

Walter E. Longo  
Vikram Reddy  
Riccardo A. Audisio  
*Editors*

# Modern Management of Cancer of the Rectum

Second Edition

 Springer

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*To Janice, Ashleigh, William  
Mary Frances and Matthew  
And  
Frank, Mary Lou  
Frankie, Peter and Christine*

– Walter E. Longo

*To my wonderful children  
Maya and Alok  
Of whom I am the proudest*

– Vikram B. Reddy

*To Monica for her immense patience*

– Riccardo A. Audisio



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## Foreword

Since the last edition of *Modern Management of Cancer of the Rectum*, there has been great progress in all matters to do with rectal cancer. Much has come from formal systematic prospective clinical research based on evermore refined preoperative staging and changes in management strategies, including developments in chemoradiotherapy and surgery. Genetic analysis has demonstrated that large-bowel cancer is at least three diseases. The blank genetic picture of 30 years ago is gradually being filled in by an extraordinary amount of new information. Preoperative staging has achieved a high degree of accuracy, which can predict the histopathological examination of the excised specimen in most cases. This has changed the management strategy regarding the integration of chemoradiotherapy with surgery, whether major or local. Treatment has been opened up dramatically through chemoradiotherapy as primary treatment, by which patients experiencing a complete response are followed without surgery or undergo local excision at the site of the primary tumour. This approach still needs validation, and there are now several prospective studies examining this question.

There is much focus in the book on the identification of risk factors which determine the cancer-specific outcome of patients with rectal cancer. These include preoperative staging of lymph nodes before and after chemoradiotherapy, which is still one of the most important factors influencing multidisciplinary management. The book deals with all forms of treatment, from that aimed with curative intent to the management of palliative disease. All types of treatment of colorectal cancer are considered, including any form of chemoradiotherapy and the newly applied brachytherapy. The numerous operations for rectal cancer are also dealt with in detail, with equivalence given to local and radical procedures. The growing interest in the treatment of pelvic recurrence and metastatic disease receives considerable attention. There are chapters on follow-up, rare colorectal tumours, revisional surgery and quality of life after treatment. Further chapters include discussion of the technique focussing on restorative resection, lateral-node dissection and laparoscopic, compared with robotic, surgery.

*Modern Management of Cancer of the Rectum* deals with every aspect of rectal cancer. Its overall view is delivered by an internationally recognised panel of experts, all of whom are leaders in their field. The referencing is excellent, supplying a bibliography including classical publications leading on to an invaluable list of modern citations. The book is well laid out, with



excellent tables and illustrations. As a statement of the present position regarding all aspects of rectal cancer, it is an up-to-date account by experts.

London, UK

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## Preface to the Second Edition

The premise of the second edition of *Modern Management of Cancer of the Rectum* is a revision and update of a gradually changing field, in which the surgeon, medical oncologist, and radiation oncologist cannot function without the others. In the 13 years since the last edition, several advances in medical oncology and surgical techniques have changed the management of rectal cancer, and every chapter of this edition reflects these changes, while adding new ones about the burden of disease, relevant anatomy, role of laparoscopy and robotics, anorectal reconstruction, and remedial surgery. We hope that this book will become an important reference material for the newest data regarding rectal cancer and its management. Expert authors from all around the world have dedicated their precious time to create outstanding chapters on all aspects of the management of rectal cancer.

We trust that this book will provide practicing surgeons, surgeons in training, oncologists, radiation oncologists, and all others who diagnose and treat this malignancy with up-to-date information that will ultimately allow for a better management of each of our patients.

In producing this book, we would like to acknowledge our mentors for their inspiration and teaching, our patients who made us want to persevere in our advancements, our students so that they may be better than us, and our families for their support and understanding. We would like to acknowledge our utmost appreciation and gratitude to our authors, to our publishers, and to Joni Fraser at Springer for making this book possible.

