3, 4] guidelines. Target coverage was assessed as the percentage of prescribed dose covering 100% of the CTV; both global point doses and maximum doses covering 2% of the CTV were compared. OAR dose constraints were evaluated at V40Gy, V60Gy, and V65Gy for the rectum and at V50Gy for the bladder. The eviQ [3, 4] guidelines for assessing femoral head dose are V35Gy ≤ 100%, V45Gy < 60%, and V60Gy < 30%, but since all plans easily achieved these constraints, mean doses were determined for the purposes of this study. For each of the five cases, mean values were derived for dose covering 100% of the CTV for XiO S&S, Monaco S&S, and Monaco VMAT plans. Mean values were also derived for the three rectal dose-volumes as well as V50Gy for the bladder.

IMRT prescription aims were similar for retrospective planning. In order of layering, IMRT prescriptions contained objectives to achieve CTV/PTV coverage and to control high dose areas, both in size and location (i.e., within the CTV). Rectal constraints were added to control dose at both 40 Gy and 60 Gy levels. Constraints on the bladder were used at the 50 Gy level. To control peripheral dose in the patient, dose constraints were used at three intervals concentric to the PTV.

In addition to quality, plans were evaluated for total monitor units (MU) and number of segments. Beam-on times were recorded during dose validation checks. Times to deliver XiO plans were recorded by running the plans in quality assurance (QA) mode to enable direct comparison of beam-on times. Dose delivery QA was verified by physics staff on each plan using a 2D diode array dosimetry MapCheck2 device for S&S plans and ArcCHECK device [6] for VMAT plans (Sun Nuclear Corp., FL, USA) and included radiochromic film assessment in up to three transverse planes.

Data are presented as means (SD). For statistical assessment, paired 2-tailed t-tests (Microsoft Excel 2010) were used to compare planning systems; a probability value $P < 0.05$ was considered statistically significant.

This study received approval by the North Coast Area Health Service (NCAHS) Human Research Ethics Committee as a quality improvement initiative.

3. Results

Each plan was clinically acceptable according to eviQ [3, 4] recommendations. The mean values for CTV coverage, OAR dose-volumes, and treatment delivery parameters are shown in Table 1. Although XiO S&S results fell within clinically acceptable limits, Monaco S&S produced significantly better mean CTV coverage (99.85%) than both XiO S&S (97.98%, $P = 0.04$) and Monaco VMAT (99.44, $P = 0.02$). Mean PTV doses remained within 0.5 Gy.

Statistically significant reductions in the rectal dose-volume parameter of V40Gy were observed for Monaco S&S (mean 46.36%) compared to both XiO S&S (58.06%, $P = 0.001$) and Monaco VMAT (54.66%, $P = 0.02$). Four out of five Monaco VMAT plans showed similar reductions (though not statistically significant) over XiO S&S (Figure 1).

A reduction in the V60Gy rectal dose-volume parameter (Figure 2) was evident in each case when Monaco S&S was compared to XiO S&S (mean 19.89% versus 31.25%, $P = 0.02$). Monaco VMAT (mean 21.09%) was also significantly different to XiO S&S for this parameter (31.25%, $P = 0.02$). Three of the five plans showed a dosimetric advantage when using Monaco VMAT over Monaco S&S; however, the mean result was not significant. There were no significant differences between planning systems for the rectum V65Gy.

Regarding bladder V50Gy, percentage volumes tended to be lower for the Monaco plans; however the differences were not significant (Figure 3).

Although both Monaco VMAT and Monaco S&S showed lower mean femoral head doses, none were statistically significant except for the right femoral head when comparing VMAT to XiO (mean 11.52 Gy versus 14.76 Gy, $P = 0.03$).

Monaco-based S&S plans contained significantly fewer segments than XiO S&S (mean 78.6 versus 116.8 segments, $P = 0.02$ (Figure 4)), lower total MU (mean 677.6 MU versus 770.7 MU, $P = 0.01$ (Figure 5)), and shorter treatment delivery times (mean 5.7 min versus 7.6 min, $P = 0.03$). Monaco-based VMAT also had lower total MU (mean 676.7 MU versus 770.7 MU, $P = 0.06$) and treatment delivery time (despite larger number of segments than XiO S&S [mean 4.8 min versus 7.6 min, $P = 0.01$]). There were no significant differences in delivery times between Monaco S&S and VMAT ($P > 0.05$).

