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Present and future tense in operable rectal cancer

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Rezumat

Prezent și perspectivă în cancerul rezecabil al rectului

În ultimii 30 de ani s-a insistat în mod repetat pe excizia totală a mezorectului (TME), ca fiind cheia reducerii recurenței pelvine. Autorii s-au oprit asupra unor aspecte încă "discutabile", care invita la reflecție, având ca punct de pornire perceptele devenite de acum clasice ale lui R.J. Heald. Autorii se opresc cu precădere asupra punctelor definitorii care justifică abordarea complexă terapeutică a cancerului de rect. Sunt discutate inclusive unele aspecte încă supuse controverselor: amploarea exerezei regionale, punctele critice de risc chirurgical, atitudinea privind protecția inervației genito-urinare. În acest scop se prezintă considerații chirurgicale asupra: anatomiei rectului și mezorectului, TME și limitele sale, aspectelor de anatomie patologică privind diseminarea și gradingul tumoral, recurenței pelviene și asupra locului terapiei adjuvante. Deasemenea este analizată rata complicațiilor, cât și calitatea vieții pacientului supus TME. În final sunt avansate concluzii, parte din ele având calitatea de a oferi subiecte de studiu și de dezbatere pentru viitor.

Cuvinte cheie: cancer rect, excizia totală a mezorectului, grading tumoral, diseminare limfatică, terapie neoadjuvantă, plex hipogastric, plex pelvin

Abstract

In the last three decades it has been repeatedly insisted on the total mesorectal excision (TME), as being the key for pelvic recurrence. The authors have focused upon issues still "questionable", that invite reflection, having as a starting point now become the classic precepts of RJ Heald. The authors stop mainly on defining points that justify the complex therapeutical approach of rectal cancer. There are discussed some issues still subject to controversy: the extent of regional extirpation, critical points of surgical risk, the attitude towards the protection of genito-urinary innervation. In this purpose surgical considerations are presented on: the anatomy of the rectum and mesorectum, TME and its limits, on dissemination issues and pathology tumor grading, pelvic relapse and the place of adjuvant therapy. Complication rate is also analyzed and the quality of life of patients undergoing TME. Finally conclusions are advanced, some of them having the capacity to provide topics for future study and debate.

Key words: rectal cancer, total mesorectal excision, tumoral grading, lymph nodes involvement, neoadjuvant therapy, hypogastric plexus, pelvic plexus

Introduction

During the last 30 years, rectal cancer has continued to be a neoplasic localization that needs a surgical solution. Meanwhile, there is a high improvement of consistent neo-adjuvant therapy: radiotherapy and chemotheraphy (RCT). The aim of this general review is to emphasize the actual state of progress obtained in this combined approach and to set the perspectives with the goal to improve post therapeutical

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results. From the beginning, we state that our interest was only focused on medium and inferior rectum localizations in T1/T3 and at most N1 stages. We have chosen this limitation because the T4 stage is not viable for curative surgical therapy. Furthermore, for superior rectum localization (more than 10 cm from the anal orifice) the radical objective is ensured by the inferior resection limit which leaves a convenient rectal stump for a safe anastomosis without abdicating from the principles of oncologic surgery.

In the following article, we will point out the main aspects of interest for rectal neoplasm, focusing on debatable elements, which invite to reflections.

Considerations on the surgical anatomy of the rectum

Begining in 1986, through Heald's work, there has been a strong emphasis on the total excision of the mesorectum, stating that this is the key to success for reducing pelvic recurrence. Heald (1,2,3) has insisted on the total excision of the mesorectum (TME), an apparently new concept, for interventions by anterior access. Would this be new? Evidently not, after we go through older references. The TME has been a subject of medical literature even as far back as the 1920's. In Paris, P. Reinhold, in 1924 elaborates his PhD thesis titled "Contributions to the study of post operatory relapse factors in rectal cancer. The total excision of the rectum's fibrous sheath". The authority of E. Miles is found in the monography that appeared in London in 1926 in which TME compulsoriness is stipulated. From than on, in all monographies dedicated to rectal cancer, there is a strong emphasis on this principle.

