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A pilot study of silicone tissue expander prosthesis to protect the small bowel during radiation therapy for uterine malignancies

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ABSTRACT

A silicone tissue-expander prosthesis (STEP) connected with a subcutaneously located self-sealing valve system was introduced surgically to displace small bowel outside the treatment volume in order to decrease radiation-induced small bowel injury in 42 patients with a gynecological malignancy before radiation therapy. According to the FIGO classification, there were 13 stage IB, 19 stage IIB, 6 stage IIIB, and 4 stage IVA patients. All patients received external pelvic (n=40) or pelvic and paraaortic (n=2) radiotherapy with a median total dose of 59.4 Gy (range: 45-70.4). Intracavitary brachytherapy was given in 38 patients with a median dose of 30 Gy (range: 10-45). Overall and disease-free survival were 46% and 44%, respectively at 5 years. Acute and late toxicity were graded according to the WHO and RTOG/EORTC classification system, respectively. During external radiotherapy there were 28 patients with G0, 9 with G1 and 5 with G2 gastrointestinal toxicity. During brachytherapy, the same toxicity was G0 in 35 patients, and G1 in 6. At the end of the treatment only 5 patients had G1 gastrointestinal toxicity. No gastrointestinal toxicity was recorded at 3 and 6 months following treatment. Only three patients developed major complications requiring surgery: 2 (one small bowel obstruction and one ileus with abscess) related to STEP and one related to radiation therapy at 32 Gy (mechanical ileus) resulting with surgical correction and application of a STEP to complete her treatment. We conclude that STEP is correlated with very low rates of gastrointestinal toxicity due to major reductions of small bowel quantity within the radiation volume without any major surgical toxicity related to its placement. [Turk J Cancer 2004;34(1):11-18]

KEY WORDS:

Silicone tissue-expander prosthesis, radiotherapy, small bowel toxicity, gynecologic cancer

INTRODUCTION

Radiation therapy (RT) is widely used as a curative treatment in several gynecologic malignancies either as a primary treatment or combined to surgery (1-5). The small bowel is a major dose limiting structure during the course of pelvic radiation, especially when the doses exceed 40-45 Gy. Diarrhea is a common acute side effect encountered after intestinal irradiation in more than 70% of the patients (6,7). Late intestinal radiation toxicity (chronic malabsorption, intestinal obstruction, perforation, fistula) is rare, and

may necessitate surgical correction associated with higher morbidity and mortality (8,9). A recent randomized study of radical surgery versus radiotherapy for early stage cervical cancer showed 5% more ileal obstruction in patients treated with surgery and postoperative radiotherapy versus 1% if radiotherapy is used as the sole treatment modality (10). The aim of the radiation oncologist is to maintain the best therapeutic index in malignant disease and, therefore, avoid serious complications resulting from combined modalities. In collaboration with the Department of Gynecology and Obstetrics, we used a silicone tissue expander prosthesis (STEP) at the time of surgery removing as much as possible small bowel outside the irradiation volume in order to decrease early and late toxicity as well.

This study prospectively assesses the efficacy of tissue expanders implanted at the time of surgery for gynecologic malignancies, and appraises its efficacy in decreasing chronic intestinal toxicity with long time follow-up.

PATIENTS AND METHODS

Between 1990 and 1995, 42 patients with cervical (n=36) or endometrial (n=6) cancer including squamous-cell carcinoma (n=36), adenocarcinoma (n=4) or sarcoma (n=2) were treated. Median age was 48 years (range: 25-70). Forty-one patients underwent surgical placement of a temporary STEP connected with a subcutaneously located self-sealing valve system before RT (it was placed in one patient after mechanical ileus with inflammatory reaction at 32 Gy). This technique allows elimination of the small bowel outside the RT volume, thus, reducing the risks of acute and late small bowel toxicity. The expander is fixed within the pelvis using a vicryl mesh, and filled with 400 ml isotonic saline solution (Figure 1A and 1B). No other surgical procedure was necessary to secure the device in position. Radiation therapy (RT) was administered either exclusively (n=30) or in postoperative (n=12) setting. All patients underwent treatment-planning simulation using oral contrast medium to highlight the amount of small bowel within the radiation fields. Figure 2A, 2B, 3A, and 3B illustrate the simulation radiographies with or without STEP, respectively.

