

# Early Effect of External Beam Radiation Therapy on the Anal Sphincter: A Study Using Anal Manometry and Transrectal Ultrasound

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The early effect of pelvic irradiation on the anal sphincter has not been previously investigated. This study prospectively evaluated the acute effect of preoperative radiation on anal function. Twenty patients with rectal carcinoma received 4,500 cGy of preoperative external beam radiation. The field of radiation included the sphincter in 10 patients and was delivered above the anorectal ring in 10 patients. Anal manometry and transrectal ultrasound were performed before and four weeks after radiotherapy. No significant difference in mean maximal squeeze or resting pressure was found after radiation therapy. An increase in mean minimal sensory threshold was significant. Histologic examination revealed minimal radiation changes at the distal margin in 8 of 10 patients who underwent low anterior resection and in 1 of 3 patients who underwent abdominoperineal resection. We conclude that preoperative radiation therapy has minimal immediate effect on the anal sphincter and is not a major contributing factor to postoperative incontinence in patients after sphincter-saving operations for rectal cancer. [Key words: Rectal cancer; Preoperative radiation therapy; Anal manometry; Transrectal ultrasound]

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External pelvic radiation therapy is frequently used in the treatment of rectal cancer and other pelvic malignancies, but the early effect of radiation on the function of the anal sphincter is not known. The majority of patients with rectal cancer at our institution receive external pelvic radiation therapy to facilitate local control of their tumors. Our patients are usually elderly, and the side ef-

fects associated with pelvic irradiation have been minimal. The purpose of this study was to prospectively evaluate the early effect of preoperative high-dose radiation on the anal sphincter. Clinical assessment of anal function and results of anal manometry were compared before and after radiotherapy in patients with rectal cancer above the anal sphincter or within the anal canal. Changes in tumor stage were documented by transrectal ultrasound, and the effect of radiation on the sphincter was documented by histologic examination.

## PATIENTS AND METHODS

Between February and December 1989, 20 consecutive patients (9 men and 11 women) with rectal cancer were prospectively evaluated for early effects of pelvic irradiation on the anal sphincter. The average age was 60.2 (range 43-83) years. Pretreatment evaluation included a thorough medical history and physical examination. All patients underwent double-contrast barium enema or total colonoscopy. Tumor characteristics were assessed by digital examination, proctoscopy, and biopsy. Local tumor invasion was assessed by transrectal ultrasound and pelvic computed tomography; distant metastases were evaluated by chest x-ray and abdominal computed tomography.

All patients had biopsy-proven invasive rectal cancer ranging between 1.0 cm and 5.0 cm in diameter (average, 3.1 cm) and located within 12 cm from the anal verge (average, 7.4 cm). Microscopic examination of the initial biopsy specimen revealed that 1 patient had a well-differentiated tumor, 16 patients had moderately differentiated tumors, and 3 patients had poorly differentiated tumors.

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## Anal Manometry

All patients had anal manometry at the time of diagnosis and four weeks after completion of external beam radiation therapy. The Arndorfer® (Arndorfer Medical Specialists, Greendale, WI) hydraulic capillary perfusion system was used to perfuse a flexible, four-lumen, 140-cm polyvinyl catheter with radially positioned ports located 4 cm from the tip at 90° from one another. The catheter tip was positioned in the rectum above the sphincter with the patient in the left lateral position. The catheter was withdrawn at 1 mm/second using a reverse-gear Harvard pump screw system while constant recordings of pressure changes in each quadrant were made on a Sensor Medics™ #R-611 (Sensomedics, Anaheim, CA) multichannel recorder.

Maximal resting pressure, maximal squeeze pressure, and sphincter length were measured in all four quadrants. Rectoanal inhibitory reflex was evaluated during incremental inflation of a 60-cc latex balloon within the rectal ampulla while recording anal canal resting pressures. Sensory threshold was recorded as the first perception of rectal filling. The patient was asked to expel the air-filled 60-cc rectal balloon in the privacy of a bathroom at the end of the study.

## Radiation Therapy for Rectal Carcinoma

All patients received 4,500 cGy of external beam radiation to the pelvic region delivered in 25 fractions of 180 cGy using an 18-megavolt linear accelerator. Three or four field techniques were utilized. The distal port edge was set at least 5 cm caudad to the inferior margin of the tumor. The treated volume was above the anal canal in 10 patients and included the sphincter in the other 10 patients. Abdominoperineal resection ( $n = 3$ ) or low anterior resection ( $n = 10$ ) was performed in 13 patients after external beam radiation therapy. Endocavitary radiation was added to external radiation to treat seven patients with well-differentiated tumors less than 4 cm in size and limited to the rectal wall on ultrasound. These patients received an additional 6,000 to 9,000 cGy as local treatment to the tumor bed.

