

# Conservative alternatives to radical surgery for favorable rectal cancers



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## Introduction

Early stage rectal cancers have an excellent cure rate after radical, extirpative surgery. However there can be substantial morbidity. The lowest lying lesions, of course require an abdominoperineal resection. In addition, even when a low anterior resection can be performed, there is a substantial risk of injury, including loss of sexual function and impaired bowel or bladder function. For this reason conservative alternatives to full surgery have been considered. These are best suited for small, clinically favorable tumors. If the lesion is small enough, the primary tumor can be adequately addressed by either a limited surgical procedure or high doses of carefully confined radiation while still preserving good function. With appropriate selection criteria, the risk of subclinical disease elsewhere in the pelvis is low enough to be controlled with either no regional treatment or with moderate dose pelvic radiation in place of radical surgery.

Two approaches to the primary tumor are well established in the literature (1-12). The first is surgical, consisting of local excision of the primary cancer. The tumor is removed in one piece, usually by an en bloc procedure that takes the full thickness of the wall of the rectum. The non-surgical alternative addresses a similarly confined volume and involves high doses of low energy radiation directed to the rectal cancer. This approach, referred to as endocavitary radiation, was first popularized over two decades ago by Papillon (10) in France and subsequently by Sischy (12, 16) in the United States.

## Abstract

*Selected cases of favorable rectal cancer can be treated with less than radical surgery. The literature demonstrates that excellent local control can be achieved using either local excision or carefully confined high dose radiation to treat the primary tumor site. Two treatments to the tumor site appear equally effective: local excision (usually a full thickness en bloc procedure) or low energy (50 kVp) endocavitary radiation. For many patients treated conservatively there is also a role for external beam radiation to the pelvis which treats subclinical disease in regional nodes and around the tumor bed. The locoregional control for T1 lesions is excellent. For T2 lesions about 15% of patients can experience recurrence after conservative treatment. Close follow up of these patients is important, since local failures after conservative treatment are more amenable to salvage surgery than failures after standard radical surgery. Careful selection of cases, using endorectal ultrasound or MRI whenever possible, is important. The incidence of unexpected T3 disease or tumor at the margin of resection has been reported as high as 40% in series that do not utilize endorectal T staging.*

**Key words:** Rectal neoplasms, radiotherapy, surgery, combined modality therapy.

## Riassunto

**TERAPIE CONSERVATIVE, ALTERNATIVE ALLA CHIRURGIA RADICALE NEI TUMORI DEL RETTO A PROGNOSI FAVOREVOLE**

*In pazienti selezionati, affetti da carcinoma rettale con caratteristiche prognostiche favorevoli, è possibile eseguire modalità di trattamento chirurgico meno estese di quelli tradizionali. I risultati della letteratura dimostrano che sia l'escissione locale che il trattamento radiante ad alte dosi consentono di ottenere eccellenti risultati in termini di controllo locale. Due modalità di trattamento, in particolare, sembrano caratterizzate da simili risultati clinici: l'escissione locale (abituamente eseguita con asportazione in blocco di tutti gli strati della parete) o la radioterapia endocavitaria con radiazioni di bassa energia (50 kVp). Per la maggioranza di questi pazienti, inoltre, trova indicazione un trattamento pelvico con radioterapia a fasci esterni, in grado di controllare la malattia infraclinica nei linfonodi*

*regionali e nelle zone prossime al letto tumorale. Il controllo locoregionale nei carcinomi T1 è eccellente. Nelle lesioni T2, invece, circa il 15% dei pazienti presenta recidiva locale dopo trattamento conservativo. Uno stretto controllo clinico dopo il trattamento di questi pazienti è pertanto fondamentale ai fini dell'eventuale ricorso a chirurgia radicale "di salvataggio". Altrettanto importante è una attenta selezione dei pazienti, possibilmente basata sull'utilizzo dell'ecografia transrettale o della risonanza magnetica. Infatti, l'incidenza di carcinomi T3 "inattesi" e di margini di resezione positivi raggiunge il tasso del 40% nelle casistiche in cui non si sia fatto ricorso a metodiche di staging endorettali.*

Parole chiave: Neoplasie del retto, radioterapia, chirurgia, terapie multimodali.