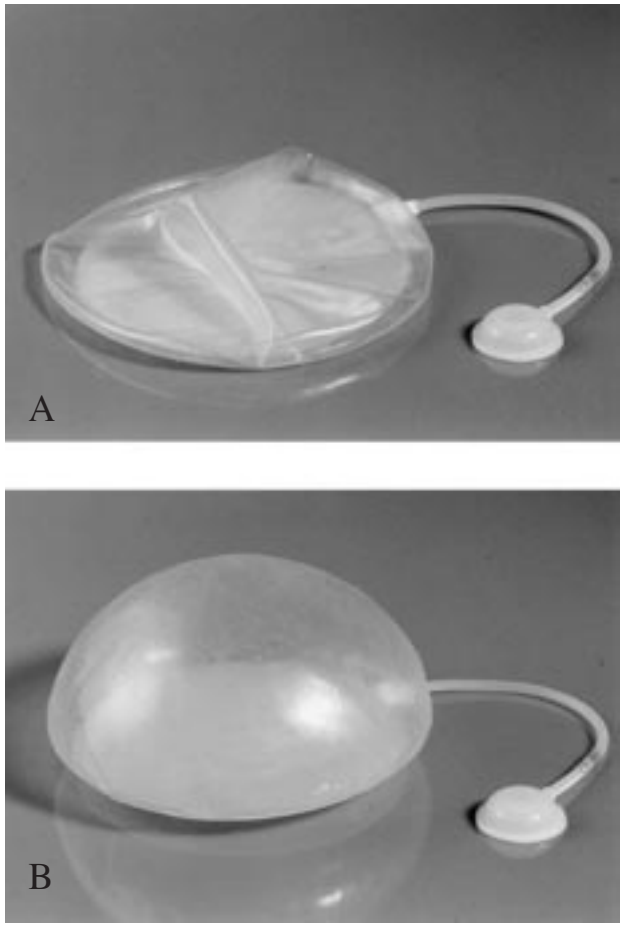

Fig 1 (A,B). Silicone tissue expander. (A): empty, (B): filled with isotonic saline solution

Two patients with local relapse and 40 with newly diagnosed tumors were treated. According to the International Federation of Gynecology and Obstetrics (FIGO) staging system, there were 13 stage IB, 19 stage IIB, 6 stage IIIB, and 4 stage IVA patients. Surgical procedure consisted of staging laparatomy in 19 patients, Wertheim operation in 5, total abdominal hysterectomy (TAH) and bilateral salpingo-oopherectomy (BSO) in 4, BSO in 11, and TAH in 4 (Table 1). Previous surgical history included appendectomy in 8 patients, appendectomy and cholecystectomy in one, hysterectomy in 5, colectomy for benign disease in one, caesarian in one, inguinal hernia in one, and tubal ligation in four patients.

All patients received external pelvic (n=40), or pelvic and paraaortic (n=2) RT with a median total dose of 59.4 (45-70.4) Gy using the standard four-field technique. The median dose per fraction of 2.0 (1.6-2.0) Gy was prescribed at the isocenter according to the ICRU recommendations