With regard to physics QA, Monaco plans were delivered with a slightly higher average pass rate of 97.7% compared to an average of 97.2% for the XiO plans.

Table 1: Comparison between XiO S&S, Monaco S&S, and Monaco VMAT treatment plans for five postprostatectomy patients: CTV coverage, OAR dose-volumes. and treatment delivery parameters (means (SD)).

Parameter	XiO S&S	Monaco S&S	Monaco VMAT
CTV 100% TD (%)	97.98 (0.01)	*‡99.85 (0.00)	99.44 (0.00)
Rectum V40Gy (%)	58.06 (0.06)	*‡46.36 (0.09)	54.66 (0.05)
Rectum V60Gy (%)	31.25 (0.04)	*19.89 (0.05)	†21.09 (0.04)
Rectum V65Gy (%)	14.29 (0.09)	11.34 (0.03)	10.35 (0.03)
Bladder V50Gy (%)	41.91 (0.13)	32.97 (0.09)	37.96 (0.08)
Lt. femoral head mean dose (Gy)	19.89 (3.78)	16.18 (1.86)	14.69 (0.93)
Rt. femoral head mean dose (Gy)	14.76 (8.40)	12.74 (7.18)	†11.52 (7.46)
Number of segments/fraction	116.8 (22.0)	*‡78.6 (8.3)	141.0 (27.0)
MU/fraction	770.7 (76.2)	*677.6 (76.3)	676.7 (29.6)
Delivery time (minutes)	7.6 (1.1)	*5.7 (0.9)	‡4.8 (0.3)

*Monaco S&S versus XiO, $P < 0.05$. †Monaco VMAT versus XiO, $P < 0.05$. ‡Monaco S&S versus Monaco VMAT, $P < 0.05$.

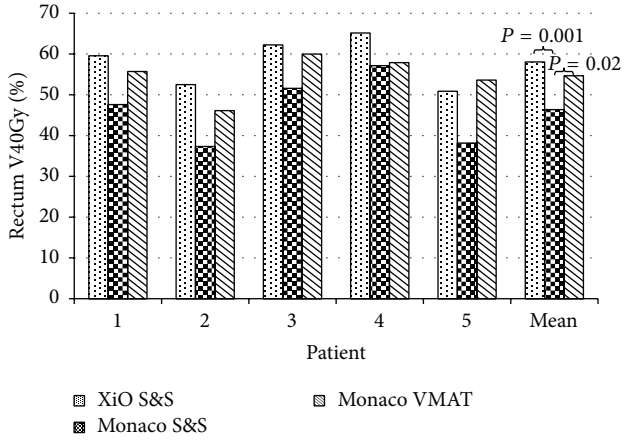

Figure 1: Comparison between XiO S&S, Monaco S&S, and Monaco VMAT treatment plans for five PPRT patients: the mean rectal dose-volume parameter of V40Gy was significantly lower in plans generated by Monaco S&S compared to both XiO S&S and Monaco VMAT.

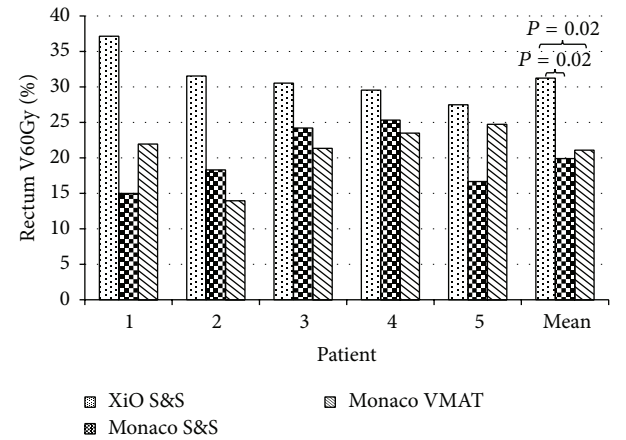

Figure 2: Comparison between XiO S&S, Monaco S&S, and Monaco VMAT treatment plans for five PPRT patients: compared to XiO S&S, the rectal dose-volume parameter of V60Gy was significantly lower in plans generated by Monaco S&S and VMAT.

