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Development of a Standardized Method for Contouring the Lumbosacral Plexus: A Preliminary Dosimetric Analysis of this Organ at Risk Among 15 Patients Treated With Intensity-Modulated Radiotherapy for Lower Gastrointestinal Cancers and the Incidence of Radiation-Induced Lumbosacral Plexopathy

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Summary

Radiation-induced lumbosacral plexopathy is likely an underreported toxicity for patients receiving pelvic radiotherapy. The lumbosacral plexus is not routinely delineated or constrained during intensity-modulated radiotherapy planning, which may lead to excessive dose dumping and rates of toxicity. These are guidelines to assist radiation oncologists in contouring this organ at risk.

Purpose: To generate a reproducible step-wise guideline for the delineation of the lumbosacral plexus (LSP) on axial computed tomography (CT) planning images and to provide a preliminary dosimetric analysis on 15 representative patients with rectal or anal cancers treated with an intensity-modulated radiotherapy (IMRT) technique.

Methods and Materials: A standardized method for contouring the LSP on axial CT images was devised. The LSP was referenced to identifiable anatomic structures from the L4−5 interspace to the level of the sciatic nerve. It was then contoured retrospectively on 15 patients treated with IMRT for rectal or anal cancer. No dose limitations were placed on this organ at risk during initial treatment planning. Dosimetric parameters were evaluated. The incidence of radiation-induced lumbosacral plexopathy (RILSP) was calculated.

Results: Total prescribed dose to 95% of the planned target volume ranged from 50.4 to 59.4 Gy (median 54 Gy). The mean (±standard deviation [SD]) LSP volume for the 15 patients was 100 ± 22 cm^3 (range, 71−138 cm^3). The mean maximal dose to the LSP was 52.6 ± 3.9 Gy (range, 44.5−58.6 Gy). The mean irradiated volumes of the LSP were V40Gy = 58% ± 19%, V50Gy = 22% ± 23%, and V55Gy = 0.5% ± 0.9%. One patient (7%) was found to have developed RILSP at 13 months after treatment.

Conclusions: The true incidence of RILSP in the literature is likely underreported and is not a toxicity commonly assessed by radiation oncologists. In our analysis the LSP commonly

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received doses approaching the prescribed target dose, and 1 patient developed RILSP. Identification of the LSP during IMRT planning may reduce RILSP. We have provided a reproducible method for delineation of the LSP on CT images and a preliminary dosimetric analysis for potential future dose constraints. © 2012 Elsevier Inc.

Keywords: Lumbosacral plexus, Contouring atlas, Radiation-induced lumbosacral plexopathy, Incidence, IMRT

Introduction

The use of intensity-modulated radiotherapy (IMRT) has increased for treatment of many pelvic malignancies, including cervical, prostate, rectal, and anal cancers, and is associated with improved normal tissue avoidance (1). Rates of rectal, urinary (2), and hematologic toxicities (3) have decreased with use of this technique. Concerns of doses to undefined organs at risk (OARs) within unspecified regions of tissue, however, have been raised.

The Advanced Technology Consortium currently mandates OAR contouring instructions for all clinical trials that allow IMRT-based treatment planning. The accurate delineation of all OARs is critical to the success of IMRT for dose avoidance to adjacent normal structures. The lumbosacral plexus (LSP) is not routinely contoured for patients receiving IMRT for pelvic malignancies, nor is it required to be reported on current Phase II protocols evaluating IMRT for the treatment of rectal or anal cancers. This may lead to a problem known as "dose dumping" (4), with higher than expected doses placed in the LSP because it is not specified as an OAR.

Radiation-induced lumbosacral plexopathy (RILSP) has been described in the literature for patients having undergone radiotherapy for pelvic malignancies. The syndrome often presents with symptoms including paresthesias, numbness, dysesthesias, pain, and lower extremity weakness (5). These debilitating symptoms are usually progressive and permanent. Most cases are described in patients treated with both external-beam and intracavitary radiotherapy for cervical cancer (6); however, reports of RILSP in patients treated for lower gastrointestinal malignancies, including rectal and anal cancers, have also been reported (7, 8).

Limiting dose to the LSP with IMRT requires accurate delineation of this OAR during treatment planning. The purpose of this study was to generate a reproducible step-wise guideline for the delineation of this OAR on axial computed tomography (CT) planning images and to provide a preliminary dosimetric analysis on 15 representative patients with rectal or anal cancers treated with an IMRT technique.