## Statistical Analysis

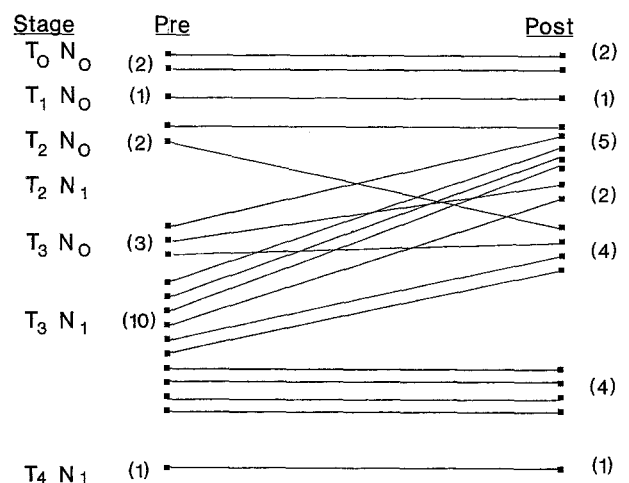
A paired Student's *t*-test was used to compare maximal resting pressure, maximal squeeze pres-

sure, sphincter length, and minimal sensory rectal volume before and after radiation therapy. The rank sum test was also used to confirm significant differences.

## RESULTS

Clinical evaluation before radiation therapy revealed complete anal continence in 17 patients, incontinence to flatus in 1 patient, and incontinence to liquid stools and gas in 2 patients. Radiation therapy did not affect the clinical perception of continence in any patient. Adverse reaction to radiation therapy was mild in most of the patients and included mild bleeding, perianal skin irritation, diarrhea, dysuria, and rectal pain.

The effect of radiation on the tumors was evaluated using transrectal ultrasound after external beam radiation therapy in 19 patients (Fig. 1). Eight patients were downstaged, 1 patient was upstaged, and in 10 patients the stage was not affected. Downstaging was most often due to shrinkage of the tumor. The single upstage on ultrasound was due to an increase in the depth of invasion of the tumor. This patient had no change of stage when pretreatment staging was compared with histologic staging. Histologic staging for the 13 patients who underwent resection revealed a decrease in tumor stage in 8 patients and no change in stage in 5 patients when compared with the pretreatment stage. The 7 patients who were treated with external and endocavitary radiation therapy had no evidence of disease after treatment.



**Figure 1.** Effect of radiation on transrectal ultrasound staging. Transrectal ultrasound staging is compared before and after preoperative radiation therapy. Numbers of patients appear in parentheses.

There was little manometric change in patients in whom the sphincter was spared irradiation (Table 1). A small decrease in resting pressure and squeeze pressure was noted. These changes are not significant, and the mean resting and squeeze pressures remained well within normal limits.

Patients in whom the sphincter was included in the irradiated field had slight decreases in resting pressure and slight increases in squeeze pressure (Table 2). Neither of these changes was statistically significant.

The maximal resting pressures, maximal squeeze pressures, and sphincter lengths for all patients before and after radiation are shown in Table 3.

The mean maximal resting and squeeze pressures were slightly decreased after radiation therapy. The sphincter length was essentially unchanged. The increase in the minimal sensory threshold after radiation, however, was found to be significant. Rectoanal inhibitory reflex was present in all patients who were evaluated before ( $n = 19$ ) and after ( $n = 20$ ) radiation therapy (Table 4). There was no change in the ability to expel a 60-cc rectal balloon following radiation therapy.

The area immediately around the tumor showed mild to moderate radiation effects (submucosal and extramural fibrosis) in all 13 patients who underwent operative therapy. Only mild changes

**Table 1.**  
Anal Manometry: Radiation Field Above Sphincter

	Before Radiation (n = 10)	After Radiation (n = 10)
Maximal resting pressure (mm Hg)	66.25	63.92
Maximal squeeze pressure (mm Hg)	149.62	138.75
Sphincter length (cm)	3.69	3.76

**Table 2.**  
Anal Manometry: Radiation Field Includes Sphincter

	Before Radiation (n = 10)	After Radiation (n = 10)
Maximal resting pressure (mm Hg)	73.25	69.12
Maximal squeeze pressure (mm Hg)	152.25	157.36
Sphincter length (cm)	3.68	3.61

**Table 3.**  
Anal Manometry: All Patients with Rectal Cancer

	Before Radiation (n = 20)	After Radiation (n = 20)
Maximal resting pressure (mm Hg)	69.75	66.52
Maximal squeeze pressure (mm Hg)	150.94	147.56
Sphincter length (cm)	3.68	3.69
Minimal sensory threshold (cc)	20.83	24.75*

\* Difference is significant,  $P < 0.05$  (Student's *t*-test).