## Results with Local Excision

The results of conservative treatment with either local excision or endocavitary irradiation are comparable (1-8). Single institution studies using local excision in combination with pelvic radiotherapy and careful patient selection report locoregional control ranging from 84 to 97% (1-5). Several series reporting the results of local excision alone (no pelvic radiotherapy) demonstrate lower locoregional control rates (60-72%) (6-8). This would suggest a role for pelvic radiotherapy for at least some patients receiving conservative treatment.

When conservative treatment is built around local excision, the procedure performed in most studies has been a full thickness removal of the involved portion of the rectum, either by a trans anal (with or without sphincterotomy), trans sacral, or trans coccygeal approach. Surgical margins should be inked. It is also important to place clips to help direct postoperative radiotherapy. More limited excisions (sparing the bulk of the muscularis propria) or piecemeal removal of the lesion have been reported as subsets of larger series (1-4, 8). In one study (1) a less than full thickness excision was limited to cases where a full preoperative workup including, trans rectal ultrasound, indicated a T1 lesion. In this study the cases with a less than full thickness excision were all locally controlled. In the other studies the impact of surgical procedure on outcome was either not detailed (2, 3) or local control was reduced 10-15% or more if there was less than a full thickness excision (4, 8).

In North America there have been two prospective, multi institutional phase II trials evaluating conservative treatment with local excision. Both called for full thickness procedures and both called for postoperative radiation and chemotherapy except if the lesion was a well or moderately differentiated T1 lesion removed with margins of at least 4 mm and with no evidence of lymphovascular invasion. For all other cases, postoperative external beam radiation was delivered in conjunction with 5 Fluorouracil based chemotherapy. The first trial, by the Radiation Therapy Oncology Group (RTOG) was completed in 1992 and called for 45 Gy to the pelvis followed by boost doses of 5 to 20 Gy depending on margin status (13). The 5 FU dose schedule was similar to anal cancer (two four day infusions at 1000 mg/m<sup>2</sup> per day). The second trial, an intergroup study conducted jointly by CALGB, RTOG, ECOG, and SWOG (14) limited the radiation boost dose to 9 Gy and used less intense chemotherapy, bolus 5 FU instead of infusional 5 FU.

The data from the first RTOG study have matured sufficiently to permit a recent publication which reports outcome with a minimum of 5 years follow up (13). This shows excellent locoregional control for T1 tumors (26/27 = 96%). For T2 and T3 tumors locoregional control was 21/25 (86%) and 10/13 (77%) respectively. The actual ability to control the T3 and T2 lesions may be oversta-

Endocavitary radiation utilizes specialized equipment which is not widely available.

For either approach the selection criteria are similar. An ideal lesion should be

- 1) freely mobile;
- 2) without evidence of extension into the perirectal fat either on digital examination or on diagnostic studies such as trans rectal ultrasound or endorectal MRI (T1 or T2 tumor);
- 3) without clinical evidence of involved nodes on physical examination or diagnostic studies;
- 4) well or moderately differentiated histology (no high grade or signet ring tumors);
- 5) less than about 3 cm in diameter.

The first four criteria minimize the chance of locoregional extension either into perirectal fat, within the rectum by submucosal lymphatics, or to regional lymph nodes. The fifth factor, the size selection factor, is important for reasons of function as well as curability. If too large a portion of the rectal circumference is either removed or treated with high doses of radiation then the functional result may be unsatisfactory.

Patients with less than ideal tumors may still be considered for conservative treatment if they are poor medical risks for radical surgery. If conservative treatment is chosen it is important to carefully balance the increased risks of tumor recurrence against the patient's medical co morbidities.