New Haven, CT, USA  
New Haven, CT, USA  
St. Helens, UK

Walter E. Longo  
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# The Evolving Treatment of Rectal Cancer

# 1

Jorge L. Reguero and Walter E. Longo

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## Abstract

Rectal cancer treatment has advanced in nearly 300 years from a hopeless, morbid outcome to potentially curative treatments with constant improvement in quality of life. This chapter briefly outlines and reviews the historical evolution of the treatment of adenocarcinoma of the rectum. The earliest procedures were mostly palliative with the first proposed resections for rectal cancer appearing in the eighteenth century. Extirpative procedures utilizing the perineal, vaginal and sacral approaches prevailed until Miles' abdominoperineal resection in 1908 revolutionized the principles for a correct oncological resection. In time, the focus of interest shifted towards less radical procedures centered on the restoration of intestinal continuity. Later on, sphincter preservation procedures and pouch surgery emerged in an attempt to achieve better functional outcomes. Heald's total mesorectal excision proposed in the 1980s represented another milestone in the treatment of rectal cancer by significantly reducing local recurrence rates. Over recent years, combined multimodality therapy and the development of laparoscopic surgery have brought major advancements to the field. In the twenty-first century, the limits of rectal cancer treatment continue to be pushed with surgery still representing the primary form of therapy for optimal oncologic and functional results.

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## Keywords

Rectal cancer • Transsacral • Kraske • Perineal approach • Lockhart-Mummery • Miles • Abdominoperineal • Heald

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## Introduction

The treatment of cancer of the rectum is historically among one of the most debated for years. This has been due to constant technical challenges, the development of novel therapies such as

neoadjuvant therapy, emerging technologies and the concern with quality of life. Many of the surgical advances in surgery have come in conjunction with sentinel milestones in medicine itself such as antisepsis, anesthesia, blood banking, critical care, microscopy, diagnostic imaging, emerging surgical technology, pharmacology, energy delivery and genetics. Regardless, the evolution of rectal cancer treatment has gone from a hopeless, morbid outcome to potentially curative treatments that are very well tolerated, with shorter hospital stays and a favorable quality of life.

The principal form of treatment for rectal cancer early on, as well as today, has been attempted surgical removal of the tumor. Many of the early treatments were unrecorded and it is difficult to give credit to every individual who contributed to the management of this disease. Other treatments evolved simultaneously so an exact chronologic review would be misleading. Once considered an incurable disease, initial attempts at treatment were often palliative, and mortality resulting from the treatment was often close to 100 %, with extremely consequential morbidity.

This chapter will briefly outline and review the historical evolution of the treatment of adenocarcinoma of the rectum. Details of procedures and outcomes of many historical landmarks such as the abdominoperineal resection, restorative procedures, local therapy, minimally invasive, robotic procedures and adjuvant therapy, among others, are found in the subsequent specific chapters contained within this textbook and from the original articles quoted.

---

## Origins of Rectal Cancer Treatment

John of Arderne is credited with first recognizing the signs and symptoms of rectal cancer in 1376 [1]. Although there appeared to be some rudimentary understanding of its natural history, no form of excisional surgery was performed for nearly another 400 years.

The earliest procedures were mostly palliative. Giovanni Morgani first proposed resection of the rectum in the eighteenth century [2].

Treating rectal cancers by some form of extirpative procedure had not been considered until then. In 1739, Jean Faget of France made history by first attempting a rectal resection [3]. He believed to be draining an ischio-rectal abscess but instead a perforated rectal cancer was encountered. Faget resected the rectum, leaving the patient with a sacral anus and a disastrous functional outcome.

The use of colostomy as a diverting procedure has been reported since ancient times and it played an early role in the management of rectal cancer. In 1776, Henry Pillmore of Rouen, France, performed the first colostomy in an adult for an obstructing “annular scirrhus” carcinoma though the patient eventually did not survive [4]. Colostomy achieved an important role when a French surgeon by the name of Amussat urged that it be the routine procedure for obstructing rectal cancer [5].

---

## Early Extirpative Procedures: Perineal, Sacral and Vaginal Approaches

Jacques Lisfranc is credited for performing the first successful excision of a rectal tumor in 1826 [1]. Within 7 years, he performed nine additional perineal or posterior resections, of which five were considered successful [2]. These were performed without anesthesia or hemostasis. The patients were asked to bear down, the rectum was everted and a limited rectal amputation then performed. This would result in an incontinent perineal anus. Most patients would not leave the hospital and succumbed to hemorrhage and sepsis. The pain was unbearable, local recurrence was common and functional outcome dismal.

Anesthesia and antisepsis advances spurred a significant development of new techniques in the following decades. In 1873, Aristide Verneuil modified Lisfranc’s perineal resection and removed the coccyx to allow for better exposure and a more radical excision [6]. The conventional perineal approach had resulted in poor exposure of the upper rectum up to that point. In 1876, Theodore Kocher pioneered the transsacral

resection with coccygectomy to excise the rectum and anastomose the colon to the anus [3, 7]. Around the same time, Paul Kraske had developed his own technique to remove the rectum, which he presented in 1885 at the Congress of the German Society of Surgery [1, 2]. He removed the coccyx and part of the left wing of the sacrum and preserved the anus and sphincters to allow for a potential anastomosis. Restoring intestinal continuity via the sacral approach was often problematic due to tension on the upper segment and inadequate blood supply. In general, the perineal and sacral approaches provided limited exposure, precluding radical resection of the tumors.