Methods and Materials

This study was reviewed and approved by our institutional review board.

Anatomic textbooks and radiologic imaging were reviewed for descriptions of the LSP within the pelvis (9). Magnetic resonance imaging (MRI)-based descriptions were primarily used because CT-based information on the LSP was limited. A board-certified radiologist (W.M.) assisted with identification of the LSP and adjacent structures on axial CT images. The LSP was referenced to identifiable bony and soft tissue landmarks beginning from the L4−5 interspace inferiorly to the level of the sciatic nerve. The referenced structures included the psoas, iliacus, piriformis, obturator internus, and gluteus maximus muscles, the common and internal iliac arteries and veins, and relevant vertebral bodies and sacral bones. The LSP is divided into three portions, referenced to the piriformis muscle: the preplexal (L4, L5, S1), which lies cranial to the piriformis; the plexal segment, which lies anterior to the piriformis; and the postplexal segment (sciatic nerve), which lies caudal to the piriformis and in the greater sciatic foramen (9).

Creating the LSP contouring guidelines was accomplished on reconstructed 1.5-mm-thick sections on contrast-enhanced diagnostic abdominopelvic CT images. A set of step-by-step guidelines for contouring the LSP on noncontrast axial CT images was devised (Table 1) to contour the LSP using a 5-mm-diameter paint tool.

Using these guidelines, the LSP was contoured on 15 representative patients having undergone IMRT treatment for rectal or anal cancer on a TomoTherapy treatment unit (Madison, WI) with total doses prescribed to cover 95% of the planned target volume from 50.4 to 59.4 Gy.

Table 1 Lumbosacral plexus contouring guidelines

1. At the L4 and L5 levels, the entire respective foramina should be included.
2. The L4 root should be contoured by including the space defined by the PM anterior and laterally, and the facet joint/posterior vertebral body elements posteriorly.
3. The L5 root should be contoured using the CIV and PM anteriorly, the IM laterally, and the vertebral body and sacrum posteriorly. Below the level of the L5 foramen, the SI joint should serve as the lateral border as well.
4. Beginning at the level of the S1 foramen, the LSP (L4/L5) and S1 lie in the area bounded by the IVs anteriorly, the IM/SI joint laterally, the sacral ala posteriorly, and medial margin of the S1 foramen medially.
5. Beginning at the level of origin of the Pfm, the LSP should be contoured in the space bounded by the IVs anteriorly, IM/iliac wing laterally, and Pfm posteriorly.
6. At the lower margin of the greater sciatic foramen, contour the space bounded by the OIM/ischial spine anteriorly, Pfm laterally, and GM posteriorly. The medial portion of the OIM should serve as the medial extent.
7. Below the Pfm, contour the space between the OIM anteriorly and the GM posteriorly. The medial and lateral extent should be 1 to 2 cm in length.
8. Contour to the level of the superior most portion of the femoral neck.

Abbreviations: PM = psoas muscle; CIV = common iliac vein; IM = iliacus muscle; SI = sacroiliac; LSP = lumbosacral plexus; IVs = iliac vessels; Pfm = piriformis muscle; OIM = obturator internus muscle; GM = gluteus maximus muscle.

Table 2 Dosimetric parameters

Patient	LSP volume (cm^3)	Maximum LSP dose (Gy)	Average LSP dose (Gy)	V30 (%)	V40 (%)	V50 (%)	V55 (%)	V60 (%)	LSP
1	138	44.5	26.8	62	26	0	0	0	No
2	128	52.3	45.6	87	77	71	0	0	No
3	77	55.3	42.7	86	83	27	2	0	No
4	71	55.2	44.3	89	71	33	0	0	Unclear
5	86	47.3	40.2	87	70	0	0	0	Unclear
6	120	52.5	42.8	93	75	14	0	0	No
7	86	49.7	27.2	48	32	0	0	0	Recurrence
8	89	51.3	38.4	71	66	58	0	0	No
9	91	52.4	37.8	69	59	50	0	0	No
10	90	48.2	24.9	52	36	0	0	0	No
11	128	58.6	41.8	92	68	5	1	0	**Yes**
12	101	52.8	26.6	32	24	16	0	0	No
13	87	54.1	36.8	76	58	12	0	0	No
14	88	58.2	34.6	63	59	28	3	0	No
15	131	55.9	41.8	94	62	12	1	0	Recurrence

Abbreviations: LSP = lumbosacral plexus; Vx (%) = (volume of LSP receiving x dose or greater/total volume of LSP) × 100%.