Selecting a conservative alternative to radical surgery is more appropriate if it can be shown that the choice is not necessarily an irreversible one—that standard surgery can still be used if the initial conservative approach fails. The literature for both local excision and endocavitary radiation demonstrates that about 1/3-1/2 of failures after conservative treatment can be salvaged with standard surgery (1-3, 8-12). This means that patients treated conservatively deserve particularly close follow up—since locoregional failure is more manageable than after standard surgery.

ted, since cases with incomplete resections were excluded from this study. The number of such cases is unknown since most patients were enrolled on the RTOG study after the local excision had been performed.

The successor intergroup phase II trial has only been reported in abstract form (14). The preliminary results from this study appear to be at least as good as those reported by the RTOG study, although cases with positive margins or T3 disease were excluded from the intergroup study. Since the RTOG study reported a 10% incidence of major late toxicity, with an additional 12% of patients requiring temporary or permanent colostomies, the lower radiation doses (45 Gy + 9 Gy boost) and less intensive (bolus 5FU) chemotherapy of the intergroup study appear to be a better choice. However, until a full report of the intergroup trial becomes available, the standards of adjuvant care for patients undergoing full thickness excision remain incompletely defined.

In selecting patients for conservative therapy with local excision, it is important to assess the extent of the primary tumor as accurately as possible before proceeding to surgery. If a full thickness excision transects the tumor there may be iatrogenic seeding of the extra rectal space. The ability to salvage such cases with subsequent surgery and/or radiation is compromised. This can be a common problem. In the intergroup study 67 (37%) of 180 enrolled cases were ruled ineligible because of positive margins, T3 disease, or otherwise inadequate surgery. The outcome of the excluded 37% of patients was not reported in the abstract by Steele et. al. (14). One single institution study (8) reported 42% of the lesions either had positive margins or were pathologically identified to be T3 tumors. To reduce the likelihood of inadequate local excision, trans rectal ultrasound or endorectal MRI should be strongly considered before selecting patients for this procedure.

### **Results with Endocavitary Radiation**

As an alternative to full thickness local excision, endocavitary radiation therapy may be considered. Small favorable lesions are treated with very high (20-30 Gy) doses of low energy radiation. The device that has been used is the Phillips 50 kVp contact unit. This is placed in an applicator cone with a 2.4 or 2.9 cm diameter. The radiation, in addition to being low energy, is generated from a target that is positioned very close (3.5 cm) to the aperture of the treatment cone. These two factors lead to a very short ranged depth dose profile, with the dose at a depth of 1 cm equal to about 1/3 the surface dose. The dose is well confined to the treatment aperture, with a very uniform distribution within the aperture (15). Because the volume treated is small, high doses can be administered with excellent tolerance. As practiced by Papillon and Sischy, lesions would be treated every few weeks until a complete response was achieved

(10, 12, 16). Although the cumulative total surface dose might appear high, treatment was very well tolerated. This was partly because of the limited volume irradiated. In addition the tumor surface that received the highest dose of radiation in the first treatment would be gone by the last treatment, thus no tissue actually received the full cumulative administered dose.

The older literature for endocavitary radiation antedated diagnostic tools such as trans rectal ultrasound. Nonetheless, there are strong parallels to the experience with local excision. For clinically ideal tumors endocavitary radiation alone has been reported to achieve local controls ranging from 86% to 91%, with ultimate local control (after salvage surgery for failures) of about 95% (9, 10, 12). However, with endocavitary radiation alone, the local control for less than ideal lesions is substantially worse, with Papillon reporting local control for 76% of ulcerated tumors and 33% of an ill defined group of "palliative" tumors (10). Similar results have been reported by others (11, 12). The poor results with less than ideal tumors recalls the inferior local control achieved with local excision alone, without the use of external beam radiotherapy.