Others experimented with transvaginal resection of rectal tumors. These techniques are, at present, of historical value. Norton reported in 1889 the excision of a tumor of the anterior rectal wall not involving the vagina. The sphincter muscles were resected along with the rectum. In 1890, MacArthur was unable to mobilize the bowel enough to bring it to the skin while operating on a patient with recurrent rectal cancer. He, therefore, sutured it to the upper vagina. Byford reported in 1896 a singular method in which the vagina was used to replace the excised portion of the rectum. The proximal and distal portions were sutured to different portions of the vagina and the vaginal opening was closed [8].

Nearly 100 years after Lisfranc initial perineal resection, Lockhart-Mummery from St Mark's Hospital in London revised the technique so it would allow for a relatively safer operation [9]. He would first perform a permanent loop colostomy and determine if the tumor was resectable. A week to 10 days later the perineal stage would take place. Removal of the coccyx with the patient in semi-prone position would allow for rectal and anal mobilization; the peritoneum was then opened and as much bowel as possible was pulled down and resected. In 1926, he reported a series of 200 patients in which an 8.5 % mortality was noted, much lower than that of the abdominoperineal resection at the time. A 50 %, 5-year survival without recurrence was observed, though it is said that he rejected about 50 % of his cases that were deemed unresectable [8, 9].

This posterior excision, as it was called, remained popular until the 1940s. The main drawback was that it left the superior lymphatics unresected; therefore, it was not an adequate cancer operation nor was it applicable for upper rectal tumors.

A small variant of the sacral resection, the York-Mason modification of the Kraske procedure, has been used to resect small distal rectal tumors through a presacral approach [10]. This technique of dividing and subsequently restoring the anal sphincter is rarely used anymore and has been replaced by either transanal procedures or ultralow resections with coloanal anastomosis.

---

## Emergence of the Abdominoperineal Resection

Early attempts at abdominal resection of tumors were experimental and performed with little attention to oncological principles. Carl Gussenbauer, an assistant to Billroth, performed the first abdominal resection of a rectal tumor with intraperitoneal closure of the distal rectum [11]. The first reported case combining abdominal and perineal approaches was performed by Vincenz Czerny in Germany [9]. In 1884, he was unable to remove a rectal cancer using a posterior perineal approach alone and decided to complete the extirpation through the abdomen by turning his patient supine. In 1904, Charles Mayo [8] first presented his technique of abdominoperineal resection (APR) at a meeting in Portland, Oregon, stressing the importance of resecting the lymphatics above the rectum, as high as the sacral promontory. The sigmoid colon was divided at that level and the inferior mesenteric artery transected as high as possible.

The problem of local recurrence was evident among surgeons at the time, including Sir William Ernest Miles. He had been a pupil of Harrison Cripps, who was well known for his work on rectal cancer and the introduction of the perineal approach in England [2, 7]. Miles had witnessed local recurrences within the pelvis in 54 of 57 of his patients excised by this mean [12]. He analyzed postmortem dissections and realized a more radical excision was needed, based on a

better and new understanding of the perirectal lymphatic spread.

In 1908, Miles described a modification of Czerny's operation and emphasized the downward, upward, and lateral spreads of the cancer, with the upward being the most important in his opinion [13, 14]. He considered even the most talented surgeons were unable to completely excise the mesorectal lymph nodes proximal to the tumor via the perineal approach. His operation started by creating a loop colostomy and dividing the bowel 2 in. below it. The distal bowel was mobilized until it could be pushed down into the pelvis and the peritoneum could be closed over it. The patient was then positioned in the right semi-prone position, the coccyx resected and the excision completed from the perineal approach. The procedure was based on five principles including resection of the rectosigmoid and its blood supply, resection of the mesorectum, removal of lymph nodes over the bifurcation of the common iliac artery, wide perineal resection including removal of the levator ani muscle and creation of an abdominal colostomy. Although his original series of 12 patients found 42 % mortality [14], seven survivors were tumor free in 1 year. In subsequent years, he was able to further reduce the mortality associated with the procedure as well as the overall recurrence rate, making the APR the standard of care for rectal tumors. Miles not only revolutionized the principles for a correct oncological resection of rectal cancers, but his approach was a landmark operation in the history of large bowel surgery.