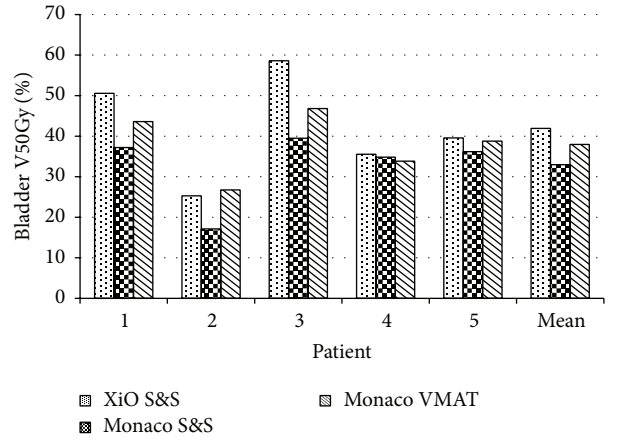

Figure 3: Comparison between XiO S&S, Monaco S&S, and Monaco VMAT treatment plans for five PPRT patients: although the bladder dose-volume parameter of V50Gy tended to be lower when using the Monaco TPS, the differences were not statistically significant.

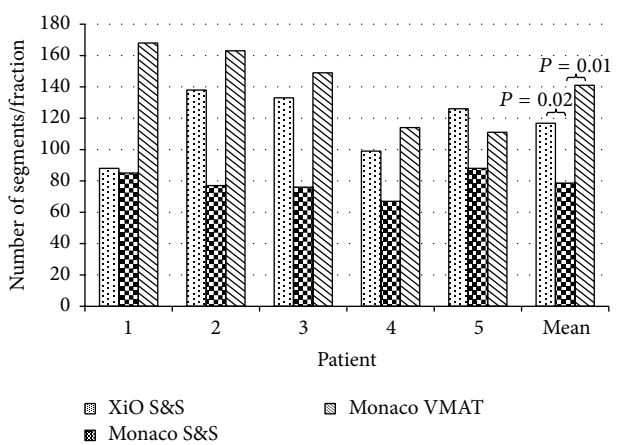

Figure 4: Comparison between XiO S&S, Monaco S&S, and Monaco VMAT treatment plans for five PPRT patients: Monaco-based S&S plans had fewer segments than both XiO S&S and Monaco VMAT.

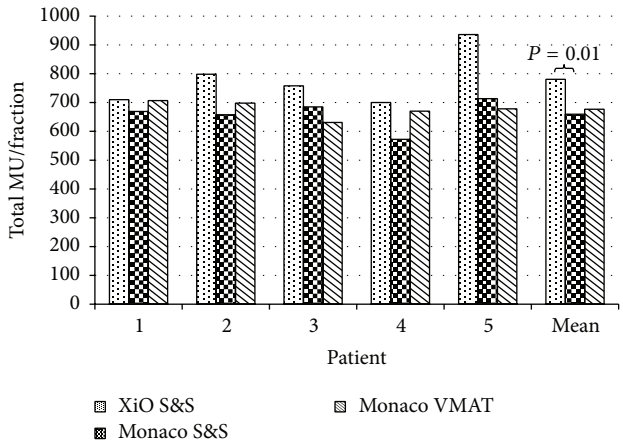

Figure 5: Comparison between XiO S&S, Monaco S&S, and Monaco VMAT treatment plans for five PPRT patients: Monaco-based S&S plans had lower total MU than XiO S&S ($P = 0.01$).

4. Discussion

Refining treatment techniques and aims are an integral part of ongoing quality improvement. The present study assessed plan quality and treatment efficiency gains in five postprostatectomy patients who were planned using the XiO TPS and retrospectively replanned using the Monaco TPS for S&S and VMAT techniques.

