Radiation enteritis: Diagnostic and therapeutic issues

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Summary

Abdominal pelvic radiation therapy can induce acute or chronic lesions in the small bowel wall, called radiation enteritis. Treatment of acute radiation enteritis is essentially symptomatic; symptoms regress when radiation is discontinued. Conversely, late toxicity can occur up to 30 years after discontinuation of radiation therapy, posing diagnostic problems. Approximately one out of five patients treated by radiation therapy will present clinical signs of radiation enteritis, including obstruction, malabsorption, malnutrition and/or other complications. Management should be multidisciplinary, centered mainly on correction of malnutrition. Surgery is indicated in case of complications (*i.e.*, abscess, perforation, fistula) and/or resistance to medical treatment; intestinal resection should be preferred over internal bypass. The main risk in case of iterative resections is the short bowel syndrome and the need for definitive nutritional assistance.

Key words : radiation enteritis, radiotherapy, small bowel iterative resections

List of abbreviations

RT: radiation therapy; **RE**: radiation enteritis;

Key points:

- Complications induced by radiation therapy on the small bowel wall, called radiation enteritis, radiation enteritis (RE)can occur up to 30 years after discontinuation of abdominal pelvic radiation.

- The diagnosis of RE is often established late because the entity is poorly understood, and clinical signs are non-specific. Management is multidisciplinary and based essentially on reversal of malnutrition.

- CT enterography has replaced small bowel follow-through examination for the morphological diagnostic strategy because it establishes a precise cartography of the lesions. Colonoscopy is indicated if colorectal involvement is suspected.

- Surgical treatment is indicated for complications and/or resistance to medical treatment; resection followed by anastomosis in healthy tissue should be preferred over internal bypass

- The development of less invasive irradiation techniques (conformational radiation with intensity modulation) and a better understanding of the natural history of RE should lead to decreased prevalence of RE, but also, shorten the interval to diagnosis, thus limiting the impact on malnutrition.

Introduction

Radiation therapy (RT) is an essential tool in the therapeutic armamentarium for cancers in the abdominal pelvic sphere (gastro-intestinal, urological and gynecological cancers) (1), used alone or associated with chemotherapy and/or surgery. Technical progress and a multidisciplinary approach have contributed to substantial improvement in the prognosis and survival of patients treated for cancer, often providing non-mutilating organ conserving solutions (1). Radio-chemotherapy has been shown to be effective for anal epidermoid cancer and frequently allows to avoid abdomino-perineal rectal resection in the treatment scheme (2).

Notwithstanding, tumor control is dependent on the dose of RT delivered. Consequently, any therapeutic scheme that includes RT must take into account the histology and the localization of the primary tumor, the adjacent anatomical structures, as well as the surgical antecedents that can modify the anatomy (3). This is particularly true for the small bowel whose location can limit the permissible dose of irradiation in patients undergoing abdomino-pelvic RT. The small bowel is extremely radiosensitive, and RT can lead to intestinal wall injury with incapacitating functional sequelae and long-lasting impairment of patient quality of life (4,5). While it has been considered difficult to avoid the consequences of such treatments in the past, the prevention of these sequelae as well as steps taken to improve quality of life of these patients have become a priority for learned societies. As is the case for evaluation of the toxicity of anti-cancer treatments, this priority is attested by the goals of the French Cancer Project 2014-2019. Nonetheless, recognition of the entity « radiation enteritis », as well as its management, remain relatively poorly understood (3,5). The goals of this literature review are to give a detailed explanation of radiation enteritis (RE) by successively examining the risk factors, the pathophysiology, the clinical expression, the medical management and the consequences of surgical treatment.

1. Risk factors for RE

Several elements related to the modalities of RT and/or to the patient predispose to RE.

1.1 Factors related to the modality of RT

The goal of RT, indicated in the management of abdomino-pelvic cancers, is to deliver an optimal dose to the “target volume” while sparing the surrounding healthy tissues as much as possible. According to the type of cancer, the optimal dose in the lesser pelvis ranges from 25 Grays (Gy) in the « Swedish schema» for rectal cancer to 76 Gy for prostate cancers (6,7). The risk of developing RE and its severity are correlated not only to the volume of irradiated small bowel but also to the dose delivered per fraction (8). This intestinal toxicity can be estimated before starting RT thanks to dose-volume histograms. According to Kavanagh et al., the five-year risk of intestinal toxicity is 50% for partial irradiation starting from 50 Gy and for complete irradiation of the small bowels starting from 40 Gy (9). Besides the total dose delivered, the modality of irradiation also constitutes a risk factor. Presently, digital technology and progress in pre-therapeutic imaging allow reconstruction of the tumor volume to be treated and allow conformation of the irradiation beam to the form of the tumor and to optimize dose delivery to the three-dimensional volume (3-D conformational radiation therapy (10,11). As an example, the rate of small bowel obstruction observed after adjuvant radiation therapy (45 Gy) for rectal cancer is six times less with 3-D conformational radiation therapy compared to a two-field technique (10).