The English pathologist Cuthbert Dukes published in 1930 that there was no significant difference between perineal and abdominoperineal operations for Stages A and B rectal cancer (negative lymph nodes, invasion into or through the bowel wall respectively); but the Miles operation was superior for Stage C (lymph node positives), because the perineal approach would leave the superior lymphatics unresected. This finding validated Miles pathologic premises [12, 15].

Several modifications of the abdominoperineal procedure popularized by Miles emerged in the following years. In 1915, Daniel Fiske Jones proposed a two-stage procedure consisting of an

initial abdominal portion followed by a perineal stage 5–7 days later under spinal anesthesia [1]. Jones considered this would decrease sepsis and he reported a mortality of 18 % in 16 patients. Gabriel, a disciple of Lockhart-Mummery, proposed in 1934 a further modification of the APR designated as a perineoabdominal excision [16]. He performed a one-stage procedure starting with a perineal excision, then turning the patient supine and mobilizing the colon through an abdominal incision. Gabriel demonstrated a significant improvement in 5-year survival figures, 30 % vs 17.9 %, for those patients found to have positive lymph nodes via a perineoabdominal excision versus the perineal approach favored by his mentor.

As others emphasized the safety of a two-stage procedure, it was not until 1938 that the one-stage procedure originally described by Miles became commonplace. There was no longer the need to reposition the patient after Sir Hugh Devine introduced the adjustable leg rests in 1937, so the operation could be performed in the lithotomy-Trendelenburg position [2]. Oswald Lloyd Davies was the first to perform a synchronous combined radical abdominoperineal resection in the lithotomy-Trendelenburg position with two teams working simultaneously [1, 2]. The speed and efficiency of the procedure vastly improved with the two-team approach. By the 1960s, the Lloyd Davies technique was the most commonly performed excisional procedure for rectal cancer with a marked reduction in mortality.

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## Advent of Restorative Procedures

With Miles' operation and principles of resection well established, the focus of interest shifted towards new procedures centered on the restoration of intestinal continuity. The abdominoperineal resection was not only considered too radical by some surgeons but it submitted patients to a permanent colostomy and frequent genitourinary dysfunction.

Some of these techniques had originated in the late nineteenth century. The first documented

attempt at restoration of intestinal continuity for rectal cancer is attributed to Reybard of Lyon when he performed a partial sigmoid resection for a colonic growth with immediate anastomosis of the ends [17]. In 1888, the “Durchzug” procedure (pull-through technique) was described by Hochenegg, in which the anorectal stump was everted, stripped of its mucosa and returned to its natural position followed by the distal colon drawn through the denuded rectum and sutured to the anal verge [7]. Despite achieving bowel continuity, this technique was not widely accepted due to the high mortality resulting from anastomotic leaks.

In 1892, Widenham Maunsell of New Zealand described a method for anastomosing the sigmoid colon to the anus [1, 17]. After dividing the anal sphincters in the posterior midline, the rectosigmoid was mobilized through the abdomen and invaginated out through the expanded anus. The tumor was resected and the two ends of the bowel anastomosed. Robert Weir, from Columbia University, New York, later modified this technique in 1901 [8]. Weir mobilized the rectosigmoid through the abdomen in similar fashion; but in contrast to Maunsell, he transected it 3 in. from the anus and pulled out the lower rectum from the perineum using an assistant. The upper bowel was dragged down through the lumen of the exteriorized everted rectum and anastomosed to it.

Babcock and Bacon offered a new procedure in 1939 and 1945 respectively, the delayed union and amputation technique, that basically involved removing the lining of the anal canal and bringing down the mobilized colon through it, leaving about 50 cm outside the body [9]. The previously divided anal sphincters were then sutured to the protruding colon and the excess intestine was removed after 2–3 weeks. With the temporary perineal colostomy, a proximal diversion was unnecessary. Bacon reported lower incidence of male impotence and fecal incontinence than with the APR, and yet similar cancer specific survival rates [9, 15]. In 1961, Turnbull and Cuthbertson from the Cleveland Clinic described their technique, a two-stage abdominoanal pull-through procedure [15, 17]. The rectum was resected, the colon pulled out through the everted rectal stump

and the rectum sutured to the seromuscular layer of the protruding colon. Ten days later, and to the patient’s relief, the bowel was finally excised above the dentate line and the end-to-end anastomoses performed.