In order to establish the value of TME it is necessary to remind what exactly is the mesorectum and its anatomy and positioning in line with the pelvic formations. The continuing of the ileo-pelvin mesocolon, the mesorectum is the most caudal portion of this structure and hosts the vessels, lymphatics and nerves of the rectum. The mesorectum confers a relative mobility of the rectum in relationship to the bone structures,and then disappears at the S4 level, where the fascia of the rectum merges with the presacrat fascia. The rectum ends at the tip of the prostate anteriorly, and about 3 cm under the tip of the coccis posteriorly, where it becomes the anal canal. The merger spot of the presacred and rectal fascias forms, on the median line the recto-sacrat ligaments, which after dissection cover the anal lifting muscles underneath which we find the perirectal inferior space (the ischio-rectal fossa). Placed totally subperitoneal, the mesorectum is divided in three distinct areas that communicate: the posterior, lateral and anterior areas. Not all compartments are well represented, the posterior one being by far the most consistent. Actually, any messo including the mesorectum is a hilum of the organ it serves, therefore a vascular limphatic and nervous gateway.

The posterior mesorectum is vascular (superior hemoroidal vessels) and lymphatic (Gerota 1 station). The lateral mesorectum, besides vascular and lymphatic hilum,also hosts nerve structures for the rectum (rectal fibers from the pelvic plexus).The anterior mesorectum is in general very lightly represented, and cannot be looked at as a hilum because the rectum does not receive anything through it. We must emphasize the fact that in the mesorectum are nervous structures that are essential to the urinary bladder, the genital organs, the rectum and the anal sphincter apparatus: superior hypogastric plexus (sympathetic T11-L1), hypogastric nerves (sympathetic), pelvic plexus or inferior hypogastric (hypogastric nerves fibers, S2-S3 sympathetic fibers, S2-S4 parasympathetic fibers,last ones known as erigentes nerves). The pelvic plexus is placed at the external level of the lateral ligaments and has average dimensions of 3/3 cm under the pelvic fascia, imediately internal of the vascular layout. From the pelvic plexus emerge nervous fibers dedicated to the rectum and bladder, also the cavernous plexus. The last one serves the prostate and seminal vesicles, using the neuro-vascular bands around the vessels of the prostathic capsula. The erection depends on the sacred parasympathetic, and ejaculation depends upon lombar sympathetic. Therefore lesions of the hypogastric plexus and nerves will result in ejaculation deficiencies (dry ejaculation), and pelvic plexus lesions account for impotence and urinary and defecation dysfunctions. (4)

TME and its limits

While the oncological resection of the colon is done in comfortable conditions,that of the rectum – which is localized profoundly in the pelvic cavity – creates real tactical and technical problems: deep dissection, the impossibility to enlarge the operation field, the existence of a sphincterian apparatus which must be spared , the risk of anal, sexual and urinary dysfunction as well as difficult anastomosis. This results in the surgeon's difficult task to take into account two major considerations that counter lapse: the radicality versus the functionality, not very easy to achieve at the same time. Initially it was suggested that the efficiency of TME is able to maintain a low relapse even without RCT. Therefore the key to pelvic recurrence will be the mesorectum and proper TME would lower local relapse from 15%-40% to 4%.

But, a recent Swedish cohort study from 1997 has noted a difference between isolated TME with 9% local relapse and TME associated with RCT with a 1.5% relapse rate (5). This made it clear that the local relapse depends on a lot of factors and is not controllable only through surgical means, no matter of the accuracy and principles of TME. This is not the place to describe the TME technique as it can be found in a multitude of papers that address the surgery of rectal neoplasm. We remind only that TME addresses only T1-T3, N1+, localized on the medium and inferior rectum. The intervention is usually with anterior access and has the next mandatory steps according to Heald (2,3):

- the ligature of the origin of the inferior mesenteric artery or of the arterial trunk under the origin of the left colic artery;
- the mobilization of the splenic flexure;
- the instrumental dissection of the mesorectum;
- the ligature of the lateral ligaments at the spot in which the medium rectal arteries enter in the mesorectum as close as possible to the nervous plane;

- the excision of the mesorectum to the anal levators, without opening the rectal fascia;
- temporary colostoma on the transvers colon;
- low anastomosis (colo-rectal) or very low anastomosis (colo-anal).