More recently, the development of conformational radiation with intensity modulation (CRIM) (**Figures 1 and 2**) produces a better benefit/risk ratio between the dose delivered and at-risk adjacent organs, as shown in a recent Cochrane review (12). Compared to conformational radiation, CRIM decreases the dose delivered to the small bowel to < 30 Gy (**Figure 3**) (13). Nonetheless, in spite of ballistic *remarkable* progress and above all the optimization conveyed by CRIM, it is impossible to treat an abdominal pelvic tumor without injuring the adjacent non-tumoral tissues, particularly, the small intestine.

1.2. Other risk factors

While the toxicity of the irradiation is determined by the total dose delivered, the fractionation, the volume of the at-risk organs included in the irradiation volume, and the consequences of irradiation depend also on intrinsic patient-related factors and to concomitant therapy; these must be taken into consideration when RT is planned.

Combining RT with chemotherapy triples the gastro-intestinal toxicity, notably in the treatment of uterine cervical cancer (14). Likewise, the addition of mitomycin to a regimen of RT and 5-fluorouracil increases late intestinal toxicity by 10 to 26% compared to RT and 5-fluorouracil alone (15). Post-operative RT is much more toxic for the gastro-intestinal tract than neo-adjuvant RT (16). Likewise, previous pelvic surgery modifies the dose-volume parameters for the small bowels and substantially increases the toxicity secondary to RT (17). Patient risk factors (smoking, arterial hypertension, diabetes) (3) or more rarely micro-angiopathies or certain hereditary diseases (ataxia- telangiectasia) can also increase intestinal toxicity. Five-year post-RT intestinal toxicity is increased almost two-fold in diabetics (28% vs. 17%) (18). The role of the acquired immunodeficiency syndrome (AIDS) is currently under debate (19). The presence of chronic inflammatory intestinal disease (IBD) increases the risk of intestinal toxicity with a prevalence ranging from 29 to 46% (20). The presence of systemic collagen vascular diseases such as lupus erythematosus or scleroderma potentiates intestinal toxicity of RT (21). BMI < 18.5 kg/m² and smoking represent risk factors for intestinal toxicity, in particular, for heavy smokers (> 1 pack/d) (22).

In sum, the toxicity of RT on the small bowels not only depends on the characteristics of the irradiation (total dose delivered, fractionation, associated chemotherapy) but also on patient-related factors (co-morbidities, surgical history…).

2. Consequences of abdominal pelvic irradiation

2.1. Pathophysiology of RE

Because of its anatomical situation, the small intestine is at risk during abdominal-pelvic irradiation. The risk is increased when the intestinal loops occupy the place of removed organ(s) after abdominal-pelvic organ resection. This is particularly the case after total hysterectomy for cancer or after proctectomy for rectal cancer, where the intestinal loops fall down into the pelvis (23).

Acute radiotoxicity corresponds to mucosal injury. The normal villous epithelium of the intestine is renewed by non-functional cells, which leads to the loss of the barrier effect, and consequently to abdominal pain and accelerated intestinal transit. Conversely, late radiotoxic effects consist of a combination of submucosal fibrosis and vascular degeneration. This chronic involvement, in particular of the muscular and serosal layers, can be uni- or multisegmental, therefore, staged, involvement (24). The lesions observed in RE are similar

to those observed in chronic inflammatory bowel disease and ischemic enteritis. The main late effect of RT is chronic diarrhea of multifactorial origin (malabsorption, microbial overgrowth, protein-losing enteropathy). To sum up, several pathophysiologic mechanisms lead to chronic intestinal inflammation that can, in turn, induce mucosal ulceration or strictures with perforation, abscess and/or fistula, and possibly cause chronic obstruction and microbial overgrowth (24).

2.2. Clinical signs of RE

Abdomino-pelvic RT results in acute toxicity in nearly 80% of patients and late toxicity in 20% (3-5). This RE is still largely not well recognized among practitioners who consider RE as a secondary manifestation of previous irradiation rather than an ongoing pathologic entity. The more recent entity, grouping together the symptoms of radiation-induced pelvic injury, is called « pelvic radiation disease » (3).