Original treatment-planning axial CT images, regions of interest, and prescription isodoses were transferred from TomoTherapy treatment-planning software and uploaded into CERR software (St. Louis, MO). No dose limitations were placed on the LSP during initial treatment planning. The LSP volumes were drawn retrospectively according to the guidelines. Various dosimetric parameters were calculated according to conditions prescribed in the initial treatment plan. The LSP volumes, maximum LSP doses, mean LSP doses, and the percentage of volume receiving ≥30, ≥40, ≥50, ≥55, and ≥60 Gy were computed and recorded (Table 2). Dose−volume histogram curves were generated using the percentage of volume receiving ≥30, ≥40, ≥50, ≥55, and ≥60 Gy and doses received by this OAR (Fig. 1).

Results

The proposed guidelines for contouring the LSP are outlined in Table 1. An example of this OAR is shown on noncontrast 3-mm axial CT treatment-planning images from one representative patient in Fig. 2. The LSP contours were successfully created on nonenhanced axial treatment-planning CT images of 15 representative patients utilizing the proposed guidelines. Disease characteristics and treatment courses for all 15 patients are listed in Table 3. Of the 15 patients, 6 were treated for rectal cancers, and 9 were treated for anal cancers. All patients were treated by IMRT on a TomoTherapy treatment unit to total prescribed doses covering 95% of the planned target volume ranging between 50.4 Gy and 59.4 Gy (median 54 Gy) in 1.8-Gy fractions. All patients received concurrent chemotherapy consisting of either a combination of 5-fluorouracil and mitomycin or 5-fluorouracil alone.

The mean (±SD) LSP volume was 100 ± 22 cm^3 (range, 71−138 cm^3). The mean maximal dose to the LSP was 52.6 ± 3.9 Gy (range, 44.5−58.6 Gy) and was >50, >55, and >60 Gy in 73%, 33%, and 0 patients, respectively. The mean average dose to the LSP was 36.8 ± 7.1 Gy. The mean irradiated volumes of the LSP were 73% ± 19% (30 Gy), 58% ± 19% (40 Gy), 22% ± 23% (50 Gy), 0.5% ± 0.9% (55 Gy), and 0 ± 0 (60 Gy). All 15 patients received doses to the LSP in excess of 40 Gy. Seventy-three percent of patients received doses to the LSP in excess of 50 Gy. Twenty-seven percent of patients received doses in excess of 55 Gy. No patients were found to have received ≥60 Gy to the LSP.

Of 15 patients, 1 (Patient 11) was found to have a clinical diagnosis of RILSP at 13 months follow-up. Diagnostic MRI imaging was taken for new-onset burning sensation and low back pain radiating down the right leg. Findings revealed perineural and lumbosacral marrow T2 hyperintensity from L5 through S3 vertebral bodies, with no evidence of tumor recurrence (Fig. 3). The patient was fully evaluated by a board-certified neurologist and excluded for other potential etiologies of lumbosacral plexopathy. Interestingly, this patient was found to have the highest maximal LSP dose (58.6 Gy) among all 15 patients evaluated in this study. This patient was managed with epidural corticosteroid injections, with symptoms gradually improving over the next several years but remaining persistent and impacting overall quality of life.

Two other patients (Patients 7 and 15) were noted to have new-onset lower extremity neurologic complaints at 19 and 33 months after treatment, respectively, and were eventually diagnosed with recurrent disease. Patient 4 developed sudden and persistent

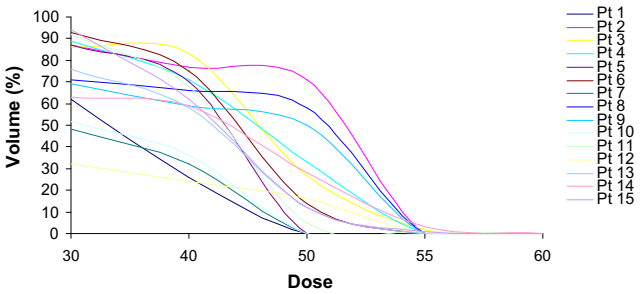

Fig. 1. Lumbosacral plexus (LSP) dose−volume histogram of percentage of volume receiving doses from 30 to 60 Gy shown for all 15 patients contoured for this study. Five patients were found to have very little to no volume of the LSP receiving >50 Gy. Ten patients were found to have LSP volumes receiving ≥50 Gy ranging between 12% and 71%. No patients were found have LSP volumes receiving ≥60 Gy.