Today it is well defined and accepted that the manual dissection of the posterior mesorectum is a "rustic surgery" that does not permit the maintaining in the extra fascial plane, and makes the "violation of the mesorectum" possible. (6)

Recently, the term "meticulous TME" was introduced, that defines a type of surgery that takes out all the mesorectum localized at 5 cm under the tumor, considering that tumoral deposits can be found in mesorectum at a distance at maximum 4 cm from the tumor. There is a contradiction here. The surgeon has the obligation to place the inferior section of the rectum at a minimum 1 cm under the tumor and the section of the mesorectum 5 cm downstream of the tumor. In fact, the result is that the mesorectum decides the distal margin of the rezection (7).

The contradiction would be in the fact that the TME must overtake with about 4 cm the rezection of the rectum at the level of the inferior section line. This gesture brings the organ sacrifice in the vecinity of the sphincterian apparatus, 3 cm of the anal orifice. Therefore, low rectal tumors are classified in 3 categories: low (2 cm from the anal-rectal line), very low (less than 1 cm) and ultra low (in the anal canal). In these types of rectal cancer localized under 5 cm from the anal orifice, we take in to account rectal amputation or partial/total conservation of the sphincterial apparatus. Following this idea,it could be taken into account to abdicate from the lymphatic system surgery in favor of functional surgery. It's true that neoplasic secondaries do not overtake 1-2 cm under the inferior limit of the tumor but lymphatic involvements do not follow this rule. For these low tumor locations, inter-sphincterian resections are performed, wich implies keeping 1-2 cm of anal stump, by conserving the external sphincter and partially the internal one (the constrictor fascicullum of levator ani). Obviously these gestures are followed by a colo-anal low or very low anastomosis which is highly demanding, but once the anal levators are passed downstream of the tumor, the excision does not remove the lymphatic tissue of the perirectal inferior space (ischio-rectal fossa), this not being more than an organ surgery, and not a system surgery. It is now practiced a sort of "heroic anastomosis", ultra low, with the only goal to keep an anatomical evacuation way. We will further on elaborate this subject when discussing the morbidity of the rectum surgery.

On executing a TME, there are 6 critical nervous risk poins, that the surgeon must know and avoid: The plexus of the inferior mesenteric artery, at the place of it's origin from the aorta, the superior hypogastric plexus at L5 level, the hypogastric nerves, the pelvic plexus and the erector nerves, the cavernous plexus-structures found under the pre-sacrat fascia or the endo-pelvin one. The technical ways of avoiding a lesion in these structures are well coded, in essence we must maintain an internal plan of the presacral fascia, the endopelvis fascia and the Denonvilliers fascia. (8,9)

Anatomo-pathological aspects

The anatomo-pathological role of appreciating the correctness of the surgical exeresis in neoplasms has risen more and more. From 1992, thanks to Quirke (10,11), we can appreciate the adequate or inadequate character of the resection in rectum surgery. He has set the predictive and essential role of the extension degree of the resection at the rectum and mesorectum level in order to reduce local relapse. Therefore the main predictive factors for recurrence are: circumferential dissemination and distal dissemination. Cranial dissemination is not taken in to consideration because the most unable surgical act succeeds in properly eliminating the rectum and mesorectum from above the tumor. The final resolution is in the ability of the surgeon to lift the recto-colic piece with the whole "cuff" that contains both the circumferential and caudal dissemination. For caudal secondaries, it has been convened that a 2cm margin of safety under the tumor is sufficient. More delicate than this is the problem of circumferential invasion in the atmosphere of the rectal sheath and outside of it. Of the components of appreciating a dissemination, we take into account: direct lateral invasion, lymphatic and venous extension (7,8,12,13).