Acute RE

Acute intestinal toxicity includes all toxic involvement occurring within the three months following irradiation, with maximal prevalence between the 4th and 5th week. It associates intestinal functional disorders such as diarrhea, abdominal pain, and weight loss. In case of associated radiation proctitis, bleeding per anum, rectal pain or even episodes of anal incontinence can be observed (25). It may be necessary to modify the RT plan according to the degree of toxicity, as symptoms should resolve after discontinuation (26).

Chronic RE

Late toxicity is less prevalent between 18 and 60 months after irradiation but cases have been reported as early as three months or as late as 30 years (27). Although difficult to determine with precision, the prevalence of chronic RE 10 years after irradiation ranges from 10 to 20% (3,5,28). The most frequently observed symptoms include chronic diarrhea (again multifactorial in origin, *i.e.*, increased propulsive malabsorption of biliary salts and/or microbial overgrowth) (3-5). Diarrhea worsens in case of associated loss of sigmoid-rectal compliance. Obstruction is often similar to the Koenig syndrome observed in Crohn's disease, related to ileal stricture. Because of the delay in diagnosis and long-standing character of symptoms, malabsorption is very frequently observed in RE. Consequently, parenteral nutrition, potentially in a specialized nutritional assistance unit, may be necessary in case of insufficient compensation and/or diagnostic delay. Last, RE can be diagnosed based on findings at emergency operation for complications (*i.e.*, obstruction, abscess, perforations, fistulas) (29). Just as an example, following RT for rectal cancer, obstruction and fistula are observed in 0.8 to 13% and 0.6 to 4.8% of cases, respectively (3-5).

2.3. Imaging in chronic RE

When RE is suspected, imaging is necessary to confirm the diagnosis, to identify the single or multisegmental site of involvement, and to search for a potential complication and/or associated pelvic involvement (colorectal stricture, ureteral dilation) (3-5). Imaging is essential to rule out cancer recurrence, whenever surgical treatment is considered. While colonoscopy is necessary to rule out sigmoid colonic involvement associated with terminal ileal involvement (the most common area of radiation), endoscopic exploration of the small bowel is generally incomplete. Considered the gold standard only twenty years ago, the radiologic small bowel follow-through (SBFT) examination has been replaced in recent years

by CT with oral contrast or even MRI with oral contrast (entero-MRI) (30-32). Indeed, these two investigations provide precise mapping of intestinal involvement (short or long segment, single or multiple strictures, distance between the most distal stricture and the ileocecal valve) and determine its upstream impact, or even detect complications such as fistulas or abscesses (Figures 4A and 4B). IV contrast enhancement along with GI-contrast enteroclysis enhances the contrast between the intestinal wall and the luminal contents while intravenous contrast injection also highlights inflammatory signs within the mesentery (31). Entero-MRI has the advantage over entero-CT scans of being a non-irradiating examination, but it is not widely available (32). Finally, video capsule endoscopy has been described but it must be preceded by a patency type test to be sure the capsule will pass without impacting and causing obstruction.

3. Therapeutic strategies

3-1. Prevention

The main goal is to limit small intestinal injury within the irradiation field. The dose/volume ratio can be adapted thanks to progress in RT and the development of CRIM (12). Nonetheless, irrespective of the irradiation modality, the position of the small intestine can be problematic, especially in case of post-operative enterocele. Some technical tricks have been described to prevent the small bowel from falling into the pelvic cavity such as omentopexy to fill the pelvic space (33), or fixation of the greater omentum to the pelvic brim posteriorly and to the bladder anteriorly. Of note, the thickness or quality of omental tissue may be insufficient and pediculization might create the risk of internal hernia. Or the omentum may simply not be available because of previous surgery. In these cases, mammary implants or « expanders » (**Figures 2 and 3**) have been used; Sugarbaker in the 1980's described their use to exclude the small bowel from the pelvic cavity (34). However, these devices have to be adapted to the pelvic space because vein compression, giving rise to deep venous thrombosis and pulmonary embolism has been reported (35). Another alternative is to use absorbable mesh such as Vicryl® mesh suspended between the pelvic brim and the bladder to form a sort of sling between the abdominal and pelvic cavities, to prevent the descent of the small bowel loops. These meshes can be inserted laparoscopically (36). This type of procedure can be considered in case of elytrocele, previous hysterectomy or enterocele when pre-operative CT scan identifies small bowel in the pelvis.

3-2 Place for medical treatment

3.2.1 Symptomatic treatment

The therapeutic strategy focuses essentially on symptoms, particularly on diarrhea: motility medication in case of dysmotility-related diarrhea, biliary acid chelators to bind bile salts and antibiotics for microbial overgrowth (3-5). Nonetheless, diarrhea is amplified when the sigmoid-rectum is involved, and in this case, treatment of associated radiation proctitis is indicated (25).