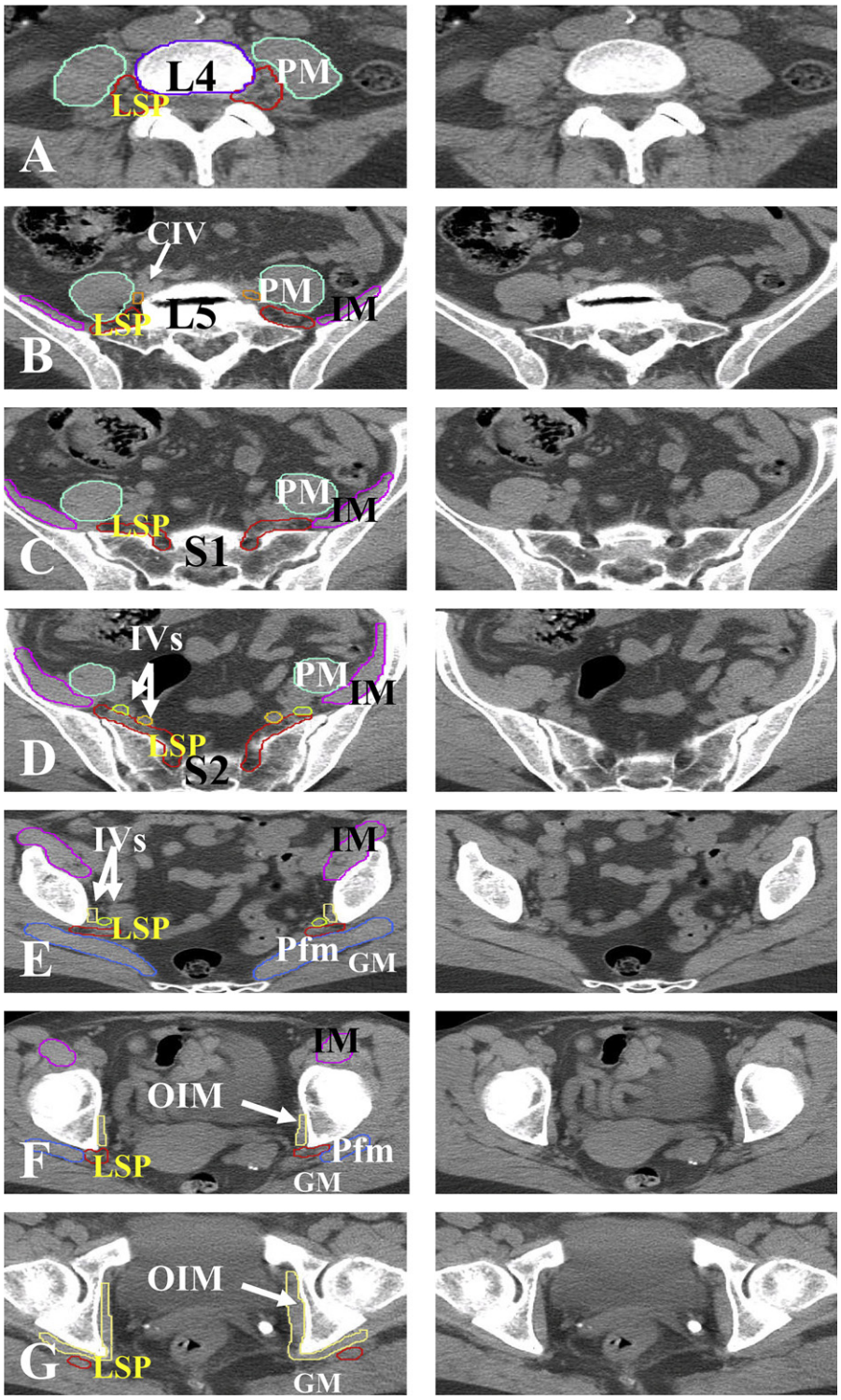

Fig. 2. Axial sections from the L4 vertebral body to the level of femoral neck showing lumbosacral plexus (LSP) contours. (A) L4 vertebral body level. The LSP is bounded by the psoas muscle (PM) anteriorly and laterally, and the L4 vertebral body posteriorly and medially. (B) L5 vertebral body level. The LSP is bounded by the common iliac vein (CIV) anteromedially, PM anteriorly, iliacus muscle (IM) and sacroiliac (SI) joint laterally, posterior vertebral body elements posteriorly, and the vertebral body neural foramina medially. (C) S1 level. The LSP is bounded by the PM anterolaterally, IM laterally, sacral ala posteriorly, and the medial portion of S1 neural foramina medially. (D) S2 level. The LSP is bounded by the iliac vessels (IVs) anteriorly, PM/IM/SI joint laterally, sacral ala posteriorly, and the medial portion of S2 neural foramina medially. (E) Level of superior aspect of piriformis muscle (Pfm). The LSP is bounded by the IVs anteriorly and Pfm posteriorly. (F) Level of ischial spine. The LSP is bounded by the obturator internus muscle (OIM) and ischial spine anteromedially, Pfm laterally, and the gluteus maximus (GM) muscle posteriorly. (G) Level of femoral neck. The LSP is bounded by the lateral portion of OIM anteriorly and GM posteriorly.

Table 3 Tumor, target, treatment course, and time to last follow-up

Patient	Stage	Site	Prescribed dose, total (Gy); fraction (Gy/d)	Concurrent chemotherapy	Time from completion to last follow-up (mo)
1	IIIB (T3N2)	Anal canal	54; 1.8	Yes (5-FU/mitomycin)	27
2	IV (T4NX M1)	Rectal	50.4; 1.8	Yes (5-FU)	11
3	IIIB (T3N2)	Anal canal	54; 1.8	Yes (5-FU/mitomycin)	23
4	IIIB (T3N3)	Anal canal	54; 1.8	Yes (5-FU/mitomycin)	27
5	II (T2N0)	Anal canal	54; 1.8	Yes (5-FU/mitomycin)	24
6	IIIB (T2N2)	Anal canal	54; 1.8	Yes (5-FU/mitomycin)	4
7	IIIA (T1N1)	Anal canal	54; 1.8	Yes (5-FU/mitomycin)	25