The surgeons and the pathologists had the job to redefine the surgical anatomy of the rectum, so that finding the "happy plan" or the "holy plan" in order to make a dissection, to be able to remove the rectum with a complete lymphatic cuff. (3)

J. MacFarlane (1993), an ardent supporter of TME, strengthens the idea that "the meticulous TME contains the entire area of tumor dissemination" and regulates that: manual dissection should not be performed, as it is an "rustic surgery" and the total appreciation of TME falls on the pathologist. (6)

Thus, some sort of competence audit of the pathologist has been reached, the only one capable of appreciating the precision of the surgical resection. (14) The integer, "untouched" by the surgeon fascia of the rectum should be easily recognized on the resected piece. According to Quirke (11) there are 3 degrees of appreciating the precision of the resection. The 3-rd degree implies a correct excision, outside the rectal sheath,being in the same time the real TME: intact mesorectum with shiny surface given by its own fascia, and which does not get narrow at the inferior pole of the piece, while getting close to the rectum *(Fig. 1)*. The 2nd degree presupposes some defects of the mesorectum surface, as well as the tendency of its caudal margin to get cone-shaped. Finally, the 1st degree, completely inadequate, because the mesorectum has large defects on "fascia propria" , having a conic aspect on the inferior pole which suggests that the dissection plan is to close to the rectum boundaries. In order to appreciate the oncological value of the excision there is an precise protocol to treat the surgical piece, introduced by Quirke. (11) It is not our aim to present the protocol but it must be learnt and practiced by the pathologist. It is important to note that the vertical and circumferential security margins, having no cancer deposits, must be taken into consideration: minimum 4 cm of integer mesorectum from under the tumor and minimum 1mm of lateral tissue from any tumor deposit, including the lymph node structures.

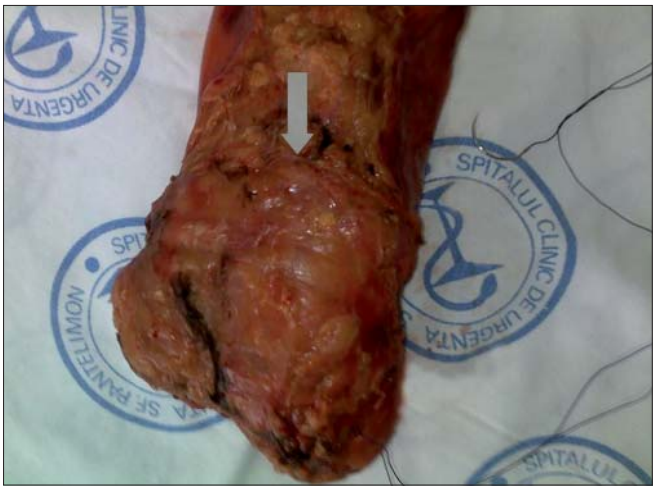

Figure 1. *Total mesorectal excision*

By taking into account these anatomo-surgical rules a decrease of the local recurrences has been obtained, from 36% for TME - 1st degree, up to 4-10% for TME - 3rd degree, in fact the only accurate TME. Here are two comparative studies, published 30 years apart. In the year 2000, through TME, for Dukes A and B rectal neoplasm, the following outcomes were obtained: 81% survival rate at 5 years, 3,7 local recurrence, 85% anal continence and 13% anastomotic fistulas (1,2). For the same point of vue, but 30 years before, the Lahey clinic communicates 73% surviving rate at 5 years, taking into account that the preoperatively RCT did not make the rule the way it does nowadays. It can be considered that the surviving rate is, amazingly, almost the same.

Moreover, some aspects concerning the neoplastic dissemination and the tumor grading (histological differentiation) must be underlined. These two criteria are compulsory in the prognosis assessment. It is relatively easy to establish the tumor direct dissemination in the axis of the rectum - up to 5 cm above and up to 2 cm below the tumor. The lateral dissemination is obviously realized towards the mesorectum and to its lateral side.

The lateral lymphatic dissemination mostly appears in the medium rectum and inferior rectum cancers, 20% of the secondaries being recorded in intern iliac groups, mostly in the patients with a positive 1 station (mesorectum nodes)(15). It is somehow strange that at this large percentage (20%) of interest of the lateral pelvic groups, the same procedure as in the cervical cancer, where these stations are obligatorily removed is not used. In fact, according to the anatomy, the pelvic viscera are sleeved in the so-called sacral-rectal-genital retinaculum,a lympho-conjunctive structure, including the vascular-nervous content. This extra-visceral space, which the mesorectum, the paracystium and the paracolpos are part of, communicates with the retroperitoneum, having no anatomical obstruction. According to classical anatomy, the 1st ganglion station for the pelvic organs can be found in the vicinity of them, but the 2nd stations are, in the end, joined. Nevertheless, the surgical approach for the medium and inferior rectum neoplasms is different compared to the ones for genital or bladder neoplasms, as far as unbinding to perform a N2 excision is concerned, for the first ones. The clearly stated oncologic principle does not seem to be taken into consideration in rectal cancer: it is compulsory that the next non-invaded ganglion station be removed: in N1+, N2 must be removed. The oncological principle also functions as a rule in gastric neoplasms. Even more, it seems like it is constantly ending up with the D2 dissection and sometimes D3.

