Lumbosacral plexus: An unattended organ at risk in irradiation of pelvic malignancies

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y virtue of inverse planning and improved target conformality, intensity-modulated radiation therapy (IMRT) reduces radiation dose to normal organs at risk (OARs) in the vicinity of the target, while allowing delivery of high doses to the tumor and regional lymph nodes. As a result, IMRT can reduce side effects by conforming the dose to avoid normal, uninvolved tissues, which may correlate with an improved toxicity profile.1 Rates of rectal, urinary and hematological toxicities have decreased with the use of this technique.^{2,3} However, dose to OARs that are not contoured remains an area of

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Lumbosacral plexus (LSP) is such an organ that is not routinely contoured for patients undergoing IMRT for pelvic malignancies. This may lead to dose dumping, with higher than expected doses placed in the LSP because it is not specified as an OAR.4 Radiation-induced injury to the LSP (RILSP) in pelvic malignancies is a rare but severely debilitating complication of pelvic irradiation, causing lower limb weakness, numbness and paresthesia. Presentation of RILSP injuries occurs as early as 3 months to several years after radiation completion. While the estimated frequency of RILSP is 0.3% to 1.3%,^{5,6} the true incidence of this complication is under-reported. Neurologic deficits are irreversible and no effective therapy other than supportive care has been found. A standardized method for LSP delineation was devised by Yi et al for patients treated with IMRT for rectal and anal cancers.⁷ In this study, we retrospectively evaluated the dose distribution to the LSP in patients with rectal carcinoma treated with IMRT where no specific dose constraint was used regarding the LSP.

Materials and Methods

Fifteen consecutive patients with rectal cancer who were treated with IMRT at our institute from January 2015 to August 2015 were included in the study. Eligibility criteria were: histologically proven rectal cancer, no evidence of distant metastases, no previous history of pelvic irradiation, and whole-pelvis radiation using IMRT. Patients with uncontrolled diabetes were excluded from the study. LSP was delineated in every patient from the L4-L5 interspace to the level of the sciatic nerve on the planning CT scan of 2 mm slice thickness by the radiation oncologist with the assistance of a radiologist, using the anatomic atlas developed by Yi et al. The LSP was contoured in relation to anatomic landmarks, which included the psoas



FIGURE 1. (A-D) Axial sections of a planning CT scan from the level of the L4 vertebral body to the femoral head, representing the muscles and lumbosacral plexus in relation to the anatomic landmarks.



FIGURE 2. Digitally reconstructed radiograph depicting the lumbosacral plexus.

major, iliacus, piriformis, obturator internus, gluteus maximus muscles, and vertebral bodies and sacral bones.

The axial slices of the planning CT scan of a representative patient at various

levels are shown in Figure 1, and the lumbosacral plexus is digitally reconstructed, as shown in Figure 2. Dose-volume histogram curves were created using a percentage of volume of the LSP receiving 30 Gy, 40 Gy, 50 Gy, 55 Gy and doses received by LSP, as shown in Figure 3. No dose limitation had been placed for this organ during initial treatment planning. After delineation, the dose-volume histogram of each patient was evaluated, and the total LSP volume; mean LSP dose; maximum LSP dose; and percentage of volume receiving 30 Gy, 40 Gy, 50 Gy, and 55 Gy were estimated.

Clinical and disease characteristics of all 15 patients are listed in Table 1. All patients were treated with IMRT on a dual-energy linear accelerator (6 MV and 15 MV) using 9-field dynamic IMRT with beams at 40-degree intervals. Prescribed dose covered 95% of the PTV, ranging from 50.4 to 66.6 Gy in 1.8 to 2 Gy per fraction. All but 2 patients received concurrent chemotherapy in the form of a 5-fluorouracil injection and leucovorin rescue, or oral capecitabine.

Results

As shown in Table 2, the mean LSP volume was 59.84 cc (range: 33-77.7 cc), mean dose to the LSP was 45.5 Gy (range: 39.7-55.5 Gy), and maximum

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FIGURE 3. LSP dose volume histogram of the percentage of volume receiving doses from 30-55 Gy for all 15 patients.

dose to the LSP was 55.67 Gy (range: 36.6-63.8 Gy). Mean volume percentages of the LSP 30 Gy, 40 Gy, 50 Gy, 55 Gy were 84.6%, 78.16%, 55.04% and 0%, respectively. All patients received doses > 50 Gy, and no patient was found to receive > 55 Gy to the LSP.