**Table 4.**  
Anal Sphincter Function

	Before RT		After RT	
	Above Sphincter (n = 10)	Within Sphincter (n = 10)	Above Sphincter (n = 10)	Within Sphincter (n = 10)
Rectoanal reflex (+/-)	10+	10+	10+	10+
Balloon expulsion (+/-)	7+ (3 ND*)	7+/1- (2 ND)	9+ (1 ND)	8+/1- (1 ND)
Minimal sensory threshold (cc)	17.78	23.88	21.50	28.00

\* ND = not done.

of radiation proctitis (submucosal fibrosis) were seen at the distal resection margin in 8 of the 10 patients who underwent low anterior resection. The sphincter in one of the three patients who underwent abdominoperineal resection showed acute inflammation but no fibrotic changes. The remainder of the patients who underwent operative therapy had minimal to no changes that could be attributed to radiation injury in the distal margin (low anterior resection) or the sphincter (abdominoperineal resection). There was minimal evidence of radiation vasculitis in the areas of the tumors that were usually ulcerated. No evidence of either chronic or acute radiation injury was noted in the distal resection margins of any of the operative specimens.

## DISCUSSION

The standard excisional operations for rectal cancer are associated with high pelvic recurrence rates, which vary according to the stage and grade of the tumor.<sup>1-3</sup> Experience with preoperative adjuvant radiotherapy in the treatment of rectal cancer demonstrates improved local control and possibly improved survival.<sup>4-10</sup> The effect of radiation on lateral margins and local lymph node metastases may be responsible for this finding. The immediate tumor-shrinking effect of external beam radiation therapy was demonstrated in this study by transrectal ultrasound staging (42 percent downstaged) and by operative staging (62 percent downstaged) when compared with staging before radiation therapy. The complete disappearance of the cancer in seven patients after endocavitary treatment also supports this finding. Pelvic irradiation, however, is associated with a variable degree of injury to the rectum and other pelvic organs.<sup>11, 12</sup> The dose of radiation, mode of delivery, and depth of penetration determine the severity of early and late complications.<sup>12</sup> Newer linear accelerators minimize complications by delivering focused doses of radiation with minimal surface and superficial tissue injury.

The early effect of radiation on the function of the rectum and anal sphincter is not known. The acute effect of radiation causes vasodilatation in response to endothelial damage to the small blood vessels.<sup>13</sup> Microscopic features often include epithelial meganucleosis, lack of mitotic activity, and patchy fibroblastic proliferation in the lamina propria.<sup>14</sup>

Manometric evaluation revealed the presence of a rectoanal inhibitory reflex in all patients studied before and after radiation therapy. Therefore, it is unlikely that the neurologic pathway of the internal sphincter is damaged by irradiation in the early phase following treatment. The minimal volume necessary to evoke rectal sensation was greater after radiation therapy compared with pretreatment values. There was no difference between patients with radiation fields above the sphincter and those with portals including the sphincter. This difference was significant only when both groups were analyzed together. This increase in the minimal sensory threshold represents decreased rectal and anal canal sensation immediately following radiotherapy. Edema and inflammation in the mucosa may prevent nerve-ending response to balloon inflation. Pelvic irradiation was also found to be associated with small decreases in maximal resting and squeeze pressures that were not significant. The increased susceptibility of the external sphincter to radiation injury is not explained in the current study. Pudendal nerve latencies may be beneficial to document nerve injury in future studies.

A significant decrease in rectal volume, compliance, resting pressure, and sphincter length has been found to occur in chronic radiation injuries of the rectum.<sup>15, 16</sup> Histologic examination showed damage to the myenteric plexus and smooth muscle hypertrophy. Varma *et al.*<sup>16</sup> assessed the function of anal sphincter activity in 10 patients with symptomatic chronic radiation proctitis resulting from radiotherapy for prostatic carcinoma. A significant decrease in maximal resting pressure and sphincter length with abnormal latency of the rectoanal reflex was found in these patients as compared with healthy volunteers. It will be important to evaluate pudendal nerve function in patients with chronic radiation injury as well.

In the assessment of anal sphincter function, it is important to differentiate the potential injury caused by sphincter-saving operations from that caused by radiation. A low pelvic dissection close to the anorectal ring with primary restoration of bowel continuity may interfere with the function of anal sphincter activity. The anorectal function has been investigated following coloanal sleeve anastomosis for chronic radiation injury to the rectum.<sup>17</sup> Postoperative decreases in maximal resting pressure, compliance, and sphincter length were found when compared with a matched control

group. Maximal squeeze pressure of the external anal sphincter was unaffected. This suggests that only internal sphincter injury should be expected after irradiation. However, no evaluation of the sphincter was made after irradiation but before surgery. Therefore, it is important to be able to document that only minimal injury to the sphincter is caused by external irradiation of the pelvis and to differentiate the effect of radiation from surgical trauma to the sphincter.

### CONCLUSION

The early effect of radiation on anal sphincter function was evaluated in the present study before operative treatment was undertaken. The only significant finding was an increase in the minimal sensory volume detected during inflation of a rectal balloon. There was only slight reduction in resting and squeeze pressures after radiation was directed at the sphincter. Repeat manometry in the group of patients who did not undergo operations may reveal the chronic nature of sphincteric injury caused by external radiation for rectal cancer. Preoperative radiation therapy for rectal cancer has minimal immediate effects on the anal sphincter and should not affect functional outcome after colorectal anastomosis.

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