At Washington University we have utilized a combination of external beam radiotherapy and endocavitary radiation for two decades. Our initial experience with endocavitary radiation alone showed good overall survival, however when patients with tumors that were larger than 3 cm but otherwise ideal were treated, more than half required salvage surgery (17-19). A marked improvement for these not quite ideal tumors was seen when external beam radiotherapy was given prior to the endocavitary radiation: the local control of such lesions improved to about 80%, with an ultimate local control (including the contribution of salvage surgery) of about 90% (17-19). The use of external beam radiotherapy prior to endocavitary radiation serves to shrink the primary tumor bed (rendering it more accessible to the endocavitary device) as well as addressing subclinical disease in regional nodes.

The availability of trans rectal ultrasound has improved our ability to select patients for conservative treatment. Birnbaum reviewed the results of ultrasound staged tumors treated at Washington University with external beam radiation therapy and endocavitary radiation (20). She found that the outcome for T1 tumors was excellent, with 100% controlled without the need for salvage surgery. For T2 tumors, external beam plus endocavitary radiation controlled 21/25 (86%) with 90% ultimately NED after salvage surgery. For T3 lesions 53% (19/36) were controlled with radiation, with salvage surgery increasing the ultimate NED rate to 64%. These results, for clinically staged tumors, are almost identical to the results for pathologically staged lesions treated with local excision and chemoradiation in the RTOG study (see above) (13). The two reports suggest that T1 lesions are very well served by conservative treatment.

Compared with radical surgery, T2 tumors may have a slightly impaired control rate with conservative treatment, although the ultimate control rate after including the contribution of salvage surgery is acceptable. Unless the patient is unfit for surgery, T3 lesions do not appear to be as well served with conservative treatment.

In recent years we have seen an increasing number of patients referred after undergoing trans anal (but not trans mural) removal of all macroscopic disease. These patients had presented with sessile tumors of uncertain malignancy status. All macroscopic disease was removed because that would have been adequate treatment if these lesions prove to contain no invasive cancer. However, when invasive cancer was demonstrated, further treatment was needed to address the risk of residual cancer in the tumor bed and in regional nodes. We have treated 54 such cases with a combination of external beam radiotherapy (20 Gy/5 fractions for ultrasound T1 lesions and 45 Gy/25 fractions for ultrasound T2) and endocavitary radiation (two fractions of 30 Gy mucosal surface dose 6-8 weeks after completing external beam radiation). The endocavitary radiation is used to replace full thickness removal of the rectal wall. These patients have had excellent tumor control (51/54 = 94% with one of the three local failures a second malignancy developing 7 cm above the initial lesion) and no major morbidity.

## Conclusions

Conservative treatment with either local excision or endocavitary radiation is a suitable alternative to radical surgery for selected cases of invasive rectal cancer. The most suitable lesions are small T1 tumors. Mobile, small T2 lesions may also be considered for this treatment, however the patient needs to understand that there may be a 10-15% greater risk of recurrence and should agree to very close follow up post treatment. T3 lesions or bulky T2 lesions are not generally suitable for conservative treatment. However if the patient is at high medical risk for surgery, a course of external beam radiation to attempt to shrink the tumor enough for local treatment can be considered.

Except, possibly, for very early T1 lesions, the local treatment should address the full thickness of the rectal wall deep to the tumor site-either by performing a trans mural excision or using endocavitary radiation. External beam radiotherapy addresses the risk of subclinical foci of cancer near the tumor bed (but beyond the field of the endocavitary radiation or local excision) as well as in regional lymph nodes. As such it is an important part of the treatment of most cases. The exception is selected early lesions, particularly if a full thickness excision demonstrates clear margins, T1 disease, and no negative histologic findings.

Finally the importance of careful selection must be repeated. This includes a careful physical examination inclu-

ding rigid proctoscopy and assessment of tumor size and mobility. In addition, evaluation of the T stage with endorectal ultrasound or MRI should be very strongly considered.

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