During the second half of the twentieth century, restoration of intestinal continuity by means of primary anastomosis evolved through the abdominosacral resection championed by Localio [18]. He placed the patient in the right lateral position with the hips flexed, thus avoiding the need for repositioning between the abdominal and sacral portions of the procedure. The abdominal incision was made above the left inguinal ligament, the resection was completed from the sacral approach and a primary anastomosis performed with a 4–5 cm distal stump [8, 18].

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## Sphincter Preservation and Pouch Surgery

Many surgeons were in disagreement with Miles’ oncologic principle regarding downward lymphatic spread as an important pathway for rectal cancer propagation. By preserving the sphincters a radical downward resection could be avoided and therefore better functional outcomes would be achieved.

In 1910, the American surgeon Donald Balfour described a technique of anterior resection through an abdominal approach with the construction of an end-to-end anastomosis between the rectum and the sigmoid colon [2, 8]. In this setting he utilized a “tube support” for the anastomosis after accidentally injuring the sigmoid colon during a procedure. He later suggested his operation could have a role in cancer resections. This technique never gained widespread acceptance due to the high mortality rate related to anastomotic leaks.

The French surgeon Henri Hartmann offered an alternative operation for the treatment of cancer of the middle to upper rectum. In 1921 he described an anterior resection without end anastomosis for high rectal lesions [3]. After resecting the involved segment and its mesentery, the rectum was inverted and left in place.

This procedure succeeded in removing the tumor with establishment of a colostomy and avoided the perineal dissection. It was associated with less blood loss and lower mortality than the abdominoperineal resection. The main disadvantage was the necessity of a permanent colostomy. The Hartmann's resection is frequently applied today in the initial management of complicated sigmoid diverticulitis.

Experience with sphincter preservation multiplied after surgeons returned to practice from World War II. In 1948 Claude Dixon of the Mayo Clinic shifted the focus of rectal cancer surgery from the abdominoperineal resection to sphincter sparing procedures with the reintroduction of the anterior resection [7, 19]. The safety of his approach was confirmed when he reported the results of 400 patients with a mortality rate of 2.6 % and a 5-year survival of 64 %. His operation was designed either as a three-stage procedure when a colostomy was created before resection or as a two-stage procedure with a colostomy created at the time of resection and a hand-sewn anastomosis, using one row of sutures posteriorly and two rows anteriorly. Anterior resection came to be accepted as the standard of care for cancer of the upper and middle third of the rectum, although this approach was not applicable for cancers of the lower third (distal 5 cm). Experience with proximal rectal cancers led to the use of this technique on more distal tumors. The low anterior resection (LAR) was distinguished from high resections by an extraperitoneal rectal anastomosis and was initially associated with more complications.

One of the biggest developments in the evolution of sphincter-saving procedures was a better understanding of distal margins of tumor resection. In 1951, Goligher, Dukes and Bussey had established a safe oncological margin of 5 cm [2, 15]. Interestingly, only 2 % of tumors in 1,500 specimens reviewed spread more than 2 cm. This "safe margin" was quickly challenged in 1953 when Quer proposed a 2.5 cm distal margin after discovering spread greater than 1.5 cm in only one of 89 specimens [2]. Pollett and Nichols found further evidence for a safe distal margin of 2 cm [20]. They published in 1983 the analysis of

334 rectal cancer specimens with different distal margins of <2 cm, 2–5 cm and >5 cm, where they discovered no survival difference over 5 years. The knowledge that distal margins of 2 cm did not compromise survival or local control provided the rationale for further developments in surgical technique in the late 1970s. This permitted sphincter preservation for tumors of the distal rectum that did not invade the anal sphincter mechanism. In more recent years, Moore analyzed patients undergoing a restorative procedure with distal margins <1 cm or >1 cm and found no difference in oncologic outcome [21].

In 1972, Sir Alan Parks described an important modification of the pull-through technique that allowed for sphincter preservation even in low-lying tumors without compromising oncologic results [22]. The entire rectum was mobilized in a low anterior or abdominoperineal resection, and the colon was anastomosed to the anorectum through the dilated anal canal, avoiding the potentially damaging eversion required in previous pull-through procedures. In his series, all 76 patients underwent restoration of bowel continuity, ten patients developed pelvic sepsis but there were no deaths and only 50 % reported good functional outcomes [23].