In addition, Moynihan's statement (1908) that "The surgery of cancer does not mean the surgery of the organs, but the surgery of the lymphatic system", seems to remain valid.

The examination of the margins of the resection specimen is mandatory in order to make sure that the "margin free" exists. As far as the lymphatic determinations are concerned, it is unanimously appreciated the fact that positive ganglions represent the most accurate factor in the process of prognosis (13).

The importance of the tumor grading is unfortunately, ignored, most of the times, meaning that it is not given the same credit as the neoplasm dissemination has. The pre-operative grading should be taken into account concerning the prognosis and especially when choosing the degree of lymphatic and rectum-mesorectum excision (16).

Pelvic recurrence

The source of the local recurrences resides in: the cranio-caudal extension of the excision, the lateral extension of the resection, the tumor grading. TME has reduced the recurrence from 40% to 5-10% in conventional surgery and has increased the survival rate to 5 years, from 45-50% to 75%(6,12). A major merit in the reduction of recurrences is attributed without any doubt to the RCT.

The importance of neoadjuvant therapy

The RCT value,which tumor regression owes to, is unanimously accepted. RCT allows the surgeon to reanalyze the stage of the rectum neoplasm before the time it was scheduled for surgery. RCT reduces the rate of recurrences and has permitted the lowering of the anastomoses, therefore, a more functional surgery by preserving the sphincter. The local recurrence after unirradiated TME is situated on a scale, to 8,2% and after irradiated TME to 2,4%(17). In order to obtain the tumor regressions RT is used on short term (25 Gy in 5 days) or on long term (50 Gy in 4-5 weeks). Most of the surgeons appreciate the long term RT more, being the most efficient in tumor and ganglion regression of the locally advanced cancers (5).

There are 5 degrees of tumor regression after RCT, established by Bazzetti (1996)(16):

- R1 - total regression (the absence of residual cells);
- R2 - almost complete regression (rare residual cells);
- R3 - partial regression (a more severe fibrosis than the neoplasic cellularity);
- R4 - insufficient regression (the neoplasic cells overcome the fibrosis);

R5 - absence of regression.

The goal of any radiotherapist is to achieve R1, which is recorded in approximately 6% of the cases, whilst R2 is achieved in 73% of the cases(13). The survival rate of up to 3 years in these two categories is of 90-95%, while in the rest the survival rate lowers to 55%. It is obvious that the surgeon who has the chance of operating more patients in the R1 -2 group will also have satisfactory results. The determination of the degree of regression in the multimodal treatment is based upon: the T reduction and the reduction of the adenopathies evaluated by doing an endorectal ultrasound and a MRI. Unfortunately, only 40- 60% of the tumors regress and are reconverted through RCT (16). At present, there are no major studies, which can give information regarding the histopathological changes after different variants of RCT, meaning about the components of necrosis, fibrosis, vascular injuries, peritumoral inflammatory processes, etc. (5,13,17)

Even though the RCT is very successful in the field of tumor regression, no reductions of the distant metastatic dissemination risk are obtained. As far as the postoperative RCT is concerned, it is advisable only in cases of perirectal extensions (T3) and in N+ outside the mesorectum.

Results of TME surgery

Undoubtedly, the surgical radicalism is necessary and it presupposes the lymphatic system surgery, on the ground of preoperatory preparation through RCT. However, the radicalism, which the reduction of the local recurrences is based on, is opposed to the quality of life indicators of the patient. Which is the price of these incontestable successes?