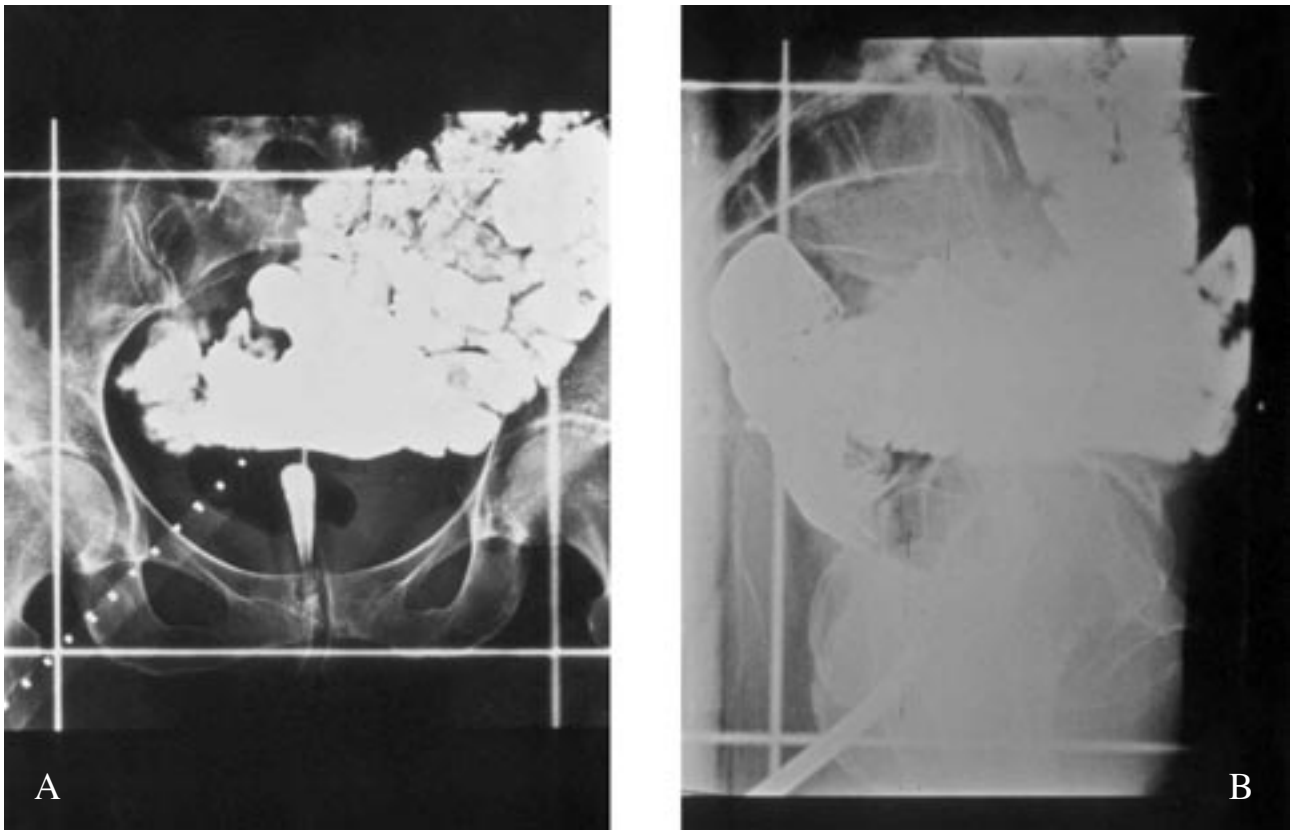

Fig 2 (A,B). Simulation films illustrating the importance of small bowel volume within the irradiation volume. (A): AP/PA fields; (B): lateral fields