The development of surgical staplers constituted another breakthrough for sphincter preservation surgery. In 1975, Fain first described his experience with the Soviet designed circular stapling apparatus for rectal cancer anastomosis [24]. Mark Ravitch, an American pediatric surgeon, capitalized on this finding and introduced circular stapling devices in the United States, facilitating technical success of low pelvic anastomosis [9]. In 1977, the circular stapler enabled the creation of low colorectal or coloanal anastomosis without increased leak rates when compared to hand-sewn anastomosis [15].

Furthermore, to avoid a colostomy in surgery for very low rectal cancer, intersphincteric resection (ISR) with coloanal anastomosis was developed in the 1980s. This procedure includes removing all or part of the internal sphincter and restoring bowel continuity for rectal cancers involving or located next to the anal canal [9]. Due to the catastrophic potential consequences of



anastomotic leak in these low anastomoses, especially in the setting of an irradiated field, a defunctioning stoma is performed in most cases. A recent systematic review of the technique revealed acceptable oncologic outcomes but often-imperfect functional results [25].

One of the main drawbacks to the low colorectal or coloanal anastomosis that were being performed with increasing frequency was the poor functional outcome, with fecal urgency, soiling and incontinence following the loss of the rectal reservoir. In 1986, Lazorthes and Parc proposed the creation of a colonic reservoir combined with the coloanal anastomosis to compensate for the loss of reservoir in the neorectum [26, 27]. The colonic J-pouch showed short and long term functional improvements over straight anastomosis and fewer anastomotic leaks. Fazio [28] championed the coloplasty as an alternative to colonic J-pouch reservoir in an effort to improve reservoir capacity and decrease morbidity, especially in the setting of inadequate colonic length, diverticular disease or when the colonic J-pouch would not fit into a narrow pelvis. Pouch surgery has continued to evolve to present times with standardization of technical aspects and refinements in construction to achieve better functional outcomes.

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## **Total Mesorectal Excision and Autonomic Nerve Preservation**

From the establishment of the anterior resection by Dixon in the 1940s to the 1970s, the blunt or manual presacral pelvic dissection for rectal cancer constituted the technique of choice. This type of dissection risked violation of the mesorectum along undefined planes, leaving residual cancer-containing mesorectum within the pelvis. Worldwide, 5-year survival rates of only 45–50 % for all curable stages were reported at the time and local recurrence rates of 30–40 % were expected [12].

Quirke revealed on his study that more than a quarter of specimens had positive lateral wall margins with 85 % developing local pelvic recurrence [29]. It was Quirke, in 1986, who brought

forward the importance of lateral tumor spread of primary rectal cancer. He also identified the fact that inadequate circumferential resection margin led to the development of locally recurrent rectal cancer and was associated with poor survival. This brought to the forefront the importance of sharp dissection in the pelvis, replacing the conventional resection technique of blunt dissection.

Heald recognized that the midline hindgut (rectum) and its mesorectum were embryologically derived together [30]. In 1982, he introduced the concept of “total mesorectal excision” (TME) technique, which involved sharp en bloc resection of the tumor and mesorectal tissue to the level of the levator muscles. Later, Hida supported with his work the rationale for TME by demonstrating that the principal field of lymphatic spread is contained within the mesorectum [31]. He confirmed the fact that rectal cancer is a disease of the supralelevator compartment and that Miles’ cylindrical concept was wrong. The TME technique by sharp dissection in the avascular plane between the mesorectum and surrounding tissues reduced the risk of excessive blood loss, decreased local recurrences from 12 to 20 % to less than 4 % and allowed for ultralow resections with coloanal anastomosis [32]. Heald achieved disease-free survival rates of 80 and 78 % at 5 and 10 years respectively. The TME technique continued to be easily reproduced with similar survival rates; it has relegated the radical APR to very few patients, representing another milestone in the treatment of rectal cancer [15].

Now that cure rates had increased and disease free survival was on the rise, the focus of attention shifted towards improving quality of life for patients after treatment. Damage to the pelvic autonomic nerves was felt to be inevitable part of the radical surgery for rectal cancer. In Japan, Tsuchiya, Hojo and Moriya pioneered the concept of nerve identification and preservation [2, 7]. New resection techniques allowed preservation of the hypogastric nerves, inferior hypogastric plexus and pelvic splanchnic nerves and with that, preservation of the autonomic innervation of the urogenital organs. Postoperative sexual and urinary dysfunctions

were subsequently reduced from more than 50 % to 10–28 % [15]. In America, Warren Enker combined the nerve preserving principle with the TME technique resulting in intact urogenital function in 90 % of patients with intact oncologic results [7]. Moriya demonstrated on his Dutch series of 47 patients how nerve preservation did not compromise the radical nature of mesorectal excision [33].