8	IIIC (T3N2)	Rectal	50.4; 1.8	Yes (5-FU)	23
9	IIIB (T3N1)	Rectal	50.4; 1.8	Yes (5-FU)	None
10	II (T2N0)	Anal canal	50.4; 1.8	Yes (5-FU/mitomycin)	41
11	II (T2N0)	Anal canal	57; 1.8	Yes (5-FU/mitomycin)	57
12	IIIB (T3N1)	Rectal	50.4; 1.8	Yes (5-FU)	5
13	IV (T4NXM1)	Rectal	59.4; 1.8	Yes (5-FU)	23
14	IIIC (T3N2)	Rectal	55.8; 1.8	Yes (5-FU)	25
15	IIIB (T3N3)	Anal canal	59.4; 1.8	Yes (5-FU/mitomycin)	37

Abbreviation: 5-FU = 5-fluorouracil.

burning dysthesias in the bilateral upper groin and thigh region 1 month after completion of therapy. These symptoms were evaluated by MRI, which demonstrated no evidence of recurrent or persistent disease. Additionally, there were no radiation changes that could unequivocally account for the patient's neurologic symptoms, and thus the diagnosis remains unclear at the time of this study. Patient 5 also developed new-onset left leg pain 22 months after therapy completion. At the time of this study no further radiologic or neurologic workup has been completed.

Discussion

Much of what is understood about radiation-induced toxicity of peripheral nerve plexi has come from experience gained with intraoperative radiotherapy in animal experiments. Radiation-induced peripheral nerve injury is thought to include two phases, including direct effects on neuronal electrophysiology and histochemistry, followed by later fibrotic changes (10).

In humans, radiation-induced plexopathies have best been described in patients having received radiotherapy for the treatment of breast cancer. Increases in both total dose and dose per fraction have been associated with increased rates of developing radiation-induced plexopathy and have been observed in breast cancer survivors having received as little as 50 Gy (11). Our group has previously developed a Radiation Therapy Oncology Group (RTOG)-endorsed brachial plexus contouring atlas to help better identify and avoid this OAR.