3.2.2. Nutritional management

This is an essential component of management of patients with RE, ranging from simple dietetic counseling associated with correction of deficiencies to nutritional supplementation. Home-based parenteral nutrition can be indicated in RE, either

intermittently because of repeated episodes of obstruction responsible for malabsorption and malnutrition, or definitively, in case of intestinal failure related to short gut syndrome after multiple iterative resections (37). Indeed, home-based parenteral nutrition is not exceptional in the adult, and for severe forms, a previous French series reported a 36% 5-year actuarial survival starting at the first consultation (38).

3.2.3. Management of obstruction

Except for complications that require surgery, medical treatment should be privileged, combining nasogastric suction decompression, fluid and electrolyte replacement and parenteral nutrition (3-5). Intravenous steroids seem to potentiate the efficacy of parenteral nutrition over 4-8 weeks. In a small-sample randomized study comparing this association to eight weeks of renutrition alone for RE complicated by chronic partial obstruction or malabsorption, the authors observed the addition of steroids to have a positive effect on clinical and biological nutritional parameters (39). Moreover, in responders, symptomatic recurrence within two years was observed more often in patients who did not receive steroid therapy (39). In sum, the combination of intravenous steroid therapy and parenteral nutrition is more effective and decreases the risk of recurrence.

3.2.4. Place of hyperbaric oxygen therapy

To the best of our knowledge, only two randomized studies have been published on this topic, with discordant results. While one study (HORTIS) reported improvement in fecal incontinence, urgency, and pain in the hyperbaric arm (40), the second, HOT2 blinded study, did not show any significant benefit on gastrointestinal symptoms or quality of life based on validated questionnaires at 3, 6, 9 and 12 months, respectively (41). Of note, the restricted number of hyperbaric oxygen chambers limits the accessibility to this treatment.

3.2.5 Other treatments

With regard to glutamine, an intestinal trophic factor, a recent meta-analysis including 13 randomized trials did not show any significant effect of this treatment on the prevention and treatment of severe RE (42).

In sum, because of the multiplicity and the heterogeneity of symptoms of RE, the progressive worsening of quality of life of these patients, taking into account the usual delay from RT to diagnosis, and the poor understanding of the disease by general practitioners, a multidisciplinary team approach including a gastroenterologist and specialized nurse seems most appropriate, in agreement with the recent decisional algorithm validated by the ORBIT randomized trial (43).

3.3. Place of surgical treatment

3.3.1 Indications and procedures

Surgical management is indicated in complicated and/or severe RE, or cases refractory to medical treatment. This is the case of one third of patients with chronic RE (44).

At the present time, there is no consensus concerning the surgical strategy with regard to intestinal resection or enteric bypass. In the absence of perforation and/or fistula, the indications for resection and bypass are theoretically identical. Nonetheless, the disadvantage of internal bypass, although seemingly simpler and quicker to perform, is that the diseased bowel remains in place with the risk of bleeding, abscess, perforation and bacterial translocation. Taking into account the natural history of RE (multiple lesions, frequent recurrence, iterative resections), extended and/or repeated resections can ultimately lead to a short gut syndrome with intestinal insufficiency; the patient should be informed of this possibility (45).

The older series of surgical treatment for RE reported high morbidity and mortality rates, ranging from 30 to 50% and 10 to 15%, respectively (46,47). However, caution is warranted in the interpretation of the morbidity data in these older series because peri-operative management has evolved radically, particularly, with respect to peri-operative renutrition.

3.3.2. Results

Few surgical series have been published as can be seen in **Table 1** (46-52). In these series, the majority of patients were female, aged between 51 and 60 years old who had undergone irradiation for pelvic cancer. Radiation was performed post-operatively in more than two-thirds of cases, with the dose ranging from 50 to 58 Gy. RE most commonly involved the ileo-cecal region while colorectal involvement was noted in up to 40% of cases. While intestinal obstruction was the main indication for surgery, two series reported emergency operations in 24 and 46% of cases, respectively (**Table 1**). Intestinal resection *via* laparotomy was performed in 60 to 100% of cases (Table 2), but the feasibility of laparoscopy was evaluated in one series (53). Mortality was ≤ 5% in most studies, and the overall morbidity ranged from 22-75% of cases. In the Beaujon Hospital series, three out of four patients experienced complications, the authors' explanation being that half of patients underwent emergency or semi-emergency operation (48). In three series, major post-operative complications (Dindo-Clavien ≥ 3) occurred in 19-29% of the cases and required re-operation in 3-13% of patients. In the multicenter center French Associations for Research Association study, post-operative mortality was significantly higher after emergency operation (11% *vs*. 1%, $p<0.05$) (46). In the literature, the independent risk factors in multivariable analysis were arterial hypertension and blood loss >200ml in the series of Huang *et al*. (51), ASA score ≥3, pre-operative anemia, and peri-operative transfusion in the series of Li *et al*. (50).