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## Combined Multimodality Therapy

Since the early 1900s, radiation therapy (RT) has had a major role in the treatment of rectal cancer. In 1914, Symonds first reported the use of radium bromide in a patient with rectal cancer achieving complete regression of the tumor [7, 12]. For the next 60 years postoperative pelvic RT was used mainly as a mean to decrease the incidence of pelvic recurrence over surgery alone, but did not show any improvement in overall survival [15]. George Binkley, the first Chief of the Rectal Service at Memorial Sloan-Kettering Cancer Center, introduced multimodality RT in the 1920s. Originally intended for non-surgical candidates, significant tumor regression was observed in patients receiving radiation that went on to have resection, prompting Binkley to recognize the value of radiation as an adjuvant treatment [12]. It was precisely at Memorial Sloan-Kettering where Stearns, Deddish and Quan observed that resected, lymph node positive patients with preoperative RT, had a higher 5-year survival than patients without preoperative radiation concluding that preoperative radiation would be useful in patients with locally advanced rectal cancer. The past few years have confirmed that preoperative RT should be the standard in rectal cancer, based on several large trials. In 2001, the Dutch Colorectal Cancer Group showed significantly better local recurrence rates for RT plus TME versus TME alone, 2.4 and 8.2 % respectively [34]. Overall survivals at 2 years were not different. Preoperative RT has since been shown to downstage and reduce the

bulk of the primary tumor, rendering sphincter saving procedures possible [15].

In 2004, Sauer, from the German Rectal Cancer Study Group, compared preoperative and postoperative chemoradiation therapy in locally advanced rectal cancer patients, showing improved local control with less toxicity in the preoperative group [35]. It is precisely the use of combined modality therapies (CMT) in recent years that has achieved the greatest reduction in local failure when compared to RT alone (50 %), and improvement in survival rates (10 %) [15]. Neoadjuvant chemoradiation treatment has improved sphincter conservation and in conjunction with TME offers a reduction in the incidence of local recurrence; but this occurs at the expense of long-term compromise of sexual and bowel function outcomes. Multimodality treatment of rectal cancer, with the combination of radiation therapy, chemotherapy, and surgery has become the preferred approach to locally advanced rectal cancer.

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## Other Forms of Therapy: Local Treatments and Transanal Excision

Transanal excision through an operating proctoscope or by dilating the anus and using retractors has been advocated by surgeons for the occasional small, exophytic, movable and well-differentiated lesion [17]. However, in the first half of the twentieth century, local treatment of rectal cancers was really a necessity spurred by the high mortality of the extirpative procedures in vogue.

Concerns about seeding viable tumor cells prompted electrocoagulation to be the preferred treatment. Strauss advocated electrocoagulation in 1935 for palliation in poor-risk patients with carcinoma of the rectum, and in those patients with extensive lesions, although his indications were gradually broadened to include almost all stages of carcinoma of the rectum [8]. His results appeared to have little impact until Madden and Kandalaf, and subsequently Crile and Turnbull

reported more favorable outcomes in 1967 and 1972 respectively [17].

Cryosurgery has been utilized by Gage and Fritsch for palliation of symptoms in patients with inoperable rectal cancers. Disadvantages of this technique include hemorrhage, discharge of necrotic tissue and malodorous secretions. Endocavitary radiation was championed by Papillon in 1973 as an alternative to surgery for potentially curable lesions [15]. It involved delivery of high radiation doses using a special device inserted through a large diameter proctoscope. Total dose was anywhere from 8,000 to 15,000 rads over a 4–10 week period at a dose of 1,000–2,000 rads per session. These were highly selected patients who met with a 70 % 5-year cure and 10–15 % local recurrence rate [17].

Local excision is an alternative, less invasive approach to early rectal cancer; but, from the oncologic standpoint, it results in closer resection margins and it does not allow for sampling of lymph nodes [36]. Adequate methods of local staging utilizing either intrarectal ultrasound or pelvic MRI have allowed a small group of patients with distal rectal tumors to be candidates for a transanal local excision. Emerging technology allowing improved exposure has made transanal approaches more feasible. Transanal endoscopic microsurgery (TEM) was first introduced in 1983, allowing for resection of adenomas and early rectal carcinomas not suitable for local or colonoscopic excision, and that would otherwise require major surgery [37]. It permitted full-thickness excision and closure of the rectal defect of lesions as proximal as the pelvic brim. There is still much controversy about the long-term results and indications.