The protocol followed for target coverage at the time of data collection was that 99%-100% of the CTV be covered by the prescribed dose and a minimum of 95% of the PTV be covered by 95% of the prescribed dose; this defined our standard for normalizing plans for comparison. For every patient investigated, Monaco S&S plans improved CTV dose coverage compared to both XiO S&S and Monaco VMAT. Mean PTV dose variation remained within 0.5 Gy for XiO and both Monaco TPS techniques. Although global maximum point doses showed variations of up to 1.2 Gy, the differences in maximum doses covering 2% of volumes were negligible. With mean PTV dose variation limited to 0.5 Gy coupled with negligible differences in maximum doses, it was demonstrated that Monaco did not increase CTV coverage by simply producing higher dose plans.

Monaco S&S was significantly superior to both VMAT and XiO for rectal V40Gy, and both Monaco techniques were superior to XiO for V60Gy. Since a study by Iyengar et al. [7] demonstrated the association between rectal dose and late complications, the statistically significant improvements in rectal doses by using Monaco were also clinically significant. Bladder V50Gy was not significantly different between planning systems. All systems provided very low femoral head doses (well within eviQ recommendations), with a small advantage to Monaco VMAT over XiO.

For the patients in this study, Monaco S&S yielded superior results compared to both Monaco VMAT and XiO. A study conducted by Qi et al. [5] concluded that "the use of biological models in treatment planning optimization can generate IMRT plans with significantly improved normal tissue sparing with similar or slightly increased dose heterogeneity in the target." Considering the improvements in OAR doses using Monaco's biological cost functions, confirmed both in this study and in an independent evaluation by Semenenko et al. [8], there may be scope in the future to dose escalate PPRT since both five-year biochemical relapse-free survival and disease-free survival were significantly higher (83% versus 71% ($P = 0.001$) and 94% versus 88% ($P = 0.005$), resp.) in a cohort of patients who received 70 Gy [9]. The biological cost functions of the Monaco TPS can lead to further reductions in OAR doses once target objectives have been met, resulting in a plan that can be better than what was asked for in the IMRT prescription.

In our experience, the visualization and analysis tools of the Monaco TPS have assisted in troubleshooting. In most cases, clinically acceptable plans were achieved in shorter time frames compared to XiO, although this was not formally evaluated. Planning templates developed prior to clinically rolling out the Monaco TPS generally gave excellent results. If plans were not clinically acceptable after the first optimization and segmentation, only relatively minor adjustments were needed to finalize plans. Minor adjustments included shrink margins to control high dose regions (either size of high doses or moving hot spots away from the anterior rectal wall) and segmentation properties to increase the minimum MU per segment, thereby reducing the number of total segments per fraction and daily delivery time.

It is important to note the similarities in the XiO and Monaco prescriptions used. Both had CTV/PTV objectives with minimum and maximum goals (Monaco used the target equivalent uniform dose (EUD) and quadratic overdose cost functions for targets). However, to control dose within the target/s, XiO requires additional planning contours (e.g., expansions and/or contractions) that need to be generated prior to planning. Monaco's shrink margins achieve the same effect without additional contouring. Shrink margins applied to cost functions determine the voxels to which the cost functions apply. Dose-volume rectal constraints were also used; XiO prescriptions had a constraint on the actual rectum and another on a volume created on the posterior one-third of the rectum to reduce dose away from the PTV, while Monaco prescriptions used a shrink margin applied to a parallel cost function to control rectal dose. To control dose to the normal tissue adjacent to the PTV (i.e., patient excluding target volumes), XiO used three PTV expansion contours while the Monaco prescription contained dose constraints on quadratic overdose cost functions with corresponding shrink margins. While both XiO and Monaco prescriptions contained target objectives and OAR dose constraints, Monaco allows alteration of the voxels to which the elements of the prescription apply without the need for additional contouring, saving time and making fine-tuning easier and more efficient.