Long-term follow-up was evaluated in three series, ranging from 40 to 71 months (Table 2). Although the difference was not statistically significant, survival was superior after intestinal resection compared to internal bypass (71% vs. 51%, ns) in the multicenter French Association for Research study (46). In the Beaujon Hospital experience, survival was significatively influenced by the presence or not of residual tumor at the time of initial surgery (median: 71 versus 24 months, $p=0.001$) (48). Actuarial survival was 97, 78 and 55% at 1, 5 and 10 years, respectively. In multivariable analysis, the risk factors for mortality were age > 60 years at the time of diagnosis of RE, an ASA score > 3, and residual malignancy (54). In patients with two or three of these risk factors, non-surgical treatment should be

privileged, relying on endoscopic tube gastrostomy and parenteral nutrition. In the series from Asia by Chen et al., the risk factors for early death were age > 65 years, residual malignancy at the time of resection, and recurrence less than one year after surgery for RE (54).

3.3.3. Re operation for recurrrence

Because of the natural history of RE, iterative resections can be necessary because of symptoms refractory to medical treatment and/or complications, which occur in between 6 and 61% of patients (**Table 2**). Recurrent obstruction requiring surgery occurs more frequently after conservative treatment compared to initial resection (46,51). In the Beaujon Hospital experience, the prevalence of recurrent obstruction requiring surgery was 37%, 54% and 59%, at 1, 3 and 5 years, respectively (48). In multi-variable analysis, emergency operation, male sex, and anastomotic fistula were independent risk factors for relapse. The only protective factor was initial ileocecal resection (RR: 4.48) (48).

Conversely, extensive first-line intestinal resection can expose the patient to the short gut syndrome and mandate nutritional assistance. Resorting to parenteral nutrition because of intestinal failure is necessary in 12 to 50% of patients (**Table 2**). In the Beaujon Hospital series, the probability of being dependent on parenteral nutrition was 66, 55 and 43% at 1,2 and 3 years, respectively (54). In the RE setting, parenteral nutrition-dependence worsens the prognosis (55). RE is a rare but severe cause of intestinal failure and impacts patient survival. Although the difference was not statistically significant, survival at 1, 5 and 10 years was decreased compared to patients with intestinal failure of another cause (78, 58 and 48% versus 85, 74 and 70%, respectively) (55); of note, none of the deaths were related to a complication of parenteral nutrition.

In summary, surgical treatment of RE is indicated only for complications and/or for intractable disease that is refractory to medical treatment. Compared to internal bypass, intestinal resection with anastomosis in healthy tissues decreases the rate of recurrent obstruction without increasing morbidity. In case of ileo-cecal resection for ileal stricture (the most frequent indication for surgery), ileocolic anastomosis to the transverse colon decreases the risk of anastomotic leakage. Nonetheless, non-surgical treatment has its place in patients with two of the following three criteria (age>60 years, ASA score >3 and unresectable residual tumor), with a preference for endoscopic tube gastrostomy and parenteral nutrition.

Conclusions

RT is part of the therapeutic armamentarium for abdomino-pelvic cancers today but radiation of healthy adjacent tissues, particularly the small intestine, must be minimized. Intestinal toxicity, initially acute, can become chronic after several months or years, and seriously compromise the quality of life of patients. The diagnosis of RE is difficult and requires a multi-disciplinary management plan, based on treatment of symptoms and correction of malnutrition. Surgery is reserved for complications and for intractable disease unrelieved by medical treatment; resection should be preferred over internal bypass (**Figure 5**). While the prognosis of patients with RE has improved greatly, better information to

practitioners and patients should allow optimal management as underscored in the “ORBIT” randomized trial (43).

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Legends to Figures

Figure 1 Dosimetric axial and sagittal slices for anal canal cancer

Axial and sagittal slices corresponding to 3-dimensional conformational radiation with intensity modulation (3D-CRT) (**1A and 1B**) and intensity-modulated radiation therapy (CRIM or IMRT) (**1C and 1D**): the latter decreases small bowel irradiation (circled in red) and bladder (circled in yellow)

PTV = previsional target volume; OGE= external genital organs; Gy=Gray ; OAR=organs at risk
3D = 3-dimensional conformational radiation therapy
IMRT= intensity-modulated radiation therapy

Figure 2: axial and sagittal slices of radiation therapy with conformational radiation with intensity modulation **(CRIM) without (A and C) and with space expander in the Douglas pouch (B and D)**
The expander decreases the irradiation of the small bowel (circled in red).
PTV: previsional target volume

Figure 3: Dose-volume histogram comparing 3-D conformational radiation therapy (3D-CRT) and intensity-modulated radiation therapy (CRIM) **for anal canal cancer without (full line) and with expander (dotted line)**

CRIM and expander decrease the dose delivered to the small bowel, without decreasing the target volume (tumor), or the dose delivered to the small bowel
Example: the small bowel volume irradiated at 45 Gray (V45) is nil with CRIM + expander, versus 38 cc with CRIM alone and 425 cc with 3D-CRT.