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## The Emergence of Minimally Invasive Procedures

Over the past 20 years, the development of laparoscopic surgery brought a major advancement in the treatment of colorectal cancer. Laparoscopic surgery of the colon was first reported in 1991

[38]. At present, its benefit to patients with colon cancer has been well established by numerous randomized studies. The procedure results in earlier recovery of bowel function, reduced blood loss, less postoperative pain and decreased length of hospitalization when compared to open colectomy. Despite this success in colon cancer treatment, the use of laparoscopic resection requires careful consideration to oncologic principles and functional outcomes. Also, the consequences of conversion to an open procedure need to be considered. The United Kingdom Medical Research Council trial of conventional versus laparoscopic assisted surgery in colorectal cancer (CLASSIC) reported a conversion rate of 34 % in rectal cancer surgery with comparable complication rates and no difference in 3 year overall survival, disease free survival and recurrence rates [39].

With laparoscopic surgery for colon cancer recognized as oncologically equivalent to conventional open surgery, could the same be said of laparoscopic surgery for rectal cancer? One of the major concerns is whether or not a good total mesorectal excision can be achieved. With the information provided on laparoscopic rectal cancer surgery from various centers, a few large multicenter trials have been initiated. In the United States, the American College of Surgeons Oncology Group trial (ACOSOG-Z6051) is a phase III prospective randomized trial comparing laparoscopic assisted resection with open resection for rectal cancer. The trial began in August 2008 is currently nearing completion. A second major randomized trial, the COLOR II, is conducted in Europe [40]. Current evidence suggests that laparoscopic rectal cancer resection benefits patients with earlier return of bowel function, reduced blood loss and shorter hospital stay. There is little data to make any conclusions on the effect of laparoscopic resection for rectal cancer on genitourinary function. In general, laparoscopic rectal cancer resection is now considered safe and feasible but only experienced, trained surgeons should practice it. Robotic-assisted surgery for rectal cancer has demonstrated good short term and midterm outcomes; this technique

has been performed with acceptable morbidity and a low rate of positive circumferential resection margin with effective local control.

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## Surgery for Locally Recurrent Disease

Though the incidence of loco-regional recurrence after primary resection has been substantially reduced with optimized surgery and adjuvant therapy, local failure rates are still significant. It is common knowledge that the choice of surgical therapy for salvage of these patients depends on the initial procedure performed as well as the location of the tumor. If initially a restorative procedure was performed, an APR is often required; a re-restorative procedure could be possible but often frowned upon.

In current series, about half of recurrences are limited to the pelvis, thus a significant number of patients can be considered for curative re-excision. Involvement of both anterior and posterior pelvic structures is usually managed by pelvic exenteration, first described by Brunschwig in the 1960s [41]. His results were characterized by high mortality and poor survival. Involvement of the sacrum requires a more radical procedure such as the abdominosacral resection popularized as a two-stage procedure by Wanebo [42]. Today, because of routine use of neoadjuvant therapy, the understanding of the principles of TME and optimized surgery, local recurrence rates have substantially decreased. Over the last 20 years, especially with the ability of intraoperative radiotherapy, survival has improved and morbidity is less, though the operations remain technically challenging.

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## Future Perspectives

In the twenty-first century, the limits of rectal cancer treatment continue to be pushed. Rectum saving therapy, avoiding the morbidity associated with major resection treatment, has been touted. Chemoradiation utilized in the preoperative setting was readily accepted and moreover,

refinement in techniques of energy delivery, and improvements in chemo-sensitizers resulted in an increased number of “complete responders”. As some of these patients may be looking at a large pelvic procedure with no residual tumor in the specimen, Habr-Gamma aimed to omit surgery completely from rectal cancer treatment [43]. Her series, as well as others’, showed promising results; however, long-term data is not complete.

The practice of robotic rectal cancer resection is on the rise. Efforts are directed to further investigate its role in long-term outcomes.

Although recurrent rectal cancer is somewhat less frequent than in the past, future techniques to salvage patients both following minimal access and radical procedures will be an important hurdle. It is apparent today that personalized medicine and genomics will be a large part of medical care. As the genetics of those likely to respond or not to various therapies continues to be elucidated, surgeons will need to collaborate with geneticists, radiation oncologists and medical oncologists in a multidisciplinary fashion. Until proven otherwise, surgery will continue to be the primary form of therapy for optimal oncologic and functional results. Fortunately, the goals of complete removal of the tumor with anal sphincter preservation, decreased treatment morbidity with relatively normal postoperative bowel and pelvic function and high curative rates have been met.

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