Discussion

Radiation-induced plexopathies are relatively more common in the form of brachial plexopathies in patients receiving irradiation for breast carcinoma as compared to lumbosacral plexopathies. Increases in total doses and dose per fraction have been associated with heightened risks of radiation-induced brachial plexopathy, and have been seen in breast cancer survivors with a dose of 50 Gy/25 fractions.⁸ Also, there

are concerns about brachial plexopathy while treating unresectable superior sulcus tumors as well as head and neck cancers. Amini et al showed that in patients treated for superior sulcus tumors, a median plexus dose of > 69Gy and a maximum dose of 75 Gy to > 2 cc are strong predictors of plexopathy.9 Fraction size is the single most important predictor of this chronic toxicity and, therefore, SBRT for apical NSCLC also carries a significant risk of brachial plexopathy.¹⁰ Compared to brachial plexopathy, few cases of LSP have been described in the literature. Tolerance to the spinal cord and cauda equina (TD5/5), from which LSP arises, has been estimated at 47 Gy and 60 Gy,11 respectively, for full volume irradiation. Most cases have been described

in patients receiving a combination of external-beam radiation therapy and intracavitary brachytherapy in cervical carcinoma. Higher incidence has been found in patients receiving 70 Gy to 80 Gy to the LSP.¹² Although RILSP is much more common in cervical carcinoma, a few cases have also been seen in patients with lower gastrointestinal malignancies, including rectal and anal cancers. It has also been noted that radiosensitivity of peripheral nerves is increased by concomitant chemotherapy, particularly with taxanes and platinum drugs.¹³ Hence, we must be cautious when using doses of 50 Gy to 60 Gy with concurrent chemotherapy. Although, the exact mechanism is not clear, it is thought to be associated with localized ischemia and subsequent

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| Table 1. Clinicopathological and treatment characteristics | | | | | | | | | | | |
|--|---------|------------|---------------|-------------|-------------------------|--|--|--|--|--|--|
| Serial No. | Age/sex | Stage | | Dose | Concurrent chemotherapy | | | | | | |
| 1 | 70y/M | pT3N0 cM0 | Postoperative | 50.4Gy/28fr | Cap Capecitabine | | | | | | |
| 2 | 61y/M | pT3N2 cM0 | Postoperative | 50.4Gy/28fr | Cap Capecitabine | | | | | | |
| 3 | 37y/M | cT4bN0M0 | Preoperative | 50.4Gy/28fr | Inj Leucovorin + 5FU | | | | | | |
| 4 | 76y/F | cT4N0M0 | Radical | 66.6Gy/37fr | Inj Leucovorin + 5FU | | | | | | |
| 5 | 49y/M | cT2N0M0 | Preoperative | 50.4Gy/28fr | Inj Leucovorin + 5FU | | | | | | |
| 6 | 62y/M | pT3N2b cM0 | Postoperative | 50.4Gy/28fr | Cap Capecitabine | | | | | | |
| 7 | 23y/F | cT3N2aM0 | Preoperative | 50Gy/25fr | Inj Leucovorin + 5FU | | | | | | |
| 8 | 56y/M | pT3N1 cM0 | Postoperative | 50.4Gy/28fr | Cap Capecitabine | | | | | | |
| 9 | 36y/M | cT3N0M0 | Preoperative | 50.4Gy/28fr | Inj Leucovorin + 5FU | | | | | | |
| 10 | 57y/F | pT2N1ccM0 | Postoperative | 50.4Gy/28fr | No | | | | | | |
| 11 | 48y/M | pT3N0 cM0 | Postoperative | 50.4Gy/28fr | Inj Leucovorin + 5FU | | | | | | |
| 12 | 64y/M | pT2N1acM0 | Postoperative | 60Gy/30fr | No | | | | | | |
| 13 | 50y/M | pT3N1 cM0 | Postoperative | 50.4Gy/28fr | Inj Leucovorin + 5FU | | | | | | |
| 14 | 57y/M | cT3N2M0 | Preoperative | 50.4Gy/28fr | Cap Capecitabine | | | | | | |
| 15 | 78y/M | pT3N1M0 | Postoperative | 54Gy/30fr | No | | | | | | |