PTV = previsional target volume

Figure 4A: Abdomino-pelvic CT scan axial slice: long small bowel stricture 16 years after radiation therapy (white arrow)

Figure 4B: CT scan with injection (axial slice) showing short small bowel stricture 10 years after radiation therapy (white arrow)

Figure 5: Decision tree for management of patients with radiation enteritis

TPN: Total parenteral nutrition, MRI: Magnetic resonance imaging, CT: Computed tomography, NGT: Nasogastric tube

Volume cible/OAR	Objectifs/contraintes	3D	IMRT
PTV	V95(%)	96.7	95.2
grêle	V15Gy (cc)	871	884
	V45Gy (cc)	425	38
vessie		45.8	36.7
Têtes fémorales	Dose moyenne (Gy)	23.8	19.8
OGE		46.9	28.9
Queue de cheval		46.5	23

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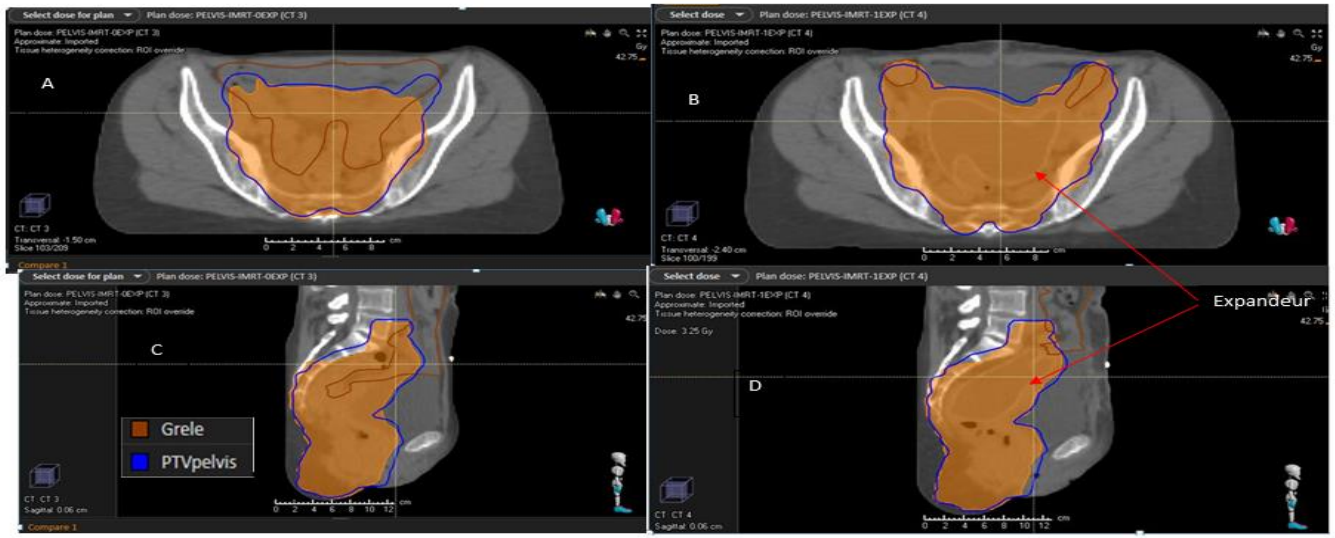