TME is most frequently accompanied by anastomotic fistulas and the post-operatory morbidity reaches 25-50%, in the same time being dominated by anastomotic dehiscences in 20% of the cases (12). Moreover, the anastomotic leak brings 6-22% of the total cases of post-operatory mortality. That is why the protective colostomy is made after the TME, this operation's purpose being to reduce the risk of the fistulas to 3-8%, but, in the same time, the stoma implies up to 15-30% of its own complications (2). It clearly results that the surviving rate and the local recurrence are the main elements in judging the therapeutic success. However, beside these two major elements, the third one is not less important - the quality of life (QL) offered to the patient who has been subjected to a surgery. Comparing the rectum amputation with TME, some authors do not record differences in the QL and others tend to be in favor of TME (18,19).

The surgery of the rectum includes possible nervous risks, responsible for urinary disorders, anal and sexual dysfunctions. The more TME is extended, especially the extramesorectal one, the more accentuated these dysfunctions will be. Disorders are the result of the involuntary or voluntary nervous interceptions. The lesions of the hypogastric plexus and of the hypogastric nerves are responsible for the ejaculation disorders (dry ejaculation). Partial or total pelvic plexus lesions are followed by impotence and urinary disorders. Even more, the lower the anastomosis, the more frequent are the defecation disorders (15,20,21,22,23,24,25).

Systematizing, post-operatorily the patient may deal with the following damages of the QL:

Anorectal disorders 80%:

- erratic defecation 44%;
- imperious defecation 40%;
- constipation 20%;
- partial incontinence 15%;
- total incontinence 5% /.

All these defecation disorders improve post-operatory, after 1-2 years. (13)

Urinary disorders 30-70%:

- incontinence;
- imperious micturitions;
- frequent micturitions;
- dysuria;
- incomplete chronical retention.

Most of these disorders are temporary. (13,15)

Sexual disorders 60-70%:

- ejaculation disorders 60%;
- erectile disorders 65%.

The more the anastomosis lowers, the more accentuated these three categories of disorders will be. Certainly, RCT also has a participation share in the genesis of these disorders. It can be affirmed that the elements, which decide the QL, are the location and the stage of the tumor, the amplitude of the lymphatic curage, the level of the anastomosis and the amplitude of the adjuvant treatment.

As far as the mortality rate is concerned, this is similar after TME and conventional surgery and it is situated at 5-6%. (2,12)

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After this review of the actual problems of the rectal cancer surgery, we can draw certain conclusions, each of them representing in fact, subjects of reflection in the future:

1. The anterior mesorectum does not contain vascular, nervous or lymphatic structures, being a poor represented conjunctive adipose lama, located in the back of Denonvilliers fascia.
2. The nervous hilum of the rectum is located in the rectum wings and in the posterolateral-extra-mesorectal areas.
3. There is only the lymph-node 1 station in the mesorectum.
4. The cancers of the medium and inferior rectum precociously involve the mesorectum, directly or by metastases, it's lymphatic systems and frequently (20%) the station 2 - pelvic, iliac, obturator nodes.
5. In the cancers of the anterior rectal wall, the inconsistency of the mesorectum can impose the excision prior to the Denonvilliers fascia, in the extra-mesorectal plane, with the risk of urogenital disorders.
6. The excision of the rectum must assure minimum 1 cm inferior to the tumor and minimum 4 cm from the under tumoral mesorectum.
7. The principle of lymphatic system surgery, according

to which the first uninvaded ganglion station is obligatorily lifted, must be respected. This is regularly respected vertically,but laterally there is no consistence because TME only removes the station 1; a proper resection would also impose extended dissection in N1+ situations,accepting nervous risk for the pelvic plexus and the hypo-gastric nerves.

8. The preoperative tumoral grading must be taken into consideration when determining the type of ganglionar and resection extension. In the poor differentiated neoplasms, the dissemination overcomes the macroscopically visible margins of the tumor with over 1 cm. The lateral dissemination towards the iliac ganglionar groups appears more frequently in medium and low cancers, which are low differentiated or with positive mesorectal ganglions.
9. Pre-operatory RCT is mandatory because it assures the tumoral and lymphatic regression,the growth of the resection, the local control of the recurrences and the surviving rate improvement. Post-operatory RCT is valid only for the extensions outside the sheath of the rectum or with mesorectal positive nodes.
10. RCT does not replace the insufficiencies of the surgical act but it considerably improves the results of a correct surgery.
11. The objective of maintaining the sexual dynamics and the one of saving the anal-sphincter complex do not have to be accomplished by ignoring the oncological principles.

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