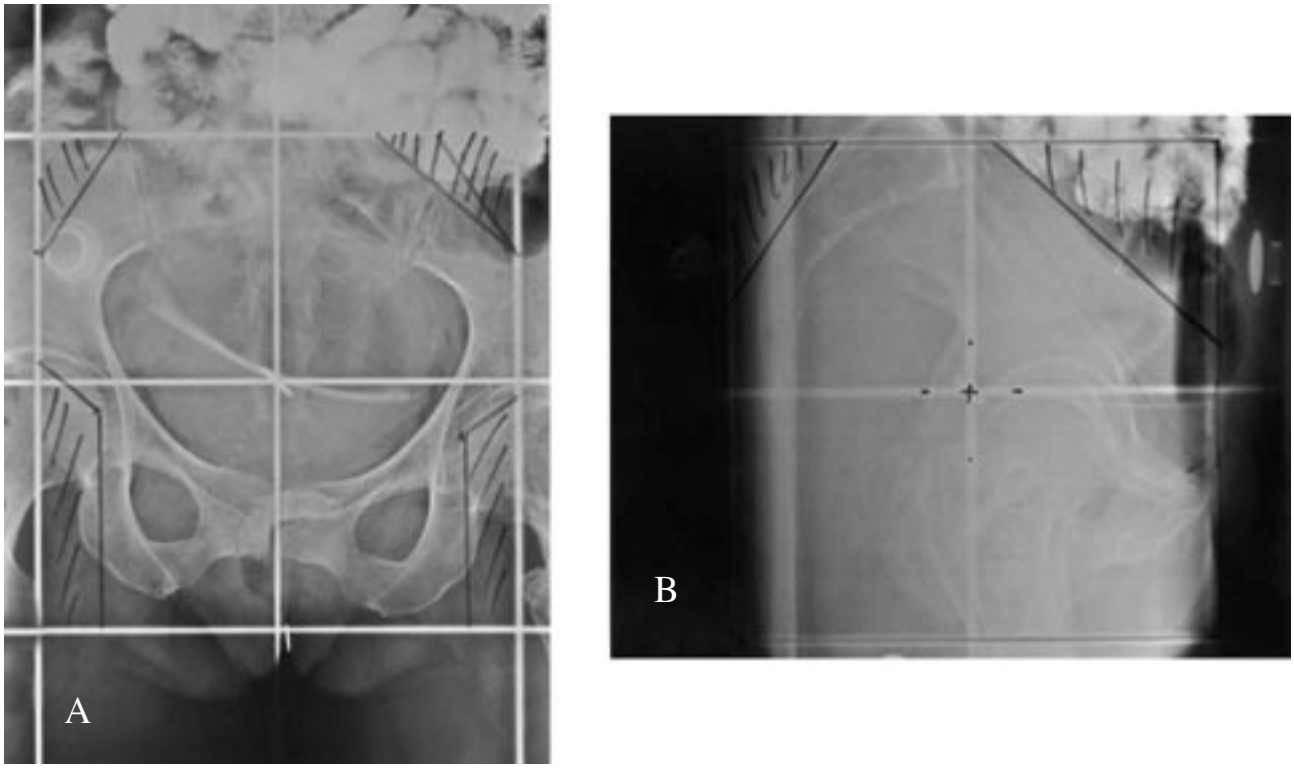

Fig 3 (A,B). Simulation films after introduction of STEP; there is an upward displacement of the small bowel outside the treated volume. (A): AP/PA fields, (B): lateral fields

(11). All patients were treated with at least 6-MV photons from a linear accelerator. STEP does not alter the isodose distribution because its density is similar to the density of human tissues. Six patients included in this study were treated according to a local protocol combining hyperfractionated RT (1.6 Gy/fraction) and cisplatin-based chemotherapy.

lntracavitary brachytherapy boost using a cesium source was given in all but 2 patients with a median dose of 30 (10-45) Gy according to the Manchester system. Brachytherapy was started at the end of external pelvic RT in 33 patients, during external RT in 6, and before external RT in one. Median AP/PA field surface was 270 (164-879) cm^2, and median lateral opposed field surface 204 (159-318)

Table 1
Characteristics of 42 patients

	N	(%)
FIGO-stage		
IB	13	31
IIB	19	45
IIIB	6	14
IVA	4	10
Grade		
1	20	47
2	18	43
3	4	10
Tumor site		
Cervix	36	86
Corpus	6	14
Histology		
Carcinoma	40	95
Sarcoma	2	5
Type of surgery		
LAP	19	45
BSO	11	26
Wertheim	5	12
TAH+BSO	4	10
Previous surgical history		
Appendectomy	8	19
Hysterectomy	5	12
Tubal ligation	4	10
APP+cholecystectomy	1	2
Colectomy	1	2
Caesarean	1	2
Inguinal hernia	1	2

LAP: laparotomy; BSO: bilateral salpingo-oopherectomy; TAH: total abdominal hysterectomy; FIGO: International Federation of Gynecology and Obstetrics; APP: appendectomy

Table 2
Radiation Therapy (RT)

	N	(%)
RT indications		
Exclusive RT	30	71
Postoperative RT	12	29
Type of RT		
Pelvic RT	40	95
Paraaortic RT	2	5
RT technique	**Median**	**Range**
Total dose (Gy)	59.4	45.0 - 70.4
Dose (Gy)/fraction	2.0	1.6 - 3.2
Field surface (cm^2)		
AP/PA	270	164 - 879
Lateral	204	159 - 318
Smal bowel surface (cm^2)		
AP/PA	6	0 - 107
Lateral	0	0 - 2
Brachytherapy dose (Gy)	30	10 - 45

AP/PA: anteroposterior and posteroanterior

cm^2. Median measured small bowel surface was 6 (0-107) cm^2 in the AP/PA fields, and 0 (0-20) cm^2 in the lateral fields (Table 2). The median follow up was 75 months (range: 2-9 years).

RESULTS

As of January 1999, the 5-year overall, and disease-free survivals were 46% and 44%. Acute and late toxicities were graded according to World Health Organization (WHO) and European Organization of Research and Treatment of Cancer/Radiation Therapy and Oncology Group (EORTC/RTOG) criteria, respectively (12). During external RT, there were 28 patients with G0, 9 with G1, and 5 with G2 gastrointestinal system (GIS) toxicity (Table 3). During brachytherapy, GIS toxicity was G0 in 35 patients, and G1 in 6. At the end of the treatment, only 5 patients had G1 GIS toxicity. No GIS toxicity was recorded either at 3 and 6 months following treatment, or until the end of the whole follow-up period. Only three patients developed major complications requiring surgery (none of them had previous surgery): two (one small bowel obstruction and one ileus with abscess) were related to STEP, and one was related to previous surgical interventions and RT (mechanical ileus with inflammatory reaction at 32 Gy) resulting with surgical correction and application of a STEP to complete her treatment.