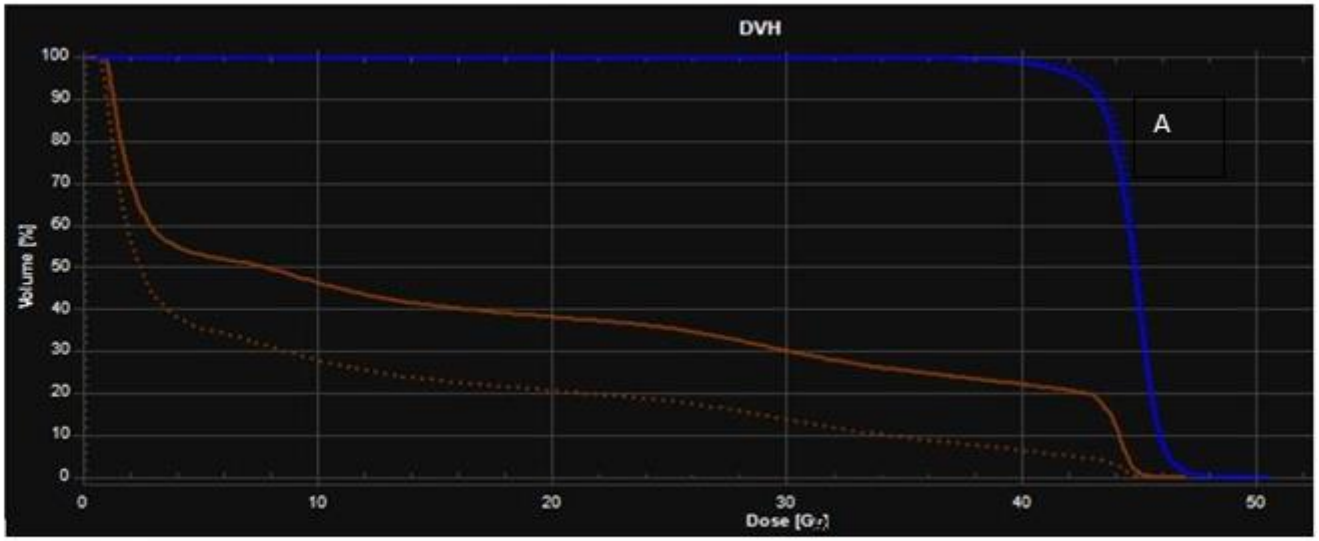

Volume cible/OAR	Objectifs/contraintes	3D	IMRT	B	
			Sans expandeur		avec expandeur
PTV	V95(%)	96.7	95.2		97
grêle	V15Gy (cc)	871	884		434
	V45Gy (cc)	425	38		0

Figure 5

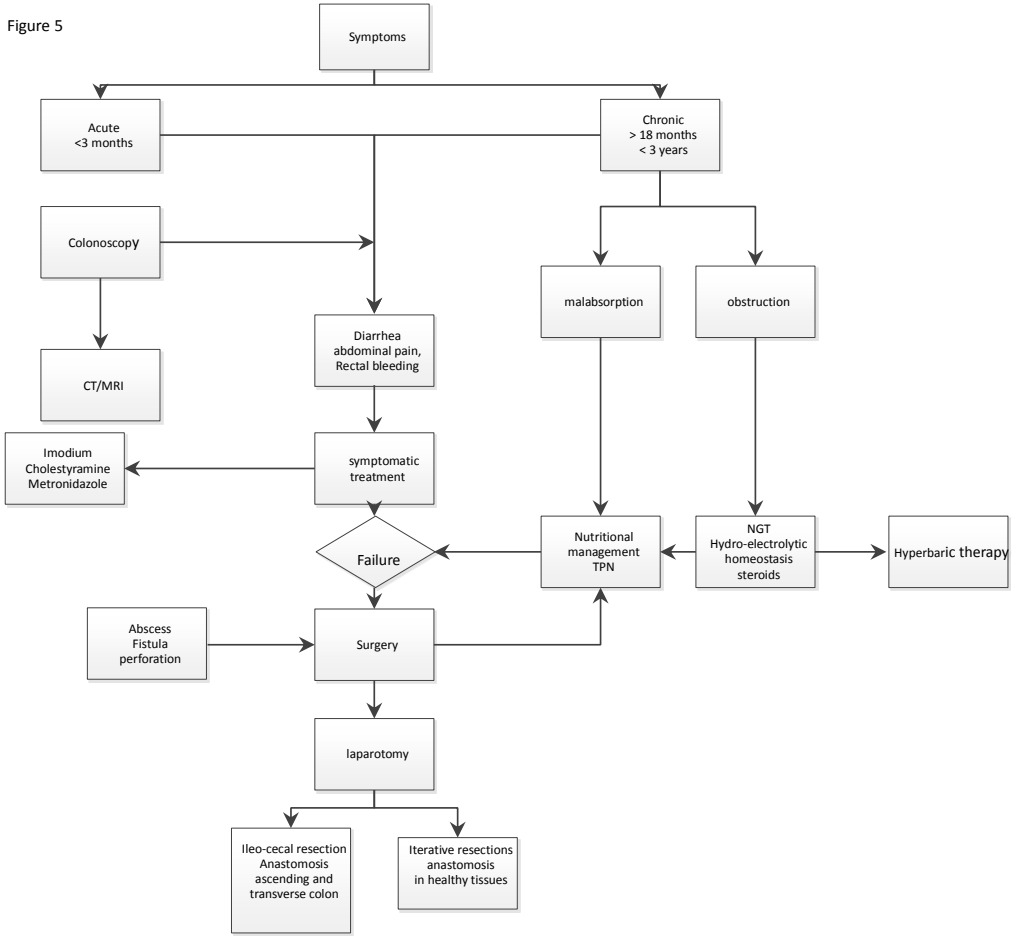
Symptoms
Acute
<3 months
Chronic
> 18 months
< 3 years
Colonoscopy
malabsorption
obstruction
Diarrhea
abdominal pain,
Rectal bleeding
CT/MRI
Imodium
Cholestyramine
Metronidazole
symptomatic
treatment
Failure
Nutritional
management
TPN
NGT
Hydro-electrolytic
homeostasis
steroids
Hyperbaric therapy
Abscess
Fistula
perforation
Surgery
laparotomy
Ileo-cecal resection
Anastomosis
ascending and
transverse colon
Iterative resections
anastomosis
in healthy tissues