Templates provide preset values for treatment machine information, isocenter location, calculation parameters, structures and layering order, structure properties, segment shape properties, and prescription information. Creation of templates not only reduces planning times but also provides and maintains greater consistency between planners. Both

XiO and Monaco templates used in this study contained CTV/PTV objectives, as well as constraints on the rectum and normal tissue surrounding the targets. As dose to the bladder was controlled under normal tissue constraints, the bladder structure does not appear in template prescriptions. While templates for both XiO and Monaco provide good starting points for planning, plans using Monaco were closer to be clinically acceptable after initial calculations than for XiO. Monaco templates were created during initial investigations and subsequently applied to other patients to see if one template could provide a class solution for the majority of cases. In most cases, the utilization of templates in Monaco produced plans that were clinically acceptable without alterations. For plans that did not meet our planning criteria first time, only minor adjustments (as previously described) were required to produce plans with improved CTV coverage, greater OAR sparing, and more efficient delivery time (Table 1). The ability to apply a template to define such a vast range of parameters means that once structures have been defined, the template can be applied and optimization can be started in a shorter amount of time. Our experiences showed that templates should be kept simple and contain parameters that achieve a reasonable result in the majority of cases. As well as dose factors, segmentation was also considered in template creation, as superior dosimetry could be achieved but at a cost of a higher number of segments and/or MU, leading to longer delivery times. Template segmentation aims to produce plans that contain a reasonable number of segments and total MU that can be efficiently delivered.

The results following extensive commissioning of Monaco clearly indicated that the Monte Carlo model and algorithm more accurately models the linear accelerator beam dosimetry for nonsegmented static fields. The treatment delivery QA results in this study indicate that after segmentation the overall delivery accuracy of the Monaco plans is marginally better than for the equivalent XiO plans but achieved with significantly less MU and treatment time.

A reduction in occurrence of plan QA failure and necessity to replan further improved efficiency and maximized the use of resources for both planning and physics staff. The VMAT dynamic-leaf model (Monaco V2.03) resulted in a 3–5% cumulative dose discrepancy which was measured during the dosimetry verification QA phase and confirmed by vendor notification; for this reason, QA results for VMAT plans did not form part of this study. The beam models were subsequently revised by the vendor and the dynamic delivery limitation was corrected for later versions of Monaco. There was a small increase in physics QA time required for VMAT compared to Monaco S&S of approximately 15–20 minutes per patient.

Monaco-based S&S delivery beam-on times were lower due to fewer segments and lower total MU. Shorter delivery time reduces the chance of intrafraction movement and therefore increases treatment accuracy since dose uncertainties for both targets and OAR are amplified with increased exposure time [10]. Segment properties were investigated to discern whether adjustments could be made to further reduce the number of segments and therefore reduce treatment time, without compromising target coverage. Initial results with VMAT demonstrated faster delivery times compared to Monaco S&S, though these results were not statistically significant.

As Monaco S&S offered improvements at both planning and treatment levels, and after considering the dose discrepancies observed with VMAT plans generated by Monaco V2.03, VMAT has not been implemented for PPRT. VMAT may offer further time savings in treatment delivery compared to Monaco S&S; however the small added benefit may be outweighed by poorer CTV coverage and higher rectal doses. Utilizing multiple VMAT arcs may improve CTV and OAR sparing; however Monaco v2.03 did not allow bidirectional treatment delivery of multiple arcs, that is, treatment delivery limited to clockwise gantry rotation; a second arc required the gantry to return to the original start position before delivery, leading to an increase in treatment time. As we were assessing quality and efficiency gains, VMAT did not seem feasible with this particular version of Monaco. Further research in this area is warranted since the dose discrepancy in Monaco v2.03 has been rectified and bidirectional delivery is now possible. Sale and Moloney [11] concluded that single- and double-arc VMAT (using Varian treatment planning system version 8.6 (Palo Alto, CA USA)) consistently resulted in favorable or slightly superior dosimetry when compared with static gantry IMRT for prostate cases. Additionally, Davidson et al. [12] found that VMAT resulted in reductions in treatment times with 15–38% fewer MU over IMRT.

5. Conclusion

The dosimetric advantages of IMRT over 3D conformal radiotherapy are well established; Monaco S&S IMRT has further demonstrated statistically significant increases in CTV coverage while reducing rectal doses compared to both XiO S&S IMRT and VMAT in PPRT. Monaco S&S delivery times are comparable to single arc VMAT; both Monaco techniques resulted in significantly faster delivery times than XiO S&S plans. Given the advantages of Monaco S&S IMRT over the other systems, and considering the discussed issues with VMAT v2.03, we have implemented Monaco S&S for all postprostatectomy planning with ongoing plan auditing to assess and refine IMRT planning templates.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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