STEP caused discomfort in two patients necessitating volume reduction of the saline solution.

The surgical removal of the tissue expander under local anesthesia was done immediately following the end of treatment without complications in all patients.

Table 3
Acute and late radiation-related toxicities according to the WHO and RTOG/EORTC scoring systems, respectively

	G0 (%)	G1 (%)	G2 (%)	G3 (%)	G4 (%)
Acute					
Diarrhea	28 (67)	9 (21)	5 (12)	-	-
Skin	-	40 (95)	2 (5)	-	-
Late					
Small bowel	-	-	-	-	2 (5)

WHO classification: grade 0, absence of diarrhea; grade 1, transient diarrhea <2 liquid stools/day; grade 2, tolerable diarrhea >2 liquid stools/day; grade 3, intolerable diarrhea necessitating a specific treatment or cessation of irradiation; grade 4, hemorrhagic diarrhea or dehydratation
EORTC/RTOG: European Organization of Research and Treatment of Cancer/Radiation Therapy and Oncology Group, Grade 4: surgical intervention

DISCUSSION

Radiation therapy is largely used in gynecologic malignancies as a single treatment modality, or combined to surgery with or without chemotherapy (10, 13-20). Following hysterectomy, the small intestine moves into the pelvis. Small intestine being a highly radiosensitive organ in the abdomen and the pelvis and major side effects are observed when RT doses exceed 40-45 Gy (21-23). Acute side effects during RT cause patient discomfort but can also alter therapeutic results by increasing overall treatment time leading to late complications such as chronic radiation enteropathy (24-26). Late intestinal radiation injury is rare, and can result with chronic malabsorption syndrome (partial or complete obstruction, perforation, or fistula). Important acute small bowel toxicity can lead to severe late toxicity, therefore, affecting patient's quality of life. Management of patients with such sequel generally requires surgical correction by experimental hands because of high postoperative morbidity (27).

A number of approaches have been used in order to displace the small intestine outside of the irradiation volume using small bowel contrast during simulation, manoeuvres in displacing small bowel, thiol compounds as radioprotector (30), prostaglandin inhibitors or sucralfat, non surgical methods as patient positioning (prone, supine, decubitus, Trendelenburg), external compression and bladder distension during treatment, and conformal treatment planning using individualized normal-tissue blocks (6, 28-35). Surgical techniques include omental sling, uterine retroversion, use of an absorbable mesh sling or the placement of a removable pelvic spacer (36-38).

The insertion of a STEP into the abdominal cavity to displace small bowel from the pelvic irradiation field has been utilized first by Sugarbaker in the management of advanced or recurrent rectal carcinoma (39). Our technique and initial experience using the same device is reported elsewhere and, to our knowledge, it is the largest prospective series in the gynecologic cancer setting (40,41).

Herbert et al. (42), in their series of 14 patients using STEP, reported acute G1 or G2 GIS toxicity according to the RTOG criteria in 5 patients, and G2 GIS toxicity requiring medication in 4 patients. Another study from the Fox Chase Center using STEP in 34 patients was started in 1989, and published in 1994 (43). In their updated results including 57 patients with gastrointestinal and gynecologic malignancies, they reported overall 16 complications

associated with STEP (abscess in 4 patients, abscess and fistula in 1, fistula after removal of STEP in 4, early STEP withdrawal in 5, fill-port tubing erosion in 1, and capsule mistaken for bladder in 1) (44).

In series without STEP, symptoms of acute GIS toxicity including G2 or G3 diarrhea occur in more than 70% of patients undergoing pelvic irradiation (45,46). In our series, only 5 patients (12%) had G2 acute GIS toxicity confirming the efficiency of STEP in excluding the small intestine outside the treatment volume. Only 2 patients (5%) developed major late toxicity requiring surgery (one small bowel obstruction and one ileus with abscess). The reason for this low rate of late GIS toxicity is probably related to the homogeneity of our series including only gynecologic tumors without major abdominal surgery for GIS tumors compared to other series.

This prospective study demonstrated that the placement of STEP before RT in patients with gynecologic malignancies resulted with decreased irradiated small bowel volume and, therefore, very low rates of acute and late gastrointestinal toxicity.

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