Can Bladder Late Complications be predicted in Cervical Cancer HDR Brachytherapy?

R. Zakariaee, C. Aquino-Parsons, G. Hamarneh, C. J. Brown, M. Gaudet, P. Lim, I. Spadinger

**Purpose:** Multi-fraction high-dose-rate (HDR) brachytherapy (BT) is an important element in the treatment regimen for locally advanced carcinoma of cervix. While standard treatment planning guidelines have been established for dose-volume-histogram (DVH) based thresholds for the surrounding organs at risk (OAR), there are still high-grade complications observed in these OAR that cannot be explained by the traditional DVH parameters. In our centre, the practice of changing the bladder volume between fractions has been applied with the aim of reducing toxicity by shifting the location of high-dose regions on the bladder from fraction to fraction. In this study, we investigate the effectiveness of this practice, as well as the correlation of bladder toxicity with selected non-dosimetric parameters and bladder neck accumulated dose.

**Materials and Methods:** The treatment planning data for 57 cervical cancer patients treated with five 600 cGy HDR BT sessions were evaluated retrospectively. The bladder outer and inner surfaces were carefully contoured on CT scans for each fraction to create a “bladder wall” structure. The bladder neck was also identified in all scans. The bladder wall contours were registered using a previously validated deformable registration method, and the deformation map was used to locally accumulate the dose contributions from each fraction. Bladder neck accumulated dosimetric parameters ($\text{acBND}_{2\text{cc}}$, $\text{acBND}_{0.5\text{cc}}$, and $\text{acBND}_{0.1\text{cc}}$, i.e. minimum accumulated dose in the volumes of the corresponding size centered on bladder neck) were then calculated. Bladder wall volume (Wvol) and percentage variation in the total volume of the bladder (BlVol%) were also recorded.

Bladder late toxicity was evaluated using LENT-SOMA questionnaires collected from the patients following treatment. Following NCI CTAE guidelines, urinary complications were assessed in terms of dysuria, urgency, frequency, nocturia, incontinence and stream. Overall toxicity grades were calculated by averaging the scores in each category and rounding to the nearest integer (possible range: 0-4). Patients with toxicity grade 2 and higher were categorized as Cases and those with grades of 0-1 as Controls. The differences between Case and Control means were determined for Wvol, BlVol%, $\text{acBND}_{2\text{cc}}$, $\text{acBND}_{0.5\text{cc}}$, and $\text{acBND}_{0.1\text{cc}}$ parameters. The individual grades for dysuria, urgency, incontinence and stream, which were assumed to be indicative of “bladder neck” complications, were also studied independently against the $\text{acBND}_{n\text{cc}}$ parameters.
Results: The final data set consisted of 14 Cases and 43 Controls. The mean BlVol% for the Controls (27.1±2) was significantly higher (p=0.044) than that of the Cases (19.7±4), as expected. The mean Wvol for the Controls (46.6±1 cc) was significantly lower (p=0.042) that that of the Cases (53.3±3 cc). A suggestion of correlation (p=0.090) was found between acBND_{0.1cc} and the overall toxicity grades. Among the individual urinary complications, only incontinence showed significant correlations with acBND_{0.1cc} and acBND_{0.5cc} (p=0.037 and 0.036, respectively), with less significant correlation with acBND_{2cc} (p=0.062).

Conclusions: The results of this study suggest that urinary incontinence after BT for cervical cancer correlates with the total dose to a small volume around the bladder neck. This study also suggests that changing the bladder volume between HDR BT fractions can lead to a measurable improvement in bladder late complications. It was also found that a larger total bladder wall volume, which may indicate a thicker bladder wall, increases the likelihood of bladder toxicity. While the underlying reasons for this effect are yet to be determined, this finding may open up new perspectives for mitigating bladder late side effects in HDR cervix brachytherapy.