| Table 2. Dosimetric parameters of lumbosacral plexus | | | | | | | | | | |
|--|------------|-----------|----------|-------|-------|-------|-------|--|--|--|
| Serial No. | LSP volume | Mean dose | Max dose | V30Gy | V40Gy | V50Gy | V55Gy | | | |
| 1 | 77.7 | 41.66 | 53.7 | 79 | 75 | 60 | 0 | | | |
| 2 | 54.3 | 45.25 | 53.68 | 91 | 81 | 53 | 0 | | | |
| 3 | 87 | 47.7 | 53.7 | 94 | 84.6 | 65 | 0 | | | |
| 4 | 60 | 42 | 69 | 81 | 79 | 24 | 0 | | | |
| 5 | 75 | 43 | 55.5 | 82 | 76 | 62 | 0 | | | |
| 6 | 59.3 | 48 | 54.2 | 95 | 89.4 | 70 | 0 | | | |
| 7 | 33 | 44 | 54.2 | 92 | 84 | 33.2 | 0 | | | |
| 8 | 54.4 | 48.4 | 55.1 | 95 | 86.6 | 67 | 0 | | | |
| 9 | 50.3 | 44.8 | 54.55 | 86.5 | 77.8 | 59.6 | 0 | | | |
| 10 | 67.6 | 44.8 | 54 | 87.9 | 79.2 | 61.5 | 0 | | | |
| 11 | 55.8 | 46.5 | 54.4 | 90.6 | 87.6 | 65.9 | 0 | | | |
| 12 | 69.2 | 39.7 | 64 | 66.4 | 64.2 | 60.4 | 0 | | | |
| 13 | 53.9 | 43.2 | 63.8 | 73.8 | 70.8 | 64.8 | 0 | | | |
| 14 | 55.5 | 55.5 | 36.6 | 70.7 | 55.5 | 2.5 | 0 | | | |
| 15 | 44.6 | 48.18 | 58.7 | 84.3 | 81.7 | 77 | 0 | | | |

soft-tissue fibrosis caused by microvascular insufficiency.14 Clinical manifestations include painless weakness in the lower limbs, which is bilateral in 80% of the patients, and paresthesia. Sensory loss occurs in 50% to 75% of the patients. Deep-tendon reflexes are almost always abnormal at the knee and ankle. Distal lower extremities are more frequently affected compared to proximal counterparts. Differential diagnoses to consider are neoplastic lumbosacral plexopathy, diabetic lumbosacral plexopathy, degenerative joint disease, and chemotherapy-induced plexopathy. Because the management of these entities differs, it is important to distinguish the cause. Management of RILSP is difficult and there are no established guidelines. As mentioned, neurological changes are usually irreversible, which underscores the importance of prevention. Principal treatment remains symptomatic and options include pain management with oral opioids, steroids, and local peripheral nerve blocking agents. Other supportive management includes pharmacotherapy in the form of anticoagulants, antiepileptics, tricyclic antidepressants, etc. Hyperbaric oxygen is another management strategy to improve the symptoms of RILSP.15

As we have seen in our study, all patients received doses to the LSP approaching the target dose, because no constraint was placed at the time of planning. This article is an attempt to spread awareness of the need to contour the LSP and prevent dose dumping and formation of hotspots in this structure, thereby minimizing the risk of associated toxicity.

A major drawback of this study is lack of clinical correlation of dose distribution

in LSP and late toxicity. Recruitment of more patients, evaluation of other pelvic malignancies where higher radiation doses are used—either dose escalation in prostate malignancies by external-beam radiation therapy only or a combined use of external-beam radiation therapy and brachytherapy as in gynecologic malignancies—and a further clinical correlation will be the next step to further strengthen this study.

Conclusion

The success of radiation oncology has lengthened patient survival but, in turn, has increased the chances of neurological toxicities. The lack of definitive treatment of these neurological complications is a call to do as much as possible to prevent them. One of the most important prevention strategies is limiting the radiation dose to the structures implicated in the causation of this pathology. A significant step toward this goal is to begin contouring and limiting the dose to the LSP in pelvic malignancies receiving IMRT, and limiting the mean dose to < 45 Gy.

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