Table 1: Review of the literature

Author	Year	N of patients	Type of cancer n(%)			RTT characteristics				Pre-operative nutrition n (%)	Delay between RTT-S	Indication for surgery	
			Gastro-intestinal	Gynecology	urology	Dose	Pre	Post	CTT (%)		months	AIO	Fistula
Regimbeau[46]	2001	109	28(26)	68(62)	8	55+/-17	5	66	14(13)	65(60)		89(82)	8(7)
Onodera[47]	2005	48	2(4)	43(90)	3							39(81)	
Lefevre[48]	2011	107				50(40-115)		98		31(29)	31	82(77)	14(13)
Zhu[49]	2012	156	57(37)	89(57)	10	58+/-16	8	131	86(55)		31+/-49	112(72)	42(27)
Li[50]	2013	158	37(64)	112(73)	4	56+/-16	4	136		60(38)			
Huang [51]	2016	404	105(26)	282(70)	17	52+/-15	7	331	239(59)	350(87)	20+/-35	300(74)	80(20)
Reddy[52]	2018	50	4(8)0	45(90)	1		40	10			8		

N = number; RTT = radiation therapy; pre = pre-operative: post = post-operative CTT: chemotherapy; S = surgery; AIO = acute intestinal obstruction

Table 1 cont'd

author	year	N of patients	Age	M/F n	ASA n (%) II/III/IV	Emergency n (%)	Site of lesions n			
							Ileum/ileocecal	colorectal	diffuse	
Regimbeau[46]	2001	109	59+/-15	20/89		27(25)	51	12	45	
Onodera[47]	2005	48	58.6	5/43						
Zhu[48]	2012	156	51+/-11	52/104			74	6	12	
Lefevre[49]	2011	107	57	13/94	50/52 (46.7/48.5)	50(47)				
Li[50]	2013	158	51	32/126	91/48/8 (57/30.3/)		158		34	
Huang [51]	2016	404	51+/-11	94/310	251/133/20 (62/33/5)		167	24	22	
Reddy[52]	2018			3/47			31			

M/F male/female ; ASA: American Society of Anesthesiologists

Table 2: Review of the literature: short term and long-term outcome for surgery of radiation enteritis

Author	Operative procedure		Length* n (%)	Mortality n (%)	Overall morbidity n (%)	AF n (%)	Re-op n (%)	Mean hospital stay days	Follow-up months	Death n (%)			Reoperation for recurrence n (%)	PN n (%)
	Bypass or stoma	Resection	<150 cm							Total	cancer	Int/ins		
Regimbeau[46]	42	65	21(19)	5 (5)	33 (30)	11 (10)			40+/-52	26(28)	15(16)		40(45)	32(36)
Onodera[47]	9	39		2(4)	10(22)	0			47		12(25)			
Lefevre[48]	24	83		1(1)	80(75)	12(11)	14(13)	21	71	51(48)	19(17)	10(1)	65(61)	53(50)
Zhu[49]	99	35	5(4)		35(26)	8(6)		40+/-28						
Li[50]	0	158	10(6)	3 (2)	90(57)		13 (8)	13	20		19(12)		6(6)	12(12)
Huang[51]	53	351	36 (9)	4 (1)	206 (51)	19(5)	11 (3)	18+/-17	42	25(7)	20(5)	3(1)	22(6)	
Reddy [52]		31	1(3)	5 (16)				14						

AF= anastomotic fistula; ; Re-op =Re-operation; Réc =récidive chirurgicale ; NPT = nutrition parentérale totale ; Ins. Int. = insuffisance intestinale ;
Longueur* = longueur d'intestin grêle restant après chirurgie