Unlike radiation-induced brachial plexopathy, there are very few reports of RILSP described in the literature. The true incidence of RILSP is likely underreported because it is not a toxicity commonly evaluated for by radiation oncologists, and symptoms are often overlooked given the prevalence of lower back pain. Tolerance to the spinal cord and cauda equina (TD 5/5), from which the LSP arises, has been estimated at 47 Gy and 60 Gy, respectively, for full-volume irradiation (12). Most cases have been described in patients receiving radiotherapy with a combination of both external-beam radiotherapy and intracavitary brachytherapy for the treatment of cervical cancer. Of those reported to have developed RILSP, the estimated dose to the LSP has been estimated to fall between 70 and 80 Gy (6). There are also reports of patients developing RILSP after radiotherapy for the treatment of lower gastrointestinal (GI) malignancies, including rectal and anal cancers. The reported cases have described patients treated with concurrent chemoradiotherapy to total doses ranging between 50 and 60 Gy (7, 8). It has been proposed that the radiosensitivity of peripheral nerves is likely enhanced by concomitant chemotherapy and other drugs (13). With radiotherapy doses typically reaching >50 Gy with concomitant chemotherapy in the treatment for rectal, anal, and gynecologic cancers, it is important to consider this late sequela during treatment planning.

Clinical manifestations of RILSP often include an initial presentation of painless weakness, which occurs bilaterally in up to 80% of patients, from 3 months to many years after the completion of radiotherapy, though the median symptom-free interval has been cited at 5 years (14). Pain is initially observed in only approximately 10% of patients but will eventually affect up to 50% of patients (5). Symptoms associated with RILSP

Fig. 3. Representative axial T2-weighted magnetic resonance imaging slice at the S1 vertebral body level with diffuse marrow and perineural foraminal T2 hyperintensity, indicative of radiation-induced edema and fibrosis.

are nonspecific and are often confused with those resulting from age-related processes. It is important to distinguish RILSP from lumbosacral plexopathy due to other causes because management differs for each. Etiologies that must be excluded include those that are due to degenerative joint processes, diabetes-related, chemotherapy-induced, and plexopathy from recurrent tumor. Efforts have been made for radiographic differentiation of radiation- vs. tumor-induced plexopathy by MRI, with T2 hyperintesity changes in immediately adjacent tissues reflecting radiation-induced edema and fibrosis (15). Other tests that may be helpful include positron emission tomography scans and electromyography (16, 17).

The management of RILSP is very difficult and often refractory, which highlights the importance of prevention. Treatment goals include adequate pain control and preservation of remaining neurologic function. Physical therapy, assistance devices for ambulation, and pain management with oral narcotics and local peripheral nerve blocking agents are often used. Other pharmacologic agents that may be helpful include anticoagulants, antiepileptics, tricyclic antidepressants, and corticosteroids. Hyperbaric oxygen has also been reported to improve symptoms of radiation-induced plexopathy (18).

Prior studies have demonstrated reduced dose and toxicity to surrounding normal structures for the treatment of cervical (19), rectal (20), and anal cancers (21) when using IMRT. The role of IMRT is currently being evaluated in two open Phase II clinical trials for the treatment of patients with locally advanced rectal (RTOG 0822) and anal (RTOG 0529) cancers. Neither study requires the LSP to be included in treatment plan submission to the Image-guided Therapy Center and may lead to a problem known as "dose dumping" (4) and allocation of "hot spots" to undefined and unconstrained regions near the treated volumes, potentially leading to excessive doses to the LSP.

Interestingly, our patient with RILSP (Patient 11) was found to have the highest maximal LSP dose (58.6 Gy) among all 15 patients that were evaluated. This illustrates how dose dumping may be an elusive problem in regions that are not clearly delineated during treatment planning. Two other patients had symptoms consistent with the syndrome, making for a 7%−20% incidence among our study group. Among these 3 patients the mean maximal dose to the LSP was 53.7 Gy, and mean average LSP dose was 42.1 Gy, which were higher than the means for the entire cohort.

A major limitation of our study is the small size of our cohort because IMRT for rectal and anal cancers has been recently adopted at our institution. Because no attempt was made to definitively identify dosimetric parameters that increase the risk for RILSP, future studies will be needed to better define this. Another limitation of our study is the limited duration of follow-up for some patients. Thus, with longer follow-up more patients may eventually develop RILSP, given its tendency for late occurrence.

Conclusion

In conclusion, several case reports of RILSP have been described in the literature for patients having undergone pelvic irradiation for lower GI or gynecologic malignancies. The true incidence of this debilitating, permanent, and often refractory sequela is likely underreported. We found at least 1 patient in our small sample having developed this potentially avoidable toxicity. In our cohort the LSP commonly received doses approaching the prescribed target dose. With increasing use of IMRT for treatment of lower GI, gynecologic, and genitourinary malignancies, dose dumping may lead to increased rates of this toxicity if the LSP remains undelineated in future treatment plans. Therefore, we have provided a reproducible step-wise method for accurate delineation of the LSP on radiation treatment-planning CT images.

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